

ROLE OF MOTOR CORTEX CELLS IN CONTROL OF OPERANTLY CONDITIONED MUSCLE ACTIVITY

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INTRODUCTION

In the primate, precentral motor cortex plays an important role in both the learning and execution of voluntary limb movements, particularly those involving discrete patterns of muscle activity. A better understanding of the neural mechanisms underlying voluntary movements seems a prerequisite to the eventual goal of understanding the neural mechanisms of operant conditioning per se, i.e., how the occurrence of a reinforcing stimulus changes the probability of an operant response. The role of motor cortex cells in voluntary control of limb muscles has been elucidated recently by studies of neural activity in behaving animals, operantly conditioned to perform relevant motor responses. The functional relations between cortical cells and limb muscles are particularly well elucidated by experiments that test for constraints in their interactions.

The degree to which voluntary muscle responses can be differentiated appears to have definite limits. While different limb muscles may be activated in various combinations during voluntary movements, different motoneurons within a muscle cannot be activated so independently: their relative recruitment order is to a large extent fixed by inherent physiological constraints. The existence of comparable constraints in relative activation of motor cortex cells and motor units would be of some consequence to any final explanation of voluntary movement. This question is addressed by observations of cell and muscle activity during operantly conditioned response patterns.

This chapter reviews experimental evidence from a variety of studies in humans and monkeys that suggest differences in the degree to which

activity of motor units and motor cortex cells may be independently controlled.

CONSTRAINTS IN RELATIVE RECRUITMENT ORDER

Motor Units

Initial experiments on the voluntary control of single motor units in human muscles had suggested a remarkable ability to recruit different motor units independently. For example, Harrison & Mortensen (1962) found that a human subject with auditory feedback could activate any one of six motor units in tibialis anterior independently of the others. These motor units were recruited at low force levels and "slight changes of the foot or leg were sometimes effective" in their isolation. Similar observations were reported by Basmajian (1973), who asked human subjects to fire different motor units in hand muscles at will. Under isometric conditions, however, in which limb movements are eliminated, the relative recruitment order of different motor units is more difficult to reverse. Whether or not two motor units can be activated independently depends on their critical firing level—i.e., the level of muscle force at which the unit normally begins to fire. Under isometric conditions, awake human subjects found it difficult to change the relative recruitment order of motor units whose critical firing levels differed appreciably (Henneman et al., 1976). Although the lower threshold unit could variably be activated in isolation, it was not possible to discharge the higher threshold unit without coactivating the lower threshold unit.

These apparently discrepant reports may be explained in part by the observation that when the subject is free to move, the motor unit recording electrode may be repositioned in the muscle and may therefore be isolating different motor units at different times and may record different waveforms for the same motor unit (Thomas et al., 1978).⁵ The regular recruitment order of motor units under controlled isometric conditions has been confirmed in a number of different laboratories (Henneman et al., 1976; Milner-Brown et al., 1973; Tanji & Kato, 1973; Thomas et al., 1978). However, there remains some evidence that the recruitment order observed during slower movements may be reversed during quick, rapid responses (Hanerz, 1973). Nevertheless, when recruitment was systematically related to peak ballistic force, Desmedt & Godaux (1976) found the same recruitment order for ballistic and slow contractions. It seems, therefore, that on balance the experimental evidence indicates a limit in the degree to which motor units of a muscle can be independently controlled.

Motor Cortex Cells

Just as motor unit discharge can be studied as an operant response, so can activity of cells in precentral motor cortex. Experiments in which single motor cortex neurons were operantly reinforced indicate that

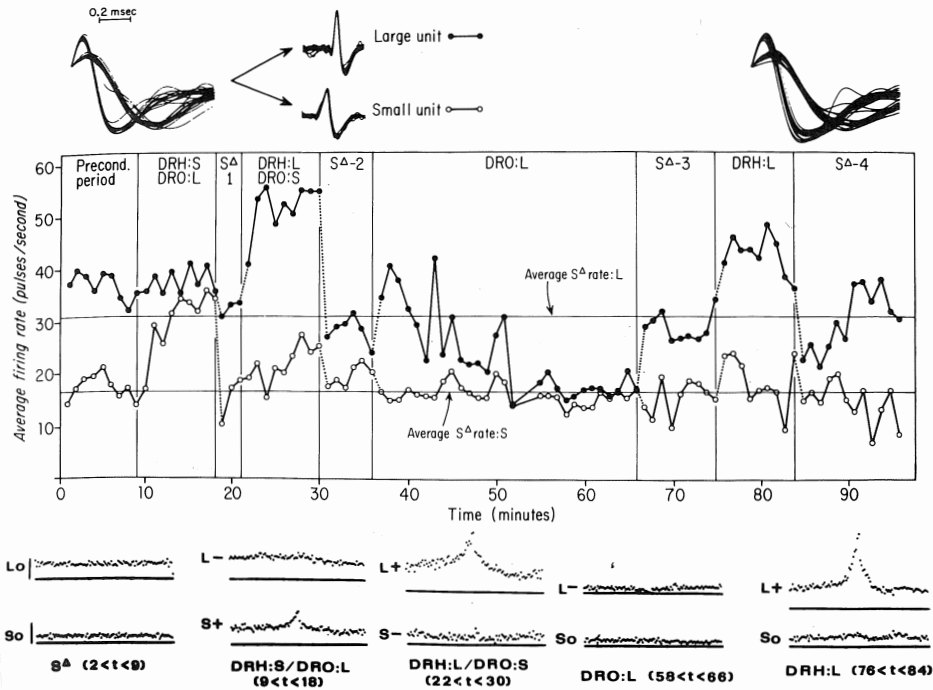


Fig. 1. Operant conditioning of a pair of adjacent motor cortex cells related to knee movement. Insets at top illustrate action potentials of large (L) and small (S) units, whose firing rates are plotted in 1-min intervals. During "Operant level" and S^{Δ} periods, the reinforcement and meter feedback were turned off. During the "DRH:S/DRO:L" period, high rates of the small unit and simultaneous suppression of the large unit were reinforced; the reverse contingency was in effect during "DRH:L/DRO:S." During DRO:L, suppression of activity in the large unit was reinforced with no contingency on the small unit. Response averages (bottom) show time histograms of large and small unit rates for 2-sec periods aligned around feeder discharge; these were compiled during the time interval indicated in parentheses. Vertical bars calibrate 50/sec firing rate. (Fetz & Baker, 1973.)

conditioned monkeys could voluntarily activate virtually any motor cortex cell (Fetz & Baker, 1973; Schmidt et al., 1977; Wyler et al., 1975, 1980). In contrast to motor units of a muscle, adjacent motor cortex cells that were associated with a given movement could often be independently controlled. Figure 1 illustrates a pair of precentral cells that were consistently coactivated with active flexion of the knee and were both driven by passive extension of the knee. To test whether the monkey could activate the cells

independently, we presented a differential schedule rewarding the monkey for increasing the firing rate of one cell and simultaneously reducing the activity of the other. As shown in Fig. 1, the monkey readily increased the activity of either cell without increasing the firing rate of the other. Moreover, the animal could also suppress cell firing as well as increase it. Similar results were obtained with other pairs of precentral cells, suggesting that the activation of motor cortex cells associated with a given joint may be more flexible than the recruitment of motor units of a given muscle. However, since the muscles to which these cells may have been linked remain unknown, the dissociation of adjacent motor cortex cells may be more analogous to the dissociation of adjacent muscles.

In studies rewarding the activity of motor cortex cells, the monkeys often performed some limb movement in association with the operant bursts of cell activity (Fetz, 1974; Schmidt et al., 1977; Wyler & Burchiel, 1978). These associated movements often became quite specific and sometimes dropped out as bursts of the same unit continued to be reinforced. Some precentral cells were activated in operant bursts with no associated movements or muscle activity (Fetz & Baker, 1973; Fetz & Finocchio, 1975).

Recruitment of Motor Cortex Cells Vs. Muscles

To test the relation of single motor cortex cells to specific forearm muscles directly, we operantly reinforced various patterns of isometric activity (Fetz & Finocchio, 1975). Figure 2 illustrates a representative precentral neuron that was consistently coactivated with the biceps muscle and with a wrist flexor under several different behavioral conditions. Isolated activation of biceps muscle produced clear coactivation of the cell (Fig. 2C), and operant reinforcement of unit activity with no contingency on the muscles produced coactivation of biceps, as well as wrist muscles (Fig. 2E). As might be expected, this unit was also coactivated with biceps during active elbow flexion. Yet, when the unit-biceps coactivation was directly tested by operantly rewarding its dissociation, the monkey activated the unit without coactivating any muscles (Fig. 2F). This degree of flexibility was revealed only when it was specifically tested. All the motor cortex cells that were similarly tested could be readily activated without coactivating any of the muscles that had been previously associated with the cell.

The reverse dissociation—muscle activation in the absence of motor cortex cell activity—was not so readily achieved. Figure 2G illustrates the response patterns obtained with this schedule; although the monkey increased the relative amount of biceps activity, this was still accompanied by some activity in the unit. It remains possible that the inability to suppress the cortical cell activity did not reflect a physiological constraint, but rather was due simply to behavioral causes. This last schedule was presented after the monkey had worked many hours on other schedules, so the fact that he did not achieve greater unit suppression may be attributable to satiation or fatigue.

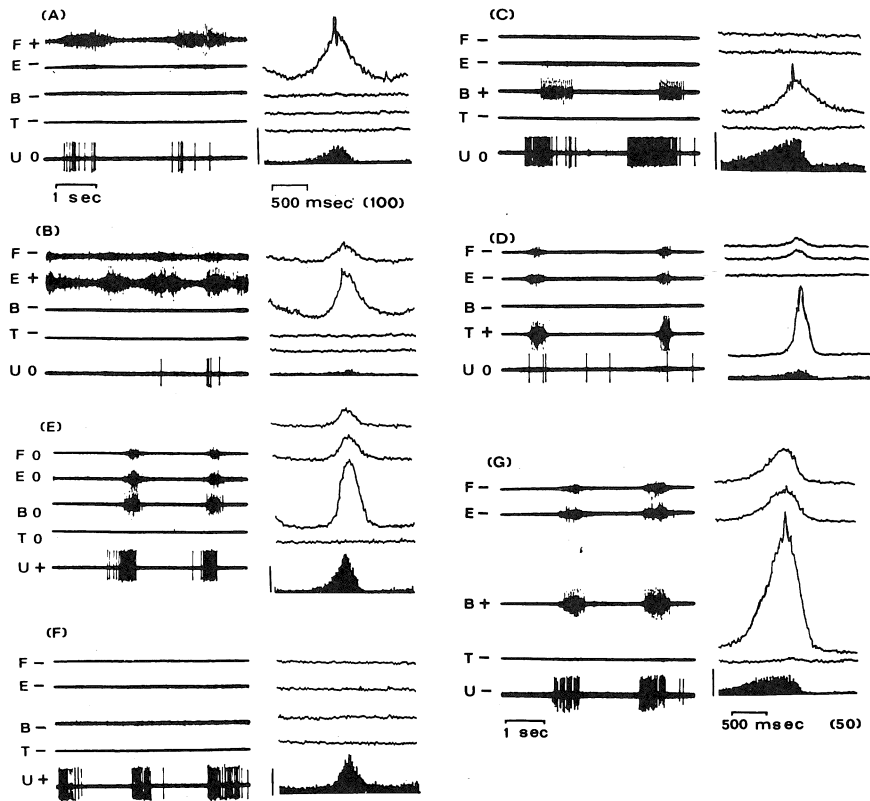


Fig. 2. Operantly conditioned response patterns of precentral cell and four contralateral forearm muscles. Response trials at left illustrate successive reinforced activity patterns and response averages at right show profile of reinforced responses. These isometric responses were performed with the elbow angle fixed at 90° and the wrist at 180° . The muscles include flexor carpi radialis (F), extensor carpi radialis (E), biceps (B) and triceps (T). A "+" indicates elements whose activation was rewarded; a "-" indicates elements whose simultaneous suppression was required; 0 indicates elements whose activity was not included in the reinforcement contingency. (A-D) differential reinforcement of isolated bursts of EMG activity in each arm muscle with no contingency on the cortical unit activity; (E) operant unit bursts reinforced with no contingency on the muscle; (F) reinforcement of operant unit bursts and simultaneous muscle suppression; (G) response pattern when isolated biceps activity and simultaneous unit suppression were reinforced. Vertical bars calibrate firing rate of 50/sec. (Fetz & Finocchio, 1975.)

It is relevant to note that even if the monkey had suppressed this unit during activation of the biceps, there could be a simple explanation. The unit might have been associated with a synergist muscle, such as brachialis, that could be activated independently, or it might not have had any output to muscles whatsoever. To resolve such questions, we need an independent means of determining the output connections of cells under behavioral conditions. Such a test is provided by the technique of spike-triggered averaging of EMG activity (Woody & Black-Cleworth, 1973; Fetz & Cheney, 1979).

RELATIVE RECRUITMENT OF CM CELLS AND THEIR TARGET MUSCLE

In monkeys performing alternating flexion and extension of the wrist, it has been possible to identify those motor cortex cells that have output effects on agonist muscles by compiling spike-triggered averages of rectified EMG activity (Fetz & Cheney, 1979, 1980). Certain precentral cells generate a clear postspike facilitation (PSF) of motor unit activity consisting of a transient increase in the average EMG level, reaching a peak at about 10 msec after the spike. The latency and magnitude of such facilitation are consistent with the expected effects of corticomotoneuronal linkage, so we refer to the cells generating clear PSF as CM cells. To optimize chances of detecting CM cells, we recorded activity of several muscles simultaneously and found that over half of the CM cells facilitate more than one target muscle. The relative activation of CM cells and their target muscles is of particular interest, since the PSF indicates a direct correlational linkage.

The firing patterns of CM cells during ramp-and-hold wrist movements fall into four characteristic response patterns (Fig. 3). The most common type (59% of CM cells) is the phasic-tonic pattern, characterized by a phasic burst of activity at onset of movement, followed by a steady discharge during the static hold period. The next most common response pattern (28%) is tonic activity during the hold period, without any burst of activity at onset. The remaining CM cells have a gradually increasing firing rate during the hold period, which may or may not be preceded by a burst at onset.

With regard to the issue of their relative recruitment order, we have noted two conditions under which CM cells are active without their target muscles. As illustrated in Fig. 3, during ramp-and-hold movements many CM cells typically begin their firing pattern well before activation of their target muscles. Figure 4 plots the time of onset of activity in CM cells relative to onset of their target muscles. Many CM cells, particularly those whose firing begins with a burst, increased their firing rate several hundred milliseconds before their facilitated motor units became active. This would suggest that even motor cortex cells with direct linkages to motoneurons may be activated in the absence of any peripheral activity. The second condition in which CM cells can be activated without their target muscles is in response to adequate natural stimulation--usually

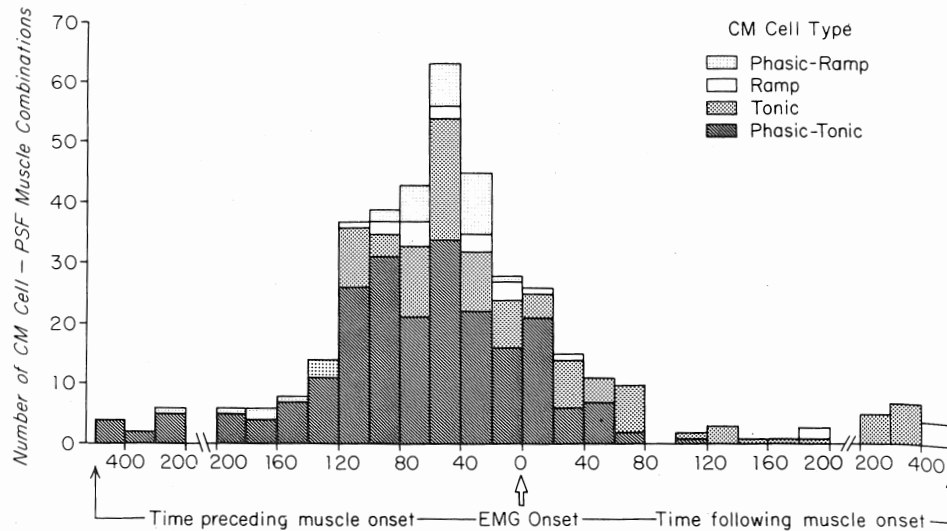


Fig. 4. Onset times of CM cell activity relative to onset of EMG activity in muscles facilitated by each cell. Origin of abscissa indicates time of onset of target muscle activity, and histogram plots relative onset time of CM cell preceding and following muscle onset (msec). Response pattern of CM cells during ramp-and-hold movements is indicated separately by shading. For CM cells that facilitated several muscles, the relative latencies are plotted for each muscle. (Cheney & Fetz, 1980.)

passive joint movements that stretch their target muscles. Since cortico-motoneuronal EPSPs are not sufficiently large to activate the motoneurons by themselves, it is understandable that CM cells could be activated without necessarily recruiting their target muscles into activity.

There is also some evidence for the reverse dissociation, namely, activation of target muscles without activation of the CM cells that facilitate them. Under certain response conditions the target muscles were found to be activated in the relative absence of CM cell activity, viz., when the movement was ballistic rather than a controlled ramp-and-hold movement. Some CM cells observed under both types of movement conditions showed an appreciable discharge when the monkey carefully performed the ramp-and-hold movements; but when, in apparent frustration with the task, he alternately flexed and extended the wrist rapidly, the same CM cells remained paradoxically inactive, although their target muscle exhibited the most intense EMG activity (Cheney & Fetz, 1980). Presumably, the motor units activated during the ballistic responses included those that the CM cells facilitated; if so, this could indicate that the target motor units could be activated in the relative absence of CM cell activity during ballistic movements.

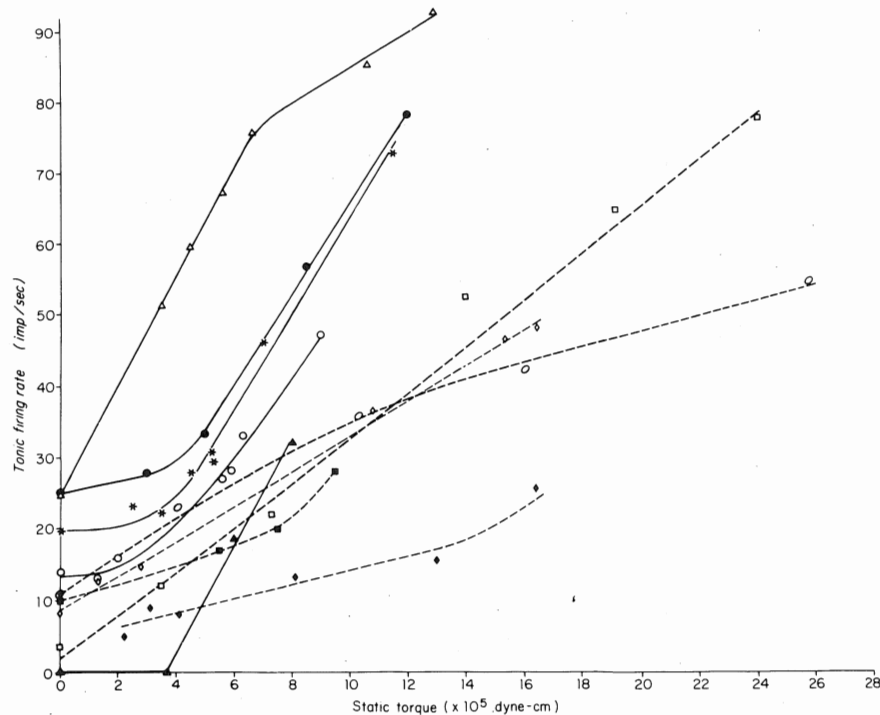


Fig. 5. Tonic firing rate of CM cells during static hold period plotted as a function of active torque. Representative examples of CM cells related to extension (—) and flexion (- - -). Most CM cells were active even at lowest levels of active force; only one CM cell (\blacktriangle) was recruited into activity at higher levels of static torque. (Fetz & Cheney, 1979.)

Even during controlled ramp-and-hold movements, there was some evidence of target muscle activity without CM cell firing. Some CM cells whose firing pattern had no burst at onset began to fire after their target muscles had become active (Fig. 4). When the activity of CM cells was documented during generation of increasing amounts of active force during the hold period, only one CM cell was recruited at a higher level of static force than its target muscle. While single motor units of agonist muscles are recruited sequentially as force is increased (Milner-Brown et al., 1973; Tanji & Kato, 1973), most CM cells appear to be recruited at the lowest levels of active force. They contribute to higher levels of force more by increasing their firing rate than increasing the number of active CM cells (Fig. 5). One observed exception was a CM cell that became active at higher force levels, well after its target muscles had been recruited into activity (\blacktriangle in Fig. 5). It may be possible to search out more such CM cells that are activated after their target muscles, but most of the CM cells observed to date were recruited at the lowest levels of muscular force.

Under normal conditions, then, the activation of CM cells without their target muscles occurs more commonly than the reverse dissociation. The final determination of the degree to which CM cells and their target muscles can be independently controlled awaits direct operant conditioning of their activity. This will confirm whether any CM cell can be bidirectionally dissociated from the motoneurons that it facilitates.

CONCLUSIONS

Taken together, these results suggest that precentral motor cortex cells undergo a much greater variety of activity than is reflected in the activity of motoneurons. The modulation of motor cortex cells without peripheral muscle activity has also been observed under other behavioral conditions. Following a cue for a delayed response, some precentral cells fire in anticipation of an intended movement (Tanji & Evarts, 1976; Thach, 1977). It seems likely that considerable subthreshold activity involved in integration and initiation of learned voluntary movements occurs in precentral motor cortex. The fact that many pyramidal tract neurons discharge more intensely with fine controlled movements than with ballistic responses (Fromm & Evarts, 1977; Cheney & Fetz, 1980) suggests that these cortical cells are particularly concerned with control of discrete learned movements. The interactions between motor cortex cells and muscles can be further analyzed by the application of operant conditioning techniques to control their activity directly.

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