5

Motor Systems: The Organization of Action

INTRODUCTION

Sensory systems provide the inputs to cognitive processes, and motor systems deliver the physical behavioral output that expresses cognitive goals. Thus, understanding the organization of motor systems is essential for understanding the organization of cognitive systems, which ultimately manifest perception, attention, emotion, and the consequences of decisions in action. All body movements are generated by the stimulation of skeletal muscle fibers by lower motor neurons whose cell bodies are located in the brainstem and spinal cord. Lower motor neuron activity is coordinated by interneurons in local circuits. Although such local circuits can produce simple reflexive movements on their own, they are governed by descending projections from upper motor neurons in the cerebral cortex and brainstem. These descending influences modulate the activity of local circuits to produce and coordinate complex sequences of movements that make up purposeful, goal-directed actions. This higher-order control of movement is mediated by upper motor neurons in the primary motor cortex and other premotor areas of the frontal and parietal lobes.

Neurons in motor cortex and premotor areas contribute critically to cognitive functions such as the planning and initiation of complex sequences of movements, the selection of behavioral goals for action, and the learning and remembering of new movement sequences. Thus, higher motor areas enhance the complexity and efficacy of behavior. All of these higher motor areas themselves are monitored and modulated by two other key motor systems—the cerebellum and the basal ganglia. Major functions of the cerebellum are to correct errors in ongoing movements and to learn new motor skills. Major functions of the basal ganglia are to gate motor commands and to facilitate simple forms of learning. The complex neural processing carried out by the basal ganglia and cerebellum also influences cognitive functions that are not directly expressed in motor activity, including motivation, emotion, and decision making.

■ INTRODUCTORY BOX APRAXIA

The importance of cognition for action is keenly apparent when the ability to plan movements or carry out motor programs is compromised. Such deficits are known as apraxias. *Apraxia*–Greek for "without act or deed"–is a loss of the ability to execute learned voluntary movements, especially complex sequences of movements, despite the motivation and physical capability to perform the actions.

Apraxias can take several forms. Ideomotor apraxia, for example, is an inability to voluntarily perform a learned action when presented with the appropriate objects, an inability to imitate what someone else is doing, or an inability to follow verbal instructions. An afflicted person might be unable to follow the command to wave goodbye, but able to properly wave when a familiar person leaves the room. Or she might be unable to pantomime combing her hair when given a comb and asked to pretend using it, but able to comb her hair when she wants to.

Ideational apraxia is the inability to carry out sequential tasks involving the use of tools or objects in the proper order. Patients with this form of apraxia might put on their shoes before putting on their socks or strike a candle against the side of a matchbox rather than striking a match and using it to light the candle.

A particularly vexing form of apraxia is verbal apraxia, which results in difficulty producing speech. Verbal apraxia can afflict both adults and children, the latter having potentially devastating consequences for learning and socialization.

Although the causes of apraxia remain largely unknown, ideational and ideomotor apraxia have been linked to damage of the parietal and premotor cortex, typically on the language-dominant side. Such damage can result from neurological insults such as stroke or ischemia, as in the case of ideomotor apraxia, or from the more diffuse degeneration that is associated with diseases such as Alzheimer's disease or Parkinson's disease. Unfortunately, the prognosis for apraxia is rather grim. Some recovery can be made with physical therapy or occupational therapy, particularly in younger patients, yet many people suffering from apraxia never recover and become dependent on communicative aids and assistive devices. Despite this rather bleak outlook, some people with apraxia, particularly children, do recover or adapt to the condition, especially in its milder forms.

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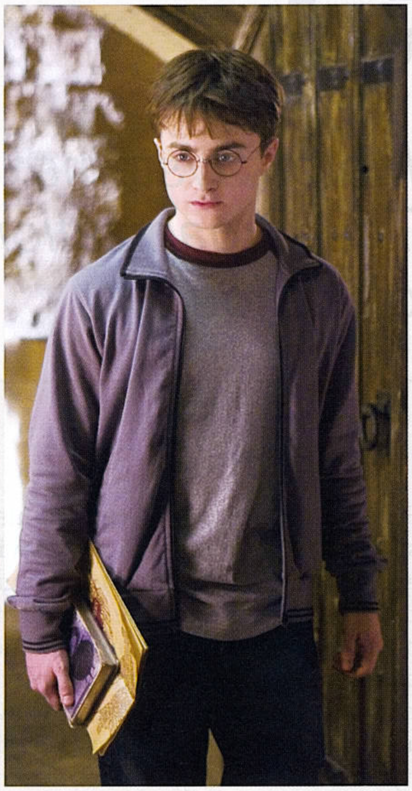


Example of mild apraxia. Actor Daniel Radcliffe, best known for his portrayal of the young wizard Harry Potter in the film series, struggles to tie his shoes because of a mild case of apraxia, sometimes referred to as dyspraxia.

Motor Control Is Hierarchical

Behavioral and theoretical studies of motor control strongly support a hierarchical model of the neural systems that organize action. The notion of hierarchical organization is vividly illustrated by the observation that complex movements, such as signing one's name, preserve distinctive features such as shape and style even when performed by different muscle groups. For example, the Russian physiologist Nikolai Bernstein asked people to sign their name with a pen held in the dominant (usually right) hand, and then with the pen attached near the wrist, elbow, or shoulder; with the pen attached to the right shoe; and even with the pen held in the mouth. Although penmanship was clearly sloppier and larger in scale under these decidedly unnatural conditions, the signature remained remarkably similar in overall form (**Figure 5.1**).

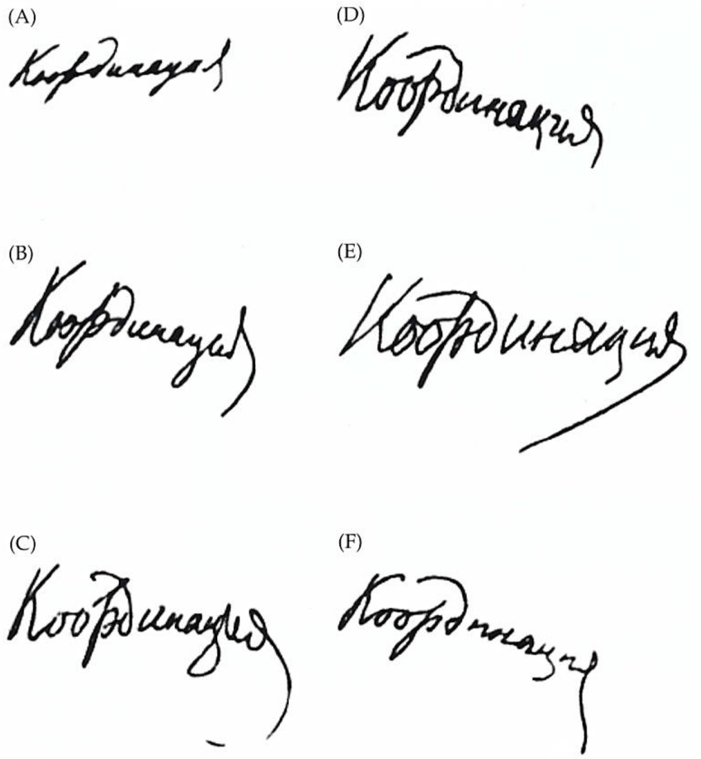


Figure 5.1 Behavioral evidence for motor programs These signatures were made with a pen held in the right hand (A), attached at the right wrist (B), attached at the elbow (C), attached at the shoulder (D), attached to the right shoe (E), and held in the teeth (F). Note the remarkable similarity in form retained by all the signatures. (From Bernstein 1947.)

Such observations support the notion that complex behaviors are organized at several levels. At the highest level are **motor programs**, which are sets of commands to initiate a sequence of movements. Such motor programs are distinguished by the fact that they are more or less ballistic, in the sense that they do not strictly depend on incoming sensory information. Moreover, as demonstrated by Bernstein's handwriting experiment, motor programs are independent of the actual muscle groups used to carry them out. Finally, motor programs originate within the central nervous system itself, rather than arising directly from sensory signals from the periphery.

By contrast, at the lowest level of the motor control hierarchy are elementary behavioral units that directly activate muscles. As described in the remainder of this chapter, a variety of intermediate processing levels intervene between motor programs and the elementary units of motor control. Such intermediate processing in the motor system translates motor programs into the precisely coordinated sequences of motor neuron activation and suppression that are needed to generate the patterns of muscle contraction and relaxation responsible for complex behavior.

Anatomical organization of motor systems

Hierarchical models of motor control can be loosely mapped onto neuroanatomically and neurophysiologically distinct elements of the central nervous system. At a broad level, the neural circuits controlling skeletal movements can be thought of as being made up of four distinct but interacting subsystems: lower motor neurons in the spinal cord and brainstem; upper motor neurons in the cortex and brainstem; the cerebellum; and the basal ganglia (**Figure 5.2**).

At the lowest level are circuits within the spinal cord and brainstem, composed of **lower motor neurons** and **local circuit neurons**. Lower motor neurons

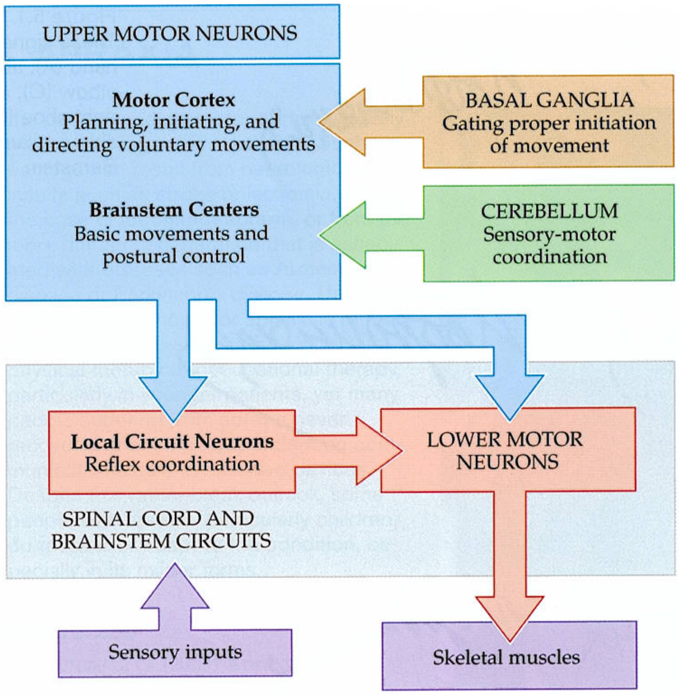


Figure 5.2 Overall organization of the human motor system Four systems–upper motor neurons in the cortex and brainstem (blue), lower motor neurons in the spinal cord and brainstem (red), the cerebellum (green), and basal ganglia (brown)–make essential and distinct contributions to motor control.

in the gray matter of the spinal cord and brainstem send axons out of the central nervous system to directly innervate skeletal muscle fibers, and they can be considered synonymous with the elementary behavioral units already mentioned. Lower motor neurons begin to fire action potentials immediately preceding contraction of the muscles they innervate; thus, their activity is directly correlated with movement of the relevant body part (**Figure 5.3**). Motor neurons involved in fine motor control, such as those used to move the fingers or control the position of the eyes, innervate far fewer muscle fibers than do motor neurons involved in gross movements of larger muscles, such as those used to move the legs during walking and running. Local circuit neurons, on the other hand, provide synaptic input to lower motor neurons and contribute to the local coordination of lower motor neuron activity. This is especially important for the coordination of reflexes engaged by rhythmic activities like walking and chewing (**Box 5A**).

At higher levels of the motor system, **upper motor neurons** in the cerebral cortex and brainstem provide descending control of local circuitry in the spinal cord and brainstem. The other two components of the motor system—the

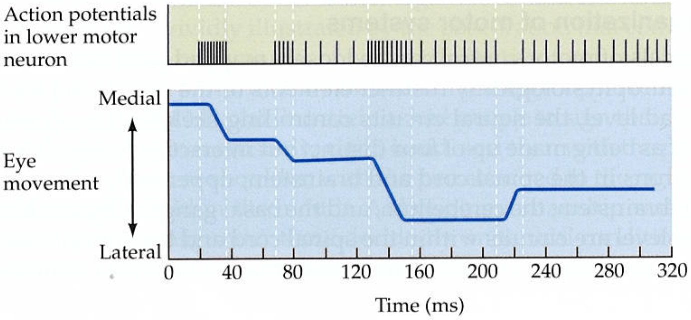


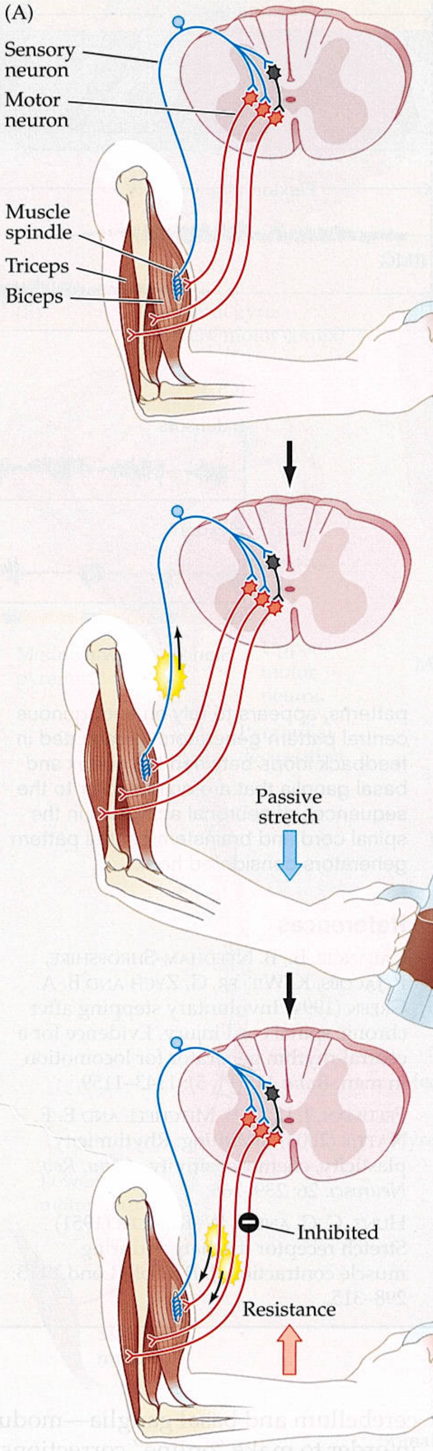
Figure 5.3 Activity of lower motor neurons predicts muscle contraction and ultimately movement In the example here, the upper trace shows a recording from a lower motor neuron that innervates one of the eye muscles, causing the eye to rotate laterally. Note that the rate of action potentials is directly correlated with the amplitude and direction of the eye movement. (After Fuchs 1967.)

■ BOX 5A REFLEXES, CENTRAL PATTERN GENERATORS, AND RHYTHMIC BEHAVIORS

The fundamental unit of behavior is the reflex. Reflexes connecting the muscles to the spinal cord and then back to the muscles provide simple yet powerful mechanisms for controlling basic behavior (Figure A). Key components are local circuit neurons within the spinal cord that help connect incoming sensory information to appropriate motor neurons that enable movement. In fact, activation of the appropriate sets of local circuit neurons can generate complex patterns of muscle contraction and relaxation that result in rather sophisticated behavior. For example, the spinal cord (and brainstem) contains circuits capable of producing coordinated movements of the limbs with no input from the brain. Not surprisingly, these local circuits can also produce and sustain even more complex movements that are not simply reflexive responses to sensory inputs. Experimental work in a variety of animals has shown that rhythmic movements such as locomotion and swimming are actually produced by local spinal cord circuits known as central pattern generators.

Walking, to take a specific example, is a rhythmic behavior in which each foot moves from the stance phase, where it is in contact with the ground, to the swing phase, in which it is lifted and brought forward to begin the next stance phase. These phases of locomotion are associated with bursts of activity in extensor muscles during the stance phase and in flexor muscles during the swing phase (Figure B). Cats that have undergone surgical transection of the spinal cord anterior to the motor neurons controlling the hind limbs can nonetheless walk relatively normally on a treadmill. Their gait continues to follow the normal stance-swing-stance pattern, and the extensor and flexor muscles show coordinated bursts of activity typically associated with the stance and swing phases in normal animals (Figure C). Remarkably, cats with transected spinal cords can also adjust their walking speed when the treadmill is sped up or slowed down. When the sensory fibers entering the spinal cord via the dorsal roots are cut, however, the cat can continue to walk on the treadmill but can no longer adjust its gait or avoid obstacles.

These experiments, and others like them, demonstrate that the spinal cord and brainstem contain circuitry capable of controlling the timing and coordination



Reflexes and central pattern generators. (A) A stretch reflex. *(Figures B and C on next page.)*

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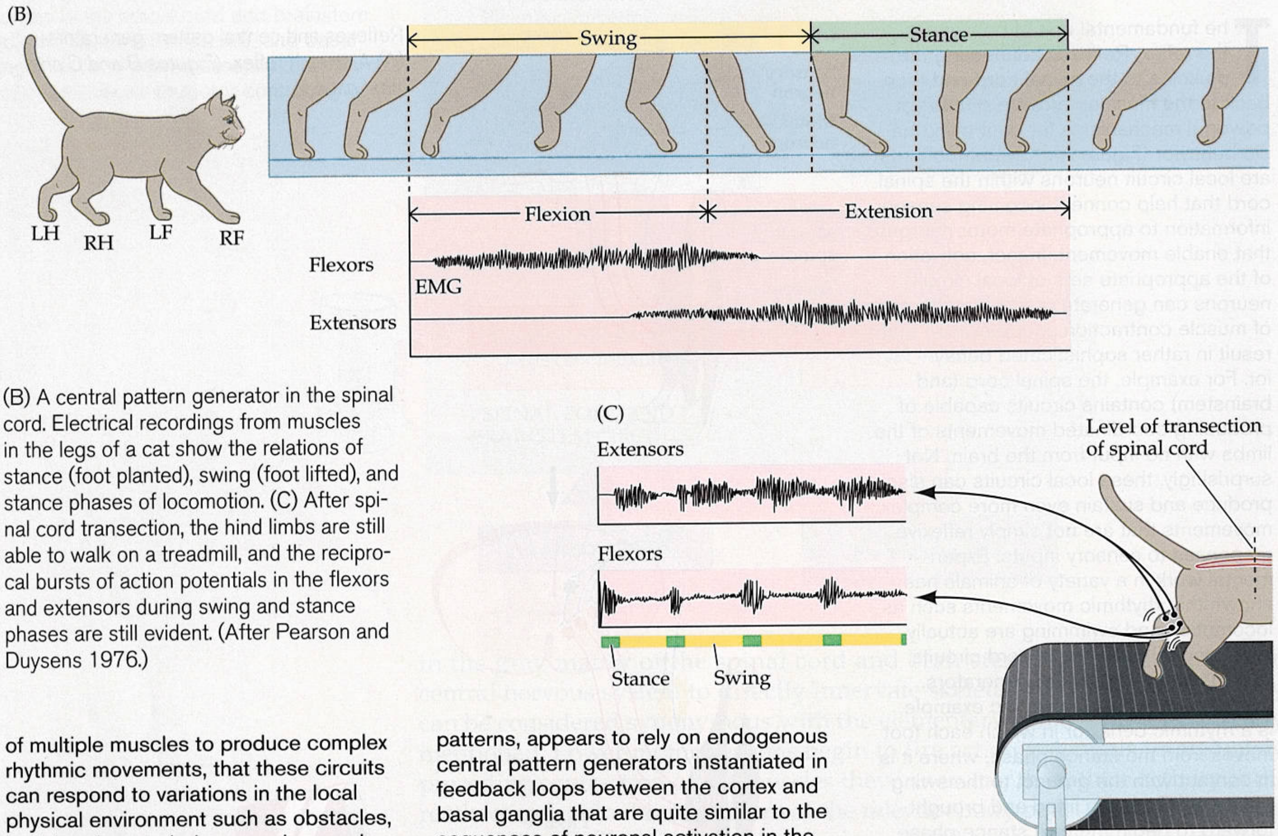
■ BOX 5A *(continued)*



(B) A central pattern generator in the spinal cord. Electrical recordings from muscles in the legs of a cat show the relations of stance (foot planted), swing (foot lifted), and stance phases of locomotion. (C) After spinal cord transection, the hind limbs are still able to walk on a treadmill, and the reciprocal bursts of action potentials in the flexors and extensors during swing and stance phases are still evident. (After Pearson and Duysens 1976.)

of multiple muscles to produce complex rhythmic movements, that these circuits can respond to variations in the local physical environment such as obstacles, and that the needed processing can be performed in the absence of any input from higher brain centers.

Once evolution has generated a neural solution to a particular motor problem, the same mechanisms are often applied in new contexts to solve similar problems. Thus, central pattern generators, which evolved originally to mediate basic rhythmic functions such as swimming, walking, or swallowing, serve important roles in more complex, often cognitive, motor behaviors. For example, spoken language is arguably the most complex cognitive behavior generated by the brain, yet all human languages rely on the same basic motor processes for generating meaningful utterances (see Chapter 12). Verbal sequencing, much like the sequencing of other complex movement patterns, appears to rely on endogenous central pattern generators instantiated in feedback loops between the cortex and basal ganglia that are quite similar to the sequences of neuronal activation in the spinal cord and brainstem central pattern generators considered here.

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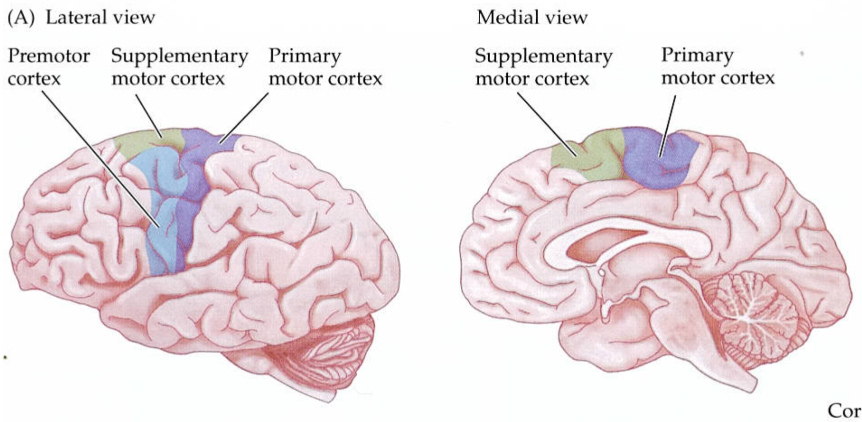
cerebellum and basal ganglia—modulate the activity of upper motor neurons in order to make "online" corrections in response to perturbations in ongoing movements and to help initiate goal-directed movements, respectively. The localization of motor programs remains an active area of investigation.



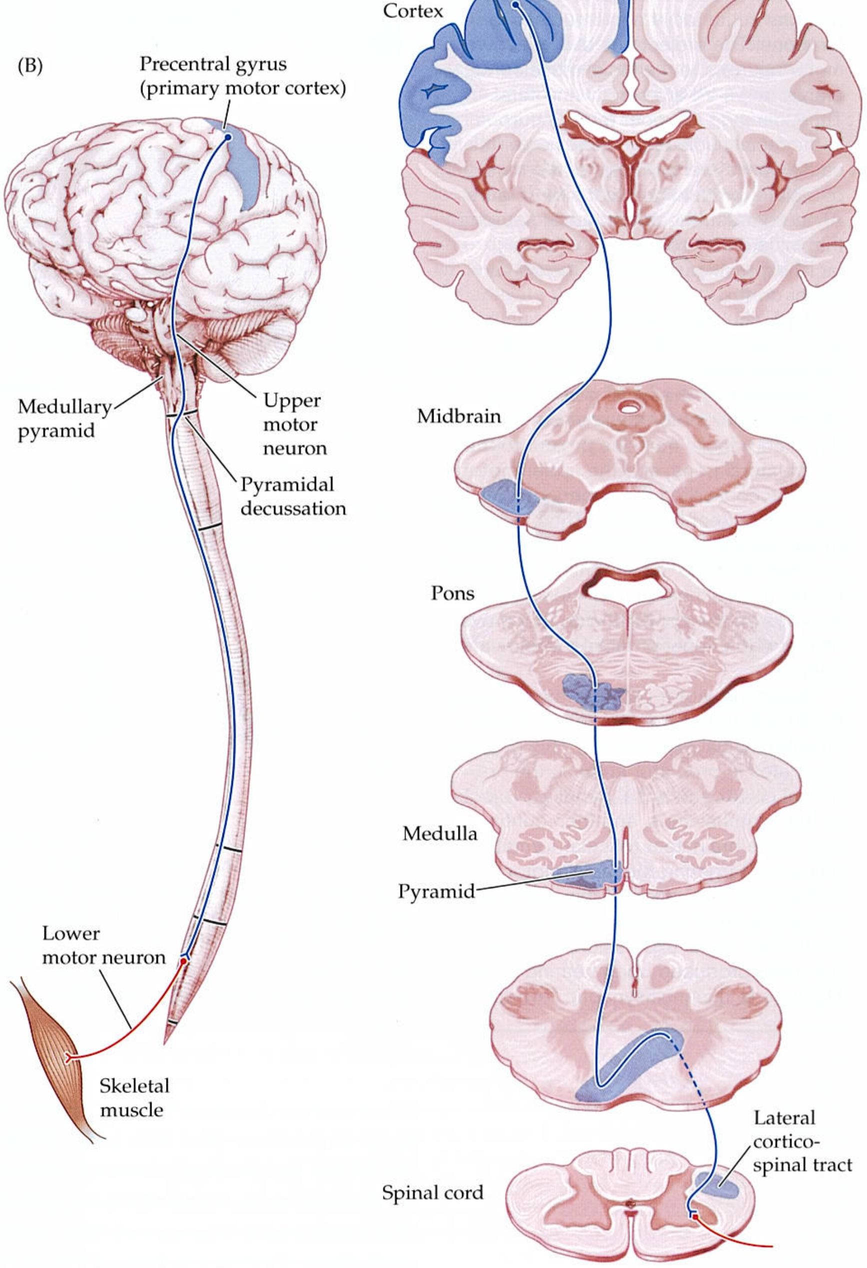


Figure 5.4 Upper motor neuron pathways (A) The primary motor cortex and premotor cortical areas. The primary motor cortex is located in the precentral gyrus. The motor and supplemental premotor areas are more rostral in the frontal lobe. (B) Descending pathways from the primary motor cortex. Pathway to the spinal cord and the lateral corticospinal tract in cross section.

Cortical Pathways for Motor Control

As we saw in the preceding discussion, the spinal cord and brainstem contain circuitry capable of generating an array of complex motor behavior. These subcortical systems serve animals with limited behavioral repertoires quite well, but in primates and other animals in which evolution has favored more demanding behaviors, the brain has evolved correspondingly complex higher motor centers capable of initiating and coordinating the local circuits and lower motor neurons that generate movements more directly.

Descending projections from the cerebral cortex to brainstem and spinal cord originate from upper motor neurons within the **primary motor cortex** and the adjacent **premotor cortical areas**, including the **premotor cortex** and **supplementary motor cortex** (**Figure 5.4**; see also the Appendix). In addition to having anatomical differences, the primary motor cortex is distinguished from other premotor areas by the very low intensity of current needed to evoke movements by electrical stimulation. The fact that low electrical current intensities applied to primary motor cortex can evoke movements indicates that the upper motor neurons of this area have relatively direct access to local circuit neurons and lower motor neurons in the brainstem and spinal cord.

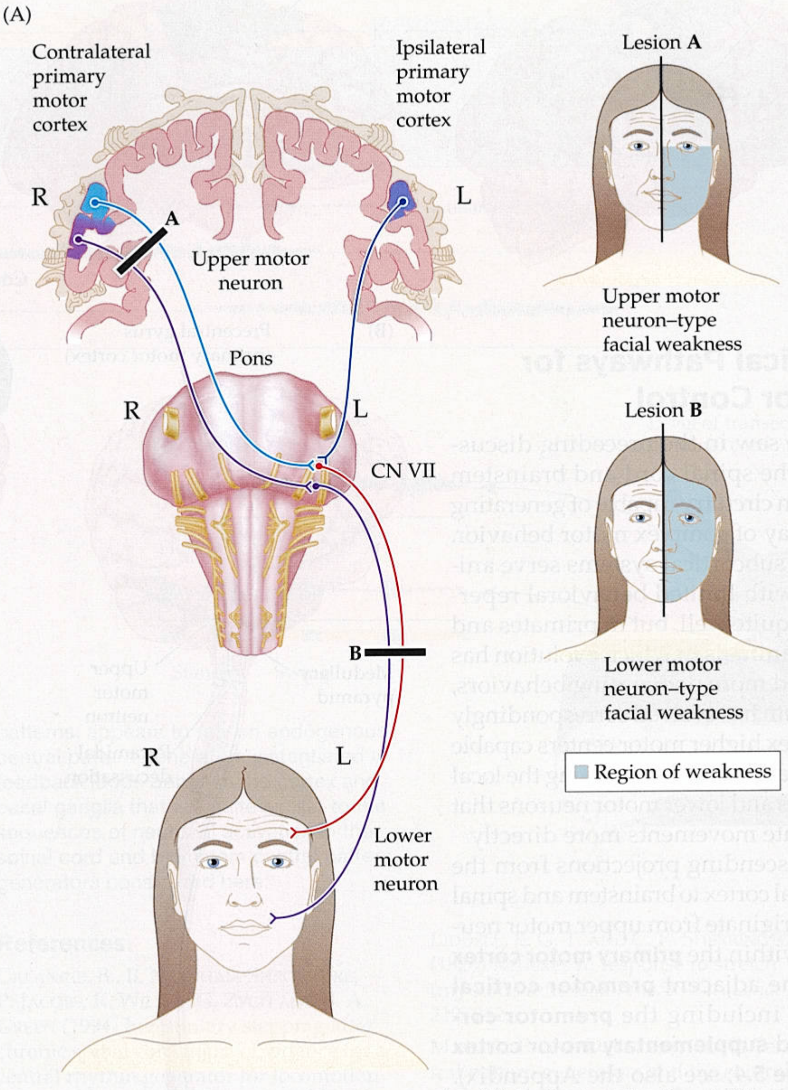
The axons of the upper motor neurons in the primary motor cortex that

BOX 5B MOTOR CONTROL OF FACIAL EXPRESSIONS

The neural control of facial expressions provides a fascinating and instructive example of how upper and lower motor neurons are coordinated to generate useful behavior, and how some aspects of emotion play into the generation of facial movements. The muscles of facial expression, including those that elevate the corners of the lips in a smile and raise the eyebrows in surprise, are under the direct control of lower motor neurons in the facial nerve nucleus in the pons. The projections of these lower motor neurons to the facial muscles via cranial nerve VII are strictly unilateral. Thus, damage to upper motor neurons in the facial nucleus or to the nerve itself causes unilateral paralysis of the muscles of facial expression on that side (Figure A). In contrast, the upper motor neurons that initiate and coordinate voluntary facial expressions reside in the primary motor cortex.

A particularly common, and usually reversible, form of such facial paralysis known as Bell's palsy is caused by inflammation of the facial nerve. Notably, the upper motor neurons controlling the inferior facial muscles project to the contralateral pons, and the upper motor neurons controlling the superior facial muscles project bilaterally. Thus, damage to the portion of the primary motor cortex corresponding to movements of the face results in weakness of the inferior facial muscles on the opposite side, but movements of the superior facial muscles are spared.

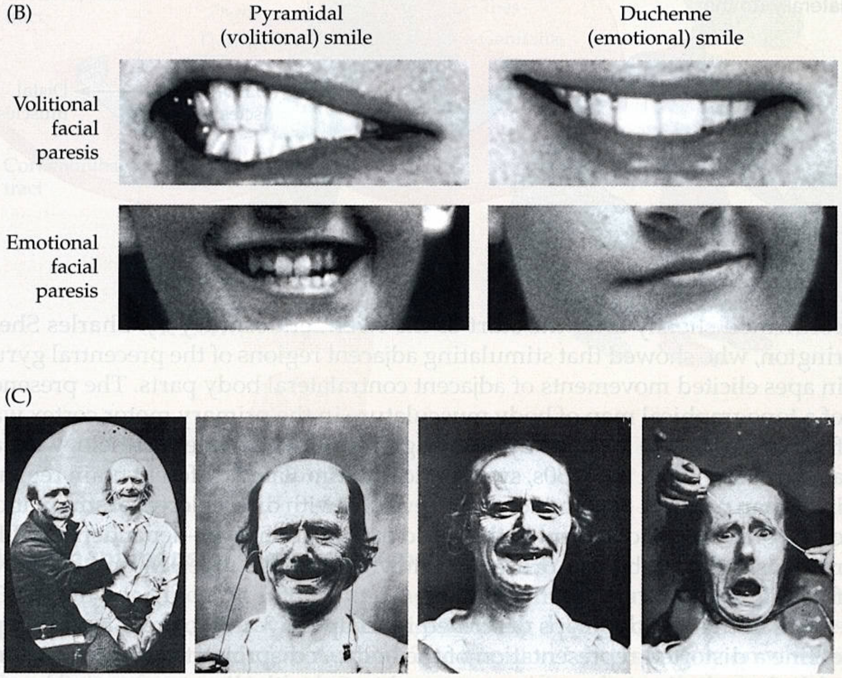
A second motor pathway more closely linked to emotion contributes to largely involuntary facial expressions. This pathway originates in premotor areas in the prefrontal cortex and basal ganglia, projects to the hypothalamus, and then continues to the brainstem reticular formation, ultimately targeting the facial motor nuclei in the pons. Activation of this pathway by an emotional experience evokes involuntary facial expression, such as the smile produced upon hearing a joke. Damage to this multisynaptic “extrapyra-



Voluntary and emotional control of facial expression. (A) Anatomical circuit controlling voluntary facial expression. Lower motor neurons in the pons project to the muscles of the upper and lower face. Upper motor neurons projecting to the pons are unilateral for the lower face, but bilateral for the upper face. A unilateral lesion to the facial nucleus in the pons results in complete paralysis of the face on the same side, whereas a unilateral lesion in the lateral part of the primary motor cortex results in paresis of the lower face on the opposite side due to bilateral projections serving the upper facial muscles.

innervate neurons in the brainstem, such as those controlling the muscles of facial expression (**Box 5B**), branch off at appropriate levels, and those continuing to the spinal cord coalesce and descend through the **medullary pyramids** (so named for their triangular appearance) in the pyramidal tract. The majority of corticospinal fibers cross the midline, or *decussate*, at the caudal end of the medulla and enter the lateral corticospinal tract in the spinal cord (see Figure

BOX 5B *(continued)*



(B) Voluntary and emotional paresis of the face. Lesions to the face representation in primary motor cortex lead to unilateral weakness in smiling on command (left). Lesions to the emotional pathway for facial expression lead to an inability to smile in response to a joke, while voluntary smiling remains intact (right). (C) Duchenne de Boulogne's pioneering study of "faradization," or electrical stimulation, of the facial muscles. The patient in the photographs had lost sensation in the face and thus did not feel the effects of stimulation. Compare the stimulated "smile" (second from left) with the emotional smile (third from left).

midal" pathway (the voluntary pathway is referred to as the pyramidal pathway because it travels in the pyramids in the caudal medulla) renders patients unable to spontaneously express emotions in the face, although they can still produce symmetrical voluntary facial expressions (Figure B). Conversely, patients with damage to upper motor neuron pathways have difficulty voluntarily moving the muscles of the lower part of the contralateral face but nonetheless can smile, frown, or cry normally in response to emotional stimulation.

These distinctions between the pathway for voluntary facial expression and spontaneous, emotional facial expression were first described by the French neurologist and physiologist G. B. A. Duchenne de Boulogne, who photographed subjects producing facial expressions in response to direct electrical stimulation of the muscles and in response to emotional stimulation (Figure C). Duchenne de Boulogne demonstrated that some facial muscle groups, such as the orbicularis oculi, can be activated involuntarily only by subjective emotional experience—an expression known as the Duchenne smile. A forced or voluntary smile does not activate this muscle group, thus appearing strained and unnatural. The distinctions between voluntary and emotional facial expression pathways are often painfully obvious in the contrived facial expressions worn when we are less than sincere.

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5.4B), and they terminate within the gray matter of the cord at levels appropriate to the distal muscles that they serve. A small minority of corticospinal fibers remain uncrossed, forming the medial or ventral corticospinal tract; these axons terminate within the medial spinal cord gray matter on both sides (after crossing through the spinal cord commissure). These medial corticospinal projections, as suggested by the loci of their targets, are involved in control of the midline (proximal) musculature (**Figure 5.5**).

Organization of the primary motor cortex

Early studies conducted in the late nineteenth century showed that electrical stimulation of the primary motor cortex in the precentral gyrus on one side of the primate brain evokes muscle contractions on the opposite side of the body. This apparently topographical organization of the primary motor cortex was

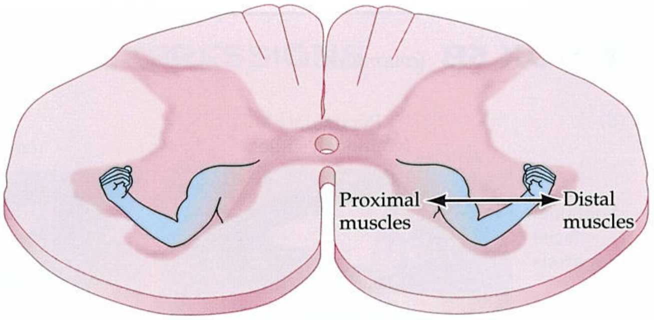


Figure 5.5 Organization of the lower motor neurons in a cross section of the cervical spinal cord Motor neurons innervating proximal muscles (i.e., those closest to the shoulder) are located medially (close to the midline); those innervating distal muscles (toward the digits) are located laterally (to the right or left).

confirmed shortly after the start of the twentieth century by Charles Sherrington, who showed that stimulating adjacent regions of the precentral gyrus in apes elicited movements of adjacent contralateral body parts. The presence of a topographical map of body musculature in the primary motor cortex was further verified in humans by Sherrington's student Wilder Penfield, who, as a neurosurgeon in the 1930s, systematically stimulated different brain regions in human patients. Such motor maps revealed with direct electrical stimulation of the brain are also evident in the blood oxygenation level–dependent (BOLD) response when subjects are asked to move their lips, finger, thumb, elbow, or foot (**Figure 5.6**).

As in the sensory maps described in Chapters 3 and 4, these motor maps define a distorted representation of the body. A disproportionately large area of the lateral primary motor cortex was devoted to the lips, tongue, and hands; and a much smaller area of the dorsal and medial primary motor cortex was devoted to the lower extremities and genitalia (**Figure 5.7**). Thus, the amount of cortical space devoted to motor function corresponds to the capability of that area to exercise fine motor control, and it underscores the principle that more sophisticated processing is always reflected in a greater allocation of cortical space.

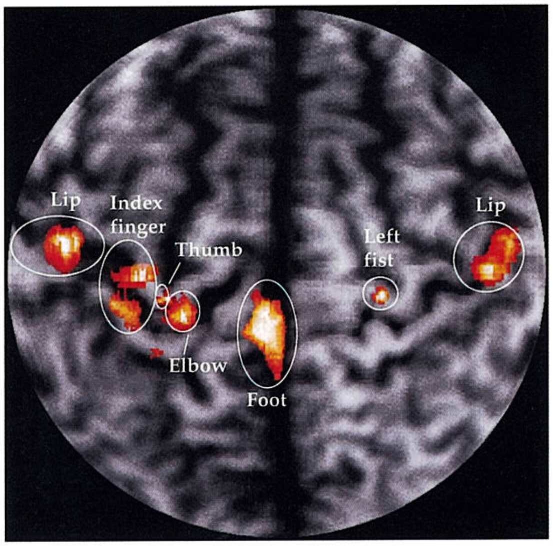


Figure 5.6 Moving different body parts activates different parts of the primary motor cortex in humans Human subjects lay on their back in an fMRI scanner with their eyes closed, while their heads and proximal limbs were secured in order to minimize involuntary movements. Subjects were asked to perform the following movements in succession: elevate the foot at the ankle, flex and extend the right elbow, make a fist with the right hand, tap the right thumb and index finger together, make a fist with the left hand, and purse the lips. The BOLD signal revealed neural activation most laterally for the lips, most medially for the foot, and in between for movements of the hands and fingers—in good accordance with the motor maps generated by intracranial electrical stimulation in human surgical patients. (After Lotze et al. 2000.)

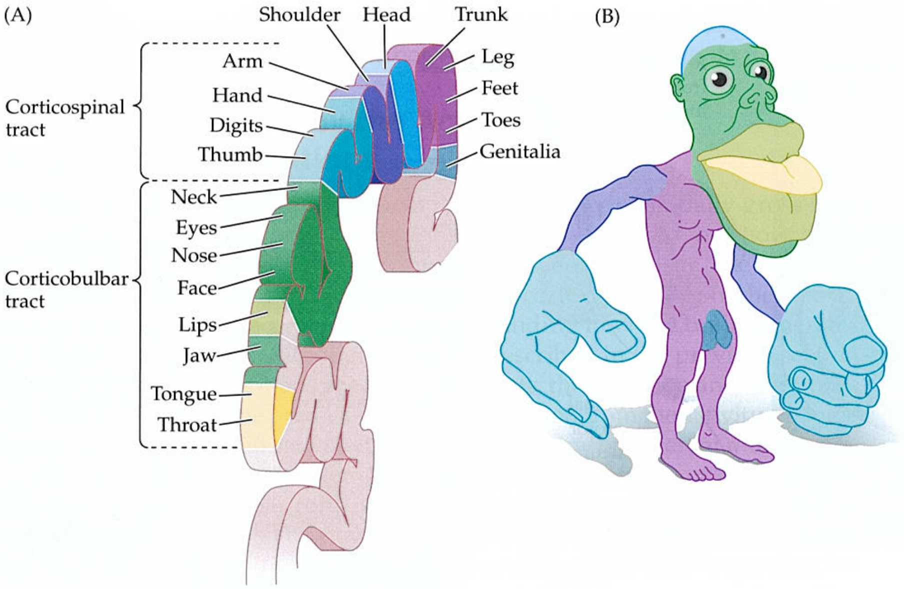


Figure 5.7 The distorted map of the body's musculature in the primary motor cortex (A) The primary motor cortex (M1) is located just in front of the brain's central sulcus. Regions controlling motor responses in different parts of the body are shown here in relative size and sequence. (B) The proportions of the homunculus show the parts of the body relative to their represented size in the primary motor cortex. (After Breedlove et al. 2007.)

Movement maps in the primary motor cortex

Especially pertinent to understanding how cognitive functions relate to the generation of motor behavior is the long-standing debate about the role of these motor maps in producing movement. The question centers largely on whether the activity of neurons in these motor maps specifies what to do (a motor command) or how to do it—the particular patterns of muscle activity necessary to generate the forces required for a particular movement.

Early studies in monkeys using low-intensity electrical stimulation suggested that the primary motor cortex might contain a map of individual muscles. However, later electrical stimulation studies in monkeys confirmed reports by Penfield and Sherrington that activation of some portions of the primary motor cortex evokes coordinated, multijoint movements (**Figure 5.8**). This observation is what would be expected, given that descending projections from the primary

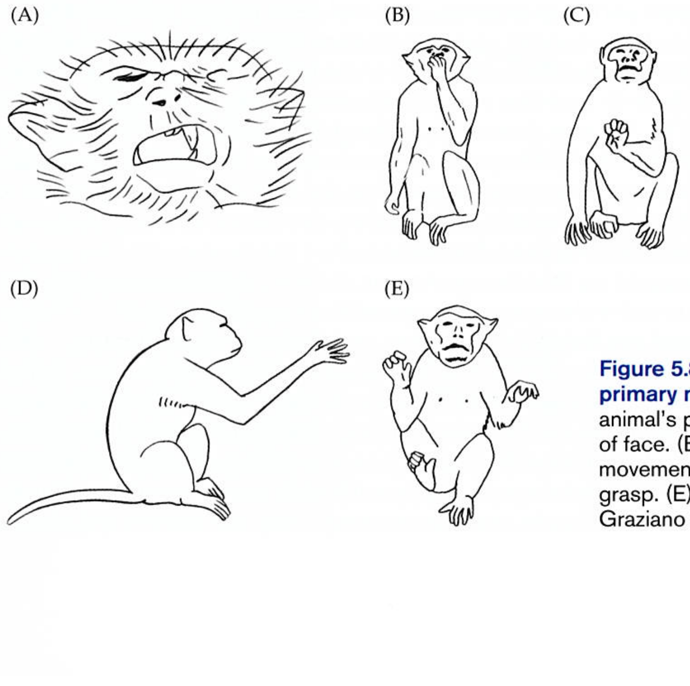


Figure 5.8 Complex movements evoked by stimulation of the primary motor cortex in the monkey Each drawing represents the animal's posture at the end of the stimulation. (A) Defensive-like posture of face. (B) Hand to mouth. (C) Manipulation-like shaping of fingers and movement of hand. (D) Outward reach with hand open, as if shaping to grasp. (E) Climbing- or leaping-like posture involving all four limbs. (After Graziano 2006.)

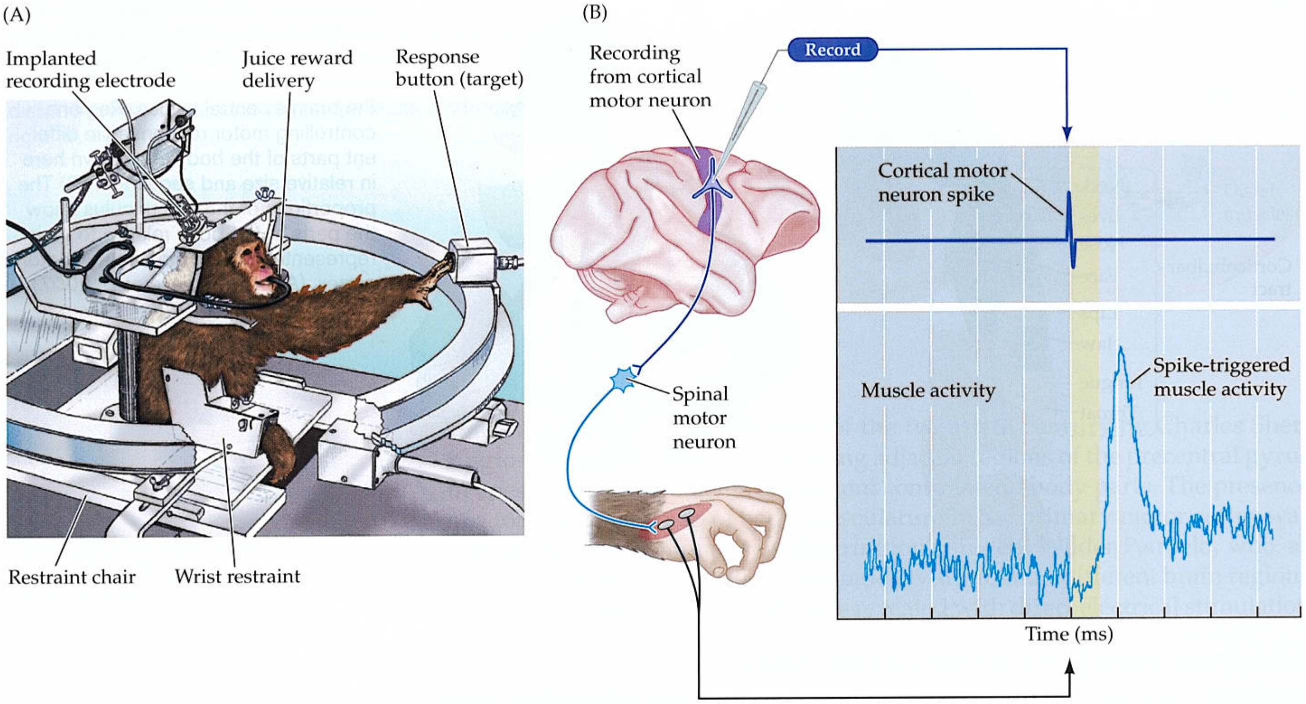


Figure 5.9 Determining the role of cortical motor neurons in generating movements (A) Experimental setup for recording from monkey primary motor cortex neurons in relationship to reaching. (B) As indicated in the diagram and sample recording, neurons in the primary motor cortex fire before movements occur. Movement onset is defined by the increase in the activity of the muscles in the electromyogram (EMG). (A after Evarts 1981; B after Porter and Lemon 1993.)

motor cortex target mainly local circuits in the brainstem and spinal cord rather than the lower motor neurons themselves.

Electrophysiological recordings from single neurons in the primary motor cortex of monkeys have largely supported the conclusion that movements and not muscles are represented in motor maps. In the late 1960s, neuroscientist Edward Evarts and his colleagues pioneered the technique of implanting electrodes in the motor cortex of monkeys that had been trained to reach toward cued targets in order to receive rewards (**Figure 5.9A**). The electrical signals generated by neurons were then compared to the muscle fiber action potentials recorded from the arm muscles, as well as to recordings of the direction and force generated by the arm during movement (**Figure 5.9B**). Evarts's group found that most neurons in the primary motor cortex fired action potentials in relation to a subset of movements, and that the firing rate corresponded to the changes in force generated by the muscles during movement. Moreover, many of these neurons began to discharge before the movements themselves were initiated, suggesting that their activation did not cause movement directly.

Commands to move the eyes are generated in a similar set of circuits comprising the **frontal eye fields** in the cortex and the superior colliculus in the midbrain, which then project to the brainstem reticular formation, which organizes and coordinates activation of the extraocular muscles by lower motor neurons in the brainstem (as discussed earlier). These and other observations are all consistent with the idea that higher motor centers, including the primary motor cortex and the frontal eye fields, provide both motor command signals that engage lower-level circuits to produce coordinated movements and signals that indicate, to some degree, how forceful these movements should be. That is, these upper motor neurons specify both what to do and how to do it.

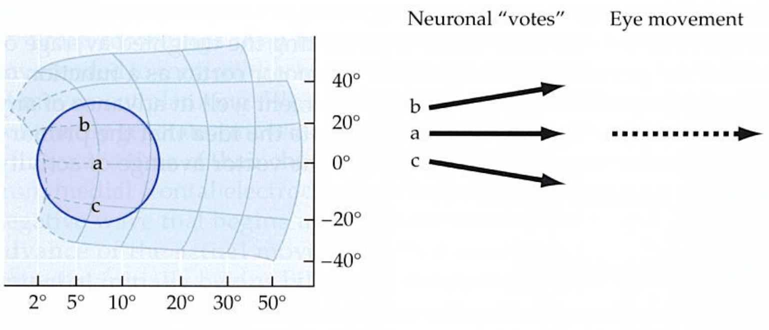
Coding Movements by the Activity of Neuronal Populations

The motor maps discussed in the previous section are essentially gross anatomical descriptions of how the motor system is organized, but how these maps are related to coordinated movements is not entirely clear. The relatively coarse tuning of neurons in the primary motor cortex and other higher movement centers presents a problem for understanding how the brain generates a particular movement. Although the work described in the previous section provided evidence that maps specify movements, the direction and amplitude of a movement cannot be predicted with any precision from the activity of single neurons, which are often activated during a wide array of different movements.

One solution to this problem is the idea that the activity of hundreds or perhaps thousands of neurons is averaged in computing the desired movement. Early work focused on maps of eye movements because the oculomotor system, by virtue of its simplicity, is a useful model for sorting out the principles governing more complex movements. Movements of the eyes are also under the control of higher movement centers, although the organization of these pathways is distinct from that of higher pathways that control limb movements.

The study of eye movements is facilitated by the fact that the local circuits in the brainstem coordinating eye movements are under the direct control of neurons in the **superior colliculus**, an easily accessible layered structure in the midbrain. Electrical stimulation in the intermediate and deep layers of the superior colliculus in monkeys produces coordinated gaze shifts, and single neurons in these layers fire action potentials just before the rapid, ballistic eye movements known as **saccades** begin (Figure 5.10A). Moreover, electrical stimulation at any site evokes a saccade with a particular direction and

(A) Normal



(B) Inactivated

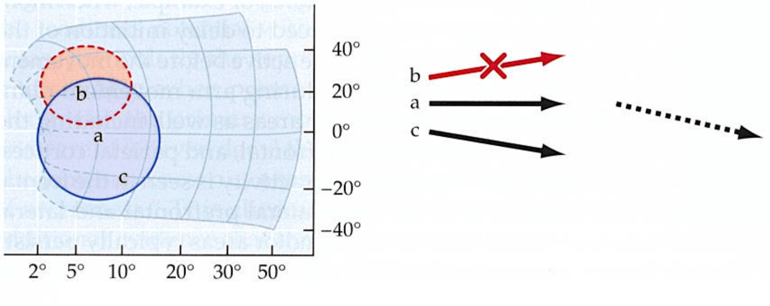


Figure 5.10 Population coding (A) Topographical map showing eye movements in the superior colliculus. Movement amplitude is coded in increasing steps from left to right, and movement direction is coded on the vertical axis. The light purple region is the zone of neurons activated preceding a movement 5 degrees to the right of the zone marked "a." (B) Pharmacological inactivation of the zone centered on "b" (red circle) in a monkey results in a shift in the weighted average of collicular activity, as well as the endpoint of the eye movement. (After Lee et al. 1988.)

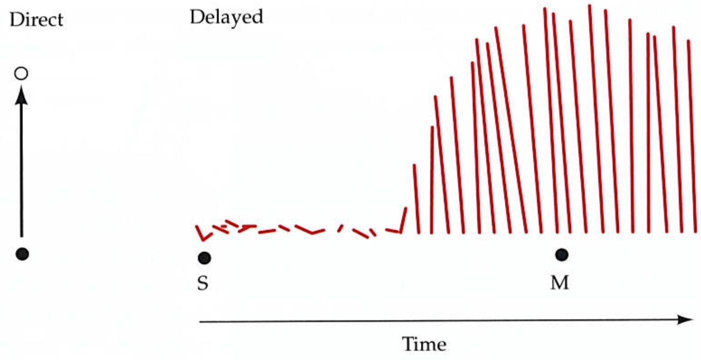


Figure 5.11 Population vectors in the primary motor cortex Each line indicates the direction and amplitude of an arm movement decoded from the activity of a population of neurons recorded in the primary motor cortex. The time of the trials proceeds from bottom to top; S indicates the cue for movement, and M indicates the onset of movement. Movement in direct response to a cue results in immediate generation of a population vector specifying the movement. Delayed movement evokes a population vector specifying the movement hundreds of milliseconds before movement onset. (After Georgopolous et al. 1986.)

amplitude, whereas stimulation at nearby sites evokes saccades with slightly different vectors. Thus, the superior colliculus contains a topographical map of eye movements, much like the topographical maps of skeletal movements in the primary motor cortex (see Figure 5.7A).

Each superior colliculus neuron is thought to vote for its range of movements, with the weight of the vote cast determined by how strongly the neuron fired. The weighted votes would then be averaged across the population to arrive at the vector for the desired movement. To test this idea, small portions of the map of eye movements in the superior colliculus were reversibly inactivated in monkeys trained to look toward visual targets for fruit juice rewards. Following inactivation, eye movements were systematically biased away from the inactivated portion of the collicular map, as would be expected if movements were specified by the weighted average of the activity of all the neurons in the superior colliculus (**Figure 5.10B**). This experiment provided the first functional support for the notion that the brain achieves precise movements by averaging together the activation of large populations of coarsely tuned neurons.

The idea that precise movements are encoded by averaging the activity of many coarsely tuned neurons has been extended to the primary motor cortex. Neurons in the primary motor cortex are broadly tuned to generate a range of movement directions and amplitudes, firing strongly for some movements but weakly or not at all for others. A vector representing the weighted average of activity across the population of neurons in the motor cortex as a function of time (**Figure 5.11**) specifies the impending movement well in advance of any activity in the muscles. This observation supports the idea that the primary motor cortex encodes intended movements by the vector average of activity across the active neuronal population.

Planning Movements

Although many movements are more or less automatic in response to a sensory stimulus, other actions are planned in advance and their initiation held off until the circumstances are appropriate for their execution. For example, when monkeys are cued to reach toward a target but are forced to delay initiation of the reach, neurons in the primary motor cortex become active before the movement is initiated. Anticipatory activation of neurons during arm movement planning has been observed in a number of premotor areas as well, including the premotor, supplementary motor, dorsolateral prefrontal, and parietal cortices.

In the case of visual orienting movements, such activity is seen in the frontal and supplementary eye fields, and in the dorsolateral prefrontal and lateral parietal cortices. Planning-related activity in premotor areas typically persists when movement cues are removed and ceases when monkeys are cued to stop

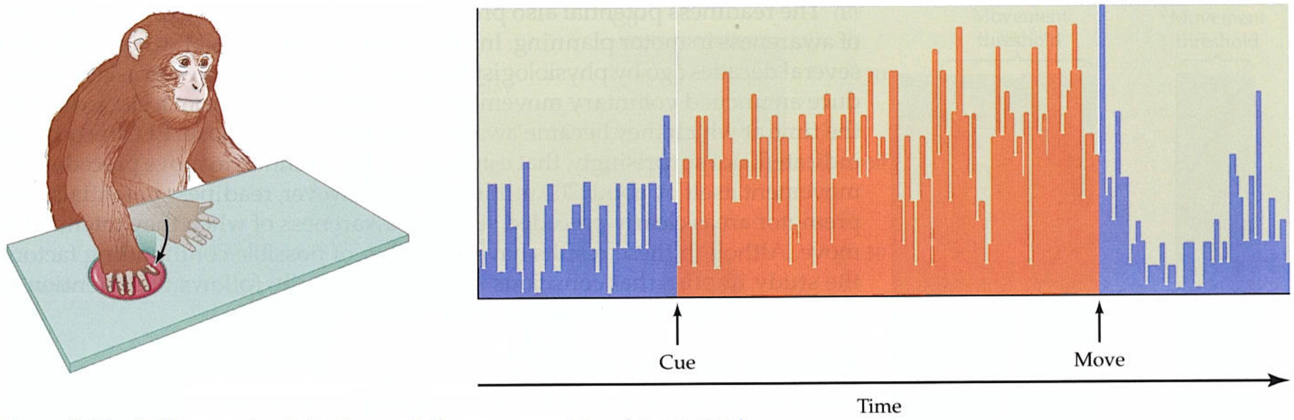


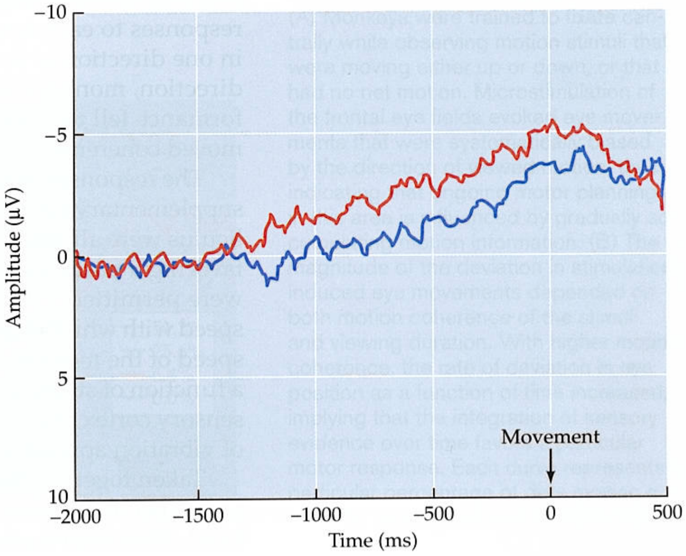
Figure 5.12 Evidence of anticipatory activity as a correlate of movement intention in the premotor cortex The histogram shows neuronal firing as a function of time in a monkey cued to reach toward a target after a delay (red). Neuronal activity continues from the cue until the movement, suggesting a neural correlate of the intention to reach toward the target.

planning the movement, thus suggesting a role in intention (**Figure 5.12**). One indication of the functional role of these premotor areas is that planning-related neuronal activity typically begins even earlier in these areas than in the primary motor cortex (or the superior colliculus for saccades).

These observations support the idea that motor areas are hierarchically organized, with premotor areas providing more abstract planning information related to behavioral goals, which is then translated into the intention to perform specific movements in the primary motor cortex (and the superior colliculus for visual orienting movements). Thus, higher motor areas appear to serve a functional role in specifying the motor program discussed earlier. Motor intention signals in the primary motor cortex are then translated by downstream local circuits in the brainstem and spinal cord into neural activity that specifies the patterns of muscle contraction necessary to accomplish the intended movements.

Scalp recordings from humans (see Chapter 2) have tended to confirm this hierarchical organization of movement planning. When subjects are asked to voluntarily generate a movement—for example, lifting a finger at a time of their choosing—EEG recordings from medial frontal electrodes show a pronounced negative wave that begins up to several seconds in advance of the actual movement. This **readiness potential** initially begins bilaterally over premotor areas, but later it becomes enhanced over the primary motor cortex contralateral to the finger movement (**Figure 5.13**). Neuroimaging studies have identified the readiness potential with activation in premotor areas, particularly the supplementary motor areas. Interestingly, when premotor areas are damaged along with the primary motor cortex, patients are unaware of (or even deny) their inability to move—a phenomenon known as **anosognosia**, meaning "loss of awareness." This clinical observation provides additional evidence that the premotor cortex is the source of motor planning and intentional awareness.

Figure 5.13 Readiness potential These EEG recordings were taken from scalp electrodes over premotor and supplementary motor cortices in human subjects asked to voluntarily move a finger. EEG amplitude when subjects attend to their own movement (blue) increases several seconds in advance of the actual movement. EEG amplitude when subjects attend to the urge to move–the readiness potential (red)–is enhanced relative to the movement potential. Readiness potentials begin later in the contralateral primary motor cortex, consistent with a hierarchical progression of motor intention. (After Eagleman 2004.)



The readiness potential also provides a means of further exploring the role of awareness in motor planning. In a famous but controversial study conducted several decades ago by physiologist Benjamin Libet, subjects were asked to produce an uncued voluntary movement and then estimate (from a clock display) the time at which they became aware of the intention to move. EEG recordings indicated, not surprisingly, that estimates of the intention to move preceded the movement itself by about 200 milliseconds. However, readiness potentials over premotor areas clearly preceded subjects' awareness of when they intended to move. Although these results have a number of possible confounding factors, the study implies that conscious awareness actually follows the intention to move rather than preceding and thus causing it.

Selecting goals for action

At any given moment, several competing or alternative behavioral goals might be options for motor planning. For example, on approaching a stoplight that just turned yellow, a driver might either slow to stop, or accelerate to get through the intersection before the light turns red. The neural processes responsible for selecting a course of action to reach a goal (e.g., getting to the destination faster) and generating the relevant movement have come under increasing scrutiny as researchers have realized the importance of cognitive contexts for motor behaviors. Most such studies have focused on the processes that link sensory information to motor output.

Early electrophysiological studies in monkeys demonstrated that neurons in a variety of premotor areas where planning-related activity occurs respond to sensory cues used to guide movements. Moreover, these responses to sensory cues can be enhanced or diminished if the stimulus is made more or less likely to be the target of a movement. Subsequent work showed that such sensory-motor linkage is graded by the quality of information guiding the movement integrated over time. For instance, neurophysiologists William Newsome and Michael Shadlen provided evidence that neuronal responses in a number of premotor areas involved in saccadic eye movements are systematically related to the weight of sensory evidence favoring a particular movement. In these experiments, monkeys were trained to judge the net direction of motion in a field of moving dots and report this evaluation by shifting their gaze to a specific target if they judged the motion to be in one direction and a different target if they saw motion in the opposite direction (**Figure 5.14A**). Newsome and Shadlen systematically manipulated the quality of the evidence favoring responses to each target by changing the fraction of dots moving coherently in one direction or another. When about 50 percent of the dots moved in one direction, monkeys were nearly always correct in their responses; their performance fell to chance levels, however, when less than 5 percent of the dots moved coherently.

The responses of neurons in the posterior parietal cortex, frontal eye fields, supplementary eye fields, dorsolateral prefrontal cortex, and even superior colliculus were all found to be modulated by the strength of the motion stimulus favoring a particular eye movement response (**Figure 5.14B**). When monkeys were permitted to move their eyes as soon as they had made a decision, the speed with which neuronal activity in the parietal cortex increased matched the speed of the monkeys' eye movement responses. Similar graded responses as a function of stimulus quality have been reported in the higher-order somatosensory cortex and premotor areas in monkeys trained to report the frequency of vibration applied to the forearm by pushing a button.

Taken together, these studies imply that neurons in a number of premotor areas specify movements in a graded manner as sensory evidence is accumulated. This hypothesis was tested directly by applying microstimulation to

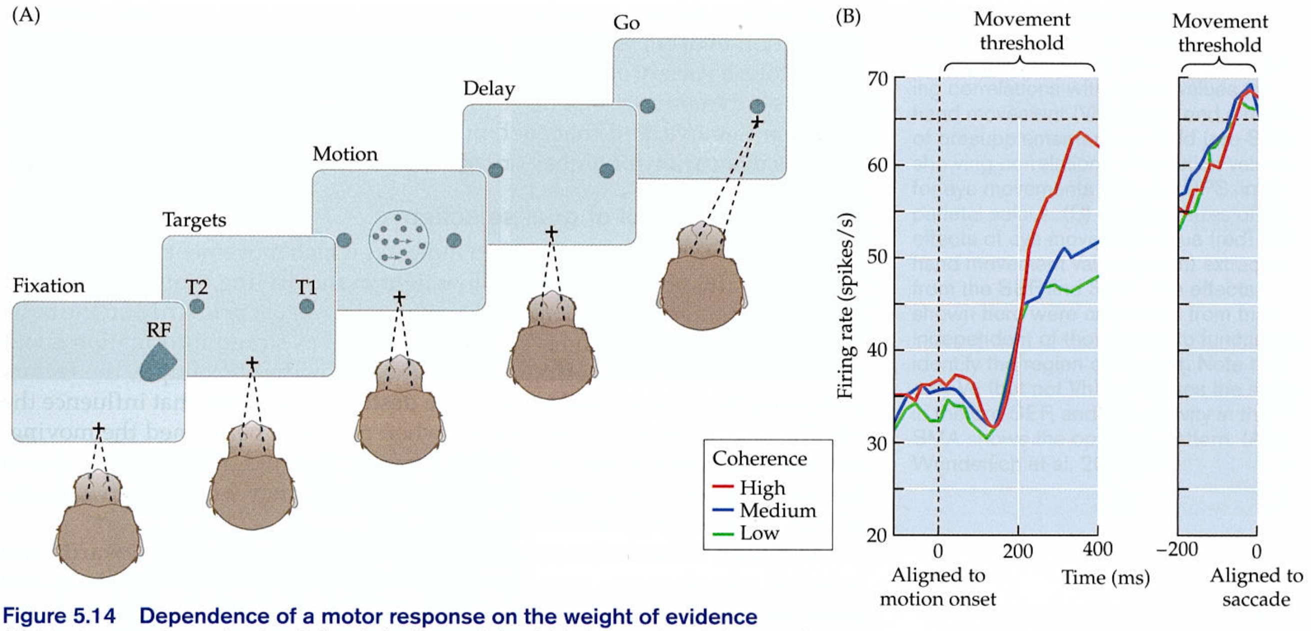


Figure 5.14 Dependence of a motor response on the weight of evidence (A) Monkeys performed a visual discrimination task in which, by moving their eyes, they reported the direction of motion in a field of randomly moving dots. One target was in the response field (RF) of a neuron in the posterior parietal cortex; the other was in the opposite visual field. (B) The firing rate of neurons in posterior parietal cortex increased when monkeys viewed dots moving toward the target in the RF. The rate of increase over time was directly proportional to motion coherence, or the weight of evidence favoring an eye movement to the RF target. The relation between firing rate and motion coherence reflects the integration of motion over time. (After Roitman and Shadlen 2002.)

the frontal eye fields while monkeys performed the dot discrimination task illustrated in Figure 5.14A. Stimulation in this area evoked saccadic eye movements at short latencies, but the endpoints of the movements were systematically biased by the pattern of motion the monkeys saw (**Figure 5.15A**). Moreover, the amount of bias gradually increased as monkeys viewed the motion longer, as well as when the fraction of coherently moving dots was gradually increased (**Figure 5.15B**). When the locations of the movement targets were not revealed

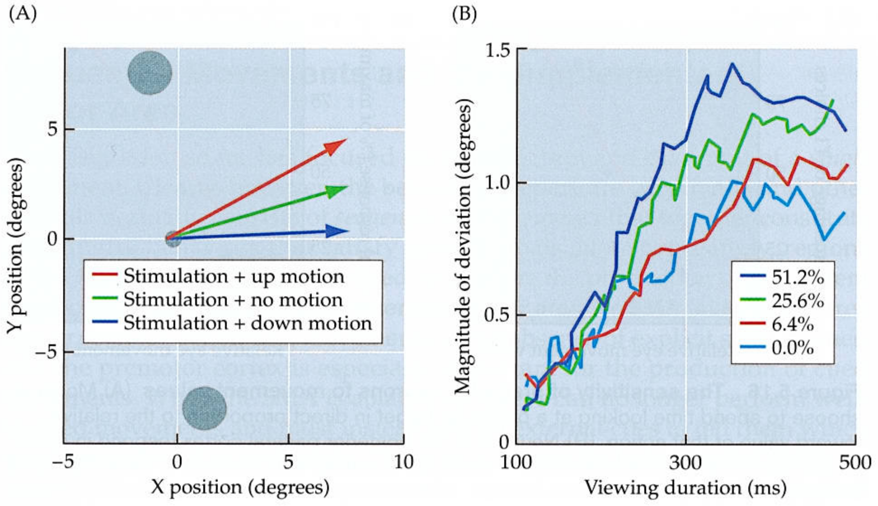


Figure 5.15 Graded conversion of sensory percepts into action (A) Monkeys were trained to fixate centrally while observing motion stimuli that were moving either up or down, or that had no net motion. Microstimulation of the frontal eye fields evoked eye movements that were systematically biased by the direction of viewed motion, thus indicating that ongoing motor planning in this area is influenced by gradually accumulating motion information. (B) The magnitude of the deviation in stimulation-induced eye movements depended on both motion coherence of the stimuli and viewing duration. With higher motion coherence, the rate of deviation in eye position as a function of time increased, implying that the integration of sensory evidence over time favors a particular motor response. Each curve represents a particular percentage of dots moving coherently. (After Gold and Shadlen 2000.)

in advance of the dot stimulus, however, dot motion had very little effect on stimulation-evoked saccades.

All told, a variety of observations support the conclusion that motor preparation is a dynamic, competitive process linking sensory information to the intention to move, and that such processing entails the graded activation of neurons in a variety of higher-order premotor cortical (and subcortical) areas.

Motivational control of goal selection

Although sensory stimulation often indicates which movement should be produced (e.g., the response to the yellow light in the driving example described in the previous section), people must often select a goal primarily on the basis of additional, far more complex stimuli, as well as stored information about the likely state of the environment (in the yellow-light example, the factors indicating the relative need to get to the destination quickly that influence the significance of the stimulus). Indeed, when monkeys performed the moving-dot task illustrated in Figure 5.14, they reported their judgments not because of the stimulus per se, but because if they responded, they would receive squirts of fruit juice—highly desirable treats.

Although behavior is typically directed toward acquiring rewards and avoiding punishments, very little is understood about the mechanisms that guide the motor system to select goals that satisfy such biological motivations. This question was tackled directly in a series of studies by neurobiologists Paul Glimcher and Michael Platt designed to understand how internal motivations shape the responses of neurons in the posterior parietal cortex (**Figure 5.16**). They trained monkeys to choose between looking at two visually identical lights and then, across a series of trials, systematically varied either the probability or the amount of fruit juice reinforcement the monkeys received for looking at one light versus the other. Platt and Glimcher found that neurons in the posterior parietal cortex were sensitive to the **reward value** of shifting gaze to a particular target, which depended on both the probability and the magnitude of the juice reward associated with that target.

Neurons in a number of premotor areas, including the dorsolateral prefrontal cortex, supplementary eye fields, frontal eye fields, and posterior cingulate cortex have also been found to be sensitive to movement value. Further, fMRI studies of people choosing between movements of different value have found similar scaling of activation by movement value. In one study, scientists asked

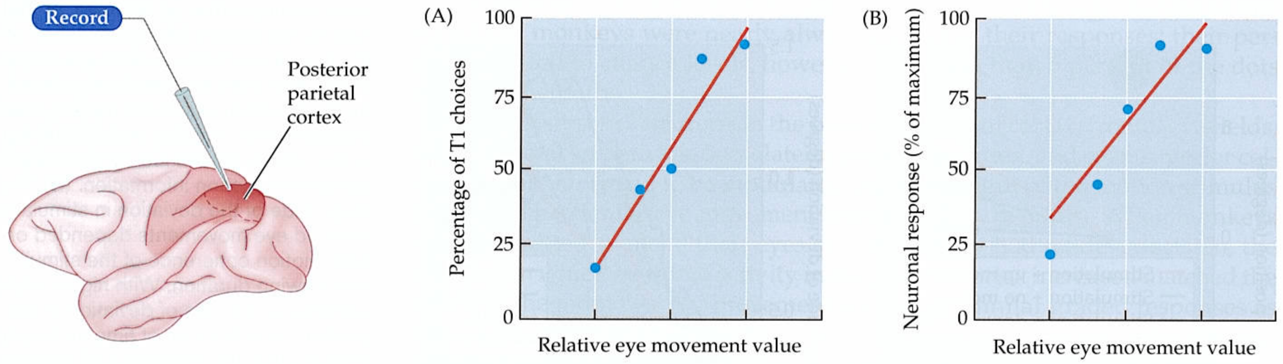


Figure 5.16 The sensitivity of premotor neurons to movement values (A) Monkeys choose to spend time looking at a particular target in direct proportion to the relative reward value of that action. (B) Neurons in the posterior parietal cortex respond in direct proportion to the relative reward value associated with an eye movement. (After Platt and Glimcher 1999.)

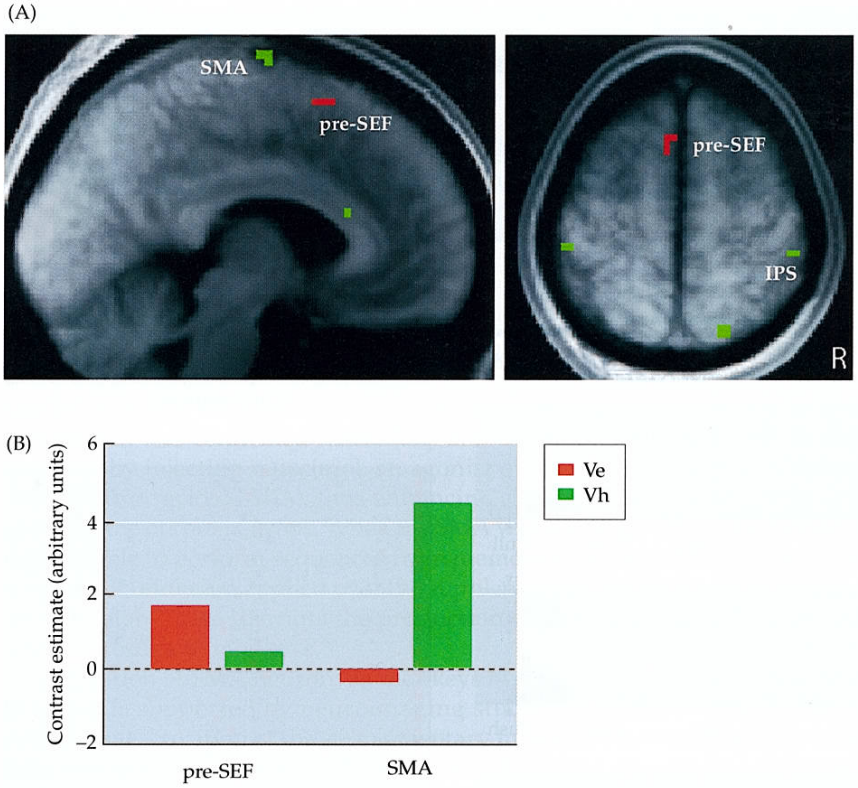


Figure 5.17 Action value signals in the human brain (A) Region of the supplementary motor area (SMA) showing correlations with action values for hand movement (Vh; green) and a region of presupplementary eye field (pre-SEF) showing correlations with action values for eye movements (Ve; red). IPS, intraparietal sulcus. (B) Average sizes of the effects of eye movement value (red) and hand movement value (green) extracted from the SEF and SMA. The effects shown here were calculated from trials independent of those used to functionally identify the region of interest. Note that only Ve (but not Vh) modulates the signal in the pre-SEF, and that activity in the SMA shows the opposite pattern. (After Wunderlich et al. 2009.)

people to choose between an eye movement and a hand movement, each of which varied in value across trials. As expected, people generally tended to choose the more valuable option. Importantly, activity in the supplementary eye field (**Figure 5.17**) tended to vary with the value of the eye movement, whereas activity in the supplementary motor area tended to vary with the value of the hand movement, paralleling the findings from single-neuron recording studies done in monkeys. Together, these studies suggest that selecting a movement goal involves scaling neuronal responses associated with each possible movement by that movement's value, thereby biasing the motor system to produce a movement that best satisfies biological motivations such as acquiring rewards or avoiding punishments.

Sequential Movements and the Supplementary Motor Area

The discussion so far has focused on the selection and planning of a *single* movement. Clearly, however, the behavioral repertoire of humans and other animals normally consists of *sequences* of movements that together constitute meaningful behaviors that satisfy specific goals. Not surprisingly, regions of the frontal cortex are specialized to support the production of movement sequences. As a rule, the **supplementary motor area**, or **SMA** (also called area 6) is crucial for generating movements in the absence of explicit sensory cues, and the premotor cortex is especially important for the production of cued movements. When the SMA is ablated, monkeys can no longer perform well-learned movements and must instead rely on external cues to tell them which movement should be performed. The reverse is true for lesions of the premotor cortex, which selectively disrupt visually guided movements but do not affect

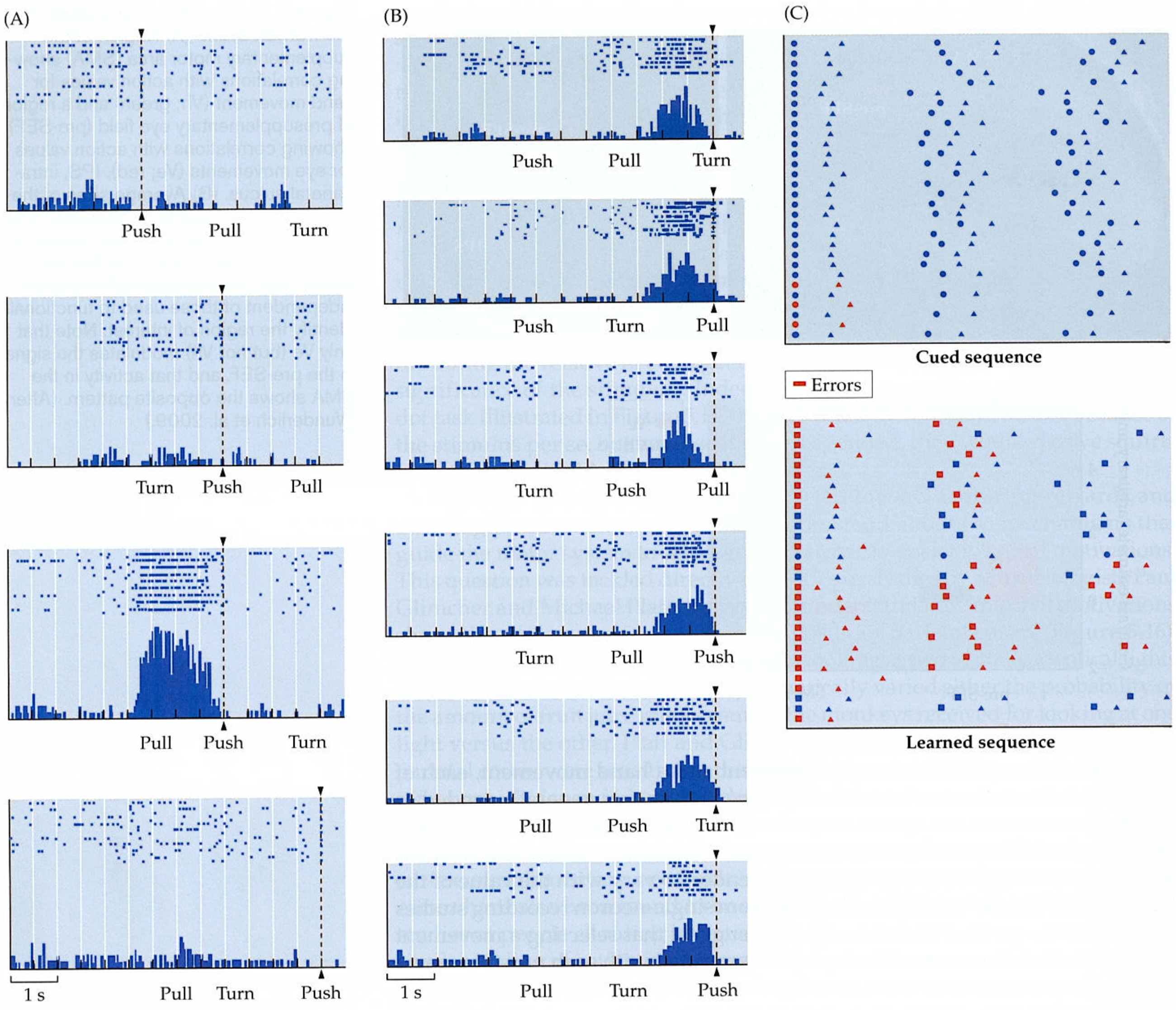


Figure 5.18 Neuronal responses mediating action sequences (A) The SMA neuron recorded here responds selectively to the sequence "pull, push, turn." (B) In this case, the SMA neuron responds selectively to the last movement in a sequence, independent of the type of movement required. (C) Pharmacological inactivation of the SMA causes errors in producing learned sequences but not explicitly cued sequences of movements. (After Tanji and Shima 1994.)

well-learned responses that can be made in the absence of sensory cues. These results suggest a functional dissociation between the premotor cortex and the supplementary cortex for producing cued and uncued movements, respectively.

A similar logic applies to the production of movement sequences, which requires the ability to generate action in the absence of external cues specifying each individual movement. In an important and revealing experiment, physiologist Jun Tanji and colleagues trained monkeys to make a sequence of arm movements based on a visual cue. For example, a red light might mean "push, pull, turn," whereas a green light might mean "turn, push, pull." Note that the visual cues specify which sequence of movements to make rather than cuing any single movement directly. Tanji and his group then recorded from SMA neurons while monkeys performed this sequence generation task.

Tanji's group found that many neurons in the SMA were selectively activated when a particular action embedded within a sequence was performed (**Figure 5.18A**). Moreover, many neurons responded only for a particular action sequence, irrespective of the type of movement (**Figure 5.18B**). For example, some neurons

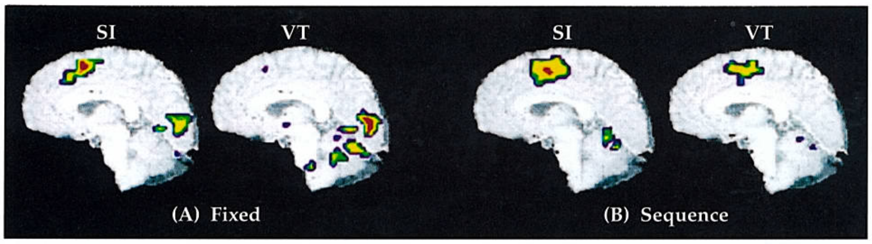


Figure 5.19 Activation of the human supplementary motor cortex when subjects intentionally generate sequences of finger movements These fMRI data were gathered from a single human subject asked to repeatedly touch index finger to thumb (A) or to generate a learned sequence of finger-to-thumb movements (B), cued either internally (SI) or by a visual stimulus (VT). (From Deiber et al. 1999.)

responded to the second movement in the sequence, whereas others responded to the third. These observations suggest that SMA neurons convey information needed to guide the production of a sequence of reaching movements. This supposition was confirmed when Tanji and colleagues reversibly deactivated the SMA by injecting muscimol, an agonist of the neurotransmitter gamma-aminobutyric acid (GABA), thus enhancing local inhibitory connections and silencing the output neurons. When the SMA was silenced in this way, monkeys were unable to perform sequences from memory (**Figure 5.18C**). Transcranial magnetic stimulation applied over the supplementary motor cortex in humans (see Chapter 2) also disrupts the production of manual sequences, in accord with the results in monkeys.

Activation of SMA neurons in monkeys by internally generated sequences of action is supported by neuroimaging studies in humans demonstrating preferential activation of the supplementary motor cortex during self-initiated finger movements, compared with visually triggered movements. Moreover, such modulations were even stronger when subjects generated sequences of movements rather than repeating the same movement over and over (**Figure 5.19**). Together, these observations support the conclusion that the supplementary motor area provides relatively abstract motor intention signals that control the internally guided production of sequences of actions, whereas the prefrontal cortex plays a more important role in the initiation and termination of movement sequences. The primary motor cortex then issues sequences of commands that activate pools of motor units in the brainstem and spinal cord to produce the desired movements.

Sensory-Motor Coordination

Another key issue in understanding motor control concerns the transformations needed to translate spatial and textural information gleaned from sensory inputs into appropriate motor commands. For example, shifting gaze to a visual target is a relatively trivial computational problem, mainly because the vector representing the locus of retinal stimulation relative to the fovea is aligned with the vector representing the amplitude and direction of an eye movement that directs the fovea to the target. This happy marriage of sensory and motor coordinates does not, however, apply to other sensory-guided movements. Thus, reaching toward a visible target such as a cup of coffee requires translating the retinal location of the target into a location anchored to the position of the hand.

To do this, the retinal vector must in some way be combined with information about the position of the eye in the head, the head's position with respect to the rest of the body, and the hand and arm relative to everything else. Similarly complex coordinate transformations are needed in order to look accurately in the direction of an auditory stimulus, scratch an itch, walk to a geographically challenging destination, or undertake innumerable other routine challenges that require translations from one or more frameworks to another. Thus, in

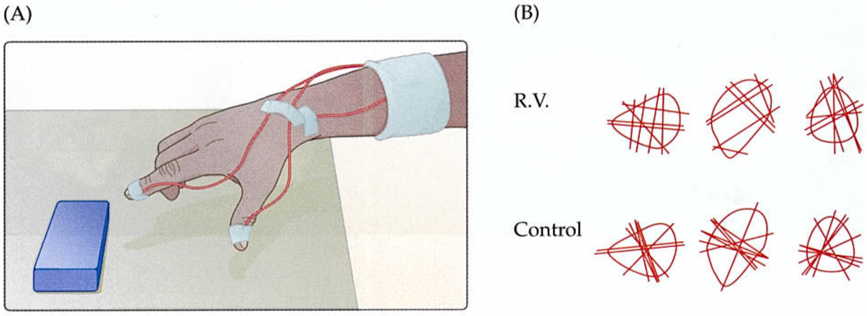


Figure 5.20 Deficits in visually guided reaching and grasping caused by parietal lesions (A) The reaching and grasping of objects is measured by electrodes hooked up to the subject's finger, thumb, and wrist. (B) Lines connect the precision grip made with thumb and forefinger for a patient with parietal lesion (R.V.) and a control subject. The optimal grasp crosses the center of mass of the object. (A after Goodale, http://psychology.uwo.ca/faculty/goodale/research/index.html; B after Milner and Goodale 1995.)

addition to selecting, planning, and initiating movements, neural mechanisms must use sensory information to compute the appropriate spatial coordinates for guiding movements.

Several lines of evidence suggest that the parietal cortex is crucial for sensory-motor coordination. In partial support of this idea, damage to the parietal cortex in humans can disrupt both reaching and saccades—a clinical syndrome known as **optic ataxia**. The spatial errors that arise from this condition reveal a failure to correctly integrate information about the locations of the eye, hand, and target. Disruptions in sensory-motor integration are also manifest when patients with parietal lesions attempt to grasp objects (**Figure 5.20**). Compared to control subjects without lesions, such patients fail to grasp objects accurately across their centers of mass. These errors invariably lead to difficulties in actually picking up objects—a deficit also found in monkeys following pharmacological inactivation of the parietal cortex.

The observation of such deficits following parietal damage, along with the observation that damage to the lateral temporal cortex typically disrupts object identification and naming (anosognosia), led neurobiologists Mel Goodale and David Milner to suggest that the dorsal visual stream may be particularly important for using vision to guide movement, whereas the ventral visual stream may be specialized for object identification (see Chapter 3). Endorsing this idea, patients with temporal lobe damage may have difficulty describing the orientation of a mail slot (i.e., vertical or horizontal) but no trouble putting an envelope into it, while patients with parietal damage typically have no trouble naming objects, despite finding it difficult to reach for and grasp them.

In sum, lesion data from human patients support the idea that the parietal cortex is a critical locus for the integration of visual, eye position, and limb position data necessary to produce coordinated movements of the eyes and hands. Note, however, that complex computations like transforming retinal coordinates into object-centered coordinates may not be made explicitly. Because the circuitry that enables complex motor behavior has evolved simply to associate complex inputs with complex outputs on the basis of evolutionary success, neuronal computations such as those underlying coordinate transformations may never be understood explicitly.

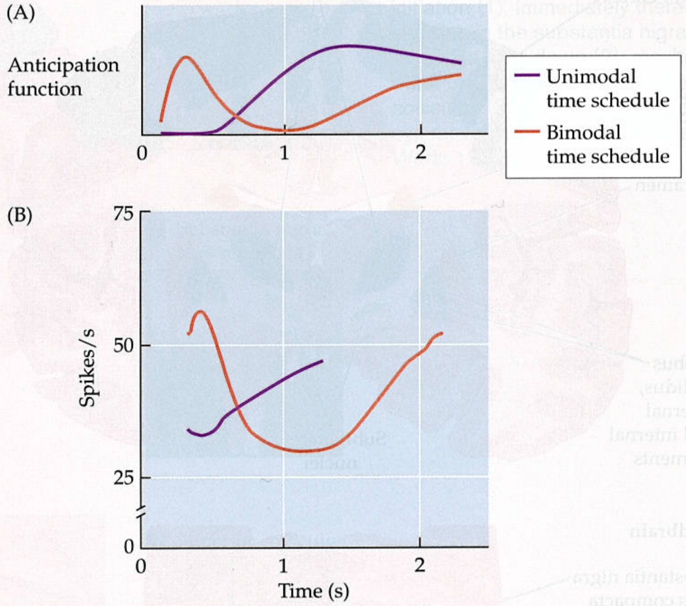
Initiation of Movement by the Basal Ganglia

The motor cortex (and for eye movements, the superior colliculus) comprises a more or less hierarchical set of circuits responsible for selecting, planning, and initiating sequences of movements that satisfy goals. At the same time, an important set of subcortical circuits in the **basal ganglia** appears to serve as a **gating** mechanism, inhibiting potential movements until they are fully

BOX 5C MOTOR SYSTEMS AND INTERVAL TIMING

In addition to the overall ability of the brain to adjust numerous functions to daily cycles of light and dark, it is essential for humans and other animals to keep time on much shorter scales, allowing them to anticipate predictable events that have biologically important consequences. Interval timing is the ability to keep track of time on the order of seconds to minutes, and nearly all aspects of human behavior require this sort of temporal judgment. Changing lanes on a highway, catching a ball, cooking an omelet, playing a musical instrument, and telling a joke all require accurate tracking of temporal intervals.

The dependency of such behaviors on timing suggests an intimate relationship between the initiation and coordination of action and the sense of time. In fact, interval timing appears to depend on neural circuits involved in the coordination and initiation of action, including the basal ganglia and its inputs from prefrontal cortex, and the cerebellum. For example, lesions of the basal ganglia (the substantia nigra, caudate, and putamen in particular) disrupt the ability of rats to reproduce temporal intervals by pressing a bar. Further, patients with damage to the basal ganglia (e.g., in Huntington's or Parkinson's disease) show increased variability in timing tasks in both millisecond and second ranges. Endorsing a role for basal ganglia function in interval timing is the observation that dopaminergic drugs systematically speed up or slow down the sense of the passage of time, as revealed by the behavior of humans or rats instructed to reproduce elapsed temporal intervals. Other brain regions involved in motor coordination also appear to be involved in timing. Patients with cerebellar damage perform various time production and discrimination tasks poorly when they receive no feedback about the accuracy of their responses.



Timing signals in evolving motor commands. Monkeys waited for a "go" cue to initiate a saccadic eye movement to a target to receive a juice reward. In separate blocks of trials, the "go" signal was either unimodally distributed or bimodally distributed in time. (A) Behavioral anticipation functions computed from reaction times for the unimodal (purple) and the bimodal (red) time schedule, demonstrating that monkeys had an internal sense of when movements were most likely to be requested. (B) Average neural activity recorded during waiting period for the "go" signal under the bimodal (red) and the unimodal (purple) time schedule. (After Janssen and Shadlen 2005.)

The close link between timing and motor behavior is also evident in the buildup of activity in neurons in the lateral intraparietal area (LIP) when monkeys plan a saccadic eye movement at a specific time. LIP neurons typically ramp up their activity in anticipation of movement initiation, reaching a peak just at movement onset (Figure A). When monkeys are confronted with different temporal dependencies, or hazard rates, between the onset of cues specifying where and when to move, the buildup of activity in LIP neurons anticipates the "go" cue, thus betraying the monkey's sense of elapsing time (Figure B). Such signals may be critical for initiating ballistic movements under time pressure—whether catching an insect to eat, swinging at a 90-mile-per-hour fastball, or flatpicking a guitar. Together, the behavioral and neurobiological evidence suggests that motor systems take advantage of the temporal structure of the environment to anticipate, initiate, and coordinate behavior and, further, that such processes may be responsible for our own subjective sense of time.

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appropriate for the circumstances in which they are to be executed. By helping to coordinate movement timing, the basal ganglia also appear to play an important role in the subjective sense of time (**Box 5C**).

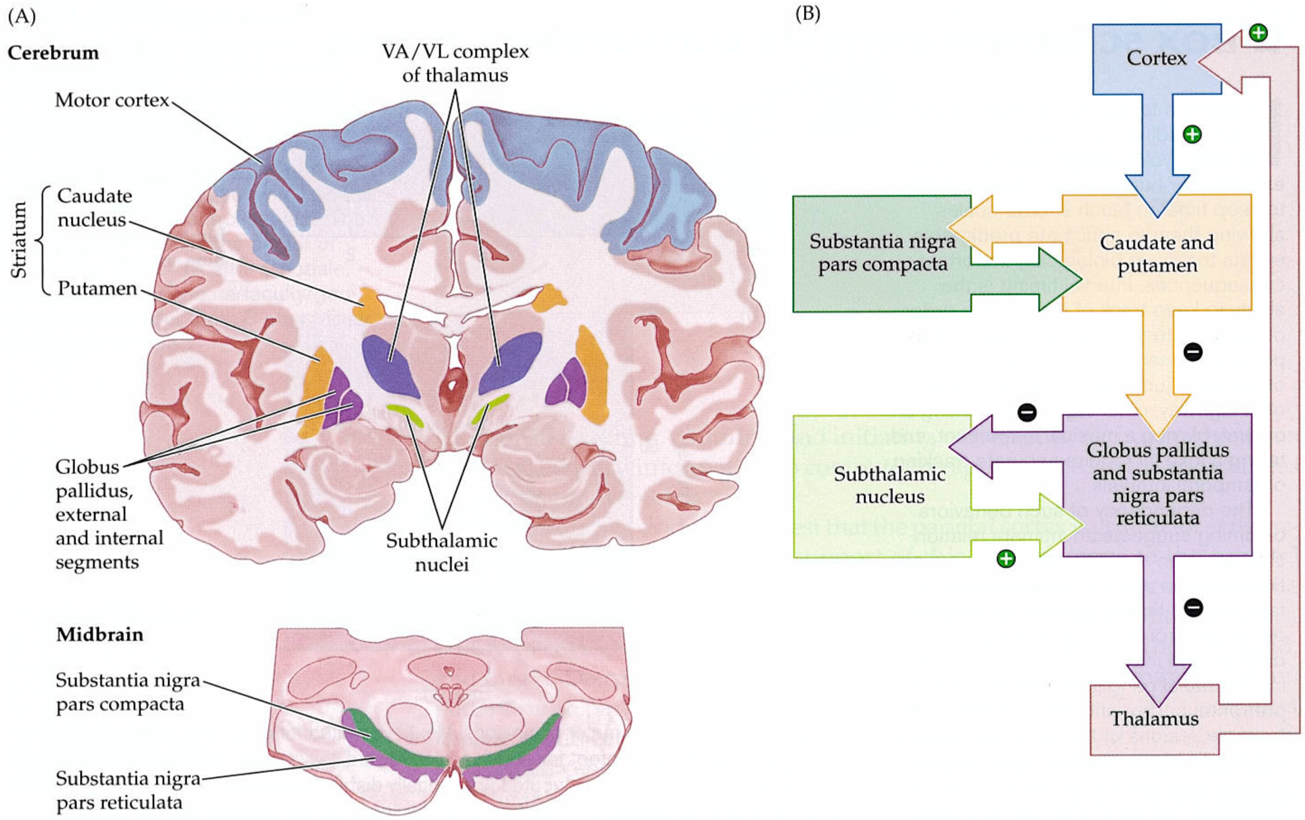

Figure 5.21 The basal ganglia loop that starts and stops movements (A) Coronal section through the human forebrain showing the principal components of the basal ganglia. The caudate and putamen (orange) are the zones receiving the main inputs to the basal ganglia. The globus pallidus (purple) provides the principal output, which projects to the ventral anterior and ventrolateral (VA/VL) nuclear complex of the thalamus, which in turn projects to the motor cortex. The substantia nigra pars reticulata in the midbrain serves as the output nucleus for the basal ganglia circuits controlling eye movements. (B) Pro-jections from the cortex excite neurons in the caudate and putamen, which then inhibit neurons in the globus pallidus and substantia nigra pars reticulata. This effect suppresses tonic inhibition of the thalamus by the globus pallidus, thereby further exciting the cortex. The substantia nigra pars compacta provides modulatory dopaminergic inputs to the basal ganglia, and a circuit through the subthalamic nucleus serves a secondary role in releasing movement.

The basal ganglia are made up of three principal nuclei: the **caudate** and **putamen** (known collectively as the **striatum**), and the **globus pallidus** (Figure 5.21A). In addition, two other nuclei—the subthalamic nucleus and the substantia nigra pars compacta—make important contributions to basal ganglia function. Nearly all cortical areas project to the basal ganglia, principally through the caudate and putamen. The globus pallidus is the output nucleus of the basal ganglia and modulates the activity of cortical neurons via a relay through the thalamus. Activation of the caudate and putamen inhibits the globus pallidus, thereby releasing the thalamus and its cortical targets from tonic inhibition (Figure 5.21B). The net effect of basal ganglia activation is thus excitation of cortical neurons. The balance of excitatory and inhibitory effects of the basal ganglia releases and coordinates desired movements. Circuits projecting through the caudate to the **substantia nigra pars reticulata** (**SNr**) and on to the superior colliculus serve a similar braking function for saccades.

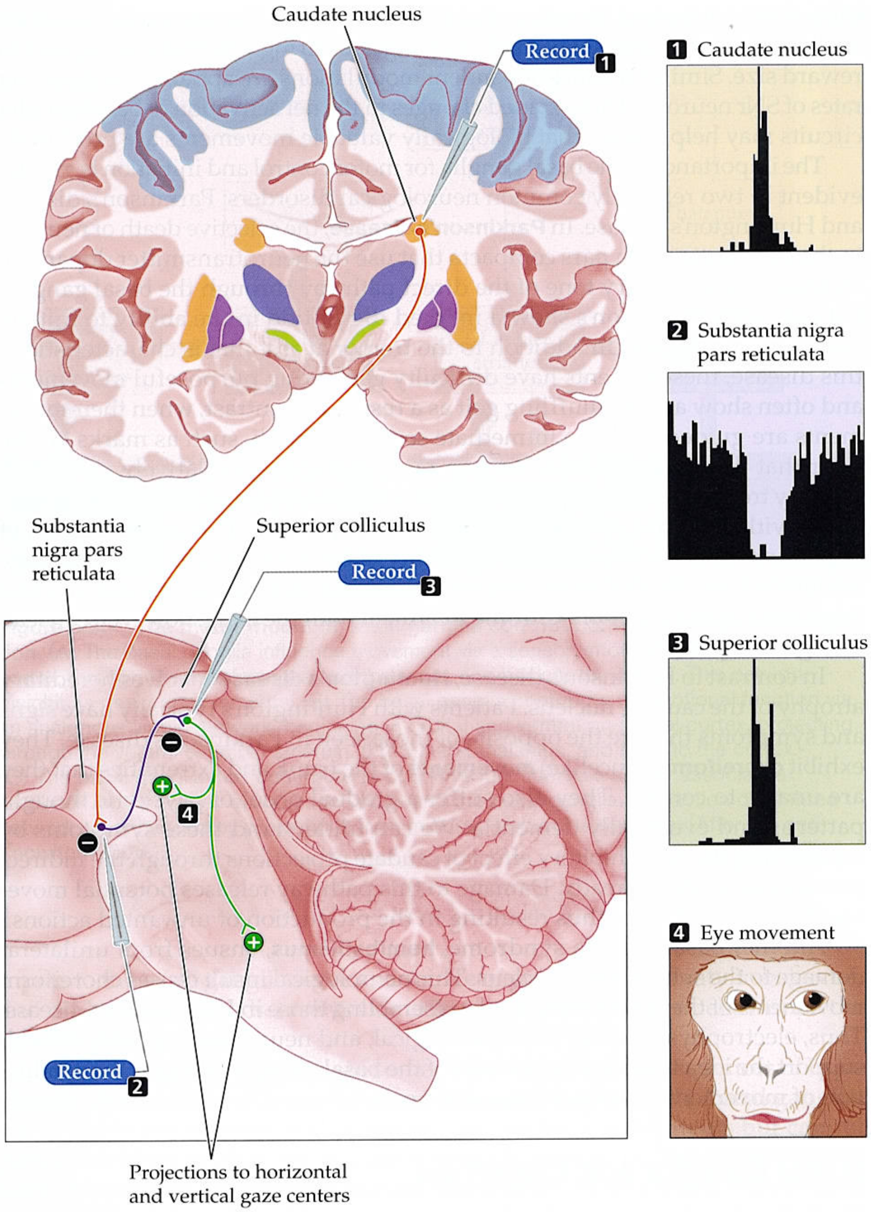

Figure 5.22 The superior colliculus–basal ganglia relationship Neurons in the caudate nucleus fire bursts of action potentials just before eye movement initiation (1). Immediately thereafter, neurons in the substantia nigra pars reticulata shut down (2), resulting in a burst of action potentials in the superior colliculus (3) and the production of an eye movement (4). (After Hikosaka and Wurtz 1989.)

The role of the basal ganglia in movement inhibition and initiation has been examined directly in monkeys trained to make eye movements to visible and remembered targets while recording from neurons in the SNr, the analogue of the globus pallidus output circuit for eye movements. In one study, SNr neurons fired tonically until just before saccade onset, when they abruptly ceased firing for the duration of the movement (Figure 5.22). At about the same time, neurons in the superior colliculus associated with the saccade began firing action potentials.

When the superior colliculus is released from tonic inhibition by injection of the GABA agonist muscimol into the SNr, monkeys cannot suppress unwanted saccades. These results indicate that one important function of the basal ganglia is to inhibit undesired movements and permit desired ones. More recent work, however, has suggested that this "braking function" is not all or none. When the rewards delivered for successful saccade performance are varied, neurons in the caudate nucleus show graded changes in firing rate that correspond to reward size. Similar reward-dependent modulations are apparent in the firing rates of SNr neurons. Thus, graded changes in the net activation of basal ganglia circuits may help ensure that biologically valuable movements are produced.

The importance of the basal ganglia for motor control and initiation is vividly evident in two relatively common neurological disorders: Parkinson's disease and Huntington's disease. In **Parkinson's disease**, the selective death of neurons in the substantia nigra pars compacta that use the neurotransmitter dopamine increases the excitatory tone of the direct pathway through the basal ganglia. Patients with Parkinson's show a marked disruption in the ability to initiate voluntary movement. In addition to the tremor at rest that is characteristic of this disease, these patients have difficulty generating purposeful movements and often show a slow, shuffling gait as a result. By contrast, when their movements are guided by more immediate sensory stimuli, such as marks on the floor that the patient is asked to step over, gait appears relatively normal. A primary treatment for Parkinson's disease remains supplementation of dopamine levels with L-dopa, a synthetic precursor to dopamine. This augmentation of dopamine function helps restore the ability of the basal ganglia to release tonic inhibition from the thalamus, thereby enhancing motor cortex excitability and improving motor function. Chronic treatment with the drug, however, can lead to cognitive problems.

In contrast to Parkinson's disease, **Huntington's disease** involves hereditary atrophy of the caudate nucleus. Patients with Huntington's typically have signs and symptoms that are the opposite of those seen in Parkinson's disease. They exhibit **choreiform** (dancelike) **movements** of the trunk and extremities that they are unable to control. They also suffer a gradual onset of psychotic thought patterns and eventually dementia. We can understand these symptoms by considering the net inhibitory effect of caudate projections through the indirect pathway described already. Damage to this pathway releases potential movements from inhibition, thus resulting in the production of unwanted actions.

Another basal ganglia syndrome, **hemiballismus**, ensues from unilateral damage to the subthalamic nucleus. This neurological insult causes choreiform movements of the contralateral limbs resembling those in Huntington's disease. Thus, electrophysiological, pharmacological, and neurological patient data all support the idea that a main function of the basal ganglia is to gate the production of movements directed to specific goals.

Basal Ganglia and Cognition

The motor deficits associated with basal ganglia dysfunction, tragically evident in Parkinson's and Huntington's diseases, lead inexorably to the conclusion that these structures play a critical role in gating movement. Some of the problems with these diseases and their treatment, however, seem explicitly cognitive, and recent neurophysiological and neuroimaging findings appear to confirm this implication. Anatomical studies have also demonstrated the existence of several nonmotor pathways through the basal ganglia, including a limbic or emotional channel and an associative or cognitive channel (Figure 5.23).

These separate pathways appear to serve distinct but related functions in emotion and cognition, and these roles are especially prominent in humans and other primates. According to this view, the same principles governing movement disinhibition in the motor pathway apply to emotional or cognitive processing in the limbic and associative channels. Each channel thus comprises a feedback loop beginning in the cortex, projecting through the basal ganglia, and ultimately providing excitatory feedback to the cortex. In this model, cortical

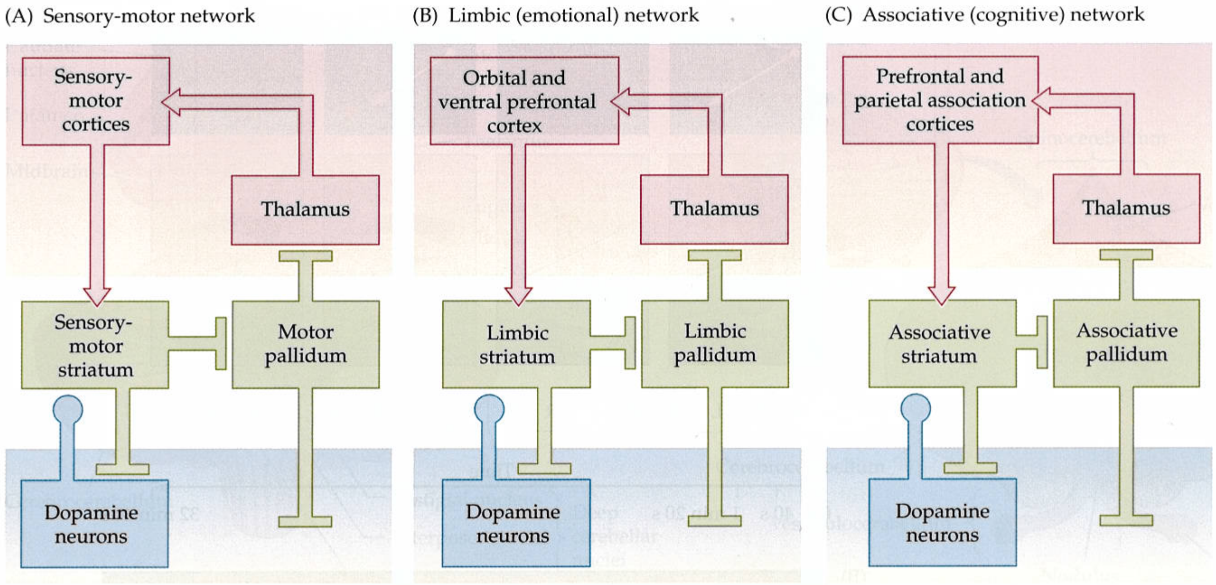

Figure 5.23 The motor model of basal ganglia contributions to emotion and cognition (A) The basal ganglia influence movement via a sensory-motor network from the cortex, through the basal ganglia and thalamus, and back to the cortex. This network disinhibits desired movements. (B) The basal ganglia contribute to emotional function via an analogous limbic network, beginning in orbital and ventral prefrontal cortex, projecting through the ventral or limbic striatum, through the thalamus, and back to the cortex. (C) The basal ganglia may contribute to cognitive function via a similar associative feedback loop between association cortex and the basal ganglia. The action of all three networks is enhanced by projections from midbrain dopamine neurons. (After Yin and Knowlton 2006.)

inputs to the basal ganglia serve as a source of potential variability in behavior, and the basal ganglia themselves contribute to the selection of behavior on the basis of prior outcomes.

This framework helps explain some of the nonmotor consequences of basal ganglia dysfunction. For example, animals with lesions of the basal ganglia, particularly the caudate and putamen, can perform movements but cannot perform or learn new actions to acquire rewards or avoid punishments. Patients with Parkinson's disease, who exhibit diminished basal ganglia functioning because of dopaminergic dysfunction, also show impairments in probabilistic classification tasks that require subjects to make predictions based on a series of cues. Similar impairments in learning and memory follow damage to prefrontal regions projecting to the associative basal ganglia pathway, and, as noted, one of the hallmarks of Huntington's disease is psychotic thought processes. The ability to produce learned sequences of movements is also disrupted in patients with damage to the basal ganglia, and this disruption is evident in both Parkinson's disease and Huntington's disease.

Neuroimaging studies have confirmed that the basal ganglia are activated when human subjects learn new movement sequences. In one typical study, subjects were asked to perform a task in which they were required to manipulate a joystick with the right hand (**Figure 5.24A**). During some blocks of trials, the mapping between the joystick movement and the direction of movement of a target cursor on a computer screen was shifted by 90 degrees. When brain activity was compared between blocks of trials requiring such motor

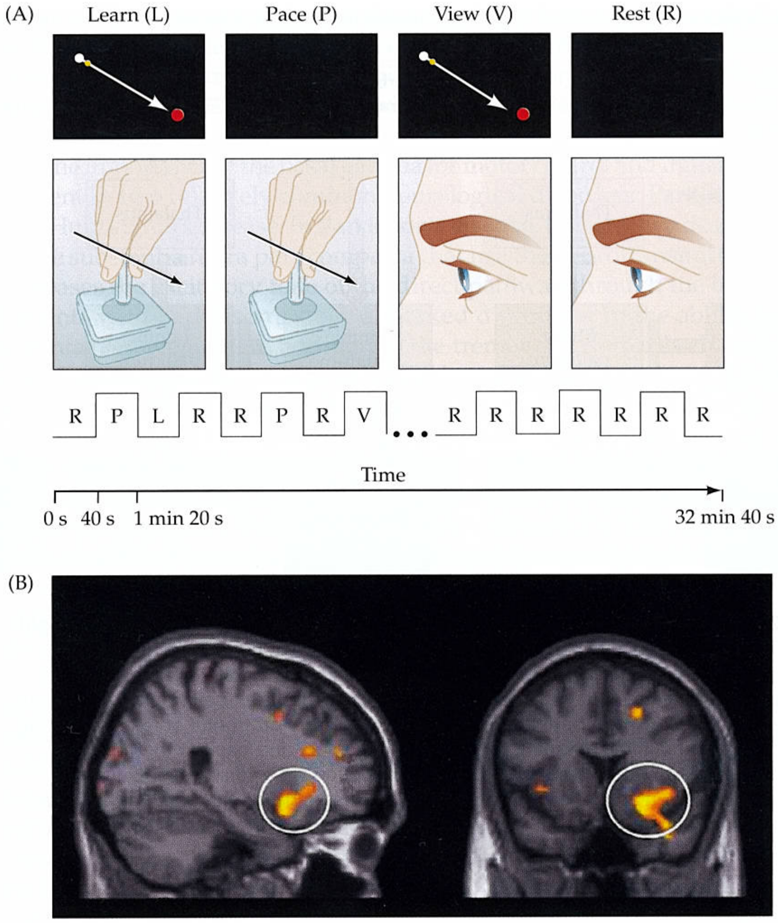

Figure 5.24 The contribution of the basal ganglia to motor learning (A) Human subjects grasped a joystick to move a cursor on a computer screen. In some blocks of trials ("Learn"), the direction of cursor movement and the direction of joystick movement were offset by 90 degrees. In other blocks of trials, subjects simply moved the cursor without feedback ("Pace"), watched the cursor move by itself ("View"), or rested ("Rest"). (B) Functional MRI activation during motor learning was strongest in the putamen (circled). (After Graydon et al. 2005.)

adaptation and blocks of trials in which movements were produced without visual feedback, the putamen was selectively activated (**Figure 5.24B**). These observations, and others like them, endorse the idea that the basal ganglia play a broad role in linking sensory events and motor actions, while also helping to suppress undesirable movements and to initiate movements that satisfy goals.

Neurophysiological studies in animals, as well as neuroimaging in humans, have also demonstrated that basal ganglia neurons are modulated by the anticipation of reward, thus linking this network to the adaptive modification of behavior based on outcomes—the computational basis of reinforcement learning (see Chapters 10 and 14). Such studies also suggest that addictive behavior could reflect the "hijacking" of this basal ganglia system by chemicals that activate receptors associated with reward. Specifically, cue-induced craving could ensue from the unconscious association of environmental cues present during drug consumption with pathological reward modulation of basal ganglia cognitive

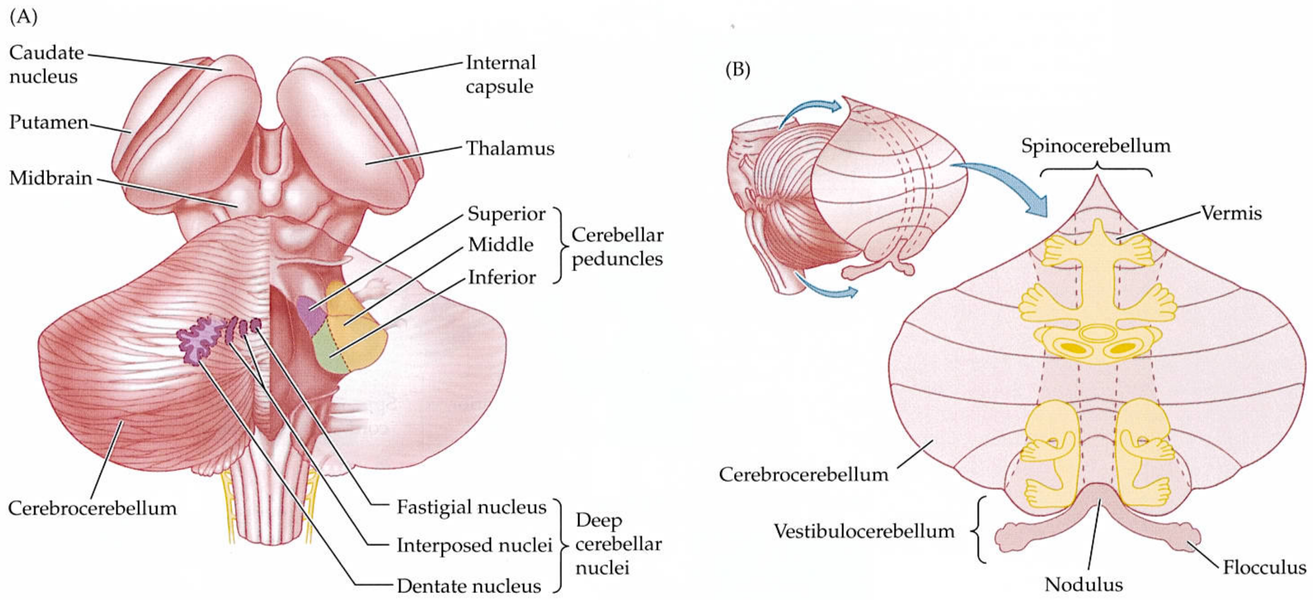

Figure 5.25 Organization of the cerebellum (A) The cerebellum consists of an outer cortex of neurons, deep nuclei, and large fiber tracts, known as *peduncles*, coursing in and out. Inputs to the cerebellum arrive via the middle and superior cerebellar peduncles, and the deep nuclei project out of the cerebellum via the inferior and superior cerebellar peduncles. (B) The cerebellar cortex can be divided into the spinocerebellum, which receives inputs from the spinal cord; the cerebrocerebellum, which receives inputs from the cerebral cortex via the pons; and the vestibulocerebellum, consisting of the flocculus and nodulus, which receives inputs from the vestibular nuclei. The spinocerebellum is organized topographically according to inputs from spinal cord neurons carrying proprioceptive information. In contrast with upper motor neurons of the cortex and basal ganglia, cerebellar circuits mediate movements of the ipsilateral musculature.

pattern generators. In any event, these and other studies hint at the powerful influence of the basal ganglia on a wide range of cognitive behavior.

Error Correction and Motor Coordination by the Cerebellum

Circuits within the brainstem help coordinate lower-level reflex circuits in the spinal cord and brainstem motor nuclei to make the anticipatory postural adjustments needed to accommodate movements, correct posture for ongoing changes in balance, and coordinate more complex multijoint movements. Supplementing the brainstem circuits that mediate these aspects of motor coordination, another specialized set of neural circuitry has evolved to provide additional control of sensory-motor interactions. The key component at the center of this circuitry is the **cerebellum**, a large, foliated structure that sits atop the pons in the brainstem (**Figure 5.25**). The cerebellum is responsible for online error corrections necessary to produce smoothly coordinated, skilled movements.

Exquisitely organized circuits of specialized neurons within the cerebellar cortex (**Figure 5.26A**) appear to compute the net error between ongoing motor commands issued by the motor cortex and the actual movements being produced. These error signals are relayed back to the frontal and parietal cortices via projections from the dentate nucleus (the deep nuclear output structure for

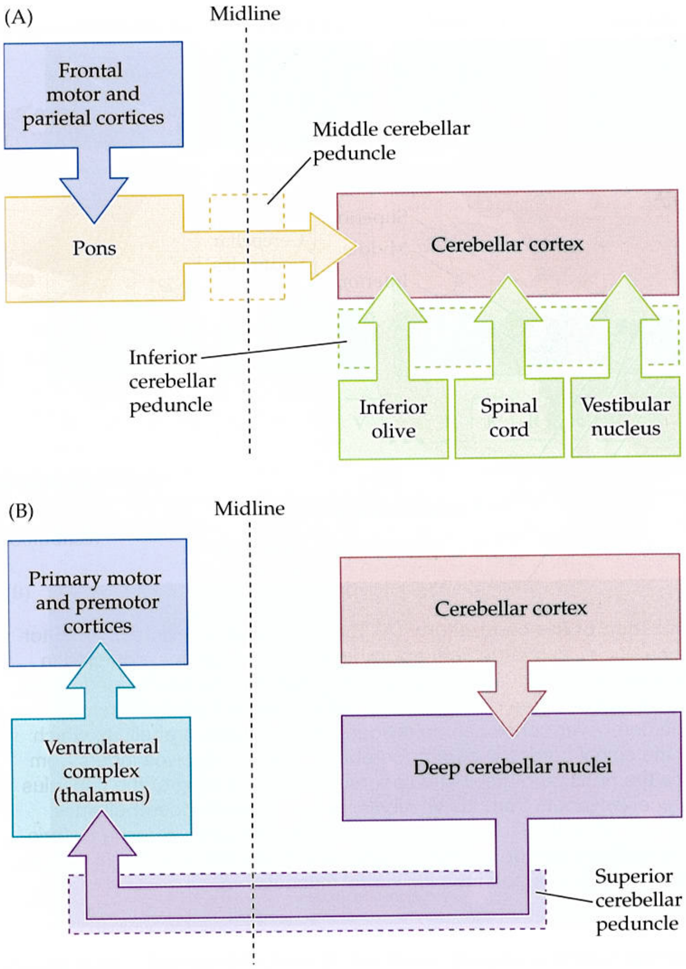

Figure 5.26 Cerebellar inputs and outputs These block diagrams illustrate the inputs (A) and major outputs (B) of the cerebellum.

the cerebrocerebellum) to the ventrolateral complex of the thalamus (**Figure 5.26B**). As a result, damage to the cerebellum causes an inability to perform smooth movements.

Lesions of the medial cerebellar vermis result in a condition known as *truncal ataxia* (uncoordinated, disorganized movement), which is characterized by a wide-based, unsteady gait similar to that of someone who has had too much alcohol to drink. Damage to the lateral cerebellum, on the other hand, disrupts the sensory coordination of limb movements and is known as *appendicular ataxia*. A useful clinical test of appendicular ataxia requires patients to point from their nose to the clinician's finger and back again (**Figure 5.27**). Patients with damage to the ipsilateral cerebellum show halting, uncoordinated movements of the hand and arm; this deficit is called **intention tremor** because it is evident only during voluntary movements. The jerky movements of appendicular ataxia appear to result from disruptions in the normal smooth compensation for ongoing errors in finger trajectory.

The role of the cerebellum in correcting ongoing errors in order to coordinate smooth movement extends to correcting errors during motor learning. In short,

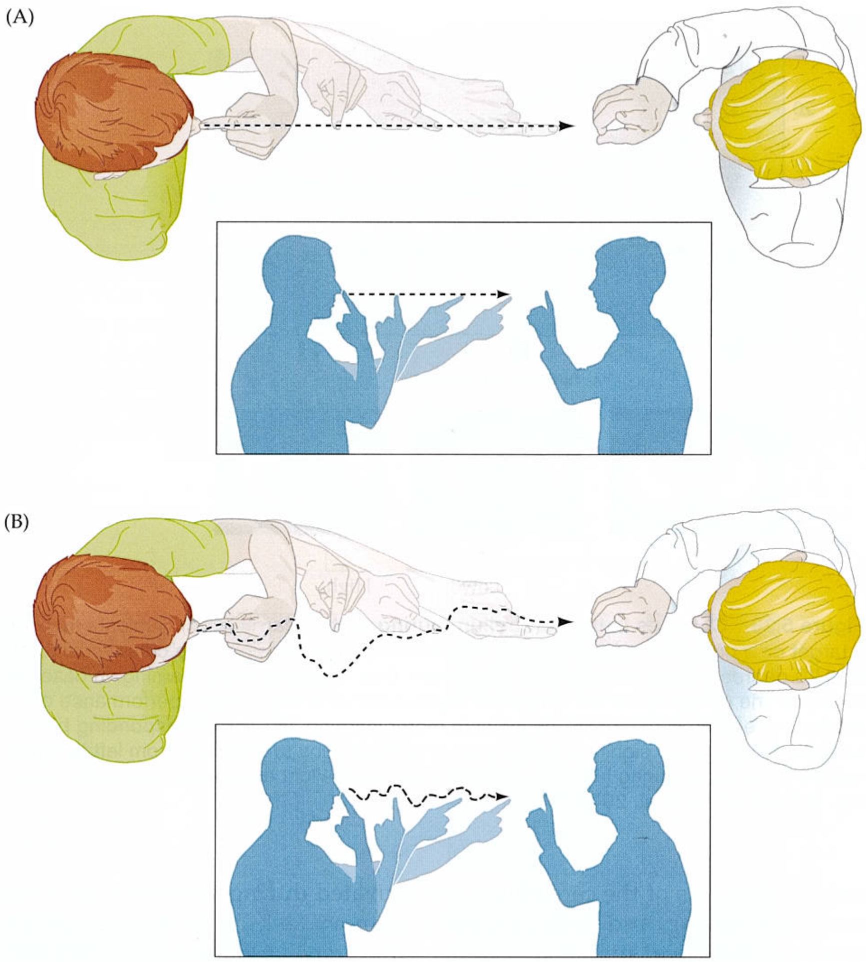

Figure 5.27 **Cerebellar ataxia** Patients are asked to point rapidly from the clinician's finger to their own nose and back again. (A) Normal subjects point smoothly and rapidly from nose to finger and back again. (B) Patients with cerebellar ataxia produce irregular, jerky movements, known as *intention tremor*, when reaching from nose to finger and back again. (After Blumenfeld 2010.)

lesions that damage the cerebellum disrupt the ability to learn new motor skills. Moreover, the cerebellum is activated during motor learning. When subjects are asked to track a target on a computer screen and the target randomly jumps to another position at the end of each trial, motor error during tracking is initially quite large but improves with practice (**Figure 5.28**). Activation in the cerebellum parallels this change in performance, peaking during initial learning and declining with improvement in performance.

Cerebellar Contributions to Cognitive Behavior

Traditionally, the cerebellum and its canonical circuitry have been considered a strictly motor structure providing error correction during motor acts and motor learning. With the advent of modern neuroimaging, however, it has become increasingly clear that the cerebellum contributes to cognitive processing

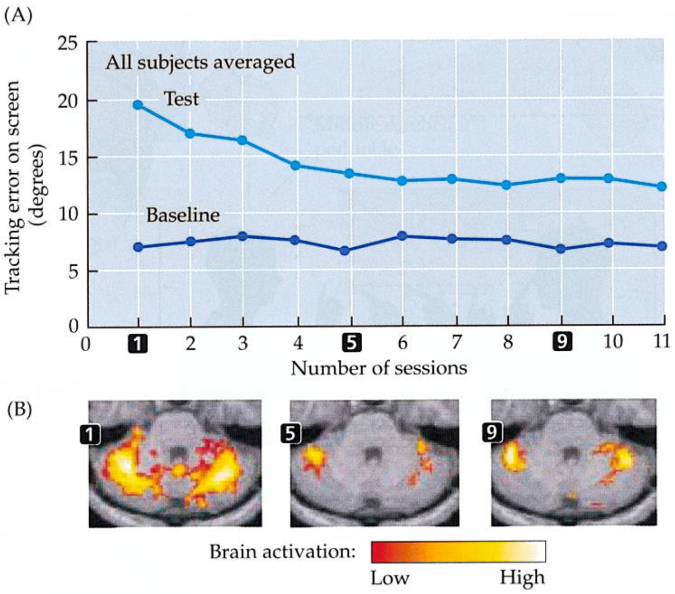

Figure 5.28 Changes in the cerebellum during motor learning (A) Subjects tracked a target on a computer screen using a mouse. During test sessions, the cursor was rotated 120 degrees about the center of the screen, thus requiring motor learning. In baseline sessions, the cursor remained unrotated. Improvements in the average performance of subjects over time in test sessions indicate motor learning. (B) The corresponding brain activation maps show significant activation in test sessions (decreasing from left to right) relative to baseline during learning. Activity in the cerebellum decreased with motor learning. (After Imamizu et al. 2000.)

as well. Portions of the cerebellum are activated during nonmotor learning, attention, timing, and verbal working memory tasks. Furthermore, recent neuropsychological studies of patients with cerebellar damage have reported deficits in speech, learning rates, timing, and working memory. Problems in orienting attention in autistic individuals have also been linked to abnormalities in the cerebellum.

Despite all this evidence, it is not clear how or why the cerebellum participates in cognitive functions. One proposal is that the computational power of the cerebellum as an efficient and accurate error correction device has simply been harnessed to serve cognitive functions that also require error correction (**Figure 5.29**). This model assumes that the cellular architecture repeated throughout the cerebellum can be used to perform the same computation on any set of inputs. For the motor system, these inputs would arise in the primary and premotor cortices, and the output would be a feedforward prediction of the sensory consequences of the impending movement. For cognitive tasks, the inputs would arise in the prefrontal cortex and specify intended cognitive operations, and the output would be the predicted cognitive consequences of the operation. Such predictions would then be compared against actual cognitive consequences, and the resulting error signals would be used to update both future cognitive operations and the internal models of their outcomes.

Support for this general class of models comes from the observation that, in addition to the heavy inputs from the motor and premotor cortices, the prefrontal cortex has massive connections to the cerebellum via the pontine nuclei. In fact, prefrontal inputs to the cerebellum in humans are at least as prominent as inputs from motor and premotor cortex. Moreover, prefrontal

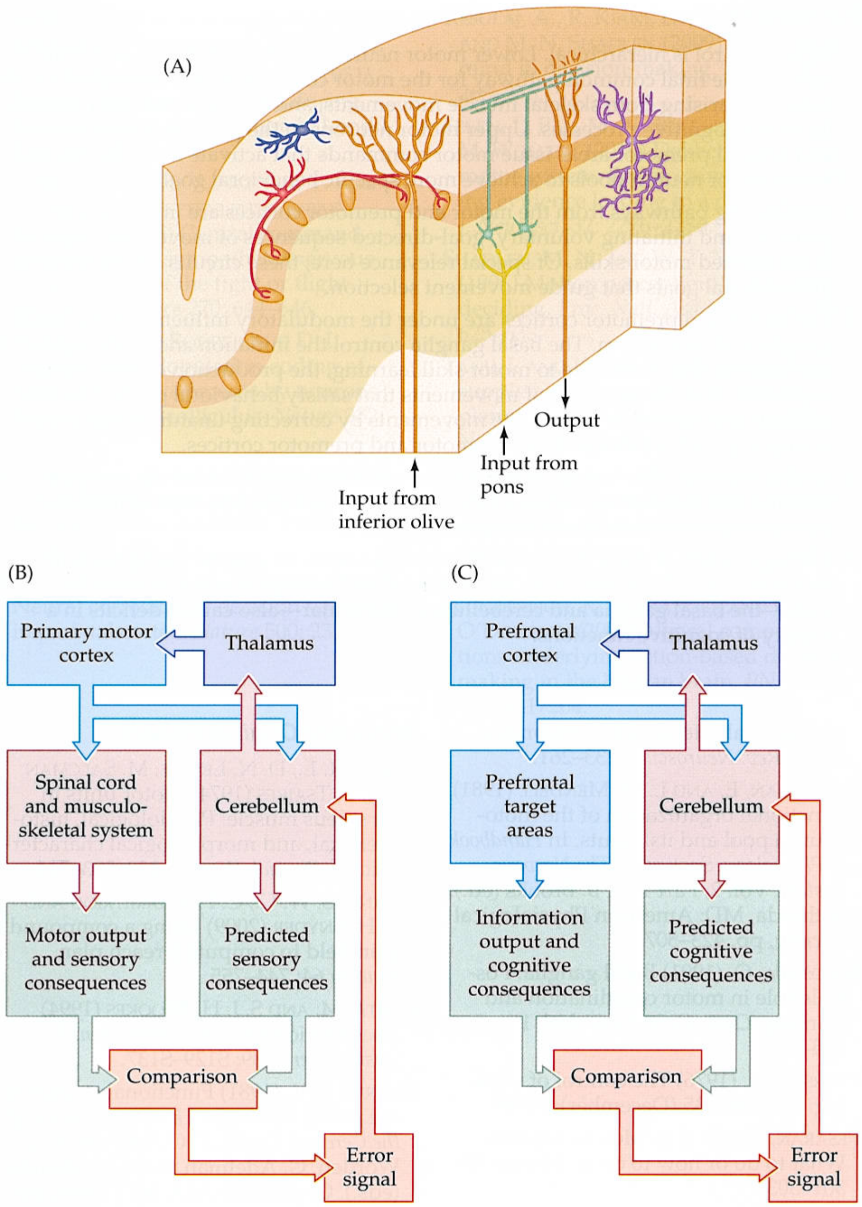

Figure 5.29 Model of cerebellar contributions to cognition (A) The canonical circuitry of the cerebellar cortex. Inputs to the cerebellar cortex arrive from the pons and inferior olive, a brainstem relay nucleus. (B) Model of cerebellar feedforward simulation and error correction of motor commands. The cerebellum computes the predicted sensory consequences of movement. The error between the predicted and actual consequences of movement is then fed back into the cerebellum to update future predictions. (C) The same model applied to cognitive processing. The cerebellum computes the predicted cognitive consequences of cognitive operations, and the error between predicted and actual cognitive outcomes is used to refine future predictions. (After Ramnani 2006.)

inputs to the cerebellum are more developed in humans than in non-human primates, and these differences parallel differences in cognitive complexity across species (see Chapter 15). Cognitive operations instantiated in prefrontal circuits feeding to the cerebellum might rely on the highly stereotyped cellular architecture of the cerebellum to provide fast, accurate, and automatic "simulations" of the output of these cognitive operations. This conjecture is supported by the observation that prefrontal circuits show reduced activation during the course of learning, whereas cerebellar circuits become more active. The cerebellum may thus provide another example in which neural circuitry originally adapted to one purpose is co-opted for another; that is, the circuitry for motor control (see Figure 5.29B) is co-opted for use in cognitive information processing (see Figure 5.29C).

Summary

1. Motor control is hierarchical. Lower motor neurons in the spinal cord and brainstem are the final common pathway for the motor commands that determine behaviors arising from skeletal muscle movements, and they are thus the effectors for many cognitive processes. Upper motor neurons in the primary motor cortex and cortical premotor areas issue motor commands that activate local circuits and lower motor neuron pools to achieve more specific behavioral goals.
2. Descending pathways from the motor and premotor cortices are important in planning and initiating voluntary, goal-directed sequences of movement, especially for learned motor skills. Of special relevance here, these circuits are sensitive to motivational goals that guide movement selection.
3. The motor and premotor cortices are under the modulatory influence of the basal ganglia and cerebellum. The basal ganglia control the initiation and stopping of movements and contribute to motor skill learning, the production of movement sequences, and the selection of movements that satisfy behavioral goals. The cerebellum acts further to coordinate movements by correcting unanticipated errors in ongoing motor processing in the motor and premotor cortices.
4. Acting together, the various motor circuits mediate production of the complex intrinsic and learned sequences of movement that are characteristic of human motor behaviors that express cognitive goals.
5. Damage to any of these motor control circuits results in specific disruptions in movement planning, initiation, or coordination. Damage to some of these circuits—the basal ganglia and cerebellum in particular—also causes deficits in a variety of cognitive functions.

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