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Changes in Human Alpha-Motoneurone Excitability Following Mechanical Muscle Stimuli*

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Summary. Short mechanical stretches given to partially activated human abductor digiti minimi muscle (ADM) evoke early (M1) and late (M2) reflex responses. Transcranial magnetic brain stimuli were used to evoke compound muscle action potentials in ADM and hence to estimate motoneuronal excitability at various times after mechanical stimuli. There was no evidence that Ia volleys produce additional facilitation in motoneurones of muscles which are already voluntarily activated. However, the inhibitory phase between M1 and M2 was associated with a reduction in size of muscle responses from brain stimuli. This may reflect reduced Ia input, polysynaptic Ia inhibition or Renshaw inhibition.

Key words: Long loop reflex – Magnetic brain stimulation – Muscle spindles – Renshaw inhibition

Introduction

Painless transcranial stimulation of the human motor cortex can be achieved with an intense time-varying magnetic field (Barker and Jalinous 1985). The magnetic field is generated in a coil which is centred over the vertex. A corticospinal volley evoked by the magnetic field reaches motoneurones of small hand muscles after an estimated latency of 5.7 ms. The latency to abductor digiti minimi muscle (ADM) is roughly 21 ms (Hess et al. 1987). Small mechanical stimuli with a rising velocity of 200 mm/s excite muscle spindles when applied to the proximal interphalangeal joint of the abducted fifth digit to cause stretching of the ADM. They produce a scalp somatosensory evoked potential (SEP) with the first components N1 at 27 ms and P1 at 33 ms latency (A) (Claus et al. 1988). With the ADM contracted these stimuli also produce an early M1 and a late M2 reflex response in the muscle. M1 is likely to be a monosynaptic spinal reflex (Davies 1987), while M2 is thought to be a transcortical long loop response (Lee and Tatton 1975). The purpose of this investigation was to test the effect of these mechanical stimuli on the excitability of motoneurones as assessed by the size of compound muscle action potentials (CMAPs) evoked by transcranial brain stimulation.

Since M1 is thought to be a monosynaptic spinal reflex response, the latency from ADM to its spinal motoneurones, as well as the motor conduction time from motoneurones to ADM, can be estimated by the formula B = (M1 latency − 1)/2, assuming a synaptic delay of 1 ms at the motoneurone and similar afferent and efferent conduction times. This conduction time is estimated to be 17 ms (SD2.5, $n = 6$). If latency B is subtracted from the M2 latency, then the result will be a latency (C). At this moment (C), the M2 volley can be assumed to have arrived at ADM motoneurones, no matter what the central pathway of the long reflex loop is. A transcranial stimulus would excite the motor cortex simultaneously with afferent impulses from mechanical muscle stimulation, if it were given at a time interval equal to the latency of the SEP. Furthermore, the corticospinal volley after transcranial brain stimulation would arrive at ADM motoneurones simultaneously with the M2 volley after mechanical stimulation, if the interval between both stimuli was equal to D (D = M2 latency − [B + 5.7]). As would be expected, A and D are similar because the afferent pathway of the SEP is thought to be similar to that of the long loop. The central motor conduction time should be the same following either a long loop vol-

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ley or a volley after transcranial brain stimulation. After an interval of E (E = M1 latency − [B + 5.7]) arrival of the corticospinal volley following brain stimulation should coincide with the M1 volley at spinal motoneurones. When M1 or M2 peak latencies are used in the formulae E and D instead of onset latencies (see Fig. 1) one might expect the maximum of M1 and M2 volleys to be at the spinal motoneurones. The beginning of M2 marks the end of a phase of inhibition, or lack of excitation, between M1 and M2 known as I1 (Jenner and Stephens 1982).

Methods

Experiments were carried out in six healthy subjects (aged 23–61, mean 37 years) with the ADM exerting a steady isometric contraction of 5% of the maximum force. This was measured by a strain gauge and monitored by an ultraviolet recorder. Recordings were made from the right ADM with surface cup electrodes (amplification 2 mV/division, bandpass 20 Hz–2 kHz). Transcranial magnetic stimuli (10% above the threshold for obtaining a response in the relaxed muscle) were given with the coil of the magnetic stimulator centred over the vertex (Barker and Jalinous 1985). This stimulus intensity remained constant throughout the experiment. At the beginning and end of the session, stimuli were given both with ADM relaxed and with ADM exerting 5% contraction (no mechanical stimulus). The other brain stimuli (with ADM exerting 5% contraction) were given at random intervals of 6–40 ms after the mechanical muscle stimulus (rise time 200 mm/s, 100 ms, 1 mm). Four stimuli were given each time to calculate the average CMAP amplitude and the area of the negative phase. The long loop reflex was also recorded from each subject's right ADM after mechanical stimulation (averaging of 50–80 rectified responses). In the six subjects the onset latency of M1 was 33 ± 5 ms, with a peak latency of 40 ± 5 ms and the onset latency of M2 was 55 ± 6 ms with a peak latency of 67 ± 6 ms. The stimulus intervals for the corticospinal volley to arrive simultaneously with reflex volleys at spinal motoneurones, as calculated by formulae E and D, are: onset M1 11.5 ± 2.5 ms; M1 peak 18.1 ± 2.4 ms; onset M2 32.8 ± 3.8 ms; M2 peak 45.1 ± 3.7 ms.

The amplitude and area values of responses were compared with those recorded at the end of the experiment (5% muscle contraction but no mechanical stimulation, marked with an arrow in Fig. 1) using Wilcoxon's test.

The subjects were members of staff who gave their informed consent. The procedures were approved by the Ethics Committee of the National Hospitals for Nervous Diseases.

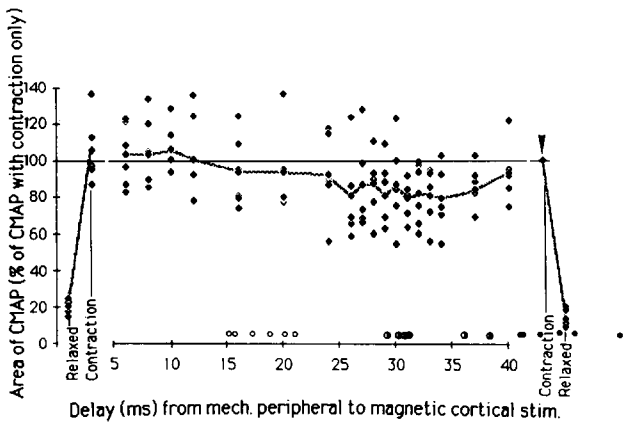

Fig. 1. Area of compound muscle action potentials (CMAPs) normalized to the area of the CMAP obtained during 5% contraction but without mechanical stimulation at the end of the experiment *(arrow)* is plotted against the time interval (ms) between a mechanical muscle stimulus and a magnetic cortical stimulus. Each *diamond* represents the mean of four responses in one subject. The times at which spinal motoneurones would be participating in M1 (○), I1 (◑) and M2 (●) are indicated just above the X axis for comparison

Results and Discussion

Muscle contraction alone produced an approximately five-fold enlargement of CMAPs (at beginning and end: relaxed mean areas 3 ± 1.5 and 2 ± 1.2 m V × ms, contraction 15 ± 4.5 and 14 ± 5.2 m V × ms). The results with ADM contracted and relaxed did not differ at the beginning and end of the experiment. No additional facilitation of CMAPs was seen after mechanical stimulation compared with the recording with contraction alone (Fig. 1, arrow). At interstimulus intervals calculated by E for the peak of M1 volleys being at the spinal motoneurones simultaneously with corticospinal volleys the CMAPs were not enlarged (mean values between 94% and 106% of those without mechanical stimulation, Fig. 1). However, at intervals between 26 and 37 ms the CMAPs as measured by amplitude or area were significantly smaller (mean areas 79%–88%, $P < 0.001$).

With an interstimulus interval of ≥ 33 ms the corticospinal volley is thought to arrive at spinal motoneurones simultaneously with the M2 volley. Therefore the responses to brain stimulation returned to 94% at an interval of 40 ms. However, the mean interval for simultaneous arrival with the M2 peak is 45 ms (not investigated in this experiment).

Another series of experiments was therefore performed to examine this time difference separately. In four of the subjects magnetic stimuli were applied 6 ms, 30–34 ms (onset M2, D) and 43–46 ms (peak M2, D) after the muscle tap. At 6 ms the descending volley was thought to have arrived at motoneurones before Ia impulses. This was used as a reference value. At 30–34 ms the descending volley was likely to arrive at motoneurones within the I1 period, and an inhibition of CMAPs was suspected. Finally, at 43–46 ms, simultaneous arrival of descending pyramidal tract impulses with the M2 peak volley could produce facilitation at the same motoneurones (Fig. 2). Ten responses were averaged at each stage and the amplitude values at 6 ms were set at 100%. At 30–

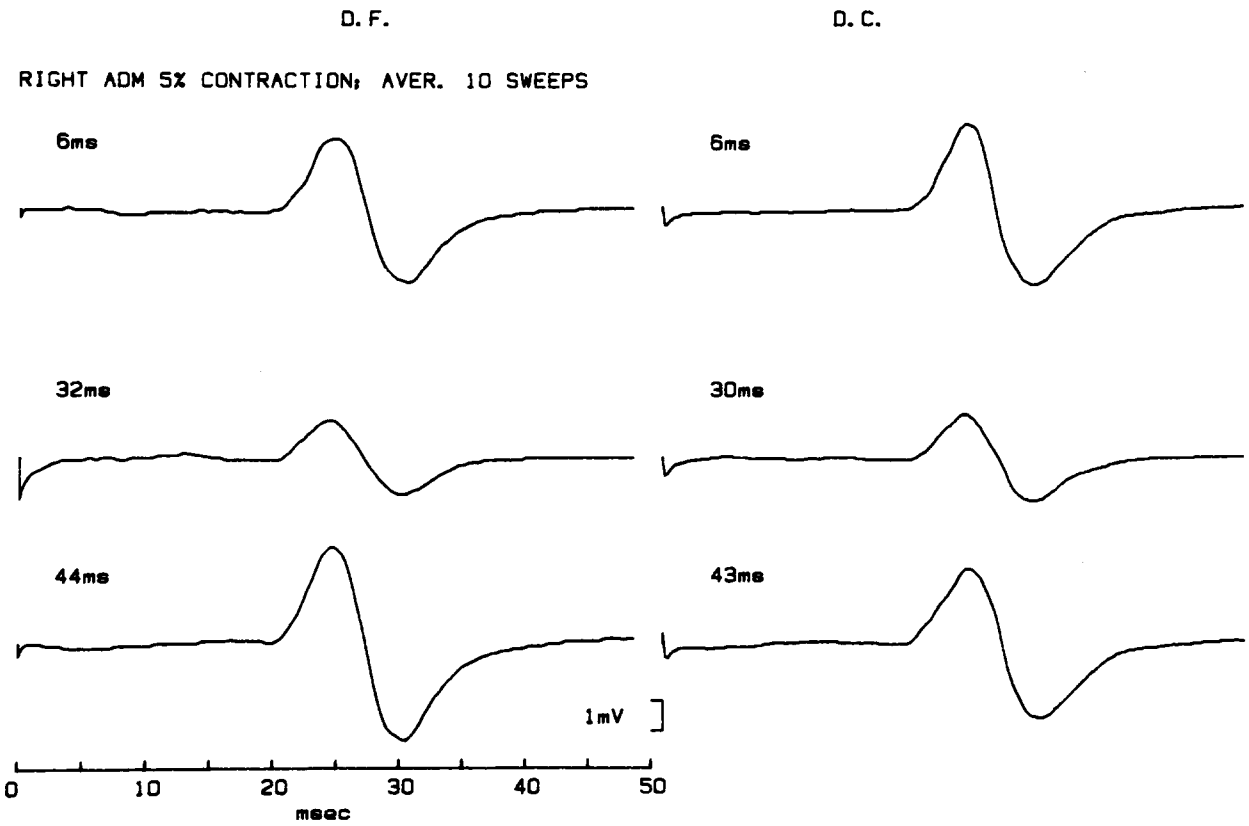

Fig. 2. Averaged ($n = 10$) CMAPs from abductor digiti minimi muscle exerting 5% maximum voluntary contraction after mechanical stimuli given at times calculated to be before spindle primary volleys have reached motoneurones *(upper traces)*, when the motoneurones are between M1 and M2 *(middle traces)* and finally when the motoneurones are maximally involved in the production of M2 *(lower traces)*. Examples from two subjects are shown

34 ms the amplitudes were reduced to 39%–93% (mean 66%), confirming the attenuation seen in Fig. 1. At 43–46 ms no facilitation was seen (amplitudes 86%–126%, mean 104%). With a steady muscle contraction, therefore, neither an early nor a late facilitation of the response to brain stimulation was seen.

It is likely that the input evoked by mechanical stimulation could not produce any further effect since the spinal motoneurones had already been brought to threshold by voluntary muscle activation. Ia afferents could well excite motoneurones, producing M1 and M2 responses which are not exactly time locked to transcranial stimuli. An increase of the excitability of motoneurones which did not fire cannot be detected by this method. The period of CMAP attenuation coincides with the period I1 in the spinal motoneurones (I1 calculated by formula D). The potential's attenuation is due either to a lack of excitation of spinal motoneurones between M1 and M2 or inhibition. I1 after mechanical stimulation can be due to lack of Ia excitation (Merton 1951). However, the pause in discharge of the spindles is often much briefer than the twitch causing it. Furthermore, inhibition of motoneurones could be the cause of the reduction in CMAP size. This inhibition could be a Ia mediated polysynaptic spinal inhibition, or due to afferents from spindle secondaries or cutaneous afferents (flexor reflex afferents) (Jenner and Stephens 1982; Katz and Pierrot-Deseilligny 1982; Lundberg et al. 1987; Rothwell 1987). In two subjects 25 min of ischaemia of the right fifth digit produced numbness. The attenuation of CMAPs after brain stimuli given 30 ms after mechanical stimulation was applied distally to the rubber cuff was still apparent, however (CMAP amplitudes, average of 20 sweeps each, before ischaemia 39% and 25%, after ischaemia 47% and 34%). Therefore, skin afferents are not likely to be the only cause of the attenuation of CMAPs. Renshaw recurrent inhibiton (Lee and Tatton 1975) may last up to 50 ms and thus this possibility cannot be excluded. Finally, postexcitatory hyperpolarization of alpha-motoneurones may play a role.

The stimulus offered here is relatively specific for spindle primaries; these may be important because the phenomenon was also seen with a very short

stimulus (8 ms duration, 0.9 mm amplitude) equivalent to one vibration phase of 125 Hz (two subjects, average of 20 sweeps each, 6 ms and 30 ms intervals, at 6 ms CMAP amplitudes 100%, at 30 ms amplitudes 45% and 36%). Thus when experimental conditions are such that short and long latency stretch reflexes can be produced, then stimulation of the motor cortical areas does not convincingly reveal any periods of enhanced excitability, either of the cortex or the cord. However, we have been able to demonstrate a period of reduced excitability corresponding to the inhibitory phase between M1 and M2.

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