CORTICOMOTONEURONAL CELLS CONTRIBUTE TO LONG-LATENCY STRETCH REFLEXES IN THE RHESUS MONKEY

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(Received 24 June 1983)

SUMMARY

1. To test the hypothesis that a transcortical reflex contributes to the stretch-evoked long-latency electromyographic (e.m.g.) response we documented the responses of identified corticomotoneuronal (c.m.) cells and their target muscles to perturbations of active wrist movements. Macaque monkeys performed ramp-and-hold wrist movements against elastic loads, alternating between flexion and extension zones; brief (25 ms) torque pulses were intermittently applied during the hold period.

2. C.m. cells were identified by a clear post-spike facilitation in spike-triggered averages of forelimb muscle e.m.g. activity. Activity of c.m. cells and twelve wrist and digit flexor and extensor muscles was recorded during: (a) active ramp-and-hold wrist movements, (b) passive ramp-and-hold wrist movements, and (c) torque perturbations applied during the hold phase of active flexion and extension which either lengthened or shortened the c.m. cell's target muscles.

3. Muscle-lengthening perturbations evoked a reproducible pattern of average e.m.g. activity in the stretched muscles, consisting of two peaks: the first response (M1) had an onset latency of 11.2 ± 2.1 ms (mean ± s.d.), and the second (M2) began at 27.9 ± 5.1 ms. Torque perturbations which shortened the active muscles also evoked a characteristic e.m.g. response consisting of an initial cessation of activity at 13.5 ± 3.4 ms followed by a peak beginning at 33.9 ± 3.0 ms.

4. The responses of twenty-one c.m. cells which facilitated wrist muscles were documented with torque pulse perturbations applied during active muscle contraction. Twenty of twenty-one c.m. cells responded at short latency (23.4 ± 8.8 ms) to torque perturbations which stretched their target muscles.

5. For each c.m. cell–target muscle pair, transcortical loop time was calculated as the sum of the onset latency of the c.m. cell's response to lengthening perturbations (afferent time) and the onset latency of post-spike facilitation (efferent time). The mean transcortical loop time was 30.4 ± 10.2 ms, comparable to the mean onset latency of the M2 peak (27.9 ± 5.1). The duration of a c.m. cell's response to torque perturbations provides a further measure of the extent of its potential contribution to the M2 muscle response. In all cases but two, the c.m. cell response, delayed by the latency of the post-spike facilitation, overlapped the M2 e.m.g. peak.

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6. In addition to responding to perturbations which stretched their target muscles, as predicted by the transcortical stretch reflex hypothesis, eight of eighteen c.m. cells also responded at short latency (22.0 ± 7.4 ms) to perturbations which shortened their target muscles. These excitatory responses were appropriately timed to contribute to the long-latency e.m.g. peak in their target muscles evoked by muscle-shortening perturbations. The functional consequence of the long-latency coactivation of flexors and extensors is a stiffening of the joint, to which these bidirectionally activated c.m. cells contribute.

7. Seventeen of nineteen c.m. cells responded to passive wrist movements. Of these, ten responded to wrist rotation in only one direction and seven responded bidirectionally. Seven of the unidirectionally responsive cells were activated by passive movements which stretched their target muscles; three were activated for passive and active movements in the same direction.

8. Since c.m. cells respond at appropriate times to mediate the long-latency e.m.g. response and demonstrably facilitate motoneurone firing probability, the burst of c.m. cell activity following torque perturbation should contribute to the long-latency stretch reflex. This causal involvement was further confirmed by spike-triggered averages of e.m.g. selectively compiled during torque pulse responses; action potentials evoked by torque pulses effectively facilitated the long-latency muscle response.

We conclude that c.m. cells contribute to the stretch-evoked long-latency e.m.g. response and therefore function as the efferent limb of a transcortical reflex loop.

INTRODUCTION

Rapid stretch of an actively contracting muscle evokes a sequence of reflex electromyographic (e.m.g.) responses (Tatton, Forner, Gerstein, Chambers & Liu, 1975; Marsden, Merton & Morton, 1976; Villis & Cooke, 1976; Cooke & Eastman, 1977; Evarts & Vaughn, 1978; Tatton, Bawa, Bruce & Lee, 1978; Bawa & Tatton, 1979; Tatton & Bawa, 1979; Lee & Tatton, 1982). The short latency of the earliest of the reflex peaks, termed M1 (Tatton et al. 1975), suggests that it is mediated by a spinal stretch reflex. The existence of longer-latency reflex components is widely acknowledged, but their number and mechanism remain debated. A second reflex e.m.g. response to muscle stretch (M2) is clearly separable from any subsequent voluntary response. The longer latency of M2 suggests it may be mediated by a longer feedback loop than M1, possibly involving supraspinal centres. Phillips (1969) proposed that a transcortical stretch reflex loop may act together with the spinal stretch reflex to compensate for unexpected disturbances in load. According to this hypothesis, the longer latency of M2 would result from the additional transmission time between spinal cord and motor cortex. Indeed, the latency of M2 for different muscles increases with the distance between the muscle and the brain (Melvill-Jones & Watt, 1971; Marsden et al. 1973, 1976). Furthermore, cortical lesions in the monkey abolish or reduce M2 (Tatton et al. 1975; Lenz, Tatton & Tasker, 1983) and eliminate the corresponding long-latency facilitation of the H reflex (Chofflon, Lachat & Ruegg, 1982).

In accordance with predictions of the transcortical loop hypothesis, motor cortex
cells respond to inputs from muscle receptors (Albe-Fessard & Liebeskind, 1966; Phillips, Powell & Wiesendanger, 1971; Wiesendanger, 1973; Murphy, Wong & Kwan, 1975; Hore, Preston, Durković & Cheney, 1976; Lemon, Hanby & Porter, 1976; Fetz, Finocchio, Baker & Soso, 1980). Moreover these responses are servo-like in that their amplitudes are graded in proportion to the magnitude of muscle stretch (Sakai & Preston, 1978). In awake animals motor cortex cells have been amply demonstrated to respond to load perturbations, often at latencies appropriate for a contribution to the M2 e.m.g. response (Evarts, 1973; Evarts & Tanji, 1974, 1976; Conrad, Meyer-Lohmann, Matsunami & Brooks, 1975; Porter & Rack, 1976; Tanji & Evarts, 1976; Evarts & Fromm, 1977; Wong, Kwan & Murphy, 1979). Despite this wealth of circumstantial evidence (cf. Desmedt, 1978) a causal relationship has never been established between motor cortex cell activity and any component of the stretch-evoked e.m.g. response.

Recently, several reports have challenged the notion that M2 is mediated by a transcortical loop. Segmented peaks in the e.m.g. response of biceps and triceps to muscle stretch have been demonstrated in decerebrate as well as spinal cats and primates (Ghez & Shinoda, 1978; Tracey, Walmsley & Brinkman, 1980; Miller & Brooks, 1981; Lenz et al. 1983). One plausible mechanism is suggested by the observation that muscle spindle afferents may exhibit multiple bursts in response to quick stretch of their parent muscles (Hagbarth, Young, Hagglund & Wallin, 1980; Tracey et al. 1980; Hagbarth, Hagglund, Wallin & Young, 1981). These bursts may be initiated by mechanical oscillations in muscle evoked by a single stretch (Eklund, Hagbarth, Hagglund & Wallin, 1982a, b). A late contribution from slowly conducting afferents, such as group II afferents, must also be considered (Matthews, 1983). These reports indicate that multiple e.m.g. responses may be evoked in proximal muscles in the absence of cerebral cortex and other supraspinal centres, and suggest that they may simply represent sequential or delayed spinal stretch reflexes. Clearly, the multiple e.m.g. responses evoked in intact, awake animals may involve different neural mechanisms from those observed in spinal animals. Therefore, the role of motor cortex in mediating e.m.g. responses to stretch remains to be documented under normal conditions.

The efferent limb of the postulated transcortical stretch reflex is formed by corticospinal neurones whose discharge facilitates activity of motoneurones, either directly as in the case of corticomotoneuronal (c.m.) cells or indirectly through the action of spinal interneurones. The activity of these cells provides the final test of the transcortical loop hypothesis. In awake monkeys, c.m. cells and their target muscles may be identified by their characteristic post-spike facilitation of average e.m.g. activity (Fetz & Cheney, 1978, 1980); during normal limb movement c.m. cells clearly contribute to generating active muscle force (Cheney & Fetz, 1980). In these experiments, we tested the response of twenty-one identified c.m. cells to torque perturbations which stretched or shortened the cell's target muscles. Twenty cells responded at short latency to these torque perturbations. Furthermore, their responses were timed appropriately to contribute to the M2 e.m.g. response.
Training procedures

Three Rhesus monkeys, weighing 3–5 kg, were trained to perform alternating wrist movements requiring ramp-and-hold wrist displacements into flexion and extension target zones. The monkeys were required to hold within each target zone for 1–2 s to receive an apple sauce reward. The target zone for extension was usually 20–30°; that for flexion was 30–40°. Zero position was that at which the hand and forearm were aligned.

During performance of the task, the monkey was seated in a primate chair and its right forearm was placed in a restraint. The hand, with fingers extended, was held between padded plates which were attached to the shaft of a torque motor. To ensure moderate amounts of e.m.g. activity, all active movements were performed against elastic loads, which generated opposing torques proportional to displacement from the zero position.

Load perturbations consisted of torque pulses applied during the hold phase of the task, when cortical cell and muscle activity were relatively steady. Torque perturbations were generated by applying 25 ms rectangular pulses as signals to the servo control circuitry of the torque motor. The amplitude of the torque pulse signal was adjusted to produce a transient wrist displacement of 5–10° at velocities from 200 to 400 deg/s. The wrist torque deflexion associated with this displacement varied as a function of the load against which the monkey worked; however, the torque deflexion was generally in the range 0.1–0.2 N m.

The monkeys were not trained to respond in any particular way to the occurrence of an unexpected load perturbation. Nevertheless, the perturbation seldom provoked a 'let go' response; instead the monkey maintained tonic e.m.g. activity and, if necessary, quickly returned the wrist to the target zone. Torque pulses were applied unpredictably with an average of one torque pulse per two to ten responses.

Four torque pulse conditions were investigated: wrist flexing and extending torque pulses were applied during the hold phases of both flexion and extension. Flexion torque pulses transiently flexed the wrist, thus stretching the extensors and shortening the flexors; extension torque pulses did the opposite.

The responses of c.m. cells to passive movements of the wrist were also investigated. During passive movements, all active movement cues (lights and bell tones) were turned off and the monkey sat quietly at rest. Ramp-and-hold passive movements with velocities and amplitudes similar to those of active movements were generated by driving the torque motor servo mechanism with a trapezoidal control signal. Standard passive movements were symmetrical about the zero position and generally had amplitudes in the range of ±20–40° and velocities in the range of 50–400 deg/s. In addition, the responses of some c.m. cells to low-amplitude (±5–15°) high-velocity (400–600 deg/s) passive movements were documented to define better the minimal onset latency of the cell's response. In all cases, the qualitative features of the cell's response were the same for both rates of passive movement. Passive movements were well tolerated by the monkey and usually were not contaminated by background e.m.g. activity; those instances in which sustained background e.m.g. activity was present were excluded from the analysis.

Surgical procedures

After the monkey had been trained to acceptable performance levels (which took 3–4 months) a cortical recording chamber and head restraint nuts were attached to the monkey's skull under halothane anaesthesia. The recording chamber allowed exploration of a 20 mm diameter circle, centred over the precentral hand area (4 mm anterior to the bregma, 18 mm lateral to the mid line). Both recording chamber and head restraint cap nuts were fastened to the skull with vitallium screws and dental cement. In one monkey, a concentric bipolar stimulating electrode was placed in the pyramidal tract ipsilateral to the site of cortical recording to test the axonal projection of cortical cells. Antidromic responses of pyramidal tract neurones were usually confirmed by the collision technique (Fetz & Cheney, 1980).

Following initial exploration of the precentral cortex and location of neurones related to wrist movement, e.m.g. recording electrodes were implanted under halothane anaesthesia. Pairs of multistranded stainless-steel wires (AS-632 Bioflex insulated wire, Cooner Sales Company, Chatsworth, CA) were inserted percutaneously with a hypodermic needle into the bellies of each
of twelve muscles acting at the wrist. These muscles were: extensor carpi ulnaris, extensor digitorum communis, extensor digitorum 2 and 3, extensor digitorum 4 and 5, extensor carpi radialis longus, extensor carpi radialis brevis, flexor carpi radialis, flexor digitorum profundus, flexor carpi ulnaris, palmaris longus, pronator teres, and flexor digitorum sublimis. The anatomical relationships of these muscles are illustrated in a previous paper (Fetz & Cheney, 1980). The muscle location of e.m.g. wires was tested by observing wrist and finger movements elicited by trains of low-intensity intramuscular stimuli applied through the wires. After confirming that all e.m.g. wires were properly located, the leads were attached to the monkey's forearm with medical adhesive tape. These implants provided stable e.m.g. recording for several weeks and were well tolerated by the monkeys.

Fig. 1. Identification of corticomotoneuronal (c.m.) cells using spike-triggered averaging of rectified e.m.g. activity. Left, records of c.m. cell activity and e.m.g. activity of a target muscle during a single ramp-and-hold wrist extension. Right, c.m. cell action potential followed after conduction delay by a c.m. excitatory post-synaptic potential (e.p.s.p.) in a target motoneurone (drawing) and post-spike facilitation (p.s.f.) obtained from the c.m. cell–muscle pair whose activities are illustrated on the left.

Recording and analysis of data

While the monkey made wrist movements against moderate to heavy elastic loads, cortical neurones in the left precentral gyrus were recorded with a tungsten micro-electrode. Action potentials of task-related neurones that fired during either flexion or extension and exhibited tonic discharge during the static hold period were used to compute spike-triggered averages of rectified e.m.g. activity from six coactivated wrist muscles. C.m. cells were identified by their transient post-spike facilitation of motor unit firing probability in spike-triggered averages of rectified e.m.g. activity.

The spike-triggered averaging method used to identify c.m. cells is illustrated in Fig. 1. Shown on the left is the activity of a motor cortex neurone and the e.m.g. activity of a wrist extensor muscle associated with one ramp-and-hold wrist extension response. Spike-triggered averages were computed from all spikes occurring during such ramp-and-hold movements. Movements with superimposed load perturbations were excluded from these averages to eliminate any synchronized activation of cell and muscle activity evoked by the torque pulses. The spike-triggered average (right) includes an analysis period from 5 ms before the cortical spike to 25 ms after it; this includes a base line and the post-spike facilitation of e.m.g. associated with the cortical cell spikes. The record on the right illustrates the effects mediated by a c.m. cell. Each spike of the c.m. cell will produce, after a conduction delay, an excitatory post-synaptic potential (e.p.s.p.) in its target motoneurones. These individual e.p.s.p.s are too small to fire each motoneurone consistently, but will increase their probability of firing. This enhanced firing probability may be detected as a transient post-spike facilitation of multi-unit e.m.g. activity. The facilitation shown in Fig. 1 begins about 6 ms after the cortical spike, rises to a peak and then declines to pre-trigger base-line levels.
The shape of such post-spike facilitation is a function of several factors, including the wave form of the facilitated motor unit potentials, the number of facilitated motor units, the conduction velocities of target a-motoneurones, and the wave form of the c.m. e.p.s.p.s. The existence of post-spike facilitation was evaluated in spike-triggered averages of 2000 events or more, and its reproducibility could be confirmed by compiling several consecutive averages.

All data, including unit activity, torque and position signals, and e.m.g.s were recorded on magnetic tape for subsequent off-line analysis. The activity of c.m. cells during active movement as well as their response to torque pulses and passive movements were evaluated from average histograms of unit firing rate compiled with analogue averages of rectified e.m.g. activity, wrist torque and wrist position. Such averages included ten to fifty responses and were computed by triggering the PDP 8/e computer from the onset of active movement, passive movement or the torque pulse signal. For averages of active movement responses, the histogram bin width was typically 10 ms; the sampling rate for analogue signals was 100 Hz. For averages of torque pulse and passive movement responses the histogram bin width was typically 2 ms; the sampling rate for analogue signals was 500 Hz.

The magnitudes of peaks in the averages could be quantified by calculating a 'percentage increase' over base line of the bins in a chosen interval. Letting $B$ be the average of base-line values, and $C$ the average of values in a comparison interval, the percentage increase of the comparison values was calculated as:

$$\% \text{ increase} = \frac{C - B}{B} \times 100.$$  

RESULTS  

Properties of corticomotoneuronal (c.m.) cells  

A task-related motor cortex neurone was identified as a c.m. cell if its action potentials were followed by a clear post-spike facilitation of rectified e.m.g. activity in spike-triggered averages. This study concerns twenty-one c.m. cells whose responses to load perturbations and passive movements were adequately documented. Many of these neurones facilitated several synergistic target muscles acting on the wrist and fingers. Twelve fired during wrist extension and nine during flexion. The peak-to-noise ratios of the post-spike facilitation (Fetz & Cheney, 1980) for the most strongly affected target muscle of these twenty-one c.m. cells ranged from 1·3 to 7·6 with a mean of 3·3 ± 1·7. Representative post-spike facilitations for many of these c.m. cells were illustrated in a previous paper (Cheney & Fetz, 1980, Figs. 5, 7 and 8), in which the cells were identified by the same nomenclature. The response patterns of these neurones during active ramp-and-hold wrist movements were characterized as phasic–tonic (nine), tonic (ten) or ramp (three). These cells also contributed causally to generating active force, since their tonic discharge increased with the level of static torque (Cheney & Fetz, 1980).

Responses of c.m. cells and target muscles to load perturbations  

The transcortical stretch reflex hypothesis predicts that c.m. cells should respond to torque pulses which lengthen the cell’s target muscles. Fig. 2 illustrates the response of a c.m. cell, one of its target muscles, plus wrist torque and position when a flexion torque pulse was applied during the hold period of wrist extension. The torque pulse in Fig. 2 produced a transient 8° deflexion of the wrist towards flexion and elicited a sharp burst of c.m. cell activity, during which firing rates reached instantaneous frequencies of 400 Hz. Target muscle e.m.g. activity also showed a burst followed by a brief pause, then returned to its tonic base-line level.
The time course of these responses is shown more clearly in averages aligned with the torque pulse (Fig. 3). The e.m.g. response consists of two distinct peaks labelled M1 and M2. As in most cases, the area under M2 (here, 330% above base line) exceeded the area under M1 (207% above base line). During its peak response, activity of the c.m. cell increased to an average of 120 impulses/s over a period of 31 ms. The response of the c.m. cell began at 17 ms, about 11 ms before the onset of M2 in its target muscle. The spike-triggered average of e.m.g. activity of this muscle at the right shows that it was facilitated by the c.m. cell.

The spike-triggered averages used to define the cell's facilitated target muscles were compiled during unperturbed wrist movements, when e.m.g. activity was relatively stationary. To prove that the spikes evoked by the torque pulse did indeed contribute to the M2 response, we also compiled averages triggered selectively from the spikes evoked by the perturbation. Fig. 4 compares the spike-triggered averages of two extensor muscles, compiled separately for only those spikes which followed the torque pulses (right) and for only the spikes during the static hold, exclusive of the torque pulse responses (left). These averages, shown at the same gain, indicate that the post-spike facilitation was considerably enhanced following the torque pulse. The spikes associated with the torque pulse response not only facilitated the cell's target muscle (extensor digitorum 4 and 5) more effectively, but also generated clear post-spike facilitation in a synergist muscle (extensor carpi ulnaris) which was not facilitated during the static hold.

Half of the c.m. cells were activated only by perturbations which lengthened the target muscle and not by shortening perturbations. Fig. 5 shows the pattern of torque
Fig. 3. Average response of a c.m. cell (SW 53-3) (top) and its target muscle (extensor digitorum 4 and 5) evoked by transient muscle-lengthening torque perturbation applied during active extensions (left). Spike-triggered average (right) shows the post-spike facilitation of this muscle following the cortical spike. In this and subsequent Figures the number of events averaged is shown at the bottom right. The peak amplitudes are 0·11 N m for torque and 13° for position.

Fig. 4. Spike-triggered averages of extensor muscle e.m.g. activity compiled separately during static wrist extension (left) and during the torque pulse responses (right). Top shows autocorrelograms of trigger spikes. The spike-triggered averages of a target muscle of this cell (ED 4,5, extensor digitorum 4 and 5) and a non-target muscle (ECU, extensor carpi ulnaris) are shown at the same gains. Black bars denote intervals used for base line (first 10 ms of sweep) and post-spike facilitation (p.s.f.). The mean percentage increase of the bins in the p.s.f. interval over base line for extensor digitorum 4 and 5 was 5·0 % during the static hold and 13·9 % during the torque pulse. For extensor carpi ulnaris the corresponding percentage increases were 3 % and 19·6 %. Same cell as in Figs. 3 and 6.
Fig. 5. Torque pulse perturbation responses of a c.m. cell (SI 120-1) and three extensor muscles, including two of its target muscles (ED 4,5, extensor digitorum 4 and 5; EDC, extensor digitorum communis). Flexion torque pulses (top) lengthened this cell's target muscles; extension torque pulses (bottom) shortened them. Torque pulses were applied while the monkey held a constant position against a moderate load in either the extension zone (left) or flexion zone (right). Extensor muscles were active at left but inactive at right. This cell's torque pulse sensitivity was unidirectional in that it responded only to perturbations which stretched the target muscles. Calibration bar for torque, 0-1 N m; position, 10°. ECR-L, extensor carpi radialis longus.

pulse responses of one of these cells, with the responses of two of its target muscles: extensor digitorum communis and extensor digitorum 4 and 5. Torque pulses which stretched the active target muscles during extension (top left) consistently evoked M1 and M2 muscle e.m.g. peaks and a burst of c.m. cell firing with an onset latency intermediate between the onset of M1 and M2. Similar lengthening torque pulses applied when the wrist was flexed and the target muscles were inactive (top right) also evoked a clear burst of c.m. cell activity. Although extensor muscle activity was
negligible during wrist flexion, the flexion torque pulse evoked M1 and M2 e.m.g. responses in extensor carpi radialis and extensor digitorum communis, and a long-latency response in extensor digitorum 4 and 5.

Torque pulses that shortened target muscles applied during wrist extension (bottom left) produced no change in the activity of this c.m. cell, but did evoke a consistent response in its target muscles: an initial suppression followed by excitation. Similarly, muscle-shortening torque pulses applied when the wrist was flexed evoked no response from this c.m. cell (bottom right). A cell responding strictly in accordance with a transcortical stretch reflex loop might be expected to pause after muscle-shortening perturbations; however, the cell in Fig. 5 showed no such pause. Only three of the nineteen c.m. cells tested showed reciprocal inhibition to muscle-shortening...
torque pulses. Nevertheless, the excitatory responses of c.m. cells like the one in Fig. 5 are consistent with the functioning of a transcortical stretch reflex.

Other c.m. cells were excited at short latency by all torque pulses—not only perturbations which stretched the target muscles but also those which shortened them. The response pattern of one such neurone is illustrated in Fig. 6 (same neurone as in Figs. 3 and 4). This c.m. cell strongly facilitated four target muscles: extensor digitorum communis, extensor digitorum 2 and 3, extensor digitorum 4 and 5, and extensor carpi radialis longus. Consistent with the transcortical stretch reflex hypothesis, this cell responded briskly to flexion torque pulses applied during active extension and flexion (Fig. 6, top). However, this c.m. cell also responded with a burst to perturbations which shortened the target muscles (Fig. 6, bottom). These neural responses were just as intense and had onset latencies (17 ms) similar to the responses to lengthening perturbations (17·5 ms). Extension torque pulses applied when the wrist was extended (bottom left) evoked an initial e.m.g. suppression (mean latency 14 ms), consistent with removal of excitatory spindle afferent input to motoneurones. This pause was followed by brisk excitation at a mean latency of 35 ms. When applied with the wrist flexed and the extensors inactive (lower right) the extension torque pulses elicited relatively weak long-latency e.m.g. responses, and a clear c.m. cell response at 18 ms. These bidirectional c.m. cell responses are consistent with the long-latency muscle responses evoked under all four conditions, although the response to perturbations which shortened the muscle would seem inappropriate for generating a movement opposing the perturbation.

The response properties of all twenty-one c.m. cells are summarized in Table 1. Eighteen of twenty-one recorded c.m. cells were tested under both muscle-lengthening and muscle-shortening torque pulse conditions. One of these eighteen cells did not respond to torque pulses (which did evoke M2 responses in its target muscles). Of the remaining seventeen, nine increased their activity only for muscle-lengthening perturbations, and showed either no change (six) or a decrease (three) for muscle-shortening torque pulses. The remaining eight c.m. cells were activated by torque pulses which lengthened the target muscles (mean latency 22·5 ± 7·6 ms) and also by the muscle-shortening torque pulses at similar short latencies (22·0 ± 7·4 ms). Table 1 also includes the cells’ antidromic latency to pyramidal tract stimulation and the strength of the post-spike facilitation in their most clearly facilitated target muscles (Fetz & Cheney, 1980). The Table also gives each cell’s response pattern during active ramp-and-hold movement. We see no consistent relation between a c.m. cell’s responses to torque pulses and its response pattern during active movement, its conduction velocity or target muscles.

**Effect of torque pulse duration**

One may question whether the c.m. cell and muscle responses to brief (25 ms) torque pulses are entirely related to torque pulse onset or whether some components of these responses may be related to pulse termination or to discontinuities in the torque trajectory. To investigate this question we perturbed muscles with torque pulses of different durations. Fig. 7 (left) shows the responses of an extension c.m. cell and two strongly facilitated target muscles to muscle-lengthening torque pulses of 25 and 200 ms, applied during wrist extension. The structure and latency of the early muscle
Table 1. Summary of c.m. cell responses during active movements, passive movements and torque perturbations

<table>
<thead>
<tr>
<th>C.m. cell</th>
<th>P.s.f. strength</th>
<th>P.t. lat. (ms)</th>
<th>Response type</th>
<th>Active movement</th>
<th>Passive movement</th>
<th>Torque pulses applied during</th>
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<tr>
<td>SI 130-2</td>
<td>M</td>
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<td>SW 54-1</td>
<td>S</td>
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<td>F E</td>
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<td>+ +</td>
<td>F E</td>
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<tr>
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<td>P/T</td>
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<td>0 +</td>
<td>F E</td>
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<tr>
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<td>F E</td>
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<tr>
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<td>+ +</td>
<td>F E</td>
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<td>F E</td>
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<td>R</td>
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C.m. cells are identified by the same symbols used in previous papers (Fetz & Cheney, 1980; Cheney & Fetz, 1980). The second column gives the strength of post-spike facilitation in the target muscle(s) most strongly facilitated, rated as strong (S), moderate (M) or weak (W). The third column gives antidromic latency to pyramidal tract stimulation (in ms), or whether the cell gave no response (NR) or was not tested (NT). The fourth column indicates response patterns during active ramp-and-hold responses: phasic/tonic (P/T), tonic (T) or ramp (R). Remaining columns summarize responses to flexion (F) or extension (E) movements as excitation (+), inhibition (−), no response (0) or not tested (NT).

and c.m. cell responses were virtually the same for both torque pulse durations, indicating that these responses can be attributed to inputs generated at the onset of the torque pulse. The onset latencies of the c.m. cell’s responses were similar for loading (29 ms) and unloading (27 ms) perturbations. After their initial onset, the torque records show a discontinuity in their rising phase: a transient pause beginning at about 11 ms, followed by a second fast rise starting at 15–16 ms. Peripheral receptors activated by this pause may well have generated afferent input contributing to subsequent events.

Passive movement responses

Torque perturbations test the c.m. cell’s response to afferent inputs during active movements. It is also of interest to compare the responses of c.m. cells to passive movements when the target muscles are inactive. Fig. 8 shows the passive movement
Fig. 7. C.m. cell and target muscle responses to lengthening and shortening torque pulses of two different durations: 25 ms (top) and 200 ms (bottom). This cell strongly facilitated the two muscles shown (ED 4,5, extensor digitorum longus; EDC, extensor digitorum communis), as well as two others. Each set of records is an average of ten responses. Calibration for torque, 0-1 N m; position, 10°.

responses of neurone SI 120-1, whose torque pulse responses were consistent with the transcortical stretch reflex hypothesis (Fig. 5). Passive wrist flexion produced a brisk, short-latency excitation, whereas passive wrist extension did not. Thus, the passive movement responses of this cell match its responses to torque perturbations and both are consistent with mediation by afferents from stretch receptors in the cell’s target muscles and/or their synergists.
Fig. 9 shows the passive movement responses of cell SW 53-3, which facilitated extensor muscles and responded equally well to perturbations in both directions (Fig. 6). Two rates of passive movement are shown: fast (500 deg/s) and slow (200 deg/s). The former stretched the extensor muscles sufficiently fast to evoke a segmental stretch reflex, whereas slow flexion evoked no muscle response. Both passive flexion and passive extension elicited equally strong, short-latency bursts of

cell activity. Responses to fast passive movements were stronger than those to slow movements and had slightly earlier onset latencies as measured from the earliest deflexion in the torque record. Therefore, the bidirectional passive movement responses of this c.m. cell match its bidirectional torque pulse responses, but appear inconsistent with mediation by stretch receptors of the cell's target muscles.

Table 1 summarizes the passive movement responses of all nineteen c.m. cells investigated. Two cells were unresponsive to passive movements; one of these was also unresponsive to perturbations of active movement. Of the seventeen responsive cells, ten responded to movements in only one direction and seven responded bidirectionally. Of the ten unidirectional cells, seven were activated by passive movement in the direction opposite to the active movement with which the cell was related and three were activated by passive and active movement in the same direction. Although fourteen of seventeen responsive c.m. cells responded to passive movements which stretched their target muscles, consistent with a transcortical
stretch reflex hypothesis, the seven bidirectional cells also responded to passive movements in the opposite direction.

For eleven of eighteen fully tested c.m. cells, the torque pulse and passive movement responses were in complete agreement. Two c.m. cells responded to passive movements in the direction opposite to that of the torque pulse which activated them; four cells responded bidirectionally under one condition and unidirectionally under the other; and one was activated by torque pulses but not by passive movements.
Cutaneous inputs

The sensitivity of four of the twenty-two c.m. cells to cutaneous inputs was tested by mechanically stimulating the glabrous and hairy skin of the hand. (Since e.m.g. leads were taped to the forearm, this region was inaccessible to exploration of receptive fields.) None of the four c.m. cells tested had cutaneous receptive fields on the hand or wrist region. One of these, illustrated in Figs. 6 and 9, was activated in all four torque pulse conditions and by both passive flexion and extension.

![Graph showing histograms summarizing the onset latencies of c.m. cell and muscle responses to perturbations that lengthened target muscles.](image)

Fig. 10. Histograms summarizing the onset latencies of c.m. cell and muscle responses to perturbations that lengthened target muscles. Top, latencies of c.m. cell responses to muscle-lengthening perturbations. Middle, sum of c.m. cell onset and post-spike facilitation onset (transcortical loop time) 3, weak; 4, moderate; *, strong. Bottom, onset latencies of M1 (3) and M2 (4) responses in target muscles following muscle-lengthening torque pulses.

Timing of c.m. cell and muscle activity

These results demonstrate that all responsive c.m. cells are activated by perturbations which stretch the cell's target muscles. But is the timing of this activity appropriate to contribute to the M2 e.m.g. peak? To evaluate the relative timing we measured the afferent and efferent conduction times for each c.m. cell and compared their sum with the latency of the M2 e.m.g. response in its target muscles. These measurements are illustrated in Fig. 3 for the response of cell SW 53-3 and its target...
muscle to the muscle-lengthening torque pulse applied during wrist extension. The conduction time in the afferent limb of the transcortical loop is the onset latency of the c.m. cell response relative to onset of the torque pulse; for cell SW 53-3 this was 17.0 ms. The minimum transmission time of the efferent limb is given by the onset latency after the spikes of the facilitation produced in the cell's target muscles; the

spike-triggered average, on the right, reveals a facilitation onset latency of 7.6 ms. Transcortical loop time is the sum of c.m. cell onset latency and post-spike facilitation onset latency (24.6 ms). In comparison, the M2 e.m.g. onset latency was 27.9 ms, slightly longer than the transcortical loop time.

Fig. 10 summarizes similar measures for twenty responsive c.m. cells and their facilitated target muscles. The top histogram shows the distribution of c.m. cell onset latencies, the middle histogram gives the sum of c.m. cell onset latency and target muscle post-spike facilitation onset latency for each facilitated muscle (transcortical loop time), and the bottom histogram is the distribution of onset latencies of the M1 and M2 e.m.g. responses for the same target muscles. The transcortical loop time for many early c.m. cells is appropriate to contribute to the initiation of the M2 response, although many other c.m. cells would contribute after the initiation of M2. The mean loop time of cells in the early peak of the distribution is slightly less than the mean of the M2 onset latency distribution.

C.m. cells producing strong, moderate and weak post-spike facilitation are distinguished in the histogram of transcortical loop time in Fig. 10. It is noteworthy that the loop times which overlap or precede the M2 e.m.g. onsets are primarily those of c.m. cells which produced strong or moderately strong post-spike facilitation and which, therefore, would have produced the greatest facilitation of motoneurones.

The scatter plot of Fig. 11 compares the transcortical loop time for each c.m. cell
with the M2 e.m.g. onset of its target muscles. Each point represents one c.m. cell–target muscle pair. The dashed line represents the points for which the loop time equals the onset latency of the M2 response. Twenty-six of fifty-eight c.m. cell–target muscle combinations had loop times within \( \pm 5 \) ms of the M2 e.m.g. onset time. However, cells with loop times shorter than M2 would also have contributed to the subliminal facilitation of target motoneurones before overt activation.

Moreover, many c.m. cells with loop times greater than the M2 onset latency would also have contributed to M2, since the total durations of the c.m. cell and M2 muscle responses overlapped. A better representation of target muscle facilitation produced by the c.m. cell response could be obtained by convolving the c.m. cell’s torque pulse response with its average post-spike facilitation. Since the duration of post-spike facilitation is short relative to the duration of the c.m. cell response, this convolution can be approximated by delaying the c.m. cell response by the latency of the facilitation peak (about 10 ms). Of thirty-seven c.m.–target muscle pairs for which response durations were measured, the estimated total period of c.m. cell facilitation of muscle activity overlapped with the corresponding M2 response in thirty-five cases. The total period of muscle facilitation was estimated as c.m. cell response duration delayed by the latency of post-spike facilitation. The mean duration of the c.m. cell response \((35 \pm 15.3 \text{ ms, mean } \pm \text{S.D.})\) was greater than the mean duration of the M2 response \((25 \pm 12.4 \text{ ms})\), so a larger fraction of the M2 response overlapped with the cell response (77 \%) than vice versa (58 \%). Of the non-overlapping portions of the c.m. cell responses, 30 \% preceded target muscle M2 onset while 70 \% followed M2 termination. Nevertheless, after accounting for loop time and response duration, the responses of nearly all c.m. cells are consistent with the cell contributing to some part of the M2 e.m.g. response.

DISCUSSION

Cortical contribution to the long-latency stretch reflex

A major objective of these experiments was to determine whether motor cortex cells causally contribute to the generation of the long-latency M2 e.m.g. response. To contribute to M2, a candidate cell must not only respond to a perturbation at the appropriate time, but must also facilitate the activity of muscles exhibiting M2. Spike-triggered averaging of e.m.g. activity makes it possible to identify those cortical neurones whose discharge facilitates muscle activity, and to assess the magnitude and distribution of such facilitation. As discussed previously (Fetz & Cheney, 1980), strong post-spike facilitation is probably mediated by monosynaptic corticomotoneuronal connexions, and we refer to such cells as c.m. cells. Since these c.m. cells could form the efferent limb of a transcortical reflex loop, their responses to torque perturbations are particularly relevant. Our primary finding was that nearly all c.m. cells responded at short latency to torque perturbations which stretched the cell’s active target muscles.

For these c.m. cells it was also possible to determine the transcortical loop time, i.e. the sum of the afferent transmission time (the onset latency of the neuronal response following torque perturbation onset) and efferent transmission time (the onset latency of average e.m.g. facilitation following the spike discharge of the c.m.
cell). Many c.m. cells, especially those producing strong post-spike facilitation, had loop times compatible with a role in the initiation of M2. Moreover, the response of nearly all c.m. cells overlapped with some part of the corresponding M2 response. Thus, the timing of c.m. cell responses relative to M2, combined with the documented facilitation of muscle activity by these cells, indicates that a transcortical loop involving c.m. cells does contribute to the long-latency stretch reflex.

The causal contribution of c.m. cells to the M2 response could be directly confirmed by e.m.g. averages selectively triggered from spikes evoked by the torque pulse (Fig. 4). Such a selective average showed a stronger post-spike facilitation than averages compiled during the static hold, both for the cell's target muscles and also for a normally unfacilitated synergist. This enhanced facilitation following the torque pulse probably results from recruitment of additional motoneurones and interneurones which were brought closer to threshold by synchronous inputs. The fact that the post-spike facilitation still has a distinct onset indicates that it is mediated by outputs from the c.m. cell rather than by other coactivated cells. Since the number of available spikes associated with torque pulses was usually limited, and since the interpretation of their facilitation is compromised by synchronous activation of many cells, we routinely used spike-triggered averages compiled during the static hold period to define the onset and distribution of post-spike facilitation.

The demonstrated contribution of c.m. cells to the long-latency M2 response does not deny the potential involvement of additional mechanisms. Since motoneurone firing results from the summation of all inputs to the motoneurone pool, we concur with the view (Villis & Cooke, 1976; Lee & Tatton, 1982) that M2 may well be mediated by multiple pathways. The relative contribution of motor cortex may be greater for distal than proximal muscles (Marsden et al. 1976; Lenz et al. 1983), consistent with the greater excitatory effect of c.m. cells on motoneurones of distal muscles (Phillips, 1969). Our current evidence confirms that one contribution to forelimb M2 is a transcortical reflex.

C.m. cell and muscle responses to shortening perturbations

An unexpected finding in these experiments was the fact that half of the c.m. cells not only responded to torque perturbations which stretched their target muscles but were also activated by perturbations which shortened them. Such paradoxical responses seem inconsistent with the functioning of a transcortical stretch reflex whose purpose is to compensate for load perturbations by generating opposing movements. These excitatory responses to shortening perturbations had onset latencies comparable to latencies for muscle-lengthening perturbations, so they could not have been generated by a burst of afferent input at torque pulse termination. The initial response of the shortened muscles was inhibition, consistent with removal of excitatory spindle input, so it seems unlikely that spindle afferents in the shortened muscles were initially excited. However, spindle afferents may respond to oscillations triggered by unloading torque pulses, due to resonant properties of the musculo-tendinous system (Eklund et al. 1982a, b).

Following the initial period of e.m.g. suppression the shortened muscles consistently exhibited a peak in e.m.g. activity comparable in latency to the M2 of lengthening perturbations (Figs. 5–7). This peak could not have been mediated by afferent input
from torque pulse termination since it had the same latency in responses to 200 ms torque pulses as in responses to 25 ms pulses (Fig. 7). One factor which may have contributed to this peak would be mechanical oscillations of the muscle triggered by torque pulse onset. Another factor may have been removal of Ib inhibition, a mechanism Crago, Houk & Hasan (1976) felt was responsible for a phase of muscle excitation during shortening in human experiments. Our evidence indicates that another contribution comes from the bidirectionally sensitive c.m. cells whose responses to shortening perturbations were appropriately timed to contribute to the long-latency e.m.g. peak in their target muscles.

The activation of bidirectional c.m. cells and their target muscles by perturbations which shortened the muscles is consistent with their correlational linkage, but appears inconsistent with the hypothesis that the function of the transcortical reflex is simply to generate movement opposing the perturbations. The observed reflex co-contraction of agonist and antagonist muscles would result in a stiffening of the wrist joint, producing an increased resistance to displacement by subsequent perturbations. Thus, the observed response patterns of c.m. cells are consistent with a contribution of the transcortical reflex to stabilization of the joint by increasing its stiffness. Such increases in stiffness have been measured directly for the elbow joint of human subjects instructed to resist sustained torque changes (Kwan, Murphy & Repeck, 1979). Our findings indicate that a similar reflex increase in wrist stiffness may be produced by co-contraction of forelimb flexors and extensors at M2 latencies; moreover, many c.m. cells contribute to this by facilitating their target muscles for both lengthening and shortening perturbations.

**Passive movement responses**

The peripheral receptors providing input to c.m. cells were further tested by imposing passive wrist movements and by exploring the hand for cutaneous receptive fields. Almost all c.m. cells responsive to passive movement (fourteen of seventeen) responded at short latency to passive wrist movements which stretched their target muscles. Such responses are consistent with the hypothesis that c.m. cells may be activated by input from stretch receptors in their target muscles. However, seven c.m. cells were additionally activated by mild passive movements which shortened their target muscles. These bidirectional responses to mild passive movements, like the responses to perturbations during active movements, are not readily explained in terms of a simple stretch reflex feed-back system from muscle spindles of target muscles. It remains possible that delayed input from spindle receptors in the shortened muscles could be generated by mechanical oscillations; these inputs could produce excitatory responses in the c.m. cells. (The absence of comparable monosynaptic activation of homonymous muscles could be the result of reciprocal inhibition from their stretched antagonists.) In any case, the initial pause in spindle input evoked by muscle shortening could be expected to generate a comparable pause in c.m. cell activity; only three of the eighteen c.m. cells exhibited such a pause.

Alternatively, the bidirectional c.m. cells may have received input from stretch receptors in both flexor and extensor muscles or from another type of receptor similarly activated by both flexion and extension movements, such as cutaneous receptors (Fetz et al. 1980). One c.m. cell responding bidirectionally to torque pulses
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(Fig. 6) and passive movements (Fig. 9) could not be activated by cutaneous stimulation of the hand or wrist, suggesting that such cutaneous inputs were not involved in its responses. The bidirectionally responsive c.m. cells were intermingled with the unidirectional cells; they were not located in separate regions of the precentral gyrus, as demonstrated for neurones responsive to cutaneous and deep inputs (TANJI & Wise, 1981; Strick & Preston, 1982).

The responses of about half of the c.m. cells (seven of seventeen) to passive movements did not agree in all respects with their responses to torque perturbations during active movements; most of these differences are attributable to additional responses evoked by the torque pulses, possibly associated with a greater number of peripheral receptors activated or a greater degree of central excitability during active movements.

Relation between torque pulse and active movement responses

Prior studies of torque pulse responses of motor cortex neurones have emphasized those neurones which exhibit reciprocal response patterns—excitation with movement in one direction and inhibition with movement in the opposite direction. Conrad et al. (1975) found that about 61% of motor cortex cells (including identified pyramidal tract neurones) with a predominantly reciprocal relation to active elbow movements also showed reciprocal responses to oppositely directed torque pulses. Two-thirds of these discharged in association with active movements and torque pulses in opposite directions, consistent with participation in load-compensating reflexes; and one-third discharged with active movements and torque pulses in the same direction. Another 30% of their task-related cells responded similarly to both flexion and extension torque pulses.

Evarts & Tanji (1976) reported that pyramidal tract neurones with a reciprocal relation to active elbow movements were more common than those with a reciprocal relation to oppositely directed torque pulses (41% compared with 20%). They also found that 39% of pyramidal tract neurones reciprocally related to active movements were reciprocally related to torque pulses, and that 90% of these discharged in association with active movements in the opposite direction to those evoked by torque pulses.

Since these studies included motor cortex cells potentially affecting diverse muscles, it seemed relevant to determine whether c.m. cells with known target muscles show more specific torque pulse responses. All our c.m. cells were reciprocally related to active wrist movements (Cheney & Fetz, 1980). Half of these responded only to torque pulses opposing the active movements; the other half discharged similarly for both flexion and extension torque pulses. In contrast to previous studies only three of the nine unilaterally activated c.m. cells showed a strictly reciprocal response pattern (excitation for one torque pulse and inhibition for the opposite); six unidirectional c.m. cells increased their activity for one direction of perturbation, and showed no change for the opposite (Fig. 5). Thus, even c.m. cells with known output effects on agonist muscles exhibit diverse relations between their responses to active movements and torque pulses.

In conclusion, we feel that the present evidence confirms that c.m. cells causally contribute to the long-latency responses to muscle stretch in primate forearm
muscles. This does not deny the existence of potential contributions of other mechanisms, such as repetitive input from primary afferents (Tatton et al. 1978; Tracey et al. 1980; Hagbarth et al. 1981; Eklund et al. 1982a,b) or delayed input from secondary afferents (Matthews, 1983) or long loops via other supraspinal reflex centres. When comparable evidence of their causal contribution is obtained, it may become possible to assess the relative contribution of peripheral and descending systems.

The authors thank Ms Linda Carr for typing the manuscript, Mr Jerrold Maddocks for technical assistance and Mr Wade Smith for programming help. This work was supported by N.I.H. grants NS 12542, NS 5082 and RR00166.

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