Muscle Fields and Response Properties of Primate Corticomotoneuronal Cells

E.E. FETZ and P.D. CHENEY

Department of Physiology and Biophysics, and Regional Primate Research Center, University of Washington, Seattle, WA 98195 (U.S.A.)

INTRODUCTION

The role of motor cortex cells in control of movement and posture depends not only on their activity during relevant behavioral responses but also on the target cells that are affected by this activity. Analysis of precentral cell responses during active and passive movement has revealed two major sources of input, central and peripheral; however, the functional significance of this activity remains uncertain as long as its output destinations are unknown. We have, therefore, investigated those precentral cortex cells whose output effects on the activity of motor units could be confirmed by cross-correlation techniques. Spike-triggered averages (STA's) of rectified EMG activity have revealed that action potentials of certain precentral neurons are followed by a transient postspike facilitation (PSF) of average motor unit activity (Fetz et al., 1976). Such cells would therefore contribute rather directly to control of muscle activity. Since the latency and time course of the PSF suggest that they are mediated by direct corticomotoneuronal (CM) connections, we have referred to these as CM cells. The present review summarizes the evidence concerning the distribution of PSF in different forelimb muscles and the response properties of these cells during controlled ramp-and-hold wrist movements.

METHODS

To provide prolonged periods of coactivation of wrist and finger muscles with cortical cell activity, monkeys were trained to alternately flex and extend the wrist against elastic loads. Thus, displacement of the wrist from a neutral center position required proportional active torques. The hand was held with fingers extended between padded plates which could rotate about a shaft aligned with the wrist. The movement trajectory consisted of a phasic ramp followed by a static hold in an electronically detected hold zone for at least 1 sec (cf. figures). EMG activity of six flexor and six extensor muscles was monitored with pairs of stainless steel electrodes implanted in the belly of each muscle. The muscles were identified both by their anatomical location and by characteristic movements evoked by stimulating through the electrode pairs. As indicated below, recordings were confirmed to be of independent motor units by cross-correlating the EMG activity. The specific muscles that were

sampled and illustrated include extensor digitorum communis (EDC); extensors carpi radialis brevis and longus (ECR-B and ECR-L); extensor carpi ulnaris (ECU); flexors digitorum profundus and sublimis (FDP and FDS); flexors carpi radialis and ulnaris (FCR and FCU) and palmaris longus (PL).

Action potentials of precentral cortex cells that fired during flexion or extension were used to compile STA's of the full-wave rectified EMG activity of six covarying agonist muscles. The rectification was intended to eliminate cancellation of positive and negative components of any motor unit potentials that might appear at variable latencies after the cortical spike. The STA's included a minimum of 2,000 events, although more were often included to reduce the noise. The analysis period was typically 30 msec, 5 msec before to 25 msec after the spike.

RESULTS

Distribution of PSF in different forelimb muscles

Examples of cells producing postspike facilitation in coactivated wrist and finger muscles are illustrated in the first three figures. The cell in Fig. 1 fired consistently during extension of the wrist. STA's of two of the six covarying extensor muscles showed clear PSF (EDC and ED 4,5); in addition, two other muscles also showed evidence of a weaker augmentation of EMG activity after the spike. The remaining two muscles showed no significant spike-related effect in the number of events averaged (4,600).

The cell in Fig. 2 covaried with wrist flexion and produced PSF in three of the wrist flexor muscles recorded with implanted electrodes, as well as in EMG recorded with

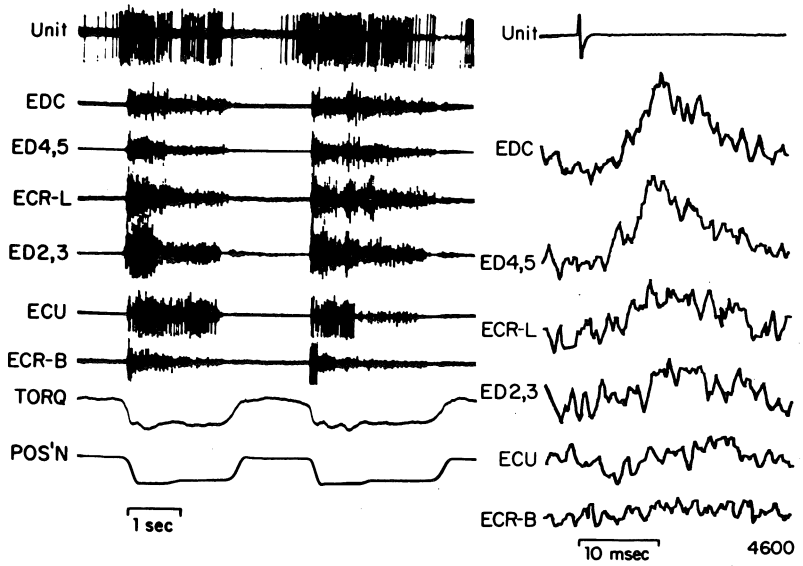

Fig. 1. Responses of an extension-related CM cell during successive wrist movements against a spring-like load (left). Muscles are identified in text; bottom traces illustrate active torque and wrist position. At right are averages of the rectified EMG activity, triggered from 4,600 action potentials of the cell. As shown by position of the unit spike at top, the analysis interval included 5 msec preceding the spike and 25 msec after the spike. In this and subsequent figures the number of events averaged is given beneath the average. (From Fetz and Cheney, 1978).

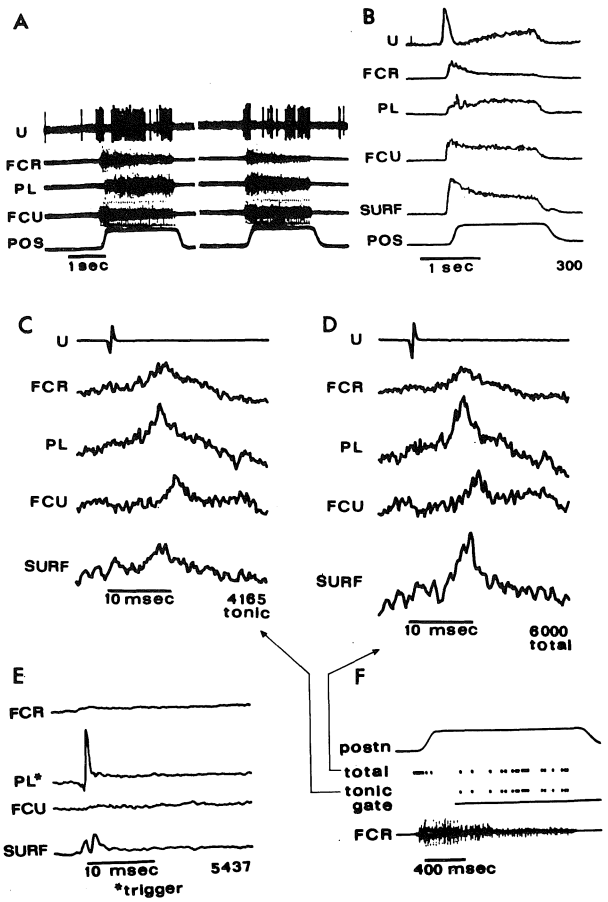

Fig. 2. CM cell related to flexion of the wrist. A) Responses of cortical unit (U), implanted flexor muscles, and wrist position (POS). B) Average of 300 flexion responses, aligned at onset of flexion movement. Unit activity shows pattern characteristic of "phasic-ramp" cells, i.e., a phasic burst of activity at movement onset, followed by gradually increasing discharge during static hold period. Averages of full-wave rectified EMG activity recorded from implanted muscles and by surface electrodes (SURF). C) Spike-triggered averages of rectified EMG activity compiled for action potentials occurring during the static hold period. D) STA's compiled for action potentials occurring during both phasic movement and static hold periods. E) Averages of rectified EMG activity triggered from motor units recorded in PL muscle; as in STA's, analysis interval was 30 msec. F) Single flexion response illustrating gating of unit pulses used to compile STA in C. Dot rasters below position trace show pulses for all action potentials (total) and those occurring during static hold period (tonic); gate signal began 200 msec after end of phasic movement. (From Fetz and Cheney, 1978.)

surface electrodes. Response averages aligned on the phasic flexion movement (Fig. 2B) indicate that this unit exhibited an unusually strong peak of activity at movement onset, when muscle activity was initiated. This unit provides a particularly convincing example of the fact that PSF is not simply an artifactual consequence of averaging non-stationary EMG activity. Excluding from the triggering events all action potentials occurring during the initial peak and compiling STA's only from those action potentials occurring during the static hold period (using the gating procedure illustrated in Fig. 2F) resulted in the clear PSF's shown in Fig. 2C. In comparison, STA's that were triggered from *all* action potentials, including those at movement

onset, showed similar effects (Fig. 2D); the larger PSF in the records from PL and SURF in Fig. 2D may be due to the contribution of larger motor units at onset or to enhanced effectiveness of brief interspike intervals. Similar controls with other units confirmed that PSF was not a consequence of changing levels of EMG activity.

In a total of 2,242 STA's, we observed 483 instances of PSF (21%). The average onset latency after the cortical spike was 6.7 ± 2.9 msec (mean ± SD). This is consistent with known conduction times in pyramidal tract neurons (PTN's) and motoneurons. In the macaque monkey, the latency of antidromic responses evoked from stimulating the pyramidal tract (minimum 0.7 msec) (Evarts, 1965) and from cervical spinal cord (1.3 msec) (Humphrey and Rietz, 1978) indicates that the conduction from cortex to cervical levels could be as fast as 1.1 msec (assuming a 0.2 msec utilization time); minimal conduction for motoneurons to muscles could be 3.5 msec. Most PSF latencies were longer than the sum of these minimal conduction times from cortex to muscle. As shown in Fig. 2C and D, the same cell could produce PSF in different muscles with different latencies, probably attributable to different conduction times of the relevant motoneurons. The rise time of the PSF peak (3.2 ± 1.8 msec) and decay time back to base line (7.0± 3.0 msec) would depend on several factors, including the number of motor units affected, their conduction times, the shape of their muscle fiber potentials and the time course of the CM-EPSP's. The time after the cortical spike when facilitation was greatest, i.e., the latency of the PSF peak, was on average 10.2± 3.0 msec. The amplitude of this peak relative to base line level was measured for representative samples of PSF. The peaks of the PSF ranged from 12.4% of base line for strong PSF to an average 5.7% for weak PSF. Of course, these values are somewhat arbitrary since they depend on the number of motor units recorded and the amplitude of their recorded potentials as well as on the strength of any underlying cross-correlation.

Most of the cells exhibiting PSF proved to be PTN's when tested. In fact, there was a correlation between the antidromic PT latency and PSF latency: slow PTN's produced PSF at relatively longer latencies after the spike. Fast PTN's produced primarily short-latency PSF but some also produced PSF of longer latency. Of all the PTN's correlated with five or six muscles, 55% exhibited signs of postspike facilitation in at least one of the muscles.

When STA's were compiled simultaneously for multiple muscles, cells that produced PSF generally facilitated more than one muscle. Of 370 precentral neurons that covaried strongly with flexion or extension and were used to compile STA's of five or six covarying forelimb muscles, 160 (43%) produced PSF in at least one muscle and on this basis were defined as CM cells. Of these, 112 (70%) produced PSF in more than one muscle (29% in two muscles, 23% in three, 11% in four, 4% in five and 3% in six).

The set of facilitated muscles represents those muscles whose activity is statistically affected by action potentials of the cell, and may be referred to as the cell's "muscle field" (Fetz and Cheney, 1978). If these PSF's are mediated by monosynaptic CM connections, then the cells that produce them are cortico-motoneuronal cells also in the anatomical sense, and their muscle field would represent their target muscles, i.e., the muscles whose motoneurons are contacted by terminals of the cell. Existence of divergent terminals of PTN's has been demonstrated electrophysiologically in primates by antidromic activation from different motor nuclei (Asanuma et al., 1979). Whether all monosynaptic CM connections are sufficiently potent to produce detectable cross-correlations, and conversely, whether some of the observed correlations

may be mediated by indirect connections via other cells, remains an important unresolved issue. At this point, it seems technically simpler to determine the set of muscles whose activity is facilitated by the cell rather than the set of motoneurons that are anatomically contacted by the cell. Indeed, the set of facilitated muscles would seem to be a functionally more significant measure of the output effects of the cortical cell than the distribution of the underlying synaptic connections, which may or may not produce detectable effects

The method used to sample EMG activity will of course influence the extent of the observed muscle field. STA's can only detect effects in muscles that are coactivated with the unit. The extent of facilitation in different muscles could be mistakenly exaggerated if the same motor units were recorded redundantly through different EMG electrode pairs. Therefore, this possibility was routinely tested in all experiments by cross-correlating muscle activity. Compiling averages of rectified EMG activity triggered from motor units of each muscle revealed the extent to which the same units might have been picked up by adjacent leads. For example, Fig. 2E shows that when EMG averages were triggered from motor units in PL, only the surface-recorded activity revealed a peak simultaneously with the triggering peak in PL, confirming that the surface electrodes (over PL) had picked up some of the same units. However, there was no sign of a comparable peak in averages of either of the two adjacent flexor muscles, FCR or FCU. This, plus similar averages triggered from each of the other muscles, confirmed that the implanted electrodes had, indeed, recorded independent motor units. Such "cross-correlation" of muscle recordings was done routinely when multiple PSF's were observed. In a few cases, EMG-triggered averages revealed evidence that some units had been recorded in common; in those cases, one of the redundant EMG records was eliminated from the data base. Thus, the distribution of PSF in different forelimb muscles was not artifactually exaggerated by redundant EMG recording.

On the other hand, since the sample of motor units was limited, the extent of the cells' muscle fields could easily have been underestimated. Implanted leads recorded perhaps 10% of the total motor units of the muscle; if the CM cells facilitated specific motor units within the pool, as suggested by recent evidence (Jankowska et al., 1975), recordings that showed no evidence of PSF might have missed detecting possible facilitation of other motor units in the same muscle. Moreover, additional muscles that were not sampled could also have contained facilitated motor units. Thus, the extent of the cell's muscle field may have been underestimated by the limited sampling of motor unit potentials.

Response patterns of CM cells

Since the PSF represents the average effect of the action potentials of CM cells on muscle activity, the net effect of a given firing pattern of such a cell may be estimated by convolving the PSF with its firing rate. Thus, the response patterns of a CM cell during wrist movements would produce a directly proportional augmentation of the firing probability of its facilitated motor units. To quantify the firing pattern of CM cells during controlled ramp-and-hold wrist movements, monkeys were trained to displace the wrist against elastic loads of different stiffness. On the basis of their phasic response during the ramp movement and their tonic firing during the static hold period, all CM cells could be classified into four basic types. Every CM cell exhibited some degree of activity during the static hold period, firing either at a constant rate

("tonic" types; cf. Figs. 3 and 4) or with gradually increasing rates ("ramp" types; cf. Fig. 2B). In contrast, many other precentral cells fired only phasically at onset of movement, but exhibited no maintained discharge during the hold period; none of these cells ever produced any postspike facilitation in the recorded muscles. The CM cells were further subdivided according to the presence of a phasic peak of activity at the onset of movement (Figs. 2B and 3) or the absence of such enhanced activity at the beginning of movement (Fig. 4). Thus, on the basis of their dynamic and static responses during the ramp-and-hold wrist movements all CM cells could be classified into one of four basic types: phasic-tonic (59%), tonic (28%), phasic-ramp (8%) and ramp (5%). These patterns were related to the torque response, since they occurred whether or not the response involved proportional wrist displacement, i.e., whether the response was isotonic or isometric (Cheney and Fetz, 1978). Clearly those cells with an enhanced phasic peak of activity at onset of movement would provide particularly effective input to activate motoneurons.

Relation of CM cells to active torque

The relation of activity of motor cortex cells to active force and joint displacement was first investigated by Evarts in monkeys trained to displace a handle against different loads. He found that the firing rate of many PTN's was related to the active force or to changes in force (Evarts, 1968). Similar results have been obtained by others

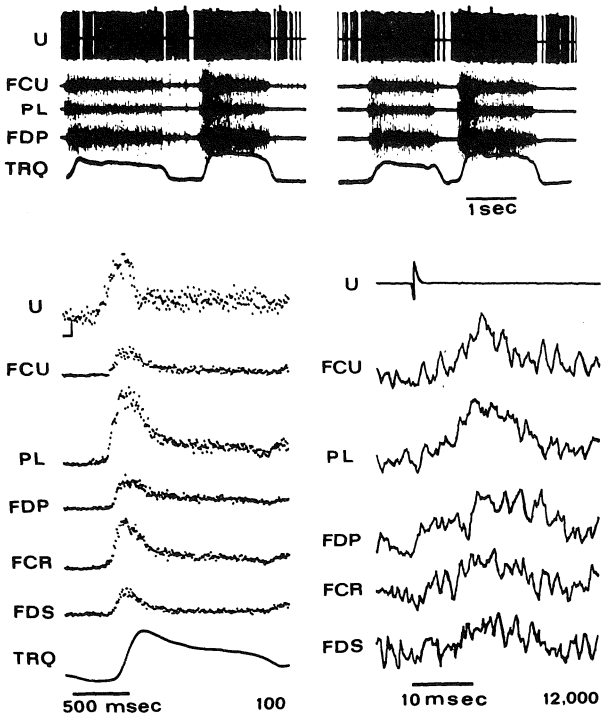

Fig. 3. Flexion-related CM cell facilitating activity of 5 muscles. Top: representative responses during flexion movements, illustrating higher firing rate at greater levels of active torque. Bottom left: response average of unit and rectified EMG activity of implanted flexor muscles, and torque. The firing pattern of this unit is characteristic of "phasic-tonic" CM cells. Bottom right: STA of rectified EMG activity, showing some PSF in each muscle.

(Humphrey et al., 1970; Hepp-Reymond et al., 1978; Smith et al., 1975; Schmidt et al., 1975), although the exact proportions and interpretations differ. Since some of the variation in results may be due to differences in cell types recorded and in their projections, it seemed worth re-investigating this issue with CM cells, whose output effects on specific agonist muscles could be independently confirmed by STA's. Accordingly, monkeys were trained to make the ramp-and-hold wrist movements into the same hold zone but against elastic loads of different stiffness. Separate response averages were compiled for movements involving the same displacement but different degrees of active torque. The firing rate of CM cells was consistently higher when the monkey exerted a greater amount of active torque as illustrated by the single trials in Fig. 3 and the response averages in Fig. 4. Since the onset of movement involved overcoming inertial loads of unknown magnitude, it was difficult to quantitatively interpret the phasic discharge at movement onset. However, the tonic firing rate during the static hold period occurs when activity in central and peripheral circuits has reached a relatively steady-state condition. We therefore measured the tonic firing rate as a function of static torque for CM cells from response averages; representative results are plotted in Fig. 5 for cells related to flexion and extension. All CM cells had a range over which tonic firing rate increased linearly with active static torque. The slope of this linear portion (i.e., the increment in firing rate per increment in static torque) was consistently greater for cells related to extension than for cells related to

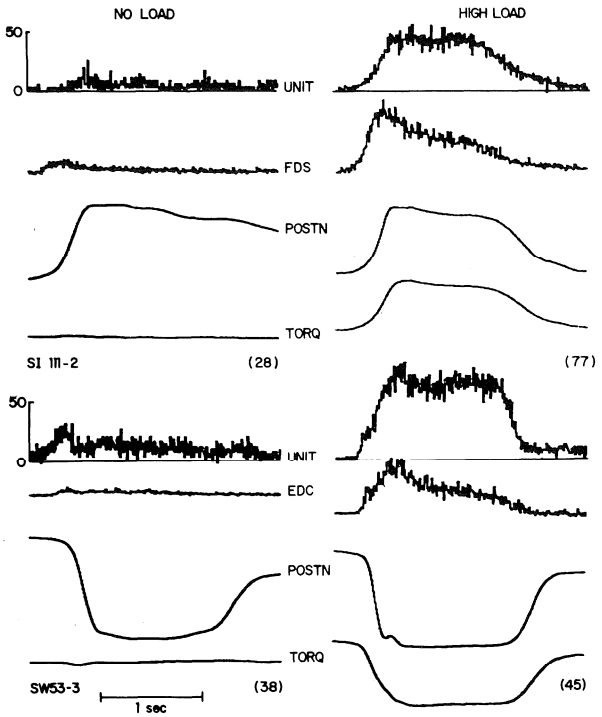

Fig. 4. Relation of CM cell activity to active torque. Response averages of a flexion-related cell (top) and extension-related cell (bottom) during comparable wrist displacements against no external load (left) and against stiff elastic load (right). Also shown is average EMG activity of one of the covarying agonist muscles which exhibited PSF. Response pattern of flexion-related cell (top right) is characteristic of "tonic" CM cells.

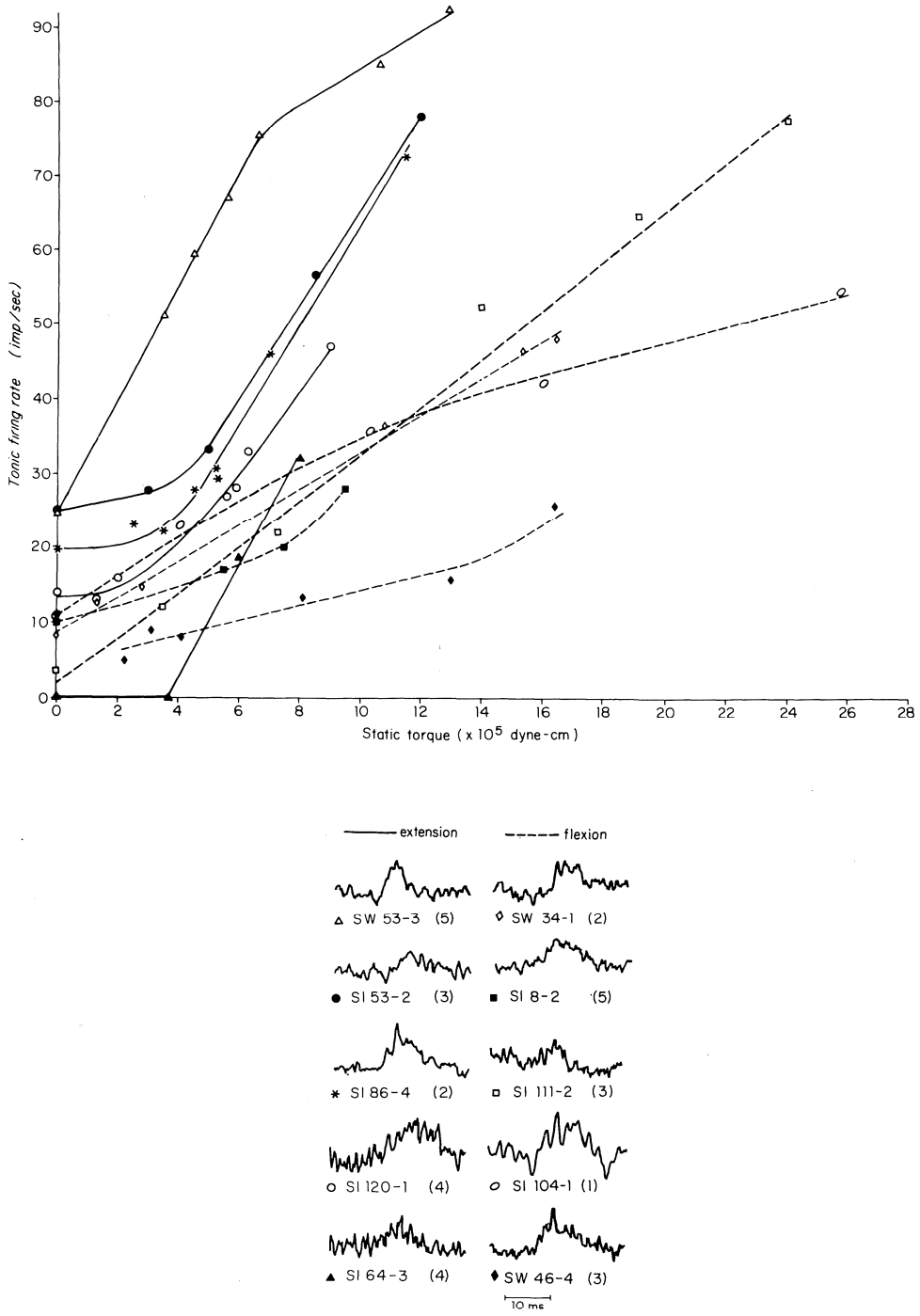

Fig. 5. Tonic firing rate of CM cells during static hold period plotted as function of active torque; representative examples of CM cells related to extension (solid lines) and flexion (dashed lines). Each point represents a measurement from a response average. Below: examples of PSF in one of the facilitated muscles for each cell plotted at left. Number of facilitated muscles is given in parentheses.

flexion (means: 4.8 vs 2.5 imp/sec/10^5 dyne-cm). These differences in load sensitivity between flexion-and extension-related cells may be due partly to differences in mechanical factors such as the radius over which the torque is exerted and to differences in internal loads between flexion and extension. Alternatively, there may also be inherent differences in the effects of CM cells related to flexor and extensor musculature (cf. Clough et al., 1968). Similar differences in load sensitivity were observed under isometric conditions.

Since CM cells have firing rates which increase with active torque and since their activity demonstrably facilitates agonist motoneurons, they clearly contribute causally to producing active force. In the range studied, their contribution to increases in force seems to be more through increments in firing rate than to recruitment of additional CM cells. One clear example of a CM cell recruited into activity at higher load levels is illustrated in Fig. 5; the rest were active to some degree even at the lowest levels of external load. Of course, some of this activity may be related to overcoming internal load, such as stretching the antagonist muscles.

In addition to their role in generating static torque, many CM cells may also respond phasically to perturbations of the wrist, and may participate in a transcortical reflex postulated to subserve load compensation. They responded to passive joint movements which stretched their facilitated muscles and during active movements they responded to load torque pulses at latencies consistent with a contribution to the M2 response (Cheney and Fetz, 1978). All CM cells exhibited at least those responses consistent with the load compensation hypothesis, i.e., they responded to perturbations which lengthened the facilitated muscle. However, half of the CM cells also showed additional responses to load perturbations in which their output would not be appropriate for load compensation. This would suggest that other systems in addition to the cortico-motoneuronal cells could be significantly involved in load compensation.

SUMMARY

In monkeys alternately flexing and extending the wrist against elastic loads, cortico-motoneuronal (CM) cells were identified by characteristic post-spike facilitation (PSF) of averaged forelimb muscle activity. Spike-triggered averages of rectified EMG activity of five to six covarying agonist muscles revealed that action potentials of 43% of strongly covarying motor cortex cells (n = 370) were followed by PSF of at least one muscle. The mean latency of such PSF was 6.7 ± 2.9 msec. The "muscle field" of such CM cells, defined as the set of muscles exhibiting PSF, could include only one muscle (30% of cells) or two (29%) or more (41%).

On the basis of their dynamic and static responses during the ramp-and-hold wrist movements, CM cells could be classified into four basic types: phasic-tonic (59%), tonic (28%), phasic-ramp (8%) and ramp (5%). During the static hold period the "tonic" cells fired at constant rates, while activity of "ramp" cells increased gradually. In addition, some cells of each group exhibited larger phasic responses at onset of movement.

When monkeys exerted different degrees of static torque, the tonic firing rate of CM cells increased linearly as a function of torque over much of the range. In the linear range, the increment in firing rate per increment in static torque was about twice as great for extension-related cells as for flexion-related cells. For the responses

studied, the contribution of CM cells to active torque was more through increases in firing rate than recruitment of additional CM cells. Most CM cells also responded to passive movements and load perturbations which stretched their facilitated muscles.

ACKNOWLEDGEMENTS

We gratefully acknowledge the technical assistance of Mr. Jerrold D. Maddocks in many phases of this work and the collaboration of Dr. Dwight German in early stages of this research. This research was supported by Grants RR 00166, NS 5082, NS 12542 and US0966 from the National Institutes of Health, U.S. Public Health Service.

REFERENCES

Asanuma, H., Zarzecki, P., Jankowska, E., Hongo, T. and Marcus, S. (1979) Projections of individual pyramidal tract neurons to lumbar motoneuron pools of the monkey. *Exp. Brain Res.*, 34: 73–89.

Cheney, P.D. and Fetz, E.E. (1977) Comparison of spike-triggered averages and stimulus-triggered averages of forearm muscle activity from identical motor cortex sites in behaving animals. *Neurosci. Abstr.*, 3: 269, no. 852.

Cheney, P.D. and Fetz, E.E. (1978) Functional properties of primate corticomotoneuronal cells. *Neurosci. Abstr.*, 4: 293, no. 918

Clough, J.F.M., Kernell, D. and Phillips, C.G. (1968) The distribution of monosynaptic excitation from the pyramidal tract and from primary spindle afferents to motoneurons of the baboon's hand and forearm. *J. Physiol. (Lond.)*, 198: 145–166.

Evarts, E.V. (1965) Relation of discharge frequency to conduction velocity in pyramidal tract neurons. *J. Neurophysiol.*, 28: 216–228.

Evarts, E.V. (1968) Relation of pyramidal tract activity to force exerted during voluntary movement. *J. Neurophysiol.*, 31: 14–27.

Fetz, E.E. and Cheney, P.D. (1978) Muscle fields of primate corticomotoneuronal cells. *J. Physiol. (Paris)*, 74: 239–245.

Fetz, E.E., Cheney, P.D. and German D.C. (1976) Corticomotoneuronal connections of precentral cells detected by post-spike averages of EMG activity in behaving monkeys. *Brain Res.*, 114: 505–510.

Hepp-Reymond, M.C., Wyss, U.R. and Anner, R. (1978) Neuronal coding of static force in the primate motor cortex. *J. Physiol. (Paris)*, 74: 287–291.

Humphrey, D.R. and Corrie W.S. (1978) Properties of pyramidal tract neuron system within a functionally defined subregion of primate motor cortex. *J. Neurophysiol.*, 41: 216–243.

Humphrey, D.R., Schmidt, E.M. and Thompson, W.D. (1970) Predicting measure of motor performance from multiple cortical spike trains. *Science*, 170: 758–762.

Jankowska, E., Padel, Y. and Tanaka, R. (1975) Projections of pyramidal tract cells to α-motoneurones innervating hindlimb muscles in the monkey. *J. Physiol. (Lond.)*, 249: 637–667.

Schmidt, E.M., Jost, R.G. and Davis, K.K. (1975) Reexamination of the force relationship of cortical cell discharge patterns with conditioned wrist movements. *Brain Res.*, 83: 213–223.

Smith, A.M., Hepp-Reymond, M.C. and Wyss, U.R. (1975) Relation of activity in precentral cortical neurons to force and rate of force change during isometric contractions of finger muscles. *Exp. Brain Res.*, 23: 315–332.