

The sites of neural adaptation induced by resistance training in humans

Timothy J. Carroll, Stephan Riek and Richard G. Carson

Perception and Motor Systems Laboratory, The School of Human Movement Studies, The University of Queensland, Brisbane, Queensland 4072, Australia

Although it has long been supposed that resistance training causes adaptive changes in the CNS, the sites and nature of these adaptations have not previously been identified. In order to determine whether the neural adaptations to resistance training occur to a greater extent at cortical or subcortical sites in the CNS, we compared the effects of resistance training on the electromyographic (EMG) responses to transcranial magnetic (TMS) and electrical (TES) stimulation. Motor evoked potentials (MEPs) were recorded from the first dorsal interosseous muscle of 16 individuals before and after 4 weeks of resistance training for the index finger abductors ($n = 8$), or training involving finger abduction–adduction without external resistance ($n = 8$). TMS was delivered at rest at intensities from 5 % below the passive threshold to the maximal output of the stimulator. TMS and TES were also delivered at the active threshold intensity while the participants exerted torques ranging from 5 to 60 % of their maximum voluntary contraction (MVC) torque. The average latency of MEPs elicited by TES was significantly shorter than that of TMS MEPs (TES latency = 21.5 ± 1.4 ms; TMS latency = 23.4 ± 1.4 ms; $P < 0.05$), which indicates that the site of activation differed between the two forms of stimulation. Training resulted in a significant increase in MVC torque for the resistance-training group, but not the control group. There were no statistically significant changes in the corticospinal properties measured at rest for either group. For the active trials involving both TMS and TES, however, the slope of the relationship between MEP size and the torque exerted was significantly lower after training for the resistance-training group ($P < 0.05$). Thus, for a specific level of muscle activity, the magnitude of the EMG responses to both forms of transcranial stimulation were smaller following resistance training. These results suggest that resistance training changes the functional properties of spinal cord circuitry in humans, but does not substantially affect the organisation of the motor cortex.

(Received 7 June 2002; accepted after revision 19 July 2002; first published online 16 August 2002)

Corresponding author T. J. Carroll: Neurophysiology Laboratory, E-427 Van Vliet Centre, Faculty of Physical Education and Recreation, University of Alberta, Edmonton, Canada T6G 2H9. Email: tcarroll@ualberta.ca

Training involving repetitive movements against a large resistance is known to enhance muscular strength, and the intramuscular adaptations that occur in response to this 'resistance training' have been well described (for reviews see Timson, 1990; Abernethy *et al.* 1994; Baldwin & Haddad, 2001). Although it has long been suspected that resistance training is also accompanied by adaptations in the CNS that play an important role in the development of strength, the precise nature of the neural responses to resistance training is unknown (e.g. Sale, 1988; Moritani, 1993; Enoka, 1997; Carroll *et al.* 2001a; Gandevia, 2001). Since it is now well established that motor learning is accompanied by changes in the functional organisation of the cerebral cortex (e.g. Martin & Morris, 2001), it seems reasonable to presume that resistance training may induce changes in the organisation of the cortex. However, it has recently been shown that the repetitive execution of a simple movement does not induce substantial adaptation in the motor cortex in monkeys (Plautz *et al.* 2000). Furthermore,

Remple *et al.* (2001) reported that repetition of a difficult task that requires a new movement technique to be learned and refined induces a similar degree of cortical adaptation, regardless of whether the training movements are performed against high or low resistance in rats. These studies suggest that the systematic repetition of simple movements with low force and velocity requirements does not cause substantial, long-lasting (i.e. beyond a few hours after exercise) cortical adaptation, and that increasing the force required to execute a new task during skill learning does not markedly affect the degree of cortical adaptation that occurs. The question remains, however, whether training involving the repetitive execution of a simple movement against a large resistance has the capacity to cause adaptations in the motor cortex. In the present experiment, we investigated whether resistance training induces relatively long-lasting changes in the functional properties of the corticospinal pathway in humans.

The specific aim of the present experiment was to determine whether resistance training changes the input–output properties of the corticospinal pathway at rest and during muscle activation. In order to investigate whether resistance training causes adaptations at cortical or subcortical sites along the corticospinal pathway, we determined the effect of training on the magnitude of responses to transcranial magnetic stimulation (TMS) and transcranial electrical stimulation (TES) during background muscle activation. The mechanism by which descending corticospinal volleys are elicited differs between TMS and TES. A large proportion of the muscular response to TMS of the upper limb muscles is brought about by trans-synaptic excitation of corticospinal cells, which results in one or more ‘indirect’ descending volleys, or I waves (Mazzocchio *et al.* 1994; Edgley *et al.* 1997; Di Lazzaro *et al.* 1998a,b). Compared with TMS, a greater proportion of the corticospinal neurones activated by TES are depolarised directly by the electrical stimulus, probably at an axonal site two or three nodes distant to the axon hillock, resulting in a so-called ‘direct’, or D wave (e.g. Di Lazzaro *et al.* 1998a, 1999). The responses to TES are therefore less strongly influenced by the excitability state of the motor cortex than those to TMS. It was anticipated that the present experiment, which investigated changes in the evoked responses to both TES and TMS, would allow us to determine whether the adaptations to resistance training occur to a greater extent at cortical or subcortical sites in the CNS.

METHODS

Participants

Sixteen individuals (aged 22–36 years; 15 male, 1 female) volunteered for this experiment. The participants were randomly allocated to either a resistance-training condition ($n = 8$) or to a condition involving unresisted movement ($n = 8$). All of the participants were right handed according to the Edinburgh Handedness Inventory (Oldfield, 1971). Each individual gave written, informed consent to participate in the study, the procedures for which conformed to the Declaration of Helsinki and were approved by the University of Queensland Medical Research Ethics Committee.

General procedure

Twelve training sessions were performed by the participants over a 4 week training period (three sessions per week). Before and after the training period, each volunteer participated in an experimental session involving transcranial and peripheral nerve stimulation. The final experimental session was conducted between 48 and 96 h after the last training session. Participants were seated in a dentist’s chair, with their forearm and hand supported by a custom-built device (Fig. 1A). The device restricted movement of the wrist and hand, and allowed measurement of abduction torque about the second metacarpo-phalangeal joint via a torque transducer aligned co-axially with the joint. Motor evoked potentials (MEPs) were recorded from the first dorsal interosseous muscle (FDI) at rest and during background contraction. During the resting trials, TMS was applied at a range

of stimulation intensities from just below the threshold intensity for eliciting a response at rest to the maximal output of the stimulator. During the active trials, TMS and TES were applied at the active threshold intensity while the participants exerted finger abduction torque at a range of levels from 5 to 60 % of their maximum capacity.

Training programme

The experimental device used during the stimulation sessions (Fig. 1A) was also used to apply resistance during training. The second metacarpo-phalangeal joint was aligned co-axially with the main shaft of a pulley system. Weights were attached to the terminal pulley in a manner that applied a resistance to abduction movements of the index finger at a point 5 cm from the axis of joint rotation. Thus, in order to rotate the device shaft at a steady pace, the subjects were required to perform shortening and lengthening muscle actions with index finger abductors. A potentiometer was attached in series with the main shaft of the training device in order to record the joint position during training. The calibrated output of the potentiometer was amplified and displayed in real time to provide visual feedback to the participants. They were required to move their fingers between 20 deg of finger abduction and 15 deg of finger adduction. The participants were instructed to move steadily throughout the prescribed range, so that they controlled the load at all times. Four trials, each consisting of six complete finger abduction–adduction cycles, were completed in each training session. All training loads were scaled to each individual’s maximal dynamic strength (as determined prior to training); the load was increased from 70 % of maximum in steps of 5 % whenever three sessions had been completed with the previous load. Participants in the unresisted-training group performed the same number of movements, through the same range, but without external resistance.

Maximal voluntary contraction

The peak torque recorded in either of two trials was taken as the maximal voluntary contraction (MVC). Participants were instructed to increase torque steadily for 2 s and then to exert maximal torque for 3 s. Verbal encouragement and visual feedback of the torque exerted were provided.

EMG recordings and peripheral nerve stimulation

The surface EMG was recorded from the FDI via Ag/AgCl electrodes (1 cm in diameter) positioned respectively over the motor point of the muscle and the metacarpo-phalangeal joint of the index finger. The reference electrode was attached over a bony prominence on the distal part of the radius. Signals were band-pass filtered (30–1000 Hz), and amplified (gain \times 200–1000) by a Grass (P511) amplifier. EMG data were sampled at 5000 Hz by a 12 bit National Instruments board (AT-MIO-16E-10) and saved to disk.

Maximal compound muscle action potentials (maximal M waves) were elicited by surface electrical stimulation of the ulnar nerve. A Digitimer DS7A constant-current stimulator applied current to the nerve via Ag/AgCl electrodes fixed just proximal to the wrist. The intensity of stimulation was increased from a subliminal level until there was no increase in the peak-to-peak magnitude of the M wave with increasing intensity. For the stimulations that were recorded, the output of the stimulator was set to 1.5 times the current required to elicit a maximal response. Eight maximal M waves were recorded in a single trial at the beginning and at the end of the experiment. The interstimulus interval was randomly varied between 6 and 8 s during each trial.

Transcranial stimulation procedures

MEPs were elicited via a Magstim 200 magnetic stimulator with a figure of eight coil (outside diameter of each loop = 7 cm) and a Digitimer D180A electrical cortical stimulator (output 0–1200 V). For TMS, the stimulating coil was oriented so that the axis of intersection between the two loops was oriented at approximately 45 deg to the sagittal plane. It was anticipated that this arrangement induced posterior-to-anterior current flow across the motor strip in the primary motor cortex. The optimal position for eliciting MEPs in the contralateral FDI was established and marked directly on the scalp. The lowest stimulation intensity at which potentials of peak-to-peak amplitude greater than 50 μV were evoked in at least three out of five trials was taken as the passive threshold. During threshold determination and all subsequent passive trials, auditory feedback of the EMG signal was provided to the participants at high gain. MEPs were not considered for threshold determination if muscle activity was detected prior to the stimulus. During the trials conducted at rest, 10 stimuli were applied at the following levels: 0, 5, 10, 15, 20, 30 and 40 % of the stimulator output above the threshold intensity, at 100 % of the stimulator output, and at 5 % of the stimulator output below threshold. MEPs were recorded in three successive trials comprising 3, 3 and 4 stimuli (for a total of 10 stimuli) at each intensity. At least 2 min was allowed between successive trials. The stimulation intensities were randomly ordered within each trial and the interstimulus interval was randomly varied between 6 and 8 s. Care was taken to ensure that the coil was held at the correct position on the scalp before each trial by verifying that stimulation at the passive threshold evoked a small response.

Following the passive trials, the TMS and TES intensities required to elicit MEPs of between 250 and 450 μV while the participants exerted torque at 2 % of their MVC were determined. It was not possible to obtain MEPs of lesser amplitude than 250 μV that could be reliably distinguished from the background EMG, even when responses were averaged over a number of trials. TES and TMS intensities were adjusted until the mean amplitudes of 10 MEPs evoked by each form of stimulation were within 50 μV of each other. These stimulus intensities were used for all subsequent trials. For TES, cup electrodes (8 mm diameter, gold-plated) were fixed to the scalp with an adhesive and filled with conducting gel. The cathode was placed on the vertex and the anode was placed over the left hemisphere 7 cm lateral to the vertex on the interaural line. Care was taken to ensure that participants were capable of relaxing their face, scalp and upper arm muscles during TES trials.

During the active trials, target torque levels were set at 5, 10, 20, 30, 40, 50 and 60 % of each participant's MVC. Two TMS and two TES stimuli were applied at each level of contraction in each of five trials. The TES and TMS were randomly intermingled and the order in which the targets were presented was also random. The interstimulus interval was varied randomly between 7 and 9 s. At the beginning of each trial, the target on the torque-feedback indicator was set to 5 % MVC below zero. Participants were instructed to relax during this time. After approximately 3 s, the target was set to the required torque level (5–60 % MVC). The participants were required to steadily increase finger abduction torque to the level of the target and then to maintain torque as close as possible to the target until they received a transcranial stimulus. The target was typically acquired within 2 s of its presentation. Either TMS or TES was delivered 4–6 s after the target was presented. After stimulation, the target was set to 5 %

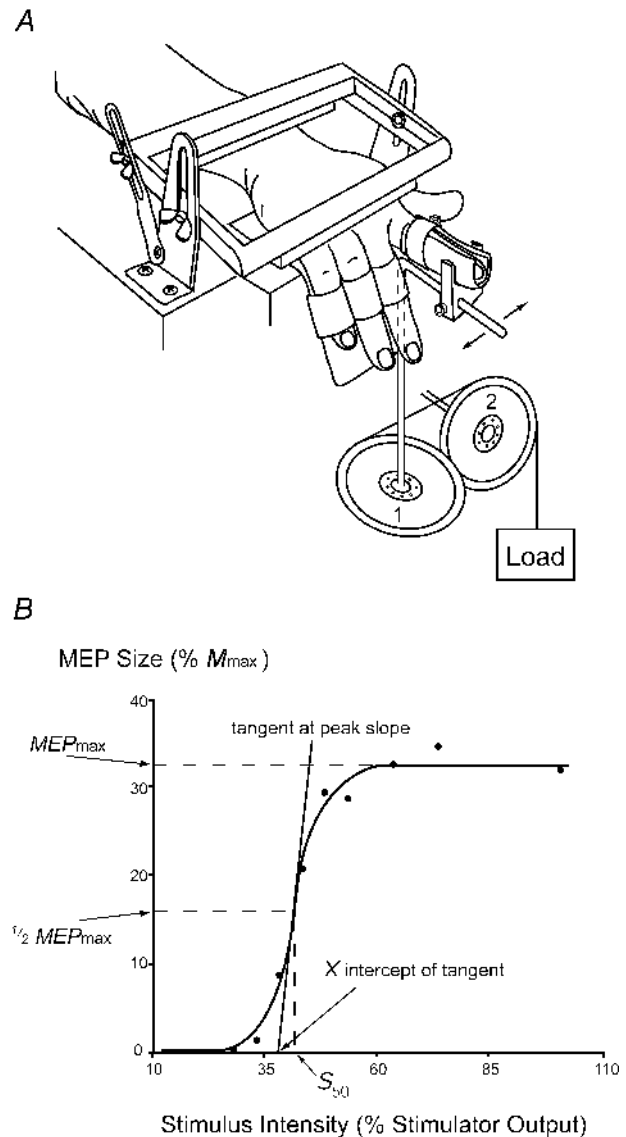


Figure 1. The experimental set-up and plot of motor evoked potential (MEP) size versus stimulus intensity for a single individual

A, the device used to restrain the hand during the experiments and to apply loads during resistance training. The finger made contact with the horizontal section of the L-shaped main shaft. The vertical section of the shaft was fixed in series with pulley 1, which rotated in the horizontal plane. An inextensible wire was fixed between pulley 1 and pulley 2. Pulley 2 was oriented in the vertical plane. Weights were hung from an additional wire that was attached to pulley 2. During training, a potentiometer was aligned in series with pulley 1. For static trials in the experiments, the wire between pulleys 1 and 2 was disconnected and a torque transducer was aligned in series with pulley 1. B, an example of a sigmoid fit to an MEP size versus stimulus intensity plot for an individual participant. The peak slope of the function is its tangent at S_{50} . MEP_{max} , maximal MEP amplitude; M_{max} , maximal M-wave amplitude. Adapted with permission from Elsevier Science from Carroll *et al.* (2001b).

MVC below zero, and the participant was instructed to relax until the next target was presented.

Data processing

Each recording was inspected at high resolution to identify the beginning and end of the MEP or M wave. For the passive trials, the EMG trace prior to the stimulus was also examined. Any trials containing EMG activity were excluded from further analysis. The response latency and duration, the peak-to-peak amplitude of the evoked potentials, the integral of the full-wave-rectified evoked potentials and the root mean square (r.m.s.) of the EMG signal from 45 to 5 ms prior to the stimulus were obtained. We subsequently report MEP size as the peak-to-peak amplitude of the evoked responses; however, in all cases, the results based upon the integral of the rectified MEPs were comparable to those that are reported for the peak-to-peak amplitude. As a further precaution against the inclusion of responses in which there was voluntary muscle activity, only resting trials in which the r.m.s. of the EMG from 45 to 5 ms prior to the stimulus was lower than a criterion level were included for further analysis. The maximum acceptable r.m.s. EMG level was determined independently for each experimental session, and was based on the amplitude of the electrical noise in the raw EMG traces. The criterion was typically set between 5 and 10 μV . All EMG recordings are expressed as a percentage of the magnitude of the maximal M wave.

For the passive trials, the mean amplitude was determined for the MEPs at each stimulus intensity. Stimulus intensity was plotted against response magnitude, and the data were fitted with the following three parameter sigmoid function:

$$\text{MEP}(s) = \frac{\text{MEP}_{\max}}{1 + e^{m(S_{50} - S)}}$$

where MEP_{\max} is the maximum MEP defined by the function, m is the slope parameter of the function, S is stimulus intensity and S_{50} is the stimulus intensity at which the MEP size is 50% of the maximal MEP. This equation is a variation of the logistic equation (MacMillan & Creelman, 1991), and is identical to a sigmoid equation that has been used previously and referred to as the 'Boltzmann equation' (Capaday, 1997; Devanne *et al.* 1997; Capaday *et al.* 1999; Kealin-Lang & Cohen, 2000). We have demonstrated previously that the parameters of this equation can be obtained reliably in testing sessions conducted on different days (Carroll *et al.* 2001b). We obtained four variables from the function in order to characterise the input-output properties of the corticospinal pathway. The slope parameter of the sigmoid function was taken as a general measure of the excitability of the pathway. This variable describes the rate of increase in response magnitude relative to the maximal MEP size, with increasing stimulus intensity. We also calculated the peak slope of the function to provide an indication of the maximal rate of increase in MEP magnitude with stimulus intensity (see Fig. 1B). The maximum response magnitude of the sigmoid function (i.e. function parameter MEP_{\max}) was taken as an indication of the peak of the input-output relationship. The variable obtained from the input-output function that indicated the stimulus intensity necessary to elicit a threshold response was the stimulus intensity defined by the X intercept of the tangent to the function at the point of maximal slope (i.e. at S_{50}).

The peak-to-peak amplitude of individual MEPs recorded during active trials was plotted against both the r.m.s. of the EMG activity (normalised to maximal M-wave amplitude, M_{\max}) and the

average finger abduction torque from 45 to 5 ms prior to the stimulus. Individual MEPs were not plotted if they could not be clearly discriminated from the background EMG activity. A similar proportion of the total number of responses collected was included in the analysis before (pre) and after (post) training (pre = 82.3%, post = 84.5%). The average MEP at each target force level was also calculated so that comparisons could be made between the responses obtained before and after training.

Statistics

Parameters of the linear regression and sigmoid equations were analysed via repeated-measures ANOVA with planned comparisons between pre- and post-training for each group. TES and TMS data were analysed separately. Mean MEP magnitudes obtained during the active trials were analysed via repeated-measures ANCOVA with mean finger abduction torque (relative to MVC) recorded at each level of contraction as the covariate. The ratios of MEP amplitude to the r.m.s. EMG or absolute torque in the period immediately prior to the stimulus at each target torque level were analysed via repeated-measures ANOVA. Planned comparisons were made between the data obtained at pre- and post-training for each target level of contraction and group. Effect sizes (f) were calculated following Cohen (1969). Effect sizes of 0.2, 0.5 and 0.8 indicate small, moderate and large effects, respectively. Data are presented as means \pm S.D.

RESULTS

The isometric strength of the index finger abductors increased significantly in response to resistance training (pre = 2.21 ± 0.66 Nm, post = 2.95 ± 0.95 Nm; 33.4% increase, $f = 1.20$, $P < 0.05$), but not to unresisted training (pre = 2.20 ± 0.62 Nm, post = 2.47 ± 0.40 Nm; 12.3% increase, $f = 0.44$, $P = 0.09$). The peak torque elicited in response to a supramaximal stimulus of the ulnar nerve was not significantly affected by resistance training (pre = 0.074 ± 0.053 Nm, post = 0.083 ± 0.033 Nm; 12.6% increase, $f = 0.19$, $P > 0.2$).

The relationship between MEP magnitude and stimulus intensity during the passive trials was clearly sigmoidal, both before and after training (see Fig. 1B and Carroll *et al.* 2001b for examples of sigmoid fits to MEP size *versus* stimulus intensity relationships for individual subjects). The median proportion of the variance accounted for by the sigmoid fit was 97% on both occasions. None of the input-output parameters of the corticospinal pathway at rest were significantly affected by either training intervention (Table 1). In all cases, the effect sizes for the comparisons between values obtained before and after training were below 0.34.

The latency of the responses to TES during background contraction was significantly shorter than that for TMS responses (TES latency = 21.5 ± 1.4 ms; TMS latency = 23.4 ± 1.4 ms; $P < 0.05$; Fig. 2A). The linear regressions of MEP size on absolute torque accounted for 61% of the variance for TMS MEPs and 49% of the variance for TES MEPs. The slope of the relationship between MEP

Table 1. The effect of training on the input–output parameters of the corticospinal pathway at rest

Training group		RT	UT
Slope parameter (<i>m</i>)	Pre	0.20 ± 0.05	0.28 ± 0.15
	Post	0.18 ± 0.06	0.25 ± 0.13
MEP _{max} (% <i>M</i> _{max})	Pre	18.23 ± 11.09	22.83 ± 12.32
	Post	16.58 ± 10.24	26.62 ± 13.04
Peak slope (% <i>M</i> _{max} % stimulator output ⁻¹)	Pre	0.94 ± 0.61	1.67 ± 1.45
	Post	0.78 ± 0.62	1.97 ± 2.04
X intercept of peak slope (% stimulator output)	Pre	37.65 ± 8.33	44.25 ± 10.98
	Post	38.51 ± 9.02	41.66 ± 8.60
Threshold (% stimulator output)	Pre	38.63 ± 7.09	39.38 ± 6.05
	Post	37.00 ± 7.78	38.88 ± 6.47

Mean ± s.d. values for the input-output parameters of the corticospinal pathway under resting conditions before (Pre) and after training (Post) for the two groups. UT = unresisted-training group, RT = resistance-training group, MEP_{max} = maximal motor evoked potential, *M*_{max} = maximal M-wave amplitude.

amplitude and the absolute torque exerted immediately prior to both the TMS and TES stimuli was significantly lower following training for the resistance-training group (TMS: pre = 24.7 ± 17.8 % *M*_{max} Nm⁻¹, post = 15.3 ± 4.3 % *M*_{max} Nm⁻¹, *f* = 0.83, *P* < 0.05; TES: pre = 28.5 ± 10.6 % *M*_{max} Nm⁻¹, post = 15.1 ± 11.8 % *M*_{max} Nm⁻¹, *f* = 0.73, *P* < 0.05) but not the unresisted-training group (TMS: pre = 22.5 ± 12.7 % *M*_{max} Nm⁻¹, post = 20.8 ± 7.6 % *M*_{max} Nm⁻¹, *f* = 0.14, *P* > 0.2; TES: pre = 27.8 ± 20.1 % *M*_{max} Nm⁻¹, post = 21.7 ± 14.2 % *M*_{max} Nm⁻¹, *f* = 0.34, *P* > 0.2; Fig. 2B). Similar results were obtained for comparisons of the relationship between EMG activity recorded in the period immediately prior to the stimulus and the MEP size (data not reported).

The linear regressions of MEP size *versus* background EMG activity and torque suggest that the functional properties of the corticospinal pathway were altered in response to resistance training, such that for a particular absolute level of background contraction, the magnitude of the compound EMG response to transcranial stimulation was smaller following training. However, it is conceivable that a change in the slope of the relationship between MEP amplitude and background contraction may have occurred due to adaptations that affect the input–output properties of the pathway over a relatively specific range of contraction levels. From inspection of the scatter plots of individual participants, it appeared that there was a greater disparity in MEP size before and after training at the higher levels of contraction. Furthermore, a reduction in the proportion of the variance accounted for by the linear regressions that approached statistical significance (Wilcoxon matched pairs, *P* < 0.1 for three out of four comparisons) was apparent for the resistance-training group after training. The important question is:

did the reduction in the magnitude of MEPs relative to EMG or torque occur over the entire range of background contraction levels?

In order to investigate directly the range of background contraction levels for which MEP size was reduced at a given absolute level of EMG or torque following resistance training, we expressed the average MEP size as a proportion of both the average EMG activity and the average absolute torque prior to the stimulus at each target level of torque. The ratio of MEP size to absolute torque was significantly reduced in response to resistance training at 40 and 50 % MVC for TES (40 % MVC, *f* = 0.95, *P* < 0.05; 50 % MVC, *f* = 1.34, *P* < 0.05) and at 40, 50 and 60 % MVC for TMS (40 % MVC, *f* = 0.53, *P* < 0.05; 50 % MVC, *f* = 0.67, *P* < 0.05, 60 % MVC, *f* = 1.08, *P* < 0.05) responses. Although the effects were only statistically significant at the high torque levels, reductions in the MEP size *versus* absolute torque ratios of similar magnitude were apparent at all of the target levels for both forms of stimulation (Fig. 3). The variability of the response magnitudes was higher at the low levels of contraction, as has been reported previously (e.g. Rothwell *et al.* 1991), and this probably contributed to the non-significant results. There were no large or statistically significant differences between pre- and post-training for the unresisted-training group. The comparisons between pre- and post-training for MEP amplitude expressed as a proportion of EMG activity followed a similar pattern.

In order to determine whether resistance training resulted in a decrease in MEP size at any individual contraction level relative to MVC, we plotted the average MEP magnitude at each of the target torque levels (Fig. 4). A plateau in the relationship between MEP amplitude and the target level of torque was apparent at the higher target

levels. The plateau occurred at a lower target torque for the resistance-training group following training for both TMS and TES responses. The amplitude of the responses to TMS and TES was also greater at 50 and 60 % MVC before training, although the effect only achieved statistical significance at 50 % MVC for TMS MEPs (TMS at 50 % MVC, $f = 1.01$, $P < 0.05$; at 60 % MVC, $f = 0.74$, $P = 0.06$; TES at 50 % MVC, $f = 0.59$, $P = 0.11$; at 60 % MVC, $f = 0.69$, $P = 0.14$). None of the changes in MEP size at the target torques of 40 % MVC and below were statistically

significant, and the effect sizes were all lower than 0.35 (except for TMS at 5 % MVC, $f = 0.51$). The magnitude of evoked responses to TMS and TES was therefore similar before and after training when the comparison was made on the basis of the torque exerted relative to MVC, although there was a tendency towards a reduction in MEP amplitude at the higher torques. These data further illustrate that for a particular absolute level of torque or EMG activity, the MEP size was reduced following training over the entire range of contraction strengths investigated,

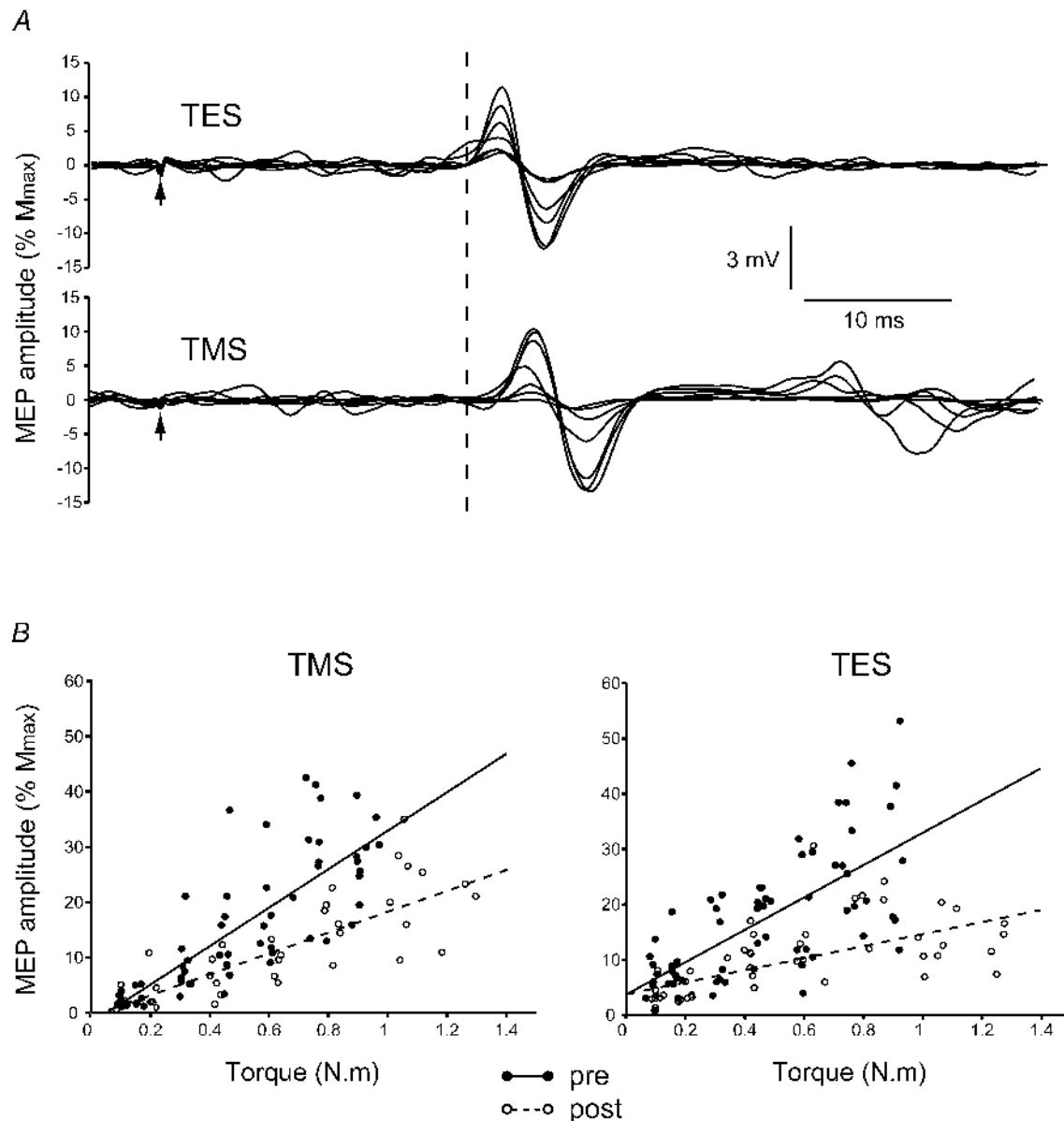


Figure 2. Responses to transcranial magnetic (TMS) and electrical (TES) stimulation at various levels of voluntary contraction

A, mean MEPs recorded in response to TMS and TES at each of the levels of voluntary contraction for an individual participant. The small arrows illustrate the stimulus artefacts. Note that the onset latency, specified by the dashed line, is approximately 2 ms shorter for the TES responses. B, linear regressions of MEP amplitude on the absolute torque exerted from 45 to 5 ms prior to the stimulus for an individual participant in the resistance-training group before (pre) and after training (post) for the two methods of stimulation.

since both the absolute torque exerted and the EMG activity recorded at each target torque level were considerably greater after training. The absolute torque exerted was significantly greater following resistance training at all target levels ($P < 0.05$; $f_{range} = 0.76\text{--}1.30$).

DISCUSSION

Our results demonstrate that a programme of resistance training that increases strength also alters the input–output properties of the corticospinal pathway. In particular, the slope of the linear regressions of MEP size on the level of background torque exerted prior to the stimulus was smaller following training for both TMS and TES responses. Furthermore, the ratios of MEP size to absolute torque and background EMG activity were considerably smaller for the entire range of contraction strengths investigated after resistance training, although the differences were only statistically significant at the higher target torques (i.e. 40, 50 and 60 % MVC, see Fig. 3). These results indicate that at each of the levels of muscle

contraction investigated in the present experiment, the magnitude of the compound EMG response to transcranial stimulation was smaller following resistance training.

The observation of a reduction in MEP amplitude at a particular level of background contraction in response to resistance training implies either that fewer motoneurons were activated by the descending volleys, or that a greater degree of cancellation of motor unit action potentials occurred at the muscle membrane following training. In relation to the second possibility, it is now well established that maximal MEP amplitudes are considerably smaller than M_{max} , even though maximal MEPs recruit nearly all of the motor units within a muscle (Magistris *et al.* 1998; Bühler *et al.* 2001). The amplitude of maximal MEPs is smaller because the firing time of each of the motoneurons that are activated by a descending corticospinal volley elicited by transcranial stimuli varies by a few milliseconds (e.g. Olivier *et al.* 1995). The variation in the precise time of motoneurone firing results in an asynchronous arrival of motoneurone action potentials at

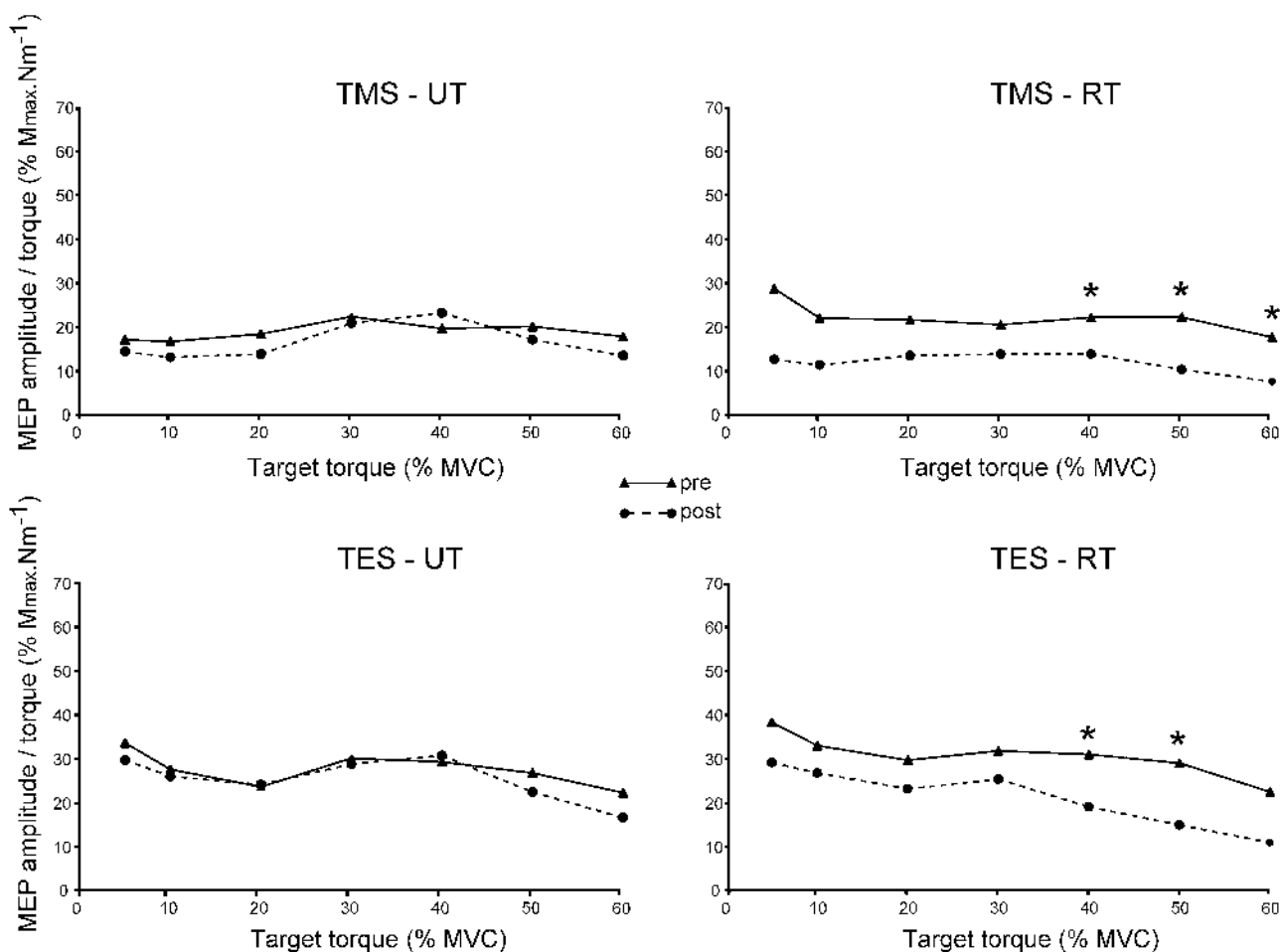


Figure 3. Mean ratios of MEP amplitude divided by the absolute torque versus target torque

Mean ratios of MEP amplitude divided by the absolute torque exerted from 45 to 5 ms prior to the stimulus at each target torque level before and after training for the two methods of stimulation and the two training groups. UT, unresisted-training group; RT, resistance-training group. * Significant difference pre-training versus post-training ($P < 0.05$).

the neuromuscular junction, which ultimately leads to phase cancellation of the motor unit action potentials that are recorded at the muscle membrane. An increase in the degree of phase cancellation seems an implausible explanation for the changes in MEP amplitudes during background contraction seen in the present experiment, as there was no reduction in the magnitude of the maximal MEP or slope of the input–output relationship at rest. Any changes in the shapes of the motor unit action potentials or in the distribution or strength of corticospinal inputs to the motoneurone pool, that could influence the degree of phase cancellation, would affect MEP size both at rest and during background contraction.

The alternative explanation for the reduction in MEP amplitude at a particular level of background contraction following resistance training is that fewer motoneurons were activated by the descending corticospinal volleys arising from transcranial stimulation. It is possible that fewer motoneurons were recruited after resistance training because of a reduction in the magnitude of the descending volleys. If this were the case, it would imply that resistance training caused a reduction in the relative

excitability of corticospinal cells for a particular level of muscle activity. Although we cannot exclude the possibility that resistance training has the capacity to alter corticospinal cell excitability, this alternative cannot account for our results, because the reduction in the gain of the relationship between MEP size and background activity was of similar magnitude for TES and TMS responses. Furthermore, the degree of reduction in the ratios of MEP magnitude to both the absolute torque exerted and the background EMG activity was also comparable for the TMS and TES responses. The latency of the responses to TES was approximately 2 ms shorter than that for TMS responses (Fig. 2A), which suggests that an additional synapse was involved in the conduction of descending volleys elicited by TMS to the periphery compared with TES. This confirms that at the stimulus intensities used in our experiment, much of the peripheral response to TES originated from a D wave that would be unaffected by changes in cortical excitability (Di Lazzaro *et al.* 1999). The balance of evidence suggests, therefore, that a large proportion of the effect of resistance training on MEP amplitude in the present experiment was due to changes in the functional properties of circuitry within the spinal

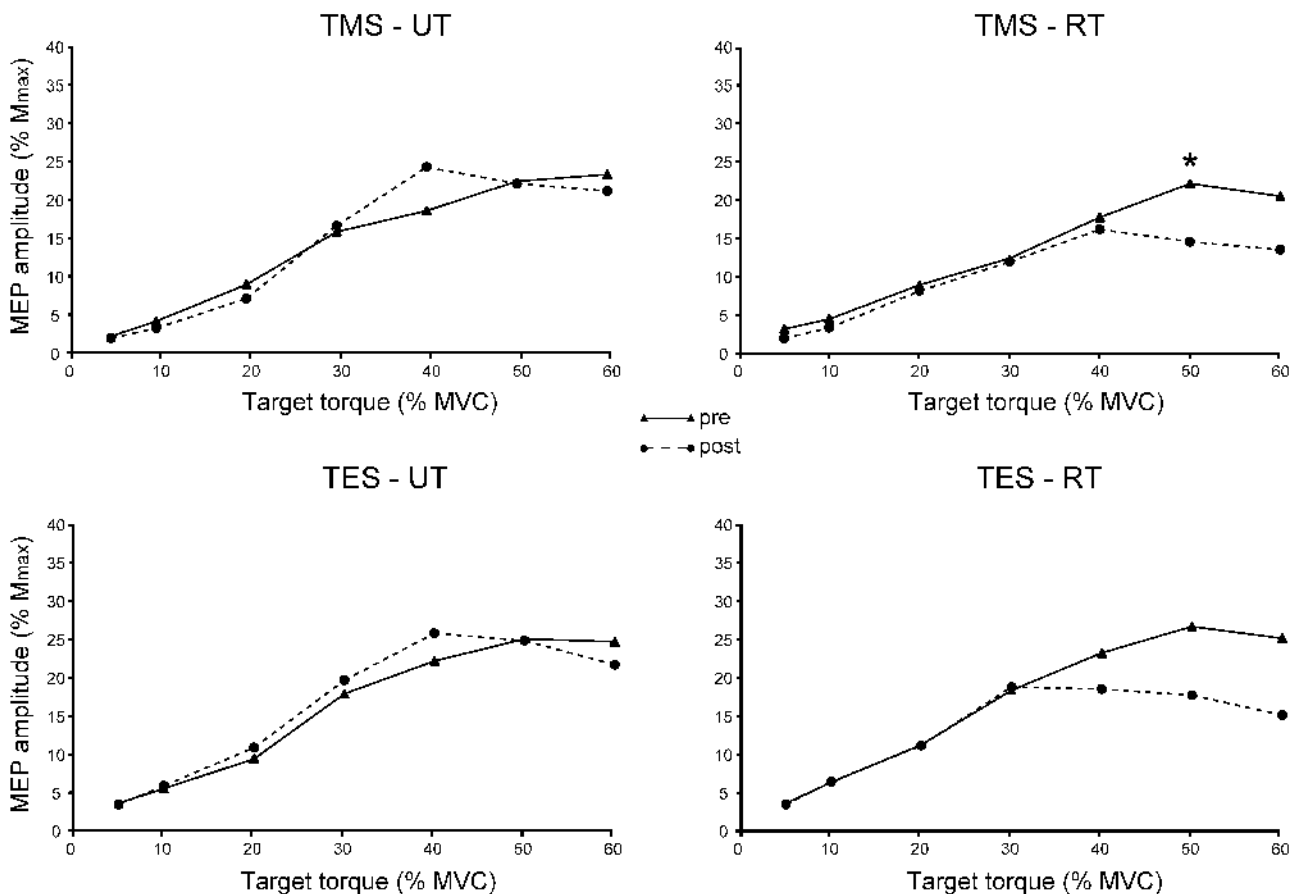


Figure 4. Effect of training on mean MEP amplitude at each target torque level

Mean MEP amplitude at each target torque level before and after training for the two methods of stimulation and the two training groups. * Significant difference pre-training *versus* post-training ($P < 0.05$).

cord. Specifically, resistance training altered the organisation of the central nervous system such that a corticospinal input of a given magnitude activated fewer motoneurons during muscle contraction than were recruited prior to training.

There are a number of possible mechanisms that could underlie a reduction in the number of motor units activated by transcranial stimulation for a given level of background contraction. These include: changes in the efficacy of synapses between corticospinal cells and motoneurons, changes in the influence of interneuronal circuitry on the descending volleys or the excitability of the motoneurons, or alterations to the intrinsic properties of the motoneurons themselves. The lack of change in the properties of the corticospinal pathway at rest, however, suggests that the adaptation underlying changes in MEP size during activity is specifically associated with the neural processes that operate during muscle contraction. This would mitigate against the possibility that adaptations that affect the transmission of impulses across corticomotoneuronal synapses or the difference between the resting membrane potential and firing threshold of motoneurons contributed to the reductions in MEP size for a given level of background contraction, since these factors would be expected to change the input–output properties of the pathway at rest. More likely explanations are an increase in the inhibitory effect of interneuronal circuitry on the descending volleys or motoneurons, or changes in the intrinsic firing properties of motoneurons that reduced their responsiveness to a given synaptic input during tonic firing. Since Nielsen & Petersen (1994) found no evidence that ‘classical’ presynaptic inhibition occurs at the synapses between corticospinal fibres and soleus muscle motoneurons, any inhibition of the descending corticospinal volleys is likely to act via the parts of the volley that are transmitted to the motoneurons via non-monosynaptic pathways. In this respect, it is clear that corticospinal transmission to motoneurons is influenced by activity in di- and oligosynaptic pathways (see McCrea, 1992; Peirrot-Dessigney, 1996 for reviews). In particular, both inhibitory (Cowan *et al.* 1986) and excitatory (Burke *et al.* 1994; Mazevet *et al.* 1996; Alstermark *et al.* 1999) disynaptic pathways are thought to affect the responses to cortical stimulation in human upper limbs, although the importance of the excitatory pathways is the subject of considerable debate, especially for primate hand muscles (Porter & Lemon, 1993; Maier *et al.* 1998; Olivier *et al.* 2001). It is also conceivable that interneuronal circuits could exert a postsynaptic inhibitory influence on motoneurons that receive some excitatory input but are not firing tonically, and thereby reduce the magnitude of the MEP.

In order to understand how changes in the intrinsic firing properties of motoneurons could affect their responsiveness

to a given level of excitatory drive, it is necessary to consider the biophysical factors that determine the response of motoneurons to a particular synaptic input. These factors were recently discussed in detail by Matthews (1999). Information sufficient only to support our argument is presented in brief here. The response properties of a motoneuron are determined by the difference between its resting membrane potential and firing threshold potential, as well as the input resistance of the membrane and the amount of synaptic current applied to it. The trajectory of the membrane’s after-hyperpolarisation potential also has an important influence on the response characteristics of a motoneuron during tonic firing. The response probability of a motoneuron to a test stimulus increases as it receives excitatory input in a sigmoidal manner, and either falls or reaches a plateau when it begins to fire (Matthews, 1999). Thus, if we consider the response of a group of motoneurons with a similar recruitment threshold, the greatest response to a test stimulus of any intensity will occur when the highest number of motoneurons receive a level of excitatory drive that is just insufficient to induce tonic firing (i.e. when the ‘subliminal fringe’ is largest).

When the motoneuron is firing tonically, computer simulations (Jones & Bawa, 1997; Matthews, 1999) and experiments (Kudina, 1988; Piotrkiewicz *et al.* 1992; Jones & Bawa, 1995; Olivier *et al.* 1995) have shown that for a test stimulus of given magnitude, the firing probability is greatest at the lowest firing frequencies. There exists some controversy regarding the range of firing frequencies over which this inverse relationship between firing rate and probability of firing will hold. However, the important conclusion in the present context is that for a test stimulus of given magnitude, the response of a group of motoneurons that are firing at a range of frequencies will be inversely related to the mean firing rate. When the responses of motoneurons with different membrane characteristics are considered, the trajectory of the membrane after-hyperpolarisation potential also has a strong influence on firing probability. For two motoneurons firing at the same rate, the probability of firing in response to a test stimulus will be greater for the neuron with an after-hyperpolarisation potential of shorter duration or lower magnitude (Jones & Bawa, 1997). This is because decreasing the time constant of the after-hyperpolarisation potential increases the proportion of time that the membrane potential is close enough to threshold for the test stimulus to initiate an action potential.

The previous discussion indicates that the reduction in MEP size that we observed at a specific level of contraction could have been caused by changes in the firing rate of motoneurons and/or their intrinsic firing properties.

Either an increase in firing rate or an increase in the duration or amplitude of the after-hyperpolarisation potential trajectory would reduce the response probability of individual motor units and therefore reduce the magnitude of the compound MEP. Furthermore, changes in the after-hyperpolarisation potential trajectory of motoneurons have been identified previously in response to motor training. Carp & Wolpaw (1994) reported both that the firing threshold potential for motoneurons and the amplitude of the after-hyperpolarisation potential were increased in primates that were exposed to an H-reflex conditioning protocol. Similarly, Beaumont & Gardiner (2002) found that the slow-type motoneurons of rats that engaged in daily treadmill running for 12 weeks had greater after-hyperpolarisation potentials than those of sedentary controls. Although these experiments involved 3–6 months of training that was very different to the training performed in the present experiment, their data confirm that the intrinsic properties of motoneurons exhibit the potential for adaptation in response to motor training.

An additional observation that follows from the discussion of factors that determine the response properties of motoneurons to a test stimulus is that the level of contraction at which the entire population of motor units receiving input from the transcranial volley had been recruited was lower after training. This is because the MEP with the greatest magnitude should occur when all of the motoneurons that receive input from the transcranial stimulus are receiving excitatory input, but the size of the subliminal fringe comprising the highest threshold motoneurons is maximal. The peak MEP occurred at approximately 50 % MVC before training (Fig. 4), which is consistent with previous reports that suggest that almost all FDI motor units are tonically active by approximately 50 % of the MVC, and further increases in torque are achieved via increasing the rate of motor unit firing (Milner-Brown *et al.* 1973; De Luca *et al.* 1982, 1996; Spiegel *et al.* 1996). Since the peak MEP occurred at a lower percentage of MVC following resistance training (30–40 % MVC; Fig. 4), there is evidence that the level of contraction at which the entire population of motor units receiving input from the transcranial volley had been recruited was lower after training.

We found that resistance training increased the strength and changed the input–output properties of the corticospinal pathway. The question remains as to whether the particular mechanisms underlying the corticospinal effects were related to the increases in strength. The lack of substantial change in the twitch torque recorded in response to supramaximal stimulation of the ulnar nerve suggests that the strength increase was not solely due to changes in the intrinsic ability of the muscle fibres to

generate force. However, the evidence is not beyond question, because the ulnar nerve innervates both the dorsal and palmar interossei. The net torque recorded about the second metacarpo-phalangeal joint will therefore be the difference between the abduction and adduction forces generated respectively by the dorsal and palmar interossei. Although this means that the twitch torque effects that we observed were not solely due to the properties of the FDI, our results indicate that the intrinsic force-generating capacity of the finger abductors did not change significantly relative to that of the index finger adductors. Since the finger abductors were the focus of the resistance-training programme, this suggests that an increase in the intrinsic force-generating capacity of the trained muscles is unlikely to completely account for the increase in strength. Although this suggests that some other, probably central, factor was responsible for the strength changes, it is not possible to determine whether these central adaptations were related to those underlying the changes in MEP size.

In summary, the results of the present experiment demonstrate that resistance training alters the functional properties of the corticospinal pathway in humans. We found that the magnitude of the evoked responses to transcranial stimulation was reduced for a given absolute level of torque or EMG activity following resistance training. The findings suggest that resistance training causes changes in the organisation of the synaptic circuitry in the spinal cord, but does not substantially affect the functional properties of the motor cortex. The results extend those of recent animal studies in which it was suggested that the repetitive execution of simple or well-learned movements has little impact on the organisation of the motor cortex (Plautz *et al.* 2000) and that the degree of cortical adaptation that accompanies motor learning is similar regardless of whether the training movements are executed against small or large resistances (Rempel *et al.* 2001). The present data suggest that the reorganisation of the corticospinal motor pathway that occurs in response to the repetitive execution of simple movements against a large resistance is independent of that which occurs during motor learning.

REFERENCES

- ABERNETHY, P. J., JURIMAE, J., LOGAN, P., TAYLOR, A. W. & THAYER, R. (1994). Acute and chronic response of skeletal muscle to resistance exercise. *Sports Medicine* **17**, 22–38.
- ALSTERMARK, B., ISA, T., OHKI, Y. & SAITO, Y. (1999). Disynaptic pyramidal excitation in forelimb motoneurons mediated via C(3)–C(4). propriospinal neurons in the *Macaca fuscata*. *Journal of Neurophysiology* **82**, 3580–3585.
- BALDWIN, K. M. & HADDAD, F. (2001). Effects of different activity and inactivity paradigms on myosin heavy chain gene expression in striated muscle. *Journal of Applied Physiology* **90**, 345–357.

- BEAUMONT, E. & GARDINER, P. (2002). Effects of daily spontaneous running on the electro-physiological properties of hindlimb motoneurons in rats. *Journal of Physiology* **540**, 129–138.
- BÜHLER, R., MAGISTRIS, M. R., TRUFFERT, A., HESS, C. W. & ROSLER, K. M. (2001). The triple stimulation technique to study central motor conduction to the lower limbs. *Clinical Neurophysiology* **112**, 938–949.
- BURKE, D., GRACIES, J. M., MAZEVET, D., MEUNIER, S. & PIERROT-DESEILLIGNY, E. (1994). Non-monosynaptic transmission of the cortical command for voluntary movement in man. *Journal of Physiology* **480**, 191–202.
- CAPADAY, C. (1997). Neurophysiological methods for studies of the motor system in freely moving human subjects. *Journal of Neuroscience Methods* **74**, 201–218.
- CAPADAY, C., LAVOIE, B. A., BARBEAU, H., SCHNEIDER, C. & BONNARD, M. (1999). Studies on the corticospinal control of human walking. I. Responses to focal transcranial magnetic stimulation of the motor cortex. *Journal of Neurophysiology* **81**, 129–139.
- CARP, J. S. & WOLPAW, J. R. (1994). Motoneurone plasticity underlying operantly conditioned decrease in primate H-reflex. *Journal of Neurophysiology* **72**, 431–442.
- CARROLL, T. J., RIEK, S. & CARSON, R. G. (2001a). Neural responses to resistance training: implications for movement control. *Sports Medicine* **31**, 829–840.
- CARROLL, T. J., RIEK, S. & CARSON, R. G. (2001b). Reliability of the input-output properties of the corticospinal pathway obtained from transcranial magnetic and electrical stimulation. *Journal of Neuroscience Methods* **112**, 193–202.
- COHEN, J. (1969). *Statistical Power Analysis for the Behavioural Sciences*. Academic Press, New York.
- COWAN, J. M., DAY, B. L., MARSDEN, C. & ROTHWELL, J. C. (1986). The effect of percutaneous motor cortex stimulation on H reflexes in muscles of the arm and leg in intact man. *Journal of Physiology* **377**, 333–347.
- DE LUCA, C. J., FOLEY, P. J. & ERIM, Z. (1996). Motor unit control properties in constant-force isometric contractions. *Journal of Neurophysiology* **76**, 1503–1516.
- DE LUCA, C. J., LEFEVER, R. S., MCCUE, M. P. & XENAKIS, A. P. (1982). Behaviour of human motor units in different muscles during linearly varying contractions. *Journal of Physiology* **329**, 113–128.
- DEVANNE, H., LAVOIE, B. A. & CAPADAY, C. (1997). Input-output properties and gain changes in the human corticospinal pathway. *Experimental Brain Research* **114**, 329–338.
- DI LAZZARO, V., OLIVIERO, A., PROFICE, P., INSOLA, A., MAZZONE, P., TONALI, P. & ROTHWELL, J. C. (1999). Effects of voluntary contraction on descending volleys evoked by transcranial electrical stimulation over the motor cortex hand area in conscious humans. *Experimental Brain Research* **124**, 525–528.
- DI LAZZARO, V., OLIVIERO, A., PROFICE, P., SATURNO, E., PILATO, F., INSOLA, A., MAZZONE, P., TONALI, P. & ROTHWELL, J. C. (1998a). Comparison of descending volleys evoked by transcranial magnetic and electric stimulation in conscious humans. *Electroencephalography and Clinical Neurophysiology* **109**, 397–401.
- DI LAZZARO, V., RESTUCCIA, D., OLIVIERO, A., PROFICE, P., FERRARA, L., INSOLA, A., MAZZONE, P., TONALI, P. & ROTHWELL, J. C. (1998b). Effects of voluntary contraction on descending volleys evoked by transcranial stimulation in conscious humans. *Journal of Physiology* **508**, 625–633.
- EDGLEY, S. A., EYRE, J. A., LEMON, R. N. & MILLER, S. (1997). Comparison of activation of corticospinal neurons and spinal motoneurons by magnetic and electrical transcranial stimulation in the lumbosacral cord of the anaesthetised monkey. *Brain* **120**, 839–853.
- ENOKA, R. M. (1997). Neural adaptations with chronic physical activity. *Journal of Biomechanics* **30**, 447–455.
- GANDEVIA, S. C. (2001). Spinal and supraspinal factors in human muscle fatigue. *Physiological Reviews* **81**, 1725–1789.
- JONES, K. E. & BAWA, P. (1995). Responses of human motoneurons to Ia inputs: effects of background firing rate. *Canadian Journal of Physiology and Pharmacology* **73**, 1224–1234.
- JONES, K. E. & BAWA, P. (1997). Computer simulation of the responses of human motoneurons to composite IA EPSPS: effects of background firing rate. *Journal of Neurophysiology* **77**, 405–420.
- KAELIN-LANG, A. & COHEN, L. G. (2000). Enhancing the quality of studies using transcranial magnetic and electrical stimulation with a new computer-controlled system. *Journal of Neuroscience Methods* **102**, 81–89.
- KUDINA, L. P. (1988). Excitability of firing motoneurons tested by Ia afferent volleys in human triceps surae. *Electroencephalography and Clinical Neurophysiology* **69**, 576–580.
- MCCREA, D. A. (1992). Can sense be made of spinal interneuron circuits? *Behavioral and Brain Sciences* **15**, 633–643.
- MACMILLAN, N. A. & CREELMAN, C. D. (1991). *Detection theory: A User's Guide*, p. 190. Cambridge University Press, Cambridge, UK.
- MAGISTRIS, M. R., ROSLER, K. M., TRUFFERT, A. & MYERS, J. P. (1998). Transcranial stimulation excites virtually all motor neurons supplying the target muscle. A demonstration and a method improving the study of motor evoked potentials. *Brain* **121**, 437–450.
- MAIER, M. A., ILLERT, M., KIRKWOOD, P. A., NIELSEN, J. & LEMON, R. N. (1998). Does a C3–C4 propriospinal system transmit corticospinal excitation in the primate? An investigation in the macaque monkey. *Journal of Physiology* **511**, 191–212.
- MARTIN, S. J. & MORRIS, R. G. (2001). Cortical plasticity: It's all the range! *Current Biology* **11**, R57–59.
- MATTHEWS, P. B. C. (1999). The effect of firing on the excitability of a model motoneurone and its implications for cortical stimulation. *Journal of Physiology* **518**, 867–882.
- MAZEVET, D., PIERROT-DESEILLIGNY, E. & ROTHWELL, J. C. (1996). A propriospinal-like contribution to electromyographic responses evoked in wrist extensor muscles by transcranial stimulation of the motor cortex in man. *Experimental Brain Research* **109**, 495–499.
- MAZZOCCHIO, R., ROTHWELL, J. C., DAY, B. L. & THOMPSON, P. D. (1994). Effect of tonic voluntary activity on the excitability of human motor cortex. *Journal of Physiology* **474**, 261–367.
- MILNER-BROWN, H. S., STEIN, R. B. & YEMM, R. (1973). Changes in firing rate of human motor units during linearly changing voluntary contractions. *Journal of Physiology* **230**, 371–390.
- MORITANI, T. (1993). Neuromuscular adaptations during the acquisition of muscle strength, power and motor tasks. *Journal of Biomechanics* **26**, suppl. 1, 95–107.
- NIELSEN, J. & PETERSEN, N. (1994). Is presynaptic inhibition distributed to corticospinal fibres in man? *Journal of Physiology* **477**, 47–58.
- OLDFIELD, R. C. (1971). The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* **9**, 97–113.
- OLIVIER, E., BAKER, S. N., NAKAJIMA, K., BROCHIER, T. & LEMON, R. N. (2001). Investigation into non-monosynaptic corticospinal excitation of macaque upper limb single motor units. *Journal of Neurophysiology* **86**, 1573–1586.
- OLIVIER, E., BAWA, P. & LEMON, R. N. (1995). Excitability of human upper limb motoneurons during rhythmic discharge tested with transcranial magnetic stimulation. *Journal of Physiology* **485**, 257–269.

- PIERROT-DESEILLIGNY, E. (1996). Transmission of the cortical command for human voluntary movement through cervical propriospinal premotoneurons. *Progress in Neurobiology* **48**, 489–517.
- PIOTRKIEWICZ, M., CHURIKOVA, L. & PERSON, R. (1992). Excitability of single firing human motoneurons to single and repetitive stimulation (experiment and model). *Biological Cybernetics* **66**, 253–259.
- PLAUTZ, E. J., MILLIKEN, G. W. & NUDO, R. J. (2000). Effects of repetitive motor training on movement representations in adult squirrel monkeys: role of use *versus* learning. *Neurobiology of Learning and Memory* **74**, 27–55.
- PORTER, R. & LEMON, R. N. (1993). *Corticospinal Function and Voluntary Movement*. Oxford University Press, Oxford, UK.
- REMPLE, M. S., BRUNEAU, R. M., VANDENBERG, P. M., GOERTZEN, C. & KLEIM, J. A. (2001). Sensitivity of cortical movement representations to motor experience: evidence that skill learning but not strength training induces cortical reorganization. *Behavioural Brain Research* **123**, 133–141.
- ROTHWELL, J. C., THOMPSON, P. D., DAY, B. L., BOYD, S. & MARSDEN, C. D. (1991). Stimulation of the human motor cortex through the scalp. *Experimental Physiology* **76**, 159–200.
- SALE, D. G. (1988). Neural adaptation to resistance training. *Medicine and Science in Sports and Exercise* **20**, S135–S145.
- SPIEGEL, K. M., STRATTON, J., BURKE, J. R., GLENDINNING, D. S. & ENOKA, R. M. (1996). The influence of age on the assessment of motor unit activation in a human hand muscle. *Experimental Physiology* **81**, 805–819.
- TIMSON, B. F. (1990). Evaluation of animal models for the study of exercise-induced muscle enlargement. *Journal of Applied Physiology* **69**, 1935–1945.

Acknowledgements

The authors thank Professor John Rothwell, Professor Simon Gandevia, Dr James Tresilian and Dr Guy Wallis for advice during the design of experiments and the preparation of the manuscript, and Ben Tathem, Andrew Lonergan, Jon Shemmel, Dr Victoria Galea, Benjamin Barry and Matthew Forner for assistance with data collection. The work was funded by the Australian Research Council.

Author's present address

S. Riek: Human Movement Studies Unit, Charles Sturt University, Bathurst, NSW 2795, Australia.