Functional Relations between Primate Motor Cortex Cells and Arm Muscles

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That the motor cortex plays a significant role in performance of limb movements is clear from the paresis produced by its ablation, the muscle contractions evoked by its stimulation (Asanuma & Rosen, 1972; Chang, Ruch, & Ward, 1947), the known corticomotoneuronal connections of many pyramidal tract cells in the primate (Kuypers, 1960; Phillips & Porter, 1964; Porter & Hore, 1969; Preston & Whitlock, 1961), and the covariation of motor cortex cell activity with movements (Evarts, 1967; Fetz, 1974; Fetz, Cheney, & German, 1976; Fetz & Finocchio, 1975; Fetz, Finocchio, Baker, & Soso, 1974; Humphrey, Schmidt, & Thompson, 1970). Yet the details of the functional relations between specific motor cortex cells and contralateral limb muscles remain relatively unresolved. In comparison, our understanding of the functional organization of cells in sensory systems is relatively well developed, primarily due to the ease of determining their receptive fields and deducing the necessary degrees of convergence and divergence between cells at successive levels. We know relatively little concerning hierarchical relations between cells in motor systems. In the primate, single spinal motoneurons receive a convergence of monosynaptic input from a "colony" of corticomotoneuronal (CM) cells, whose spatial distribution may extend over wide areas of cortex (Phillips & Porter, 1964). The degree to which terminals of single CM cells may diverge to different motoneurons remains unknown; in the absence of concrete evidence it has been commonly assumed that CM cells project to motoneurons of only one muscle.

To investigate the functional relations between individual motor cortex cells and arm muscles, we have recorded their activity in alert monkeys trained to perform appropriate behavioral responses. These experiments have employed two basic types of observations. Consistent *covariation* between activity of motor cortex cells and arm muscles during specific motor responses have been documented as evidence for *functional relations*. More

recently, *cross-correlations* between cell and muscle activity have been used to statistically detect the existence and extent of *functional connections.*

The covariations between cell and muscle activity have been observed during three types of motor responses: controlled active and passive limb movements, and operantly reinforced patterns of muscle activity and of cell activity. To investigate the relation of cell activity to parameters of limb movement, we trained monkeys to alternately flex and extend the elbow or wrist against a programmed load (Fetz, Finocchio, Baker, & Soso, 1974). Many cells became active prior to and during either flexion, extension, or both. The responses of the same cells during comparable passive movements were also investigated, to document the sensory input from peripheral receptors. Most primate motor cortex cells responded to passive movement of one or more joints (75%); relatively few could be driven by cutaneous stimulation (8%) and some had no demonstrable sensory input (17%). Responses to passive joint movements could originate in muscle stretch receptors or in joint receptors, and it was not always possible to resolve these. Usually these cells also fired repeatedly during active movements of the same joint. For some cells the effective active movement was in the *opposite* direction as the effective passive movement. If the output of such cells contributes to activation of agonist muscles during active movements and if their sensory input during passive movements derives from stretch receptors of the same muscles, such cells would clearly be involved in a cortical "stretch" reflex. For other cells the effective active movement was in the *same* direction as the effective passive movement. Such a pattern would be consistent with input from joint receptors which undergo the same activation during active and passive movements. If such cells contribute to activation of agonist muscles, they could clearly be involved contribute to activation of agonist muscles, they could clearly be involved in a "positive" cortical feedback loop. We have observed both types of cells in roughly equal proportion, as well as many others with more complex patterns, e.g., activation during passive and active movements in both directions (Fetz, Finocchio, Baker, & Soso, 1974). Such diversity of active and passive responses precludes any simple conclusions concerning one predominant input-output relation for the majority of motor cortex cells.

The observation of cell activity during controlled limb movements provides only limited evidence concerning which muscles the cell may be functionally related to since many muscles are usually coactivated in a stereotyped pattern. To determine how single motor cortex cells are related to individual forelimb muscles, monkeys were trained to isometrically contract each of four representative arm muscles in isolation (Fetz & Finocchio, 1975). Each cell was observed during relatively isolated contractions of a flexor and extensor muscle of wrist and elbow. Most cells were found to be coactivated with more than one muscle. Some cells were activated with two antagonistic muscles of the same joint; others fired with both wrist and elbow muscles; still others exhibited the same pattern with all four muscles, as if more related to the occurrence of a response than its topography. These observations suggest

that single motor cortex cells may have a higher order relation to muscles than the one-to-one relation of motoneurons.

Similar conclusions were reached in experiments in which activity of the cortical cell was reinforced and correlated muscle activity observed (Fetz, 1969; Fetz, 1974; Fetz & Baker, 1973). By training the monkey to activate individual motor cortex cells in "operant bursts", the movements in which that cell fired could be qualitatively observed. For some cells these movements were quite generalized and variable; for other cells the movements were relatively specific and repeatable; still other cells were activated with no observable concomitant motor responses (Fetz & Baker, 1973). Under isometric conditions, the set of muscles which were coactivated with operant unit bursts -- called the cell's "motor field" -- often included several different arm muscles (Fetz & Finocchio, 1975). These motor fields were usually different for different cells, even in the same region of motor cortex. The fact that many muscles were usually coactivated with a given cell is again consistent with a higher order functional relation with several muscles.

Some precentral units were observed to covary consistently with the same muscles under several different behavioral conditions: active limb movement, isolated muscle activity, or operantly reinforced unit bursts. When the stability of such a consistent unit-muscle correlation was tested by operantly reinforcing its dissociation, the monkey readily fired the cortical cell in the absence of any movement or muscle activity (Fetz & Finocchio, 1975). This suggests that unit-muscle correlations may be shown to be quite flexible when their dissociation is differentially reinforced.

Although consistent covariation between activity of a precentral cell and contralateral arm muscle may suggest a functional relationship, it can never prove the existence of an anatomical connection. Since the effect of one motor cortex cell is subthreshold for activating a motoneuron (Phillips & Porter, 1964; Porter & Hore, 1969), consistent coactivation is neither necessary nor sufficient to establish a functional connection. To investigate whether monosynaptic connections between PT cells and motoneurons can be statistically detected in chronic animals, we applied the post-spike averaging technique of Mendell and Henneman (1971) as a convenient approximation to a true cross-correlation (Fetz, Cheney, & German, 1976). To provide prolonged periods of coactivation, monkeys were trained to flex and extend the wrist against a programmed load. Triggering the averager from action potentials of the cortical cell and summing rectified EMG activity, we found, for a small proportion of cells which covaried strongly with the movements, a clear transient facilitation of muscle activity following the cortical spikes. The latency and time course of such enhanced post-spike probability was entirely consistent with those expected from monosynaptic connections. In simultaneous recordings from different synergistic muscles of the wrist, these facilitations could appear in up to five different muscles. This suggests that the set of muscles whose motoneurons are contacted by a CM cell -- the cell's "muscle field" -- may include at least all the recorded

synergists of one joint. For some cells, the post-spike facilitation appeared in only one of the recorded muscles, suggesting these cells had more specific projections.

In summary, the fact that single motor cortex cells may consistently covary with several different muscles suggests a functional relation with diverse groups of forelimb muscles; the fact that post-spike averages reveal facilitation of multiple muscles suggests that corticomotoneuronal cells can send terminal projections to motoneurons of different synergistic muscles.

References

Asanuma, H., & Rosen, I. Topographical organization of cortical efferent zones projecting to distal forelimb muscles in the monkey. *Experimental Brain Research*, 1972, *14*, 243-256.

Chang, H.T., Ruch, T.C., & Ward, A.A., Jr. Topographical representation of muscles in motor cortex of monkeys. *Journal of Neurophysiology*, 1947, *10*, 39-56.

Evarts, E.V. Representation of movements and muscles by pyramidal tract neurons of the precentral motor cortex. In M.D. Yahr and D.P. Purpura (Eds.), *Neurophysiological Basis of Normal and Abnormal Motor Activities*, Hewlett, New York: Raven Press, 1967.

Fetz, E.E. Operant conditioning of cortical unit activity. *Science*, 1969, *163*, 955-957.

Fetz, E.E. Operant control of single unit activity and correlated motor responses. In M. Chase (Ed.), *Operant Control of Brain Activity*, Los Angeles, California: UCLA Press, 1974 , 61-89.

Fetz, E.E., & Baker, M.A. Operantly conditioned patterns of precentral unit activity and correlated responses in adjacent cells and contralateral muscles. *Journal of Neurophysiology*, 1973, *36*, 179-204.

Fetz, E.E., Cheney, P.D., & German, D.C. Corticomotoneuronal connections of precentral cells detected by post-spike averages of EMG activity in behaving monkeys. *Brain Research*, 1976, *114*, 505-510.

Fetz, E.E., & Finocchio, D.V. Correlations between activity of motor cortex cells and arm muscles during operantly conditioned response patterns. *Experimental Brain Research*, 1975, *23*, 217-240.

Fetz, E.E., Finocchio, D.V., Baker, M.A., & Soso, M.J. Responses of precentral "motor" cortex cells during passive and active joint movements. *Society for Neuroscience Abstracts*, 1974, *200*.

Humphrey, D.R., Schmidt, E.M., & Thompson, W.D. Predicting measures of motor performance from multiple cortical spike trains. *Science*, 1970, *170*, 758-762.

Kuypers, H.G.J.M. Central cortical connections to the motor and somatosensory cell groups. An experimental study in the rhesus monkey. *Brain*, 1960, *83*,161-184.

Mendell, L.M., & Henneman, E. Terminals of single Ia fibers: Location, density and distribution within a pool of 300 homonymous motoneurons. *Journal of Neurophysiology*, 1971, *34*, 171-187.

Phillips, C.G., & Porter, R. The pyramidal projection to motoneurons of some muscle groups of the baboon's forelimb. *Progress in Brain Research*, 1964, *12*, 222-242.

Porter, R., & Hore, J. Time course of minimal corticomotoneuronal excitatory postsynaptic potentials in lumbar motoneurones of the monkey. *Journal of Neurophysiology*, 1969, *32*, 443-451.

Preston, J.B., & Whitlock D.G. Intracellular potentials recorded from motoneurons following precentral gyrus stimulation in primates. *Journal of Neurophysiology*, 1961, *24*, 91-100,