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Ipsilateral motor cortical responses to TMS during lengthening and shortening of the contralateral wrist flexors

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Abstract

Unilateral lengthening contractions provide a greater stimulus for neuromuscular adaptation than shortening contractions in the active and non-active contralateral homologous muscle, although little is known of the potential mechanism. Here we examined the possibility that corticospinal and spinal excitability vary in a contraction-specific manner in the relaxed right flexor carpi radialis (FCR) when humans perform unilateral lengthening and shortening contractions of the left wrist flexors at the same absolute force. Corticospinal excitability in the relaxed right FCR increased more during lengthening than shortening at 80 and 100% of maximum voluntary contraction (MVC). Short-interval intracortical inhibition (SICI) diminished during shortening contractions and it became nearly abolished during lengthening. Intracortical facilitation (ICF) lessened during shortening but increased during lengthening. Interhemispheric inhibition (IHI) to the “non-active” motor cortex diminished during shortening and became nearly abolished during lengthening at 90% MVC. The amplitude of the H-reflex in the relaxed right FCR decreased during and remained depressed for 20 s after lengthening and shortening of the left wrist flexors. We discuss the possibility that instead of the increased afferent input, differences in the descending motor command and activation of brain areas that link function of the motor cortices during muscle lengthening vs. shortening may cause the contraction-specific modulation of ipsilateral motor cortical output. In conclusion, ipsilateral M1 responses to TMS are contraction-specific; unilateral lengthening and shortening contractions reduced contralateral spinal excitability but uniquely modulated ipsilateral corticospinal excitability and the networks involved in intracortical and interhemispheric connections, which may have clinical implications.

Keywords

Motor cortex; spinal excitability; cross education

Introduction

Lengthening and shortening contractions are an integral part of human voluntary movements and are routinely used in exercise prescription for athletic, clinical and elderly populations as a means to maintain skeletal muscle function. Chronic training with lengthening contractions have been demonstrated to provide a greater stimulus for neuromuscular

adaptation resulting in larger gains in skeletal muscle hypertrophy and changes in neural adaptation (Hortobágyi *et al.*, 1996, for example). Interestingly, a bout of high intensity contractions can result in temporary muscle damage; however when this bout is repeated in the following weeks a reduction in the magnitude of damage is observed (Howatson and van Someren, 2007) that is not evident following initial bouts of shortening contractions. The mechanisms responsible for this adaptation have been suggested to be, at least in part, due to neural plasticity (Lee and Carroll, 2007). Chronic unilateral lengthening contraction training has been shown to provide greater improvements in strength and EMG activity than shortening contractions (Hortobágyi *et al.*, 1997) in the inactive contralateral homologous muscle. In addition a single bout of high intensity lengthening contractions also provide protection to the inactive contralateral homologous muscle (Howatson and van Someren, 2007) and intuitively it seems these adaptive phenomena are likely mediated by neural mechanisms that remain to be elucidated.

Activation of the ipsilateral motor cortex (M1) and the excitability of the corticospinal path targeting the resting hand increase during unilateral voluntary isometric contractions. These responses increase with contraction intensity as shown by EEG (Crone *et al.*, 1998; Urbano *et al.*, 1998), fMRI (Rao *et al.*, 1993; Shibasaki *et al.*, 1993; Cramer *et al.*, 1999), MEG (Salmelin *et al.*, 1995), PET (Kawashima *et al.*, 1998), and TMS studies (Hess *et al.*, 1986; Meyer *et al.*, 1995; Tinazzi & Zanette, 1998; Muellbacher *et al.*, 2000; Liepert *et al.*, 2001; Stinear *et al.*, 2001; Hortobágyi *et al.*, 2003; Perez & Cohen, 2008). Much less is known about the effects of effortful unilateral contractions comprising of muscle lengthening and shortening on the corticospinal excitability in the ipsilateral M1 and the resting contralateral homologous muscle. Corticospinal and spinal excitability are significantly less in the actively lengthening compared with shortening arm and foot muscles of healthy humans (Abbruzzese *et al.*, 1994; Sekiguchi *et al.*, 2001; Nordlund *et al.*, 2002; Sekiguchi *et al.*, 2003; Gruber *et al.*, 2009). These task-dependent changes are presumably due to differences in excitability of the motoneuron pool (Abbruzzese *et al.*, 1994) and in the gain of the corticospinal tract during lengthening compared with shortening contractions (Sekiguchi *et al.*, 2001; Sekiguchi *et al.*, 2003). In addition, EMG (Grabiner & Owings, 2002), EEG (Fang *et al.*, 2001) and TMS (Gruber *et al.*, 2009) studies suggest that the descending commands associated with lengthening and shortening are also different. For example, there was a 21% greater ratio of motor evoked potentials-to-cervicomedullary motor evoked potentials during lengthening vs. isometric contractions, suggesting a reduction in spinal excitability and an increase in motor cortical excitability during lengthening compared with isometric muscle contractions (Gruber *et al.*, 2009). Together, there are multiple lines of evidence for task-specific corticospinal and spinal control during muscle lengthening and shortening.

Here we examine the possibility that corticospinal and spinal excitability vary in the resting right wrist flexors according to whether intact humans perform controlled lengthening or shortening contractions using unilateral left wrist flexion. This hypothesis emerged from the studies that showed task-specificity of the corticospinal and spinal excitability in the contracting muscle (Abbruzzese *et al.*, 1994; Sekiguchi *et al.*, 2001; Nordlund *et al.*, 2002; Sekiguchi *et al.*, 2003; Gruber *et al.*, 2009) and from chronic exercise studies that reported task-specific responses in motor output in the resting non-exercised limb after unilateral practice using lengthening vs. shortening contractions (Housh *et al.*, 1996; Hortobágyi *et al.*, 1997; Farthing & Chilibeck, 2003). We were especially interested in determining task-specificity in networks of cortical neurons in the ipsilateral M1 that are involved in short intracortical inhibition (SICI) and facilitation (ICF) and in the GABA-ergic projections that mediate interhemispheric inhibition (IHI) from the active to the “non-active” M1. To aid the localization of any task-specific effect, we also measured spinal excitability in the resting right flexor carpi radialis (FCR) during lengthening and shortening of the left wrist flexors. In addition to providing novel information about this phenomenon, elucidating the potential

mechanisms might have implications for exercise prescription and rehabilitation protocols for individuals who suffer from a unilateral orthopaedic or neurological pathology. Therefore the aim of this investigation was to examine the task specific responses to transcranial magnetic brain stimulation and peripheral nerve stimulation in the resting flexor carpi radialis of the right wrist during lengthening and shortening contractions of the left wrist flexors.

Methods

Participants

Forty-one right-handed (Oldfield, 1971) healthy volunteers (26 men, 15 women) with an average age, height, mass, and body mass index of $21.5 (\pm 2.75)$ years, $1.75 \text{ m} (\pm 0.09)$, $79.2 (\pm 12.13) \text{ kg}$, and $24.1 (\pm 3.20) \text{ kg}\cdot\text{m}^{-2}$, respectively, participated in the study. Thirty-one subjects (21 males, 10 females) completed the TMS experiments and 10 subjects (5 males, 5 females) completed the H-reflex experiments. Several subjects participated in more than one experiment conducted at least 5 days apart. Each experiment lasted approximately one hour. All subjects gave their written informed consent to the experimental procedure, which was approved by the University and Medical Center Institutional Review Board. The study was performed in accordance with the Declaration of Helsinki.

General experimental protocol

In each experiment subjects performed left wrist flexion using lengthening and shortening contractions while the right arm remained at rest. Motor cortical function of the ipsilateral (left) M1 was evaluated at rest and during voluntary contraction using different TMS protocols. All experiments were conducted at the same absolute force during lengthening and shortening. The maximal force in Newtons was noted for each subject during maximal voluntary contraction (MVC) of the left wrist flexors during shortening. Then, as needed in each experiment, we computed a given percent of this absolute force and subjects performed both shortening and lengthening contractions at the same absolute force. For example, if a subject's MVC during shortening contraction was 200 N, 80% of this value is 160 N, which was the target force during shortening and lengthening. The same general experimental protocol and set-up was used in experiments that assessed spinal excitability in the resting right flexor carpi radialis (FCR) using H-reflexes.

Experimental setup

Participants sat comfortably at a table with the active (left) forearm resting upon the surface and held in place by foam-padded blocks to prevent extraneous movements during contractions. The hand was held in a neutral position in the sagittal plane with the thumb upper-most and the fingers extended. An isokinetic dynamometer (Kin-Com, Chattanooga, TN, USA) was configured to enable lengthening and shortening contractions of the wrist flexors in the transverse plane over the table surface. Subjects performed wrist flexion by pressing at the metacarpophalangeal joint on a plastic covered manipulandum that projected vertically downward toward the table surface from the dynamometer's lever arm. Visual feedback of the target forces was provided using the dynamometer's monitor. The resting (right) upper limb was placed in comfortable position on the table surface, on a towel or a pillow if necessary. Surface EMG was recorded from the left and right FCR. The distance between the axis of rotation and the transducer was kept at a constant length between conditions for each subject but was adjusted between subjects to account for anatomical differences. The TMS stimulus to the left M1 (ipsilateral to the active wrist flexors) or the peripheral electrical stimulus to the right median nerve was delivered in all experiments when the left wrist was at 0° position. The target forces were set at the same absolute or relative forces within-subjects and between subjects (see below). Relative to the 0° neutral

position, lengthening contractions started at 20° of wrist flexion by the subjects resisting the manipulandum. Shortening contractions started with the wrist in 20° of extension. Contraction velocity was 20°·s⁻¹. Data acquisition was initiated when the subject applied 1% of maximal voluntary force to the manipulandum.

Electromyography (EMG)

Surface EMG was recorded from the left and right FCR to quantify the electrical activity during voluntary contractions of the left FCR and motor evoked potentials (MEP) in the right FCR. After the skin surface was shaved, cleaned with alcohol, and abraded with LemonPrep, two shielded Ag-AgCl disk electrodes (8 mm diameter, model E258S, Biopac Inc., Goleta, CA, USA) were taped on the muscle belly (inter-electrode distance, 2 cm) and one electrode as ground was fixed on distal styloid process of the radius. Surface EMG was band-passed filtered at 10 to 500 Hz, amplified 1000× (model EMG100C, Biopac Inc., Goleta, CA, USA) and then sampled at 5 kHz (CED Power 1401, Cambridge Electronics Design, Cambridge, UK) and recorded on a personal computer. MEPs were analyzed for peak-to-peak amplitude with custom software (Signal, v.3.0, Cambridge Electronics, Cambridge, UK). EMG activity from the contracting and resting FCR were rectified and smoothed with a 20-ms moving window and the mean EMG activity computed for 100 ms window prior to the stimulation artifact.

Transcranial magnetic stimulation of the motor cortex

MEPs were produced by transcranial magnetic stimuli delivered from a magnetic stimulator (part number 3010, Magstim 200², Magstim, Dyfed, UK) through a high power 2nd generation figure-of-eight remote control coil (loop diameter 9 cm, SN 059, part number 3192, Magstim, Spring Gardens, Wales, UK) with a monophasic current waveform of about 2.24 T peak strength. Paired pulses were produced with the addition of a second Magstim 200² stimulator equipped with a BiStim² timing module (part number 3021) and the pulses were delivered through the same 9-cm coil. TMS was delivered to the optimal scalp position for the activation of the right FCR overlying left M1 as this hot spot correlates well with stimulation of Brodmann's area 4 (Mills *et al.*, 1992). The coil was held with the handle pointing backwards and 45° away from the midline. Resting motor threshold (rMT) was measured as a percent of the stimulator output where the lowest stimulation intensity produced an MEP of ≥ 50 µV on at least five of 10 consecutive stimulations (Rossini *et al.*, 1994). In the interhemispheric experiment, the hotspot and rMT were determined for each FCR as described above. In these experiments we used two custom built figure-of-eight coils (loop diameter 6 cm, type SP 15859 and SP 15860, model D60 mm flat, Magstim, Spring Gardens, Wales, UK). Strong unimanual voluntary contractions often produce unintended mirror EMG activity in the contralateral muscles (Muellbacher *et al.*, 2000; Hortobágyi *et al.*, 2003). Subjects received standard instructions 10 s prior to each effort and were frequently reminded to relax all other muscles during left wrist flexions. Trials with mirror activity greater than 25 µV in the right FCR were excluded from the analyses.

Single-pulse experiments

We conducted two experiments in separate sessions. One determined the effects of contraction intensity on MEP amplitude recorded from the resting right FCR during shortening and lengthening contraction of the left wrist flexors at the same absolute force corresponding to 20, 40, 60, 80, and 100% of the shortening MVC force (n = 11). TMS was delivered at an intensity of 1.6 of rMT. A total of seven MEPs were evoked in each of the 5 runs (contraction intensities): one during the contraction and six at rest after the contraction every 5 s. Using seven MEPs allowed us to minimize the number of TMS pulses delivered and still ensured that the MEPs returned to control level after the contraction (Hortobágyi *et al.*, 2003). The amplitude of the last MEP in each run was used to normalize the remaining 6

trials. The second experiment examined the effects of TMS intensity (1.0, 1.2, 1.4, 1.6, and 1.8, times rMT) on MEP size during shortening and lengthening contraction ($n = 11$). The contraction intensity was set at 90% of shortening MVC force. The order of contraction intensity in the first experiment and the order of stimulation intensity in the second experiment were randomized between subjects. We also rotated the order of lengthening and shortening contraction blocks between subjects. To confirm that corticospinal excitability was not different between conditions immediately preceding contractions we completed a recruitment curve (also randomized within and between subjects) to ensure corticospinal excitability was similar between conditions.

Short-interval intracortical inhibition (SICI) and facilitation (ICF)

In a separate experiment, we measured SICI and ICF in the right FCR at rest and when the left wrist flexors performed a lengthening and a shortening contraction at $20^{\circ}\cdot\text{s}^{-1}$ and 90% MVC ($n = 10$). We used a method previously described in detail (Kujirai *et al.*, 1993; Muellbacher *et al.*, 2000). The conditioning stimulus was set at about 80% of rMT, an intensity that does not affect spinal excitability (Di Lazzaro *et al.*, 2001). Because a second peak of ICF can also affect SICI (Ziemann *et al.*, 1998) and muscle contraction can facilitate the size of the MEP produced by the test stimulus (Muellbacher *et al.*, 2000), we adjusted the stimulation intensity to keep the size of the test stimulus constant at about 0.3 mV at rest and during the contraction. The test stimuli were delivered 2 and 10 ms after the conditioning stimulus for SICI and ICF, respectively. Because there are two distinct phases of inhibition (Fisher *et al.*, 2002), we used the 2-ms interstimulus (Kujirai *et al.*, 1993) interval to avoid a mixture of the two phases. Ten test stimuli, 10 SICIs, and 10 ICFs were presented at random at rest and repeated 2 times to establish the stimulation parameters. After measurements at rest, 10 test stimuli, 10 SICIs, and 10 ICFs were presented in one block of lengthening contractions. After 5 minutes of rest, a second block was completed using shortening contractions. There were 10 s of pause between trials within a block. The order of lengthening and shortening contraction was systematically rotated between subjects. Similarly to Muellbacher *et al.* (2000), we also assessed intracortical excitability with a conditioning stimulus set at 90% of rMT, a stimulus intensity that is less likely to produce changes in motoneuron excitability at the spinal level, and found similar results at 80 and 90% conditioning stimulus ($n = 4$, data not shown).

Interhemispheric inhibition

In a separate experiment, we measured IHI from right M1 to left M1 (ipsilateral to contraction) in the right FCR during lengthening and shortening contraction of the left wrist flexors at 50 and 90 % MVC ($n = 8$). The right FCR was always at rest. A suprathreshold conditioning stimulus was set at an intensity that elicited about 60% of inhibition (Ferber *et al.*, 1992). The conditioning stimulus was adjusted by changing the stimulator output so that the conditioning MEP in the left FCR was ~0.45 mV at rest (increasing stimulator output in some cases up to 100% stimulator output) and during contraction of the left wrist flexors (reducing stimulator output) (Chen, 2004). In order to match the size of the conditioning MEP across conditions, we had to select volunteers with low rMT and high responses to TMS. We also adjusted the test stimulus delivered to the left M1 so that it produced about ~0.2–0.4 mV test MEPs in the right FCR. The conditioning stimulus was delivered 10 ms before the test stimulus (Ferber *et al.*, 1992). The two coils were positioned at the optimal location for activating the left and right FCR. The positions were marked on the subjects' scalp with ink. The handles of the coils pointed 45° backward and laterally relative to the midsagittal line. Twenty test stimuli and 20 IHI were presented randomly at rest and repeated twice to establish the stimulation parameters. After measurements at rest, 10 test stimuli and 10 IHI were presented during lengthening at 50 and 90% MVC, respectively. After 3–4 minutes of rest, 10 test stimuli and 10 IHI were presented during shortening

contractions at 50 and 90% MVC, respectively. In all conditions, there was a 10 s pause between trials. The order of lengthening and shortening contractions and the order of 50 and 90% contraction intensity were both systematically rotated between subjects. We also conducted a control experiment in 4 volunteers without adjusting for the size of conditioning stimulus while keeping the size of the test stimulus constant.

Peripheral electrical stimulation

In a separate experiment, we measured the Hoffman reflex (H-reflex) in the right FCR at rest and when the left wrist flexors performed a lengthening and a shortening contraction at $20^{\circ}\cdot\text{s}^{-1}$ at 100% MVC of shortening force ($n = 10$). We placed subjects' right wrist in an optimal position (Baldissera *et al.*, 2000) to evoke H-reflexes by single electrical stimuli delivered to the right median nerve through water-soaked gauze-covered button electrodes, the cathode 5 cm proximal to the anode, in the cubital space (duration 1 ms, Digitimer DS7, Welwyn Garden City, Hertfordshire, UK). First, we determined the appropriate stimulating electrode location and identified the H-reflex in the FCR based on its latency and recruitment curve. Next, we determined the maximal amplitude of the H-reflex. Finally, the stimulation intensity was set to produce an H-reflex that corresponded to approximately 50% of the maximal H-wave (Hortobágyi *et al.*, 2003). During blocks of trials, H-reflexes were evoked at 5 s intervals. Action potentials were analyzed for peak-to-peak amplitude. A total of 9 H-reflexes were evoked in each of the 5 runs: one during contraction and eight at rest after the contraction every 5 s. The amplitude of the last 3 H-reflexes in each of the 5 runs were averaged and used to normalize the remaining 6 trials. Compared with 7 TMS pulses, we used 9 H-reflexes because a previous study showed that H-reflexes recover slower than MEPs and they can be also more variable (Hortobágyi *et al.*, 2003).

Statistical analyses

Data are expressed as mean $\pm$ SD. In each experiment, we used a repeated-measures ANOVA to determine if the position of the wrist, the level of force, and EMG activity in the contracting left and relaxed right FCR were similar during lengthening and shortening contraction of the left wrist flexors. To determine the effect of contraction intensity, we used a Contraction Mode (lengthening, shortening) by Contraction Intensity (20, 40, 60, 80, 100% MVC) repeated-measures ANOVA. To determine the effect of stimulation intensity, we used a Contraction Mode (lengthening, shortening) by Stimulation Intensity (1.2, 1.4, 1.6, 1.8, 2.0) repeated-measures ANOVA. We used a Contraction Mode (lengthening, shortening) by Stimulation Condition (Test, SICI, ICF) repeated-measures ANOVA to test the effect of contraction mode on intracortical excitability. In the IHI experiment, we tested the effect of muscle contraction on IHI with a repeated-measures ANOVA with five levels (rest, lengthening and shortening at 50 and 90% MVC). The H-reflex data were analyzed with Condition (lengthening, shortening) by Trial (6) ANOVA with repeated measures on both factors. Tukey's post-hoc contrast was used to determine the means that were significantly different at $p < 0.05$.

Results

Table 1 shows that the experimental conditions were similar during lengthening and shortening contractions in terms of joint position and force produced by the left wrist flexors and the background EMG activity in the resting right FCR when the TMS produced the MEPs at five contraction intensities. The data suggest that at the time of TMS to the left M1 the position of the left wrist was at the neutral position (0°) during lengthening and shortening. The force exerted by the left wrist flexors was also similar during lengthening and shortening, indicating that we successfully matched the force levels between the two contraction modes. Further, the EMG activity of the left FCR as a percent of maximal EMG

recorded during an MVC was 8.4% (± 5.5) lower during lengthening than shortening contractions ($F_{1,10} = 18.6$; $P = 0.021$). The background EMG activity in the right, resting FCR was negligible ($0.006 \text{ mV} \pm 0.001$) and it was similar when the left wrist flexors performed lengthening or shortening contractions and did not vary with contraction intensity. Fatigue did not bias the data; a comparison of MVCs measured in 6 subjects before and after the experiment produced a mean change of 3.3% (± 5.2), $t_{10} = 1.2$; $P = 0.229$).

Figure 1A shows a representative example for a single subject and the group data in Figure 1B shows that the size of the MEPs recorded from the right, resting FCR produced by TMS in the ipsilateral (left) M1 increased with increasing contraction intensities (main effect, $F_{4,40} = 34.0$; $P = 0.001$). In addition, a significant interaction ($F_{4,40} = 3.2$, $P = 0.025$) revealed a greater increase in MEP amplitude during lengthening than shortening contractions at higher intensities (80% and 100%), equating to 15.6% and 21.9%, respectively ($P < 0.05$).

Table 2 shows that experimental conditions were similar during lengthening and shortening contractions of the left wrist flexors at 5 MEP stimulation intensities. The left wrist was in a similar position (neutral, 0°) between lengthening and shortening conditions and between different stimulation intensities when TMS was delivered. The force was also similar between lengthening and shortening contractions and was well matched between stimulation intensities. Furthermore, the EMG activity of the left FCR (as a percent of EMG recorded during an MVC) was 5.5% lower during lengthening than shortening contractions and did not vary with TMS intensity. The negligible EMG activity in the resting right FCR was $0.015 \text{ mV} \pm 0.011$; during left wrist flexion EMG in the right FCR was similar during lengthening and shortening and did not vary with TMS intensity.

Figure 2 shows the interaction in MEP size between stimulation intensity and the two modes of muscle contraction. The size of the control MEPs, i.e., given at rest (refer to Figure 2A), was similar in the experiment using lengthening and shortening, but did increase with stimulation intensity ($F_{4,40} = 5.5$; $P = 0.001$), demonstrating that corticospinal excitability was similar between conditions before the contractions. MEP size was similar during lengthening and shortening contractions, but increased continuously with stimulation intensities during shortening and stabilized at mid-intensities during lengthening (interaction, $F_{4,40} = 2.7$; $P = 0.046$).

Table 3 shows the position, force, and EMG data recorded when a TMS test stimulus was delivered to the left M1 alone and in combination with a conditioning stimulus 2 ms (SICI) and 10 ms (ICF) before the test stimulus during lengthening and shortening contractions of the left wrist flexors. There were no significant contraction, stimulation condition or interaction effects in wrist position. In addition the target force was similar between the two contraction modes stimulation conditions, without an interaction between these two factors. During contraction of the left wrist flexors, there was 6.2% less EMG during lengthening than shortening contractions ($F_{1,10} = 7.3$; $P = 0.023$). The incidental EMG in the right FCR activity was small and of a similar magnitude when the left wrist flexors performed lengthening and shortening contractions. We kept the size of the test pulse constant at rest and adjusted the stimulation intensity during contractions; at rest the size of the test pulse was also similar during lengthening and shortening contractions.

Although we isolated the left wrist in a myograph, extraneous movement during forceful flexion of the wrist could activate muscles that stabilize the elbow and shoulder; differences in the level of co-activation between lengthening and shortening might affect MEP size. Consequently, we measured the surface EMG activity of left and right anterior deltoid

muscle ($n = 6$) during lengthening and shortening contraction of the left wrist flexors. Activation of the left and right deltoid, respectively, was similar when the left wrist flexors performed lengthening and shortening contractions but, as expected, the activation of the deltoid was higher on the contracting left side (0.0225 ± 0.021) than the resting right side (0.0108 ± 0.0195) ($F_{1,5} = 4.5$; $P = 0.029$).

Figure 3A shows representative data in a single subject and Figure 3B shows the group data for SICI and ICF. There was a significant ($F_{2,18} = 6.4$; $P = 0.008$) Contraction mode by Stimulation condition interaction, illustrating that SICI of $53.5\% (\pm 7.25)$ at rest diminished during shortening ($69.0\% \pm 7.16$) and further diminished during lengthening contraction ($92.0\% \pm 11.12$) ($P < 0.05$). In addition, ICF of $135.1\% (\pm 7.32)$ at rest diminished during shortening ($116.2\% \pm 11.20$) but increased during lengthening ($158.1\% \pm 15.42$) ($P < 0.05$).

Table 4 shows the stimulation, recording, and mechanical characteristics for the experiment that determined IHI from the right M1 to left M1 during lengthening and shortening contractions of the left wrist flexors. The size of the contralateral conditioning stimulus given to the right M1 and recorded in the left FCR was similar at rest and during left wrist flexion with lengthening and shortening contractions at 50 and 90% of MVC. The size of the test stimulus was also similar at rest and during the four conditions of muscle contraction. At the time of the contralateral conditioning stimulus during left wrist flexion with lengthening and shortening contractions at 50 and 90% MVC, the position of the left wrist joint and the EMG activity in the relaxed right FCR were similar ($P = 0.171$). The level of force produced at 50% MVC and 90% MVC during lengthening and shortening conditions was similar between contraction types. The level of EMG activity during wrist flexion with lengthening was smaller ($F_{1,7} = 32.1$; $P = 0.001$) compared with shortening contraction, respectively, at 50% and 90% MVC. Figure 4 shows the condition main effect for IHI ($F_{4,28} = 30.9$; $P = 0.001$). Compared with rest MEP ($58.7\% \pm 9.30$), IHI did not change during left wrist flexion with lengthening or shortening contractions at 50% MVC. However, during wrist flexion with shortening at 90% MVC, IHI diminished (78.5 ± 9.99) relative to rest and with lengthening IHI further diminished (95.0 ± 11.06) relative to rest and 50% MVC ($P < 0.05$). In a further experiment ($n = 4$), the size of the conditioning pulse was not adjusted, and as expected, IHI significantly increased during lengthening and shortening contractions at both 50% and 90% MVC ($P < 0.05$).

When the H-reflex was evoked, the position of the left wrist was similar during lengthening ($0.13 \pm 0.06^\circ$) and shortening ($0.03 \pm 0.02^\circ$) contractions and, as intended, the forces were also similar (lengthening: 81.4 ± 16.6 N, shortening: 82.3 ± 19.9 N). As expected, the EMG activity in the contracting FCR was lower during lengthening (0.023 ± 0.012 mV) than shortening (0.034 ± 0.009 , $F_{1,9} = 14.8$; $P = 0.014$). The size of the control H-reflexes used for normalization of the H-reflex measured during contraction were similar and averaged 0.55 ± 0.06 mV (lengthening) and 0.60 ± 0.08 mV (shortening). Fig. 5 shows that independent of the type of muscle contraction of the left wrist flexors, the amplitude of the H-reflex in the resting right FCR was depressed to ~65% of control and remained depressed for 20 s after contraction (Time main effect, $F_{8,72} = 20.0$; $P = 0.001$).

Discussion

We found that the corticospinal output to a resting hand differed whether the contralateral unimanual motor task involved forceful lengthening or shortening contractions. Further experiments showed that SICI was significantly diminished during lengthening contractions when compared to shortening and resting conditions. ICF increased during lengthening contractions but decreased during shortening compared to rest. IHI was diminished during shortening and further diminished during strong lengthening contractions. The amplitude of

the H-reflex became depressed during and remained depressed for about 20 s after both types of contraction. These observations demonstrate that effortful unilateral lengthening and shortening contractions uniformly depress contralateral spinal excitability (H-reflex) and uniquely modulate the ipsilateral motor cortical excitability and the networks involved in intracortical and interhemispheric connections. The findings provide a mechanistic basis for task-specific differences between lengthening and shortening contractions. Previous studies reported adaptive responses to occur following acute and chronic exercise using unilateral lengthening muscle actions. Therefore, the present data provide a potential mechanistic basis for these observations that have implications for exercise prescription in healthy and pathological populations.

Corticospinal excitability

Studies utilizing EEG (Crone *et al.*, 1998; Urbano *et al.*, 1998), fMRI (Rao *et al.*, 1993; Shibasaki *et al.*, 1993; Cramer *et al.*, 1999), MEG (Salmelin *et al.*, 1995), PET (Kawashima *et al.*, 1998), and TMS (Hess *et al.*, 1986; Meyer *et al.*, 1995; Tinazzi & Zanette, 1998; Muellbacher *et al.*, 2000; Liepert *et al.*, 2001; Stinear *et al.*, 2001; Hortobágyi *et al.*, 2003; Perez & Cohen, 2008; Uematsu *et al.*, 2010) provide evidence that activation of the ipsilateral motor cortical areas and the excitability of the corticospinal path targeting the resting hand increase during contralateral unilateral voluntary isometric contractions and these responses increase with contraction intensity. The findings of the present study extend these observations to effortful lengthening and shortening contractions of the wrist flexors in intact humans. Unlike isometric contractions, dynamic motor activity at low forces and phasic movements in reaction time paradigms can inhibit excitability in M1 ipsilateral to the movement (Leocani *et al.*, 2000; Liepert *et al.*, 2001; Weiss *et al.*, 2003). In the present study, the recruitment curves recorded during lengthening and shortening contractions at increasing contraction intensity revealed a monotonic increase in ipsilateral M1 excitability (Fig. 1). Our working hypothesis was that the mechanisms contributing to the control of corticospinal output to the contralateral homologous (resting) wrist flexors occur in a task-dependent fashion during lengthening and shortening contractions of the opposite wrist flexor muscles. This idea evolved from observations that showed task-dependent adaptations (Housh *et al.*, 1996; Hortobágyi *et al.*, 1997; Farthing & Chilibeck, 2003; Howatson & van Someren, 2007) and variations in corticospinal and spinal excitability in a muscle actively lengthening and shortening (Nardone *et al.*, 1989; Abbruzzese *et al.*, 1994; Sekiguchi *et al.*, 2001; Carson *et al.*, 2002; Nordlund *et al.*, 2002; Sekiguchi *et al.*, 2003; Gruber *et al.*, 2009; Uematsu *et al.*, 2010), although this has not been reported in the ipsilateral M1. For example, in arm and foot muscles of healthy humans, corticospinal and spinal excitability was significantly lower during lengthening than shortening contractions (Abbruzzese *et al.*, 1994; Sekiguchi *et al.*, 2001; Nordlund *et al.*, 2002; Sekiguchi *et al.*, 2003; Gruber *et al.*, 2009). These task-dependent changes were attributed to differences in excitability of the motoneuron pool (Abbruzzese *et al.*, 1994) and to reductions in maximum excitation level and the gain of the corticospinal tract during lengthening compared with shortening contractions (Sekiguchi *et al.*, 2001; Sekiguchi *et al.*, 2003).

The recruitment data (Fig. 1) in the resting contralateral wrist, however, revealed a different pattern compared with the data in the actively contracting muscles in previous studies (Leocani *et al.*, 2000; Liepert *et al.*, 2001; Weiss *et al.*, 2003). We observed similar MEP size at 20, 40, and 60% MVC contractions but 15.6% and 21.9% greater MEPs in the resting right FCR while the left wrist flexors performed lengthening compared with shortening contractions. Because at the time TMS produced the MEPs, the right hand was motionless and the associated EMG activity (Zijdewind *et al.*, 2006) in the right FCR was minimal and similar when the left wrist flexors lengthened and shortened, afferent feedback from the right wrist muscles played minimal, if any role, in modulating MEP size. Therefore, we

suspect that the observed task-specificity in the corticospinal excitability emanated through interhemispheric effects as such mechanisms can modulate the corticospinal responses to TMS (see below) (Avanzino *et al.*, 2007; Lee *et al.*, 2007; Perez & Cohen, 2008, 2009).

While MEP size increased more during forceful lengthening than shortening contractions at constant TMS intensity, corticospinal excitability revealed a different pattern when subjects produced a strong contraction in combination with TMS intensity increasing from 1.0 to 1.8 of rMT (Fig. 2). Under these conditions corticospinal excitability increased two-fold and then plateau during lengthening but increased nearly three-fold during shortening contractions. These data suggest that the ipsilateral, left, M1 had a greater capacity to respond to TMS during shortening than lengthening contractions of the left wrist flexors. The data obtained in the present study during lengthening contractions resemble the plateau observed in the abductor pollicis brevis during isometric contraction reported previously (Muellbacher *et al.*, 2000). While in this latter study F-wave amplitude also increased in the resting hand during contralateral muscle contractions favoring the interpretation of MEP facilitation mainly occurring subcortically (Muellbacher *et al.*, 2000) (see also (Gerloff *et al.*, 1998)), the absence of change in brainstem stimulation-produced MEPs and the depression of H-reflex in our previous (Hortobágyi *et al.*, 2003) and in the present study (Fig. 5) raise the possibility that the location of MEP modulation occurred predominantly at the motor cortical level. These data also point to a role the ipsilateral motor cortex may play in contralateral adaptations after acute and chronic unilateral exercise training with high intensity eccentric contractions (Housh *et al.*, 1996; Hortobágyi *et al.*, 1997; Farthing & Chilibeck, 2003; Howatson & van Someren, 2007). Methodological differences are unlikely to account for the observed task-specificity in MEPs because when TMS produced the MEPs, the conditions were similar during lengthening and shortening contractions in terms of position of the left wrist joint, the level of absolute force produced by the left wrist flexors, absence of fatigue, co-activation of the deltoid muscle, and the associated EMG activity in the right FCR (Zijdewind *et al.*, 2006) in the resting right FCR (Tables 1, and 2).

Involvement of the ipsilateral motor cortex

The present data are the first to document the task-specific modulation of SICI and ICF evoked in the ipsilateral M1 during contralateral lengthening and shortening contractions of the wrist flexors in intact humans. It is thought that regardless whether it is evoked in the ipsi- or contralateral M1 by paired-pulse focal TMS, SICI is mediated by GABA_A receptors of neurons forming cortico-cortical networks (Kujirai *et al.*, 1993; Ziemann *et al.*, 1996b; Ridding & Rothwell, 1999). Muscle contraction at increasing intensities reduces and relaxation increases SICI in the ipsi- and contralateral M1 (Buccolieri *et al.*, 2004; Perez & Cohen, 2008, 2009), suggesting that the modulation arises from the motor cortex. Our data now show that SICI in the ipsilateral M1 decreases but this diminished response is substantially greater during lengthening than shortening contractions of the wrist flexors. We performed these paired-pulse experiments only at high intensity contractions because our preliminary experiments revealed no modulation in SICI at any contraction intensities below 90% MVC (data not shown). Thus, our data agree with previous studies showing a diminished response in SICI at high contraction intensities (Muellbacher *et al.*, 2000; Perez & Cohen, 2008), but not at low intensities of 30% MVC (Perez & Cohen, 2008). This discrepancy suggests dynamic (present study) versus static contractions (Muellbacher *et al.*, 2000; Perez & Cohen, 2008) have a different effect on SICI. Previous research has speculated that modulation of SICI may be activity-dependent (Perez & Cohen, 2008), which then influences corticospinal excitability in the ipsilateral M1 (Ziemann *et al.*, 1996a; Buccolieri *et al.*, 2004). It seems possible that the observed task specificity is because intracortical GABAergic inhibitory interneuron activity is reduced or blunted during higher intensity lengthening contractions. Task specificity of ICF has been rarely studied and its

interpretation is complex (Muellbacher *et al.*, 2000; Soto *et al.*, 2006; McCombe Waller *et al.*, 2008) probably because its mechanism is more complex than SICI as it is mediated by more than one neurotransmitter, including glutamate, dopamine, GABA (Ziemann *et al.*, 1996b; Nakamura *et al.*, 1997; Reis *et al.*, 2006). In general, our SICI and ICF data fit with the model that during effortful unimanual contractions the ipsilateral M1 becomes more excitable due to diminishing SICI and strengthening ICF (Muellbacher *et al.*, 2000).

Interhemispheric effects

We found that IHI in M1 ipsilateral to the contraction diminished during shortening and further diminished during forceful lengthening contractions. Overall, these findings agree with the model, suggesting that forceful voluntary muscle contractions tend to reduce IHI from the active to the non-active M1 (Perez & Cohen, 2008). Because of the related diminished response of SICI and IHI in the ipsilateral M1 in the present experiments and in a previous study (Perez & Cohen, 2008), it is also likely that an interaction between intracortical and interhemispheric connections regulates the excitability of the M1 ipsilateral to the contraction (Murase *et al.*, 2004; Duque *et al.*, 2007). This interaction is more evident at high contraction intensities and more so during lengthening contractions. Together, these data support the activity-dependent modulation of inhibitory mechanisms in the control of the inactive limb during unimanual tasks (Perez & Cohen, 2008, 2009). A key difference between shortening and lengthening contraction is that lengthening is associated with increased Ia activity (Burke *et al.*, 1978). Therefore, in the current experiments the most obvious source for a differential modulation of IHI would be the crossed sensory effects due to this increased Ia activity. However, careful examination of previous data on crossed sensory effects elicits a more complex picture. Results from previous studies suggest a model in which decreased sensory input reduces IHI and increased sensory input deepens IHI. For example, a reduced sensory state by anesthesia of the hand and forearm increased MEPs of muscles in the opposite hand and reduced IHI in the hemisphere contralateral to anesthesia (Werhahn *et al.*, 2002a; Werhahn *et al.*, 2002b). In contrast, increased sensory input by vibrating the right wrist extensors at 80 Hz for 4 s with 0.5 mm amplitude significantly decreased the excitability of corticospinal projections to the opposite wrist flexors (Kossev *et al.*, 2001). While proprioceptive input from a hand muscle also decreased the corticospinal excitability of the contralateral homologous muscle, and deepened SICI and IHI (Swayne *et al.*, 2006), vibration, mixed nerve stimulation, and pure sensory nerve stimulation produced no changes in the excitability of corticospinal projections to the opposite wrist flexors (Hortobágyi *et al.*, 2003). The overall picture emerging from these studies, i.e., increased sensory input to one hand decreases the excitability of corticospinal projections to the opposite hand, is thus not compatible with the current data because increased sensory state during muscle lengthening (Burke *et al.*, 1978) of the left wrist flexors produced increases and not reductions in IHI and in the excitability of corticospinal projections to the right wrist. Clearly, more work is needed to elucidate the precise effects and mechanisms of the nature and magnitude of unilateral sensory stimulation of a muscle on the homologous muscle pair in the opposite limb.

Although the present data do not allow us to determine the mechanism, we speculate that perhaps the task-specific modulation of corticospinal excitability and the excitability of networks involved in SICI, ICF, and IHI in the ipsilateral M1 are not related to the differences in the sensory input during lengthening and shortening but to the differences in the crossed effects of the descending command. Studies examining EMG (Grabiner & Owings, 2002), EEG (Fang *et al.*, 2001), and TMS (Gruber *et al.*, 2009) uniformly suggest that the descending command associated with lengthening and shortening is different. For example, EEG studies showed that although the elbow flexor muscle activation was lower during lengthening than shortening contractions, the amplitude of movement-related cortical

potentials in the cortical areas associated with movement planning, execution, and feedback from the peripheral systems were all higher during lengthening than shortening contractions (Fang *et al.*, 2001). The higher cortical signal during lengthening vs. shortening contraction suggests that neural command associated for planning and programming of movements using lengthening vs. shortening contraction are different, and require greater neural resources and perhaps such differences can mediate the contraction-specific crossed effects. In addition, the 21% greater ratio of motor evoked potentials-to-cervicomedullary motor evoked potentials during lengthening vs. isometric contractions also suggest the spinal excitability is reduced while motor cortical excitability is actually increased during lengthening compared with isometric muscle contractions (Gruber *et al.*, 2009). Confirming these EEG and TMS studies, there were also significant differences in the surface EMG activity measured in the target muscles before the onset of lengthening and shortening contractions, providing evidence at the effector level for the CNS implementing a different motor command for lengthening vs. shortening contractions (Grabner & Owings, 2002). Finally, the positive correlation between the size of MEPs in the contralateral and ipsilateral M1 during unimanual isometric contractions adds to the argument that contraction-specific modulation may occur at the level of motor command (Perez & Cohen, 2009). As an extension of these EMG, EEG, and TMS studies, the possibility also exists that the task-specific modulation in the ipsilateral M1 is due to a differential activation of brain areas subserving the ipsilateral M1 during lengthening and shortening contractions. Perhaps the task-specific modulation of corticospinal excitability and the excitability of the networks involved in SICI, ICF, and IHI in the ipsilateral M1 are caused by unique inhibitory and facilitatory influences from the dorsal premotor and posterior parietal cortices in the contralateral (involved) (Civardi *et al.*, 2001) and in the ipsilateral (uninvolved) M1 (Mochizuki *et al.*, 2004; Koch *et al.*, 2007; Baumer *et al.*, 2009).

We must note that the above discussion relied on the IHI measurements being made with the size of the conditioning and test stimulus kept constant across conditions. Four subjects also performed a control experiment without adjusting the size of the conditioning stimulus; under these conditions the conditioning pulse produced, as expected, substantially higher conditioning pulse sizes supporting previous studies that showed an increase in IHI (Ferber *et al.*, 1992; Perez & Cohen, 2008). Remarkably, even under these conditions task specificity was still evident, so that the magnitude of IHI was less during lengthening than shortening contractions. Consequently, these IHI data collectively suggest that the GABAergic transcallosal connections have influenced corticospinal excitability in a contraction-specific manner.

Spinal excitability

In addition to responses to TMS, we also examined spinal excitability in the resting right arm during lengthening and shortening contractions of the left wrist flexors. Similarly to Uematsu *et al.* (2010), who used low intensity contractions ($\leq 30\%$ MVC), we found no evidence for task specificity in spinal excitability as reflected by the amplitude of the H-reflex. Indeed, instead of facilitation akin to the Jendrassik maneuver, we observed a depression of $\sim 65\%$ compared to the control, lasting 20 s after contraction (Fig. 5). The present data confirm findings from previous studies also reporting a large depression in spinal excitability in the resting contralateral muscle during unilateral isometric contraction of the homologous wrist flexors (Hortobágyi *et al.*, 2003; Uematsu *et al.*, 2010) and ankle plantarflexors and dorsiflexors (Bikmullina *et al.*, 2006). The emerging picture is that such side-to-side inhibition occurs in homologous muscle pairs under a variety of conditions comprising low- and high-intensity phasic and tonic voluntary contractions in intact humans (Jankowska *et al.*, 1978; Delwaide & Pepin, 1991; Sabatino *et al.*, 1994; Carson *et al.*, 2004) and these crossed spinal circuits seem to remain unaffected by chronic exercise training

(Lagerquist *et al.*, 2006; Fimland *et al.*, 2009), shifting the mechanism of cross education from spinal to supraspinal loci (Gruber *et al.*, 2009). The reasons behind this inhibition and why it lasts so long after the contraction are still unclear but presynaptic inhibition was suggested to mediate it (Hortobágyi *et al.*, 2003).

There are several limitations to the present study. To avoid fatigue by repeated high-intensity muscle contractions it was not possible to collect multiple types of measurements in the same subject and therefore we could not perform correlation analyses. The cross sectional nature of the present findings limits projections to, and interpretation of, chronic cross education studies. Further, the dissociation of H-reflexes (decrease) and MEP amplitude (increase) in right FCR during and after contraction of the left FCR is perhaps unusual. H-reflexes test a different (only partially overlapping) fraction of alpha-MNs compared to the MEP (Morita *et al.*, 1999), so a potential further test using high-intensity TMS or electrical stimulation at the level of the cervicomedullary junction would have provided direct activation of the corticospinal tract. Consequently, the results are confined to measures of cortical and spinal excitability, as we did not perform any experiments targeting the spinal motoneurons using cervicomedullary stimulation. Previous literature using these techniques showed a degree of task specificity may exist in the contracting muscle, but motor cortical excitability was increased and spinal excitability was reduced in the contralateral (involved) M1 (Gruber *et al.*, 2009). Furthermore, in previous work (Hortobágyi *et al.*, 2003), we examined the response to cervicomedullary stimulation in the uninvolved (resting) muscle and did not show an effect in the resting FCR. Although a task specific cervicomedullary paradigm remains to be elucidated, it seems likely from our data that task specific differences lie, at least in part, at a cortical level.

Some inconsistency surrounds the possibility that corticospinal excitability might be different during passive lengthening and shortening in the wrist flexors making comparisons between conditions difficult (Chye *et al.*, 2010); however others (Abbruzzese *et al.*, 1994) have shown there to be no difference in corticospinal excitability between contraction modes in the elbow flexors. Both these investigations examined the involved (active) M1, whereas we examined the ipsilateral (uninvolved) M1. However, a recent fMRI investigation (Sehm *et al.*, 2010) showed that the ipsilateral (uninvolved) M1 has little or no activation (fMRI) at low intensities, which was further supported by a trivial amount of mirror EMG activity (~2% above baseline) whilst conducting a unilateral isometric contraction at 70% MVC. It therefore makes the expectation unlikely that differences in corticospinal excitability of the active M1 during passive shortening or lengthening of the ipsilateral wrist muscles would bias or contribute to the observed differences at high intensity contractions. Finally, future experiments will have to examine the spatial specificity of the responses to TMS and peripheral nerves stimulation in agonist and antagonist muscle pairs, between upper and lower limbs, and between dominant and non-dominant limbs to provide further insights into neural organization of laterality and interactions between limbs (Slivko & Teteryatnik, 2005).

In conclusion, these data are consistent with the hypothesis that ipsilateral responses to TMS vary according to the type of muscle contraction, but the nature of this specificity is the opposite of the responses observed in the contralateral M1 reported previously. This specificity appears to be characterized by a higher ipsilateral M1 output and a shift to lower interhemispheric and intracortical inhibition and heightened facilitation during lengthening compared with shortening, which may have clinical implications.

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References

- Abbruzzese G, Morena M, Spadavecchia L, Schieppati M. Response of arm flexor muscles to magnetic and electrical brain stimulation during shortening and lengthening tasks in man. *Journal of Physiology*. 1994; 481:499–507. [PubMed: 7738841]
- Avanzino L, Teo JT, Rothwell JC. Intracortical circuits modulate transcallosal inhibition in humans. *J Physiol*. 2007; 583:99–114. [PubMed: 17556392]
- Baldissera F, Bellani G, Cavallari P, Lalli S. Changes in the excitability of the H-reflex in wrist flexors related to the prone or supine position of the forearm in man. *Neurosci Lett*. 2000; 295:105–108. [PubMed: 11090985]
- Baumer T, Schippling S, Kroeger J, Zittel S, Koch G, Thomalla G, Rothwell JC, Siebner HR, Orth M, Munchau A. Inhibitory and facilitatory connectivity from ventral premotor to primary motor cortex in healthy humans at rest—a bifocal TMS study. *Clin Neurophysiol*. 2009; 120:1724–1731. [PubMed: 19683960]
- Bikmullina RK, Rozental AN, Pleshchinskii IN. Modulation of soleus H-reflex during dorsal and plantar flexions in the human ankle joint. *Human Physiology*. 2006; 32:593–598.
- Buccolieri A, Abbruzzese G, Rothwell JC. Relaxation from a voluntary contraction is preceded by increased excitability of motor cortical inhibitory circuits. *J Physiol*. 2004; 558:685–695. [PubMed: 15181164]
- Burke D, Hagbarth KE, Lofstedt L. Muscle spindle activity in man during shortening and lengthening contractions. *J Physiol*. 1978; 277:131–142. [PubMed: 148511]
- Carson RG, Riek S, Mackey DC, Meichenbaum DP, Willms K, Forner M, Byblow WD. Excitability changes in human forearm corticospinal projections and spinal reflex pathways during rhythmic voluntary movement of the opposite limb. *J Physiol*. 2004; 560:929–940. [PubMed: 15331684]
- Carson RG, Riek S, Shahbazzpour N. Central and peripheral mediation of human force sensation following eccentric or concentric contractions. *J Physiol*. 2002; 539:913–925. [PubMed: 11897860]
- Chen R. Interactions between inhibitory and excitatory circuits in the human motor cortex. *Exp Brain Res*. 2004; 154:1–10. [PubMed: 14579004]
- Chye L, Nosaka K, Murray L, Edwards D, Thickbroom G. Corticomotor excitability of wrist flexor and extensor muscles during active and passive movement. *Hum Movement Sci*. 2010; 29:494–501.
- Civardi C, Cantello R, Asselman P, Rothwell JC. Transcranial magnetic stimulation can be used to test connections to primary motor areas from frontal and medial cortex in humans. *Neuroimage*. 2001; 14:1444–1453. [PubMed: 11707100]
- Cramer SC, Finklestein SP, Schaechter JD, Bush G, Rosen BR. Activation of distinct motor cortex regions during ipsilateral and contralateral finger movements. *J Neurophysiol*. 1999; 81:383–387. [PubMed: 9914297]
- Crone NE, Miglioretti DL, Gordon B, Sieracki JM, Wilson MT, Uematsu S, Lesser RP. Functional mapping of human sensorimotor cortex with electrocorticographic spectral analysis. I. Alpha and beta event-related desynchronization. *Brain*. 1998; 121(Pt 12):2271–2299. [PubMed: 9874480]
- Delwaide PJ, Pepin JL. The influence of contralateral primary afferents on Ia inhibitory interneurons in humans. *J Physiol*. 1991; 439:161–179. [PubMed: 1895236]
- Di Lazzaro V, Oliviero A, Profice P, Meglio M, Cioni B, Tonali P, Rothwell JC. Descending spinal cord volleys evoked by transcranial magnetic and electrical stimulation of the motor cortex leg area in conscious humans. *J Physiol*. 2001; 537:1047–1058. [PubMed: 11744776]
- Duque J, Murase N, Celnik P, Hummel F, Harris-Love M, Mazzocchio R, Olivier E, Cohen LG. Intermanual Differences in movement-related interhemispheric inhibition. *J Cogn Neurosci*. 2007; 19:204–213. [PubMed: 17280510]

- Fang Y, Siemionow V, Sahgal V, Xiong F, Yue GH. Greater movement-related cortical potential during human eccentric versus concentric muscle contractions. *J Neurophysiol.* 2001; 86:1764–1772. [PubMed: 11600637]
- Farthing JP, Chilibeck PD. The effect of eccentric training at different velocities on cross-education. *European Journal of Applied Physiology.* 2003; 89:570–577. [PubMed: 12756570]
- Ferbert A, Priori A, Rothwell JC, Day BL, Colebatch JG, Marsden CD. Interhemispheric inhibition of the human motor cortex. *J Physiol.* 1992; 453:525–546. [PubMed: 1464843]
- Fimland MS, Helgerud J, Solstad GM, Iversen VM, Leivseth G, Hoff J. Neural adaptations underlying cross-education after unilateral strength training. *European Journal of Applied Physiology.* 2009
- Fisher RJ, Nakamura Y, Bestmann S, Rothwell JC, Bostock H. Two phases of intracortical inhibition revealed by transcranial magnetic threshold tracking. *Exp Brain Res.* 2002; 143:240–248. [PubMed: 11880900]
- Gerloff C, Cohen LG, Floeter MK, Chen R, Corwell B, Hallett M. Inhibitory influence of the ipsilateral motor cortex on responses to stimulation of the human cortex and pyramidal tract. *J Physiol.* 1998; 510:249–259. [PubMed: 9625881]
- Grabner MD, Owings TM. EMG differences between concentric and eccentric maximum voluntary contractions are evident prior to movement onset. *Exp Brain Res.* 2002; 145:505–511. [PubMed: 12172662]
- Gruber M, Linnamo V, Strojnik V, Rantalainen T, Avela J. Excitability at the motoneuron pool and motor cortex is specifically modulated in lengthening compared to isometric contractions. *J Neurophysiol.* 2009; 101:2030–2040. [PubMed: 19193768]
- Hess CW, Mills KR, Murray NM. Magnetic stimulation of the human brain: facilitation of motor responses by voluntary contraction of ipsilateral and contralateral muscles with additional observations on an amputee. *Neurosci Lett.* 1986; 71:235–240. [PubMed: 3785745]
- Hortobágyi T, Hill JP, Houmard JA, Fraser DD, Lambert NJ, Israel RG. Adaptive response to muscle lengthening and shortening in humans. *J Appl Physiol.* 1996; 80:765–772. [PubMed: 8964735]
- Hortobágyi T, Hill JP, Lambert NJ. Greater cross education following training with muscle lengthening than shortening. *Med Sci Sports Exerc.* 1997; 29:107–112. [PubMed: 9000162]
- Hortobágyi T, Taylor JL, Russell G, Petersen N, Gandevia SC. Changes in segmental and motor cortical output with contralateral muscle contractions and altered sensory inputs in humans. *J Neurophysiol.* 2003; 90:2451–2459. [PubMed: 14534271]
- Housh TJ, Housh DJ, Weir JP, Weir LL. Effects of eccentric-only resistance training and detraining. *International Journal of Sports Medicine.* 1996; 17:145–148. [PubMed: 8833718]
- Howatson G, van Someren KA. Evidence of a contralateral repeated bout effect after maximal eccentric contractions. *European Journal of Applied Physiology.* 2007; 101:207–214. [PubMed: 17534644]
- Jankowska E, Padel Y, Zarzecki P. Crossed disynaptic inhibition of sacral motoneurons. *J Physiol.* 1978; 285:425–444. [PubMed: 745104]
- Kawashima R, Matsumura M, Sadato N, Naito E, Waki A, Nakamura S, Matsunami K, Fukuda H, Yonekura Y. Regional cerebral blood flow changes in human brain related to ipsilateral and contralateral complex hand movements--a PET study. *Eur J Neurosci.* 1998; 10:2254–2260. [PubMed: 9749754]
- Koch G, Fernandez Del Olmo M, Cheeran B, Ruge D, Schippling S, Caltagirone C, Rothwell JC. Focal stimulation of the posterior parietal cortex increases the excitability of the ipsilateral motor cortex. *J Neurosci.* 2007; 27:6815–6822. [PubMed: 17581969]
- Kossev A, Siggelkow S, Kapels H, Dengler R, Rollnik JD. Crossed effects of muscle vibration on motor-evoked potentials. *Clin Neurophysiol.* 2001; 112:453–456. [PubMed: 11222966]
- Kujirai T, Caramia MD, Rothwell JC, Day BL, Thompson PD, Ferbert A, Wroe S, Asselman P, Marsden CD. Corticocortical inhibition in human motor cortex. *J Physiol.* 1993; 471:501–519. [PubMed: 8120818]
- Lagerquist O, Zehr EP, Docherty D. Increased spinal reflex excitability is not associated with neural plasticity underlying the cross-education effect. *J Appl Physiol.* 2006; 100:83–90. [PubMed: 16357081]

- Lee M, Carroll TJ. Cross education: possible mechanisms for the contralateral effects of unilateral resistance training. *Sports Med.* 2007; 37:1–14. [PubMed: 17190532]
- Lee H, Gunraj C, Chen R. The effects of inhibitory and facilitatory intracortical circuits on interhemispheric inhibition in the human motor cortex. *J Physiol.* 2007; 580:1021–1032. [PubMed: 17303638]
- Leocani L, Cohen LG, Wassermann EM, Ikoma K, Hallett M. Human corticospinal excitability evaluated with transcranial magnetic stimulation during different reaction time paradigms. *Brain.* 2000; 123(Pt 6):1161–1173. [PubMed: 10825355]
- Liepert J, Dettmers C, Terborg C, Weiller C. Inhibition of ipsilateral motor cortex during phasic generation of low force. *Clin Neurophysiol.* 2001; 112:114–121. [PubMed: 11137668]
- McCombe Waller S, Forrester L, Villagra F, Whittall J. Intracortical inhibition and facilitation with unilateral dominant, unilateral nondominant and bilateral movement tasks in left- and right-handed adults. *J Neurol Sci.* 2008; 269:96–104. [PubMed: 18336839]
- Meyer BU, Roricht S, Graf von Einsiedel H, Kruggel F, Weindl A. Inhibitory and excitatory interhemispheric transfers between motor cortical areas in normal humans and patients with abnormalities of the corpus callosum. *Brain.* 1995; 118(Pt 2):429–440. [PubMed: 7735884]
- Mills KR, Boniface SJ, Schubert M. Magnetic brain stimulation with a double coil: the importance of coil orientation. *Electroencephalogr Clin Neurophysiol.* 1992; 85:17–21. [PubMed: 1371739]
- Mochizuki H, Huang YZ, Rothwell JC. Interhemispheric interaction between human dorsal premotor and contralateral primary motor cortex. *J Physiol.* 2004; 561:331–338. [PubMed: 15459244]
- Morita H, Baumgarten J, Petersen N, Christensen LO, Nielsen J. Recruitment of extensor-carpi-radialis motor units by transcranial magnetic stimulation and radial-nerve stimulation in human subjects. *Exp Brain Res.* 1999; 128:557–562. [PubMed: 10541752]
- Muellbacher W, Facchini S, Boroojerdi B, Hallett M. Changes in motor cortex excitability during ipsilateral hand muscle activation in humans. *Clin Neurophysiol.* 2000; 111:344–349. [PubMed: 10680571]
- Murase N, Duque J, Mazzocchio R, Cohen LG. Influence of interhemispheric interactions on motor function in chronic stroke. *Ann Neurol.* 2004; 55:400–409. [PubMed: 14991818]
- Nakamura H, Kitagawa H, Kawaguchi Y, Tsuji H. Intracortical facilitation and inhibition after transcranial magnetic stimulation in conscious humans. *J Physiol.* 1997; 498(Pt 3):817–823. [PubMed: 9051592]
- Nardone A, Romàno C, Schieppati M. Selective recruitment of high-threshold motor units during voluntary lengthening of active muscles. *Journal of Physiology.* 1989; 409:451–471. [PubMed: 2585297]
- Nordlund MM, Thorstensson A, Cresswell AG. Variations in the soleus H-reflex as a function of activation during controlled lengthening and shortening actions. *Brain Res.* 2002; 952:301–307. [PubMed: 12376192]
- Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia.* 1971; 9:97–113. [PubMed: 5146491]
- Perez MA, Cohen LG. Mechanisms underlying functional changes in the primary motor cortex ipsilateral to an active hand. *J Neurosci.* 2008; 28:5631–5640. [PubMed: 18509024]
- Perez MA, Cohen LG. Scaling of motor cortical excitability during unimanual force generation. *Cortex.* 2009; 45:1065–1071. [PubMed: 19243741]
- Rao SM, Binder JR, Bandettini PA, Hammeke TA, Yetkin FZ, Jesmanowicz A, Lisk LM, Morris GL, Mueller WM, Estkowski LD, et al. Functional magnetic resonance imaging of complex human movements. *Neurology.* 1993; 43:2311–2318. [PubMed: 8232948]
- Reis J, John D, Heimeroth A, Mueller HH, Oertel WH, Arndt T, Rosenow F. Modulation of human motor cortex excitability by single doses of amantadine. *Neuropsychopharmacology.* 2006; 31:2758–2766. [PubMed: 16794570]
- Ridding MC, Rothwell JC. Afferent input and cortical organisation: a study with magnetic stimulation. *Exp Brain Res.* 1999; 126:536–544. [PubMed: 10422717]
- Rossini PM, Barker AT, Berardelli A, Caramia MD, Caruso G, Cracco RQ, Dimitrijevic MR, Hallett M, Katayama Y, Lucking CH. Non-invasive electrical and magnetic stimulation of the brain,

- spinal cord and roots: basic principles and procedures for routine clinical application. Report of an IFCN committee. *Electroencephalogr Clin Neurophysiol.* 1994; 91:79–92. [PubMed: 7519144]
- Sabatino M, Sardo P, Ferraro G, Caravaglias G, La Grutta V. Bilateral reciprocal organisation in man: focus on IA interneurone. *J Neural Transm Gen Sect.* 1994; 96:31–39. [PubMed: 7857589]
- Salmelin R, Forss N, Knuutila J, Hari R. Bilateral activation of the human somatomotor cortex by distal hand movements. *Electroencephalogr Clin Neurophysiol.* 1995; 95:444–452. [PubMed: 8536573]
- Sehm B, Perez MA, Xu B, Hidler J, Cohen LG. Functional neuroanatomy of mirroring during a unimanual force generation task. *Cereb Cortex.* 2010; 20:34–45. [PubMed: 19435709]
- Sekiguchi H, Kimura T, Yamanaka K, Nakazawa K. Lower excitability of the corticospinal tract to transcranial magnetic stimulation during lengthening contractions in human elbow flexors. *Neurosci Lett.* 2001; 312:83–86. [PubMed: 11595340]
- Sekiguchi H, Nakazawa K, Suzuki S. Differences in recruitment properties of the corticospinal pathway between lengthening and shortening contractions in human soleus muscle. *Brain Res.* 2003; 977:169–179. [PubMed: 12834877]
- Shibasaki H, Sadato N, Lyshkow H, Yonekura Y, Honda M, Nagamine T, Suwazono S, Magata Y, Ikeda A, Miyazaki M, et al. Both primary motor cortex and supplementary motor area play an important role in complex finger movement. *Brain.* 1993; 116(Pt 6):1387–1398. [PubMed: 8293277]
- Slivko ÉI, Teteryatnik EV. Effects of contralateral afferent stimulation on H-reflex in humans. *Neurophysiology.* 2005; 37:372–378.
- Soto O, Valls-Sole J, Shanahan P, Rothwell J. Reduction of intracortical inhibition in soleus muscle during postural activity. *J Neurophysiol.* 2006; 96:1711–1717. [PubMed: 16790603]
- Stinear CM, Walker KS, Byblow WD. Symmetric facilitation between motor cortices during contraction of ipsilateral hand muscles. *Exp Brain Res.* 2001; 139:101–105. [PubMed: 11482835]
- Swayne O, Rothwell J, Rosenkranz K. Transcallosal sensorimotor integration: effects of sensory input on cortical projections to the contralateral hand. *Clin Neurophysiol.* 2006; 117:855–863. [PubMed: 16448846]
- Tinazzi M, Zanette G. Modulation of ipsilateral motor cortex in man during unimanual finger movements of different complexities. *Neurosci Lett.* 1998; 244:121–124. [PubMed: 9593504]
- Uematsu A, Endoh Obata H, Kitamura T, T.Hortobágyi T, Nakazawa K, Suzuki S. Asymmetrical modulation of corticospinal excitability in the contracting and resting contralateral wrist flexors during unilateral shortening, lengthening and isometric contractions. *Exp Brain Res.* 206:59–69. [PubMed: 20730420]
- Urbano A, Babiloni C, Onorati P, Carducci F, Ambrosini A, Fattorini L, Babiloni F. Responses of human primary sensorimotor and supplementary motor areas to internally triggered unilateral and simultaneous bilateral one-digit movements. A high-resolution EEG study. *Eur J Neurosci.* 1998; 10:765–770. [PubMed: 9749740]
- Weiss AC, Weiller C, Liepert J. Pre-movement motor excitability is reduced ipsilateral to low force pinch grips. *J Neural Transm.* 2003; 110:201–208. [PubMed: 12589578]
- Werhahn KJ, Mortensen J, Kaelin-Lang A, Boroojerdi B, Cohen LG. Cortical excitability changes induced by deafferentation of the contralateral hemisphere. *Brain.* 2002a; 125:1402–1413. [PubMed: 12023328]
- Werhahn KJ, Mortensen J, Van Boven RW, Zeuner KE, Cohen LG. Enhanced tactile spatial acuity and cortical processing during acute hand deafferentation. *Nat Neurosci.* 2002b; 5:936–938. [PubMed: 12219095]
- Ziemann U, Bruns D, Paulus W. Enhancement of human motor cortex inhibition by the dopamine receptor agonist pergolide: evidence from transcranial magnetic stimulation. *Neurosci Lett.* 1996a; 208:187–190. [PubMed: 8733301]
- Ziemann U, Lonnecker S, Steinhoff BJ, Paulus W. Effects of antiepileptic drugs on motor cortex excitability in humans: a transcranial magnetic stimulation study. *Ann Neurol.* 1996b; 40:367–378. [PubMed: 8797526]

- Ziemann U, Tergau F, Wassermann EM, Wischer S, Hildebrandt J, Paulus W. Demonstration of facilitatory I wave interaction in the human motor cortex by paired transcranial magnetic stimulation. *J Physiol.* 1998; 511:181–190. [PubMed: 9679173]
- Zijdewind I, Butler JE, Gandevia SC, Taylor JL. The origin of activity in the biceps brachii muscle during voluntary contractions of the contralateral elbow flexor muscles. *Exp Brain Res.* 2006; 175:526–535. [PubMed: 16924489]

Figure 1.

Representative examples of motor evoked potentials (MEP) produced by TMS applied to the ipsilateral, left, M1 and recorded in the right (inactive) flexor carpi radialis (FCR) in one subject (**A**) during muscle contraction of the left wrist flexors at 20, 40, 60, 80, and 100% of shortening MVC. The top tracing within each signal pair shows the surface EMG activity recorded from the left FCR during contraction (solid line) and at rest (dashed line). The lower tracing within each signal pair shows the MEPs produced by TMS in the relaxed right FCR when the left wrist flexors contracted (solid lines) and at rest (dashed lines).

B. Group data. Excitability of the ipsilateral, left, M1 during lengthening and shortening contraction of the left wrist flexors at 20 %/s. Vertical axis, MEP amplitude produced by

TMS during muscle contraction relative to MEPs measured during rest. Open bars, lengthening contraction, filled bars shortening contraction. * $p < 0.05$ between shortening and lengthening contraction ($n = 11$).

Figure 2.

Excitability of the ipsilateral (left) M1 during rest (panel A) and during contraction (panel B) of the left wrist flexors under lengthening and shortening conditions. The experiments were conducted at the same absolute force (90% of shortening MVC). **A:** * compared with MEP amplitudes at other stimulation intensities ($p < 0.05$). **B:** † compared with MEP amplitudes at all other TMS stimulation intensities and compared with MEPs during shortening contraction ($p < 0.05$). ‡ compared with MEP amplitudes at lower TMS stimulation intensities and compared with MEPs during shortening contraction ($p < 0.05$). * compared with MEPs at all other TMS stimulation intensities ($p < 0.05$).

Figure 3.

Representative examples of the effects of muscle contraction of the left wrist flexors on intracortical inhibition (SICI) and facilitation (ICF) produced by TMS in the ipsilateral, left, M1 in one subject (**A**). The top tracing within each signal pair shows the surface EMG activity recorded from the left flexor carpi radialis; TMS was delivered to the ipsilateral, left, M1. The lower tracing within each signal pair shows the motor evoked potential when a TMS test stimulus was given by itself (Test) and when a conditioning stimulus preceded the test stimulus by 2 (SICI) and 10 ms (ICF) at rest and when the left wrist flexor performed a lengthening (Len) and shortening (Sho) contraction at 20 %/s. The experiments were conducted at the same absolute force during lengthening and shortening, expressed as 90%

of shortening MVC. **B.** Group mean ($\pm$ SD) data show the interaction between muscle contraction of the left wrist flexors ($n = 10$). Horizontal dashed line denotes control as 100%. * all different from one another $p < 0.05$.

Figure 4.

Interhemispheric inhibition (IHI) from right M1 to left M1 at rest and during muscle contraction of the left wrist flexors. The condition main effect suggests that IHI from right M1 to left (ipsilateral) M1 did not diminish at 50% MVC but IHI diminished (* $p < 0.05$) during shortening at 90% MVC relative to rest. During lengthening, IHI further diminished relative to all the other conditions († $p < 0.05$). Experiments were conducted at the same absolute force during lengthening and shortening, expressed as 50 and 90% of shortening MVC. Horizontal dashed line denotes control as 100%. S = shortening, L = lengthening.

Figure 5.

The effects of lengthening and shortening contraction (dashed box) of the left wrist flexors on the amplitude of the H-reflex recorded from the resting right flexor carpi radialis during contraction and at rest for 40 s after contraction. * $p < 0.05$ relative control value of 100%, indicated by the dashed horizontal line.

Position and force of the left wrist and EMG activity of the left and right FCR during lengthening and shortening contractions of the left wrist flexors at five target forces.

Table 1

		Target force, % Shortening MVC									
		20		40		60		80		100	
Variable		L	S	L	S	L	S	L	S	L	S
Position, °	Mean	-0.22	0.38	0.29	0.22	0.29	-0.38	0.23	0.56	-0.22	0.51
	±SD	0.67	0.94	0.91	0.92	0.85	0.76	0.70	0.74	0.76	0.77
Force, N	Mean	23.4	16.1	44.3*	41.1*	62.4*	59.5*	87.2*	90.4*	104.1	104.5*
	±SD	8.17	7.96	18.38	13.64	15.83	8.17	34.38	34.78	36.68	35.83
EMG, %	Mean	16.2	22.3	33.9*	43.9*	51.7*	66.3*	81.7*	86.3*	89.6	96.2*
	±SD	8.44	12.34	19.66	13.32	21.22	23.04	16.56	22.82	28.32	25.53
EMG, mV	Mean	0.005	0.005	0.005	0.006	0.006	0.006	0.006	0.006	0.006	0.007
	±SD	0.001	0.002	0.002	0.001	0.001	0.001	0.001	0.001	0.001	0.001

In these experiments the level of force was set as the same absolute force during lengthening and shortening and are expressed as a percent of maximal voluntary shortening contraction force;

L and S, lengthening and shortening contraction of the left wrist flexors; Position, ° - position of the left wrist. Neutral position is 0° and positive values indicate flexion; Force, N - measured force in Newtons, matched between L and S at 5 levels of shortening MVC; EMG, % - EMG activity in the left FCR as a percent of EMG recorded during an MVC; EMG, mV - EMG activity of the resting right FCR during L and S of the left wrist flexors

* greater than at lower intensities for the same contraction mode (p < 0.05).

Table 2

Position and force of the left wrist and EMG activity of the left and right FCR during lengthening and shortening contractions of the left wrist flexors at five levels of TMS intensities.

TMS intensity, % rMT												
Variable		1.2		1.4		1.6		1.8		2.0		
		L	S	L	S	L	S	L	S	L	S	
Position, °	Mean	-0.11	0.28	0.18	0.19	-0.22	-0.10	0.17	0.28	0.22	0.30	
	±SD	0.73	1.12	0.75	1.11	0.74	1.06	0.73	1.14	0.67	1.17	
Force, N	Mean	89.9	92.6	86.8	89.4	90.7	94.2	90.3	92.1	87.2	89.1	
	±SD	12.04	8.74	13.05	16.43	9.35	9.72	10.15	9.71	12.53	12.07	
EMG, %	Mean	87.5	88.6	79.5	84.6	79.0	91.9	86.9	93.6	85.8	87.4	
	±SD	25.40	11.98	23.59	32.98	32.08	29.83	33.73	36.51	21.10	23.48	
EMG, mV	Mean	0.012	0.014	0.016	0.015	0.017	0.019	0.017	0.018	0.011	0.011	
	±SD	0.008	0.010	0.013	0.090	0.014	0.015	0.013	0.016	0.006	0.007	

The level of force in these experiments was set at the same absolute force during shortening and lengthening, determined as 90% of shortening MVC

rMT, resting motor threshold; L and S, lengthening and shortening contraction of the left wrist flexors; Position, ° - position of the left wrist. Neutral position is 0°. and positive values indicate flexion; Force, N - measured force in Newtons, matched between L and S at 90% of shortening MVC; EMG, % - EMG activity in the left FCR as a percent of EMG recorded during MVC; EMG, mV - EMG activity of the resting right FCR during L and S of the left wrist flexors

* greater than at lower intensities for the same contraction mode (p < 0.05)

Table 3

Position and force of the left wrist and EMG activity of the left and right FCR during lengthening and shortening contractions of the left wrist flexors in combination with a TMS test stimulus and a test stimulus conditioned with a conditioning stimulus 2 (SICI) and 10 milliseconds (ICF).

Variable		TS		SICI		ICF	
		L	S	L	S	L	S
Position, °	Mean	-0.40	0.36	0.42	0.37	-0.17	-0.17
	±SD	0.13	0.11	0.13	0.34	0.21	0.55
Force, N	Mean	88.6	89.1	89.8	89.9	88.6	87.5
	±SD	9.24	8.10	8.32	8.15	10.49	8.07
EMG, %	Mean	80.1	84.6*	77.9	83.9*	78.5	82.7*
	±SD	10.12	10.87	8.58	10.18	8.56	9.94
EMG, mV	Mean	0.005	0.005	0.004	0.006	0.006	0.006
	±SD	0.001	0.002	0.003	0.003	0.002	0.003

TS, test stimulus given to the left M1 during lengthening (L) and shortening (S) contraction of the left wrist flexion; SICI, ICF, intracortical inhibition and facilitation during L and S of the left wrist flexors; Position, ° - position of the left wrist. Neutral position is 0° and positive values indicate flexion; Force, N - measured force in Newtons, matched between L and S at 90% of shortening MVC; EMG, % - EMG activity in the left FCR as a percent of EMG recorded during MVC; EMG, mV - EMG activity of the resting right FCR during L and S of the left wrist flexors

* greater than lengthening ($p < 0.05$).

Table 4

Stimulation, recording, and mechanical characteristics to determine interhemispheric inhibition during wrist flexion with lengthening and shortening contraction.

Variable	Rest	50%MVC		90%MVC	
		L	S	L	S
CCS, mV	Mean	0.46	0.47	0.44	0.42
	±SD	0.12	0.12	0.09	0.13
TS, mV	Mean	0.29	0.33	0.35	0.30
	±SD	0.05	0.19	0.16	0.14
Position, °	Mean	-0.23	-0.14	-0.27	0.11
	±SD	0.33	0.23	0.14	0.20
Force, N	Mean	50.0	52.7	88.2	90.0
	±SD	4.13	11.04	9.62	22.21
EMG, %	Mean	41.7	50.6	89.9	93.2
	±SD	9.32	10.88	15.47	15.14
EMG, mV	Mean	0.004	0.005	0.004	0.004
	±SD	0.001	0.032	0.001	0.001

CCS, mV - contralateral conditioning stimulus delivered to the right M1; TS, mV - test stimulus delivered to the left M1; L and S, lengthening and shortening contraction of the left wrist flexors; Position, ° - position of the left wrist. Neutral position is 0° and positive values indicate flexion; Force, N - measured force in Newtons, matched between L and S at 50 and 90% of shortening MVC; EMG, % - EMG activity in the left FCR as a percent of EMG recorded during MVC