

# INTRACORTICAL RECORDING OF BRAIN ACTIVITY FOR CONTROL OF LIMB PROSTHESES

Donald R. Humphrey and Leigh R. Hochberg  
Laboratory of Neurophysiology, Emory University School of Medicine  
Atlanta, GA

## ABSTRACT

Evidence is reviewed from neurophysiological studies of the motor cortex in primates in relation to the question of whether signals derived directly from this and similar regions of the brain might be used for control of assistive devices.

## HISTORICAL BACKGROUND

The concept of using signals derived directly from the brain to control prosthetic devices gained impetus in the late 1960s. Researchers in rehabilitation medicine had suggested that electromyographic (EMG) potentials from non-paralyzed muscles might be useful for the control of artificial limbs (1). At about this same time, neurophysiologists were developing techniques for recording the discharge of neurons in the brains of alert, subhuman primates performing learned movements (2).

Stimulated by these seemingly unrelated lines of research, Dr. Karl Frank, an eminent scientist at the National Institute of Neurological Diseases and Stroke (NINDS), reasoned that techniques might be developed for safe, long-term recording from neurons within the human brain. If so, signals derived directly from cells in the motor control regions of the brain could then be used to control either movements of artificial limbs or movements produced by direct electrical stimulation of paralyzed muscles. To pursue this goal, he established the Laboratory of Neural Control within the NINDS in 1968, and the extramural, Neural Prosthesis (NP) Program in the early 1970s. A major goal of both was the application of neurophysiological and electrical engineering methods to rehabilitation medicine: specifically, the development of neurally controlled prostheses for paralyzed persons. Frank also envisioned prostheses for certain deaf or blind persons, consisting of sensor-controlled stimulation of appropriate auditory or visual centers in the brain.

Through Frank's laboratory and projects funded by the NP Program, the field of neural prosthetics gained momentum. These efforts were subsequently sustained and expanded by Drs. F.T. Hambrecht and W. Heetderks, the current directors of the NP Program. The Program now supports neural prosthetic research at laboratories both in the U.S. and abroad, research that is leading to technical innovations that will advance neural prosthetics and

related areas of basic neuroscience for decades to come. An early history of the development of this field may be found elsewhere (3).

## SELECTING SITES FOR THE DERIVATION OF CONTROL SIGNALS

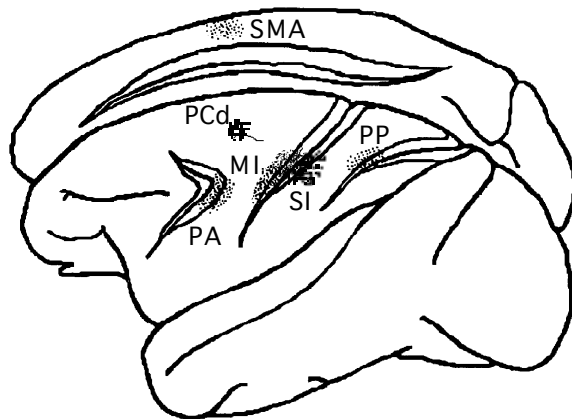
It is not a "given", however, that signals derived directly from the brain will in all or even many cases be the most desirable for prosthesis control, particularly when less invasive options are available. For example, small, voluntary movements about the shoulder have been used to control electrical stimulation of paralyzed muscles in the forearm and hand of patients with cervical spinal cord injuries, thus restoring some useful movements of the hand (4). Also, EMG signals from muscles of the upper arm and shoulder have been used to control artificial hands for amputees. Examples of this type and excellent discussions of the problems involved in the myoelectric control of prostheses are provided by Stein *et al.* (5). The success in using such signals for "non-natural" purposes is a vivid illustration of the "plasticity" of the brain in neuromuscular control; i.e., of how readily it learns to modify the signals sent to a set of muscles so that their activities become appropriate for a new task. Further, at the current state of the art, the ease and lower risk in deriving EMGs makes their use clearly preferable to any attempt to derive control signals directly from the brain.

Then why persist in research aimed at these attempts? There are several reasons. First, useful EMG signals may not in some cases be available: for example, in patients with injury to the high cervical spinal cord. Second, if technical problems can be overcome, the "richness" with which the body musculature and the parameters of movement are represented in circumscribed, accessible regions of the brain, makes the derivation of signals from them theoretically attractive. For example, the areas of the cerebral cortex that normally control voluntary movements of the arm and hand are thought to be *comparatively* intact after spinal injury, as is the contractile apparatus of paralyzed muscles; the primary deficit is an interruption of the spinal pathways which connect brain and muscle. Might not it be possible, then, to *artificially* reconnect them; i.e., to record signals directly from motor control regions of the cortex, process them as required, and use them to control movements produced by direct, electrical stimulation

of paralyzed muscles? Additionally, would not signals from brain areas that would normally control a set of (now-paralyzed) muscles be more natural for such control than EMG signals derived from other muscles? Though changes are known to occur in brain and muscle after spinal cord injury that make the answers to these questions more complex than they first appear, the presumed answers are nonetheless part of the rationale that motivates researchers in this field.

### ARM-HAND AREAS OF THE CEREBRAL CORTEX

The cerebral cortex of each hemisphere in primates contains several areas that are involved in voluntary control of the arm and hand. The locations of these regions in the macaque brain are shown in Figure 1. These areas are extensively interconnected. In addition, each gives rise to pathways (corticospinal, cortico-bulbo-spinal) to the spinal centers that organize and drive muscle activity in the arm. Not all of these areas however, are involved in controlling arm-hand movements at all times; instead, the active subset appears to depend on the behavioral context in which an arm-hand movement occurs.



**Figure 1. Arm-hand motor areas of the cerebral cortex.** The locations of six of these areas (dotted regions) are shown on a drawing of the macaque monkey cerebral cortex. The drawing shows the lateral surface and a mirror-image of the medial surface of one cerebral hemisphere. Major sulci are drawn partly open, to show the extensions of the arm-hand regions into their depths. Abbreviations: PA= postarcuate, PCd=precentral dimple, MI=precentral, SI=somatosensory, PP=posterior parietal, and SMA =supplementary motor areas. Adapted from Humphrey and Tanji (7).

For example, electrical stimulation of cells in the postarcuate area (PA in Figure 1) may evoke hand movements. Yet, neurons in this area appear to discharge in relation to movements of the

contralateral hand only if it is brought toward the face for oral exploration of an object, or for ingesting food (6). Movement-related cells in other regions may show more or less context dependence. In addition, the areas differ in their responsiveness to visual and auditory stimuli, and in the nature of the "commands" that they appear to issue in generating and controlling movement; detailed discussions of these differences may be found elsewhere (7). The important point here is that the optimal site(s) for deriving prosthesis control signals may be any one or even a combination of several of these regions, depending on the control parameters that are required, and the importance of visual and auditory feedback.

All of these cortical sites are surgically accessible, in particular those more lateral in the hemisphere. At present, however, most is known about the properties of the precentral (MI) motor area. Moreover, cells in this region normally participate in the control of *all* voluntary movements of the arm and hand, regardless of the behavioral context in which they occur. For these reasons, it is currently a preferred site for research on the use of brain signals for motor prosthesis control.

### Topographic Organization of the Precentral Motor Cortex

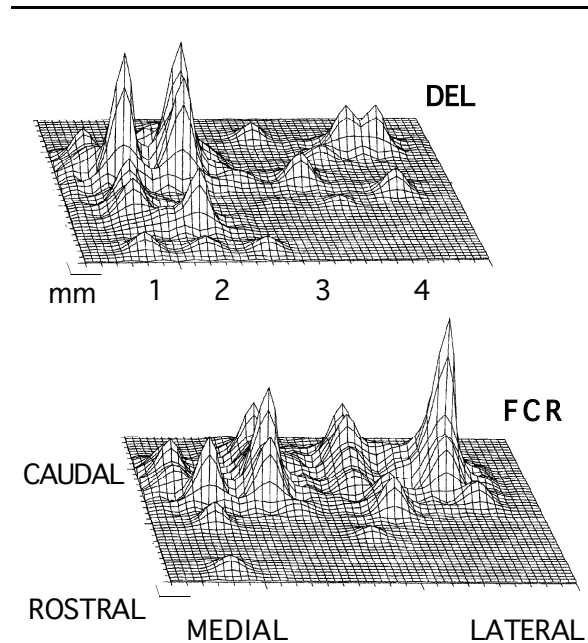
The brain region from which control signals are to be derived should ideally contain a topographic representation of the muscles to be controlled, or of the fundamental movements to be produced. By "topographic", we mean that neurons in a particular zone are related primarily to control of a particular muscle, a small set of functionally linked muscles, or a simple movement. While zones with different motor functions can overlap, it is best if they are partially separate, thus comprising a map of the motor periphery with identifiable topography. This requirement is necessary, of course, for optimal placement of recording electrodes into regions which are known to control particular muscles or movements.

The precentral gyrus of primates, often referred to as the *primary* or *MI* motor cortex, meets this requirement. The organization of MI has been studied extensively with electrical stimulation methods, with the features revealed depending in part on the methods used; reviews of this history may be found elsewhere (8). Here, we need only summarize evidence from recent studies with unanesthetized primates, in which the motor cortex has been mapped with stimulating microelectrodes, and with observations of both evoked movements and EMG activity (7-11). These studies support the following generalizations.

(1) With respect to evoked *movements*, the arm-hand region of MI has a rough topographic organization. Regions which control movements about the shoulder, elbow, wrist, or of the digits, overlap; moreover, there are multiple sites from which movements about a particular joint can be evoked. However, the overlap between these zones is not complete.

(2) When the evoked activity of single *muscles* is observed, this topography changes. Single muscles are "represented" at, i.e., may be activated from, many more sites in MI than the evoked movement maps suggest. These sites are not, however, distributed randomly. Our studies have shown that, when the maps for muscles acting at different joints along the arm are superimposed, they congregate in what appear to be three to four complete maps of the major muscles of the arm. These representations appear as rostrocaudally oriented bands, lying chiefly along the anterior bank of the central sulcus. Moreover, when compared to the movement maps, each composite muscle map for the arm coincides roughly with a major region for producing movements about a particular joint. For example, the major movement zone for the shoulder has outputs not only for affecting shoulder muscles, but also muscles acting about the elbow and the wrist. Conversely, the zone from which wrist movements are most easily evoked contains outputs which affect muscles acting about the elbow and the shoulder (7,8,11). As noted elsewhere (7), this arrangement would allow a particular movement zone to control both the primary muscles for producing that movement, and also the synergistic muscles at the same and adjacent joints that must be active simultaneously to stabilize the limb as movement occurs. Data from one monkey which illustrates this form of muscle representation are shown in figure 2.

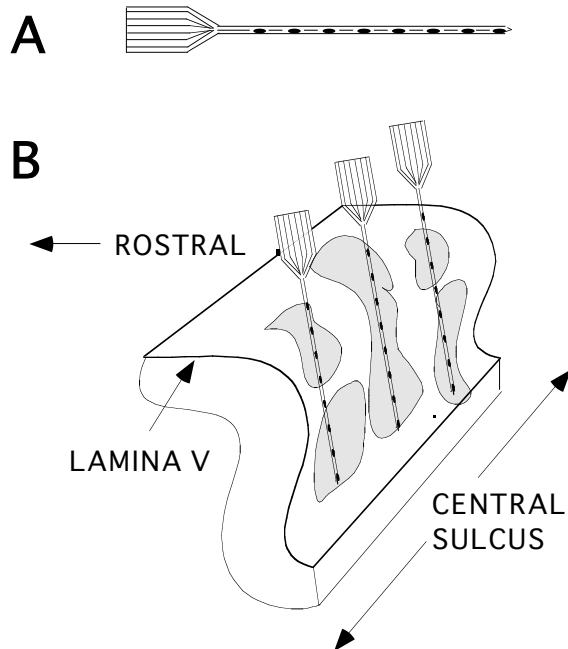
While the functional significance of this organization is not completely clear, it can nonetheless be exploited for research purposes. For example, the rostrocaudal arrangement of each arm-muscle map along the anterior bank of the central sulcus offers a particular advantage. A multichannel electrode with recording pads at several sites along its length can be inserted parallel to the central sulcus, so that it samples neural activity at many points along one of the arm muscle maps. In this way, signals can be derived along a single penetration that encode not only particular movements, but also their underlying muscle synergies; either or both can then be exploited for control purposes. This concept is illustrated schematically in Figure 3. Currently, we are using electrodes with exactly this feature, kindly supplied to us by Dr. Kenneth Wise and his colleagues at the University of Michigan integrated circuit laboratories.



**Figure 2. Comparison of maps for shoulder and wrist muscles.** Each map shows reciprocal threshold values (a measure of the strength of motor output) as a function of the location of the stimulating site in Lamina V of MI. Maps are shown for a shoulder muscle (lateral deltoid or DEL) and for a wrist flexor muscle (flexor carpi radialis or FCR). Rostrocaudal and mediolateral directions are indicated. Most of the peaks in both maps lie in the anterior bank of the central sulcus. Note that the peaks for both muscles occur in four, rostrocaudally oriented bands (labeled 1-4). Peaks in the FCR map are most prominent laterally, and those in the DEL map medially, but both have representations in all four bands. For comparison, stimulation in bands 1 and 2 produced shoulder and/or elbow joint movements, those in bands 2 and 3 elbow and/or wrist movements, and those in band 4 finger/wrist movements.

Before leaving this topic, an important property of such cortical motor (and also sensory) representations must be noted. Current studies suggest that the representations are not static; i.e., they do not reflect *completely* "hardwired" or unmodifiable neural connections. Rather, while certain general features may be fixed, the details of the maps depend in part upon individual somatosensory and motor "experiences". Thus, they appear in part to be dynamically maintained, with the details of the map reflecting the synaptic "weights" or "efficacies" of afferent and intrinsic inputs to resident neurons (12,13). These "weights" are altered by sensory and motor experience, perhaps comprising part of the basis for skill acquisition. This means, of course, that the cortical "map" of the body musculature may be significantly different in an amputee or a quadriplegic

patient from his or her pre-injury map; further, maps may differ significantly in detail across individuals.



**Figure 3. Matching recording electrodes to motor cortex maps.** A. Design of a long electrode with multiple recording pads distributed along its shaft, for use in recording from several sites along one penetration. B. Insertion of these electrodes along each of the band-like arm representations (shaded regions) allows the recording of neural signals related to several muscles along the arm, as well as to movements at different joints.

Thus, ways must be found to map out cortical regions for electrode implantation in *each individual who is a candidate for a cortically controlled prosthesis*. The importance of research directed at this problem is discussed below.

### Control Parameters in the Discharge of Motor Cortex Neurons

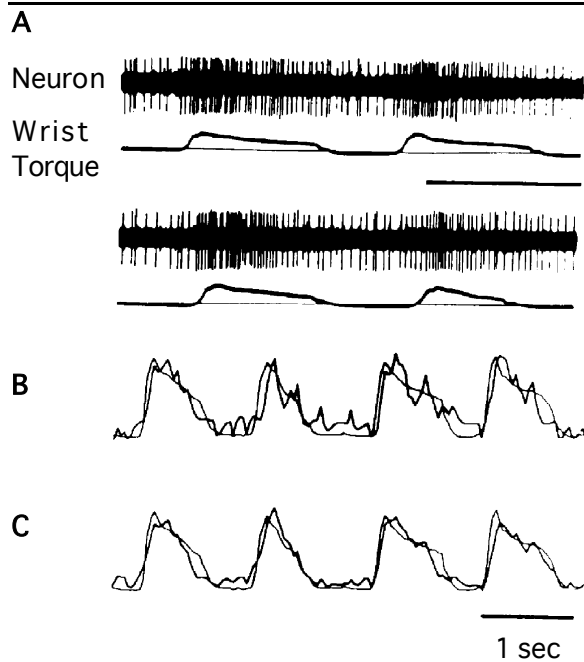
In normal voluntary movements, a number of variables are sensed and controlled by the brain. These include, but are not limited to, the following:

- (1) *Joint positions*, synthesized both at rest and during movement to give limb posture and position;
- (2) *End effector (hand) position* in relation to the body and to nearby objects;
- (3) *Movement kinematics* (direction, velocity);
- (4) *Movement force* (muscle tension and sense of effort);
- (5) *Joint/limb impedance* (as signaled by levels of co-contraction of joint stabilizing muscles).

Studies with monkeys trained to make arm movements under differing requirements of displacement, velocity, and load have shown that correlates of all of these variables can be found in the movement-related discharge of MI neurons (see 7 for review). Indeed, it is the apparent encoding of so many parameters of movement in MI cell discharge that makes it such an attractive site for study of a brain controlled motor prosthesis. Some examples of the accuracy with which motor parameters can be simulated or predicted by the discharge of MI neurons may help to illustrate this point.

More than twenty years ago, Humphrey *et al.* (14,15) showed that the discharge of only 3-5 selected cortical neurons could be used to simulate - in real time - the net wrist torques generated by voluntary, isometric contractions of the wrist muscles by the trained monkey. This was viewed at the time as remarkable, for the prevailing opinion was that too little was known about neural signal processing in the cortex and spinal cord to allow such simulation. Moreover, many thousands of cortical and spinal neurons are known to be involved in producing such contractions. Yet, a surprisingly accurate simulation was accomplished with the signals of only a few selected corticospinal neurons, using rather simple mathematical procedures. The latter consisted of: (a) introduction of a time delay between neural discharge and simulated joint torque (muscle tension), equal to the sum of neural conduction, synaptic transmission, and muscle excitation times; (b) a summation of the weighted discharge frequencies of the cells, as might occur biologically if their outputs converged onto a common set of spinal neurons; and (c) low-pass filtering of this sum, with a filter whose properties simulated the mechanical or contractile time constants of the wrist muscles. An example of one of these simulations is shown in Figure 4.

As encouraging as these simulations seemed at the time, however, they were trivial in view of those that would be required to simulate natural movements of the arm and hand. Because of its multiple joints and directions of joint movement, the arm has multiple degrees of freedom. Moreover, movements about one of these joints and the stabilization of non-moving, supporting joints is produced by the intricately orchestrated activities of some 19 major muscles in the arm. Because of this complexity, researchers have sought to identify parameters in the discharge of MI cells that might relate quantitatively to some higher order variable that would more simply describe a multi-joint movement (16-18). Fortunately, such a variable has been identified: it is the direction in space of a reaching movement or, alternatively, the path followed by the hand (so-called "end-effector") during such a movement.

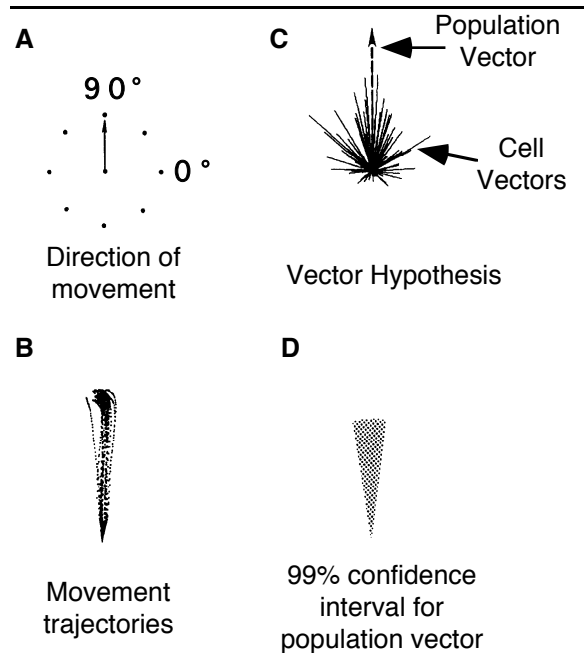


**Figure 4 Simulation of motor output from cortical cell discharge.** **A.** Discharge of a single cortico-spinal cell (upper trace) during generation of isometric wrist torques transients (lower trace), for four consecutive wrist muscle contractions. Extensor torque is upwards. **B.** Simulation of the recorded torque using the smoothed discharge frequency of the cell shown. The lighter trace shows the same torque transients shown in A, while the irregular, darker trace is the simulated torque, computed as described in the text. **C.** The match is improved when the summed discharge rates of five, simultaneously recorded cortical cells is used in the simulation. Adapted from Humphrey (15).

Georgopoulos *et al.* (16,17) were the first to discover that the discharge of some motor cortex neurons is related to the direction of reaching. As a population, the cells appear to encode and perhaps control movement direction. For example, the discharge rate of any one of these cells is maximal during reaching in a particular direction, falling off as a cosine function as the hand movement deviates from this "preferred" direction.

An important feature of the observed population of these neurons, however, is that the "preferred" directions differed for different cells. Georgopoulos *et al.* proposed, therefore, that the activity of this cell population could "encode", or be a command signal for, the direction of reaching (16,17). For example, as the focus of peak activity shifted across the population of these cells, the direction of reaching would correspondingly change. To illustrate this hypothesis, Georgopoulos *et al.* estimated how a population of the cells would behave during a

particular reaching movement, using data from cells recorded sequentially during many repetitions of movements in a series of eight different directions. To do this, each cell's preferred direction was first identified by a unit vector. This vector was then weighted by the relative changes observed in the cell's pre-movement firing rate, as the animal reached in a particular direction. These weighted vectors were then summed across all observed cells, for each reaching direction. The resulting "population vector" was found to predict closely the actual direction of reaching for the eight directions studied. An example of these computations for one such movement is shown in Figure 5.



**Figure 5. Predicting the direction of reaching from cell population discharge.** **A.** The direction of the movement to be predicted: the animal extends its arm, moving its hand in a direction straight ahead of its body. **B.** Display of the trajectories of the hand recorded during several of these movements. **C.** The directions of the weighted cell discharge vectors for a sample population of MI neurons. The discharge of each cell was recorded sequentially, with electrode movements from cell to cell while the animal repeated the movement many times. The resulting population vector (sum of the weighted cell vectors) points in the direction of reaching. **D.** Confidence interval for the computed population vector. Adapted from Georgopoulos *et al.* (17). Used with permission.

The hypothesis that the discharge of some motor cortex cells might control the *direction* of reaching was strengthened further by two additional discoveries. First, the cell population discharge vector was found to predict accurately the direction

of a movement some tens to hundreds of milliseconds *before the movement actually began*, giving credence to the belief that it is in fact a command signal for directional reaching (17). Second, it also predicted accurately the changes in hand path that an animal made when it was required to alter the direction of a reaching movement in progress; again, changes in the predicted direction led those of the actual movement (17). In fact, the correlation of MI cell discharge with hand path is sufficiently high that it can predict the path of a monkey's hand on a computer touch screen, as it traces out a figure by tracking a moving target cursor with its finger (19).

The implications of these studies for brain control of an arm prosthesis are profound. For example, if one could record from a number of these cells simultaneously, the "population discharge vector" could be used to estimate the desired path of a hand movement. This movement could then be produced (in real-time) by the most efficient muscle stimulation or actuator manipulations available. That is, it would not be necessary to simulate in detail the complex patterns of muscle activity that would normally be required to produce these movements.

Unfortunately, however, we do not as yet know how these "directionally tuned neurons" are distributed in the brain. For example, how many of these cells exist per unit volume in MI cortex? Do those with similar directional "tuning" occur in clusters, or are they randomly distributed throughout MI? Could a sufficient number of them be detected by electrodes placed in MI at surgery, without having to search the cortex with numerous electrode penetrations as the patient performs arm movements? All of these are questions that must be answered by future research, if the promise of these elegant neurophysiological studies for cortical control of an arm-hand prosthesis is to be realized.

### **Plasticity of Motor Cortex Discharge**

We turn now to an important consideration. Is the discharge of motor cortex cells sufficiently "plastic", i.e., modifiable through learning, to be easily adapted by a patient for control of a "new limb"? The proximity of these cells to the final output of the motor system, and the fact that new motor skills can be learned throughout one's lifetime, suggest an obvious affirmative answer. However, there are hidden complications when one considers how these modifications are produced.

With appropriate auditory and visual feedback, for example, animals can learn to vary the discharge of cortical cells so that their activity controls directly some external device; for example, the position of a pointer on a meter, or of a cursor on a computer screen (20,21). Moreover, it has been known for

decades that brain injured patients can learn new movements to accomplish tasks that were previously performed by muscles that are now paralyzed. The examples given earlier of the use of EMG signals from shoulder muscles to control an artificial hand, or the stimulation of paralyzed forearm muscles, are instances of such compensation.

These adaptations depend strongly, however, upon somatosensory feedback. When monkeys learn to manipulate devices controlled directly by the discharge of motor cortex cells, for example, they make small, often unnoticed movements of the body parts which these cells normally control (22). Moreover, those cells whose discharge is most easily modified are those that control the wrist and hand, where the density of sensory receptors in the arm is highest, and from which sensory feedback would be maximal. These observations suggest that sensory feedback from the arm and hand is important in an animal's ability to modify the discharge of MI cells and couple this discharge to movements of some external device. In agreement, lesions of somatosensory feedback pathways in the dorsal columns of the spinal cord greatly diminish an animal's capacity to modify MI cell discharge, under the training paradigms used (23). Other investigators have found that dorsal column lesions also impair voluntary movement, but for only one to two weeks, after which skilled arm-hand movements returned (24).

Additional research on the role of somatosensory feedback in the adaptability of cortical cell discharge is therefore needed. If the findings summarized above are confirmed, other neuronal populations or brain sites must be considered as sources of signals for prosthesis control. New imaging technologies hold promise for identifying sites in the human cerebral cortex whose activity may be less controlled by sensory feedback than is MI, and which would, therefore, be important candidate sites for derivation of prosthesis control signals (25,26).

### **DIRECTIONS FOR FUTURE RESEARCH**

We conclude this brief review with consideration of two areas in which new research is needed. The first of these aims at a better understanding of how sensorimotor regions of the brain are modified by spinal cord injury. The second relates to the very difficult problem of finding brain signals that have sufficient information for extraction of useful control parameters, and which are stable for the years to decades that realization of a neural prosthesis will require.

#### ***1) Brain imaging studies of candidates for a neural prostheses***

To study the feasibility of a neurally controlled motor prosthesis, we and others have focused on regions of the primate cortex that have a high degree of topography, strong movement-related cell discharge, and other useful properties. That is, we have attempted to maximize our probability of success by studying brain regions whose properties would be "ideal" for prosthesis control. It is time, however, to research the more realistic case; namely, motor regions in the brains of patients with spinal cord injury. Recent advances using functional imaging of the brain to study voluntary movement processes in normal subjects can clearly be extended to accomplish this goal (25,26).

In the patient with spinal cord injury, it is very likely that cortical motor areas have been reorganized extensively; there are some data available from magnetic stimulation of the motor cortex in such patients to illustrate this point (27). With cervical cord injuries, somatic sensory pathways are often damaged and corticospinal axons, which mediate voluntary movements, may be severed. At present, we do not know if corticospinal cells will survive this insult. Animal studies suggest that they may degenerate within one to two years after cervical axotomy (28), but the transection in humans is farther from the cell body than is the case in these studies. More cells may thus survive in humans. As a result of these changes in input and output, the synaptic organization of the cortical motor areas will change significantly. In such cases, it is not clear to what extent the MI motor cortex will still be a viable site for derivation of control signals.

We badly need, therefore, more functional imaging studies of brain activity during voluntary movement in normal patients, so that we have a database to compare with those from the neurological patient. We can then carry out similar studies with paralyzed patients who *imagine* or *try* to move body parts that are no longer under their control. In this way, we can identify the sites of cortical activity - wherever these might be - that correlate with each type of imagined movement. A study of this type will, in fact, be needed for each patient who is a candidate for a brain-controlled, motor prosthesis.

### **2) Finding stable neural signals for prosthesis control**

Many investigators have assumed that signals recorded from single neurons will be the most useful for prosthesis control. There are several reasons for this assumption. First, neurons with different control functions may be intermingled in the cortex, or their distributions may overlap significantly. By isolating the discharge of single neurons, those with different functions can be separated, and control signals can be derived from the most appropriate. Second, single

neuron spikes are of sufficient amplitude and have sufficient frequency (discharge rate) modulation to be suitable for real-time control. That is, averaging of activity over several trials or "attempts" to make a movement, often done to improve signal-to-noise ratios when electroencephalographic (EEG) signals are studied, is not necessary. Thus, significant delays between brain commands for movement and the occurrence of that movement - which can only impair motor performance - can be avoided. Finally, by recording from many neurons simultaneously, one may be able to extract several parameters that would be useful for prosthesis control. Recognition of these advantages has spurred attempts to develop long-term, single neuron recording methods, and techniques for on-line separation of the discharge of many simultaneously recorded neurons.

But single neurons die - at a rate of some 50,000/day in the normal adult human brain - and they are easily injured by electrodes that must be in close proximity to them to isolate their spike activity. To date, we know of only one case in which recordings have been obtained from the same, clearly identified neuron for more than three weeks (29). Thus, a way of obtaining long-term, stable signals with adequate real-time information content is at present unavailable.

We should note that some researchers have found that externally recorded EEG potentials may be useful for prosthesis control, where the actuator functions are simpler than those required for a limb prosthesis (see, for example, Wolpaw, this volume). This approach has the advantage of being non-invasive, and it is useful with current technologies. A clear disadvantage, however, is that extraction of a useful signal may require averaging over many brain events, thus precluding its use for the real-time control of movement.

We need additional research, therefore, into alternative approaches. One of these may consist of multi-unit recordings. By using electrodes with appropriate tip or pad sizes, one can record "multi-unit" potentials from small groups of active neurons. Though of smaller amplitude than single unit spikes, and containing the spikes of cells with perhaps differing motor functions, these multi-unit potentials may nonetheless correlate better with certain motor commands than with others. Moreover, by recording at many sites, one may be able improve this specificity by using spatial patterns of cell activity. Finally, multi-unit potentials may be recordable for longer periods of time than are single neuron spikes. For these reasons, we are now pursuing the multi-unit approach in our laboratory; only time will tell if it is a reasonable compromise.

## ACKNOWLEDGEMENTS

Supported by contract N01-NS-1-2308 from the Neural Prosthesis Program.

## REFERENCES

- (1) Vodovnik, L.; Long II, C.; Reswick, J.B.; Lippay, A., and Starbuck, D. (1965) Myo-electric control of paralyzed muscles. *IEEE Trans. Biomed. Eng.*, BME-12: 169-172.
- (2) Evarts, E.V. (1966) Pyramidal tract activity associated with a conditioned hand movement in the monkey. *J. Neurophysiol.*, 19: 1011-1027.
- (3) Frank, K. and Hambrecht, F.T. (1977) Present status of neural prostheses: visual, auditory, and motor. *Clin. Neurosurg.*, 24: 337-346.
- (4) Mauritz, K.H. and Peckham, H.P. (1987) Restoration of grasping functions in quadriplegic patients by Functional Electrical Stimulation (FES). *Int. J. Rehabil. Res.*, 10 (Suppl 5): 57-61.
- (5) Stein, R.B.; Charles, D. and Walley, M. (1983) Bioelectric control of powered limbs for amputees. *Advances in Neurology*, 39: 1093-1108.
- (6) Rizalotti, G.; Gentilucci, M.; *et al.* (1987) Neurons related to goal-directed motor acts in inferior area 6 of the macaque monkey. *Exp. Brain Res.*, 67: 220-224.
- (7) Humphrey, D.R. and Tanji, J. (1991) What features of voluntary motor control are encoded in the neuronal discharge of different cortical motor areas. In, *Motor Control: Concepts and Issues*, edited by D.R. Humphrey and H.-J. Freund. New York: John Wiley & Sons, pp. 413-444.
- (8) Humphrey, D.R. (1986) Representation of movements and muscles within the primate precentral motor cortex: historical and current perspectives. *Fed. Proc.*, 45: 2687-2699.
- (9) Waters, R.S.; Samulack, D.D.; Dykes, R.W and McKinley, P.A. (1990) Topographic organization of baboon primary motor cortex: face, hand, forelimb, and shoulder representation. *Somatosens. Mot. Res.*, 7: 485-514.
- (10) Donoghue, J.P.; Leibovic; and Sanes, J.N. (1992) Organization of the forelimb area in squirrel monkey primary motor cortex: representation of individual digit, wrist, and elbow muscles. *Exp. Brain Res.*, 89: 1-19.
- (11) Kwan, H.C.; MacKay, W.A.; Murphy, J.T.; and Wong, Y.C. (1978) Spatial organization of primate precentral cortex in awake primates. II. Motor outputs. *J. Neurophysiol.*, 41: 1120-1131.
- (12) Merzenich, M.M.; Recanzone, G.; *et al.* (1988) Cortical representational plasticity. In *Neurobiology of Neocortex*, edited by P. Rakic and W. Singer. New York: John Wiley & Sons, pp. 41-67.
- (13) Donoghue, J.P. and Sanes, J.N. (1994) Motor areas of the cerebral cortex. *J. Clin. Neurophysiol.*, 11(4): 382-396.
- (14) Humphrey, D.R.; Schmidt, E.M.; and Thompson, W.D. (1970) Predicting measures of motor performance from multiple cortical spike trains. *Science*, 179: 758-762.
- (15) Humphrey, D.R. (1972) Relating motor cortex spike trains to measures of motor performance. *Brain Res.*, 40:7-18.
- (16) Georgopoulos, A.P.; Kalaska, J.F.; Caminiti, R.; and Massey, J.T. (1982) On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. *J. Neurosci.*, 2: 1527-1537.
- (17) Georgopoulos, A.P.; Kalaska, J.F.; Caminiti, R.; and Massey, J.T. (1984) The representation of movement direction in the motor cortex: single cell and population studies. In *Dynamic Aspects of Neocortical Function*, edited by G.M. Edelman, W.M. Cowan, and W.E. Gall. New York: John Wiley & Sons, pp. 501-524.
- (18) Soechting, J.F. and Lacquaniti, F. (1981) Invariant characteristics of a pointing movement in man. *J. Neurosci.*, 1: 710-720.
- (19) Schwartz, A.B. (1993) Motor cortical activity during drawing movements: population representation during sinusoid tracing. *J. Neurophysiol.*, 70: 28-36.
- (20) Fetz, E.E. and Finocchio, D.V. (1972) Operant conditioning of isolated activity in specific muscles and precentral cells. *Brain Res.*, 40: 19-24.
- (21) Schmidt, E.M. ; McIntosh, J.D.; and Durelli, L. (1978) Fine control of operantly conditioned firing patterns of cortical neurons. *Exp. Neurol.*, 61: 349-369.
- (22) Wyler, A.R. and Burchiel, K.J. (1978) Factors influencing accuracy of operant control of pyramidal tract neurons in monkey. *Brain Res.*, 152: 418-421.
- (23) Wyler, A.R.; Burchiel, K.J.; and Robbins, C.A. (1979) Operant control of precentral neurons in monkeys: evidence against open loop control. *Brain Res.*, 171: 29-39.
- (24) Asanuma, H. and Arissian, K. (1982) Motor deficits following interruption of sensory inputs to the motor cortex of the monkey. *EEG Clin. Neurophysiol.*, Suppl. 36: 415-21.
- (25) Stephan, K.M.; Fink, G.R.; Passingham, R.E. *et al.* (1995) Functional anatomy of the mental representation of upper extremity movements in healthy subjects. *J. Neurophysiol.*, 73: 373-386.
- (26) Kawashima, R.; Roland, P.R.; and O'Sullivan, B.T. (1994) Fields in human motor areas involved in preparation for reaching, actual reaching, and visuomotor learning: a positron emission tomography study. *J. Neurosci.*, 14: 3462-3474.
- (27) Cohen, L.G.; Bandinelli, S; Topka, H.R. *et al.* (1991) Topographic maps of human motor cortex in normal and pathological conditions: mirror movements, amputations, and spinal cord injuries. *EEG & Clin. Neurophys.*, Supplement. 43: 36-50.
- (28) McBride, R.L.; Harper, W.B.; and Feringa, E.R. (1990) Axotomized corticospinal neurons cannot be



## Intracortical Recordings for Prosthesis Control

retrogradely labeled with fluoro-gold one year after spinal cord transection. *Soc. Neurosci. Abstr.*, 16: 984.

(29) Schmidt, E.M.; Bak, M.J.; and McIntosh, J.S. (1976) Long-term chronic recording from cortical neurons. *Exp. Neurol.*, 52: 496-506.

Donald R. Humphrey, Ph.D.  
Professor of Physiology and Neurology  
Emory University School of Medicine  
Atlanta, GA 30322  
phone: (404) 727-0346  
fax: (404) 727-2648  
e-mail: drh@physio.emory.edu