Excitability at the Motoneuron Pool and Motor Cortex Is Specifically Modulated in Lengthening Compared to Isometric Contractions

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1Neuromuscular Research Center, Department of Biology of Physical Activity, University of Jyväskylä, Jyväskylä, Finland; 2Institute of Sport and Sport Science, University of Freiburg, Freiburg, Germany; 3Department of Training and Movement Science, University of Potsdam, Potsdam, Germany; 4Laboratory of Biomechanics, University of Ljubljana, Ljubljana, Slovenia; and 5Department of Mechanical Engineering, University of Lappeenranta, Lappeenranta, Finland

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Gruber M, Linnamo V, Strojnik V, Rantalainen T, Avela J. Excitability at the motoneuron pool and motor cortex is specifically modulated in lengthening compared to isometric contractions. J Neurophysiol 101: 2030–2040, 2009. First published January 28, 2008; doi:10.1152/jn.91104.2008. Neural control of muscle contraction seems to be unique during muscle lengthening. The present study aimed to determine the specific sites of modulatory control for lengthening compared with isometric contractions. We used stimulation of the motor cortex and corticospinal tract to observe changes at the spinal and cortical levels. Motor-evoked potentials (MEPs) and cervicomedullary MEPs (CMEPs) were evoked in biceps brachii and brachioradialis during maximal and submaximal lengthening and isometric contractions at the same elbow angle. Sizes of CMEPs and MEPs were lower in lengthening contractions for both muscles (by ~28 and ~16%, respectively; P < 0.01), but MEP-to-CMEP ratios increased (by ~21%; P < 0.05). These results indicate reduced excitability at the spinal level but enhanced motor cortical excitability for lengthening compared with isometric muscle contractions.

INTRODUCTION

According to muscle models, the force during a maximum lengthening contraction should exceed force during a maximum isometric contraction by ~50% due to short range stiffness (Rack and Westbury 1974). For in vivo experiments, higher lengthening forces were only observed at the very beginning of muscle lengthening with preactivated muscles (Komi et al. 2000; Linnamo et al. 2002, 2003, 2006) but not for the whole range of motion (Aagaard et al. 2000; Komi et al. 2000; Linnamo et al. 2002, 2003, 2006; Pinniger et al. 2000; Seger and Thorstensson 2000; Westing et al. 1991). This inability to reach the maximal potential force level in the later phase of lengthening has been attributed to a failure of muscle activation (Babault et al. 2001; Loscher and Nordlund 2002; Pinniger et al. 2000; Seger and Thorstensson 2000; Webber and Kriellaars 1997; Westing et al. 1990).

Only a few studies have examined the underlying mechanisms of muscle activation failure during maximum lengthening contractions. Duclay et al. (Duclay and Martin 2005) found depressed H-reflexes but unchanged V-waves as compared with isometric and shortening contractions. Loscher and Nordlund (2002) reported unchanged areas of motor-evoked potentials (MEP) elicited by transcranial magnetic stimulation (TMS) when they compared maximal lengthening and shortening elbow flexions (Loscher and Nordlund 2002). For submaximal contraction levels, similar findings were presented regarding the depression of H-reflexes (Abbruzzese et al. 1994; Nordlund et al. 2002; Romano and Schieppati 1987). However, unlike in maximal contractions, reduced MEPs were reported for submaximal lengthening compared with shortening contractions (Abbruzzese et al. 1994; Sekiguchi et al. 2001, 2003). Consequently, it seems appropriate to assume that neural control of lengthening contractions may be unique (for review, see Enoka 1996).

There is a difference in neural control between submaximal lengthening contractions, where motor output has to be controlled carefully by the CNS, and maximal lengthening contractions, where maximal voluntary drive is required but could result in damage to the muscle (Avela et al. 1999; Chen et al. 2003; Cramer et al. 2007; Nosaka et al. 2002). Nevertheless, for both maximal and submaximal lengthening contractions, it was hypothesized that a unique control scheme might mainly act at the spinal level (Aagaard et al. 2000; Abbruzzese et al. 1994; Duclay and Martin 2005; Loscher and Nordlund 2002; Sekiguchi et al. 2001, 2003). However, because of methodological limitations, these studies could not refer directly to the site (cortical and/or spinal) of the observed changes. Therefore the aim of this study was to identify the location of neural mechanisms (cortical vs. spinal) involved in the modulatory control of submaximal and maximal lengthening contractions.

We evoked motor responses by electrical stimulation at the cervicomedullary junction (CMEP) and by TMS over the primary motor cortex during submaximal and maximal isometric and lengthening contractions in biceps brachii (BB) and brachioradialis (BR) muscles. Based on the assumption that the corticospinal tract is free from presynaptic control (Jackson et al. 2006; Nielsen and Petersen 1994) and that the CMEP for the elbow flexor muscles contains a dominant monosynaptic component (Petersen et al. 2002), changes in CMEPs reflect alterations at the spinal motoneuron pool itself, whereas changes in the ratio of CMEP to MEP area reflect effects at the motor cortex.

The fact that CMEPs are considered to be free of presynaptic inhibition (in contrast to H-reflexes) and work well during maximal contractions [in contrast to motor potentials evoked by transcranial electric stimulation (TES)], makes the comparison of MEPs with CMEPs the most direct possibility to...
identify modulatory actions at the cortical versus spinal level during strong muscle contractions (for review, see Taylor and Gandevia 2004). In the present study, we hypothesized that specific modulations at the motoneuron pool and motor cortex would be evident for lengthening compared with isometric contractions.

**Methods**

Nine people (aged 22–47, 3 females) participated in the study. They had no history of serious injuries of the right hand, arm, or shoulder and no seizures, neurosurgery, or metal or electronic implants in their skull. The participants were familiar with the testing device and had previously experienced lengthening contractions with the intention to resist maximally. However, they were not engaged in athletic or specific eccentric training at the time of the measurements.

**Ethical approval**

All subjects gave their informed consent prior to the measurements. The experiments were approved by the ethics committee of the University of Jyväskylä and conformed to the standards set by the latest revision of the Declaration of Helsinki.

**Muscle torque**

The measurement of elbow flexor torque was similar to that described in earlier papers (Komi et al. 2000; Linnamo et al. 2006). Participants sat in a chair. The lever arm was equipped with a strain gauge transducer. This transducer was adjusted for each participant to avoid any pain during maximal contractions. The distance between the axis of rotation of the lever arm and the force transducer was measured to calculate torque. Measurements were performed isometrically at a 110° elbow angle and dynamically at an elbow angle between 80 and 140° with a constant velocity of 1 rad/s (see Fig. 2).

Passive torque curves were recorded prior to the measurements to measure the gravity-dependent torques produced only by the weight of the arm. The EMG signals were checked throughout the whole movement to ensure that no muscle activity was present. After the experiments, these passive torque curves were subtracted from measured torque curves during the experiment to obtain active torque values.

**Electromyography**

Electromyographic (EMG) activity was recorded from the BB, BR and triceps brachii (TB) muscles of the right arm using self-adhesive electrodes (Blue Sensor N-00-S, Medicotest). The electrodes were adjusted on the muscle belly in accordance with the underlying muscle fiber direction (interelectrode distance = 20 mm; interelectrode resistance <2 kΩ). Alignment of the electrodes was checked according to the shape of the M-wave. It was ensured that each subject showed a smooth bipolar shaped M-wave during 50% and maximal voluntary contractions. The signals were filtered (10 Hz to 1 kHz), amplified (500 times, amplifier NL824-153, Digitimer, Welwyn, Garden City, UK) and sampled at 5 kHz through an AD-Interface (CED 2701 with Signal software, Cambridge Electronic Devices, Cambridge, UK).

**Stimulation methods (Stim)**

Motor responses were recorded for elbow flexor muscles (BB and BR) with stimulation at the brachial plexus to evoke maximal compound muscle action potentials (maximal M-wave = $M_{\text{max}}$), stimulation between the mastoids (cervicomedullary stimulation = CMS) to activate the cervicomedullary junction and evoke short-latency responses in the arm muscles (CMEP), and TMS over the motor cortex to elicit MEPs.

**Brachial Plexus Stimulation.** Single electrical stimuli were delivered to the brachial plexus to evoke maximal M-waves ($M_{\text{max}}$) in BB and BR (pulse duration = 1 ms; constant current; MEB-5304K, Nihon Kohden, Tokyo, Japan). The cathode (Unomedical, 4560M; Unomedical, Stonehouse, UK) was placed in the supraclavicular fossa and the anode (V-Trodes, No. 2702, 2 in round, Mettler Electronics, Anaheim, CA) on the acromion. The intensity used to evoke $M_{\text{max}}$ at rest in both muscles was doubled (40–70 mA) for stimulation during the experiments.

**Cervicomedullary Stimulation.** Transmastoid electrical stimulation was delivered via electrodes (Unomedical, 4560M; Unomedical) attached to the skin over the mastoid processes with the cathode on the left side (pulse duration = 100 μs; constant current; D7A, Digitimer, Welwyn). Such stimulations are able to activate axons in the corticospinal tract at the level of the cervicomedullary junction. As a result of this activation, short-latency responses in the arm muscles, termed CMEPs, can be observed (for review, see Taylor and Gandevia 2004). To be sure that activation did not shift toward the ventral roots of motor axons when stimulation intensity and contraction strength were increased, we analyzed latencies of CMEPs carefully throughout the experiment. Stimulator output (180–395 mA) was set during 50% isometric MVC to produce responses with peak-to-peak amplitudes in BB of 66 ± 9% of $M_{\text{max}}$ (BR: 57 ± 20% $M_{\text{max}}$).

**Transcranial Magnetic Stimulation.** MEPs were evoked in the BB and BR muscles of the right arm (Magstim 200, SA34 0HR; Magstim, Whitland, UK). A circular coil (Magstim St/N135, 14 cm OD) was positioned over the motor cortex of the left hemisphere to evoke MEPs. It was orientated to induce a posterior-to-anterior current in the underlying cortical area. The coil was adjusted during rest to determine the optimal position. Thereafter it remained in this position throughout the whole experiment. This was ensured by attaching the coil to a helmet and securing the helmet to the chair (3-point fixation). In addition, the scalp was marked and positions of markings in relation to the coil were checked during and after each contraction. Stimulus intensities ranged between 40 and 60% of maximum stimulator output. Intensities were adjusted at 50% of isometric MVC to produce MEPs in BB with peak-to-peak amplitudes of 69 ± 7% $M_{\text{max}}$ (BR: 50 ± 8% $M_{\text{max}}$).

The intensity of TMS was individually adjusted during 50% isometric MVCs to ensure that motor responses following CMS and TMS were comparable in size [amplitudes and areas of MEPs and CMEPs were not statistically different; BB amplitudes: $P = 0.166$; BB areas: $P = 0.097$; BR amplitudes: $P = 0.248$; BR areas: $P = 0.602$; paired Student t-test]. After adjusting the intensity, two stimuli with a 20% higher intensity were evoked to ensure that preset CMEP and MEP peak-to-peak amplitudes could increase by >10% of their value (normalized to $M_{\text{max}}$). This ensured that MEPs and CMEPs were below their plateau values during 50% isometric MVCs (input-output property in the corticospinal tract) to identify both decreased and increased responsiveness at the motor cortex during lengthening and maximal contractions. The stimulation intensities for both TMS and CMS were then kept constant throughout the experiment.

**Experimental procedures**

After subjects gave informed consent to participate in the study, EMG electrodes were placed on the muscles and interelectrode resistance was checked. Thereafter electrodes for brachial plexus stimuli were placed. Then participants were positioned in an adjustable chair. The trunk was fixed to the chair with safety seat belts. The forearms was supinated and fixed to a custom-made isokinetic elbow extension device (Komi et al. 2000). The elbow joint was aligned to the axis of rotation to prevent any movement of the lower arm in relation to the
level arm of the system. The upper body was positioned so that participants performed elbow flexion and extension as naturally as possible. The maximal range of movement was set to an elbow angle between 80° and 140° (180° = fully extended elbow) and secured with mechanical stoppers. After positioning, participants were allowed to do some submaximal contractions to become accustomed to the testing procedure. Thereafter three isometric MVCs were performed at elbow angles of 110° and 80°. The mean maximal torque values of these trials were calculated, and the 50% isometric MVC torques were displayed as two lines on an oscilloscope along with the actual torque during the subsequent experiment.

M-waves were then evoked at rest at an elbow angle of 110° in BB and BR by stimulating the brachial plexus. We analyzed peak-to-peak amplitudes and determined the stimulation intensity that evoked $M_{\text{max}}$ in resting conditions, whereby no further increase in M-wave occurred with increasing stimulation intensity. This intensity was then doubled, and three stimulations were performed at this intensity during isometric contractions of 50% MVC. Peak-to-peak amplitudes of $M_{\text{max}}$ were analyzed, and the mean value was calculated. Thereafter electrodes were placed for CMS and the stimulation intensity was adjusted to result in CMEP peak-to-peak amplitudes of ~70% of $M_{\text{max}}$ during isometric contractions of 50% MVC. Finally, we positioned the helmet and the coil for TMS and adjusted the stimulation intensity to evoke MEPs of similar amplitudes to CMEPs. The coil was attached to the helmet to ensure that the position of the coil remained constant relative to the skull during the measurements. The helmet was upheld by a device mounted to the chair to maintain a constant head position throughout the whole experiment and prevent participants from bearing the weight of the helmet and coil (Fig. 1A).

During the experiment, participants performed lengthening and isometric elbow flexions in a dynamometer at 50 and 100% of MVC. Lengthening contractions commenced after initial isometric contraction to the preset activation level. For contractions at 50% of MVC, the participants were asked to align the actual torque displayed on an oscilloscope in front of them with a line that was set to exactly 50% of MVC. Five hundred milliseconds to 1 s after they reached the target level (50% MVC), the ergometer was triggered, and participants performed the lengthening contraction with the intention of maintaining a constant level of effort. For maximal contractions, participants were instructed to contract maximally and to maintain this level until the end of the lengthening phase. The ergometer was again triggered 500 ms to 1 s after the participants reached their isometric MVC. The initial isometric contraction was performed at an elbow angle of 80°. In the case of a following elbow extension, participants were instructed to maintain a constant contraction intensity throughout the lengthening phase. All isometric measurements and stimulations were performed at an elbow angle of 110° (see Fig. 2). After contractions of 50% MVC a break of ≥1 min was allowed. After maximal contractions a break of ≥2 min was mandatory.

To minimize the total number of contractions, participants performed three trials for each target torque level. This resulted in a total of 48 contractions [3 repetitions * 2 contraction intensities (maximal and submaximal) * 2 contraction modes (isometric and lengthening) * 4 (3 stimuli)] stimulation at the brachial plexus, stimulation between...
the mastoids, stimulation over the motor cortex (+ control)]. These contractions were performed in three blocks, each with 16 unique contractions. In each of these blocks, contractions were randomized. Participants were informed about the contraction mode and thereafter instructed to aim for 50% MVC or MVC torque level, which was displayed on a monitor at eye level. Participants were not informed about the upcoming stimulation.

In three of the nine subjects, nine additional isometric contractions were performed at the end of the protocol to evoke $M_{\text{max}}$, CMEPs, and MEPs at matched background activity (BGA) levels during submaximal contractions. To find the appropriate isometric contraction strength, the BGA of BB and BR for submaximal lengthening contractions was analyzed. Thereafter the subjects had to contract isometrically while the torque level displayed on the screen was steadily increased until BGA level of the isometric contractions matched the 50% lengthening contractions. After we adjusted torque levels individually, stimulations were applied in a randomized order during isometric contractions with $\geq$2-min rest between contractions.

**Data analysis**

Peak-to-peak amplitudes and areas of $M_{\text{max}}$, CMEPs, and MEPs were calculated between the initial deflection (= latency of evoked potential) of the EMG from baseline to the second crossing of the horizontal axis (= duration of evoked potential; Fig. 1C). Results for peak-to-peak amplitudes and areas were similar but only areas are reported. For each participant, the mean areas of three trials at a given contraction intensity and mode were calculated. CMEPs and MEPs were normalized to the mean $M_{\text{max}}$ values recorded during contractions of the same intensity and mode. Torque was normalized to the
mean of the three isometric MVC contractions without stimulation. Torque levels and background EMG activities (BGA as mean amplitude voltage) for BB, BR, and TB were calculated over a 100 ms period prior to stimulation. BGA was normalized to the mean $M_{\text{max}}$ values (calculated as mean amplitude voltage) of the evoked potential recorded during contractions of the same intensity and mode.

**Repeatability and stability**

One decisive point of the present study was to compare unfatigued isometric and lengthening maximal contractions. Our pilot studies showed that not more than ~20–30 maximal contractions could be performed without inducing fatigue, even with 2 min breaks between the contractions. As an additional limitation, no more than three stimulations for each contraction mode, intensity, and stimulation type could be elicited. Therefore we had to ensure high repeatability and stability of the performed trials. Analyses were performed separately for stimulations as well as contraction modes and intensities. Values for Cronbachs Alpha showed high repeatability throughout the experiment for BGA BB (0.855–0.961), BGA BR (0.702–0.923), torque (0.942–0.999), $M_{\text{max}}$ BB (0.970–0.985), $M_{\text{max}}$ BR (0.909–0.968), CMEP BB (0.889–0.952), CMEP BR (0.838–0.938), MEP BB (0.731–0.945), and MEP BR (0.826–0.950). Univariate tests of repeated measures for each contraction mode, intensity, and stimulation type could be elicited. Therefore we had to ensure high repeatability and stability of the performed trials. Analyses were performed separately for stimulations as well as contraction modes and intensities. Values for Cronbachs Alpha showed high repeatability throughout the experiment for BGA BB (0.855–0.961), BGA BR (0.702–0.923), torque (0.942–0.999), $M_{\text{max}}$ BB (0.970–0.985), $M_{\text{max}}$ BR (0.909–0.968), CMEP BB (0.889–0.952), CMEP BR (0.838–0.938), MEP BB (0.731–0.945), and MEP BR (0.826–0.950). Univariate tests of repeated measures for these parameters using time (3) as the within-subjects factor and comparing the first, second, and third trials resulted in no statistically significant differences ($P$ always $> 0.05$).

**Statistics**

Group data are presented as means ± SD unless otherwise stated. Paired $t$-test were used to reveal differences in torque and BGA of BB, BR, and TB in time intervals of 100 ms prior to stimulations for lengthening versus isometric contractions, and to compare latencies and durations of evoked potentials, as well as sizes of CMEPs and MEPs (normalized to $M_{\text{max}}$) for submaximal isometric contractions. One-way repeated-measures (ANOVA) with Bonferroni corrected post hoc tests were used to test differences between contraction modes (isometric and lengthening), intensities (submaximal and maximal), and muscles (BB and BR) for normalized CMEPs, MEPs, and MEP-to-CMEP ratios. The level of significance was set to $P = 0.05$ (2-tailed).

**RESULTS**

**Torque and BGA**

For lengthening contractions, a marked increase in EMG level lasting ~200 ms was observed after the onset of muscle lengthening (Fig. 2). For submaximal lengthening contractions with 50% preactivation level, EMG started to rise at 20.0 ms for BB and 22.6 ms for BR after the onset of movement. EMG increased almost to the level exhibited in maximal contractions. For maximal lengthening contractions, it was not possible to determine a distinct onset of the EMG rise. Elbow angles were identical at the time of stimulation. Torque, BB, BR, and TB BGA for isometric MVCs did not differ from lengthening MVCs, whereas contractions performed with 50% preactivation, and the effort required to maintain this 50% level throughout the lengthening contraction, resulted in significantly increased torques and BGA levels in BB and BR, but reduced activity of the TB (Table 1).

**Evoked potentials**

Stimulations were delivered at the brachial plexus and between the mastoids as well as over the motor cortex to elicit potentials in the EMG of BB and BR during maximal and submaximal isometric and lengthening contractions. Figure 3 shows superimposed M-waves, CMEPs, and MEPs in one subject for BB. For this participant, MEPs and CMEPs were reduced for lengthening contractions compared with isometric contractions ($P$ always $> 0.05$; Table 2). Moreover, no differences were found between normalized sizes of CMEPs and MEPs for BB and BR for this subject were lower for lengthening contractions compared with isometric contractions ($P$ always $> 0.05$; Table 2). The level of significance was set to $P = 0.05$ (2-tailed).

**Sizes of CMEPs**

Analysis of repeated measures for CMEPs revealed no differences between maximal and submaximal contractions ($P = 0.240$) or between BB and BR ($P = 0.334$), but CMEPs were significantly lower for lengthening contractions compared with isometric contractions ($43 ± 11$ and $59 ± 14% M_{\text{max}}; P = 0.001$). Bonferroni-corrected post hoc tests showed that sizes

**Table 1. Torque and background activity (BGA) of biceps brachii (BB), brachioradialis (BR), and triceps brachii (TB)**

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<tr>
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<th>BB</th>
<th>BR</th>
<th>BB</th>
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<tbody>
<tr>
<td>Torque, Nm</td>
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<tr>
<td>MVC ISO</td>
<td>50.2 ± 18.2</td>
<td>0.297</td>
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<tr>
<td>MVC ECC</td>
<td>52.4 ± 20.0</td>
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<tr>
<td>50% ISO</td>
<td>27.0 ± 10.3</td>
<td>0.002</td>
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<tr>
<td>50% ECC</td>
<td>32.9 ± 13.2</td>
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<tr>
<td>BGA BB, mV</td>
<td></td>
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<tr>
<td>MVC ISO</td>
<td>0.55 ± 0.26</td>
<td>0.473</td>
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<tr>
<td>MVC ECC</td>
<td>0.56 ± 0.21</td>
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<tr>
<td>50% ISO</td>
<td>0.27 ± 0.20</td>
<td>0.004</td>
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<tr>
<td>50% ECC</td>
<td>0.41 ± 0.15</td>
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<tr>
<td>BGA BR, % $M_{\text{max}}$</td>
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<tr>
<td>MVC ISO</td>
<td>7.8 ± 3.0</td>
<td>0.785</td>
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<tr>
<td>MVC ECC</td>
<td>7.6 ± 2.9</td>
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<tr>
<td>50% ISO</td>
<td>3.5 ± 1.7</td>
<td>0.007</td>
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<tr>
<td>50% ECC</td>
<td>5.1 ± 2.1</td>
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<tr>
<td>BGA TB, mV</td>
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<tr>
<td>MVC ISO</td>
<td>0.11 ± 0.08</td>
<td>0.056</td>
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<tr>
<td>MVC ECC</td>
<td>0.10 ± 0.07</td>
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<tr>
<td>50% ISO</td>
<td>0.05 ± 0.02</td>
<td>0.005</td>
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<td></td>
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<tr>
<td>50% ECC</td>
<td>0.03 ± 0.01</td>
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Differences between maximal voluntary muscle torque obtained at a 110 elbow angle (angle of stimulation) for isometric (MVC ISO) and lengthening (MVC ECC) contractions and submaximal isometric (50% ISO) and lengthening (50% ECC) contractions were tested with paired Student $t$-tests.

**References**

Sizes of MEPs

Analysis of repeated measures for MEPs revealed no differences between maximal and submaximal contractions ($P = 0.577$), but MEPs were significantly lower for BR compared with BB ($58 \pm 12$ vs. $69 \pm 14$% $M_{\text{max}}$; $P = 0.008$) and during lengthening contractions compared with isometric contractions ($58 \pm 16$ vs. $68 \pm 9$% $M_{\text{max}}$; $P = 0.007$). Bonferroni-corrected post hoc tests showed that sizes of MEPs were lower during maximal lengthening contractions for BB by $19 \pm 23$% ($P = 0.041$) and for BR by $20 \pm 14$% ($P = 0.002$) compared with maximal isometric contractions. For submaximal contractions the respective post hoc tests did not show any significant differences ($P$ values always $> 0.05$).

MEP-to-CMEP ratios

For MEP-to-CMEP ratios, analysis of repeated measures revealed no differences between contraction intensities ($P = 0.342$) or between BB and BR ($P = 0.340$), but MEP-to-CMEP ratios were significantly higher for lengthening compared with isometric contractions ($1.27 \pm 0.41$ vs. $1.05 \pm 0.21$; $P = 0.039$). However, Bonferroni-corrected post hoc tests showed no significant differences for specific comparisons ($P$ values always $> 0.05$).

Evoked potentials for submaximal contractions

with matched BGA

Additional measurements at slightly higher isometric contraction strength were performed in three of the nine participants to match BGA to that of submaximal lengthening contractions (BB: $0.34 \pm 0.18$ mV for isometric and $0.35 \pm 0.18$ mV for lengthening; BR: $0.23 \pm 0.07$ mV for isometric and $0.25 \pm 0.06$ mV for lengthening; TB: $0.05 \pm 0.01$ mV for isometric and $0.06 \pm 0.02$ mV for lengthening). Torque values

FIG. 3. Superimposed EMG responses of a single subject to brachial plexus ($M_{\text{max}}$), cervicomedullary electrical (CMEP) and transcranial magnetic stimulation (MEP) for biceps brachii. Left: isometric contractions (ISOs); right: lengthening contractions (LENS) of the same target torque. - - -, timing of stimulation. [arrow], onset of $M_{\text{max}}$ (top traces), CMEPs (middle traces), and MEPs (bottom traces). ↓, 2nd reflex response that can follow corticospinal tract stimulation during maximum or near maximum voluntary contractions (see Taylor et al. 2001). For this subject, the response was regularly observed during isometric MVCs but only for 1 of the 3 lengthening maximal contractions. Please note that CMEPs and MEPs are lower during lengthening compared with isometric contractions whereas maximal M-waves do not differ.
were higher for lengthening (63.3 ± 1.0% MVC) than isometric (54.2 ± 0.6% MVC) contractions. Mean values for CMEP and MEP sizes expressed in %M_max were higher in isometric (CMEP BB: 66 ± 9 and BR 66 ± 8; MEP BB: 73 ± 11 and BR 51 ± 4) than lengthening contractions (CMEP BB: 53 ± 10 and BR 46 ± 09; MEP BB: 51 ± 13 and BR 42 ± 6).

**DISCUSSION**

This study provides new data on the neural control of lengthening muscle contractions. We compared areas of CMEPs and MEPs between lengthening and isometric contractions to differentiate between mechanisms acting at the spinal and cortical levels. The size of the MEP reflects excitability and neuron properties at the motor cortex and the spinal motoneuron pool, whereas the CMEP only relates to spinal motoneuron properties. It should be acknowledged that MEPs and CMEPs may activate motoneurons differently because the MEP involves multiple volleys and the CMEP only a single volley. Therefore motor-unit potentials after TMS are more dispersed and some motoneurons may discharge more than once, which can affect the size of potentials averaged from surface EMG (Keenan et al. 2006). However, recent studies provide no evidence that these differences might affect the susceptibility of CMEPs or MEPs to changes in spinal excitability specifically. Martin et al. (2006) found comparable changes in MEPs and CMEPs with changes in contraction strength and stimulation intensity, which indicate similar responses of MEPs and CMEPs to changes at the spinal level. Taylor et al. (2002) reported an occlusive interaction between responses to CMS and descending action potentials evoked by TMS at short interstimulus intervals in BB. This observation is consistent with the two stimuli activating some of the same corticospinal axons for this muscle. Based on the assumption that CMEPs and MEPs of similar size recruit the motoneuron pool of BB and BR in a similar manner, lower CMEPs and increased MEP-to-CMEP ratios in lengthening compared with isometric contractions indicate that properties of motoneurons as well as of neurons located at the motor cortex were modulated differently during lengthening versus isometric contractions in the present study. These modulations will be discussed with respect to contraction strength and possible underlying mechanisms.

**FIG. 5.** Relationship between size of evoked potential (MEP and CMEP) and level of prestimulus EMG of 1 subject. Same subject and figure layout as in Fig. 4. Bigger responses during isometric contractions compared with lengthening contractions were found over the whole range of prestimulus EMG levels.
Maximal contractions

During maximal lengthening contractions, higher torques compared with isometric contractions could be expected because short-range stiffness should contribute considerably to overall muscle forces for the lengthening muscles (Rack and Westbury 1974). Unlike in vitro muscle preparations but in accordance with previous in vivo studies (Aagaard et al. 2000; Komi et al. 2000; Linnamo et al. 2002, 2003, 2006; Seger and Thorstensson 2000; Westing et al. 1991), lengthening torques did not exceed isometric torques for the whole range of motion in the present study (Fig. 2 and Table 1). Studies that used superimposed mechanical (Webber and Kriellaars 1997), peripheral electrical (Babault et al. 2001; Beltman et al. 2004; Pinniger et al. 2000; Seger and Thorstensson 2000; Westing et al. 1990), or TMS (Loscher and Nordlund 2002) showed that the torque of maximal lengthening contractions can be significantly increased. Therefore the disparity between the expected and effectively measured torque was mainly attributed to an activation failure that, in consequence, limits recruitment and/or discharge rates of motor units during maximal lengthening contractions. The fact that CMEPs but not MEP-to-CMEP ratios were lower during maximal lengthening compared with isometric contractions indicates that any activation failure in the present study was located exclusively at the spinal level (Fig. 6). Consequently, we suggest that voluntary descending drive from the motor cortex toward the muscle did not limit force production during maximal voluntary lengthening contractions.

Submaximal contractions

Lengthening submaximal contractions were started with a preactivation level of 50% MVC at an 80° angle and performed with the intention of maintaining the level of effort throughout the lengthening phase of the contraction (Linnamo et al. 2002). The lengthening phase was characterized by steep rises in BB and BR EMG with onsets that are well in line with latencies of stretch reflexes in these muscles (see Table 2 in Yamamoto and Ohtsuki 1989). Therefore it can be assumed that EMG increases were caused by discharges of muscle spindles as a consequence of muscle lengthening (Burke et al. 1978). This increase was much more pronounced in submaximal compared with maximal precontractions, which is in accordance with the fact that Ia input could recruit additional motoneurons in submaximal conditions but not during maximal contractions where the whole motoneuron pool should already be recruited (Kukulka and Clamann 1981). Higher EMG and torque levels were observed throughout the lengthening movement (Fig. 2). Bonferroni-corrected post hoc tests showed no significant increases for MEP-to-CMEP ratios, and therefore the present study provides no direct evidence for a higher cortical excitability during submaximal lengthening contractions, whereas reduced CMEPs indicate that modulatory changes occurred exclusively at the motoneuron pool (Fig. 6). It should be noted that unlike in maximal contractions, BGA of BB, BR, and TB, as well as torque, were not matched for submaximal lengthening and isometric contractions (Fig. 2 and Table 1). We evoked CMEPs with an area of approx. 60% $M_{\text{max}}$ during 50% MVC and found no differences in size during MVCs with the same stimulation intensity (Fig. 6). This is well in line with the results of Martin et al. (2006; their Fig. 3A). Based on their results, CMEP and MEP sizes could be expected to increase from 50% MVC up to ~75% MVC for such a stimulus intensity but then decrease to reach approximately the sizes measured at 50% MVC for MVC itself. As a consequence, the present study’s submaximal lengthening contractions, which resulted in slightly higher torques and BGA for BB and BR compared with isometric contractions of 50% MVC, should not result in reduced but rather in increased CMEPs and MEPs. To enable a more direct measure of this behavior, we added an additional protocol. In three subjects, we matched BGA during submaximal isometric (~54% MVC) and lengthening (~63% MVC) contractions and found similarly lower values for CMEPs and MEPs. Our data suggest that reductions in CMEPs and MEPs during lengthening contractions were not primarily a result of varying BGA (Fig. 5).

This conclusion is in line with previous studies that compared rather weak lengthening and shortening contractions for elbow flexor muscles (Abbruzzese et al. 1994; Sekiguchi et al. 2001). Abbruzzese et al. (1994) investigated evoked potentials after TMS and TES as well as peripheral nerve stimulation (H-reflex via the radial nerve) in the BB and BR muscles. During weak lengthening contractions, motor responses for TES, TMS, and H-reflex were significantly reduced compared with shortening contractions at similar levels of BGA. Such a uniform variation across contraction types between evoked potentials that involve cortical as well as peripheral pathways indicates that the mechanisms are probably located at the motoneuron pool itself. While Abbruzzese et al. (1994) used a constant stimulus intensity (1.5 times motor threshold at rest) for TMS, Sekiguchi et al. (2001) investigated the input-output property of the corticospinal tract (Devanne et al. 1997). MEP sizes for all stimulus intensities were significantly smaller during weak lengthening contractions for BR, whereas there were no differences regarding threshold levels. These results indicate mechanisms that are able to

<table>
<thead>
<tr>
<th>MVC ISO</th>
<th>MVC ECC</th>
<th>50% ISO</th>
<th>50% ECC</th>
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</thead>
<tbody>
<tr>
<td>M_{\text{max}}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency BB</td>
<td>4.4 ± 0.4</td>
<td>4.4 ± 0.5</td>
<td>4.6 ± 0.4</td>
</tr>
<tr>
<td>Latency BR</td>
<td>6.2 ± 0.8</td>
<td>6.2 ± 0.5</td>
<td>6.4 ± 0.5</td>
</tr>
<tr>
<td>Duration BB</td>
<td>23.3 ± 2.4</td>
<td>23.6 ± 2.3</td>
<td>25.4 ± 2.3</td>
</tr>
<tr>
<td>Duration BR</td>
<td>22.2 ± 2.5</td>
<td>22.8 ± 4.1</td>
<td>23.7 ± 3.2</td>
</tr>
<tr>
<td>CMEP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency BB</td>
<td>8.2 ± 0.4</td>
<td>8.3 ± 0.6</td>
<td>8.2 ± 0.6</td>
</tr>
<tr>
<td>Latency BR</td>
<td>10.1 ± 0.5</td>
<td>10.1 ± 0.8</td>
<td>10.3 ± 0.8</td>
</tr>
<tr>
<td>Duration BB</td>
<td>20.5 ± 4.8</td>
<td>18.0 ± 3.3</td>
<td>22.5 ± 1.9</td>
</tr>
<tr>
<td>Duration BR</td>
<td>20.0 ± 5.6</td>
<td>17.0 ± 2.4</td>
<td>21.1 ± 4.1</td>
</tr>
<tr>
<td>MEP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latency BB</td>
<td>10.9 ± 0.4</td>
<td>10.5 ± 0.5</td>
<td>11.0 ± 0.6</td>
</tr>
<tr>
<td>Latency BR</td>
<td>12.5 ± 1.0</td>
<td>12.5 ± 0.7</td>
<td>12.7 ± 0.7</td>
</tr>
<tr>
<td>Duration BB</td>
<td>24.1 ± 3.9</td>
<td>23.8 ± 4.3</td>
<td>27.8 ± 2.6</td>
</tr>
<tr>
<td>Duration BR</td>
<td>22.7 ± 5.3</td>
<td>22.7 ± 4.9</td>
<td>25.7 ± 4.8</td>
</tr>
</tbody>
</table>

Latencies and durations were compared between isometric and lengthening contractions at MVC and 50% MVC. CMEP: cervicomedullary MEP.
suppress the subliminal fringe of the corticospinal tract during lengthening contractions. The comparison of CMEPs and MEPs in the present study provides more direct evidence that these mechanisms may act mainly at the spinal level.

Modulatory mechanisms during maximal lengthening contractions

Recently the influence of discharge rate and recruitment of motor units during voluntary isometric contractions on the size of CMEPs and MEPs was discussed in great detail (Martin et al. 2006). Martin et al. (2006) found a concurrent increase followed by a reduction in CMEP and MEP size when increasing contraction strength of isometric elbow flexion from 50% MVC up to MVC. Furthermore, they observed that the size of either CMEPs or MEPs depended not only on contraction strength but also on stimulus intensity. Both findings are well in line with predictions drawn from motoneuron modeling (Matthews 1999). For the comparison of maximal contractions in this study, it seems appropriate to assume that all motoneurons of BB and BR were recruited when we evoked the motor responses (Kukulka and Clamann 1981). Based on this assumption, alterations in CMEP and MEP areas could be related

FIG. 6. Group data showing areas of MEPs and CMEPs normalized to $M_{\text{max}}$ obtained for maximal and submaximal isometric contractions compared with those obtained during lengthening contractions. Data from 9 subjects are pooled and mean ± SE values are shown. A: submaximal contractions; B: results for maximal contractions. Left: evoked potentials for BB during isometric and lengthening contractions; right: results for BR. Analysis of repeated measures revealed decreased CMEPs and MEPs ($P < 0.01$) and increased MEP-to-CMEP ratios ($P < 0.05$) during lengthening compared with isometric contractions. In post hoc analysis, CMEPs were always lower in lengthening compared with isometric contractions, whereas MEPs only decreased during maximal contractions. Post hoc analysis revealed no differences for comparisons between MEPs during submaximal contractions and MEP-to-CMEP ratios. Evoked potentials in BB and BR displayed the same behavior.

# $P < 0.05$ CMEPs or MEPs different to isometric.
to changes in discharge rates of already recruited motoneurons. Once recruited, a motoneuron should become effectively more refractory and therefore less excitable by increasing the discharge rate as a result of its afterhyperpolarization trajectory. This was predicted by mathematical models (Jones and Bawa 1997; Matthews 1999) and tested in single human motoneurons by peripheral stimulation of the Ia afferents (Jones and Bawa 1995) as well as TMS of the corticospinal tract (Olivier et al. 1995). Recently Martin et al. (2006) mainly attributed their observation of decreasing CMEPs with increasing isometric contraction strength from 75% MVC toward MVC to this mechanism. They argued that once all motoneurons are recruited with a given stimulus intensity, a further increase in contraction strength can only decrease the overall response. Thus for maximal contractions, the reduction in CMEPs found in the present study during lengthening contractions could reflect increased discharge rates of already recruited motoneurons. However, this is rather unlikely because higher firing frequencies for lengthening contractions compared with isometric contractions should result in much higher maximal torques as suggested by classical in situ stimulation data reported by Rack and Westbury (1974). Moreover, in studies that examined single motor units at given torque levels during lengthening contractions compared with isometric contractions, unchanged (Pasquet et al. 2006) or even lower discharge rates were reported (Howell et al. 1995; Tax et al. 1989). Reduced firing frequencies could explain the deficit in maximal torque but assuming full motoneuron recruitment these alterations should result in increased and not in reduced CMEPs (Martin et al. 2006).

A possible explanation for reduced CMEPs is selective recruitment of motoneurons. If we assume selective recruitment of motoneurons as a neural strategy to control overall motor output during lengthening contractions, the inhibitory control has to be very powerful to ensure that these motoneurons will not become recruited by maximal voluntary drive or enhanced Ia afferent input during muscle lengthening. In that case, inhibition of specific motoneurons could be so strong that it was not possible to recruit them via corticospinal volleys used in the present study. Consequently, this would explain decreases in CMEP and MEP sizes, respectively. However, there is no direct evidence for selective recruitment during maximal lengthening contractions. Until now, such behavior was only observed during submaximal or rather weak lengthening contractions when a light weight has to be lowered (Howell et al. 1995; Nardone et al. 1989). Nardone et al. (1989) described selective recruitment of high-threshold motor units in soleus and gastrocnemius muscles during rather weak lengthening contractions. Howell et al. (1995) found similar recruitment patterns for the human first dorsal interosseous muscle. It was speculated that the functional advantage could be a silencing of low-threshold motor units and concurrently reduced reflexive muscle contractions via Ia afferent contributions, which allows central mechanisms more freedom to control muscle contraction (Nardone et al. 1989). It should be noted that such a control scheme might not only depend on contraction strength but could be muscle specific as well. In recent studies, no specific derecruitment of low-threshold motoneurons was observed for BB or tibialis anterior during lengthening compared with isometric or shortening contractions (Kossev and Christova 1998; Pasquet et al. 2006; Sogaard et al. 1996; Stotz and Bawa 2001; Tax et al. 1989).

The present study did not aim to clarify specific alterations in recruitment and firing properties. However, reduced CMEPs showed that the responsiveness of motoneurons was reduced for any peripheral or corticospinal input in lengthening compared with isometric contractions. This behavior cannot be explained by higher firing rates of motoneurons during lengthening compared with isometric contractions, which suggests that inhibition of motoneurons may mainly operate at the spinal level. There are various mechanisms that could diminish spinal excitability. However, the comparison of CMEPs and MEPs provides no evidence that could favor any of these mechanisms nor does it exclude any as a possible candidate. According to previous studies, the potential mechanisms most likely to explain inhibition of spinal motoneurons may be Ib afferent inhibitory input from Golgi tendon organs (Aagaard et al. 2000) and the setting of motoneuron excitability by supraspinal structures (Abbruzzese et al. 1994; Sekiguchi et al. 2001).

From a functional perspective, the purpose of inhibiting motoneurons during lengthening muscle contractions could be to control muscle force. For submaximal contractions, this mechanism may enable the adjustment of muscle force to the requirements of the task, thus facilitating proper execution of the movement. For maximal lengthening contractions, this mechanism is powerful enough to reduce maximal eccentric force values considerably. However, any inhibition of motoneurons should decrease the number of active motor units and thus increase the stress (force per unit area) on these units above the level perceived during maximal isometric contractions (Please note that eccentric MVC was similar to isometric MVC in the present study). The weakest half-sarcomeres in active myofibrils would take up most of the total length change until the point of no myofilament overlap. As a result, in these half-sarcomeres, the force in passive structures would balance the force produced by still intact cross-bridges of adjacent sarcomeres (for review, see Prosk and Morgan 2001). For repeated lengthening contractions, this could lead to a considerable number of disrupted sarcomeres, causing muscle damage that has been demonstrated to occur after this kind of exercise (Avela et al. 1999; Chen et al. 2003; Crameri et al. 2007; Nosaka et al. 2002). It can be speculated that increased maximal eccentric strength accompanied by increased agonistic EMG, as has been reported to occur after only one training session (Linamno 2002), is related to neural adaptations that result in the removal of some of the inhibitory setting at the spinal level (Linamno et al. 2002). Moreover, such adaptations can explain increased voluntary maximal eccentric strength and increased agonistic EMG after high-intensity strength training (Aagaard et al. 2000) and in eccentrically trained athletes (Amiridis et al. 1996).

In conclusion, the present study showed that the responsiveness of motoneurons was reduced for any peripheral or corticospinal input in lengthening compared with isometric contractions, indicating inhibition of spinal motoneurons. The observed reduction in CMEPs indicates that spinal excitability was considerably lower in lengthening than isometric contractions, whereas a moderate increase in MEP/CMEP ratio indicates that cortical excitability was slightly higher. We suggest that increased cortical excitability results in extra excitatory descending drive during muscle lengthening to compensate for spinal inhibition. This indicates changes in neural control of muscle activity for both spinal and cortical sites in lengthening compared with isometric contractions.
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