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Strength Training of One Limb Increases Corticomotor Excitability Projecting to the Contralateral Homologous Limb

Dawson J. Kidgell, Mark A. Stokes, and Alan J. Pearce

The contralateral transfer of strength following unilateral strength training (ULS) is thought to be due to changes within the nervous system. Using transcranial magnetic stimulation (TMS) we compared corticospinal responses following ULS of the right biceps brachii (BB) projecting to the untrained left BB. Motor evoked potentials (MEPs) were recorded from both BB of 23 individuals pre and post 4 weeks heavy load (80% of 1RM) ULS of right BB. TMS was delivered at intensities below active motor threshold (AMT) to saturation of the MEP (MEPmax). ULS resulted in a 28% increase in 1RM right BB strength, resulting in a 19.2% increase in contralateral strength of the left BB ($p = .0001$). There was a significant increase in MEP amplitude of 30.3% ($p = .03$), 33% ($p = .05$), and 26.5% ($p = .01$) at AMT, 20% above AMT and MEPmax respectively. No significant differences in silent period were seen at AMT, 20% above AMT or MEPmax. This study has demonstrated increased corticospinal excitability projecting to the untrained arm following heavy load ULS.

**Keywords**: Strength training, Contralateral Transfer of Strength, Transcranial Magnetic Stimulation, Corticomotor excitability.

A common observation that underscores the complexity of neuromuscular interactions between homologous limbs is the phenomenon of cross-education. Initially described by Scripture et al. (1894) whereby unilateral motor training of one limb improves motor task performance of the contralateral limb, there is good evidence to support cross-education in strength training of upper and lower limbs using various muscular contraction and movement types (Adamson et al. 2008; Brown et al. 1990; Cannon and Cafarelli 1987; Farthing et al. 2007; Farthing and Chilibeck 2003; Finland et al. 2009; Hortobágyi et al. 1997; Hortobágyi et al. 1999; Lee et al. 2009; Scripture et al. 1894; Shaver 1975; Yue and Cole 1992).

A recent meta analysis of randomized, controlled cross-education studies focusing on strength, found a mean increase of 7.8% in muscle strength of the contralateral homologous muscle (Munn et al. 2004). However, Munn et al. (2004)
presented data from studies ranging from a reduction of 2.7% (Meyers, 1966) to an increase of 21.7% (Carolan and Cafarelli 1992), and suggested that the exclusion of an adequate control measure, not only underpowers most studies but may also explain the inconsistent findings. Typical control measures have included the comparison of within-subjects’ strength between the trained and untrained limbs. Carroll et al. (2006) suggested that with such a design, the changes in contralateral strength may be due to familiarization. Using this procedure, it has been demonstrated that repeated exposure to muscle testing can improve performance through learning (Gleeson and Mercer 1996). Given that these studies have not included a separate control group (Adamson et al. 2008; Garfinkel and Cafarelli 1992; Meyers 1966) it is possible that as the participants are strength training a single arm, they are becoming familiar with the movement pattern, thus biasing the posttesting period. A potential approach to overcome this problem and obtain more objective data concerning the cross-education effect would be to randomize participants into two groups (experimental and control) and then compare the increases in strength of the contralateral untrained limbs between groups (Carroll et al. 2006; Munn et al. 2004). Despite these methodological differences (Munn et al. 2004), considerable evidence illustrates that the cross-education effect exists; however the exact mechanisms underlying the cross-transfer of strength remains unclear, although neural adaptations have been implicated (Carroll et al. 2006; Lee et al. 2009).

In an attempt to explain the neural contribution to cross-transfer of strength (Fimland et al. 2009), it has been suggested that 10% (Carpenter 1985; Nyberg-Hansen and Rinvik 1963) to 30% (Nathan et al. 1990) of pyramidal tract neurons do not decussate providing ipsilateral corticospinal projections. Recently, it has been demonstrated using the combined techniques of fractional anisotropy and paired-pulse transcranial magnetic stimulation (TMS), functional connectivity between primary motor cortex (M1) hand areas in both hemispheres (Wahl et al. 2007). Taken together, neuro-anatomical studies have provided a structural explanation for ipsilateral projection and interhemispheric integration underpinning physiological mechanisms for the cross-education effect.

In determining neurophysiological mechanisms for cross-education, studies have employed TMS to investigate corticospinal excitability. Hortobágyi et al. (2003), showed increased motor evoked potentials (MEPs), but depressed H-reflex excitability, in homologous right limb wrist flexors and extensors following moderate, 50% maximal voluntary contraction (MVC), to strong (75% MVC) acute voluntary contractions of the left limb. These authors suggested an increased excitability in the M1 with little to no change in the motoneuron pool. More recently, Lee et al. (2009) demonstrated an increase in voluntary activation of the opposite untrained limb following four weeks of isometric strength training of the right wrist extensor muscles. Twitch interpolation, using TMS, was used to assess the changes in cortical voluntary activation of the untrained wrist extensors. Following training there was a significant increase in strength of the trained (31.5%) and untrained wrist extensors (8.2%) which was accompanied by a significant decrease in twitch amplitude (35%) contributing to a significant increase in voluntary activation (2.9%). The finding of a reduced amplitude of the superimposed twitch following the strength training period was interpreted as increased motor cortical output to the untrained wrist extensors (Lee et al. 2009).
There is evidence to suggest that during a unilateral contraction, there is bilateral activation of the M1, termed motor irradiation (Carson 2005; Hortobágyi 2005; Hortobágyi et al. 2003; Muellbacher et al. 2000; Perez and Cohen 2008; Stedman et al. 1998; Todor and Lazarus 1986). Todor and Lazarus (1986) suggest that the degree of motor irradiation to the contralateral limb is conditional to the level of neural drive directed to the muscles undergoing the movement. More recently, Perez et al. (2008) demonstrated, using paired-pulse TMS, bilateral motor cortical activity during unilateral wrist flexion and increased MEPs of the ipsilateral motor pathway with increasing force output. Therefore, with interhemispheric connections between the cortices via the corpus callosum, along with ipsilateral and contralateral corticospinal projections, there are many potential sites within the nervous system that could contribute to the cross-transfer of strength (Carroll et al. 2006).

A further question raised within cross-education research is attributing the effects of cross-education to strength training or practice of a motor skill. Zhou (2000) and Farthing (2009) suggested that cross-education is consequential to the specificity to the prescribed training, and indeed has been shown to occur during both motor skill training (Schulze et al. 2002) and following strength training (Teixeira and Caminha 2003). Evidence for cross-education being related to motor skill acquisition come from studies that have shown maximal contralateral strength gains when the movement tested is the same as the training movements (Hortobágyi et al. 1997). Similarly, studies that have employed unfamiliar movements as part of the strength training regimen have also shown cross-education effects. Farthing et al. (2007) using functional magnetic resonance imaging demonstrated an enlarged region of activation in the contralateral sensorimotor cortex and activation of the ipsilateral temporal lobe of the untrained limb, proposing that the temporal lobe may be important for the cross-transfer of strength; however, the effect of incremental learning, particularly in light of using an unfamiliar movement exercise, could not be discounted.

However, despite current evidence supporting the cross-education phenomenon coming from strength training and motor skill acquisition literature, it remains unknown whether heavy load (80% of 1-RM) unilateral strength training has the capacity to increase corticospinal excitability projecting to the untrained limb. Therefore, our study was designed to extend on previous work by investigating the neural mechanisms underpinning the cross-education effect with heavy load (80% 1-RM), controlled (timing of each repetition, 3 s concentric/4 s eccentric) unilateral strength training using a between groups design (Munn et al. 2004). The primary objective was to determine whether cross-education strength training induces changes in corticospinal excitability and inhibition projecting to the untrained limb. The general aims of the investigation were to compare the changes in the input-output properties of the corticospinal pathway following ULS. The specific aims of the study were to compare the changes in TMS active motor threshold (AMT), MEP latency, MEP amplitude, MEP\textsubscript{max}, and silent period (SP) duration, at and 20% above AMT, to assess the influence of heavy load unilateral strength training on the contralateral transfer of strength. It was anticipated that the current study would allow us to determine the responses that occur within the contralateral corticospinal pathway projecting to the untrained limb.
Methods

Organization of the Study

Twenty six healthy participants (26.8 ± 7.3 years, 12 males, and 14 females) were systematically (by gender) and randomly assigned into either a strength training (6 males, 20.3 ± 3.4 years and 7 females, 24.5 ± 3.0 years) or a control group (6 males, 27.6 ± 7.9 years and 7 females, 29 ± 6.2 years). All participants were right-handed, as assessed by the Edinburgh handedness inventory (Oldfield 1971), and none of the subjects had participated in any kind of strength training in the past two years. Participants gave written informed consent and all procedures were approved by the University Human Research Ethics Committee. Participants assigned to the strength training group were required to undertake 12 supervised strength training sessions over a four-week training period. Participants assigned to the control group completed no training. At the beginning and at the end of the training period each subject participated in a testing session that involved: (1) strength testing to evaluate maximal voluntary dynamic elbow flexor muscle strength (1-RM) and maximal root mean square electromyography (rmsEMG) during an isometric MVC; and (2) single pulse TMS applied to both hemispheres projecting to the right and left BB. All testing post-training was conducted within 48 hr of the final supervised strength training session.

Maximum Strength Testing

Participants in both groups performed a standard unilateral 1-RM test for the right and left arm. Following the protocol of Munn et al. (2005b), participants were asked what they believed their 1-RM elbow flexion strength was and this load served as their initial starting weight. Participants performed the 1-RM test standing, holding a weighted dumbbell with one hand, with their elbow in full extension, forearm supinated, and the opposite arm placed behind their back while standing against a wall to prevent excessive body movement. Participants were then asked to flex their arm and lift the dumbbell as if doing a standard "biceps curl". If the trial was successful, the weight of the dumbbell was increased accordingly (.5 kg increments) on each trial after a three-minute recovery to minimize the development of muscular fatigue (Munn et al. 2005a). This procedure continued until the subject could no longer complete one repetition and their prior trial served as their 1-RM elbow flexion strength (Munn et al. 2005b).

Arm circumference:

To determine whether there was any change in muscle hypertrophy as a result of the strength training program, arm circumference of the right and left upper arm was measured with a tape measure. Specifically, arm circumference was determined at the largest circumference of the upper arm while participants attempted a strong contraction of the elbow flexors in a shortened position, with the shoulder at 90° flexion and the forearm 45° to the upper arm (Munn et al. 2005a).

Strength Training Procedures

The strength training group performed heavy load strength training (80% of their 1-RM) of the right elbow flexors only, three times per week for four weeks (12
sessions in total). All training was supervised within the laboratory and participants were instructed to train in the same way as tested, that is, with the contralateral limb placed behind their back to reduce possible activation of the muscles during training. Biceps curls with a dumbbell were performed by undertaking flexion-extension movements of the elbow with the forearm supinated. The participants performed four sets of 6–8 repetitions at 80% 1-RM with a three-minute recovery period between sets (Munn et al. 2005a). Participants were required to perform each repetition with a repetition timing of 3 s concentric and 4 s eccentric, as data suggests that this repetition timing produces the greatest transfer in strength (Hortobágyi et al. 1997; Munn et al. 2005a). The principle of progressive overload was employed throughout the training period to maximize the training response (Peterson et al. 2005). Specifically, when participants could complete four sets of 8 repetitions, at the beginning of the next training session, the training weight (kg) was increased by 5%.

**Contralateral Strength Transfer**

The contralateral transfer of strength was quantified according to the procedure of Carroll et al. (2006). The transfer was determined by the difference in change in mean strength of the untrained left arm in the control group and the experimental group post training. The calculation was performed as follows:

$$\left( \frac{E_{Post} - E_{Pre}}{E_{Pre}} - \frac{C_{Post} - C_{Pre}}{C_{Pre}} \right) \times 100$$

Where $E_{Post}$ refers to mean post training 1-RM strength for the experimental group’s untrained arm, $E_{Pre}$ refers to mean pre training 1-RM strength for the experimental group’s untrained arm, $C_{Post}$ refers to mean post training 1-RM strength for the control group’s untrained arm, and $C_{Pre}$ refers to mean pre training 1-RM strength for the control group’s untrained arm.

**Electromyography and Transcranial Magnetic Stimulation**

Surface EMG activity was recorded from the left and right BB muscle using bipolar Ag-AgCl electrodes. Two electrodes were placed 2 cm apart over the BB muscle, located by manual muscle testing and placed over the belly of the muscle, with the third reference electrode (ground electrode) placed over the bony prominence at the elbow (lateral epicondyle). The area of electrode placement was prepared by shaving and cleaned with 70% isopropyl alcohol. The site was marked with permanent marker and continually maintained by the investigator and participant, to ensure no differences in electrode placement occurred relative to the innervation zone before and after the four week training period. EMG signals were amplified (1000×) with bandpass filtering between 10 Hz and 1 kHz and digitized at 1.5 kHz for 500 ms using custom-designed software (National Instruments V4.0). The surface rmsEMG was calculated from a 500 ms segment occurring during the asymptote of the MVC (Griffin and Cafarelli 2007; Wilson et al. 1993b). To obtain the MVC, participants were seated in a chair with the elbow flexed to 90°, as measured by an electronic goniometer (Biometrics, USA), and with their hand in a supinated position. A dynamometer (Microfet², USA) was positioned on a modifiable bench so the dynamometer was inside the participant’s forearm at the level of the wrist.
The participant was then instructed to flex the elbow against the dynamometer as forcefully as possible for 3 s. Three attempts, with a two-minute rest between each attempt were performed. This procedure was repeated for the participant’s other arm. The trial with the highest MVC and rmsEMG level was recorded and subsequently used to determine background muscle activity during the TMS protocol. The standard criteria for measurement of MVCs were fulfilled and included a period of familiarization (before data collection) and verbal encouragement, feedback of rmsEMG displayed on a computer monitor at eye level, standardized verbal encouragement provided by the investigators and the rejection of a trial in the case the participant felt it was not a maximal effort (Gandevia 2001).

TMS testing followed the established protocols of Byrnes et al. (1999), Pearce et al. (2000) and Wilson et al. (1993). MEPs were evoked by TMS of the contralateral motor cortical area projecting to the BB using a Magstim 200² stimulator (Magstim Co, UK), with a 70 mm figure of 8 coil placed tangential to the skull in an antero-posterior direction. For reliability of coil placement, participant’s wore a snugly fitting cap, positioned with reference to the nasion-inion and interaural lines (Byrnes et al. 1999; Hortobágyi et al. 2008; Pearce et al. 2000; Wilson et al. 1993b). The cap was marked with sites at 1 cm spacing in a latitude-longitude matrix to ensure reliable coil position throughout the testing protocol and for repeated testing sessions over the period of the study. The cap was checked constantly to ensure that no changes in cap position occurred. Sites near the estimated center of the BB area (4–7 cm lateral to the vertex) were explored to determine the site at which the largest MEP amplitude was observed, via visual inspection of the MEP waveform (Figure 1). This site was defined as the “optimal” site (Pearce et al. 2000; Wilson et al. 1993a). At the optimal site, MEP stimulus-response curves were measured by delivering two sets of five TMS stimuli at intensities (5% of stimulator output steps) from a level below the participant’s AMT until the plateau of MEP amplitude (i.e., until the amplitude did not increase with increased stimulation). AMT was defined as the intensity at which an MEP could be obtained with at least five of the 10 stimuli with a peak-peak amplitude being greater than 200μV during 10% of MVC rmsEMG (Rogasch et al. 2009). MVC rmsEMG was determined from the participant who performed an isometric MVC of their BB muscle on the bench with their elbow flexed to 90° and was used to control for background muscle activity during TMS trials. Each set of five stimuli were delivered during a controlled, low level voluntary contraction of the BB muscle at 10% (± 3%) of MVC rmsEMG (Pearce et al. 2000; Wilson et al. 1993a). Feedback of the participant’s rmsEMG level was displayed on a computer monitor positioned 1.5m away at eye level using custom-built software (National Instruments V4.0). Each stimulus was delivered in random intervals every 10–12 s to avoid stimulus anticipation and 30 s rest was provided between each set of stimuli to reduce the possibility of muscular fatigue.

Data and Statistical Analyses

All MEPs collected (n = 10, two sets of five 500 ms recordings, at each stimulus intensity from below participant’s AMT to MEP max, see Figure 1 for an example) were displayed and averaged online for visual inspection, in determining the optimal site, and then stored off-line for further analysis.
Stimulus-response curves were constructed according to the protocol of Carroll et al. (2002). Stimulus intensity was plotted against MEP amplitude, and the data were fitted with a three parameter sigmoid equation:

$$MEP(s) = \frac{MEP_{max}}{1 + e^{m(S50-s)}}$$

Where $s$ is stimulus intensity, $m$ is the estimated slope, $S50$ is the estimated peak slope, and $MEP_{max}$ is the measured maximum the participant’s MEP amplitude reached in a given trial. A nonlinear data fit iterative model to each participant’s data using SPSS17.0 (SPSS Inc, Chicago, Ill) was applied. This procedure estimated the values for $m$ and $S50$ and provided a measure of the curves fit to the data. All iterative fits significantly fitted the data.
All data were first screened to ensure they were normally distributed. To have sufficient data to test for questions of normality, all data from 68 trials were used to establish the distributional properties. No variable’s z-score of skew or kurtosis was excessive. Further, Kolmogorov-Smirnov tests suggested the variables $S50$ ($KS = 0.07, p = .2$) and $MEP_{max}$ ($KS = 0.1, p = .08$) were clearly normally distributed, while $m$ was apparently nonnormal, ($KS=0.1, p = .01$) however; this violation appeared to be only mild from examination of frequency histograms and detrended Q-Q plots, and was not considered sufficient to warrant a more conservative analytic strategy than used herein. Consequently, it was decided to treat the data as essentially normal in distribution. To identify changes in the input-output properties of the corticospinal pathway, the slope and plateau values of the stimulus-response curve was used to characterize the physiological strength of the corticospinal connections projecting to the left and right BB (Boroojerdi et al. 2001; Carroll et al. 2002). Latency was calculated from stimulus artifact to MEP onset; MEP peak-to-peak amplitude and SP duration (onset of MEP to return of uninterrupted EMG) were cursoried and measured for both motor cortices (Byrnes et al. 1999; Pearce and Kidgell 2009; Williams et al. 1992; Wilson et al. 1993a; Wilson et al. 1993b). Furthermore, MEP sweeps ($n = 10$) obtained at AMT, 20% above AMT and $MEP_{max}$ were analyzed to quantify changes in membrane excitability and corticospinal cell recruitment following the strength training intervention (Hallett 2007).

To test the hypothesis that unilateral strength training increases contralateral strength and corticospinal excitability, a two-way ANOVA, and Fisher’s least significant difference (LSD) procedure for post hoc testing, for each arm was used to compare group interaction (trained vs. control) by testing session (pre vs. post) for each dependant variable (elbow flexion strength, rmsEMG, MEP latency and amplitude, and SP duration). Pearson’s correlation coefficient was used to determine correlations between changes in corticospinal excitability and changes in contralateral strength. Data are presented as means ($\pm SD$) and the level of significance used for all tests was set at $p \leq .05$.

**Results**

All participants in the training group completed all training sessions, however three participants (1 male and 2 females) in the control group were not able to complete the posttesting session and subsequently their data were not used. No significant differences were observed in muscle girths between groups pre training (right arm trained group pre 31.9±5.6 cm versus control group pre 31.3 ± 5.2 cm, $p = .4$; left arm trained group pre 31.3 ± 4.9 cm versus control group pre 30.9 ± 6.2 cm, $p = .5$). No significant differences in arm girths were observed within and between groups following the training period (right arm trained group post 32.2 ± 4.9 cm versus control group post 31.4 ± 3.3 cm, $p = .3$; left arm trained group post 31.2 ± 4.7 cm versus control group post 31.5 ± 3.1 cm, $p = .3$).

**Voluntary Muscle Strength**

There were no significant differences in dynamic elbow flexion strength (1-RM) at baseline between the control and trained groups in both right and left arms (right arm: $p = .7$; left arm: $p = .3$). Dynamic elbow flexion mean strength increased by 28% ($p = .0001$) in the trained (right) arm (11.5 ± 4.5 kg to 14.8 ± 5.2 kg) and a 19.2%
(\(p = .0001\)) increase in strength to the untrained (left) arm (11.3 ± 4.9 kg to 13.7 ± 5.4 kg; Figure 2). There was a significant correlation between the percentage of strength gained in the trained right limb and the percentage of the contralateral transfer of strength to the untrained left limb \((r = .67, p = .01; \text{Figure 3})\). There were no significant differences in voluntary strength for the control group (right arm: 13.3 ± 4.2 kg to 13.2 ± 4.3 kg, \(p = .34\); left arm: 11.8 ± 3.9 kg to 12.0 ± 3.8 kg, \(p = .1\), Figure 2).

**Figure 2** — Average 1-RM strength (± SD) data for the strength-training and control groups left untrained arm and right trained arm. The bars on the left represent pretraining absolute strength and the bars on the right represent post training absolute strength. There was a 19.2% increase in unilateral left strength and a 28% increase in unilateral right strength for the trained group. * Indicates statistical significance \((p < .05)\) from pretraining values.

**Figure 3** — Strength changes for the elbow flexors of the trained and contralateral limb in trained subjects after four-weeks of heavy load controlled unilateral strength training, expressed as a percentage of pretraining strength \((r = .67; p < .05)\).
rmsEMG

There were no significant differences at baseline for group mean left and right BB MVC rmsEMG activity between the groups (control, left arm: .39 ± .12 mV; trained, left arm: .52 mV ± .22 mV, \( p = .1 \); control, right arm: .41 ± .24 mV; trained, right arm: .50 mV ± .20 mV, \( p = .5 \)). There were also no differences following training to pretraining values within or between the groups (control, left arm: .37 ± .12 mV; trained, left arm: .60 mV ± .22 mV, \( p = .1 \); control, right arm: .41 ± .21 mV; trained, right arm: .58 mV ± .17 mV, \( p = .5 \)). Further, no interaction was found between groups by training (\( p = .7 \)). Similarly, no differences were observed between rmsEMG at 10% of MVC contraction pre and post testing sessions (pre control, left arm: .04 ± .01 mV; pre trained, left arm: .05 mV ± .02 mV, \( p = .2 \); post control, left arm: .04 ± .01 mV; post trained, left arm: .06 ± .02 mV; pre control, right arm: .04 ± .02 mV; pre trained, right arm: .05 ± .02 mV; \( p = .4 \); post control, right arm: .04 ± .02 mV; post trained, right arm: .05 mV ± .01 mV, \( p = .5 \)).

Latency

No significant differences in latency duration were seen between groups at 20% above AMT at pretraining (right M1, \( p = .8 \); left M1, \( p = .2 \)). Following the training intervention, there was no significant difference in latency duration pre vs. post training in both trained (right M1: 13 ± .8 ms vs. 12.8 ± .5 ms, \( p = .8 \); left M1: 13 ± .8 ms vs. 12.9 ± .3 ms, \( p = .3 \)) and control groups (right M1: 12.9 ± .5 ms vs. 12.8 ± .5 ms, \( p = .8 \); left M1: 12.9 ± .50 ms vs. 12.8 ± .5 ms, \( p = .4 \)).

Active Motor Threshold and Motor Evoked Potentials

Mean group data for the control and the trained groups for percentage of stimulator output at AMT are shown in Table 1. There were no significant differences at pretraining for the percentage of stimulator output at AMT within and between the trained and control groups left (\( p = .3 \)) and right M1 (\( p = .7 \)). Following the training period, there were no significant differences for percentage of stimulator output at AMT between the trained and control groups (control left M1 vs. trained left M1; \( p = .8 \); control right M1 vs. trained right M1; \( p = .9 \), Table 1).

Table 1 displays the mean data for both the control and the trained group for mean MEP amplitude at AMT, and 20% above AMT and MEP$_{max}$. There was no significant difference in mean MEP amplitude at AMT at baseline between groups (right M1: \( p = .9 \); left M1: \( p = .16 \)). MEP amplitude at AMT increased by 53% (\( p = .01 \)) in the left M1 and increased by 30.3% (\( p = .03 \)) in the right M1 in the trained group following the training intervention. There were no significant differences (\( p = .3 \)) in the mean MEP amplitude at AMT in the right M1 and left M1 (\( p = .3 \)) in the control group following the training intervention. Further, there were no interaction effects between the groups (\( p = .2 \)). There were no significant differences in the estimated slope (\( m \)) of the input-output curve following strength training in the trained group (pre: 0.15 AU ± 0.05 AU; post: 0.14 AU ± 0.03 AU; \( p = .3 \)) for the right M1. There were also no significant differences in \( m \) for the left M1 (pre: 0.16 AU ± 0.06 AU, post: 0.15 AU ± 0.05 AU, \( p = .4 \)). Furthermore, no significant differences were identified for S50 following the training intervention for the right or left M1 (right M1: pre; 4.3 AU ± 3.4 AU, post; 4.5 AU ± 3.3 AU, \( p = .8 \); left M1: 4.5 AU ± 3.3 AU, \( p = .7 \));
Table 1  Mean data (± SD) for percentage of stimulator output at AMT (%), MEP amplitude at AMT, 20% above AMT, MEP\textsubscript{max} (mV), SP duration (msec) at 20% above AMT and at MEP\textsubscript{max} (sec), before and following the four week strength training intervention for the control and trained groups.* represents significant difference to pre training values (p < 0.05).

<table>
<thead>
<tr>
<th></th>
<th>Stimulator Output at AMT (%)</th>
<th>AMT Amplitude (mV)</th>
<th>MEP Amplitude (mV) @ 20% above AMT</th>
<th>Max MEP (mV)</th>
<th>SP Duration (msec) at 20% above AMT</th>
<th>SP Duration (msec) at Max MEP (Mv)</th>
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<tbody>
<tr>
<td><strong>Control</strong></td>
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<tr>
<td>Right M1</td>
<td>48.57 ± 5.5</td>
<td>0.75 ± 0.43</td>
<td>1.73 ± 1.12</td>
<td>99.91 ± 18.5</td>
<td>112.56 ± 14.5</td>
<td>111.99 ± 14.5</td>
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<tr>
<td>Left M1</td>
<td>49.37 ± 6.7</td>
<td>0.93 ± 0.72</td>
<td>2.76 ± 1.83</td>
<td>99.65 ± 12.8</td>
<td>115.75 ± 14.2</td>
<td>114.23 ± 15.0</td>
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<tr>
<td><strong>Trained</strong></td>
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<tr>
<td>Right M1</td>
<td>48.4 ± 8.9</td>
<td>*1.16 ± 0.72</td>
<td>*3.06 ± 1.56</td>
<td>101.04 ± 23.9</td>
<td>111.07 ± 15.9</td>
<td>113.54 ± 18.8</td>
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<tr>
<td>Left M1</td>
<td>50.0 ± 10.4</td>
<td>*1.26 ± 0.82</td>
<td>*3.26 ± 2.45</td>
<td>107.93 ± 23.9</td>
<td>112.07 ± 17.3</td>
<td>107.86 ± 22.4</td>
</tr>
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</table>
4.9 AU ± 3.7 AU, post; 5.6 AU ± 4.8 AU, p = .6). There was a moderate, but non-significant, correlation between the amplitude of MEPs at AMT in the right M1 and changes in strength of the untrained left limb (r = .42, p = .06). Following strength training, there was a significant correlation between the amplitude of MEPs at 20% above AMT in the right M1 and the change in strength of the untrained left limb (r = .57, p = .04). In addition, there was also a significant correlation between the amplitude of MEPs at 20% above AMT in the left M1 and the change in strength of the untrained left limb (r = .62, p = .02). There were no difference in mean MEP amplitude at 20% above AMT at pretraining between groups (right M1: p = .20; left M1: p = .4). There were no significant differences (p = .4) in MEP amplitude of the right M1 in the control group at 20% above AMT, however, there was a 33% increase in MEP amplitude in the right M1 for the trained group (p = .05). There were also no significant differences (p = .6) in MEP amplitude of the left M1 at 20% above AMT in the control group, however, there was a 33% increase (p = .05) in the trained group following the intervention. No significant interaction effect was observed between the groups (right M1: p = .93; left M1: p = .1). There were no significant differences in mean MEP_{max} amplitude at pretraining between groups (right M1: p = .6; left M1: p = .4, see Table 1). Following the training intervention, there was a 26.5% increase in the amplitude of the MEP_{max} in the right M1 (p = .01; Figure 4) and a 38% increase in the left M1 (p = .02) in the trained group. There were no significant (p = .8) differences detected for the control group or any significant interaction effects (right M1: p = .9; left M1: p = .3).

Silent Period Duration:
Table 1 shows all SP data of the two groups’ pre and post training intervention. No significant differences in SP duration were observed between groups at 20% above AMT at pretraining (right M1: p = .8; left M1: p = .2, Table 1). Following the training intervention, there was a small nonsignificant reduction in mean SP duration in the trained group (right M1: 4.2%, p = .7; left M1: 2.8%, p = .5) while there were no significant change in SP duration in the control group following the training intervention (right M1: .05% decrease, p = .7; left M1: 3.1% increase, p = .5, Table 1). No significant differences were seen in the mean duration of the SP at MEP_{max} between groups at baseline (right M1: p = .9; left M1: p = .4). Following training, there was a small nonsignificant reduction in mean SP duration at MEP_{max} in the trained group (right M1: 5.2%, p = .7; left M1: 3.9%, p = .3). No differences in SP duration at MEP_{max} were observed following the training intervention within the control group (right M1: .5% decrease, p = .7; left M1: 1.3% decrease, p = .3).

Discussion
This study extends on existing evidence supporting contralateral strength and corticomotor changes following a period of unilateral strength training. The major findings from the current study are that four weeks of heavy load dynamic strength training for the right elbow flexors, in participants with no strength training experience, increased dynamic 1-RM strength for both the right trained (28% increase) and left untrained (19.2% increase) upper limbs. In the absence of muscle hypertrophy, we have demonstrated an increase in corticospinal excitability (MEPs) projecting to
the untrained left arm, with no significant differences observed in latency duration or corticospinal inhibition (SP).

The contralateral transfer of strength observed in this study is greater than recent investigations that have used a similar between subjects design, reporting a contralateral strength transfer of 7% (Lee et al. 2009) and 9% (Munn et al. 2005b). The large difference in the cross-transfer of strength between this study and that of Munn et al. (2005b) may be due, in part, to using the preferential direction of transfer, being right to left in right handed participants (Farthing et al. 2005), as well as the methodology of the strength training employed. For example, Munn et al. (2005) used an identical protocol in terms of volume and intensity of training; however, they employed a faster repetition scheme of 1 s concentric and 1 s eccentric whereas the current study employed a repetition cycle of 3 s concentric and 4 s eccentric. The rationale for using a slow controlled repetition protocol has been based primarily on previous research suggesting greatest cross-education of strength from slow controlled repetitions (Hortobágyi et al. 1997; Munn et al.
The repetition timing for training was also chosen following recent studies demonstrating increased corticospinal excitability during motor tasks when the level of precision required to complete the task has been altered by slowing and purposefully controlling the movement (Pearce and Kidgell 2010). Farthing and Chilibeck (2003) investigated cross-transfer of strength in the untrained limb following isokinetic strength training, also focusing on the eccentric component of the movement. However, these investigators demonstrated increased cross-transfer following high velocity training, which contradicts the findings in this study. Methodological differences may also explain contrary findings as the current study trained participants using free weights whereas Farthing and Chilibeck (2003) employed an isokinetic training regimen. In light of these differences, both the current study and Farthing and Chilibeck (2003) still employed muscle actions that were high intensity and this may be an important factor in the cross-transfer of strength. Furthermore, the change in contralateral strength observed in the present study is larger compared with the recent study by Lee et al. (2009). The observed differences may largely be related to the strength training paradigm employed. Lee et al. (2009) employed isometric contractions of the extensor carpi radialis brevis, while the current study adopted a dynamic strength training protocol, whereby the timing of each repetition was controlled and as such may have resulted in the observed differences. Furthermore, dynamic strength training that involves both concentric and eccentric contractions has been shown to increase strength when compared with isometric strength training alone and this may also account for the observed differences in contralateral strength (Brown et al. 1988; Higbie et al. 1996).

The observation of increased MEP amplitude projecting to the untrained left arm suggests increased excitability of neurons in the M1 as well as by the excitability of the spinal motor neuron pool (Rothwell et al. 1991); supporting the findings and the suggestion by Hortobágyi et al. (2003) that a general increase in motor cortical excitability occurs following strong voluntary contractions. It has been suggested that excitatory motor cortical activity during strong unilateral contractions diffuse from the active M1 to the “inactive” M1 through inter-hemispheric pathways (Farthing 2009; Zhou 2000). Neuro-imaging and TMS studies have shown mechanisms whereby unilateral motor activity is associated with bilateral activation of both the left and right M1 (Carson 2005; Cramer et al. 1999; Muellbacher et al. 2000) via increased excitability of existing intrinsic horizontal pathways within the M1. Corticospinal cells within layer II and III of the M1 form a broad, intrinsic horizontal projection system (Mountcastle 1997). Rioult-Pedotti et al. (1998) provided the first line of evidence that motor activity leads to an increase in strength of horizontal cortical connections within the M1 as demonstrated by an increase in amplitude of field potentials via micro stimulation of corticospinal cells. Given that high force unilateral voluntary contractions have been shown to affect the efficacy of neural circuits controlling the untrained limb (Carson et al. 2004; Hortobágyi et al. 2003; Sohn et al. 2003) the results suggest that the strength training program employed in the current study increased the neural excitability of the contralateral homologous muscle due to chronic changes in synaptic connectivity within specific neural circuits between hemispheres that contribute to the ability to generate force. The adaptations observed within the right M1 may have contributed in some capacity to the contralateral transfer of
strength to the left arm, as we have demonstrated a moderate to strong correlation between the change in MEP amplitude and change in strength of the untrained arm.

In this study, repeated strong and controlled voluntary contractions may have also induced a motor learning effect contributing to increased corticospinal excitability at stimulus intensities at and above AMT. A general consensus exists in the literature that cross-education of strength might be similar to cross-education of motor skill acquisition (Carroll et al. 2002; Farthing 2009; Lee and Carroll 2007; Zhou 2000). Carroll et al. (2002) has put forward that strength training is a form of motor learning, in the sense that participants are required to learn to produce muscle recruitment patterns associated with optimal performance of the task. Other authors concur that short-term increases in strength stem from improved coordination between opposing muscles (Enoka 1997; Olafsdottir et al. 2008). Moreover, Farthing et al. (2007) have affirmed that skill learning does not induce muscle hypertrophy but still contributes to strength gains. As first proposed by Parlow and Kinsbourne (1989), the cross-activation model suggests that motor task or skill memory engrams are stored in both hemispheres following unilateral skill acquisition. It has also been suggested that adaptations associated with skill learning involve changes in cortical synapse number and/or synaptic strength (Jones 1999; Jones et al. 1999; Muellbacher et al. 2001). While it is not possible from the current study to determine the precise underlying mechanism responsible for the changes in corticospinal excitability, the novel aspect of the strength training program employed (i.e., high intensity strength training, with controlled timing of each repetition) in untrained participants, lead to some form of neural adaptation, as a result of both strength and skill training influences.

Limitations in the current study include quantifying muscle activity in the contralateral limb during the training period and the technique of magnetic stimulation. It has been suggested that contralateral increases in strength may arise as a result of contraction of muscles in the untrained limb during unilateral training (Carolan and Cafarelli 1992; Hortobágyi et al. 1997). We did not collect EMG data in the untrained limb while participants undertook strength training, and therefore cannot discount the possibility that participants were coactivating limb musculature, despite instructing participants to keep their arm behind their back. However, more recent studies (Evetovich et al. 2001; Fimland et al. 2009; Lee et al. 2009) have published similar findings of strength increases of the contralateral limb without within-training EMG data. Furthermore, the observation of no change in maximum rmsEMG pre and post training is consistent with the findings of Evetovich et al. (2001) and Lee et al. (2009). A second limitation of this study was that only single-pulse TMS and contralateral MEP responses were recorded, limiting the conclusions that can be drawn from the data, particularly in relation to the questions of adaptation occurring at the cortical or spinal levels and the influence of ipsilateral projection changes. However, previous research has shown that the mechanisms underpinning increases in cross-education of strength are unlikely to occur at subcortical and spinal levels. For example, Hortobágyi and colleagues (2003) following acute high intensity contractions (80–100% of MVC) showed increases in MEPs, but not in cervicomedullary MEPs (CMEPs) which remained unaffected, or H-reflex which showed depression (Fimland et al. 2009). Similarly, Lagerquist et al. (2006) demonstrated a 17.6% increase in strength of the contralateral untrained limb in the absence of modifications in spinal cord excitability.
Alterations in ipsilateral inhibition have been previously documented in unimanual motor tasks and alter depending on the involvement of distal or proximal muscles (Harris-Love et al. 2007), movement complexity (Avanzino et al. 2008) and motor learning acquisition (Perez et al. 2007). Recently, Perez and Cohen (2008) demonstrated unilateral activity-dependant changes in M1 ipsilateral projection using paired and triple-pulse TMS technique which can access intracortical inhibitory circuits that use the neurotransmitter γ-aminobutryic acid (GABA). The single pulse TMS method can also be used to assess GABA_B receptors (Chen 2004; Siebner et al. 1998) reflected as the SP duration on the EMG. The present investigation, found no change in the duration of the SP in either hemisphere at 20% above AMT and at MEP_max, suggesting that there were no changes in cortical inhibition. However, this may not mean that the level of inhibition has not altered, but rather a failure of the single-pulse technique to show changes in intracortical inhibition. It has been suggested (Foltys et al. 2003; Hortobágyi 2005) that an association exists between the intensity of M1 activation and the amount of inhibition in the contralateral M1. With the current study employing high intensity training of a repetitive nature, the left M1 may have influenced and altered the right M1 excitability via a reduction in the level of inhibition. Although SP duration did not alter, changes were observed in corticospinal excitability in the M1 projecting to the untrained arm above AMT which may be due to decreases in inhibition reflecting greater excitation (i.e., MEP amplitude increases) in the contralateral corticospinal pathway (Foltys et al. 2003; Hortobágyi 2005). It is intended that further research will investigate ipsilateral projection in elbow flexors following a period of high-intensity strength training using a between groups design.

In conclusion, the results of the current study demonstrate that high intensity unilateral strength training increases strength, in the absence of muscle hypertrophy, and alters the functional properties of the corticospinal pathway projecting to the untrained arm in healthy humans. The present data suggests that adaptation of the corticospinal pathway is reflective of the specific nature of the strength training employed, but is also likely to be due to motor learning adaptations. Although we have demonstrated increased corticospinal excitability, the results do not discount that additional adaptations may have also occurred within neural structures not confined to the M1 and corticospinal pathway. Further research should investigate ipsilateral corticospinal excitability and inhibition, using a similar training intervention.

References


