Motor control in simple bimanual movements: a transcranial magnetic stimulation and reaction time study

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Abstract

Objective: Simple reaction time (RT) can be influenced by transcranial magnetic stimulation (TMS) to the motor cortex. Since TMS differentially affects RT of ipsilateral and contralateral muscles a combined RT and TMS investigation sheds light on cortical motor control of bimanual movements.

Methods: Ten normal subjects and one subject with congenital mirror movements (MM) were investigated with a RT paradigm in which they had to move one or both hands in response to a visual go-signal. Suprathreshold TMS was applied to the motor cortex ipsilateral or contralateral to the moving hand at various interstimulus intervals (ISIs) after presentation of the go-signal. EMG recordings from the thenar muscles of both hands were used to determine the RT.

Results: TMS applied to the ipsilateral motor cortex shortened RT when TMS was delivered simultaneously with the go-signal. With increasing ISI between TMS and go-signal the RT was progressively delayed. This delay was more pronounced if TMS was applied contralateral to the moving hand. When normal subjects performed bimanual movements the TMS-induced changes in RT were essentially the same as if they had used the hand in an unimanual task. In the subject with MM, TMS given at the time of the go-signal facilitated both the voluntary and the MM. With increasing ISI, however, RT for voluntary movements and MM increased in parallel.

Conclusions: Ipsilateral TMS affects the timing of hand movements to the same extent regardless of whether the hand is engaged in an unimanual or a bimanual movement. It can be concluded, therefore, that in normal subjects simple bimanual movements are controlled by each motor cortex independently. The results obtained in the subject with MM are consistent with the hypothesis that mirror movements originate from uncrossed corticospinal fibres. The alternative hypothesis that a deficit in transcallosal inhibition leads to MM in the contralateral motor cortex is not compatible with the presented data, because TMS applied to the motor cortex ipsilateral to a voluntary moved hand affected voluntary movements and MM to the same extent. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Transcranial magnetic stimulation; Reaction time; Mirror movements; Bimanual movements

1. Introduction

Simple reaction time (RT) can be influenced by transcranial magnetic stimulation (TMS). In a series of experiments Pascual-Leone and co-workers have observed both an increase and a shortening of RT, dependent on both the site and the intensity of stimulation (Pascual-Leone et al., 1992a,b). RT was delayed by suprathreshold TMS delivered over the contralateral motor cortex at an intensity high enough to induce motor-evoked potentials in muscles involved in the response. In contrast subthreshold TMS over the same scalp position decreased RT. In addition, it has been demonstrated that the delay in RT produced by suprathreshold TMS increases the nearer the application of TMS approached the expected response onset (Day et al., 1989; Ziemann et al., 1997).

Up until now no systematic investigation has been performed with regard to the influence of TMS in a RT paradigm which required a bimanual response. Hand movements are controlled mainly by the contralateral hemisphere (Brinkman and Kuypers, 1972). Co-ordinated bimanual movements, therefore, require interhemispheric coupling of the relevant motor areas. It has been argued that an
unified motor command may be released in bimanual performance (Kelso et al., 1979). In a goal-directed drawer opening task which requires a high degree of interlimb coordination the hypothesis of a higher-order area organizing interactions at lower levels could be supported by Wiesendanger and co-workers (Perrig et al., 1999; Serrien and Wiesendanger, 2000). Whether simple bilateral movements are similarly controlled is not yet clear. At present it is a matter of debate whether one cortical area presides over the operation of both hemispheres in bimanual movements or whether there are two centres, one in each hemisphere. The importance of the supplementary motor area (SMA) for the performance of bimanual movements has been demonstrated both in studies performed in patients with lesions of the SMA as well as in functional imaging studies (Chan and Ross, 1988; Sadato et al., 1997). Recent studies in monkeys, however, have indicated that the primary motor cortex also contains a significant number of neurons which are active in bimanual movements (Aizawa et al., 1990; Donchin et al., 1998). In addition it has been shown that repetitive TMS to the ipsilateral motor cortex can induce timing errors in complex finger movements (Chen et al., 1997). In this study we investigated whether simple and symmetrical bimanual movements are controlled separately by the respective contralateral hemisphere. If TMS over the motor cortex affects ipsilateral and contralateral RT differentially, this can be taken as evidence that the motor cortices in both hemispheres act independently in simple bimanual movements.

Bimanual finger movements occur incidentally in subjects with congenital mirror movements (MM). In congenital MM, voluntary movements are accompanied by unintended movements in homologous muscles on the other body side. The neuroanatomical and neurophysiological basis of these MM has been much discussed. The origin of MM has been related to the existence of a considerable number of uncrossed corticospinal fibres or, alternatively, to a bilateral activation of both motor cortices (Britton et al., 1991; Cohen et al., 1991; Mayston et al., 1997; Leinsinger et al., 1997). Neurophysiological studies indicate that there are differences between MM which occur occasionally during effortful or complex movements in normal subjects and those which occur in patients with complex syndromes such as Klippel-Feil and X-linked Kallmann’s syndrome. Using the same technique Mayston and co-workers have related MM in patients with X-linked Kallmann’s syndrome to activity in uncrossed corticospinal tracts whereas in normal subjects MM were produced by simultaneous activation of crossed corticospinal pathways originating from both left and right motor cortices (Mayston et al., 1997, 1999). There are, however, otherwise completely healthy subjects who exhibit MM during simple effortless movements (Fellows et al., 1996). To identify the hemisphere responsible for this type of congenital MM we applied the reaction time paradigm to a subject with congenital MM. We expected that if the corticospinal neurons responsible for the execution of both voluntary and MM are located in the same hemisphere, TMS would affect the timing of both movements to a similar degree.

2. Subjects and methods

2.1. Subjects

We investigated 10 healthy subjects (aged between 23 and 38 years), who were right-handers according to the Edinburgh Handedness Inventory (Oldfield, 1971). None of the subjects showed MM during simple or rapid movements of the thumbs.

The subject with MM was a 25-year-old medical student who had no neurological disorders until mirror movements were found in a screening examination for a neurophysiological study. His motor development was normal. He learned successfully to play the piano and the flute at the age of 12 years and typewriting at the age of 17. There were no reports of MM in his family. MM were only seen in hand muscles of both hands, and were most prominent while moving the middle finger. MM could not be observed in the lower extremities. The presence of mirror movements were assessed according to the criteria of Woods and Teuber (1978). On this ranking score the subject rated 4 points for voluntary right-hand movements and 3 points for performance with the left hand. The subject was right-handed as determined by the Edinburgh Handedness Inventory. An MRI scan of the brain revealed no structural abnormalities. All subjects gave informed consent for participating in this study, which was approved by the Ethics Committee of the Aachen Medical Faculty.

2.2. Transcranial magnetic stimulation and reaction time

The subjects were seated in a comfortable chair with elbows slightly flexed. The room light was dimmed and subjects used earplugs to avoid distraction. A personal computer with a 17 inch monitor, on which the visual stimuli were presented, was placed 60 cm in front of the subjects. A white rectangle of $5 \times 5$ cm size which appeared for 100 ms on a grey background was used as go-signal. The interval between each go-signal was randomly varied between 5 and 6 s. Subjects were instructed to respond to each visual stimulus by a fast thumb opposition movement. The onset of the movement was determined by recording rectified electromyographic activity from both thenar muscles (ThM) with surface electrodes in a muscle-tendon setting. Signals were amplified, filtered and saved for further off-line analysis. Before the actual experiments the subjects were given several practice trials until stable RTs could be obtained. RT without TMS was used as the baseline condition. To investigate the influence of TMS on RT, different interstimulus intervals (ISIs) between the presentation of the go-signal and the magnetic stimulus were chosen. ISIs of 0, 50 and 100 ms between the go-signal and TMS were applied.
before the predicted movement onset. Eight trials were recorded for the baseline condition as well as for each ISI. The ISIs were randomly varied. In the first set of experiments subjects were instructed to move the right or the left hand. In the second series they had to perform a symmetrical thumb opposition movement with both hands.

TMS was delivered with a Magstim 200 (Magstim Co. Ltd., UK). A figure-of-8 coil with two loops (each loop with an outer diameter of 9 cm) was used. This device delivers monophasic pulses with a maximum magnetic field strength of 2.2 Tesla. The personal computer that presented the visual stimuli was used to trigger a Viking EMG device (Nicolet Viking I) and the magnetic stimulator. The coil was placed tangentially on the skull over the motor cortex with the handle pointing occipitally and laterally. This orientation provides a posterior to anterior current flow perpendicular to the course of the central sulcus (Brasil-Neto et al., 1992).

The optimal site for eliciting maximal hand motor responses in the contralateral ThM was located in each subject. The resting motor threshold was determined for both ThM and defined as the minimum stimulator output producing 3 motor-evoked potentials of at least 100 μV in 6 consecutive stimulations (Rossini and Caramia, 1988). To look for ipsilateral EMG responses following TMS the motor cortex was stimulated with an intensity of 75% of stimulator output in each subject. During the RT trials TMS was delivered with 120% of the individual resting motor threshold of the respective hemisphere. During the session the coil was fixed with a self-made mounting device and the coil position was checked between trials.

In order to control for non-specific TMS effects on RT, TMS was applied over the vertex with the coil held either parallel to the skull (vertex stimulation) or with the coil held perpendicular to the skull, so that no electric current was induced in the brain (sham stimulation). In 10 subjects these control conditions were tested for ISIs of 0 and of 100 ms during an unimanual RT task.

2.3. Statistical evaluation

For statistical evaluation the RTs of 8 trials were averaged for each condition. In normal subjects repeated measures variance analysis was used to reveal if simple main effects and interactions between the conditions existed. We first tested for differences in RT of baseline conditions. The conditions were: (1) unimanual or bimanual task, (2) right or left hand movement. In a second step active TMS conditions were tested for statistical differences. We defined the conditions as follows: (1) unimanual or bimanual task, (2) performing hand (left or right), (3) stimulation side (ipsilateral or contralateral to movement) and (4) stimulation condition (TMS with a delay of 0, 50 or 100 ms with respect to the visual go-signal). Significance level for simple main effects and interactions was set at \( P < 0.05 \). To correct for degrees of freedom, intrasubject effects were tested with the Mauchly test and the Greenhouse-Geisser correction factor was used. \( t \)-Tests, paired for TMS stimulation condition, were used to compare the RTs for the different TMS conditions and the baseline condition. The threshold for significance was set at \( P < 0.01 \). For the subject with MM the differences between RT of the intentionally and unintentionally moved hand were calculated.

Since it is known from the literature (Day et al., 1989) that RTs are increasingly delayed with increasing ISI between go-signal and TMS, gradients of linear regression were calculated for the RT in relation to the ISI. To test for statistical significant differences of the gradients the test for polynomial trends was used \( (P < 0.05) \).

3. Results

3.1. Transcranial magnetic stimulation of the motor cortex

After discharging the coil over the left or the right hemisphere motor-evoked potentials (MEP) could be recorded in the contralateral ThM of all normal subjects. In none of the normal subjects was it possible to obtain MEP from the ipsilateral ThM. TMS delivered at 120% of motor threshold evoked MEPs with an amplitude ranging from 0.2–1.5 mV. The mean latencies of left- and right-sided MEPs did not differ significantly.

In the subject with MM MEP of the contralateral and the ipsilateral ThM could be recorded after stimulation of either hemisphere. The amplitude of the contralateral MEP (cMEP) exceeded that of the ipsilateral MEP (iMEP) in all trials. Three consecutive stimulations of the left hand motor area yielded a MEP with a mean amplitude of 2.86 ± 0.21 mV (SD) at the right ThM and of 0.72 ± 0.10 mV at the left ThM. MEP with a mean amplitude of 5.15 ± 0.71 mV at the left ThM and 0.82 ± 0.12 mV at the right ThM were obtained following stimulation of the right motor cortex. The mean latencies of the MEPs after stimulating the left hemisphere were 21.3 ± 0.3 ms for right ThM and 24.5 ± 0.2 ms for left ThM. Discharging the coil over the right hemisphere produced a MEP in the left ThM after 21.5 ± 0.7 ms and after 20.6 ± 0.8 ms in the ipsilateral, right ThM.

3.2. Reaction time studies

3.2.1. Reaction time without TMS

The unimanual and bimanual RT tasks were performed in 10 subjects. The mean RTs without TMS are summarized in Table 1. Repeated measures variance analysis revealed no statistical difference either between the unimanual or bimanual task \( (F = 3.246, P = 0.105) \) or between left or right hand performance \( (F = 2.232, P = 0.169) \).

During the bimanual task the mean difference in movement onset between the right and left hand was less than 10 ms in 8 subjects. In two subjects movement onset in the left
hand preceded right hand movement, on average, by 11 and 12 ms.

3.2.2. Reaction time with TMS

When subjects were instructed to perform a bimanual movement in response to the go-signal, TMS induced changes in the RT which were essentially the same as if they used the respective hand in an unimanual task (Fig. 1). Repeated measures variance analysis revealed no significant simple main effect for the unimanual or bimanual task ($F = 2.676, P = 0.136$) or performing hand (left or right) ($F = 4.810, P = 0.06$).

TMS to the motor cortex induced a delay of RT in the contralateral hand when TMS was delivered 50 or 100 ms after the go-signal. In the ipsilateral hand TMS induced a

![Diagram](image-url)

**Fig. 1.** TMS effects on RT during a unimanual (A, $n = 10$) and bimanual (B, $n = 10$) task (left thumb: □, right thumb: ●). TMS applied to the contralateral (■) or ipsilateral (○) motor cortex affects RT differentially. Contralateral TMS delays RT. A TMS pulse applied with an ISI of 0 ms to the motor cortex ipsilateral to a movement decreased RT significantly during the unimanual and bimanual task. The linear regression lines (---) calculated for the unimanual and the bimanual task are significantly steeper for contralateral than for ipsilateral TMS. Statistically significant changes are marked with an asterisk.

**Table 1**

<table>
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<th>Subject</th>
<th>Unimanual Right</th>
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<th>Bimanual Right</th>
<th>Bimanual Left</th>
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<td>1</td>
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<td>155 ± 16</td>
<td>154 ± 12</td>
<td>154 ± 9</td>
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<tr>
<td>2</td>
<td>114 ± 5</td>
<td>116 ± 7</td>
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<td>139 ± 8</td>
<td>127 ± 9</td>
<td>153 ± 12</td>
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<td>4</td>
<td>111 ± 2</td>
<td>114 ± 4</td>
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<td>Mean ± SD</td>
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<td>165 ± 40</td>
<td>172 ± 42</td>
<td>171 ± 41</td>
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</tbody>
</table>

Hand movement sequencing, on average, by 11 and 12 ms.
facilitation of RT when go-signal and TMS were given simultaneously (Fig. 1). An increase or decrease in RT had no effect on the pattern of the recorded EMG activity. The mean amplitude and duration of the EMG burst were unaltered in all experiments. Repeated measures variance analysis revealed a significant simple main effect for TMS stimulation with different ISIs ($F = 259.9; P < 0.001$) and a significant simple main effect for stimulated hemisphere (contralateral or ipsilateral to movement) ($F = 19.5; P = 0.002$). Further analysis of interaction showed a significant interaction of stimulated hemisphere and TMS stimulation with different ISIs ($F = 5.24; P = 0.016$).

t-Tests for the unimanual condition revealed a significant facilitation of RT if TMS was delivered to the ipsilateral hemisphere at go-signal presentation. A mean decrease of 53.8 ± 22.9 ms ($P < 0.001$) was found for the left hand and a mean decrease of 52.7 ± 33.7 ms ($P = 0.001$) was observed for the right hand. A significant increase in RT was apparent when TMS was applied 100 ms after go-signal presentation. The EMG onset on the left side was delayed by 60.3 ± 51.8 ms ($P < 0.005$) and on the right side by 40.1 ± 34.5 ms ($P = 0.006$).

Fig. 2. RT of the left (rectangle) and right (circle) hand during an unimanual task. Neither TMS applied over vertex (□, ○) nor sham stimulation (■, ●) with different ISIs (0 and 100 ms) affected RT significantly. In contrast active TMS over the ipsilateral motor cortex (grey squares, circles) with an ISI of 0 ms decreased RT significantly (*) and active TMS over the contralateral motor cortex (grey squares, circles) with an ISI of 100 ms increases RT significantly (*) compared with baseline conditions (■, ○).

Fig. 3. EMG of the subject with mirror movements in response to an unimanual (A±C) or bimanual (D) reaction time task. (A) The EMG burst of a voluntary movement of the right thumb (R) is accompanied by a mirror EMG burst (mEMG) on the left side (L). The latencies of the EMG onset are similar on both sides. (B) TMS applied 100 ms after go-signal presentation to the left hemisphere evokes a motor-evoked potential in the contralateral (cMEP) and the ipsilateral (iMEP) thenar muscles and delays the onset of the voluntary EMG burst and the mEMG burst. (C) In contrast, the same stimulation of the left hemisphere produced only a slight delay when the subject performed a voluntary movement with the left hand. During a bimanual movement (D) stimulation of the left hemisphere only slightly delayed the onset of the EMG on the right side, but the recorded EMG seemed to consist of two parts. The first part starting with a slight delay (mEMG) may represent the involuntary movement, which accompanies the voluntary movement of the opposite hand and the second part (EMG) may represent the delayed voluntary movement. For each task (A±D), 8 trials are superimposed.
Tests for the bimanual condition revealed a significant facilitation of RT at the hand ipsilateral to TMS if applied with an ISI of 0 ms. A mean decrease of $48.5 \pm 24.7$ ms ($P < 0.001$) was found for the left hand and a mean decrease of $55.2 \pm 36.2$ ms ($P = 0.001$) was observed for the right hand. A significant increase in RT was observed on the side contralateral to TMS applied 100 ms after go-signal presentation. The EMG onset of the left side was delayed by $56.6 \pm 64.4$ ms ($P = 0.01$) and of the right side by $48.3 \pm 48.0$ ms ($P = 0.005$).

When ISI and RT were correlated the linear regression line revealed a steeper slope for TMS applied to the contralateral hemisphere compared with ipsilateral stimulation (test for polynomial trends; $F = 19.5, P = 0.02$).

3.2.3. Control conditions

Control conditions (vertex stimulation, sham stimulation) were performed during an unimanual task. Active TMS over motor cortex and control conditions were compared with repeated measures variance analysis which used the following conditions: (1) right or left hand; (2) sham stimulation, stimulation at vertex and active stimulation; (3) ISI of 0 and 100 ms. $t$-Tests were subsequently performed to test for significant differences between baseline conditions and stimulation conditions (sham/active TMS). Repeated measures variance analysis revealed a simple main effect for different ISIs ($F = 145.77, P < 0.001$) and the interaction of ISI and stimulation condition ($F = 117.6, P < 0.001$). $t$-tests revealed no significant difference between the control conditions (sham and vertex stimulation) and the baseline conditions (Fig. 2).

3.3. Unimanual task in the subject with congenital mirror movements

During unimanual thumb movements an EMG burst could be recorded in both the intentionally and the unintentionally moved hand. The EMG burst of the MM was smal-
ler in amplitude and shorter in duration for both hands (Fig. 3A). During voluntary movements with the right hand the MM in the left hand followed with a delay of $7.8 \pm 8.3$ ms while a mean delay of $23.3 \pm 10.8$ ms was observed during voluntary movements with the left hand. The difference between onset of voluntary movement and of MM was statistical significant (two-tailed Wilcoxon test for paired samples, $P < 0.01$) for both hands.

A magnetic pulse delivered ipsilateral or contralateral to a voluntary movement with an ISI of 0 ms caused a decrease in RT in both hands (Fig. 4). The relation of the EMG onset of voluntary movement and MM changed if TMS was applied to the hemisphere contralateral to the intended movement. Moving the left hand voluntarily decreased the difference between EMG onset of voluntary movement and of MM to $-0.9 \pm 0.4$ ms and to $-7.4 \pm 2.1$ ms if the right hand was moved voluntarily. Exactly the same difference in EMG onset between voluntary movements and MM could be observed when TMS was applied 50 or 100 ms after go-signal presentation. TMS of the motor cortex ipsilateral to the voluntary movement did not change the temporal relation of the EMG bursts in both hands.

Compared with the facilitation induced by TMS given simultaneously with go-signal presentation, RT was delayed for an ISI of 100 ms after both contralateral or ipsilateral stimulation (Figs. 3B,C and 4). The regression lines relating the timing of the magnetic stimulus and the RT for voluntary movements and MM were nearly identical for ipsilateral and contralateral stimulation (Fig. 4).

3.4. Bimanual movements in the subject with MM

During the bimanual task without TMS a nearly simultaneous EMG burst onset of left and right thumb movement could be recorded (mean difference $2.2 \pm 4.5$ ms). TMS during the bimanual task did affect RT and additionally caused a change of the EMG burst pattern. RT was significantly shortened in both hands when TMS was delivered at go-signal presentation (Fig. 5). With an ISI of 50 or 100 ms RT was successively delayed compared with an ISI of 0 ms (Fig. 5). The slopes of the regression lines for left and right hand movement were again nearly identical (96% for TMS applied to the right hemisphere and 89% for TMS applied to the left hemisphere).

TMS induced changes in the pattern of the EMG bursts. During a bimanual task the EMG recorded in one hand consisted both of the large intended muscle activity of this hand as well as of the smaller unintended EMG activity accompanying the movement of the contralateral arm. Due to the TMS-induced delay of the voluntary component of the EMG burst the unintended ‘mirror’ component could be visually segregated: Inspection of the EMG trace revealed a smaller EMG component representing the mirror movement which preceded the larger EMG burst characteristic of the intended movement by 30 ms (Fig. 3D).

4. Discussion

4.1. Reaction time studies in normal subjects

We have confirmed previous studies (Day et al., 1989; Pascual-Leone et al., 1992b; Masur et al., 1996) by showing that simple RT in normal subjects can be influenced by TMS. The amount of facilitation or slowing of RT depended on which motor cortex was stimulated and on the timing of the TMS pulse. It has been argued that the TMS-induced facilitation is due to ‘intersensory facilitation’ (Terao et al., 1997). The phenomenon of intersensory facilitation describes the fact that simple RT can be shortened if the cue signal is accompanied by a second stimulus in another modality (Bernstein et al., 1969; Nickerson, 1973). Sham stimulation or TMS applied over the vertex, however, had no significant effects on RT, which makes it unlikely that a
‘non-TMS-specific’ increase in the subject’s ability to react to a given stimulus is the explanation for the observed facilitation. Instead it has been suggested that transcallosal connections are responsible for the shortening of RT after ipsilateral motor cortex stimulation (Pascual-Leone et al., 1992b). TMS has been assumed to prepare M1 neurons via transcallosal connections and to enhance the information transfer between set-related neurons in the premotor cortex and movement-related neurons of the opposite motor cortex. Our data are compatible with such an interpretation.

In our study TMS applied with ISIs of 50 and 100 ms increasingly delayed RT after contralateral and ipsilateral stimulation. This finding is consistent with earlier observations (Day et al., 1989; Pascual-Leone et al., 1992b). Such a TMS-induced delay of voluntary movements has so far only been observed with TMS applied to the part of the motor cortex which generates the subsequent movements (Palmer et al., 1994). Stimulation of motor areas other than the primary motor cortex, such as the SMA, did not affect RT (Ziemann et al., 1997).

TMS applied to the motor cortex after go-signal presentation delayed contralateral RT and, to a smaller degree, ipsilateral RT. The amount of the observed delay was the same, regardless of whether subjects performed unimanual or bimanual movements. If one primary motor cortex controlled movements in both hands during a bimanual movement, it would have been expected that ipsilateral RT in an unimanual and a bimanual task should be differentially affected. The regression lines calculated for the TMS-dependent changes in RT, however, were nearly identical for unimanual and bimanual movements. The timing of simple bimanual movements would therefore seem to be controlled by each primary motor cortex independently. These findings support a recently published fMRI study which showed similar levels of activation of the sensorimotor cortex area regardless whether the hand moved by itself or together with the other hand during a bimanual task (Jäncke et al., 2000).

In addition, we found no evidence for a consistent hemispheric dominance for simple RT in our very homogeneous study population of right-handed young men. In more complex bimanual movements evidence for cerebral dominance has indeed been found. During a bimanual circular tracking task, the right hand leads the left by some 25 ms (Stucchi and Viviani, 1993). This asynchrony has been attributed to a functional dominance of the left hemisphere, with the other hemisphere receiving time-keeping information via transcallosal connections.

With simple unimanual movements an asymmetrical activation of the respective ipsilateral hemisphere has been observed. When subjects performed simple finger movements with the left hand the movement-related EEG potentials of the ipsilateral motor cortex area were greater than the ipsilateral sensorimotor cortex activation seen with right hand movements (Urbano et al., 1998; Babiloni et al., 1999). In addition, patients with left-hemisphere lesions have a more severe deficit of the ipsilateral hand compared with patients with right-hemisphere lesions (Haaland and Harrington, 1989). A more pronounced activation of the left motor cortex area with simple ipsilateral finger movements has been reported in studies using fMRI (Kim et al., 1993) and magnetoencephalography (Kristeva et al., 1991). Others, however, found no significant difference in the degree of ipsilateral motor cortex activity during left or right hand movements (Volkman et al., 1998). The functional significance of the activity in ipsilateral motor areas which has been found to increase with increasing complexity of the movement is unclear at present (Wexler et al., 1997). It may even be possible that the activity in the ipsilateral motor cortex seen with functional imaging techniques is inhibitory in nature. Our observation that TMS to the left or right motor cortex has the same effects on ipsilateral and contralateral RT makes it unlikely that the left motor cortex has a significant control over the timing of simple movements of the left hand. Otherwise, a significant slowing of the RT of the left hand would be expected with left motor cortex TMS.

If the control of movements in the bimanual RT task was hemispherically lateralized one would expect a consistent difference in RT between both hands, because the RT in the hand ipsilateral to the ‘motor-dominant’ cortex should be delayed by the transcallosal processing time compared with the RT in the contralateral hand. In our study, like in previous studies (Kaluzny et al., 1994), no such differences were encountered, making the concept of ‘motor dominance’ in simple symmetrical movements unlikely. Further experiments are required to investigate at what stage of movement complexity motor planning becomes lateralized.

4.2. Reaction time studies in the subject with congenital mirror movements

In the subject with congenital MM, TMS evoked MEPs in ipsilateral and contralateral thenar muscles with a latency difference of less than 4 ms. In addition the cortical stimulation sites for evoking MEPs of maximum amplitude were the same for ipsilateral and contralateral muscles. These findings can be taken as clear neurophysiological evidence for the existence of a significant number of uncrossed corticospinal fibres in our subject. It is, however, unclear to what extent the uncrossed corticospinal fibres participate in the execution of MM. A number of studies have tried to unravel the neurophysiological mechanism of MM in patients with Kallmann’s syndrome who are characterized by MM associated with hypogonadism and anosmia. Some authors suggested a reduction of transcallosal inhibitory activity resulting in a simultaneous activation of both motor cortices (Forget et al., 1986; Danek et al., 1992). A simultaneous activation of both motor cortices in patients with MM has also been postulated by Shibasaki and Nagae (1984) who found bilateral movement-related cortical potentials in response to intended unilateral hand movements. In addi-
tion, neuroimaging studies have described an activation of both the contralateral and ipsilateral motor cortex in subjects with congenital MM and in subjects with Kallmann’s syndrome (Cohen et al., 1991; Krams et al., 1997). The results of our study, however, suggest that MM originate in the ipsilateral hemisphere: TMS given at different interstimulus intervals influenced the latency of both the voluntarily and the unintentionally moved hand to the same extent: this was evident in the identical slope of the regression lines. In normal subjects performing bimanual movements the increase in RT was always larger for the contralateral hand. If MM originated in the contralateral motor cortex as has been suggested, it would be expected that TMS over the motor cortex ipsilateral to a voluntary movement delayed MM to a much greater extent than voluntary movements.

In unconditioned RT tasks the onset of voluntary movements preceded MM by some 15 ms. This almost simultaneous EMG onset (maximum recordable difference of 30 ms) in homogeneous muscles has been described in subjects with congenital MM but not in patients with acquired MM (Forget et al., 1986; Cohen et al., 1991). TMS applied to the motor cortex ipsilateral to a voluntary movement did not affect this stable shift in the onset of voluntary movements and MM. TMS to the motor cortex contralateral to a voluntary movement, however, changed the relative timing of the voluntary and MM irrespective of the interstimulus interval between go-signal and TMS. The increase in RT was larger for voluntary than for MM. Cincotta and co-workers have described a decrease in the length of the cortical silent period in hand muscles in a subject with MM, which has been taken as evidence for an abnormal bilateral activation of the hand motor cortex (Cincotta et al., 1996). Since there is a direct correlation between the length of the cortical silent period and the delay in movement onset (Roicik et al., 1993; Ziemann et al., 1997) these results are also compatible with the alternative hypothesis that voluntary and MM are generated in the same hemisphere. It could well be that ipsilaterally projecting corticospinal neurons are less susceptible to the TMS-induced delay than contralaterally projecting neurons which are responsible for the voluntary movements. With increasing interstimulus interval between go-signal and TMS, RT for mirror and voluntary movements increase in parallel, which strongly argues for a generation of both movements in one hemisphere. Our results, therefore, extend the careful neurophysiological investigations by Mayston and co-workers performed in patients with Kallmann’s syndrome who found clear evidence for a common synaptic drive from one motor cortex to homologous muscles of both hands (Mayston et al., 1997).

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