

Voluntary Movement: Motor Cortices

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The Primary Motor Cortex Is Dynamic and Adaptable

Highlights

IN THIS CHAPTER, WE DESCRIBE HOW the cerebral cortex uses sensory information from the external world to guide motor actions that allow the individual to interact with the surrounding environment. We begin with a general description of what we mean by the term voluntary movement and some theoretical frameworks for understanding its control, followed by the basic anatomy of the cortical circuits involved in voluntary motor behavior. We then consider how information related to the body, external space, and behavioral goals is combined and processed in parietal cortical regions. This is followed by a discussion of the

role of premotor cortical regions in selecting and planning motor actions. Finally, we examine the role played by the primary motor cortex in motor execution.

Voluntary Movement Is the Physical Manifestation of an Intention to Act

Animals, including humans, have a nervous system not just so that they can sense their world or think about it, but primarily to interact with it to survive and reproduce. Understanding how purposeful actions are achieved is one of the great challenges in neuroscience. We focus here on the cerebral cortical control of voluntary motor behavior, in particular voluntary arm and hand movements in primates.

In contrast to stereotypical fixed-latency reflexive responses that are automatically triggered by incoming sensory stimuli (Chapter 32), voluntary movements are purposeful, intentional, and context-dependent, and are typically accompanied, at least in humans, by a sense of “ownership” of the actions, the sense that the actions have been willfully caused by the individual. Decisions to act are often made without an external trigger stimulus. Moreover, the continuous flux of events and conditions in the world presents changing opportunities for action, and thus voluntary action involves choices between alternatives, including the choice not to act. Finally, the same object or event can evoke different actions at different times, depending on the current context.

Throughout evolution, these features of voluntary behavior have become increasingly prominent in higher primates, especially in humans, indicating that the neural circuits controlling voluntary behavior in primates are adaptive. In particular, evolution has resulted in an increasing degree of dissociation of the physical properties of sensory inputs from their behavioral salience to the individual. Adaptation of the control circuits also enhances the repertoire of voluntary motor actions available to a species by allowing individuals to remember and learn from prior experience, to predict the future outcomes of different action choices, and to adopt new strategies and find new solutions to attain their desired goals. Volitional self-control over how, when, and even whether to act endows primate voluntary behavior with much of its richness and flexibility and prevents behavior from becoming impulsive, compulsive, or even harmful.

Voluntary behavior is the physical manifestation of an individual’s intention to act on the environment, usually to achieve a goal immediately or at some point in the future. This may require single nonstereotypical

movements or sequences of actions tailored to current conditions and to the longer-term objectives of the individual. The ability to use fingers, hands, and arms independent of locomotion further helps primates, and especially humans, exploit their environment. Most animals must search their environment for food when hungry. In contrast, humans can “forage” by using their hands to cook a meal or simply enter a few numbers on a cellphone to order food for delivery. Because large areas of the cerebral cortex are implicated in various aspects of voluntary motor control, the study of the cortical control of voluntary movement provides important insights into the purposive functional organization of the cerebral cortex as a whole.

Theoretical Frameworks Help Interpret Behavior and the Neural Basis of Voluntary Control

The neural processes by which individuals acquire information about their environment and the relationship of their body to it, decide how to interact with the environment to achieve short- or long-term goals, and organize and execute the voluntary movement(s) that will fulfill their goals are traditionally partitioned into three analytic components: Perceptual mechanisms generate an internal representation of the external world and the individual within it, cognitive processes use this internal model of the world to select a course of action to interact with its environment, and the chosen plan of action is then relayed to the motor systems for implementation. This serial view of the brain’s overall functional organization has long dominated neuroscience; this textbook, for example, has separate sections dedicated to perception, cognition, and movement.

The brain must transform a goal into motor commands that realize the goal. For example, taking a sip of coffee requires the brain to convert visual information about the coffee cup and somatic information about the current posture and motion of your arm and hand into a pattern of muscle contractions that moves your hand to the cup, grasps it, and then lifts it to your mouth. Many behavioral and modeling studies suggest that this could be accomplished by a series of transformations of sensorimotor coordinates that convert the retinal image of the cup into motor commands (Figure 34–1A).

Variants of this sensorimotor transformation model have guided the design and interpretation of many studies on the control of voluntary arm movements. Neural recording studies, including many that will be described here, have found possible neural correlates of the motor parameters and sensorimotor transformations presumed to underlie movement

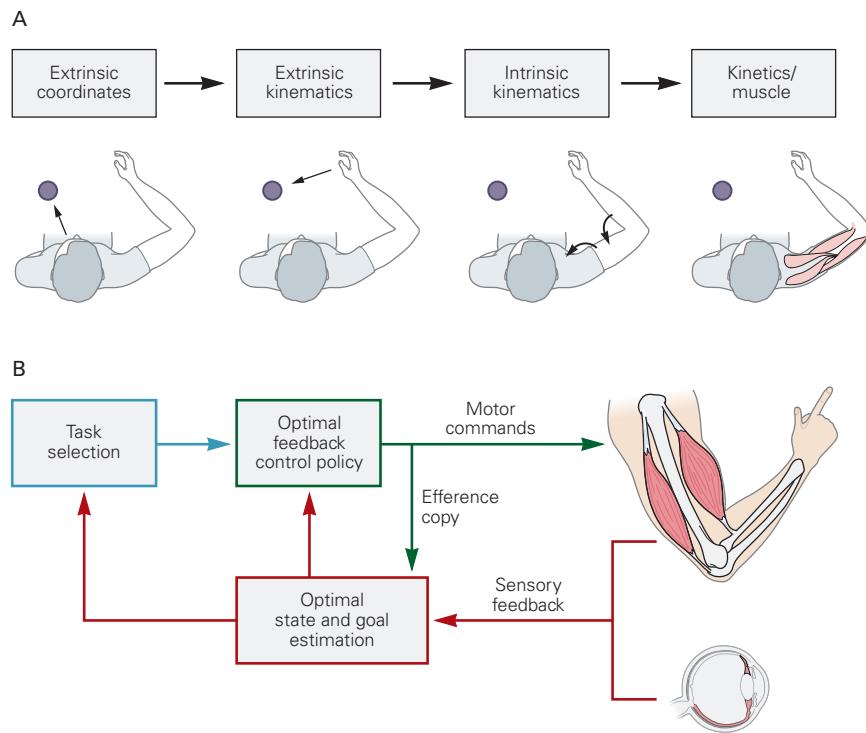


Figure 34-1 Theoretical frameworks for interpreting neural processing during voluntary motor actions.

A. The concept of sensorimotor transformations addresses the basic problem that tasks such as reaching to a visual target require the brain and spinal cord to convert sensory information about the spatial location of the target, initially represented in retinal coordinates, into patterns of muscle activity to move the limb to the target object. It is assumed that this sensorimotor transformation involves the use of intermediary representations—representation of the location of the target object relative to the body, the spatiotemporal trajectory of the hand (extrinsic kinematics), and motion of the joints (intrinsic kinematics) necessary to reach and grasp the object—before

generating the patterns of neural activity that specify the causal forces (kinetics) or muscle activity.

B. Optimal feedback control recognizes three key processes for control. Optimal state and goal estimation (red box) integrates sensory feedback from various modalities along with an efference copy of motor commands to estimate the present position and motion of the body and objects in the world. Task selection (blue box) involves processes that identify behavioral goals based on internal desires and information about the state of the body and the world. Control policy (green box) determines the feedback gains, operations, and processes necessary to generate motor commands to control movement.

planning and execution. This conceptual framework is an example of a *representational model* of brain function. Just as the activity of neurons in primary sensory areas appears to encode specific physical properties of stimuli, the sensorimotor transformation model assumes that the activity of neurons in the motor system explicitly encodes or represents specific properties and parameters of the intended movement.

However, the sensorimotor transformation model has important limitations. Among them, the parameters and coordinate systems typically used in such models were imported from physics and engineering, rather than derived from the physiological properties of biological sensors and effectors. Furthermore, the model places all emphasis on strictly serial feed-forward computations and delegates feedback circuits

primarily to the detection and correction of performance errors after they are committed. The model also requires that every temporal detail of a movement be explicitly calculated before the motor system can generate any motor commands. Another limitation is its rigidity; it assumes that the same sequence of computations controls every movement in every context. Finally, this approach has not addressed how the proposed sensorimotor transformations could be implemented by neurons.

In recent years, theoretical studies of the motor system have been moving away from strictly representational models to more dynamical causal models. This approach begins with the premise that the functional architecture of motor control circuits evolved to generate movements, not to represent their parameters.

These circuit properties were acquired by evolutionary changes in neural circuitry and by experience-dependent adaptive processes during postnatal development that produce the patterns of synaptic connectivity within the neural circuits that are necessary to generate the desired movements. Spinal and supraspinal motor circuits ensure that spinal motor neurons generate the appropriate muscle contraction signals across task conditions without relying on computational formalisms such as coordinate transformations.

One such theoretical framework is optimal feedback control (Figure 34–1B; and see Chapter 30). There are many different forms of optimal control, and each captures important aspects of control. Optimal feedback control, as the name implies, emphasizes the importance of feedback signals for the planning and control of movements. It is optimal in the sense that it emphasizes the importance of the behavioral goal and the current context in determining how best to plan and control movements. This flexibility can explain how human motor performance can be both highly variable and yet successful.

The optimal feedback control framework also divides the control of voluntary movements into three key processes: state estimation, task selection, and control policy (Figure 34–1B). State estimation involves forward internal models that use efference copies of motor commands and external sensory feedback to provide the best estimate of the present state of the body and the environment (Chapter 30). Task selection involves the neural processes by which the brain chooses a behavioral goal in the current context and what motor action(s) might best attain that goal. This selection can be based on the sensory evidence supporting alternative actions and alternate options to attain the goal, and on other factors that influence the optimal response such as motivational state, task urgency, preferences, relative benefits versus risks, the mechanical properties of the body and environment, and even the biomechanical costs of different action choices. Finally, the control policy provides the set of rules and computations that establish how to generate the motor commands to attain the behavioral goal given the present state of the body and the environment. Importantly, the control policy process in optimal feedback control is not a series of pure feedforward computations to calculate every instantaneous detail of a desired movement trajectory and associated muscle activity patterns before movement onset. Instead, it involves context- and time-dependent adjustments to feedback circuit gains that allow the spatiotemporal form of muscle activity to emerge dynamically in real time as part of the control process underlying movement generation.

The sensorimotor transformation and optimal feedback control models are not mutually incompatible hypotheses. Optimal feedback control explains certain features of motor behavior but is largely agnostic as to the neural implementation for control. It assumes that motor circuits are dynamical systems that attain desired goals under varying task constraints. As a result, a given neuron may contribute to sensorimotor control in different task conditions, but its activity may not correspond to a specific movement parameter in a definable coordinate framework. In contrast, sensorimotor transformation models do not fully explain how real-time movement control is implemented by motor circuits, but emphasize the need to convert information from sensory signals to motor commands.

Even if the neural control system is dynamical, the system it controls—the musculoskeletal plant—is a physical object that must obey the universal physical laws of motion. Thus, neural activity should show correlations with those physical parameters and laws that will help to infer how those neurons are contributing to voluntary motor control, even if they are not attempting to encode those terms. Indeed, experimental tasks that dissociate different types of movement-related information have revealed important differences in how neural activity in different cortical motor regions correlates with different movement properties and different aspects of movement planning and execution. Finally, we can impose arbitrary volitional control on how we move. For example, we can choose to make an unobstructed reaching movement efficiently along a straight path to the target or whimsically along a complex curved path even though there is no obstacle to avoid and the movement is energetically costly. The experimental challenge is to reveal how the brain can implement this willful control with neurons and neural circuits.

Many Frontal and Parietal Cortical Regions Are Involved in Voluntary Control

Here we describe the regions of frontal and parietal cortex that convert sensory inputs into motor commands to produce voluntary movement. We then examine the neural circuits involved in the voluntary control of arm and hand movements that are prominent components of the motor repertoire of primates. We focus on studies in the rhesus monkey (*Macaca mulatta*), as much of our knowledge of the cortical control of the arm and hand comes from this species and the neural circuitry underlying human voluntary control appears to have a similar organization. Many other neural structures, including the prefrontal cortex, the basal ganglia, and

cerebellum, also play critical roles in the global organization of goal-directed voluntary behavior (Chapters 37 and 38).

Several different nomenclatures have been used in partitioning the precentral, postcentral, and parietal cortex, based on regional differences in cytoarchitectonic and myeloarchitectonic details, cortico-cortical connectivity, the distribution of different marker molecules, and regional differences in neural response properties. Here we will use some of the more widely accepted terminology without describing approximate homologies among the various nomenclatures.

Based on the pioneering cytoarchitectonic studies of humans by Brodmann, the different lobes of the monkey's cerebral cortex were divided into smaller regions, including two in precentral cortex (areas 4 and 6), four in the postcentral cortex (areas 1, 2, 3a, and 3b), and at least two in the superior and inferior parietal cortex (areas 5 and 7). While these cytoarchitectonic divisions persist in the literature, subsequent anatomical and functional studies have radically changed the view of how the precentral and parietal cortices are organized (Figure 34–2).

Current maps usually place the *primary motor cortex* (M1), the cortical region most directly involved in motor execution in primates, in Brodmann's area 4. Brodmann's area 6 is now typically divided into five or six functional areas that are principally involved in different aspects of the planning and control of motor actions of different parts of the body. Arm-control regions include the *dorsal premotor cortex* (PMd) and *predorsal premotor cortex* (pre-PMd), in the caudal and rostral parts of the dorsal convexity of lateral area 6, respectively. Hand-control regions include the *ventral premotor cortex* (PMv), found on the ventral convexity of area 6, which has been further divided into two or three smaller subregions. A variety of functions related to motor selection, sequencing, and initiation have been found in medial premotor cortical regions. These include a region on the medial surface of the cortical hemisphere that was originally called the secondary motor cortex by Woolsey and colleagues, who discovered it, but is now called the *supplementary motor area*. This region is in turn split into two regions, a *supplementary motor area proper* (SMA) in the caudal part and a *presupplementary motor area* (pre-SMA) in the rostral part. Outside of Brodmann's area 6, three additional motor areas, the dorsal, ventral, and rostral cingulate motor areas (CMAd, CMAv, and CMAr, respectively), are also involved in motor selection but have not been as well studied as more lateral premotor areas.

The *primary somatosensory cortex* (S-I; including areas 1, 2, 3a, and 3b) is located in the anterior

postcentral gyrus. It processes cutaneous and muscle mechanoreceptor signals from the periphery and transmits that information to other parietal and precentral cortical regions (Chapter 19). Like area 6, Brodmann's parietal areas 5 and 7 are now divided into several regions within and adjacent to the intraparietal sulcus (IPS), each of which integrates various types of sensory information about the body or spatial goals for voluntary motor control. These include parietal lobe areas PE and PEc on the rostral or superior bank, and PF, PFG, PG, and OPT on the caudal, inferior bank. Areas inside the IPS include the anterior, lateral, medial, and ventral intraparietal areas (AIP, LIP, MIP, and VIP, respectively) as well as intraparietal area PEip and higher visual area V6A.

These precentral, postcentral, and parietal cortical regions are interconnected by complex patterns of reciprocal, convergent, and divergent projections. The SMA, PMd, and PMv have somatotopically organized reciprocal connections not only with M1 but also with each other. Both the SMA and M1 receive somatotopically organized input from S-I and the dorsorostral parietal cortex, whereas PMd and PMv are reciprocally connected with progressively more caudal, medial, and lateral parts of the parietal cortex. These somatosensory and parietal inputs provide the primary motor and caudal premotor regions with sensory information related to behavioral goals, target objects, and the position and motion of the body that is used to plan and guide motor acts.

In contrast, pre-SMA and pre-PMd project to SMA and PMd but do not project to M1 and are only weakly connected with the parietal lobe. They instead have reciprocal connections with prefrontal cortex and so may impose more arbitrary context-dependent control over voluntary behavior. Prefrontal cortex is also connected with other premotor cortical regions.

The control of hand and arm motor actions is implemented by partially segregated parallel circuits distributed across several parietal and precentral motor areas. Hand motor function is generally supported by frontoparietal circuits that are located more laterally, notably AIP and PMv. In contrast, proximal arm motor function is supported by circuits that are more medial, notably parietal areas PE and MIP and precentral areas PMd, SMA, and pre-SMA.

Descending Motor Commands Are Principally Transmitted by the Corticospinal Tract

Older textbooks often referred to the primary motor cortex (M1) as the "final common path." Other

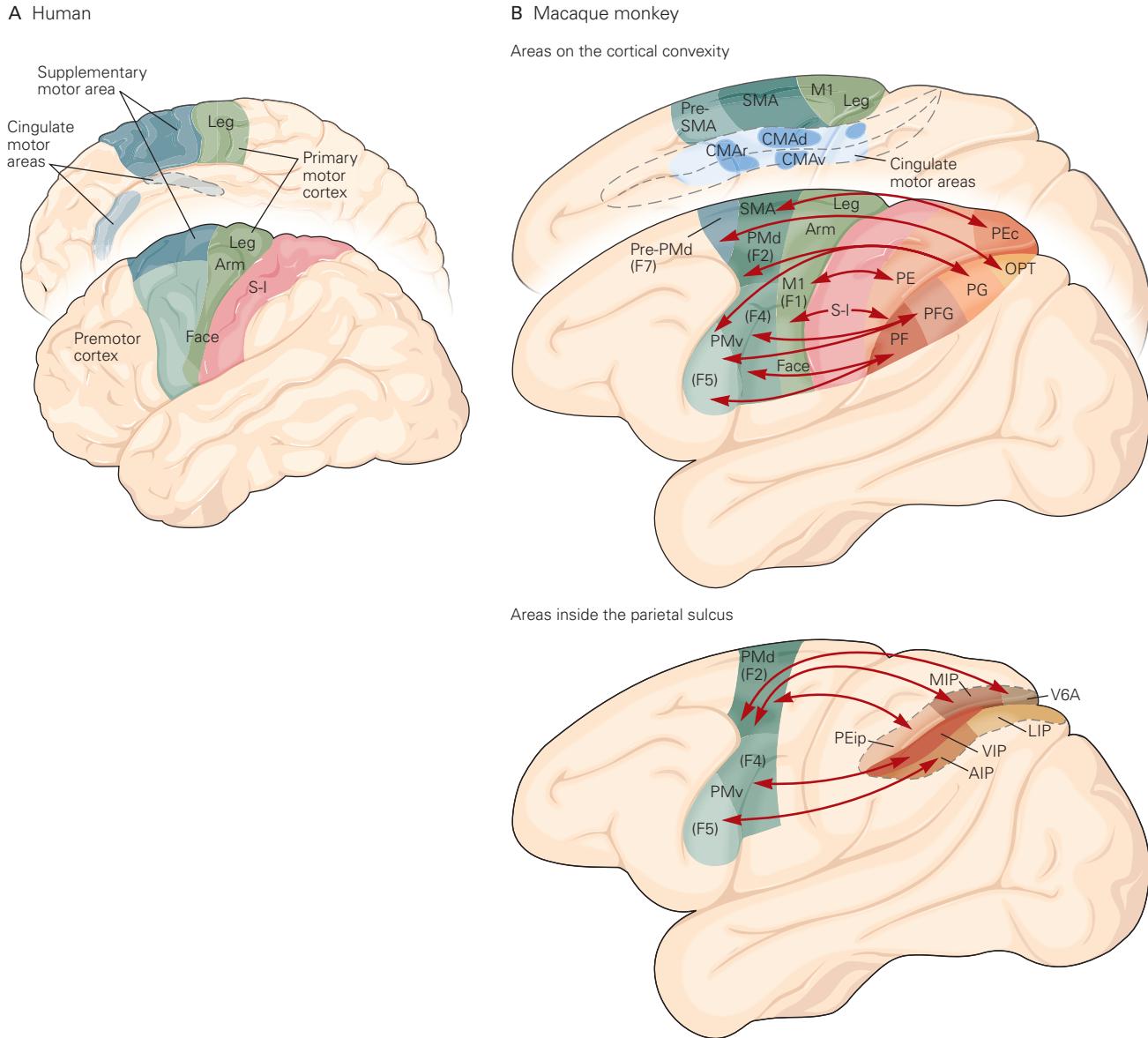


Figure 34-2 Parietal and frontal motor areas that support voluntary control. For illustration purposes, the intraparietal sulcus is opened in the bottom panel. The parietal areas are designated in Constantin von Economo's terminology by the letter P (parietal), followed by letters instead of numbers to indicate the cytoarchitectonically different areas. Areas PF and PFG roughly correspond to Brodmann's area 7b, and areas PG and OPT to Brodmann's area 7a. Areas inside the intraparietal sulcus include the anterior, lateral, medial, and ventral intraparietal areas (AIP, LIP, MIP, VIP, respectively), as well as the PE intraparietal area

cortical motor areas were thought to influence voluntary movements via their projections to M1, which then formulated the descending motor command that was transmitted to the spinal cord. This is not correct.

(PEip) and visual area 6A (V6A). Arrows show the patterns of the principal reciprocal connections between functionally related parietal and frontal motor areas. (Abbreviations: CMAr, rostral cingulate motor area; CMAv, ventral cingulate motor area; CMd, dorsal cingulate motor area; F, frontal; M1, primary motor cortex; OPT, occipito-parieto-temporal; P, parietal; PE, PF, and PFG are parietal areas according to the nomenclature of von Economo; PMd, dorsal premotor cortex; PMv, ventral premotor cortex; Pre-PMd, predorsal premotor cortex; S-I, primary somatosensory cortex; SMA, supplemental motor area.)

Several cortical motor regions outside of M1 project to subcortical areas of the brain as well as to the spinal cord in parallel with the descending projections from M1. The key descending pathway for

voluntary control is the *pyramidal tract*, which originates in cortical layer V in a number of precentral and parietal areas. The pyramidal tract contains axons that terminate in brain stem motor structures (the *corticobulbar tract*) and axons that project down to the spinal cord (*corticospinal tract*). Precentral areas include not only M1 but also SMA, PMd, PMv, and the cingulate motor areas (Figure 34–3). Descending fibers from S-I and parietal areas, including PE and PFG, also travel in the pyramidal tract. The pre-SMA and pre-PMd do not send axons directly to the spinal cord; instead, their descending outputs reach the spinal cord indirectly through projections to other subcortical structures.

Most corticospinal tract axons originating in one hemisphere cross to the other side of the midline (decussate) at the pyramid in the caudal medulla, and from there project to the spinal cord itself, forming the lateral corticospinal tract. A small portion does not decussate and forms the ventral corticospinal tract. Many corticospinal axons in primates, and virtually all corticospinal axons in other mammals, terminate only on spinal interneurons and exert their influence on voluntary movement indirectly through spinal interneuronal and reflex pathways. In monkeys, all corticospinal axons from premotor cortical areas and many from M1 terminate on interneurons in the spinal intermediate zone, whereas postcentral and parietal areas target interneurons in the dorsal horn. The terminal endings of a sizeable portion of the corticospinal axons arising from M1 in primates, but not other mammals, arborize at their targets and synapse directly on spinal alpha motor neurons that in turn innervate muscles; these M1 neurons with direct monosynaptic projections to spinal motor neurons are called *corticomotoneuronal cells*.

Any voluntary arm movement can have destabilizing effects on the rest of the body due to mechanical interactions between body segments. Thus, control of voluntary arm movements requires coordination with neural circuits responsible for the control of posture and balance. This is mediated by descending projections from cortical motor areas to the reticular formation, which in turn project to the spinal cord via the reticulospinal tract (Chapters 33 and 36).

Imposing a Delay Period Before the Onset of Movement Isolates the Neural Activity Associated With Planning From That Associated With Executing the Action

Voluntary movement requires the intervention of a number of neural processes between the arrival of salient sensory inputs and the initiation of an appropriate motor response. With the development in the 1960s of

single-cell recording in the cerebral cortex of awake animals, tasks that experimentally manipulate different attributes of movements have been used to study every cortical area involved in the control of arm and hand movements to try to identify neural correlates of the presumed control processes in each area.

In “reaction-time” tasks, animals make a prespecified response when they detect a particular stimulus, such as reaching to a target when it appears (Figure 34–4A). The stimulus informs the animal both what movement to make and when to make it. However, reaction times in such tasks are typically short, often less than 300 ms, and most or all putative planning stages leading up to the initiation of the movement are accomplished within that brief time. This makes it very difficult to discern what kinds of information are represented in the activity of the neurons at each given moment and thus to what processes they are contributing (Figure 34–4B).

However, a critical feature of voluntary behavior is that movement initiation is not obligatory the instant an intention to act is formed. This volitional control over the timing of movement has been exploited by so-called “instructed-delay” motor tasks (Figure 34–4A), in which an instructional cue informs the animal about specific aspects of an impending movement such as the location of a target, but the animal must withhold the response until a delayed stimulus signals when to make the movement. This protocol allows researchers to dissociate in time the neural processes associated with the early stages of planning the intended act from those that are directly coupled in real time to the initiation and control of the movement.

As expected, neurons in all the movement-related cortical areas discharge prior to and during movement execution in reaction-time tasks (Figure 34–4B), and their activity correlates systematically with different properties of movements, such as their direction, velocity, spatial trajectory, and causal forces and muscle activity. Critically, however, many neurons in the same areas also signal information about an intended motor act during an instructed-delay period long before its initiation (Figure 34–4B). Thus, even though planning and execution are distinct serial stages in voluntary motor control, they are not implemented by distinct neural populations in different cortical areas. Moreover, even a well-trained monkey will occasionally make the wrong movement in response to an instructional cue. In those trials, the activity during the delay period generally predicts the erroneous motor response that the monkey will eventually make. This is compelling evidence that the activity is a neural correlate of the monkey’s motor intentions, not a passive sensory response to the instructional cues.

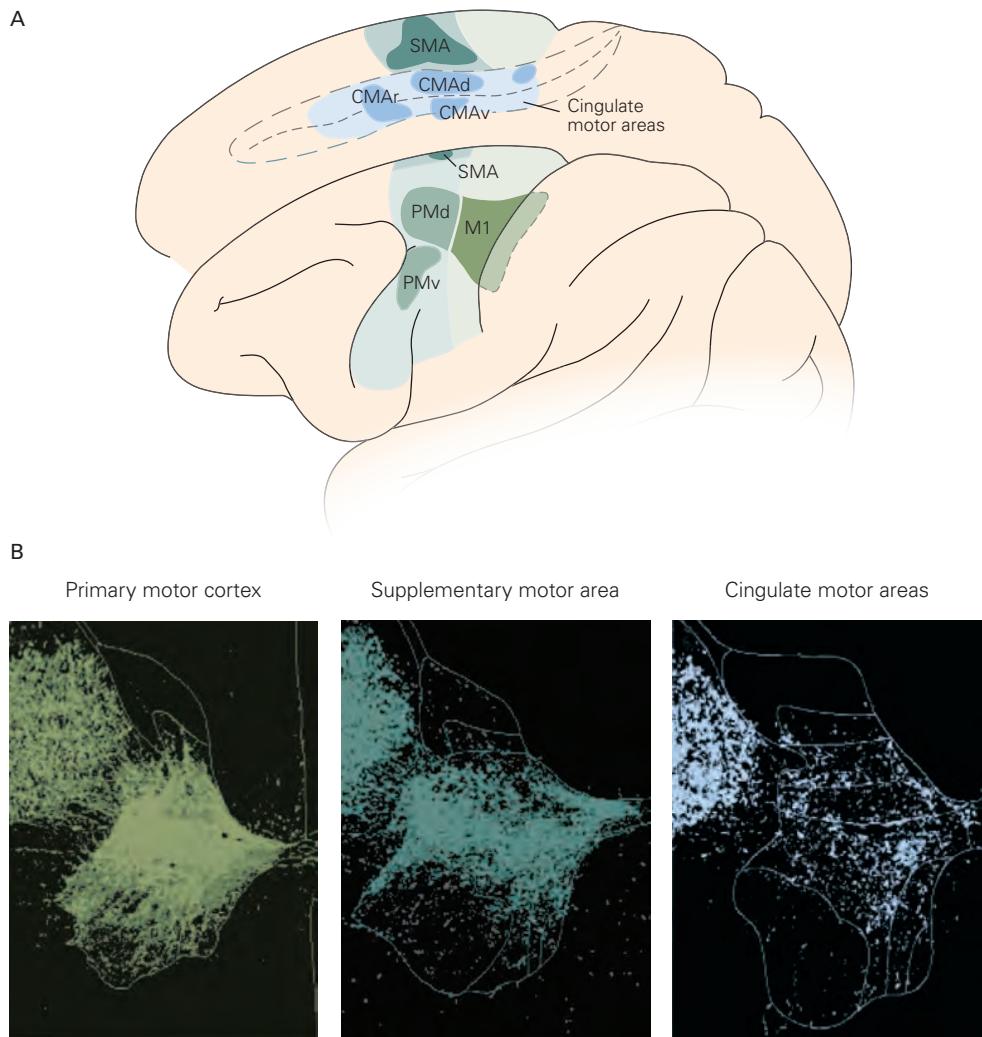


Figure 34-3 Cortical origins of the corticospinal tract. (Reproduced, with permission, from Dum and Strick 2002. Copyright © 2002 Elsevier Science Inc.)

A. Corticospinal neurons that modulate muscle activity in the contralateral arm and hand originate in the parts of the primary motor cortex (**M1**) motor map and many subdivisions of the premotor cortex (**PMd**, **PMv**, **SMA**) that are related to arm and hand movements (indicated by the darker zones). The axons from these areas project into the spinal cord cervical enlargement (see part B). Corticospinal fibers projecting to the leg, trunk, and other somatotopic parts of the brain stem and spinal motor system originate in the other parts of the motor and premotor cortex, indicated by the lighter zones. (Abbreviations: **CMAd**, dorsal cingulate motor area; **CMAr**, rostral cingulate motor area; **CMAv**, ventral cingulate motor area; **M1**, primary motor cortex; **PMd**, dorsal premotor cortex; **PMv**, ventral premotor cortex; **SMA**, supplementary motor area.)

B. Transverse sections of the spinal cord at the level of the cervical enlargement in monkeys after injection of the anterograde tracer horseradish peroxidase into different arm-related cortical motor regions to label the distribution of corticospinal axons arising from each cortical region. The corticospinal axons from the primary motor cortex (*left*), supplementary motor area (*middle*), and cingulate motor areas (*right*) all terminate on interneuronal networks in the intermediate laminae (V–VIII) of the spinal cord. Only the primary motor cortex contains corticospinal neurons (corticomotoneuronal cells) whose axons terminate directly on spinal motor neurons in the most ventral and lateral part of the spinal ventral horn (Rexed's lamina IX). Rexed's laminae I to IX of the dorsal and ventral horns are shown in faint outline in each section. The dense cluster of labeled axons adjacent to the dorsal horn (*upper left*) in each section are corticospinal axons descending in the dorsolateral funiculus, before entering the spinal intermediate and ventral laminae.

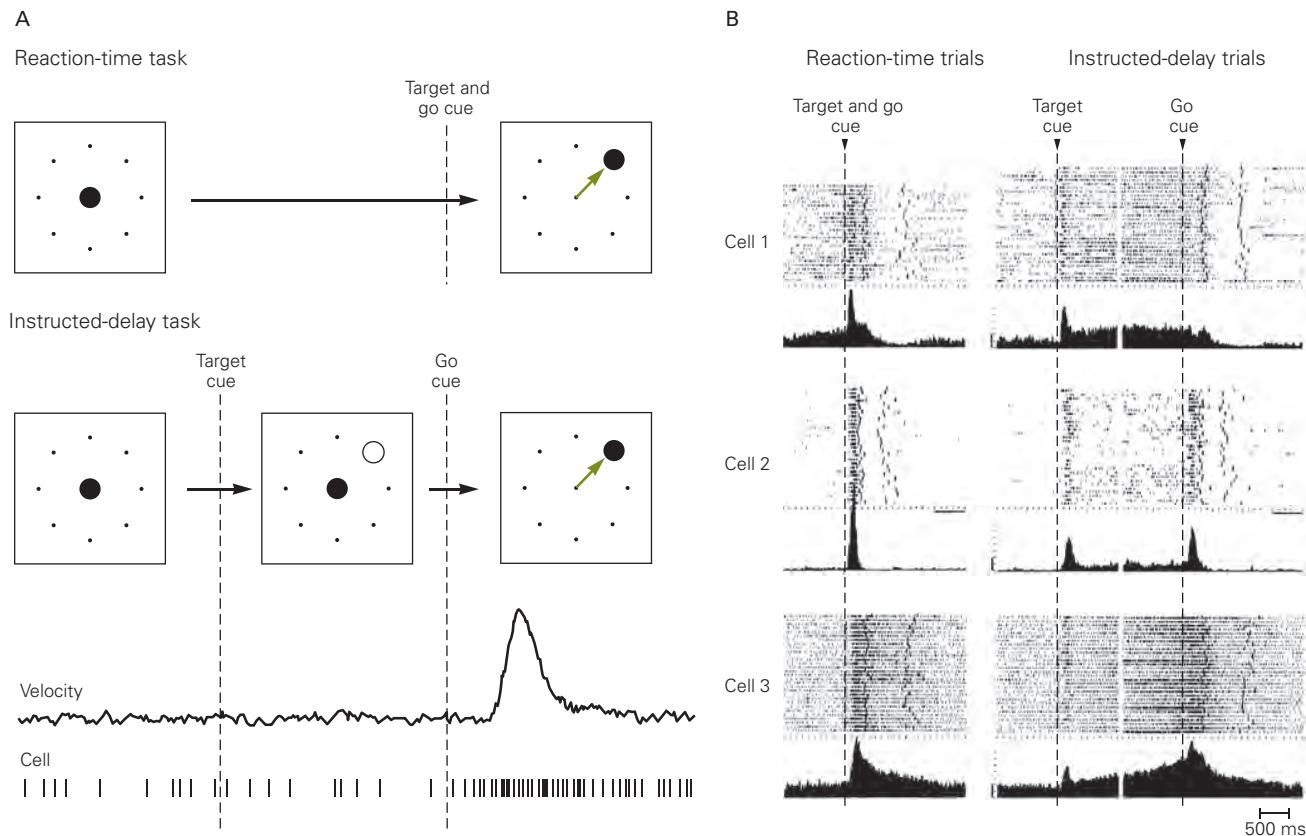


Figure 34-4 Neural processes related to movement planning and movement execution can be dissociated in time. (Reproduced, with permission, from Crammond and Kalaska 2000.)

A. In a *reaction-time task*, a sensory cue instructs the subject both where to move (target cue) and when to move (go cue). All neural operations required to plan and initiate the execution of the movement are performed in the brief time between the appearance of the cue and the onset of movement. In an *instructed-delay task*, an initial cue tells the subject where to move, and only later is the go cue given. The knowledge provided by the first cue permits the subject to plan the upcoming movement. Any changes in activity that occur after the first cue but before the second are presumed to be neural correlates of the planning stage.

B. Movement planning and execution are not completely segregated at the level of single neurons or neural populations in a given cortical area. Raster plots and cumulative histograms show the responses of three premotor cortex neurons to

movements in each cell's preferred direction during reaction-time trials and instructed-delay trials. In the raster plots, each row represents activity in a single trial. The thin tics in each raster row represent action potentials, and the two thicker tics show the onset and end of movement. In reaction-time trials, the monkey does not know in which direction to move until the target appears. In contrast, in instructed-delay trials, an initial cue informs the monkey where the target lies well in advance of the appearance of a second signal to initiate the movement. During the delay period, activity in many premotor cells shows directionally tuned changes that signal the direction of the impending delayed movement. The activity in cell 1 appears to be strictly related to the planning phase of the task, for there is no execution-related activity after the go signal in the instructed-delay task. The other two cells show different degrees of activity related to both planning and execution.

Parietal Cortex Provides Information About the World and the Body for State Estimation to Plan and Execute Motor Actions

Sensory information is essential for selecting appropriate and effective actions. Before drinking from a cup, the brain uses visual input to identify which object is the cup, where it is located relative to the body, and its physical properties such as size, shape, and handle orientation.

In addition, information about the current posture and motion of the arm and hand is provided by integrating proprioceptive signals from the limb with efference copies of motor commands (Chapter 30). Finally, cutaneous signals are critical when interacting manually with objects, such as grasping and lifting the cup.

Several lines of evidence implicate the parietal cortex as a key brain region in sensory processing for motor action. The parietal lobe, especially PE, PEip, and MIP,

receives strong somatic sensory inputs about body posture and movement from S-I. Several parietal regions along and within the IPS are major components of the dorsal visual pathway, which processes visuospatial information about objects that guides arm and hand movements while reaching to, grasping, and manipulating them. The parietal lobe is also reciprocally interconnected with precentral cortical motor areas to provide the precentral cortex with signals for the sensory guidance of movement and to receive efference copies of motor commands from those same precentral areas. Finally, human subjects with lesions of the posterior parietal cortex often demonstrate specific impairments in using sensory information to guide motor action (Box 34-1).

The Parietal Cortex Links Sensory Information to Motor Actions

We experience the space that surrounds us as a single unified environment within which objects have specific locations relative to each other and to ourselves. Classical neurology suggested that the parietal lobe constructed a unified multimodal neural representation of the world by integration of inputs from different sensory modalities. This single map of space was assumed to provide all the information necessary both for spatial perception and for the sensory guidance of movement, and so was shared by the different motor

circuits that controlled different parts of the body, such as the eyes, arm, and hand.

However, the idea that the parietal cortex contains a single topographically organized representation of space is incorrect. Instead, the posterior parietal cortex contains several distinct functional areas that work in parallel and receive different combinations of sensory and motor inputs related to the guidance of movement of different effectors, such as the eyes, arm, and hand. Neurons in these areas are often multimodal, with both visual and somatic sensory receptive fields, and also discharge preferentially prior to and during movements of a specific effector. Each functional area is connected to frontal motor regions involved in control of the same effectors. Finally, each region is not topographically organized in the familiar sense of a faithful point-to-point representation of surrounding space, but rather comprises a complex mixture of neurons with different sensory inputs that may contribute to the multisensory integration required to guide motor actions with the environment.

Body Position and Motion Are Represented in Several Areas of Posterior Parietal Cortex

The S-I and adjacent superior parietal cortex regions PE, MIP, and PEip are a major source of proprioceptive and tactile sensory information about the position and motion of body parts. Neurons in S-I areas 1 and 2

Box 34-1 Lesion Studies of Posterior Parietal Cortex Lead to Deficits in the Use of Sensory Information to Guide Action

Naturally occurring or experimentally induced lesions have long been used to infer the roles of different neural structures. However, the effects of lesions must always be interpreted with caution. It is often incorrect to conclude that the function perturbed by an insult to a part of the motor system resides uniquely in the damaged structure or that the injured neurons explicitly perform that function. Furthermore, the adverse effects of lesions can be masked or altered by compensatory mechanisms in remaining, intact structures. Nevertheless, lesion experiments have been fundamental in differentiating the functional roles of brain regions.

Behavioral studies by Goodale, Milner, Rossetti, and others on patients with parietal cortical damage have led to the conclusion that a primary function of the parietal lobe is to extract sensory information about the external world and one's own body for the planning and guidance of movements. Such studies have shown that patients with

lesions of certain parts of the parietal lobe suffer specific deficits in the ability to direct their arm and hand accurately to the spatial location of objects and to shape the orientation and grip aperture of the hand prior to grasping it.

They have also shown a particularly severe deficit in the ability to make rapid adjustments to their ongoing reach and grasping actions in response to unexpected changes in the location or orientation of the target object. This visual guidance of action is provided by visual signals that are routed through the dorsal visual stream and may operate in parallel with and independently of perceptual processes evoked by the visual inputs that are routed simultaneously through the ventral visual stream in the temporal lobe. For instance, whereas our visual perception of the size and orientation of objects can be deceived by certain perceptual illusions, the motor system often behaves as if it is not fooled and makes accurate movements.

typically respond to tactile input from a limited part of the contralateral body or to movements of one or a few adjacent joints in specific directions.

In contrast, many PE and MIP neurons discharge during passive and active movements of multiple joints. Some cells also respond during combined movements of multiple body parts, including bilateral movements of both arms. Many PE and MIP neurons also have large tactile receptive fields whose responses are modulated by context during limb movement or posture. For instance, a neuron with a tactile receptive field that covers the entire glabrous (palmar) surface of the hand may only respond to physical contact with an object when the hand is close to the body and not when it touches the object with the arm fully extended.

These findings indicate that while area 1 and 2 neurons encode the positions and movements of specific body parts, superior parietal neurons integrate information on the positions of individual joints as well as the positions of limb segments with respect to the body. This integration creates a neural “body schema” that provides information on where the arm is located with respect to the body and how different arm segments are positioned and moving with respect to one another. This body schema is critical for selecting how to attain behavioral goals and for ongoing control of movement.

For instance, a key requirement for efficient reaching is knowledge of where the arm is before and during the reach. Monkeys with experimental lesions in Brodmann's area 2 and the adjacent superior parietal lobule (area 5 or PE) show deficits in reaching to and manipulating objects under proprioceptive and tactile guidance without vision. Human patients with similar lesions show the same deficit, without the spatial neglect that is a common consequence of more lateral lesions in the inferior parietal lobe.

Spatial Goals Are Represented in Several Areas of Posterior Parietal Cortex

Functional areas within the IPS are strongly implicated in the processing of spatial, especially visual, information relevant to action. Each of these areas has unique ways of representing objects and spatial goals relative to the body and contributes to controlling motor actions of different parts of the body. For instance, many neurons in the lateral intraparietal area (LIP) receive visual input from extrastriate cortical areas. Their receptive fields are fixed in retinal coordinates and shift to new spatial locations whenever the monkey changes its direction of gaze. Neural responses also often increase when the animal attends to a stimulus within the receptive field even without looking

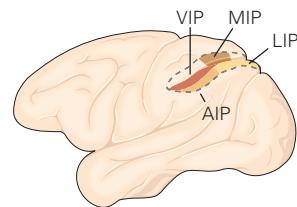
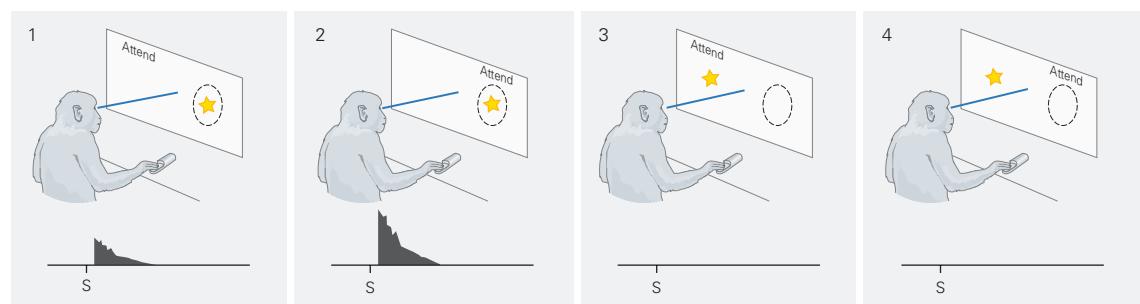
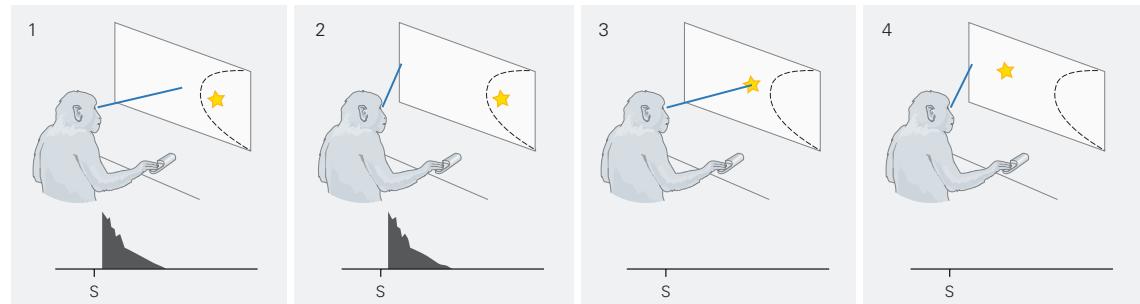
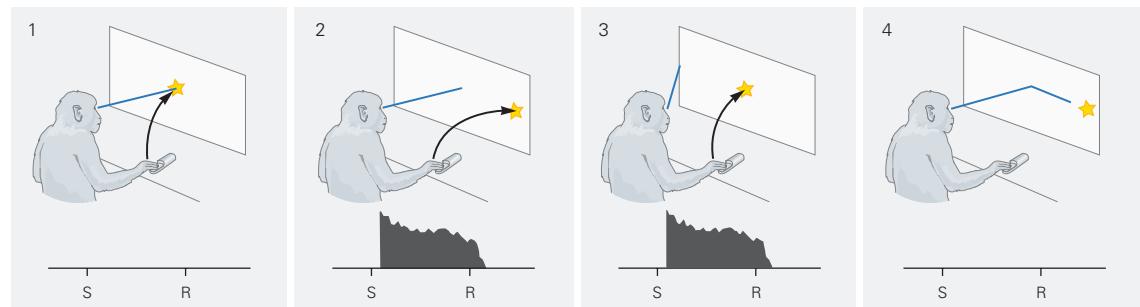
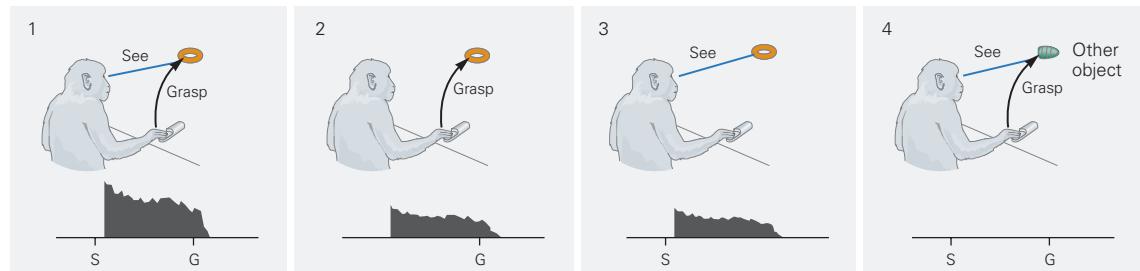
at it, and they often discharge prior to a saccade that is directed toward a visual stimulus in their receptive field (Figure 34–5A; and see Chapter 35).

Several parietal regions are preferentially implicated in the control of arm and hand movements. For instance, the most medial regions of the superior parietal cortex, areas V6A and PEc, receive input from extrastriate visual areas V2 and V3. Many V6A and PEc neurons have visual receptive fields in retinal coordinates, but their activity is also frequently modulated by the direction of gaze, the current arm posture, and the direction of reaching movements.

The ventral intraparietal area (VIP) in the fundus of the IPS receives inputs from two components of the dorsal visual stream, the medial temporal cortex and medial superior temporal cortex, which are involved in the analysis of optic flow and visual motion. Many VIP neurons respond to visual stimuli and somatosensory stimuli with receptive fields on the face or head and, in some cases, on the arm or trunk. Neural activity is in head-centered coordinates, as somatosensory and visual information remains in register even if the eyes move to fixate different spatial locations (Figure 34–5B). Some VIP neurons respond to both visual and tactile stimuli moving in the same direction, whereas others are strongly activated by visual stimuli that move toward their tactile receptive field but only if the path of motion will eventually intersect the tactile receptive field. These neurons may allow the monkeys to link the location and motion of objects in their immediate peripersonal space with different parts of their body.

Another area of parietal cortex related to reaching is the parietal reach region (PRR). The PRR likely corresponds to the medial intraparietal cortex (MIP) and adjacent arm-control parts of the superior and inferior parietal cortex. The activity of many PRR neurons varies with the location of reach targets relative to the hand. However, this signal is not fixed to the current location of the hand or target but rather on the current direction of gaze (Figure 34–5C). Each time the monkey looks in a different direction, the reach-related activity of PRR neurons changes, even if the location of the target and hand and the required reach trajectory do not change. In contrast, the reach-related activity of many neurons in areas PE and PEip is less related to gaze and more strongly related to the current hand position and arm posture. PE and PEip neurons thus provide a more stable signal about the location of the reach target relative to the current position of the hand compared to PRR.

Finally, neurons in the anterior intraparietal area (AIP) are primarily implicated in object grasping and manipulation by movements of the hand. Many AIP neurons are preferentially active while reaching for

**A Lateral intraparietal area (LIP)****B Ventral intraparietal area (VIP)****C Medial intraparietal area (MIP)****D Anterior intraparietal area (AIP)**

and grasping objects of particular shapes, sizes, and spatial orientations, and often even while viewing those objects before grasping them (Figure 34–5D). There is a broad range of neural response properties, from neurons that respond almost exclusively to visual input about the objects but not to the grasping actions to neurons that discharge only during the hand movements themselves even in the dark. This suggests that the AIP contains neural circuits that begin to transform visual information about the physical properties of an object that are relevant to how it could be handled—what James Gibson has called the object's *affordances*—into appropriate hand actions (Chapter 56).

A fascinating discovery about the parietal cortex is that the receptive fields of neurons can be altered by individual experience, such as tool use. Monkeys were trained to retrieve food pellets that were out of normal reach of the arm and hand by using a rake-shaped tool. Many VIP neurons normally respond to visual objects when they are either located near the current position of the hand or anywhere within reach with the arm. After training, their visual receptive fields transiently expand to incorporate the tool when the monkey grasps it, as if the distal end of the tool had become a functional extension of the monkey's own hand and arm (Figure 34–6).

Internally Generated Feedback May Influence Parietal Cortex Activity

The delays involved in the transmission of visual and somatic feedback about arm movements from the periphery to cortical circuits can lead to oscillations

or even instabilities in real-time sensorimotor control. One theoretical solution to this problem is to use a forward internal model to make predictive estimates of body motion based on internal efference copies of outgoing motor commands as well as from slower peripheral feedback signals (Chapter 30).

Several lines of evidence suggest that parietal cortex circuits, along with the cerebellum (Chapter 37), may implement a similar solution. Many reach-related neurons in PE, MIP, and PRR are active not only in response to passive sensory inputs but also before the onset of movement and during the instructed-delay period of delayed-reaching tasks. These responses suggest that these neurons process centrally generated signals about motor intentions prior to movement onset. This premovement activity is often interpreted as evidence that the parietal cortex generates feedforward signals that contribute to the early planning of movements. However, an alternate interpretation is that the premovement activity is driven by an efference copy of the motor command for the intended movement that is transmitted into the parietal cortex via its reciprocal connections with precentral motor areas. This combination of peripheral sensory inputs and central efference copies could permit some parietal reach-related circuits to compute a continuously updated estimate of the current state of the arm and its position relative to the behavioral goal. This estimate could be used to make rapid corrections for errors in ongoing arm movements.

Whether the parietal circuits are primarily involved in the formation of a subject's motor intentions or in

Figure 34–5 (Opposite) Neurons in the parietal cortex of the monkey are selective for the location of objects in the visual field relative to particular parts of the body. Each histogram represents the firing rate of a representative neuron as a function of time following presentation of a stimulus. In each diagram, the line emanating from the eyes indicates where the monkey is looking.

A. Neurons in the lateral intraparietal area have *retina-centered* receptive fields. The strength of the visual response depends on whether the monkey is paying attention to the stimulus (S). The neuron fires when a light is flashed inside its receptive field (dotted circle) (1). The response is more robust if the monkey is instructed to attend to the location of the stimulus (2). The neuron does not fire if the stimulus is presented outside the receptive field, regardless of where attention is directed (3, 4).

B. In the ventral intraparietal area, some neurons have *head-centered* receptive fields. This is determined by keeping the head in a fixed position while the monkey is instructed to shift its gaze to various locations. This neuron fires when a light appears to the right of the midline of the head (1, 2). It does not fire when the light appears at another location relative to the head, such as the midline or to the left. (3, 4). The critical

contrast is between situations 1 and 4. The retinal location of the light is the same in both (slightly to the right of the fixation point), yet the neuron fires in 1, when the stimulus is to the right of the head, but not in 4, when the stimulus is to the left of the head.

C. In the medial intraparietal area, neurons are selective for the *retina-centered* direction of the reach (R) and fire when the monkey is preparing to reach for a visual target. This neuron fires when the monkey reaches for a target to the right of where he is looking (2, 3). It does not fire when he reaches for a target at which he is looking (1) or when he moves only his eyes to the target at the right (4). The physical direction of the reach is not a factor in the neuron's firing: It is the same in 1 and 3, and yet, the neuron fires only in 3.

D. In the anterior intraparietal area, neurons are selective for objects of particular shapes and fire when the monkey is looking at or preparing to grasp (G) an object. This neuron fires when the monkey is viewing a ring (3) or making a memory-guided reach to it in the dark (2). It fires especially strongly when the monkey is grasping the ring under visual guidance (1). It does not fire during viewing or grasping of other objects (4).

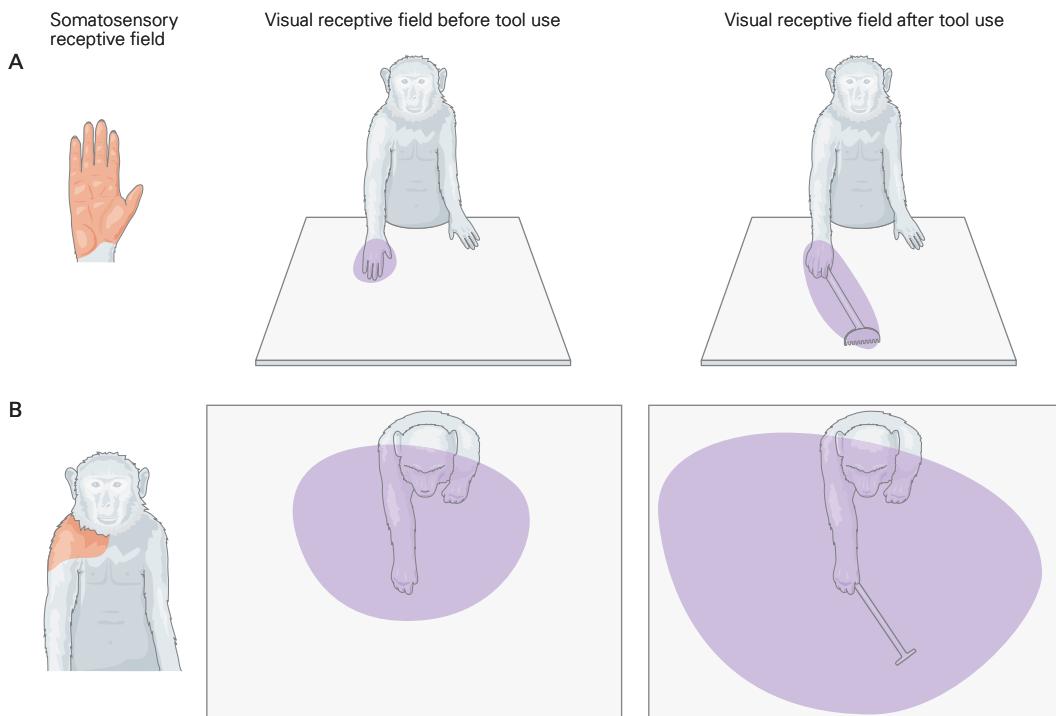


Figure 34–6 Some neurons in the parietal cortex of the monkey have receptive fields that dynamically expand once a tool is grasped. (Adapted from Maravita and Iriki, 2004. Copyright © 2003 Published by Elsevier Ltd.)

A. The orange area on the hand (*left*) indicates the somatosensory receptive field for a neuron. The purple area (*middle*) indicates the neuron's visual receptive field (vRF) region around the hand. The vRF is anchored to the hand and changes spatial location whenever the monkey moves its arm. The vRF expands

when the monkey grasps a rake after it has learned how to use the rake to reach for objects in the workspace (*right*).

B. A single neuron that has a shoulder-centered bimodal somatosensory (orange) and visual (purple) receptive field is illustrated. The vRF for this neuron (*middle*) is larger than the one shown in part A, possibly reflecting the potential workspace related to whole-arm function. The vRF also expands to incorporate the extended workspace permitted by use of a rake (*right*).

state estimation will depend on the origin of its pre-movement activity. If it is mainly generated within the parietal cortex itself, this will strongly implicate the parietal cortex in the planning of intended movements. In contrast, if it is primarily driven by an efference copy relayed from precentral motor areas, this would strongly implicate the parietal circuits in state estimation, including predicting how the arm should move in response to the motor command.

Premotor Cortex Supports Motor Selection and Planning

As outlined at the beginning of this chapter, a decision to act in a particular way in a given situation is shaped by many factors, including sensory information about objects, events, and opportunities for action from the

environment, body position and motion, internal motivational states, prior experiences, reward preferences, and learned arbitrary rules and strategies linking sensory inputs to motor actions. There can be many reasons why you want to drink some coffee, and that desire can be fulfilled by actions ranging from simply reaching out to your full coffee cup to making coffee at home or going to a café.

Frontal premotor cortical regions just rostral to M1 play an important role in early movement planning or task-selection processes. Many neurons in those areas, such as the PMd neurons shown in Figure 34–4, generate activity during instructed-delay tasks that reflect the motor intentions of the monkey and even the factors that influenced those action choices. The different premotor cortical regions are presumed to make different but overlapping contributions to motor selection and planning. For instance, the lateral premotor

cortex, including PMd and PMv, have traditionally been implicated in actions initiated and guided by external sensory inputs. In contrast, medial premotor areas, including SMA, pre-SMA, and CMA, have been implicated in the control of self-initiated movements as well as the suppression of actions. However, the distinction between their respective contributions is not absolute.

Medial Premotor Cortex Is Involved in the Contextual Control of Voluntary Actions

Clinton Woolsey's pioneering electrical stimulation studies showed that, in addition to the motor map in M1, the medial wall of the frontal cortex contains an array of neurons that also regulate body movements. This medial motor map, now called the supplementary motor area (SMA), includes the entire contralateral body but is coarser than the detailed map in M1, as described later. Strong stimulus currents are required to evoke movements, which are often complex actions such as postural adjustments or stepping

and climbing and can involve both sides of the body. Today, there is agreement that this region contains two areas that have distinct cytoarchitectonic characteristics, axonal connections, and functional properties: a more caudal SMA proper and a more rostral presupplementary motor area (pre-SMA), which we will collectively call the supplementary motor cortex (SMC).

The SMC has been implicated in many aspects of voluntary behavior, although its contribution remains controversial. Several lines of evidence support a role in self-initiated behavior. In humans, electrical stimulation of SMC below the threshold for movement initiation can evoke an introspective sense of an urge to move that does not arise during M1 stimulation. Lesions of SMC produce problems initiating desired movements or suppressing undesirable movements (Box 34-2). Moreover, recordings of slow cortical potentials at the surface of the skull during the execution of self-paced movements show that the initial potential arises in the frontal cortex as much as 0.8 to 1.0 second before the onset of movement. This signal, named the *readiness*

Box 34-2 Lesions of Premotor Cortex Lead to Impairments in the Selection, Initiation, and Suppression of Voluntary Behavior

Lesions of the supplementary motor area (SMA) and presupplementary motor area (pre-SMA) and the prefrontal areas connected with them produce deficits in the initiation and suppression of movements. Initiation deficits manifest themselves as loss of self-initiated arm movements, even though the patient can move when adequately prompted. This deficit can involve movement of parts of the body (*akinesia*) contralateral to the region and speech (*mutism*).

Deficits in movement suppression, in contrast, include the inability to suppress behaviors that are socially inappropriate. These include compulsive grasping of an object when the hand touches it (*forced grasping*), irrepressible reaching and searching movements aimed at an object that has been presented visually (*groping movements*), and impulsive arm and hand movements to grab nearby objects and even people without conscious awareness of the intention to do so (*alien-hand* or *anarctic-hand syndrome*).

Another striking syndrome is *utilization behavior*, in which a patient compulsively grabs and uses objects without consideration of need or the social context. Examples are picking up and putting on multiple pairs of glasses or reaching for and eating food when the

patient is not hungry or when the food is clearly part of someone else's meal.

These deficits in the initiation and suppression of actions may represent opposite facets of the same functional role for SMA and especially pre-SMA in the conditional or context-dependent control of voluntary behavior.

Lesions affecting premotor cortex also lead to impairments in the selection of motor actions. For example, when a normal monkey sees a tasty food treat behind a small transparent barrier, it readily reaches around the barrier to grasp it. However, after a large premotor cortex lesion, the monkey may persistently try to reach directly toward the treat and so repeatedly strikes the barrier with its hand, rather than making a detour around the barrier.

More focal lesions or inactivation of the ventral premotor cortex perturbs the ability to use visual information about an object to shape the hand appropriately for the object's size, shape, and orientation before grasping it. Focal lesions of the dorsal premotor cortex affect the ability to learn and recall arbitrary sensorimotor mappings or conditional stimulus-response associations, whereas supplementary motor cortex lesions impede the ability to learn and recall temporal sequences of movement.

potential, has its peak in the cortex centered in SMC. Because it occurs well before movement, the readiness potential has been widely interpreted as evidence that neural activity in this region is involved in forming the intention to move, not just in executing movement.

Neurons in both SMA and pre-SMA discharge before and during voluntary movements. Unlike M1 neurons, the activity of most SMA neurons is less tightly coupled to particular actions of a body part and appears instead to be associated with more complex, coordinated motor acts of the hand, arm, head, or trunk. Compared to SMA neurons, pre-SMA neurons often begin to discharge much earlier in advance of movement onset and are less tightly coupled to the execution of movements.

The SMC has been implicated in the so-called *executive control* of behavior, such as operations required to switch between different actions, plans, and strategies. For example, in monkeys, some SMC neurons discharge strongly when a subject is presented with a cue instructing it to change movement targets or to suppress a previously intended movement. The

SMC may therefore contain a system that can override motor plans when they are no longer appropriate.

The SMC has also been implicated in the organization and execution of movement sequences. Some SMC neurons discharge before the start of a particular sequence of three movements but not before a different sequence of the same three movements (Figure 34–7). Other neurons discharge only when a particular movement occurs in a specific position in a sequence or when a particular pair of consecutive movements occurs regardless of their position in the sequence. In contrast, some other SMC neurons discharge only when the monkey makes the movement that occurs in a particular ordinal position of a sequence (eg, only the third) irrespective of its nature or how many movements remain to be executed in the sequence.

These seemingly disparate functions may reflect a more general role of the SMC in *contextual control* of voluntary behavior. Contextual control involves selecting and executing those actions deemed appropriate on the basis of different combinations of internal and external cues as well as withholding inappropriate actions in

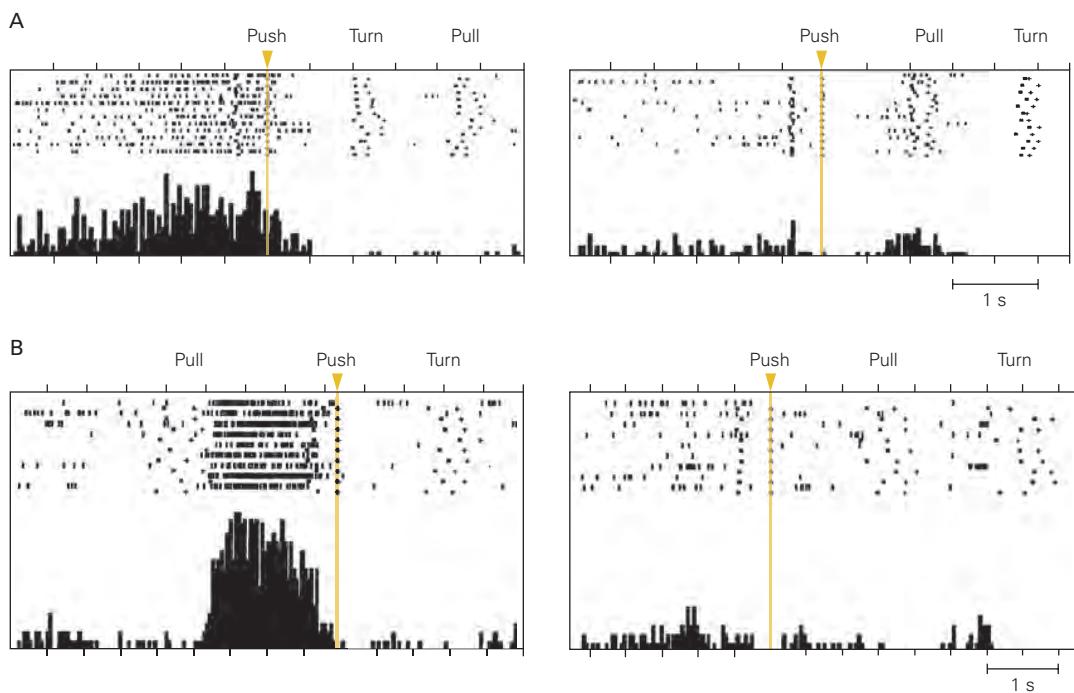


Figure 34–7 Some neurons in the supplementary motor complex of monkeys encode a specific sequence of motor acts. (Adapted, with permission, from Tanji 2001. Copyright © 2001 by Annual Reviews.)

A. A neuron discharges selectively during the waiting period before the first movement of the memorized sequence push-pull-turn (*left*). When the sequence is push-pull-turn (*right*), the cell remains relatively silent, even though the first movement in

both sequences is the same (push). Triangles at the top of each raster plot indicate the start of the push movement.

B. Records of a neuron whose activity increases selectively during the interval between completion of one motor act, a pull, and the initiation of another act, a push. The cell is not active when a push is the first movement in the sequence or when pull is followed by turn.

a specific environmental or social context. It also can involve organizing the sequence of actions required to achieve a particular goal. Contextual control likely also involves contributions from other neural circuits such as regions of the prefrontal cortex and the basal ganglia.

The cingulate motor areas (CMA) may also contribute to the contextual control of behavior. CMA appears to be involved in selecting alternate actions following motor errors or in response to changing reward contingencies. For example, monkeys were trained to push or turn a handle in response to a noninstructive trigger signal. Initially, the monkeys received a large reward if they made the same movement (pushing or turning the handle) in sequential trials. After several trials, the reward size began to decrease. If the monkeys then switched to the other movement, the reward size returned to maximum once that movement was repeated for several trials. The best strategy for the monkeys, therefore, was to switch between repetitions of either pushing or turning the handle as soon as they detected a reduction in reward size.

In this task, some neurons in the rostral CMA responded during the interval between the reception of reward and the start of the next trial. On trials with a reduced reward, task-related activity in these neurons did not change when the monkeys made the same movement in the next trial; their activity only changed when the monkeys switched to the other movement in the next trial. Importantly, those same neurons did not show the same response change when a visual cue instructed the monkeys to change movements in the next trial. This suggests that these rostral CMA neurons were preferentially involved in the voluntary decision to switch and move to the alternate goal based on action outcomes (reward size), but not by visual instructions to switch.

Dorsal Premotor Cortex Is Involved in Planning Sensory-Guided Movement of the Arm

Some of the first neural evidence that the lateral premotor cortex, including PMd and PMv, plays a crucial role in the selection and planning of sensory-guided motor actions came from recording studies by Ed Evarts, Steven Wise, and colleagues in the 1980s. These studies showed that many premotor neurons emitted brief short-latency discharge bursts in response to instructional cues that signaled specific movements, or sustained activity during the instructed-delay period between the appearance of the instructional cue and a second cue that permitted the instructed movement (Figure 34–4).

This activity reflects information about the intended act, including the spatial location of the target, the direction of arm movement, and other

movement attributes. Importantly, PMd delay-period activity can reflect the intention to reach to a particular location with either the contralateral or ipsilateral arm, even though the biomechanical details of the two arm movements are very different. This suggests that PMd activity can signal the intention to generate a motor act independent of the effector used to generate the action, in an extrinsic spatial coordinate framework consistent with a prediction of the sensorimotor coordinate transformation model of motor planning. Imaging studies have likewise found evidence for an extrinsic spatial representation of finger-tapping sequences made with either hand in human premotor cortex.

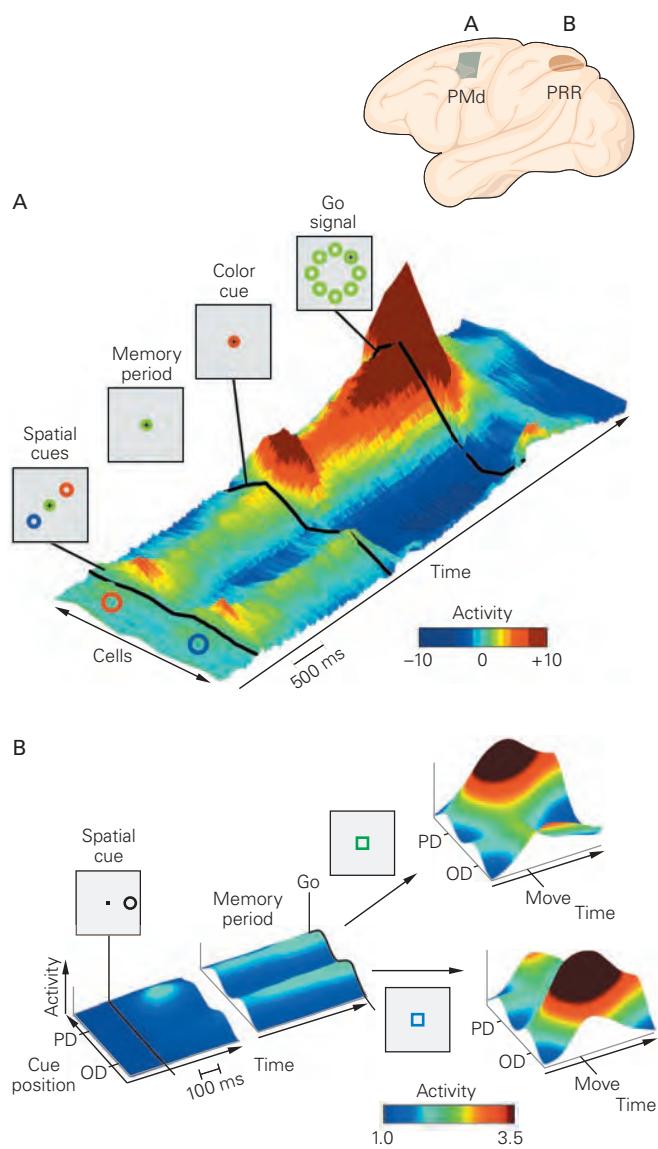
Selection of an appropriate action from among multiple alternatives is a critical aspect of voluntary control. Delay-period activity in PMd can reflect that process. For example, in one experiment, recordings were made from PMd neurons in monkeys during a task in which the animals first received two colored spatial cues that identified two potential targets for reaching in opposite directions. After a memorized-delay period, a new centrally-located color cue informed the monkeys which of the spatial cues was the correct target. Following the first instruction, neural activity in PMd signaled both potential-reaching movements, but immediately after the second instruction, activity in PMd signaled only the monkeys' reaching choice (Figure 34–8A). This showed that PMd can prepare multiple potential motor actions prior to the final decision about which action to take. Subsequent studies suggest that this might be limited to no more than three to four simultaneous potential actions. Reach-related neurons in parietal area PRR also contribute to the preparation for two potential motor actions before the final action decision is made (Figure 34–8B), revealing how this process is distributed across multiple arm movement-related cortical neural populations.

PMd neurons can also signal a deliberate decision not to move. Many PMd neurons generate directionally tuned activity during an instructed-delay period when a colored visual cue at a target location instructs a monkey to reach to the target, but decrease their activity when a different colored cue at the same location instructs the monkey to refrain from reaching to it. This differential activity is an unequivocal signal, seconds before the action is executed, about the monkey's intention to reach in a particular direction or not to move in response to an instructional cue (Figure 34–9). Interestingly, many neurons in the parietal area PE/MIP studied in the same task continue to generate directionally tuned activity during the delay period even after the instructional cue to withhold

Figure 34–8 Activity of reach-related cortical neurons in monkeys during a target selection task reflects potential movements to different targets as well as the chosen direction of reach.

A. The three-dimensional colored surface depicts the mean level of activity of a population of dorsal premotor cortex (PMD) neurons with respect to baseline in a task in which a monkey must choose one of two color-coded reach targets in each trial. Cells are sorted along one axis (labeled “cells”) based on their preferred movement direction (neurons located at the red and blue circles prefer movements at 45° and 215°, respectively). Diagrams beside the neural response profile display the stimuli presented to the monkey at different times during the trial. Red and blue cues provide information about potential actions; green cues guide the monkeys through different stages of each trial but provide no information about what reach to make. Shortly after the start of each trial, two potential reach targets (blue and red spatial cues) appear in opposite locations relative to the starting position of the arm (green circle) for 500 ms and then disappear. After a memorized delay period, the color of the starting circle changes to either red or blue (color cue), indicating to the monkey which is the correct target, in this case at 45°. After a further delay period, the go signal (green circles at all eight possible target locations) instructs the monkey to begin reaching to its chosen target. During the period of target uncertainty between the appearance of the two spatial cues and the central color cue, PMd neurons that prefer the two potential reach movements (red and blue circles) are simultaneously activated, whereas neurons that prefer other movements are inactive or suppressed, so that the entire PMd population encodes the two potential reach actions. As soon as the color cue appears to identify the correct target, the PMd neural activity changes rapidly to signal the reach movement chosen by the monkey. Had the color cue designated the target at 215°, the neurons preferring that target (blue circle) would increase their activity, and the neurons preferring the target at 45° (red circle) would decrease their activity (not shown). (Reproduced, with permission, from Cisek and Kalaska 2010. Copyright © 2010 by Annual Reviews.)

B. In a second study of neural activity in the parietal reach region (PRR), the format of data is the same as in part A. In this study, the monkey is presented with a single spatial cue that instructs it to prepare to reach either to the cue’s location (PD) or in the opposite direction (OD). After a random memorized delay period, a color cue specifies whether the reach should be to the remembered location of the spatial cue (green; PD) or in the OD (blue). PRR neural activity is sorted according to the preferred movement direction of each neuron, as in part A. Population activity initially specifies the spatial cue location but then reflects both potential movement directions during the remainder of the memorized delay period. Shortly after the color cue appears, the activity quickly shifts to reflect the chosen reach direction, either the PD or OD. (Reproduced, with permission, from Klaes et al. 2011. Copyright © 2011 Elsevier Inc.)



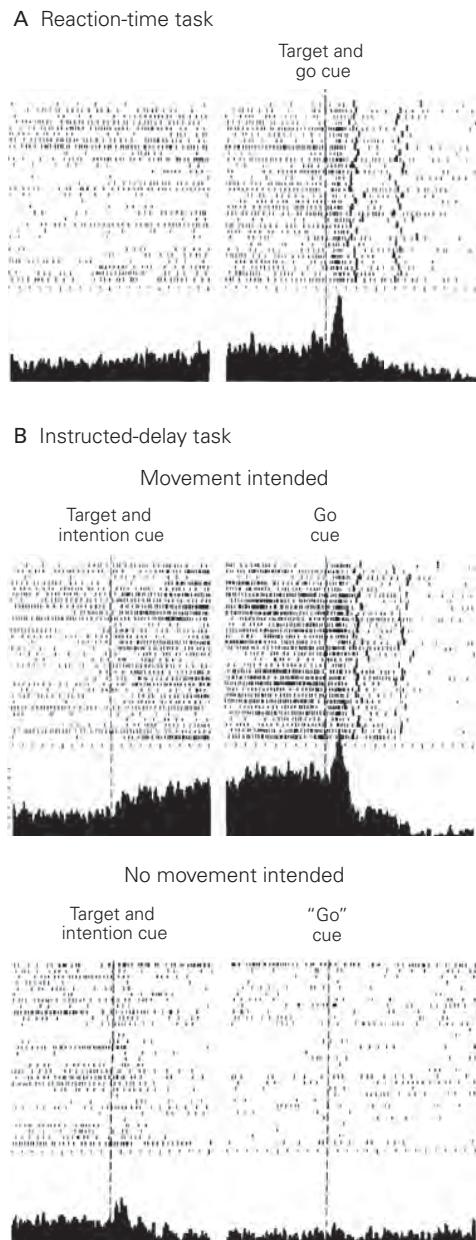


Figure 34–9 Decisions about response choices are evident in the activity of premotor cortex neurons in the monkey. (Reproduced, with permission, from Crammond and Kalaska 2000.)

- A. In a reaction-time task (reaching), a cell exhibits gradually increasing tonic firing while waiting for the appearance of a target. When the target appears (go cue), the cell generates a directionally tuned response.
- B. In an instructed-delay task, when a monkey is shown the target and instructed to move once the go cue appears, the cell generates a strong directionally tuned signal for the duration of the delay period before the go cue (**top**). When the monkey is shown the target and instructed not to move when the go cue appears, the cell's activity decreases (**bottom**).

reaching, suggesting that the parietal cortex retains a representation of potential actions that ultimately are not executed.

Many neurons in premotor cortex also discharge during movement execution. Given this close proximity of planning- and execution-related activity, even at the level of individual neurons, a major question is why planning-related neural activity does not immediately initiate a movement. What prevents the movement from being executed prematurely? It does not appear that planning-related activity simply fails to exceed a minimum threshold required to initiate the movement or that there is a separate overt braking mechanism that must be released to allow the movement to begin.

A different way to interpret neural processing during the planning and execution of reaching that might provide answers to such questions comes from a dynamical-systems perspective. The idea is that cortical motor circuits form a dynamical system whose distributed activity patterns evolve in time as a function of their initial state, input signals, and stochastic neural response variability (“noise”). Activity patterns during different stages of planning and execution thus reflect different states of the network, including a specific state during the delay period that can prepare the movement but not activate muscles (Figure 34–10). The overall similarity of the population-level activity patterns during repetitions of the same movement shows that the entire population undergoes a coordinated pattern of co-modulation of activity during the planning and execution of the movement, determined by the synaptic connectivity within the neural circuit.

Dorsal Premotor Cortex Is Involved in Applying Rules (Associations) That Govern Behavior

Behavior is often guided by arbitrary rules that link specific symbolic cues to particular actions. When driving your car, you must perform different actions depending on whether a traffic light is green, amber, or red. In monkeys that have learned to associate arbitrary cues with specific movements, many cells in premotor areas respond selectively to specific cues. For instance, in order to select the correct target in the two-target study in Figure 34–8, the monkeys had to apply a rule that mapped color to target location provided by the two sequential instructional cues.

The PMd is implicated in the acquisition of new movement-related associations or rules. In one experiment, recordings from PMd neurons were made while the monkeys learned the association between four unfamiliar visual cues and four different movement

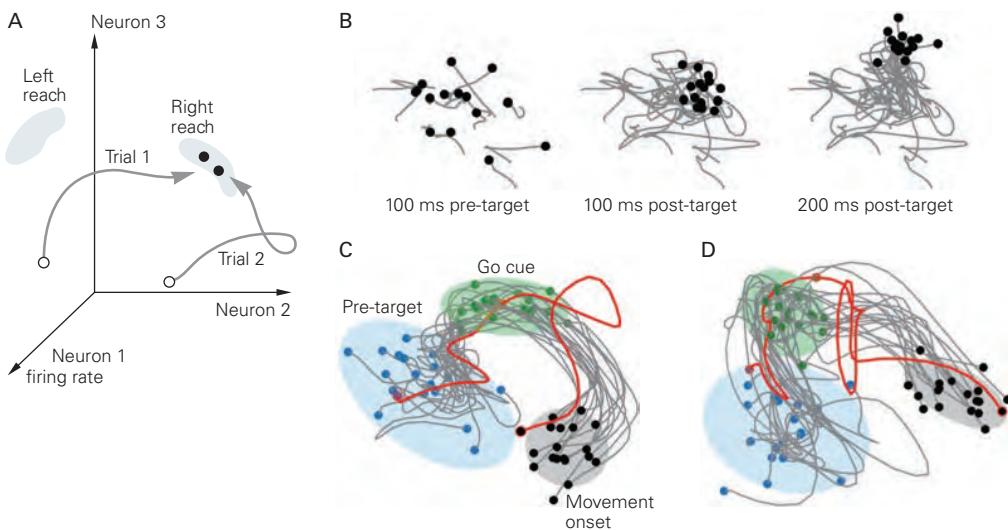


Figure 34–10 The time-varying neural activity in the dorsal premotor cortex of monkeys during different stages of the planning and execution of a movement can be viewed as transitions between different activation states. (Adapted, with permission, from Churchland MM et al. 2010. Stimulus onset quenches neural variability: a widespread cortical phenomenon. *Nat Neurosci* 13:369–378. Copyright © Springer Nature.)

A. A schematic illustration of how the simultaneous activity of neurons can be viewed as a trajectory through a multi-neuron activity “state space.” The time-varying activity level of three simultaneously recorded neurons is represented along three axes, which defines a three-neuron state space. A specific plan (reach left or reach right) requires different combinations of preparatory firing rates for the three neurons (**gray zones**). Prior to the formation of the intention to move left or right, the baseline activity of the three neurons occupies a region in state space that is associated with holding the arm in its current position (**open circles**, for two different trials). When an instruction appears to make a reach to the right, the combined activity of the three neurons changes in a coordinated fashion, creating time-varying “neural trajectories” (**gray arrows**) that converge on the region of state space that is associated with generating a rightward movement (**filled circles** within the “right reach” **gray zone**).

B. Projection of the simultaneous activity of a large population of dorsal premotor cortex (PMd) neurons onto a two-dimensional state space shortly before (pre-target) and after (post-target) the appearance of a reach target cue in a task in which the reach movement must be delayed until a subsequent go cue is presented. **Gray lines** show the temporal evolution of the neural trajectories during the earliest part of movement preparation from 200 ms before target cue until the specified pre- or post-target time (**black dots**) in 15 different trials to the same target location. Neural activity initially meanders randomly within the region of state space associated with the starting posture of the arm (**left**). It then begins to converge onto a smaller region of the state space shortly after the reach target instruction appears (**center**) and begins to evolve along

the neural trajectory associated with entering the preparatory state for the reach (**right**).

C. A more complete illustration of the neural trajectories recorded during 18 different repeated trials to the same target in this delayed reaching task from the initial pre-target postural state to the onset of movement. **Blue dots** indicate activity while holding the arm in the starting posture 100 ms before appearance of the target instruction onset. Once the target instruction appears, the neural trajectories evolve toward a region of state space associated with the preparatory activity state during the delay period (**green zone**), where it dwells until a go cue appears that allows the monkey to initiate the withheld movement (**green dots**). While in this reach-preparatory part of the state space during the delay period, the arm stays at the start position because PMd activity in that part of state space is not capable of activating muscles (ie, it is “output-null”). When the go cue appears, the neural trajectories unfold toward a different region of state space associated with the initiation of the intended reach movement (**gray zone** and **black dots**). The neural activity can only cause the muscle activity for the intended movement when it enters this “output-potent” zone of state space. The trial-to-trial variability of the neural trajectories can account for intertrial variability in movement kinematics and reaction times. One outlier trial (**red**) had a long reaction time and followed a more complex and time-consuming neural trajectory from the **green** to the **gray** zone. The output-null preparatory (**green**) and output-potent movement-initiation (**gray**) zones for reaches to different target locations occupy different regions of the total population state space distinct from those associated with this reach target.

D. Data are for the same target location as in part C but were recorded on a different day. The neural trajectory structure is fundamentally similar for the same movements between recording sessions. Differences in the overall pattern of activity can be explained by interday differences in the activity of individual neurons and differences in the composition of the recorded neural population between sessions.

directions. Although the monkeys' choices were initially random, they learned the rules within a few dozen trials. The monkeys made an arm movement in response to each cue; during the early "guessing" phase of learning, the activity of many PMd neurons was weak but gradually increased in strength and directional tuning as the monkeys learned which cue signaled which movement. Other neurons showed a reciprocal decline in activity as the rules were acquired. These changes in activity during learning reflected both the movement choices and the rising level of knowledge of the rules linking cues with actions.

The nature of the rule can also have a strong effect on neural responses. In monkeys that have been trained to choose between several possible movements based on a spatial rule (a visual cue's location) or a semantic rule (a cue's arbitrarily designated meaning independent of its location), many prefrontal and PMd neurons are preferentially active when the animal chooses a movement using one rule but not the other. This shows that the neural activity is related not just to a particular cue or action but also to the association between them.

Premotor areas are involved in the implementation of even abstract rules. For example, monkeys were trained in a task that required two decisions, one perceptual and the other behavioral, that had no prior association. In each trial, the monkeys first had to decide whether two sequentially presented visual images were the same or different (*a match/nonmatch perceptual decision*). In some trials, a *rule cue* presented at the same time as the sample visual image instructed the monkeys to move their hand if the two images were identical and to refrain from moving if they differed (*a go/no-go motor decision*); in other trials, the rule was reversed—move if the images differ and do not move if they match. Neural activity in PMd after the test visual images were presented was correlated more strongly to the motor decision than the perceptual decision in each trial, but both decisions were expressed in PMd. More strikingly, PMd activity was also correlated with the match/non-match *behavioral rule* during the delay period between the two visual images that guided the motor decision after the test image appeared (Figure 34–11). These results suggest that PMd has a major role in applying rules that govern the appropriateness of a behavior and in making behavioral decisions according to the prevailing rules. Neural recordings in prefrontal cortex during the same task (not shown) found a strong representation of the physical identity of the visual images, but weaker and later correlates of the behavioral rule and the motor decision than in PMd.

Ventral Premotor Cortex Is Involved in Planning Motor Actions of the Hand

The most lateral part of the premotor cortex, area PMv, is reciprocally connected with parietal cortex areas AIP, PF, and PFG and the secondary somatosensory area. Electrical stimulation shows that PMv contains extensively overlapping circuits that control hand and mouth movements.

Like AIP neurons, many PMv neurons appear to contribute to the control of hand actions based on the physical affordances offered by target objects. These neurons tend to fire preferentially during certain stereotypical hand actions, such as grasping, holding, tearing, or manipulating objects. Many neurons discharge only if the monkey uses a specific type of grip, such as a precision grip, whole-hand prehension, or finger prehension (Figure 34–12). Precision grip is the type most often represented. Some PMv neurons discharge throughout the entire action, while others discharge selectively at particular stages of one type of prehension, such as during the opening or closing of the fingers.

Another striking property of PMv neurons is that their discharge often correlates with the goal of a motor act and not with the individual movements forming it. Thus, many PMv neurons discharge when grasping an object is executed with effectors as different as the right hand, the left hand, and even the mouth. Conversely, a PMv neuron may be active when an index finger is flexed to grasp an object but not when the animal flexes the same finger to scratch itself.

Premotor Cortex May Contribute to Perceptual Decisions That Guide Motor Actions

A series of studies provide evidence that cortical motor areas not only represent the sensory information that guides voluntary movements but also express the neural operations necessary to make and act on perceptual decisions. Monkeys were trained to discriminate the difference in frequency between two brief vibratory stimuli applied to one finger and separated in time by a few seconds. The animals had to decide whether the frequency of the second stimulus was higher or lower than the first and to report their perceptual decision by reaching out to push one of two buttons with the other hand.

The decision-making process in this task can be conceived as a chain of neural operations: (1) encode the first stimulus frequency (f1) when it is presented; (2) maintain a representation of f1 in working memory during the interval between the two stimuli; (3) encode the second stimulus frequency (f2) when it is

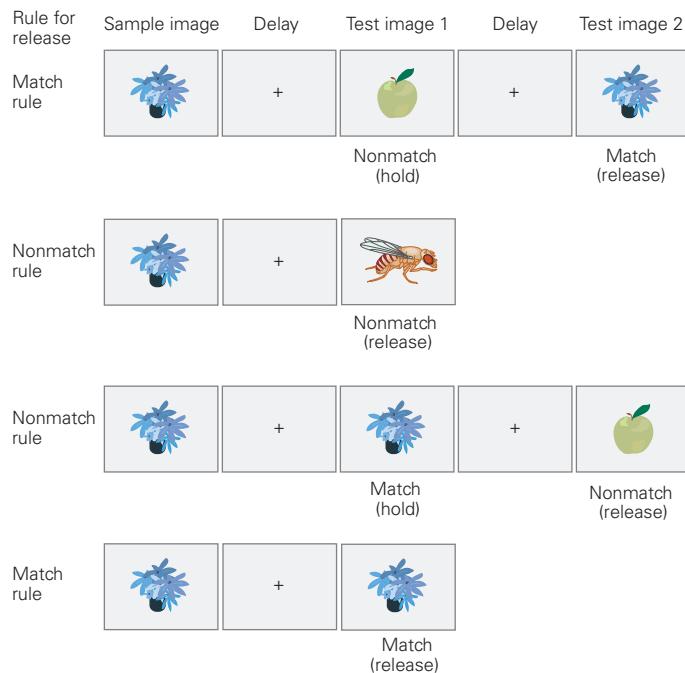
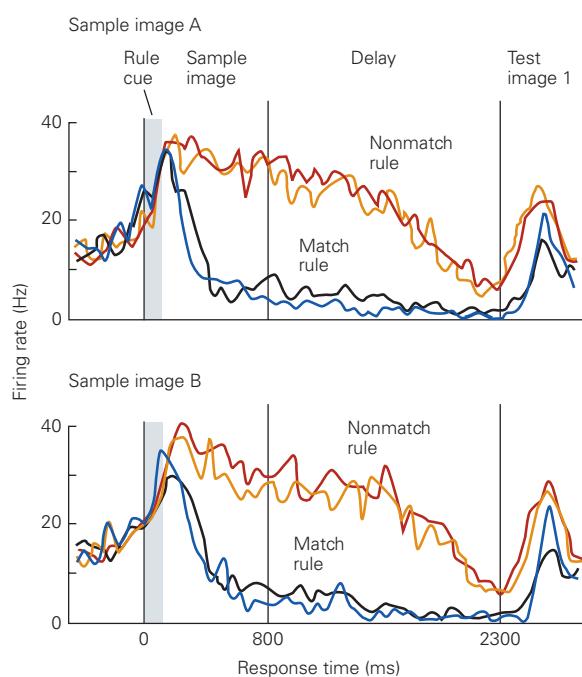
A Delayed match-to-sample task**B Premotor neurons show rule-dependent activity**

Figure 34-11 Premotor cortex neurons in the monkey choose particular voluntary behaviors based on decisional rules. (Reproduced, with permission, from Wallis and Miller 2003.)

A. A monkey must make a decision about whether to release a lever or keep holding it based on two prior decisions: a perceptual choice, whether a test image is the same as or different from a sample image presented earlier, and a behavioral choice, whether the current rule is to release the lever when the test image is the same as the sample (match rule) or when it is different (nonmatch rule). The monkey is informed of the behavioral rule that applies in each trial by a rule cue, such as an auditory tone or juice drops, which is presented for 100 ms at the same time as the onset of the sample image at the start of the trial.

presented; (4) compare f₂ to the memory trace of f₁; (5) decide whether the frequency of f₂ is higher or lower than that of f₁; and finally, (6) use that decision to choose the appropriate movement of the other hand. Everything prior to the last step would appear to fall entirely within the domain of sensory discriminative processing.

While the monkeys performed the task, neurons in the primary (S-I) and secondary (S-II) somatosensory cortices encoded the frequencies of the stimuli while they were presented. During the interval between f₁ and f₂, there was no sustained activity in S-I representing the memorized f₁ and only a transient representation in S-II, which vanished before f₂ was presented.

B. A neuron in the dorsal premotor cortex has a higher discharge rate whenever the nonmatch rule is in effect during the delay between the presentation of the first and second images. The responses to two different sample images (upper and lower plots) were recorded from the same cell, indicating that the rule-dependent activity is not altered by changing the images. Nor, as shown by the pairs of curves associated with each rule, does activity depend on the type of rule cue (auditory tone or juice drops). (Tone cue trials: orange and blue curves; juice cue trials: red and black curves). Other dorsal premotor cortex cells (not shown) respond preferentially to the match rule over the nonmatch rule. The differential activity of the neuron up to presentation of the test image reflects the rule that will guide the animal's motor response to the test image, not the physical properties of the visual stimuli or the motor response.

Strikingly, however, the activity of many neurons in the prefrontal cortex, SMC, and PMv scaled with the frequencies of f₁ and f₂ while they were being delivered. Furthermore, some prefrontal and premotor neurons showed sustained activity proportional to the frequency of f₁ during the delay period between f₁ and f₂. Most remarkably, many neurons in those areas, especially in PMv, encoded the *difference* in frequency between f₂ and f₁ independently of their actual frequencies when f₂ was delivered (Figure 34-13). This centrally generated signal is appropriate to mediate the perceptual discrimination that determines which button to push. Neurons that encoded the f₂-f₁ difference were absent in S-I and were far more common in SMC and PMv than in S-II.

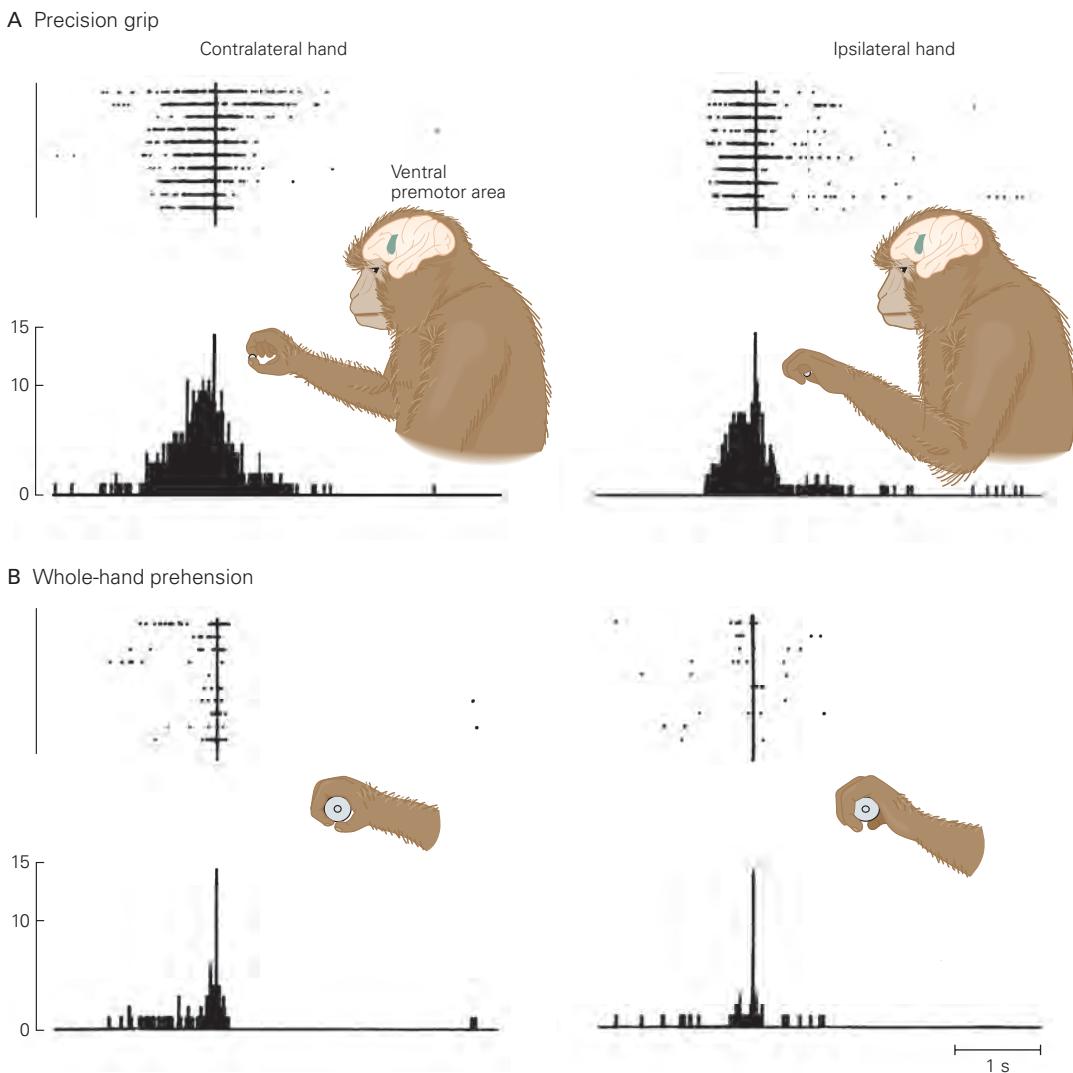


Figure 34–12 Some neurons in the ventral premotor cortex of a monkey discharge selectively during one type of grasping. This neuron discharges vigorously during a precision grip with the thumb and index finger of either the right or the left hand but very weakly during whole-hand prehension with either hand.

Raster plots and histograms are aligned (vertical line) with the moment the monkey touches the food (A) or grasps the handle (B). (Reproduced, with permission, from Rizzolatti et al. 1988. Copyright © Springer-Verlag 1988.)

Several Cortical Motor Areas Are Active When the Motor Actions of Others Are Being Observed

Some premotor and parietal areas can be activated when no overt action is intended, such as when an individual is asked to imagine performing a certain motor act. This phenomenon, termed *motor imagery*, has been demonstrated in humans using functional brain imaging. The neural activity evoked by motor imagery presumably reflects brain mechanisms associated with motor planning and preparation that have been disassociated from its overt execution.

A second condition in which cortical motor circuits are activated without intending overt action is when an individual observes another individual performing motor acts that are part of her own motor repertoire. The control of behavior and social interaction depends greatly on the ability to recognize and understand what others are doing and why they are doing it. Such understanding could result from a high-order visual perceptual analysis of the nature of the observed behavior and by drawing inferences about the motivation and purpose of the behavior based on

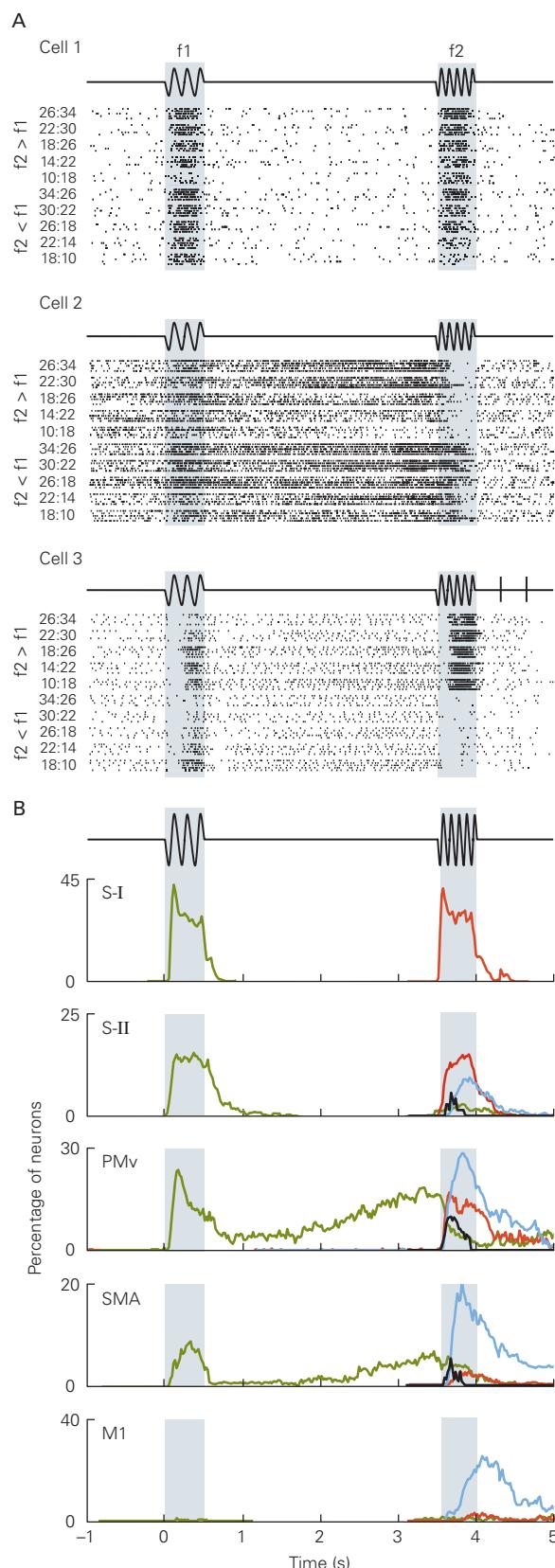
one's own experience. An alternative explanation is the *direct-matching hypothesis*, the idea that observation of the actions of others activates motor circuits in the observer that control similar motor actions. According to this hypothesis, empathetic activation of motor circuits could provide a link between the observed actions and the observer's stored knowledge of the nature, motives, and consequences of similar actions that they had performed in the past.

Striking evidence in support of the direct-matching hypothesis was provided by the discovery of a remarkable population of neurons called mirror neurons, first in PMv and later in the parietal AIP of monkeys. Mirror neurons discharge both when the monkey actively grasps and manipulates objects and when it observes similar actions performed by another monkey or the experimenter (Figure 34–14). Mirror neurons typically do not respond when a monkey simply observes a potential target object or when it observes mimed arm and hand actions without a target object. Some parietal mirror neurons can even differentiate the ultimate goal of similar observed actions, such as grasping and picking up food to eat it versus putting it into a cup.

Figure 34–13 (Right) Neural activity in ventral premotor cortex in monkeys expresses the operations required to choose a motor response based on sensory information. (Adapted, with permission, from Romo, Hernández, and Zainos 2004. Copyright © 2004 Cell Press.)

A. These records of three neurons in the ventral premotor cortex of a monkey were made while the animal performed a task in which it had to decide whether the second of two vibration stimuli (**f1** and **f2**, applied to the index finger of one hand) was of higher or lower frequency than the first. The choice was signaled by pushing one of two buttons with the nonstimulated hand. The frequencies of **f1** and **f2** are indicated by the numbers on the left of each set of raster plots. Cell 1 encoded the frequencies of both **f1** and **f2** while the stimuli were being presented but was not active at any other time. This response profile resembles that of many neurons in the primary somatosensory cortex. Cell 2 encoded the frequency of **f1** and sustained its response during the delay period. During the presentation of **f2**, the neuron's response was enhanced when **f1** was higher than **f2** and suppressed when it was lower. Cell 3 responded to **f1** during stimulation and was weakly active during the delay period. However, during exposure to **f2**, the cell's activity robustly signaled the difference **f2**–**f1** independently of the specific frequencies **f1** and **f2**.

B. Histograms show the percentage of neurons in different cortical areas whose activity correlated at each instant with different parameters during the tactile discrimination task. Green shows the correlation with **f1**, red the correlation with **f2**, black the interaction between **f1** and **f2**, and blue the correlation with the difference between **f2**–**f1**. (Abbreviations: M1, primary motor cortex; PMv, ventral premotor cortex; S-I, primary somatosensory cortex; S-II, secondary somatosensory cortex; SMA, supplementary motor area.)



Neural-recording and brain-imaging studies show that humans are also endowed with a mirror-like mechanism to match observed actions with actions encoded in their motor system. This activity arises in various areas of cortex, including the rostral inferior parietal lobule, IPS, PMv, and posterior sector of the inferior frontal gyrus.

Cortical motor circuits appear to be involved in understanding and predicting the outcomes of observed events. In one experiment, PMd neurons implicated in the selection of reaching targets using visual cues (Figure 34–8) also discharged when monkeys simply watched the same cues and cursor motions on the monitor while an unseen party performed the task. The monkeys received a free juice reward when the cursor moved to the correct target but not if it moved to the wrong target. The monkeys began to lick the juice tube shortly after the cursor started to move to the correct target well before the juice was actually delivered, but

quickly removed their mouth from the tube when the cursor moved toward the wrong target. This behavior showed that the monkeys correctly interpreted what they saw and accurately predicted its consequences.

Remarkably, the activity of most of the task-related PMd neurons was strikingly similar whether the monkeys used visual cues to plan and make arm movements or simply observed the visual events and predicted their outcome. Those neurons stopped responding during observation if no reward was delivered after correct trials or if the animal was sated and not interested in drinking juice. This showed that the neurons were not simply responding to the sensory inputs, but instead were processing the observed sensory events to predict their ultimate outcome for the monkey, namely the likelihood of a free juice reward.

This activation in connection with passive observation supports the idea that activation of premotor

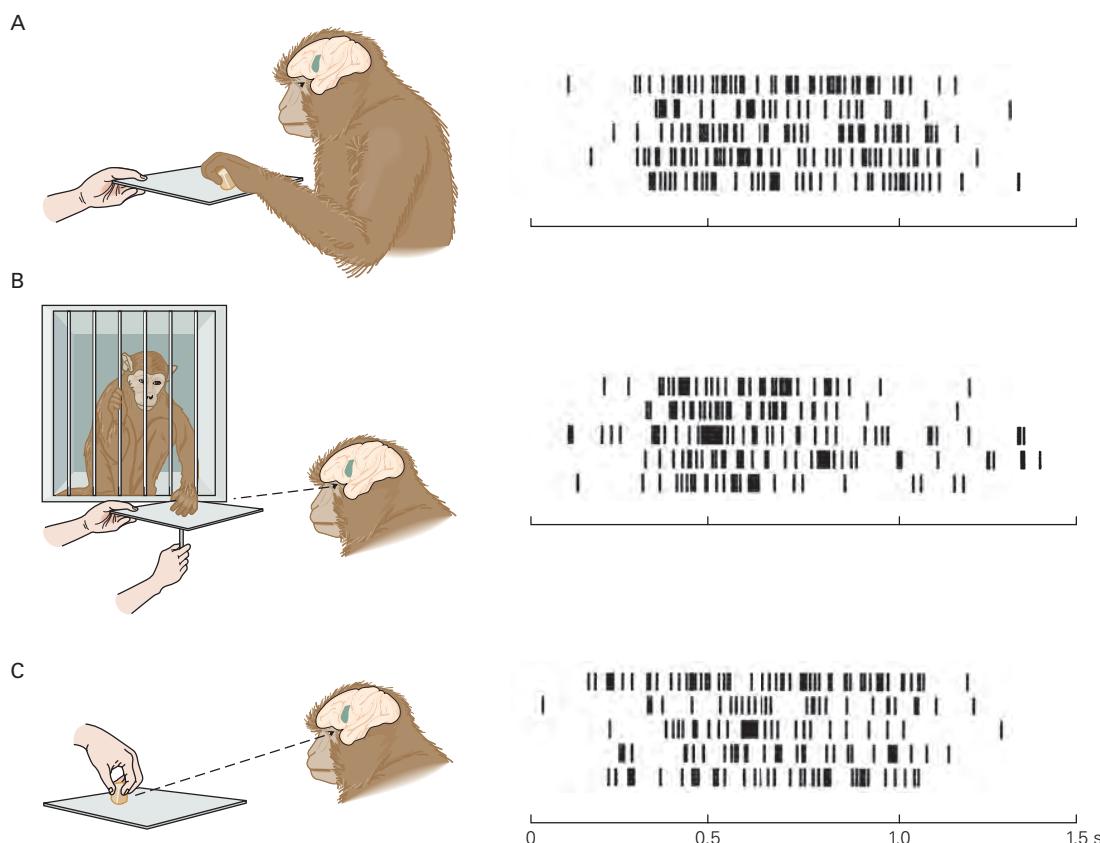


Figure 34–14 A mirror neuron in the ventral premotor cortex (area F5) of a monkey. (Reproduced, with permission, from Rizzolatti et al. 1996. Copyright © 1996 Elsevier Science B.V.)
 A. The neuron is active when the monkey grasps an object.
 B. The same neuron is also excited when the monkey observes another monkey grasping the object.

C. The neuron is similarly activated when the monkey observes the human experimenter grasping the object.

Time zero in the cell activity rasters corresponds approximately to the time of presentation of the object to grasp (panel A) or the onset of the observed grasping actions (panels B and C).

circuits in nonmotor contexts may contribute to understanding the nature and consequences of observed events in the environment. It has also been implicated in the ability of human subjects to learn new motor skills simply by observing a skilled person perform the same actions. Moreover, dysfunction of the mirror-neuron system in young children may contribute to some of the symptoms of autism.

Many Aspects of Voluntary Control Are Distributed Across Parietal and Premotor Cortex

While we have described the roles of premotor areas in parietal and precentral cortex separately, it must be

emphasized that major sensorimotor control processes are shared across multiple cortical regions via their reciprocal interconnections.

For instance, the neural processes that link the physical affordances of target objects to appropriate hand actions are distributed across parietal area AIP, premotor area PMv, and M1, with visuospatial aspects of the process more prominent in AIP and motor components more prevalent in precentral cortex (Figure 34–15). Likewise, as already noted, neural correlates of reach target selection in PRR (Figure 34–8B) strikingly resemble those reported in PMd (Figure 34–8A).

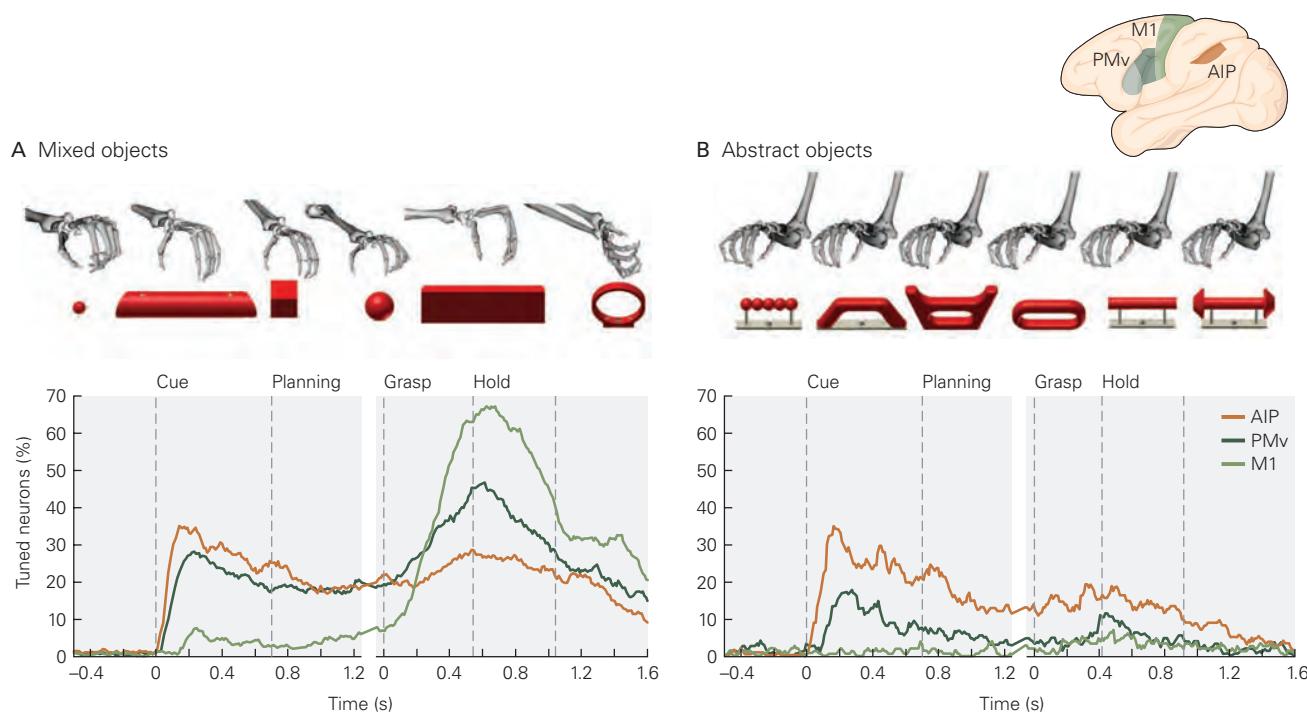


Figure 34–15 Visuomotor processing of object shape is distributed across several cortical areas in the monkey. (Reproduced, with permission, from Schaffelhofer and Scherberger 2016.)

A. A set of “mixed” objects elicit different visual responses and require different motor responses to grasp them. The plots show the percentages of neurons in the anterior intraparietal areas (AIP; orange), ventral premotor cortex (PMv; dark green), and primary motor cortex (M1; light green) that significantly modulated their response as a function of object identity across time. Monkeys were first shown the object to grasp (cue and planning periods) and then allowed to reach to, grasp, and hold the object (grasp and hold periods). The proportion of neurons that varied their activity across object types (tuned neurons) during the cue and planning periods was greatest in

AIP and least in M1, indicating that sensitivity to object visual shape was most prominent in AIP. During motor action (grasp and hold periods), the reverse pattern was observed, with many neurons in PMv and especially M1 displaying a strong dependence on the different grasping actions required to hold onto the different objects.

B. A set of “abstract” objects elicit different visual responses but require similar motor responses to grasp them. As with the “mixed” object set, many AIP neurons varied their activity as a function of object shape during the cue and planning periods, but fewer PMv and almost no M1 neurons showed sensitivity to observed object shape. During motor action (grasp and hold periods), very few PMv and M1 neurons showed any difference in activity as a function of the shape of the different objects, all of which required the same grasping action.

The Primary Motor Cortex Plays an Important Role in Motor Execution

Once an individual has decided on a behavioral goal, motor commands must then be communicated to muscles to move the body. The complexity of this problem cannot be underestimated as it requires precise control of the spatiotemporal patterns of activity of large numbers of muscles acting across many joints to achieve the behavioral goal, while also accounting for the complex, nonlinear mechanical properties of the musculoskeletal system and forces and loads imposed by the environment. These detailed patterns of muscle activity are coordinated by spinal motor neurons and interneuronal circuits (Chapter 32). However, the primary motor cortex (M1) plays an important role in generating the motor commands that control that spinal activity, including essential information necessary to select and control the timing and magnitude of muscle activity.

The Primary Motor Cortex Includes a Detailed Map of the Motor Periphery

The idea that a local region of the cerebral cortex contains a motor map of the body dedicated to voluntary motor control dates back to the work of the English neurologist John Hughlings Jackson in the middle of the 19th century. He reached this conclusion while treating patients with epileptic seizures that were characterized by recurring spasmodic involuntary movements that sometimes resembled fragments of purposive voluntary actions and that progressed systematically to include different parts of the body during each seizure episode (Chapter 58). Later in the 19th century, improved anesthesia and aseptic surgical techniques allowed direct experimental study of the cerebral cortex in experimental animals. Using those new methods, Gustav Fritsch and Eduard Hitzig in Berlin and David Ferrier in England showed that electrical stimulation of the surface of a limited area of cortex in different anesthetized mammalian species evoked movements of parts of the contralateral body. In monkeys, the electric currents needed to evoke movements were lowest in a narrow strip along the rostral bank of the central sulcus, the same region now called primary motor cortex.

Their experiments demonstrated that within this strip of tissue stimulation of adjacent sites evoked movements in adjacent body parts, starting with the foot, leg, and tail medially, and proceeding to the trunk, arm, hand, face, mouth, and tongue more laterally. When they lesioned a cortical site at which stimulation had evoked movements of a part of the body,

movement of that body part was perturbed or lost after the animal recovered from surgery. These early experiments showed that the motor cortex contains an orderly motor map of major parts of the contralateral body and that the integrity of the motor map is necessary for voluntary control of the corresponding body parts. Studies in the first half of the 20th century on many species by Clinton Woolsey and on humans undergoing surgery by Wilder Penfield demonstrated that the general topographic organization of the rostral bank of the central sulcus is conserved across many species (Figure 34–16). One important observation was that the motor map is not an exact point-to-point reproduction of the body's anatomical form. Instead, the most finely controlled body parts, such as the fingers, face, and mouth, are represented by disproportionately large areas, reflecting the larger number of neurons needed for fine motor control.

Today the best-studied regions of the map are those parts controlling the arm and hand and reveal far more complexity than conveyed in the classic diagrams shown in Figure 34–16A,B. First, neurons controlling the muscles of the digits, hand, and distal arm tend to be concentrated within a central zone, whereas those controlling more proximal arm muscles are located in a horseshoe-shaped ring around the central core (Figure 34–16C). Second, stimulation sites overlap extensively, allowing control of muscles acting across different joints; conversely, each muscle can be activated by stimulating many sites dispersed across the arm/hand motor map. Finally, local horizontal axonal connections link different sites across the motor map, likely allowing coordination of activity across the map during the formation of motor commands.

Some Neurons in the Primary Motor Cortex Project Directly to Spinal Motor Neurons

As already noted, while many corticospinal axons in primates terminate only on spinal interneurons, others also synapse directly onto spinal motor neurons. These corticomotoneuronal (CM) cells are found only in the most caudal part of M1 that lies within the anterior bank of the central sulcus. There is extensive overlap in the distribution of the CM cells that project to the spinal motor neuron pools innervating different muscles (Figure 34–17A).

CM cells are very rare or absent in nonprimate species and become a progressively larger component of the corticospinal tract in primate phylogeny from prosimians to monkeys, great apes, and humans. In monkeys, more CM cells project to the motor pools for muscles of the digits, hand, and wrist than to

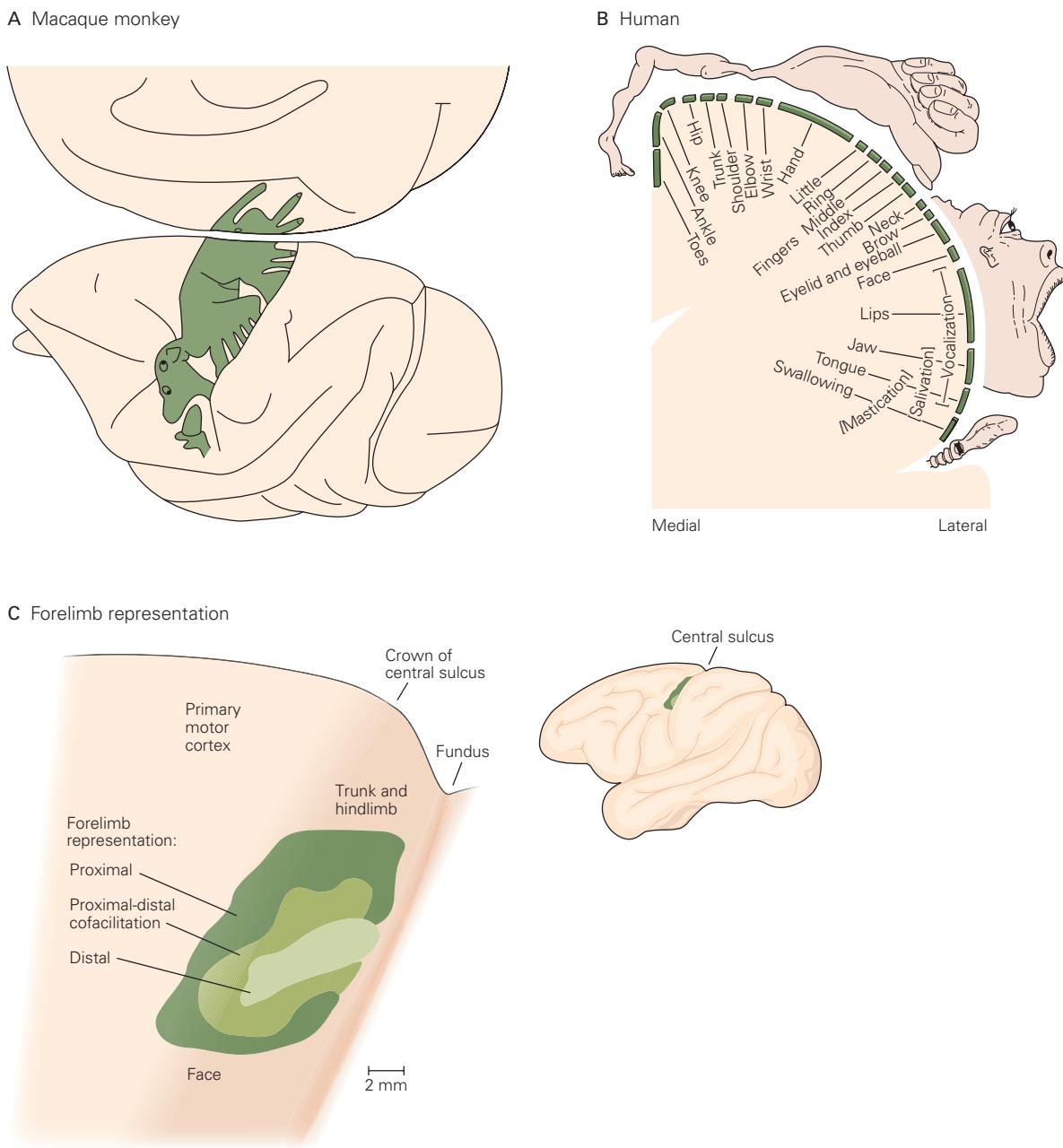


Figure 34–16 The motor cortex contains a topographic map of motor output to different parts of the body.

A. Studies by Clinton Woolsey and colleagues confirmed that the representation of different body parts in the monkey follows an orderly plan. Motor output to the foot and leg is medial, whereas the arm, face, and mouth areas are more lateral. The areas of cortex controlling the foot, hand, and mouth are much larger than the regions controlling other parts of the body.

B. Wilder Penfield and colleagues showed that the human motor cortex motor map has the same general mediolateral organization as in the monkey. However, the areas controlling the hand and mouth are even larger than in monkeys, whereas the area controlling the foot is much smaller. Penfield

emphasized that this cartoon illustrated the relative size of the representation of each body part in the motor map; he did not claim that each body part was controlled by a single separate part of the motor map.

C. The arm motor map in monkeys has a concentric, horse-shoe-shaped organization. Neurons that control the distal arm (digits and wrist) are concentrated in a central core (**pale green**) surrounded by neurons that control the proximal arm (elbow and shoulder; **dark green**). The neuron populations that control the distal and proximal parts of the arm overlap extensively in a zone of proximal-distal co-facilitation (**intermediate green**). (Reproduced, with permission, from Park et al. 2001. Copyright © 2001 Society for Neuroscience.)

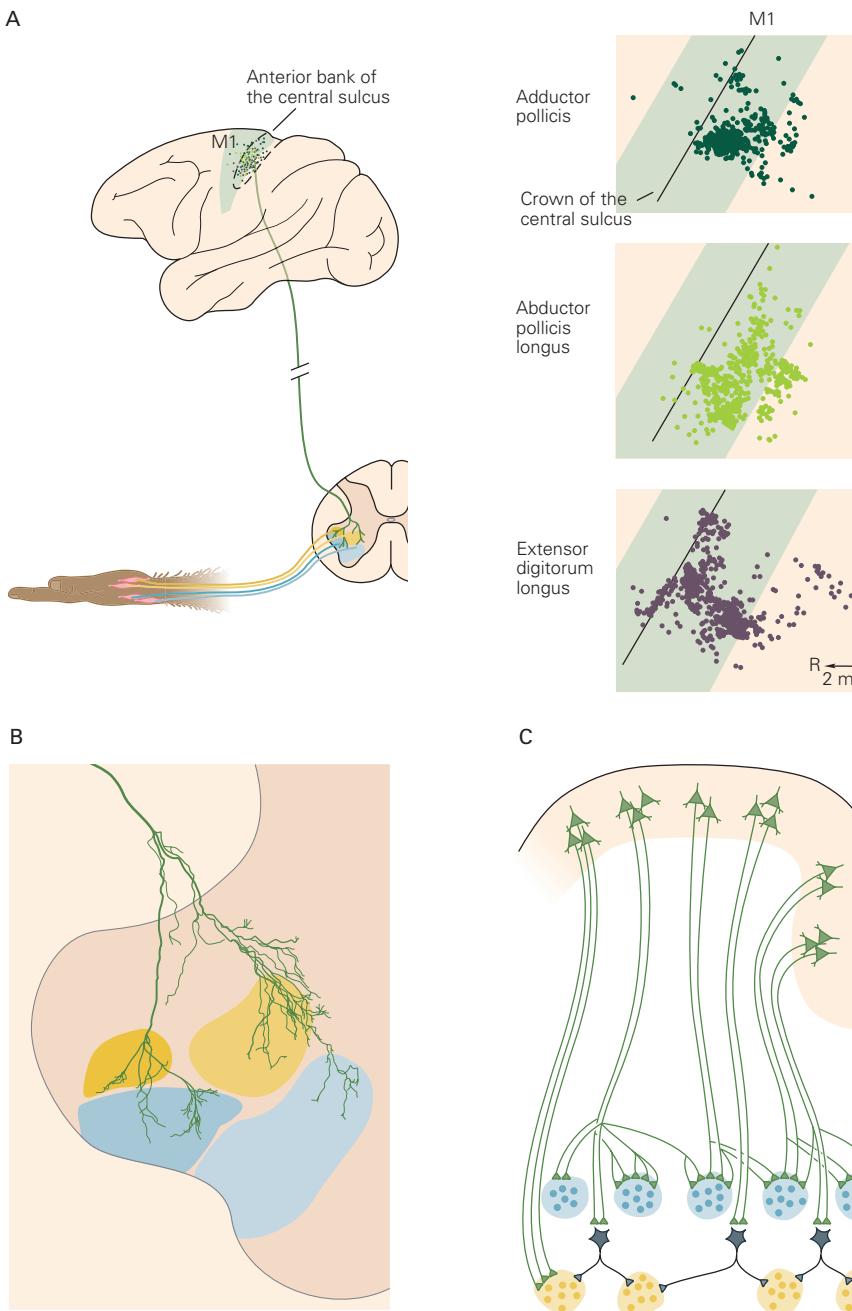


Figure 34-17 Corticomotoneuronal cells activate complex muscle patterns through divergent connections with spinal motor neurons that innervate different arm muscles.

A. Corticomotoneuronal (CM) cells, which project monosynaptically to spinal motor neurons, are located almost exclusively within the anterior bank of the central sulcus in the caudal part of the primary motor cortex (M1). The CM cells that control a single hand muscle are widely distributed throughout the arm motor map, and there is extensive overlap of the distribution of neurons projecting to different hand muscles. The distributions of the cell bodies of CM cells that project to the spinal motor pools that innervate the adductor pollicis, abductor pollicis longus, and extensor digitorum communis (shown on the right) illustrate this pattern of wide distribution and extensive overlap of CM cells projecting to different muscles. (Abbreviations: **M**, medial; **R**, rostral.) (Reproduced, with permission, from Rathelot and Strick 2006.)

B. A single CM axon terminal is shown arborized in the ventral horn of one segment of the spinal cord. It forms synapses with the spinal motor neuron pools of four different intrinsic hand muscles (yellow and blue zones), as well as with surrounding interneuronal networks. Each axon has several such terminal arborizations distributed along several spinal segments. (Reproduced, with permission, from Shinoda, Yokota, and Futami 1981.)

C. Different colonies of CM cells in the primary motor cortex terminate on different combinations of spinal interneuron networks and spinal motor pools, thus activating different combinations of agonist and antagonist muscles. Many other corticospinal axons terminate only on spinal interneurons (not shown). The figure shows CM projections largely onto extensor motor neuron pools. Flexor motor pools receive similar complex projections (not shown). (Adapted, with permission, from Cheney, Fetz, and Palmer 1985.)

those for more proximal parts of the arm. The terminal of a CM cell axon often branches and terminates on spinal motor neurons for several different agonist muscles and can also influence the contractile activity of still more muscles through synapses on spinal interneurons (Figure 34–17B,C). This termination pattern is organized to produce coordinated patterns of activity in a *muscle field* of agonist and antagonist muscles. Most frequently, a CM cell axon directly excites the spinal motor neurons for several agonist muscles and indirectly suppresses the activity of some antagonist muscles through spinal inhibitory interneurons (Figure 34–17C). The fact that CM cells are more prominent in humans than in other species may be one of the reasons why lesions of M1 in humans have a more profound effect on voluntary motor control compared to other mammals (Box 34–3).

The complexity of the motor map in M1—as revealed by short trains of electrical stimuli and anatomical and neurophysiological studies of direct and indirect M1 descending outputs targeting single muscles and small muscle groups—shows how motor commands from M1 to the spinal motor apparatus are

able to control movements of every part of the body, with special focus on the fingers, hand, arm, face, and mouth in primates.

Activity in the Primary Motor Cortex Reflects Many Spatial and Temporal Features of Motor Output

As already noted, a given action such as reaching for an object can be described on many levels, ranging from the hand's spatial trajectory and velocity to its joint-centered causal forces and muscle activity (Figure 34–1A). Representational models assume that the motor system directly plans and controls specific parameters of movement. They predict that different neural populations encode the intended movement in a parameter space (ie, hand or joint motion or joint muscular torque) and perform the transformations between them. Dynamical models predict that neural circuits control movements through changes in their activation state from its current state to the desired final state. As their activity changes across time, correlates of various parameters and properties of the intended movement can be observed in the activity

Box 34–3 Lesions in Primary Motor Cortex Lead to Impairments in Motor Execution

The effects of primary motor cortex (M1) lesions differ across species. Large lesions in cats do not cause paralysis; the animals can move and walk on a flat open surface. However, they have severe difficulties using visual information to navigate within a complex environment, avoid obstacles, or climb the rungs of a ladder. In cats, the pyramidal tract neurons in M1 are much more strongly activated when an animal must modify its normal stepping motion to clear an obstacle under visual guidance than during normal unimpeded locomotion over a flat, featureless surface (Chapter 33).

Large M1 lesions in monkeys have more drastic consequences, including initial paralysis and usually the permanent loss of independent movements of the thumb and fingers. Monkeys nevertheless recover some ability to make clumsy movements of the hands and arms and to walk and climb.

More focal lesions of M1 typically result in muscle weakness, slowing and imprecision of movements, and discoordination of multi-joint motions, perhaps as a result of selective perturbations of the control circuitry for specific muscles or muscle groups. Lesions limited to part of the motor map, such as the contralateral arm,

leg, or face, lead to paralysis of that body part. There is diminished use of the affected body part, and movements of the distal extremities are much more affected than those of the proximal arm and trunk.

The severity of the deficits also depends on the level of required skill. Control of fine motor skills, such as independent movements of the fingers and hand and precision grip, is abolished. Any residual control of the fingers and the hand is usually reduced to clumsy, claw-like, synchronous flexion and extension motions of all fingers, not unlike the unskilled grasps of young infants. Remaining motor functions, such as postural activity, locomotion, reaching, and grasping objects with the whole hand, are often clumsy.

In humans, large motor cortex lesions are particularly devastating, resulting in severe motor deficits or complete paralysis of affected body parts, usually with limited potential for recovery. This presumably reflects the increased importance in humans of descending signals from M1 onto spinal interneuronal circuits and spinal motor neurons and a diminished capacity of other cortical and subcortical motor structures to compensate for the loss of those descending M1 signals.

of single neurons and neural populations. However, the activity of most neurons reflects a combination of parameters that does not correspond to any identifiable parameter in any specific coordinate framework.

Despite their different assumptions, both perspectives suggest that one can infer the possible contribution of different neurons and different neural structures to motor control by studying how their activity correlates with different parameters of movements. The activity of M1 neurons has been intensively studied since the 1960s to try to reveal, for instance, whether M1 generates a high-level signal about the hand motion or a lower-level kinetic signal more related to the causal forces and muscle activity.

Knowledge about the nature of the control signals generated by M1 also helps to clarify the role of other motor structures, notably the spinal cord. If M1 encodes specific information about muscle activity patterns, less computational processing would be necessary at the spinal level. In contrast, if M1 mainly encodes higher-level information about the intended movement, the spinal cord would have to perform the processes that convert this global signal into detailed patterns of muscle activity.

However, one of the major experimental challenges in identifying how M1 controls movement is the fact that virtually all movement-related parameters are intercorrelated through the laws of motion. As a consequence, a particular muscular force (kinetics) will cause a specific motion (kinematics) given an initial condition (posture, movement) of the body. As a result, if one recorded neural activity while a monkey makes reaching movements in different directions, a neuron that theoretically signals the spatial direction of movement will also inevitably show a correlation with the direction of causal forces. Likewise, the contractile activity of a muscle will co-vary systematically with the spatial direction of movement even though it is clearly generating the causal forces. Unless the task design adequately dissociates these different classes of parameters, it will yield ambiguous information about the functional role of each neuron.

Edward Evarts was the first to examine this issue in the 1960s, in pioneering single-neuron recordings in monkeys while they made simple flexion/extension movements of the wrist. Using a system of pulleys and weights, he applied a load to the wrist of the monkey that pulled the wrist in either the direction of flexion or extension in different trials. This required the monkey to alter the level of wrist muscle activity to compensate for the load while making the movements. As a result, the kinematics (direction and amplitude) of wrist movements remained constant, but the kinetics (forces and muscle activity) changed with the load.

Using a microelectrode, he located single neurons in the M1 motor map that modulated their activity when the monkey made movements of the wrist without the external load. In some neurons, their discharge increased during wrist flexion (*preferred movement direction*) and was suppressed during extension, whereas others displayed the opposite pattern. This movement-related activity typically began 50 to 150 ms before the onset of agonist muscle activity, supporting a causal link between M1 neural activity and movement. When a load was applied, many M1 neurons increased their activity when the load resisted movement in their preferred direction and decreased activity when the load assisted the movement (Figure 34–18). These changes in neural activity paralleled the changes in muscle activity required to compensate for the external load.

Subsequent studies have confirmed that the activity of many M1 neurons varies systematically with the magnitude of muscle force output. This is best shown in tasks in which monkeys generate isometric forces against immovable objects that prevent movement. The activity of many M1 neurons, including CM cells, varies with the direction and level of static isometric output forces generated across a single joint, such as the wrist or elbow, as well as during precise pinches using the thumb and index finger (Figure 34–19A). At least over part of the tested range, these responses vary linearly with the level of static force.

Most natural behaviors involve multi-joint, multi-muscle actions. For instance, reaching movements of the arm in different directions requires different patterns of coordinated motions at the shoulder and elbow. Proximal limb muscle activity during reaching shows a roughly cosine pattern of activity with maximal activity in a specific movement direction, its preferred movement direction, that gradually diminishes as the angle between the desired direction of reach and the muscle's preferred direction increases (Figure 34–20A). Like the proximal arm muscles, single neurons related to shoulder and elbow movements respond in a continuously graded fashion during movements in different reach directions centered on a preferred direction of maximal activity (Figure 34–20B). Different neurons have different preferred directions that cover the entire directional continuum around the circle, and during any given movement, neurons with a wide range of preferred directions discharge at different rates.

As Ed Evarts had shown in single-joint tasks, much of the M1 activity during reaching is closely related to the causal kinematics. For instance, in monkeys trained to make reaching movements in eight directions while compensating for external loads that pulled the arm in different directions, the reach-related activity of both

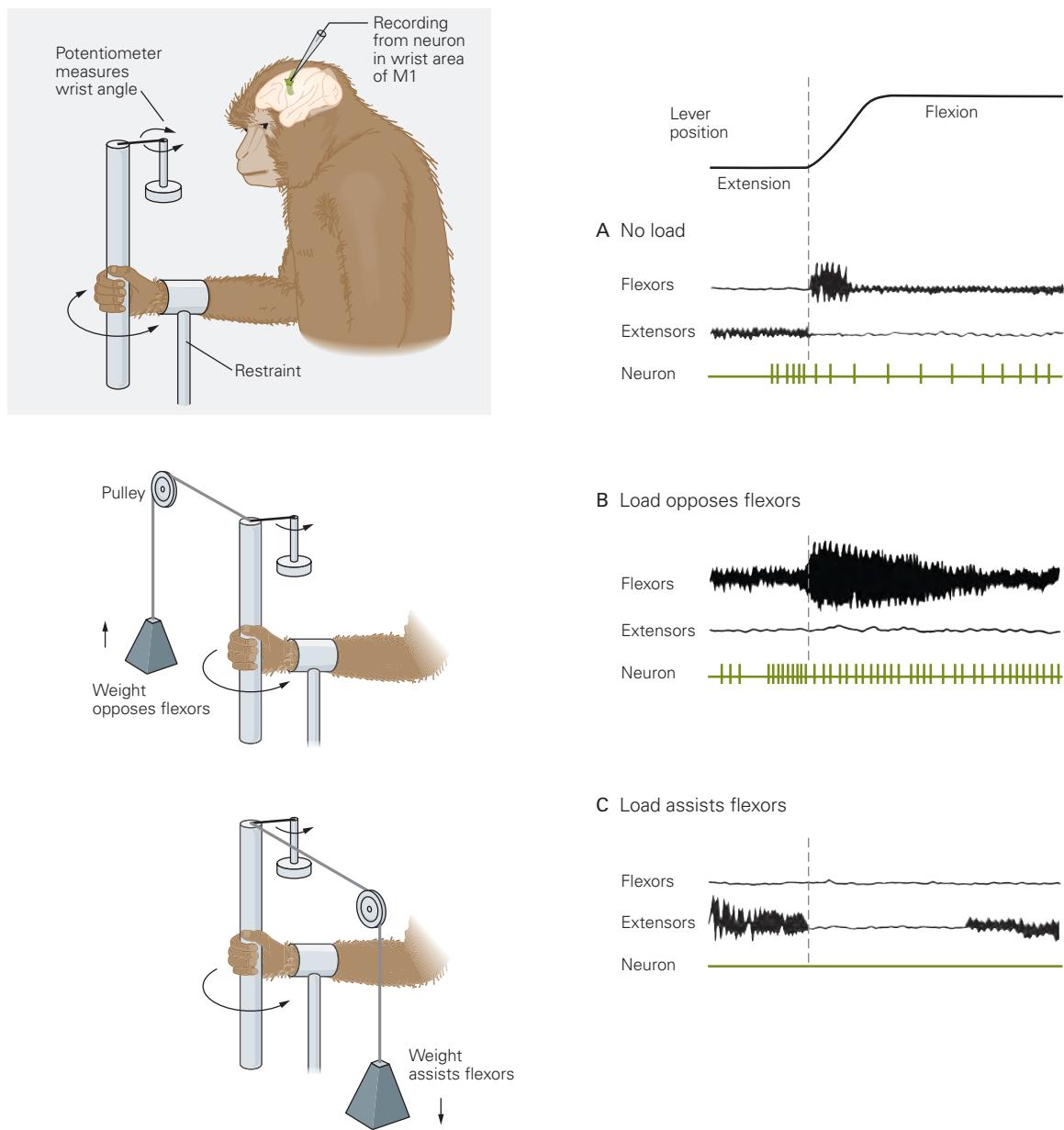


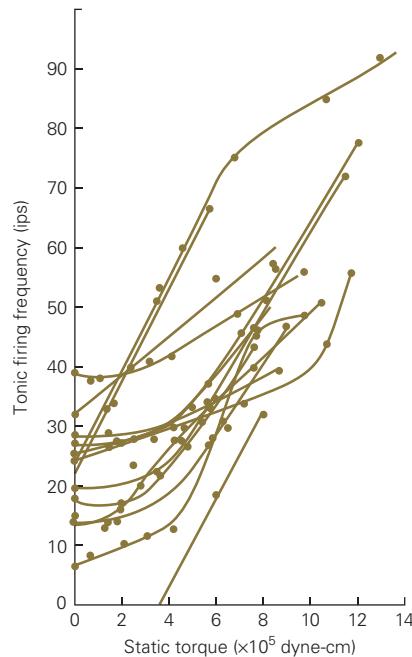
Figure 34-18 Activity of a motor cortex neuron correlates with changes in the direction and amplitude of muscle forces during wrist movements. The records are from an M1 neuron with an axon that projected down the pyramidal tract. The monkey flexes its wrist under three load conditions. When no load is applied to the wrist, the neuron fires before and during flexion (A). When a load opposing flexion is applied, the activity of the flexor muscles and the neuron increases

proximal-arm muscles and many M1 neurons changed systematically with the direction of the external loads and the corresponding corrective forces that the monkeys had to generate for each reach direction. Both muscle and neural activity increased when the load

(B). When a load assisting wrist flexion is applied, the flexor muscles and neuron fall silent (C). In all three conditions, the wrist displacement is the same, but the neural activity changes as the loads and compensatory muscle activity change. Thus, the activity of this motor cortex neuron is better related to the direction and level of forces and to muscle activity exerted during the movement than to the direction of wrist displacement. (Adapted from Evarts 1968.)

resisted movements in their preferred directions and decreased when the loads assisted those movements. In addition, when a monkey uses its whole arm to exert constant isometric force levels in different directions at the hand, the activity of many M1 neurons varies

A Neuronal activity increases with the amplitude of static torque



B Neuronal activity varies with the direction of isometric force

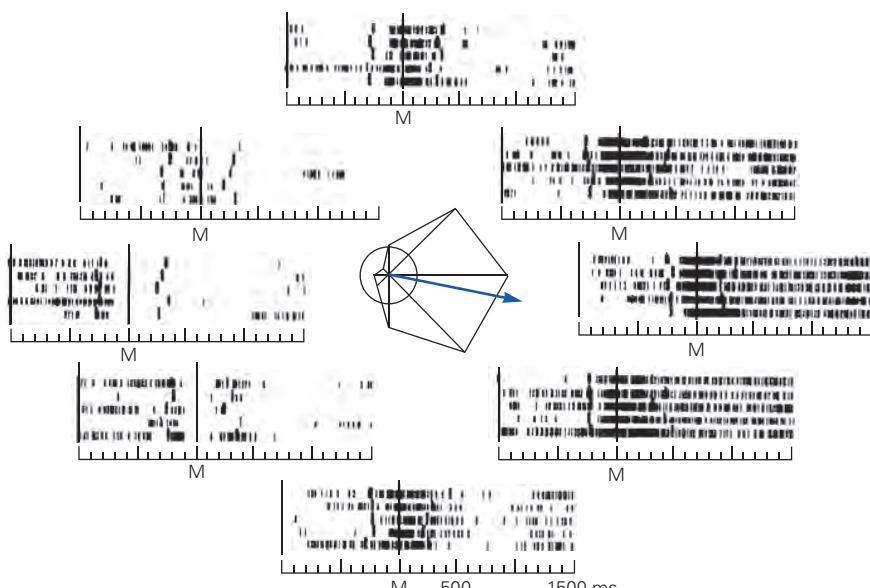


Figure 34-19 Activity in many primary motor cortex neurons correlates with the level and direction of force exerted in an isometric action.

A. The activity of many primary motor cortex neurons increases with the amplitude of static torque generated across a single joint. The plot shows the tonic firing rates of several different corticomotoneuronal cells at different levels of static torque exerted in the direction of wrist extension. Other motor cortex neurons show increasing activity with torque exerted in the direction of wrist flexion, and so would show response functions with the opposite slope (not shown). (Reproduced, with permission, from Fetz and Cheney 1980.)

B. When a monkey uses its whole arm to push on an immovable handle in its hand, the activity of some primary motor

cortex neurons varies with the direction of isometric forces. Each of the eight raster plots shows the activity of the same primary motor cortex neuron during five repeated force ramps in one direction. Each row shows the pattern of spikes during a single trial of the task. The position of each raster of activity corresponds to the direction in which the monkey is generating isometric forces on the handle. The onset of the force ramp is indicated by the vertical line labeled M. The thick ticks on the left of that line in each row indicate when the target appeared on a computer monitor, telling the monkey the direction in which it should push on the handle. The central polar plot illustrates the directional tuning function of the neuron as a function of the direction of isometric forces. (Reproduced, with permission, from Sergio and Kalaska 2003.)

systematically with force direction, and the directional tuning curves for isometric force resemble those for activity during reaching movements (Figure 34-19B).

The complex and nonlinear properties of multi-segmented limbs present a major control problem for the motor system. For instance, one can make reaching movements with similar hand trajectories but different arm geometries that require changes in the causal joint-centered torques and muscle activity. In one experiment, when monkeys made horizontal reaching movements along the same planar spatial hand trajectories while holding the arm in different spatial orientations (ie, elbow raised versus lowered), the activity of proximal-arm muscles and many M1 neurons showed corresponding changes in the strength and directional

tuning of their reach-related activity. This indicates that the M1 neurons generate signals that take into account the changes in intrinsic limb biomechanics during the reaching movements.

Similarly, arm movements toward or away from the body require much larger angular motion at the shoulder and elbow joints compared to movements to the right or left. In contrast, muscular torques tend to be larger for movements to the right and left. Both of these factors influence the amount of muscle activity required to move the limb, which can be quantified by a single term, joint muscular power (joint angular velocity multiplied by net muscular torque about that joint). With the limb in the horizontal plane, joint power is greatest for movements away from the body and slightly to the left,

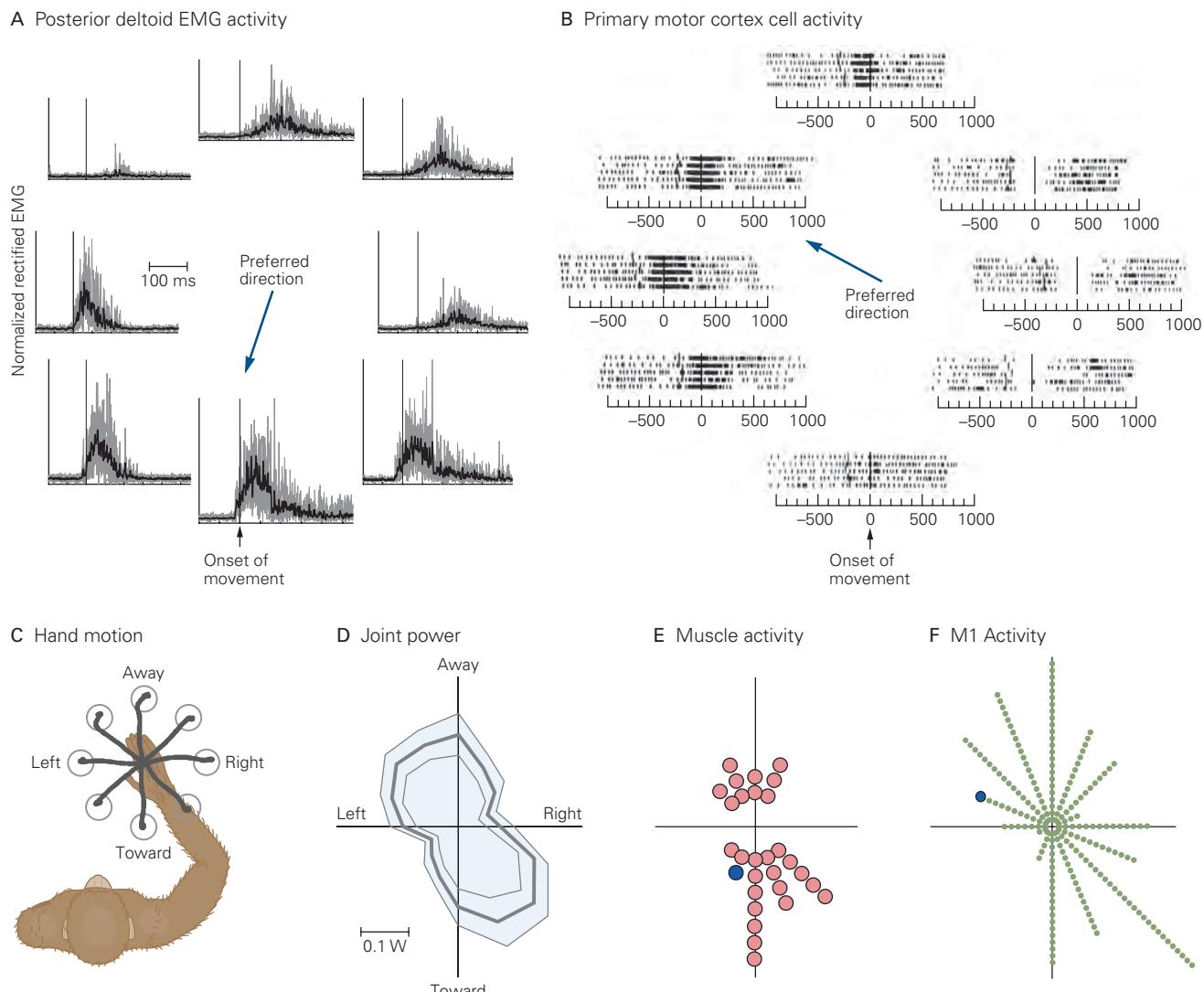


Figure 34–20 Limb muscles and primary motor cortical neurons are broadly tuned to the direction of reaching.

A. Plots show the activity of posterior deltoid of the right arm, a shoulder extensor, during arm movements in eight directions (see panel C) (central panel displays mean hand trajectories). The muscle is initially maximally active for movements at 270° (towards the body, preferred direction = 250°) and diminishes for movements in other directions. Black lines denote the mean activity of the muscle across multiple trials, and data are aligned on movement onset (vertical thin line). (Abbreviation: EMG, electromyography.)

B. Raster plots show the firing pattern of a single primary motor cortex neuron during whole-arm movements in eight directions. The neuron discharges at the maximal rate for movements near 135° and 180° and at lesser intensities for movements in other directions. The cell's lowest firing rate is for movements opposite the cell's preferred direction. Each row of thin ticks in each raster plot represents the activity in a single trial, aligned at the time of movement onset (time 0); thick ticks, time of target appearance. (Reproduced, with permission,

from Georgopoulos et al. 1982. Copyright © 1982 Society for Neuroscience.)

C. Hand trajectories when reaching from a central position in the horizontal plane.

D. Peak joint power (joint muscular torques multiplied by joint velocity) for movements performed in different spatial directions (shoulder and elbow power added together).

A large amount of power is required to reach away from the body and to the upper left and to reach toward the body and to the lower right. (Right X-axis is at 0°.)

E. Preferred directions of proximal-limb muscles tend to be for movements that require greater muscular power, reflecting the obvious link between muscle use and the physical requirements of the motor task. Each dot represents an individual muscle binned into 22.5° sectors; the blue dot represents the preferred direction of the muscle displayed in panel A.

F. Distribution of preferred directions of neurons in primary motor cortex (M1). Each dot represents an individual neuron, and the blue dot represents the preferred direction of the neuron displayed in panel B. (Adapted, with permission, from Scott et al. 2001.)

and toward the body and to the right (Figure 34–20C,D). This bias in the physics of limb movement leads to a bias in the preferred directions of shoulder and elbow muscles, which tend to be maximally active in these same directions (Figure 34–20E). Correspondingly, the distribution of preferred directions of neurons in M1 also parallels this bias, with neurons tending to have preferred directions either away and slightly to the left or toward and to the right (Figure 34–20F). Thus, the physics of the limb dictates the pattern of muscle activity needed to generate movement, and this in turn is reflected in the pattern of neural activity in M1.

The impact of limb physics on M1 activity extends to the level of muscle-related signals. The activity of some single M1 neurons, including CM cells, can be correlated with specific components of the contraction patterns of different muscles during such diverse tasks as isometric force generation, precision pinching of objects between the thumb and index finger, and complex reaching and grasping actions (Figure 34–21). These findings highlight how M1 contributes to the specification of muscle activity patterns for motor actions, including onset times and magnitudes. Nevertheless, the final pattern of muscle activity will only be generated by the spinal motor neurons since they alone take into account the additional influence of other descending supraspinal inputs and local spinal interneuronal processes.

All the studies described so far related the activity of single M1 neurons to motor output. However, voluntary motor control is implemented by the simultaneous coordinated activity of many neurons throughout the motor system. Their activity is noisy, varying stochastically between repetitions of the same movement. Furthermore, their broad symmetrical movement-related tuning curves introduce a high level of uncertainty as to what the limb should do in response to the ambiguous signal generated by each neuron.

A simple computational approach was developed to extract a unique signal about each reaching movement by pooling the heterogeneous single-neuron activity of the recorded M1 population. The activity of each neuron is represented by a vector pointing in its preferred direction; the length of the vector varies as a function of its mean discharge rate during reaches in each direction. This vector notation implies that an increase in the activity of a given M1 neuron evokes changes in activity in the spinal motor apparatus and muscles that causes the arm to move along a path corresponding to the neuron's task-related preferred direction; the strength of that single-neuron influence varies systematically with the difference between the neuron's preferred direction and the desired movement (Chapter 39, Figure 39–6). When the reach-related

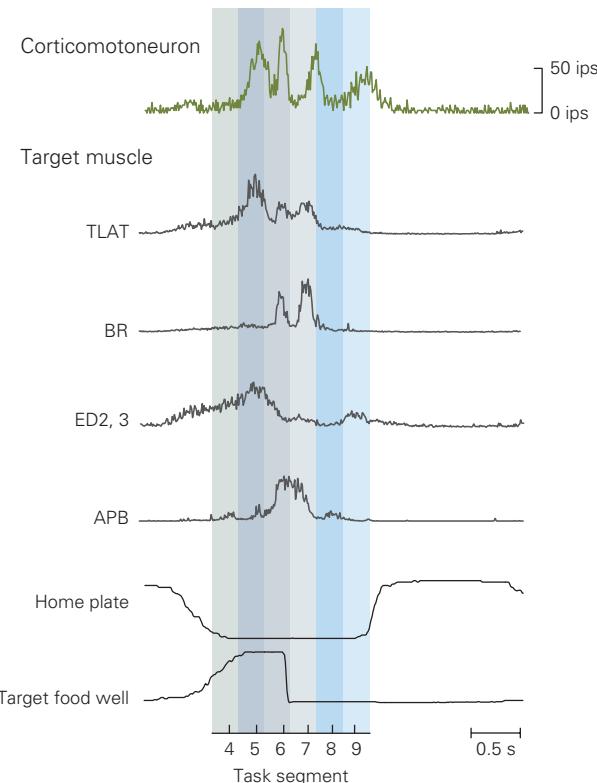


Figure 34–21 The activity of some primary motor cortex neurons can be correlated with particular patterns of muscle activity. Bursts of activity in a single corticomotoneuron during a reach-and-grasp movement to retrieve food pellets from a small well are correlated with bursts of contractile activity in several of its target muscles at different times during the movement. (Abbreviations: APB, abductor pollicis brevis; BR, brachioradialis; ED2, 3, extensor digitorum 2, 3; ips, impulses per second; TLAT, lateral triceps.) (Reproduced, with permission, from Griffin et al. 2008.)

activity of about 250 M1 neurons was represented by variable-length vectors for each of the eight reach directions and summed, the direction of the net resultant *population vectors* varied systematically with the actual reach directions (Figure 34–22A).

The novel insights of this analysis were that the control of a given reach movement involves coordinated changes in the activity of M1 neurons distributed throughout the M1 arm motor map and that their pooled activity clearly distinguishes the unique identity of each of the reach actions generated by the eight different distributed patterns of population activity. Subsequent studies demonstrated that “instantaneous” population vectors extracted from the pooled activity of large populations of M1 neurons during sequential 20-ms time bins from the start to the end of movement predicted the continually changing trajectory of the

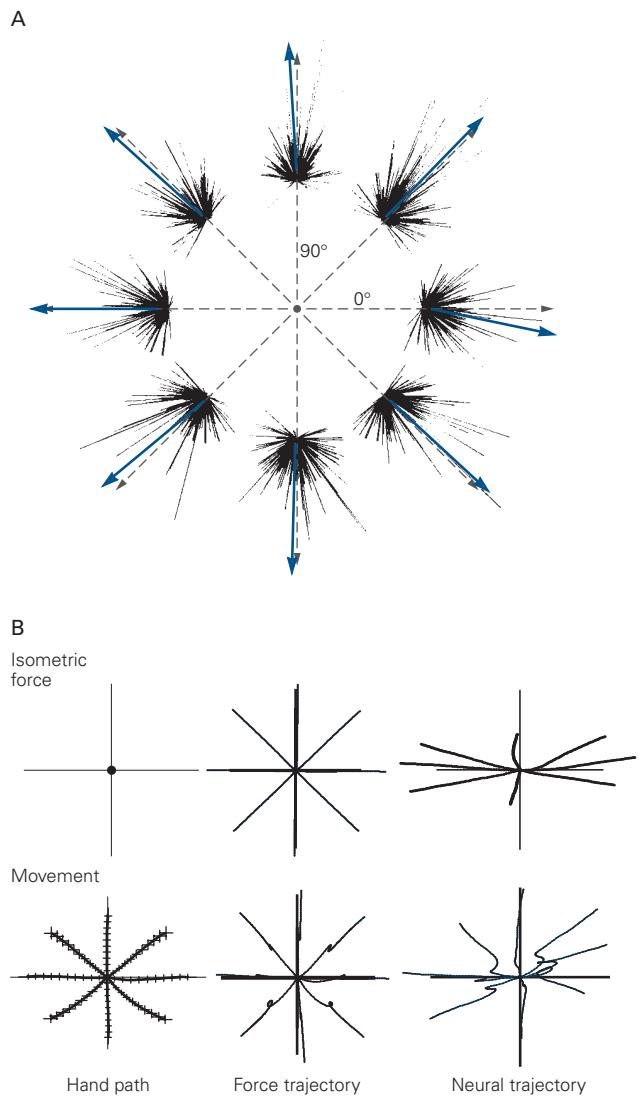


Figure 34-22 Population codes relate M1 activity to different properties of movement.

A. The eight single-neuron vector clusters (thin black lines) and the population vectors (blue arrows) represent the activity of the same population of cells during reaching movements in eight different directions. Each single-neuron vector points in the neuron's preferred movement direction, and its length is proportional to the discharge of the neuron during that movement. The population vectors were calculated by vectorial addition of all the single-cell vectors in each cluster; dashed arrows represent the direction of movement of the arm. (Reproduced, with permission, from Georgopoulos et al. 1983.)

B. Comparison of hand kinematics and kinetics and neural population activity in an isometric task and when moving a handle with a large mass. Force and neural trajectories were generated by linking sequences of 20-ms output force vectors or neural population vectors tip-to-tail for each direction of force or movement output. (Reproduced, with permission, from Sergio et al. 2005.)

arm motions 100 to 150 ms into the future while monkeys made reaching movements or traced spirals on a computer monitor. This showed that the simple vector notation could be used to extract from the activity of populations of neurons a signal about intended motor output even on a moment-to-moment basis. These findings were anticipated by a prescient study in 1970 by Donald Humphrey and colleagues, who showed that the appropriately summed activity of three to five M1 neurons was better correlated to the temporal patterns of motor output during single-joint movements than was the signal of any of the single neurons.

Subsequent studies used the population-vector decoder algorithm to provide further insight into neural processing in M1. In one study, the activity of proximal arm-related M1 neurons was recorded while monkeys performed two tasks (Figure 34-22B). In the first task, they generated isometric force ramps in eight different spatial directions uniformly distributed at 45° intervals in a horizontal plane against a rigid handle that they held in their hand, without arm movements. A 20-ms population-vector decoder was used to extract the net directional bias of the pooled activity of many M1 neurons, and the result showed that these pooled signals varied systematically with the direction of output forces throughout the duration of the force-ramp generation, even though there were no movements. However, unlike the actual uniformly distributed directions of the forces generated by the monkey at the hand, the decoded population-vector signals were skewed toward the *x*-axis. This showed that the M1 activity reflected the nonlinear relationship between causal shoulder muscle torques and measured isometric forces at the hand resulting from the complex biomechanical properties of the arm (see Figure 34-20).

In the second task, the monkeys made reaching movements of the arm in the same eight directions to move a heavy handle. This required an initial accelerative force in the direction of movement and then a transient reversal of the direction of forces to decelerate the movement of their arm and the mass as it approached the target. The decoded M1 population-vector signals in this task varied dramatically through time. They were directed initially toward the target but then transiently reversed just before the peak of hand velocity. This showed once again that the M1 activity was more closely correlated with the time course of causal forces generating the reaching movements, including their transient directional reversal, than to the uninterrupted motion of the hand toward the target. They also found that correlates of the forces to generate reaching were strongest in M1, weaker in PMd, and largely absent in PE/MIP. This indicated that, unlike M1,

reach-related neurons in area PE/MIP generated a reliable signal about stable arm postures and the kinematics of arm movements independent of the underlying causal forces and muscle activity.

Finally, one study has shown that reliable signals about the time-varying activity of proximal-arm muscles during reaching movements can be extracted from the activity of a population of simultaneously recorded M1 neurons. Another study found that the pooled activity of M1 neurons that fire selectively in connection with either shoulder or elbow movements can predict the changes in onset times and levels of contractile activity of the shoulder or elbow muscles during reaches in different directions.

These studies showed that the pooled activity of many M1 neurons is a rich and reliable source of signals about different time-varying attributes of whole-arm movements. This provided an important conceptual foundation for the development of more sophisticated decoder algorithms in brain-machine interfaces that make use of the movement-related information available in the simultaneous activity of many M1 neurons to allow subjects to control the actions of neuroprosthetic devices by covert modulations of M1 neuron activity without overt limb movements (Chapter 39).

Primary Motor Cortical Activity Also Reflects Higher-Order Features of Movement

Activity in M1 is not correlated only with causal forces and muscle activity. Many studies, beginning with those of Ed Evarts, that have attempted to dissociate kinematic from kinetic properties of motor outputs have found that the activity of some M1 neurons varies with the direction of movement but is only weakly influenced or not influenced at all by changes in output forces. Such neurons appear to preferentially signal the kinematic aspects of limb motion.

Changes in behavioral task can influence the relationship between M1 activity and motor output. One study has highlighted how contextual changes in an isometric force task altered the coding of force magnitude by M1 neurons. Either the order of forces or the range of expected forces results in changes in the activity in M1. They suggested that M1 neurons could dynamically adjust their relationship to output forces to optimize precision of control as a function of the range of forces that would be encountered in a given context. Another study found that many CM neurons may discharge intensely when monkeys performed precisely controlled force tasks with low force levels but are relatively inactive when the monkeys generate powerful contractions of the same muscles to make

brisk, back-and-forth movements of the handle. Likewise, a study demonstrated that CM cells in M1 could be very active when monkeys generated a precision-pinch grip of the thumb and index finger with relatively low force output, but were much less active or nearly silent when the animals generated much larger forces with a power grip involving the entire hand.

Still another study has shown that some M1 neurons that respond to loads applied to the limb during postural control can lose this load sensitivity as soon as the monkey makes a reaching movement to another spatial target, and vice versa. That is, those neurons can reflect output forces during postural control, but reflect only kinematics during movement. This change in the cell's response occurs quite abruptly, about 150 ms before the onset of movement. Importantly, any neurons that are sensitive to loads during both posture and movement will retain the same motor field across behaviors; that is, if the neuron responds only to shoulder flexor loads during postural control, it will respond only to shoulder flexor loads during reaching.

Even a simple change in the metrics of limb movement can have a large influence on M1 activity. In a study of monkeys making slow or fast reaching movements in different directions from a central target to peripheral targets, proximal limb muscles displayed relatively simple scaling of their activity patterns, reflecting increased forces for faster and longer reaches. In contrast, M1 neurons displayed a broad range of changes in their activity patterns that rarely paralleled the pattern of changes observed for muscles.

Activity in neurons can also correlate with higher-level features of movement such as the nature of an upcoming motor action. This was demonstrated in a study in which monkeys were trained to make wrist movements to three targets in a row starting from one extreme, stopping at a central position, and then finishing at the other extreme. Visual cues instructed the monkeys when to make each movement. Because the task used a predictable sequence of wrist movements, the monkeys knew before the visual cues appeared what would be the next direction of movement. While many M1 neurons signaled the current wrist posture or the direction of each movement while they were being performed, some M1 neurons reliably signaled the next movement in the sequence before the visual cue appeared. Many subsequent studies have confirmed that M1 neurons can signal impending intended movements, although these planning-like signals are not as prominent in M1 as in premotor cortical areas.

In summary, neural recording studies have revealed a diverse range of response properties within

and across movement-related cortical areas, with stronger correlations to causal movement kinetics in M1 and to higher-order motor parameters in premotor and parietal cortex. However, these experimental findings have not yet led to a single unifying hypothesis about how cortical motor circuits control voluntary movements. Part of this uncertainty may result from inadequacies in experimental task design.

Representational motor-control models have interpreted these complex results as evidence of the transformations between different levels of representation of intended movements performed by neural populations distributed across different cortical motor areas. In contrast, nonrepresentational motor-control models such as optimal feedback control argue that these same results can only be interpreted as evidence of when and where neural correlates of different motor output parameters emerge in the dynamical activity distributed across cortical motor areas but do not shed much insight into the underlying neural computations. This illustrates the experimental challenges still confronting researchers as they try to reverse engineer the cortical motor circuitry to reveal its internal computational organization.

Sensory Feedback Is Transmitted Rapidly to the Primary Motor Cortex and Other Cortical Regions

Postcentral and posterior parietal cortex provide much of the sensory information related to the position and motion of the body and the location of spatial goals that is important in voluntary motor control, although the cerebellum is likely another important source (Chapter 37).

The type of afferent information transmitted to M1 differs between the proximal and distal portions of the limb. Afferent input from cutaneous and muscle sensory neurons is equally prevalent for hand-related neurons, reflecting the importance for both sources of sensory feedback when grasping and manipulating objects with the hand. Muscle afferents provide the major source of feedback from the proximal limb. Information from muscles is more prevalent in the rostral M1, whereas cutaneous input is more common in the caudal M1. Muscle afferent feedback to M1 is surprisingly rapid as it takes as little as 20 ms for M1 neurons to respond following a mechanical disturbance to the limb. Analogous to reaching, neural activity is broadly tuned to the direction of the mechanical disturbance.

Sensory feedback supports our ability to make rapid goal-directed corrections for motor errors that arise during movement planning and execution or are caused by unexpected disturbances of the limb. When a perturbing mechanical load is applied to the limb, the

motor system generates a multipeaked compensatory electromyographic response, beginning with a short-latency stretch response (20–40 ms after the perturbation), followed by a long-latency response (50–100 ms) and then a so-called “voluntary” response (≥ 100 ms). The short latency of the initial response indicates that it is generated at the spinal level. The response is relatively small and stereotyped, and its intensity scales with the magnitude of the applied load. In contrast, motor corrections beginning in the long-latency epoch (50–100 ms) are modulated by a broad range of factors necessary to attain a behavioral goal, including the physics of the limb and environment, the presence of obstacles in the environment, the urgency of the goal, and properties of the target, including alternate goals. These context-dependent features suggest the long-latency feedback epoch is an adaptive process in which the control policy (ie, feedback gains) is adjusted based on the behavioral goal, as predicted by the optimal feedback control model.

The ability of the motor system to rapidly generate these goal-directed long-latency motor responses is supported by a transcortical feedback pathway. Neural activity across frontoparietal circuits responds rapidly to mechanical disturbances to a limb, and the pattern of activity across the cortex depends on the behavioral context. Perturbation-related activity is observed in all cortical regions beginning at approximately 20 ms after the disturbance even if the monkey is distracted by watching a movie and does not have to respond to the disturbance (Figure 34–23A,B). If the monkey is actively maintaining its hand at a spatial goal, there is an immediate increase in the neural response in parietal area PE following the disturbance, followed shortly thereafter by changes in activity in other cortical regions (Figure 34–23A,B). If the disturbance is a cue that instructs the monkey to move to another spatial target, then M1 activity reflects the need for a more vigorous response if the disturbance knocks the hand away from the target compared to knocking the hand into the target (Figure 34–23C). In contrast, perturbation-related activity in PE remains similar regardless of target location.

The Primary Motor Cortex Is Dynamic and Adaptable

One of the most remarkable properties of the brain is the adaptability of its circuitry to changes in the environment—the capacity to learn from experience and to store the acquired knowledge as memories. When human subjects practice a motor skill, performance improves.

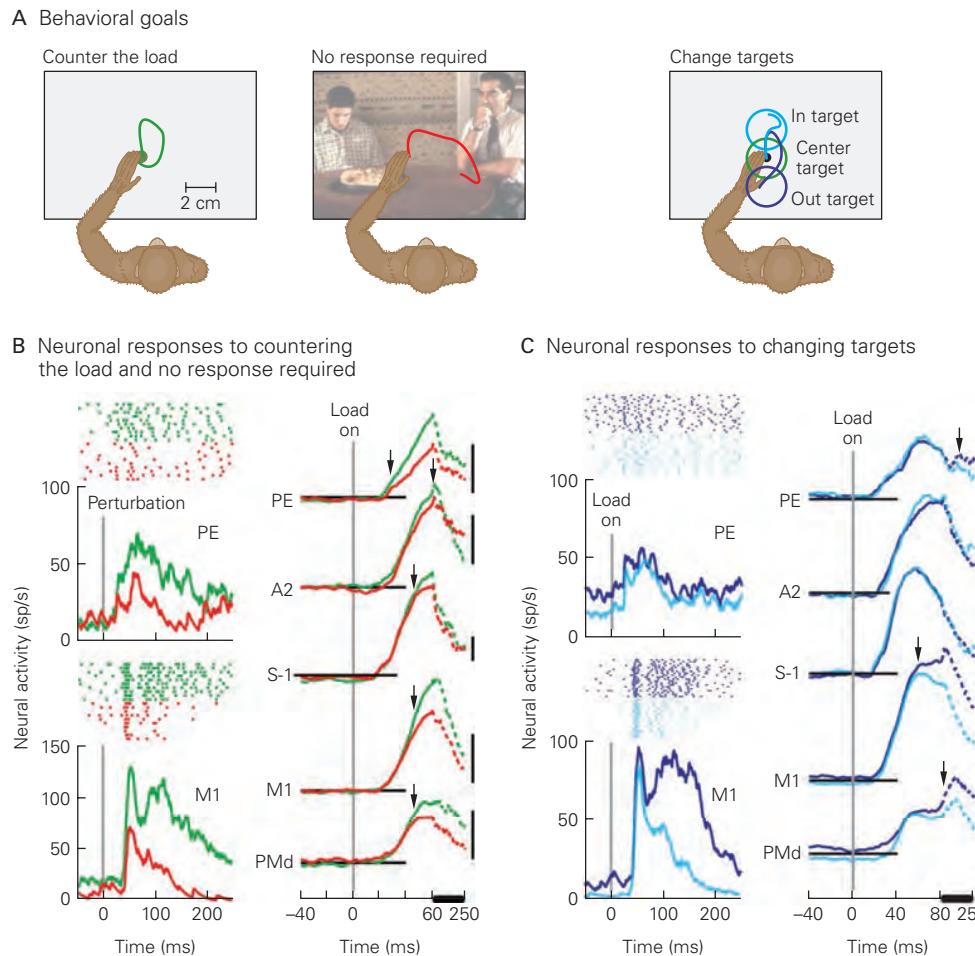


Figure 34–23 Changes in behavioral goals alter rapid sensory feedback to parietal and frontal motor cortices. (Reproduced, with permission, from Omrani et al. 2016. Part A photo is from the film American Pie and is reproduced, with permission, from Universal Studios. © 1999, Universal Pictures, All Rights Reserved.)

A. In the experiment described here, the responses of cortical regions to mechanical loads randomly applied to the arm are compared. In the *left* panel, motor corrections return the hand to the spatial goal following the disturbance (**green hand trajectory**). In the *middle* panel, the monkey watches a movie and does not have to respond to the disturbance, leading to the hand remaining to the right following the disturbance (**red hand trajectory**). In the *right* panel, the monkey places its hand at a central start target, and one of two other targets is also presented. The disturbance applied to the limb is a cue for the monkey to move to this second target with its position being either in the direction of the disturbance (**cyan “in target” trajectory**) or away from the disturbance (**blue “out target” trajectory**).

B. Left: Response of a neuron in PE and in M1 when a mechanical load was applied to the limb and the monkey had to counter the load and return the hand to a spatial target (**green**) or was not required to respond to the disturbance (**red**). **Right:**

Population signals in each cortical region in response to perturbations. Note how all cortical areas show an increase in activity approximately 20 ms after the applied load. **Arrows** denote when activity was different when the monkey had to respond to the disturbance (**green curve**) as compared to not being required to respond to the disturbance (**red curve**). Note that PE is the first to show a difference in activity between the two conditions. Other cortical areas show changes at 40 ms or later. **A2** is a subregion of **S-1**. (For B and C: Vertical scale bars, 20/ spikes/s); Activity between 60–250 ms (thick horizontal line) compressed for visualization purposes.)

C. Left: Responses of single neurons in PE and M1 when a mechanical load was a cue and instructed the monkey to move to another target. The disturbance either pushed the hand toward the target (**cyan**) or away from it (**blue**). **Right:** Population signals based on perturbation-related activity in each cortical region for the “in target” and “out target” conditions. The initial responses are similar for both “in target” and “out target” disturbances across all cortical areas, and **arrows** denote when there is a difference in activity between conditions. M1 is the first to display an increase in activity for the “out target” disturbance just prior to changes in muscle activity moving the hand to the spatial target.

Motor experience can also modify the motor map. In monkeys trained to use precise movements of the thumb, index finger, and wrist to extract treats from a small well, the area of the motor map in which intracortical microstimulation (ICMS) could evoke

movements at these joints was larger than before training (Figure 34–24). If a monkey did not practice the task for a lengthy period, its skill level decreased, as did the cortical area from which the trained movements could be elicited by ICMS. Similar modifications of the

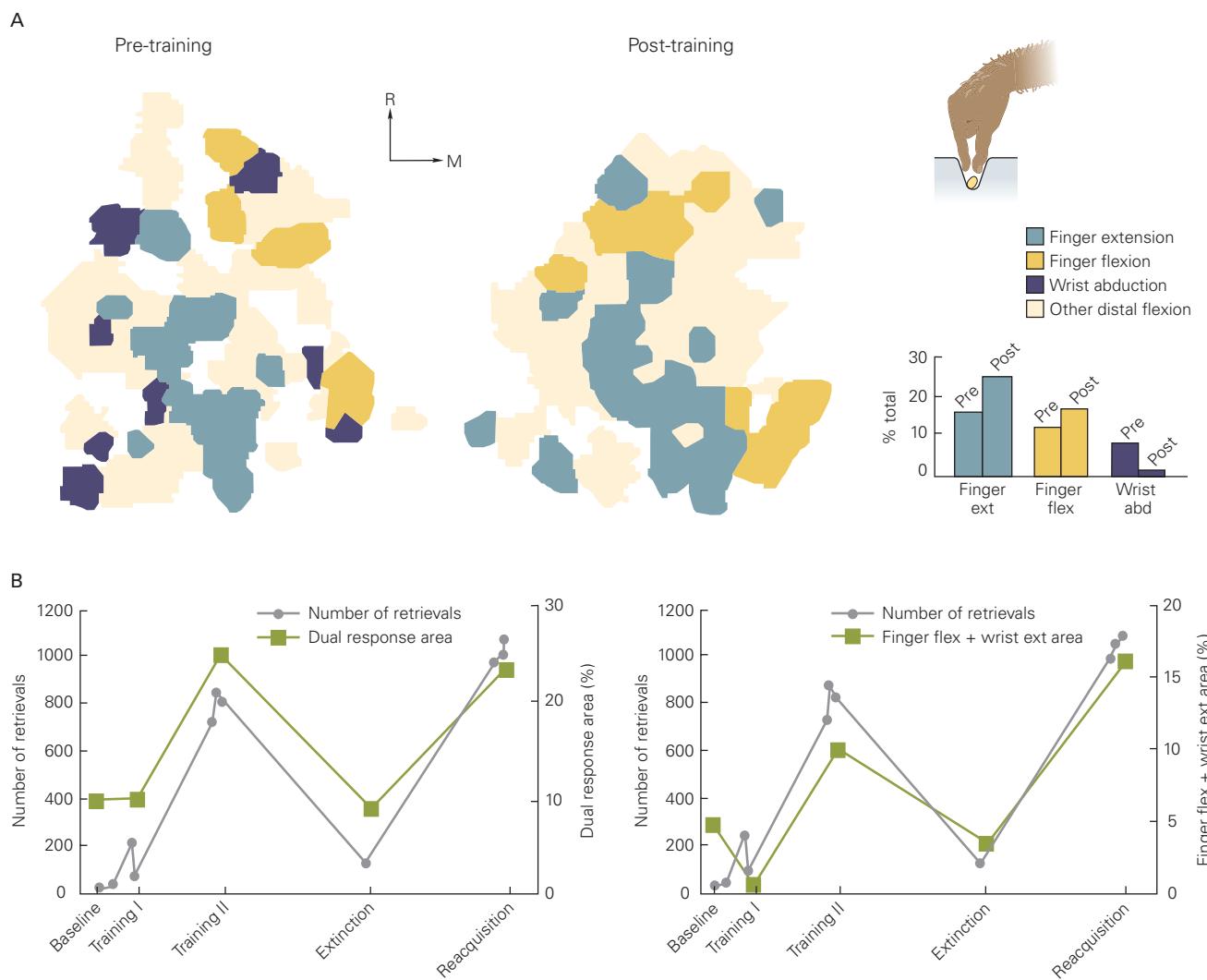


Figure 34–24 Learning a motor skill changes the organization of the M1 motor map. (Reproduced, with permission, from Nudo et al. 1996. Copyright © 1996 Society for Neuroscience.)

A. Motor maps for the hand in a monkey before and after training on retrieval of treats from a small well. Before training, areas of the motor map that generate index finger and wrist movements occupy less than half of a monkey's motor map. After training, the area from which the trained movements can be evoked by intracortical microstimulation expands substantially. The area of the map from which one could elicit individuated movements such as finger extension and flexion has expanded considerably, while the areas controlling wrist abduction, which this monkey used less in the

new skill, became less prominent. (Abbreviations: M, medial; R, rostral.)

B. The areas of the motor output map parallel the level of performance (number of successful pellet retrievals) during acquisition of the motor skill and extinction (due to lack of practice). Two areas were tested: a "dual response" area (*left plot*), from which any combination of finger and wrist motions could be evoked, and an area from which the specific combination of finger flexion and wrist extension could be evoked (*right plot*). Both areas increased as the monkey's skill improved with practice and decreased as the monkey's skill was extinguished through lack of practice. These data are from a different monkey than the one in part A but trained for same task.

cortical representation of practiced actions in humans have been demonstrated by functional imaging and transcranial magnetic stimulation.

At least some of the processes contributing to these changes to the motor map are local to M1 itself. One of the mechanisms contributing to the cortical reorganization underlying improved reach-to-grasp performance in rodents involves changes in synaptic strength similar to long-term potentiation and depression within the local horizontal connections linking different parts of the arm motor map. It has been shown that spike-triggered ICMS could cause specific alterations to the M1 motor output map even without specific training. For instance, one study first identified two different cortical sites (A and B) that caused contractions of different muscles (muscle A and muscle B, respectively) when electrically stimulated. They then recorded the activity of a neuron at site A; whenever that neuron fired, they stimulated site B. Within a day or two of this ICMS conditioning at site B, electrical stimulation of site A was able to cause simultaneous contractions of both muscles A and B. The change likely resulted from a spike-timing dependent increase in synaptic strength that was limited to the horizontal cortical projection from site A to site B. Electromyographic responses elicited by ICMS at a third site that did not receive similar conditioning did not change, confirming that the effect was not generalized.

Motor adaptation to visual or mechanical disturbances has been studied extensively in human subjects (Chapter 30). Neural-recording studies have demonstrated that these alterations lead to changes in the activity of M1 neurons in monkeys as the animals adapt to the perturbations. For instance, when monkeys make reaching movements in a predictable external force field that pushes on the arm in a direction perpendicular to the direction of movement, their initially curved reach trajectories get straighter. As this adaptation evolves, large increases gradually arise in the activity of M1 cells whose preferred directional tuning is opposite to the applied force field. The magnitude of such adaptation-dependent changes in activity diminishes progressively as the angle between the force direction and cell preferred direction increases, following a cosine-like function. This shows that the adaptive changes were specific to the neurons that would make the greatest contribution to compensate for the external force field.

Another example of selective changes in M1 activity during motor learning comes from a visuomotor learning study in which visual feedback from a computer monitor is rotated 90° clockwise such that movements of a monkey's arm to the right result in

downward movement of the cursor. Initially, the monkeys make arm movements in the original direction aimed at the visual target location, with corrections made online after movement onset. However, with practice, the monkeys begin to move in a new direction rotated counterclockwise to the visual target so that the cursor moves directly to the target. When training occurs for only one direction, learning generalizes poorly to other directions, suggesting that the adaptive changes occur only in neurons that evoke the adapted movement. The tuning curves of neurons with preferred directions near the learned direction were altered during training, whereas neurons with other preferred directions were not affected by the training. This confirmed that the adaptation was local, consistent with the findings of the force-field adaptation study, and explained why adaptation to the visuomotor rotation in one direction generalized poorly to other directions.

Motor-error signals in the precentral cortex also play an important role in trial-by-trial motor adaptation based on feedback learning. In one study with monkeys, an adjustable prism was used to displace the apparent location of the reach target in the environment. Visual feedback of the target and arm were blocked during the reaching movements, leading to systematic errors in touching the target. The monkeys were allowed to see visual feedback of the position of the hand relative to the target for a brief period of time at the end of movement (Figure 34–25). Activity in M1 and PMd during that brief period of visual feedback after movement reflected the direction of reach end-point errors and could be involved in adapting reaching movements to correct these errors. To test that hypothesis, ICMS was then used in M1 and PMd to simulate those error responses and showed that the monkeys began to make adaptive changes in their reaching movements to compensate for the simulated errors even though no reaching error was actually made.

Some motor skills are relatively easy to learn, such as compensation for a visuomotor rotation. Others, however, are very difficult to learn. Recent studies examined this discrepancy by first measuring the activity of a population of M1 neurons as the monkey moved a cursor on a computer screen using a brain-machine interface and a neural activity decoder. This population-level mapping between M1 activity and cursor motion was then altered by changing the association between the directional tuning of each neuron and cursor motion in the decoder. When the altered decoder mapping retained the normal co-modulation structure of neural activity, as would be the case for instance if the mapping between the activity of all

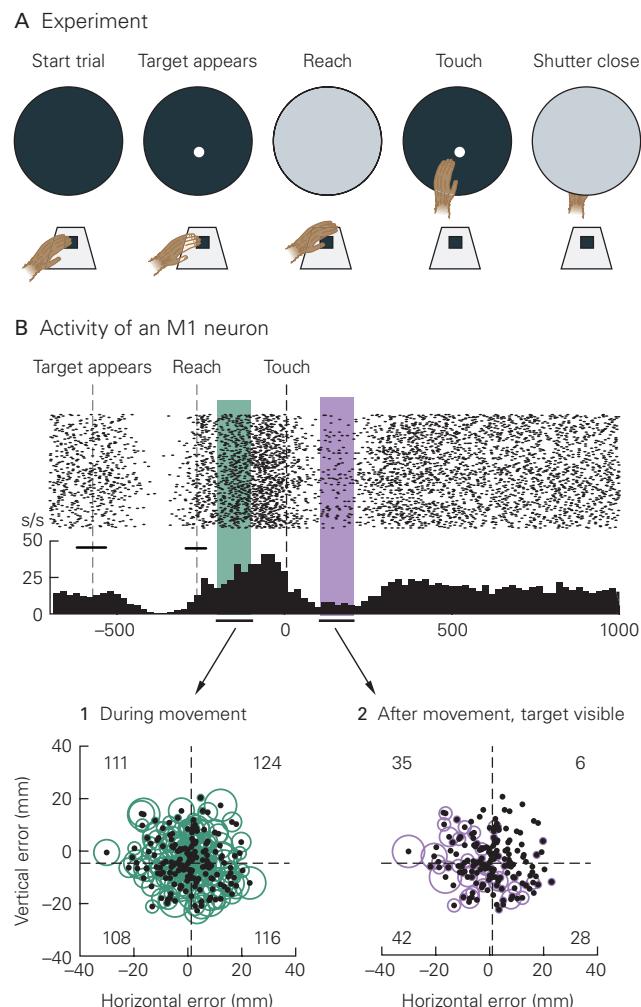
Figure 34–25 (right) Error signals in the primary motor cortex drive adaptation. After a movement is complete, M1 activity reflects the error between the spatial target and final hand position. (Reproduced, with permission, from Inoue, Uchimura, and Kitazawa 2016. Copyright © 2016 Elsevier Inc.)

A. Monkeys made reaching movements to spatial targets on a touch screen. On each trial, adjustable prism goggles shifted the viewed position of the spatial target by a variable amount during the movement, while a shutter blocked vision of the monkey's hand and the target. Feedback of the final hand position was only provided for 300 ms after contact with the touch screen at the end of movement.

B. Top: Discharge response of a typical M1 neuron. Raster plots and spike-timing histograms are aligned with the initial screen contact (touch).

1. Distribution of reach endpoint errors (black dots) where the origin represents the center of the target. Diameters of green circles denote the firing rate of the neuron during each movement (green bar in B); the firing rates were unrelated to the subsequent endpoint error. The numbers in each quadrant indicate the summed spike activity during movements that ended in the corresponding quadrant; they are all nearly equal.

2. Same as in part B except purple circles denote firing rate 100 to 200 ms after movement while the monkey can see its hand while touching the screen (purple bar in part B). The circles and spike counts show that the firing rate is greatest for endpoint errors down and to the left relative to the position of the target (0,0), revealing that the neural activity during this postmovement period is strongly modulated by visual feedback of reach endpoint error.



neurons and cursor motions was rotated clockwise by 45°, the monkeys showed significant adaptation to the perturbation within a few hundred trials during a single recording session. In contrast, when the perturbation required the monkeys to learn a more complex “unnatural” remapping, for instance, random clockwise and counterclockwise rotations of the apparent directional tuning of neurons by different amounts, the monkeys showed little ability to recover proficient cursor control over several hundred trials in a single recording session. Importantly, another study found that monkeys could eventually master an “unnatural” change in an M1 neural activity decoder mapping if they could practice with the same altered decoder over several days, indicating that they could learn a new neural co-modulation structure if allowed enough experience with it. These studies reinforce how neural circuits in these cortical motor regions are critical for motor skill learning.

The studies just described used brain-machine interfaces and neural decoders to explore how single neurons and neural populations contribute to motor skill learning. This technology promises to be an increasingly important research tool for developing new insights into the neural mechanisms of voluntary motor control and motor skill learning (Chapter 39).

Highlights

1. Voluntary motor behavior implements an individual's intentional choice or decision to move within, and to interact physically with objects in, the environment. A hallmark of human motor action is the breadth of skills we possess and, when highly practiced, the ease and automaticity of these actions.
2. Voluntary motor control has long been separated into two stages—planning and execution—that

- can be dissociated in time. Neural recording studies have found correlates of these two stages differentially distributed across many movement-related cortical areas.
3. The overall computational problem that the motor system must resolve to control voluntary movement is to convert sensory information about the current state of the world and the body into plans for action and ultimately into patterns of muscle activity that generate the causal forces required to execute the desired movement(s), while avoiding or correcting for errors.
 4. Representational models of voluntary motor control such as the sensorimotor coordinate transformation hypothesis assume that the motor system directly plans and controls specific features or parameters of intended movements. Single neurons and neural populations express those parameters in their activity and perform definable computations to effect the transformations between the controlled movement parameters in corresponding coordinate frameworks.
 5. Dynamical systems models of voluntary motor control, in contrast, assume that motor circuits find empirical solutions for the computations underlying the planning and execution of movements by evolutionary and individual adaptive processes. One recent theory, optimal feedback control, proposes that planning and execution of voluntary movements involve three functional processes, namely, state estimation, task selection, and a control policy. Single neurons and neural populations contribute to voluntary motor control by participating in the computations underlying these three processes.
 6. Distributed frontoparietal circuits in cerebral cortex play a pivotal role in voluntary control. There are substantial reciprocal axonal interconnections between frontal and parietal cortical regions, partially segregated based on body part (eg, hand, arm, eye). Frontal motor and parietal cortical regions both directly influence spinal processing through the corticospinal tract and indirectly through brain stem descending pathways.
 7. Posterior parietal cortex plays a prominent role in identifying potential goals and objects in the environment, state estimation of the body, and sensory guidance of motor actions. Important sources of sensory signals are transmitted from visual cortex through the dorsal visual pathway and from primary somatosensory cortex. Behavioral goals and objects are represented in many parietal subregions, but how they are represented (relative

to the orientation of the eye, head, or arm) varies across subregions. The presence of multiple representations provides a rich basis for defining the movement-relevant properties and the locations of objects in the world and relative to the body that can be used to select and guide movement.

8. Premotor and prefrontal cortices play a prominent role in task selection and motor planning. The dorsal and ventral premotor regions are often implicated when external sensory information plays a dominant role in selecting motor actions. In contrast, more medial premotor regions, such as the supplementary and cingulate motor areas, may play a more dominant role when internal desires are more critical in selecting and initiating a motor action. However, this dichotomy is not absolute, and multiple premotor and prefrontal cortical areas all contribute to the control of voluntary behavior in a broad range of contexts and conditions.
9. Primary motor cortex in primates has a representation of the entire body along its mediolateral axis, with larger cortical territories associated with the hand and face relative to other body parts. This cortical region also provides a large component of the corticospinal tract and has projections to both interneurons and alpha motor neurons in the spinal cord.
10. Neural activity that reflects the causal forces and the spatiotemporal features of muscle activity necessary to move the limb is particularly prominent in the primary motor cortex and can be rapidly altered to correct movement errors or to compensate for displacements of the limb away from the desired movement if the limb is perturbed. However, neural activity in primary motor cortex can also show more complex properties, reflecting changes based on the behavioral context, performance goals and constraints, and features such as movement kinematics. These properties of primary motor cortex activity may reflect the formation of a task-specific control policy within the motor system.
11. Although parietal, premotor, and primary motor cortical regions play prominent roles in state estimation, motor planning, and motor execution, respectively, they are not uniquely responsible for any one aspect; they are instead distributed to some degree across most or all of these cortical regions.
12. The cortical motor system is adaptive and can undergo changes in its functional architecture to adapt to long-term changes in the physical

- properties of the world and the body, as well as acquire, retain, and recall new motor skills.
13. New technologies such as large-scale multi-neuron recording and imaging methods, enhanced multi-neuron activity decoding algorithms, and optogenetic control of the activity of specific neural populations will lead to deeper insights into the functional architecture of cortical motor circuits.

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