Cortical control of motor behavior at the cellular level

Apostolos P. Georgopoulos and James Ashe

Veterans Affairs Medical Center, Minneapolis, Minnesota and
University of Minnesota Medical School, Minneapolis, Minnesota, USA

The studies reviewed in this paper describe the relations of single-cell
activity in central motor structures to complex visuomotor tasks and
document the fact that various cortical areas process visuomotor
information in parallel. Moreover, the studies provide clear evidence that
the map in the motor cortex is modifiable and dynamically maintained.

Introduction

The search for an understanding of the cellular mechanisms underlying the cortical control of movement has relied on two major techniques, namely recordings of single-cell activity during motor performance, and motor mapping by electrical stimulation. The first technique provides a direct link between cell activity and motor behavior, whereas the second describes the functional organization and somatotopic arrangement of cortical areas controlling motor output. Significant new results have been obtained in both these fields during the past year.

Recordings of single-cell activity and motor behavior

Preparation, initiation and execution of movement

A number of cortical and subcortical structures are intimately involved in motor function, including the motor cortex and various premotor areas, the basal ganglia, and the cerebellum. Do these areas function serially and independently, each dealing with a particular aspect of motor control, or do they contribute in varying degrees to all aspects of movement? One way to answer this question is to record from these areas during the performance of the same motor task. Alexander and Crutcher [1••–3••] have examined the activity of single cells in the motor cortex, the supplementary motor area (SMA), and the putamen in the monkey during the performance of an instructed task that involved movements at the elbow. The monkey first moved the forearm in the direction (flexion/extension) indicated by a visual stimulus (right/left). Then, the forearm returned to the initial position and a preparatory period ensued at the end of which the stimuli at both positions (right and left) were turned on. The monkey was required to move the forearm in the direction of the previous movement. The task was performed in the presence of loads opposing flexion

or extension; thus the same movement was produced by a different set of muscles, and the effect of the intended direction of movement on neural activity was dissociated from the effect of the muscle pattern that was dictated by the loads applied. The authors found that many of the cells in the motor cortex (37%, n = 202), the SMA (55%, n = 222), and the putamen (33%, n = 317) showed changes in activity during the preparatory period. These changes were selective, in anticipation of elbow movements in a particular direction (87% in motor cortex, 86% in SMA, and 78% in putamen) and were independent of the loading conditions (83% in motor cortex, 80% in SMA, and 84% in putamen). A relation of neural activity to visual signals was observed when the visually defined direction was dissociated from the direction of the upcoming joint movement [2••]. In the usual task, the visual instruction (target), and the monkey's cursor and forearm all moved in the same direction, whereas in the dissociation task the forearm moved in the opposite direction from that of the cursor (and target). It was found that the activity of a good proportion of cells in the motor cortex (40%), SMA (36%), and putamen (38%) showed selective discharge prior to all pre-planned movements of the cursor toward one or the other direction (right or left in the visual display), irrespective of whether the limb movement involved extension or flexion of the elbow.

The findings summarized above show that the changes in activity observed in central motor structures during tasks that involve visually guided movements may not relate exclusively to upcoming peripheral motor events (e.g. muscle contractions), but instead may reflect higher order processing of visuomotor information. The results also indicate that the three structures studied (motor cortex, SMA and putamen) participate in parallel to visuomotor processing.

The relations of the motor cortex and the SMA to upcoming motor events have also been investigated in a study by Chen et al. [4•] with regard to the preparation and execution of movements. They found that motor cortical

---

Abbreviations
GABA—γ-aminobutyric acid; SMA—supplementary motor area.

cell activity is related more to the execution of movement, whereas activity in the SMA is related more to the preparation of movement. It is remarkable, however, that qualitatively, the two areas are concerned with both aspects of movement, that is preparation and execution. These findings, together with those of Alexander and Crutcher [1••–3••] suggest that the initiation of movement is subserved by a distributed system rather than a strictly hierarchical one.

Coding of static force in precision grip

A study by Wannier et al. [5•] has compared in a rigorous and quantitative fashion the relations of single-cell activity in the motor and somatosensory cortices to static force levels exerted by monkeys in a precision grip. Recordings in the motor cortex confirmed previous results [6]. A new finding was that although cells in the somatosensory cortex were active during the task, they did not seem to be concerned with force initiation; they could very well be participating in the fine control of force exerted, however. The problem of continuous isometric force control is important, as is the role of feedback. This is the first study to provide detailed information about the possible cortical mechanisms underlying the control of force through feedback.

Directional coding

A number of studies [7••,8•,9••] have focused on the relations between single cell and neuronal population activity, and the direction of motor output (movement or static force). The quantitative studies of the relations between single-cell activity in cortical areas and direction of arm movement in space were initiated a decade ago using movements in a two-dimensional space [10]. These studies were later extended to movements in three-dimensional space [11,12]. The main finding was that the activity of single cells in the motor cortex was directionally and broadly tuned with respect to the direction of reaching; cell activity was most intense for reaching in a particular direction (the cell's 'preferred direction') and decreased progressively for movements made farther away from this direction. In addition, the changes in cell activity were found to relate to the direction and not the endpoint of the reaching movement [13]. The preferred directions differed for different cells and were distributed in the whole directional continuum. The activity of a number of cells in the motor cortex was also found to be tuned with respect to the direction of the static loads [14], whereas other cells showed no tonic activity during load application. It is interesting that the load effect, when present, was statistically additive to that of movement [14].

These data indicate that a given cell participates in the generation of movements in various directions. It therefore follows that, conversely, a movement in a particular direction will involve the activation of a whole popula-

tion of cells. A unique coding scheme of the direction of movement by the neuronal ensemble has been proposed that considers the motor cortical command for the direction of reaching as an ensemble of vectors [11,15,16], each of which represents the contribution of a directionally tuned cell. A particular vector points in the cell's preferred direction and has a length proportional to the change in cell activity associated with a particular movement direction. The vector sum of these weighted cell vectors (the 'neuronal population vector') then points at or near the direction of the movement [11,15,16].

Three papers have extended these observations and ideas in several important ways [7••,8•,9••]. Caminiti et al. [7••] have investigated the effect of the origin of the movement on the preferred direction of motor cortical cells. They trained monkeys to reach to eight targets placed at the corners of three cubes located in different areas of space, such that the centers of the cubes were on a horizontal line in front of the animal. Each cell was then studied during each of the 24 (eight movement directions multiplied by three cubes) movements. It was found that the cell's preferred direction tended to shift by approximately 10–15° on average, in the horizontal plane. Remarkably, there was no systematic shift in the sagittal or frontal planes. As this shift in preferred direction was similar to the shift in the orientation of the arm at the starting position, the results indicate an influence of the orientation of the arm on the preferred direction. Is such an influence observed for the direction of the population vector as well? Interestingly, this is not the case. The population vector pointed in the appropriate direction in all three cubes without being biased in any plane. Very similar results have been obtained from recordings in the premotor cortex [8•].

In summary, the studies by Caminiti et al. [7••,8•] have documented an effect of arm orientation on the cell's preferred direction and extended the directional coding analysis to the premotor cortex. This coding has already been shown in area 5 of the parietal cortex [14,17], and in the cerebellum [18].

Kalaska et al. [9••] have addressed the effect of static loads on the steady-state cell activity of cells in parietal area 5. This effect had already been thoroughly investigated in the motor cortex [14], where it was found that a good proportion (66.1%) of cells were sensitive to the direction of applied static loads. In contrast, the effect was very weak in area 5 [9••], in that both the proportion of cells showing the effect (11.1%), and the amplitude of modulation of their activity, were appreciably lower than those in the motor cortex. Given that cells in both parietal area 5 and the motor cortex show directional tuning during movements, Kalaska et al. [9••] have proposed that this directional modulation may reflect a kinematic (i.e. purely spatial) signal in area 5 and a mixture of kinematic and dynamic (i.e. torque-related) signals in the motor cortex. This is an interesting idea that has a direct bearing on the planning and implementation of movement.

Complex visuospatial behavior

A study by Hocherman and Wise [19••] has focused on the relations between single-cell activity in the motor cortex and premotor areas (including the SMA and dorsal and ventral premotor cortex) and aspects of memorized handpaths on a working surface. In this study, monkeys were required to reproduce a trajectory outlined on the plane by a series of light emitting diodes, after the diodes had been turned off. The trajectories were such that the same end position could be reached by a straight-line trajectory or by curved trajectories. A rich variety of patterns of cell activity were found in all areas studied. The important finding was that these patterns appeared to reflect various influences, including the selection of a motor path from memory. These results add further weight to the view that precentral motor fields cooperate in motor planning and execution, and that, conversely, these functions are represented in a distributed fashion across the different cortical areas.

Neural correlates of hand preshaping

The relation of neuronal activity in parietal area 7 to preshaping of the hand during a task that involves reaching towards and manipulating an object has been addressed by Taira et al. [20••]. The manipulation was controlled by using several kinds of manipulanda. The reaching movement was the same in all cases as the manipulanda were always placed in the same position in front of the animal. The monkeys had to reach towards the manipulandum and then perform a certain operation on it dictated by the shape and orientation of the manipulandum itself (e.g. a lever to be pulled by the hand, a button to be pushed, a switch placed within a groove to be pulled by the thumb and index finger, and a freely accessible switch to be pulled by all fingers). The major finding was that single cells showed preferential activation with certain manipulanda, although the activity was graded across the different cases. Moreover, cell activity changed gradually as the orientation of the manipulandum, e.g. the lever, was changed, dictating a different shaping of the hand and forearm for the same basic operation (pulling the lever). It is interesting that 69 % of the cells related to hand preshaping in the dark further modulated their activity when the manipulandum was visible. This suggests that these parietal cells may be concerned with matching movement patterns to the characteristics of the objects that are to be manipulated. This is the first rigorous study of the neural mechanisms underlying visuomotor planning and coordination in the hand preshaping domain, and one that opens an exciting field for future investigations.

Electrical stimulation and mapping

Electrical stimulation of the motor cortex leads to motor responses in corresponding parts of the body. This method has been used to construct somatotopic motor maps of the motor cortex, to study their organization and

dynamic maintenance, and to effect changes in the map through repeated stimulation.

Motor mapping

A thorough re-evaluation of the motor representation in the motor cortex of the baboon has been performed by Waters et al. [21•]. They constructed a detailed cortical map by electrical microstimulation. There were two major findings: first, that movements are multiply represented, confirming recent results from other studies on the multiple representation of muscles [22] and joint movements [23]; and second, that there are silent zones of the motor cortex, that is parts of the cortex from which microstimulation does not evoke a response. This is a novel finding that raises new questions about the possible functions of cells in these zones with respect to integrating motor function in the motor cortex.

Re-organization of the motor map

Although early studies suggested that motor representation in the motor cortex might be flexible and change over time [24], it was commonly thought that the connection between the motor cortex and target muscles was fixed [25]. The concept of a rigid organization of the motor system has been at variance with observations on the plasticity of cortical representations in the visual [26], somatosensory [27], and olfactory [28] systems, in which cortical reorganization has been shown following disruption of sensory input during a critical period of development [29], or in the case of the somatosensory system, following manipulations in the neonate or adult animal [27].

Donoghue and Sanes [30,31] had previously demonstrated that motor cortical maps could reorganize in neonatal rats following forelimb amputation. In a more recent series of studies [32••,33••] the authors have examined the motor cortical organization in adult rats following forelimb amputation or facial nerve transection. Normal adult rats have distinct contiguous areas within the motor cortex which, when stimulated, cause movement of the contralateral forelimb, vibrissae or eye/eyelid. Stimulation 2–4 months after forelimb amputation showed that the representation of the contralateral shoulder within the forelimb area had increased and that these movements were elicited at the same or at a lower threshold level than in normal animals [32••]. Areas of cortex that would have been associated with distal forelimb responses in normal animals, yielded vibrissa movement in the treated animals. In animals that had had a facial nerve transection the normal vibrissal area was replaced by eye/eyelid and forelimb response areas. The authors studied the rapidity of the reorganization by recording the responses immediately before and for 10 h after facial nerve transection [33••]. An electrode placed in the vibrissal area did not elicit any response when stimulated immediately after nerve section. However, within 4 h, and in some cases as early as 1 h after transection, stimulation in this area produced electromyographic responses

in the contralateral forelimb that were similar in magnitude to responses obtained when stimulating in the forelimb area. This response persisted for up to 10 h after section. Remapping of the forelimb motor cortex area after transection showed that the boundary had shifted 1 mm into what had previously been identified as a vibrissal area.

These studies demonstrate that connections between motor cortical areas and muscles are not fixed, and that the connections are subject to modification not only in the developing animal but also in the adult. The rapidity with which the reorganization occurs is remarkable. These studies have changed our concept of the motor system as a rigid anatomic structure into one in which various influences can change the functional pathways within the structure. It is not yet clear how these changes are modulated.

Dynamic maintenance of the motor map

It is now clear that new patterns of organization can occur in the motor cortex within hours of a peripheral nerve lesion [32••,33••]. Jacobs and Donoghue [34••] proposed that this functional reorganization might be caused by a change in the balance between existing inhibitory/excitatory intracortical connections; a prominent role of γ-aminobutyric acid (GABA), the main inhibitory neurotransmitter within the cortex, has been demonstrated. The authors microstimulated the motor cortex of adult rats to delineate the areas related to movement of the vibrissae and the forelimb. They then microstimulated in the vibrissal area while iontophoretically releasing the GABA antagonist bicuculline in the adjacent forelimb area. The electrical stimulation now elicited electromyograph responses in the forelimb in addition to the vibrissae. The effect was reproducible, was maintained for the duration of the infusion, and diminished and then disappeared following the infusion. The bicuculline did not cause a general increase in cortical excitability, as judged by microstimulation thresholds, nor did it spread more than 660 μm from the release site. The hypothesis is that there is a system of excitatory intracortical connections between motor cortical output neurones. This connection is not usually functionally expressed because the intracortical fibers also stimulate local inhibitory neurones. When the local inhibitory neurones are themselves inhibited by bicuculline, the excitatory connections become manifest. These studies show that the motor map in the motor cortex is not the result of a static permanent connectivity, but relies for its maintenance on a dynamic interplay between neurones in the local circuit. Inhibitory mechanisms appear to play a major role in this function.

The functional nature of the motor map in the motor cortex has also been studied by Nudo *et al* [35•]. In their study, the motor responses elicited by microstimulation changed over time, following a 3–4 h period of microstimulation in a particular locus. This procedure resulted in an enlargement of the field from which motor responses could be elicited that were similar to those

evoked by stimulating at the locus. Thus, repeated microstimulation results in a change of the boundaries of the somatotopic map, supporting the view that the motor cortical map is dynamically maintained.

Concluding remarks

It is clear from the studies discussed in this review that the motor cortex is quite complex with respect to both the functional properties of its cells and the mechanisms by which its motor map is maintained. It is therefore more appropriate, and more useful, to regard this structure in the whole behavioral–motor repertoire with the intricate plasticity mechanisms that govern its functional organization, rather than limit its role as a pure muscle controller. Moreover, the complexity of the motor cortex should be regarded within the context of the complexity of premotor and parietal areas. The challenge now is to understand visuomotor behavior in an integrated manner across the diverse cortical areas involved.

Acknowledgements

References and recommended reading

Papers of special interest, published within the annual period of review, have been highlighted as:
•   of interest
••   of outstanding interest

1.   ALEXANDER GE, CRUTCHER MD: **Preparation for Movement:**
••   **Neural Representation of Intended Direction in Three Motor Areas of the Monkey.** *J Neurophysiol* 1990, 64:133–150.
Directionally selective preparatory activity was documented in the motor cortex, the SMA, and the putamen. The effect of loading on the preparatory activity was negligible. The results indicate that preparatory activity is distributed, related to visuomotor processing, but not exclusively to muscle activation.

2.   ALEXANDER GE, CRUTCHER MD: **Neural Representations of**
••   **the Target (Goal) of Visually Guided Arm Movements in Three Motor Areas of the Monkey.** *J Neurophysiol* 1990, 64:164–178.
Target-related neurons were found in the motor cortex, the SMA, and the putamen. These findings reflect the sophisticated visuomotor processing taking place in these motor structures.

3.   CRUTCHER MD, ALEXANDER GE: **Movement-Related Neuronal**
••   **Activity Selectively Coding Either Direction or Muscle Pattern in Three Motor Areas of the Monkey.** *J Neurophysiol* 1990, 64:151–163.
Movement-related cells that were muscle-like or directional were found in all three areas. This is the first time that rigorous dissociations between muscles, movements and visual targets have been carried out in the areas studied.

4.   CHEN D-F, HYLAND B, MAIER V, PALMERI A, WIESENDANGER M:
•   **Comparison of Neural Activity in the Supplementary Mo-**

tor Area and in the Primary Motor Cortex in Monkeys. *Somatosens Mot Res* 1991, 8:27–44.

Properties of SMA neurones were found to be very similar to neurones in the motor cortex, although the motor cortex neurones seemed to relate more to movement execution than planning.

5.   WANNIER TMJ, MAIER MA, HEPP-REYMOND M·C: Contrasting
•   Properties of Monkey Somatosensory and Motor Cortex Neurones Activated During the Control of Force in Precision Grip. *J Neurophysiol* 1991, 65:572–588.

A detailed investigation of force coding in somatosensory and motor cortex using the precision grip paradigm.

6.   SMITH AM, HEPP-REYMOND M-C, WYSS UR: Relation of Activity in Precentral Cortical Neurons to Force and Rate of Force Change During Isometric Contractions of Finger Muscles. *Exp Brain Res* 1975, 23:315–332.

7.   CAMINITI R, JOHNSON PB, URBANO A: Making Arm Movements
••   within Different Parts of Space: Dynamic Aspects in the Primate Motor Cortex. *J Neurosci* 1990, 10:2039–2058.

A study of directional tuning of motor cortical cells while reaching within various parts of space. The preferred direction of single cell shifts in the horizontal plane with the orientation of the arm. This is the first report on the influence of the orientation of the arm on a cells preferred direction.

8.   CAMINITI R, JOHNSON PB, GALLI C, FERRAINA S, BURNOD Y,
•   URBANO A: Making Arm Movements within Different Parts of Space: the Premotor and Motor Cortical Representation of a Coordinate System for Reaching at Visual Targets. *J Neurosci* 1991, 11:1182–1197.

A study of directional tuning and neuronal population coding in the premotor cortex. Cell and population properties were very similar to those in the motor cortex. An additional finding was that the preferred directions of single cells shifted with the orientation of the arm, whereas the direction of movement predicted by the neuronal population vector did not.

9.   KALASKA JF, COHEN DAD, PRUD'HOMME M, HYDE ML: Parietal
••   Area 5 Neuronal Activity Encodes Movement Kinematics not Movement Dynamics. *Exp Brain Res* 1990, 80:351–364.

Unlike motor cortex, only a few cells in parietal area 5 are related to the direction of static loads. Area 5 appears to be related to movement kinematics rather than movement dynamics.

10.   GEORGOPOULOS AP, KALASKA JF, CAMINITI R, MASSEY JT: On the Relations Between the Direction of Two-Dimensional Arm Movements and Cell Discharge in Primate Motor Cortex.
•   *J Neurosci* 1982, 2:1527–1537.

11.   GEORGOPOULOS AP, SCHWARTZ AB, KETTNER RE: Neuronal Population Coding of Movement Direction. *Science* 1986, 233:1416–1419.

12.   SCHWARTZ AB, KETTNER RE, GEORGOPOULOS AP: Primate Motor Cortex and Free Arm Movements to Visual Targets in Three-Dimensional Space. I. Relations Between Single Cell Discharge and Direction of Movement. *J Neurosci* 1988, 8:2913–2927.

13.   GEORGOPOULOS AP, KALASKA J, CAMINITI R: Relations Between Two Dimensional Arm Movements and Single Cell Discharge in the Motor Cortex and Area 5: Movement Direction Versus Movement Endpoint. *Exp Brain Res Suppl* 1985, 10:176–184.

14.   KALASKA JF, COHEN DAD, HYDE ML, PRUD'HOMME M: A Comparison of Movement Direction-Related Versus Load Direction-Related Activity in Primate Motor Cortex, Using a Two-Dimensional Reaching Task. *J Neurosci* 1989, 9:2080–2102.

15.   GEORGOPOULOS AP, CAMINITI R, KALASKA JF, MASSEY JT: Spatial Coding of Movement: a Hypothesis Concerning the Coding of Movement Direction by Motor Cortical Populations. *Exp Brain Res Suppl* 1983, 7:327–336.

16.   GEORGOPOULOS AP, KETTNER RE, SCHWARTZ AB: Primate Motor Cortex and Free Arm Movements to Visual Targets in Three-Dimensional Space. II. Coding of the Direction of Movement by a Neuronal Population. *J Neurosci* 1988, 8:2928–2937.

17.   KALASKA JF, CAMINITI R, GEORGOPOULOS AP: Cortical Mechanisms Related to the Direction of Two-Dimensional Arm Movements: Relations in Parietal Area 5 and Comparison with Motor Cortex. *Exp Brain Res* 1983, 51:247–260.

18.   FORTIER PA, KALASKA JF, SMITH AM: Cerebellar Neuronal Activity Related to Whole-Arm Reaching Movements in the Monkey. *J Neurophysiol* 1989, 62:198–211.

19.   HOCHERMAN S, WISE SP: Effects of Hand Movement Path on
••   Motor Cortical Activity in Awake, Behaving Rhesus Monkeys. *Exp Brain Res* 1991, 83:285–302.

The neural mechanisms underlying the planning and execution of two-dimensional handpaths from memory were studied in motor and premotor cortical areas. Cell activity in all areas studied reflected the complexity of the task, including motor memory.

20.   TAIRA M, MINE S, GEORGOPOULOS AP, MURATA A, SAKATA H:
••   Parietal Cortex Neurones of the Monkey Related to the Visual Guidance of Hand Movement. *Exp Brain Res* 1990, 80:351–364.

The authors have found that some neurons in the parietal cortex are related to the preshaping of hand movement and are concerned with matching the pattern of a movement to the shape of the object to be manipulated.

21.   WATERS RS, SAMULACK DD, DYKES RW, MCKINLEY PA: Topo-
•   graphic Organization of Baboon Primary Motor Cortex: Face, Hand, Forelimb, and Shoulder Representation. *Somatosens Mot Res* 1990, 7:485–514.

This study shows that muscles are multiply represented within the motor cortex. In addition, there are a number of silent zones that do not elicit motor responses with microstimulation.

22.   DONOGHUE JP, LEIBOVIC SL, SANES JN: Organization of Muscle Representations in Primate Forelimb Motor Cortex. In *Neuroscience Integrative Functions: a Symposium Honoring Vernon B. Mountcastle.* Baltimore: Book of Abstracts 1989, abstract no. 44.

23.   HUMPHREY DR, MITZ AR: Multiple, Joint-Weighted Representations of the Arm Within the Precentral (MI) Motor Cortex of the Macaque Monkey. In *Neuroscience Integrative Functions: a Symposium Honoring Vernon B. Mountcastle.* Baltimore: Book of Abstracts 1989, abstract no. 59.

24.   LEYTON ASF, SHERRINGTON CS: Observations on the Excitable Cortex of the Chimpanzee, Orangutan and Gorilla. *Q J Exp Physiol* 1917, 11:135–222.

25.   CRAGGS MD, RUSHTON DN: The Stability of the Electrical Stimulation Map of the Motor Cortex of the Anaesthetized Baboon. *Brain* 1976, 99:575–600.

26.   HUBEL DH, WIESEL TN: Binocular Interaction in Striate Cortex of Kittens Reared with Artificial Squint. *J Neurophysiol* 1965, 28:1041–1059.

27.   KALASKA J, POMERANZ B: Chronic Paw Deafferentation Causes an Age-Dependent Appearance of Novel Responses from Forearm in 'Paw Cortex' of Kittens and Adult Cats. *J Neurophysiol* 1979, 42:618–633.

28.   WILSON DA, SULLIVAN RM, LEON M: Single Unit Analysis of Post-Natal Olfactory Learning: Modified Olfactory Bulb Output Response Patterns to Learned Attractive Odors. *J Neurosci* 1987, 7:3154–3162.

29.   HUBEL DH, WIESEL TN: The Period of Susceptibility to the Physiological Effects of Unilateral Eye Closure in Kittens. *J Physiol (Lond)* 1970, 206:419–436.

30.   DONOGHUE JP, SANES JN: Neonatal Peripheral Nerve Injury Reorganizes Representation Pattern in Motor Cortex. *Proc Natl Acad Sci USA* 1987, 84:1123–1126.

31. DONOGHUE JP, SANES JN: Organization of Adult Motor Cortex Representation Following Neonatal Forelimb Nerve Injury in Rats. *J Neurosci* 1988, 8:3221–3232.

32. SANES JN, SUNER S, DONOGHUE JP: Dynamic Organization of
•• Primary Motor Cortex Output to Target Muscles in Adult Rats. I. Long Term Patterns of Reorganization Following Motor and Mixed Peripheral Nerve Lesions. *Exp Brain Res* 1990, 79:479–491.
Motor cortical reorganization can occur following amputation or motor nerve transection in adult rats, establishing the plasticity of the motor cortex in adults. This and [33••] are the first reports on the reorganization of the motor cortex following nerve lesions.

33. DONOGHUE JP, SUNER S, SANES JN: Dynamic Organization of
•• Primary Motor Cortex Output to Target Muscles in Adult Rats. II. Rapid Reorganization Following Peripheral Nerve Lesions. *Exp Brain Res* 1990, 79:492–503.
Reorganization of the motor map can occur within hours of nerve transection. This suggests that local changes within the cortex are responsible for the process.

34. JACOBS KM, DONOGHUE JP: Reshaping the Motor Cortical
•• Maps by Unmasking Latent Intracortical Connections. *Science* 1991, 251:944–947.

The motor effects of microstimulation of the motor cortex can be changed by injecting bicuculline (a GABA antagonist) locally in the cortex. This suggests that the organization of the motor map is dynamic and depends on intact intracortical GABA-mediated inhibitory mechanisms.

35. NUDO RJ, JENKINS WM, MERZENICH MM: Repetitive Microstim-
• ulation Alters the Cortical Representation of Movements in Adult Rats. *Somatosens Mot Res* 1990, 7:463–483.
Repeated microstimulation of the motor cortex resulted in a change of the boundaries of the motor map. This indicates that the map is dynamically maintained and is probably activity-dependent.

AP Georgopoulos, Brain Sciences Center (11B), Veterans Affairs Medical Center, One Veterans Drive, Minneapolis, Minnesota 55417 and Department of Physiology, University of Minnesota Medical School, Minneapolis, Minnesota 55455, USA.

J Ashe, Brain Sciences Center (11B), Veterans Affairs Medical Center, One Veterans Drive, Minneapolis and Department of Neurology, University of Minnesota Medical School, Minneapolis, Minnesota 55417, USA.