Responses of ankle extensor and flexor motoneurons to transcranial magnetic stimulation

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INTRODUCTION

Stimulation of the precentral motor cortex with transcranial magnetic or electrical stimulators produces clear short latency responses in the target muscles of contralateral limbs. The responses, or motor evoked potentials (MEPs), may be observed with surface electromyographic (EMG) recordings or with peristimulus time histograms (PSTHs) constructed from responses of single motor units of the muscle (Day et al. 1987). These responses are suggested to result from activation of fast corticospinal neurons that make monosynaptic connections with spinal motoneurons (Palmer and Ashby 1992). The corticomotoneuronal (CM) connections activated by transcranial magnetic stimulation (TMS) have a systematic synaptic pattern such that TMS recruits motoneurons of a pool according to the size principle (Bawa and Lemon 1993). Motoneurons that do not receive meaningful monosynaptic connections from the cortex fail to exhibit clear and sharp response peaks. Based on this assumption, the relative strengths of CM connections have been mapped in the upper limb motoneurons by Palmer and Ashby (1992). Based on the same premise, it has been argued that soleus motoneurons do not show clear responses because they receive weak or no CM connections (Brouwer and Qiao 1996; Brouwer et al. 1992). The presence of only diffused, poorly defined peaks have been reported in PSTHs of soleus motor units by Nielsen and Petersen (1995), even though the same groups have reported clear response peaks for motor units of the neighboring ankle flexor, tibialis anterior (Brouwer and Qiao 1995; Morita et al. 2000). Besides weak excitatory connections to soleus, these authors report that only a very small percentage of soleus motoneurons receive excitatory connections (18%, Brouwer and Qiao 1995) while the majority of TA motoneurons are excited monosynaptically. Such random monosynaptic connections to a few soleus motoneurons would lead to poor control of this large postural muscle. The importance of these monosynaptic connections cannot be undermined even if the reflex and polysynaptic descending connections are strong.

In the upper limb, the density of CM connections decline from distal to proximal muscles (Palmer and Ashby 1992). Soleus and tibialis anterior do not have such a relationship as both act on the ankle joint. However, soleus is a slow anti-gravity muscle while TA is not. Would that explain the differences in responses observed to date? The purpose of the following study was to examine the nature of both population and single motor unit responses of soleus and TA motoneurons in normal adult subjects. Portions of this work have been presented as a poster (Bawa et al. 2001).

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METH ODS

Detailed data are reported from ten subjects in the age range 20–57 yr (3 female, 5 male) including three of the authors. Ten additional subjects were tested in one-time short experiments with surface EMG only. These experiments were approved by the Ethics Committee on Human Experiments at Simon Fraser University.

Surface EMG recording

The subject sat comfortably in a straight back chair with knees at approximately 150° and ankles at approximately 100°. Electromyographic (EMG) activities of soleus and tibialis anterior of the right leg were recorded with pairs of Ag-AgCl electrodes. For soleus, electrodes were positioned on the midline of the leg, just below where the two heads of gastrocnemius muscle end. Electrodes for the tibialis anterior were positioned at the same height from the sole of the foot as the soleus electrodes, although occasionally TA electrodes were positioned a bit higher over the middle of the muscle belly. These signals were preamplified (Grass P15 AC preamplifiers, U. S. A.) and filtered (30 Hz–3 KHz).

Single motor unit recording

Single motor unit (SMU) activity was recorded with a pair of stainless steel wires, 25–30 μm in diameter. These wires were embedded in a 25-gauge hypodermic needle, which acted as the carrier for the recording wires and floated freely in the muscle. Activity from these electrodes was preamplified (Grass P15 AC preamplifiers) and filtered (100 Hz–10 KHz).

H reflexes and M wave

To elicit H-reflexes in soleus, the posterior tibial nerve was stimulated at the popliteal fossa with bipolar stimulating electrodes using a Grass S88 stimulator and Grass SIU5 isolation unit. Pulse width of the stimulus was 1 ms, and a wide range of stimulus intensities were applied starting from that needed to obtain the threshold value of the H or the M wave to the highest value required for a maximum M wave (M max). This range of stimulus intensity also provided the maximum value of H reflex (H max). The normalized value of H max/M max was computed for each subject.

Transcranial magnetic stimulation

The area of the motor cortex representing the right lower leg was stimulated with Magstim 200 (Magstim Company Ltd., U. K.) placing the center of the large double cone coil slightly left of the midline. In a few initial experiments, a Dantec MagPro stimulator with a 14.5 cm diameter, cup shaped coil was used, but much higher stimulus intensities were required to elicit responses.

Procedures

To record MEPs of soleus and TA muscles in the surface EMG, the subject was asked to relax during stimulation of the left precentral cortex. Starting at 30% of the maximum output of the stimulator (1.4 Tesla is the maximum output with the large double cone coil), stimulus intensity was increased until a clear, short latency (onset 20–30 ms) response was observed in the soleus. Stimulus intensity was varied around this value for various parts of the experiment. For input/output relationships of MEPs (intensity versus response amplitude), stimulus intensity was increased from threshold to between 70 and 80%.

For SMU activity from soleus or tibialis anterior muscle, the subject’s foot was stabilized for isometric recordings. The subject contracted the muscle under observation until a discernible motor unit potential could be seen and heard. Starting with 30% intensity, stimulus was applied to the cortex at a rate of 0.2/s. The timing of the stimulus was random with respect to the spikes of the motor unit. Since the shape and duration of the PSTH peak was unknown, random stimulation was preferred over spike triggered stimulation (Olivier, Bawa and Lemon 1995). The stimulus intensity was adjusted to allow clear responses of the tonically firing unit to be observed. The goal was to obtain approximately 100 responses at one single stimulus intensity. Responses of some motor units were examined at more than one stimulus intensity.

Data recording

All data comprising surface EMG, SMU activity and stimulus triggers were recorded on a video tape (Vetter digital PCM Recorder, Model 4000A, Rebersburg, PA) for off-line analysis. The bandwidth of the recorder for the EMG channels was DC–7 KHz and that for the SMU channel was DC–15 KHz. Data were analyzed off-line using SPIKE2 and SIGNAL software from Cambridge Electronic Design Ltd. (U.K.)

Data analysis

Each motor unit was converted into a TTL pulse with two in-series Bak time-voltage window discriminators (Bak, U. S. A.). Both for SIGNAL and SPIKE2, surface EMG was sampled at 1.0 KHz while single motor unit data were acquired at 10 KHz. SIGNAL was used for averaging MEPs for experiments with surface EMG recordings only. For the rest of the experiments, raw single motor unit records, associated TTL pulses, stimulus triggers, and surface EMG records from TA and soleus muscles were digitized simultaneously using SPIKE2 software. Once data were acquired on the computer, spike shapes were compared with corresponding TTL pulses. Wrongly discriminated pulses were corrected. Any spurious pulses on stimulus channel were also deleted. Surface EMG records were rectified and averaged using either SPIKE2 or SIGNAL. For spike activity, peristimulus time histograms (PSTHs) were constructed between the spikes and stimulus triggers using a 1.0 ms binwidth (except for Fig. 7). To determine firing rate, a first order interval histogram was constructed for each motor unit using 1.0 ms binwidth. The peak or the mode value has been provided as the interspike interval (ISI) in the Results.

Statistics

To establish the presence and duration of a PSTH peak, two statistical methods were used so that we could compare our values with those in the literature. The first was the χ² test (χ² test). For each of the 1 ms bins in the PSTH between 20 and 60 ms (post stimulus time), it was determined if the observed counts were significantly (P < 0.05) greater than the average count per bin in the background period −50 to −2 ms prior to stimulus. The width of the response peak was taken from the time of the first significant bin to the last significant bin irrespective of whether the in-between bins had significant activity. The reason for this is that due to the presence of subpeaks with TMS there are bins with zero or insignificant activity, but the total peak width includes these bins. The second test for significance of the peak was similar to the one use by Brouwer and Qiao (1995) and will be referred to as 3SD test. For this test, the mean and the SD of the background activity (−50 to −2 ms prestimulus time) were computed for each histogram. Bin activity was considered significant if the number of counts in a bin were greater than the mean plus three SDs of the background counts per bin. Again, the peak width was calculated from the first significant bin to the last significant bin irrespective of the significance of the in-between bins. The χ² test for bin counts is very stringent whereas the 3SD test occasionally gave false positive results. Therefore we first determined the peak with χ² test, did the 3SD test for 5 bins before and 5 bins extending

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beyond the peak determined by \( \chi^2 \) test. Once peak width was determined, the response probability (\( P_r \)) was calculated using the method given in Bawa and Lemon (1993) for both the peak defined by the \( \chi^2 \) test and the peak defined by the 3SD test. Response probability is defined as the number of counts in the response peak per stimulus.

**Corrections for onset of PTH peak**

The motor unit potential recorded with intra-muscular microelectrode samples only a few muscle fibers of the motor unit and, hence, has a very short-duration. There can be substantial delays within the muscle between when a motor unit is activated and when the microelectrode picks up the activity. This delay depends on where in the muscle the tip of the microelectrode is located. The delay between the start of the electrical activity of the whole motor unit and the TTL used to construct the PTH was calculated by spike triggered averaging of the unrectified surface EMG with respect to the TTL (Milner-Brown and Stein 1975). The averaged activity is the compound action potential of the whole motor unit. Once the onset of the peak was determined by applying the statistical methods, it was corrected by the amount of delay between the onset of the motor unit action potential and the TTL. These delays ranged from 1 to 18 ms. The peak onset time for each PTH is reported after this correction.

**Results**

**Surface EMG responses**

Detailed observations of MEPs from surface EMG are presented from nine subjects. The stimulus threshold to observe soleus responses ranged from 30% to 70% of the maximum available stimulus intensity. The stimulus intensity was rarely increased beyond 75% because of discomfort to the subject.

An example of concomitantly recorded MEPs of soleus and tibialis anterior muscles, when the subject was completely at rest, are shown in Fig. 1 for three different stimulus intensities. The onset and duration of MEPs were the same in both muscles at all three intensities; this was true for three other intermediate intensities tested. As can be seen from this figure, when the subject was at rest, the amplitude of TA responses were larger than those of soleus (note different scales for the two muscles).

To compare relative amplitudes of TA and soleus responses, MEPs were recorded from five subjects at five to eight different stimulus intensities. Individual and mean values of the MEPs for all five subjects are shown in Fig. 2 using different scales for the two muscles. For each subject the slope of the input/output curves were always higher for the TA than for soleus. The same is true for the population curves.

Very frequently a second peak was observed in soleus with an onset latency of around 90 to 100 ms, the onset latency of the second peak varied considerably depending on the subject and the posture of the subject. The amplitude of the second peak increased with increasing stimulus intensity as can be seen by comparison of panels A through C in Fig. 1.

To determine the origin of the second (late) peak, namely whether it is reflex in origin or results from descending pathways, additional tests were carried out. The peak was seen only...
under nonisometric conditions as shown in Fig. 3 (A, C, E). When the subject’s foot was fixed to make the contraction of ankle flexors and extensors isometric, the second peak was abolished (Fig. 3B). In a second test, the tibialis anterior tendon was vibrated with a 120 Hz physiotherapy vibrator. The primary soleus and TA peaks were not affected much, while the second soleus peak was either reduced or abolished (Fig. 3D). In other tests not shown in the figure, when stimulus was applied with the ankle flexed passively thus stretching the soleus muscle, the second peak increased in magnitude. On the other hand, when soleus was shortened passively, the peak was reduced or abolished. In one subject, electrical stimulation of the common peroneal nerve, distal to the neck of the fibula, produced a soleus peak at 70 ms. The second peak in soleus with TMS also appears at 70 ms after the onset of TA MEP, thus linking this peak to stretch reflex of soleus (Vals-Solé et al. 1994).

**Single Motor Unit Responses**

Data are reported from a total of 81 motor units from 5 subjects, 42 from soleus and 39 from tibialis anterior. Some units in each muscle were examined with multiple stimulus intensities resulting in 51 PSTHs for soleus and 45 PSTHs from TA. Stimulus intensities ranged from 40 to 75% for soleus motor units and from 38 to 47% for TA motor units. In one subject, stimulus intensities for evoking clear responses in TA were much lower than those required to produce similar responses in soleus motor units, while in the other four subjects the intensities used for the two muscles were in the same range.

The number of stimuli used to construct each of the 51 soleus PSTHs ranged from 27 to 154 (mean ± SD; 103 ± 34), and for the 45 TA PSTHs the number ranged from 46 to 192 (117 ± 30). The number of stimuli varied for several reasons: the unit was lost during a ten minute run, an additional unit started to discharge halfway through the run of a targeted unit or several of the stimuli had to be ignored when the responses were not clear. The onset and duration of peaks were different depending on the statistic used to define the peak. Using the \( \chi^2 \) test: onset of soleus peaks ranged from 24 to 42 ms (30.9 ± 4.6), onset of TA peaks ranged from 22 to 41 ms (27.3 ± 3.6); peak duration for soleus ranged from 1 to 20 ms (6.9 ± 4.2), and for TA it ranged from 1 to 9 ms (5.1 ± 2.1); response probability \( P \) for soleus ranged from 0.05 to 0.80 (0.43 ± 0.18) and for TA it ranged from 0.1 to 0.77 (0.45 ± 0.18). Using the 3SD criterion: onset of soleus peaks ranged from 22 to 38 ms (29.7 ± 4.3), for TA it ranged from 21 to 38 (25.9 ± 3.4); peak duration for soleus ranged from 2 to 22 ms (10.0 ± 4.4), for TA it ranged from 3 to 15 ms (7.8 ± 2.6); response probability \( P \) for soleus ranged from 0.18 to 0.93 (0.52 ± 0.18), and for TA it ranged from 0.19 to 0.83 (0.52 ± 0.17). Similar \( P \) values for soleus and TA indicates that both motoneuron populations were tested with comparable amplitudes of EPSPs.

Clear response peaks were observed for all TA motor units. But contrary to what has been reported in the literature (Broswer and Qiao 1995; Morita et al. 2000; Nielsen and Petersen 1995), we also observed clear responses for each of the soleus motor units that we recorded. Figure 4 illustrates examples of

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**FIG. 3.** Source of second soleus peak. In control responses when the subject was at rest and the foot was not constrained (allowing nonisometric contractions of ankle extensors and flexors), there are short latency response peaks in soleus and TA starting around 26 ms. In soleus there is a second peak starting around 88 ms in this subject as shown in panels A, C, and E. When the subject’s foot was constrained for isometric contractions, the second peak in soleus was abolished (panel B). When 120 Hz vibration was applied to the tendon of TA muscle, the second peak in soleus was reduced (panel D) without affecting the short latency peaks in soleus or TA. Isometric conditions were tested between controls A and C while vibration condition was tested between controls C and E. The ordinate values give the average value of the EMG response/bin, binwidth = 1 ms. Time 0 marks application of TMS stimulus. \( n = \) number of responses, averaged in each panel.

**FIG. 4.** Response peaks in soleus. Response peaks from four soleus motor units from four different subjects are illustrated to show the pattern of sub-peaks observed within the response peaks. The ordinate values show the total number of spikes per bin for N stimuli, binwidth = 1 ms. Motor units were firing with interspike intervals of 230 ms (subject 1), 167 ms (subject 2), 152 ms (subject 3) 190 ms (subject 4). These were the mode values of the first order interval histograms. The top horizontal bars show peak widths according to the 3SD criterion: while lower horizontal bars show peak widths according to \( \chi^2 \) criterion. \( P \) values for subjects 1, 2, 3, and 4 are 0.729, 0.396, 0.638, 0.647 with 3SD criterion, and 0.665, 0.372, 0.560, 0.586 with \( \chi^2 \) criterion, respectively.
response peaks from soleus motor units from four subjects. Each peak stands clearly above the background activity and is segmented into two sub-peaks. These sub-peaks were not always clearly demarcated for every PSTH but are shown here to illustrate the nature of sub-peaks (when observed) in soleus responses. The lower horizontal bar indicates the duration of the peak according to the $\chi^2$ criterion while the upper bar is according to the 3SD criterion.

Having observed clear PSTH response peaks for soleus motor units, the question arose whether each motor unit in the muscle, in both soleus and TA, responds to the same stimulus. Figure 5 shows data from three simultaneously (but randomly picked by the electrode) recorded units from soleus and Fig. 6 shows similar data from three TA motor units. Each of the three units in soleus and each of the three units in TA exhibited clear response peaks in corresponding PSTHs. The mean firing rates (impulses/s) of the three soleus units were 5.9 (unit 1), 3.0 (unit 2) and 5.3 (unit 3); the corresponding peak widths were 7 ms, 8 ms and 14 ms respectively according to 3SD criterion, and 5 ms, 4 ms and 9 ms respectively by $\chi^2$ criterion. For the TA motor units in Fig. 6, the mean firing rates in impulses/s were 7.5 (unit 1), 6.8 (unit 2) and 9.7 (unit 3); peak widths were 9 ms, 7 ms and 7 ms respectively by 3 SD criterion, and 2 ms, 6 ms and 4 ms respectively by $\chi^2$ criterion. These data suggest that soleus and TA motor units behave very similarly to cortical stimulation, and every unit within each muscle responds to TMS in a qualitatively similar fashion. Concomitantly firing motor units from soleus were analyzed for eight more sets (2–3 units per set), results were similar to those reported in Fig. 5. Two additional sets were analyzed for TA with similar results. A few of the units analyzed in these sets responded only phasically during the response peak. Such units were clearly higher threshold units compared with the ones that the subject discharged tonically with voluntary effort.

In the upper limb, the response probability increases with increase in stimulus (Bawa and Lemon 1993). The same was found to be true for the 5 soleus and 5 TA motor units tested for multiple stimulus intensities in this study. PSTHs of a soleus motor unit and corresponding averaged surface EMG responses are illustrated for four stimulus intensities in Fig. 7. For the range of stimulus intensities tested for this motor unit (58% to 65%), the duration of the surface EMG peak (D1) did not change with intensity. Each excitatory peak was followed by depression. The duration of this post peak depression (D2) decreased with decreasing stimulus intensity. For the single motor unit, the corrected onset of the peak was 27 ms for all four intensities, but the duration of the peak had a trend to first increase and then decrease with decreasing stimulus intensity (10 ms, 14 ms, 11 ms, and 6 ms by 3 SD criterion for 65%, 60%, 58%, and 55%, respectively). As seen for surface EMG, the postpeak silent period was clearly longest and deepest for the strongest stimulus.

SOLEUS RESPONSES TO TMS AND 1a AFFERENTS. In addition to the detailed experiments above, a few short experiments were conducted on a larger number of subjects. A total of eighteen subjects were tested for soleus responses to TMS (Magstim 200). Three of the 18 subjects tested did not show any short latency MEPs, even with background voluntary facilitation of soleus. In the rest of the subjects, responses were observed even under resting conditions, but the threshold to evoke MEPs varied considerably.

Soleus is a slow postural muscle with strong stretch reflexes and H-reflexes. Is there an inverse relationship between the threshold for response to TMS and the $H_{\text{max}}/M_{\text{max}}$ ratio? In ten subjects between the ages of 20 and 30 yr, we recorded the $H_{\text{max}}/M_{\text{max}}$ ratio and the threshold for response to TMS. Age limits were put on this group since the threshold to TMS responses increases with age (personal observations) and the $H_{\text{max}}/M_{\text{max}}$ ratio decreases with age (Chalmers and Knutzen 2000). Two of the three subjects who produced no clear soleus responses, had a $H_{\text{max}}/M_{\text{max}} > 0.9$ indicating a greater percentage of 1a afferent fibers with large diameters. On the other hand, a third subject who did not show a soleus response also had a very small H reflex ($H_{\text{max}}/M_{\text{max}} < 0.1$). Some subjects had a very low threshold for response to TMS (<30%) and...
high $H_{max}/M_{max}$ values. Thus no relationship between $H_{max}/M_{max}$ and threshold for response to TMS was found. These limited data suggest that there is no relationship between the strength of monosynaptic cortical and reflex control of the postural muscle. However, this conclusion should be taken with precaution. A clear answer can be obtained, not with H-reflexes, but by examining the gain of stretch reflexes.

DISCUSSION

Transcranial magnetic stimulation studies on human subjects have clearly shown excitation of limb muscles on the contralateral side. The list of various muscles tested is compiled in Rothwell et al. (1991). There is one exception, and that is the soleus muscle. Most of the studies demonstrated excitation of all upper limb motoneurons, excitation of the ankle flexor, tibialis anterior, and inhibition of the ankle extensor, soleus. However, a few studies have shown clear excitation of soleus with surface EMG recordings (Capaday et al. 1999; Maertens de Noordhout et al. 1999; Valls-Sole et al. 1994). Our observations agree with these latter studies. The onset latency and duration of MEPs are shown to be similar for TA and soleus muscles (Morita et al. 2000; Valls-Sole et al. 1994). Valls-Sole et al. (1994) have shown that soleus MEPs have a slightly shorter onset latency during voluntary activation of soleus, and TA peaks can be slightly earlier when TA is voluntarily activated. If the short latency MEPs in TA are assumed to be of corticomotoneuronal origin, the same might apply for soleus from the MEP studies. Since surface EMG can pick up activity of several neighboring muscles, single motor unit studies would provide a clearer answer.

Single motor unit results

CORTICOMOTONEURONAL CONNECTIONS TO SOLEUS MOTONEURONS. Brouwer et al. (1992), Brouwer and Qiao (1995), and Nielsen and Petersen (1995) recorded responses from soleus and tibialis anterior motor units. While response peaks in PSTHs of TA motor units were very clear and very similar to those reported in the upper limbs, response peaks of soleus motor units were either not observed or were poorly defined (diffused) in appearance. Of all the motor units tested, only a small percentage of the motor units showed excitatory peaks: 18% of 62 units studied by Brouwer and Qiao (1995), and 37% of 27 soleus units reported by Nielsen and Petersen (1995). From these observations, the authors concluded that soleus essentially lacks corticomotoneuronal connections, and that cortical connections to soleus involve mostly polysynaptic pathways. In our experiments, no difference was observed between the responses of TA or soleus motor units as indicated by very similar $P_r$ values. Analysis of all sets of concomitantly firing units showed that if one unit responded with an excitatory peak, all other simultaneously recorded units did as well. That is, all soleus units responded with an excitatory peak, which is contrary to the results reported by Brouwer and Qiao (1995) and Nielsen and Petersen (1995). Most of the units analyzed in our study were low threshold ($<10\%\text{ MVC}$), but a few reached thresholds $\leq30\%\text{ MVC}$. The units responding just phasically during the response peak were also of relatively higher threshold, thus providing us with the nature of CM connections to a good sample of the soleus pool. If all motoneurons of this large muscle did not receive weighted ex-
citatory input as other motoneuron pools do, it would cause serious control problems for this postural muscle.

Using transcranial electrical stimulation (TES), Maertens de Noordhout et al. (1999) made a strong argument for the presence of corticomotoneuronal connections to all muscles tested, which included soleus. Since TES produces clear D wave and no I waves, the authors were able to estimate the rise times of monosynaptic EPSPs in all muscles tested, including the TA and soleus. The values were 1.13 ms for TA and 1.14 ms for soleus, indicating similar positioning of corticomotoneuronal synapses onto the two populations of motoneurons. On the other hand, of all the muscles tested, soleus had the smallest response. This observation can be interpreted as soleus requiring higher stimulus intensity to produce a response compared with its anatomical neighbor TA, as observed by us. Therefore it is proposed that the poorly defined PSTH peaks, or absent soleus responses (Brouwer and Qiao 1995; Morita et al. 2000; Nielsen and Petersen 1995) may be due to weak stimulus intensities used in these studies. Morita et al. (2000) reported observing short latency peaks in soleus motor units at very strong voluntary background contractions. In our study, most of the peaks were constructed for low threshold units firing at the lowest possible rates and background contraction was generally very low (<10% MVC as perceived by the subject). An important difference to point out is the way stimulus was applied with respect to motor unit spikes. The random mode of stimulation used by us gives a true profile of the PSTH peak, whereas when the applied stimulus is triggered by the preceding motor unit spike (Morita et al. 2000), it affects the shape of the earlier part of the peak, particularly the wide peaks observed for the lower limb motor units. Low stimulus intensities combined with spike-triggered stimulus may have resulted in narrow or nonexistent peaks.

Inhibition of soleus reported by other authors is not surprising either (Rothwell et al. 1991). Inhibition of voluntary activity is observed at low stimulus intensities even for the upper limb muscles. Only when intensity is increased does one see the excitatory peak (Davey et al. 1994). Since higher intensities are required for soleus compared with those for TA, inhibition or a lack of clear excitation of soleus motoneurons would result if the same stimulus intensity were used for the two muscles. In fact, we did observe inhibition of soleus units with low intensity stimulus. With adequate stimulus, when each response was examined, we saw no difference in the pattern of responses between the upper limb (Bawa and Lemon 1993) and lower limb motoneurons. Clear inhibition, indicated by a very long silent period after the stimulus, was frequently observed for motoneurons belonging to all motoneuron pools, even though the averaged response for each motoneuron was excitatory.

**Peak widths of soleus and TA PSTH peaks.** The peak widths reported in the upper limbs are approximately 5 ms (4.6 ± 1.7 ms for intrinsic hand muscles, Miller 1991). Using 3SD test, Brouwer and Qiao reported TA peaks in the range 2.4 ± 0.1 ms (59 units), and soleus peaks in the range 3.3 ± 0.4 (62 units). Using $\chi^2$ test, Nielsen and Petersen (1995) reported soleus peak width in the range 2–5 ms for their 27 motor units. In the present work, the mean duration with 3SD test was 7.8 ± 2.6 ms for TA and 10.0 ± 4.4 ms for soleus. These values are much higher than those reported by Brouwer and Qiao. Using $\chi^2$ test, our values are higher than those given by Nielsen and Petersen. These values are much higher than those for the upper limb motoneurons in normal human subjects. When the soleus response was segmented into sub-peaks, we never observed more than two clear sub-peaks (Fig. 4). In the upper limbs, sub-peaks are <2 ms in duration (Miller 1991). If we consider sub-peaks in Fig. 4, a sub-peak could be as long as 8 ms (second peak for Subject 1). As for the upper limb, we assume that the sub-peaks originate from D and I waves. If D and I waves were all to travel in the fast CM axons, then the peak width should not be different in the upper and lower limbs, there should be very little dispersion between successive waves from cervical to the lumbar regions. How do we explain the differences in the peak widths and widths of sub-peaks for the lower limb motoneurons? Probably several factors contribute to the peak width. According to Edgley et al. (1997), fast CM axons have a lower threshold for D waves while the slow axons have a lower threshold for I waves. If D and I waves travel in axons of different conduction velocities, the dispersion between successive waves would increase with distance from the cortex. This is proposed to be the reason for the longer duration of response peaks in PSTHs constructed for lumbar motoneurons. Factors which could cause longer peaks in soleus compared with those in TA motoneurons are: (1) weaker connections onto soleus motoneurons would produce weaker EPSPs, which in turn result in longer duration of PSTH peaks (Fetz and Gustaffson 1983), (2) slower motoneurons produce slower EPSPs and hence longer PSTH peaks, and (3) polysynaptic pathways may contribute to soleus peaks (Nielsen and Petersen 1995).

**Latency and duration of PSTH peaks.** In Fig. 7 we reported a slight decrease in peak width at the highest stimulus intensity. This should not be taken as a universal observation. The peak latency and duration depends on the motoneuron firing rate, the afterhyperpolarisation (AHP) of motoneuron, the strength and duration of the synaptic volley, and excitability of the cortex and spinal cord. Therefore to compare the effect of stimulus strength on the latency or duration between motoneurons of different subjects, or of different pools or even within the same pool, is difficult. With the presence of multiple sub-peaks of a PSTH, the response probability $P_r$ will always increase (unless it reaches maximum) with increasing stimulus intensity. But a shift in latency and change in peak width (increase or decrease) depends on many factors. When stimulus intensity is increased, one observes all possibilities such as: an increase in $P_r$ without shift in onset latency or change in duration; an increase in $P_r$ with an increase in duration and decrease in latency; an increase in $P_r$ with no decrease in latency, but a decrease in duration. For example, if a small intensity evokes a D wave and the motoneuron responds to this D wave, then we already may have the shortest peak latency, and there may not be a further shift in latency with increasing stimulus intensity. In fact, the latency may stay the same, and as $P_r$ increases, the duration will decrease because the motoneuron will respond more frequently to the D wave, and therefore less to the subsequent I waves. If on the other hand the weak stimulus does not evoke a D wave, or the motoneuron is not responsive to the D wave, then the peak onset is late. However, if slightly higher stimulus intensity produces a response to D wave, then one will observe a shortening of the peak latency while $P_r$ increases. Because of
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POSTEXCITATORY INHIBITION. Figure 7 shows that the postexcitatory inhibition does not last 150 ms, at least in soleus. This is found because the only way to produce a silent period of 150 ms is by presynaptic inhibition (Hultborn et al. 1987). The question arises: if both TA and soleus are active at the same time, why does only soleus show this activity. There are two possible reasons: first, that TA is always activated more strongly than the soleus muscle (Fig. 3), thus TA contracts more strongly flexing the ankle and stretching soleus; the second reason is suggested to be a higher gain stretch reflex in soleus than in TA. Such peaks may be extremely important in interpretation of data from other experimental paradigms. For example, if such a peak is subliminal in conditioning-testing experiments, a large test response may simply be the result of superposition of test and (subliminal) reflex activity, and hence, misinterpreted.

CONCLUSIONS

Soleus receives corticomotoneuronal connections like other motoneuron pools innervating the limb muscles. The difference is that the connections are relatively weak in many subjects, however all motoneurons receive excitatory connections for systematic recruitment as motoneurons in other muscles do. The existence of a large range of stimulus intensities to elicit MEPs in subjects 20–30 yr of age suggests a large variability in the strength of CM connections onto soleus motoneurons. The onset and duration of MEPs in the ankle extensor soleus and the ankle flexor TA were very similar suggesting qualitatively similar cortical connections. On the other hand, input-output relations of concomitantly recorded MEPs indicates much stronger connections onto the ankle flexor TA motoneurons, which is opposite of what has been shown for the wrist muscles. Fetz and Cheney (1980) showed stronger CM connections onto wrist extensors than onto wrist flexors. Functionally, this is not the opposite; wrist flexors and ankle extensors are antigravity muscles and may depend more on segmental reflexes. Single motor unit PSTH peaks in the lower limb muscles are of longer duration than in the upper limbs, otherwise no clear difference was observed in their input-output properties, post peak depression, or any other activation patterns.

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