

The Cortical Control of Movement Revisited

Review

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Recently, we found that electrical stimulation of motor cortex caused monkeys to make coordinated, complex movements. These evoked movements were arranged across the cortex in a map of spatial locations to which the hand moved. We suggest that some of the subdivisions previously described within primary motor and premotor cortex may represent different types of actions that monkeys tend to make in different regions of space. According to this view, primary and premotor cortex may fit together into a larger map of manual space.

Introduction

How does the primate cerebral cortex control movement? During the past century, three interrelated hypotheses have dominated the research. These hypotheses remain in debate and are now thought to be at least partly incorrect. They are: (1) Primary motor cortex, located on the precentral gyrus, contains a topographic map of the body. The foot is represented at the top of the cerebral hemisphere, the mouth is represented at the bottom, and other body parts are systematically arranged between (see Figure 1A). (2) Each point in the map specifies the tension in a single muscle or, perhaps, a small related group of muscles. The pattern of activity across the map thus specifies a pattern of muscle tensions across the body, resulting in the desired movement. (3) The cortical motor areas are organized in a hierarchical fashion. Premotor cortex (see Figure 1B) projects to and controls primary motor cortex, which in turn projects to and controls the spinal cord.

These three familiar views of motor cortex were summarized as long ago as 1938 by Fulton. Since then, a growing body of evidence has cast some doubt on all three hypotheses:

(1) Investigators failed to find the hypothesized orderly map of the body in primary motor cortex (Sanes and Schieber, 2001). Instead, the somatotopy is fractured and intermingled (e.g., Penfield and Boldrey, 1937; Woolsey et al., 1952; Gould et al., 1986; Nudo et al., 1992; Donoghue et al., 1992; Schieber and Hibbard, 1993; Sanes et al., 1995). A broad organization can be discerned, with a hindlimb region located medially, a face region located laterally, and a forelimb region in-between. These three regions overlap to some extent. Whether there is any somatotopic organization within each of these broad regions is still in debate. In the forelimb region, the fingers are represented in an intermingled fashion and overlap at least partly with a repre-

sentation of the arm (Donoghue et al., 1992; Schieber and Hibbard, 1993; Park et al., 2001).

(2) It is now understood that each site in cortex does not control one muscle. The connectivity is more complex. Some investigators suggest that neurons in motor cortex may influence high-level aspects of movement, such as direction or velocity of the hand through space (Georgopoulos et al., 1986, 1989; Caminiti et al., 1990; Reina et al., 2001). Others suggest that joint angle is coded in motor cortex (Scott and Kalaska, 1995, 1997) or that muscle tension is coded, perhaps in a complex fashion in which each location in cortex influences many muscles (Evarts, 1968; Cheney et al., 1985; Donoghue et al., 1992; Kakei et al., 1999; Todorov, 2000; Cabel et al., 2001). All of these possibilities have some evidence in support of them, and the debate has not yet been resolved. Indeed, almost every movement parameter that has been tested has been found to be encoded by motor cortex neurons.

(3) The hierarchical organization among the cortical motor areas is in question. The division between primary motor and premotor cortex is notoriously fuzzy; it may be more of a gradient than a border. Damage to the primary motor area does not cause a general loss of the ability to move; instead, it results in a specific deficit in fine manual coordination (e.g., DennyBrown and Botterell, 1947; Travis, 1955; Kermadi et al., 1997; Rouiller et al., 1998). Since Fulton (1938), many new motor areas have been described, including the supplementary motor area (Penfield and Welch, 1949; Woolsey et al., 1952) the cingulate motor areas (He et al., 1995), and many subdivisions of the premotor cortex (e.g., Wise et al., 1997; Rizzolatti and Luppino, 2001). The hierarchical relationship among these areas is not certain, because most of them project to the spinal cord in complex, overlapping patterns (e.g., Murray and Coulter, 1981; Dum and Strick, 1991, 1996; Maier et al., 2002). Thus, the notion of a “primary” motor area is in question because there is no single motor area that provides the output from cortex to the spinal cord.

In order to address some of these unresolved questions, we electrically microstimulated sites in motor cortex of monkeys (Graziano et al., 2002). Each site was stimulated for half a second, on the approximate time-scale of a monkey’s normal arm and hand movements. This stimulation caused the monkey to enact complex, coordinated movements, such as reaching, grasping, or pantomiming a flinch from a nearby object. The evoked movements were arranged across the cortical surface in a rough map of spatial locations to which the movements were directed. The map included parts of both primary motor and premotor cortex. Primary motor cortex emphasized hand locations in central space and manipulatory postures of the fingers and wrist. Premotor cortex emphasized other regions of manual space, such as grip postures near the mouth or reaching postures in lateral space. These results surprised us at first, because they could not be predicted from the traditional hypotheses about motor cortex control. The traditional hypotheses, however, do not easily account for much of the

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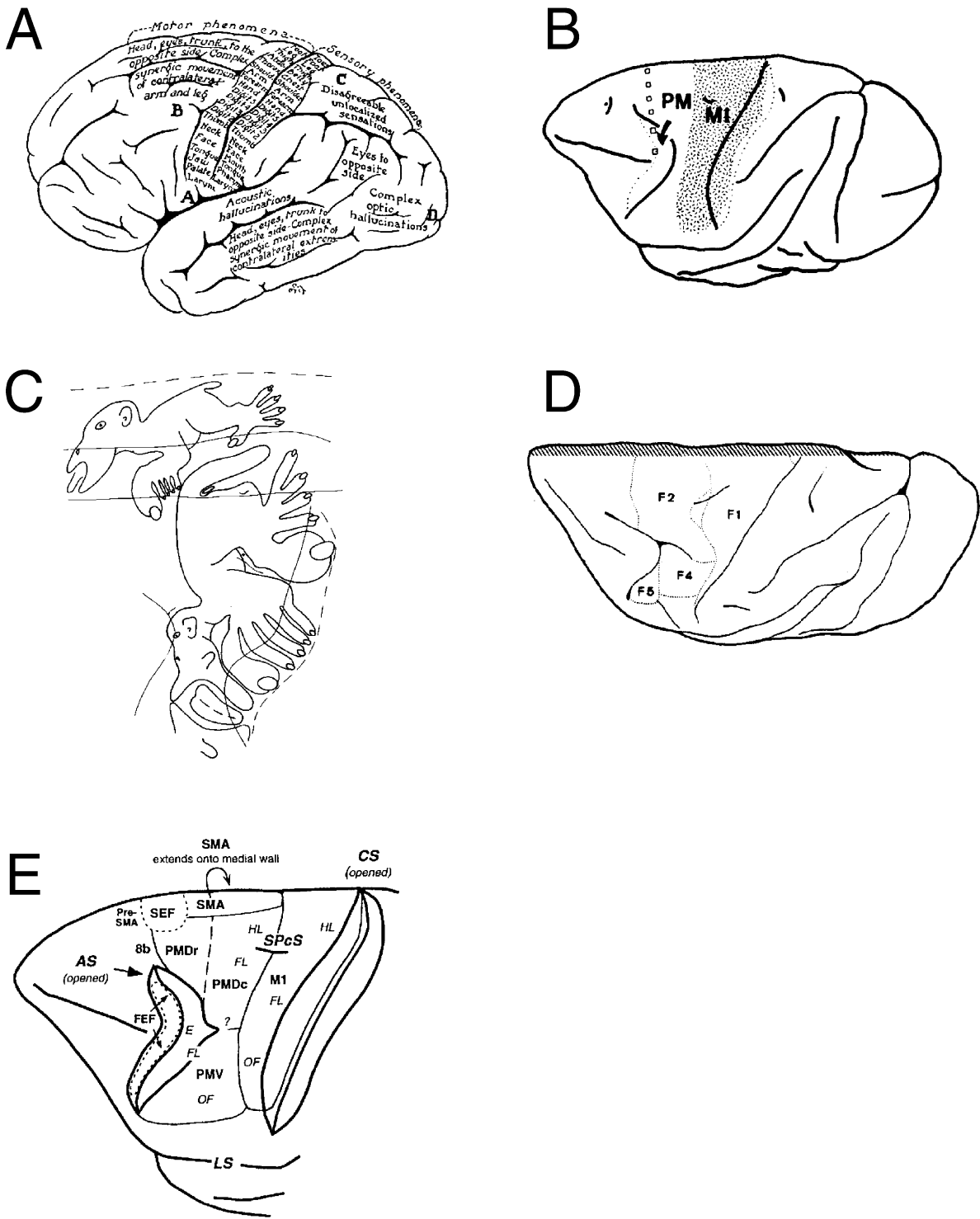


Figure 1. Five Views of the Organization of Motor Cortex

(A) Foerster's map of the somatotopy in the human motor cortex, based on surface electrical stimulation. Cited in Fulton (1938, p. 403).

(B) The primary motor strip (labeled M1) and a more anterior, premotor strip (PM) in the monkey. (Adapted from Wise, 1985).

(C) Woolsey's view of a single motor map (MI) on the precentral gyrus and a second motor map (MII) on the medial wall of the hemisphere (adapted from Woolsey et al., 1952). Note that in Woolsey's map, the fingers and toes occupy the region that is traditionally termed primary motor cortex.

(D) Subdivisions of the monkey precentral gyrus according to Matelli et al. (1985).

(E) Subdivisions of the monkey precentral gyrus according to Wise et al., 1997.

previous data. In this review, we suggest that the map of movements that we obtained closely matches the previous data and may provide a new framework for understanding the functions of the primary motor and premotor areas and their relationship to each other.

The stimulation technique that we used is common in the study of many brain areas but different from methods traditionally used in studies of motor cortex. We therefore begin this review with a discussion of the electrical stimulation technique and its relationship to traditional views of motor cortex. We then briefly describe our results suggesting that certain parts of primary motor and premotor cortex may fit together into a single map of complex postures. Finally, we discuss how this map relates to the previous literature.

Microstimulation on a Behavioral Timescale to Study Brain Function

The use of electrical stimulation to study motor cortex dates back at least to Fritsch and Hitzig (1870), who used stimulating electrodes on the surface of the dog brain to demonstrate a rough somatotopic organization. Over the next 80 years, a large number of experiments obtained similar results in monkeys, apes, and humans (e.g., Ferrier, 1873; Foerster, 1936; Fulton, 1938; Penfield and Boldrey, 1937; Woolsey et al., 1952).

Asanuma and colleagues pioneered the method of using low currents delivered to cortex through a micro-electrode (e.g., Stoney et al., 1968; Asanuma, 1975; Asanuma and Arnold, 1975; Asanuma et al., 1976). This technique was subsequently used by many others (e.g., Strick and Preston, 1978; Sessle and Wiesendanger, 1982; Weinrich and Wise, 1982; Kurata, 1989; Sato and Tanji, 1989; Huntley and Jones, 1991; Stepniewska et al., 1993; Wu et al., 2000). Most of these experiments used brief trains of electrical pulses, each train typically less than 20 ms, to evoke a muscle twitch.

By extending the stimulation trains to longer durations, we were able to observe complex, coordinated movements (Graziano et al., 2002). The twitch evoked by a short train appeared to be the beginning of the longer movement evoked by the longer train. Why then did experimenters limit themselves to short stimulation trains?

Asanuma and Arnold (1975) outlined two reasons for using brief trains when stimulating cortex. One reason was to limit the cellular damage that might occur with the accumulation of electric charge. This difficulty has since been solved. Most studies now use biphasic pulses, consisting of a negative followed by a positive phase. In this procedure, the charge is balanced, and thus higher currents and longer trains can be safely used (Tehovnik, 1996).

A second reason to limit stimulation to a brief train of pulses was to try to control the spread of neuronal signals through the motor network (Asanuma, 1975; Asanuma and Arnold, 1975). This attempt to control the spread of signal was the result of a lack of understanding about the functioning of networks. Whereas the projection from motor cortex to the spinal motor neurons was understood to be important, the interconnections with the cerebellum, basal ganglia, red nucleus, thalamus, parietal lobe, and supplementary motor cortex, and the

projections of many of these areas to the spinal cord, were largely ignored, and their recruitment by electrical stimulation of motor cortex was seen as an artifact. Likewise, lateral connections within motor cortex were seen as an experimental nuisance. Short stimulation trains were used in the hope that they would somehow channel the signal directly from motor cortex to the spinal motor neurons while avoiding the other, unwanted connections through the network. This technique, however, became controversial. It was discovered that even a single pulse of electrical current applied to the cortex recruited widespread circuits (Jankowska et al., 1975). Long stimulation trains caused even more recruitment of circuits. Thus, it appeared to be impossible to channel the activity along one pathway through the motor network while blocking it from other, connected pathways through the same network.

When electrical stimulation was used to study the function of brain systems outside of motor cortex, the method was altered. No attempt was made to channel the activity along one or another pathway. Rather, the signal was assumed to follow the existing pattern of connections. This spread of signal through the network was viewed as a necessary part of the technique rather than as something to control or avoid. The stimulation trains were typically applied on the same timescale as the behavior under study, because these train durations usually evoked behaviors that were similar to natural behaviors. For example, in the superior colliculus, a complete saccadic eye movement unfolds during stimulation trains of about 80 ms, whereas shorter stimulation trains result in truncated saccadic eye movements (Stanford et al., 1996). Stimulation trains up to 400 ms in the superior colliculus evoke coordinated movements of the head and eyes resembling natural gaze shifts (Freedman et al., 1996). In the hypothalamus of rats and primates, stimulation trains ranging from 10 s to 3 min are used to evoke feeding and mating behaviors; the behavior pattern stops when the stimulation train stops (e.g., Caggiula and Hoebel, 1966; Hoebel, 1969; Quaade et al., 1974; Okada et al., 1991). In one of the few studies to apply longer stimulation trains to motor cortex, Huang et al. (1989) stimulated the orofacial part of motor cortex and found that stimulation trains up to 3 s evoke rhythmic jaw movements similar to chewing, while shorter stimulation trains evoke muscle twitches. In visual and somatosensory cortical areas, stimulation on a behavioral timescale can influence an animal's perceptual judgements (Salzman et al., 1990; Britten and van Wezel, 1998; DeAngelis et al., 1998; Romo et al., 1998).

In this type of experiment, the directly stimulated tissue is thought to influence a wide network of neurons: the network influences behavior, and the behavior can be measured. It is hoped that this effect on behavior is at least similar to the effect caused by naturally occurring neuronal activity. However, electrical stimulation is non-physiological and thus should always be interpreted with caution. It can presumably activate neurons in unnatural patterns. The technique is most convincing when the evoked behaviors (1) resemble naturally occurring behaviors, (2) are organized in the brain in an orderly functional architecture, and (3) match other known properties of the brain area.

We used this method of electrical stimulation on a

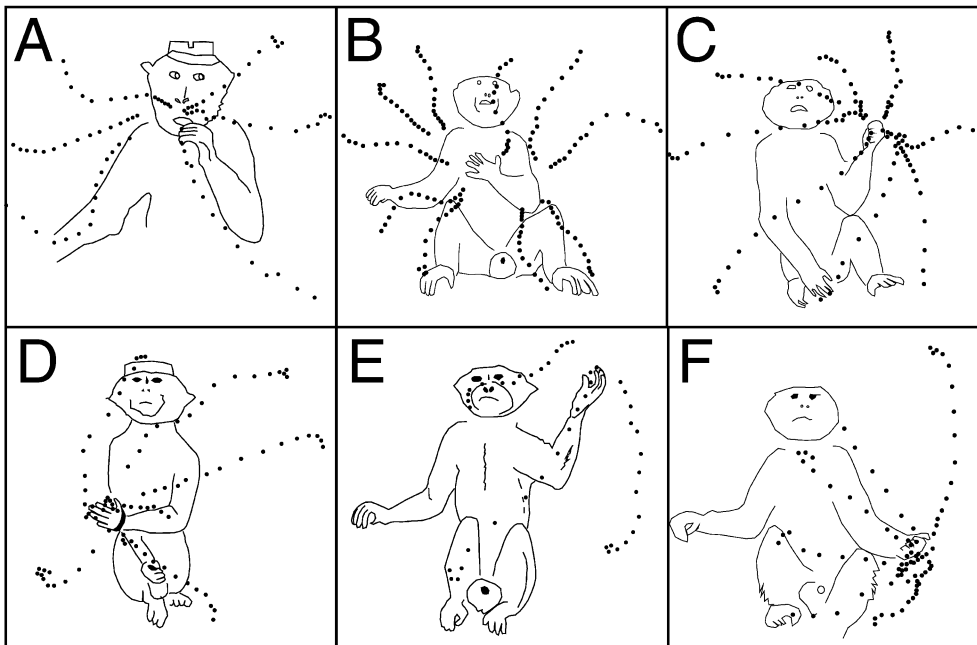


Figure 2. Six Examples of Complex Postures Evoked by Stimulation of the Precentral Gyrus

Stimulation of each cortical site in the right hemisphere evoked a different final posture of the left hand and arm. Drawings were traced from video footage taped at 30 frames per second. The dotted lines show the frame-by-frame position of the hand during stimulation. Regardless of the starting position, stimulation caused the hand to move toward a specific final position.

behavioral timescale in order to study the function of motor cortex (Graziano et al., 2002). To each site in cortex, we applied a train of biphasic pulses for 500 ms, approximating the time course of the neuronal activity that normally accompanies movement (e.g., Georgopoulos et al., 1986) and also approximating the time course of the reaching and grasping movements that monkeys typically perform (e.g., Georgopoulos et al., 1986; Reina et al., 2001). These stimulation trains were thus ten to twenty times longer than those generally used in previous experiments in motor cortex. When we applied short stimulation trains (50–100 ms), we evoked muscle twitches that were arranged across cortex in an intermingled fashion with little clear topography, matching previous reports (e.g., Gould et al., 1986; Donoghue et al., 1992). When we applied longer, half-second stimulation trains, the “twitches” unfolded into coordinated, complex movements that were arranged across the cortex in a map.

A Map of Complex Postures Evoked by Microstimulation in Motor Cortex

In this section, we describe the complex movements evoked by stimulation of motor cortex on a behaviorally relevant timescale (Graziano et al., 2002). First, we describe the results of two example sites. Then, we summarize the three main findings.

On stimulation of one site (Figure 2A), the contralateral hand closed into a precision grip posture with the fingers together and slightly curled and the tip of the thumb against the side of the forefinger (a typical precision grip for a monkey); the wrist and forearm rotated such that the point of the grip faced the mouth; the elbow and

shoulder rotated such that the hand moved smoothly to the mouth, in a manner and with a velocity profile that matched the monkey’s normal hand-to-mouth movements; and the mouth opened. All of these movements occurred simultaneously. The hand moved to the mouth, regardless of its starting position. Once the hand reached the space in front of the mouth, it stayed at that location; the hand, arm, and mouth remained stuck in this final posture until the end of the stimulation train. This movement was repeatable and consistent across hundreds of trials.

Stimulation of another site (Figure 2B) caused the contralateral elbow and shoulder to rotate such that the hand moved to a position about 10 cm in front of the chest; the hand opened into a splayed posture with the fingers straight and separated from each other, and the forearm supinated such that the open palm was aimed toward the monkey’s face. For this site as for the last site, stimulation evoked the same final posture, regardless of the direction of motion required to reach the posture.

Stimulation of other cortical sites evoked other complex movements (e.g., Figures 2C–2F). These movements had a machine-like repeatability over hundreds of trials. If an obstacle was placed between the hand and the final stimulation-evoked hand position, stimulation caused the same machine-like movement, resulting in the hand hitting the obstacle and pressing against it. That is, stimulation never caused the hand to move around the obstacle in an adaptive fashion. The stimulation-evoked movements did not appear to depend on the behavioral state of the monkey. A similar movement was obtained whether the monkey was sitting quietly, spontaneously moving, reaching toward food targets, or

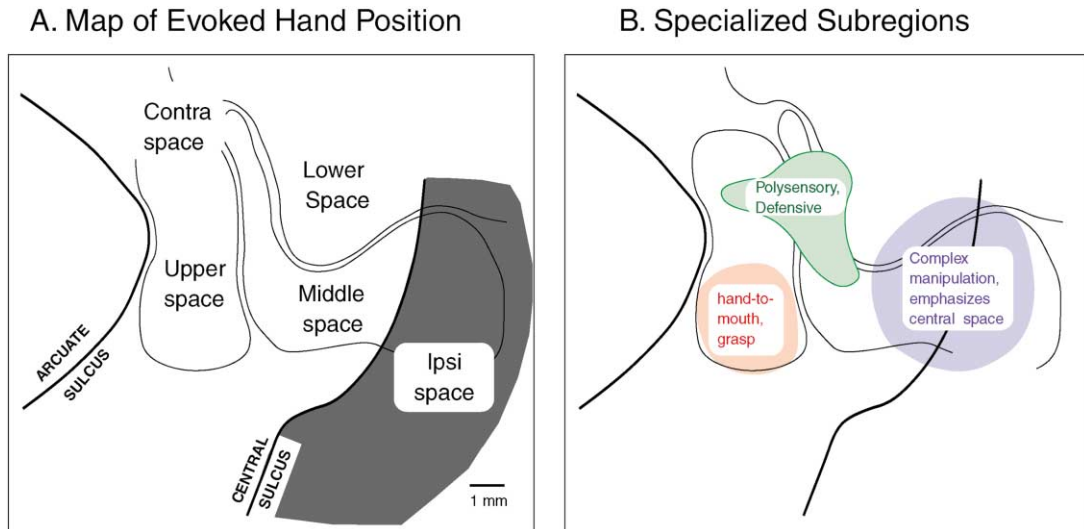


Figure 3. A Map of Postures in the Precentral Gyrus Obtained with Microstimulation on a Behavioral Timescale

(A) Stimulation at different cortical sites caused the hand to move to different positions in the space around the body. The shaded region indicates the buried cortex in the anterior bank of the central sulcus.

(B) Subregions within the map of hand position that had specialized properties. The region labeled “Polysensory, defensive” (green) may correspond functionally to the dorsal part of area F4 (see Figure 1D). The region labeled “Hand-to-mouth, grasp” (red) may correspond to part of area F5 (see Figure 1D). The region labeled “Complex manipulation, emphasizes central space” (blue) may correspond to the representation of the fingers in Woolsey’s map (see Figure 1C). It also may correspond to the primary motor forelimb representation. (Adapted from Graziano et al., 2002. The maps have been mirror-reversed from the original to facilitate comparison with the maps shown in Figure 1.)

anesthetized with a barbiturate. The stimulation-evoked movements had three basic properties:

(1) Stimulation caused the relevant joints to move into a specific final posture, regardless of the starting posture. The joints then remained in that final configuration until the stimulation train ended. Thus, we did not evoke sequences of movements or repetitive movements. We did not evoke a specific direction of movement; opposing directions of movement could be obtained depending on the starting position. Many of the evoked postures appeared to have obvious behavioral significance, such as putting food in the mouth or defending the side of the head from a threat.

(2) Sites that involved movement of the arm were arranged across the precentral gyrus to form a rough map of evoked hand positions. This map is summarized in Figure 3A. The map contained some degree of local disorder. The organization was not apparent over a distance of a few millimeters and became apparent only over greater distances. Hand position was clearly not the only variable specified by stimulation of each site. The posture of the entire arm and sometimes of the wrist and fingers was specified. The acceleration and speed with which the joints converged on the final posture also varied from site to site. Hand position, however, appeared to be the parameter that varied systematically across the cortical surface.

(3) This single map of hand position encompassed both primary motor cortex and parts of the adjacent premotor cortex, extending from the anterior bank of the central sulcus forward to the arcuate sulcus. Neither primary motor nor premotor cortex by itself contained a complete map of hand positions in space. Primary motor cortex corresponded mainly to an enlarged repre-

sentation of the central space in front of the chest. As described in a later section, we suggest that the specialized anatomical and physiological properties of primary motor cortex may be related to the complex manipulation of objects that is most commonly performed in this part of the workspace.

Other maps in the brain also have specialized subregions. For example, primary visual cortex contains a foveal representation that is different in its neuronal properties and anatomical connections from the peripheral representation. A naive investigator might think that the foveal representation is a separate visual area at a more primary level of processing, with its smaller receptive fields and greater emphasis on visual detail. However, the foveal representation and the peripheral representation are encompassed by a single map of visual space. Furthermore, the two regions are not separated by a clear border but rather grade into each other. In the same fashion, we suggest that some of the specialized subregions that have been identified in the precentral gyrus may belong together in the larger context of a map of postures.

Movement Variables Controlled by Motor Cortex *Complex Mapping from Cortex to Muscles*

A traditional view of motor cortex is that it contains a map of the body’s musculature (e.g., Fulton, 1938; Asanuma et al., 1976). Activity at each location in the map causes an increase in tension in the corresponding muscle. A more recent view is that each point in cortex ultimately connects to many muscles, and likewise, each muscle is connected to many points in cortex (e.g., Cheney et al., 1985; Donoghue et al., 1992; Todorov, 2000; Sanes and Schieber, 2001). In this view, activity

at a location in cortex should result in a change in tension in a distributed set of muscles.

Cheney et al. (1985) recorded the activity of single neurons in motor cortex and, simultaneously, measured the activity of muscles in the arm. They obtained what they called "spike triggered averages" or the average effect on muscle activity caused by each action potential of the neuron being studied. For many neurons, each action potential was followed by a minute but measurable change in more than one muscle. For a subset of neurons, each action potential appeared to cause an increase in activity in one group of muscles and a simultaneous decrease in activity in the opposing set of muscles. These results suggested that each neuron in motor cortex was connected in a complex way to the periphery and might contribute to forelimb movements that required the coordinated contraction of some muscles and relaxation of others.

Our stimulation results suggest an even more complex relationship between cortex and muscles. Stimulation of a site in cortex can drive the arm one direction or another, depending on the starting position, in order to arrive at a single final position. This result suggests that different sets of muscles may become active depending on the initial position of the arm. We confirmed this complex mapping from cortex to muscles by recording the electromyographic (EMG) activity of upper arm muscles evoked by stimulation (Graziano et al., 2002; C.S.R. Taylor et al., 2002, Soc. Neurosci., abstract). We found that the EMG activity varies depending on the starting position of the arm. With one start position, a muscle may act as an agonist and show one pattern of EMG activity, typically a short latency burst. With another start position, the same muscle during stimulation at the same brain site may act as an antagonist and show a different pattern of activity, typically a longer latency burst, or a drop in activity followed by a rise, or no activity at all. Thus, motor cortex may influence movement at the level of muscles, but it does so in a complex way. The mapping of cortical sites to muscles is not only many to many, as previous experiments have already demonstrated, but the mapping also appears to change depending on the starting position of the joints, at least in the case of upper arm muscles.

Coding of Higher-Order Movement Parameters

Georgopoulos and colleagues (1986) trained monkeys to reach in various directions from a central starting position and found that neurons in motor cortex responded during the reach. Each neuron generally responded most during one direction of reach and responded less well during neighboring directions. That is, the neurons were tuned to the direction of reach. Though each neuron was broadly tuned, the authors pointed out that a population of such neurons could collectively provide precise spatial information about the direction of reach.

Other experiments by Georgopoulos et al. (1992) suggested that the code for movement in motor cortex must be more complex than a simple direction code. Many groups have since demonstrated that the firing of motor cortex neurons is correlated with parameters such as the angles of joints, the force applied by the arm muscles, and the velocity of the hand movement in space (Kalaska et al., 1989; Caminiti et al., 1990; Scott and

Kalaska, 1995, 1997; Kakei et al., 1999; Reina et al., 2001; Cabel et al., 2001).

Scott and Kalaska (1995, 1997) showed that the directional preference of most neurons changed when the monkey was required to maintain an unusual arm posture, with the elbow raised. Thus, the neurons seemed sensitive to the posture of the entire arm and how that posture changed over time rather than reflecting only the changing position of the hand in space. Scott and colleagues speculated that motor cortex neurons may control so-called intrinsic variables, such as muscle force and joint angle, rather than extrinsic variables, such as the position or movement of the hand in external space. Other experiments (Kakei et al., 1999) suggest that the firing of motor cortex neurons is correlated with both intrinsic and extrinsic variables, at least for wrist movements.

These single-neuron experiments have the limitation that they test the correlation between neuronal activity and a restricted set of simple movements. Neurons that encode complex movements might produce a confusing and diverse pattern of results when filtered through these simpler tasks. Electrical stimulation can help to resolve this difficulty, because it is a causal technique rather than a correlational one. It is possible to measure the movement that is ultimately caused by activity at a location in motor cortex.

Does electrical stimulation of motor cortex specify hand location in space, individual joint angles, or the muscle forces involved in producing a particular velocity profile? Our results suggest that all of these aspects of movement may be specified. Stimulation of each site within the arm and hand representation evoked a movement to a specific, final posture. Because the arm posture was specified, the location to which the hand moved was also specified. However, each site did not appear to encode only hand location, independent of the joint angles that composed the arm posture. There are many postures of the arm that can correspond to the same hand location, and stimulation of one site specified only one arm posture. Thus, our results agree closely with the findings of Scott and Kalaska (1995, 1997) in that the posture of the arm, not merely the position or movement of the hand, appeared to be of critical importance.

Dynamic aspects of movement such as the acceleration of the hand also appeared to depend on the cortical site that was stimulated. For example, for a hand-to-mouth movement, the velocity profile of the hand was appropriate for putting food in the mouth without damaging the face (e.g., 20 cm/s at peak speed for one stimulation site). For a protective movement in which the hand moved to an upper lateral position and turned outward as if to block an impending threat to the head, the velocity was remarkably fast, appropriate for a defensive gesture (230 cm/s at peak speed for one stimulation site).

These stimulation results suggest that movement control in motor cortex might be organized in terms of behaviorally useful actions aimed toward a goal posture. In this case, asking whether the control is extrinsic, intrinsic, kinematic, or dynamic may be the wrong question. It may be all of those, perhaps to different degrees for different types of movement.

Postural Coding as a General Method of Movement Control

The idea of movement control by means of postural coding is not new. It has been particularly successful in the study of speech and of facial expressions. In speech, each phoneme may be defined by a posture of the vocal tract including the mouth, tongue, and larynx (Fowler et al., 1980). To produce a phoneme, the speaking apparatus moves toward this final posture. It does not need to achieve the final posture, but only to move toward it. For example, in this view, a given vowel "is an equivalence set of gestures that are equivalent because they all aim toward some particular limiting shape and length of the vocal tract" (Fowler et al., 1980). Speech is composed of a sequence of these gestures toward defined postures. Why should speech have evolved in this fashion? One possibility is that the mechanisms for speech were built on a preexisting mechanism for motor control, one that emphasized the specification of complex, behaviorally useful postures. When we stimulated in the ventral part of the precentral gyrus, in the mouth and face representation, we often caused the lips and tongue to move toward specific postures (Graziano et al., 2002). For example, at one site, stimulation caused the mouth to open about 2 cm and the tongue to move to a particular location in the mouth. Regardless of the starting posture of the tongue or jaw, stimulation evoked a movement toward this final configuration. This type of posture may be useful to a monkey for eating but could also be an evolutionary precursor to the phoneme.

Facial expressions appear to be controlled in a manner strikingly similar to the phonemes in spoken language. An emotional expression is conveyed by the movement of the facial musculature toward a particular posture (Ekman, 1993). A frown, a smile, an angry expression, a surprised expression, a disgust face, all these can be categorized by their archetypal final postures. However, even a subtle movement toward this postural endpoint will vividly express an emotion. Thus, again, the system appears to operate by means of a repertoire of postures toward which movements are made.

Could limb movements also be controlled at some level by means of a stored set of postures? Rosenbaum and colleagues (1995) proposed a model for limb control that uses linear combinations taken from a basic set of stored postures. The map of postures that we evoked by electrical stimulation in motor cortex could provide a basis for this method of limb control. The map in motor cortex is similar to a map of leg postures evoked by electrical stimulation of the spinal cord in frogs and rats (Giszter et al., 1993; Tresch and Bizzi, 1999); thus, the spinal cord might also control movement partly at the level of posture.

In motor control, there is a subtle but important distinction between specifying a final posture and specifying a trajectory that is aimed toward a final posture. An example of a control algorithm that specifies only the final posture is the equilibrium position hypothesis. According to this hypothesis, limb movement is controlled by specifying *only* a final set of muscle tensions (Bizzi et al., 1984). If the muscles acquire that set of tensions and maintain them in a steady state, the limb will move to the desired final posture and remain there.

The equilibrium position hypothesis is now known to be incorrect. During a limb movement to a specified posture, the muscles do not acquire a fixed set of tensions but rather perform a complex dance of activity, resulting in a smooth path (e.g., Hallett et al., 1975; Bizzi et al., 1984; Cooke and Brown, 1990). This complex pattern of muscle activity depends on both the initial and final position of the arm. Thus, the entire trajectory of the arm is specified, not only the desired final configuration.

The stimulation-evoked postures that we found in motor cortex follow the pattern of muscle activation observed during normal movement rather than the pattern predicted by the equilibrium position hypothesis. Stimulation evokes a complex pattern of muscle activity in the upper arm that resembles the interplay between agonist and antagonist muscles observed during natural movement. This pattern of muscle activity depends on the starting position of the arm. Thus, stimulation specifies more than just a final posture; it specifies the entire, coordinated trajectory that is aimed toward the final posture.

Relationship between Primary Motor and Premotor Cortex

The frontal cortex contains many proposed areas thought to be part of the motor network (e.g., Matsuzaka et al., 1992; Picard and Strick, 1996; Wise et al., 1997; Rizzolatti and Luppino, 2001). Some of these areas are diagrammed in Figures 1D and 1E. These areas include primary motor cortex, ventral premotor cortex (sometimes divided into areas F4 and F5), dorsal premotor cortex (sometimes divided into a caudal and a rostral part), supplementary motor cortex, a presupplementary motor area, and a set of motor areas on the medial wall of the hemisphere.

When we electrically stimulated motor cortex, we found a single map of arm postures (Figure 3A) that encompassed the precentral gyrus, covering the forelimb representation in primary motor cortex and premotor cortex including ventral premotor cortex (F4 and F5) and dorsal premotor cortex (probably mainly the caudal division). These areas appeared to form a complete, unitary map of the position of the hand in space. How can this single map be reconciled with the mosaic of separate areas described within this region of cortex?

The map of postures appeared to contain specialized subregions with somewhat different functions (Figure 3B). These subregions included the representation of hand location in central space, emphasizing complex manipulation (roughly matching the primary motor hand area); the representation of hand location near the mouth, emphasizing grip postures of the fingers and open postures of the mouth (roughly matching the dorsal, posterior part of area F5); and a multimodal region in the center of the map, emphasizing defensive movements (roughly matching the dorsal part of area F4). Thus, the map that we obtained with electrical stimulation is not only consistent with previous findings but also provides a possible organizing principle. The subregions may differ because they emphasize the types of actions that monkeys tend to make in different regions of space. In the following sections, we discuss these different subregions in greater detail.

A Manual Fovea: The Use of Central Space for Manipulation

We recently videotaped monkeys in their home cages in the laboratory and also monkeys in group cages at the Bronx Zoo (M.S.A. Graziano and D.F. Cooke, 2002, Soc. Neurosci., abstract). We then analyzed the tapes frame-by-frame to study the types of movements typically generated by the monkey motor system. We soon realized that the most common function of the arm and hand was not to reach (13.9% of total time) but rather to maintain a posture, for example, while holding an object or supporting the body's weight (86.1% of time). Of the total time that monkeys used their hands to grasp or manipulate small objects such as food or toys, 96.8% of this time was spent with the hand poised in central space either in front of the chest (57.6%) or in front of the mouth (39.2%). Grasping and manipulating small objects was almost never performed in other parts of the workspace. On those occasions when the monkey did reach outside of central space to grasp a small object, it immediately brought the object into central space for further manipulation. Once an object was brought within the central space in front of the chest, the monkey typically held it with one or both hands in a precision grip (thumb against forefinger) or a power grip (a fist), rotated the object by pronating or supinating the forearm, rubbed the object with one hand against the open palm of the other hand, hit the object against a hard surface, or opened one hand in a splayed posture with the palm directed toward the face, possibly to inspect the palm after contact with the object. Punctuated throughout these manipulations of the object in central space, the monkey also raised the object briefly to the mouth and bit it while still holding it with a grip posture of the hand. Thus, the hand was generally in a grip posture when near the mouth and in a large variety of complex postures involving the wrist, the forearm, and the independent use of the fingers when in the space in front of the chest.

We hypothesized that these behavioral trends should be reflected in the map of postures that we observed in motor cortex. This turned out to be the case. Within the map of hand position, two subregions appeared to emphasize the control of the fingers, wrist, and forearm. One subregion corresponded to hand locations at the mouth. Stimulation within this region always caused the hand to shape into a grip posture. The hand generally moved to the mouth with great spatial precision, usually reaching the same final position within a few centimeters. At most sites within this hand-to-mouth part of the map, stimulation also caused the mouth to open. Rizzolatti et al. (1988) recorded from single neurons in this area, which they termed F5, and concluded that it is specialized for controlling grip postures of the hand and movements of the mouth. Neurons in F5 also appear to be involved in movements of the arm, especially toward the mouth. Rizzolatti and colleagues (Rizzolatti et al., 1988; Murata et al., 1997; Fogassi et al., 2001) argue that this part of cortex serves the general function of coordinating grip postures in any region of space. On the basis of our data, we argue that it is biased toward grip postures associated with bringing the hand to the mouth, though of course it may also contribute to other functions.

The second subregion of the map that emphasized the control of the hand corresponded to hand locations in a large area of space in front of the chest. Stimulation within this part of the map evoked a variety of hand postures, including a grip with the thumb against the forefinger, a fist, an open hand with all five digits splayed, rotations of the wrist, and also a pronation or supination of the forearm, matching the natural behavior of monkeys within this region of their manual workspace. In this part of the map, the representation of hand position appeared to be especially coarse. If the hand was in a peripheral location, stimulation drove it toward central space. If the hand was already within a large central region of space, stimulation often had no observable effect on hand location. At several sites, stimulation evoked only a posture of the fingers and wrist but did not affect the position of the arm. Thus, this part of the map emphasized the fine control of the wrist, fingers, and forearm and had a relatively imprecise representation of arm position that favored central space. This part of cortex corresponded to the primary motor forelimb representation. As described in the next section, the primary motor forelimb representation has long been known to emphasize the control of manual dexterity. On the basis of our data, we suggest that this emphasis on manual dexterity is paired with an emphasis on hand locations in central space in front of the chest, the monkey's "manual fovea" in which manipulation is most commonly performed. Just as the fovea on the retina is reflected in every stage of visual processing in the brain, the "manual fovea" may have profound implications for the neuronal control of the hand and arm.

A similar concept of a manual or motor fovea was proposed by Tillery et al. (1994), who found that in human subjects, fine spatial control of the hand was most accurate in a restricted region of space in front of the chest. They suggested that the exact location of the manual fovea was consistent within each subject but varied among subjects.

Fulton and Woolsey on the Organization of Motor Cortex

It was once thought that the giant pyramidal cells in layer 5 of motor cortex, the Betz cells, formed the principal output from the cortex to the spinal cord. Fulton (1938) called them a "funnel" for information to flow from cortex to the spinal cord. The Betz cells are most common in the posterior part of the precentral gyrus and within the central sulcus. This region of cortex was therefore assumed to be a "primary" motor area, in that it controlled the spinal cord directly. The more anterior "premotor" cortex was assumed to connect to and instruct "primary" motor cortex and thus influence the spinal cord in an indirect fashion. Consistent with this view, electrical stimulation could evoke movements at a much lower current level in primary motor than in premotor cortex (Fulton, 1938).

This view, that the precentral gyrus could be divided into a posterior, primary area and a more anterior, premotor area, soon appeared to be an oversimplification. Most of the differences between the posterior and anterior areas are graded, providing no clear border between them. The anterior area, Fulton's premotor area, turned out to be a collection of functionally different subregions (Wise et al., 1997; Rizzolatti and Luppino, 2001). The

posterior area, Fulton's primary motor area, turned out not to be necessary for the control of movement. Damage to it affected mainly fine manual coordination (e.g., DennyBrown and Botterell, 1947; Travis, 1955; Kermadi et al., 1997; Rouiller et al., 1998).

Fulton's primary motor area also turned out not to be the only motor area to project directly to the spinal cord. Instead, a range of other cortical areas, including premotor cortex, supplementary motor cortex, and motor areas on the medial wall of the hemisphere, project to the spinal cord (Murray and Coulter, 1981; Dum and Strick, 1991, 1996; Maier et al., 2002). The Betz cells may serve a specific function—one speculation is that, in the forelimb representation, they are related to the dexterity of the fingers—but whatever their function, they do not appear to act as a “funnel” providing the output from cortex to the spinal cord. As Lassek found in 1941 (Lassek, 1941), the Betz cells in monkeys account for only about 3.4% of the efferent fibers coursing through the pyramidal tract to the spinal cord.

It was originally thought that the shoulder, upper arm, forearm, and fingers were represented in a sequential fashion in a dorsal-to-ventral map (see Figure 1A). Woolsey (Woolsey et al., 1952) was one of the first to point out that, if there is an organization to the forelimb representation, it is partly an anterior-posterior one. He suggested that the fingers were represented in the posterior part of the gyrus and within the central sulcus, whereas the upper arm, shoulder, and trunk were represented in a more anterior part of the gyrus (Figure 1C). This emphasis on the fingers in a posterior part of the gyrus has been confirmed by others (e.g., Lemon and Porter, 1976; Wong et al., 1978; Kwan et al., 1978; Gentilucci et al., 1988; Park et al., 2001). Whether there is a true somatotopy, however, is in debate. The finger representation may be partly intermingled with the control of the wrist, arm, and shoulder (Gould et al., 1986; Donoghue et al., 1992; Park et al., 2001). The anterior region of the precentral gyrus does not appear to contain a simple representation of the upper arm and shoulder as Woolsey thought but rather contains a heterogeneous collection of subregions, including one that emphasizes different types of grip (Rizzolatti and Luppino, 2001).

Thus, neither Fulton's view of two somatotopic maps, each arranged vertically (Figure 1B), nor Woolsey's view of a single somatotopic map of the arm arranged horizontally (Figure 1C) captures the complexity of the data. We suggest that the data fit the map of postures that we found with electrical stimulation (Figure 3). According to this map, within the forelimb representation, the posterior part favors central space and thus emphasizes manipulation. The anterior part represents a diverse set of functions performed by the arm and hand in other regions of space, including grip postures of the hand near the mouth, reaches toward peripheral targets, and defensive gestures.

A Specialized Anatomical and Physiological Machinery for the Control of Manipulation

As described above, on the basis of the map of stimulation-evoked postures, we suggest that the posterior part of the precentral forelimb region is a “manipulation” area rather than a “primary motor” area. Damage to this part of cortex results in a permanent loss of fine finger coordi-

nation (e.g., DennyBrown and Botterell, 1947; Travis, 1955; Kermadi et al., 1997; Rouiller et al., 1998). The large pyramidal cell bodies and the high proportion of monosynaptic connections to spinal motor neurons, once thought to be hallmarks of a primary motor function, are now known to be correlated with the control of the musculature of the fingers, hand, and wrist (Bortoff and Strick, 1993; Lawrence, 1994; Maier et al., 1997; Lemon et al., 1998). Probably as a result of the large cell bodies and more direct connections to spinal motor neurons, this region of cortex has low thresholds for electrically evoking movements. The thresholds are especially low for finger movements. For example, in the anterior bank of the central sulcus, currents as low as 4 microamps can evoke movements of the fingers (e.g., Asanuma et al., 1976; Gentilucci et al., 1988). An especially high proportion of neurons in this cortical region have small tactile receptive fields on the fingers and respond during passive and active movements of the fingers (Lemon and Porter, 1976; Wong et al., 1978; Gentilucci et al., 1988).

Primates that are relatively less prehensile, such as squirrel monkeys, have a less pronounced pattern of direct connections to spinal motor neurons demarcating this “primary” motor cortex (Maier et al., 1997; Lemon et al., 1998). Bucy (1935) compared the motor cortex in a range of species and concluded that, in the more prehensile animals, the motor forelimb area was more differentiated, with the giant Betz cells concentrated in the posterior part, whereas in the less prehensile animals, the differentiation was less clear.

In summary, the posterior part of the precentral gyrus has a specialized pattern of anatomical projections, cytoarchitectonics, electrical thresholds, and single neuron properties. These specializations are often interpreted as evidence of a primary motor area. However, another interpretation is that these features are part of a specialized machinery for the control of manipulation, with an emphasis on central space.

Preparatory Activity in Primary Motor and Premotor Cortex

Perhaps the best evidence for Fulton's hierarchy, in which premotor cortex controls primary motor cortex, comes from studies of motor preparation. A standard way to study motor preparation is to record the activity of neurons while the monkey performs a delayed movement task (e.g., Weinrich and Wise, 1982; Weinrich et al., 1984; Godschalk et al., 1985; Kurata, 1989; Requin et al., 1990; Riehle, 1991). In the typical task, a sensory cue specifies the movement that should be made; then, after a delay period, a “go” signal instructs the monkey to make the movement. During such a task, some neurons in primary motor and premotor cortex respond to the sensory cue and maintain a high firing rate during the delay period before the movement. These neuronal responses are thought to reflect the preparation for movement. Such preparation-related or “set” responses are more common in dorsal premotor cortex. The transition from premotor to primary motor cortex is gradual.

The relationship between these results and the single map of stimulation-evoked postures is not clear at this point. One possibility, of course, is that premotor cortex is indeed at a higher level in a motor hierarchy and that the map of postures is misleading. Another possibility

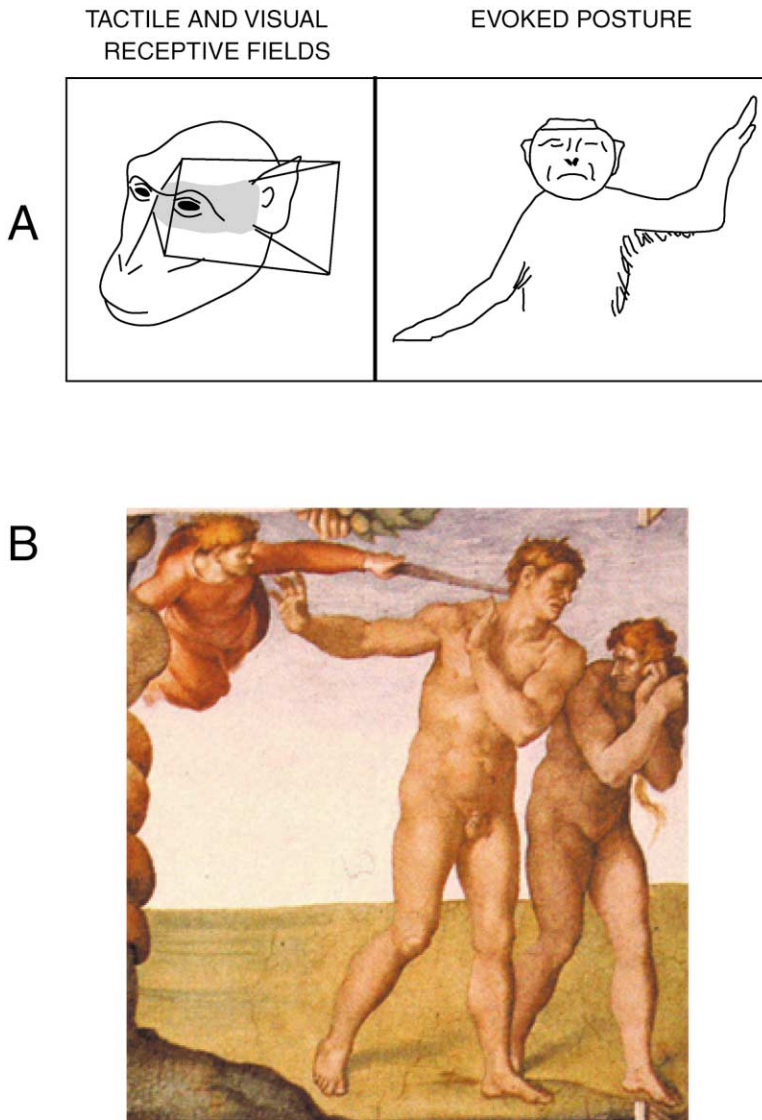


Figure 4. Defensive Postures in Monkey, Man, and Woman

(A) The first panel shows the tactile receptive field (shaded) and the visual receptive field (boxed) of neurons at a site within the polysensory zone on the precentral gyrus. Electrical stimulation of this site caused the monkey to move rapidly into a defensive posture, shown in the second panel. This posture included a facial grimace, a squinting of the eye, a turning of the head away from the side of the sensory receptive fields, a hunching of the shoulders, a fast thrusting of the hand into the space beside the head, and a turning of the hand such that the palm faced outward, away from the head.

(B) A similar defensive posture shown in a detail from Michelangelo's *Fall and Expulsion from Eden*.

is that the parts of premotor cortex in which set-related responses are most common lie outside the boundaries of the single map of postures found in our stimulation study. Indeed, set-related responses appear to be especially common in the rostral part of dorsal premotor cortex (see PMDr in Figure 1E), an area that might not be included in the map of stimulation-evoked postures.

A third speculation is that the differences between primary motor and premotor cortex may be the result of specializations within a single map. In this view, the parts of the map that represent peripheral hand locations may also emphasize the processing of visual target information and the planning of reaches. Since this part of the map overlaps dorsal premotor cortex, it may explain the high incidence of visual and set-related activity in this region of cortex.

Multimodal Neurons and the Coding of a Margin of Safety

As described in the previous section, neurons in both primary motor and premotor cortex respond to visual stimuli if the monkey is trained to make specific move-

ments in reaction to those stimuli. At least some neurons in premotor cortex, however, respond to visual stimuli in untrained monkeys and even in anesthetized ones (Rizzolatti et al., 1981; Fogassi et al., 1996; Graziano et al., 1997). These untrained visual responses are clustered in a relatively small zone that lies just posterior to the bend in the arcuate sulcus (Graziano and Gandhi, 2000). It is sometimes termed F4 (Gentilucci et al., 1988), though the polysensory responses appear to be concentrated in the dorsal part of F4. It is also sometimes termed ventral premotor cortex, or PMv (Graziano et al., 1997), though again the polysensory responses are concentrated within only one part of PMv. Here we refer to the specific region that responds to multiple sensory modalities as the polysensory zone. Most neurons in the polysensory zone have a tactile receptive field on the contralateral face, shoulder, arm, or torso. About half of the neurons are also visually responsive. The visual receptive field is typically adjacent to the tactile receptive field and extends 5–30 cm outward from the body surface. Some of these bimodal, visual-tactile cells

respond best to tactile stimuli swept across the skin in a particular direction and have a matching directional preference in the visual modality. Cells that have a tactile receptive field on the side or back of the head also often respond to auditory stimuli in the space near the tactile receptive field, within about 30 cm of the head (Graziano et al., 1999). Thus, neurons in the polysensory zone represent the space immediately surrounding the body through touch, vision, and sometimes audition.

The polysensory zone is embedded in the middle of the postural map that we observed. Stimulation within the polysensory zone evoked movements that were consistent with defending the body against nearby threatening objects (Graziano et al., 2002). Different movements were evoked depending on the location of the sensory receptive fields. For example, at some sites, the neurons had a tactile receptive field on the side of the head and a visual receptive field near the side of the head. Stimulation of this type of site evoked movements consistent with defending the side of the head from an impending threat. These movements included a squint and facial grimace that was more pronounced on the side of the sensory receptive field, a turning of the head away from the side of the sensory receptive field, a rapid movement of the hand to an upper lateral location as if blocking an object in the sensory receptive field, and a turning outward of the palm (see Figure 4). At other sites, the neurons had a tactile receptive field on the arm and a visual receptive field near the arm. Stimulation of this type of site evoked a fast withdrawal of the arm behind the back. These movements resulted in the hand reaching a final position in lower space, generally beside the thigh or hip.

These different types of movement were arranged in a topographic map. Sites for which the hand moved to upper lateral space, as if defending the side of the head, were located in the anterior part of the polysensory zone. Sites for which the hand moved to a lower location behind the back were located in the posterior part of the polysensory zone. Thus, the topography within the polysensory zone appeared to be continuous with the topography of the larger map within which the polysensory zone was embedded. That is, although the polysensory zone may be functionally distinct, it is also part of the larger map of arm postures.

Similar neuronal responses to tactile and visual stimuli have been described in area VIP in the parietal lobe. Area VIP receives convergent input from many cortical regions, including visual, somatosensory, and motor areas (Maunsell and Van Essen, 1983; Lewis and Van Essen, 2000). VIP neurons typically have a tactile receptive field on the contralateral side of the face and a visual receptive field that corresponds spatially (Colby et al., 1993; Schaafsma and Duysens, 1996; Duhamel et al., 1997, 1998). About half of the neurons respond best to nearby visual stimuli, within 30 cm of the tactile receptive field (Colby et al., 1993). The tactile and visual modalities generally share the same directional preference (Colby et al., 1993). Thus, almost identical response properties have been found in VIP and the polysensory zone, although the proportions of cell types are somewhat different. This similarity is especially interesting because VIP projects to the precentral gyrus, and its main area

of projection appears to be the polysensory zone (Lupino et al., 1999; Lewis and Van Essen, 2000).

We recently found that stimulation of area VIP evoked defensive movements similar to those evoked by stimulation of the polysensory zone (D.F. Cooke et al., 2002, Soc. Neurosci. abstract). Stimulation of cortex surrounding area VIP did not evoke the same movements. One hypothesis is that areas VIP and the polysensory zone form part of a pathway that is specialized for encoding nearby space and defending the body.

Summary

In this review, we discussed the hypothesis that the precentral gyrus contains a representation of complex, behaviorally meaningful postures. Stimulation of a site in cortex causes the relevant body parts to move from any initial configuration toward a single final posture. In the forelimb representation, these postures are arranged in a rough topographic map of hand location in the space around the monkey's body. This map encompasses many proposed areas within the precentral gyrus, including primary motor cortex and several subdivisions of premotor cortex. These different subdivisions, described by others, appear to match specialized parts of the postural map.

The map of arm postures is embedded in a larger, rough map of the monkey's body. At more ventral sites, the face and mouth are recruited. At more dorsal sites, the leg and foot are recruited. Although electrical stimulation in these other regions evoked postures, such as a reaching posture of the leg and foot or a posture of the mouth and tongue, we do not know if these postures are arranged in any topographic map. At present, our data suggest only that the hand and arm representation contains a map of space to which actions are directed.

A final caveat is in order. Motor cortex is obviously highly complex and may control movement by means of many overlapping strategies. This complexity is reflected in the diverse effects of stimulation, including movement of the hand to a location in space, movement of joints toward a final posture, movement at different speeds, and an emphasis on controlling the hand and fingers in certain regions of cortex. At the single-neuron level, even more diversity has been found in coding schemes for movement. The coding scheme may even vary depending on the type of movement or the part of the map studied. For example, the manipulation of objects may employ a specialized anatomical and physiological machinery in which the cortex exerts an especially direct control over spinal motor neurons. It is probably incorrect to assign a single motor-control algorithm to motor cortex. Here we suggest that one of possibly many strategies used by motor cortex involves a topographic map of postures that are of behavioral relevance to the animal.

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