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Changes in motor cortical excitability during human muscle fatigue

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1. The excitability of the motor cortex was investigated during fatiguing contractions of the elbow flexors in human subjects. During sustained contractions at 30 and 100% maximal voluntary force (MVC), the short-latency electromyographic responses (EMG) evoked in biceps brachii and brachioradialis by transcranial magnetic stimulation increased in size. The reduced EMG in the elbow flexors following the evoked muscle potential (silent period), increased in duration during a sustained MVC but not during 30% MVCs nor during a sustained MVC of a remote muscle (adductor pollicis).

2. When the blood supply to brachioradialis was blocked with a sphygmomanometer cuff at the end of a sustained MVC, the changes in EMG responses to transcranial stimulation rapidly returned to control values. This suggests that changes in these responses during fatigue were not mediated by small-diameter muscle afferents.

3. Tendon vibration during sustained MVCs indicated that the changes in the responses to magnetic cortical stimulation were not mediated by reduced muscle spindle inputs.

4. Muscle action potentials evoked in brachioradialis by electrical stimulation at the cervicomedullary junction did not increase in size during sustained MVCs. Thus, growth of the cortically evoked responses during sustained MVCs reflects a change in cortical excitability. Although the silent period following cervicomedullary stimulation lengthened, it remained substantially shorter than the cortically evoked silent period.

5. The altered EMG responses to transcranial stimulation during fatigue suggest both increased excitation and increased inhibition in the motor cortex. As these changes were unaffected by manipulation of afferent input they presumably result from intrinsic cortical processes and/or altered voluntary drive to the motor cortex.

Transcranial magnetic stimulation can be used to examine the motor output in human subjects. Stimulation over the motor cortex evokes both excitatory and inhibitory responses in the EMG of contracting muscle. The short-latency motor-evoked potential (MEP) is a compound muscle action potential with an onset latency consistent with a rapidly conducting monosynaptic pathway. It is believed to arise from direct and trans-synaptic activation of cortico-spinal neurones and is influenced by the excitability of the motor cortex and the α-motoneurone pool (Amassian, Stewart, Quirk & Rosenthal, 1987; Day *et al.* 1989). A period of near-silence of the EMG follows the MEP. At least the latter part of this silent period is due to inhibition of motor cortical output (Edgley, Eyre, Lemon & Miller, 1990; Inghilleri, Berardelli, Cruccu & Manfredi, 1993; Roick, von Giesen & Benecke, 1993) and thus the duration of the silent period reflects the strength of inhibition within the cortex (Priori, Berardelli, Inghilleri, Accornero & Manfredi, 1994*a*; Priori, Berardelli, Inghilleri, Polidori & Manfredi, 1994*b*).

With voluntary contraction, MEPs are increased in size compared with those evoked from relaxed muscle and this reflects increased excitability at both cortical and spinal levels (Hess, Mills & Murray, 1987; Mazzocchio, Rothwell, Day & Thompson, 1994). However, fatiguing exercise may diminish cortical excitability. Brasil-Neto and colleagues (Brasil-Neto, Pascual-Leone, Valls-Solé, Cammarota, Cohen & Hallet, 1993; Brasil-Neto, Cohen & Hallet, 1994) demonstrated a decrease in MEPs immediately after subjectively fatiguing exercise, along with changes in the responses to repeated cortical stimulation.

We stimulated the motor cortex during sustained isometric contractions and found that the MEP increased in size while the silent period increased in duration with muscle fatigue. These changes seem to result from events at a cortical level. The role of these cortical changes in modifying muscle force is considered in the accompanying paper (Gandevia, Allen, Butler & Taylor, 1996). Preliminary results have been presented (Gandevia, Butler, Allen & Taylor, 1994).

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METHODS

Ten normal volunteers (aged 23–42 years, 3 female) were studied. All procedures were undertaken with the approval of the local ethics committee and the written consent of each volunteer was obtained. Subjects sat with the right arm held at the wrist in an isometric myograph which measured the force of elbow flexion (transducer linear to 2 kN; Xtran, Melbourne, Australia). The elbow was flexed to 90 deg with the forearm vertical and supinated (Fig. 1*A*). A light-emitting diode (LED) array gave subjects feedback of force and subjects were encouraged verbally throughout all contractions.

Stimulation

Motor responses were elicited by stimulation at two different sites. (1) Motor cortex: transcranial magnetic stimuli were delivered via a round coil (13 cm o.d.) over the vertex (stimulus intensities 70–100% output; Magstim 200, Magstim Co., Dyfed, UK). The coil, held by a helmet, stimulated the left hemisphere preferentially. Stimulus intensity was adjusted for each subject so that a silent period of 180–200 ms followed the MEP in contracting muscles. This length of silent period exceeds the duration of the silent period following direct corticospinal stimulation and is likely to result from inhibition at a cortical level (Inghilleri *et al.* 1993; confirmed here). (2) Cervicomedullary junction: single electrical stimuli (50 μs duration, 550–750 V; model D180, Digitimer Ltd, Welwyn Garden City, Herts, UK) were delivered through 9 mm Ag–AgCl electrodes fixed over the right (cathode) and left mastoids (Ugawa, Rothwell, Day, Thompson & Marsden, 1991).

Protocol

Transcranial magnetic stimulation. Subjects ($n = 7$) performed five brief isometric elbow flexions (2–3 s duration) at intervals of ~1 min. These control efforts were followed by a 2 min sustained contraction. Finally, a series of brief contractions were performed at 0·5, 1, 2 and 3 min after the sustained contraction to monitor the recovery of responses (Fig. 1*B*). During each brief contraction, a single transcranial magnetic stimulus was given, whereas during the sustained effort, stimuli were delivered every 10–15 s. Each subject made contractions at 30, 60 or 70% (mean 64%) and 100% MVC in separate sessions. Stimulus intensity for each subject was constant in all sessions and the order of contraction strengths was randomized. When the stimulus was delivered during the contractions, an EMG 'silence' followed the MEP and force declined. Subjects were instructed to regain their target force as fast as possible. EMG was recorded from biceps brachii and brachioradialis through surface electrodes. EMG signals were amplified (53 Hz–1 kHz) and sampled with the force signal at 5 kHz from 50 ms before to 500 ms after each stimulus. Data were recorded on disk for off-line analysis (1401 interface; Cambridge Electronic Design, Cambridge, UK).

Cervicomedullary junction stimulation. In three subjects, cervicomedullary stimulation alternated with transcranial stimulation. Stimulus intensities were adjusted so that the short-latency muscle action potentials evoked by cervicomedullary stimuli matched the peak-to-peak amplitudes of MEPs. Following ten brief MVCs (5 with cervicomedullary and 5 with transcranial stimulation), subjects performed a 2 min sustained MVC during which cervicomedullary and magnetic cortical stimuli were alternated every 15 s.

Cortical stimulation during muscle fatigue maintained by ischaemia. In four subjects, a sphygmomanometer cuff was placed around the upper arm prior to the start of the sequence of elbow flexions. After 1·25–1·75 min of the sustained MVC, the cuff was inflated to 300 mmHg to block arterial blood flow, and maximal effort was maintained until one further transcranial stimulus had been delivered. The cuff remained inflated until two brief contractions with superimposed cortical stimuli were performed at 0·5 and 1 min after the end of the sustained MVC. Additional magnetic stimuli were delivered during brief maximal flexions after the cuff was deflated.

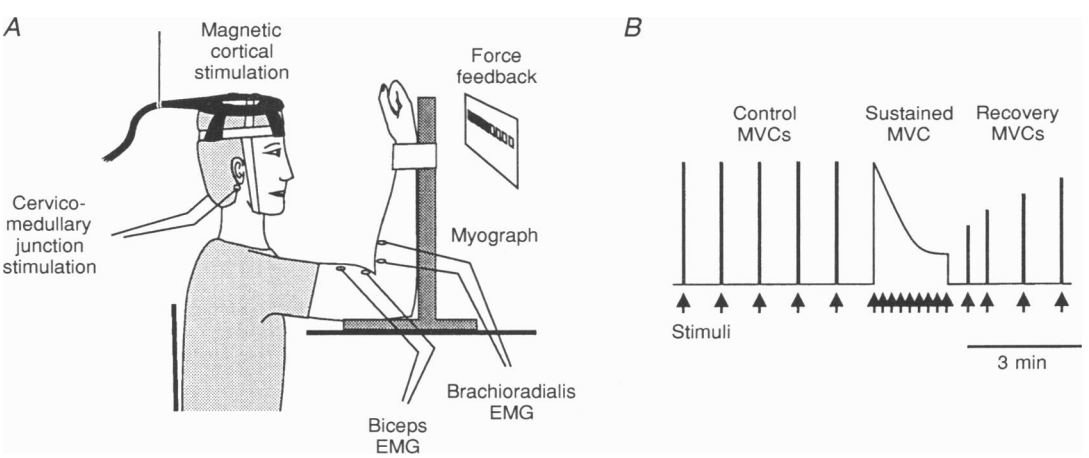

Figure 1. Experimental arrangement

A, subject seated with the right arm in a myograph. Force feedback was provided. EMGs from biceps brachii and brachioradialis were recorded. Stimuli were delivered to the cervicomedullary junction through electrodes over the mastoids or to the cortex via a magnetic coil. *B*, subjects initially performed brief maximal voluntary contractions (MVCs, 2–3 s duration). During each contraction, a stimulus was given (arrows). Subjects then performed a sustained MVC (1·5–2 min duration). Stimuli were delivered every 10–15 s. Additional brief MVCs with superimposed stimuli were performed during the recovery period.

Effect of tendon vibration on EMG responses to cortical stimulation. Vibration was introduced at the end of a sustained MVC to increase input from large-diameter muscle afferents in five subjects. Vibration (125 Hz) was applied to the distal tendon of biceps brachii with a hand-held pneumatic vibrator and was sufficient to cause a tonic vibration reflex in relaxed or submaximally contracting muscle. Vibration started before each of the final two transcranial magnetic stimuli during the sustained effort, and continued for a few seconds until subjects recovered force output after the stimulus. Control cortical stimuli were given during brief MVCs both with and without vibration. All but the final contractions during recovery were performed with vibration.

Specificity of changes in EMG responses to cortical stimulation. To determine whether a sustained MVC of a different muscle altered the responses to transcranial magnetic stimulation in biceps brachii, four subjects made a sustained MVC of the right adductor pollicis while EMG was recorded with surface electrodes over adductor pollicis and right biceps brachii. Subjects received visual feedback of the force of thumb adduction and elbow flexion. Control transcranial stimuli were delivered during brief MVCs in which the thumb adductors and elbow flexors contracted simultaneously. A sustained MVC of adductor pollicis was then performed with cortical stimuli delivered at 15 s intervals. Before the first stimulus and final two stimuli during the sustained MVC of adductor pollicis, subjects concurrently made a brief maximal elbow flexion. Efforts during recovery consisted of simultaneous brief contractions of both muscles.

Data analysis

The area of each MEP was measured automatically between cursors that encompassed the potentials evoked by all stimuli in each experiment. The duration of the silent period was measured by cursor and was taken as the interval from the stimulus to the return of continuous EMG. Repeated measures analyses of variance with *post hoc* testing (Student–Newman–Keuls) were performed. Significance was set at the 5% level. In the text, group data are stated as means ± S.D., whereas in figures, means ± S.E.M. are shown.

RESULTS

Motor-evoked potentials (MEPs)

Short-latency EMG potentials evoked by magnetic cortical stimulation were measured during a 2 min voluntary contraction of elbow flexors at 30, 64 and 100% MVC. In biceps brachii, MEPs during control contractions ranged from 3·6 to 13·9 mV (mean peak-to-peak amplitudes; $n = 7$), and in brachioradialis, from 3·6 to 8·6 mV. For each level of contraction, the area of the MEP grew over the course of the sustained effort in biceps brachii (Fig. 2) and brachioradialis. This increase was greatest during the MVC when the MEP in biceps brachii increased to 156 ± 51% of control values and in brachioradialis to 178 ± 68%. The increase in mean MEP area did not occur gradually, but reached a plateau by about 30–45 s into the maximal contraction. During sustained contractions, particularly in maximal efforts, the potentials broadened and often increased in amplitude (Fig. 3*B*). Because of the background EMG, it was not possible to document formally the durations of MEPs or any shifts in latency.

Silent period

Each MEP was followed by near-silence in the EMG of biceps brachii and brachioradialis (the 'silent period'). During

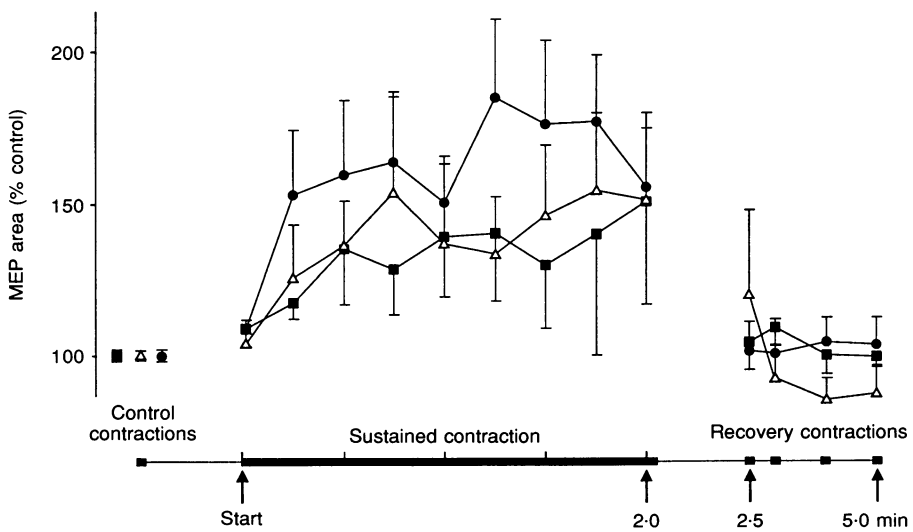

Figure 2. Area of MEPs in biceps brachii during sustained elbow flexions

Values obtained during contractions at 30 (■), ~60 (△) and 100% MVC (●; $n = 7$). Area of MEP is expressed as a percentage of that during brief control contractions of the same strengths. Each control point is from five values in each subject. MEP area increased during the 2 min isometric contractions at each strength, and this was most marked for the MVC. After the fatiguing contractions, MEP area during a brief contraction returned to control levels within 0·5–1·0 min. Comparable data were obtained for MEPs in brachioradialis.

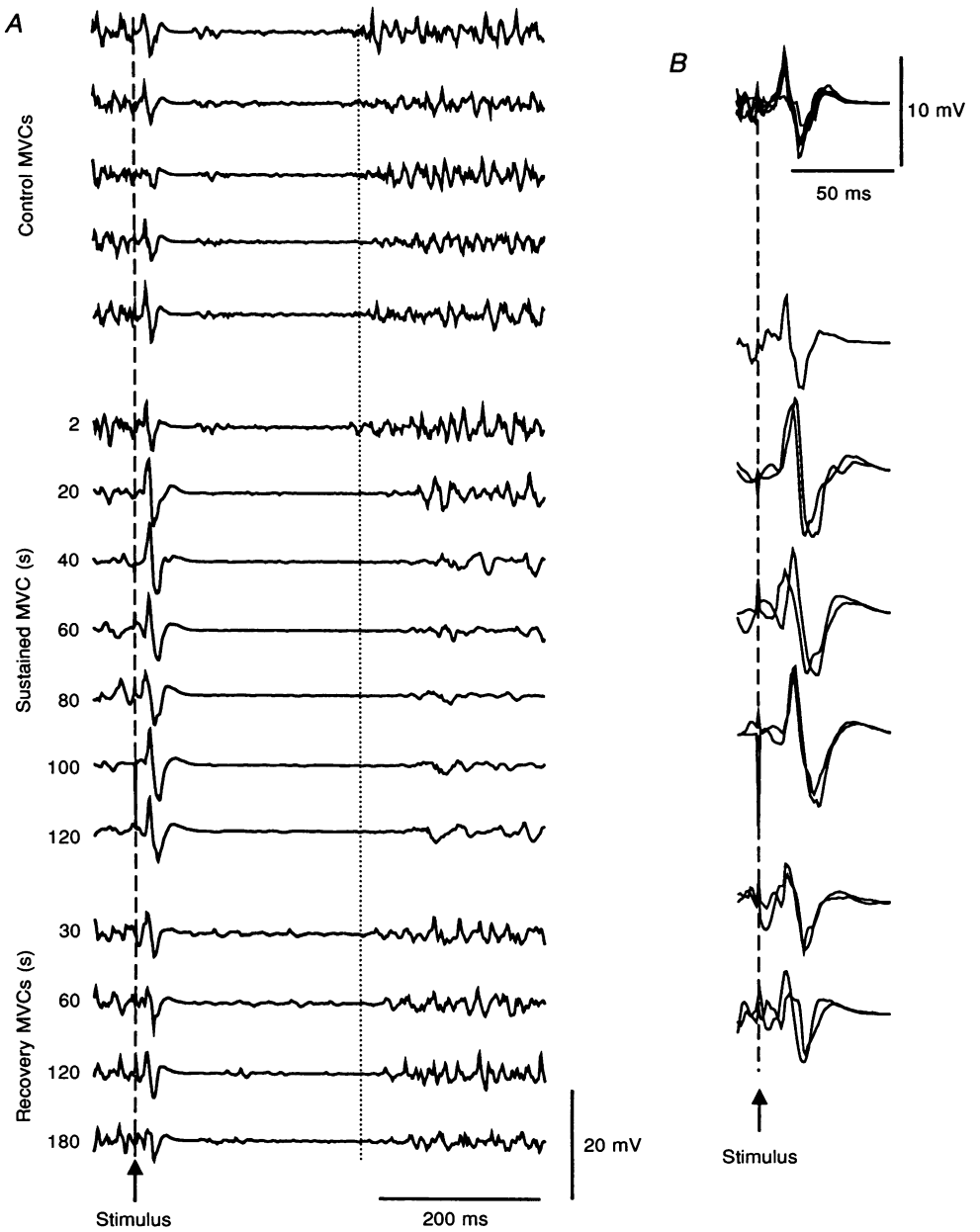

Figure 3. EMG following magnetic cortical stimulation during MVCs

A, biceps brachii EMG from one experiment. Upper five traces during brief control MVCs. Middle seven traces during a sustained 2 min MVC and lower four traces during recovery. Dashed line shows the time of stimulation. Dotted line shows the mean latency for return of continuous EMG in control trials and, thus, marks the end of the control silent period. The silent period lengthens during the sustained MVC and quickly recovers. EMG silence is not absolute during the so called 'silent period' in control trials. This small-amplitude variable activity (from ~65 ms post-stimulus) disappears during the sustained contraction and reappears during recovery. The MEP (just to right of dashed line) is variable but increases during the sustained contraction and recovers within 30 s. MEPs are shown on a larger scale in *B*. The five control responses are superimposed, as are sequential pairs during the sustained MVC and recovery.

brief control contractions, the strength of contraction (30, 64 and 100% MVC) did not alter the mean duration of the silent period (biceps brachii: 213, 212 and 216 ms; brachioradialis: 208, 213 and 222 ms; $P > 0{\cdot}9$; $n = 7$). However, after 30 s of sustained MVC, the silent period had extended by 53 ± 28 ms in biceps brachii (Figs 3*A* and 4) and 45 ± 25 ms in brachioradialis. Continued contraction maintained this lengthening of the silent period but did not increase it further. By 30 s after cessation of the effort, the silent period had returned to control lengths.

In contrast to the changes seen with maximal efforts, the silent period duration did not alter during sustained 30% MVCs. During contractions of intermediate strength (64% MVC), the silent period lengthened significantly (Fig. 4). In individual subjects, the silent period became longer when the target force required near-maximal effort but because this occurred at different times for each subject, the grouped data show a more progressive change.

In the unfatigued muscle the silent period after the MEP began with initial abolition of EMG. However, following this (starting at 50–110 ms post-stimulus) there was a small amount of activity which may reflect long-latency responses to the cortical stimulus (Holmgren, Larsson & Pedersen, 1990; Dimitrijević, Kofler, McKay, Sherwood, Van der Linden & Lissens, 1992). During sustained MVCs, this EMG within the silent period disappeared. It recovered after the contraction but more slowly than silent period duration (Fig. 3, see also Fig. 6).

Cervicomedullary junction stimulation

In three subjects, an electrical stimulus between the mastoids evoked a short-latency response in brachioradialis (latencies during MVC: 10·4, 10·6 and 14·8 ms) by exciting the corticospinal tract at the cervicomedullary junction (Ugawa *et al.* 1991). Electrical transmastoid stimuli and magnetic cortical stimuli that evoked similar amplitude motor potentials (transmastoid: 2·4–7·9 mV; cortical: 3·5–7·9 mV) were delivered alternately during a sustained MVC. Motor potentials evoked by transmastoid stimuli did not change in the same way with the sustained contraction as those evoked by cortical stimuli ($P < 0{\cdot}001$). The area of MEPs increased during the contraction ($P < 0{\cdot}05$), whereas the area of the muscle potentials evoked by transmastoid stimulation did not differ significantly from control levels (Fig. 5*B*). Thus, the increases in MEP area during a sustained contraction result from changes in excitability of the motor cortex.

Following transmastoid stimulation, a period of relative silence of EMG also occurred. This was much shorter than that following magnetic cortical stimulation despite the similar sizes of evoked EMG potentials. In brief MVCs, the silent period was 78 ± 27 ms ($n = 3$) following transmastoid stimulation and 205 ± 51 ms after cortical stimulation. During the sustained MVC, the silent period evoked by corticospinal tract stimulation lengthened (Fig. 5*A*), as did the magnetically evoked silent period. At the end of the contraction, the transmastoid stimulation silent period had

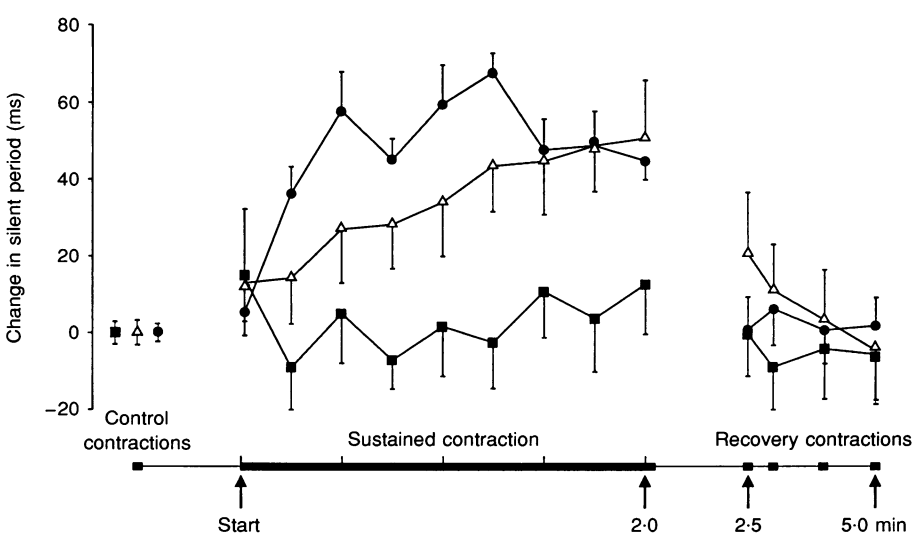

Figure 4. Increase in the silent period in biceps brachii during sustained elbow flexions of different strengths

The change in duration of the silent period from its duration in matched control contractions, is plotted for contractions at 30 (■), ~60 (△) and 100% MVC (●; $n = 7$). Positive values indicate an increase in duration. The silent period increased during the sustained 60 and 100% MVCs but not during the 30% MVC. The silent period returned to control duration after 0·5–1·0 min of recovery.

increased by 27 ± 15 ms and the cortical stimulation silent period by 52 ± 26 ms. However, despite its increase in duration, even the longest EMG silence seen after transmastoid stimulation was more than 60 ms shorter than the duration of the control cortically evoked silent period. Thus, any spinal inhibition following the magnetically evoked motor potential is likely to have ceased before the resumption of voluntary output from the motor cortex and so is unlikely to contribute to the increase in duration of the cortically evoked silent period.

Responses during muscle fatigue maintained by ischaemia

Blocking blood supply to brachioradialis after the end of the sustained MVC prevented recovery of voluntary force output from the low level of about 30% of initial maximum (Merton, 1954; cf. Gandevia *et al.* 1996). However, despite maintained ischaemia, MEP size which had grown during the sustained MVC ($P < 0{\cdot}05$) returned to control levels (160 ± 38 to 93 ± 28% of initial MEP area at 1 min after MVC end; $n = 4$). The duration of the silent period also recovered rapidly. At the end of the sustained MVC, the duration of the silent period had increased to 260 ± 43 ms from its initial 220 ± 42 ms ($P < 0{\cdot}05$), whereas after 30 s of relaxation its duration was reduced to 207 ± 38 ms, and after 1 min, to 225 ± 29 ms. This suggests that the altered EMG responses are not associated with fatigue-related firing of small-diameter muscle afferents.

Effect of tendon vibration on EMG responses to cortical stimulation

Vibration of the biceps brachii tendon was used to augment muscle afferent input near the end of a sustained MVC (1·5 min duration) in five subjects. Tendon vibration excites muscle spindle afferents which discharge progressively less during a sustained isometric contraction (Macefield, Hagbarth, Gorman, Gandevia & Burke, 1991). Vibration had no effect on MEP area or silent period duration during control contractions or at the end of a sustained MVC (Fig. 6). In brief control MVCs, vibration made no consistent change to the maximal voluntary force, MEP area or silent period duration ($P > 0{\cdot}3$). Of the last four cortical stimuli during the sustained contraction, the earlier two were without vibration, whereas the latter two were

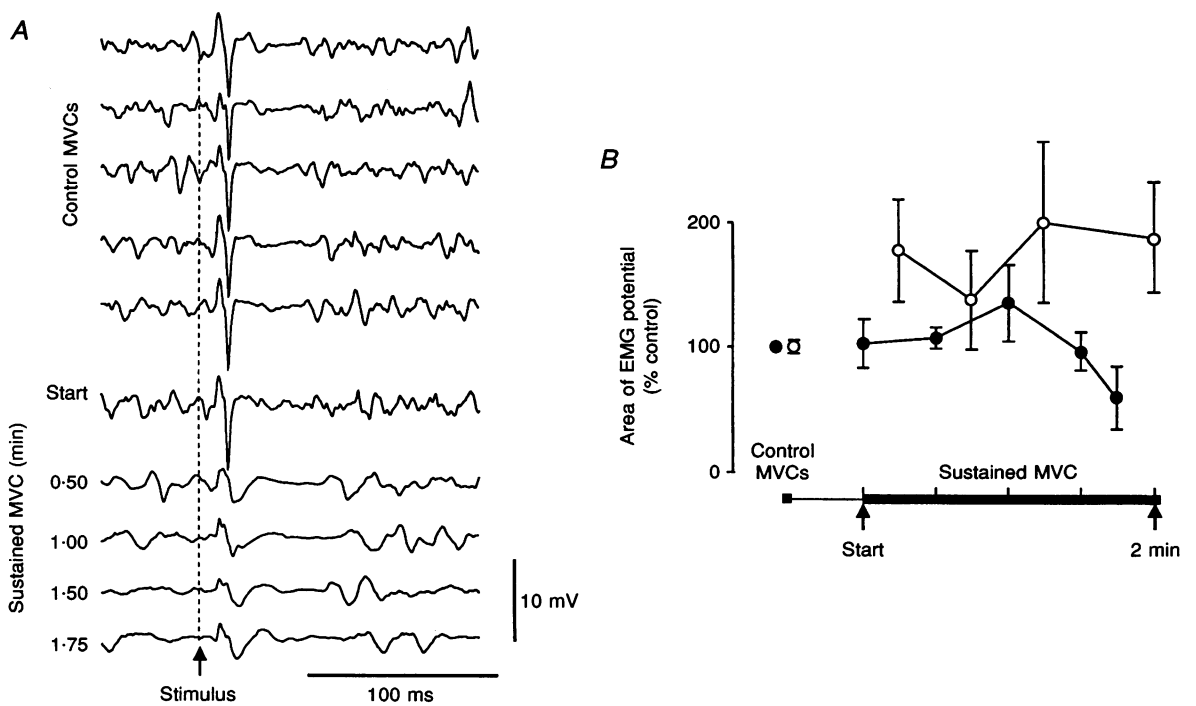

Figure 5. Responses in brachioradialis EMG following cervicomedullary junction stimulation

A, upper five traces were recorded during brief control MVCs and the remaining traces during a sustained MVC. Dashed line indicates the time of stimulation. Muscle action potentials evoked by the stimuli decrease in amplitude during the sustained MVC. The short silent period increases in duration. *B*, area of EMG potentials evoked in brachioradialis by cervicomedullary junction stimulation or by motor cortical stimulation. Area of the motor potentials is expressed as a percentage of the averaged area of potentials elicited during control MVCs. Area of cortically evoked potentials (○) increases during the sustained MVC, whereas the area of the potentials elicited by transmastoid stimulation (●) does not.

with vibration. No differences were found between the areas of the evoked motor potentials ($P > 0{\cdot}3$) or between the durations of the silent periods ($P > 0{\cdot}5$). Differences in voluntary force production with vibration were not investigated during fatigue.

Specificity of changes in EMG responses

A sustained MVC of another muscle in the same arm did not affect the duration of the silent period in biceps brachii. Although the simultaneous MVCs were difficult to perform, the silent period in adductor pollicis lengthened during its sustained contraction and this was maintained when a brief MVC of elbow flexors was performed concurrently near the end of the sustained MVC of the thumb adductor (Fig. 7). The silent period in adductor pollicis (220 ± 26 ms) increased by 35 ± 22 ms ($P < 0{\cdot}05$). In contrast, the silent period (148 ± 46 ms) in biceps brachii, which was not involved in the sustained maximal effort, was unchanged.

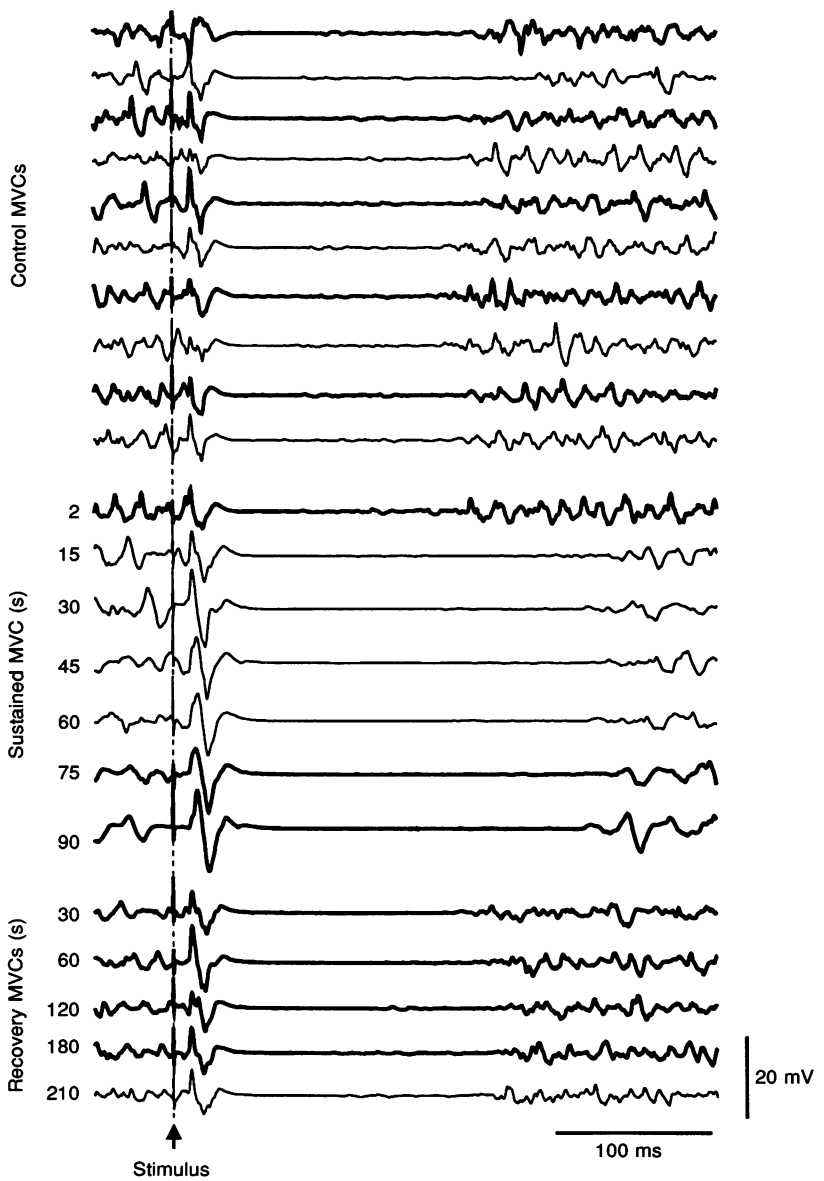

Figure 6. Effect of vibration of the biceps brachii tendon on cortically evoked EMG responses during fatigue

EMG from biceps brachii in one subject. Thick traces are those with vibration prior to, and throughout, the record. There was no vibration for the other records. Traces recorded sequentially during brief control MVCs, a sustained MVC and during recovery. Vibration did not alter the duration of the silent period or the amplitude of MEPs during control, sustained or recovery contractions.

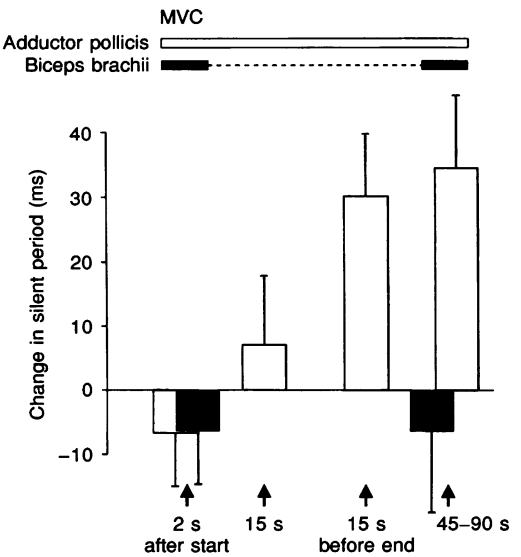

Figure 7. Effect of a sustained MVC of a different muscle on silent period in biceps brachii

Change in silent period duration compared with the mean of five control values for each subject is plotted for adductor pollicis (□) and biceps brachii (■; $n = 4$). Positive values indicate that the duration was longer than control. Because the duration of sustained contraction of adductor pollicis varied between subjects, the changes in silent period duration for stimuli delivered close to the start and end of each subject's contraction were averaged. Thus, the initial value is for the silent period elicited by a stimulus delivered at the start, and the second value for 15 s after the start, of the MVC. The third value is for 15 s before, and the fourth immediately before, the end of the sustained contraction. At the start and end of the sustained MVC of adductor pollicis, subjects added a brief MVC of the elbow flexors. The silent period in adductor pollicis lengthens over the sustained effort but the silent period measured for biceps brachii during the brief concurrent contractions did not change.

DISCUSSION

MEP

A magnetic cortical stimulus elicits a larger MEP in contracting muscle than in relaxed muscle (Hess *et al.* 1987). However, we report a further increase in MEP size with continued contraction. During sustained MVCs, MEPs grow but potentials evoked by corticospinal stimulation do not. Thus, the growth is likely to reflect events at a cortical level and suggests increased excitability of the motor cortex. Large-diameter muscle afferents can facilitate responses to magnetic stimulation of the motor cortex (Day, Riescher, Struppler, Rothwell & Marsden, 1991; Deuschl, Michels, Berardelli, Schenk, Inghilleri & Lücking, 1991) but firing of muscle spindle afferents declines during sustained isometric contractions (Macefield *et al.* 1991) and should decrease cortical excitability. Small-diameter muscle afferents fire during fatigue but despite their continued firing when the muscle was held ischaemic, the size of MEPs returned to control levels. Thus, it is likely that an increase in voluntary drive rather than changes in afferent input causes the increase in MEP size during sustained efforts. This is consistent with psychophysical findings of increasing subjective effort during a sustained 'maximal' contraction (e.g. Gandevia, Killian & Campbell, 1981). MEPs also grew during submaximal sustained contractions but we did not examine the extent to which this was mediated by cortical or spinal changes. Yet, even for the weakest sustained contractions (30% MVC), subjects reported increasing effort to maintain the target force and this suggests increasing cortical output. Recordings in monkeys provide supporting evidence for increased motor cortical activity during fatigue. Cortical cells with monosynaptic connections to biceps brachii and brachioradialis motoneurones show, on average, an increase in firing during fatigue induced by repeated isometric elbow flexions (Maton, Fourment & Belhaj-Saïf, 1994).

Silent period

During sustained maximal contractions of the elbow flexors, the silent period lengthened in the contracting muscle but not in muscles that did not take part in the MVC. Similar lengthening of the silent period during fatigue of tibialis anterior has been noted but without an apparent increase in size of the MEP (McKay, Stokić, Sherwood & Dimitrijević, 1994). Although inhibition at the

spinal level may contribute to the initial EMG silence following transcranial magnetic stimulation, the later part of the silent period is probably due to reduced cortical output (Fuhr, Agostino & Hallett, 1991; Inghilleri *et al.* 1993; Triggs, Cros, Macdonell, Chiappa, Fang & Day, 1993). Changes in the duration of the silent period may reflect changes in intracortical inhibition (Priori *et al.* 1994). When fatigue-related input from small-diameter muscle afferents was maintained by ischaemia after a fatiguing contraction, the silent period still recovered to control duration. Thus, any spinal inhibition from these afferents was not the cause of the prolonged silent period in sustained MVCs. The fall in muscle spindle firing during a sustained contraction and consequent decreased excitatory input to both the motoneurone pool and motor cortex did not cause the prolonged silent period. The silent period did not recover with augmentation of spindle input by tendon vibration at the end of sustained MVCs. These findings make it unlikely that changes in spinal excitability caused the increase in silent period duration with fatigue, and also suggest that changes in afferent input to the cortex were not responsible. During sustained submaximal contractions, silent period lengthening occurred only if, with fatigue, subjects needed to exert near-maximal effort to maintain the target force. Increased inhibition may occur in a limited area of motor cortex and then only if it is driven to perform near-maximally.

The MEP results from direct and trans-synaptic stimulation of corticospinal neurones (Amassian *et al.* 1987), whereas the silent period derives from inhibitory interneurones which limit the discharge of corticospinal neurones (Krnjević, Randić & Straughan, 1966*a*, *b*). Magnetic stimuli might activate inhibitory interneurones directly, or trans-synaptically via inputs from cortical and subcortical regions (Krnjević *et al.* 1966*a*; Kujirai *et al.* 1993). Recurrent inhibition through corticospinal collaterals is likely to account for only a small part of the inhibition following a cortical stimulus (Krnjević *et al.* 1966*a*). In our study, recurrent inhibition through antidromic activation of the corticospinal tract may have contributed to the silent period following stimulation of the cervicomedullary junction and this may explain why it also lengthened during a sustained MVC, although it remained much shorter than the magnetically evoked silent period. The lengthening of the silent period during sustained MVCs paralleled the growth in MEP area. Together, these changes suggest paradoxically both increased excitation and increased inhibition in the motor cortex during fatigue. However, different cortical elements cause the excitatory and the inhibitory responses (Wassermann, Pascual-Leone, Valls-Solé, Toro, Cohen & Hallett, 1993; Davey, Romaiguère, Maskill & Ellaway, 1994). It is as if the threshold for excitation of each of these decreases during fatigue.

Fatigue is an exercise-induced decrease in maximal voluntary force and some of this decline is attributed to processes within the central nervous system. The findings reported here demonstrate complex changes in cortical excitability during fatigue. However, they do not indicate whether these changes affect force production. The changes in force that result from stimulation of the motor cortex during MVCs are reported in the following paper (Gandevia *et al.* 1996). Although motor cortical output is suboptimal during fatigue, changes in the excitability of the motor cortex may not contribute to the decrease in voluntary force.

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