Output of Human Motoneuron Pools to Corticospinal Inputs During Voluntary Contractions

P. G. Martin, S. C. Gandevia, and J. L. Taylor

Prince of Wales Medical Research Institute and the University of New South Wales, Sydney, Australia

Submitted 23 November 2005; accepted in final form 7 February 2006

INTRODUCTION

Every voluntary muscle contraction involves an increase in “excitability” at the motor cortex and at the motoneuron pool. Voluntary contraction increases the size and number of corticospinal volleys evoked by transcranial magnetic stimulation (TMS) of the motor cortex. The total amplitude of descending epidural volleys in conscious humans increases by 50% during maximal voluntary contractions (MVCs) compared with rest (Di Lazzaro et al. 1998b). This suggests that motor cortical excitability increases with increasingly strong voluntary contractions. Furthermore, the excitatory response to motor cortical stimulation recorded from the muscle (motor evoked potential, MEP) increases dramatically during weak contractions (e.g., Hess et al. 1987; Kischka et al. 1993; Taylor et al. 1997; Thompson et al. 1991). This has been attributed to increased excitability of motor cortical output cells and motoneurons during voluntary contraction (e.g., Cowan et al. 1986; Di Lazzaro et al. 1998b; Kaneko et al. 1996; Mazzocchio et al. 1994; Taylor et al. 2002; Ugawa et al. 1995).

In contrast, during strong contractions, the size of MEPs can decline (Todd et al. 2003, 2004). For voluntary forces >50% MVC, MEPs in biceps brachii decrease progressively to maximal forces. This paradox indicates that, for this muscle, the excitability of either the motor cortex or motoneuron pool does not continue to increase across the entire contraction range. Because the response to magnetic stimulation of the motor cortex is dominated by transsynaptically evoked output from corticospinal neurons (e.g., Di Lazzaro et al. 1998a; Edgley et al. 1997; Rothwell et al. 1991), the decrease in MEPs during strong contractions may arise from changes in the excitability of cortical neurons. However, models suggest that motoneuron responsiveness declines at high firing rates (Jones and Bawa 1994; Matthews 1996, 1999). Understanding these mechanisms is crucial to understanding how cortical and spinal levels interact to produce voluntary forces of different strengths. It is also needed to interpret changes in cortical or motoneuronal “excitability” during contractions at any strength.

To differentiate cortical and motoneuronal mechanisms underlying changes in “corticospinal excitability” across a wide range of voluntary contractions, we stimulated the motor cortex as well as the descending corticospinal pathways to elicit responses in biceps and brachioradialis. Corticospinal synapses appear to lack presynaptic inhibition (Nielsen and Petersen 1994) and thus responses to corticospinal tract stimulation likely reflect changes only in the corticospinal path and the motoneurons. We also examined responses in an intrinsic hand muscle to cortical stimulation during strong contractions. We hypothesized that MEPs in the hand muscle would also decrease in size at high voluntary forces. Furthermore, if motoneuronal mechanisms were responsible, differences between muscles in recruitment and rate coding of force output might be important in determining the magnitude of the reduction. Although biceps continues to recruit motor units beyond 90% MVC (De Luca et al. 1982; Kukulka and Clamann 1981) few motor units in an intrinsic hand muscle are recruited above 50% MVC (Milner-Brown et al. 1973; Moritz et al. 2005). Further increases in voluntary force rely on increasing motor unit firing rates. Thus we expected that decreases in MEP size would be more marked in the hand muscle than in biceps. Preliminary results were previously presented (Gandevia et al. 2005; Martin et al. 2005).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
METHO DS

Three experiments were conducted to assess responses elicited by stimulation of the motor cortex (motor evoked potentials, MEPs) and descending corticospinal pathways (corticomedullary evoked potentials, CMEPs) during isometric flexion of the elbow or isometric abduction of the index finger. A total of 13 healthy adult volunteers (four females; 34 ± 10, mean age ± SD) participated. Five subjects were studied on two or more occasions. The procedures were approved by the local ethics committee and the study was conducted according to the Declaration of Helsinki. All subjects gave their informed consent to participate. The three studies are described under Protocol below. Because many of our conclusions rely on the level of voluntary contraction in the various protocols, we use the adjectives strong for contractions >50% MVC and very strong for those >75% MVC.

Force and EMG recordings

Many of our experimental procedures and recording techniques are similar to those described previously (Gandevia et al. 1999; Taylor et al. 2000; Todd et al. 2003). For elbow flexion the subject sat with the right arm held at 90° in an isometric myograph (Fig. 1A). Electromyographic (EMG) activity was recorded from biceps brachii and brachioradialis using self-adhesive electrodes (Ag–AgCl, diameter 10 mm). One electrode was placed over the midbelly of each muscle and the other over the tendon. For index finger abduction, the index finger was placed firmly in a ring connected to an immovable bar and strain gauge (Fig. 1B). The subject was seated on a chair with the right forearm pronated and positioned on a table with the elbow flexed at a right angle and the hand open. The forearm and third to fifth fingers were restricted with a strap and metal brace, respectively. EMG activity was recorded from first dorsal interosseous (FDI) with one electrode placed over the muscle belly and the other electrode over the second metacarpophalangeal joint. EMG activity from biceps, brachioradialis, and FDI was filtered (16–1,000 Hz) and the signals, as well as torque (experiments 1 and 2) or force (experiment 3), were sampled at 2 kHz for off-line analysis using customized software (CED 1401 with Signal and Spike2 software; Cambridge Electronic Design, Cambridge, UK).

Stimulation

Recordings were made of the motor responses in the elbow flexor muscles to stimulation at the brachial plexus, stimulation between the mastoids, and magnetic stimulation over the motor cortex. Responses to ulnar nerve stimulation and magnetic stimulation over the motor cortex were recorded from the hand muscle.

BRACHIAL PLEXUS STIMULATION. To evoke maximal compound muscle action potentials [maximal M-wave (Mmax)] in biceps brachii and brachioradialis single electrical stimuli were delivered to the brachial plexus with a cathode in the supracleavicular fossa (Erb’s point; 2.5 cm above the clavicle and a third of its length from the medial end) and an anode on the acromion (200-μs duration; constant current; DS7AH, Digitimer, Welwyn Garden City, Hertfordshire, UK). The intensity of stimulation (42–216 mA, experiment 1; 60–168 mA, experiment 2) was set ≥20% above that needed to produce Mmax in both muscles.

ULNAR NERVE STIMULATION. To evoke Mmax in FDI single electrical stimuli were delivered to the ulnar nerve with a cathode and anode placed anteriorly and posteriorly, respectively, 3 cm proximal to the wrist (200-μs duration; constant current). The stimulus intensity was 20% above that required to evoke Mmax (30–114 mA).

TRANSCRANIAL MAGNETIC STIMULATION. A circular coil (13.5-cm outside diameter) positioned over the vertex elicited MEPs recorded from biceps and brachioradialis or FDI (Magstim 200, Magstim, Dyfed, UK). The direction of current flow in the coil preferentially activated the left motor cortex. Stimulus intensities for experiment 1 were between 40 and 80% of maximum stimulator output to evoke responses in biceps with an amplitude of 65–80% Mmax (70 ± 5%, mean ± SD) during contractions at 50% MVC. In experiment 2 the intensity was reduced (25–55% of maximal stimulator output) to elicit smaller responses in biceps of 30–50% Mmax (45 ± 5%) during 50% MVCs. Finally, in experiment 3 the intensity was between 37 and 60% of stimulator output to evoke responses in FDI of 40–60% Mmax (51 ± 8%) during 50% MVCs.

CERVICOMEDULLARY STIMULATION. The corticospinal tract was stimulated by passing a high-voltage electrical current (duration 100μs, Digitimer D180) between cup electrodes filled with conductive gel and glued to the skin (1–2 cm posterior and superior to the tip of the mastoid processes with the cathode on the left side) (Gandevia et al. 1999; Ugawa et al. 1991). Activation occurs at the cervicomedullary junction and evokes large, short-latency responses in the arm muscles, termed CMEPs. The stimulus activates many of the same axons as motor cortical stimulation because the single volley evoked by transmastoid stimulation can largely occlude the response to cortical stimulation (Taylor et al. 2002). A significant proportion of the motoneuronal response to cervicomedullary stimulation appears to be monosynaptic for both the hand muscles and the more proximal biceps (Petersen et al. 2002; Ugawa et al. 1991). The stimulator output (285–450 V, experiment 1; 323–413 V, experiment 2) was set during 50% MVCs to produce responses in biceps (mean amplitude 80 ± 9% Mmax, experiment 1; 37 ± 10% Mmax, experiment 2), the peak-to-peak amplitude of which approximated that of the responses to cortical stimulation. The amplitude of MEPs and CMEPs during 50% MVCs was not different within each experiment (P > 0.05; paired t-test). Stimulus intensity remained constant throughout the protocol. The latency of responses was monitored carefully to ensure that high-stimulation intensities did not activate the motor axons at or near the
ventral roots. A jump in latency of about 2 ms occurs when the site of stimulation spreads from descending tracts to the ventral roots (Taylor and Gandevia 2004).

Protocol

EXPERIMENT 1. The first experiment assessed large MEPs and CMEPs during voluntary contractions of the elbow flexors. Subjects (n = 7) performed three brief (1–2 s) control MVCs. The peak force of each MVC was measured and three submaximal target forces of 50, 75, and 90% MVC were set on a visual feedback display. Subjects then performed four pairs of test contractions in pseudorandom order, with 1–3 min rest between pairs to avoid fatigue. Each pair involved a brief MVC (1–2 s) followed 6 s later by a submaximal contraction of the same duration (Fig. 1C). During each contraction, stimulation of the motor cortex, brachial plexus, or cervicomedullary junction was delivered. Fifteen pairs of contractions were performed for each type of stimulation with five contractions at each of the three submaximal target forces.

EXPERIMENT 2. To assess the effect of stimulus intensity on the size of the evoked responses at different contraction strengths in biceps, subjects (n = 5) performed an identical protocol to experiment 1 with lower stimulus intensities for both cortical and cervicomedullary stimulation.

EXPERIMENT 3. To determine whether changes in the size of the MEP during contractions of different strengths were also apparent in other muscles, responses in FDI during abduction of the index finger were assessed. The protocol was similar to experiment 1 but additional target forces of 10 and 25% of MVC were added and CMEPs were not elicited. To minimize the number of contractions the repetitions for each submaximal target force were reduced to four. Thus subjects (n = 7) performed 40 pairs of contractions with either cortical or ulnar nerve stimulation.

Data analysis

The areas of MEPs, CMEPs, and Mmax were measured between cursors appropriately positioned for all potentials elicited by the same stimulus during contractions of similar strength. The cursors encompassed a region from the initial deflection from baseline to the second crossing of the horizontal axis (Fig. 1D). For each subject, mean areas for five trials (four in experiment 3) at each stimulus intensity and contraction strength were calculated. MEPs and CMEPs were normalized to the mean Mmax values recorded during contractions of the same strength. The absolute reduction in the size of responses across contraction strengths was calculated for each subject by subtraction of the normalized MEP or CMEP during MVCs from the largest responses, irrespective of the contraction strength at which these occurred. For each subject, torque or force was normalized to the mean of the five strongest contractions during the entire experimental session (62 ± 15 Nm, experiment 1; 61 ± 14 Nm, experiment 2; 40 ± 10 N, experiment 3).

Statistics

Group data are presented as means ± SD in the text and the means ± SE are shown in the figures (with n in the legends). Statistical analysis involved one-way repeated-measures ANOVA to test differences between contraction strengths. Post hoc discrimination between means was made with the Student–Newman–Keuls procedure. Paired t-tests were used to compare the magnitude of the maximum decrement of the MEP and CMEP. Unpaired t-tests were used to compare these decreases between the two stimulus strengths and muscle groups. The contraction strengths at which the largest normalized responses occurred are expressed as median values for the group of subjects. Mann–Whitney rank sum tests were performed to assess the differences between the two stimulus strengths and muscles for the contraction strength at which these largest responses occurred. Statistical significance was set at P < 0.05.

RESULTS

MEPs and CMEPs elicited by high-intensity stimulation

In the first experiment, stimulation was applied to the motor cortex and corticospinal tract to elicit large responses in biceps with a peak-to-peak amplitude >65% Mmax while subjects made strong voluntary elbow flexions (>50% MVC). Figure 2A shows typical superimposed EMG responses in biceps elicited by high-intensity corticospinal tract (CMEPs) and motor cortical stimulation (MEPs), as well as Mmax. For this subject, the area of potentials shows a consistent and progressive reduction from the weakest to strongest contractions for both biceps (Fig. 2B, left) and brachioradialis (Fig. 2B, right). Raw EMG traces comparing the sizes of responses during contractions at 50% MVC and during maximal contractions

![Figure 2](http://jn.physiology.org/)

**FIG. 2.** EMG responses to motor cortical, cervicomedullary, and brachial plexus stimulation for biceps and brachioradialis. A: single-subject data showing superimposed EMG responses in biceps brachii after motor cortical stimulation (MEP, left traces), cervicomedullary stimulation (CMEP, middle traces), and peripheral nerve stimulation (Mmax, right traces) during contractions of 50% and 100% MVC. Dashed horizontal lines indicate peak responses. Up arrows indicate timing of stimulation. Down dot arrow shows a transcortical reflex response that can follow corticospinal tract stimulation (see Taylor et al. 2001). B: corresponding data for the same subject plotted as areas of MEPS (filled circles) and CMEPS (open circles) during 50, 75, 90, and 100% MVC in biceps (left) and brachioradialis (right). Forces are shown as a percentage of the mean of the 5 largest contractions for the subject recorded during the entire experiment.
show that MEPs and CMEPs as well as $M_{\text{max}}$ were reduced (Fig. 2A). Because there were systematic changes in $M_{\text{max}}$ with contraction strength, MEPs and CMEPs were normalized to $M_{\text{max}}$ and pooled for the group of subjects to show mean changes in the responses (Fig. 3). With high-intensity stimulation the size of both MEPs and CMEPs reached a peak during 75% MVCs in biceps (areas 98 ± 10 and 86 ± 7% $M_{\text{max}}$, respectively; mean ± SD) and in brachioradialis (75 ± 14 and 73 ± 13% $M_{\text{max}}$, respectively). During maximal efforts, MEPs decreased to 76 ± 10% $M_{\text{max}}$ in biceps (Fig. 3A, filled circles) and to 51 ± 12% $M_{\text{max}}$ in brachioradialis (Fig. 3B, filled circles), significantly smaller than during contractions at other strengths ($P < 0.01$). Similarly, during maximal efforts, CMEPs declined to 60 ± 13% $M_{\text{max}}$ in biceps (Fig. 3A, open circles) and to 50 ± 17% $M_{\text{max}}$ in brachioradialis (Fig. 3B, open circles). Again, these were smaller than potentials at all other contraction strengths ($P < 0.05$). For both elbow flexor muscles, the reduction in area of the CMEP and MEP with stronger contractions was similar.

MEPs and CMEPs elicited by low-intensity stimulation

In a second experiment the intensities for cortical and corticospinal tract stimulation were reduced to obtain responses in biceps with a peak-to-peak amplitude <50% $M_{\text{max}}$. With the low-intensity stimulus, changes in MEPs and CMEPs in biceps with stronger contractions (>50% MVC) were less marked. MEPs and CMEPs were largest during 90% MVCs (64 ± 13 and 42 ± 13% $M_{\text{max}}$, respectively) and were significantly reduced during MVCs (56 ± 10 and 30 ± 14% $M_{\text{max}}$, respectively; $P < 0.05$; Fig. 3A, triangles). This reduction was similar for MEPs and CMEPs. Results for brachioradialis are not included because these small potentials were difficult to differentiate from ongoing EMG at high contraction strengths.

MEPs and CMEPs elicited by low- and high-intensity stimulation

In biceps, reductions in the sizes of MEPs and CMEPs across contraction strengths were larger for the high stimulus intensity ($P < 0.05$). In addition, the largest responses were elicited at stronger contraction strengths for the low-intensity stimulus ($P < 0.05$). Thus the largest MEPs and CMEPs occurred during 90% MVCs for weak stimulation, as opposed to 75% MVCs during high-intensity stimulation.

MEPs in first dorsal interosseous

To determine the influence of motor unit recruitment and rate coding on the reduction in MEPs during strong contractions, responses to cortical stimulation were elicited during contractions of the first dorsal interosseous (FDI). Figure 4A shows typical superimposed responses from one subject to cortical and ulnar nerve stimulation. In Fig. 4B the mean MEPs with different contraction strengths are shown normalized to $M_{\text{max}}$ for the group of subjects. As for biceps and brachioradialis, MEPs decreased in size during strong contractions (>50% MVC) of FDI. MEPs were reduced from 82 ± 12% $M_{\text{max}}$ during 50% MVCs to 50 ± 12% $M_{\text{max}}$ during maximal efforts. This was significantly smaller than for all other contraction strengths ($P < 0.001$). However, the magnitude of the depression in the MEP for contractions >50% MVCs was larger in FDI than in biceps, regardless of the stimulus intensity used to evoke responses in biceps. In FDI, the MEP was reduced by 35 ± 14% $M_{\text{max}}$, which was about threefold greater than the 12 ± 6% $M_{\text{max}}$ reduction in biceps with low-intensity stimulation ($P < 0.01$). This effect was also evident, but less pronounced, when comparisons were made with responses in biceps to high-intensity stimulation (35 ± 14 vs. 23 ± 7% $M_{\text{max}}$, $P < 0.05$). In addition, the largest MEPs in FDI occurred at weaker contraction strengths when compared with biceps. The largest responses in FDI occurred during 50% MVCs compared with peak responses in biceps at 75% MVCs during high-intensity stimulation ($P < 0.05$) and 90% MVCs ($P < 0.001$) during weak stimulation.

DISCUSSION

This study shows that motoneuron responses to corticospinal stimulation decline during very strong voluntary efforts (>75% MVC). The effect underlies a decrease in the MEP and
probably relates to changes in motor unit firing and recruitment occurring concurrently during progressively stronger efforts. Over the range of contraction strengths from 50 to 100% MVC, the MEP in biceps (normalized to $M_{\text{max}}$) decreased by about 25% $M_{\text{max}}$ with a similar attenuation in brachioradialis. The MEP in a hand muscle (FDI) also decreased about (35% $M_{\text{max}}$) during strong finger abductions (>50% MVC). A reduction in the size of the CMEP in the elbow flexors suggests that effects below the level of the motor cortex are responsible for the reduction in evoked output during strong contractions. As a significant proportion of the CMEP is monosynaptic for biceps (Petersen et al. 2002) and is not subject to presynaptic inhibition (Nielsen and Petersen 1994), it is likely that the changes are mediated by mechanisms at the motoneuron pool.

Changes occurring within the cortex can affect the MEP. During weak contractions (<50% MVC) the size of the MEP increases partly as a result of increased cortical excitability (e.g., Di Lazzaro et al. 1998b; Kaneko et al. 1996; Mazzocchio et al. 1994; Taylor et al. 2002; Ugawa et al. 1995). Conversely, the responsiveness of single motor units of distal muscles firing at moderate rates (<12 Hz) declines, an effect variably attributed to either cortical (Brouwer et al. 1989) or motoneuronal properties (Olivier et al. 1995). However, the present study shows that during the more rapid firing that occurs during very strong contractions, properties of the motoneuron, and not the cortex, limit motoneuronal output evoked by cortical stimulation. This is indicated by similar reductions in CMEPs and MEPs with increasing contraction strength. One consideration when comparing MEPs and CMEPs is that stimuli applied to the motor cortex and corticospinal tracts activate motoneurons differently. The MEP involves multiple descending volleys as opposed to the single volley responsible for the CMEP. Thus activation of many motoneurons in the MEP depends on temporal summation and the motor unit potentials, which constitute the MEP, are more dispersed than in the CMEP. The dispersion of action potentials producing the MEP could lead to phase cancellation of action potentials, thus reducing the size of the MEP (Keenan et al. 2006). In addition, stimuli may cause some motoneurons to discharge more than once, particularly for high stimulus strengths. Changes in these repetitive discharges could contribute to reductions in the size of the MEP. Finally, changes in the distribution of D- and I-waves evoked by cortical stimulation cannot be ruled out (e.g., Di Lazzaro et al. 1998b; Rothwell et al. 1991). However, it is not clear that these differences at the motoneuron level or in the muscle should make the MEP more or less susceptible than the CMEP to decreases with increased contraction strength. On the contrary, we found that comparable reductions in MEPs and CMEPs occurred for both weak and strong stimulation and for potentials evoked in biceps and brachioradialis.

Changes at the motoneuron pool with increased contraction strength

The reduction in the size of the CMEP with stronger contractions reflects the inability of some motoneurons to fire in response to the excitatory input. A likely mechanism is that with increased contraction strength some motoneurons become effectively refractory as a result of the trajectory of their afterhyperpolarization. Recovery of motoneuronal excitability after an action potential is influenced by firing rate, with motoneurons having an exponential return to threshold at low rates and a more linear approach during rapid firing. This has been described for cat motoneurons (e.g., Baldissera and Gustafsson 1974; Schwindt and Calvin 1972) and in models (Jones and Bawa 1997; Matthews 1996, 1999). The afterhyperpolarization trajectory affects the ability of a stimulus to elicit an action potential. Low-frequency firing increases the probability of eliciting a spike as the time available for excitation is greater if the membrane potential approaches threshold slowly (Jones and Bawa 1997, 1999; Matthews 1996). This fits with the response of single motoneurons to Ia (Jones and Bawa 1995; Kudina 1988; Piotrkiewicz et al. 1992) and corticospinal volleys (Bawa and Lemon 1993; Brouwer et al. 1989; Olivier et al. 1995) during moderate firing (between 9 and 15 Hz). Our data extend the idea of reduced responsiveness of individual motoneurons during rapid firing to the entire motoneuron pool. However, in contrast to modeling, our results show that with strong contractions the responsiveness of the motoneuron pool does not plateau as predicted but continues to fall (Matthews 1999). Near-maximal contractions would equate to mean firing rates of >26 Hz in biceps and 31 Hz in FDI (Bellemare et al. 1983; Seki and Narusawa 1996).

Although changes in the afterhyperpolarization trajectory associated with rapid firing are probably the main factor explaining the reduced responsiveness of the motoneuron pool, the recruitment of motor units is likely to be an important determinant of the contraction level at which a reduced response is observed. Our results show that stimulus intensity had a substantial effect on changes in CMEPs and MEPs with increased contraction strength. For biceps, responses evoked by low-intensity stimuli grew up to 90% MVC, whereas they
were largest at 75% MVC for strong stimuli. In addition, the decline in the size of potentials was more marked with strong stimuli. The different effects of contraction strength on responses to strong and weaker stimuli are consistent with the influence of motor unit recruitment occurring concurrently with increased firing rates. This behavior is predicted by a model of responses to Ia input proposed by Capaday and Stein (1987). The model suggests that as the percentage of active motoneurons increases the percentage of units recruited by the input should decline. However, when the excitatory postsynaptic potential is small the reflex output should increase over a much greater range of the motoneuron pool excitation level than when it is large (Capaday and Stein 1987). Whereas more rapid firing of motoneurons will decrease the overall EMG response to the stimulus, additional recruitment has mixed effects. Increased drive recruits more high-threshold motoneurons and brings others closer to threshold. The motoneurons near threshold contribute positively to the excitatory response of the motoneuron pool. Thus in 50% MVCs, both weak and strong stimuli should elicit responses from some motor units recruited by voluntary drive, and some of those not yet recruited, but the proportion of each should be smaller for the weaker stimulus. With increasing contraction strength, for both stimuli, the response from motoneurons that increased their firing rate should decrease, whereas that from inactive motoneurons should increase. However, once all the inactive units respond to the stimulus, further increases in contraction strength can only decrease the total response. This will occur at a lower contraction strength for the strong stimulus. In biceps, the strong stimulus probably activated most of the units not recruited by voluntary effort during contractions of 50–75% MVC.

Whereas biceps continues to recruit motor units beyond 90% MVC (De Luca et al. 1982; Kukulka and Clamann 1981), intrinsic hand muscles recruit few motor units beyond 50% MVCs (Milner-Brown et al. 1973; Moritz et al. 2005). The MEP in FDI behaved differently to biceps and brachioradialis with increased contraction strength. For FDI, the largest responses occurred during weaker contractions and showed larger reductions with strong contractions. These results support our suggestion that rate coding and recruitment are important in determining the response of the motoneuron pool to test stimuli. For FDI, most motoneurons are recruited by 50% MVC. Therefore further increases in force and thus firing rate decrease MEP size.

Changes at the motor cortex with increased contraction strength

Because high firing rates during strong voluntary contractions appear to limit the responsiveness of spinal motoneurons, one might expect similar limitations to the response of cortical neurons. However, changes occurring at the cortex do not appear to contribute to the reduction in the size of MEPs during strong contractions. Several factors may explain the lack of effect at a cortical level. First, it is unclear what portion of the cortical neurons targeted by TMS are recruited or how fast these are firing during MVCs. During weak contractions, large changes in frequency modulation and recruitment of cortical neurons evoke small increases in force (Evarts et al. 1983), but with stronger contractions firing rates may change little (Brouwer et al. 1989; Muir and Lemon 1983). Second, cortical neurons may have intrinsic properties favoring rapid regular discharge in contrast to the long afterhyperpolarization in spinal motoneurons. Recent evidence suggests that, in the monkey, pyramidal tract neurons do not have monotonically rising trajectories but instead peak between 10 and 60 ms after the spike (Wetmore and Baker 2004).

The present study describes the behavior of the motor cortex and motoneurons over a wide range of contraction strengths. It provides evidence that the paradoxical decrease in MEP size with increased contraction strength is mediated by changes below the motor cortex, most likely at the motoneuron pool. Thus while the motoneurons become less responsive during very strong voluntary contractions, output from the motor cortex does not appear to be limited in the same way. An important implication of this work concerns the way in which changes in the cortex translate into changes in motoneuron pool output. Under passive conditions or during weak contractions any increase in motor cortical output will readily increase motoneuron recruitment and firing rates. However, with strong contractions, increased cortical output will not evoke a similar increase in motoneuron pool output, particularly if the pool operates by rate coding. Furthermore, the response of the motoneuron pool to other descending or afferent inputs will also be limited.

Acknowledgments

We are grateful to Dr. Jane Butler for helpful discussion of the manuscript.

Grants

This work was supported by the National Health and Medical Research Council of Australia.

References


