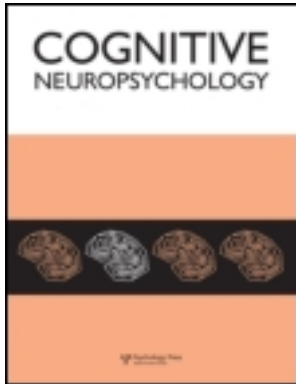


This article was downloaded by: [Tufts University]

On: 15 March 2013, At: 07:56

Publisher: Routledge

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Cognitive Neuropsychology

Publication details, including instructions for authors and subscription information:

<http://www.tandfonline.com/loi/pcgn20>

The role of the primary motor cortex in mental rotation: a TMS study

Barbara Tomasino ^a, Paola Borroni ^b, Alessio Isaja ^a & Raffaella Ida Rumiati ^{a c}

^a Scuola Internazionale Superiore di Studi Avanzati (SISSA), Trieste, Italy

^b Istituto di Fisiologia Umana II, Milano, Italy

^c Institute of Medicine, Research Center, Juelich, Germany

Version of record first published: 05 Jan 2007.

To cite this article: Barbara Tomasino , Paola Borroni , Alessio Isaja & Raffaella Ida Rumiati (2005): The role of the primary motor cortex in mental rotation: a TMS study, Cognitive Neuropsychology, 22:3-4, 348-363

To link to this article: <http://dx.doi.org/10.1080/02643290442000185>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.tandfonline.com/page/terms-and-conditions>

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae, and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand, or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

THE ROLE OF THE PRIMARY MOTOR CORTEX IN MENTAL ROTATION: A TMS STUDY

Barbara Tomasino

Scuola Internazionale Superiore di Studi Avanzati (SISSA), Trieste, Italy

Paola Borroni

Istituto di Fisiologia Umana II, Milano, Italy

Alessio Isaja

Scuola Internazionale Superiore di Studi Avanzati (SISSA), Trieste, Italy

Raffaella Ida Rumiati

*Scuola Internazionale Superiore di Studi Avanzati (SISSA), Trieste, Italy,
and Institute of Medicine, Research Center, Juelich, Germany*

Mental rotation (MR) is sustained by a network of brain regions, including parietal, pre-motor and primary motor (M1) cortices. However it is still not clear whether M1 is recruited only when individuals mentally rotate hands or whether it is also enhanced by MR of non-body parts. Here we report two experiments in which the involvement of M1 in MR of hands and letters was tested using TMS. In Experiments 1a and 1b participants were asked to judge whether two line drawings, depicting either hands or letters, were the same or mirror images of each other ($N = 112$). Subjects were presented with pairs of stimuli with the same orientation (*baseline condition*) in half of the trials, while in the other half the stimulus in the right visual field was rotated (*rotation condition*). They performed the same-different task in three experimental situations: TMS of the primary motor hand area delivered at 400 ms after stimulus onset, sham TMS, and no-TMS. We stimulated the left M1 in Experiment 1a, and the right in Experiment 1b. Results showed that in Experiment 1a participants were slower after TMS when they performed MR of hands but not of letters. In Experiment 1b we failed to find an effect of TMS on MR of hands and letters. While in Experiment 1 the stimulus to be rotated was always presented in the right visual field, in Experiment 2 it was presented either in the left or in the right visual field. Results showed that only when TMS was delivered to the left M1, participants' ability to mentally rotate right and left hands slowed down. Taken together, these findings suggest that the left but not the right M1 plays a critical role in MR of hands.

INTRODUCTION

Mental rotation (MR) is the ability to manipulate mental representations, and it can take place either in an egocentric or an object-centred reference frame. MR is performed in the absence of real

movements by imagining visual stimuli rotating into an orientation other than that in which they appear. The importance of this cognitive ability is in allowing individuals to predict the consequences of their own actions by continuously following and updating them. Several neuroimaging

Correspondence should be addressed to Raffaella Rumiati, Cognitive Neuroscience Sector, Scuola Internazionale Superiore di Studi Avanzati, SISSA, via Beirut 2–4, 34014 Trieste, Italy (Email: Rumiati@sisa.it).

studies, in which subjects had to decide whether two rotated pictures depict the same image or the mirror-image of each other has been adopted, show that MR is supported by a brain network involving *visual processing* areas, the *parietal lobe* (Cohen et al., 1996; Harris, Egan, Sonkkila, Tochon-Danguy, Paxinos, & Watson, 2000; Kosslyn, DiGirolamo, Thompson, & Alpert, 1998; Podzebenko, Egan, & Watson, 2002; Zacks, Ollinger, Sheridan, & Tversky, 2002; Zacks, Rypma, Gabrieli, Tversky, & Glover, 1999), and the *premotor cortex* (Cohen et al., 1996; Kosslyn et al., 1998; Kosslyn, Thompson, Wraga, & Alpert, 2001; Parsons & Fox, 1998). Whereas there is a general agreement that the premotor and parietal cortices are likely to be involved in MR, the role of M1 is still under debate.

IS M1 INVOLVED IN MR?

Traditionally, M1 has been thought to control voluntary movements. However, the idea that M1 can also be involved in higher motor functions has recently received support from studies using single-cell recording in the monkey (Alexander, & Crutcher, 1990; Ashe et al., 1993; Carpenter, Georgopoulos, & Pellizzer, 1999; Georgopoulos, Lurito, Petrides, Schwartz, & Massey, 1989; Pellizzer, Sargent, & Georgopoulos, 1995; Smyrnis, Taira, Ashe, & Georgopoulos, 1992; Wise, Moody, Blomstrom, & Mitz, 1998), brain imaging (Grafton, Hazeltine, & Ivry, 1995; Honda, Wise, Weeks, Deiber, & Hallett, 1998; Karni et al., 1998; Lotze et al., 1999; Tagaris, Richter, Kim, Pellizzer, & Anderson, 1998) and transcranial magnetic stimulation technique (TMS) in humans (Ganis, Keenan, Kosslyn, & Pascual-Leone, 2000). These studies suggest that M1 is engaged in motor imagery and spatial transformations, in addition to stimulus-response compatibility, plasticity, motor sequence learning and memory, and learning sensorimotor associations.

That MR, too, may in some instances require the involvement of action-related brain areas, including the M1 (e.g., Carpenter, Just, Keller, Eddy, & Thulborn, 1999; Ganis et al., 2000;

Kosslyn et al., 1998), should surprise no-one. The idea that the manipulation of mental images is associated with a motor process was already intrinsic to the definition of MR given by Shepard and Cooper (1982). They pointed out that stimuli under MR appear to move in imagery, as they would if they were *physically rotated* by the subject. This simulated manipulation can be triggered implicitly by some classes of stimuli (e.g., hands) or explicitly by a strategy. Kosslyn et al. (2001), for instance, showed that the left M1 was selectively activated *only* when subjects were explicitly asked to imagine grasping and turning the 3-D object with their own hand (i.e., the motor strategy), but not when they just imagined the object rotating in the visual space (i.e., the visual strategy). Interestingly, in a different study in which subjects were not instructed to use any given strategy (Kosslyn et al., 1998), the left M1 was found to be activated during MR of hands and not of stimuli different from body parts, such as 3-D cubes.

So far the only neuropsychological evidence suggesting the involvement of the left M1 in MR of hands has been provided by Tomasino and Rumiati (2004). These authors found that patients with a tumour in the left M1 were impaired in MR of hands and succeeded in MR of letters; in contrast, patients with a tumour invading the right M1 succeeded in both MR tasks. Further evidence supporting a critical role of the left M1 in MR is provided by Ganis et al. (2000) who, using TMS, showed that stimulating the human hand area in the left M1 at 650 ms after stimulus onset significantly slowed down the subjects' latencies when they mentally rotated hands but not feet. Based on this evidence, these authors argued that the M1 must contain motor representations.

Yet, not everybody accepts that M1 has something to do with MR. In some imaging studies the activation found in M1 during MR was explained as just being due to the subjects responding by pressing the response button (Cohen et al., 1996; Richter et al., 2000). Other studies have failed to report any M1 activation when subjects performed tasks tapping MR (Barnes et al., 2000; Harris et al., 2000; Jordan, Heinze, Lutz, Kanowski, & Jancke, 2001; Parsons et al., 1995, 1998).

The reason why there are inconsistent findings concerning the involvement of M1 may be found in the variety of stimuli being used in the studies reported above. Indeed, the nature of the stimulus seems to affect the implicit selection of a particular type of mental transformation (i.e., motor or visual). In fact, an activation of M1 was observed, when subjects were explicitly requested to use a motor strategy in a mental rotation task (Kosslyn et al., 1998; Wraga, Thompson, Alpert, & Kosslyn, 2003). By contrast, the failure to find any enhancement of M1 in the studies of Barnes et al. (2000), Harris et al. (2000), and Jordan et al. (2001) could be due to the use of abstract pictures like alphanumeric character or an abstract 3-D shape as stimuli. Such stimuli can be transformed in a visual object-centred space without requiring motor processes (Zacks et al., 2002). However, there are other studies in which the M1 cortex was found to be enhanced during MR of external abstract objects, though subjects were not explicitly instructed to use a particular strategy (Carpenter et al., 1999; Cohen et al., 1996; Lamm, Windischberger, Leodolter, Moser, & Bauer, 2001; Richter et al., 2000; Tagaris, Kim, Strupp, Andersen, Ugurbil, & Georgopoulos, 1996; Vingerhoets, Santens, Van Laere, Lahorte, Dierckx, & De Reuck, 2001). Here the idea that subjects might have spontaneously adopted a motor strategy can account for these results. One of the above studies investigated MR of body parts by comparing pictures of hands and feet (Ganis et al., 2000). Since MR of stimuli other than body parts has not been tested, nobody can yet tell whether M1 is involved in MR of hands only or of external objects as well.

In the present study we carried out two experiments in which we applied the TMS to the left and the right hand area of healthy individuals who mentally rotated hands and external objects as stimuli, free to use any strategy. Based on the findings of Kosslyn et al. (1998) and Ganis et al. (2000), who both found that the left M1 is involved in MR of hands, we predicted that TMS on this region should significantly slow down the RTs of subjects when they mentally rotate hands but not letters. We also predicted an asymmetry between the left

and the right M1 in sustaining MR of hands, with a direct involvement of the left M1 in MR of both the right and left hand stimuli. In Experiment 1a we stimulated the left M1 in one group of subjects, and in Experiment 1b the right M1 in a different group. In Experiment 2 both the left and the right M1 of the same individuals were stimulated in different blocks.

EXPERIMENT 1A: SINGLE PULSE TMS ON THE LEFT M1

If the left M1 were involved in MR of hands as stimuli, then single pulse TMS applied to the left M1 should slow down RTs during MR of hands but not of letters (Experiment 1a). Moreover we predicted that TMS over the left M1 should slow down RTs during MR of both the left and the right hand (as stimuli). This prediction is in alignment with the neuropsychological observations of patients suffering from ideomotor or ideational apraxia. The reduction in higher-level motor ability experienced by these patients affects both limbs and is typically caused by lesions of the left hemisphere (De Renzi, Faglioni, & Sorgato, 1982; De Renzi, Motti, & Nichelli, 1980). This suggests that the left hemisphere is specialised in controlling higher motor activities. Similarly, the hand area of the left M1 seems to play an essential role in the imagination of movements of both hands, as suggested by the work of Fadiga, Buccino, Craighero, Fogassi, Gallese, and Pavesi (1999).

Method

Subjects

Ten right-handed (mean age = 26 years \pm 6.4, 100/D, according to the Edinburgh Inventory, Oldfield, 1971) volunteers took part in the experiment. None of the subjects had any contraindications to TMS (e.g., metallic implants in their head or an implanted pacemaker; see Wassermann, 1998), or a history of neurological (e.g., seizures and a family history of epilepsy, chronic illnesses), psychiatric, or other medical disorders. Female

participants were not pregnant. All participants gave informed consent prior to the experiment after being informed about the TMS procedure and risks but not about the specific hypotheses of the study. The study has been approved by the SISSA Ethical Committee.

Stimuli

Subjects were presented with pairs of pictures on a computer screen and were required to judge whether stimuli of each pair were the same or different (i.e., mirror version of each other). Two experimental blocks, one of line drawings of hands ($N=28$) and the other of letters ($N=28$) were presented in a counterbalanced order across subjects. In the case of hands, the stimulus on the left side was always a left hand to avoid visuomotor interference (Ganis et al., 2000), whereas the stimulus on the right could be either a left (50%) or a right hand (50%). Hands varied for view (i.e., palms and backs of an open hand shape), handedness (i.e., left and right hands), and orientation. All ($N=56$) stimuli could have either the same (*baseline condition*) or different orientations (*rotation condition*). In the rotation condition, the stimulus on the left was always upright, whereas the stimulus on the right could appear at four different orientations (60° , 150° , 210° , and 330°). In both conditions the pair stimuli were either the same (50%) or the mirror version of each other (50%), following Ganis et al.'s study (2000). Each participant performed two sessions of each task (i.e., MR of hand shapes $N=28 \times 2$, and MR of letters $N=28 \times 2$) in each of the three experimental situations (TMS, no-TMS and sham stimulation) for a total of 336 trials.

Design and procedure

Stimuli were presented on a 14" LCD monitor with a refresh rate of 60 Hz. Stimuli, responses, and TMS triggering were generated and collected by E-prime software. Subjects sat throughout the experiment in a comfortable, reclining armchair in front of a computer screen at a distance of 90 cm. They were instructed to keep their hands still and to be as relaxed as possible. After subjects

were presented with some practice trials, they performed the experiment proper. Unlike other studies (Cohen et al., 1996; Richter et al., 2000), in which subjects responded by pressing a key, in the present study participants were required to respond verbally. Thus RTs of the subjects' voice onset (*Yes!* = same/ *No!* = mirror), and their accuracy were recorded. Of the three experimental situations, subjects performed the TMS and no-TMS in a counterbalanced order, and the sham stimulation in a different session on a different day (see Figure 1).

In each trial, the sequence of events was the following: A fixation point appeared on the screen for 200 ms, followed by the stimulus that remained visible until the response was given (see Figure 2). Single pulses of TMS were delivered at 400 ms after stimulus onset by means of a MagStim 200 Super Rapid Magnetic Stimulator (The Magstim Company, Wales, UK) on the hand area of the left motor cortex. For each trial the computer generated a TTL output pulse that triggered a stimulator (Grass Telefactor, S 88K, W. Warwick, RI, USA), and was then transferred to the MagStim with a 400 ms delay. The 400 ms delay was empirically driven. First, Iwaki, Ueno, Imada, and Tonoike (1999) showed that activity in M1 or SMA was detected (around 330–470 ms) after the activation in the occipital (at about 120–180 ms), inferior temporal (at 170–230 ms) and parietal cortices (at 200–270 ms). In addition, Ganis et al. (2000) found that TMS interfered with MR of hands at 650 ms after stimulus onset. Second, when in a pilot study we stimulated eight subjects at 250 ms after stimulus onset during a MR task, we failed to find any significant difference between the TMS and the no-TMS conditions, $F(1, 7) = 0.65, p > .05, ns$). Neither the two- nor three-way interactions were found significant (all $p > .05, ns$). RTs of MR of hands during the TMS (1036 ms) and during the no-TMS (1053 ms) conditions were similar to those of MR of letters in the same conditions (980 ms and 1005 ms, respectively).

The subject's head was restrained by a fitted support and a stereotactic apparatus held a figure-of-eight coil over the cortical focus for TMS

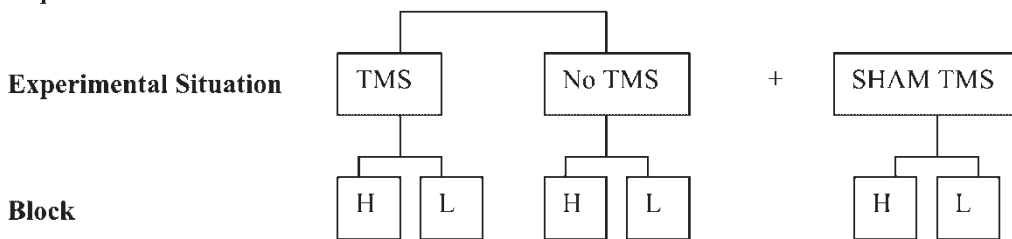
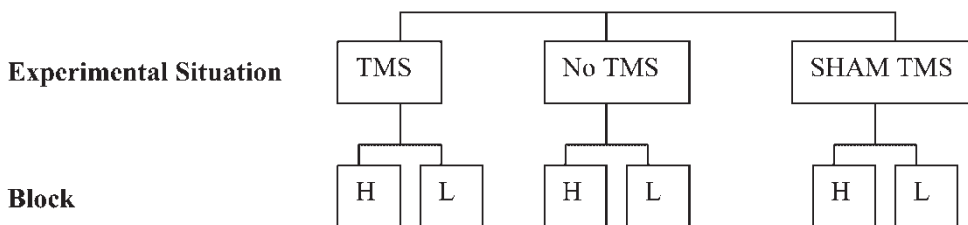
Experiment 1a**Experiment 1b and 2**

Figure 1. Experimental design in Experiment 1a (upper panel) and in Experiment 1b (lower panel) using one possible counterbalancing order (H = MR of hands; L = MR of letters).

activation of forearm muscles. The effectiveness of the TMS stimulation was verified by recording the compound muscle action potentials (CMAPs) from the right *extensor carpi radialis* muscle. The motor threshold for the target muscle was determined for each subject independently. The stimulation intensity was set at about 110% of the motor threshold and a CMAP was recorded for every single response accompanied by a TMS pulse. In the sham condition, the coil was placed more directly in front of the ear, and moved away from the surface of the head by 2 cm so that it was unlikely that the induced magnetic field would stimulate cortical neurons in M1, though the sound produced by the coil was comparable to that in the real TMS condition. The lack of effective stimulation in this condition was verified in each subject by the absence of an evoked CMAP. CMAPs were amplified, filtered (band-pass 10 to 3000 Hz), digitally converted (sampling rate 4 kHz).

Results

An ANOVA with experimental situation (TMS, sham TMS, and no-TMS), stimulus type (hands, letters), condition (baseline, rotation), and orientation (60°, 150°, 210°, and 330°) as factors was conducted on correct responses. Those trials in which subjects made an error (1.5%), RTs were 2 *SDs* above the mean for each cell (~3%), or in which the voice box was not triggered by the first response and subjects repeated the answer (2%), were not included in the analysis.

Accuracy

When stimulation was actually delivered, subjects made few errors (hands: 3.7%, letters: 3.6%), and were as accurate in carrying out the task with TMS as with no-TMS, $F(1, 9) = 0.16$, $p > .05$. No significant difference between MR of hands and letters was found, $F(1, 9) = 0.76$, $p > .05$.

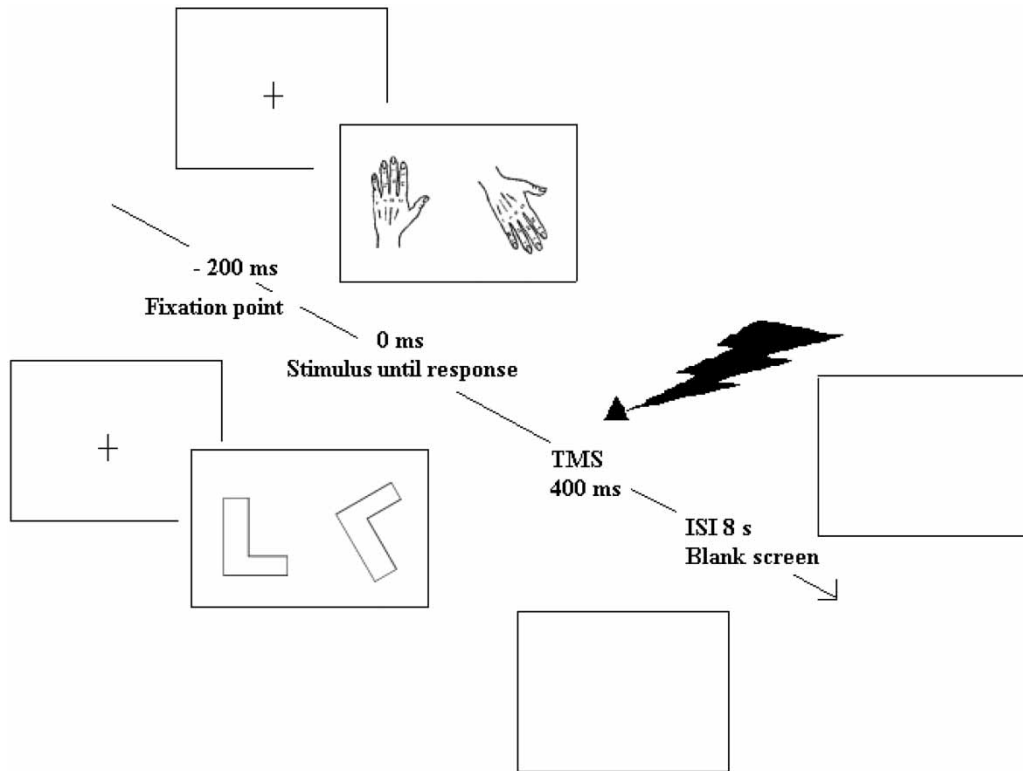


Figure 2. Sequence of events in the experiment: A fixation point appeared on the screen for 200 ms, followed by the stimulus that remained visible until the response was given. Single pulses were delivered at 400 ms after stimulus onset on the hand area of the primary motor cortex.

Reaction times

The main result was a significant three-way interaction: Experimental Situation \times Stimulus Type \times Condition, $F(2, 18) = 5.425$, $p = .014$. TMS slowed the RTs of MR of hands (i.e., in the rotation condition only, see Figure 3a), as suggested by the significant interaction Experimental Situation \times Stimulus Type \times Orientation, $F(6, 54) = 2.66$, $p = .025$. Within-subject contrasts revealed that RTs for MR of hands in the real TMS (1104 ms) were significantly slower, $F = 6.48$, $p < .05$, than those with no-TMS (999 ms), or when the sham stimulation was applied (1024 ms). RTs for MR of letters were similar in the real TMS (908 ms), in the no-TMS (956 ms), and in the sham stimulation (1019 ms).

In addition, significant main effects of condition, $F(1, 9) = 71.709$, $p < .001$, with RTs slower

in the rotation condition than in the baseline, stimulus type, $F(1, 9) = 4.925$, $p < .05$, with MR slower for hands than for letters, and orientation, $F(3, 27) = 68.43$, $p < .001$, were found (see Figure 3b). The interaction Experimental Situation \times Stimulus Type was also significant, $F(2, 18) = 10.43$, $p < .005$, with RTs for MR of hands slower in the real TMS (1013 ms) than in the sham stimulation (947 ms), and so was the interaction Condition \times Orientation, $F(3, 27) = 28.72$, $p < .001$, with increasing RTs in the rotation condition only. The main effect experimental situation, $F(2, 18) = 1.11$, $p > .05$, and all the other interactions were not significant (all $p > .05$, *ns*).

Post hoc comparisons revealed a significant difference between RTs in the sham condition and RTs in the real TMS, $t(9) = 3.3$, $p < .009$, and between RTs in the no-TMS condition and

in the TMS condition, $t(9) = 4.37$, $p < .005$, when subjects performed MR of hands. All the other planned comparisons did not reach significance.

A further ANOVA on RTs of MR of hands showed that the TMS effect was the same for left and right hands as stimuli. The interaction Experimental Situation \times Handedness was not significant, $F(1, 9) = 1.00$, $p > .05$, ns , suggesting that the stimulation to the left hand area affected MR of both ipsi- and contralateral hand images (see Figure 3c).

EXPERIMENT 1B: SINGLE PULSE TMS ON THE RIGHT M1

In Experiment 1a we showed that TMS over the left M1 slowed down MR of hands but not of letters, suggesting that the hands are stimuli that implicitly engage motor processes. Moreover we observed that MR was affected by TMS irrespective of whether the stimuli were left or right hands. The next question to ask was whether this is a prerogative of the left M1 or whether it extends to the right M1 as well. To address this

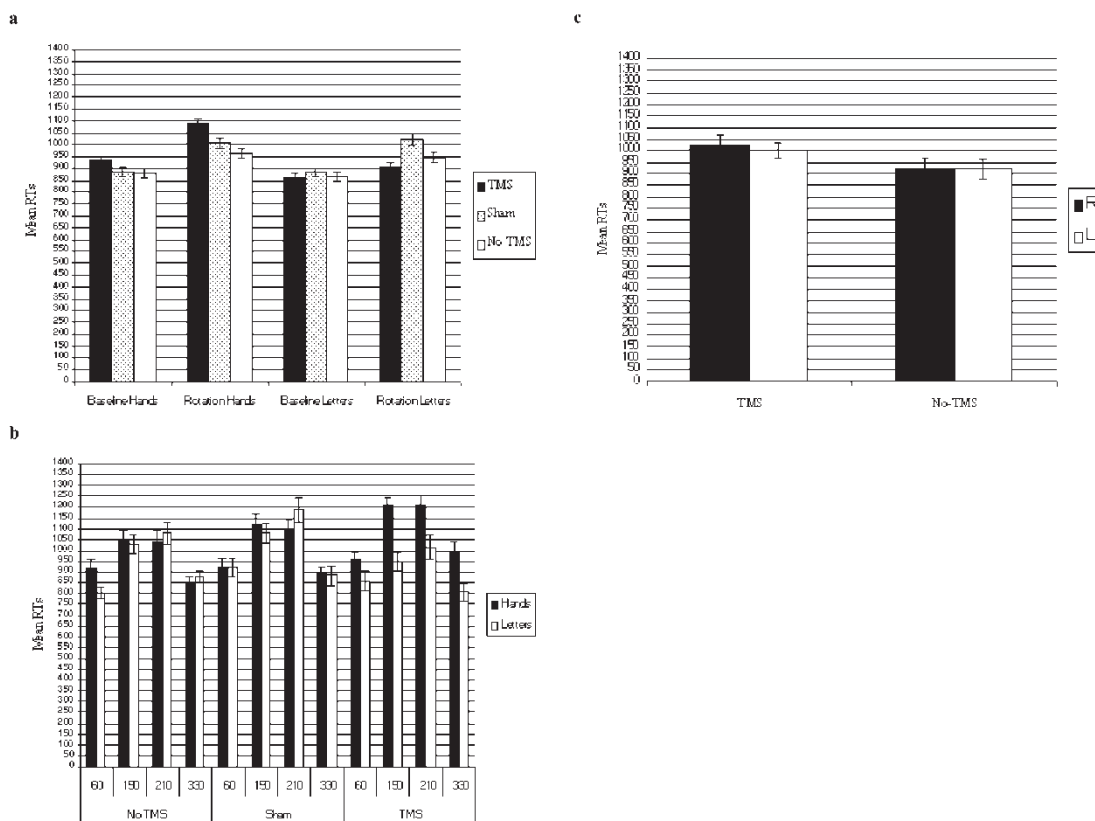


Figure 3. *a*) Experiment 1a. Mean RTs (ms) and error bars (SD) are shown. TMS over the left-hand motor area slowed the RTs in the judgment task relative to hands in the rotation condition only. *b*) Interference effect of TMS in the rotation condition only, for each of the stimulus orientations. *c*) The TMS effect was the same for MR of left and right hands as stimuli. The stimulation of the left M1 hand area slowed RTs down MR of both the ipsi- and contralateral hand stimuli.

issue in Experiment 1b we directly stimulated the right M1. Based on previous studies (Kosslyn et al., 1998; Wraga et al., 2003), single-pulse TMS to the right M1 was not expected to interfere with MR of left hands (or letters) as stimuli.

Stimuli, design, and procedure

In order to avoid possible learning effects, a different group of 10 right-handed subjects (mean age = 27.7 years \pm 5.3, 100/D, according to the Edinburgh Inventory, Oldfield, 1971) was selected for Experiment 1b. Stimuli, design, and procedure were the same as in Experiment 1a except for the fact that the hand area in the right M1 was stimulated and that the three experimental conditions were performed in the same session and were counterbalanced across subjects (see Figure 1).

Results

An ANOVA with experimental situation (TMS, sham TMS, and no-TMS), stimulus type (hands, letters), condition (baseline, rotation), and orientation (60°, 150°, 210°, and 300°) as factors was performed. As for Experiment 1a, we discarded from the analysis those trials in which RTs were 2 *SDs* above the mean for each cell (\sim 2%) as well as those in which the subject's voice did not trigger the voice box (2%).

Accuracy

Subjects were equally accurate in the baseline and the rotation conditions, $F(1, 9) = 0.84$, *ns*, irrespective of the experimental situations (TMS, sham, and no-TMS), $F(2, 18) = 2.02$, *ns*. Neither did their accuracy vary with the type of stimulus, $F(1, 9) = 0.212$, *ns*. Only the main effect of orientation was significant, $F(3, 27) = 6.77$, $p < .005$, with fewer errors at 150° and 210° stimulus orientations. None of the interactions was found significant (all $p > .05$, *ns*).

Reaction times

A significant main effect of condition, $F(1, 9) = 9.38$, $p < .05$, with slower RTs in the rotation condition, and of orientation, $F(3, 27) = 25.33$, $p < .001$, with RTs increasing as an effect of stimulus orientation (see Figure 4b), were found to be significant, as was the interaction Condition \times Orientation, $F(3, 27) = 5.54$, $p < .001$, with an increase in RTs in the rotation condition. All the other main effects—experimental situation, $F(2, 18) = 1.7$; stimulus type, $F(1, 9) = 3.27$ —and the remaining interactions did not reach significance (all $p > .05$). Post hoc comparisons between RTs concerning hands at 210° and 300° showed that subjects were slower in the TMS condition than in the sham TMS, $t(9) = 2.69$, $p < .05$, $t(9) = 2.81$, $p < .05$, respectively. None of the other comparisons reached significance.

Although we failed to observe any significant effect of TMS, we performed an ANOVA on RTs for MR of hands only in order to test whether RTs for MR of left and right hands as stimuli were different. Neither the Experimental Situation \times Handedness, $F(2, 18) = 0.807$, $p > .05$, *ns*, nor the Experimental Situation \times Condition \times Handedness, $F(2, 18) = 0.013$, $p > .05$, *ns*, interactions were found significant, suggesting that the TMS did not affect RTs for either the ipsi- or the contralateral hand stimuli.

Discussion of Experiments 1a and b

Results from Experiment 1a clearly showed that TMS on the left M1 slowed RTs during MR of hand images but not of letters. This effect was the same for left and right hands as stimuli. Furthermore, results in Experiment 1b suggested that the right motor hand area does not seem to be recruited in MR of hands, not even when individuals imagine movements of the contralateral left hand. The specialisation of the left M1 for both the left- and right-hand movements has been observed also in the context of planning and execution of movements (Chen, Cohen, & Hallet, 1997; Kim et al., 1993; Kosslyn et al., 1998), as well as in the motor imagery domain (Fadiga et al., 1999).

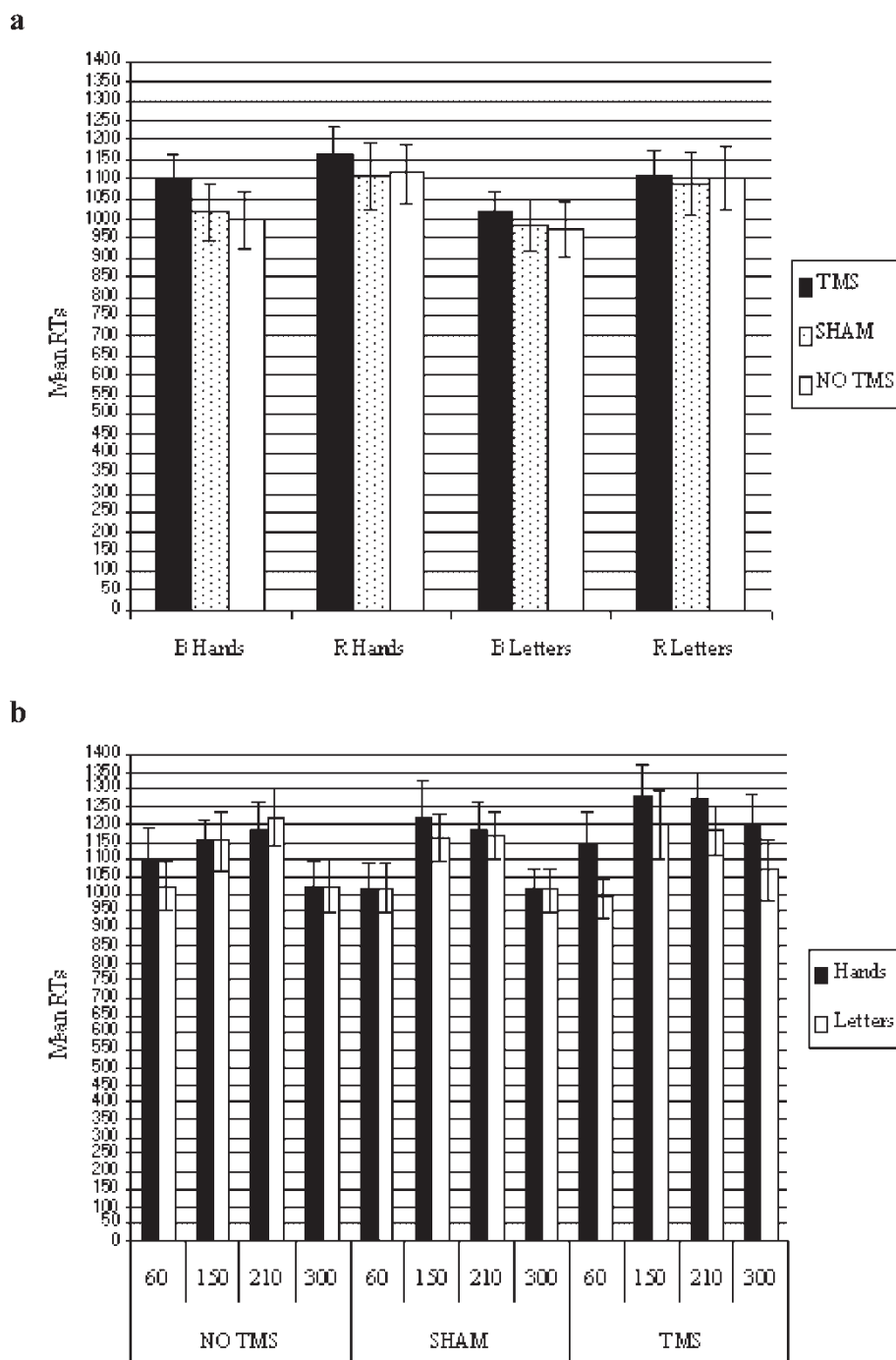


Figure 4. *a) Experiment 1b. Mean RTs (ms) and error bars (SD) are shown. TMS over the right motor hand area did not affect RTs for MR of either hands or of letters. b) RTs of the MR of hands and letters in the rotation condition only for each of the stimulus orientations.*

EXPERIMENT 2: TO-BE-ROTATED STIMULUS PRESENTED IN EITHER THE LEFT OR THE RIGHT VISUAL FIELDS

Results from Experiments 1a and 1b showed that the ability to perform MR of hands was altered when TMS was delivered to the left motor hand area but not to the same area in the right hemisphere. These results, however, may be constrained by the experimental design employed. In Experiment 1 the “comparison hand” was always presented in the left visual field, while the “rotating hand” was always shown in the right visual field, thus shading a potential role of the right motor cortex in MR. Even though this experimental design has been consistently used in many others MR studies (Cohen et al., 1996; Ganis et al., 2000; Kosslyn et al., 1998; Tagaris et al., 1996; Vingerhoets et al., 2001; Wraga et al., 2003), it could well be that the fixed location of the rotated stimulus may have influenced the participants to process all aspects of the task with the left hemisphere. To rule out the account that results in Experiment 1 were biased by the fixed location of the comparison hand we carried out an experiment in which the rotating hands (and letters) were presented in either the left or the right visual fields.

Subjects

A different group of six right-handed participants (mean age = 26.3 ± 3.3 , 100/D, according to the Edinburgh Inventory, Oldfield, 1971) took part in the experiment. None of the subjects had any contraindications to TMS (see Method section in Experiment 1). Participants gave informed consent to the experiment after being informed about the TMS procedure and risks but not about the specific hypotheses of the study.

Method and procedure

In Experiment 2, stimuli, design, and procedure were the same as in Experiment 1 except for the fact that the three experimental conditions (TMS

on the left motor hand area, TMS on the right motor hand area, and sham stimulation) were performed in the same session and were counter-balanced across subjects.

Results

An ANOVA with experimental situation (left M1 TMS, right M1 TMS, sham TMS), stimulus type (hands, letters), condition (baseline, rotation), rotating stimulus position (in the left or the right visual field), same–different (same or mirror images), and orientation (60° , 150° , 210° , and 330°) as factors was conducted on correct responses.

Accuracy

When stimulation was actually delivered, subjects made few errors (hands: 3.2%, letters: 3.4%) and they were as accurate in carrying out the task during TMS to the left and right M1 as during the sham TMS ($p > .05$). No significant difference between MR of hands and letters ($p > .05$) was found.

Reaction times

The effect of TMS was independent of whether the rotating stimulus was presented in the left or right visual field. None of the interactions were found to be significant (all $p > .05$) except for the Experimental Situation \times Stimulus Type \times Condition interaction, $F(2, 10) = 6.009$, $p = .019$, suggesting that TMS over the left M1 slowed down RTs for MR of hands only, just like in Experiment 1a (see Figure 5). The main effects of condition, $F(1, 5) = 25.37$, $p < .005$, orientation, $F(3, 15) = 23.45$, $p < .001$, and stimulus type, $F(1, 5) = 9.832$, $p < .05$, were significant. All the other main effects were not significant (all $p > .05$, n.s.). The Stimulus Type \times Rotating Stimulus Position, $F(1, 5) = 12.8$, $p < .05$, Condition \times Orientation, $F(3, 15) = 11.606$, $p < .001$, Condition \times Same–Different, $F(1, 5) = 15.568$, $p < .05$, and the Stimulus Type \times Condition \times Orientation, $F(3, 15) = 4.36$, $p < .05$, interactions were all found significant.

Within-subject contrasts revealed that RTs were slower in the rotation than in the baseline condition, $F(1, 5) = 25.37, p < .005$, increased with the increase of the stimulus angle, $F(1, 5) = 62.38, p < .005$ for 60° vs. 150° , $F(1, 5) = 1.68, p > .05$, *ns* for 150° vs. 210° , and $F(1, 5) = 16.14, p < .05$ for 210° vs. 60° , and slowed down during MR of hands with respect to letters, $F(1, 5) = 9.8, p < .05$. In addition, subjects were slower when hands were presented in the right visual field, but were slower when letters were presented in the left visual field, $F(1, 5) = 12.821, p < .05$.

Discussion of Experiment 2

Results in Experiment 2 proved that the left primary motor cortex does play a critical role in MR of hands. Moreover, we demonstrated that the hemispheric lateralisation within the M1 cortex during MR tasks is not simply a consequence of the position in the visual field (i.e., left or right) of the rotating stimulus. A lateralisation effect has

been found also in Kawamichi, Kikuchi, Endo, Takeda, and Yoshizawa's (1998) and in Parsons et al.'s (1995) studies in which a single hand was tachistoscopically presented to right-handed subjects in either the left or the right visual field. In these studies a stronger activation in the left premotor cortex, but not in M1, was observed, irrespective of the visual field or body side of the hand stimulus. The role of the left and the right M1 will be addressed in the General Discussion.

GENERAL DISCUSSION

Left M1 is involved in MR

The main finding of the present study is that the ability of healthy subjects to perform MR of hands but not of letters was affected by the temporary disruption of the neural activity in the left motor hand area by means of single-pulse TMS. The finding that the left M1 is recruited in MR of

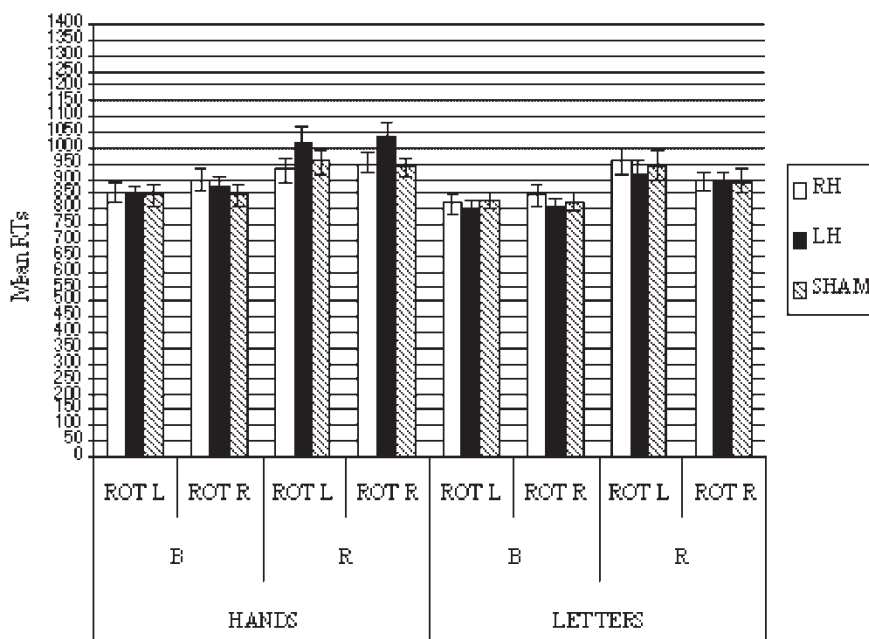


Figure 5. Experiment 2: Mean RTs (ms) and error bars (SD) are shown. TMS over the hand motor area of the right-hand, the left-hand, and the sham stimulation when stimuli were presented in the left (Rot L) or the right visual field (Rot R).

hands is consistent with some neuroimaging results (Kosslyn et al., 1998) and with a previous TMS study (Ganis et al., 2000) in which MR of hands and feet but not of external objects was studied.

This specificity should not be taken as evidence that discrete brain areas are selectively recruited according to the *type of stimulus* to be rotated. Neuropsychological (Tomasino & Rumiati, 2004) and neuroimaging (Kosslyn et al., 2001) studies have shown that the left M1 is recruited not just for body parts such as hand shapes, but also for non-body-part stimuli such as 3D cubes, providing that subjects use a *motor strategy* in MR. In particular, Tomasino and Rumiati found that patients with left M1 lesions exhibited a selective deficit when solving MR of either hands or external objects only when instructed to use a motor strategy (i.e., as a consequence of their manual activity).

In the present study, subjects were free to apply one or the other strategy, with the instructions requiring them to mentally rotate the stimulus on the right, and decide whether it was the same or a mirror image of the other one. Since an interference effect due to stimulation was obtained only during MR of hands, we argue that hands *implicitly* require a mental motor transformation. This account is consistent with the activation of M1 found in some brain imaging studies in which subjects mentally simulated a motor act (Abruzzese, Trompetto, & Schieppati, 1996; Decety et al., 1994; Gerardin et al., 2000; Lang et al., 1994; Lotze et al., 1999; Porro et al., 1996; Roth et al., 1996; Stephan et al., 1995).

By contrast, since TMS did not interfere with MR of letters, we argue that alphanumeric characters do not implicitly require a mental motor strategy (i.e., viewer-based), but rather a visuospatial strategy (i.e., object-based). This view is compatible with Harris and Miniussi's (2003) finding that MR of external objects is lateralised to the right parietal lobe. In their study, subjects performed MR of alphanumeric characters while undergoing repetitive TMS. While the right parietal lobe stimulation slowed down the MR performance, the left parietal stimulation did produce no significant interference. We therefore suggest that the

type of stimulus (i.e., hands or external objects) may implicitly triggers one or the other strategy (i.e., motor or visual respectively; see also Tomasino & Rumiati, 2004), and that the left M1 supports the former.

Left M1 is involved in simulating the movements of both left and right hands

We showed that the left M1 plays an essential role in MR of both the left and the right hands. In sharp contrast with Parsons et al.'s (1995) study in which M1 was not found activated, we demonstrated the involvement of the left M1 cortex in MR when the rotating hand is fixed in the right visual field (Experiment 1a) as well as when it is shown randomly in the left and right visual fields (Experiment 2). However, in Parsons et al.'s study, where the visual and the somatic processing were dissociated by presenting left-hand stimuli to the right hemisphere and right-hand stimuli to the left hemisphere, the authors found that the activation in SMA and in the premotor cortex was stronger in the left hemisphere, regardless of whether the hand was left or right. We proposed here that the left hemisphere specialisation for MR of both the ipsi- and contralateral hand movements is consistent with the specialisation of left hemisphere for higher motor control of both left and right limbs. Consistently, ideomotor and ideational apraxia affect both limbs and it is typically caused by lesions of the left hemisphere (DeRenzi et al., 1980, 1982).

Right M1 hand area does not seem to be involved in MR

The stimulation of the right M1 did not interfere with MR of hands not even when the subjects simulated the rotation of the contralateral hand. This functional left–right asymmetry within M1 is consistent with neuroimaging results (e.g., Kosslyn et al., 1998; Wraga et al., 2003) in which the right M1 hand area was not found activated during MR of hands and with an fMRI study by Porro et al. (1996), in which an activation of the left and right M1 was found while subjects performed

kinaesthetic motor imagery involving the contralateral hand, with a greater activation in the left MI during left-hand movement and imagery.

Our results are at variance with the view that the right M1 would play a role in MR at least of the left-hand movements (Chen et al., 1997). In fact, when we stimulated the right M1 hand area we failed to find a significant effect on MR of either hands, though RTs tended to be slower in the TMS than in the sham or in the no-TMS conditions. One interpretation holds that the right M1 hand area participates in MR of hands, but its involvement is weaker than that of the left M1. If we interfere with the neuronal activity of the right M1, the effect may not reach significance because the left M1 can, alone, complete MR. Likewise Beisteiner, Hollinger, Lindinger, Lang, and Berthoz (1995) recorded direct current (DC) brain potentials during a motor imagery task and found that they were larger in the left than in the right hemisphere both when subjects performed or imagined performing hand movements.

Which computations are sustained by the M1?

Overall our findings strengthen the idea that the left M1 hand area, whose primary function is known to be the execution of hand movements, is involved in at least one type of MR. Thus within the brain network supporting MR, the left M1 can be recruited at a final stage of the object rotation. The interference produced by the TMS was found at about 400 ms after stimulus onset and there are other studies reporting M1 involvement at 650 ms (Ganis et al., 2000) or even later at 900 ms (Thayer, Johnson, Corballis, & Hamm, 2001, using ERPs). These differences in between-studies timing can be explained by different stimuli used (i.e., open hand shapes and finger configurations). MR of open hand shapes is known to require a rotation on the picture plane. By contrast, MR of finger configurations might involve the simulation of a movement through a longer trajectory, and for this reason, more time is needed.

We do not wish to claim that M1 represents a module in the brain dedicated to MR. We share the view that MR is performed by a host of subprocesses sustained by different parts of the brain (visual areas, parietal lobe, and premotor cortex). However, depending on the nature of the task, various components of this network may become more or less important. What does M1 do then? The parietal lobe plays a role in processing the 3D visual information in ego-, allo- and object-centred reference frames; it can select the movement, guide attention to motor performance, and anticipate the consequences of the action by simulating the movement. This information is then transferred to premotor areas, involved in the planning of motor acts, and probably to M1. M1 may contribute to MR during somatotopic, dynamic remapping, a process in which individuals mentally track and continuously update the transformation of the hand motor image by comparing the actual position of their own hands to the final position of the hand stimulus. It is known from neurophysiological studies that M1 neurons code the intended direction of the movements (e.g., Georgopoulos et al., 1989). Thus the fact that subjects usually report kinaesthetic feelings specific to the imagined limb suggests that this representation is of a kinaesthetic-motor type.

PrEview proof published online 10 January 2005

REFERENCES

- Abruzzese, G., Trompetto, C., & Schieppati, M. (1996). The excitability of the human motor cortex increases during execution and mental imagination of sequential but not repetitive finger movements. *Experimental Brain Research*, 111, 465–72.
- Alexander, G. E., & Crutcher, M. D. (1990). Neural representations of the target (goal) of visually guided arm movements in three motor areas of the monkey. *Journal of Neurophysiology*, 64, 164–178.
- Ashe, J., Taira, M., Smyrnis, N., Pellizzer, G., Georgakopoulos, T., Lurito, J. T., & Georgopoulos, A. P. (1993). Motor cortical activity preceding a memorized movement trajectory with an orthogonal bend. *Experimental Brain Research*, 95, 118–130.

- Barnes, J., Howard, R. J., Senior, C., Brammer, M., Bullmore, E. T., Simmons, A., Woodruff, P., & David, A. S. (2000). Cortical activity during rotational and linear transformations. *Neuropsychologia*, 38, 1148–1156.
- Beisteiner, R., Hollinger, P., Lindinger, G., Lang, W., & Berthoz, A. (1995). Mental representations of movements. Brain potentials associated with imagination of hand movements. *Electroencephalography Clinical Neurophysiology*, 96, 183–193.
- Carpenter, A. F., Georgopoulos, A. P., & Pellizzer, G. (1999). Motor cortical encoding of serial order in a context-recall task. *Science*, 283, 1752–1757.
- 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.
- Chen, R., Cohen, L. G., & Hallett, M. (1997). Role of the ipsilateral motor cortex in voluntary movement. *Canadian Journal of Neurological Science*, 24, 284–291.
- 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.
- Decety, J., Perani, D., Jeannerod, M., Bettinardi, V., Tadary, B., Woods, R., Mazziotta, J. C., & Fazio, F. (1994). Mapping motor representations with positron emission tomography. *Nature*, 371, 45–52.
- De Renzi, E., Faglioni, P., & Sorgato, P. (1982). Modality specific and supramodal mechanisms of apraxia. *Brain*, 105, 301–312.
- De Renzi, E., Motti, F., & Nichelli, P. (1980). Imitating gestures. *Archives of Neurology*, 37, 6–10.
- Fadiga, L., Buccino, G., Craighero, L., Fogassi, L., Gallese, V., & Pavesi, G. (1999). Corticospinal excitability is specifically modulated by motor imagery: A magnetic stimulation study. *Neuropsychologia*, 37, 147–158.
- 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.
- Georgopoulos, A. P., Lurito, J. T., Petrides, M., Schwartz, A. B., & Massey, J. T. (1989). Mental rotation of the neuronal population vector. *Science*, 243, 234–236.
- Gerardin, E., Sirigu, A., Lehericy, S., Poline, J. B., Gaymard, B., Marsault, C., Agid, Y., & Le Bihan, D. (2000). Partially overlapping neural networks for real and imagined hand movements. *Cerebral Cortex*, 10, 1093–1104.
- Grafton, S. T., Hazeltine, E., & Ivry, R. (1995). Functional mapping of sequence learning in normal humans. *Journal of Cognitive Neuroscience*, 7, 497–510.
- Harris, I. M., Egan, G. F., Sonkkila, C., Tochon-Danguy, H. J., Paxinos, G., & Watson, J. D. G. (2000). Selective right parietal lobe activation during mental rotation. *Brain*, 123, 65–73.
- Harris, I. M., & Miniussi, C. (2003). Parietal lobe contribution to mental rotation demonstrated with rTMS. *Journal of Cognitive Neuroscience*, 15, 315–323.
- Honda, M., Wise, S. P., Weeks, R. A., Deiber, M. P., & Hallett, M. (1998). Cortical areas with enhanced activation during object centred spatial information processing: A PET study. *Brain*, 121, 2145–2158.
- Iwaki, S., Ueno, S., Imada, T., & Tonoike, M. (1999). Dynamic cortical activation in mental image processing revealed by biomagnetic measurement. *NeuroReport*, 10, 1793–1797.
- Jordan, K., Heinze, H. J., Lutz, K., Kanowski, M., & Jancke, L. (2001). Cortical activations during the mental rotation of different visual objects. *NeuroImage*, 13, 143–152.
- Karni, A., Meyer, G., Rey-Hipolito, C., Jezzard, P., Adams, M. M., Turner, R., & Ungerleider, L. G. (1998). The acquisition of skilled motor performance: Fast and slow experience-driven changes in primary motor cortex. *Proceedings of the National Academy of Sciences of the United States of America*, 95, 861–868.
- Kawamichi, H., Kikuchi, Y., Endo, H., Takeda, T., & Yoshizawa, S. (1998). Temporal structure of implicit motor imagery in visual hand-shape discrimination as revealed by MEG. *NeuroReport*, 9, 1127–1132.
- Kim, S., Ashe, J., Hendrich, K., Ellermann, J. M., Merkle, H., Ugurbil, K., & Georgopoulos, A. P. (1993). Functional magnetic resonance imaging of motor cortex: Hemispheric asymmetry and handedness. *Science*, 261, 615–617.
- 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.
- Kosslyn, S. M., Thompson, W. L., Wraga, M., & Alpert, N. M. (2001). Imagining rotation by endogenous versus exogenous forces: Distinct neural mechanisms. *NeuroReport*, 12, 2519–2525.
- Lamm, C., Windischberger, C., Leodolter, U., Moser, E., & Bauer, H. (2001). Evidence for premotor cortex activity during dynamic visuospatial imagery from single-trial functional magnetic resonance imaging

- and event-related slow cortical potentials. *NeuroImage*, 14, 268–83.
- Lang, W., Petit, L., Hollinger, P., Pietrzyk, U., Tzourio, N., Mazoyer, B., & Berthoz, A. (1994). A positron emission tomography study of oculomotor imagery. *NeuroReport*, 5, 921–924.
- Lotze, M., Montoya, P., Erb, M., Hulsmann, E., Flor, H., Klose, U., Birbaumer, N., & Grodd, W. (1999). Activation of cortical and cerebellar motor areas during executed and imagined hand movements: An fMRI study. *Journal of Cognitive Neuroscience*, 11, 491–501.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia*, 9, 97–113.
- Parsons, L. M., & Fox, P. T. (1998). The neural basis of implicit movements used in recognizing hand shape. *Cognitive Neuropsychology*, 15, 583–615.
- Parsons, L. M., Fox, P. T., Downs, J. H., Glass, T., Hirsh, T. B., Martin, C. C., Jerabeck, P. A., & Lancaster, J. L. (1995). Use of implicit motor imagery for visual shape discrimination as revealed by PET. *Nature*, 375, 54–58.
- Pellizzer, G., Sargent, P., & Georgopoulos, A. P. (1995). Motor cortical activity in a context-recall task. *Science*, 269, 702–705.
- 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.
- Porro, C. A., Francescato, M. P., Cettolo, V., Diamond, M. E., Baraldi, P., Zuiani, C., Bazzocchi, M., & Prampero, P. E. (1996). Primary motor and sensory cortex activation during motor performance and motor imagery. *Journal of Neuroscience*, 16, 7688–7698.
- 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.
- Roth, M., Decety, J., Raybaudi, M., Massarelli, R., Delon-Martin, C., Segebarth, C., Morand, S., Gemignani, A., Decorps, M., & Jeannerod, M. (1996). Possible involvement of primary motor cortex in mentally simulated movement: A functional magnetic resonance imaging study. *NeuroReport*, 7, 1280–1284.
- Sekiyama, K., Miyauchi, S., Imaruoka, T., Egusa, H., & Tashiro, T. (2000). Body image as a visuomotor transformation device revealed in adaptation to reversed vision. *Nature*, 407, 374–377.
- Shepard, R. N., & Cooper, L. A. (1982). *Mental images and their transformations*. Cambridge, MA: MIT Press.
- Smyrnis, N., Taira, M., Ashe, J., & Georgopoulos, A. P. (1992). Motor cortical activity in a memorized delay task. *Experimental Brain Research*, 92, 139–151.
- Stephan, K. M., Fink, G. R., Passingham, R. E., Silbersweig, D., Ceballos-Baumann, A. O., Frith, C. D., & Frackowiak, R. S. J. (1995). Functional anatomy of the mental representation of upper extremity movements in healthy subjects. *Journal of Neurophysiology*, 73, 373–386.
- 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*, 29, 773–776.
- Tagaris, G. A., Kim, S. G., Strupp, J. P., Andersen, P., Ugurbil, K., & Georgopoulos, A. P. (1998). Mental rotation by functional magnetic resonance imaging at high field (4 tesla): Performance and cortical activation. *Journal of Cognitive Neuroscience*, 9, 419–432.
- Tagaris, G. A., Richter, W., Kim, S. G., Pellizzer, G., & Andersen, P. (1998). Functional magnetic resonance imaging of mental rotation and memory scanning: A multidimensional scaling analysis of brain activation patterns. *Brain Research Reviews*, 26, 106–112.
- Thayer, Z. C., Johnson, B. W., Corballis, M. C., & Hamm, J. P. (2001). Perceptual and motor mechanisms for mental rotation of human hands. *NeuroReport*, 12, 3433–3437.
- Tomasino, B., & Rumiati, R. I. (2004). Effects of strategies on mental rotation and hemispheric specialization: Neuropsychological evidence. *Journal of Cognitive Neuroscience*, 16, 878–888.
- Tomasino, B., Rumiati, R. I., & Skrap, M. (2004). *The role of the human motor hand area in mental rotation: Neuropsychological evidence*. Manuscript submitted for publication.
- 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 position emission tomography study. *NeuroImage*, 13, 381–391.

- Wassermann, E. M. (1998). Risk and safety of repetitive transcranial magnetic stimulation. *Electroencephalography Clinical Neurophysiology*, 105, 1–17.
- Wise, S. P., Moody, S. L., Blomstrom, K. J., & Mitz, A. R. (1998). Changes in motor cortical activity during visuomotor adaptation. *Experimental Brain Research*, 121, 285–299.
- Wraga, M., Thompson, W. L., Alpert, N. M., & Kosslyn, S. M. (2003). Implicit transfer of motor strategies in mental rotation. *Brain and Cognition*, 52, 135–143.
- Zacks, J. M., Ollinger, J. M., Sheridan, M. A., & Tversky, B. (2002). A parametric study of mental spatial transformations of bodies. *NeuroImage*, 6, 857–872.
- Zacks, J., Rypma, B., Gabrieli, J. D. E., Tversky, B., & Glover, G. H. (1999). Imagined transformations of bodies: An fMRI investigation. *Neuropsychologia*, 37, 1029–1040.