Effect of Low-Frequency Repetitive Transcranial Magnetic Stimulation on Interhemispheric Inhibition

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INTRODUCTION

Repetitive transcranial magnetic stimulation (rTMS) involves the application of regularly repeated magnetic pulses, and a stimulation rate of ≤1 Hz is referred to as low-frequency rTMS (Wassermann 1998). rTMS can activate or inhibit cortical activity depending on stimulation parameters and the effects of low-frequency stimulation are often opposite to those of high-frequency rTMS. Suprathreshold (Chen et al. 1997) and subthreshold (Romero et al. 2002) low-frequency rTMS reduce corticospinal excitability at the stimulation site. Reduction in cortical excitability, measured by suppression of size of motor-evoked potentials (MEPs), may last for >15 min after 15–25 min of stimulation at ~1 Hz (Chen et al. 1997; Ger-schlager et al. 2001). The neurophysiological effects of low-frequency rTMS form the basis of potential therapeutic application of rTMS in several neurological and psychiatric disorders (Hoffman et al. 2003; Siebner et al. 1999).

Cognition and smooth performance of voluntary movements is dependent on the proper functioning of the cortico-cortical excitatory and inhibitory processes. Single- and paired-pulse TMS protocols can test several different intracortical inhibitory and facilitatory processes (Chen 2004; Hallett 2000). These include short interval intracortical inhibition (SICI) and intracortical facilitation (ICF) (Kujirai et al. 1993), long interval intracortical inhibition (LICI) (Valls-Sole et al. 1992; Wassermann et al. 1996), and the contralateral silent period (cSP) (Cantello et al. 1992). rTMS have been shown to affect several of these processes, depending on the frequency and intensity of stimulation. Low-frequency rTMS may have no effect (Romero et al. 2000) or shorten the cSP (Fierro et al. 2001), possibly through decreased excitability of inhibitory cortical neurons. After subthreshold 1-Hz rTMS, there is decreased ICF without concomitant change in SICI (Pascual-Leone et al. 1998; Romero et al. 2002) although a study using suprathreshold rTMS found no change in SICI or ICF (Plewnia et al. 2003). These reports suggest rTMS has different effects on different cortical circuits.

In addition to the effects in the stimulated area, rTMS also change the excitability of other cortical areas. For example, positron emission tomography studies showed that rTMS causes blood flow changes in remote but interconnected cortical areas (Paus et al. 1997, 2001). Low-frequency rTMS of the premotor cortex decreases the excitability of the motor cortex (Gerschlager et al. 2001), and low-frequency rTMS of the motor cortex may change the excitability of the contralateral motor cortex (Gorsler et al. 2003; Plewnia et al. 2003; Schamba et al. 2003; Wassermann et al. 1998).

Interhemispheric inhibition (IHI) is a physiologic phenomenon that may help to maintain hemispheric dominance in cognitive and motor tasks by suppressing undesired activity of the opposite hemisphere. There are two methods to evaluate IHI in humans: a paired-pulse method (will be termed ppIHI) and the ipsilateral silent period (ISP). ppIHI involves applying a conditioning stimulus (CS) to the motor cortex (M1), which inhibits the size of the MEP produced by a test stimulus (TS) applied to the opposite M1 6–50 ms later (Chen et al. 2003; Ferbert et al. 1992; Gerloff et al. 1998). At interstimulus...
interhemispheric connections between both motor cortices. 

METHODS

Subjects

We studied 13 healthy volunteers (4 women and 9 men), aged 28–59 yr [40.9 ± 12.9 (SD) yr] in the main experiment. Subjects were recruited through advertisements in the community and postings within the hospital. All subjects gave their written informed consent, and the protocol was approved by the University Health Network Research Ethics Board in accordance with the declaration of Helsinki on the use of human subjects in experiments.

EMG recording

Surface EMG was recorded from the right and left first dorsal interosseous (FDI) muscles, using disposable disc electrodes placed in a tendon-belly arrangement over the bulk of the FDI muscle and the first metacarpal-phalangeal joint. The subjects were instructed to maintain muscle relaxation throughout the study, and the EMG was monitored on a computer screen and via speakers at high gain. The EMG signal was amplified (Model 2024F, Intronix Technologies, Bolton, Ontario, Canada), filtered (band-pass: 2 Hz to 2.5 kHz), digitized at 5 kHz (Micro 1401, Cambridge Electronics Design, Cambridge, UK) and stored in a laboratory computer for off-line analysis.

TMS procedure

A conditioning stimulus (CS)-test stimulus (TS) paradigm similar to that described by Ferbert et al. (1992) was used to evaluate IHI. A suprathreshold CS was delivered to the M1 followed by a suprathreshold TS delivered to the contralateral M1 at ISIs of 4, 10, and 40 ms. ISIs of 10 and 40 ms were chosen because they test different aspects of ppIHI (Chen et al. 2003), and ISIs of 4 ms may induce intrahemispheric facilitation (IHF) (Hananjima et al. 2001). Both the left-to-right ppIHI (LIHI) and right-to-left ppIHI (RIHI) were examined. ppIHIIs before rTMS are indicated by pre-LIHI and pre-RIHI and those after rTMS by post-LIHI and post-RIHI.

For the IHI studies, four Magstim 200 stimulators (Magstim, Dyfed, UK) and two Bistim modules were used. Each motor cortex was stimulated with two Magstim stimulators connected via a Bistim module to a 7-cm figure-eight coil. This setup allowed us to use different stimulus intensities for the one hemisphere in the same experimental run for the post-rTMS IHI study. The stimulators produced monophasic current.

Pre-rTMS IHI

The optimal positions for the right and left M1 to produce MEPs in the contralateral FDI muscles were determined and marked on the scalp to ensure identical placement of the coil throughout the experiment. The coil was placed tangentially to the scalp with the handle pointing backward and laterally at an approximate angle of 45° to the midsagittal line. For each M1, both the CS and TS were the minimum stimulus intensity (determined to the nearest 1% of the maximum stimulator output) that produces a peak-to-peak MEP amplitude of ≥1 mV in ≥5 of 10 trials (indicated as 1mVpre for left M1 and 1mVpre for right M1). In some subjects, it was not possible to hold both coils at the optimal positions because of the size of the coil and minor changes of coil positions were required. In these subjects, the stimulus intensities required to obtain ~1-mV MEPs were determined with the coils at the adjusted positions, and same positions were used before and after rTMS.

The test conditions are shown in Table 1. Conditions 1–3 tested pre-RIHI and conditions 4–6 tested pre-LIHI. For pre-RIHI, the MEP amplitude for the TS alone from left M1 stimulation was taken from the MEP produced by the CS in condition 2pre. Similarly, for pre-LIHI, the MEP amplitude for TS alone was taken from the MEP produced by the CS in condition 3pre. Each run consisted of 10 trials of each of the six conditions delivered in a random order (60 trials) with 6 s between trials.

rTMS procedure

rTMS of left M1 was performed with a 7-cm figure-eight coil connected to a Magstim Super Rapid stimulator. This stimulator produces biphasic currents. The coil was placed tangentially to the scalp with the handle pointing backwards and laterally at an approximate angle of 45° to the midsagittal line, and was perpendicular to the
TABLE 1. Stimulus conditions used in pre-rTMS IHI study

<table>
<thead>
<tr>
<th>Inhibition Studied</th>
<th>Condition</th>
<th>First Pulse (CS)</th>
<th>Second Pulse (TS)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>M1</td>
<td>Strength</td>
</tr>
<tr>
<td>pre-RHI</td>
<td>1pre</td>
<td>R</td>
<td>1mV_{Rpre}</td>
</tr>
<tr>
<td></td>
<td>2pre</td>
<td>R</td>
<td>1mV_{Rpre}</td>
</tr>
<tr>
<td></td>
<td>3pre</td>
<td>R</td>
<td>1mV_{Rpre}</td>
</tr>
</tbody>
</table>

| pre-LIHI          | 4pre     | L     | 1mV_{Lpre} | 4   | R     | 1mV_{Rpre} |
|                   | 5pre     | L     | 1mV_{Lpre} | 10 | R     | 1mV_{Rpre} |
|                   | 6pre     | L     | 1mV_{Lpre} | 40 | R     | 1mV_{Rpre} |

CS, conditioning stimulus; ISI, interstimulus interval; L, left; LIHI, interhemispheric inhibition from left M1 (motor cortex) to right M1; R, right; RHI, rhinal hemispheric inhibition from right M1 to left M1; TS, test stimulus; 1 mV_{Rpre}, pre-rTMS stimulus intensity over right M1 that produced a peak-to-peak major-evoked potential (MEP) amplitude of ≥1 mV from right first dorsal interosseus (FDI); 1 mV_{Lpre}, pre-rTMS stimulus intensity over left M1 that produced a peak-to-peak MEP amplitude of ≥1 mV from left FDI.

TABLE 2. Stimulus conditions used in post-rTMS IHI study

<table>
<thead>
<tr>
<th>Inhibition Studied</th>
<th>Condition</th>
<th>First Pulse (CS)</th>
<th>Second Pulse (TS)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>M1</td>
<td>Strength</td>
</tr>
<tr>
<td>post-RHI{adj}</td>
<td>1_{post}</td>
<td>R</td>
<td>1mV_{R_{post}}</td>
</tr>
<tr>
<td></td>
<td>2_{post}</td>
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<td>1mV_{R_{post}}</td>
</tr>
<tr>
<td></td>
<td>3_{post}</td>
<td>R</td>
<td>1mV_{R_{post}}</td>
</tr>
<tr>
<td>post-LIHI{adj}</td>
<td>4_{post}</td>
<td>R</td>
<td>1mV_{R_{post}}</td>
</tr>
<tr>
<td></td>
<td>5_{post}</td>
<td>R</td>
<td>1mV_{R_{post}}</td>
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<tr>
<td></td>
<td>6_{post}</td>
<td>R</td>
<td>1mV_{R_{post}}</td>
</tr>
<tr>
<td>post-LIHI</td>
<td>7_{post}</td>
<td>L</td>
<td>1mV_{L_{post}}</td>
</tr>
<tr>
<td></td>
<td>8_{post}</td>
<td>L</td>
<td>1mV_{L_{post}}</td>
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<tr>
<td></td>
<td>9_{post}</td>
<td>L</td>
<td>1mV_{L_{post}}</td>
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<tr>
<td></td>
<td>10_{post}</td>
<td>L</td>
<td>1mV_{L_{post}}</td>
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<td></td>
<td>11_{post}</td>
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<td></td>
<td>12_{post}</td>
<td>L</td>
<td>1mV_{L_{post}}</td>
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ppHII

ppHII was expressed as a ratio of the MEP amplitude for each conditioned trial to the mean unconditioned (TS alone) MEP amplitude for each experimental run. Ratios less than one indicate inhibition, and ratios greater than one indicate facilitation.

RMT. The rTMS paradigm as well as the pre-rTMS and the post-rTMS studies were otherwise identical to the main experiment.

Data analysis

The peak-to-peak MEP amplitude for each trial was measured off-line. Paired t-test were used to examine the differences between the stimulus intensities used for 1mV_{Rpre} and 1mV_{Lpre} and between amplitudes of unconditioned (TS alone) MEPS for pre- and post-rTMS.

Effect of rTMS on MEP amplitude

To examine the changes in MEP amplitudes during the rTMS period, the mean MEP amplitudes of each block of 100 stimuli (9 blocks for 900 stimuli) were expressed as a percentage of the mean amplitude of the 20 MEPS recorded prior to rTMS. Some subjects were unable to relax the target muscle during rTMS. Therefore trials with voluntary EMG activity were excluded. To avoid subjective bias in determining which trials should be rejected, the background EMG area between the TMS stimulus artifact and MEP onset was calculated for each of the 20 pre-rTMS MEPS. A trial during the rTMS was excluded if the EMG area of the same period exceeded mean ± 2 SD of the baseline EMG area. In addition, a subject was excluded from this analysis if >50 trials were rejected in an epoch of 100 consecutive trials. The effects of duration of rTMS were evaluated by repeated-measures ANOVA. If the effect of stimulus duration was significant, Fisher’s protected least-significant difference (PLSD) post hoc test was used to detect differences among different epochs of stimuli.
Effects of rTMS on Interhemispheric Inhibition

Three subjects reported mild headache after rTMS, and there were no other adverse effects. In the pre-rTMS studies, no IHI was detected in one subject at ISI of 10 ms and in two subjects at ISI of 40 ms. These subjects were excluded from the analysis of the effect of rTMS on IHI.

Changes in MEP amplitude during rTMS

The stimulation intensity for rTMS for the nine subjects was 64.0 ± 10.5% (mean ± SD) of stimulator output and the amplitude of the baseline MEP before rTMS was 1.29 ± 1.14 mV. Four subjects were unable to maintain muscle relaxation during rTMS and were excluded from the analysis of the effect of rTMS on MEP amplitude. Figure 1 shows the effect of duration of rTMS on the mean MEP amplitude in each epoch. Repeated-measures ANOVA showed a significant effect of time on MEP size (P = 0.032). Post hoc testing showed that the MEP amplitude of the last epoch of 100 stimuli was significantly lower than that of the baseline (*P = 0.007).

Changes in MEP amplitude before and after rTMS

Before rTMS, the TS to produce 1-mV MEPs for left M1 was 57.4 ± 11.7% (1mV_Lpre, Tables 1 and 2) and for right M1 was 57.9 ± 12.5% (1mV_Rpre, Tables 1 and 2) of stimulator output, which increased after rTMS to 61.6 ± 14.7% (1mV_Lpost, Table 2) for left M1 and 60.1 ± 17.0% (1mV_Rpost, Tables 2) for right M1, the difference being significant only for left M1 (P = 0.023). There was no significant difference in the amplitudes of the unconditioned MEPs (TS alone) pre- and post-rTMS (right FDI: pre-rTMS = 1.44 ± 0.92 mV (generalized by 1mV_Lpre pulse, Table 1), post-rTMS = 1.69 ± 0.84 mV (1mV_Lpost, Table 2); left FDI: pre-rTMS = 1.60 ± 1.11 mV (1mV_Rpre, Table 1), post-rTMS = 1.93 ± 1.35 mV (1mV_Rpost, Table 2).

Effect of left M1 rTMS on LIHI

The results are shown in Fig. 2. Repeated-measures ANOVA showed a significant effect of test conditions (pre-LIHI, post-LIHIadj, post-LIHI, P = 0.01) on LIHI. The effects of ISI or interaction between test conditions and ISI were not significant. Post hoc analysis showed a significantly reduced IHI for post-LIHI (P = 0.0049) and post-LIHIadj (P = 0.0169) compared with pre-LIHI, but no significant difference between post-LIHI and post-LIHIadj.

Effect of left M1 rTMS on RIHI

The results are shown in Fig. 3. Repeated-measures ANOVA showed a significant effect of test condition (pre-RIHI, post-RIHIadj, post-RIHI, P = 0.006) on RIHI. The effects of ISI or interaction between test conditions and ISI were not significant. Post hoc analysis showed a significant reduction in IHI for post-RIHI (P = 0.0015) compared with pre-RIHI, but no significant difference between pre-RIHI and post-RIHIadj and between post-RIHI and post-RIHIadj.

Effect of rTMS on interhemispheric transmission at ISI of 4 ms

In the pre-rTMS study, IHF was absent at ISI of 4 ms on both sides. The mean ratio of the conditioned to unconditioned MEP amplitude of right FDI was 0.99 ± 0.24 and that of left FDI was 0.91 ± 0.25. In the post-rTMS period, the ratios did not change significantly on both sides. Using the pre-rTMS CS, the ratios were 1.06 ± 0.36 for the right FDI and 1.07 ± 0.40.
Effects of rTMS on interhemispheric inhibition from right to left motor cortex (RIHI) at different ISIs. pre-RIHI, RIHI before rTMS; post-RIHI, RIHI after rTMS using post-rTMS adjusted test stimulus and pre-rTMS conditioning stimulus; post-RIHI adj, RIHI after rTMS using post-rTMS adjusted test as well as conditioning stimuli. Each error bar represents 1 SE. Repeated-measures ANOVA showed a significant effect of test condition (P = 0.006) on RIHI but not of ISI or any significant interaction between time and ISI. Post hoc analysis of effect of ISI did not show any significant difference in RIHI between 10 and 40 ms. Post hoc analysis of the effect of test condition on RIHI showed a significant difference between pre-RIHI and post-RIHI (P = 0.0015) but not between pre-RIHI and post-RIHI adj and between post-RIHI and post-RIHI adj.

Effect of M1 rTMS on LIHI

The results are shown in Fig. 4. Repeated-measures ANOVA showed a significant effect of test conditions (pre-LIHI, post-LIHI adj, post-LIHI P = 0.0126) on LIHI. The effect of ISI or interaction between test conditions and ISI were not significant. Post hoc analysis showed a significantly reduced LIHI for post-LIHI (P = 0.028) and post-LIHI adj (P = 0.0045) compared with pre-LIHI, but no significant difference between post-LIHI and post-LIHI adj. Because a previous study (Gilio et al. 2003) found changes only for ISI of 10 ms, we performed an additional analysis examining the effects of test conditions separately for ISIs of 10 and 40 ms. The effect of test condition was significant for ISI of 10 ms (P = 0.05) but not for ISI of 40 ms (P = 0.187).

Effect of left M1 rTMS on RIHI

Repeated-measures ANOVA showed no significant effect of test conditions (pre-RIHI, post-RIHI adj, post-RIHI P = 0.0949) on RIHI.

Effect of rTMS on interhemispheric transmission at ISI of 4 ms

Similar to the main experiment, there was no significant inhibition or facilitation pre-rTMS. The mean ratio of the conditioned to unconditioned MEP amplitude of right FDI was 0.98 ± 0.23 and that of left FDI was 0.97 ± 0.13, and there was no significant change post-rTMS.

DISCUSSION

Low frequency rTMS produced a significant reduction in the excitability of the ipsilateral M1, similar to earlier reports (Chen et al. 1997; Fitzgerald et al. 2002; Maeda et al. 2000; Muellbacher et al. 2000). This inhibitory effect persisted following rTMS because the stimulation intensity for left M1 for a 1-mV MEP from right FDI also increased significantly. Our results showed that 15 min of rTMS at 1 Hz over the left M1 significantly reduced the LIHI and to a less extent the RIHI. Because the post-rTMS assessment of IHI started 3–4 min after rTMS and lasted 12 min, this inhibitory effect on IHI lasted for ≥15 min after rTMS and affected ppiHI at both ISIs of 10 and 40 ms. Because only post-RIHI but not post-LIHI adj was significantly reduced compared with pre-RIHI, the reduction in RIHI can be reversed by slightly increasing the CS on the right M1 in the post-RIHI adj condition. There may be greater reduction of LIHI compared with RIHI as both the post-LIHI and post-LIHI adj were reduced compared with pre-rTMS values.
Interhemispheric facilitation

ISI of 4 ms was used to examine IHF. IHF is produced when the test MEPs are elicited using a posteriorly directed current at low stimulus intensities (Hanajima et al. 2001). Because we are primarily interested in ppIHI and due to the time constraints after rTMS, our testing paradigm was not optimal for eliciting IHF. This likely explains why IHF was not observed in our study. Our findings suggest that IHF was not grossly increased after rTMS and the reduction in ppIHI was probably not due to increased IHF. However, minor changes in IHF cannot be ruled out.

Previous studies on the effect of low-frequency rTMS on IHI

Our finding of decreased LIHI at ISI of 10 ms in the main experiment is similar to that of Gilio et al. (2003). However, Gilio et al. (2003) found no change in LIHI at longer intervals of 15–75 ms and no change in ISP. Moreover, Gilio et al. (2003) found that left rTMS led to increased MEP amplitude with right M1 stimulation while we found no significant change in the stimulus intensity needed to produce the same MEP as the pre-rTMS condition. The different findings may be related to different study design. While the number of pulses, stimulation frequency and the intensity of rTMS were similar (mean of 117% rest MT in Gilio et al. 2003 and 115% rest MT in the present study) in the two studies, in Gilio et al. (2003), the current direction for rTMS (handle pointing forward) was opposite to that used in our main experiment, and rTMS did not reduce the MEP size from the stimulated hemisphere. In our control experiment using the same current direction as Gilio et al. (2003), we confirmed their findings of no change in MEP amplitude from the stimulated hemisphere and reduced LIHI at ISI of 10 ms. The failure to find a significant difference between ISIs of 10 and 40 ms (no significant effect of ISI) may be related to the low number of subjects tested. Separate ANOVAs for ISI of 10 and 40 ms showed a significant effect for test condition only for ISI of 10 ms, but this point needs to be examined further in future studies. Thus our findings suggest that the rTMS with the first phase of the biphasic current inducing posterior to anterior current in the brain used in the main experiment reduce corticospinal excitability and IHI at both short and long ISIs. By contrast, rTMS with the first phase inducing anterior to posterior current (Gilio et al. 2003) has little effect on corticospinal excitability. Therefore the effects of 1-Hz rTMS on neuronal circuits are dependent on the current direction, and this should be taken into account in the design of treatment studies for neurological and psychiatric disorders using low-frequency rTMS.

Mechanism of rTMS induced changes in IHI

Because there are no known long-range inhibitory neurons that cross the corpus callosum, IHI is probably mediated by transcallosal excitatory fibers originating from the ipsilateral motor cortex that synapse with local circuits of inhibitory interneurons in the contralateral cortex, which finally inhibit the corticospinal neurons (Berlucci 1990). Therefore reduction of IHI can result from inhibition of transcallosal excitatory neurons in the originating M1 or inhibition of the inhibitory interneurons of the contralateral M1. Our results do not allow us to distinguish between these possibilities. The reduction in LIHI after left M1 rTMS can be due to inhibition of transcallosal fibers originating from the left M1 if there is reduced excitability of the transcallosal projection, similar to the changes in the corticospinal projection from the left M1. However, IHI interacts with intracortical inhibitory circuits (Daskalakis et al. 2002b) and repeated activation of transcallosal fibers by rTMS may lead to changes in inhibitory circuits in the right M1. This possibility is supported by the observation that increasing the conditioning stimulus intensity of the left M1 to compensate for the reduction in corticospinal excitability did not reverse the decreased LIHI after rTMS. It has been hypothesized that IHI may share common mechanism with LIC (Chen 2004; Daskalakis et al. 2002b), and LIC is likely related to the cSP (Wassermann et al. 1996). If this is correct, the slight reduction in RIHI can be related to the observation that 1-Hz rTMS shortens the cSP duration (Fierro et al. 2001) as these can be explained by reduced excitability of the inhibitory neurons mediating cSP and IHI in the stimulated (left) M1. However, changes in the excitability of transcallosal projection from the right M1 are also possible.

Abnormal IHI in neuropsychiatric disorders and potential therapeutic role of low-frequency rTMS

Low-frequency rTMS is being investigated as treatment of neurological and psychiatric disorders such as Parkinson’s disease (Ikeguchi et al. 2003; Okabe et al. 2003; Shimamoto et al. 2001), dystonia (Siebner et al. 1999), hemispheric neglect (Brighina et al. 2003), and schizophrenia (Hoffman et al. 1999, 2000; Rollnik et al. 2000) because of the ability to reduce cortical excitability. Our findings suggest that these treatment regimens may also affect the transcallosal pathways.

Few studies have systematically studied IHI in disease states. Reduction or imbalance of IHI has been reported in several neurological and psychiatric conditions. These include decreased ppIHI at short ISIs in schizophrenia (Daskalakis et al. 2002a), which has been described as a disorder of dysfunctional cerebral connectivity (Crow 1998), and reduced ISP in multiple sclerosis with callosal lesions (Schmierer et al. 2000), corticobasal degeneration (Trompetto et al. 2003), and writer’s cramp (Niehaus et al. 2001).

In patients suffering from acute ischemic stroke in middle cerebral artery territory, reduced intracortical inhibition and increased excitability of the unaffected hemisphere have been reported (Butefisch et al. 2003; Kimiskidis et al. 2002; Liepert et al. 2000; Manganotti et al. 2002). ppIHI from the unaffected to the affected hemisphere was found to be increased in chronic subcortical stroke just prior to movement onset (Murase et al. 2004). Such pathophysiological changes may explain the phenomena of neglect or extinction resulting from breakdown of the balance of hemispheric rivalry from unilateral hemispheric lesions (Kinsbourne 1977). There is a relative disinhibition of the unaffected hemisphere and generation of an unopposed orienting response toward ipsilesional space.

Low-frequency rTMS of the unaffected left parietal cortex has been reported to improve contralesional visuospatial hemineglect in right brain damaged patients for ≤15 days (Brighina et al. 2003). While it was suggested that this effect is due to rTMS-induced long-lasting depression of the left parietal cortex (Brighina et al. 2003), reduction in left to right IHI may...
also be involved and may help to balance transcallosal inhibitory activity. In the other conditions with asymmetrically reduced interhemispheric inhibitions, low-frequency rTMS over the side with better preserved IHI may be tested as a therapeutic option.

Reduction of IHI has been observed in professional musicians who began musical training at an early age (Ridding et al. 2000). Low-frequency (1 Hz) rTMS to the motor cortex was reported to improve ipsilateral finger movements (Kobayashi et al. 2004). These findings raise the possibility that reduction in interhemispheric inhibition induced by rTMS may improve hand dexterity.

In summary, 1-Hz suprathreshold rTMS over M1 reduces IHI. The effect is bi-directional, but it is more prominent from the stimulated to unstimulated hemisphere. Further studies on how different rTMS parameters such as frequency, stimulus intensity, and current direction affect IHI will give valuable information in designing rational treatment strategies using rTMS.

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