

## SHORT REPORT

## The effect of transcranial magnetic stimulation on movement selection

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**Objective:** To attempt to replicate previous findings that showed an influence of transcranial magnetic stimulation of the cortical motor areas on the selection of motor programmes on the contralateral side.

**Methods:** Healthy volunteers were asked to choose to make a right or left index finger extension movement freely after hearing the click produced by transcranial magnetic stimulation. The stimulation was applied to the motor areas (test), including the motor cortex, vertex, and prefrontal cortex, and in the air (control).

**Results:** There was no preference for choosing the hand contralateral to the stimulation site, in either test or control trials.

**Conclusions:** Previous results could not be reproduced. Simple magnetic stimulation of the motor areas is insufficient to affect voluntary selection of movement.

Repetitive transcranial magnetic stimulation over the motor cortex (M1) or the supplementary motor area can disrupt the motor programme for movement sequences,<sup>1,2</sup> suggesting a role of M1 as well as the midline frontal region in implementation of a motor programme. Thus modulation of M1 excitability could influence movement selection. This concept is supported by previous studies showing external bias of freely chosen movement by transcranial magnetic stimulation.<sup>3,4</sup> With recent technical advances in this type of stimulation, however, we felt that there were some limitations in the experimental setting and the interpretation of results in the earlier studies.

Brasil-Neto *et al* showed that their normal subjects more often chose the hand contralateral to the site stimulated when the reaction time was less than 200 ms.<sup>4</sup> This hand preference was only observed when transcranial magnetic stimulation was delivered to M1, but not to the prefrontal regions. They used a figure of eight shaped coil that was moved to different areas (Fz, sites 5 cm lateral to Fz, M1 bilaterally, and in the air) before giving stimulation. In this setting, subjects knew the stimulation site before the selection of movement and this might have biased their selection. In addition, their arbitrary classification of response time (200 ms) could have limited the reliability of their post hoc interpretation. Extra short responses (< 200 ms) accounted for 7% of all M1 stimulations, and less than 2% of all other area stimulations, which are too few for proper statistical analysis.

Ammon and Gandevia<sup>3</sup> used a circular coil, the centre of which was positioned over Fz. Contralateral hand preference was observed according to the direction of current flow. Subjects could not expect the direction of current flow, which would eliminate bias related to the anticipation of stimulation. However, the extraordinarily long response times of up to two to five seconds make it difficult to consider their results as the direct effect of transcranial magnetic stimulation. In addition,

it is difficult to interpret the opposite results—ipsilateral hand preference—observed in left handed subjects.

In the present study we tried to replicate previous results in order to confirm the influence of transcranial magnetic stimulation on movement selection.

## METHODS

## Subjects

We studied 11 healthy, right handed volunteers (six men and five women, mean age 38 years, range 23 to 59 years), with a different number of subjects in each experiment. Each volunteer participated in one or more experiments. All subjects gave their written informed consent for participation in the study. The experiment was approved by the institutional review board of the National Institute of Neurological Disorders and Stroke. Handedness was assessed using the Edinburgh handedness inventory.<sup>5</sup>

## Experimental procedure

The subjects sat on a chair with their forearms supported on a horizontal surface. They were asked to decide which finger to move, and to extend either their right or left index finger as quickly as possible after hearing the click produced by transcranial magnetic stimulation. They were specifically instructed to avoid repetitive selection of the same hand and to avoid constant alternation of the hands. No further instruction about selection was given. The surface electromyogram (EMG) was recorded (band pass, 10 Hz to 2 kHz) from the extensor indicis proprius muscles bilaterally, using a conventional EMG machine (Counterpoint, Dantec Electronics, Skovlunde, Denmark). The amplified EMG signal was recorded on a desktop computer for further off-line analysis. EMG responses were checked off-line. Trials with no response, responses of both hands, and response with delayed reaction time longer than one second were excluded from the data analysis (response errors). The reaction time was defined as the interval from the go signal (the click produced by transcranial magnetic stimulation) to the onset of the EMG signal in the extensor indicis proprius.

The study was composed of three different experiments. Before the experiment, each subject practiced the task approximately 20 times without data collection.

## Experiment 1: subthreshold stimulation of M1

Six volunteers participated in this experiment (four men and two women; mean age 39 years). Two figure of eight shaped coils (7 cm in diameter), each connected to a Magstim 200 magnetic stimulator (Magstim, Whitland, Dyfed, UK), were placed over M1 bilaterally (the optimal position for producing a maximal motor evoked potential (MEP) in the contralateral extensor indicis proprius). The optimal coil position was marked on the scalp, and the correct placement of the coil was checked continuously during the experiment. The intensity of the transcranial magnetic stimulation was set at 5% below each subject's resting motor threshold (RMT). RMT was

**Table 1** Number of trials selecting each hand movement

Experiment	TMS		Total No of trials	Number of trials		Number of trials with short RT*		
	Intensity	Site		Contra	Ipsi	Contra	Ipsi	RT (ms)†
Experiment 1	5% below RMT	M1	470	210 (45%)	260 (55%)	53 (45%)	66 (55%)	323 (151)
		Air	464	217 (47%)	247 (53%)	62 (49%)	75 (51%)	305 (154)
Experiment 2	Near RMT	Right	581	250 (43%)	331 (57%)	102 (53%)	89 (47%)	317 (184)
		Left	575	302 (53%)	273 (47%)	126 (51%)	120 (49%)	
Experiment 3	5% above RMT	M1	508	244 (48%)	264 (52%)	16 (38%)	26 (62%)	442 (180)
		F3/4	510	234 (46%)	276 (54%)	23 (45%)	28 (55%)	398 (151)
		Air	517	247 (48%)	273 (52%)	32 (42%)	44 (58%)	385 (170)

Contra, contralateral hand selection; ipsi, ipsilateral hand selection; M1, the motor cortex; RMT, resting motor threshold; RT, reaction time; TMS, transcranial magnetic stimulation.

\* $\leq$  200 ms in experiment 1 and 2, and  $\leq$  300 ms in experiment 3.

†Mean (SD).

defined as the lowest stimulus intensity capable of producing MEP of  $\geq 50 \mu\text{V}$  in at least five of 10 consecutive trials. Four subjects received 120 trials, in four sets of 30 stimuli, and two received 240 trials, in eight sets of 30 stimuli. The stimuli were delivered at random intervals of between five and nine seconds. Half the stimuli were given randomly to the coil placed on the left side, while the other half were delivered to the right side. Half the stimuli applied on one side were directly on the scalp over the M1 (test), while the others were done in the air at least 5 cm away from the scalp (control). The test and control sets of stimuli were randomly mixed.

#### Experiment 2: near threshold stimulation of the vertex with large round coil

Five subjects participated in this experiment (three men and two women; mean age 31 years). A circular coil (9 cm in diameter) connected to a Magstim 200 stimulator was placed over the vertex; the centre of the coil was positioned over Fz in the international 10–20 electrode placement system. In this setting, the lateral edges of the coil were therefore near M1 bilaterally. The intensity of the transcranial magnetic stimulation was set at RMT or 70% of the maximum stimulator output if no MEP was observed at this intensity. (In this setting, RMT was expected to be higher than that achieved with optimal site stimulation, because transcranial magnetic stimulation was not directly applied to that site.) MEP were measured in the right extensor indicis proprius if the current flow of the coil was in an anticlockwise direction, and the in left extensor indicis proprius with a clockwise current. Subjects received 240 trials, in eight sets of 30 stimuli, randomly applied for between five and nine seconds. Four sets of stimuli were conducted with anticlockwise current, while others were done with clockwise current. The order of stimulation sets was randomly arranged.

#### Experiment 3: suprathreshold stimulation of M1 and the prefrontal cortex

Six subjects participated in this experiment (three men and three women; mean age 40 years). The experimental settings were identical to those of experiment 1, with the exception that, in addition to M1, transcranial magnetic stimulation was also applied to both prefrontal cortices (F3 and F4). The intensity of the stimulation was set at 5% above RMT. Subjects received 270 trials, in nine sets of 30 stimuli: three sets over M1, three sets over the prefrontal cortex, and three sets in the air. The order of stimulation sets was randomly arranged.

#### Statistical analysis

We employed  $\chi^2$  analysis to test the effects of transcranial magnetic stimulation on the movement selection compared with the control condition. Probability (p) values of  $< 0.05$  were regarded as significant.

## RESULTS

Twenty six trials (2.7%) among the 960 trials in experiment 1, 44 (3.7%) among the 1200 trials in experiment 2, and 80 (4.9%) among the 1620 trials in experiment 3 were excluded from the analysis because of response errors. Transcranial magnetic stimulation did not produce any statistically significant preference in hand choice. In experiments 1 and 2, we set a “short reaction time” as 200 ms or less, according to the previous study.<sup>4</sup> However, it was set as 300 ms in experiment 3, because suprathreshold stimulation of M1 usually delayed reaction time so that there were only a few responses with 200 ms or less. The number of trials selected for each hand movement is shown in table 1. In experiments 1 and 3, hand preference in M1 and prefrontal stimulation trials was comparable to that in control trials, both in total number of trials and in trials with the short reaction time. There was a preference for selecting the hand ipsilateral to the stimulation site both in test and control trials. In experiment 2, the ipsilateral hand was more often chosen with right hemispheric stimulation, while left hemispheric stimulation was more commonly associated with contralateral hand selection. However, this difference appeared simply to reflect dominant (right) hand preference. In trials with the short reaction time, hand preference was comparable between right and left hemispheric stimulation.

## DISCUSSION

We failed to replicate previous studies showing the influence of transcranial magnetic stimulation on voluntary movement selection. In experiment 1, we tried to replicate Brasil-Neto *et al's* results<sup>4</sup> by using the same coil, the same stimulation intensity, and similar stimulation sites. Two coils were placed over both sides simultaneously, and the stimulation came from either side randomly. Thus the subject could not expect the site of forthcoming stimulation, and this eliminated bias that could have affected the previous results. We asked subjects to select and execute movements as quickly as possible, and this produced many responses with short reaction times. Even in this setting, and even limiting the analysis to trials with a short reaction time, we could not observe any hand preference contralateral to the stimulation site. Instead, there was ipsilateral hand preference. However, this phenomenon seemed unrelated to an effect of transcranial magnetic stimulation on the brain because it was also observed in control trials. In experiment 3, we used suprathreshold stimulation in which M1 was more strongly stimulated, but the results were also negative, as in experiment 1. We also failed to reproduce Ammon and Gandevia's results<sup>3</sup> in experiment 2, in which we selected the responses within one second after stimulation. There seemed to be dominant (right) hand

preference, which could explain differences in hand preference according to the subjects' handedness observed by Ammon and Gandevia.

Our results indicate that simple magnetic stimulation over M1 is insufficient to affect selection of voluntary movement. Further investigations using other methods of M1 modulation will be required to address the possible role of M1 in movement selection.

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