Evidence favouring different descending pathways to soleus motoneurones activated by magnetic brain stimulation in man

J. Nielsen and N. Petersen

Division of Neurophysiology, Department of Medical Physiology, The Panum Institute, University of Copenhagen, Blegdamsvej 3, DK-2200 Copenhagen N, Denmark

1. In resting subjects low-intensity magnetic stimulation of the brain evoked an inhibition of the soleus H reflex at short latency (conditioning–test interval, −2 to +1 ms) followed approximately 10 ms later by a period of facilitation. During voluntary dynamic or tonic plantar flexion the same stimulus evoked a facilitation with a shorter latency than the inhibition (conditioning–test interval, −5 to −1 ms).

2. At the onset of ramp-and-hold plantar flexion the short-latency facilitation was seen at lower intensities of stimulation than the long-latency facilitation in six of seven subjects. At rest and/or during tonic plantar flexion the opposite was observed in four of the subjects, whereas the two facilitations had approximately the same threshold in the remaining subjects.

3. The short-latency facilitation decreased approximately 100 ms after the onset of ramp-and-hold plantar flexion in all of eight subjects. The long-latency facilitation, in contrast, either had the same size throughout the ramp phase or even increased around the end of the ramp phase.

4. The short-latency facilitation of the reflex was significantly larger at the onset of a fast ramp-and-hold plantar flexion (10 N m (150 ms)$^{-1}$) than at the onset of a slow contraction (10 N m (600 ms)$^{-1}$), whereas the opposite was the case for the long-latency facilitation

5. As the short- and long-latency facilitations had different thresholds and were differently regulated during voluntary movement, it is suggested that they are caused by activation of different descending pathways by the magnetic stimulus.

Transcranial stimulation of the intact human brain evokes short-latency effects compatible with a monosynaptic linkage between the motor cortex and spinal motoneurones in almost all muscles (Rothwell, Thompson, Day, Boyd & Marsden, 1991). Previously, the soleus muscle has been thought to be an exception. Thus Cowan, Day, Marsden & Rothwell (1986) found a short-latency facilitation of the soleus H reflex in only one subject out of six following transcranial electrical stimulation and Advani & Ashby (1990) and Brouwer & Ashby (1991) only observed short-latency peaks in the post-stimulus time histogram of a few single voluntarily activated soleus motor units following transcranial magnetic stimulation. Similar findings have also been reported for the soleus muscle in the baboon (Uemura & Preston, 1965). The most notable effect observed in these studies was an inhibition followed by a facilitatory effect later. The descending excitatory drive to the soleus motoneuronal pool was consequently assumed to be conveyed almost exclusively by indirect polysynaptic pathways. Later studies have, however, documented that monosynaptic projections from the motor cortex to the soleus motoneuronal pool do exist in man (Brouwer & Ashby, 1992; Nielsen, Petersen, Deuschl & Ballegaard, 1993; Nielsen & Petersen, 1995) as well as in the monkey (Jankowska, Padel & Tanaka, 1975), although in man they are less easily activated by stimulation than projections to other muscles. In a preceding paper, changes in the size of the short-latency, presumably monosynaptic, facilitation of the soleus H reflex were investigated during voluntary contraction (Nielsen & Petersen, 1995). It was the purpose of the present study to investigate whether the facilitation of the H reflex described at longer latencies in previous studies (Cowan *et al.* 1986; Nielsen *et al.* 1993) is caused by activation of the same monosynaptic pathway as this short-latency facilitation or whether different descending pathways are responsible.

METHODS

The experiments were performed in fourteen subjects aged 20–56 years. The subjects gave informed consent to the experimental procedure, which was approved by the local ethics committee.

A detailed description of the methodology has been given in a preceding paper (Nielsen & Petersen, 1995) and will only be briefly summarized here. The subjects were seated in a reclining armchair with their right foot attached to a foot plate. In some experiments the subject had to perform a voluntary plantar flexion. In these experiments the torque exerted on the foot plate was recorded by a torque meter and presented on an oscilloscope in front of the subject. The subject performed either a tonic plantar flexion maintaining the torque at a pre-set level (usually 10 N m) or a ramp-and-hold plantar flexion. In the latter case the subject initiated the contraction in response to an auditory starter signal presented every 8 s. At the same time a dot representing the torque appeared on the oscilloscope. The subject then had to make the dot follow a ramp drawn on the oscilloscope screen. The ramp began 400 ms after the starter signal and reached a torque level of 10 N m within 300 ms. The subject was requested to maintain this level of contraction for another 1–2 s.

H reflexes

The soleus H reflex was recorded by bipolar surface electrodes placed over the soleus muscle. It was evoked by stimulation of the posterior tibial nerve in the popliteal fossa. The size of the reflex was maintained constant during the different tasks (usually 15–20% of the maximal direct M-response). Conditioned and unconditioned (control) reflexes were randomly alternated. At least twenty reflex responses were averaged for each alternative. The mean and standard deviation of the responses were calculated on-line.

Conditioning stimulations

Magnetic stimulation was applied over the contralateral motor cortex. The magnetic stimulator was a MagStim 200 (MagStim Co., UK) and the coil was a prototype of the figure-8 double-cone coil. In experiments in which the stimulations were used to condition the H reflex, it was checked that the intensity of stimulation was below the threshold for eliciting a direct motor-evoked potential in the soleus muscle.

Post-stimulus time histograms (PSTHs)

Histograms of the probability of discharge of single voluntarily activated soleus motor units were constructed following magnetic stimulation of the brain or stimulation of the posterior tibial nerve (see Fournier, Meunier, Pierrot-Deseilligny & Shindo, 1986, for a detailed description of the technique). To reduce the number of triggers, the stimulations were triggered on the previous discharge of the motor unit. By changing the delay between the trigger and the stimulation, the stimulation could thus always be given at an optimum time; i.e. when the unit was not refractory due to the previous discharge. The PSTH was constructed for a window between 20 and 70 ms after the stimulations with bins of 1 ms. A histogram was also constructed in a control situation without stimulation. The spontaneous discharge probability of the unit could thus be subtracted from that resulting from the stimulation. The interval between each measurement was 4 s.

Data analysis and statistics

The means and standard errors of the mean of control and conditioned test reflexes were calculated on-line. Student's paired t test was used to test for statistical significance of differences between conditioned reflexes and control reflexes and between conditioned reflexes recorded in different situations (i.e. contraction *vs.* rest). Conditioned reflexes from all the subjects were pooled in each of the tested situations and the population mean and standard error of the mean were calculated. Differences in the population mean between the different situations were tested statistically using Student's t test. A χ^2 test was used to test for statistical significance of periods of increased firing probability in the PSTH of the single motor units.

RESULTS

H reflex experiments

Figure 1 demonstrates the time course of the effect of magnetic stimulation of the left motor cortex on the right soleus H reflex at rest (Fig. 1*A*), during tonic plantar flexion (Fig. 1*B*) and at the onset of a voluntary ramp-and-hold plantar flexion (Fig. 1*C*) in a single subject. In the latter task the ramp phase lasted 300 ms and the strength of the contraction was 10 N m. The magnetic stimulus was adjusted to 0·95 of the threshold for a direct motor-evoked potential (MEP) in each of the three tasks; i.e. to 50% of the maximum stimulator output at rest, to 40% during tonic plantar flexion and to 28% at the onset of plantar flexion. At rest the earliest discernible effect was an inhibition at a conditioning–test interval of −2 ms (i.e. when the magnetic stimulus was applied *after* the test stimulus) followed by a second and third inhibitory phase at conditioning–test intervals of +1 and + 3 ms, respectively. At least the first of these phases of inhibition is caused (at least partly) by activation of Ia inhibitory interneurones projecting to soleus motoneurones (Iles & Pisini, 1992; Nielsen *et al.* 1993). A facilitation of the reflex was not observed until the conditioning–test interval was +10 ms. It was possible to demonstrate a similar long-latency facilitation without any evidence of an earlier facilitation in six out of ten tested subjects at a similar stimulation strength. The onset of this facilitation varied between +5 and +10 ms. In the remaining four subjects a facilitation was observed at a much shorter conditioning–test interval (−5 to −1 ms). In two of these subjects this facilitation lasted for only 5–8 ms and was not followed by a later facilitation, but in the other two subjects the facilitation lasted for almost 20 ms. Whereas the facilitation observed at a conditioning–test interval of −5 to −1 ms is probably caused by activation of monosynaptic projections from the cortex to the motoneurones, the latency of the facilitation observed at conditioning–test intervals of +5 to +10 ms appear too long to be explained by the same mechanism (Cowan *et al.* 1986; Deuschl, Michels, Berardelli, Schenck, Ingilleri & Lücking, 1991; Nielsen *et al.* 1993; Nielsen & Petersen, 1995). In this paper the term 'short-latency facilitation' will be used to designate the presumed monosynaptic facilitation, which is seen at conditioning–test intervals of −5 to −1 ms (Nielsen *et al.* 1993). The term 'long-latency facilitation' will be used to designate the facilitation seen at conditioning–test intervals longer than +8 ms. This

facilitation should not be confused with the facilitation of the tibialis anterior and soleus H reflexes which is seen at a much longer latency (Holmgren, Kadanka & Larsson, 1992).

In contrast to what was observed at rest, the short-latency, presumed monosynaptic, facilitation was readily demonstrated in the subject illustrated in Fig. 1 at the onset of a ramp-and-hold plantar flexion (Fig. 1*C*) and during tonic plantar flexion (Fig. 1*B*; see also Nielsen & Petersen, 1995). During tonic contraction the facilitation lasted for more than 20 ms (Fig. 1*B*; the last part is not shown), whereas it lasted only 7–8 ms when measured at the onset of contraction (Fig. 1*C*).

To investigate whether the two facilitations were caused by activation of the same or different pathways their threshold and regulation during voluntary movement were investigated in thirteen subjects. Data from one of these subjects are presented on the left in Figs 2–4, whereas pooled data from all the subjects are presented on the right. The effect of the magnetic stimulus on the reflex was measured (i) at a conditioning–test interval at which the short-latency facilitation was seen during either strong tonic plantar flexion or at the onset of a ramp-and-hold contraction (conditioning–test interval, −3 ms in the illustrated subject) and (ii) at a conditioning–test interval shortly after the onset of the long-latency facilitation at

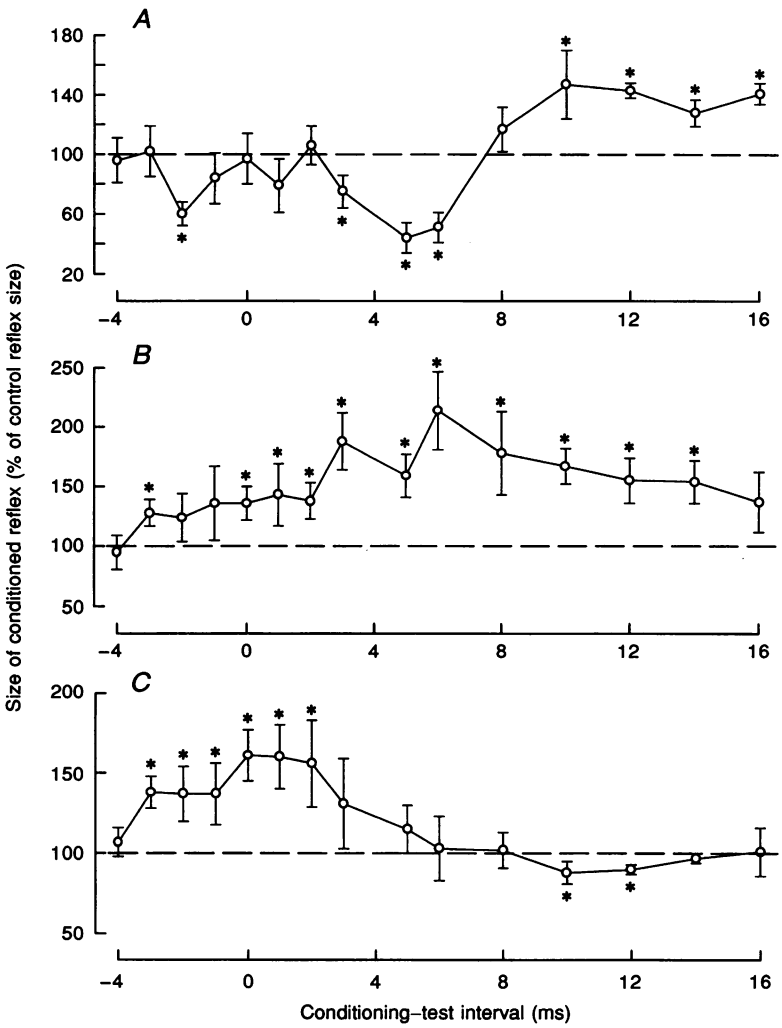

Figure 1. Time course of the effect of magnetic brain stimulation on the soleus H reflex at rest (*A*), during tonic plantar flexion (*B*) and at the onset of a ramp-and-hold plantar flexion (*C*)

The data are from a single subject. The intensity of the magnetic stimulation was decreased to 0·95 × MEP threshold (50% of maximal stimulator output in *A*, 40% in *B* and 28% in *C*). The control H reflex was adjusted to 18–20% of the maximal motor response, M_{max}, in all situations. In *B* the subject maintained a torque level of 10 N m continuously. In *C* the subject performed a ramp contraction which lasted 300 ms and reached a torque level of 10 N m. The asterisks indicate that the conditioned reflex was significantly different from the control reflex size ($P < 0·05$). Each bar represents one standard error of the mean.

rest (conditioning–test interval, 10 ms in the illustrated subject).

It was shown in Fig. 1 that the long-latency facilitation could be seen without evidence of the short-latency facilitation at rest, whereas the opposite was true at the onset of plantar flexion. In Fig. 2 this finding was investigated further by systematically changing the intensity of the magnetic stimulus in the three tasks. In the illustrated subject an MEP was evoked at a stimulus intensity of 70% of the maximum stimulator output at rest as compared to 60% during tonic contraction and 55% at the onset of contraction. As was the case for the subject in Fig. 1 the long-latency facilitation had a lower threshold (statistically significant at 50% of maximum stimulator output) than the short-latency facilitation (statistically significant at 60% of maximum stimulator output), while the subject was at rest (Fig. 2*A*). However, in contrast to the subject in Fig. 1, the long-latency facilitation also occurred at a much lower stimulation intensity (statistically significant at 45% of maximum stimulator output) than the short-latency facilitation (statistically significant at 52% of maximum stimulator output) during tonic plantar flexion (Fig. 2*C*). Consistent with the findings in the study by Nielsen & Petersen (1995), the short-latency facilitation

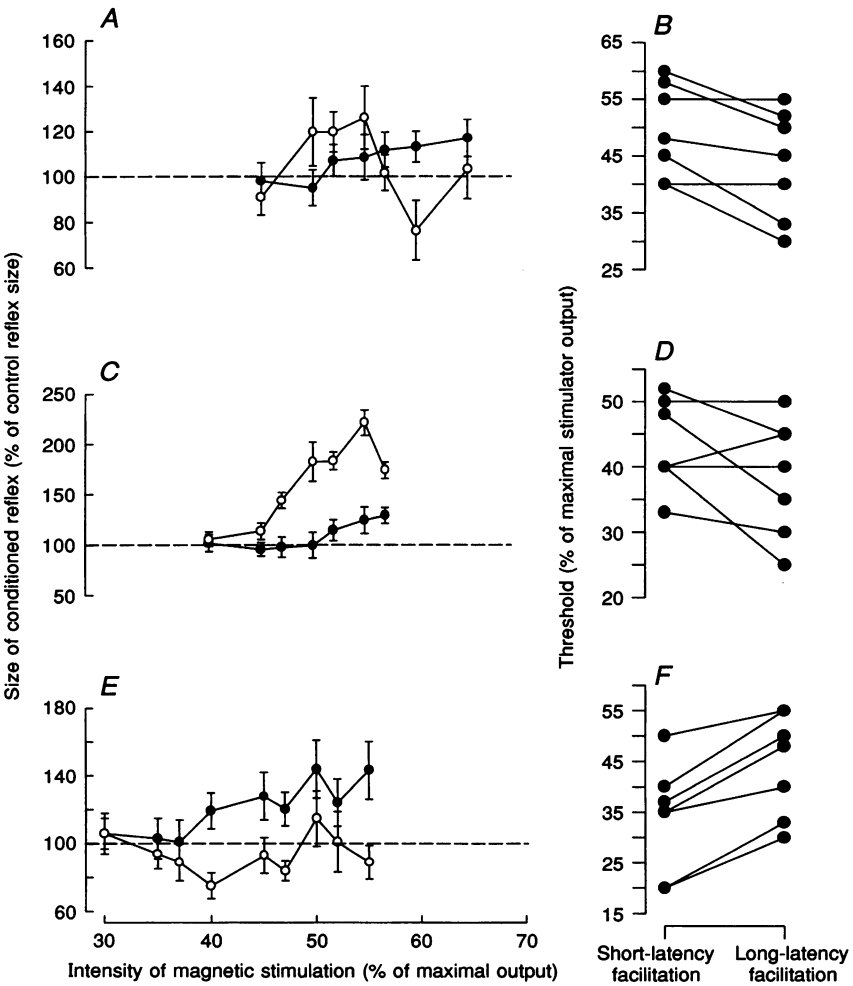

Figure 2. Comparison of the threshold of the short- and long-latency facilitation of the soleus H reflex at rest (*A* and *B*), during tonic plantar flexion (*C* and *D*) and at the beginning of a voluntary ramp-and-hold plantar flexion (*E* and *F*)

A, *C* and *E* show data from a single subject, whereas *B*, *D* and *F* show data from all the subjects. In *A*, *C* and *E* the short-latency facilitation was measured at a conditioning–test interval of −3 ms (●) and the long-latency facilitation (○) was measured at a conditioning–test interval of 10 ms. Each bar represents one standard error of the mean. In *B*, *D* and *F* the short-latency facilitation was measured within the first 0·5 ms of the onset of the earliest observed facilitation after the brain stimulation (conditioning–test interval, −5 to −2 ms). The long-latency facilitation was measured at a conditioning–test interval of 10 ms in all subjects. The data are from 7 subjects. Each line and symbol represents data from one subject.

had a very low threshold (statistically significant at 40% of maximum stimulator output) at the onset of contraction (Fig. 2*E*). In contrast, the long-latency facilitation was not seen at all, even when increasing the stimulus intensity to the threshold of the MEP. In six of seven subjects the short-latency facilitation had a lower threshold (difference more than 5% of maximal stimulator output) than the long-latency facilitation when tested at the onset of contraction (Fig. 2*F*). During tonic plantar flexion and/or at rest the opposite was the case in four of the subjects (Fig. 2*B* and *D*). In the remaining three subjects the short- and long-latency facilitation had the same threshold both at rest and during tonic plantar flexion. On average, the threshold of the short-latency facilitation was found to be significantly lower than the threshold of the long-latency facilitation when measured at the onset of contraction (34 ± 3·2 and 44 ± 3·4%, respectively; $P < 0{\cdot}001$), whereas the opposite was the case at rest (49 ± 3·1 and 44 ± 3·6%, respectively; $P < 0{\cdot}05$). There was no statistically significant difference in the threshold of the two facilitations during tonic contraction (43 ± 2·6 and 39 ± 3·4%, respectively; $P > 0{\cdot}1$).

In the experiment illustrated in Fig. 3*A* the short- and long-latency facilitations were measured at different times during and after the ramp phase of a voluntary ramp-and-hold plantar flexion (300 ms ramp; amplitude, 10 N m). The intensity of the magnetic stimulation was adjusted so that the long-latency facilitation was seen during tonic contraction, whereas only the short-latency facilitation was seen at the onset of contraction (48% of maximum stimulator output; cf. Fig. 2). The short-latency facilitation was largest at the very onset of contraction, but then decreased approximately 100 ms into the contraction (see also Nielsen & Petersen, 1995). In contrast, the long-latency facilitation was not seen until 200 ms after the *end* of the ramp and then increased slowly until it reached its tonic (high) level 300 ms later. The short-latency facilitation was thus significantly larger at the onset of contraction than during tonic contraction ($P < 0{\cdot}05$), whereas the opposite was the case for the long-latency facilitation ($P < 0{\cdot}05$).

In all subjects the short-latency facilitation decreased shortly after the onset of contraction, but the long-latency facilitation either had the same size throughout the ramp-and-hold plantar flexion (five subjects) or increased either shortly before or after the end of the ramp phase (three subjects). The short-latency facilitation was, on average, found to be significantly larger at the onset of contraction than during tonic contraction (Fig. 3*B*; 148 ± 11 and 121 ± 8%, respectively; $P < 0{\cdot}01$), whereas the opposite was the case for the long-latency facilitation (Fig. 3*C*; 118 ± 7 and 136 ± 11%, respectively; $P < 0{\cdot}05$).

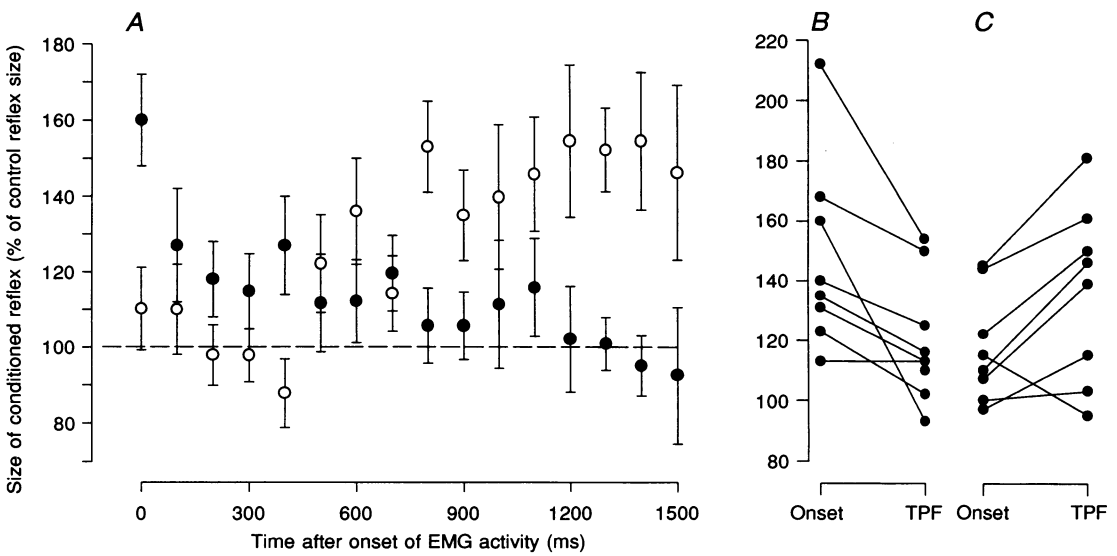

Figure 3. The size of the short- and long-latency facilitations at different times during a voluntary ramp-and-hold plantar flexion

A shows data from a single subject, whereas *B* and *C* show data from all 8 investigated subjects. In *A* the short-latency facilitation (●) was measured at a conditioning–test interval of −3 ms and the long-latency facilitation (○) was measured at a conditioning–test interval of 10 ms. Each bar represents one standard error of the mean. In *B* and *C* the short-latency and long-latency facilitations were measured as in Fig. 2*B*, *D* and *F*. Each line and symbol represents one subject. A comparison is made between the size of the short-latency facilitation (*B*) and the long-latency facilitation (*C*) at the onset of a voluntary ramp-and-hold plantar flexion (300 ms ramp phase; 10 N m amplitude) and during tonic plantar flexion (TPF).

In Fig. 4*A* the subject was instructed to perform contractions of different velocity (10 N m (150 ms)$^{-1}$, 10 N m (300 ms)$^{-1}$, 10 N m (600 ms)$^{-1}$, 10 N m (1500 ms)$^{-1}$) and the short- and long-latency facilitations were measured at the very onset of contraction. The intensity of the magnetic stimulation was maintained at 48% of the maximum stimulator output. As can be seen, the short-latency facilitation increased with the speed of the contraction (see also Nielsen & Petersen, 1995). The facilitation was thus significantly larger at the onset of the fastest contraction (10 N m (150 ms)$^{-1}$) than at the onset of the slowest contraction (10 N m (1500 ms)$^{-1}$; $P < 0{\cdot}05$). In contrast, the long-latency facilitation was not seen at all at the onset of the fast contractions, but only at the onset of the slowest contraction ($P < 0{\cdot}001$). In fact an inhibition was observed at the latency of the long-latency facilitation at the onset of the fastest contractions.

In Fig. 4*B* and *C* the size of the two facilitations is compared at the onset of a ramp-and-hold contraction in which the ramp phase lasted either 150 or 600 ms in all the nine subjects. The short-latency facilitation was significantly larger at the onset of the fast contraction than at the onset of the slow contraction (Fig. 4*B*; 153 ± 10 and 127 ± 8·3%, respectively; $P < 0{\cdot}05$), whereas the opposite was the case for the long-latency facilitation (Fig. 4*C*; 100 ± 7·6 and 144 ± 9·7%, respectively; $P < 0{\cdot}001$).

PSTHs of the discharges of single voluntarily activated soleus motor units

Evidence of two different excitatory effects on the soleus motoneurones from the motor cortex was also obtained from single motor units. Examples of the firing probability of single voluntarily activated soleus motor units following the magnetic stimulus in two different subjects are shown in Fig. 5. A large short-latency facilitation of the soleus H reflex (conditioning–test interval, −3·2 ms) was always seen during tonic plantar flexion in the subject illustrated in Fig. 5*A* and *B*, whereas only a small and variable short-latency facilitation was seen (at a conditioning–test interval of −3·0 ms) in the subject illustrated in Fig. 5*E* and *F*. In this latter subject a large long-lasting facilitation of the H reflex with an onset at a conditioning–test interval of +5 ms was the most prominent finding. As can be seen, these H reflex findings were reproduced for single motor units in the two subjects. The peak induced by stimulation of I a afferents in the tibial nerve was seen at a latency of 41 and 40 ms, respectively, in the two subjects (*C–D* and *G–H*, respectively, in Fig. 5). A peak corresponding to the short-latency facilitation should consequently be expected at latencies of 38 and 37 ms, respectively (marked by dashed lines). However, only in the subject with a large short-latency facilitation of the H reflex was a peak seen at this latency (statistically

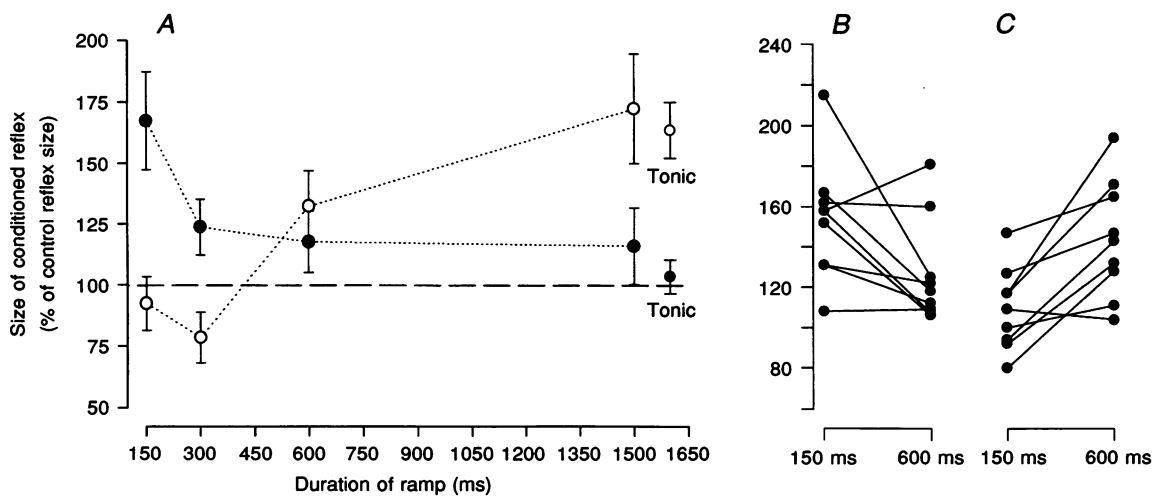

Figure 4. The size of the short- and long-latency facilitations at the onset of ramp-and-hold plantar flexions of different velocities

A shows data from a single subject, whereas *B* and *C* show data from all 9 investigated subjects. In *A* the short-latency facilitation (●) was measured at a conditioning–test interval of −3 ms and the long-latency facilitation (○) was measured at a conditioning–test interval of 10 ms. In all cases the amplitude of the ramp was 10 N m. The subject had to reach this level within either 150, 300, 600 or 1500 ms. Each bar represents one standard error of the mean. In *B* and *C* the short- and long-latency facilitations were measured as in Fig. 2*B*, *D* and *F*. A comparison is made between the size of the two facilitations (*B* and *C*, respectively) at the onset of a ramp-and-hold plantar flexion with a ramp phase lasting either 150 or 600 ms.

significant at 39–40 ms). In the other subject a period of increased firing probability was not seen until 4–5 ms after the peak induced by stimulation of Ia afferents (statistically significant at 44–50 ms), i.e. at a latency corresponding to the large long-latency facilitation of the H reflex in this subject. A peak at the latency of the short-latency facilitation was only observed in a single motor unit out of twelve in the subject with the small short-latency facilitation, whereas such a peak could be demonstrated in five out of six investigated motor units

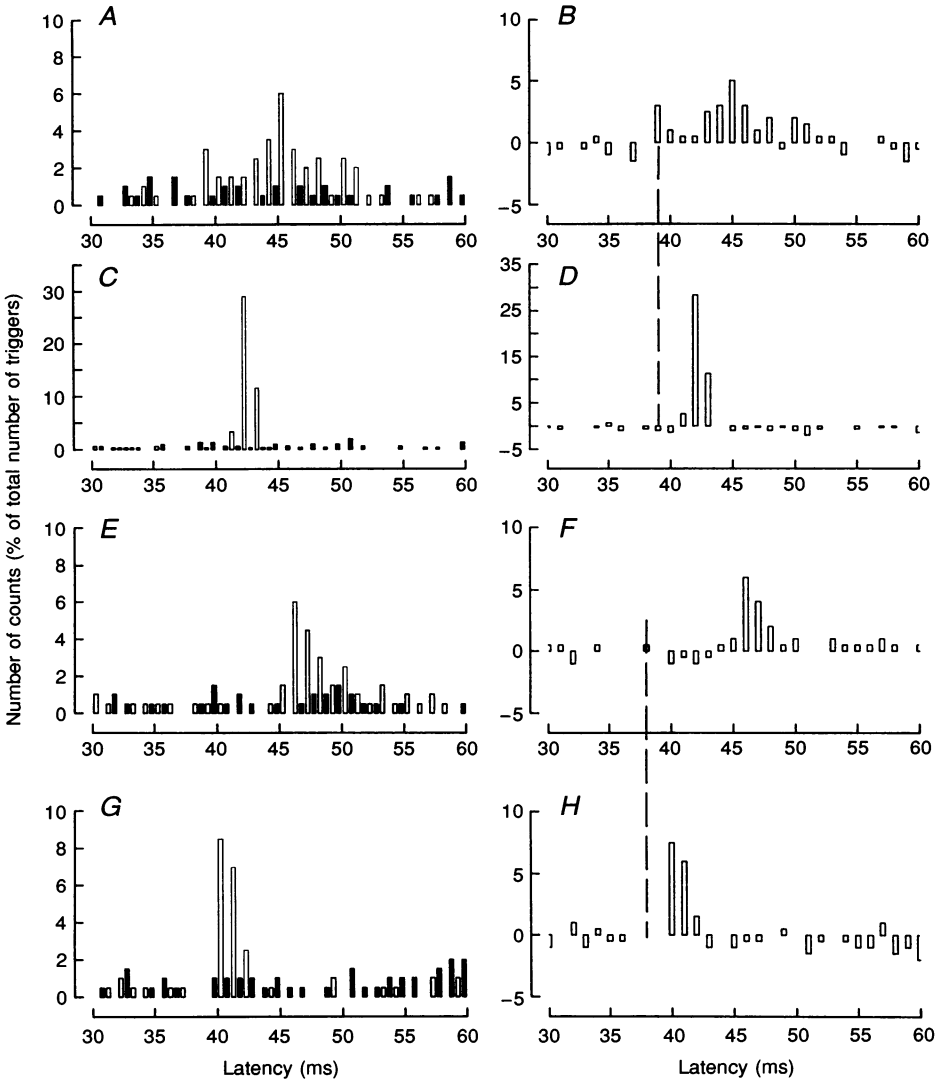

Figure 5. PSTHs of the probability of discharge of two single voluntarily activated soleus motor units (*A–D* and *E–H*, respectively) following stimulation of the posterior tibial nerve (*C–D* and *G–H*) or magnetic stimulation of the brain (*A–B* and *E–F*)

A–D and *E–F* are from different subjects. The histograms on the left show measurements in the control situation (■) and following stimulation (□). The histograms on the right show the difference between measurements with and without stimulation. The ordinate is the number of counts in each bin (1 ms) as a percentage of the total number of triggers. The abscissa is the latency following the stimulations (in ms). The intensity of the magnetic stimulation was 50% of the maximal stimulator output. The vertical dashed line in *B–D* marks the latency of the short-latency peak following the magnetic brain stimulation, whereas the same line in *F–H* marks the latency at which a peak was expected from the latency (in relation to the H reflex) of the short-latency facilitation of the soleus H reflex in the subject. The interspike interval of the motor unit in *A* and *B* was 192 ± 44 ms, whereas it was 159 ± 52 ms for the motor unit in *E* and *F*. The total number of counts was 300.

from the other subject. A total of twenty-seven motor units were studied in six subjects. We found short-latency peaks with a duration of 2–5 ms in ten of the units (37%). In fifteen units (55%) a period of increased firing probability was seen either immediately after the short-latency peak (as in the subject used for the illustration in Fig. 5*A* and *B*) or with an extra latency of 5–10 ms. In nine units this period of increased firing probability was seen without any evidence of a short-latency peak. The duration of the period of increased firing probability varied between 5 and 15 ms.

DISCUSSION

In the present study it has been demonstrated that magnetic stimulation of the brain evokes two distinct phases of soleus H reflex facilitation. These two different facilitations often had different thresholds and were regulated differently during voluntary contraction. The facilitation with the shortest latency was probably caused by activation of direct monosynaptic projections from the motor cortex to spinal motoneurones and it has been described in detail in a preceding paper (Nielsen & Petersen, 1995). The question to be answered here is whether the long-latency facilitation is also caused by activation of this pathway or whether the two facilitations reflect activation of different descending pathways.

Evidence suggesting that magnetic brain stimulation activates different descending pathways to soleus motoneurones

Several observations suggest that the latter possibility is the most likely. The long-latency facilitation (and the late period of increased firing probability in the PSTH) could first of all be observed without any evidence of an earlier facilitation. Cowan *et al.* (1986) similarly observed that electrical stimulation of the brain caused a facilitation of the soleus H reflex in resting subjects at a longer latency than in other muscles. Kernell & Wu (1967*a*, *b*) suggested that the late excitatory postsynaptic potentials (EPSPs) observed in baboon motoneurones were caused by summation of monosynaptic EPSPs evoked by multiple volleys in the same descending pyramidal tract fibres. Magnetic stimulation of the brain in man probably also elicits multiple descending volleys in the same pyramidal fibres (Day *et al.* 1987) and it could therefore be argued that the long-latency facilitation was caused by the same mechanism as in the baboon. However, in this case a continually increasing facilitation beginning at the latency of the short-latency facilitation would have been expected (cf. Fig. 1 of Kernell & Wu, 1967*b*). In fact, in the resting subject, one or two phases of inhibition were usually followed by a much larger late inhibition before the long-latency facilitation occurred (cf. Fig. 1 in the present study). While the large late inhibition may be caused by summation of multiple IPSPs evoked by activity in the same fibres, it is difficult to use the same explanation for the long-latency facilitation.

Secondly, it is difficult to reconcile the different regulatory mechanisms of the short- and long-latency facilitations during voluntary contraction with the explanation that both of them are activated by the same monosynaptic pathway. The fact that the long-latency facilitation had the lowest threshold at rest and during tonic contraction, but not at the onset of contraction strongly indicates that different pathways were responsible for the two facilitations. This view was further supported in the present study by the observations (i) that the short-latency facilitation decreased during the ramp phase of contraction, whereas the long-latency facilitation was constant or even increased, and (ii) that the short-latency facilitation was larger the faster the contraction, whereas this was not the case for the long-latency facilitation. These latter two observations could also be explained by modulation of the intervening inhibition, which is at least partly caused by activation of Ia inhibitory interneurones (Iles & Pisini, 1992; Nielsen *et al.* 1993) and which may, at least theoretically, interfere with the size and occurrence of the long-latency facilitation. However, as the inhibition is caused by an at least disynaptic linkage (Nielsen *et al.* 1993), it cannot interfere with either the size or the occurrence of the earlier presumed monosynaptic short-latency facilitation. Furthermore, to explain the observed modulation of the long-latency facilitation by modulation of the inhibition would require that the inhibition was largest at the onset of fast movements, but this is not in accordance with the established parallel control of corresponding motoneurones and Ia inhibitory interneurones during such movements (Crone & Nielsen, 1989). According to this the activity of Ia inhibitory interneurones projecting to soleus motoneurones should be depressed at the onset of soleus contraction. There are preliminary data which suggest that this is indeed the case (Y. Kagamihara, J. Nielsen & N. Petersen, unpublished observations).

The different durations of the short-latency peak and the late period of increased firing probability in the PSTH also suggest that pathways with different properties were responsible for the peaks. The short duration and large amplitude of the short-latency peaks suggests that these peaks were caused by EPSPs with a very fast rise time (Ashby & Zilm, 1982; Gustafsson & McCrea, 1984). The long duration and low amplitude of the late period of increased firing probability in contrast would be compatible with activation of a pathway evoking slowly rising EPSPs in the motoneurones.

Which pathway is responsible for the long-latency facilitation?

We have at the present time no way of deciding which pathway is responsible for the long-latency facilitation, but several different alternatives may be considered. It has recently been demonstrated that the large fast-conducting pyramidal tract cells, which are probably responsible for the short-latency facilitation, are not the only cells which have monosynaptic projections to the motoneurones (Lemon, Werner, Bennet & Flament, 1993). Some of the small pyramidal cells, which constitute 90% of the pyramidal tract, have also been demonstrated to produce spike-triggered facilitation of small hand muscles. This may suggest that they too have monosynaptic connections with the motoneurones. If activation of these cells is responsible for the long-latency facilitation, the longer latency could be explained by their slower conduction velocity, and the longer duration of the period of increased firing probability in the PSTH could be explained by a wider range of conduction velocities than occurs in the population of fast conducting pyramidal tract cells.

Another possibility is that the long-latency facilitation is caused by activation of indirect polysynaptic pathways. This could include corticorubrospinal, corticoreticulospinal as well as corticospinal pathways. In particular, the long-latency facilitation resembles the polysynaptic excitation of lumbar motoneurones evoked by stimulation of the corticospinal pathway in the cat and monkey (Lundberg & Voorhoeve, 1962; Uemura & Preston, 1965).

Similar evidence of long-latency facilitation in other muscles

We focused in the present study on the soleus muscle, as a long-latency facilitation may be seen in this muscle in some subjects without a preceding short-latency facilitation at rest and during tonic plantar flexion. This is not the case in other muscles such as the tibialis anterior or the flexor carpi radialis muscles. These muscles do, however, exhibit a short latency, but long-lasting facilitation of the H reflex during voluntary contraction (Figs 2 and 3 in Nielsen *et al.* 1993), which may indicate that a similar organization of the descending input exists to these muscles. Furthermore, Colebatch, Rothwell, Day, Thompson & Marsden (1990) have reported that they observed a peak in the PSTH of deltoid and biceps motor units at a latency of 10 ms in relation to the short-latency presumably monosynaptic peak. They emphasized that the failure to demonstrate such late (or medium-latency, as even later peaks may also be seen; Holmgren *et al.* 1992) peaks in the PSTH of motor units from distal arm muscles could be due to the size of the short-latency peak in these motor units. Large peaks in the PSTH thus inevitably produce 'shadows' of decreased firing probability at the same time as the long-latency (or medium-latency) peak should occur. It cannot therefore be excluded that similar pathways to distal arm muscles may be activated by brain stimulation.

Functional implications

In the study by Nielsen & Petersen (1995) it was suggested that the fast-conducting corticomotoneuronal cells could provide the initial command for the contraction and determine the first part of the trajectory towards a target independently of the peripheral feedback. We observed that the long-latency facilitation had a lower threshold than the earlier (presumed monosynaptic) facilitation during tonic contraction, whereas the opposite was true at the onset of contraction and in the first 100 ms of the dynamic phase of contraction. Furthermore, we found that in some subjects the long-latency facilitation increased towards the end or even after the end of the ramp phase of contraction. We suggest as a tentative hypothesis that these observations may reflect a switch of descending pathways conveying the central command. If the long-latency facilitation is, for instance, caused by activation of a polysynaptic corticospinal pathway, changes in the excitability of spinal interneurones induced by the peripheral feedback would ensure that the excitatory command reaching the motoneurones is always adjusted to take account of the information from the periphery.

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Acknowledgements

We would like to thank Professors Anders Lundberg and Hans Hultborn for reading and commenting on the manuscript. We are grateful to Robert Brownstone for scrutinizing the English. The study was supported by grants from The Danish Society of Multiple Sclerosis, the Danish Health Research Council and the Lauridtz Petersen foundation.

Received 30 August 1994; accepted 24 January 1995.