Exp Brain Res (2004) 159: 530–536
DOI 10.1007/s00221-004-1978-y

RESEARCH ARTICLES

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Different effects of fatiguing exercise on corticospinal and transcallosal excitability in human hand area motor cortex

Received: 8 April 2004 / Accepted: 5 May 2004 / Published online: 13 July 2004

Abstract Following forceful exercise that leads to muscle fatigue, the size of muscle evoked responses (MEPs) generated by transcranial magnetic stimulation (TMS) in the exercised muscle is depressed over a prolonged period. Strong evidence implicates intracortical mechanisms in this depression. As well as evoking MEPs in contralateral muscles, TMS also reduces MEPs evoked in ipsilateral muscles through interhemispheric inhibition mediated by a transcallosal pathway. Here we have sought to determine whether this effect is also depressed after exercise. Using two magnetic stimulators, the aftereffects of unilateral hand muscle exercise on the ability of TMS delivered to the hemisphere that generated the exercise were examined to i) generate MEPs in the exercised hand muscles, and ii) depress MEPs evoked by TMS pulses in contralateral (non-exercised) hand muscles. After exercise there was a significant reduction in the amplitudes of MEPs evoked by TMS in the exercised muscles ($p<0.001$). However, the same stimuli remained able to depress responses evoked by TMS to the contralateral hemisphere in the non-exercised muscles as effectively as before the exercise. We conclude that unlike the MEPs evoked by corticospinal output, interhemispheric inhibition evoked from the hemisphere that generated the exercise is not depressed after exercise. A similar differential effect on interhemispheric inhibition and corticospinal output has been reported recently for the effects of transcranial direct current (DC) stimulation of the motor cortex. Fatiguing exercise and transcranial DC stimulation may therefore engage similar intracortical mechanisms.

Keywords Corpus callosum · Interhemispheric inhibition · Intrinsic hand muscle · Motor cortex · Transcranial magnetic stimulation

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Introduction

During exercise, muscle responses to transcranial magnetic brain stimulation (TMS) are greatly enhanced, but beginning shortly after the cessation of fatiguing exercise the responses are substantially reduced for many minutes (e.g. Brasil-Neto et al. 1993, 1994; Zanette et al. 1995; Liepert et al. 1996; Gandevia et al. 1999). Several lines of evidence show that these are long-lasting changes in motor cortex excitability involving an intracortical process rather than a spinal process. After exercise, H-reflex responses and responses to transcranial electrical stimulation (TES), which can activate corticospinal neurones directly close to the soma or subcortically, do not show a prolonged depression (Brasil-Neto et al. 1993; Zanette et al. 1995; Gandevia et al. 1999), indicating that motoneuron excitability is not depressed, whereas TMS responses are. Using electrical transmastoid stimulation to activate corticospinal axons in the brainstem close to the cervicomedullary junction, Gandevia et al. (1999) described a brief depression of responses at spinal level, suggesting a potential synaptic depression at the terminals of corticospinal axons. However, this effect was relatively short lasting and responses returned to levels similar to control in less than 2 min, whereas the depression of TMS responses in the same experiments was much greater and much longer lasting.

A substantial part of the muscle response to TMS is generated by repetitive indirect activation of corticospinal axons either through intrinsic mechanisms or through presynaptic inputs (see Rothwell 1997; Di Lazzaro et al. 1999a). Direct evidence that the depression after exercise accompanies a reduction of intracortical excitability has been obtained from epidural recordings of these indirect responses to TMS (Di Lazzaro et al. 2003).

In this study we examined whether an additional effect of TMS, the inhibition of responses generated by stimulation of the contralateral hemisphere (Ferbert et al. 1992), is also depressed after exercise. A major component of this effect is interhemispheric inhibition, easily demonstrated with appropriately timed bilateral TMS pulses: muscle

evoked responses (MEPs) evoked by TMS pulses delivered to one hemisphere are reduced in amplitude by conditioning TMS pulses delivered 10–15 ms earlier to the contralateral hemisphere. Interhemispheric inhibition is generated by transcallosal connections, since it is absent or much reduced when the corpus callosum is absent or damaged (e.g. Meyer et al. 1995, 1998) and remains after subcortical lesions of the ipsilateral corticospinal tract that leave the callosal fibres intact (Boroojerdi et al. 1996). Direct evidence that the output of the contralateral cortex is reduced by interhemispheric inhibition was provided by Di Lazzaro et al. (1999b), who showed that epidurally recorded I-waves in the descending volleys evoked by TMS are depressed by preceding TMS stimuli delivered to the contralateral motor cortex.

Using bilateral TMS coils, we have examined the aftereffects of fatiguing exercise on the ability of TMS stimuli delivered to the hemisphere that generated the exercise to depress MEPs evoked by TMS delivered to the contralateral hemisphere, in the non-exercised hand. Responses in the intrinsic muscles of the left hand (evoked by TMS to the right hemisphere) were depressed over a period of more than 10 min after repetitive forceful contractions of the hand muscles. However, MEPs evoked in the homologous muscles of the right hand, which were not exercised but maintained a fixed low-level contraction, were depressed by interhemispheric inhibition as effectively as in the control period. These data resemble those recently obtained for direct current (DC) stimulation of the motor cortex (Lang et al. 2004).

Some of these results have been presented in an abstract (Winter and Edgley 2001).

Methods

Recordings

Experiments were performed on nine adult subjects (five male, four female, all right-handed, ages 21–42 years) with informed consent and Local Ethical Committee approval (University of Cambridge Human Biology Research Ethics Committee). Surface EMG recordings (bandpass 10 Hz to 2 KHz, gain 200–10,000) were taken from the thenar eminence and first dorsal interosseous (FDI) of both hands. In all of the experiments described the subjects performed the exercise with the left hand and generated weak steady forces with the right hand, in which interhemispheric inhibition was assessed. During the experiments the subjects were seated comfortably with the right forearm secured to a splint at the wrist with Velcro straps. The right hand was placed in a position such that the index finger could exert force on a strain gauge by abduction. Digits 3–5 of the right hand were fixed to the splint with Velcro straps, so that only forces exerted by the index finger could be recorded. Subjects were provided with a visual display of the forces exerted on the strain gauges on a screen and were required to maintain a fixed, low-level force (approximately 5% maximum force) throughout the experiment. In some experiments (n=5) the thumb also performed an abduction task against a lever; in others (n=4) it was relaxed. The left hand was relaxed except during the fatiguing task.

Stimulation

Two Magstim 200 stimulators (Magstim Company, Whitland, UK) were used to deliver TMS pulses. In both cases 55-mm figure-of-eight coils were used. The coils were fixed to a close-fitting motorcycle helmet from which large regions were cut out bilaterally over the fronto-parietal region permitting close access to the skull. Clamps with universal joints attached to the helmets held the coils in position. The helmet was strain relieved so that the subjects could sit comfortably for long periods without large stresses on the neck or back. Each coil was carefully positioned at the optimal position to evoke MEPs in the contralateral hand muscles before they were clamped in position. The coils were orientated so that the current flowed in an anteromedial direction, approximately 45% from the sagittal plane, and tangential to the skull. This direction evokes short latency MEPs close to threshold (see Sakai et al. 1997), and in our experience was the position at which threshold was lowest. Thresholds for evoking MEPs were determined during the weak contractions used to maintain low force level throughout the experiment and were always less than 40% of maximal stimulator output.

Test stimuli of 5–15% of stimulator output above threshold for evoking MEPs were delivered to the left motor cortex (range 35–48% stimulator output). The intensity was chosen as one that reliably evoked small MEPs in response to each stimulus. The MEPs evoked by these test stimuli were compared with MEPs evoked by trials in which conditioning stimuli were delivered to the right hemisphere. Conditioning stimuli were delivered 12 or 15 ms before the test stimuli and had intensities 30 or 40% of stimulator output above the threshold for evoking MEPs in left hand muscles during a weak contraction (range 63–77% of stimulator output). The conditioning stimulus intensities were selected to produce a consistent depression of test MEPs in the right hand.

Test (left hemisphere TMS) and conditioned (right hemisphere TMS followed 12–15 ms later by left hemisphere TMS) stimuli were delivered at interstimulus intervals of 5–8 s throughout the experiment. This low repetition rate limited the numbers of responses that could be gathered in each experiment, but was chosen since stimulation at shorter intervals can produce long-lasting depression of MEPs (see Chen et al. 1997; Muellbacher et al. 2000). We used the same conditioning stimuli (right hemisphere TMS) to assess both the post-exercise depression (of MEPs evoked in muscles of the left hand) and interhemispheric inhibition (the depression MEPs evoked by left hemisphere TMS in the non-exercised muscles of the right hand).

Exercise task

In the initial part of the experiment, test and conditioned stimuli were interleaved for a period of at least 10 min to ensure that both test and conditioned responses were consistent. At this point a fatiguing task was performed with the muscles of the left hand until the muscles were exhausted. The fatiguing task was then discontinued, the left hand relaxed, the sequence of test and conditioned stimuli resumed with the right hand muscles holding the same low-level contraction as before the exercise, and recordings continued for at least 20 min. In some initial experiments we used a static force generation exercise task, but in these small, short-lived and/or non-significant reductions in the size of the MEPs evoked in the left hand were seen. Consequently, in the main experiment we used a phasic exercise task where the subject was asked to repeatedly produce pincer grips against spring-loaded levers. In the open position the levers were separated by 10 cm, and with a forceful pinch grip they could be closed until the levers touched (finger separation 25 mm). Subjects were required to repeatedly close the levers at least once per second, until they were unable to generate sufficient force to fully close the levers. This task produced a strong sense of fatigue in the exercised muscles (thenar, intrinsic hand muscles and wrist muscles acting on the index finger).

Data sampling and analysis

Unrectified EMG data were sampled on-line (sampling rate 2.5 KHz) with Signal software (Cambridge Electronic Design Ltd). Off-line the EMG signals were rectified and the MEPs were quantified as the area under the rectified response. For analysis of grouped data, responses recorded for the 5-min period immediately preceding the exercise were compared with those from a 5-min period commencing 2 min after the end of the exercise task. We discarded the data from the first 2 min of relaxation after the fatiguing task, since Gandevia et al. (1999) showed that responses to transmastoid stimulation of corticospinal axons close to the cervicomedullary junction were depressed for up to 2 min after exercising: our assessment of the reduction in MEP size in the left hand muscles was therefore unlikely to be biased by this effect. Gandevia et al. (1999) also showed that the maximal M-wave could also be increased for a prolonged period after fatiguing exercise, and that a better estimate of MEP size after exercise would be to express MEP size as a proportion to the maximal M-wave amplitude. However, since we could obtain significant depressions of MEP amplitude post-exercise, we did not complicate the experiment with this additional measure.

To assess the effectiveness of the depression of responses in the non-exercised muscles of the right hand, the amplitudes of responses to conditioned stimuli were expressed as proportions of the amplitudes of responses to the preceding test stimulus. The depression of MEP amplitudes in individual cases was assessed by comparing the responses from the pre- and post-exercise

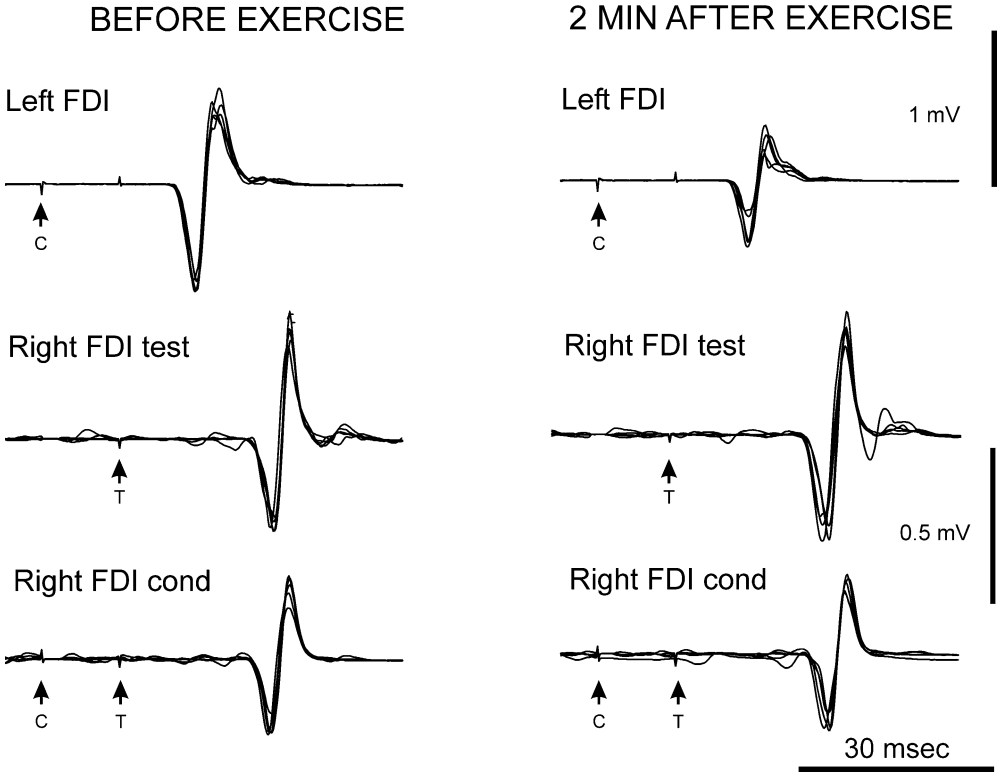

Fig. 1 Example MEPs from one experiment. Illustrative MEPs are shown from the pre-exercise (*left*) and post-exercise (*right*) periods. In each case five consecutive MEPs are overlaid. The *upper traces* show responses from the left FDI, which were evoked by the same stimuli that were used to evoke inter-hemispheric inhibition (stimulus at the *arrows* marked C). Two minutes after the exercise ended the amplitudes of these MEPs were depressed by about one third their initial values. The *middle set of traces* are unconditioned test responses recorded from the right FDI, evoked by TMS pulses delivered to the left hemisphere (stimulus at time T). The *lowermost traces* are conditioned responses recorded from the right FDI, in which conditioning stimuli delivered to the right hemisphere (at time C) preceded the test stimuli (at time T)

periods using Student *t*-tests, or if the data were not normally distributed, using Mann-Whitney Rank Sum Tests. Grouped data from pre- and post-exercise periods were compared using Student's paired *t*-tests.

Results

Depression of MEPs evoked in muscles after exercise

The design of these experiments depends on MEPs evoked in muscles of the left hand, driven from the right cortical hemisphere, being depressed after exercise. In all nine subjects the size of MEPs in the left FDI evoked by stimulation of the right cortex was significantly depressed during the 5-min period 2–7 min after exercise. The amount of depression varied between 8 and 62% (uncorrected for possible changes in maximal M wave size).

The *upper traces* in Fig. 1 show example MEPs recorded from the left FDI of one subject before and after exercise. In this case peak-to-peak amplitude of the pre-exercise MEPs were usually greater than 1 mV, being reduced to 0.7 mV or less after exercise, a reduction of approximately 30%. Changes in the amplitudes of individual MEPs in the left FDI before, during and after the exercise are shown in the *upper graph* of Fig. 2. The *grey bar* represents the time during which the exercise occurred and the MEPs are clearly larger during this period. The *horizontal lines* show the mean MEP amplitudes pre- and post-exercise; the MEP amplitude decreased by 35% after the exercise. Note that these were evoked by strong TMS stimuli, which were set at intensities 30–40% above threshold in order to reliably depress MEPs evoked by TMS of the left hemisphere. The post-exercise depression of the large MEPs evoked by these stimuli was proportionally smaller than the depression of MEPs evoked by stimuli closer to threshold. Nevertheless, in all experiments included there was a statistically significant reduction in MEP size. Comparing the values from individual subjects pre and post exercise the size of the MEPs was significantly reduced with a probability of <0.005 in all cases (Student's *t*-test or Mann-Whitney Rank Sum test). In the grouped data the reduction in the size of the MEPs after exercise was statistically significant (Paired *t*-test, $p<0.005$).

Effects of exercise on interhemispheric inhibition

The test MEPs evoked in the non-exercised right FDI and thenar muscles were considerably smaller and more variable in amplitude than the MEPs evoked by the conditioning TMS pulses in the left hand, since the stimuli were weaker (5–15% of stimulator output above MEP threshold). The conditioning stimuli produced a consistent reduction of the size of test MEPs, ranging in individual subjects from 8 to 86% in FDI and between 9 and 84% in thenar muscles, during the control (pre-exercise) period.

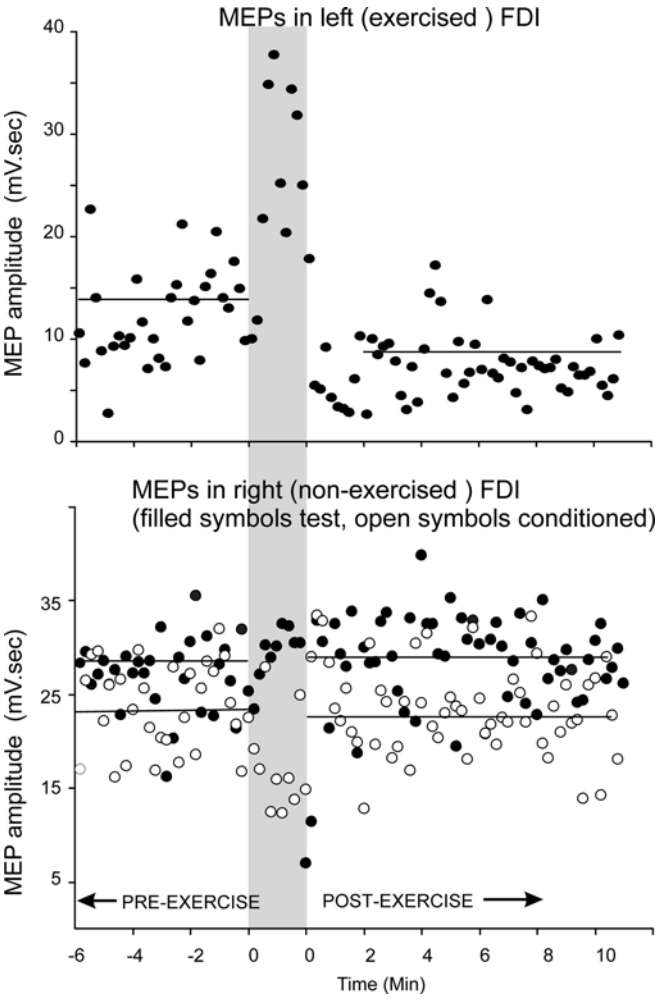

Fig. 2 MEP amplitudes followed through one experiment. Quantified MEP amplitudes (areas under rectified responses) are plotted through a period of 6 min before and 12 min after exercise (marked by the *grey bar*). The *upper graph* shows MEPs from the left FDI, which underwent the exercise. The *lower graph* shows the amplitudes of both test (*filled circles*) and conditioned (*open circles*) MEPs from the right FDI, which maintained a constant, low-level contraction. The *horizontal lines* show the mean MEP amplitudes for the pre- and post-exercise periods (excluding the first 2 min post-exercise)

Examples of test and conditioned MEPs from one subject, before and after the exercise are shown in the *lower traces* of Fig. 1. While the MEPs evoked in the exercised left FDI (*upper traces*) were clearly reduced after exercise, both the test and conditioned MEPs in the non-exercised right FDI and thenar muscles were similar in the pre- and post-exercise periods in the raw traces.

The quantified MEP amplitudes of individual responses from one experiment are shown in the *lower traces* of Fig. 2. Amplitudes of test MEPs (*filled circles*) and the conditioned MEPs (*open circles*) were of similar mean amplitude before and after the exercise. Comparisons of the test and conditioned MEP amplitudes for each subject showed no significant changes before and after exercise.

For group analysis we averaged the MEPs collected during a 5-min period preceding the exercising contrac-

tion, and compared these with values taken from a 5-min period beginning 2 min after the exercise ended. One problem with this type of analysis is that any changes in the size of the test MEPs with time, either caused by the exercising contraction in the contralateral hand, or occurring with changes in experimental conditions over time, could bias the results. For example, if the test MEPs were larger, they could include activity of different motoneurones and the effects of the conditioning stimulation may not be the same on all motoneurones—by analogy with the effects on conditioned H-reflexes (see Crone et al. 1990). However, for all nine subjects included in the study the test responses in the right FDI, which was maintained constant index finger abduction force, were not significantly different before and after exercise (Student's *t*-test or Mann-Whitney Rank Sum tests). Three other cases were excluded from the analysis because there were significant changes in test responses (an increase in two, a decrease in one).

The effectiveness of the conditioning stimuli before and after exercise is compared in Fig. 3. The *upper graph* plots the proportional reduction in amplitude of the MEPs evoked in the left (exercised) hand. The *lower graphs* plot the mean amplitudes of the conditioned MEPs, relative to the size of the test MEP (i.e. a reduction of an MEP to three quarters of its original size would give a value of 0.75) before and after exercise. There are no systematic trends in the data for the non-exercised muscles of the right hand. For the right FDI (*middle graph*) the amount of depression was less after exercise in five cases, but was greater in four cases. Before exercise, the mean ratio of conditioned to test responses was 0.60 (SEM 0.082), whereas after exercise the ratio was 0.615 (+SEM 0.065). These values are not significantly different (Student's paired *t*-test, p=0.78). For thenar muscles (*bottom graph*), the mean ratio of conditioned to test responses was 0.59 (SEM+0.084) before exercise and 0.60 (SEM+0.084) after exercise. Again these were not significantly different (Student's paired *t*-test).

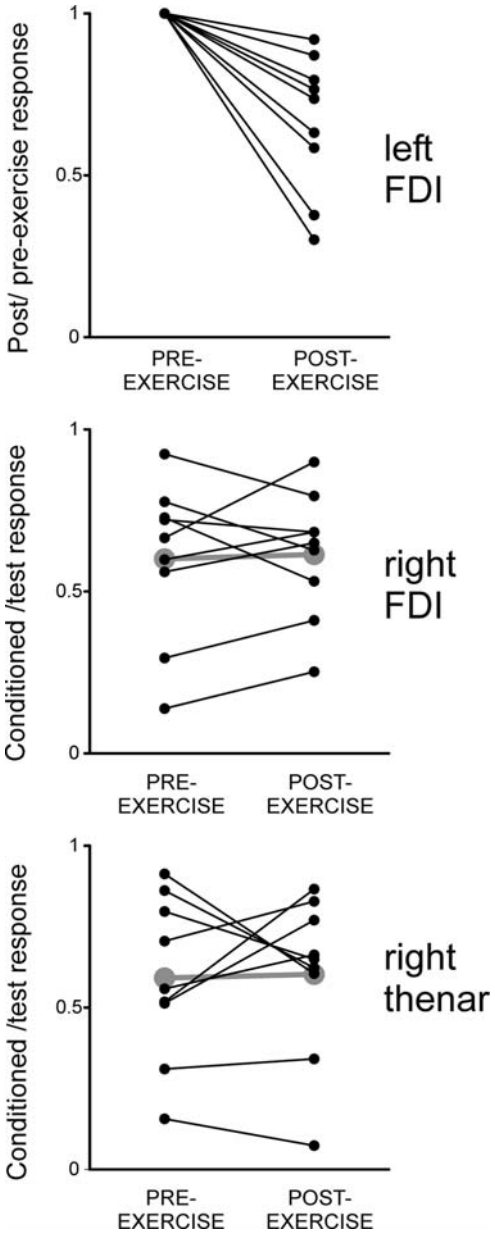

Fig. 3 Post-exercise changes in MEP amplitudes. The *upper graph* plots the depression of MEP amplitudes in left FDI after exercise, expressed as a proportion of the pre-exercise amplitude. The *lower plots* show the size of conditioned MEPs in the right hand muscles before and after exercise. In each case the conditioned response is expressed as a proportion of the mean test MEP amplitude. A decrease in interhemispheric inhibition would give higher values after exercise, and increase in interhemispheric inhibition would give lower values after exercise. The *thick grey lines* show the means of the grouped data

Discussion

The results of these experiments confirm that after fatiguing exercise of the muscles of the left hand, the responses generated in those muscles by TMS (to the right cortical hemisphere) are significantly reduced over a period of many minutes. In contrast, the same TMS pulses were still able to produce a depression of the MEPs evoked in contralateral non-exercised muscles that was not significantly different to the control values. The upshot of these experiments is therefore that the depression of TMS-evoked MEPs after exercise is evident in the circuitry generating corticospinal output destined for the contralateral muscles, but does not appear to be present in the circuitry that generates depression of responses to contralaterally applied TMS.

At first sight these results appear to differ from results described previously (Baumer et al. 2002), where a fatiguing task performed by the contralateral hand produced changes in intracortical facilitation and depression in the hemisphere contralateral to the one that generated the exercise (as measured by paired pulse TMS in the hemisphere contralateral to the one that generated fatiguing contraction). However, a key difference between these studies may be that in the present study responses in the non-exercised hand were obtained while the muscles

maintained a constant low level of force generation, rather than being relaxed. If changes in excitability of the cortex occurred, they may have been counteracted by an increased drive to maintain the constant force level. This was an important consideration, allowing interhemispheric inhibition to be assessed against constant motoneurone excitability levels (see Crone et al. 1990).

Since exercise does produce changes in the excitability of the hemisphere that generated the contraction, then changes in the contralateral hemisphere might be predicted, given that there are links between hemispheres. Nevertheless, in the large majority of subjects the amplitudes of the test MEPs evoked in contralateral hand muscles were not significantly changed. This has also been reported in other studies (Zanette et al. 1995; Baumer et al. 2002; Lang et al. 2004). Some reports have shown changes in MEPs evoked in muscles following fatiguing exercise of the homologous contralateral muscles (Bonato et al. 1996, Humphry et al. 2004). These changes were depressions, and their origin may have been through transcallosal system (either through increased inhibition or decreased facilitation). The absence of consistent effects in our study may reflect our experimental requirement that the right (non-exercised) hand maintained a steady low-level contraction to control the excitability of the motoneurones.

The major finding of this study, i.e. that interhemispheric inhibition evoked from one hemisphere was as prominent after the exercise whereas the amplitudes of the MEPs evoked in contralateral (exercised) muscles were significantly reduced, has clear implications for the mechanisms of the depression. The differential effect on the direct output of the exercised hemisphere to muscles (which was depressed) and on the interhemispheric effects on MEPs in contralateral non-exercised muscles (which were unchanged) suggests a specificity of action. Strong evidence indicates that at least a major component of the effect of TMS of one hemisphere on the contralateral one is interhemispheric inhibition, involving transcallosal axons (see Di Lazzaro et al. 1999b). The results presented here therefore suggest that the activation of the transcallosal system is as effective before and after the hemisphere generates exercise. In contrast, the output to contralateral muscles is strongly and significantly depressed. The exercise therefore had a substantial effect on the recruitment of corticospinal axons into the TMS response, but had no apparent effect on responses dependent on the recruitment of transcallosal axons.

Some evidence suggests that the inhibitory effects of stimulation of one hemisphere on responses evoked from the other reflect a partially subcortical process (Gerloff et al. 1998). However, if this is the case then the findings reported here lead to a similar conclusion: if a significant part of the inhibition were evoked subcortically, then the subcortical systems remain accessible to activation by TMS after exercise, while the effects on muscles are depressed. The effective conclusion from our results is the same: the post-exercise effects are specific to the corticospinal neurons that generate MEPs in contralateral muscles, not to those involved in depression of the responses in ipsilateral muscles.

The findings reported here on post-exercise changes in MEPs and interhemispheric inhibition have very strong parallels with recent findings with transcranial direct current (DC) stimulation of the motor cortex. While DC stimulation of one hemisphere can dramatically reduce the size of MEPS evoked by TMS stimulation of the stimulated hemisphere in contralateral hand muscles, it has recently been shown not to affect interhemispheric inhibition evoked from the stimulated hemisphere in the non-stimulated hemisphere (Lang et al. 2004). In this case interhemispheric inhibition was measured as the duration of suppression of ongoing EMG in ipsilateral hand muscles. This parallel suggests that exercise and DC stimulation may act through common intracortical mechanisms. Interestingly, transcallosal inhibition evoked in the hemisphere that received DC stimulation (evoked from the non-stimulated hemisphere) was affected. Lang et al. (2004) propose a model in which the excitatory transcallosal neurones which originate in the DC-stimulated hemisphere and target the non-stimulated hemisphere are not influenced by DC stimulation. Conversely, the inhibitory actions of the transcallosal neurones that target the DC-stimulated hemisphere are mediated by interneurones which are influenced by DC stimulation. If the post-exercise effects share a common mechanism with DC stimulation, then this would predict that interhemispheric inhibition will be changed after exercise in the hemisphere that generated the exercise.

In contrast, repetitive TMS has been reported to alter interhemispheric inhibition contralaterally to the stimulated hemisphere, either increasing or decreasing it (Wassermann 1998; Gilio et al. 2003; Gorsler et al. 2003), suggesting that repetitive TMS acts of different systems to DC stimulation and exercise.

References

Baumer T, Munchau A, Weiller C, Liepert J (2002) Fatigue suppresses ipsilateral intracortical facilitation. Exp Brain Res 146:467–473

Bonato C, Zanette G, Manganotti P, Tinazzi M, Bongiovanni G, Polo A, Fiaschi A (1996) 'Direct' and 'crossed' modulation of human motor cortex excitability following exercise. Neurosci Lett 216:97–100

Boroojerdi B, Diefenbach K, Ferbert A (1996) Transcallosal inhibition in cortical and subcortical cerebral vascular lesions. J Neurol Sci 144:160–170

Brasil-Neto JP, Pascual-Leone A, Valls-Sole J, Cammarota A, Cohen LG, Hallett M (1993) Postexercise depression of motor evoked potentials: a measure of central nervous system fatigue. Exp Brain Res 93:181–184

Brasil-Neto JP, Cohen LG, Hallett M (1994) Central fatigue as revealed by postexercise decrement of motor evoked potentials. Muscle Nerve 17:713–719

Chen R, Classen J, Gerloff C, Celnik P, Wassermann EM, Hallett M, Cohen LG (1997) Depression of motor cortex excitability by low-frequency transcranial magnetic stimulation. Neurology 48:1398–1403

Crone C, Hultborn H, Mazieres L, Morin C, Nielsen J, Pierrot-Deseilligny E (1990) Sensitivity of monosynaptic test reflexes to facilitation and inhibition as a function of the test reflex size: a study in man and the cat. Exp Brain Res 81:35–45

Di Lazzaro V, Oliviero A, Profice P, Insola A, Mazzone P, Tonali P, Rothwell JC (1999a) Direct recordings of descending volleys after transcranial magnetic and electric motor cortex stimulation in conscious humans. Suppl Clin Neurophysiol 51:120–126

Di Lazzaro V, Oliviero A, Profice P, Insola A, Mazzone P, Tonali P, Rothwell JC (1999b) Direct demonstration of interhemispheric inhibition of the human motor cortex produced by transcranial magnetic stimulation. Exp Brain Res 124:520–524

Di Lazzaro V, Oliviero A, Tonali PA, Mazzone P, Insola A, Pilato F, Saturno E, Dileone M, Rothwell JC (2003) Direct demonstration of reduction of the output of the human motor cortex induced by a fatiguing muscle contraction. Exp Brain Res 149:535–538

Ferbert A, Priori A, Rothwell JC, Day BL, Colebatch JG, Marsden CD (1992) Interhemispheric inhibition of the human motor cortex. J Physiol 453:526–546

Gandevia SC, Petersen N, Butler JE, Taylor JL (1999) Impaired response of human motoneurones to corticospinal stimulation after voluntary exercise. J Physiol 521:749–759

Gerloff C, Cohen LG, Floeter MK, Chen R, Corwell B, Hallett M (1998) Inhibitory influence of the ipsilateral motor cortex on responses to stimulation of the human cortex and pyramidal tract. J Physiol 510:249–259

Gilio F, Rizzo V, Siebner HR, Rothwell JC (2003) Effects on the right motor hand-area excitability produced by low-frequency rTMS over human contralateral homologous cortex. J Physiol 551: 563–573

Gorsler A, Baumer T, Weiller C, Munchau A, Liepert J (2003) Interhemispheric effects of high and low frequency rTMS in healthy humans. Clin Neurophysiol 114:1800–1807

Humphry AT, Lloyd-Davies EJ, Teare RJ, Williams KE, Strutton PH, Davey NJ (2004) Specificity and functional impact of post-exercise depression of cortically evoked motor potentials in man. Eur J Appl Physiol (in press DOI: 10.1007/s00421-004-1082-9)

Lang N, Nitsche MA, Paulus W, Rothwell JC, Lemon RN (2004) Effects of transcranial direct current stimulation over the human motor cortex on corticospinal and transcallosal excitability. Exp Brain Res (E-pub)

Liepert J, Kotterba S, Tegenthoff M, Malin JP (1996) Central fatigue assessed by transcranial magnetic stimulation. Muscle Nerve 19:1429–1434

Meyer BU, Roricht S, Grafin von Einsiedel H, Kruggel F, Weindl A (1995) Inhibitory and excitatory interhemispheric transfers between motor cortical areas in normal humans and patients with abnormalities of the corpus callosum. Brain 118:429–440

Meyer BU, Roricht S, Woiciechowsky C (1998) Topography of fibers in the human corpus callosum mediating interhemispheric inhibition between the motor cortices. Ann Neurol 43:360–369

Muellbacher W, Ziemann U, Boroojerdi B, Hallett M (2000) Effects of low-frequency transcranial magnetic stimulation on motor excitability and basic motor behaviour. Clin Neurophysiol 111:1002–1007

Rothwell JC (1997) Techniques and mechanisms of action of transcranial stimulation of the human motor cortex. J Neurosci Methods 74:113–22

Sakai K, Ugawa Y, Terao Y, Hanajima R, Furubayashi T, Kanazawa I (1997) Preferential activation of different I waves by transcranial magnetic stimulation with a figure-of-eight-shaped coil. Exp Brain Res 113:24–32

Wassermann EM, Wedegaertner FR, Ziemann U, George MS, Chen R (1998) Crossed reduction of human motor cortex excitability by 1 Hz transcranial magnetic stimulation. Neurosci Lett 250:141–144

Winter AP, Edgley SA (2001) Effects of muscle fatigue on transcallosal inhibition evoked by transcranial magnetic brain stimulation (TMS). J Physiol 536P

Zanette G, Bonato C, Polo A, Tinazzi M, Manganotti P, Fiaschi A (1995) Long-lasting depression of motor-evoked potentials to transcranial magnetic stimulation following exercise. Exp Brain Res 107:80–86