RESEARCH ARTICLE

Laterality of interhemispheric inhibition depends on handedness

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Abstract There is some evidence that handedness is related to lateralisation of excitability in the motor system. We investigated lateralisation of interhemispheric inhibition (IHI), motor thresholds and short interval intracortical inhibition (SICI) and facilitation (SICF) in relation to handedness in 12 right (RH) and 13 left handed (LH) subjects. Because there is some controversy as to the optimal localisation to produce IHI we also compared IHI induced by conditioning the dorsal premotor cortex (dPM) versus primary motor cortex (M1) in ten RH. IHI was stronger following conditioning the motor dominant as compared to the motor non-dominant hemisphere in RH and LH. Motor thresholds were higher when elicited over the right hemisphere than over the left in both RH and LH, while SICI and SICF showed no differences between hemispheres or dependency from handedness. We hypothesize that IHI is a function of handedness perhaps reflecting predominant usage of the dominant hand, while lateralisation of thresholds and intracortical excitability are determined by other factors.

Introduction

There is some evidence that handedness has an influence on motor cortex excitability. Using transcranial

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magnetic stimulation (TMS) short interval intracortical inhibition (SICI) and facilitation (SICF) (Civardi et al. 2000; Hammond et al. 2004; Ilic et al. 2004), and interhemispheric inhibition (IHI) differ between the right and left hemisphere in right handers (RH) (Netz et al. 1995). For instance, in RH a difference in SICI and SICF of the left and right hemisphere was reported (Civardi et al. 2000; Hammond et al. 2004). In addition to intraindividual hemispheric differences in cortical excitability such differences have also been found between RH and LH (Netz et al. 1995; Dassonville et al. 1997; Volkmann et al. 1998; Triggs et al. 1999; Yahagi and Kasai 1999; Civardi et al. 2000; Pujol et al. 2002; Ilic et al. 2004). Also, diffusion tensor magnetic resonance imaging (MRI) has revealed structural differences of the white matter underneath the precentral sulcus related to handedness (Büchel et al. 2004).

At closer inspection TMS studies of interhemispheric differences are heterogeneous. Whereas some authors reported SICI and SICF to be more pronounced and thresholds for SICI to be lower in the motor dominant hemisphere (DH) of RH (Civardi et al. 2000; Hammond et al. 2004) others found no such hemispheric differences (Cahn et al. 2003). In the study of De Gennaro (2004) there was no hemispherical difference of IHI in relation to handedness or hemisphere. On the other hand, resting motor thresholds (RMT) were lower in the DH in LH. In contrast, Netz et al. (1995) reported IHI to be stronger when conditioning the DH in RH (at an ISI of 10 ms) but not in LH.

There is good evidence that transcallosal effects crucially depend on stimulation parameters (Hanajima et al. 2001; Bäumer et al. 2006). It is becoming clear that IHI and interhemispheric facilitation (IHF) can be

elicited both by conditioning the primary motor cortex hand area (M1) and the dorsal premotor cortex (dPM) depending on the stimulation intensity and current flow of the conditioning pulse and the current flow of the test pulse. For instance, strong IHI can readily be induced using standard figure of eight coils over M1 with a medially directed current flow (De Gennaro et al. 2004; Mochizuki et al. 2004). Thresholds to produce IHI may be lower when conditioning the dPM with medially directed currents (Mochizuki et al. 2004).

To this end we investigated hemispheric differences of IHI in RH and LH at short ISIs by conditioning M1 using customised small figure-of-eight coils allowing for focal stimulation using PA directed currents. To control for the best point of eliciting IHI in RH we also studied IHI by conditioning dPM and M1 in the same way to determine the optimal site to elicit IHI with these PA directed conditioning currents.

Methods

Study design

IHI was investigated using the TMS conditioning protocol first described by Ferbert at al. (1992) in experiment 1. IHI was measured by applying conditioning TMS pulses to right M1 followed by test pulses over left M1 and vice versa in all subjects. In a *site control experiment* the effects of conditioning pulses applied to left dPM were compared with those given to left M1. Test pulses were given over right M1. SICI and SICF were compared between both hemispheres using the Kujirai paired pulse paradigm (Kujirai et al. 1993) in experiment 2.

Subjects

In experiments 1 and 2 25 healthy subjects were studied. Handedness was tested using the Edinburgh handedness inventory (EDI). Subjects were considered RH if the EDI score was ≥70 and LH if the EDI score was ≤−70. Twelve participants were RH (six female, mean age 27.5 years ± 3.4; EDI score 95 ± 3.4) and 13 LH (eight female, mean age 28.9 years ± 2.9; EDI score −88 ± 3.9). All participants gave their written informed consent prior to the study. In the *site control experiment* ten RH (five female, mean age 28.7 years ± 1.6; EDI score 94 ± 4) were studied. The experiments conformed to the standards set by the Declaration of Helsinki and were carried out with approval of the local Ethics Committee.

Recording system

Subjects were seated in a comfortable armchair that was positioned in a subject and coil holder frame. Subjects' heads were fixed by a chin rest and a neck holder, which was adjusted individually to allow for a comfortable position. Both arms were supported by a pillow to ensure that arm muscles were completely relaxed. Subjects were instructed to relax but to keep their eyes open and fixate a visual target directly in front.

EMG was recorded with silver disc surface electrodes placed in differential pairs over first dorsal interosseous (FDI) muscles bilaterally, using a belly tendon montage. In addition to the target FDI muscle where motor evoked potential (MEP) were measured contralateral FDI muscle was also recorded to capture baseline EMG activity during measurements. EMG signals were continuously monitored acoustically with loudspeakers and visually by means of an oscilloscope. The ground electrode was placed at the wrist. EMG signals were amplified and filtered (20 Hz to 1 kHz) with a D360 amplifier (Digitimer Limited, Welwyn Garden City, UK). The signals were sampled at 5,000 Hz, digitised using a laboratory interface (Micro1401, Cambridge Electronics Design (CED), Cambridge, UK) and stored on a personal computer for display and later off-line data analysis.

TMS measurements

Measurements were performed with two Magstim 200 magnetic stimulators, each connected with a figure-of-eight shaped coil with an outer winding diameter of approximately 70 mm ("baby coil"; Magstim Company, Whitland, Dyfed, UK) with handles perpendicular to the coil windings ("Branding-Iron-Style") both for conditioning pulse (CP) and test pulse (TP) to measure IHI. The small diameter and the type of handle of this coils allowed placing each coil over the optimal target site without interfering with the coil positioning on the contralateral hemisphere. For measuring SICF and SICI both stimulators were connected with one of the coils via a Y-connector. The magnetic stimulus had a nearly monophasic pulse configuration with a rise time of about 100 μs, decaying back to zero over about 0.8 ms.

The coil was placed tangentially to the scalp at a 45° angle away from the midline, approximately perpendicular to the line of the central sulcus inducing a PA current in the brain. We determined the optimal position for activation of the FDI muscles by moving the coil in 0.5 cm steps around the presumed motor

hand area of the motor cortex of both hemispheres. The sites where stimuli of slightly suprathreshold intensity consistently produced the largest MEPs with the steepest negative slope in corresponding FDI muscle (referred to as "motor hot spot"; M1) were marked with a red wax pen. TMS coils were fixed to the frame using coil holders and placed at the marked stimulation sites.

Resting motor threshold (RMT) was defined as the minimum stimulus intensity that produced an MEP of more than 50 μV in five out of ten consecutive trials. Active motor threshold (AMT) was defined as the lowest stimulus intensity at which MEPs were elicited in the tonically contracting FDI muscle of about 10% of maximum voluntary contraction. Motor thresholds where expressed as a percentage of maximum stimulator output (MSO).

RMT and AMT for FDI were determined bilaterally over M1. The intensity of the TP was set at an intensity that, when it was given alone, would evoke an EMG response of approximately 1 mV peak-to-peak size in the left FDI muscle.

Experiment 1: laterality of IHI

Both coils were positioned as described above. IHI was probed using a conditioning-test paradigm. CP were applied to left M1 and TP given to right M1 and vice versa. The CP intensity was always set at 120% of the RMT of the conditioned M1.

IHI was tested at ISIs of 6, 7, 8, and 10 ms. These five conditions (TP given alone and four CP at different ISIs) were applied randomly in a block of 70 trials. In each block the control condition (TP given alone) was tested 30 times and each of the CP-TP conditions 10 times.

Site control experiment: focality of IHI

Effects of M1 and dPM conditioning were compared. For conditioning dPM the coil was positioned 3 cm anterior to M1 in a parasagittal line based on a neuro-anatomical PET study by Fink et al. (1997) and previous TMS studies from our group (Münchau et al. 2002; Bäumer et al. 2003). The coil was again placed at a 45° angle away from the midline, inducing PA currents. The intensity of the CP was set at 120% of AMT to investigate IHI near its threshold and to minimize activation of adjacent areas. To control for co-activation of M1 during dPM conditioning we tested two different conditioning intensities over dPM. First, CP was set at 120% AMT as determined over M1 (low intensity). Second, CP was set at 120%

AMT as determined with the coil held over dPM (high intensity). Thus, the latter would produce activation of M1 with the same intensity as in the M1 stimulation condition.

Experiment 2: laterality of SICI and SICF

SICI and SICF were determined bilaterally. CP intensity was set at 90% AMT and ISIs of 2, 3, 4, 12 and 16 ms were tested. The conditioned MEPs were tested ten times at each ISI and the TP alone 20 times. Conditions were tested randomly in a block of 70 trials.

Data analysis

Measurements were made on individual trials. Mean peak-to-peak MEP amplitudes were determined. For analysis using relative MEP amplitudes the conditioned MEPs were expressed as a percentage of the mean peak-to-peak size of the unconditioned MEP.

Statistical analysis

Test stimulus intensities and unconditioned MEP amplitudes were compared between hemispheres and groups using t test. Thresholds were compared between groups using a repeated measures between groups ANOVA with factor hemisphere (left vs. right hemisphere) and a between groups factor handedness (RH vs. LH). Absolute mean MEP amplitudes of conditioned MEPs at each ISI were compared with unconditioned test MEPs using repeated measures ANOVA to test for a conditioning effect.

Comparisons between hemispheres and groups were carried out by analysing relative mean conditioned MEP amplitudes in a between groups (RH/LH) repeated measures ANOVA with factors hemisphere (right and left) and ISI (mean relative conditioned MEP amplitudes at ISIs of 6, 7, 8 and 10 ms for IHI and 2, 3, 4, 12 and 16 ms for SICI and SICF, respectively).

Addressing focality effects relative mean conditioned MEP amplitudes were compared for conditioning M1 and dPM (for both intensities in separate analyses) using repeated measures ANOVA with factors SITE (M1 vs. dPM) and ISI (mean relative conditioned MEP amplitudes at ISIs of 6, 7, 8 and 10 ms).

For all statistical analyses the Greenhouse–Geisser correction was used to correct for nonsphericity. Conditional on a significant F value in ANOVA, post hoc tests were performed (Fisher test). P value of <0.05 was considered significant. Data are given as mean ± 1 SEM.

Results

TMS thresholds, MEP intensities

Experiments 1 and 2

Analysing thresholds between hemispheres and groups ANOVA revealed a significant effect of hemisphere on RMT ($F(1, 23) = 15.6$, $P < 0.001$) and AMT $F(1, 23) = 9.6$, $P < 0.005$). There was no significant effect for the between groups factor handedness and no interaction of these factors (Fig. 1). Analysing both groups separately thresholds were higher in the right hemisphere both in RH (RMT: right M1 $42.6\% \pm 1.6$, left M1 $38.1\% \pm 2$; AMT: right M1 $27.7\% \pm 1.9$, left M1 $25.3\% \pm 1.7$) and LH (RMT: right M1 $39.8\% \pm 1.8$, left M1 $36.8\% \pm 1.7$; AMT: right M1 $27\% \pm 1.7$, left M1 $23.8\% \pm 1.3$), which reached significance for RMT in RH ($T = 3.8$; $P<0.005$) and AMT in LH ($T = 4.0$; $P < 0.005$).

This indicates that hemispheric differences of motor thresholds are independent from handedness. Test MEP intensities used over the right hemisphere (right $52.2\% \pm 2.3$; left $48.7\% \pm 2.8$ MSO) were also higher than those over the left hemisphere (right $47.2\% \pm 2.4$;

left $45\% \pm 2.1$ MSO) ($T > 2.5$; $P < 0.05$ for both groups).

Site control experiment

Similar to experiment 1 RMT and AMT were higher in the right hemisphere (RMT right $41.7\% \pm 2.2$, left $37.6\% \pm 2.2$, $T = -2.1$, $P = 0.07$; AMT right 34.8 ± 2, left 28.9 ± 1.4, $T = -3.3$, $P < 0.01$). AMT measured over left dPM ($41.3\% \pm 2.4$) was significantly higher compared with M1 ($T = 6.2$, $P < 0.001$).

Collapsing threshold data of RH of experiment 1 and the *site control experiment* ($n = 22$) both RMT and AMT were significantly higher in the right hemisphere ($T > 3$, $P < 0.005$ for both RMT and AMT).

Interhemispheric inhibition

Experiment 1

Unconditioned MEP amplitudes did not differ for the factors hemisphere or group.

IHI was present in each hemisphere in both groups comparing conditioned and unconditioned absolute MEP amplitudes (Table 1). Comparing relative conditioned MEP amplitudes between hemispheres and groups, ANOVA revealed a significant effect for the factor ISI ($F(3, 69) = 12.4$, $P < 0.0001$) and a significant interaction of the factors hemisphere and group ($F(1, 23) = 4.9$, $P < 0.05$). The interaction (hemisphere and group) indicates that laterality of IHI between hemispheres depends on handedness (Fig. 2). Post hoc tests only showed trends towards more inhibition from the DH to the motor non-dominant hemisphere (NDH) within both groups ($P < 0.15$).

Site control experiment

IHI was present after conditioning M1 with 120% AMT comparing absolute MEP amplitudes ($F(4, 36) = 2.7$; $P < 0.05$). Post hoc test revealed significant
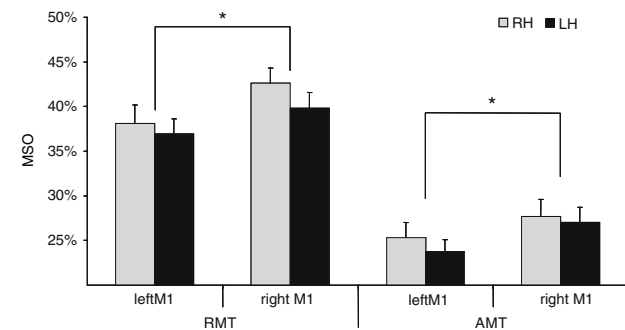

Fig. 1 Resting (RMT) and active motor threshold (AMT) of left and right hemisphere given as percentage of maximum stimulator output (MSO); mean ($\pm$SEM). *$P < 0.005$

Table 1 Interhemispheric inhibition (IHI) tested over left and right hemisphere in right (RH) and left handed (LH) subjects with conditioning pulses (CP) over the left and test pulses (TP) over right M1 and vice versa. ANOVA revealed significant inhibition for each hemisphere in both groups. Post hoc test revealed significant inhibition at certain interstimulus intervals (ISI). *P* values <0.05 were marked in italic and bold. Values are given in mV; mean ($\pm$SEM)

| | Hemisphere of | | ANOVA | TP | ISI of 6 ms | ISI of 7 ms | ISI of 8 ms | ISI of 10 ms |
	CP	TP						
RH	Left	Right	$F(4, 44) = 12.3$, $P < 0.001$	0.67 ($\pm$0.13)	**0.54 ($\pm$0.11)**	**0.46 ($\pm$0.12)**	**0.46 ($\pm$0.13)**	**0.36 ($\pm$0.09)**
	Right	Left	$F(4, 44) = 5.5$, $P = 0.001$	0.71 ($\pm$0.11)	0.68 ($\pm$0.12)	**0.55 ($\pm$0.1)**	**0.51 ($\pm$0.08)**	**0.53 ($\pm$0.09)**
LH	Left	Right	$F(4, 48) = 3.9$, $P < 0.05$	0.49 ($\pm$0.08)	0.42 ($\pm$0.11)	**0.38 ($\pm$0.12)**	**0.37 ($\pm$0.13)**	**0.35 ($\pm$0.09)**
	Right	Left	$F(4, 48) = 11.1$, $P < 0.001$	0.65 ($\pm$0.14)	**0.53 ($\pm$0.12)**	**0.45 ($\pm$0.1)**	**0.39 ($\pm$0.08)**	**0.39 ($\pm$0.09)**

Fig. 2 Interhemispheric inhibition. Relative MEP amplitudes for conditioning left M1 followed by a test stimulus over the right M1 and vice versa for right (RH) and left handed (LH) subjects. **a** Mean group values (±SEM) are shown. **b** Individual difference in IHI between hemispheres at an ISI of 10 ms are plotted for right (RH) and left handed (LH) subjects. Data are calculated by subtracting IHI (in % of mean test MEP) after conditioning right M1 from IHI after conditioning left M1
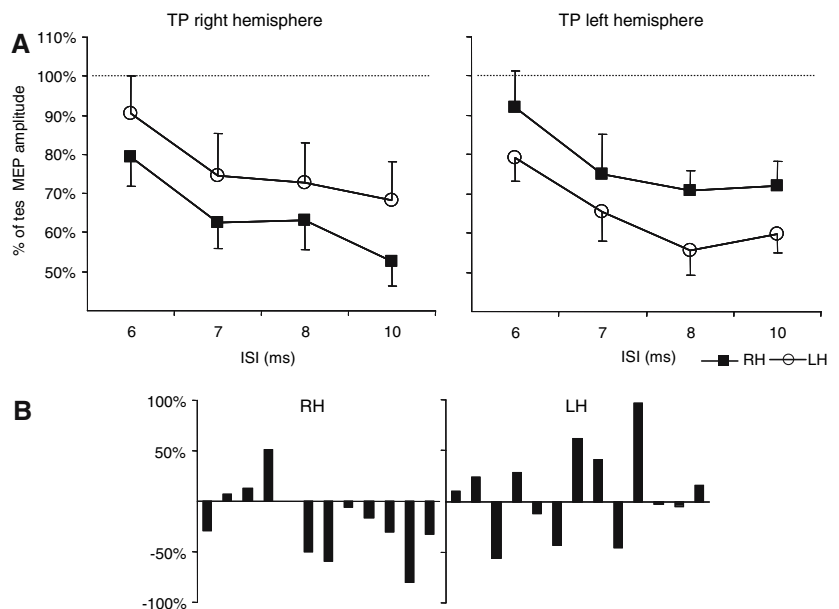
IHI at ISIs of 6, 8 and 10 ms (Fig. 3). ANOVA showed no significant effect after conditioning dPM with 120% AMT ($P = 0.22$) and AdPMT ($P = 0.14$).

Comparing relative MEP amplitudes between left M1 and dPM conditioning with 120% AMT there was a significant effect for the factor SITE ($F(1, 9) = 9.4$; $P < 0.05$) but not for the factor ISI. Also, there was no interaction of both factors. In contrast, comparison of results of the M1 conditioning (at 120% AMT) with those of the intensity adapted conditioning of dPM revealed no differences (Fig. 3). This indicates that IHI is present only after conditioning M1 but not dPM under the experimental conditions used here.

Intracortical inhibition and facilitation

Experiment 2

Unconditioned MEP amplitudes did not differ between hemispheres or groups.

Comparing absolute unconditioned and conditioned MEP amplitudes for each hemisphere and group separately ANOVA demonstrated a significant conditioning effect in both hemispheres in RH but only for the left hemisphere in LH.

Comparing relative conditioned MEP amplitudes with ANOVA the factor ISI was significant ($F(4, 132) = 5.3$, $P < 0.0001$). There was no difference between hemispheres or groups and no interaction of these factors (Fig. 4). Under the experimental conditions used in this study we did not find significant hemispherical differences of SICI and SICF related to handedness.
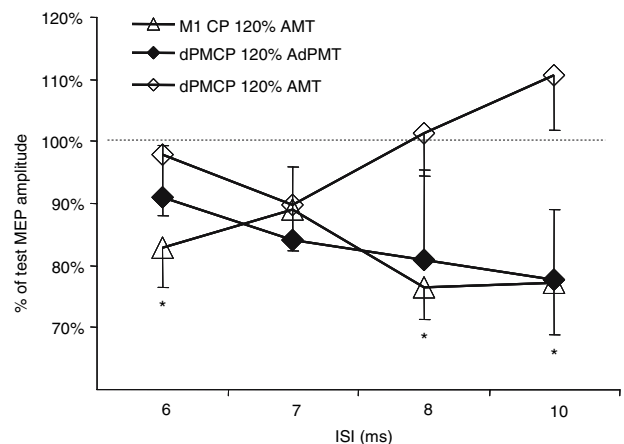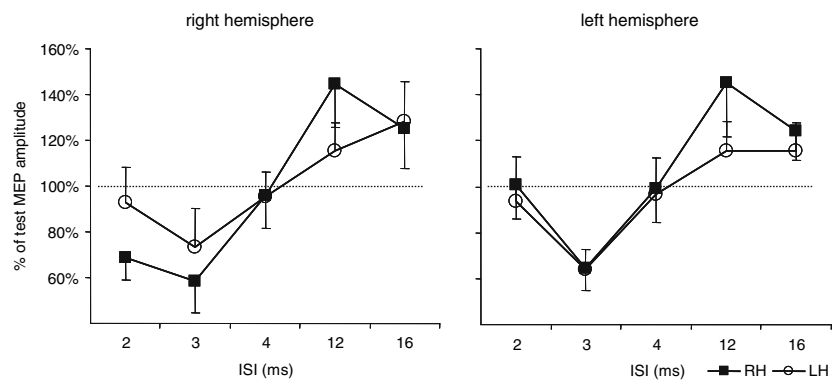

Fig. 3 Interhemispheric inhibition following dPM and M1 conditioning. Relative MEP amplitudes for conditioning left M1 and dPM followed by a test stimulus over right M1. Mean values (±SEM) are shown. *$P < 0.05$

Discussion

This study shows that asymmetries of IHI depend on handedness. The inhibitory drive from the dominant hemisphere is generally stronger than that from the non-dominant hemisphere. That is, compared with LH the inhibitory drive form the left to the right hemisphere is stronger in RH, and vice versa.

Thresholds to elicit IHI were significantly lower over M1 as compared to dPM. Motor thresholds were independent from handedness but lateralised with higher thresholds for the right hemisphere. There was no lateralisation or dependency on handedness for SICI and SICF.

IHI and handedness

In this study, hemispherical asymmetry of IHI depended on handedness. This asymmetry with stronger IHI from the DH to the NDH was reflected in the statistical interaction of the factors "Group" and the "Hemisphere" but not when IHI between hemispheres was compared within groups. This implies that hemispheric asymmetries of IHI are rather subtle. Similarly, Netz et al. (1995) reported more pronounced IHI from DH to the NDH in RH at an ISI of 10 ms but no homogeneous effects in LH. Their experimental set-up differed in that IHI was tested during tonic activation of the FDI contralateral to the target side. Also, these authors restricted their analysis to IHI at an ISI of 10 ms and did not take into account other intervals.

In contrast, De Gennaro et al. (2004) who examined a range of ISIs from 2 to 20 ms did not find a dependency of IHI on handedness or hemispherical dominance (Table 2). However, at ISIs of 6, 8, and 10 ms that were also included in the present study (Fig. 4 in de Gennaro et al. 2004) RH, but not LH, also showed an asymmetry with stronger IHI from DH to NDH.

Looking at individual data of hemispherical asymmetry of IHI at an ISI of 10 ms in RH and LH in all three studies (for this study, see Fig. 2b) a stronger drive from DH to the NDH was present in 26 out of 39 RH and 23 of 40 LH confirming that there are, albeit weak, interhemispheric differences of IHI related to handedness.

If lateralisation of interhemispherical inhibitory drive is a function of motor usage one might speculate that this drive is perhaps more homogeneous in RH, given that in a "RH world" LH are forced to use their right hand more often than RH their left hand.

IHI and focality

IHI was more readily elicited when M1 was conditioned as opposed to dPM using slightly suprathreshold

intensities. In fact, Ferbert et al. (1992) were the first to show that M1 was the optimal site for producing IHI compared with sites more lateral or medial, respectively. A recent study reported thresholds for eliciting IHI to be lower when CPs were applied to the dPM as compared to M1. More specifically, at stimulus intensities of 90% RMT IHI was present when dPM but not when M1 was conditioned (Mochizuki et al. 2004). In the present study where significant IHI was not found following conditioning dPM CP intensities were set at 120% AMT. Calculating CP intensities in relation to individual RMT in our study mean CP intensity was 93% RMT. Thus differences of CP intensities cannot account for the different results in the two studies.

However, the direction of the induced current flow differed both for the CP and the TP coil. Whereas Mochizuki et al. (2004) used medially directed currents, we applied TMS pulses resulting in anteriorly directed currents in the brain both for the test and the conditioning stimulus. Mochizuki et al. (2004) also tested anteriorly directed currents for the conditioning pulse applied over dPM and found no differences in the amount of IHI compared with medially directed currents, but they always used medially directed test stimuli. Thus, IHI probably crucially depends not only on stimulation intensities and ISI but also on the effective current flow in the brain. However, this probably mainly applies to IHI when tested with low intensity TMS. At higher intensities IHI is more robust (Chen et al. 2003). This is somewhat reminiscent of interhemispheric facilitation that can only be induced with low conditioning intensities. Here slight changes of conditioning or TP parameters can abolish conditioning effects (Hanajima et al. 2001; Bäumer et al. 2006).

Lateralisation of SICI und SICF

In this study, SICI and SICF were not lateralised. Moreover, there was no relation to handedness. This is inline with findings of Cincinelli et al. (1997), who also

Table 2 Studies where IHI was investigated in relation to handedness

Result	Interstimulus intervals	Coils	CP Intensity	Flow direction	TP Intensity	Flow direction	Reference
Significant difference with more IHI from right to left hemisphere in RH, No difference in LH	10 ms	Cadwell 45 mm	105% RMT (preactivated muscle)	n.a.	105% RMT	n.a.	Netz et al. 1995
No difference related to handedness	2,4,6,8,10,12, 14,16,18,20 ms	90 mm figure of eight	120% RMT	AP	120% RMT	AP	De Gennaro et al. 2004
Significant hemisphere × Handedness Interaction	6–10 ms	70 mm figure of eight	120% RMT	PA	120% RMT	PA	Bäumer et al. (this study)

Stimulus parameters are displayed

RMT resting motor threshold; *AP* anterior to posterior current flow in the brain; *PA* posterior to anterior current flow. *n.a.* not available

did not find intracortical excitability to differ between hemispheres in RH. Another study of Civardi et al. (2000) described lateralisation in RH with stronger SICF and less pronounced SICI in the DH. The main reason for the lack of hemispherical differences in SICI and SCIF in our study might be that we used lower intensities for the CPs, which were some 10% MSO lower than those in the study of Cirvardi et al. Because Hammond et al. (2004) found lower thresholds for eliciting SICI and SICF in the DH in RH we expected more pronounced hemispherical differences at lower CP intensities. Why this was not the case in the present study remains unclear.

Lateralisation of motor thresholds

RMT and AMT were higher in right hemispheres regardless of handedness which is in line with most previous studies (Macdonell et al. 1991; Triggs et al. 1994; Netz et al. 1995; Triggs et al. 1997; Helmich et al. 2005). However, others could not confirm this (Cicinelli et al. 1997; Civardi et al. 2000) the reason for which is unclear. Interestingly, in the study of Macdonell et al. (1991) where a clear lateralisation of motor thresholds was found in RH subjects asymmetry was greatest, i.e. thresholds were higher in the right hemisphere, in those subjects who reported less pronounced lateralisation of hand preference. This does not support the idea that handedness is the most crucial factor determining motor thresholds.

Findings in LH are even more equivocal. In some studies thresholds in LH were lower in the DH (Triggs et al. 1994; De Gennaro et al. 2004). Triggs et al. (1994) found the asymmetry with higher thresholds for the non-dominant hemisphere less pronounced in LH than in RH. De Gennaro et al. (2004) found a significant hemispherical asymmetry of the RMT in RH. However, slight threshold asymmetry in LH was not significant in post hoc analyses.

In the majority of previous studies only one factor, e.g. handedness or coil distance to the motor cortex was investigated. However, it appears that particularly in LH heterogeneous results of threshold differences are influenced by factors other than handedness including the distance between the head surface and motor cortex (Kozel et al. 2000; McConnell et al. 2001), age (Matsunaga et al. 1998) and motor performance (Triggs et al. 1997). The threshold as a measure of corticspinal excitability may find a correlate in functional MRI. In this respect, it is interesting to note that in several MRI studies addressing the activation of the sensorimotor cortex during finger movements in relation to handedness asymmetric hemispheric activation was

reported for complex finger movements but not simple motor tasks (Kim et al. 1993; Dassonville et al. 1997; Lutz et al. 2005; Klöppel et al. 2006). Thus, it appears that handedness becomes more relevant if more complex cortical networks are engaged during motor performance. As a corollary, it is possible that handedness is not reflected in "basic" properties of the motor system such as motor thresholds.

Taken together, in this study laterality of IHI was related to handedness whereas thresholds and SICI and SICF were not. Thus, intracortical parameters restricted to one hemisphere are not depended on handedness while IHI as a parameter of interhemispheric control probably is.

Conclusion

IHI depends on handedness with a more pronounced inhibitory drive from the motor dominant to the non-dominant hemisphere. Using anteriorly directed currents in the brain this inhibitory drive is more readily elicited in M1–M1 than PMd-M1 connections.

References

Bäumer T, Bock F, Koch G, Lange R, Rothwell JC, Siebner HR, Münchau A (2006) Magnetic stimulation of human premotor or motor cortex produces interhemispheric facilitation through distinct pathways. J Physiol 572:857–868

Bäumer T, Lange R, Liepert J, Weiller C, Siebner HR, Rothwell JC, Münchau A (2003) Repeated premotor rTMS leads to cumulative plastic changes of motor cortex excitability in humans. Neuroimage 20:550–560

Büchel C, Raedler T, Sommer M, Sach M, Weiller C, Koch MA (2004) White matter asymmetry in the human brain: a diffusion tensor MRI study. Cereb Cortex 14:945–951

Cahn SD, Herzog AG, Pascual-Leone A (2003) Paired-pulse transcranial magnetic stimulation: effects of hemispheric laterality, gender, and handedness in normal controls. J Clin Neurophysiol 20:371–374

Chen R, Yung D, Li JY (2003) Organization of ipsilateral excitatory and inhibitory pathways in the human motor cortex. J Neurophysiol 89:1256–1264

Cicinelli P, Traversa R, Bassi A, Scivoletto G, Rossini PM (1997) Interhemispheric differences of hand muscle representation in human motor cortex. Muscle Nerve 20:535–542

Civardi C, Cavalli A, Naldi P, Varrasi C, Cantello R (2000) Hemispheric asymmetries of cortico-cortical connections in human hand motor areas. Clin Neurophysiol 111:624–629

Dassonville P, Zhu XH, Uurbil K, Kim SG, Ashe J (1997) Functional activation in motor cortex reflects the direction and the degree of handedness. Proc Natl Acad Sci USA 94:14015–14018

De Gennaro L, Cristiani R, Bertini M, Curcio G, Ferrara M, Fratello F, Romei V, Rossini PM (2004) Handedness is mainly associated with an asymmetry of corticospinal excitability and not of transcallosal inhibition. Clin Neurophysiol 115:1305–1312

Ferbert A, Priori A, Rothwell JC, Day BL, Colebatch JG, Marsden CD (1992) Interhemispheric inhibition of the human motor cortex. J Physiol 453:525–546

Fink GR, Frackowiak RS, Pietrzyk U, Passingham RE (1997) Multiple nonprimary motor areas in the human cortex. J Neurophysiol 77:2164–2174

Hammond G, Faulkner D, Byrnes M, Mastaglia F, Thickbroom G (2004) Transcranial magnetic stimulation reveals asymmetrical efficacy of intracortical circuits in primary motor cortex. Exp Brain Res 155:19–23

Hanajima R, Ugawa Y, Machii K, Mochizuki H, Terao Y, Enomoto H, Furubayashi T, Shiio Y, Uesugi H, Kanazawa I (2001) Interhemispheric facilitation of the hand motor area in humans. J Physiol 531:849–859

Helmich RC, Bäumer T, Siebner HR, Bloem BR, Münchau A (2005) Hemispheric asymmetry and somatotopy of afferent inhibition in healthy humans. Exp Brain Res 167:211–219

Ilic TV, Jung P, Ziemann U (2004) Subtle hemispheric asymmetry of motor cortical inhibitory tone. Clin Neurophysiol 115:330–340

Kim SG, Ashe J, Hendrich K, Ellermann JM, Merkle H, Ugurbil K, Georgopoulos AP (1993) Functional magnetic resonance imaging of motor cortex: hemispheric asymmetry and handedness. Science 261:615–617

Klöppel S, van Eimeren T, Glauche V, Vongerichten A, Münchau A, Frackowiak RS, Büchel C, Weiller C, Siebner HR (2006) The effect of handedness on cortical motor activation during simple bilateral movements. Neuroimage 34(1):274–280

Kozel FA, Nahas Z, deBrux C, Molloy M, Lorberbaum JP, Bohning D, Risch SC, George MS (2000) How coil-cortex distance relates to age, motor threshold, and antidepressant response to repetitive transcranial magnetic stimulation. J Neuropsychiatry Clin Neurosci 12:376–384

Kujirai T, Caramia MD, Rothwell JC, Day BL, Thompson PD, Ferbert A, Wroe S, Asselman P, Marsden CD (1993) Corticocortical inhibition in human motor cortex. J Physiol 471:501–519

Lutz K, Koeneke S, Wustenberg T, Jancke L (2005) Asymmetry of cortical activation during maximum and convenient tapping speed. Neurosci Lett 373:61–66

Macdonell RA, Shapiro BE, Chiappa KH, Helmers SL, Cros D, Day BJ, Shahani BT (1991) Hemispheric threshold differences for motor evoked potentials produced by magnetic coil stimulation. Neurology 41:1441–1444

Matsunaga K, Uozumi T, Tsuji S, Murai Y (1998) Age-dependent changes in physiological threshold asymmetries for the motor evoked potential and silent period following transcranial magnetic stimulation. Electroencephalogr Clin Neurophysiol 109:502–507

McConnell KA, Nahas Z, Shastri A, Lorberbaum JP, Kozel FA, Bohning DE, George MS (2001) The transcranial magnetic stimulation motor threshold depends on the distance from coil to underlying cortex: a replication in healthy adults comparing two methods of assessing the distance to cortex. Biol Psychiatry 49:454–459

Mochizuki H, Huang YZ, Rothwell JC (2004) Interhemispheric interaction between human dorsal premotor and contralateral primary motor cortex. J Physiol 561:331–338

Münchau A, Bloem BR, Irlbacher K, Trimble MR, Rothwell JC (2002) Functional connectivity of human premotor and motor cortex explored with repetitive transcranial magnetic stimulation. J Neurosci 22:554–561

Netz J, Ziemann U, Homberg V (1995) Hemispheric asymmetry of transcallosal inhibition in man. Exp Brain Res 104:527–533

Pujol J, Lopez-Sala A, Deus J, Cardoner N, Sebastian-Galles N, Conesa G, Capdevila A (2002) The lateral asymmetry of the human brain studied by volumetric magnetic resonance imaging. Neuroimage 17:670–679

Triggs WJ, Calvanio R, Levine M (1997) Transcranial magnetic stimulation reveals a hemispheric asymmetry correlate of intermanual differences in motor performance. Neuropsychologia 35:1355–1363

Triggs WJ, Calvanio R, Macdonell RA, Cros D, Chiappa KH (1994) Physiological motor asymmetry in human handed-

ness: evidence from transcranial magnetic stimulation. Brain Res 636:270–276

Triggs WJ, Subramanium B, Rossi F (1999) Hand preference and transcranial magnetic stimulation asymmetry of cortical motor representation. Brain Res 835:324–329

Volkmann J, Schnitzler A, Witte OW, Freund H (1998) Handedness and asymmetry of hand representation in human motor cortex. J Neurophysiol 79:2149–2154

Yahagi S, Kasai T (1999) Motor evoked potentials induced by motor imagery reveal a functional asymmetry of cortical motor control in. Neurosci Lett 276:185–188