Effect of Transcranial Magnetic Stimulation on Bimanual Movements

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1Department of Neurology, the Neurological Institute, Taipei Veterans General Hospital, Taipei; 2Department of Neurology, National Yang-Ming University, Taipei; 3Department of Neurology, Cathay General Hospital, Taipei, Taiwan; and 4National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland

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Chen, Jen-Tse, Yung-Yang Lin, Din-E Shan, Zin-An Wu, Mark Hallett, and Kwong-Kum Liao. Effect of transcranial magnetic stimulation on bimanual movements. J Neurophysiol 93: 53–63, 2005. First published August 25, 2004; doi:10.1152/jn.01063.2003. Transcranial magnetic stimulation (TMS) of the motor cortex can interrupt voluntary contralateral rhythmic limb movements. Using the method of “resetting index” (RI), our study investigated the TMS effect on different types of bimanual movements. Six normal subjects participated. For unimanual movement, each subject tapped either the right or left index finger at a comfortable rate. For bimanual movement, index fingers of both hands tapped in the same (in-phase) direction or in the opposite (antiphase) direction. TMS was applied to each hemisphere separately at various intensities from 0.5 to 1.5 times motor threshold (MT). TMS interruption of rhythm was quantified by RI. For the unimanual movements, TMS disrupted both contralateral and ipsilateral rhythmic hand movements, although the effect was much less in the ipsilateral hand. For the bimanual in-phase task, TMS could simultaneously reset the rhythmic movements of both hands, but the effect on the contralateral hand was less and the effect on the ipsilateral hand was more compared with the unimanual tasks. Similar effects were seen from right and left hemisphere stimulation. TMS had little effect on the bimanual antiphase task. The equal effect of right and left hemisphere stimulation indicates that neither motor cortex is dominant for simple bimanual in-phase movement. The smaller influence of contralateral stimulation and the greater effect of ipsilateral stimulation during bimanual in-phase movement compared with unimanual movement suggest hemispheric coupling. The antiphase movements were resistant to TMS disruption, and this suggests that control of rhythm differs in the 2 tasks. TMS produced a transient asynchrony of movements on the 2 sides, indicating that both motor cortices might be downstream of the clocking command or that the clocking is a consequence of the 2 hemispheres communicating equally with each other.

INTRODUCTION

Bimanual coordination constitutes a large part of human movements and is characterized by precise spatial and temporal interactions between the limbs. Bimanual rhythmic coordination of the hands can be done simultaneously in the same direction (in-phase, with phase difference 0°) or in the opposite direction (antiphase, with phase difference 180°). Both in-phase and antiphase tasks are easily maintained in a stable rhythm at low frequencies, but an antiphase task often spontaneously converts to in-phase at higher frequencies (Kelso 1984). Rhythmic movements can be modulated by sensory input and descending influences from the brain stem or higher motor centers (Elble and Koller 1990).

Hemispheric dominance for motor control in humans is suggested by multiple lines of evidence. For example, in right-handers the transcallosal inhibition after transcranial magnetic stimulation (TMS) of the dominant left hemisphere was more marked than after stimulation of the nondominant right hemisphere (Netz et al. 1995). Using TMS to investigate corticospinal excitability in right-handed subjects, contralateral inhibition was more efficient for left hemisphere stimulation than for right (Leocani et al. 2000).

Interhemispheric connections appear to be important for bimanual coordination. Acallosal patients commit more errors in bimanual tapping tasks than normal subjects (Leonard et al. 1988). Interhemispheric EEG alpha coherence is increased during bimanual rhythmic tasks in children (Knyazeva et al. 1994). Interhemispheric EEG coherence increases in initial training but then decreases in a well-trained bimanual coordination task (Andres et al. 1999).

To test the influence of different inputs on an oscillation generator, the technique of phase resetting can assess whether a given input can reset the pacemaker to a fixed phase in its cycle; if it does so, then the input exerts a significant influence over the oscillator (Winfree 1980). Phase resetting can be quantified with the method of “resetting index” (RI). Using this method, the afferent influence on Parkinson tremor and essential tremor has been measured (Lee and Stein 1981). The measure is also potentially applicable to study any input on any type of repetitive activity including voluntary rhythmic movements (Wagener and Colebatch 1996). Unilateral TMS exerts both excitatory and inhibitory effects. By applying TMS to the motor cortex, it may reset Parkinson tremor, essential tremor (Britton et al. 1993; Pascual-Leone et al. 1994), orthostatic tremor (Tsai et al. 1998), palatal tremor (Chen et al. 2000), and regular voluntary muscle contraction of contralateral upper limb (Britton et al. 1993; Wagener and Colebatch 1996). The rhythm resetting is closely related to the silent period provoked by TMS (Pascual-Leone et al. 1994). This indicates that TMS modulates activity through an inhibitory effect on the neural network from the oscillator to the execution system (Britton et al. 1993; Wagener and Colebatch 1996). Here, we studied: 1) whether TMS applied to one hemisphere resets the rhythmic movements of bimanual tasks; 2) whether there is any difference between TMS disruption to ipsilateral and contralateral finger tapping; 3) whether the TMS effect differs between unimanual and bimanual rhythmic tasks; 4) whether there is any difference of the TMS effect between bimanual in-phase
and antiphase tasks; and 5) whether there is hemispheric dominance of the TMS effect on bimanual rhythmic task.

METHODS

Subjects

Six healthy right-handed volunteers (5 males, 1 female; age: 26–36 yr) were studied. Experiments were approved by the IRB and informed consent was obtained.

Electromyographic (EMG) recording

Each subject sat in front of a table and kept his/her arms on the table. Two surface electrodes, 1 cm apart, were put on the muscle belly of the extensor digitorum communis of both forearms with ground lead on one wrist. EMG activity was fully rectified and recorded 4 s before and 6 s after TMS with a band-pass 20–3K Hz and was stored in an EMG machine (Nihon Kohden, Neupack 8). After the procedure, EMG recordings could be recalled, digitally smoothed using a 5-point running mean, and averaged for further analysis.

TMS

TMS was delivered with a figure-of-eight coil (Magstim 200, Camarthenshire, UK) placed over the motor cortex, with the handle held posteriorly and oriented sagittally for focal stimulation. The precise coil position was adjusted to yield a maximal response in the target muscle at a given stimulus intensity. The appropriate coil position was marked. Motor threshold (MT) was defined in the relaxed forearm muscle as the intensity to elicit ≥5 motor-evoked potentials (MEPs) with peak-to-peak amplitude more than 100 μV in 10 consecutive stimuli. In checking for MT, we used stimulus intensities beginning at 70% of maximal output and then gradually decreased the intensity in 2% steps until appropriate MEP amplitudes were obtained. Respective MTs of the right and left forearm muscles were defined in each subject. The interval between 2 stimuli was ≥30 s.

Unilateral TMS to Contralateral and Ipsilateral Finger Tapping. Each subject was asked to maintain rhythmic tapping of the index finger of either the right or left hand at a freely chosen, comfortable rhythm. After practicing for several times, rhythm and EMG signals were monitored on the EMG machine until the rhythm was stable and EMG amplitude of each burst was similar. TMS, set at 0.5MT initially with an increment of 20% MT intensity was stable and EMG amplitude of each burst was similar. TMS, set at 0.5MT initially with an increment of 20% MT intensity was delivered randomly over the left motor cortex and then to the right motor cortex; ±20 trials were collected for each side.

Analysis

The RI was used to quantify the influence of TMS on unimanual and bimanual rhythmic movements (Lee and Stein 1981) and was also described in our previous study in palatal tremor (Chen et al. 2000). Data reduction was as follows: 1) The peaks of the last 5 EMG bursts before TMS in individual trials were identified manually; intervals between the burst peaks were measured as actual intervals. The mean of these 4 interpeak cycle intervals was the averaged interval (ave I). 2) The time between the last EMG burst before TMS and TMS was determined as a proportion of the averaged interval (%I). 3) The interval between TMS and the first EMG burst after TMS was defined as the silent period (SP) after TMS and was measured as the latency of the rhythmic movement reappearance and was also determined as a proportion of the averaged interval. 4) Intervals of the first 5 EMG bursts after TMS were also measured as a proportion of the averaged interval (I1–I5%). The predicted time for the 5 bursts after TMS was calculated from the base of the averaged time interval of the last movement burst before TMS. 5) The difference between the actual and predicted time interval of the first 5 bursts after TMS [d = (I – I/ave I)] was plotted against the time interval of the last EMG burst before TMS (%I) in each single trial (Fig. 1A). For each trial, one point was plotted in each of 5 graphs, one for each of the first 5 bursts after TMS. Because the time for delivering TMS varied randomly in each trial, the plotted points in each stimulus condition were combined to calculate 5 linear regressions, one for each of the 5 intervals after TMS. The time to deliver TMS varied randomly across trials, and the plotted points for all trials with a given stimulus condition were combined to calculate 5 individual linear regressions, one for each of the first 5 bursts after TMS. RI was defined as the average slope of the regression lines for these 5 bursts after TMS. The x-axis was the interval of the last EMG burst before TMS (%I); the y-axis was the interval of actual burst minus the predicted burst (d) (Fig. 1B). If TMS caused a prominent effect to make SP near constant, the slope would be near 1. If TMS caused no disruption, there would be no SP and the slope would be near 0. Therefore resetting was absent if RI equaled 0, and was complete if it equaled 1.

Nonparametric comparisons among groups were done with the Kruskal–Wallis test. A value of P < 0.05 was defined as statistically significant. For multiple comparisons, we used the Wilcoxon rank-sum test. Bonferroni correction was applied for multiple comparisons to ensure that the overall rate of type I errors was not >0.05. The correlation of averaged RI with magnetic intensity and tapping frequency was done by Pearson correlation test. A value of P < 0.05 was defined as statistically significant.

For visual display, 20 rectified EMG trials were averaged. Because the stimuli were delivered randomly during the movement cycle interval, the movement bursts before TMS are flattened as a result of the effect of averaging out. EMG activity after TMS shows a burst pattern as a result of this superimposition if TMS resets the rhythmic movement.

RESULTS

All subjects maintained rhythmic tapping at their freely chosen rate. The frequencies varied from 1.6 to 4.1 Hz (Table 1). Frequency analysis of intraindividual variation showed no significant difference between right and left hands in the unimanual or bimanual tasks. The rate was slightly slower in the bimanual in-phase task and slower in 3 of 6 subjects during the antiphase task, but without significant statistical difference
The variability, represented as SD, of the cycle intervals was similar in the tasks of unimanual and bimanual in-phase tasks, but was mildly increased in 3 of the 6 subjects for the antiphase task. MT for left motor cortex was 45.0 ± 3.7%, slightly lower than that for right motor cortex, 48.0 ± 3.1% (P = 0.017).

**RI**

During the unimanual task, TMS affected both contralateral and ipsilateral hand tapping and correlated well with TMS intensity (Fig. 2A). This was also shown by SP duration. RI, even at subthreshold intensities, was relatively high, which might be attributable to activity of the motor cortices during finger tapping compared with the rest state. RI was not correlated with the tapping frequency at any intensity of either hemisphere during either the unimanual or bimanual task. In the unimanual finger tapping, the contralateral RI was significantly higher than the ipsilateral RI, regardless of which hemisphere TMS was applied (left TMS: P = 0.0001; F = 37.34, right TMS: P = 0.0003; F = 14.67). Post hoc testing showed that RI was significantly less in the ipsilateral than in the contralateral hand, from 0.7 to 1.5MT (P = 0.0051 at 0.7MT; P = 0.0049 at 0.9MT; P = 0.0051 at 1.1MT; P = 0.0051 at 1.3MT; P = 0.0051 at 1.5MT) to left TMS (Fig. 2B) and from 1.1 to 1.5MT (P = 0.0004 at 1.1MT; P = 0.0001 at 1.3MT; P = 0.0001 at 1.5MT) to right TMS (Fig. 2C). When

| TABLE 1. The cycle intervals of finger tapping (ms) |
|-----------------|-----------------|-----------------|
| **Subject**     | **Right Hand**  | **Left Hand**   |
| 1                | 264.5 ± 12.2    | 266.3 ± 11.9    |
| 2                | 471.5 ± 20.9    | 475.8 ± 23.4    |
| 3                | 244.0 ± 9.6     | 248.8 ± 12.8    |
| 4                | 431.0 ± 22.2    | 435.8 ± 26.3    |
| 5                | 602.4 ± 28.6    | 605.7 ± 29.1    |
| 6                | 507.8 ± 25.8    | 504.0 ± 33.5    |

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<tr>
<th><strong>Unimanual Task</strong></th>
<th><strong>Bimanual Task</strong></th>
<th><strong>Antiphase</strong></th>
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<td>610.3 ± 29.9</td>
<td>619.0 ± 32.2</td>
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<td>500.5 ± 26.0</td>
<td>502.5 ± 29.5</td>
<td>549.5 ± 49.5</td>
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\(P = 0.94\). The variability, represented as SD, of the cycle intervals was similar in the tasks of unimanual and bimanual in-phase tasks, but was mildly increased in 3 of the 6 subjects for the antiphase task. MT for left motor cortex was 45.0 ± 3.7%, slightly lower than that for right motor cortex, 48.0 ± 3.1% (P = 0.017).
we compared the side difference for contralateral TMS on the unimanual task. RI of the right hand to left TMS was higher than that of the left hand to right TMS ($P = 0.035; F = 4.64$). Post hoc tests showed significant differences at 0.7 and 1.3–1.5MT ($P = 0.005$ at 0.7MT; $P = 0.0051$ at 1.3MT; $P = 0.0051$ at 1.5MT). There was no difference in the ipsilateral RI of TMS to either hemisphere ($P = 0.44; F = 0.44$).

In the bimanual in-phase movement, unilateral TMS modulated the rhythmic finger tapping bilaterally and simultaneously (Fig. 3A). There was a gradual increment in RI of bimanual hand movements as TMS intensity increased for stimulation of both hemispheres. Contralateral RI was higher than the ipsilateral one, whether TMS was applied to the left ($P = 0.020; F = 5.70$) or right side ($P = 0.018; F = 5.86$). For left TMS, the contralateral RI was higher than the ipsilateral one at 0.7MT ($P = 0.002$), 1.3MT ($P = 0.0015$), and 1.5MT ($P = 0.0045$). For right TMS, contralateral RI was higher at 0.9MT ($P = 0.0006$), 1.1MT ($P = 0.0021$), and 1.5MT ($P = 0.0036$). Differential resetting indicated that the hands temporarily lost synchrony after TMS. There was no hemispheric difference on
disruption of bimanual in-phase movements ($P = 0.56; F = 0.34$) (Fig. 3B).

Comparing RIs of the contralateral hand to TMS, there was less resetting in the bimanual task compared with that in the unimanual task, but this did not reach significance ($P = 0.31; F = 1.05$ in right hand to left TMS; $P = 0.41; F = 0.69$ in left hand to right TMS). However, the ipsilateral RIs to TMS in the bimanual movements were significantly higher than those in the unimanual movements. This was ascribed to a large increase in the ipsilateral RIs both to left TMS ($P = 0.0071; F = 8.32$) and to right TMS ($P = 0.015; F = 9.77$) in the bimanual task. Post hoc tests showed the ipsilateral RI in the unimanual movement was lower than that in the bimanual movement to left TMS at 1.1MT ($P = 0.0095$), 1.3MT ($P = 0.0045$), and 1.5MT ($P = 0.0018$) and to right TMS at 0.9MT ($P = 0.008$) and 1.3MT ($P = 0.007$).

There was no difference among the 5 RIs after TMS in unimanual or bimanual in-phase tasks and to TMS of either hemisphere. At higher magnetic intensities, the RI of each muscle burst after TMS gradually decreased in the contralateral hand during bimanual movements (Fig. 4A), although this trend was not significant. This was not seen in the ipsilateral hand (Fig. 4B).

**SP after TMS**

SP after TMS was correlated with RI for both uni- and bimanual in-phase tasks and for both hemispheres. Contralateral SP was significantly longer than the ipsilateral SP to left TMS ($P = 0.0021; F = 10.17$) and to right TMS ($P = 0.001; F = 15.34$) in the unimanual task. When we compared the SP at each intensity, the SP of the contralateral hand was significantly longer than the ipsilateral one at 0.7 to 1.5MT ($P = 0.0001$ at each MT) to left TMS in the unimanual task (Fig. 5A) and 0.9MT ($P = 0.047$), 1.1MT ($P = 0.008$), 1.3MT ($P = 0.003$), and 1.5MT ($P = 0.006$) to right TMS. There was no difference between the contralateral SP ($P = 0.25; F = 1.33$) or the ipsilateral SP ($P = 0.38; F = 1.05$) to left and right TMS. In the bimanual in-phase task, SP of the contralateral hand was longer than that of the ipsilateral hand when TMS was applied to either hemisphere (left TMS: $P = 0.001; F = 13.83$, right TMS: $P = 0.031; F = 4.86$) (Fig. 5B). Comparing
TMS to left or right side, there was no significant difference in contralateral SP \((P = 0.44; F = 0.60)\) or ipsilateral SP \((P = 0.48; F = 0.50)\).

**Bimanual antiphase movements**

In bimanual finger tapping, TMS produced less disruption on both hands in the antiphase task than in the in-phase task (Fig. 6A). RI of both hands with TMS to either hemisphere in the antiphase task was less than that in the in-phase task \((P = 0.0001\) in left and right TMS). There was no hemispheric difference \((P = 0.70)\) in left or right TMS in bimanual antiphase movement. There was no difference in contralateral resetting \((P = 0.65)\) or ipsilateral resetting \((P = 0.47)\) when TMS was applied to either hemisphere. The contralateral RI was larger than the ipsilateral one \((left\ TMS: P = 0.0155; right\ TMS: P = 0.0062)\). With TMS at 1.5MT to left motor cortex, the contralateral RI was \(0.130 \pm 0.016\) in antiphase movement and \(0.752 \pm 0.049\) in in-phase movement \((P = 0.0001)\). With TMS at 1.5MT to right motor cortex, the contralateral RI was \(0.116 \pm 0.040\) in antiphase movement and \(0.699 \pm 0.050\) in in-phase movement \((P = 0.0001)\). The ipsilateral RI in the antiphase movement at 1.5MT was also less \((0.030 \pm 0.016)\) in left TMS; \(0.021 \pm 0.017\) in right TMS) than that in in-phase movement \((0.629 \pm 0.073\) in left TMS; \(0.576 \pm 0.063\) in right TMS) \((P = 0.0001)\). RI for the first interval was the highest, and then declined in the following intervals in both hands during TMS to left and right hemispheres (Fig. 6B). In the in-phase movement, although there was transient suppression after TMS, both hands tapped concomitantly in the recovery phase. In the antiphase movement, although the TMS suppression phenomenon was not so marked, there was a phase transition from antiphase to in-phase immediately after TMS, especially at high intensity (Fig. 7). There was no significant change in the cycle interval before and after TMS.

**DISCUSSION**

In this study, we demonstrated that TMS disrupted unimanual and bimanual in-phase finger tapping in a self-paced rhythm. In the unimanual task, it was easier to block contralateral than ipsilateral finger tapping. In addition, the disruptive effect of left TMS to the right hand was greater than that of right TMS to the left hand. In the bimanual in-phase task, TMS...
modulated finger tapping of both hands simultaneously, whether TMS was applied to either hemisphere or applied without side differentiation. The disruption to the contralateral hand was more than that to the ipsilateral hand, which indicates that the influence of TMS to both hemispheres on rhythmic movement was similar, and that this effect was enhanced in the ipsilateral hand when the hands moved together. TMS had difficulty in affecting antiphase bimanual movement. This might be attributable to more complicated interhemispheric communication in this type of relatively complex action.

With unimanual movement, TMS more easily disrupted contralateral than ipsilateral movement. In unimanual movement, TMS disrupted contralateral rhythmic movements, as studies in normal subjects (Britton et al. 1993) and patients with Parkinson’s tremor and essential tremor (Pascual-Leone et al. 1994) have shown. TMS had far less blocking effect on ipsilateral movement in our study. This blocking might be a direct effect of TMS on the motor cortex, although sensory feedback may also play a significant role. The resetting and the SP of both the contralateral and ipsilateral hands were correlated with magnetic intensities, as the results in patients with Parkinson’s tremor and essential tremor (Pascual-Leone et al. 1994) and in palatal tremor (Chen et al. 2000) have demonstrated. Britton et al. (1993) argued that the action level was at the motor cortex because torque pulses were relatively ineffective in evoking resetting. Tremor resetting was correlated with SP, but not MEP amplitude (the muscle twitch) elicited by TMS (Pascual-Leone et al. 1994). In addition, resetting still exists when the perturbation effect is avoided and correlates with the first poststimulus EMG burst, which indicates a direct effect from TMS to the motor cortex (Wagner and Colebatch 1996). In our study, TMS at subthreshold intensity could still reset the rhythm without MEPs in the contralateral hand, and there was minimal resetting in the ipsilateral hand, even though no MEPs were measured.

Even though motor control is mainly contralateral, there are some possible reasons why TMS can influence the ipsilateral hand.

1) TMS may produce inhibitory effects on the opposite hemisphere (Ferbert et al. 1992) by the corpus callosum (Schnitzler et al. 1996) (Fig. 7A). TMS can produce an ipsilateral silent period and this appears to be mainly through transcallosal inhibition (Ferbert et al. 1992; Wassermann et al. 1991).

2) TMS may produce a transcallosal effect by influences on premotor cortices to affect the other hemisphere. Repetitive TMS over primary motor cortex can also increase supplementary motor area (SMA) activation (Siebner et al. 2001). In primates, hand representations of SMA are strongly interconnected by the corpus callosum (Rouiller et al. 1994), and lesions of the SMA can interrupt bimanual coordination (Chan and Ross 1988; Laplane et al. 1977).

3) TMS may have influence by an ipsilateral descending pathway. Positron emission tomography (PET) studies in humans demonstrate that finger or hand movements cause significant activation in the ipsilateral primary motor cortex (Blinkenberg et al. 1996; Shibasaki et al. 1993). At high stimulation intensities, TMS can elicit MEPs from ipsilateral limb muscles including the intrinsic hand muscles (Wassermann et al. 1991, 1994; Ziemann et al. 1999). This effect is
likely by an uncrossed corticospinal and/or corticoreticulospinal pathway. Therefore TMS could affect a hypothetical ipsilateral oscillator system.

With bimanual in-phase movement, the 2 hemispheres influence each other mutually because, compared with unimanual movement, it becomes more difficult to disrupt contralateral movement and easier to disrupt ipsilateral movement. The RI of the contralateral hand to TMS in the bimanual task was lower than that in the unimanual task, whereas RI of the ipsilateral hand to TMS in the bimanual task was significantly higher than that in the unimanual task. The RI difference between the 2 hands decreased more in the bimanual task than in the unimanual task. It appeared that control of bimanual in-phase movement was synchronized.

Many actions are performed in cyclic or repetitive forms. To execute such cyclic movement, time is supposed to be determined by an internal clock containing a temporal oscillator (Treisman et al. 1992, 1994). Wing and Kristofferson (1973) proposed a hierarchical 2-level model for finger tapping with a central timer to trigger a response and a motor implementation mechanism. This model was applied to the study of motor disorders (O’Boyle et al. 1996; Pastor et al. 1992; Wing et al. 1984). Results from neuroimaging studies suggested that the premotor cortices, particularly the SMA, might participate in these internal timing mechanisms. In a functional magnetic resonance imaging (fMRI) study, the primary motor cortex, SMA, premotor area, and prefrontal area were more activated in memory-timed than visually cued finger movement. This
indicated that these areas were involved in the generation of accurate timing, possibly functioning as a central clock (Kawashima et al. 2000).

In bimanual movement, there is decreased movement variation, suggesting interactions between separate left and right pacemaker systems (Helmuth and Ivry 1996). The authors of this study inferred that 2 independent timers were integrated and averaged to reduce the tapping variability. Another example is that the reaction and movement times of bimanual pointing were indistinguishable in both hands even when manual complexity was different (Kelso et al. 1979). This clearly requires bilateral interaction. When attempting to disrupt one clock, the opposite clock can maintain the rhythm relatively well, making the disruption of the clock more difficult. Such evidence appears to favor an independent clock in each hemisphere, with cross talk between the hemispheres to produce bimanual coordination (Fig. 8B).

With stimulation during bimanual movement, the 2 hands went transiently out of synchrony, suggesting that there might be independent clocks. That RI and SPs of the 2 hands were not equally disrupted demonstrates that TMS had a different influence on the 2 clocks. If there was only one clock, the disruption after TMS should be equal in the 2 hands, and this should occur in one hemisphere that is dominant in controlling the cyclic or repetitive movement.

There is an almost equal right and left hemisphere stimulation effect, indicating that there is no hemispheric dominance for running bimanual movement. In the unimanual task, TMS could interrupt the rhythm of the right hand more easily, although the difference was small. However, hemispheric dominance was minimal in the bimanual movement. In the bimanual movement, contralateral RI and SP to TMS were similar for the 2 hands. This indicates that the influence of the clocks is similar. The dominance of handedness in bimanual movements is controversial. There is evidence that the clocking systems for rhythmic movements in each hemisphere are independent of each other. There were no hemispheric differences in cortical activation in bimanual tasks in both fMRI (Toyokura et al. 1999) and PET studies (Fox et al. 1985). However, some authors argue that there is hemispheric dominance for bimanual coordination (Lang et al. 1990; Stucchi and Viviani 1993; Swinnen et al. 1996; Viviani et al. 1998).

In bimanual movement, antiphase movement was more difficult to disrupt than in-phase movement. It was difficult for TMS to reset the rhythm of the bimanual antiphase movement for either hand. The reason that TMS has more difficulty affecting the rhythmic movement in this condition might be the...
clock in the nonstimulated hemisphere. In the bimanual antiphase movement, the clocks dissociate and work independently with mutual correlation (Fig. 8C). If these clocks lost their connection completely in the antiphase movement, TMS disruption should be only in the contralateral hand, and the ipsilateral rhythm would continue. Magnetic intensity was based on the threshold of the rest state for the respective hemisphere. The actual threshold may vary in different conditions, and the TMS effect may not be comparable in both the antiphase and in-phase movements. Complex sequential finger movements recruit different brain areas, including the primary sensorimotor area, premotor area, SMA, cerebellum, and putamen (Sadato et al. 1996), and the sensorimotor cortex and SMA are activated much more for antiphase than for in-phase tasks (Immisci et al. 2001; Stephan et al. 1999; Toyokura et al. 1999).

An alternative hypothesis to TMS having a direct effect on motor cortex is that sensory feedback blocks oncoming movement. The afferent information from the perturbed hand elicited by TMS may contribute to resetting the timing signals. The interaction of the central clock with peripheral input has been difficult to determine (Elble and Koller 1990). The internal clock that determines time perception has been studied as a surrogate for this oscillator. When time intervals to be estimated are accompanied by auditory clicks that recur at certain critical rates, perturbations in time estimation occur (Treisman 1995). This indicates that the internal clock was influenced by peripheral afferents. The sensory input attributed to limb perturbation by TMS might cause a similar perturbation of timing estimation of the clock and produce a resetting of rhythm.

Other arguments are consistent with the sensory reafferent theory. 1) The phase resetting increases with TMS intensity. The degree of perturbation would be greater as TMS increases, increasing the sensory reafferent flow. The clock might be disrupted by this sensory reafferent, and when TMS is of sufficient intensity, the disruption might force the oscillation to restart. Resetting would likely be done to overcome the effects of the perturbation. Voluntary rhythm can be reset not only by TMS but also by peripheral nerve stimulation (Cobleat and Wagener 1999) and by torque pulses (Britton et al. 1992). Some reports have mentioned the influence of sensory reafference in the repetitive tapping of isochronous intervals (Aschersleben and Prinz 1995; Wing 1977). 2) The nonperturbed hand can provide an attractor for the perturbed hand and cause less phase resetting during bimanual in-phase movements. During bimanual tapping, additional tactile–kinesthetic reafferences from the other hand provide more information to decrease the variability (Drewing et al. 2002). The increased sensory reafferent might reinforce the stability of both hands and decrease the TMS blocking effect. Meanwhile, the perturbed hand might also cause a lag in the rhythm on the other hand. 3) Given the reduced spatial correspondence of the 2 hands during antiphase movements, the hand ipsilateral to the TMS is not affected by the perturbation, and thus can provide a strong reference for phase resetting or to overcome the perturbation elicited by TMS. 4) There was minimal resetting that was greater in the first interval than that in the following intervals during antiphase tapping for the hand contralateral to stimulation. Perhaps the perturbation will cause delay in the next movement, which looks like a phase reset, but instead the hand quickly returns to an antiphase mode.

However, sensory reafference cannot be the only mechanism influencing rhythmic movements. In the study of the disruption of patterns in 2-limb coordination, passive mobilization of a third limb by the experimenter affected antiphase movement more than in-phase movement (Swinnen et al. 1995). This points to the differential stability of these patterns and suggests that antiphase coordination depends more on the monitoring of kinesthetic affinements than on in-phase coordination (Swinnen et al. 1995). This result is contrasted with ours. Therefore further investigation is needed to clarify the interaction of reafferent and central effects to the central clock.

References


