CHAPTER 23

Ethologically Relevant Movements Mapped on the Motor Cortex

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DOES MOTOR CORTEX DECOMPOSE MOVEMENT INTO MUSCLES, OR INTEGRATE MUSCLES INTO MOVEMENTS?

The discovery of motor cortex is one of the landmark events in neuroscience. In 1870, Fritsch and Hitzig found that brief pulses of electrical stimulation applied to the cortex of a dog brain evoked muscle twitches. The twitch-evoking sites were arranged across the surface of the cortex to form a rough map of the body (Fig. 23.1). This map of the body was studied further in monkeys (e.g., Beevor & Horsely, 1887; Ferrier, 1874). Almost 70 years after the initial discovery of motor cortex, Penfield published his now famous study of the human motor cortex (Penfield & Boldrey, 1937), confirming that the human brain also contained a topographic map of body parts (Fig. 23.2). Although a map the body could be discerned in the motor cortex, the map was not cleanly segregated into separate muscles or rotations of separate joints. Instead, the topography was blurred and overlapped. This intermixing of muscles within the motor cortex map was reported in every major study. As shown in Figure 23.2, however, Penfield's iconic homunculus appeared to show a clean, segment-by-segment map of the body. Perhaps Penfield's summary diagram inadvertently contributed to the now widespread and inaccurate idea of a simple map of body parts laid out on the motor cortex.

The hypothesis of a segregated map of movement components was taken to its extreme by Asanuma and colleagues in their studies of the cat and monkey cortex (e.g., Asanuma & Rosen, 1972; Asanuma & Sakata, 1967; Asanuma & Ward, 1971). Rather than stimulating the surface of the cortex with large electrodes, Asanuma and colleagues inserted a microelectrode into the cortex and stimulated through its exposed tip. The volume of brain tissue directly affected by stimulation was probably less than half a millimeter in diameter. The stimulation current was reduced to its threshold, the level at which the evoked movement was barely detectable. Using this method, Asanuma and colleagues reported that each stimulation site in cortex was connected to a single muscle or in some cases two muscles. They argued for the presence of a segregated mapping of muscles on the cortex (Asanuma, 1975).

An alternative explanation exists for the results of Asanuma and colleagues. In what could be termed the "iceberg" interpretation, each site in cortex contributes to a complex movement that recruits many muscles that cross many joints. As part of the coordination of that movement, some muscles are more active than others. By lowering the electrical stimulation to threshold, by the definition of "threshold" the evoked movement is reduced until most of it is no longer detectable and only the one or two most strongly recruited muscles are still detectable above the noise.

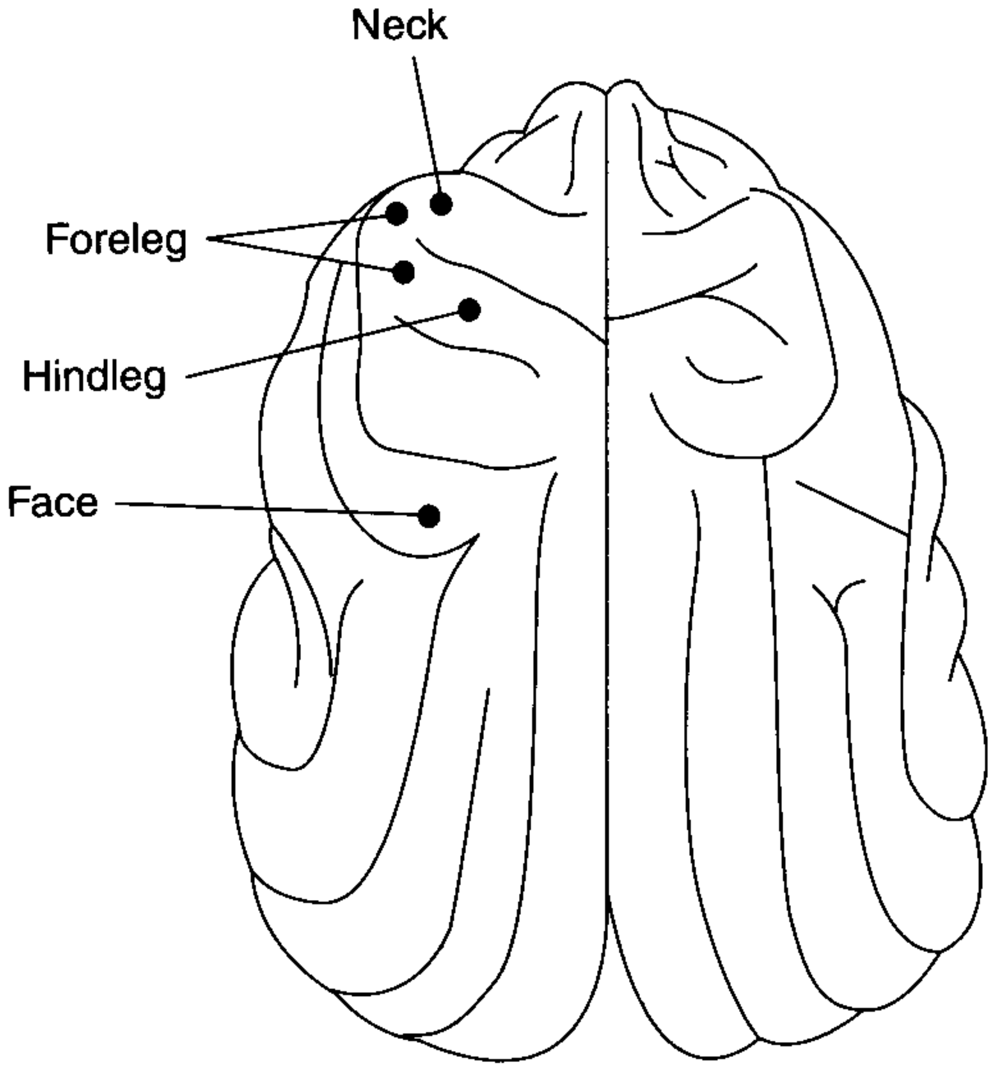

Figure 23.1 The map of stimulation-evoked movements in a dog brain. Each point indicates the approximate location of a movement center. Stimulation at or near each point evoked movements of the indicated body part. Adapted from Fritsch, G., & Hitzig, E. (1870). Uber die elektrishe Erregbarkeit des Grosshirns. Arch. f. Anat., Physiol und wissenchaftl. Mediz., Leipzig, 300–332. [On the electrical excitability of the cerebrum. Translated by G. von Bonin. In: W. W. Nowinski (Ed.), *Some papers on the cerebral cortex* (pp. 73–96). Springfield, IL: Thomas.]Used with permission.

Only the tip of the movement iceberg is measured. In this interpretation, the use of threshold stimulation by its very definition produces the misleading illusion of a muscle-by-muscle map.

Are single muscles, or combinations of muscles, controlled by the motor cortex map? The question was answered unambiguously by Cheney and Fetz (1985). They recorded the activity of neurons in the motor cortex of monkeys and the activity of muscles in the arm and hand. When a neuron in cortex fired an action potential, after a latency of approximately 5 ms, a minute effect could be observed at the muscles. By averaging the data over thousands of neuronal spikes, a clear signal could be obtained. This method of spike-triggered averaging allowed the experimenters to determine which muscles were directly affected by the firing of a neuron in cortex. The results showed that each cortical neuron could affect the activity of many muscles crossing many joints. The motor cortex did not contain a muscle-by-muscle map as suggested by Asanuma and colleagues, but instead integrated the action of muscles. Each locus in cortex, and even each neuron in cortex, affected a complex set of muscles.

One reasonable hypothesis based on the results of Cheney and Fetz is that the overlapping representation of muscles in cortex reflects the overlapping use of muscles in normal movement. In support of this hypothesis, Nudo and colleagues (1996) found that when a monkey practices a task that requires the coordinated use of two arm joints, the motor cortex develops a larger overlap in the representation of the muscles that actuate those joints. Martin and colleagues further explored the role of experience in the development of an overlapping somatotopy (Chakrabarty & Martin, 2000; Martin et al., 2005). They used microstimulation to map the motor cortex in cats. They found that at birth, the representation in motor cortex was mainly nonoverlapping. Separate joints of the forelimb were represented in discrete patches in cortex. During development, as the kitten learned to perform complex behaviors that required coordination among joints, the representations in

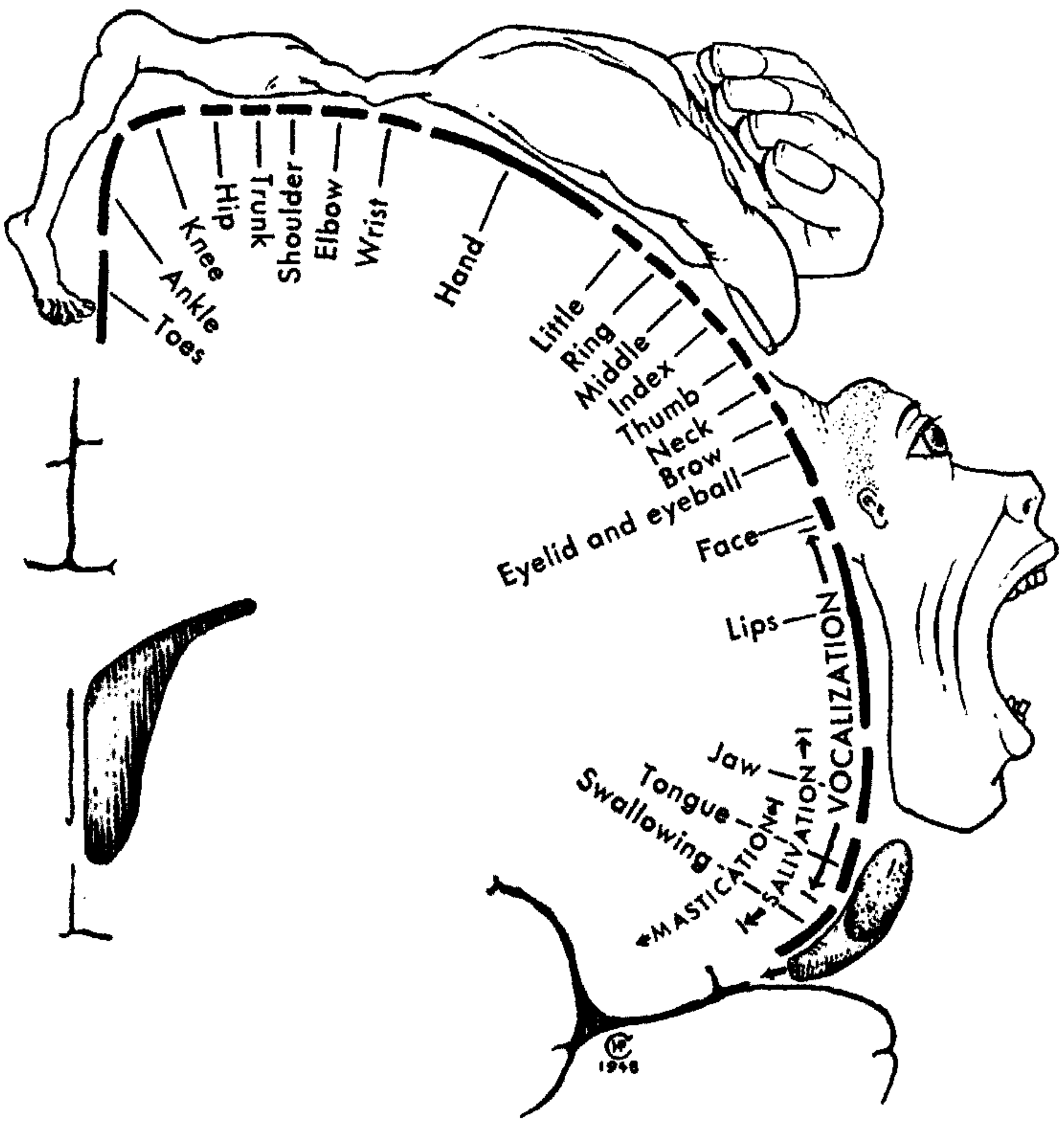

Figure 23.2 The motor homunculus of the human brain. Each point in motor cortex was electrically stimulated and the evoked muscle twitch was noted. Although each cortical point could activate many muscles, a rough body plan could be discerned. Adapted from Penfield, W., & Rasmussen, T. (1950). *The cerebral cortex of man. A clinical study of localization of function.* New York: Macmillan.

cortex developed the highly overlapped property characteristic of the adult. Individual joints were no longer typically represented in separate patches. If the kitten was prevented from practicing complex, integrated movements, the motor map did not develop the normal overlap of representations.

These results suggest that during experience the motor cortex is trained on, and comes to reflect, the movement repertoire of the animal. If an animal has a need to control individual muscles (if such an unlikely condition ever exists), the animal might well develop a motor cortex map that topographically separates the muscles. In the more common case that an animal has a need to control many muscles and joints in a coordinated fashion, such as for reaching toward an object or manipulating an object, its motor cortex develops a topography in which the relevant muscles are represented in an integrated fashion.

Recently we electrically stimulated the motor cortex in monkeys and found the often confirmed, overlapping map of muscles (Cooke & Graziano, 2004a,b; Graziano et al., 2002, 2005). However, we then extended the electrical stimulation to a duration that was behaviorally relevant. We stimulated for half a second at a time, approximating the duration of a monkey's reaching or grasping, instead of stimulating for the more typical duration of less than 50 ms. Neurons in motor cortex are not normally active in 50-ms bursts but instead, to a first approximation, are active throughout the duration of a movement. This use of electrical stimulation on a behavioral time scale is a standard method used to study brain areas outside of motor cortex. It is responsible for fundamental results such as the mapping of eye movement areas of the brain, the discovery of emotional and motivational functions of the hypothalamus, and the demonstration that cortical sensory processing causes sensory perception (e.g., Bruce et al. 1985; Caggiula & Hoebel, 1966; Hess, 1957; Hoebel, 1969; King & Hoebel, 1968; Robinson, 1972; Robinson & Fuchs, 1969; Salzman et al., 1990; Schiller & Stryker, 1972). Within motor cortex research, however, the technique of stimulation on a behaviorally relevant time scale had not been systematically explored.

Using the longer stimulation in motor cortex, we found that the muscle twitches unfolded into complex actions. Stimulation caused the monkey to perform movements that were common in its normal repertoire. Some of these movements are drawn in Figure 23.3, traced from video footage. They included ethologically relevant behaviors such as closing the hand in a grip while bringing

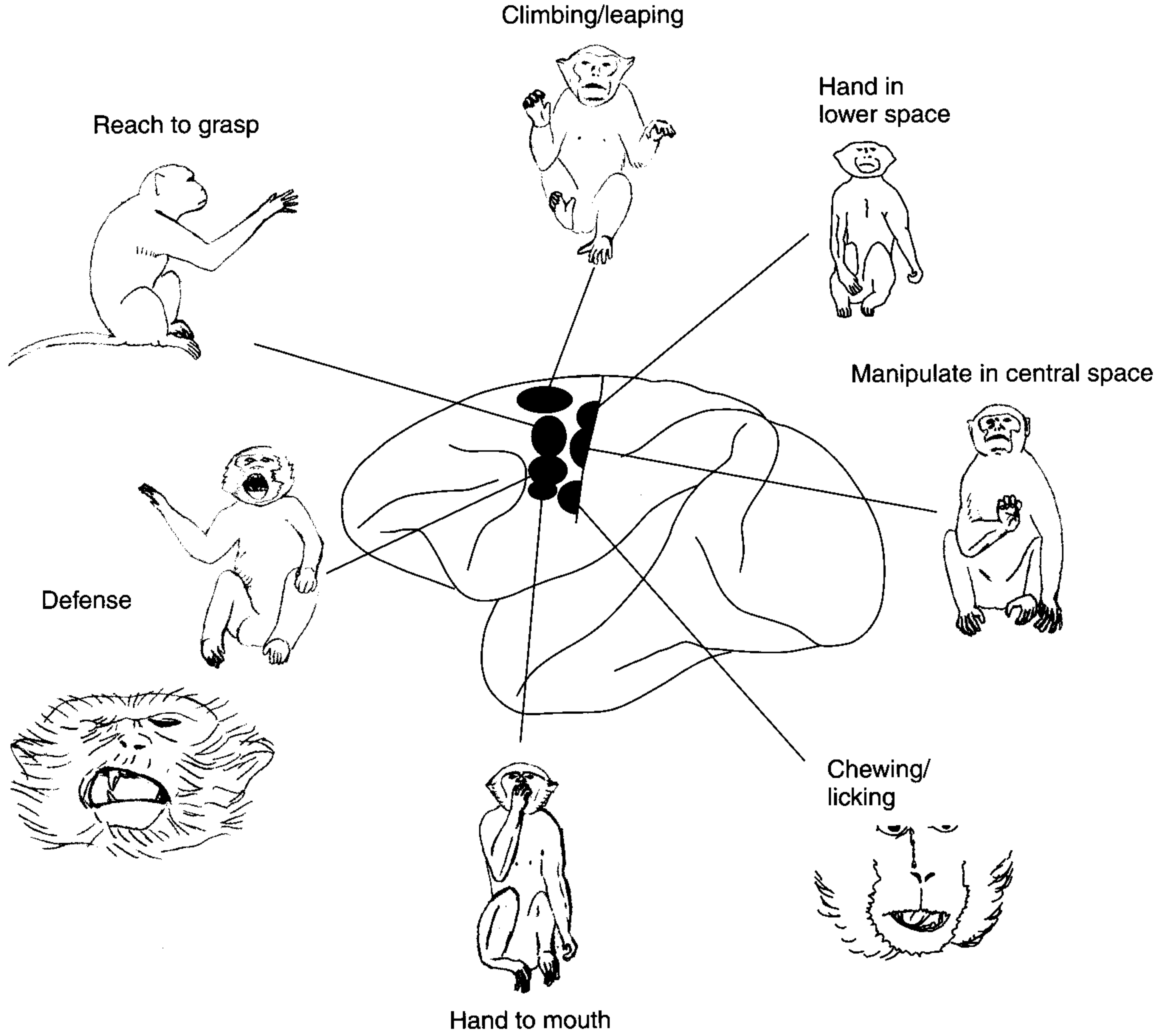

Figure 23.3 Action zones in the motor cortex of the monkey. Seven common categories of movement evoked by electrical stimulation of the cortex on the behaviorally relevant time scale of 0.5 seconds. Images traced from video frames. Each image represents the final posture obtained at the end of the stimulation-evoked movement. Within each action zone, movements of similar behavioral category were evoked. Based on results from Graziano, M. S. A., Taylor, C. S. R., & Moore, T. (2002). Complex movements evoked by microstimulation of precentral cortex. *Neuron, 34,* 841–851; and Graziano, M. S. A., Aflalo, T., & Cooke, D. F.. (2005). Arm movements evoked by electrical stimulation in the motor cortex of monkeys. *Journal of Neurophysiology, 94,* 4209–4223. Used with permission.

the hand to the mouth and opening the mouth; extending the hand away from the body with the grip opened as if in preparation to grasp an object; bringing the hand inward to a region just in front of the chest while shaping the fingers, as if to manipulate an object; squinting the facial muscles while turning the head sharply to one side and flinging up the arm, as if to protect the face from an impending impact; and moving all four limbs as if leaping or climbing. The behavioral repertoire of the animal seemed to be rendered onto the cortical sheet.

The evoked movements were also roughly arranged across the cortex according to the location in space to which the movement was directed. The height of the hand was most clearly mapped across the cortical surface. Stimulation of the lower (ventral) regions of cortex commonly drove the hand into upper space, and stimulation of upper (dorsal) regions of cortex commonly drove the hand into lower space (Fig. 23.4). Again, an important aspect of the animal's action repertoire was mapped across the cortex.

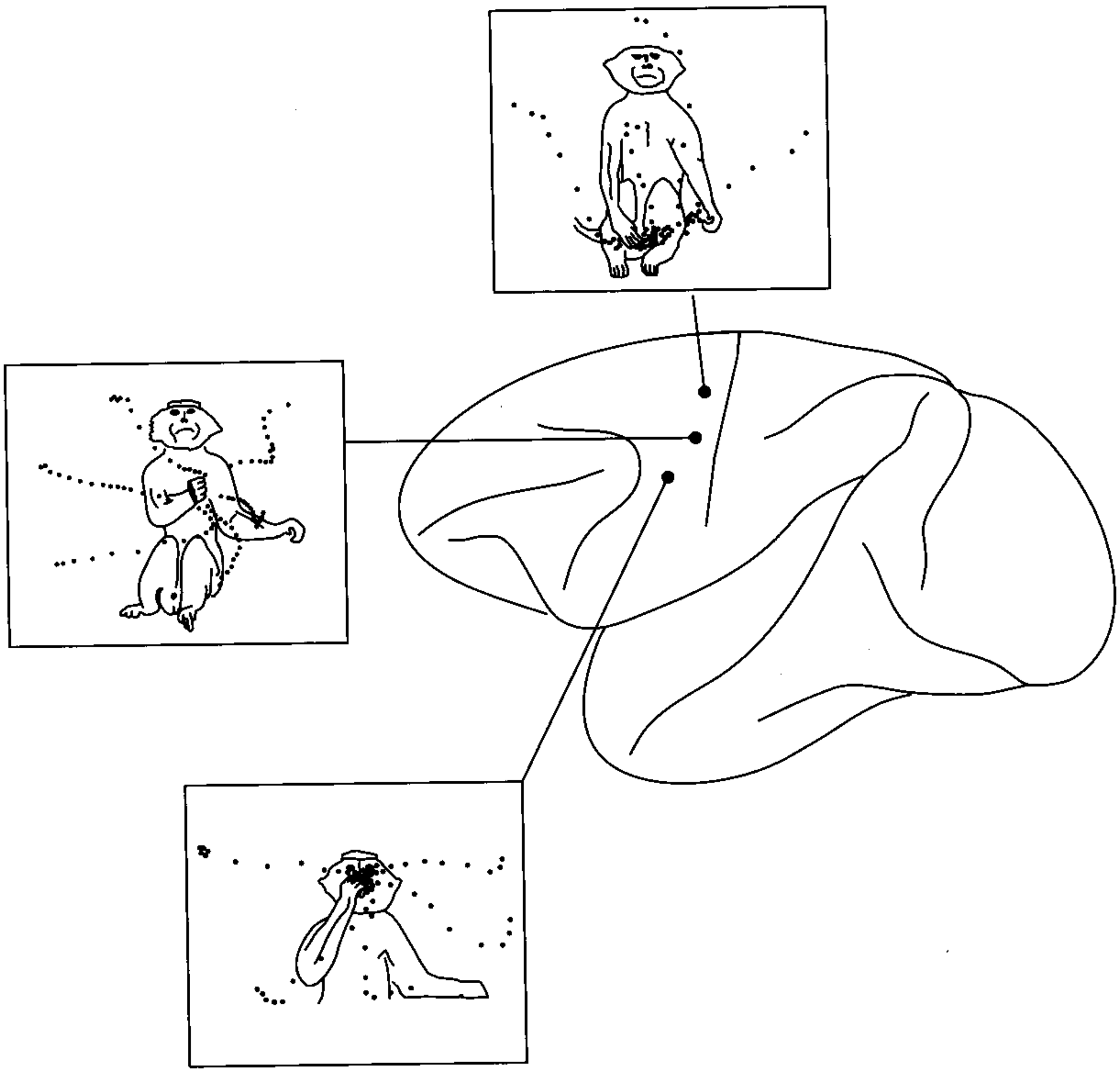

Figure 23.4 Progression of spatial locations to which hand movements are directed. Within the arm representation of the monkey motor cortex, electrical stimulation in dorsal cortex tended to drive the hand into lower space; stimulation in ventral cortex tended to drive the hand into upper space; and stimulation in intermediate cortical locations tended to drive the hand to intermediate heights. Each image is a tracing of the final posture obtained at the end of a stimulation-evoked movement. Each dotted line shows the trajectory of the hand during the 0.5-second stimulation train. Dots show the position of the hand in 30-ms increments. These trajectories show the convergence of the hand from disparate starting locations toward a final location. Based on results from Graziano, M. S. A., Taylor, C. S. R., & Moore, T. (2002). Complex movements evoked by microstimulation of precentral cortex. *Neuron, 34,* 841–851; and Graziano, M. S. A., Aflalo, T., & Cooke, D. F.. (2005). Arm movements evoked by electrical stimulation in the motor cortex of monkeys. *Journal of Neurophysiology, 94,* 4209–4223. Used with permission.

Just how closely the stimulation-evoked movements mimic natural movements is still uncertain. The muscles are activated in combinations that apparently mimic normal behavior. However, the temporal pattern of muscle activity is time-locked to the stimulation train and often does not have the smooth, bell-shaped modulation of normal movement (Cooke & Graziano, 2004a; Taylor et al., 2002). It is therefore probably not correct to think of the stimulation as triggering a complete and natural motor plan. Rather, the motor cortex network appears to have learned the statistics of natural behavior, and the electrical stimulation reveals that statistical structure and the manner in which different zones of cortex emphasize different parts of the movement repertoire.

DIMENSIONALITY REDUCTION AS A THEORY OF TOPOGRAPHIC ORGANIZATION

As described previously, a traditional view of the motor cortex is that it contains a map of the body. This map was famously depicted by Penfield (Fig. 23.2). The traditional topographic scheme, however, does not capture the actual pattern of overlaps, fractures, re-representations, and multiple areas separated by fuzzy borders. A commonly accepted parcellation of motor cortex into functionally different areas is shown in Figure 23.5 (e.g., Dum & Strick, 2002; He et al., 1995; Luppino et al., 1991; Matelli et al., 1985; Matsuzaka et al., 1992; Preuss et al., 1996; Rizzolatti & Luppino, 2001). This scheme, however, also suffers from the problem of overlap. Although the motor cortex is clearly heterogeneous, the changes across the cortical sheet are more graded than absolute. A clean division into separate areas with separate functions is almost certainly incorrect, especially since the specific functions supposedly localized to these distinct areas are largely unknown and the functions that have been tested tend to be found to some degree in all motor areas tested.

Based on our stimulation results, we proposed a different underlying topographic principle: the reduction of the many-dimensional space of the animal's movement repertoire onto the two-dimensional surface of the cortex

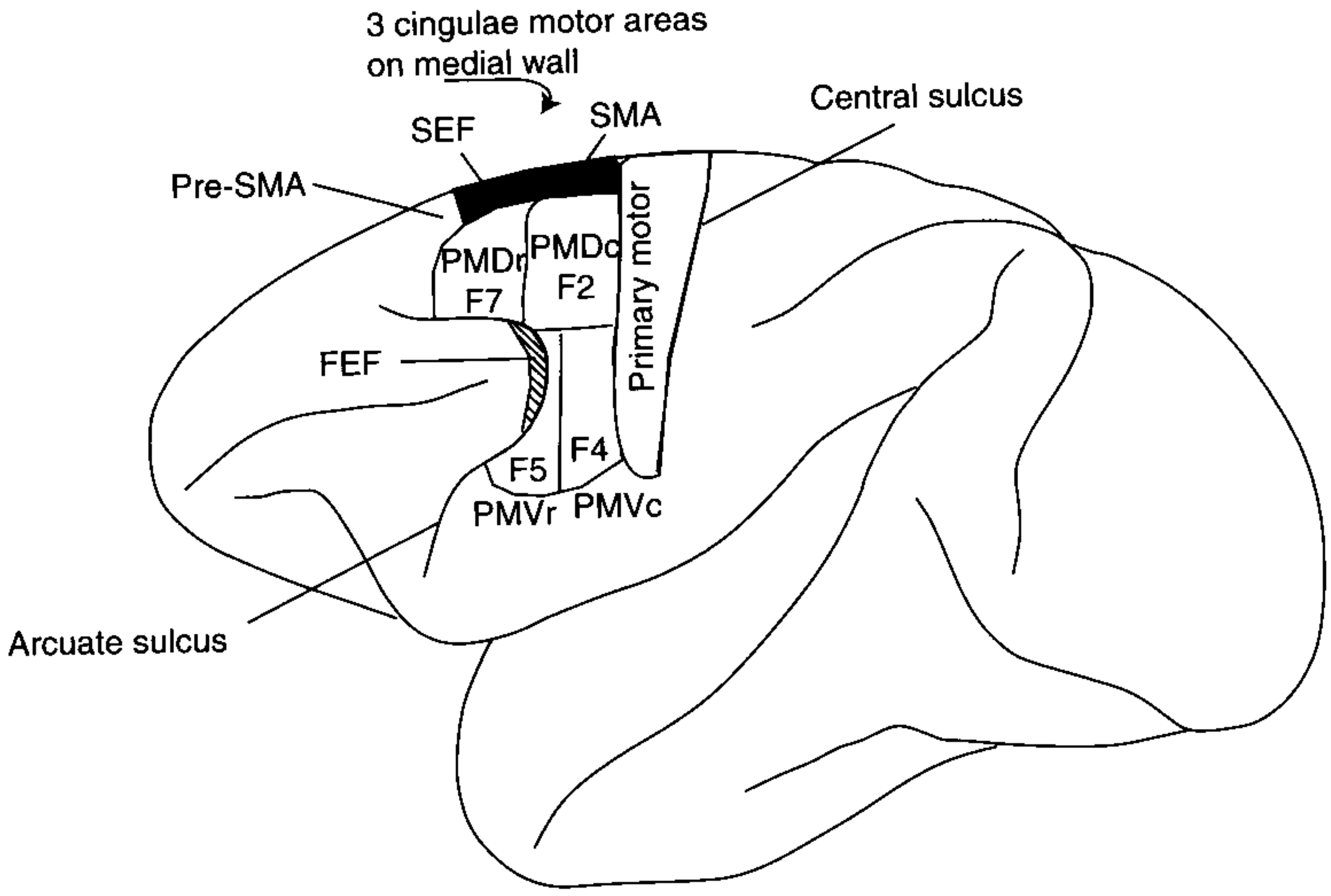

Figure 23.5 Some commonly accepted divisions of the cortical motor system of the monkey. PMDr, dorsal premotor cortex, rostral division, also sometimes called Field 7 (F7); PMDc, dorsal premotor cortex, caudal division, also sometimes called Field 2 (F2); PMVr, ventral premotor cortex, rostral division, also sometimes called Field 5 (F5); PMVc, ventral premotor cortex, caudal division, also sometimes called Field 4 (F4); SMA, supplementary motor area; SEF, supplementary eye field, a part of SMA; pre-SMA, presupplementary motor area; FEF, frontal eye field.

(Aflalo & Graziano, 2006). In this principle, local continuity is optimized. Information processors that need to interact are arranged physically near each other in cortex, presumably gaining a connectional advantage. One could term this principle of cortical organization the rule of "like attracts like." However, perfect continuity is not possible because the movement repertoire is highly dimensional and the cortical sheet is only two-dimensional. Therefore, the optimum solution for local continuity is not a perfect solution, but rather a compromise of many conflicting constraints.

In our proposal, the map of actions in Figure 23.3 is not by itself correct. It is present in the data, but the pattern is noisy and approximate. The map of the body shown in Figure 23.2 is also not by itself correct, but is noisy and blurred, as all motor cortex researchers have noted. The map of hand location shown in Figure 23.4 is also an approximate one, present statistically but overlapping and blurred. The height of the hand is most clearly mapped across the cortical surface, but even this dimension is noisily mapped. Our proposal is that many potential ways to parameterize movement are rendered onto the cortical sheet simultaneously, resulting in a compromise that does not neatly follow any single scheme.

We tested a mathematical model (Aflalo & Graziano, 2006; Graziano & Aflalo, 2007) that collapsed an approximate description of the monkey's movement repertoire onto a two-dimensional sheet following the principle of maximizing local continuity. The model followed the method of Kohonen for self-organizing maps (Kohonen, 1982, 2001). The model was able to reconstruct organizational features of the cortical motor system, including the outlines of the body map as in Figure 23.2, the clustering of movement categories as in Figure 23.3, and an approximate mapping of hand position as in Figure 23.4. In addition, the dimensionality reduction resulted in a rough division of the motor cortex into zones with different properties, closely following the outlines of the primary motor area, dorsal and ventral premotor areas, supplementary motor area, frontal eye field, and supplementary eye field, as in Figure 23.5. The details of how and why different movement types were naturally pushed to different zones in cortex are described more fully in Graziano and Aflalo (2007). The theory of a dimensionality reduction, in which the animal's movement repertoire was flattened onto the cortex, was astonishingly successful in explaining the organizational intricacies of a large swath of cortex, totaling about 20% of the macaque cortical mantle.

ACTION ZONES WITHIN MOTOR CORTEX

The following sections describe in detail the complex movements evoked by stimulation of different zones within the motor cortex of monkeys, and the manner in which these movements resemble actions in the monkey's normal behavioral repertoire.

Hand-to-Mouth Movements

Stimulation within a restricted zone in the precentral gyrus evoked a characteristic hand-to-mouth movement. Five components were typical of this movement. The grip aperture closed in the hand contralateral to the electrode; the forearm supinated and the wrist flexed, such that the grip was aimed at the mouth; the elbow flexed and the shoulder rotated such that the hand moved precisely to the mouth; the mouth opened; and when the head was released from the headbolt and allowed to turn freely, stimulation caused a rotation of the head to a forward-facing position, contributing to the alignment of the mouth and the hand. These five movement components occurred simultaneously in a coordinated fashion resembling the monkey's own voluntary hand-to-mouth movements.

Although the movements resembled voluntary actions in some respects, they clearly were not true voluntary movements of the monkey's but were driven by the stimulation. Typically, the movement could be obtained on every stimulation at short latency with mechanical reliability for hundreds of trials, with no adaptation or degradation. Similar movements could be evoked in anesthetized animals, though the movements were weaker and required greater current. A short stimulation, such as a 100-ms stimulation, evoked the initial part of the action, a slight closing of the hand, a slight twitching of the hand upward in the direction of the face, and a slight opening of the mouth. This truncated movement, by itself, makes no behavioral sense. It is best described as a twitch. It makes sense, however, if interpreted as the initial segment of a larger movement that has not had time to unfold. Longer stimulations, such as for 300 ms, allowed more of the movement to unfold, but rarely allowed the hand to reach the mouth. Yet longer stimulation of 500 ms almost always allowed the hand to reach the mouth in an apparent completion of the movement. Stimulations longer than 500 ms, such as those of 1,000 ms, typically caused the hand, arm, and mouth to freeze at the final configuration, as if the movement had been completed and the activated circuit were maintaining the final posture. When the stimulation train was extended beyond 1 second, almost always the animal appeared to overcome the stimulation effects and take back some degree of control of its arm. Once the stimulation train stopped, however, and then was reinitiated, the hand would move directly back to the mouth.

If the monkey was reaching toward a piece of food at the time of stimulation onset, the hand would close on empty air and come to the mouth. If the monkey had just grasped a piece of food, stimulation would drive the clenched hand to the mouth and cause the hand to freeze at the mouth, the food securely gripped in the fingers and the mouth stuck open, until the end of the stimulation train, at which time the animal would finally be released from the stimulation-evoked posture and put the food in its mouth. If an obstacle was placed between the hand and the mouth, stimulation caused the hand to move along a direct path toward the mouth and bump against the obstacle, pressing against it throughout the remainder of the stimulation, without moving intelligently around the obstacle. Therefore, although the stimulation evoked a movement of great complexity and coordination, the complexity was also limited. The movement resembled a fragment of behavior that was mechanically produced by the stimulated circuitry without intelligent flexibility.

Not all sites within the hand-to-mouth zone resulted in the same movement. For example, depending on the cortical site, stimulation drove the hand to one side of the mouth or the other, and caused the mouth to open more on the side that the hand approached, as if the monkey were placing a piece of food into the side of the jaw, as the animals often do in normal behavior. Not only did the exact position of the hand vary from site to site, but the type of hand grip also varied. For some stimulation sites the hand shaped into an apparent precision grip, the thumb against the side of the forefinger (typical of a macaque precision grip). For other stimulation sites, the hand shaped into what we called a hamburger grip, the four fingers against each other and opposed to the thumb, with a gap between, as if for gripping a larger object. These variations suggested that the zone of cortex was not uniform and not dedicated to producing a single movement, but instead probably contributed to a range of movements that fell within the large class of interactions between the hand and the mouth. In normal monkey behavior, the hand is often brought to the mouth to put in food, take out food, manipulate a piece of food that is in the mouth, scratch the lips, pick at the teeth, push food out of the cheek pouches, and so on.

It is unlikely that the collection of components in a hand-to-mouth movement co-occurred by chance. Even putting aside the specific combination of body parts, the hand closes rather than opens (50% chance); the mouth opens rather than closes (50% chance); the forearm supinates, aiming the grip at the mouth, rather than pronates, aiming the grip away from the mouth (50% chance); the hand moves within about 5 cm of the mouth, a ball of space accounting for about 1% of the total workspace of the hand (1% chance); and the head turns to a forward position, within about 5% of its range of motion (5% chance). Multiplied, these conservatively estimated probabilities yield a *P* value of 0.00005. We must dispense with the occasionally suggested interpretation that the evoked movements are chance collections of twitches rather than meaningful fragments of the behavioral repertoire.

In all monkeys tested, the hand-to-mouth sites were clustered in a lateral, anterior zone probably within the ventral premotor cortex. Whether they are in the caudal or rostral division is unclear. Every monkey tested thus far had a hand-to-mouth zone, but the exact location varied somewhat, especially in the rostrocaudal dimension. Our current interpretation is that the hand-to-mouth sites are more likely to lie within a ventral anterior part of F4 as defined by Matelli and colleagues (1985) and that the dorsal part of F4 emphasizes a different type of action, the defensive movement.

Defensive Movements

In a specific zone in the precentral gyrus, neurons typically respond to tactile stimuli on the face and arms and to visual stimuli looming toward the tactile receptive fields (Fogassi et al., 1996; Gentilucci et al., 1988; Graziano et al., 1997; Rizzolatti et al., 1981). Some of the neurons are trimodal, responding also to auditory stimuli in the space near their tactile receptive fields (Graziano et al., 1999). Because of these distinctive sensory properties, we refer to this cortical region as the polysensory zone (PZ). Although all monkeys tested have a PZ, it varies among animals in size and precise position (Graziano & Gandhi, 2000). It is typically located just posterior to the bend in the arcuate sulcus. In the terminology scheme of Matelli and colleagues (1985), it probably corresponds to the dorsal part of premotor area F4 where similar polysensory neurons have been reported (Fogassi et al., 1996; Gentilucci et al., 1988).

Stimulation within this zone evokes movements that closely resemble a natural defense of the body surface such as to an impending impact or unexpected touch. For example, at some sites, the neurons had tactile receptive fields on the side of the face contralateral to the electrode and visual receptive fields in the space near that side of the face. Stimulation of these sites evoked a defensive action that included eight components: a blink, stronger or exclusively on the contralateral side; a squinting of the musculature surrounding the eye; a lifting of the upper lip in a facial grimace that wrinkled the cheek upward toward the eye; a folding of the contralateral ear against the side of the head; a shrugging of the shoulder, either stronger on or exclusively on the contralateral side; a rapid turning of the head away from the contralateral side; a rapid lifting of the arm, sweeping the hand and forearm into the contralateral space near the face as if blocking or wiping away a potential threat; and a centering movement of the eyes (Cooke & Graziano, 2004a; Graziano et al., 2002). These movement components match point for point the components of a normal defensive reaction such as when the monkey's face is puffed with air (Cooke & Graziano, 2003).

At other sites, neurons had a tactile receptive field on the arm and hand and a visual response to objects looming toward the arm and hand. Stimulation caused a fast retraction of the hand to the side or back of the torso. In general, the movement evoked from a site within PZ seemed appropriate for defending the part of the body covered by the tactile and visual receptive fields of the neurons.

We observed apparent summation between the stimulation-evoked defensive-like movements and actual defensive movements. In the summation test, we lowered the stimulating current to a point near or below threshold until a subtle movement was obtained only on some trials. We then puffed air on the monkey's face, or presented some other noxious stimulus such as a ping pong ball thrown at the animal, evoking a defensive reaction. Within a second after the actual defensive reaction, we then stimulated the site in PZ. Under this condition, the stimulation evoked a robust, super-threshold defensive reaction. The actual defensive movement seemed to prime the system such that a low stimulating current in PZ could evoke a large effect.

One possibility is that the stimulation of sites in PZ evoked a noxious sensory percept to which the monkey then reacted. This possibility is difficult or impossible to rule out because the monkey cannot self-report. However, some observations suggest that it is unlikely. Although the stimulation evoked an apparent defensive reaction, as soon as the stimulation train ended the reaction ended and the monkey returned to feeding itself or playing with toys. A brief stimulation, such as for 50 ms, evoked a correspondingly brief movement, shorter than any behaviorally normal defensive reaction; a long stimulation, such as for 1,000 ms, evoked a correspondingly sustained movement that terminated abruptly at the end of the stimulation. An actual noxious stimulus, such as an air puff or a ping pong ball thrown at the face, did not result in such tight time-locking to the stimulus, but instead resulted in an extended reaction including general agitation and threats to the experimenter. Moreover, the defensive-like movements evoked by stimulation could be still evoked under anesthesia, even when the anesthesia was so deep that the animal did not react to noxious stimuli.

In order to further test the role of PZ in the coordination of defensive movements, we disinhibited neuronal activity in PZ by injecting the chemical bicuculline and inhibited neuronal activity by injecting the chemical muscimol (Cooke & Graziano, 2004b).

When bicuculline was injected into PZ, not only did the local neuronal activity increase, but the neurons also began to fire in intense spontaneous bursts of activity with approximately 5 to 30 seconds between bursts. Each spontaneous burst of neuronal activity was followed at short latency by the standard set of defensive-like movements, including blinking, squinting, flattening the ear against the side of the head, elevating the upper lip, shifting the head away from the sensory receptive fields, shrugging the shoulder, rapidly lifting the hand into the space near the side of the head as if to block an impending impact, and centering the gaze. Chemical stimulation of neurons within PZ, therefore, produced the same effect as electrical stimulation. This result may seem expected. If electrical stimulation of PZ evokes a set of movements, then surely chemical stimulation should too. However, chemical stimulation is in some ways a more specific manipulation, affecting local neuronal receptors. It does not stimulate fibers of passage or induce antidromic activation. The result of chemical stimulation in PZ, therefore, is an important confirmation and strengthens the findings from electrical stimulation.

In addition to evoking defensive-like movements by inducing bursts of neuronal activity, bicuculline also altered the monkey's actual defensive reaction to an air puff directed at the face. After the injection of bicuculline into PZ, the monkey gave an exaggerated defensive reaction to the air puff. The magnitude of the defensive reaction, as measured by facial muscle activity, was approximately 45% larger after bicuculline injection than before injection. Even gently bringing a Q-tip toward the face, normally evoking little reaction from the monkey, evoked a pronounced defensive reaction in the monkey with a bicuculline-treated PZ. Muscle activity during chewing, threat faces, and eyebrow movement were not elevated. The effect was limited to the defensive reaction. When muscimol was injected into PZ, thereby inhibiting neuronal activity, the monkey's defensive reaction to the air puff was reduced. The magnitude of the defensive reaction, as measured by facial muscle activity, was approximately 30% smaller after muscimol injection than before injection. Injections into surrounding cortical tissue outside of PZ did not affect the defensive response to an air puff. These chemical manipulations therefore strengthen the case for PZ as a sensory-motor interface related to the defense of the body surface, a cortical region to which the appropriate visual, tactile, and auditory information is supplied, and from which emerges the motor command to produce spatially directed defensive reactions.

Manipulation Movements

Stimulation of another cluster of sites evoked an especially varied and complex set of movements that involved the fingers, wrist, and often the arm and shoulder, contralateral to the electrode. The movements resembled the types of actions that monkeys typically make when manipulating, examining, or tearing objects. The finger movements included an apparent precision grip (thumb against forefinger), a power grip (fist), or a splaying of the fingers. In some cases a supination or pronation of the forearm occurred, rotating the grip one direction or the other. Also in some cases the wrist flexed or extended. A common action for monkeys is to splay the fingers of one hand, orient the palm toward the face, and examine the splayed hand, perhaps searching for stray granules of food. This splayed-hand posture, with the palm oriented toward the face, was often evoked on stimulation within this cortical zone. Monkeys commonly manipulate objects in a region of central space within about 10 cm of the chest. Stimulation within this cortical zone often evoked a movement of the shoulder and arm that brought the hand into this central region of space. A common action for monkeys when manipulating objects is to tear the object or pull it in two, the two hands pulling rapidly from central space toward lateral space while the forearms supinate and the hands are tightly gripped. Stimulation within this zone of cortex also sometimes evoked just such a movement, though only in the contralateral limb.

These sites were clustered in a posterior zone that lay partly on the gyral surface and partly on the anterior bank of the central sulcus. This cluster probably corresponds to the traditional primary motor hand representation. It may also correspond to the central hand region in the motor cortex maps of Kwan and colleagues (1978) and Park and colleagues (2001). We suggested that this cortical zone may represent a "manual fovea," a repertoire of movements that is related to the manipulation of objects and that is heavily biased toward but not exclusively limited to hand locations in a central region of space in front of the chest (Graziano et al., 2004).

Reach-to-Grasp Movements

For some cortical sites stimulation evoked an apparent reach in which the wrist straightened, the fingers opened as if to grasp, the forearm pronated to orient the grip outward, and the hand extended away from the body. In some cases the hand extended to a region of space as far as 25 cm distant from the body, at arm's length. In other cases the hand converged on a location at a lesser distance, with the elbow partially flexed, as if the hand were reaching to a closer object. In all of these cases stimulation caused a convergence to the final posture from a range of initial postures. These apparent reaching sites tended to be located on the gyral surface just anterior to the "central space/manipulation" zone and dorsal to the "defensive" zone. Because of this relative location, the reach-related sites probably lie within the dorsal premotor cortex, within its caudal division (PMDc), where a high proportion of neurons respond in relation to reaching movements (e.g., Crammond & Kalaska, 1996; Hocherman & Wise, 1991; Johnson et al., 1996; Messier & Kalaska, 2000). Typically stimulation of more rostral sites did not evoke reliable or clear movements.

Hand in Lower Space

A commonly evoked movement involved a placement of the hand in lower space near the feet, typically with the forearm pronated such that the palm faced down or inward toward the body. These stimulation-evoked movements resembled a common part of the monkey's behavioral repertoire in which the hand was braced on the ground (Graziano et al., 2004). These sites were typically found just dorsal to the central space/manipulation sites.

Mouth Movements

The aforementioned movement categories were evoked from the large arm and hand sector of the lateral motor cortex. When we stimulated in cortex ventral to the arm and hand representation, we obtained movement of the jaw, lips, and tongue, as expected on the basis of the standard body map described for the monkey motor cortex (Woolsey et al., 1952). The mouth movements often appeared to be coordinated and of behavioral significance. For example, stimulation of one site caused the jaw to attain a partially open position, the lips to purse slightly toward the contralateral side of the mouth, and the tongue to move until the tip was placed in a contralateral and slightly protuberant position. The final oral posture evoked from this site resembled an action to acquire a bit of food just outside the mouth on the contralateral side. We looked for but did not find any obvious cortical map in the mouth representation in terms of the spatial location around the mouth toward which the tongue and lip movement was directed. We also did not obtain movements that looked like threat displays, fear grimaces, or any other social displays. It is likely, however, that we failed to discover many of the movement types in the mouth representation, since we did not explore it as extensively as we did the arm and hand representation. We rarely obtained rhythmic chewing-like jaw movements, perhaps because we usually stimulated for 0.5 seconds instead of the 3 seconds used by Huang and colleagues (1989), who reported rhythmic chewing movements.

Climbing/Leaping

In a medial and anterior region, stimulation evoked especially complex movements that involved bilateral action of the arms and legs, movements of the torso, and movements of the tail, often simultaneously from one site. These complex, whole-body sites correspond roughly to the supplementary motor area (SMA), a cortical region on the crown of the hemisphere and extending slightly onto the lateral side, just anterior to the primary motor leg representation. Others have also obtained bilateral movements of multiple body parts on stimulating in this area of cortex (e.g., Foerster, 1936; Luppino et al., 1991; Penfield & Welch, 1951; Woolsey et al., 1952).

Subjectively, the movements resembled climbing or leaping postures. For example, stimulation of one site caused the left foot to press down against the floor of the primate chair; the right foot to lift and reach forward with the toes shaped as if in preparation to grasp; the left hand to reach toward a lower, lateral position while shaped as if in preparation to grasp; the right hand to reach toward a position above the head while shaped as if in preparation to grasp; and the tail to curl to one side. The long-tailed macaques in our experiments do not have prehensile tails. Instead, they use their long, stiff tails mainly as balance devices during locomotion, and therefore the tail movements evoked by stimulation of SMA are consistent with a possible role in locomotion.

Stimulation within the SMA did not always evoke movements of all four limbs. For example, stimulation of another site in the right hemisphere caused the hips to turn to the left side, the left foot to reach out and down as if stepping to a position lateral to and slightly behind the body, and the left arm to reach to a lateral position as if to grasp a support.

Although we sometimes tested stimulations extended to 1 second or more, we did not observe any cyclical stepping movements. Instead, the movements resembled the complex adjustments of body and limb often seen when monkeys are navigating a complex environment. The climbing-like movements, however, were restricted by the primate chair in which the animal was tested and therefore could never be compared directly to the normal climbing, leaping, or complex locomotor movements of a monkey.

COMPLEX MOVEMENTS REPORTED IN OTHER STUDIES

Although our studies of motor cortex were the first to systematically map the movement repertoire onto the cortical surface, many experiments before and since have reported that electrical stimulation of specific, motor-related structures can evoke highly complex, species-typical behavior. Some of these studies are reviewed below.

Midbrain

In a now classic study, electrical stimulation of a midbrain nucleus in the cat resulted in patterned locomotor behavior (Shik et al., 1969). The exact role of this mesencephalic locomotor nucleus, its relationship to spinal and cortical control of locomotion, is still unknown.

Electrical stimulation has long been used to study maps of motor output in the superior colliculus or, as it is called in nonmammals, the optic tectum. The map of saccadic eye movements in cats and monkeys is perhaps the bestknown stimulation result in the colliculus (Guitton et al., 1980; Robinson, 1972; Schiller & Stryker, 1972). However, other complex species-typical behaviors can be evoked. Stimulation of the optic tectum in salamanders evokes a coordinated movement in which the animal orients to a spatial location, reaches out with the forepaws, and opens the mouth as if to acquire prey (Finkenstadt & Ewert, 1983). In rats, stimulation of the part of the map that represents lower visual space evokes orienting movements of the head as if the animal were acquiring an object on the ground in front of it, and stimulation of the part of the map that represents upper visual space evokes retracting, defensive-like movements (Dean et al., 1989). These movements are consistent with the exigencies of normal life for a rat, in which food is found on the ground in lower visual space and enemies attack from above.

Spinal Cord

Giszter and colleagues (1993) electrically stimulated sites in the spinal cord of frogs and studied the effect on the hindleg. The frog's ankle was fixed in a range of different spatial locations. For each ankle location, the force evoked by stimulation was measured. These stimulation-evoked forces formed a convergent force field pointing toward a single location in space, suggesting that if the ankle were free to move, the foot would move to that spatial terminus. Different stimulation sites resulted in convergent force fields aimed at different spatial locations.

Our results on stimulating the monkey motor cortex are similar in that stimulation caused the limb to converge from a range of initial locations toward a specific final location. Presumably, the cortical stimulation operates by recruiting spinal circuitry. If the Giszter et al. result is applicable to the monkey spinal cord, then our results may depend on spinally mediated force fields. The cortical stimulation, however, appears to recruit a higher-order or more integrated version of the spinal force fields. We typically found convergence of many joints from different body segments. For example, a hand-to-mouth movement involves a coordination of output that passes through the spinal cord (for the control of the hand, arm, and shoulder) and through the facial nucleus (for the control of the head and mouth).

Cortex

Several studies have confirmed the essential phenomenon of complex movements evoked from the motor cortex, and have now extended the results to other species of animals.

In the rat, species-typical behavior can be evoked by stimulation of motor cortex. Brecht and colleagues (2004) found that intracellular stimulation of a single cortical neuron evoked rhythmic whisking movements. Cramer and Keller (2006) suggested that the cortically controlled whisking actions are mediated by a projection from the motor cortex to a subcortical central pattern generator that in turn controls the whiskers.

Haiss and Schwarz (2005) found that the rat motor cortex contains two adjacent zones related to the whiskers. Stimulation of one zone on a behavioral time scale (500 ms) evoked rhythmic whisking similar to normal exploratory movements. Stimulation of the other zone for 500 ms evoked a retraction of the whiskers on the contralateral side, a closure of the contralateral eye, a facial grimace, and sometimes a lifting of the contralateral forepaw to the space beside the face. These results suggest that the rat motor cortex, like the monkey motor cortex, may be organized into zones that emphasize different ethologically useful actions, in this case exploratory whisking for one zone and defensive actions for the other zone.

Ramanathan and colleagues (2006) stimulated the rat motor cortex on a behaviorally relevant time scale (500 ms) and obtained reaching and grasping movements of the forepaws. Moreover, when a reaching zone in cortex was lesioned, the rat's ability to reach was compromised. When the rat was retrained to reach, the motor cortex was found to have reorganized such that reaching could be electrically evoked from new cortical sites. After this rehabilitation, the ability of the rat to perform the behavior correlated with the amount of cortex that, when stimulated, evoked the behavior. These results strongly support the view that the motor cortex is organized to control complex, meaningful behavior; that different behaviors are emphasized in different regions of cortex; and that these behaviors can be assessed through electrical stimulation.

In the cat motor cortex, Ethier and colleagues (2006) found that stimulation on a behaviorally relevant time scale (500 ms) evoked a variety of forepaw movements including apparent reaching and hooking of the paw as if to acquire an object.

Stepniewska and colleagues (2005) stimulated the motor and parietal cortex of galagos using the behaviorally relevant time scale of 500 ms. They evoked complex movements that resembled fragments of the animal's normal behavioral repertoire. Different categories of movement were evoked from different cortical zones. The parietal lobe could be segmented into functional zones including a hand-to-mouth zone, a defensive zone, and a reaching zone. Similar results were obtained in the motor cortex, but were not studied in as much detail.

In macaque monkeys, stimulation of the ventral intraparietal area (VIP) evokes movements that resemble defensive reactions (Cooke & Graziano, 2004a; Cooke et al., 2003; Graziano et al., 2002; Thier & Andersen, 1998). The evoked movements are similar to those evoked from PZ in the motor cortex. VIP is anatomically connected to PZ (Lewis & Van Essen, 2000; Luppino et al., 1999), and neurons in VIP respond preferentially to tactile stimuli on the face and to visual and auditory stimuli near the face, much like neurons in PZ (e.g., Colby et al., 1993; Duhamel et al., 1998; Schlack et al., 2005). One possibility is that VIP and PZ are part of a larger sensory-motor circuit that contributes to the maintenance of a margin of safety around the body (Graziano & Cooke, 2006).

SUMMARY

The monkey motor cortex does not appear to decompose movement into the action of separate muscles. Instead, the control of muscles is extensively overlapped in the cortex, effectively allowing for the construction of complex, behaviorally meaningful movements. Electrical stimulation of different zones within cortex tends to evoke different categories of movement that resemble actions in the monkey's normal repertoire.

The complex topography within motor cortex roughly follows several different possible organizational schemes, including a map of the body, a spatial map of hand location, a cluster map of ethologically relevant categories of action, and a set of commonly designated areas with fuzzy borders and largely unknown functions. One possible way to reconcile these many organizational schemes, each one of which captures some of the data, is to hypothesize that the cortex is a best-fit rendering of the highly dimensional movement repertoire on the two-dimensional cortical sheet. In this view, various individual dimensions that are of importance in the movement repertoire are mapped across cortex in noisy, partial topographies. No single dimension of movement is perfectly mapped across the cortical surface because of a compromise among multiple constraints. The underlying principle of organization, in this view, is not a map of one or another dimension, but a rendering of the many-dimensional movement space onto the cortex.

It is not yet clear to what extent this ethological organization of the motor cortex is built in through evolution, and to what extent it is learned during development and adulthood as the animal learns its motor repertoire. The distinct connections and anatomical structure of different zones within motor cortex argue for some built-in organization shaped through evolution to serve the behavioral repertoire. The modifications to the map that occur with experience demonstrate that at least some of the cortical organization reflects learning.

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