Increases in corticospinal responsiveness during a sustained submaximal plantar flexion

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Submitted 25 November 2008; accepted in final form 8 May 2009

Hoffman BW, Oya T, Carroll TJ, Cresswell AG. Increases in corticospinal responsiveness during a sustained submaximal plantar flexion. J Appl Physiol 107: 112–120, 2009. First published May 14, 2009; doi:10.1152/japplphysiol.91541.2008.—Studying the responsiveness of specific central nervous system pathways to electrical or magnetic stimulation can provide important information regarding fatigue processes in the central nervous system. We investigated the changes in corticospinal responsiveness during a sustained submaximal contraction of the triceps surae. Comparisons were made between the size of motor-evoked potentials (MEPs) elicited by motor cortical stimulation and cervicomedullary motor-evoked potentials (CMEPs) elicited by magnetic stimulation of the descending tracts to determine the site of any change in corticospinal responsiveness. Participants maintained an isometric contraction of triceps surae at 30% of maximal voluntary contraction (MVC) for as long as possible on two occasions. Stimulation was applied to the motor cortex or the cervicomedullary junction at 1-min intervals during contraction until task failure. Peripheral nerve stimulation was also applied to evoke maximal M waves (Mmax) and a superimposed twitch. Additionally, MEPs and CMEPs were evoked during brief contractions at 80%, 90%, and 100% of MVC as a nonfatigue control. During the sustained contractions, MEP amplitude increased significantly in soleus (113%) and medial gastrocnemius (108%) muscles and, at task failure, matched MEP amplitude in the prefatigue MVC (~20–25% Mmax). In contrast, CMEP amplitude increased significantly in medial gastrocnemius (51%), but not in soleus (63%) muscle and, at task failure, was significantly smaller than during prefatigue MVC (5–6% Mmax vs. 11–13% Mmax). The data indicate that cortical processes contribute substantially to the increase in corticospinal responsiveness during sustained submaximal contraction of triceps surae.

lower limb; central nervous system; muscle; transcranial magnetic stimulation; electromyogram

Fatigue can be defined as any exercise-induced reduction in the force-producing capability of a muscle and can be mediated by peripheral and central factors (15, 16, 45). Fatigue processes therefore begin shortly after the initiation of muscle contraction, whether or not the functional objective of the task can still be achieved (6). Peripheral fatigue, which refers to the impairment of processes distal to the neuromuscular junction that contribute to fatigue, contrasts with central fatigue and limitations attributable to processes proximal to the neuromuscular junction (16). Although central fatigue is known to substantially contribute to reductions in force-generating capacity in many functional situations, the central nervous system processes underpinning central fatigue are not well understood.

To understand the central processes of fatigue, the responsiveness of specific central nervous system pathways can be tested using electrical or magnetic stimulation during or after exercise bouts. The size of motor-evoked potentials (MEPs), evoked by transcranial magnetic stimulation (TMS) over the cortex, reflects the responsiveness of the motor cortex and spinal neurons to a given stimulus intensity (46–48). In contrast, cervicomedullary MEPs (CMEPs), evoked by magnetic or electrical stimulation at the cervicomedullary junction, are affected only by the responsiveness of spinal neurons to the stimulation (41, 46, 50, 52). In combination, these two measures can provide information about the responsiveness of the motor cortex, inasmuch as collision studies indicate that the techniques stimulate the same corticospinal axons (35). Thus, comparisons between the amplitude of MEPs and CMEPs during a fatiguing contraction can identify the location of changes in corticospinal responsiveness.

The central and peripheral mechanisms of fatigue have typically been examined during isolated muscle contractions involving maximal [i.e., maximal voluntary contractions (MVCs)] or submaximal (i.e., submaximal voluntary contractions) torques. In a sustained MVC, the torque produced is greatest at the beginning of the contraction and progressively falls throughout the remainder of the contraction. Motor unit recruitment and firing rates are greatest at the beginning of the contraction (14), subsequently dereruitment occurs, and firing rates decline (4). It has been found that, during sustained MVCs of the elbow flexors, MEP amplitude increases (47–49), whereas CMEP amplitude decreases (9), over time. The CMEP amplitude of triceps brachii also declines after a sustained elbow extension MVC (37). These findings suggest that, during sustained maximal contractions of the upper arm muscles, motor cortex responsiveness increases and the responsiveness of the spinal motoneuron pool is decreased.

During fatigue tests involving submaximal voluntary contractions, subjects are typically required to perform a contraction at a specific submaximal torque until they are no longer able to voluntarily produce the required torque. The number of motor units recruited at the beginning of a submaximal contraction depends on the strength of the contraction but increases over time as the force developed by the initially recruited motor units declines (33). Furthermore, the firing rate of active motor units can increase, decrease, or remain constant at different stages throughout the contraction, depending on the specific task context (1, 3, 18, 27). During submaximal fatigue tasks of the elbow flexors, MEP amplitudes increase during exercise at 5, 15, 20, 30, 50, and 64% of MVC (26, 30, 43–45, 48), indicating an increase in corticospinal responsiveness. In contrast to the situation during maximal contractions, Lévêné et al. (30) showed that the amplitude of CMEPs also increases during a sustained 50% MVC of the elbow flexors. The percent change in CMEP and MEP amplitude was similar, suggesting...
a large spinal contribution to the increase in corticospinal responsiveness (30). However, because few studies have compared the fatigue responses of MEPs with those of CMEPs, especially during submaximal contractions, the observation that maximal and submaximal contractions can affect corticospinal responsiveness in different ways highlights the need to analyze central fatigue mechanisms in both types of contraction.

The motor unit recruitment properties of the muscle targeted during a fatiguing contraction may also affect how corticospinal responsiveness changes. For example, during brief, nonfatiguing contractions, there are differences in the range of contraction strengths over which MEP or CMEP amplitudes increase. In biceps brachii, which recruits motor units up to ~90% of MVC (29), MEP and CMEP amplitudes increase with increasing torque production up to ~75% of MVC and subsequently decrease at higher contraction strengths (36). In contrast, MEPs and CMEPs evoked in triceps surae are largest at the highest contraction strengths (80% and 100% of MVC) (40), and there is evidence from an animal study that motor unit recruitment in triceps surae continues to 100% MVC (21). Thus it appears that motor unit recruitment can influence corticospinal responsiveness during brief contractions. This suggests that differences between muscles, in the range of contraction strengths over which motor unit recruitment occurs, may also influence corticospinal responsiveness during sustained fatiguing contractions and highlights the need for investigation of corticospinal responsiveness during central fatigue in multiple muscle groups.

Therefore, the aim of this study was to assess corticospinal responsiveness to magnetic stimulation at two distinct sites (the cortex and the cervicomedullary junction) during a sustained submaximal voluntary contraction of the triceps surae at 30% of MVC. This task has previously been shown to produce central fatigue of sufficient magnitude to be considered a major contributor to task failure (11, 31, 32). We tested the hypothesis that corticospinal responsiveness increases through- out sustained submaximal contraction of the plantar flexors and that a large proportion of this increase is mediated at the spinal level.

METHODS

Subjects. Seven men and three women (29.5 ± 4.6 yr old, 173.3 ± 7.0 cm, 72.6 ± 10.6 kg), who were healthy and had no history of neuromuscular disease or illness, volunteered to participate in the study. The protocol was approved by a local university ethics committee and conducted according to the Declaration of Helsinki. All subjects provided written informed consent.

Protocol. Each participant attended two testing sessions separated by ≥2 wk. TMS was used to assess corticospinal responsiveness during one session, and cervicomedullary magnetic stimulation was applied in the other session. The order of the testing sessions was randomized across subjects. Except for the site at which magnetic stimulation was applied, the protocol performed during each session was identical. Because only one magnetic stimulation unit was available, it was not possible to apply TMS and cervicomedullary magnetic stimulation in a single session; therefore, rapid application of multiple stimuli to different body regions and at different stimulus intensities was not permitted.

Experimental set-up. Subjects lay prone on a bench with the right foot strapped to a foot plate that was attached to a torque transducer. The ankle was positioned at 90°, and the knee was extended to ~175°. Subjects could view a computer monitor that displayed their plantar flexion torque in relation to specified target levels.

Prefatigue task measurements. Before the fatigue task, a number of set-up and control measurements were made. Maximal M waves (M_{max}) were evoked in soleus (Sol) and medial gastrocnemius (MG) muscles by application of electrical peripheral nerve stimulation to the tibial nerve. Current was delivered with a constant-current stimulator (model DS7AH, Digitimer) and passed from a cathode (Ag-AgCl electrode, 24 mm diameter; Tyco Healthcare Group) placed on the optimal site of stimulation within the popliteal fossa to an anode (coal rubber pad, 10.2 × 4.6 cm; Empi) positioned across the lower anterior aspect of the thigh, just proximal to the patella. Current was gradually increased until M_{max} was evoked; that is, the peak-to-peak amplitude of the M wave in Sol and MG failed to increase with further increases in current. Once M_{max} was found in both muscles, the intensity was further increased by 20% (supramaximal peripheral nerve stimulation) to reduce the effects of activity-dependent axonal hyperpolarization (7, 8). Supramaximal peripheral nerve stimulation was used at this intensity for the remainder of the experiment as a double pulse with an interstimulus interval of 15 ms. The waveform produced by the second pulse was measured to obtain the M_{max} amplitude.

Subjects performed three brief (3- to 4-s) isometric plantar flexion MVCs (Fig. 1A), each separated by ≥1 min to avoid fatigue. During each MVC, supramaximal peripheral nerve stimulation was applied at peak torque to produce a superimposed twitch and, also, at rest, 2 s after the MVC was completed, to produce a resting twitch. The superimposed twitch was measured as the difference between the peak value of the twitch during the MVC and the torque produced immediately before the twitch. The resting twitch was measured as the peak value of the twitch during rest. The size of the interpolated twitch (39) can be used to determine the level of voluntary activation using the following equation: [1 − (superimposed twitch/resting twitch)] × 100 (51). Voluntary activation produced by the subjects during the MVC was very close to 100% [97.12 ± 5.70% (mean ± SD)]. Maximal evocable torque was estimated by linear extrapolation of the torque vs. voluntary activation relation to the torque value corresponding to 100% voluntary activation (16). All torque targets used throughout the experiment were set as a percentage of the maximal evocable torque to reduce any variation in the duration of the sustained contractions caused by low voluntary activation during MVC.

Magnetic stimulations were performed using a 12-cm double-cone coil and a magnetic stimulator (model 2002, MagStim). The optimal location and intensity of stimulation were determined while subjects performed brief (3- to 4-s) isometric plantar flexions at 30% of their MVC. For TMS, the coil was positioned slightly left of the vertex of the head, with the current running through the center of the coil from anterior to posterior. The intensity was altered to find the intensity at which a ~100- to 200-μV Sol MEP became visible compared with the background EMG in three of five trials. An intensity of 120% of threshold was used for the remainder of the experiment. For cervicomedullary magnetic stimulation, the coil was positioned over the mastoid processes at the back of the neck and oriented so that the current flowed through the center of the coil from proximal to distal. The intensity was altered until a Sol CMEP could be discriminated from the background EMG with use of the smallest stimulation intensity. Inasmuch as this threshold intensity was close to the maximum output for the magnetic stimulator in most subjects, this threshold intensity was used for the remainder of the cervicomedullary magnetic stimulation protocol.

Subjects performed nine brief (3- to 4-s) high-torque isometric plantar flexions with superimposed magnetic stimulation (Fig. 1A). Three contractions were randomly performed at each of the three following levels: 80%, 90%, and 100% of MVC. Between contractions, subjects rested for ≥1 min to minimize the effects of fatigue. After the final contraction, subjects rested for ≥5 min to minimize any residual effects on the fatigue task.
Throughout the contraction, stimulations separated by 10 s, followed by a supramaximal peripheral nerve stimulation pulse 2 s later, were applied at the beginning and at 1-min intervals.

Sustained isometric plantar flexion contraction at 30% of MVC until torque level dropped below 28.5% of MVC for 3 consecutive seconds. Two magnetic stimulations separated by 10 s, followed by a supramaximal peripheral nerve stimulation pulse 2 s later, were applied at the beginning and at 1-min intervals throughout the contraction.

Fatigue task. Subjects maintained an isometric plantar flexion at 30% of the predicted MVC until the contraction could no longer be sustained, which was defined as the point at which the torque fell below 28.5% of MVC for 3 consecutive seconds (Fig. 1B). Verbal encouragement was given to each subject throughout the fatigue task.

Magnetic and electrical stimulations were applied in sets throughout the fatigue task, with a set containing two magnetic stimulations (TMS or cervicomedullary magnetic stimulation) separated by 10 s followed by one supramaximal peripheral nerve stimulation 2 s later. Stimulation sets occurred at the beginning of the fatigue task and at 1-min intervals until task failure (Fig. 1B).

**EMG and torque recordings.** EMG activity from Sol and MG was recorded with two electrode configurations: a pseudo-monopolar electrode configuration to measure the evoked motor potentials and a bipolar electrode configuration to measure background EMG. For the pseudo-monopolar configuration, active electrodes (Ag-AgCl, 24 mm diameter; Tyco Healthcare Group) were placed ~3 cm distal to the middle of the belly on MG and Sol, and reference electrodes were placed on the Achilles tendon slightly proximal to the calcaneous. The bipolar configuration consisted of a pair of electrodes (interelectrode distance = 24 mm) positioned slightly proximal to the monopolar electrode on each muscle. EMG recordings were amplified 100 times (model NL 844 preamplifier, Digitimer) and band-pass filtered between 10 and 1,000 Hz (model NL 900L, Digitimer). Plantar flexor torque was measured using a torque transducer (Maywood Instruments, Hampshire, UK) and amplified (model BK 1-5, Nobel Elektronik). The torque and EMG signals were sampled at 100 and 2,000 Hz, respectively, and subjected to analog-to-digital conversion with a 16-bit analog-to-digital converter (Micro 1401 mk-II, Cambridge Electronic Design) and commercially available software (Spike2, Cambridge Electronic Design).

Data analysis. MEPs, CMEPs, and M-wave peak-to-peak amplitudes were measured using custom scripts developed in Spike2. The peak-to-peak amplitudes of the three MEPs and CMEPs evoked at 80%, 90%, and 100% of MVC were averaged at each contraction level. During the sustained contraction, the peak-to-peak amplitudes of the two magnetically evoked responses within a stimulation set were averaged and normalized to the M_max in that set.

MEG was analyzed by determination of the average root-mean-square (RMS) amplitude over a 0.5-s period. The EMG produced during the brief MVCs was measured during the 0.5-s period where torque was highest for the contraction. In the fatigue trial, EMG was measured in the 0.5-s period before each magnetic stimulation within a stimulation set. The average of these two values was determined and used as the EMG value for that stimulation set.

Twitch torque evoked by the supramaximal peripheral nerve stimulation in a stimulation set was measured as the difference between the peak value of the twitch and the baseline torque immediately before the stimulation. For quantification of the torque fluctuations during the sustained 30% of MVC, the torque signal was band-pass filtered between 5 and 30 Hz using a fourth-order, zero-lag Butterworth filter. Torque fluctuation was then calculated from the RMS amplitude of the exerted torque relative to the target torque at 1-s intervals for each subject.

The initial time of each stimulation set was converted to a percentage of 100% of each subject’s time to task failure. The data were then sorted into bins, with the first stimulation set for each subject as 0% of time to task failure and the final stimulation set as 100% of time to task failure. The other stimulation sets were binned at 20% intervals with a bin width of ±10%. If two stimulation sets fell within the same bin, the values were averaged.

**Statistical analysis.** Before differences in the data were examined, Shapiro-Wilk’s W tests were performed to identify the normality of different variables. Two-way repeated-measures ANOVAs were performed for both muscles to examine the effects of time on MEP and CMEP amplitude during the sustained contraction and to examine the effects of contraction strength on MEP and CMEP amplitude during the brief nonfatigue contractions. One-way ANOVAs were performed for both muscles to examine the effects of time on M_max, twitch torque, torque fluctuations, and EMG during the sustained contraction. Planned comparisons (25) were used to test between 0% and 20%, 0% and 40%, 0% and 60%, 0% and 80%, and 0% and 100% of time to task failure. Depending on the normality of the variables tested, Student’s t-test or Wilcoxon’s signed-rank test was used to compare MEPs and CMEPs during 100% MVCs with those at the start and the end of the sustained contraction. These comparisons were made to examine whether MEPs or CMEPs had grown throughout the sustained contraction relative to control evoked responses during a nonfatigue MVC. Dependent t-tests were also used to compare the EMG at task failure with the EMG during the brief MVC for both muscles and to compare time to task failure between the two sessions.

All group data in RESULTS are presented as means ± SD; group data in Figs. 2, 3, 6, and 7 are presented as means ± SE. Significant differences were established at P ≤ 0.05.
RESULTS

Time to task failure, muscle activity, and torque measures. The mean plantar flexion torque produced during the sustained contractions was 36.6 ± 7.3 N·m (29.5 ± 0.6% of MVC) and 38.0 ± 6.6 N·m (29.6 ± 0.7% of MVC) for the TMS and cervicomedullary magnetic stimulation trials, respectively. The mean time to task failure for the TMS trials was not significantly different from that for the cervicomedullary magnetic stimulation trials (434 ± 84 and 399 ± 94 s, respectively, P = 0.2). Consequently, data from TMS and cervicomedullary magnetic stimulation trials were pooled for subsequent data analysis where appropriate (i.e., except for the TMS and cervicomedullary magnetic stimulation evoked responses).

The RMS amplitude of the torque fluctuations increased throughout the sustained contraction from 0.09 ± 0.02 N·m at 0% of time to task failure to 0.26 ± 0.11 N·m at 100% of time to task failure (Fig. 2A). There was a significant main effect with time \([F_{(5,54)} = 17.3, P < 0.05]\), and planned comparisons revealed significant increases between 0% of time to task failure and 80% and 100% of time to task failure \((P < 0.05)\).

The RMS amplitude of EMG in Sol increased steadily throughout the sustained contraction from 23.4 ± 8.8% of MVC at 0% of time to task failure to 37.9 ± 11.4% of MVC at 100% of time to task failure (Fig. 2B). A significant main effect with time was found \([F_{(5,54)} = 4.5, P < 0.05]\), and there were significant increases in EMG amplitude from 0% of time to task failure to 80% and 100% of time to task failure \((P < 0.05)\). Sol EMG amplitude was significantly smaller at 100% of time to task failure than during the brief, prefatigue MVC \((P < 0.05)\).

The RMS amplitude of EMG in MG was 19.8 ± 5.7% of MVC at 0% of time to task failure and 36.5 ± 18.8% of MVC at 100% of time to task failure (Fig. 2C). Little change in MG EMG amplitude occurred during the first half of the contraction, whereas a substantial increase was observed over the second half of the contraction. There was a significant main effect with time \([F_{(5,54)} = 5.5, P < 0.05]\) and significant increases in EMG RMS amplitude in MG from 0% to 80% and 100% of time to task failure \((P < 0.05)\). EMG amplitude in MG was significantly smaller at 100% of time to task failure than during the brief, prefatigue MVC \((P < 0.05)\).

Superimposed twitch and \(M_{\text{max}}\) measures. The mean superimposed twitch amplitude increased slightly during the first 20% of the sustained contraction and, thereafter, decreased continuously to reach 61.0 ± 15.0% of its original size at 100% of time to task failure (Fig. 3A). This final superimposed twitch \((19.8 ± 3.9 \text{ N·m})\) was much larger than the superimposed twitch during the prefatigue MVC \((2.6 ± 3.8 \text{ N·m})\), which is exemplified by twitch recordings from a single subject in Fig. 4. A significant main effect with time was found for superimposed twitch amplitude \([F_{(5,54)} = 15.4, P < 0.05]\). The superimposed twitch was significantly lower at 60% than at 0% of time to task failure \((P < 0.05)\) and remained lower until 100% of time to task failure \((P < 0.05)\). There were no significant main effects with time for \(M_{\text{max}}\) amplitude in Sol \([F_{(5,54)} = 0.7, P = 0.63; \text{Fig. 3B}]\) or MG \([F_{(5,54)} = 0.15, P = 0.98; \text{Fig. 3C}]\), as exemplified by \(M_{\text{max}}\) traces from a single subject in Fig. 5.

Corticospinal responsiveness during the sustained contraction. MEP amplitude in Sol increased throughout the contraction from 13.0 ± 8.5% of \(M_{\text{max}}\) at 0% of time to task failure to 23.0 ± 9.0% of \(M_{\text{max}}\) at 100% of time to task failure (Fig. 6A). CMEP amplitude also increased throughout the contraction: from 3.5 ± 1.0% of \(M_{\text{max}}\) at 0% of time to task failure to 5.8 ± 4.0% of \(M_{\text{max}}\) at 100% of time to task failure. Significant main effects were found with time and stimulation location on Sol evoked potential amplitude \([F_{(5,35)} = 9.2\) and \(F_{(1,7)} = 88.9, \text{respectively, } P < 0.05]\). Furthermore, there was a significant interaction effect between time and stimulation location \([F_{(5,35)} = 2.5, P < 0.05]\). Although the significant main effect of time suggests a general increase in evoked potential ampli-

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Fig. 2. A: torque fluctuation during the fatigue task, measured as root-mean-square (RMS) amplitude error from the target at 30% of MVC, normalized to torque fluctuation at 0% of time to task failure. Values are means (solid line) ± SE (dotted lines). B and C: soleus (Sol) and medial gastrocnemius (MG) RMS EMG amplitudes during the fatigue task normalized to the EMG produced during a brief, prefatigue MVC. Values are means ± SE.
tude over the contraction, the planned comparisons only revealed significant changes for MEPs between 0% and 100% of time to task failure ($P = 0.05$). There were no other significant changes from 0% of time to task failure in MEP or CMEP amplitude, although the trend toward an increase in Sol CMEP amplitude (Fig. 6A) from 0% of time to task failure approached statistically significant levels at 80% ($F(1,7) = 4.6, P = 0.07$) and 100% ($F(1,7) = 3.8, P = 0.09$) of time to task failure.

The MEP amplitude in MG was $10.4 \pm 4.0\%$ of $M_{\text{max}}$ at 0% of time to task failure and increased predominantly over the final two-thirds of the contraction to reach $20.5 \pm 10.7\%$ of $M_{\text{max}}$ at 100% of time to task failure (Fig. 6B). MG CMEP amplitude increased steadily over the entire contraction: from $3.6 \pm 1.1\%$ of $M_{\text{max}}$ at 0% of time to task failure to $5.0 \pm 2.0\%$ of $M_{\text{max}}$ at 100% of time to task failure. There were significant time and stimulation location main effects [$F(5,35) = 9.4$ and $F(1,7) = 60.8$, respectively, $P \leq 0.05$] and a significant interaction effect between time and stimulation location for evoked potential size [$F(5,35) = 6.1, P \leq 0.05$]. Planned comparisons revealed significant differences in MG MEP amplitude between 0% and 60%, 0% and 80%, and 0% and 100% of time to task failure ($P \leq 0.05$). For MG CMEPs, there was a significant difference between CMEP size at 0% and 100% of time to task failure ($P \leq 0.05$). Figure 5 shows traces of MEPs and CMEPs in MG at the start to the end of the sustained contraction for a single subject.

Corticospinal responsiveness during brief high-torque contractions. There were minimal changes in MEP and CMEP amplitude during the brief contractions at 80, 90, and 100% of MVC (Fig. 7A). For Sol, there was no significant main effect

Fig. 3. A: superimposed twitch amplitude evoked via supramaximal peripheral nerve stimulation during the fatigue task normalized to the superimposed twitch at the beginning of the contraction. B and C: Sol and MG maximal M wave ($M_{\text{max}}$) peak-to-peak amplitude changes during the fatigue task normalized to the corresponding values at the start of the contraction. Values are means ± SE.
for contraction strength on the size of the evoked potentials \([F_{(2,18)} = 0.4, P = 0.66]\). Inasmuch as evoked potentials obtained during the 100% MVC showed the highest values, they were used as the nonfatigue control response for comparison with the evoked responses at 0% and 100% of time to task failure. The Sol MEP at 100% of time to task failure (22.7 ± 9.2% of M\text{max}) was similar to that during the 100% MVC (25.2 ± 10.4% of M\text{max}, \(P = 0.57\)), whereas Sol MEP was significantly smaller at 0% of time to task failure (13.2 ± 8.5% of M\text{max}) than during the 100% MVC (\(P \leq 0.05\)). CMEP amplitude was significantly smaller at 0% (3.6 ± 1.1% of M\text{max}) and higher at 100% (5.0 ± 2.0% of M\text{max}) of time to task failure than during the 100% MVC (13.3 ± 3.7% of M\text{max}, \(P \leq 0.05\)).

**DISCUSSION**

To assess the effect of a submaximal fatiguing contraction on corticospinal responsiveness in the lower limb, we evoked MEPs and CMEPs in Sol and MG during a sustained plantar flexion at 30% of MVC. In both plantar flexor muscles, MEP amplitude increased over the course of the fatigue task compared with the control MVC MEP. However, the growth of the two responses differed during the fatigue task. In contrast to the results for upper limb muscles, this suggests a substantial contribution to the enhanced corticospinal responsiveness observed during a sustained submaximal contraction of the triceps surae.

Central fatigue. A large superimposed twitch remained in response to supramaximal peripheral nerve stimulation at task...
failure (~7 times larger than during the prefatigue MVC), which indicates that central factors contributed to task failure, inasmuch as the superimposed twitch during fatigue did not approach that attained in prefatigue MVCs (33). Furthermore, the EMG amplitude produced at the end of the sustained submaximal voluntary contraction failed to reach the level achieved during a brief MVC (31–33). Although amplitude cancellation effects occur in surface EMG through a range of contraction strengths (24), the magnitude of this effect is unlikely to account for the entire ~60% difference between MVC EMG and task failure EMG. Both of these factors show that central fatigue occurred during the sustained 30% MVC of triceps surae, which is characteristic of most sustained submaximal voluntary contraction protocols (11, 31, 43, 45). Torque fluctuation was also measured throughout the sustained contraction to indicate that the central processes of torque production were affected. It is thought that increased excitatory drive to the motoneuron pool leads to oscillations in the stretch-reflex arc and bursts of motor unit firing. It is this bursting of motor unit firing that causes the increased fluctuations in torque production at ~8–10 Hz (11, 31, 33). As such, the nearly threefold increase in torque fluctuation found in this experiment is another indication that central processes were altered during the fatiguing contraction. It can be assumed that the present findings represent the typical effects of a sustained 30% MVC of triceps surae, inasmuch as the durations of the contractions were similar between testing sessions and are comparable to those in past experiments involving a similar fatigue task (11, 31).

**Corticospinal responsiveness.** Increases in MEP amplitude for SOL and MG show increased corticospinal responsiveness during the sustained submaximal voluntary contraction of triceps surae. Furthermore, MEP amplitude at task failure was similar to MEP amplitude evoked during a brief MVC, whereas MEPs were significantly smaller at the start of the submaximal voluntary contraction than during an MVC. Increases in corticospinal responsiveness during a sustained submaximal voluntary contraction have been reported previously for the elbow flexors (45). To assess whether the corticospinal effects were mediated at the spinal and/or cortical level, changes in MEP amplitude were compared with changes in CMEP amplitude (50). The effects of the sustained submaximal voluntary contraction on CMEP amplitude were mixed. The trend toward an increase in SOL CMEP amplitude was not statistically significant, whereas the increase in MG CMEP amplitude was significant. However, CMEP amplitude at task failure remained significantly smaller than CMEP amplitude evoked during a control MVC in both muscles. The data suggest that a small spinal contribution to the increase in corticospinal responsiveness is likely, since CMEPs are unaffected by cortical factors. The CMEP changes are in contrast with the consistent increases in MEP amplitude during the submaximal voluntary contraction and similarity in MEP amplitudes elicited at task failure and during a control MVC. Thus the data indicate that a substantial proportion of the increase in corticospinal responsiveness observed during the sustained submaximal voluntary contraction of triceps surae was mediated by processes at the cortical level.

Corticospinal responsiveness at the cortical and spinal levels has been examined in the muscles of the upper arm during a sustained submaximal voluntary contraction. In a sustained 50% MVC of the elbow flexors, MEP and CMEP amplitudes increased at a similar rate over the first 40% of the contraction and then plateaued (30). These results suggest that corticospinal responsiveness changes almost entirely at the spinal level in the upper limbs. Differences in neural control mechanisms between the upper arm and the lower leg muscles may underlie the differences in corticospinal responses to fatigue. It has been suggested that the corticospinal projections onto SOL motoneurons are weaker than those onto other muscles such as tibialis anterior (2) and biceps brachii (12) and that it is not possible to evoke large CMEPs in SOL, even with strong electrical currents applied to the thoracic spine (35). Therefore, at a given stimulation intensity, magnetically evoked responses will be larger in upper arm muscles than in the triceps surae, which may explain the differences in corticospinal responsiveness of various muscles during fatigue.

It has been suggested that the contraction range over which motor unit recruitment persists, which differs between muscles, influences the range of contraction strengths over which the amplitude of evoked potentials continues to grow (40). It has been shown that as the firing rate of a tonically active motor unit increases, the probability that the motor unit will fire for a given excitatory stimulus will decrease (23, 28). Simulations suggest that, because of the exponential afterhyperpolarization trajectory of motoneurons (38) or the widening and deepening of the afterhyperpolarization period (22), the responsiveness of a motor unit will decrease. As such, the amplitude of evoked potentials, which are affected by the probability of motor unit firing and motor unit recruitment, will be influenced by the muscle-specific contraction strength range over which motor unit recruitment occurs. It is expected that evoked potential amplitude will increase up to or close to the contraction strength at which all motor units are recruited and then decrease in amplitude, inasmuch as increased firing rate has a greater effect on evoked potential size (36, 40). In the biceps brachii, in which new motor units are recruited up to ~90% of MVC (29), MEP and CMEP amplitudes increase up to ~75% of MVC but, subsequently, decrease at higher contraction levels (20, 36). In contrast, there is a progressive increase in SOL MEP amplitude over ~80% of the contraction range followed by a plateau to 100% MVC (40). Although the range of contraction strength over which additional motor units are recruited is yet to be determined in human SOL, animal data show that SOL motor units are recruited across the entire range of contraction strengths (21). This suggests that the muscle-specific upper limit of motor unit recruitment influences the relationship between MEP/CMEP amplitude and contraction strength during brief nonfatiguing contractions. As such, the growth of evoked potentials during sustained submaximal fatiguing contractions may also be affected by different upper limits of motor unit recruitment between muscles. This may partly explain the differences in corticospinal responsiveness between the elbow flexors and triceps surae during fatigue.

One factor that may influence the comparison between MEP and CMEP responses is the respective size of the responses at the beginning of the sustained contraction. In the present study, at the commencement of the contraction, MEPs were slightly larger than CMEPs in SOL and MG by 9.5% and 6.8% of M_max, respectively. This difference in amplitude is considered to be small in relation to the full range of M_max and, as such, a comparable proportion of the motor unit pool was probably
activated by the two methods of magnetic stimulation. However, it is not possible to know the precise proportion of the pool activated in either case because of nonlinearities in the motor unit recruitment vs. evoked potential relation. Furthermore, it appears that the influence of nonmatched responses is greater when responses are quite large (>70% of $M_{max}$) (36) than when responses are small, as in the present study (40). As such, the degree of similarity in the initial amplitude of the responses evoked by the two methods of magnetic stimulation enabled us to assess changes due to fatigue.

Although the present study adds to the evidence that MEP and CMEP amplitudes increase during a sustained submaximal voluntary contraction, the corticospinal responses to a sustained MVC appear to differ. During a 2-min sustained MVC of the elbow flexors, CMEP amplitude decreases in biceps brachii and brachioradialis (9) and MEP amplitude increases (49). We speculate that differences in spinal responsiveness between submaximal voluntary contractions and MVCs might be due to the differences in motor unit recruitment and firing rate between the two types of contractions. In a sustained MVC, motor unit recruitment and firing rate should be greatest at the beginning of the contraction, when maximum torque is produced (14), and then, immediately, torque production and motor unit firing rate decrease (4, 5, 17, 34, 42, 53). In a sustained submaximal voluntary contraction, the number of motor units recruited on initiation of the contraction is dependent on its force (13) but should increase over time as additional motor units are recruited to compensate for a reduction in the force-generating capacity of the originally active units. Concomitantly, motor unit firing rates can increase, decrease, or remain constant during a submaximal voluntary contraction (1, 3, 10, 18, 19, 27). These differences in motor unit recruitment and firing rate may influence the responsiveness of the corticospinal pathway at the spinal level differently between sustained MVCs and submaximal voluntary contractions.

In conclusion, MEP and CMEP amplitude increased in MG during a sustained submaximal contraction at 30% of MVC, whereas MEP size only increased in Sol. Furthermore, CMEP amplitude failed to increase sufficiently during the sustained contraction to match the amplitude of the evoked response recorded during a prefatigue MVC, whereas MEP amplitude at task failure was similar to that evoked during a control MVC. This suggests a substantial cortical contribution to the increases in corticospinal responsiveness during a submaximal fatiguing contraction of the triceps surae.

REFERENCES


J Appl Physiol • VOL. 107 • JULY 2009 • www.jap.org


