Distribution of Ia effects onto human hand muscle motoneurones as revealed using an H reflex technique

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1. The possibility of eliciting H reflexes in relaxed hand muscles using a collision between the orthodromic impulses generated by magnetic cortical stimulation and the antidromic motor volley due to a supramaximal (SM) peripheral nerve stimulus was investigated in seven subjects.

2. Magnetic stimuli, applied through a circular coil (outer diameter, 13 cm) centred at the vertex, evoking EMG responses of 3–5 mV amplitude in the relaxed abductor digiti minimi (ADM) muscle, and SM test stimuli to the ulnar nerve at the wrist producing a direct maximal motor response (M_{max}) in the ADM muscle, were given either alone or combined.

3. In all subjects, combined cortical and SM ulnar stimulation produced a response after the M_{max} with the latency of an H reflex evoked by the ulnar stimulus. This response occurred only within interstimulus intervals (1–20 ms) compatible with collision in the motor axons. The response behaved like an H reflex being time-locked to the SM ulnar stimulus, facilitated by voluntary activation of ADM muscle, depressed by vibration (4 s, 100 Hz) of ADM tendon and by a submotor-threshold ulnar nerve stimulus applied 50 and 80 ms before the combined stimulation, respectively.

4. In some subjects, it was also possible to distinguish an earlier response preceding the H reflex by 3 ms. Evidence is given that this response is probably of cortical origin.

5. Varying the intensity of magnetic stimulation resulted in a non-linear relationship between the H reflex size and the size of the cortical response. When the latter was between 5–25% of M_{max}, H reflexes were small (2·5–7·5% of M_{max}); with cortical responses between 25–50% of M_{max}, there was a steep increase in H reflex amplitude (10–30% of M_{max}). We suggest that this behaviour is due to an uneven distribution of Ia effects within the motoneurone pool.

H reflexes may be recorded in several muscles of the leg and arm but only exceptionally can they be evoked in the resting intrinsic muscles of the human hand (see Schieppati, 1987). This difficulty may arise for the following reasons. (a) Motor axons may have similar or lower thresholds to stimuli than Ia fibres. Consequently, H reflex discharges elicited by sensory inputs would be prevented, by collision with antidromic impulses, from reaching muscles and being detected. (b) Ia connections to these motoneurones may be weak, as inferred from studies in cat (Fritz, Illert, de la Motte, Reeh & Saggau, 1989) and in man (Marsden, Merton & Morton, 1976). The excitatory postsynaptic potentials (EPSPs) induced by the Ia fibre inputs would not be sufficiently large to depolarize the motoneurone membrane to the firing level in the resting state, but a discharge may be evoked if transmission in the reflex pathway is increased, as during post-tetanic potentiation (Hagbarth, 1962), or the excitability of the motoneurone pool is raised, as during a voluntary contraction (Upton, McComas & Sica, 1971; Stanley, 1978; Buller, Garnett & Stephens, 1980). (c) Concomitant inhibitory processes set up by a mixed afferent input may be present, which would cancel out the excitatory effects of primary muscle spindle afferents, as suggested by Buller *et al.* (1980). (d) There may be a skewed distribution of Ia effects in the pool (excitation being prevalent among high-threshold motor units), which would not be detected by classic H reflex testing, i.e. using stimuli of subthreshold intensity for motor nerves insufficient to activate all Ia fibres.

In the present study, we have investigated the possibility of eliciting a short-latency reflex response in intrinsic hand muscles using a collision between the orthodromic impulses generated by magnetic cortical stimulation and the antidromic motor volley due to a supramaximal (SM) peripheral nerve stimulus. The axons in which collision has occurred are freed from the effects of the antidromic volley and can let pass a reflex response produced by the discharge of the respective motoneurones activated by the large Ia volley concomitantly set up by the SM peripheral nerve stimulus. We show here that H reflexes can indeed be revealed using this approach and that the gain of these reflexes changes according to whether low- or high-threshold motor units are recruited.

A preliminary account of these findings has been presented to The Physiological Society (Mazzocchio, Scarpini & Rossi, 1994).

METHODS

The experiments were performed on a total of seven normal volunteers who gave their informed consent; they were five males and two females with ages ranging from 22 to 38 years. The procedures were approved by the University Hospital Ethics Committee. Subjects were seated comfortably in an armchair with their left hand and forearm firmly secured on a wooden board. All recordings were made from the left abductor digiti minimi (ADM) muscle using silver–silver chloride cup electrodes of 0·7 cm diameter taped over the belly and tendon of the ADM muscle. The EMG recordings were amplified, filtered (3 Hz to 2 kHz) and stored on floppy disk for later analysis using a commercial EMG/evoked potential machine (Medelec 'Sapphire'; Old Woking, Surrey, UK). Relaxation of the left ADM muscle was monitored acoustically by surface EMG recording (0·1 mV D^{-1}).

Transcranial magnetic stimuli were delivered with a Magstim 200 (Magstim Co., Whitland, Dyfed, UK) using a 13 cm external diameter coil centred at the vertex with the inducing currents clockwise when viewed from above. At maximum output of the device, the field generated at the centre of the coil was 1·5 T. The lowest intensity that gave a reproducible response was defined as threshold for excitation of the totally relaxed ADM muscle. In five subjects, the threshold fell between 40 and 65% of the maximum output of the stimulator, while in two it was about 80%. The ulnar nerve was stimulated supramaximally at the wrist through a bipolar electrode (0·7 ms rectangular pulses). Initially, brain stimuli 20–25% above threshold were delivered in the resting condition about once per eight seconds. Such intensities and rate of stimulation yielded motor-evoked potentials (MEP) of 2·5–4·5 mV amplitude. In random trials, cortical and SM ulnar nerve stimuli were delivered either alone or combined with various time intervals between them. If the SM ulnar shock preceded the magnetic stimulus, time intervals were defined as negative. At each interstimulus interval, eight to twelve trials were performed with the muscle relaxed in all the subjects. In three subjects, further trials were also performed with the muscle slightly contracted (10% of maximum). In all subjects, blocks of trials were conducted at rest with varying intensities of magnetic stimulation using a fixed interstimulus interval (5 ms) between the cortical shock and the SM ulnar stimulus. The data from the two subjects whose threshold value was very high were not included because they were not representative of a comparable range of magnetic stimulus intensities.

In three subjects, a long-lasting vibration (4 s, 100 Hz) was applied to the relaxed left ADM muscle proximal to the metacarpophalangeal joint by an electromagnetic mechanical stimulator (Bruel and Kjaer model 4809, Nærum, Denmark) driven by monophasic rectangular pulses of 2 ms duration. The amplitude of vibration was such as not to produce a muscle contraction of the ADM muscle. Transcranial shocks were given 50 ms after the beginning of the vibration stimulus and at intervals of 5, 10 and 15 ms before the SM ulnar shock. Trials were collected before, during and after the vibration stimulus. In three subjects, a conditioning stimulus was applied to the ulnar nerve and was delivered through the same electrodes used for the SM stimulus. The intensity of such stimulus was just below the motor threshold. The intervals between the conditioning ulnar stimulus and the SM ulnar stimulus were 5 and 80 ms, respectively.

In one subject, a large H reflex from the ADM muscle could be exceptionally obtained by stimulating the ulnar nerve at the wrist with an intensity below the threshold for activation of the motor axons. A conditioning electrical stimulus was applied to the median nerve at the wrist through a bipolar electrode (0·5 ms rectangular pulses). The intensity of such stimulus was below the motor threshold and produced no current spread to the ulnar nerve. Also, two ring electrodes were attached to the index finger for digital nerve stimulation, the cathode proximal and the anode distal to the proximal interphalangeal joint. The stimulus strength was twice the perception threshold. The threshold of the direct motor response and of sensation was determined at the beginning of each experiment and checked regularly throughout the experiment. Control ADM H reflexes were randomly alternated to H reflexes conditioned by either the median nerve stimulus or digital stimulation using different time intervals between conditioning and test stimuli.

RESULTS

Figure 1*A* shows a MEP of about 4 mV in the ADM muscle produced by a magnetic stimulus 25% above threshold applied at the vertex in a relaxed healthy subject. Figure 1*B* shows a direct motor response of maximum size produced by a SM stimulus applied to the ulnar nerve at the wrist. Figure 1*C* shows the result of combining the two types of stimulation, the brain shock preceding the SM ulnar shock by 8 ms. Under these conditions, the antidromic response set up in every motor fibre stimulated by the SM stimulus should collide with the corticospinal volley due to the magnetic stimulus. At the same time, part of the SM antidromic volley should be eliminated by the magnetic volley, clearing the α-fibres for unblocked EMG activity. Indeed, the MEP disappeared and extra EMG activity remained following the direct motor response. The activity consisted of two responses. (a) The first was an early and small response (see arrow in Fig. 1*C*), the onset and peak of which

were at about 18 and 23 ms, respectively, from the SM stimulus artifact or 25 and 30·5 ms, respectively, from the magnetic stimulus artifact. The shape of this response was very similar to the last part of the MEP before it returned to baseline (see arrow in Fig. 1*A*); it will be henceforth referred to as the E (early) response. (b) The second response was a later and larger response, which, if measured from the SM stimulus artifact, started at about 28 ms, peaked at 30 ms and ended at about 35–36 ms; if measured from the brain stimulus artifact, the onset was at about 35 ms and the peak at 37 ms. This response was called H for reasons which will be made clearer below.

Figure 2*A* shows the variations of both responses when the SM stimulus relative to the brain stimulus was shifted in the same subject at rest. The E response was not evident at all the intervals examined. It became apparent with a 4 ms interval, was very clear between 7 and 9 ms, and became difficult to recognize between 10 and 15 ms because a substantial part of it fell in the direct motor response from the ulnar shock. Nevertheless, it was clearly time-locked to the brain stimulus rather than to the SM stimulus and occurred 4–5 ms later than the MEP shown in Fig. 1*A*. It could be clearly distinguished in the relaxed muscle in three out of seven subjects. In contrast, the H response was time-locked to the SM ulnar stimulus; it was also much more stable and evident at almost all the time intervals used. The latency values of the H response were very similar to those of the H reflex that could be obtained at rest in one of the subjects (not illustrated). Figure 2*B* illustrates the amplitude variations of the H response when the time interval separating the magnetic stimulus and the SM ulnar stimulus was increased. The H response was always observed in relaxed muscles when this interval was changed from 1 to 20 ms. This is the range within which collision between the antidromic volley set up by the SM ulnar shock and the orthodromic volley set up by the cortical shock is expected to occur along the α-motor fibres. In all subjects, the size of the H response rose steeply to its maximum between 5–7 ms and progressively declined thereafter. Above 20 ms, a MEP began to appear before the direct motor response from the SM stimulus, which implied that the MEP was passing under the electrode on its way to the muscle when the SM shock was delivered. With a 0 ms interval, no clear response could be discerned in this subject. Although the brain stimulus was given simultaneously with the SM stimulus, the cortical volley should reach the cervical cord some 3–4 ms earlier than the peripheral volley from the ulnar stimulus. This was the difference between the latencies of the MEP and the H reflex evoked in relaxed muscles in this subject. Therefore, with a 0 ms delay there should still be time for collision to occur in the motor axons. These, however, having passed the corticospinal volley, are in a relative refractory state for about 2 ms (see Kimura, Yamada & Rodnitzky, 1978). During such period, further impulses would not be transmitted distally. This conduction failure may explain the low-amplitude response obtained with a 0 ms delay. Similarly, when the SM stimulus preceded the brain stimulus by 1–3 ms (not illustrated), no clear H response could be distinguished. Longer negative intervals (from −5 to −10 ms), at which the SM ulnar stimulus reached the motoneurones before the brain stimulus, gave rise to a single, large response which had the same latency as the MEP. This was presumably produced by reactivation of the α-motor fibres by the brain stimulus after collision between the orthodromic and antidromic volleys of the SM stimulus.

Figure 3*A* shows an example of the EMG responses obtained using different time intervals between the magnetic cortical stimulus and the SM stimulus under relaxed conditions and during slight tonic voluntary

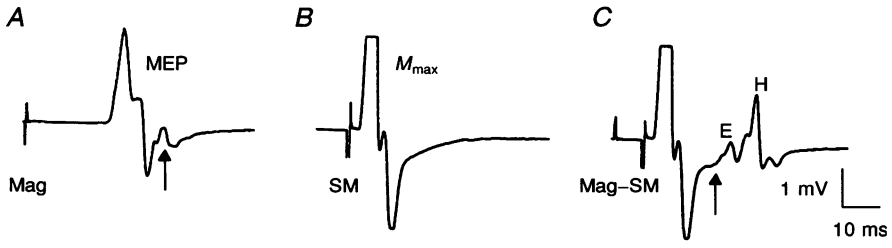

Figure 1. EMG responses from motoneurones of the relaxed ADM muscle in a representative subject

A, isolated magnetic (Mag) stimulation of the contralateral motor cortex at 80% maximum output producing a motor-evoked potential (MEP). *B*, supramaximal (SM) electrical stimulation of motor fibres of the ulnar nerve at the wrist causing maximal motor (M_{max}) response. *C*, SM stimulation of the ulnar nerve 8 ms after the cortical stimulus. Under this condition, the MEP disappears and there is additional EMG activity after the M_{max}. The latency and shape (see arrows) of the early (E) response are compatible with a cortical origin, while the subsequent response (H) has the latency of an H reflex evoked by the SM ulnar nerve stimulus. Each trace is the average of three trials.

contraction of the ADM muscle (10% of maximum voluntary effort). In this subject, the H response was not preceded by the E response at any interval at rest. However, during voluntary activity, the E response could be progressively distinguished as detaching itself from the H response and showing a clear peak of its own with longer interstimulus intervals. At 0 ms, the E response was presumably present, its peak coinciding with that of the H response. The onset of the E response was 3–4 ms later than the onset of the MEP in the active muscle and was time-locked to the brain stimulus. Compared with relaxed conditions, there was a consistent increase in the size of the H response at any time interval during voluntary effort; however, the hump-shaped curve was preserved, though

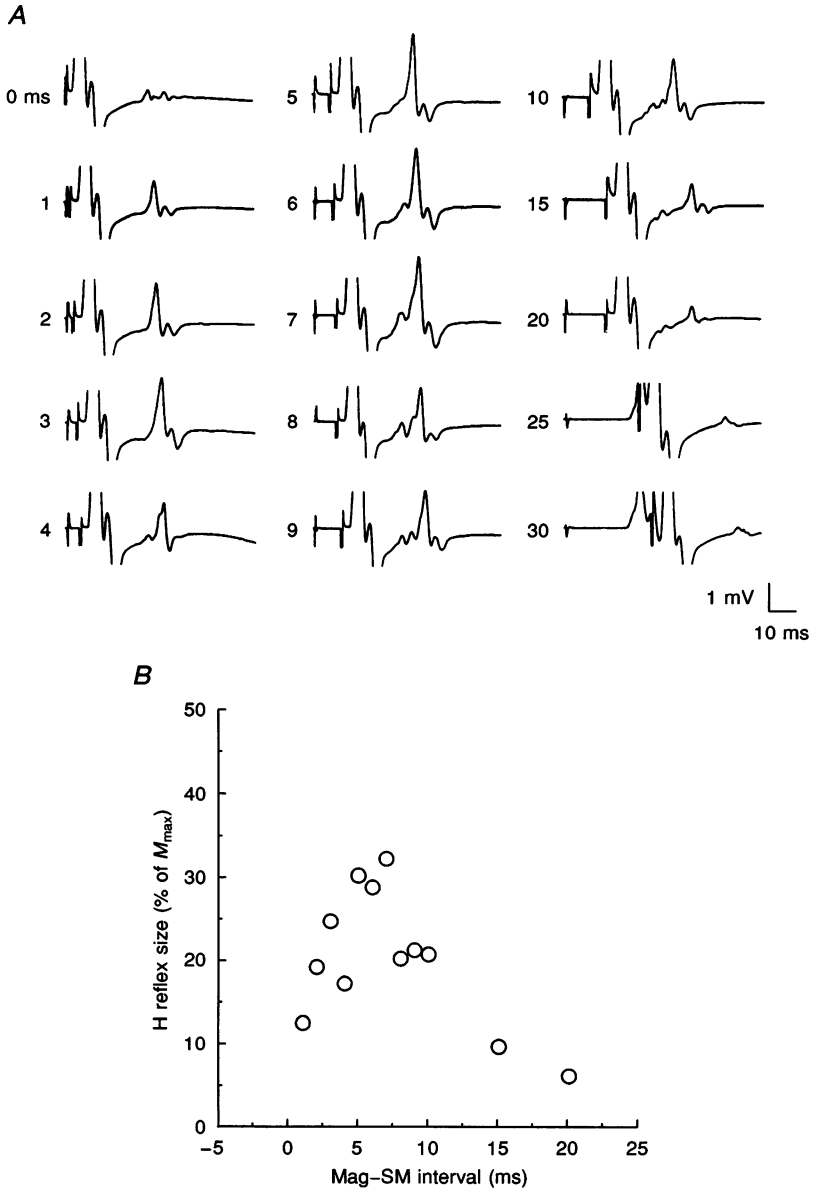

Figure 2. Variations of H reflex from the relaxed ADM muscle with changes in the Mag–SM interval

Same subject as in Fig. 1. *A*, SM ulnar stimulus preceded by Mag stimulus. The Mag–SM interval was progressively increased from 0 to 30 ms (value indicated at left of each trace); each trace is the average of three trials. Note that, in this subject, when the Mag–SM interval reached 4 ms, the E response began to appear before the H reflex. *B*, time course of the changes in H reflex size. This was measured using the falling phase of the H response and expressed as a percentage of M_{max}. Each point is the mean of five measurements; S.D. values ranged from about 5–15% of mean values.

shifted to shorter time intervals, as shown in Fig. 3*B*. In fact, maximum H amplitudes were reached between 0 and 5 ms; additionally, an H response could still be obtained using a −2·5 ms interval (SM ulnar stimulus before cortical stimulus), whereas no H response could be observed above a 17·5 ms interval, since by that time the MEP had reached the stimulating electrode when the SM stimulus occurred. This is due to the fact that shorter conduction times from the cortex to the spinal cord are obtained in activated muscles compared with resting conditions (see Rothwell, Thompson, Day, Boyd & Marsden, 1991). In this subject, the difference in time between the two conditions was 3·6 ms. Similar results were obtained in two other subjects.

Figure 4 illustrates the effects of a long vibration stimulus (4 s) applied to the tendon of the relaxed ADM muscle on the MEP (upper traces) and on the H responses (lower traces). The latter are shown at three different time intervals between the cortical stimulus and the SM stimulus. The results were obtained from the same subject

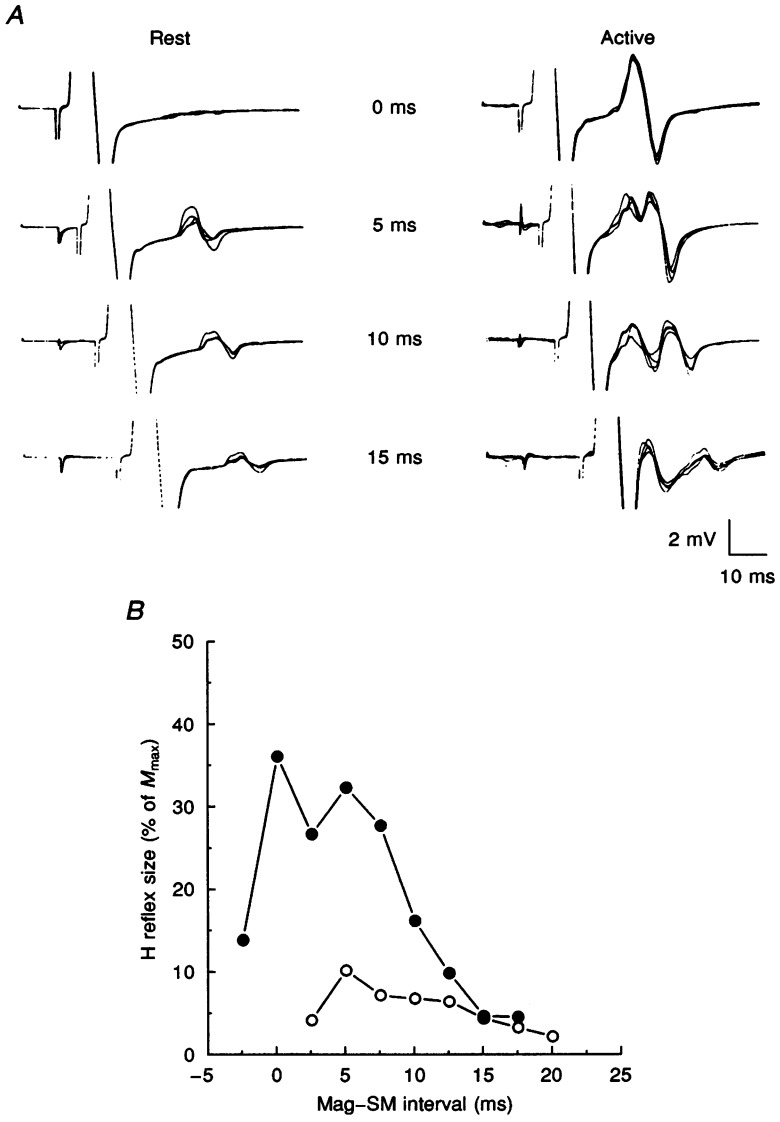

Figure 3. Comparison of ADM H reflex variations with different Mag–SM intervals under resting and active conditions

Data from another subject. *A*, SM ulnar stimulus preceded by Mag stimulus. The intensity of the Mag stimulus was the maximum possible. The Mag–SM interval is indicated in milliseconds. Note that, in this subject, the E response was not present at rest but appeared only during a tonic voluntary contraction of ADM muscle (10% of maximum). Each record shows four superimposed traces. *B*, time course of the changes in H reflex size under relaxed (○) and active (●) conditions. See legend to Fig. 2*B* for further details.

in whom there was no evidence of an E response at rest (see Fig. 3*A*). Cortical stimulus intensity corresponded to the maximum output of the magnetic stimulator. Vibration preceded the magnetic stimulus by 50 ms. In this case, no significant variation in the size of the MEP was observed as previously reported by Claus, Mills & Murray (1988). In contrast, the amplitude of the H response was almost completely depressed by the vibratory stimulus. This was observed at all the time intervals explored. Recovery of the size of the H response occurred about 1 min after the end of vibration. Similar results were seen in two other subjects.

Figure 5 shows the effect of a weak conditioning stimulus, just below the threshold for the direct motor response, applied to the ulnar nerve 5 ms (*A*) and 80 ms (*B*) before the SM stimulus, on the H response. The former (*A*), by evoking EPSPs in the motoneurones via Ia pathways, should increase the excitability of the α-motoneurones during the arrival of the SM volley; the latter (*B*), presumably via Ia afferents, should produce inhibition of H reflexes during the classic excitability cycle (see Rossi, Mazzocchio & Schieppati, 1988). The sensitivity of H reflexes to facilitation was tested on H responses of small size (1–7% of M_{max}) obtained using MEPs of relatively low amplitude (10–25% of M_{max}). There was no significant change between control and conditioned H responses at each MEP amplitude used (Fig. 5*A*). On the other hand, when the same conditioning stimulus was applied 80 ms earlier, the size of the H response was significantly depressed (Fig. 5*B*). The size of the MEP did not show significant changes between control and conditioned trials. Similar results were obtained in two other subjects.

Since the size of the MEP determined the occurrence of the H response, we studied the relationship between the H response and the MEP with increasing intensities of transcranial magnetic stimulation. Discharge of a motoneurone to a phasic excitatory input, particularly at rest, is probabilistic in nature (see Bawa & Lemon, 1993). As a result, the magnitudes of the MEP to the same magnetic stimulation intensity can be quite variable (see also Davey, Ellaway, Maskill, Anissimova, Rawlinson & Thomas, 1994). We therefore expressed the variations of H response size as a function of MEPs of increasing amplitude. Figure 6*A* shows the data from five subjects (see Methods). The interval between the magnetic shock and the SM stimulus was 5 ms. A range of MEP amplitudes between 5 and 20% of M_{max} produced small changes in the size of the H reflex (2·5–7·5% of M_{max}). In contrast, MEPs of larger size (25–50% of M_{max}) produced a steep increase in H reflex size (10–30% of M_{max}). It is known that the strength of Ia effects varies with motoneurone size so that small motoneurones with a low conduction velocity exhibit large Ia EPSPs, whereas large motoneurones with a high conduction velocity show small Ia EPSPs (see Awiszus & Feistner, 1993, for references). It has also been shown in

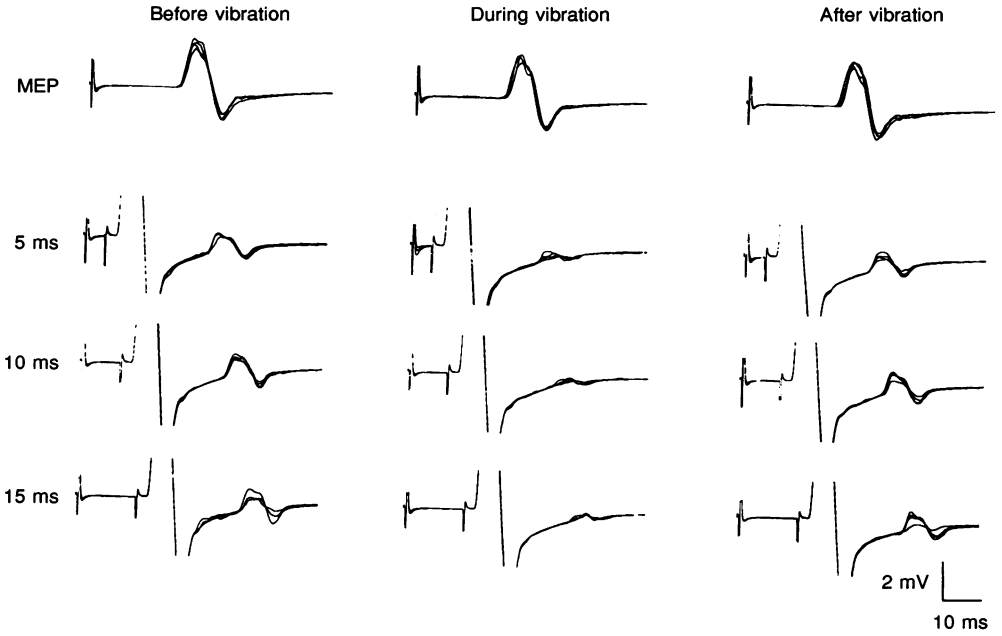

Figure 4. Effect of vibration of the ADM tendon on MEP and H reflex under resting conditions
Same subject as in Fig. 3. The vibratory stimulus (100 Hz, 4 s) was delivered 50 ms before the Mag stimulus which triggered the trace. In each panel: upper trace, isolated Mag stimulus (maximum output of the stimulator); lower traces, combined Mag and SM ulnar stimuli at different intervals. Each record shows four superimposed traces.

the monkey that, among motoneurones of the ulnar nerve, those with large Ia EPSPs tend to receive larger cortico-motoneuronal EPSPs than do cells in which the Ia EPSPs are small (Clough, Kernell & Phillips, 1968). Accordingly, the H response would be expected to reach the maximum size with low-amplitude MEPs, since these are presumably produced by the discharge of the small, low-threshold motoneurones receiving a larger amount of corticospinal EPSPs. This did not occur, the H response reaching the maximal amplitude with the largest possible MEPs.

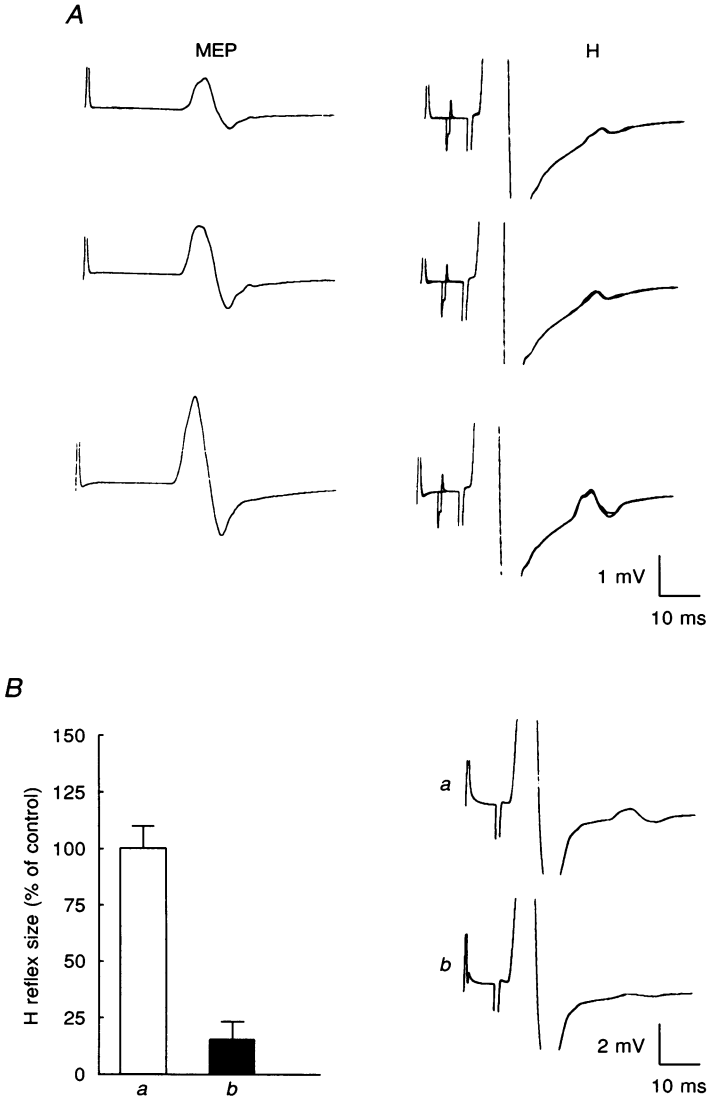

Figure 5. Effect of a conditioning ulnar nerve stimulus on the H reflex of the relaxed ADM muscle

Same subject as in Fig. 3. The intensity of the conditioning stimulus was just below the threshold for activation of motor fibres. *A*, left panel, isolated Mag stimulus of increasing intensity (between 60–80% of maximum output). Each trace is the average of eight responses. Right panel, the conditioning stimulus precedes the SM ulnar stimulus by 5 ms. The Mag–SM interval was 10 ms. Each record shows the averages of eight superimposed control and eight conditioned H reflexes. *B*, averages of twelve trials (the size of the H reflex being expressed as a percentage of its control value) and sample records (each trace was triggered by the Mag stimulus; the Mag–SM interval was 7·5 ms) show the size of the H reflex in the control situation (*a*) and when the conditioning stimulus preceded the SM ulnar stimulus by 80 ms (*b*). The difference between the two conditions is statistically significant ($P < 0{\cdot}05$; Student's two-tailed t test). Vertical bars indicate 1 S.D.

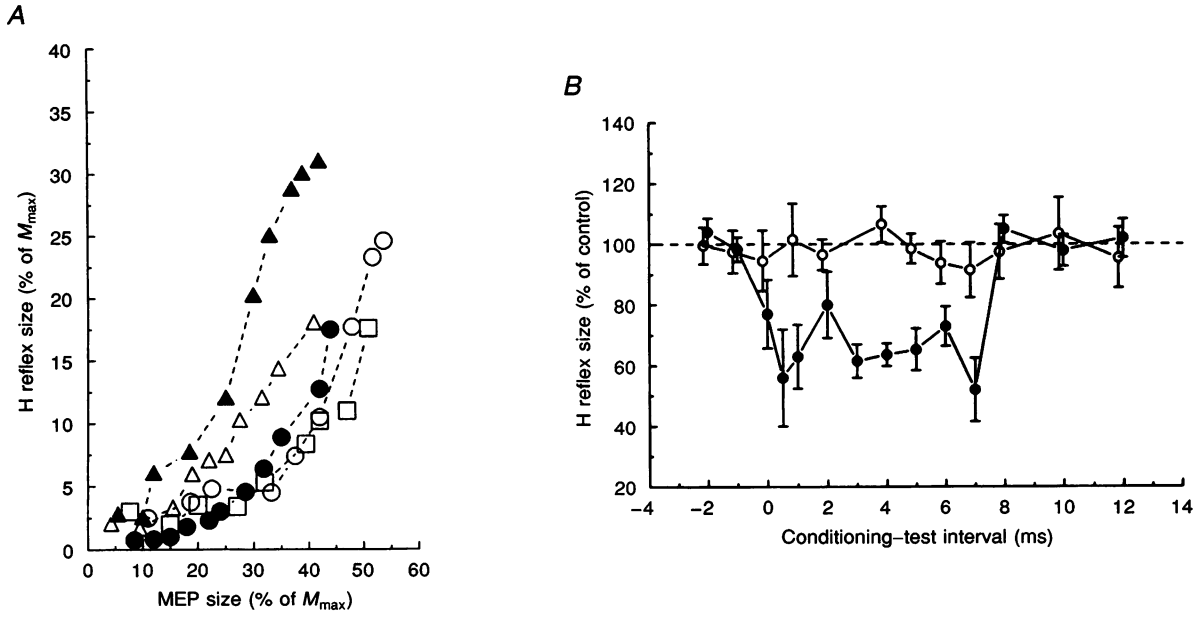

Figure 6. Variations of ADM H reflex with MEPs of increasing size under resting conditions (*A*) and effect of median and digital nerve stimulation on ADM H reflex (*B*)

A, data from five subjects. The amplitude of the H reflex (Mag preceded SM ulnar stimulus by 5 ms) is plotted against that of the MEP, both expressed as a percentage of M_{max}. Each point is the mean of 6–8 measurements; S.D. values ranged from about 5–15% of the mean values. *B*, this H reflex was exceptionally obtained in one subject at rest using submotor-threshold stimulation of the ulnar nerve at the wrist. The conditioning median (●) nerve stimulus was applied at the wrist and its intensity was just below motor threshold. The conditioning digital (○) nerve stimulation was applied to the index finger and its strength was twice the perception threshold. The size of the test H reflex, expressed as a percentage of its control value (dashed line), is plotted against the conditioning–test interval. This is negative when the test stimulus precedes the conditioning one. Each symbol represents the mean of 20 measurements. Vertical bars indicate 1 S.D.)

One possible reason for this could be the presence of an inhibitory process, induced by the SM stimulation, affecting the ADM motoneurones at very short latencies. This was investigated in the only subject in whom it was possible to elicit an H reflex from the relaxed ADM muscle with a stimulus intensity below the threshold for activating the ulnar motor axons at the wrist (see Methods). The effect of a conditioning submotor-threshold stimulation of the median nerve at the wrist on the size of this H reflex was then studied (Fig. 6*B*). Inhibition of the H reflex (●) was evident at a conditioning–test interval as early as 0 ms and was over by 8 ms. In contrast, no significant change in the size of the H reflex was observed when the conditioning stimulus was replaced by digital nerve stimulation (○). In this case, the conditioning–test intervals were corrected by subtracting the latency of the finger–wrist tract. Thus, at conditioning–test intervals of 0 ms, the volleys elicited by both stimuli should arrive at the spinal cord simultaneously, given the similar conduction velocities of low-threshold muscle and cutaneous afferents (see Macefield, Gandevia & Burke, 1989).

DISCUSSION

Combined magnetic stimulation of the scalp and SM ulnar nerve stimulation elicited additional EMG activity after the direct motor response in the relaxed ADM muscle. This consisted of a constant response (H), the onset of which was occasionally masked by the occurrence of other EMG activity (E response) preceding the H response by about 4 ms. Both responses were recorded only when there was a corticospinal volley capable of freeing the motor axons, through collision, from the antidromic motor volley set up by the SM nerve stimulation.

It has been suggested that one possible way EMG activity can appear under the above conditions is for the cortical shock to produce more than a single discharge of spinal motoneurones (Day *et al.* 1987, 1989; Hess, Mills & Murray, 1987). Assuming that a single cortical shock in man can give rise, as in monkey (Kernell & Wu, 1967), to series of descending volleys lasting up to 6–8 ms after the first volley (see Rothwell *et al.* 1991), the H response cannot be the expression of such activity since it occurred about 13 ms later than the MEP under resting conditions. On the

other hand, the E response, observed during voluntary contraction and in some cases at rest (see Figs 2 and 3), may well be due to the discharge of the same motoneurones following the arrival of succeeding corticospinal volleys not affected by the collision. Indeed, this E response occurred 4–5 ms later than the MEP elicited under either relaxed or active conditions. This value compares favourably with the estimated interval between double discharges observed in human hand muscles (see Rothwell *et al.* 1991).

The H response must then have a different origin and may result from the discharge of those motoneurones which, having fired in the MEP, have had their axons cleared from the effects of the antidromic motor volley by means of collision and are thus available for activation by the Ia afferent volley elicited by the SM stimulus. Several lines of evidence indicate that such a response is of reflex origin: (a) its latency was remarkably stable and very similar to that of the H reflex obtained using the classic technique in one of the subjects studied; (b) it was facilitated by active contraction of the ADM muscle; and (c) it was strongly inhibited by long-lasting vibration of the ADM tendon or by a conditioning group I stimulation delivered 80 ms earlier (see Rossi *et al.* 1988, for references).

The time course of the H reflex effect when changing cortical–wrist intervals showed a hump-shaped curve (see Figs 2 and 3). This may reflect a combination of two factors: first, recovery from an absolute refractory period within the motoneurones (postspike after-hyperpolarization), and second, a declining postsynaptic facilitation. Concerning the origin of the latter, it should be noted that with the H reflex obtained using collision in the motor axons only that fraction of the ADM motoneurone pool that has already discharged in response to the corticospinal volleys is tested. That is to say, the subliminal fringe created by the same corticospinal volleys will not be recruited by the SM stimulus. Therefore, the rise in the excitability of this H reflex will depend on events which follow the first corticospinal discharge, such as EPSPs elicited either by multiple descending volleys after the same cortical shock (see Rothwell *et al.* 1991; Mazzocchio, Rothwell, Day & Thompson, 1994), or by peripheral volleys after the SM stimulus itself producing central effects at very short latencies (see below and also Macefield *et al.* 1989).

The occurence of the H response at rest very much depended on the amplitude of the MEP. The relationship between their sizes with increasing intensities of magnetic stimulation was non-linear so that the recruitment gain, i.e. the number of motoneurones participating in the H response (see Kernell & Hultborn, 1990), was initially low and then became markedly increased along with the activation of new, high-threshold motor units in the MEP. There may be various reasons for such behaviour.

(a) A change in the depth of the after-hyperpolarization of the motoneurones that have fired in the corticospinal discharge. Despite the complex and phasic nature of the descending corticospinal volley generated by transcranial magnetic stimulation, recruitment of α-motoneurones under resting conditions appears to occur in an orderly size-related fashion (Bawa & Lemon, 1993). Therefore, with increasing magnetic stimulus intensity, motoneurones with shorter after-hyperpolarization might be recruited.

(b) Changes in the 'setting' of the recurrent Renshaw inhibition. Although transcranial magnetic stimulation has been shown recently to depress the activity of Renshaw cells in humans (Mazzocchio, Rossi & Rothwell, 1994) and therefore, in theory, could be one of the factors which makes the recruitment gain steeper, there is evidence suggesting a lack of recurrent inhibition in the motor nuclei of the more distal muscles of both limbs (Rossi & Mazzocchio, 1991; Katz, Mazzocchio, Penicaud & Rossi, 1993).

(c) A disproportionate increase in the total amount of descending excitatory input to the motoneurone pool. When a small cortical stimulus is given, there is relatively little continuing excitatory activity in the corticospinal tract which could summate with the H reflex; with a very strong cortical shock, there would be a large amount of persisting corticospinal facilitation of the motoneurone pool sustained by the many volleys coming down after the ones responsible for the first motoneurone discharge. The time interval between the cortical shock and the SM stimulus used to study the relationship between MEPs and H reflexes (Fig. 6*A*) and the estimated central time during which the size of the H reflex can be influenced by synaptic events (see Burke, Gandevia & McKeon, 1984) would give a total time of about 10 ms, which should allow for corticospinal EPSPs summation with increasing magnetic stimulus intensities. The steep rise in the H reflex size could be the expression of such a mechanism.

(d) Small MEPs have longer latencies at rest (see Day *et al.* 1987). Then, the motoneurones tested with the H reflex might suffer a somewhat stronger 'relative refractoriness' (earlier during their after-hyperpolarization) than with larger shorter-latency MEPs. This might be an explanation for the 'unproportionally' small H reflexes with small MEPs.

(e) A distribution of synaptic input activated by the SM stimulation favouring the recruitment of large motoneurones. If the Ia input was more effective in discharging large motoneurones than small motoneurones, this would steepen the input–output curve for the H reflex. This possibility is discussed in more detail below.

It is not possible to say whether one or all five of these reasons contributes to the steep rise in the input–output curve for H reflexes in the present experiments. Nevertheless, whatever the explanation, the findings may also have a direct bearing on the problem of why H reflexes are

so difficult to obtain in hand muscles at rest. In the past, it has often been tacitly assumed that H reflexes are absent in relaxed hand muscles because the monosynaptic Ia input to motoneurones is relatively weak (see introduction). The present experiments show that this is not the case, and that when tested appropriately, Ia input can be very powerful. We propose that the steep input–output curve is responsible for the lack of the H reflexes at rest. Effectively, the steep curve means that the Ia input is ineffective on small, low-threshold motoneurones. Why this should be the case is not clear, but of the explanations given above for the steep input–output curve only the last (e) can apply to the simple situation in which H reflexes are elicited in relaxed muscle since only that does not depend upon the effects of a prior cortical shock. We shall therefore explore this explanation in a little more detail.

There are several possible reasons why the effectiveness of Ia input could be skewed in favour of recruitment of large motoneurones. (a) The Ia terminals themselves might be distributed preferentially to large motoneurones. This would be in direct contrast to results reported in most other situations in which the Ia input is distributed evenly to motoneurones of different size (see Calancie & Bawa, 1990). (b) The anatomical distribution of Ia connections amongst the motoneurone pool may resemble that seen in other systems but the effectiveness of these connections onto motoneurones of different size could be changed by presynaptic factors or synaptic differences (Collins, Honig & Mendell, 1984; Davis, Collins & Mendell, 1985). (c) Other inputs, activated at the same time, could mask the distribution of Ia effects. Group I stimulation of median nerve fibres at the wrist elicited a short-latency inhibition of ADM motoneurones (see Fig. 6*B*). This input, by tending to cancel out Ia effects, may well be responsible for the slow rise in the excitability of ADM motoneurones, possibly explaining their low sensitivity to facilitation (see Fig. 5*A*). Presumably, a similar effect might be produced, through activation of homonymous inhibitory pathways, when testing routinely for H reflexes in hand muscles. Cutaneous input could also be important. Cutaneous fibres at the wrist have the same diameter and threshold as large diameter muscle afferents (see Macefield *et al.* 1989) and can produce a predominantly inhibitory effect on small, low-threshold motor units and an excitatory effect on high-threshold, large motor units (Garnett & Stephens, 1981; Kanda & Desmedt, 1983; Masakado, Kamen & De Luca, 1991). While a cutaneous contribution to the inhibition of the small, low-threshold motoneurones is possible, though improbable (see Fig. 6*B*), cutaneous facilitatory input would be the most likely candidate for explaining the prevalence of Ia excitation amongst large, high-threshold motoneurones.

We conclude that H reflexes are difficult to obtain in relaxed hand muscles because of the steepness of the input–output curve. This is due to a skewed distribution of Ia excitation to the motoneurone pool, which favours the discharge of large motoneurones over small motoneurones. Interestingly, in a theoretical study of the input–output relationships of a motoneurone pool model (Kernell & Hultborn, 1990), a change in output gain, as caused by synaptic input systems with an uneven distribution, is represented by a non-linear curve very similar to that obtained in the present study.

The fact that the distribution of Ia effects does not reflect the stereotyped pattern of Ia connections may perhaps point to a specific synaptic organization favouring motoneurones with fast axons. Such a differential distribution of excitation could increase the accessibility of some motor units of the hand muscles to cortical control through fast corticospinal fibres as seen during fractionated movements of the fingers involving precision grip and fine manipulation (see Johansson, Lemon & Westling, 1993; Lemon, Werner, Bennett & Flament, 1993; Maier, Bennett, Hepp-Reymond & Lemon, 1993).

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