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EFFECT OF DIGITAL NERVE STIMULI ON RESPONSES TO ELECTRICAL OR MAGNETIC STIMULATION OF THE HUMAN BRAIN

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SUMMARY

1. Reflexes were elicited in the first dorsal interosseous muscle of seven normal subjects by electrical stimulation of the digital nerves of the index finger at 3 times perceptual threshold while subjects maintained a constant voluntary contraction of the muscle. The average response in the surface-rectified electromyogram (EMG) consisted of an early inhibitory (I1) component followed by a later excitation (E2).

2. Low intensity anodal electrical or magnetic scalp stimuli were given over the motor cortex in order to elicit muscle responses within the period of the I1 and E2 reflex components.

3. Compared with control responses elicited in the absence of digital nerve stimulation, responses to electrical cortex stimulation were suppressed in the I1 period and facilitated during the E2 period of the reflex. In contrast, responses evoked by magnetic stimulation were suppressed during I1 and also for the first 10 ms or so of the E2 response. Magnetically evoked responses were facilitated during the later part of the E2 reflex.

4. Similar effects were seen when the probability of firing of single motor units was studied.

5. In three subjects, small taps were given to the abducted index finger in order to stretch the first dorsal interosseous muscle and evoke reflexes which were of comparable size to the E2 reflex evoked by digital nerve stimulation. In contrast to the experiments in which digital nerve stimuli were given, responses evoked by magnetic stimulation over motor cortex were facilitated at all times during the course of the reflex evoked when the muscle was stretched.

6. We conclude that single electrical stimuli applied to the digital nerves can reduce for a short period the excitability of motor cortex to magnetic stimulation. This occurs at a time when the same stimulus is evoking an excitatory (E2) reflex in the average surface-rectified EMG.

INTRODUCTION

Two lines of evidence have been taken to suggest that cutaneous input can modulate the excitability of the motor cortex. First, during a steady voluntary contraction, electrical stimulation of the digital nerves of the index finger, which

evokes a predominantly cutaneous afferent volley, can produce successive periods of facilitation and inhibition in the electromyographic (EMG) activity of muscles in the forearm and hand (Caccia, McComas, Upton & Blogg, 1973). In the first dorsal interosseous muscle (1DI), this modulation takes the form of an early (30–40 ms post-stimulus) period of facilitation (E1) followed by inhibition (latency 40–50 ms post-stimulus: I1) and by a later more prominent facilitation (latency 50–70 ms post-stimulus: E2). From their studies in patients with lesions in various parts of the central nervous system, Jenner & Stephens (1982) proposed that the late excitatory component (E2) was of supraspinal, transcortical origin. A second line of evidence implicating cutaneous input as a factor in modulating motor cortex excitability comes from clinical neurology. Jacksonian seizures commonly begin in the distal parts of the arm or leg and spread over several seconds to involve more proximal limb and trunk muscles before, on occasions, progressing to a generalized seizure. It is well known that some patients can stop the spread of the epileptic activity by vigorously rubbing the skin of the affected limb (e.g. Hughlings-Jackson, 1868). In these cases it seems that cutaneous input is able to inhibit motor cortex excitability, thereby preventing the fit from spreading. Extrapolating to normal subjects, this would predict that cutaneous input could decrease the excitability of motor cortex.

The purpose of the present paper was to test the ability of digital nerve input to modulate motor cortex excitability assessed by using the techniques of magnetic and electrical transcranial stimulation of the brain. If this input does reach the motor cortex, then it may be expected to modulate the size of muscle responses evoked by transcranial stimulation. Moreover, since anodal electrical stimulation through the scalp is thought to activate the axons of pyramidal output neurones directly, whereas magnetic stimulation excites them via synaptic connections or at the initial segment (Day, Dressler, Maertens de Noordhout, Marsden, Nakashima, Rothwell & Thompson, 1989; Edgley, Eyre, Lemon & Miller, 1990), there may be a differential effect of digital nerve input on the responses to these two forms of stimulation. This reasoning was used recently by Day, Riescher, Struppler, Rothwell & Marsden (1991) to support the conclusion that muscle stretch input could modulate cortical excitability during the period of the long-latency stretch reflex in man.

Several attempts have been made by other workers to address the question of cutaneous effects on motor cortex excitability. These reports have been published only in abstract form and have yielded conflicting results. In all of them the authors have assumed that the responses produced by stimulation of digital nerves are predominantly cutaneous in origin. However, although the major afferents in the digital nerves come from receptors in the skin, we can never exclude the possibility of some contribution to the effects we observe from other receptors in interphalangeal joints and tendon sheaths. The first experiments were performed by Bergamasco, Bergamini, Cantello & Troni (1987) who found that electrical stimuli applied to the index finger had no effect on the size of responses evoked in hand muscles after electrical stimulation of the motor cortex. In contrast, Delwaide & Olivier (1990) and Ashby & Palmer (1990) emphasized the predominant inhibitory effect of digital nerve input on the size of cortically evoked responses in hand muscles. Delwaide & Olivier (1990) reported that stimulation of the nerves in the index finger could decrease the amplitude of EMG responses evoked in the abductor pollicis brevis

muscle by magnetic stimulation of the cortex. The effect was observed at relatively short interstimulus intervals of 18–20 ms, which the authors argued was compatible with cutaneously evoked cortical inhibition. The same stimulus had no effect on H reflexes in a different muscle, the flexor carpi radialis. Ashby & Palmer (1990) recorded single motor units in the 1DI muscle. They showed that combined magnetic and digital nerve stimulation at an appropriate time could produce an increase in the firing probability of the unit. However, this increase was less than that predicted from the effect of the individual inputs tested alone. The precise timing of the effect was not explored. Finally, Deuschl, Michels, Berardelli, Schenck, Inghilleri & Lucking (1991), using magnetic and electrical stimulation of the brain combined with H reflex testing, recently suggested that stimulation of the predominantly cutaneous superficial radial nerve can raise the excitability of motor cortex. Again, the precise timing of the effect on the cortex was not studied.

One of the difficulties in interpreting results of digital or superficial radial nerve effects on magnetically evoked responses is that their size depends on the excitability of both cortex and spinal cord. A failure to compensate correctly for any changes in the spinal motor neurone threshold or recruitment order could result in incorrect estimation of cortical excitability changes. In the present experiments, like those of Day *et al.* (1991) on the stretch reflex, we have used both anodal electrical and magnetic stimulation of motor cortex in order to localize excitability changes to the cortical level. In addition, in order to compensate for digital nerve effects on the recruitment order of spinal motoneurones, we have compared EMG responses from surface electrodes with those seen when single motor units were studied. A preliminary report of the present results has been presented to the Physiological Society (Day, Dressler, Maertens de Noordhout, Marsden, Nakashima, Rothwell & Thompson, 1988).

METHODS

Subjects were seven healthy volunteers, aged 28–43 years, all of whom were members of the Institute staff. They gave informed consent and the procedures had the approval of the local Ethical Committee. No lasting side effects were noted in any individual.

In all experiments the conditioning stimulus was a single electrical shock applied to the digital nerves of the index finger through ring electrodes strapped around the middle and distal phalanges. The electrodes were then covered with tape to prevent the electrode gel from drying out. Pulses of 0·5 ms duration were given at an intensity of about 3 times sensory threshold. Perceptual threshold was monitored at regular intervals throughout the experiment, and the stimulus intensity adjusted if necessary. Stimuli were applied to the motor cortex via either an electrical or magnetic stimulator. The electrical stimulator was a prototype of the Digitimer D180 kindly made for us by Mr H. B. Morton. Stimuli with a time constant of 50 μs were applied through disc electrodes fixed to the scalp with collodion. The stimulating anode was placed 7 cm lateral to the vertex and the cathode was placed at the vertex. The magnetic stimulator was a prototype of the Novametrix 200, made for us by Dr A. Barker and colleagues at the University of Sheffield. The stimulating coil had a mean diameter of 9 cm, centred over the vertex, with current in the coil flowing anticlockwise as seen from above. Surface EMG activity was recorded using silver–silver chloride surface electrodes from the right first dorsal interosseous muscle (1DI). The reference electrode was placed on the lateral aspect of the first metacarpophalangeal joint; the active electrode was placed over the motor point of the muscle. Conventional needle electrodes (Medelec unipolar disposable type DMC25) were used to monitor single motor unit activity in the 1DI muscle. In all experiments the subject was instructed to maintain a steady voluntary isometric contraction against a strain gauge to approximately 5% maximum voluntary contraction. EMG signals were amplified with a

Devices type 3160 preamplifier bandpass filtered (−3 dB at 0·8 Hz and 2·5 kHz), and recorded by a PDP12 computer using programs devised by Mr H. B. Morton.

In the first series of experiments surface EMG recordings from the 1DI muscle were used to monitor the effect of digital nerve conditioning stimuli on the size of EMG responses evoked by electrical or magnetic stimulation of the motor cortex. At the start and end of each series of trials we investigated the time course of modulation of the on-going voluntary EMG in the manner described by Jenner & Stephens (1982). This was done by asking the subjects to maintain a steady voluntary contraction whilst a series of 512 stimuli were given to the fingers at random intervals with a mean frequency of 3 Hz. This procedure gave an indication of the time course of the excitability of spinal α-motoneurones after the digital nerve stimuli and allowed visualization of the I1 and E2 components of the cutaneous response. The E1 component was absent in most of the subjects we studied. In the main part of the experiment we intermixed digital nerve stimuli with electrical or magnetic cortical shocks at an intensity of about 5–10% supramotor threshold. Four conditions were randomized and given every 5–6 s: electrical cortical stimulus alone, magnetic cortical stimulus alone, electrical cortical stimulus plus digital nerve conditioning stimulus, magnetic cortical stimulus plus digital nerve conditioning stimulus. The interval between the cortical and digital nerve stimuli was varied between sets of trials such that the cortically evoked response came at different times between the onset of I1 and the peak of E2 as estimated in the control trials. On some occasions, six conditions were intermixed, allowing two conditioning–test intervals to be studied for both electrical and magnetic test shocks. For each conditioning–test interval, twenty control and twenty conditioned responses were evoked. The size of the cortically evoked response (measured peak to peak) obtained in the presence of a digital nerve conditioning stimulus was expressed as a percentage of the size of the response evoked by the cortical stimulus alone. The time course of modulation in the size of the cortical response was compared with the time course of the modulation of surface EMG activity produced by digital nerve stimulation alone. The average surface EMG in the 25 ms before the digital nerve stimulus was given served as the baseline level (100%) against which the EMG modulation was measured. When these comparisons were made, account was taken of the difference in latency between electrically and magnetically evoked responses in 1DI (Day, Thompson, Dick, Nakashima & Marsden, 1987; Hess, Mills & Murray, 1987).

In three subjects we compared the effect of digital nerve input and stretch input on the responses evoked in 1DI by magnetic stimulation of the brain. In these experiments the subject held his index finger abducted against a small force (2 N) offered by a torque motor pressing against the proximal interphalangeal joint. In one set of trials, electrical stimuli were applied via ring electrodes to the digital nerves in order to evoke an I1 and E2 reflex. In the second set of trials, a stretch reflex was evoked in 1DI by increasing the force in the motor to about 3 N for 200 ms. The exact force was adjusted so that the long-latency stretch reflex which it evoked was approximately the same size as the E2 reflex from digital nerve stimulation. In both sets of trials, four different conditions were intermixed. In three of the conditions, magnetic stimuli were given at random times with respect to the digital nerve or stretch inputs. These intervals were adjusted so that the magnetic shock produced EMG responses within the early period of the long-latency digital nerve and stretch reflexes. In the remaining condition, magnetic stimuli were given on their own (control trials). Before and after the trials using magnetic stimuli, averaged rectified surface EMG responses were obtained to 256 or 512 digital nerve or stretch stimuli, given at intervals of 1·5–3 s.

In a second series of experiments we investigated digital nerve influences on the cortical excitation of single motor units using the peristimulus time histogram technique (PSTH). This method has been described in detail elsewhere (Day *et al.* 1989). Briefly, single unit activity was recorded with a needle electrode inserted into the 1DI muscle. The subject concentrated on discharging a selected motor unit at about 10 Hz, with visual and audio feedback. The action potential was identified using an electronic window discriminator, and converted into a 0·25 ms pulse each time the selected unit was recruited. The computer generated an on-line histogram reflecting the firing probability at different times before and after the given stimulus. On all occasions identification of the selected unit was verified by eye on a digital oscilloscope. All EMG activity was recorded on tape so that off-line analysis could be performed if necessary.

In the first part of the experiment, a PSTH of the probability of firing of a selected motor unit was constructed in response to 1000 stimuli applied to the digital nerves of the index finger at 3

times sensory threshold. In all subjects, this evoked a late increase in firing of the motor unit at a latency comparable to the E2 period of excitation using surface EMG recording. This preliminary PSTH was needed in order to select accurately the intervals to be used between finger and cortex stimulation in the second half of the experiment.

The main part of the experiment tested the effect of digital nerve input on the response of 1DI motor units to cortical stimulation. Whilst subjects performed a voluntary contraction, three types of stimuli were given at random and intermixed with control trials. The four different conditions were: (i) cortical shock given alone, (ii) cortical shock plus a conditioning digital nerve shock, (iii) digital nerve shock given alone and (iv) control trial with no stimuli. The whole test was done using either electrical or magnetic cortical shocks and 100 trials of each condition were collected. The intensity of cortical stimuli was about 5–10% above that needed to produce a peak of increased firing probability in the single motor unit PSTH. Thus we could examine the increase in firing probability of the motor unit to the cortical shock given alone, and compare this with the increase in firing probability produced by combined cortical plus digital nerve stimuli. In order to detect whether the digital nerve stimulus had any effect on the response to a cortical shock, we used a χ^2 technique to test whether the increase in excitability produced by combined cortical plus digital nerve shocks was equal to the excitability change predicted from the sum of effects produced by cortical stimulation alone plus digital nerve stimulation alone. For each motor unit studied, two intervals between the conditioning finger stimulus and cortical shocks were used, such that the peak of increased firing produced by cortical stimuli fell either at the onset or at the peak of the late facilitation (E2) evoked by the digital nerve shock given alone. Seven different motor units from five normal subjects were studied in this part of the experiment.

RESULTS

Surface recordings

Figure 1 illustrates the main finding in averaged data from one subject. The subject held the 1DI contracted throughout the experiment using about 5% maximum voluntary contraction. The top trace shows the rectified EMG response in the 1DI to 512 electrical stimuli applied to the index finger. The I1 and E2 components are visible starting 45 and 55 ms respectively after the start of the sweep. The lower traces show the average (of twenty trials each) unrectified EMG responses to single magnetic (middle trace) or anodal electrical motor cortex stimulus (lower trace) given at different times during the course of the reflex. When the magnetic stimulus was timed such that the response occurred within the E2 component of the digital nerve reflex, it was smaller than control. In contrast, responses to anodal electrical stimulation were the same or larger when evoked during the E2 reflex as compared with control.

The average results from seven normal subjects are shown in Fig. 2. The graphs compare the time course of the surface rectified EMG with the time course of changes in the size of responses elicited by anodal electrical or magnetic stimuli over the motor cortex. The average rectified EMG shows the I1 and E2 components described by Caccia *et al.* (1973), which seem to reach a maximum at about 53 and 68 ms respectively. The size of the EMG responses elicited by anodal cortical stimulation follows almost exactly the same time course, being suppressed during the period of the I1 component and facilitated during the period of the E2 component. The size of magnetically evoked responses follows quite a different time course. The responses were suppressed during the period of I1 inhibition. They were also suppressed for the first part of the E2 reflex at about 60–65 ms. During the later part of the E2 reflex, they were facilitated.

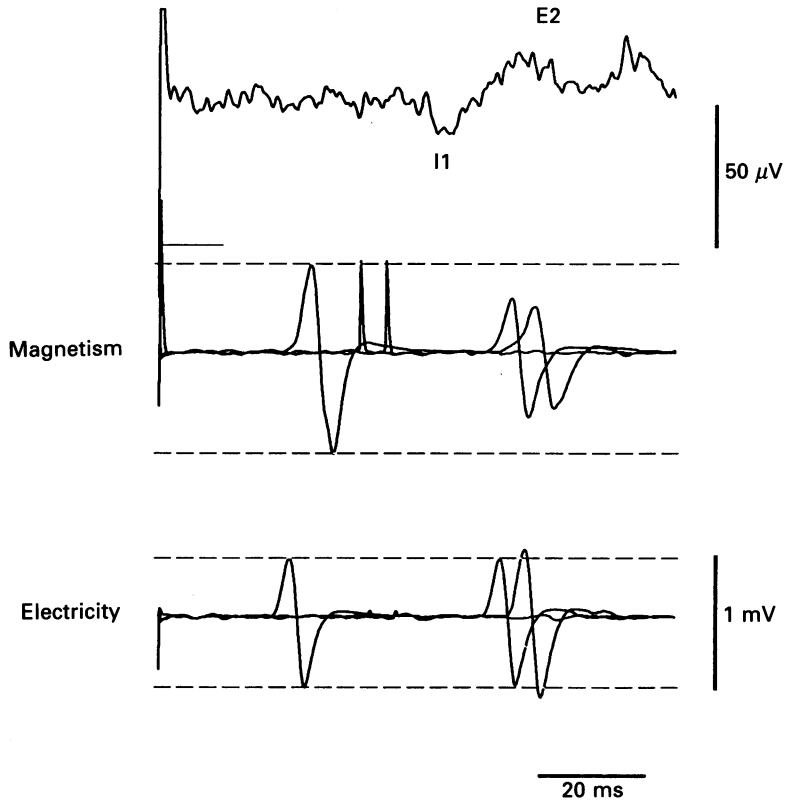

Fig. 1. Comparison of the effect of a cutaneous conditioning shock to the digital nerves of the index finger on surface EMG responses in the 1DI produced by magnetic or electrical stimulation of the brain. Data are from one subject who made a tonic background contraction of about 5% maximum voluntary force throughout. The upper trace shows the averaged rectified surface EMG response to 512 index finger stimuli applied at the start of the sweep. The short horizontal line indicates the baseline level of activity. The I1 and E2 periods of the cutaneous response are visible. The middle trace shows superimposed average (of twenty) unrectified EMG responses to magnetic brain stimuli given at three different times during the sweep (indicated by the sharp vertical artifacts). The largest, control, response was evoked when the magnetic stimulus was applied at $t = 0$ ms and was recorded on trials in which no cutaneous shock was given. When the stimulus was applied later, so that the responses occurred within the time period of the E2 reflex, the size of the response to the cortical stimulus was reduced. The bottom trace shows a similar superimposition of responses to anodal electrical brain stimuli applied at three different times during the sweep. The control response, evoked by a stimulus at $t = 0$ ms in trials in which no cutaneous shock was given, is slightly smaller than the second of the two responses evoked within the period of the E2 reflex. The horizontal dashed lines in the middle and lower trace indicate the vertical amplitude of the first control response to cortical stimulation. The 1 mV calibration bar applies to both the middle and bottom traces.

These results contrast with those observed by Day *et al.* (1991), who used muscle stretch to condition cortically evoked EMG responses. They found that magnetically evoked responses were always facilitated when they coincided with the long-latency period of the stretch reflex. There was no suggestion that the responses were

inhibited at any time during the course of the reflex. However, there are two differences between these data with stretch and the present results: (1) Day *et al.* (1991) used a different muscle, the flexor digitorum profundus rather than the 1DI; (2) the long-latency stretch reflex which they examined was generally much larger

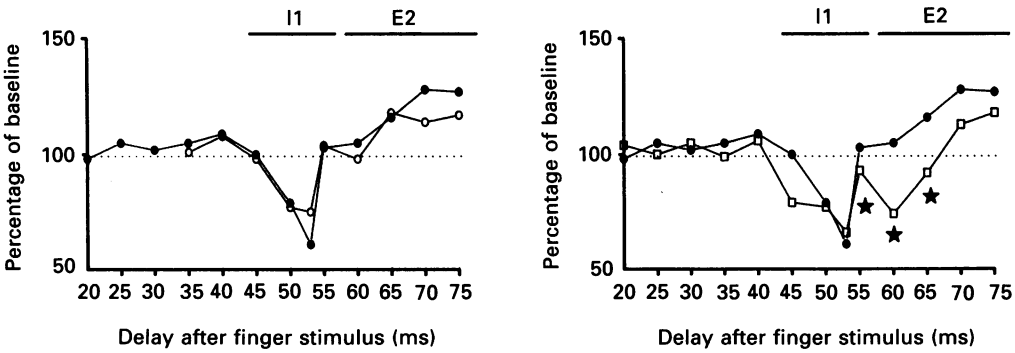

Fig. 2. Comparison between the average (from seven subjects) time course of the I1 and E2 cutaneous reflex (●) and the time course of cutaneous effects on EMG responses evoked by anodal electrical (left graph, ○) and magnetic (right graph, □) stimulation of the brain. The average time course of the cutaneous reflex was made by expressing the instantaneous rectified EMG level in each subject at each time point as a percentage of the average background EMG in a 25 ms period before the cutaneous stimulus. The size of anodal electrically or magnetically evoked responses with onset latencies at the time points shown was expressed as a percentage of the size of control responses evoked in trials in which no cutaneous stimulus was given. Only at those times marked by stars (★) was the suppression of magnetically evoked response different to the effect on the surface-rectified EMG (Student's paired t test on average data from each subject; $P < 0{\cdot}05$).

with respect to the background level of EMG activity than the rather small E2 reflexes evoked by digital nerve stimulation in the present experiments. In order to compare the effects of muscle stretch and digital nerve input more directly, we performed the following experiment on the 1DI muscle of three normal subjects. Stretch was produced by a small perturbation to the abducted index finger which was adjusted so as to evoke a long-latency stretch reflex similar in size to the E2 reflex provoked by digital nerve stimulation. The results from one subject are shown in Fig. 3: the other two subjects behaved similarly. When magnetic stimulation was timed to produce responses within the first part of the E2 reflex, the responses were smaller than in the control period. When the same stimulus was used to evoke responses in the long-latency period of the stretch reflex, then the responses were larger than in the control period. Thus, the difference between stretch and digital nerve conditioning of cortically evoked responses persists when comparisons are made in the same muscles and with the same size of long-latency reflexes.

Single motor unit studies

As shown by Garnett & Stephens (1980), stimulation of the digital nerves during a steady voluntary contraction produces changes in the firing probability of single motor units in the 1DI muscle. However, the effect on the firing pattern depends

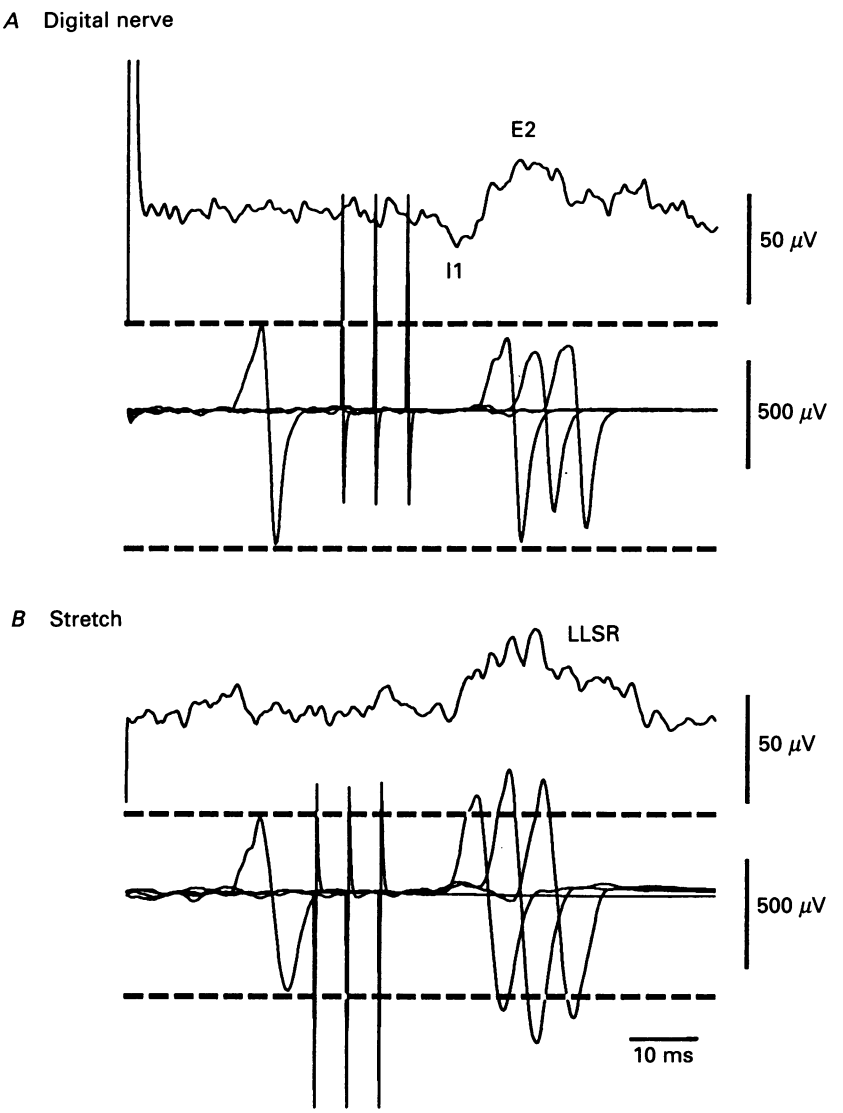

Fig. 3. Comparison in one subject of the effect of cutaneous electrical stimulation of the index finger and muscle stretch of 1DI on magnetically evoked surface EMG responses in 1DI. The top set of traces shows the effect of cutaneous stimuli (*A*), the lower set the effect of stretch stimuli (*B*). In each set, the upper trace is the average (of 256) rectified surface EMG response to cutaneous or stretch stimuli applied at the start of the sweep. The I1 and E2 components of the cutaneous reflex are visible in *A*, and the long-latency stretch reflex (LLSR) in *B*. The lower traces show superimposed responses to magnetic brain shocks applied at four different times in the sweep. The first was a control response produced by a magnetic stimulus given 5 ms before the start of the sweep in trials without any cutaneous or stretch stimulus. The horizontal dashed lines indicate the vertical height of the control response. The other three responses to magnetic brain shocks were evoked in trials with conditioning cutaneous (*A*) or stretch (*B*) stimuli. They were timed to occur within the E2 or LLSR parts of the reflex. Responses conditioned by cutaneous stimuli are smaller than control; those conditioned by stretch stimuli are larger than control.

upon the size of the motor unit. Because of this, we first constructed a PSTH for every unit to 1000 cutaneous stimuli given alone. Only units which showed a pattern of definite late (E2) facilitation were chosen for the remainder of the experiment.

Once the effect of digital nerve input was clear, we gave electrical or magnetic stimuli to the brain timed so that the cortical effect on the motor unit firing

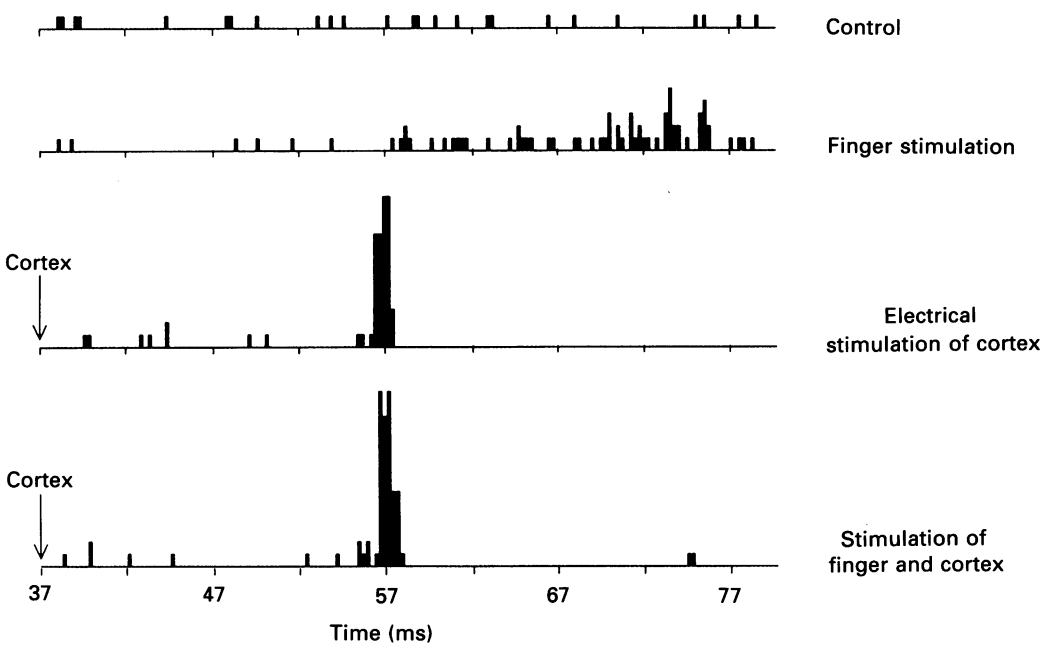

Fig. 4. PSTHs of the firing pattern of a single motor unit in 1DI under four different experimental conditions: spontaneous firing (upper trace), finger stimulation given alone at $t = 0$ ms (second trace), electrical anodal stimulation of the motor cortex given alone at $t = 37$ ms (third trace), and combined electrical stimulation of the cortex and stimulation of the digital nerves of the index finger (bottom trace). Each PSTH is constructed from 100 trials. All conditions were randomly intermixed. In the second trace, it is possible to see an increased firing of the unit which probably corresponds to the E2 response seen in surface EMG records. The third and bottom traces show the response to electrical cortical stimulation, which produced a response at about the time of the onset of E2, with and without concomitant finger stimulation. The number of counts in the 5 ms period centred on 57 ms was forty-eight for the cortical stimulus alone, and fifty-seven for the combined digital nerve and cortical stimulus (unit 1, Table 1).

probability came either at the onset, or the peak, of E2 facilitation in each particular motor unit. The size of the cortical effect under these conditions was compared with the size when the cortical shock was given alone. Due to difficulties in maintaining a single motor unit throughout the long experiments, it was not possible to study both timings with both electrical and magnetic forms of stimulation in all the units. However, the general effect was quite clear. An example is shown in Figs 4 and 5. Table 1 summarizes the results.

The effect of digital nerve stimulation on the size of peaks in firing produced by a cortical shock was not significantly different in any individual unit. However, the combined results from all seven units resembled closely those seen using surface EMG

responses. In all but one motor unit, when electrical cortical stimulation was used, the increase in firing during combined digital nerve and cortical stimulation was greater than the effect of electrical stimulation alone. In addition, the increase in firing to combined stimulation was slightly greater than the sum of increased firing

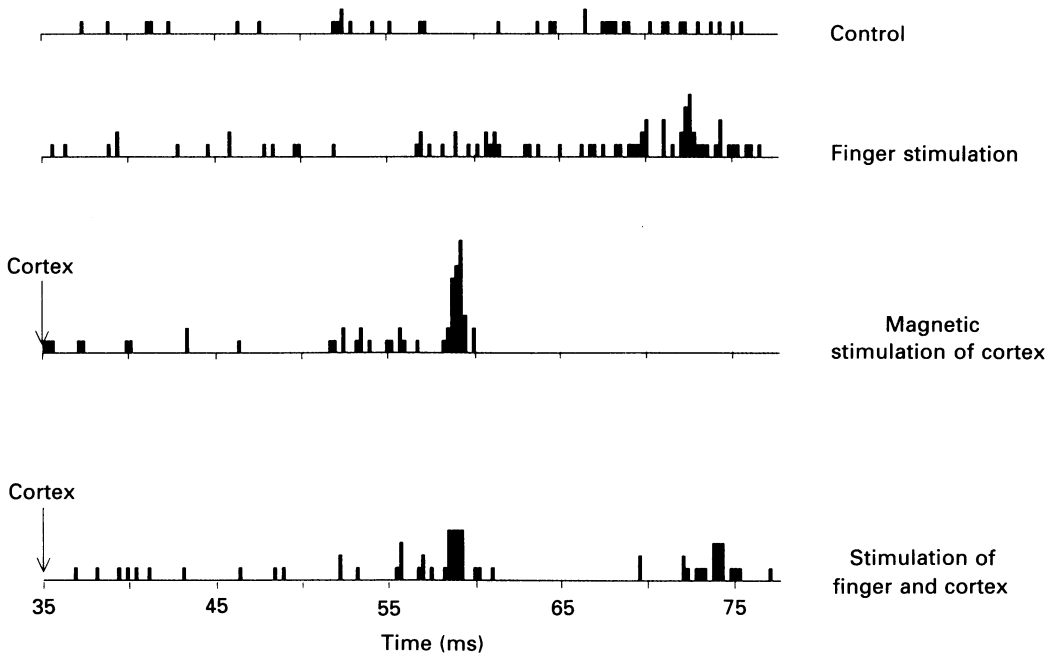

Fig. 5. PSTHs of the firing of a single motor unit in the 1DI under four different experimental conditions: spontaneous firing (upper trace), finger stimulation alone at $t = 0$ ms (second trace), magnetic stimulation of the motor cortex alone given at the beginning of the trace (third trace), and combined magnetic stimulation of the cortex with digital nerve stimulation of the index finger (bottom trace). In contrast to the data in Fig. 4, where the response to magnetic cortical stimulation was timed to coincide with the onset of the E2 period of facilitation, the number of counts in the 5 ms period around 56·5 ms was thirty-seven for cortical stimulus alone, but was only twenty-seven for combined digital nerve and cortical stimulation (unit 1, Table 1).

probability to each stimulation when given alone in all but two units (6 and 7). In contrast, when the magnetic response was timed to arrive at the onset of E2, then the increase in firing of the units was always less than the sum of the separate firing probabilities, although it was greater than or equal to the sum of firing probabilities when the stimulus was given to coincide with the peak of E2. In fact, if the stimulus was given in the period of early E2 facilitation the increase in firing during combined digital nerve and cortical stimulation was less than that to magnetic stimulation performed alone.

Thus, at the onset of E2, there was a differential effect of digital nerve stimulation on the size of PSTH peaks evoked by electrical and magnetic motor cortex stimulation: magnetically evoked responses were smaller than in control trials, whereas electrically evoked responses were larger or the same. This difference between electrical and magnetic stimulation was individually significant in three of

the seven units (χ^2 test, $P < 0{\cdot}05$) and was highly significant ($\chi^2 = 15{\cdot}4$, d.f. = 1, $P < 0{\cdot}005$) when the data from all seven units was combined. There was no difference between digital nerve effects on the responses to electrical or magnetic stimulation when given at the peak of E2 facilitation in the three units tested in this way ($\chi^2 = 0{\cdot}1$, d.f. = 1, $P > 0{\cdot}05$). Unfortunately, because of difficulties in maintaining single

TABLE 1. Change in firing of single motor units produced by digital nerve and/or cortical stimuli

Unit No.	Digital nerve†	Electrical cortex	Electrical + digital nerve	Magnetic cortex	Magnetic + digital nerve
	Period of early facilitation: E2 response				
1	6	48	57	37	27
2	6	47	54	50	26*
3	4	47	54	62	41*
4	4	31	37	50	45
5	5	37	48	81	60*
6	6	53	58	61	43
7	4	48	47	42	40
	Period of peak facilitation: E2 response				
1	7	—	—	45	59
2	—	—	—	—	—
3	5	49	55	26	36
4	5	27	34	25	38
5	—	—	—	—	—
6	6	41	52	49	55
7	—	—	—	—	—

†, electrical and magnetic stimulation were applied in separate blocks of trials, each with their own set of digital stimuli. A single value is given in the table for the number of counts evoked by this stimulus. This value is the higher (worst case) of the two totals reached in each block of trials.

*, significantly different cutaneous effect on responses to electrical and magnetic cortical stimulation (χ^2 test; $P < 0{\cdot}05$) (see text).

The table shows the number of counts in a 5 ms period of the PSTH produced by 100 electrical or magnetic stimuli given at the start (top) or peak (bottom) of E2 facilitation. Mean count for 5 ms periods in control records was five. Columns show the effect of: (i) digital nerve stimulation of the index finger given alone, (ii) electrical motor cortex stimulation alone, (iii) combined electrical and digital nerve stimulation, (iv) magnetic stimulation of the motor cortex alone, and (v) combined magnetic and digital nerve stimulation. All units were studied with cortical stimulation at the onset of E2 facilitation, but only four could be studied further with stimuli at the peak of facilitation.

motor units, it was not possible to define the duration of the effects in this part of the experiment.

DISCUSSION

A single stimulus to the digital nerves of the index finger produces in the first dorsal interosseous muscle a long-latency excitatory E2 reflex which was postulated by Jenner & Stephens (1982) to be caused by operation of a transcortical reflex. The present results show that in the time during which this E2 excitation is developing, surface EMG responses elicited by magnetic stimulation of the brain are smaller than in the control state. Similar results were obtained when the excitability of single

motor units was studied, indicating that they were not due solely to differences in the motor unit population recruited by reflex events and magnetic or electrical brain stimuli.

At what level, spinal or cortical, did this suppression of magnetically evoked EMG responses occur? In all experiments we compared the effect of a digital nerve shock on the responses evoked by electrical and magnetic stimulation of the brain. Unlike those evoked by magnetic stimulation, responses to electrical stimulation were not suppressed during the early part of the E2 reflex. Electrically evoked responses evoked in the E2 period, whether recorded in the surface EMG or in the change in probability of firing of a single motor unit, were larger than in the control state, and followed a time course similar to that of the surface-rectified EMG. As we have argued before, both electrical and magnetic forms of cortical stimulation probably activate the same population of descending corticospinal tract fibres (Day *et al.* 1989). Thus, any changes in spinal cord excitability should be seen equally well by both forms of stimulation. This is confirmed by the similarity of the changes in response to electrical and magnetic cortical stimulation delivered in the I1 period. The I1 inhibition response in the on-going EMG to digital nerve stimulation is thought to be of spinal origin (Jenner & Stephens, 1982). Both the response to electrical and magnetic cortical stimulation were inhibited by digital nerve stimulation when the brain shocks were timed to coincide with the I1 period (see Fig. 2).

Assuming that electrical cortical shocks excite pyramidal neurones distal to the initial segment, it is difficult to envisage how changes in input to the cortex could affect the EMG response to an electrical shock. During the E2 period evoked by digital nerve stimuli, the response to electrical cortical stimulation was increased in parallel with the change in EMG activity produced by the digital nerve stimulus alone (see Fig. 2). Presumably, again this was due to the change in spinal α-motoneurone excitability that accompanies the EMG changes. There is no need to invoke any effect of transcortical digital nerve influence to explain the potentiation of the response to electrical brain stimuli in the E2 period.

In contrast to the results with electrical stimulation, the responses to magnetic brain stimulation were inhibited in the early part of the E2 response. This is even more significant, bearing in mind the proposed net spinal excitation at this time. Since magnetic brain stimulation, using the strength of stimuli employed here in man, appears to excite pyramidal neurones either via synaptic connections (Day *et al.* 1989) or at the initial segment (Edgley *et al.* 1990), it is quite possible that digital nerve input to cortex could alter pyramidal neurone or cortical interneurone excitability, and therefore the response to magnetic brain stimulation. The present results suggest that the initial effect of this predominantly cutaneous input was to inhibit the motor cortex.

This was not the result we had predicted. If the excitation responsible for the E2 response travels via a transcortical pathway, as postulated by Jenner & Stephens (1982), then we might have expected cortical excitability to be enhanced during the E2 period, but it was suppressed. Can we reconcile this apparent decrease in cortical excitability with the presence of the excitatory E2 reflex evoked by the same digital nerve stimulus? There are several possible explanations although all are purely

speculative since there is no indication from experiments conducted on animals that a single afferent volley from the digital nerves would produce a short period of net inhibition in motor cortical areas. For example, the E2 reflex may not be a transcortical reflex. Although several lines of evidence suggest that the response is a transcortical phenomenon, all are equally consistent with tonic facilitation of a spinal mechanism from cortical structures. If E2 was a spinal reflex, then the apparent suppression of cortical mechanisms could occur concurrently with spinal cord excitation. Alternatively, if the E2 is indeed a cortical response then it is possible that digital nerve input produces mixed excitatory and inhibitory effects at the cortex. This input might excite elements involved in a voluntary contraction, but inhibit elements recruited by a magnetic stimulus.

Whatever the explanation, the results using stimulation of digital nerves contrasted with those obtained when muscle stretch was given by tapping the abducted index finger. In this case there was no evidence for suppression of magnetically evoked EMG responses. They were facilitated, even at the onset of the long-latency stretch reflex. Since Day *et al.* (1991) have previously argued that stretch-induced facilitation of responses to magnetic stimulation occurs at a cortical level, the implication of the present results is that afferent inputs produced by taps to the index finger and electrical stimulation of a digital nerve can have quite different effects on cortical excitability. Despite the fact that it was once thought that long-latency (transcortical) reflexes evoked by digital nerve stimulation were simpler than those evoked by muscle stretch (Jenner & Stephens, 1982), the converse may be true. Muscle stretch appears to produce a straightforward increase in cortical excitability to magnetic stimuli which lasts for the period of the long-latency reflex. Stimulation of a digital nerve produces an early inhibition which overlaps with a period of reflex facilitation. There are two possible reasons for the difference between effects of digital nerve and stretch inputs. First, the afferent fibres activated by the two forms of stimulation are different. Although both digital nerve stimulation and stretching excite cutaneous afferents, only muscle stretch excites muscle receptors. Activity in muscle afferents may therefore be important in increasing the excitability of the motor cortex to magnetic stimulation. Second, muscle stretch is a natural stimulus, whereas electrical stimulation of the digital nerves is artificial. It may well be that predominantly cutaneous reflexes evoked by natural changes in afferent input produce changes in cortical excitability which resemble more closely those evoked by muscle stretch.

In conclusion, this study has shown that a predominantly cutaneous stimulus evoked by electrical stimulation of a digital nerve can produce transient suppression of EMG responses evoked by magnetic transcranial stimulation. This effect was even observed at the level of single motor units. We conclude that the result is due to a net inhibitory action of digital nerve input on certain motor cortical mechanisms. Although unexpected, in view of the previous emphasis on cutaneous facilitatory effects to the motor cortex, the phenomenon may be related to the ability of certain neurological patients to extinguish their Jacksonian seizures by vigorous cutaneous stimulation.

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