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Corticospinal activation of internal oblique muscles has a strong ipsilateral component and can be lateralised in man

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Abstract Trunk muscles receive corticospinal innervation ipsilaterally and contralaterally and here we investigate the degree of ipsilateral innervation and any cortical asymmetry in pairs of trunk muscles and proximal and distal limb muscles. Transcranial magnetic stimulation (TMS) was applied to left and right motor cortices in turn and bilateral electromyographic (EMG) recordings were made from internal oblique (IO; lower abdominal), deltoid (D; shoulder) and first dorsal interosseus (1DI; hand) muscles during voluntary contraction in ten healthy subjects. We used a 7-cm figure-of-eight stimulating coil located 2 cm lateral and 2 cm anterior to the vertex over either cortex. Incidence of ipsilateral motor evoked potentials (MEPs) was 85% in IO, 40% in D and 35% in 1DI. Mean (\pm S.E. M.) ipsilateral MEP latencies were longer ($P<0.05$; paired t -test) than contralateral MEP latencies (contralateral vs. ipsilateral; IO: 16.1 \pm 0.4 ms vs. 19.0 \pm 0.5 ms; D: 9.7 \pm 0.3 ms vs. 15.1 \pm 1.9 ms; 1DI: 18.3 \pm 0.6 ms vs. 23.3 \pm 1.4 ms), suggesting that ipsilateral MEPs were not a result of interhemispheric current spread. Where data were available, we calculated a ratio (ipsilateral MEP areas/contralateral MEP areas) for a given muscle (IO: $n=16$; D: $n=8$; 1DI: $n=7$ ratios). Mean values for these ratios were 0.70 \pm 0.20 (IO), 0.14 \pm 0.05 (D) and 0.08 \pm 0.02 (1DI),

revealing stronger ipsilateral drive to IO. Comparisons of the sizes of these ratios revealed a bias towards one cortex or the other (four subjects right; three subjects left). The predominant cortex showed a mean ratio of 1.21 \pm 0.38 compared with 0.26 \pm 0.06 in the other cortex ($P<0.05$). It appears that the corticospinal control of IO has a strong ipsilateral component relative to the limb muscles and also shows hemispheric asymmetry.

Keywords Ipsilateral · Motor Cortex · Transcranial magnetic stimulation

Introduction

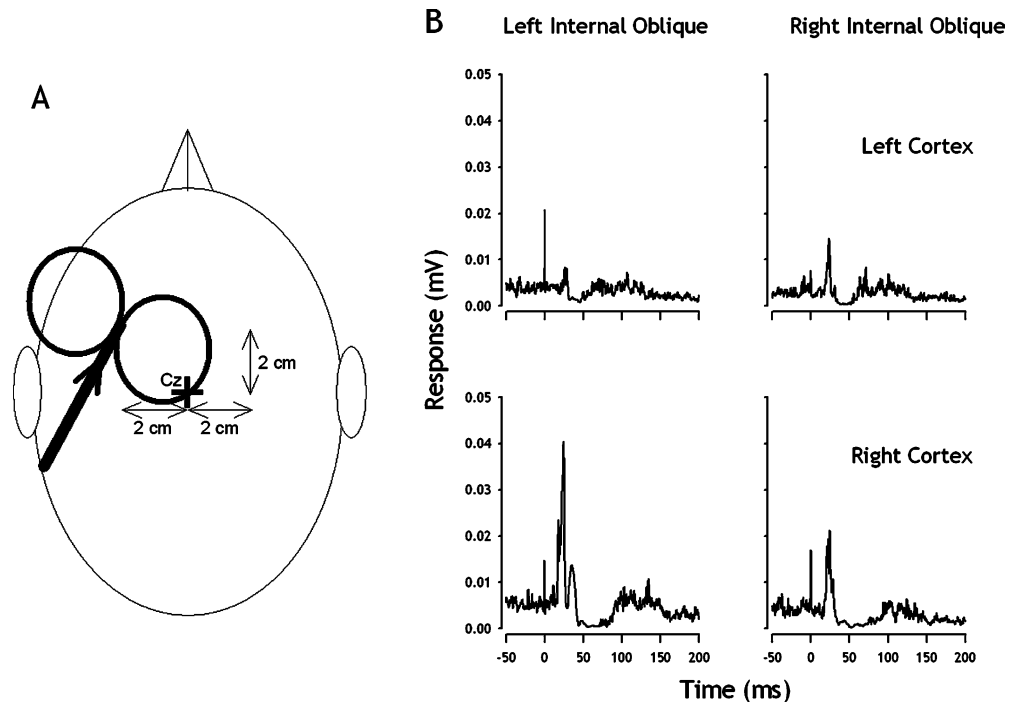
Since its introduction in 1985 (Barker et al. 1985), transcranial magnetic stimulation (TMS) has been used widely for the study of the human motor cortex and its projections to motoneurons (Day et al. 1989; Mills 1991). It is commonly accepted that TMS of one motor cortex induces motor evoked potentials (MEPs) in contralateral muscles via crossed corticospinal neurones (for review see Rothwell 1991) which descend in the lateral corticospinal tract (CST) and make up approximately 80% of the total number. The remaining 20% are uncrossed (ipsilateral) fibres which run in the anterior CST and are thought to supply proximal muscles (Porter and Lemon 1995). Indeed MEPs have been recorded from various muscles after stimulation of the ipsilateral cortex in patients with unilateral damage to one motor cortex (Carr et al. 1993) as well as in healthy subjects (Wassermann et al. 1991; Basu et al. 1994). Furthermore, Hamdy et al. (1996) showed that the muscles involved in swallowing displayed somatotopic representation in motor cortices of both hemispheres and that this representation was asymmetrical. This finding has important clinical implications since in patients with dysphagic hemispheric stroke the recovery of swallowing was found to depend on the size of the representation of the swallowing muscles in the intact hemisphere (Hamdy et al. 1996). It has been shown that it is possible to evoke MEPs, using TMS, in abdominal

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Fig. 1a, b Positioning of the stimulating coil and example MEPs. **a** The stimulating coil was positioned with its cross-over located 2 cm lateral to and 2 cm anterior to the vertex. The handle was orientated at approximately 45° from the mid sagittal plane so that the induced current in the brain flowed in an anteromedial direction. **b** Examples of rectified averaged MEPs from internal oblique muscles when either motor cortex was stimulated (20 stimuli at 80% MSO) in one subject. Note that the ipsilateral response of right internal oblique (right cortex stimulated) is larger than the contralateral response (left cortex stimulated)



muscles (Lissens et al. 1995; Tunstall et al. 2001). We have now examined the control of the abdominal muscle internal oblique in addition to a distal hand muscle (first dorsal interosseus) and a more proximal arm muscle (deltoid). The principal hypotheses in this study were: 1) there is a strong ipsilateral corticospinal drive to the internal oblique muscles and 2) cortical drive to these muscles is organised asymmetrically.

Methods

Subjects

With local ethical approval and informed consent, ten healthy subjects (three left-handed) took part in this study (mean age [\pm S.E.M.] 40.70 \pm 2.31 years, range 29–49 years, six males, four females).

Electromyography

Ag/AgCl electromyographic (EMG) recording electrodes (self-adhesive, blue sensor Q-10-A, 2 cm diameter, Medicotest) were positioned bilaterally on the *internal oblique* (IO), the middle fibres of the *deltoid* (D) and the *first dorsal interosseus* muscles (1DI). For recordings from the IO and D, pairs of electrodes were placed in line with the fibre orientation. For IO they were positioned with their centres 2 cm apart over the middle fibres of the muscle, the most lateral electrode being 1 cm medial to the anterior superior iliac spine (ASIS) and below a line joining the two ASISs (see Ng et al. 1998). For 1DI one electrode was positioned over the muscle belly and the other over the metacarpophalangeal joint of the index

finger. The EMG signals were filtered (low filter –3 db at 100 Hz and high filter –3 db at 2 KHz) and amplified ($\times 1,000$ [1DI and D]; $\times 10,000$ [IO]) before being sampled at 4 KHz by a data acquisition interface (1401 plus and Signal software; Cambridge Electronic Design, UK) connected to a PC. The use of audio feedback of the EMG signals from IO and instructions from the investigator helped the subjects to maintain consistent low-level contractions of all six muscles. For 1DI this involved making a pincer grip between the index finger and thumb. For D each arm was abducted to 45° against resistance provided by an experimenter. Subjects pulled in their abdominal wall to activate IO, a procedure known as the abdominal hollowing manoeuvre (see Beith et al. 2001).

Transcranial magnetic stimulation (TMS)

TMS was delivered using a MagStim 200 stimulator (MagStim Company, UK) connected to 7-cm figure-of-eight stimulating coil, which was positioned with its cross-over located 2 cm lateral to and 2 cm anterior to the vertex. Trial experiments showed that this coil position produced optimal contralateral activation of IO while minimizing stimulation of the opposite cortex (see Tunstall et al. 2001). The coil handle was orientated at approximately 45° from the mid-sagittal plane so that the induced current in the brain flowed in an anteromedial direction (see Fig. 1a).

The coil was placed symmetrically over left and right motor cortex in turn and the stimulus intensity was increased to a level that produced identifiable motor evoked potentials (MEPs) in ipsilateral and contralateral contracting IO. Symmetrical positioning of the stimulating coil over the two hemispheres allowed equivalent activation of the two motor cortices, so allowing comparisons of

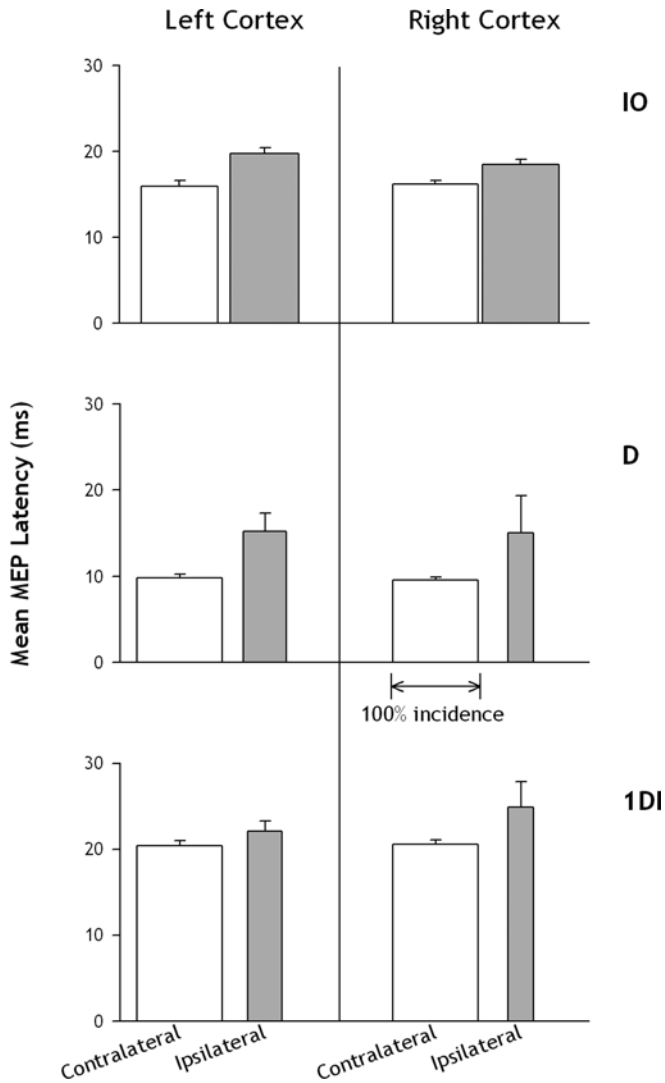


Fig. 2 Latencies and incidences of MEPs induced by ipsilateral and contralateral TMS. Mean (+ S.E.M.) MEP latencies in internal oblique (*IO*; top), deltoid (*D*; middle) and first dorsal interosseus (*1DI*; bottom). *Open bars* represent stimulation of contralateral motor cortex and *grey bars* represent ipsilateral stimulation. The width of the bars represents the incidence of the responses

responses from each cortex to a given muscle. For a given subject this stimulator strength was used for the experimental protocol (range across subjects 80–100% MSO). However, even at maximum stimulator output, one subject showed no ipsilateral MEPs (iMEPs) in either *IO*, one subject showed no iMEPs in left *IO* and one subject showed no contralateral MEPs (cMEPs) in right *IO*.

Experimental protocol and statistical analyses

In each assessment, 5–20 stimuli were delivered whilst the subject maintained low level contractions of all muscles. The number of stimuli delivered was determined by the stimulus intensity used and how well this was tolerated by the subjects (one subject 5 stimuli; two subjects 10 stimuli; seven subjects 20 stimuli). Bilateral EMG responses were recorded simultaneously from all three muscles and were

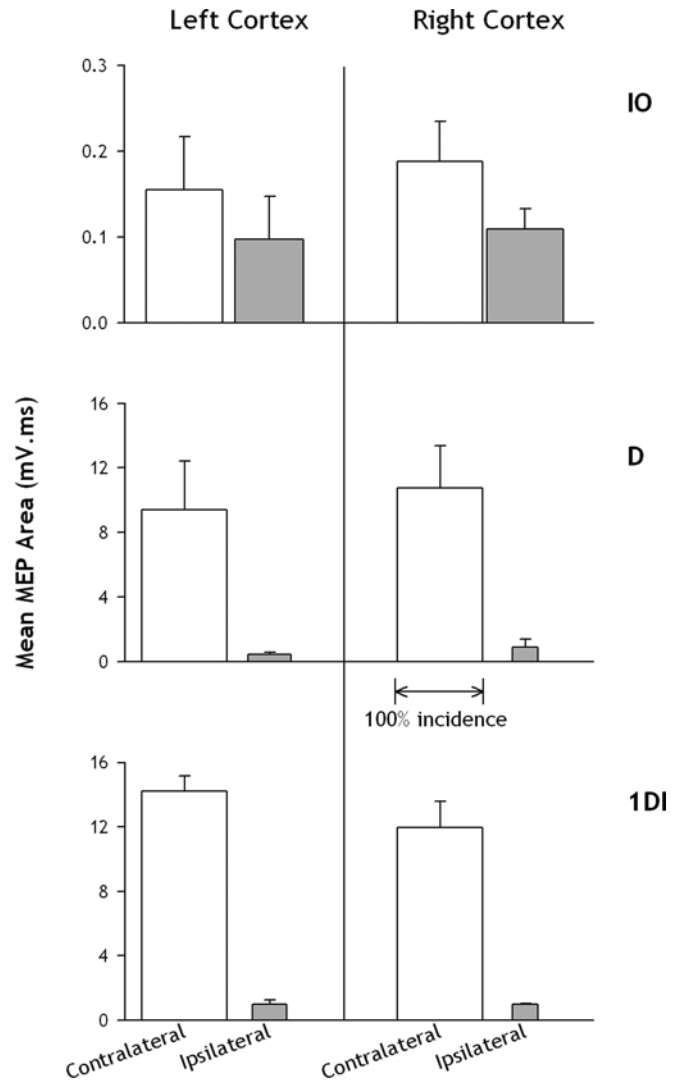


Fig. 3 Areas and incidences of MEPs induced by ipsilateral and contralateral TMS. Mean (+ S.E.M.) MEP areas in internal oblique (*IO*; top), deltoid (*D*; middle) and first dorsal interosseus (*1DI*; bottom). *Open bars* represent stimulation of contralateral motor cortex and *grey bars* represent ipsilateral stimulation. The width of the bars represents the incidence of the responses

rectified and then averaged for each trial. The times of onset and finish of the MEP were determined visually by two independent assessors and cursors positioned at these points to allow measurement of latency and area.

iMEP and cMEP latencies and areas were compared for differences using unpaired Student's *t*-test or Mann-Whitney rank sum test. A ratio was obtained for (area of iMEP)/(area of cMEP) in a given muscle. Ratio data were compared for differences using the Kruskal-Wallis one-way ANOVA on Ranks with Dunn's multiple comparison test (between the different muscles) or Mann-Whitney rank sum test (between the biased and unbiased cortices). Differences were considered statistically significant when $P < 0.05$.

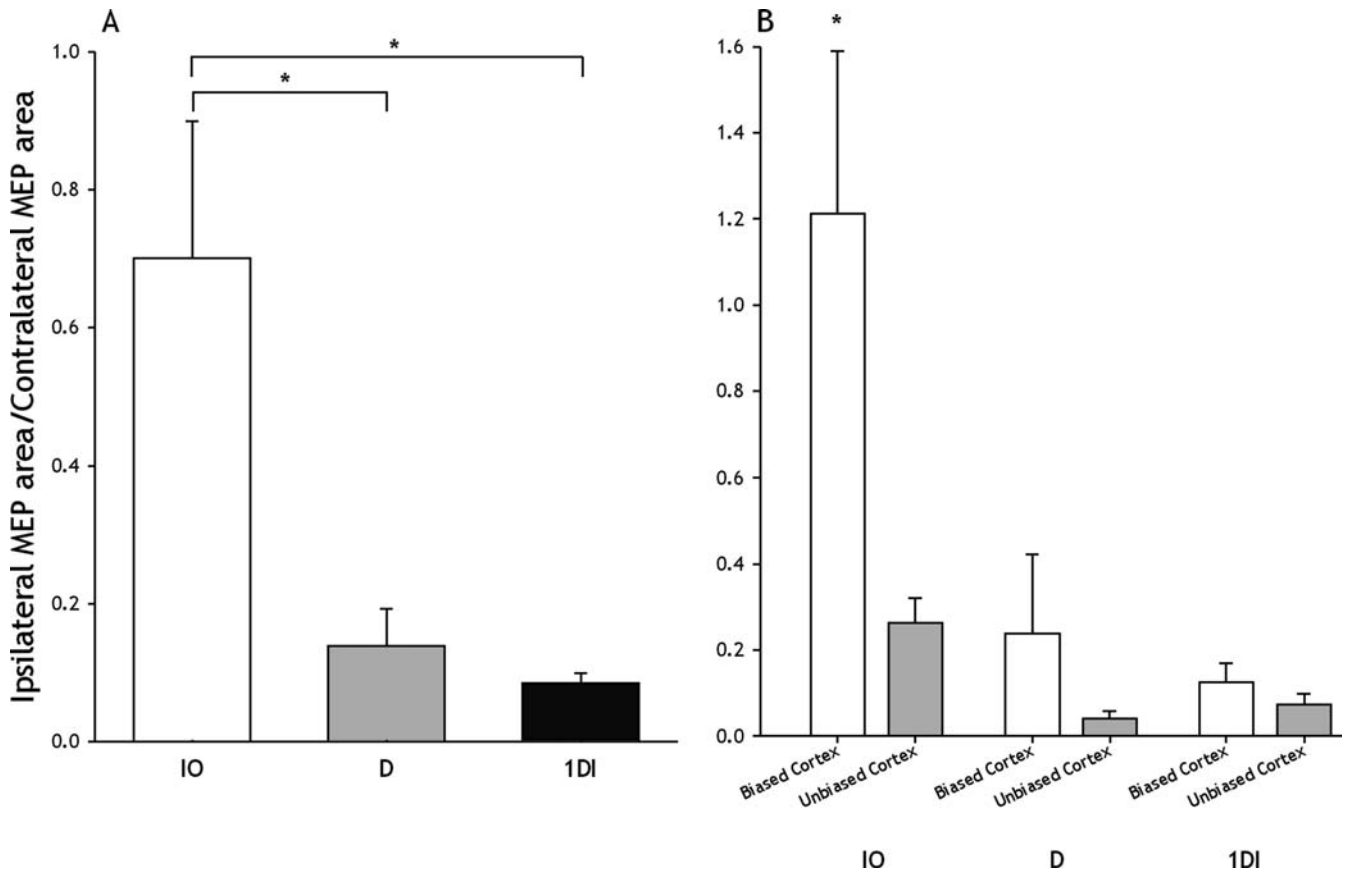


Fig. 4a, b Ratios of MEP areas to ipsilateral stimulation relative to contralateral stimulation. **a** Mean (+ S.E.M.) area of ipsilateral MEPs expressed relative to area of contralateral MEPs in internal oblique (*IO*; open bar), deltoid (*D*; grey bar) and first dorsal interosseus (*1DI*; black bar) muscles. Data are included for both left and right muscles. * $P < 0.05$; Kruskal-Wallis one-way ANOVA on

Ranks with Dunn's multiple comparison test. **b** Mean (+ S.E.M.) area of ipsilateral MEPs expressed relative to area of contralateral MEPs in the internal oblique (*IO*), deltoid (*D*), and first dorsal interosseus (*1DI*) muscles when grouped into those produced by stimulating either the biased (*open bar*) or unbiased (*grey bar*) cortex. * $P < 0.05$; Mann-Whitney rank sum test

Results

Responses were obtained in all muscles for a given side when the stimulus was applied over the contralateral motor cortex, except in one *IO*, even at 100% MSO. Figure 1b shows representative bilateral MEPs from *IO* after stimulation of both cortices.

When the stimulus was applied to the ipsilateral motor cortex, incidences of MEPs were 85% in *IO*, 40% in *D* and 35% in *1DI* (represented by the *bar widths* in Figs. 2 and 3).

Mean (\pm S.E.M.) iMEP latencies were longer ($P < 0.05$; unpaired Student's *t*-test) than cMEP latencies (cMEP vs. iMEP; *IO*: 16.1 ± 0.4 vs. 19.0 ± 0.5 ms; *D*: 9.7 ± 0.3 vs. 15.1 ± 1.9 ms; *1DI*: 18.3 ± 0.6 vs. 23.3 ± 1.4 ms; see Fig. 2).

Mean cMEP areas were not significantly different from iMEP areas in *IO* (cMEP vs. iMEP; *IO*: 0.17 ± 0.04 vs. 0.10 ± 0.03 mV.ms; $P > 0.05$; Mann-Whitney rank sum test), but were larger ($P < 0.05$) in *D* (cMEP vs. iMEP; 10.00 ± 0.19 vs. 0.62 ± 0.19 mV.ms) and *1DI* (cMEP vs. iMEP; 13.10 ± 0.95 vs. 0.97 ± 0.14 mV.ms; see Fig. 3).

The iMEP/cMEP area ratio was obtained for a given muscle, where data were available (*IO*: $n = 16$; *D*: $n = 8$; *1DI*: $n = 7$ ratios). This ratio was significantly ($P < 0.05$; Kruskal-

Wallis one-way ANOVA on Ranks with Dunn's multiple comparison test) larger in *IO* (0.70 ± 0.20) than in either *D* (0.14 ± 0.05) or *1DI* (0.08 ± 0.02), revealing a stronger ipsilateral drive to the internal oblique muscles than for either of the other two muscles (see Fig. 4a).

In one subject no iMEPs were evoked in either *IO*; in one subject no iMEPs were evoked in left *IO* and in one subject no cMEPs were evoked in right *IO*. In the seven remaining subjects comparison of the iMEP/cMEP ratios between left and right *IO* muscles revealed one to have a larger value than the other (four subjects right [two left-handed]; three subjects left [one left-handed]), which appeared to be unrelated to handedness. For example, if the ratio were 2 in the left *IO* as compared to 1 in the right *IO*, the explanation for this could be one of the following:

- 1) The ipsilateral response of left *IO* (left cortex stimulation) is larger than the contralateral response of left *IO* (right cortex stimulation), suggesting a stronger projection from the left cortex (i.e. left cortex bias)
- 2) The ipsilateral response of right *IO* (right cortex stimulation) is smaller than the contralateral response of right *IO* (left cortex stimulation), suggesting a

weaker projection from the right cortex

Both of these explanations would indicate a “bias” (stronger drive) from the left cortex to the IO muscles.

When the iMEP/cMEP ratios from the biased cortex were grouped for IO, they showed a larger ($P < 0.05$; Mann-Whitney rank sum test) mean than those from the unbiased cortex (biased vs. unbiased; 1.21 ± 0.38 vs. 0.26 ± 0.06 ; see Fig. 4b). Values for the other two muscles were (D biased vs. unbiased; 0.24 ± 0.18 vs. 0.04 ± 0.02 ; 1DI biased vs. unbiased; 0.12 ± 0.04 vs. 0.07 ± 0.02 ; see Fig. 4b). Due to the low incidences of pairs of ratios within the same subject (D=2 pairs; 1DI=2 pairs), statistical comparisons were not performed.

Discussion

The present study has revealed that TMS over the motor cortex can produce iMEPs in internal oblique (a trunk muscle). This supports earlier studies involving other trunk muscles (*pectoralis major*, Quartarone et al. 1999; *rectus abdominis*, Tunstall et al. 2001) and limb muscles (Colebatch et al. 1990; Wassermann et al. 1991; Basu et al. 1994; Netz et al. 1997; Ziemann et al. 1999; Chen et al. 2003). Furthermore, we have found that iMEPs are more readily evoked in the trunk muscle IO than in the limb muscles D or 1DI.

The presence of iMEPs in itself does not confirm the existence of an ipsilateral corticospinal projection to IO. However, the longer latencies of the iMEPs than the cMEPs in IO, D and 1DI (range 2.9–5.4 ms; see Fig. 2) are too long to be attributed to current spread to the contralateral motor cortex (Ziemann et al. 1999) and too short to be attributed to interhemispheric transcallosal conduction (Cracco et al. 1989). These latency differences are consistent with the differences (range 4–10 ms) observed in *pectoralis major* (Quartarone et al. 1999).

Furthermore, the iMEPs reported by Ziemann et al. (1999) in a patient with complete agenesis of the corpus callosum lend support to this. Therefore, it seems likely that the iMEPs reported in this study are mediated by slower conducting ipsilateral corticospinal fibres (Netz et al. 1997).

The comparable size of the iMEPs and cMEPs observed in IO contrast with the significantly larger cMEPs than iMEPs in the distal muscles D and 1DI and support further the idea that the anterior CST predominantly innervates proximal muscles (Porter and Lemon 1995). The incidence of iMEPs in 1DI and D was lower than in IO, which supports this notion. However, the focal point of the stimulation was optimised for activation of IO (see Methods) and therefore may have been sub-optimal for 1DI and D (Classen et al. 1998). Despite this, we were able to evoke cMEPs in 1DI and D muscles on all occasions in every subject, presumably because the motor cortical threshold for 1DI and D is lower than for IO. Furthermore, reference to Fig. 3 shows that cMEPs from D and 1DI were, on average, 60–90 times larger than IO

cMEPs. So, although the stimulation may not have been optimal for D and 1DI, activation of contralateral corticospinal projections was clearly very effective. We feel, therefore, that any neurones lying close-by with ipsilateral projections to D or 1DI would also receive effective stimulation. We believe that the low incidence and small size of iMEPs in these muscles reflects a weaker ipsilateral corticospinal projection.

Comparisons of the iMEP/cMEP area ratio between left and right IO muscles reveals a bias towards one cortex or another which is independent of handedness. The striking difference in ratio values between the biased and unbiased cortices (see Fig. 4b) further highlights this. Similar asymmetry has been reported in human oral, pharyngeal and oesophageal musculature involved in swallowing (Hamdy et al. 1996), although assessment of the strength of ipsilateral projections to such muscles is difficult. Our present observations of asymmetry appear to be consistent with anatomical examination of the human CSTs. In a tract tracing study of post mortem human spinal cords an asymmetry was found in the cross-sectional areas of corticospinal tracts, with a higher incidence of asymmetrical than symmetrical cords (Nathan et al. 1990).

Hamdy et al. (1996) also suggest that the dysphagia associated with hemispheric stroke may be related to cortical asymmetry. The asymmetrical cortical control of IO identified in this study may similarly affect outcome after stroke. Additionally, it may provide much needed evidence to support the design of future physiotherapeutic treatment regimes for this condition (Pollock et al. 2003).

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