20

Functional Properties of Primate Corticomotoneuronal Cells: Comparisons with Spindle Afferents and Motor Units

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A causal explanation of the neural mechanisms that generate active movement will ultimately require quantitative information on the connectivity and response properties of the mediating neurons. In their studies of the functional organization of Ia afferent fiber connections to motoneurons, Elwood Henneman and colleagues substantially advanced our understanding of this model system and, at the same time, pioneered techniques that have helped to elucidate the organization of other inputs to motoneurons. In particular, the spike-triggered averaging (STA) technique has been used to document the effects of single-fiber inputs to motoneurons (Mendell and Henneman, 1971; Fetz et al., 1979; Kirkwood and Sears, 1980; Cope, et al., 1987; see also Chapters 16, 17, and 18, this volume). In their landmark paper, Mendell and Henneman (1971) first demonstrated the elegance and power of STA to document the postsynaptic effects of single neurons: they found that Ia afferent fibers produce unitary excitatory postsynaptic potentials (EPSPs) in motoneurons with a remarkable variety of shapes and sizes; moreover, a single afferent typically distributes terminals to most homonymous and many heteronymous motoneurons. In an analogous fashion, STA of electromyographic (EMG) activity has been used in awake, behaving monkeys to identify particular motor cortex cells that have correlational links with coactivated forelimb muscles (Fetz and Cheney, 1978, 1980; Muir and Lemon, 1983; Buys et al., 1986). These so-called corticomotoneuronal (CM) cells produce post-spike facilitation of muscle activity with a time course suggesting that they make a monosynaptic connection with motoneurons. As a direct synaptic input to motoneurons, CM cells provide an interesting comparison with the segmental monosynaptic input from Ia afferent

fibers. Moreover, as the final output from motor cortex, the CM cells can also be compared in many ways with another spinal analogue, the segmental motoneurons.

DISTRIBUTION OF POSTSPIKE EFFECTS OF CM CELLS

The sequence of events mediating the postspike facilitation of EMG is illustrated in Figure 20–1. The action potentials of a premotor input cell produce monosynaptic EPSPs, which in turn increase the firing probability of the target motoneuron. The effects of unitary EPSPs on motoneuron firing probability were documented for Ia EPSPs by Cope et al. (1987). In cat lumbar motoneurons, the single-fiber EPSPs were documented by STA of membrane potential first with the motoneuron at rest. Then the motoneuron was made to fire rhythmically by current injection, and the Ia spikes and motoneuron firing were cross-correlated. As illustrated by the correlogram in Figure 20–1, single-fiber EPSPs produced an increase in motoneuron firing probability during their rising phase. The peak of the cross-correlogram between the afferent and the

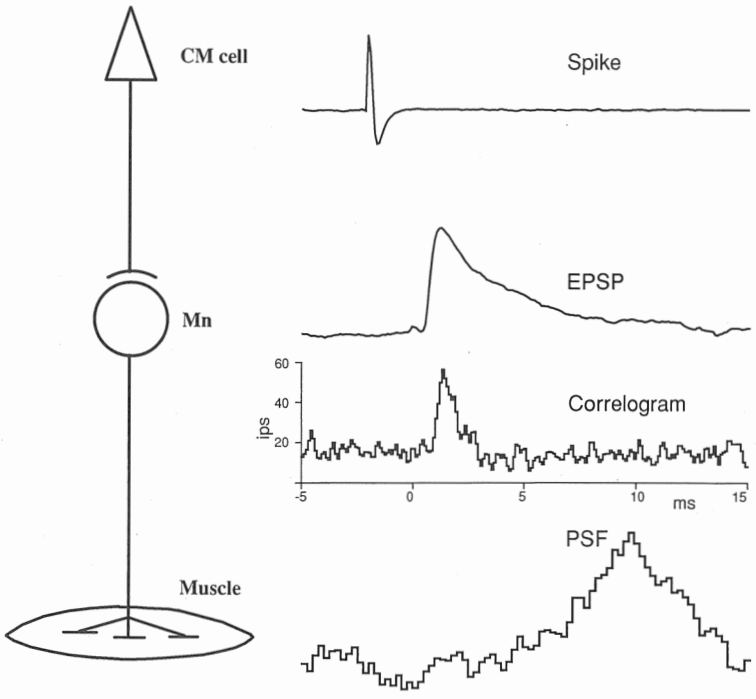

Fig. 20–1. Events mediating postspike effects of the CM cell. A monosynaptic CM connection produces an EPSP and increases the motoneuron firing probability, represented here by STA of an Ia EPSP and its associated correlogram (from Cope et al., 1987). The STA of a multiunit EMG produces postspike facilitation (PSF), representing the contribution of all facilitated motor units.

motoneuron had a shape that was largely proportional to the derivative of the EPSP and a peak area (above baseline) that was proportional to the EPSP amplitude.

The postspike facilitation of multiunit EMG would represent the contributions of many motor units. The contribution of a single motor unit to the STA would be its postspike correlogram peak convolved with the motor unit potential. In comparison to correlograms with single motoneurons, STA of EMG activity is less quantitative, but is more effective in detecting the existence of a connection because it sums the contributions of all the facilitated motor units, and the contribution of each unit to the rectified EMG is proportional to the size of its motor unit potential. A major advantage of using STA of muscle activity in behaving animals is that one can also document the normal response properties of these cells and their targets during voluntary movements. The functional interpretation of these responses becomes more meaningful when combined with such evidence of a correlational linkage.

The typical experimental situation is illustrated in Figure 20–2: the monkey makes ramp-and-hold wrist movements against an elastic load, and holds in a force zone for over a second to provide a steady level of tonic EMG activity. The action potentials of cortical cells that are modulated with the task are used to trigger averages of rectified EMG activity. Consistent postspike effects typically appear in the STA after several thousand triggers. By averaging the activity of multiple muscles simultaneously, STA has shown that single CM cells usually facilitate motor units in several synergistic muscles. About half of the CM cells facilitate only one of the six recorded muscles, and the remainder facilitate two, three, and up to all six muscles. On average, about 30–40% of the recorded coactivated muscles are clearly facilitated (Fetz and Cheney, 1980; Buys et al., 1986). These distributed effects are analogous to the divergent effects of a single Ia afferent fiber in motoneurons of heteronymous synergists as well as homonymous muscle.

Mendell and Henneman (1971) found that a single Ia afferent distributes terminals to virtually all motoneurons of the homonymous muscle. The analogous projection of single CM cells to multiple motor units *within* a muscle remains to be thoroughly documented, but some relevant evidence to date suggests that CM cells facilitate most of the motor units of their target muscles. The first evidence was based on the effects evoked by single intracortical stimuli, which produce poststimulus facilitation of EMG in stimulus-triggered averages. When multiple motor units were isolated within a muscle, cortical microstimuli of minimal intensities tended to facilitate all the recorded motor units of the muscle, including units exhibiting every type of firing pattern (Palmer and Fetz, 1985b). More recently, Mantel and Lemon (1987) cross-correlated the activity of CM cells and motor units and found that most of the motor units were facilitated by single CM cells. Thus, CM cells are likely to exert divergent effects on most, if not all, motor units of a facilitated target muscle, much like Ia afferent fibers.

In addition to their excitatory effects on motoneurons of their target muscles, both Ia afferent fibers and CM cells may exert *inhibitory effects* on antagonists of the target muscles. In the case of Ia afferents, a powerful

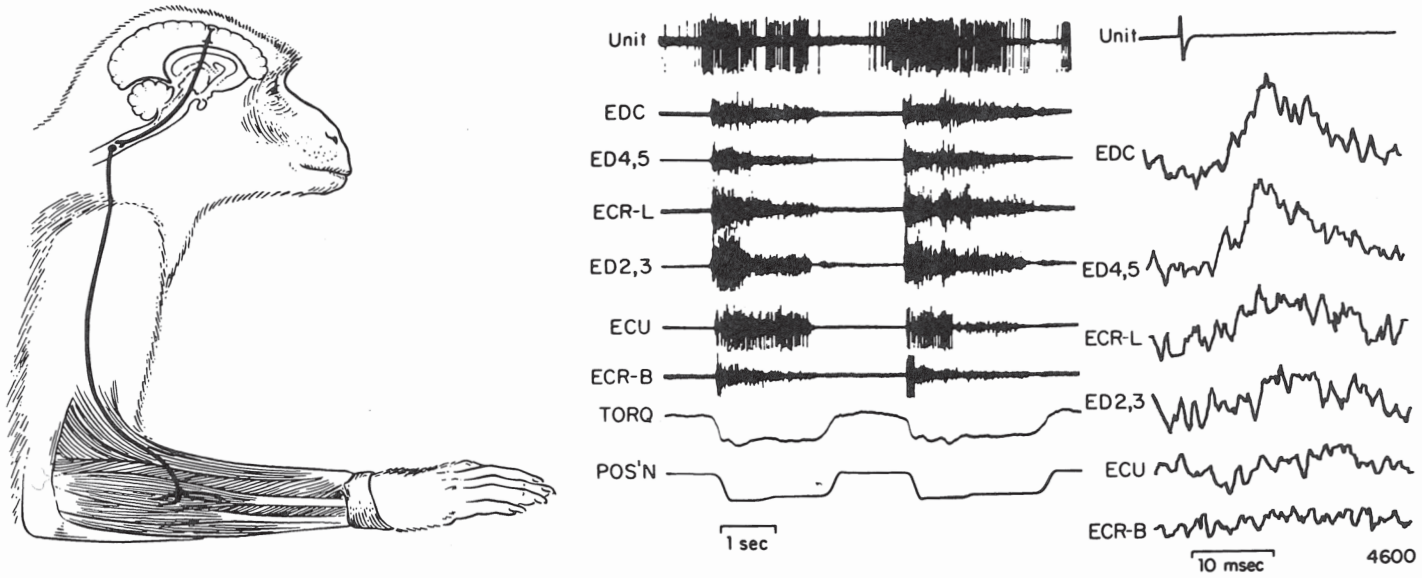

Fig. 20–2. *Left*: schematic diagram of a CM cell connected to a motoneuron of an extensor wrist muscle. *Middle*: responses of an extension-related CM cell during wrist movements against an elastic load with coactivated extensor muscles of the wrist (ECR-L; ECR-B; ECU) and the digits (EDC; ED4, 5; ED2, 3). *Right*: STAs of rectified EMG showing postspike facilitation in several target muscles. (Redrawn from Fetz and Cheney, 1978.)

reciprocal inhibition is mediated by the Ia inhibitory interneuron, which also receives monosynaptic input from corticospinal cells in the monkey (Jankowska et al., 1975). Experiments designed to test the effect of CM cells on antagonists of their target muscles have revealed reciprocal inhibition. Single intracortical microstimuli delivered at the site of CM cells typically produce poststimulus facilitation in the cell's target muscles. When delivered during the phase of movement in which the antagonists of the target muscles were active, these stimuli produced reciprocal inhibition on antagonists from about one-third of the cortical sites (Cheney et al., 1985). The postspike effects of *single* CM cells on antagonists of their target muscles are more difficult to document with STA, since the cells and antagonists are normally activated reciprocally. However, by activating CM cells with glutamate during the phase of movement in which they would normally be inactive, Kasser and Cheney (1985) showed that about one-third of the extensor-related CM cells inhibited flexor muscles, and one-sixth of the flexor CM cells produced reciprocal inhibition of extensor muscles. An example of such a reciprocal CM cell is illustrated in Figure 20–3. The averages at the top show the postspike and poststimulus effects on the forelimb muscles, illustrating facilitation of extensors and inhibition of flexors.

RESPONSE PROPERTIES OF CM CELLS: COMPARISON WITH MOTOR UNITS

In addition to elucidating the organization of divergent output effects on different target muscles, chronic recording experiments have provided new information on the *response patterns* of CM cells under normal behavioral conditions. Monkeys performed ramp-and-hold wrist movements, which were designed to reveal the relation of cell activity to phasic change in force as well as tonic sustained force. During this task, the response patterns of CM cells fell into four categories (Cheney and Fetz, 1980). The predominant cell type (half of the CM cells) exhibited a phasic-tonic discharge pattern, consisting of a phasic burst of activity at the onset of movement, followed by tonic discharge during the static hold period (Fig. 20–4). The next most frequent type (28%) was the tonic CM cell, with constant firing during the static hold period. For both types, the tonic activity was proportional to the amount of isometric force that the animal exerted. The remaining two categories of CM cells were those that showed a gradually increasing level of activity during the hold period, either with or without a preceding phasic burst of activity at the onset of movement.

The response patterns of CM cells can be contrasted with those of motor units in the agonist muscles (Palmer and Fetz, 1985a). Under similar behavioral conditions, forelimb motor units showed four types of response patterns: phasic-tonic (23%), tonic (33%), phasic (5%), and decrementing (39%). The possibility of preferential correlational links between particular types of CM cells and motor units remains to be investigated.

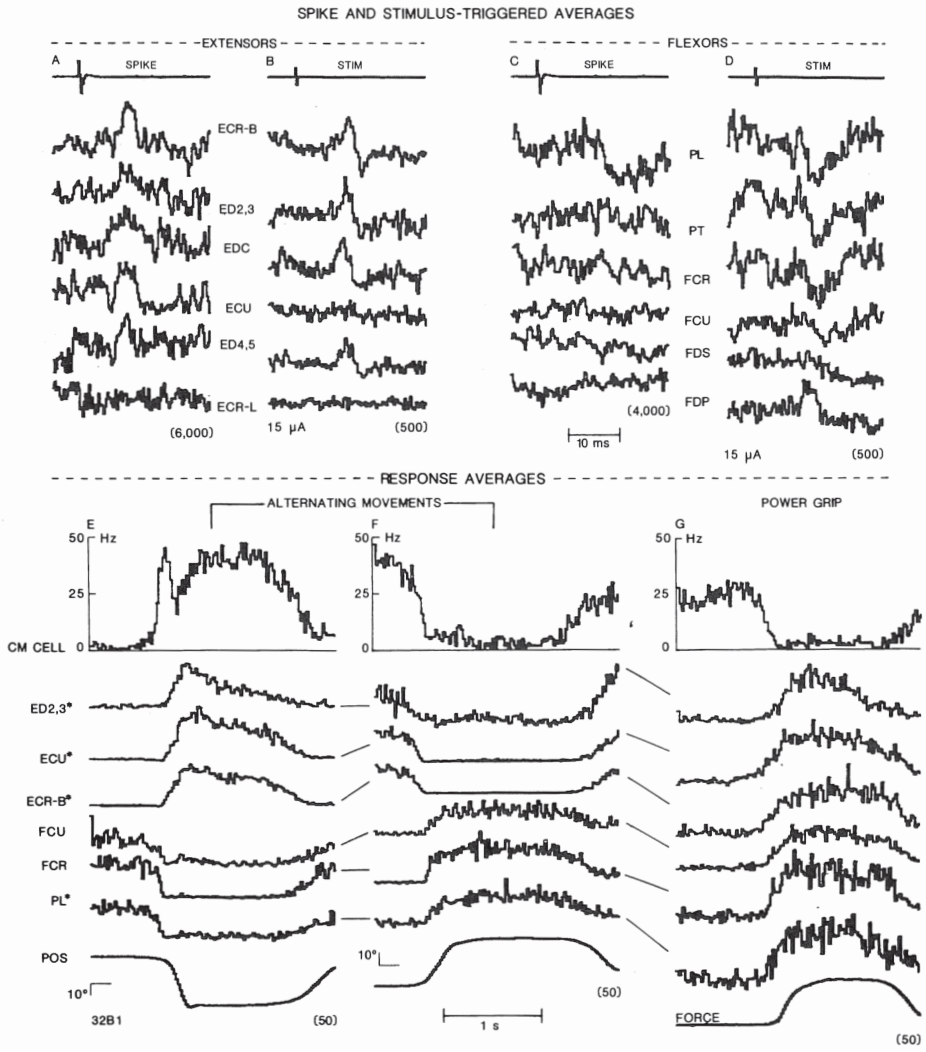

Fig. 20–3. Postspike effects of a reciprocal CM cell and its responses during alternating wrist movements and power grip. Top records show reciprocal correlational linkages of the cell: postspike facilitation of extensor muscles (A) and postspike suppression of flexors (C). These reciprocal output effects are further demonstrated by similar patterns of poststimulus effects in averages triggered from single-pulse microstimuli (15 μa) delivered at the site of this CM cell (B, D). Response averages at the bottom show that the CM cell was coactivated with its target muscles during alternating wrist movements (E, F). The cell was suppressed during cocontraction of extensors and flexors in the power grip (G). Target muscles are indicated by asterisks. In this and subsequent figures, the numbers in parentheses indicate the number of events averaged. (From Cheney et al., 1985.)

As would be expected, the tonic discharge of both CM cells and motor units is an increasing function of the amount of static force that the monkey exerts. However, there is a clear difference in the recruitment properties of CM cells and motor units as a function of active force. In accordance with Henne-

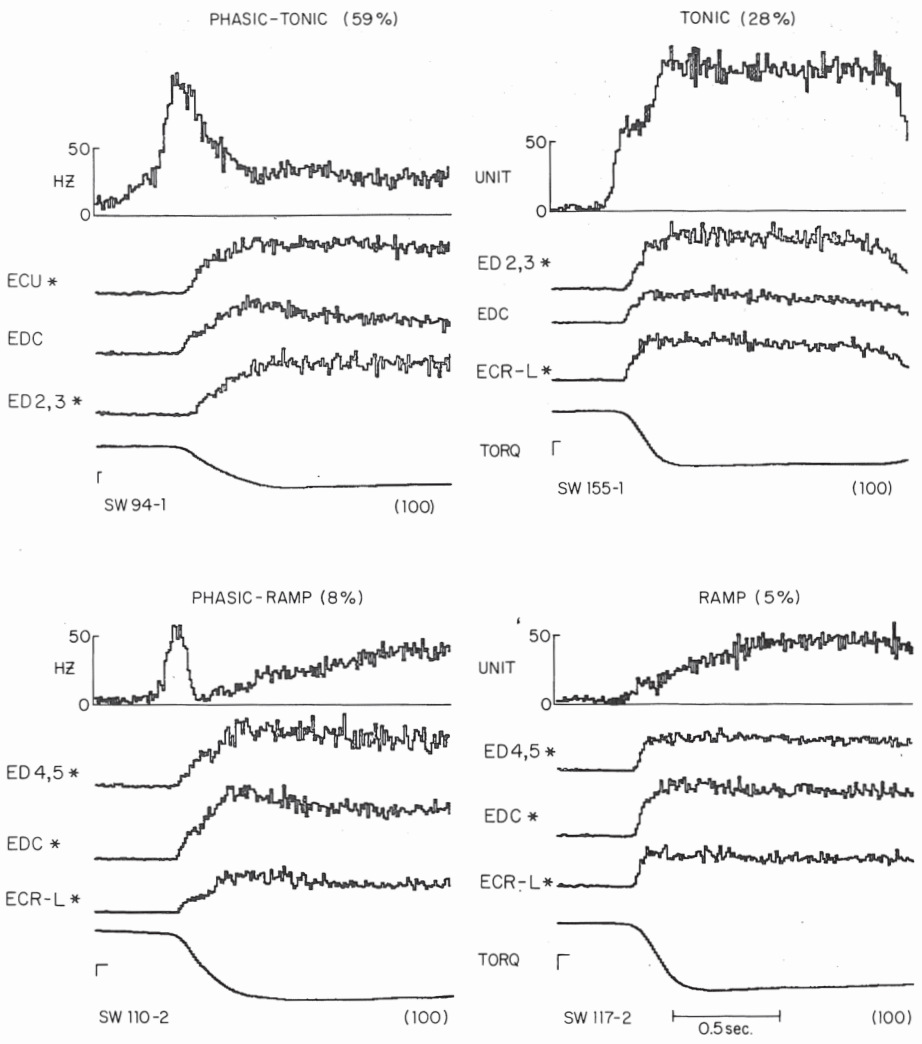

Fig. 20–4. Response patterns of CM cells and target muscles during generation of isometric ramp-and-hold torque responses. Each set shows the time histogram of CM cell activity, averages of rectified EMG (target muscles indicated by asterisk), and isometric torque. (From Cheney and Fetz, 1980.)

man's size principle, different motor units were found to be recruited into sustained activity over a range of static force levels (Palmer and Fetz, 1985a). In contrast, almost all the CM cells were active even at the lowest force levels and increased their discharge rate as a function of increasing force (Cheney and Fetz, 1980). At the upper range of forces, the CM cells tended to reach higher firing rates than the motor units, whose rates typically saturated.

Although CM cells seem to have a lower recruitment level than their target motor units, this applies specifically to well-controlled movements. CM cells are much more active during finely controlled movements than during rapid or

forceful movements, despite the fact that the latter involve greater activity in their target muscles. For example, Muir and Lemon (1983) found that CM cells were strongly modulated during a precision grip task performed with the thumb and forefinger, but, paradoxically, were less active during a power grip. Similarly, our monkeys[1] CM cells fired intensely during the ramp-and-hold tracking task, but were curiously inactive during rapid ballistic shaking of the wrist manipulandum (Cheney and Fetz, 1980). Schieber and Thach (1985) also noted that many motor cortex cells, as well as spindle afferents, exhibited enhanced activity during a precisely controlled slow tracking task. This suggests that different input systems may be preferentially recruited to activate motoneurons during different types of movements.

An example of such a dissociation between a CM cell and its target muscles is illustrated in Figure 20–3. This CM cell fired strongly in association with its facilitated extensor muscles when the monkey performed alternating ramp-and-hold movements (bottom left). However, when the monkey performed a power grip that involved coactivation of flexor and extensor muscles, this cell became entirely inactive (bottom right). In this case, the cell's inhibitory effect on the flexor muscles (top right) may provide a rationale: this post-spike suppression would be inappropriate during a response that requires coactivation of the flexor muscles. Indeed, CM cells that produced reciprocal inhibition of antagonists were more likely to decrease their activity during cocontraction of flexors and extensors than CM cells that only facilitated their target muscles (Kasser and Cheney, 1983). It seems noteworthy that during cocontraction of antagonist muscles the nervous system appears to circumvent this inappropriate inhibition by turning off the reciprocal CM cells rather than by the plausible alternative of suppressing the mediating inhibitory interneuron.

CENTRAL VERSUS PERIPHERAL CONTROL OF MOTONEURONS

The function of CM cells, as well as of other descending pathways, is commonly considered to be quite different from the function of monosynaptic input from Ia afferents. The anatomical location of supraspinal versus peripheral afferents suggests the obvious functional distinction, namely, that descending tracts provide pathways for voluntary activation of motor units, while peripheral input provides a feedback system for stabilizing muscle force in the face of changing loads. This functional dichotomy is based on the idea that CM cells are under central control during voluntary movement, whereas muscle afferents are driven predominantly by peripheral stimuli. In light of accumulating evidence, this model is now considered simplistic. In addition to being activated by peripheral events, the Ia afferents may be affected by centrally originating input via gamma bias on the spindle. This gamma bias provides a potent pathway for control of spindle activity from central sources. The remarkable experiments of Schieber and Thach (1985) suggest that Ia afferents are intensely active for finely controlled, slow tracking movements.

Similarly, CM cells are not only activated by central input (which accounts

for their activity prior to voluntary movement), but are also responsive to peripheral input from proprioceptors and cutaneous afferents. One function of this peripheral input is demonstrated by experiments in which active movements are perturbed by load changes. Stretch of an active muscle evokes responses in Ia afferents that produce a segmental reflex that helps to counteract the lengthening. This well-known myotatic stretch reflex is manifest in the early M1 EMG response following muscle stretch. The M1 is followed at longer latencies by an M2 response, sometimes called the "functional stretch reflex" (see Desmedt, 1978, for reviews). Phillips (1969) initially proposed that pyramidal tract neurons may function in a transcortical stretch reflex analogous to the segmental stretch reflex. Indeed, CM cells have been shown to contribute to M2 (Cheney and Fetz, 1984). However, there is an important difference in the responses evoked by transcortical and peripheral pathways. While Ia afferents are activated by passive stretch of their parent muscle and are inactivated by passive shortening of their parent muscle, many CM cells are activated by *both* types of movements. This bidirectional excitation of many CM cells

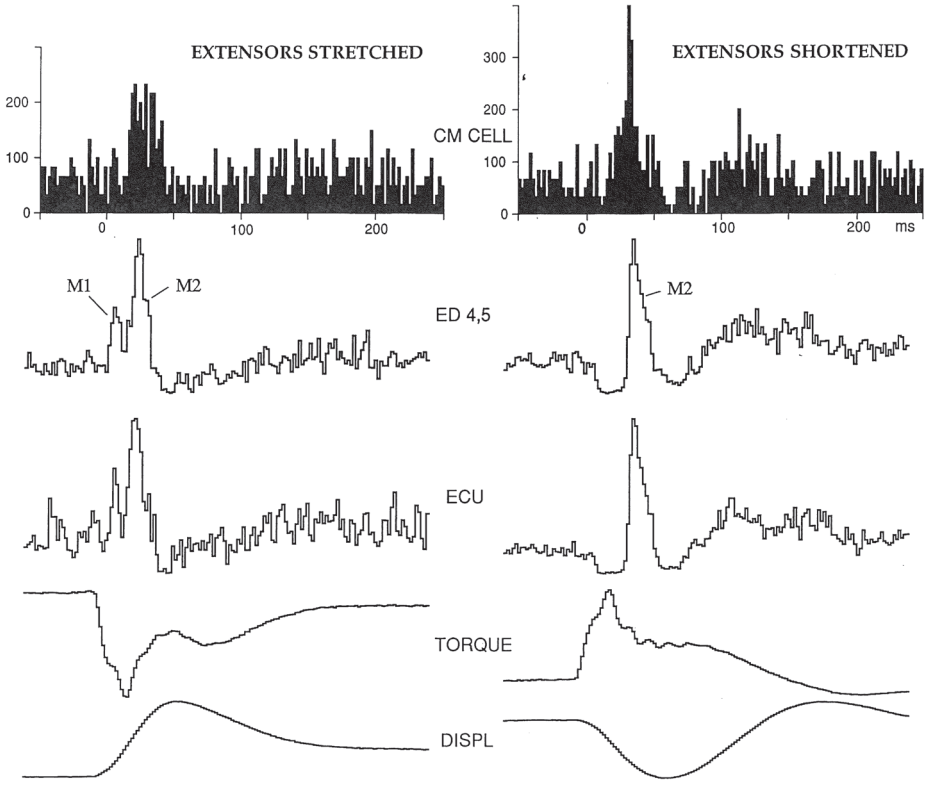

Fig. 20–5. Response of extensor CM cell and extensor muscles to brief perturbations applied during active wrist extension. This cell, like half of the CM cells, responded ubiquitously to perturbations that either stretched (left) or shortened (right) its target muscles. Note that in contrast to the reciprocal M1 response, the later M2 response was bidirectional, like the response of the CM cell.

(about half) might seem paradoxical but is in fact consistent with the observed coactivation of flexors and extensors during the functional stretch reflex. Figure 20–5 illustrates the responses of such a CM cell and its target muscle to brief load changes imposed while a monkey exerts a steady force. The initial M1 response appears only with perturbations that stretch the active muscle (left), but the later M2 response is evoked by both flexion and extension perturbations of the wrist. This bidirectional response in CM cells and muscles also serves to stabilize movements, but unlike the reciprocal stretch reflex that specifically counteracts the perturbation, such coactivation of flexors and extensors stiffens the joint. This stiffening response serves to stabilize the joint against subsequent perturbations. The involvement of motor cortex in this stabilizing reflex could provide an effective mechanism for its central modulation.

CONCLUDING COMMENTS

To summarize the points of comparison between CM cells and Ia fibers, the organization of their terminal connections appears quite analogous: Both send divergent terminals to multiple muscles, and probably most of the motoneurons in their target muscles. A distributed connection to all motoneurons of the target pool would be consistent with the recruitment of motoneurons in order of size (Henneman and Mendell, 1981). In addition, many CM cells, like Ia afferents, produce reciprocal inhibition in antagonists of their target muscles; indeed, this inhibition may be mediated by the same Ia inhibitory interneuron. Both CM cells and Ia afferents are subject to central as well as peripheral input. However, their responses to load perturbations indicate that Ia afferents mediate a stretch reflex that specifically counteracts change in muscle length, while CM cells mediate a cocontraction of flexors and extensors that stiffens the joint.

Comparisons between the responses of CM cells and motoneurons show that the CM cells are considerably more active at low levels of force. While CM cells are recruited before their target motor units during fine movements, the latter are more active than CM cells during rapid forceful movements. The ability to make these comparisons owes much to the pioneering work of Elwood Henneman and his colleagues, which provided essential information on the properties of motoneurons and Ia fibers; future work on quantitative analysis of other inputs to motoneurons will continue to employ the techniques they pioneered to investigate this model system.

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