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The involvement of primary motor cortex in mental rotation revealed by transcranial magnetic stimulation

C. Eisenegger,[1] U. Herwig[2] and L. Jäncke[1]
[1]Department of Neuropsychology, University Zurich, Treichlerstrasse 10, CH-8032 Zürich, Switzerland
[2]Psychiatric University Clinic, University Zurich, Switzerland

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Abstract

We used single-pulse transcranial magnetic stimulation of the left primary hand motor cortex and motor evoked potentials of the contralateral right abductor pollicis brevis to probe motor cortex excitability during a standard mental rotation task. Based on previous findings we tested the following hypotheses. (i) Is the hand motor cortex activated more strongly during mental rotation than during reading aloud or reading silently? The latter tasks have been shown to increase motor cortex excitability substantially in recent studies. (ii) Is the recruitment of the motor cortex for mental rotation specific for the judgement of rotated but not for nonrotated Shepard & Metzler figures? Surprisingly, motor cortex activation was higher during mental rotation than during verbal tasks. Moreover, we found strong motor cortex excitability during the mental rotation task but significantly weaker excitability during judgements of nonrotated figures. Hence, this study shows that the primary hand motor area is generally involved in mental rotation processes. These findings are discussed in the context of current theories of mental rotation, and a likely mechanism for the global excitability increase in the primary motor cortex during mental rotation is proposed.

Introduction

The generation and manipulation of mental visual images is an important psychological function for a wide range of human cognitive tasks. Shepard and Metzler developed an innovative rotation technique to make the effects of visual imagery observable (Shepard & Metzler, 1971). They found that when people compared two similar objects at different orientations, an increment of time is required for each degree of angular disparity between the objects. Recent brain imaging studies delineated those brain structures that are involved during mental rotation (e.g. Jordan *et al*., 2001; Kosslyn *et al*., 2001a; Bestmann *et al*., 2002; Harris *et al*., 2002; Wraga *et al*., 2003). In summary, it has been found that the visual dorsal stream is activated during mental rotation, including the visual areas, the parietal cortex, and premotor as well the primary motor area. The issue whether the primary motor area is directly involved in mental rotation has caused some debate because from an intuitive standpoint it is not directly understandable why motor neurons should be involved in mental manipulations of objects which, by definition, do not require action. Direct evidence for an involvement of the human primary motor cortex in mental rotation of body parts (hands and feet) came from two transcranial magnetic stimulation (TMS) studies (Ganis *et al*., 2000; Tomasino *et al*., 2005). In these studies, single pulse TMS was applied to the left primary motor hand area while the subjects performed mental rotation of pictures of hands or feet. Both studies consistently report slowing of response times when TMS pulses were applied 650 ms (Ganis *et al*., 2000) or 400 ms (Tomasino *et al*., 2005) after stimulus onset. Based on these findings both studies conclude that the primary hand motor area is specifically involved in mental rotation. However, a more recent experiment employing an elegant study protocol allowing the testing of the functional involvement of the left primary hand motor cortex at various stages of mental rotation uncovered that TMS had no direct influence on mental rotation performance regardless of the timing of TMS (Sauner *et al*., 2006). However, the corticospinal activity [as measured with motor evoked potentials (MEPs)] was differentially modulated depending on whether left-hand or right-hand drawings were mentally rotated. These results let the authors conclude that there is no time window during which the primary hand motor area makes a specific contribution to mental rotation. They, thus, propose a secondary effect of mental rotation on corticospinal activity that might not directly be related to mental rotation.

Taken together there is currently no consensus whether the primary hand motor area is directly involved in mental rotation. However, the major caveat of the above-mentioned TMS studies is that they asked the subjects to make a motor response to indicate whether the presented stimuli were same or different. Although they have asked their subjects to respond with their foot (and not with their hands) it might be that the adjacently located primary hand motor area receives some spill-over activation from the foot or leg regions. A further problem is that the above mentioned studies did not control for other cognitive functions. For example, Floel *et al*. (2003) recently showed a substantial involvement of the primary motor cortex during verbal operations (silent and loud). Thus, it is possible that at least some subjects might use verbal strategies to solve the mental rotation task causing increased corticospinal activation.

The present study was designed to use a completely different approach as compared to the above-mentioned TMS studies to studying the involvement of the primary hand area in mental rotation. First, we designed a study protocol allowing the measurement of

Correspondence: Professor Lutz Jäncke, as above.
Email: l.jaencke@psychologie.unizh.ch

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corticospinal activation in the absence of any overt motor task. In addition, we also tested whether the anticipated corticospinal activity during mental rotation is stronger than during cognitive-verbal tasks for which Floel *et al*. (2003) found very strong MEPs. It might be that verbal strategies have implicitly been used to solve mental performance and, thus, might have induced the corticospinal activations.

Materials and methods

Human subjects

Subjects were recruited by advertisements in the University and ETH Zurich. All were students with comparable socioeconomic status (21 subjects, 11 men, age range from 22 to 34, students of the University Zurich enrolled in psychology classes). Subjects were excluded from this study if information from a standardized questionnaire suggested neurological, psychiatric and medical disorders. Handedness was assessed with standard tests (Annett, 1970; Jancke, 1996). According to these tests all subjects were classified as consistent right-handed subjects (CRH). The study was approved by the local ethics committee. Each individual gave written informed consent. Tasks and testing procedures were in accordance with institutional guidelines and the study conforms to the Declaration of Helsinki (the code of ethics of the world medical association).

General experimental protocol

Subjects were seated in a comfortable chair. First, focal TMS was applied to the left M1 to measure resting motor threshold (RMT) using a figure of eight-shaped stimulating coil (diameter of each wing, 70 mm) connected to a 'Transcranial Magnetic Stimulator' (Magstim, Whitland, Dyfed, UK). The coil was placed tangentially to the scalp with the handle pointing backward and rotated away from the midline by 45°. This way, the first quarter-cycle of the cosine waveform of the current induced in the brain is directed in a posterior-to-anterior direction, while the biologically more effective following half-cycle is directed in the opposite direction. The coil was moved over the hand area of the motor cortex to determine the optimal position that consistently resulted in MEPs of maximal amplitude in the abductor pollicis brevis (APB) of the relaxed contralateral right hand. This position was marked on the scalp with a pen to ensure an identical coil placement throughout the experiment. RMT was determined to the nearest 1% of stimulator output and was defined as the minimal stimulus intensity that was sufficient to elicit MEPs greater than 50 μV peak-to-peak amplitude in at least five out of 10 trials (Rossini *et al*., 1994). The obtained stimulation position was used throughout the entire experiment. The output of the TMS pulses during the experimental sessions was adjusted to 10% above motor threshold to produce an EMG response with a mean baseline-to-peak amplitude of approximately 150–500 μV for the baseline resting condition. The subjects were required to maintain complete muscle relaxation of the hand muscles of both hands during all tasks. Background EMG activity was monitored to ensure complete muscle relaxation of hand muscles during the study (sensitivity 50 μV).

The basic principle of the experiments was to elicit ten MEPs during a resting (baseline) session and ten MEPs during various experimental sessions during which the subjects were engaged in several tasks (further details see below). The exact time point of TMS stimulation was randomly chosen with the constraint of at least 4–5 s between successive TMS pulses (see Fig. 1). Constant coil position was assured by fixing the coil to the scalp by a specially designed coil-holder. In addition, the subject's head was fixed at the back, front, and both sides of the scalp and the chin was placed and fixed on a chin holder. Thus, head movement was reduced to a minimum. All subjects wore a standard EEG-cap (Falk Minow Services, http://www.easy-cap.de) on which 32 electrode positions were marked according to the 10–20 system. In addition, surrounding C3 and C4 vertical grids were placed (2 × 2 mm) according to which the coil position was marked for evoking optimal MEPs. The evoked MEPs were recorded in the contralateral APB exactly as during RMT measurement. For each MEP the peak amplitude relative to baseline was calculated and the obtained amplitudes were averaged across the ten MEPs, thus resulting in one mean MEP for the baseline and one MEP for the experimental condition. During each session, spontaneous EMG was recorded in order to control for between-session differences with respect to background EMG.

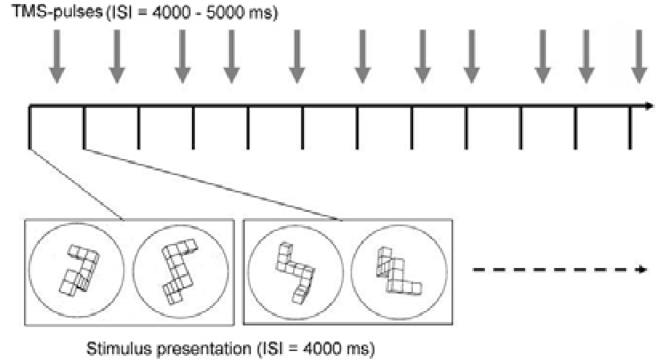

FIG. 1. TMS pulses were applied every 4–5 s. Every 4 s a different set of Shepard & Metzler cube assemblies was presented (jittered MEP elicitation).

Experiment 1

Eleven subjects (four men) with an age range of 23–30 years took part in this experiment. The experiment consisted of five different tasks that were presented in a randomized manner. Each task started with a baseline image, consisting of a fixation cross in the middle of the screen. A single task and a single baseline condition lasted exactly 50 s during which magnetic pulses were applied to the motor cortex each 4–5 s (jittered MEP elicitation). The stimulus sequence was programmed using Presentation software (Version 0.76, Neurobehavioural Systems) and it was presented on a computer screen with a 21′ flat screen. Distances to the screen were 71 ± 4 cm during the experiment. Classic Shepard and Metzler assemblies of cubes were individually placed in a circle and then rotated in different angles. In every pair, we placed a rotated version on the right and the original version of the same stimulus on the left. The pairs were presented every four seconds. Thus, 12 pairs were presented during the experimental session. The mental rotation condition was presented twice, one denoted as 'training' and the other as 'solution'. During the training condition, subjects were told that two pictures would appear and that they had to determine, as quickly but as accurately as possible, whether the two pictures were the same or mirror images. To avoid any movements interfering with the evocation of MEPs, we informed the subjects that they had 'time to practice' and that they neither had to answer manually nor orally. To ensure that the task has been solved according to the instructions, we informed the subjects that a more demanding mental rotation task would follow later. During the 'solution' condition, we simply presented the same pairs of stimuli again and informed the subjects whether the stimuli were identical or not. Most of the subjects (students enrolled in general psychology courses) were familiar with the experimental setup and have participated in similar behavioural experiments revealing the well-known relationship between angle of the rotated figures and reaction time.

No MEPs were evoked during this part of the experiment. As a control task, we used a reading aloud and a reading silently task. During reading aloud, a short text ('weather report') was presented on the computer screen and the subjects were required to read it aloud. While reading, the experimenter controlled the correct reading performance. During silent reading, a slightly modified text used in the reading aloud condition was presented on the screen and the subjects were asked to read it silently. The experimenter asked the subjects after the silent reading condition whether the subjects understood the text. All subjects performed (as expected) perfectly in these conditions.

Experiment 2

Ten subjects (seven men) with an age range of 25–32 years took part in the second experiment, which was similar to experiment 1. However, the experiment consisted of two different tasks, preceded by one baseline condition. A single task and a single baseline condition again lasted exactly 50 s during which MEPs were elicited over the left primary motor cortex. The first task was identical to experiment 1 (mental rotation). The second task involved mirrored-not-mirrored judgements of nonrotated Shepard & Metzler figures (control).

Statistical analysis

Data were analysed using nonparametric statistics. For comparing several levels simultaneously we used the Friedman ANOVA. Subsequent tests were performed using Wilcoxon and Wilcox *a-posteriori* tests corrected for multiple comparisons (Holm, 1979).

Results

Experiment 1

There was no sign of discomfort and negative emotions, which might have influenced the results. Mean motor threshold was 55.2% (SD 10.4) of stimulator intensity maximum, thus mean stimulation intensity was 60.4%. The Friedman ANOVA of the three baseline MEPs measured before each experimental session (mental rotation, reading aloud, reading silently) did not reveal any significant difference in terms of the size of the MEP amplitude for the baseline sessions ($\chi^2 = 2.36$, $n = 11$, $P = 0.307$). Thus, we calculated a mean baseline MEP amplitude across all conditions. The mean baseline MEP amplitude was then contrasted with all MEP amplitudes obtained in the experimental sessions using a Friedman ANOVA with four variables (baseline, mental rotation, reading aloud, reading silently). This test revealed a highly significant result ($\chi^2 = 20.56$, d.f. $= 3$, $P < 0.001$). Subsequent multiple *a-posteriori* tests [corrected for multiple comparisons (Holm, 1979)] using the Wilcoxon and Wilcox tests (Sachs, 1984) revealed significant increases of MEP amplitudes compared to baseline during mental rotation and reading aloud (mental rotation $z = 2.8$, $P = 0.0015$; reading aloud $z = 2.8$, $P = 0.0065$; reading silently $P = 1.77$, $P > 0.05$). In order to compare these significant MEP amplitude increases we performed a Wilcoxon test and revealed stronger MEP amplitudes during mental rotation compared to reading aloud ($z = 1.96$, $P = 0.025$) (see Fig. 2).

Experiment 2

Again, no sign of discomfort was experienced by the subjects. Mean motor threshold was 64.4% (SD 7.6), thus mean stimulation intensity was 70.8%. The baseline MEP amplitude was contrasted with the MEP amplitudes obtained in the mental rotation as well as in the control condition using a Friedman ANOVA. This test revealed a highly significant result ($\chi^2 = 16.8$, d.f. $= 2$, $P < 0.001$). Subsequent multiple *a-posteriori* tests (corrected for multiple comparisons) using the Wilcoxon and Wilcox tests (Sachs, 1984) revealed significant increases of MEP amplitudes compared to baseline during mental rotation and mental rotation control (mental rotation $z = 2.8$, $P = 0.0025$; mental rotation control $z = 1.98$, $P = 0.0235$). In order to compare these significant MEP amplitude increases we performed a Wilcoxon test and revealed stronger MEP amplitudes during mental rotation compared to reading aloud ($z = 2.803$, $P = 0.0025$) (see Fig. 3).

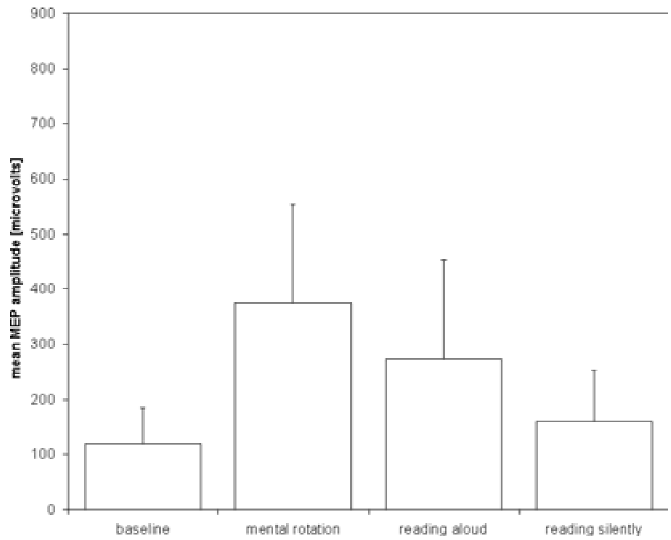

FIG. 2. Mean MEP amplitudes obtained during the average baseline and experimental conditions of experiment 1. Vertical bars indicate standard errors of the mean.

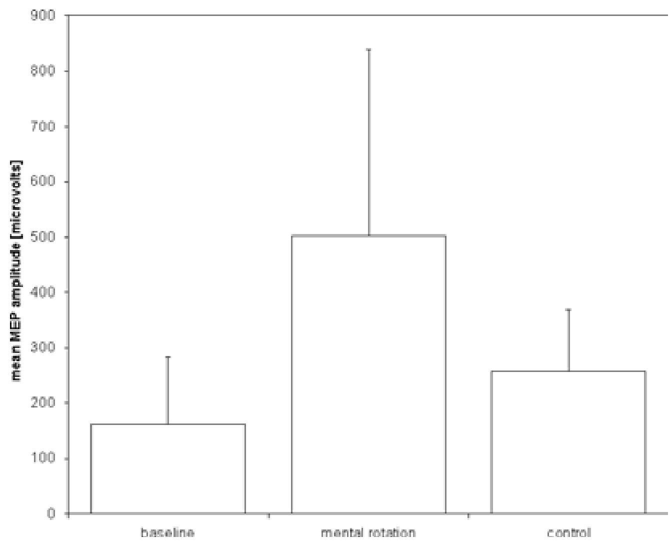

FIG. 3. Mean MEP amplitudes obtained during the average baseline and experimental conditions of experiment 2. Vertical bars indicate standard errors of the mean.

Discussion

The main finding of this study is that mental rotation of standard Shepard & Metzler figures excites the left (dominant) primary motor cortex (including the connected corticospinal pathway) as indicated by increased MEPs of the APB of the right hand. This facilitation of the motor cortex is stronger in the mental rotation condition than in the control condition (nonrotated Shepard & Metzler figures). Thus, mental rotation and the associated cognitive operations are the processes facilitating motor cortex activation and not perception of 3D-objects per se. These findings support recent studies suggesting the idea that mental rotation is accompanied by activation of the corticospinal tract (Ganis *et al*., 2000; Tomasino *et al*., 2005; Sauner *et al*., 2006). However, different to these studies in which the participating subjects have explicitly been asked for motor responses in the context of mental rotation, we avoided motor responses in order to study the influence of mental rotation on corticospinal activation independent of motor processes. Because we explicitly avoided any movements associated with mental rotation, motor preparation or motor execution could not be the driving forces behind the uncovered facilitation of the corticospinal tract. In this context it should be kept in mind that several brain imaging studies have shown that the primary motor cortex is activated during mental rotation mainly when mental rotation is accompanied by button presses or explicit answering and not during mental rotation task processing (e.g. Windischberger *et al*., 2003a, 2003b). A further interesting finding of our study is that the mental rotation related facilitation is stronger than the facilitation evoked by reading aloud or silently. Thus, verbal strategies, as one of the possible strategies for solving a mental rotation task can not explain the increased activation.

But what is the role of the motor cortex during mental rotation? Currently, three possible explanations can be given for the participation of the primary motor cortex in mental rotation: (i) a direct involvement; (ii) a strategy-dependent involvement, or (iii) a spill-over effect from adjacent brain regions directly or indirectly involved in mental rotation.

A direct involvement of M1 is supported by the monkey experiments of Georgopoulos *et al*. (1989) showing direction-sensitive neurons within M1, which might also be used for planning and imagining mental rotation operations. However, a direct support that these neural operations are implemented in the human motor cortex is lacking.

The strategy-dependent involvement of M1 in mental rotation has been proposed by Kosslyn *et al*. (2001b). They hypothesize that the primary motor cortex is involved in mental rotation because some subjects imagine rotating the stimuli using their own hand. This hypothesis has been corroborated nicely by a PET study showing activation in M1 during mental rotation when the subjects learned to imagine mental rotation by using their own hand to rotate the imagined objects (Kosslyn *et al*., 1998).

A third and most likely possibility would be that the primary motor cortex receives spill-over activations from adjacent brain regions during mental rotation. In fact many brain imaging studies found brain activations during mental rotation mostly bilaterally in the premotor and posterior parietal cortex confirming the idea that parietal and premotor areas are the main brain regions responsible for spatial transformations (Cohen *et al*., 1996; Jordan *et al*., 2001; Jordan *et al*., 2002; Windischberger *et al*., 2003a, 2003b). In this sense the primary motor cortex is only activated because of the strong interconnection between the premotor and primary motor areas. Thus, the primary motor cortex would not be the essential area involved in mental rotation but rather a subsidiary area, which is only activated when the premotor areas are activated. In other words, primary motor activation might be an epiphenomenon, or a ‘spill over’ effect of activations in closely connected cortical areas, rather than reflecting a functional role of this area in imagined spatial transformations.

Effective connectivity between the primary motor cortex and adjacent brain areas has been shown by Bestmann *et al*. (2004) who have stimulated the primary and secondary cortical motor regions using rTMS while they also performed fMRI measurements. In fact they found changed haemodynamic responses in areas connected with M1 including S1, the supplementary motor areas, the dorsal premotor cortex, the cingulum, the putamen and the thalamus. Some of these areas have been shown to increase their haemodynamic responses during mental rotation (Cohen *et al*., 1996; Tagaris *et al*., 1996; Jordan *et al*., 2001, 2003; Windischberger *et al*., 2003a, 2003b) suggesting that they are part of a larger distributed neural network involved in controlling mental rotation.

Conclusion

This study corroborates the hypothesis that the primary hand motor area and the associated corticospinal tract are activated during mental rotation performance even when no explicit motor task is required. As the present data provide no precise timing information on the processing of mental rotation in the primary motor cortex due to a jittered elicitation of MEPs, we propose that mental rotation leads to a global increase in corticospinal excitability, possibly due to a ‘spill-over’ effect from adjacent brain regions.

This corticospinal activation enhancement is even stronger than during reading aloud or silently, which are cognitive tasks for which strong activation enhancements in the corticospinal tract have been reported.

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Abbreviations

APB, abductor pollicis brevis; MEPs, motor evoked potentials; RMT, resting motor threshold; TMS, transcranial magnetic stimulation.

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