CHAPTER 5

The Motor System

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CHAPTER OUTLINE

KEY CONCEPTS

1. The contraction of skeletal muscle produces movement by acting on the skeleton.
2. Motor neurons activate the skeletal muscles.
3. Sensory feedback from muscles is important for precise control of contraction.
4. The output of sensory receptors like the muscle spindle can be adjusted.
5. The spinal cord is the source of reflexes that are important in the initiation and control of movement.
6. Spinal cord function is influenced by higher centers in the brainstem.
7. The highest level of motor control comes from the cerebral cortex.
8. The basal ganglia and the cerebellum provide feedback to the motor control areas of the cerebral cortex and brainstem.

The finger movements of a neurosurgeon manipulating microsurgical instruments while repairing a cerebral aneurysm, and the eye-hand-body control of a professional basketball player making a rimless three-point shot, are two examples of the motor control functions of the nervous system operating at high skill levels. The coordinated contraction of the hip flexors and ankle extensors to clear a slight pavement irregularity encountered during walking is a familiar example of the motor control system working at a seemingly automatic level. The stiff-legged stride of a patient who experienced a stroke and the swaying walk plus slurred speech of an intoxicated person are examples of perturbed motor control.

Although our understanding of the anatomy and physiology of the motor system is still far from complete, a significant fund of knowledge exists. This chapter will proceed through the constituent parts of the motor system, beginning with the skeleton and ending with the brain.

THE SKELETON AS THE FRAMEWORK FOR MOVEMENT

Bones are the body's framework and system of levers. They are the elements that move. The way adjacent bones articulate determines the motion and range of movement at a joint. Ligaments hold the bones together across the joint. Movements are described based on the anatomic planes through which the skeleton moves and the physical structure of the joint. Most joints move in only one plane, but some permit movement in multiple anatomic reference planes (Fig. 5.1).

Hinge joints, such as the elbow, are uniaxial, permitting movements in the sagittal plane. The wrist is an example of a biaxial joint. The shoulder is a multiaxial joint; movement can occur in oblique planes as well as the three major planes of that joint. Flexion and extension describe movements in the sagittal plane. **Flexion** movements decrease the angle between the moving body segments. **Extension** describes movement in the opposite direction. **Abduction** moves the

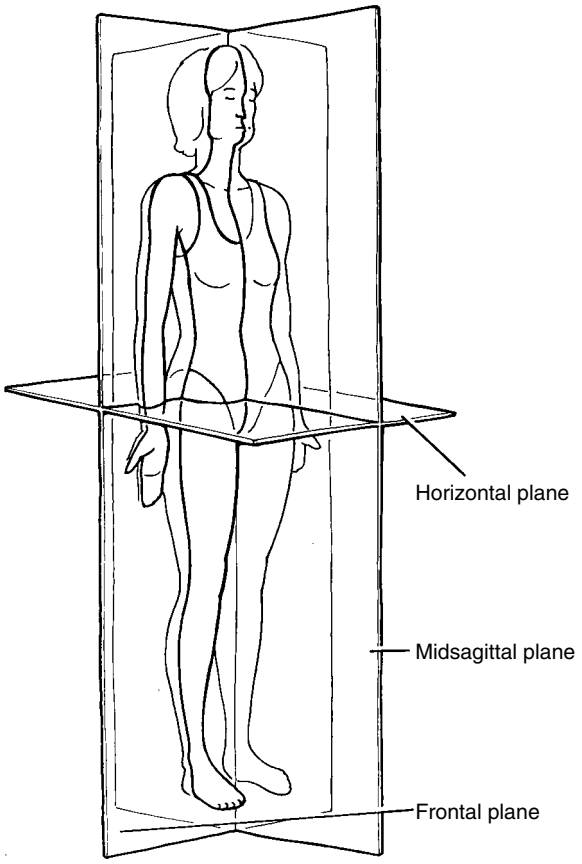

FIGURE 5.1 **Anatomic reference planes.** The figure is shown in the standard anatomic position with the associated primary reference planes.

body part away from the midline, while **adduction** moves the body part toward midline.

MUSCLE FUNCTION AND BODY MOVEMENT

Muscles span joints and are attached at two or more points to the bony levers of the skeleton. The muscles provide the power that moves the body's levers. Muscles are described in terms of their origin and insertion attachment sites. The **origin** tends to be the more fixed, less mobile location, while the **insertion** refers to the skeletal site that is more mobile. Movement occurs when a muscle generates force on its attachment sites and undergoes shortening. This type of action is termed an **isotonic** or **concentric contraction**. Another form of muscular action is a controlled lengthening while still generating force. This is an **eccentric contraction**. A muscle may also generate force but hold its attachment sites static, as in **isometric contraction**.

Because muscle contraction can produce movement in only one direction, at least two muscles opposing each other at a joint are needed to achieve motion in more than one direction. When a muscle produces movement by shortening, it is an **agonist**. The **prime mover** is the muscle that contributes most to the movement. Muscles that oppose the action of the prime mover are **antagonists**. The quadriceps and hamstring muscles are examples of agonist-antagonist pairs in knee extension and flexion. During both simple and light-load skilled movements, the antagonist is relaxed. Contraction of the agonist with concomitant relaxation of the antagonist occurs by the nervous system function of **reciprocal inhibition**. Co-contraction of agonist and antagonist occurs during movements that require precise control.

A muscle functions as a **synergist** if it contracts at the same time as the agonist while cooperating in producing the movement. Synergistic action can aid in producing a movement (e.g., the activity of both flexor carpi ulnaris and extensor carpi ulnaris are used in producing ulnar deviation of the wrist); eliminating unwanted movements (e.g., the activity of wrist extensors prevents flexion of the wrist when finger flexors contract in closing the hand); or stabilizing proximal joints (e.g., isometric contractions of muscles of the forearm, upper arm, shoulder, and trunk accompany a forceful grip of the hand).

PERIPHERAL NERVOUS SYSTEM COMPONENTS FOR THE CONTROL OF MOVEMENT

We can identify the components of the nervous system that are predominantly involved in the control of motor function and discuss the probable roles for each of them. It is important to appreciate that even the simplest reflex or voluntary movement requires the interaction of multiple levels of the nervous system (Fig. 5.2).

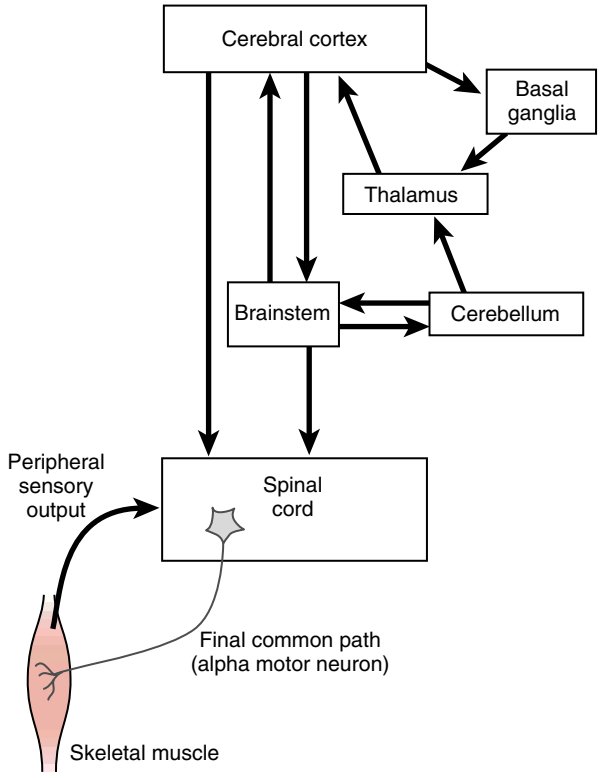

FIGURE 5.2 **Motor control system.** Alpha motor neurons are the final common path for motor control. Peripheral sensory input and spinal cord tract signals that descend from the brainstem and cerebral cortex influence the motor neurons. The cerebellum and basal ganglia contribute to motor control by modifying brainstem and cortical activity.

The motor neurons in the spinal cord and cranial nerve nuclei, plus their axons and muscle fibers, constitute the **final common path**, the route by which all central nervous activity influences the skeletal muscles. The motor neurons located in the ventral horns of the spinal gray matter and brainstem nuclei are influenced by both local reflex circuitry and by pathways that descend from the brainstem and cerebral cortex. The brainstem-derived pathways include the rubrospinal, vestibulospinal, and reticulospinal tracts; the cortical pathways are the corticospinal and corticobulbar tracts. Although some of the cortically derived axons terminate directly on motor neurons, most of the axons of the cortical and the brainstem-derived tracts terminate on interneurons, which then influence motor neuron function. The outputs of the basal ganglia of the brain and cerebellum provide fine-tuning of cortical and brainstem influences on motor neuron functions.

Alpha Motor Neurons Are the Final Common Path for Motor Control

Motor neurons segregate into two major categories, alpha and gamma. **Alpha motor neurons** innervate the **extrafusal muscle fibers,** which are responsible for force generation. **Gamma motor neurons** innervate the **intrafusal muscle fibers,** which are components of the muscle spindle. An alpha motor neuron controls several muscle fibers, 10 to 1,000, depending on the muscle. The term **motor unit** describes a motor neuron, its axon, the branches of the axon, the neuromuscular junction synapses at the distal end of each axon branch, and all of the extrafusal muscle fibers innervated by that motor neuron (Fig. 5.3). When a motor neuron generates an action potential, all of its muscle fibers are activated.

Alpha motor neurons can be separated into two populations according to their cell body size and axon diameter. The larger cells have a high threshold to synaptic stimulation, have fast action potential conduction velocities, and are active in high-effort force generation. They innervate fast-twitch, high-force but fatigable muscle fibers. The smaller alpha motor neurons have lower thresholds to synaptic stimulation, conduct action potentials at a somewhat slower velocity, and innervate slow-twitch, low-force, fatigue-resistant muscle fibers (see Chapter 9). The muscle fibers of each motor unit are homogeneous, either fast-twitch or slow-twitch. This property is ultimately determined by the motor neuron. Muscle fibers that are denervated secondary to disease of the axon or nerve cell body may change twitch type if reinnervated by an axon sprouted from a different twitch-type motor neuron.

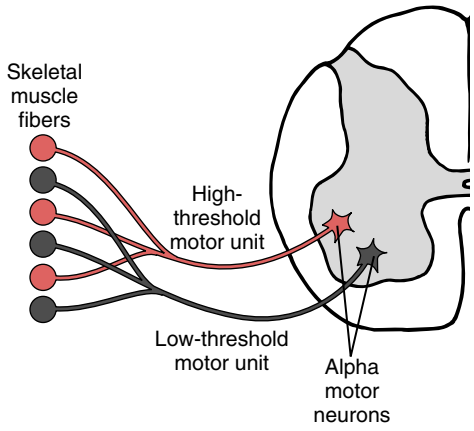

FIGURE 5.3 **Motor unit structure.** A motor unit consists of an alpha motor neuron and the group of extrafusal muscle fibers it innervates. Functional characteristics, such as activation threshold, twitch speed, twitch force, and resistance to fatigue, are determined by the motor neuron. Low- and high-threshold motor units are shown.

The organization into different motor unit types has important functional consequences for the production of smooth, coordinated contractions. The smallest neurons have the lowest threshold and are, therefore, activated first when synaptic activity is low. These produce sustainable, relatively low-force tonic contractions in slow-twitch, fatigue-resistant muscle fibers. If additional force is required, synaptic drive from higher centers increases the action potential firing rate of the initially activated motor neurons and then activates additional motor units of the same type. If yet higher force levels are needed, the larger motor neurons are recruited, but their contribution is less sustained as a result of fatigability. This orderly process of motor unit **recruitment** obeys what is called the **size principle**—the smaller motor neurons are activated first. A logical corollary of this arrangement is that muscles concerned with endurance, such as antigravity muscles, contain predominantly slow-twitch muscle fibers in accordance with their function of continuous postural support. Muscles that contain predominantly fast-twitch fibers, including many physiological flexors, are capable of producing high-force contractions.

Afferent Muscle Innervation Provides Feedback for Motor Control

The muscles, joints, and ligaments are innervated with sensory receptors that inform the central nervous system about body position and muscle activity. Skeletal muscles contain muscle spindles, Golgi tendon organs, free nerve endings, and some Pacinian corpuscles. Joints contain Ruffini endings and Pacinian corpuscles; joint capsules contain nerve endings; ligaments contain Golgi tendon-like organs. Together, these are the **proprioceptors,** providing sensation from the deep somatic structures. These sensations, which may not reach a conscious level, include the position of the limbs and the force and speed of muscle contraction. They provide the feedback that is necessary for the control of movements.

Muscle spindles provide information about the muscle length and the velocity at which the muscle is being stretched. Golgi tendon organs provide information about the force being generated. Spindles are located in the mass of the muscle, in parallel with the extrafusal muscle fibers. Golgi tendon organs are located at the junction of the muscle and its tendons, in series with the muscle fibers (Fig. 5.4).

Muscle Spindles.

Muscle spindles are sensory organs found in almost all of the skeletal muscles. They occur in

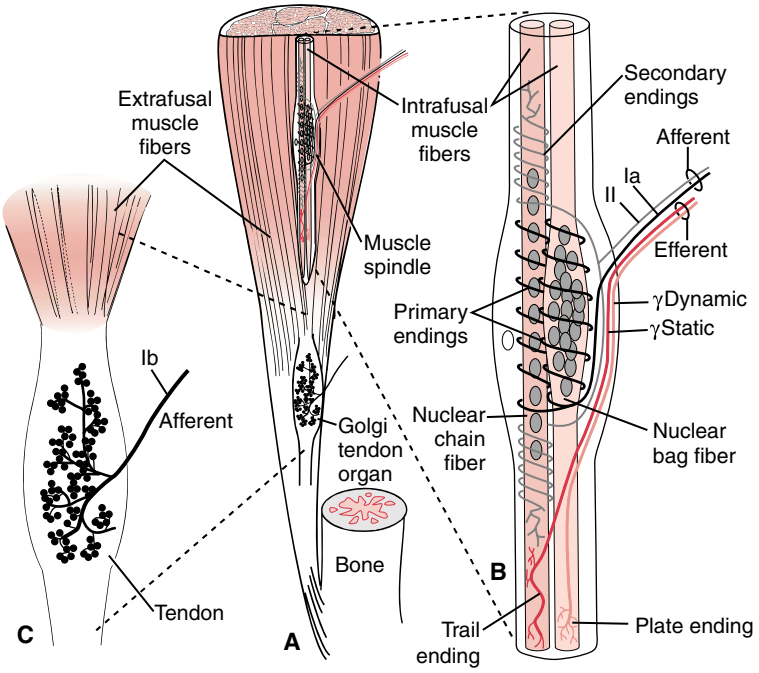

FIGURE 5.4 Muscle spindle and Golgi tendon organ structure. **A**, Muscle spindles are located parallel to extrafusal muscle fibers; Golgi tendon organs are in series. **B**, This enlarged spindle shows nuclear bag and nuclear chain types of intrafusal fibers; afferent innervation by Ia axons, which provide primary endings to both types of fibers; type II axons, which have secondary endings mainly on chain fibers; and motor innervation by the two types of gamma motor axons, static and dynamic. **C**, An enlarged Golgi tendon organ. The sensory receptor endings interdigitate with the collagen fibers of the tendon. The axon is type Ib.

greatest density in small muscles serving fine movements, such as those of the hand, and in the deep muscles of the neck. The muscle spindle, named for its long fusiform shape, is attached at both ends to extrafusal muscle fibers. Within the spindle's expanded middle portion is a fluid-filled capsule containing 2 to 12 specialized striated muscle fibers entwined by sensory nerve terminals. These intrafusal muscle fibers, about 300 μm long, have contractile filaments at both ends. The noncontractile midportion contains the cell nuclei (Fig. 5.4B). Gamma motor neurons innervate the contractile elements. There are two types of intrafusal fibers: **nuclear bag fibers**, named for the large number of nuclei packed into the midportion, and **nuclear chain fibers**, in which the nuclei are arranged in a longitudinal row. There are about twice as many nuclear chain fibers as nuclear bag fibers per spindle. The nuclear bag type fibers are further classified as bag_1 and bag_2, based on whether they respond best in the dynamic or static phase of muscle stretch, respectively.

Sensory axons surround both the noncontractile midportion and paracentral region of the contractile ends of the intrafusal fiber. The sensory axons are categorized as **primary (type Ia)** and **secondary (type II)**. The axons of both types are myelinated. Type Ia axons are larger in diameter (12 to 20 μm) than type II axons (6 to 12 μm) and have faster conduction velocities. Type Ia axons have spiral shaped endings that wrap around the middle of the intrafusal muscle fiber (see Fig. 5.4B). Both nuclear bag and nuclear chain fibers are innervated by type Ia axons. Type II axons innervate mainly nuclear chain fibers and have nerve endings that are located along the contractile components on either side of the type Ia spiral ending. The nerve endings of both primary and secondary sensory axons of the muscle spindles respond to stretch by generating action potentials that convey information to the central nervous system about changes in muscle length and the velocity of length change (Fig 5.5). The primary endings temporarily cease generating action potentials during the release of a muscle stretch (Fig. 5.6).

Golgi Tendon Organs. **Golgi tendon organs** (GTOs) are 1 mm long, slender receptors encapsulated within the tendons of the skeletal muscles (see Fig. 5.4A and C). The distal pole of a GTO is anchored in collagen fibers of the tendon. The proximal pole is attached to the ends of the extrafusal muscle fibers. This arrangement places the GTO in series with the extrafusal muscle fibers such that contractions of the muscle stretch the GTO.

A large-diameter, myelinated type Ib afferent axon arises from each GTO. These axons are slightly smaller in diameter than the type Ia variety, which innervate the muscle spindle. Muscle contraction stretches the GTO and generates action potentials in type Ib axons. The GTO output provides information to the central nervous system about the force of the muscle contraction.

Information entering the spinal cord via type Ia and Ib axons is directed to many targets, including the spinal interneurons that give rise to the **spinocerebellar tracts**. These tracts convey information to the cerebellum about the status of muscle length and tension.

Gamma Motor Neurons. Alpha motor neurons innervate the extrafusal muscle fibers, and gamma motor neurons innervate the intrafusal fibers. Cells bodies of both alpha and gamma motor neurons reside in the ventral horns of the spinal cord and in nuclei of the cranial motor nerves. Nearly one third of all motor nerve axons are destined for intrafusal muscle fibers. This high number reflects the complex role of the spindles in motor system control. Intrafusal muscle fibers likewise constitute a significant portion of the total number of muscle cells, yet they contribute little or nothing to the total force generated when the muscle con-

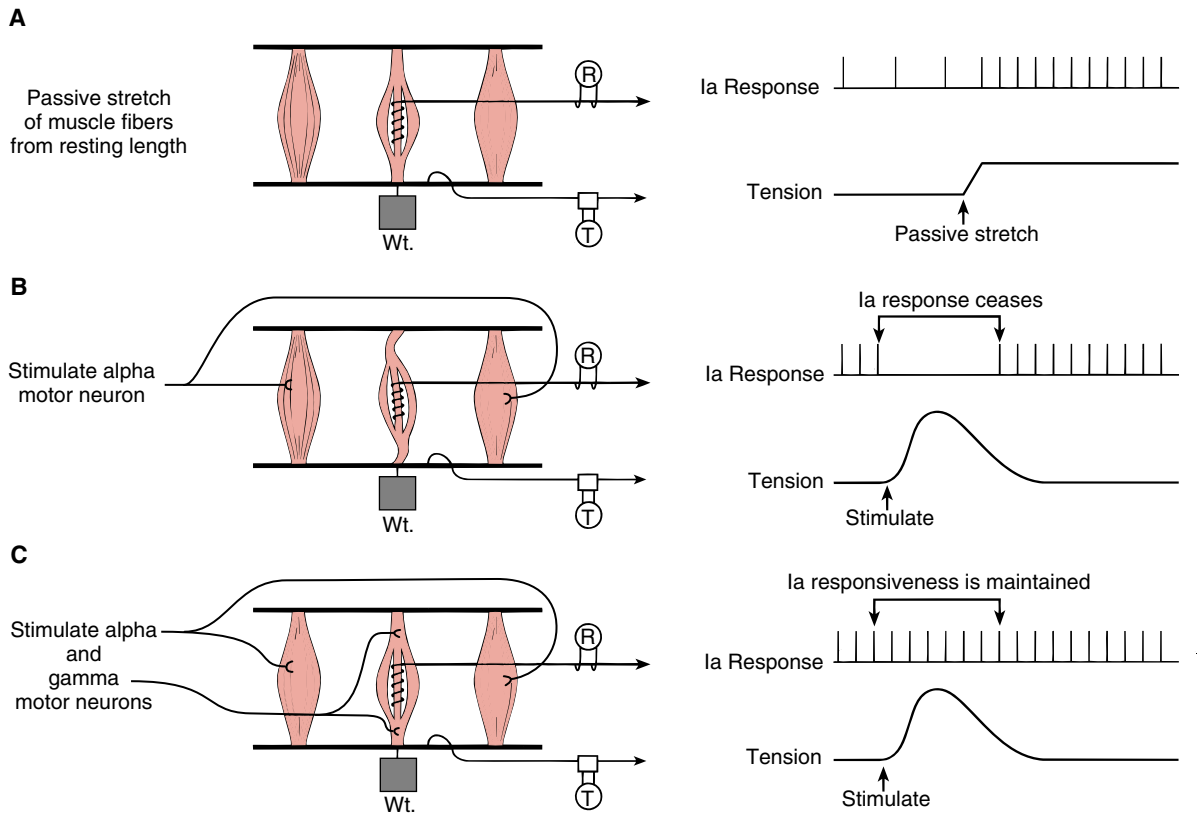

FIGURE 5.5 Action potential recording (R) from type Ia endings and muscle tension (T). **A,** The Ia sensory endings from the muscle spindles discharge at a slow rate when the muscle is at its resting length and show an increased firing rate when the muscle is stretched. **B,** Alpha motor neuron activation shortens the muscle and releases tension on the muscle spindle. Ia activity ceases temporarily during the tension release. **C,** Concurrent alpha and gamma motor neuron activation, as occurs in normal, voluntary muscle contraction, shortens the muscle spindle along with the extrafusal fibers, maintaining the spindle's responsiveness to the stretch.

tracts. Rather, the contractions of intrafusal fibers play a modulating role in sensation, as they alter the length and, thereby, the sensitivity of the muscle spindles.

Even when the muscle is at rest, the muscle spindles are slightly stretched, and type Ia afferent nerves exhibit a slow discharge of action potentials. Contraction of the muscle increases the firing rate in type Ib axons from Golgi tendon organs, whereas type Ia axons temporarily cease or reduce firing because the shortening of the surrounding extrafusal fibers unloads the intrafusal muscle fibers. If a load on the spindle were reinstituted, the Ia nerve endings would resume their sensitivity to stretch. The role of the gamma motor neurons is to "reload" the spindle during muscle contraction by activating the contractile elements of the intrafusal fibers. This is accomplished by coordinated activation of the alpha and gamma motor neurons during muscle contraction (see Fig. 5.5).

The gamma motor neurons and the intrafusal fibers they innervate are traditionally referred to as the **fusimotor system**. Axons of the gamma neurons terminate in one of two

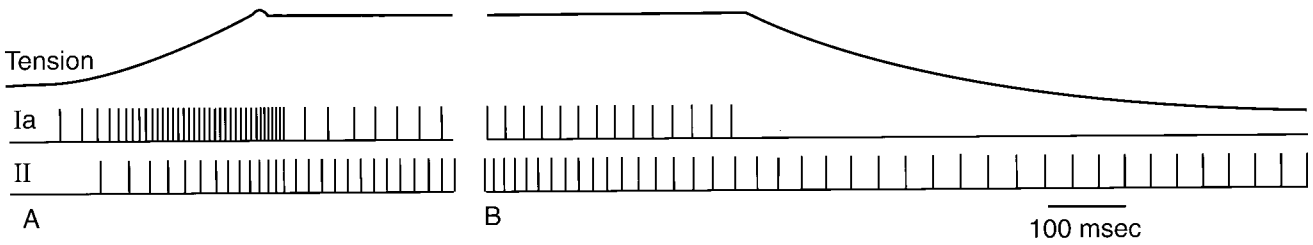

FIGURE 5.6 Response of types Ia and II sensory endings to a muscle stretch. **A,** During rapid stretch, type Ia endings show a greater firing rate increase, while type II endings show only a modest increase. **B,** With the release of the stretch, Ia endings cease firing, while firing of type II endings slows. Ia endings report both the velocity and the length of muscle stretch; type II endings report length.

types of endings, each located distal to the sensory endings on the striated poles of the spindle's muscle fibers (see Fig. 5.4B). The nerve terminals are either plate endings or trail endings; each intrafusal fiber has only one of these two types of endings. **Plate endings** occur predominantly on bag_1 fibers (dynamic), whereas **trail endings**, primarily on chain fibers, are also seen on bag_2 (static) fibers. This arrangement allows for largely independent control of the nuclear bag and nuclear chain fibers in the spindle.

Gamma motor neurons with plate endings are designated **dynamic** and those with trail endings are designated **static**. This functional distinction is based on experimental findings showing that stimulation of gamma neurons with plate endings enhanced the response of type Ia sensory axons to stretch, but only during the dynamic (muscle length changing) phase of a muscle stretch. During the static phase of the stretch (muscle length increase maintained) stimulation of the gamma neurons with trail endings enhanced the response of type II sensory axons. Static gamma neurons can affect the responses of both types Ia and II sensory axons; dynamic gamma neurons affect the response of only type Ia axons. These differences suggest that the motor system has the ability to monitor muscle length more precisely in some muscles and the speed of contraction in others.

THE SPINAL CORD IN THE CONTROL OF MOVEMENT

Muscles interact extensively in the maintenance of posture and the production of coordinated movement. The circuitry of the spinal cord automatically controls much of this interaction. Sensory feedback from muscles reaches motor neurons of related muscles and, to a lesser degree, of more distant muscles. In addition to activating local circuits, muscles and joints transmit sensory information up the spinal cord to higher centers. This information is processed and can be relayed back to influence spinal cord circuits.

The Structural Arrangement of Spinal Motor Systems Correlates With Function

The cell bodies of the spinal cord motor neurons are grouped into pools in the ventral horns. A **pool** consists of the motor neurons that serve a particular muscle. The number of motor neurons that control a muscle varies in direct proportion to the delicacy of control required. The motor neurons are organized so that those innervating the axial muscles are grouped medially and those innervating the limbs are located laterally (Fig. 5.7). The lateral limb motor neuron areas are further organized so that proximal actions, such as girdle movements, are controlled from relatively medial locations, while distal actions, such as finger movements, are located the most laterally. Neurons innervating flexors and extensors are also segregated. A motor neuron pool may extend over several spinal segments in the form of a column of motor neurons. This is mirrored by the innervation serving a single muscle emerging from the spinal cord in two or even three adjacent spinal nerve root levels. A physiological advantage to such an arrangement is that injury to a single nerve root, as could be produced by herniation of an intervertebral disk, will not completely paralyze a muscle.

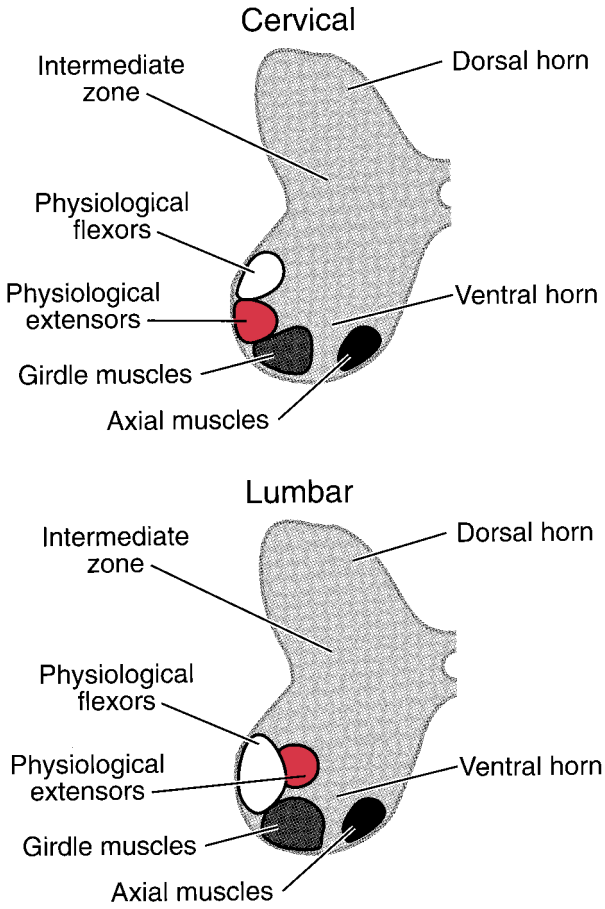

FIGURE 5.7 **Spinal cord motor neuron pools.** Motor neurons controlling axial, girdle, and limb muscles are grouped in pools oriented in a medial-to-lateral fashion. Limb flexor and extensor motor neurons also segregate into pools.

A zone between the medial and lateral pools contains interneurons that project to limb motor neuron pools ipsilaterally and axial pools bilaterally. Between the spinal cord's dorsal and ventral horns lies the intermediate zone, which contains an extensive network of interneurons that interconnect motor neuron pools (see Fig. 5.7). Some interneurons make connections in their own cord segment; others have longer axon projections that travel in the white matter to terminate in other segments of the spinal cord. These longer axon interneurons, termed **propriospinal cells**, carry information that aids coordinated movement. The importance of spinal cord interneurons is reflected in the fact that they comprise the majority of neurons in the spinal cord and provide the majority of the motor neuron synapses.

The Spinal Cord Mediates Reflex Activity

The spinal cord contains neural circuitry to generate **reflexes**, stereotypical actions produced in response to a peripherally applied stimulus. One function of a reflex is to generate a rapid response. A familiar example is the rapid, involuntary withdrawal of a hand after touching a danger-

ously hot object well before the heat or pain is perceived. This type of reflex protects the organism before higher CNS levels identify the problem. Some reflexes are simple, others much more complex. Even the simplest requires coordinated action in which the agonist contracts while the antagonist relaxes. The functional unit of a reflex consists of a sensor, an afferent pathway, an integrating center, an efferent pathway, and an effector. The sensory receptors for spinal reflexes are the proprioceptors and cutaneous receptors. Impulses initiated in these receptors travel along afferent nerves to the spinal cord, where interneurons and motor neurons constitute the integrating center. The final common path, or motor neurons, make up the efferent pathway to the effector organs, the skeletal muscles. The responsiveness of such a functional unit can be modulated by higher motor centers acting through descending pathways to facilitate or inhibit its activation.

Study of the three types of spinal reflexes—the myotatic, the inverse myotatic, and the flexor withdrawal—provides a basis for understanding the general mechanism of reflexes.

The Myotatic (Muscle Stretch) Reflex. Stretching or elongating a muscle—such as when the patellar tendon is tapped with a reflex hammer or when a quick change in posture is made—causes it to contract within a short time period. The period between the onset of a stimulus and the response, the **latency period**, is on the order of 30 msec for a knee-jerk reflex in a human. This response, called the **myotatic** or **muscle stretch reflex**, is due to monosynaptic circuitry, where an afferent sensory neuron synapses directly on the efferent motor neuron (Fig 5.8). The stretch activates muscle spindles. Type Ia sensory axons from the spindle carry action potentials to the spinal cord, where they synapse directly on motor neurons of the same (homonymous) muscle that was stretched and on motor neurons of synergistic (heteronymous) muscles. These synapses are excitatory and utilize glutamate as the neurotransmitter. Monosynaptic type Ia synapses occur predominantly on alpha motor neurons; gamma motor neurons seemingly lack such connections.

Collateral branches of type Ia axons also synapse on interneurons, whose action then inhibits motor neurons of antagonist muscles (see Fig 5.8). This synaptic pattern, called **reciprocal inhibition**, serves to coordinate muscles of opposing function around a joint. Secondary (type II) spindle afferent fibers also synapse with homonymous motor neurons, providing excitatory input through both monosynaptic and polysynaptic pathways. Golgi tendon organ input via type Ib axons has an inhibitory influence on homonymous motor neurons.

The myotatic reflex has two components: a phasic part, exemplified by tendon jerks, and a tonic part, thought to be important for maintaining posture. The phasic component is more familiar. These components blend together, but either one may predominate, depending on whether other synaptic activity, such as from cutaneous afferent neurons or pathways descending from higher centers, influences the motor response. Primary spindle afferent fibers probably mediate the tendon jerk, with secondary afferent fibers contributing mainly to the tonic phase of the reflex.

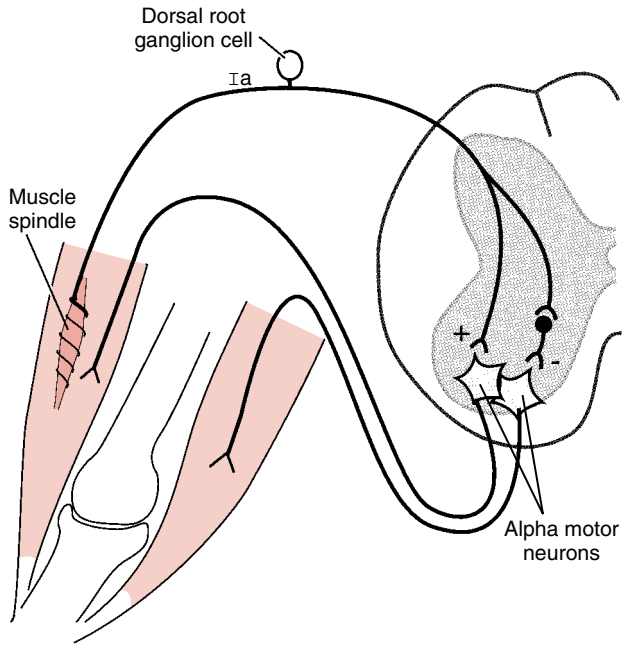

FIGURE 5.8 **Myotatic reflex circuitry.** Ia afferent axons from the muscle spindle make excitatory monosynaptic contact with homonymous motor neurons and with inhibitory interneurons that synapse on motor neurons of antagonist muscles. The plus sign indicates excitation; the minus sign indicates inhibition.

The myotatic reflex performs many functions. At the most general level, it produces rapid corrections of motor output in the moment-to-moment control of movement. It also forms the basis for postural reflexes, which maintain body position despite a varying range of loads and/or external forces on the body.

The Inverse Myotatic Reflex. The active contraction of a muscle also causes reflex inhibition of the contraction. This response is called the **inverse myotatic reflex** because it produces an effect that is opposite to that of the myotatic reflex. Active muscle contraction stimulates Golgi tendon organs, producing action potentials in the type Ib afferent axons. Those axons synapse on inhibitory interneurons that influence homonymous and heteronymous motor neurons and on excitatory interneurons that influence motor neurons of antagonists (Fig 5.9).

The function of the inverse myotatic reflex appears to be a tension feedback system that can adjust the strength of contraction during sustained activity. The inverse myotatic reflex does not have the same function as reciprocal inhibition. Reciprocal inhibition acts primarily on the antagonist, while the inverse myotatic reflex acts on the agonist.

The inverse myotatic reflex, like the myotatic reflex, has a more potent influence on the physiological extensor muscles than on the flexor muscles, suggesting that the two reflexes act together to maintain optimal responses in the antigravity muscles during postural adjustments. Another hypothesis about the conjoint function is that both of these

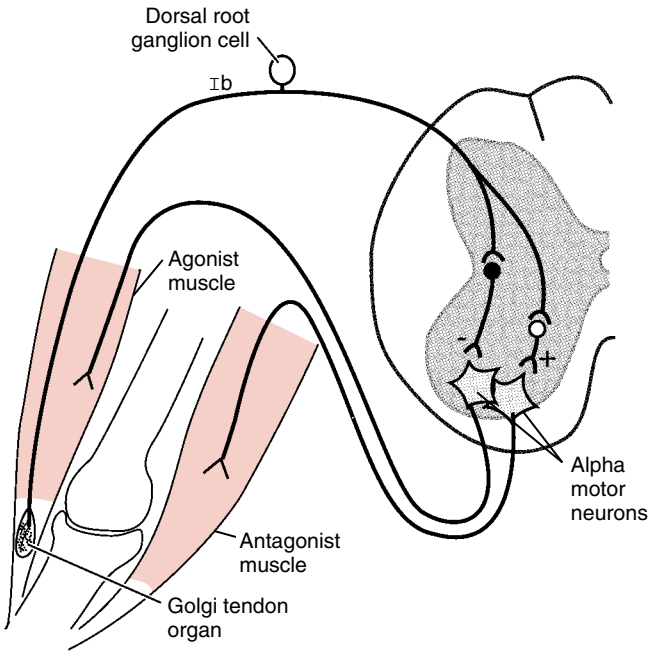

FIGURE 5.9 **Inverse myotatic reflex circuitry.** Contraction of the agonist muscle activates the Golgi tendon organ and Ib afferents, which synapse on interneurons that inhibit agonist motor neurons and excite the motor neurons of the antagonist muscle.

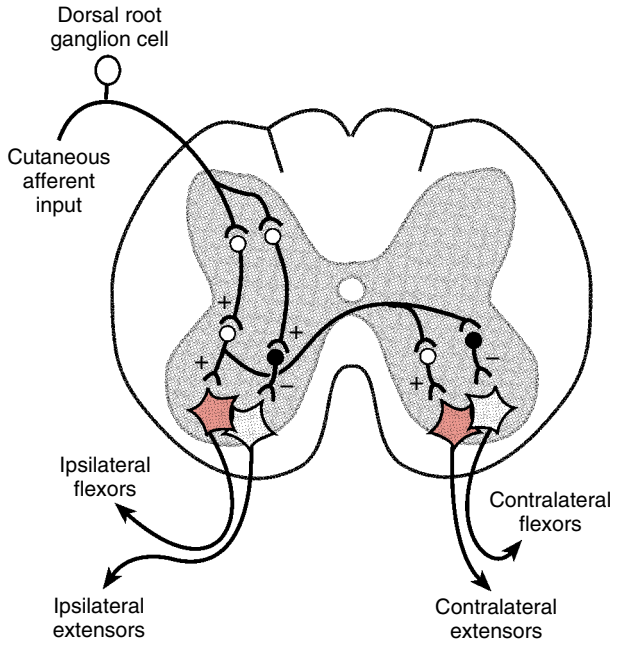

FIGURE 5.10 **Flexor withdrawal reflex circuitry.** Stimulation of cutaneous afferents activates ipsilateral flexor muscles via excitatory interneurons. Ipsilateral extensor motor neurons are inhibited. Contralateral extensor motor neuron activation provides postural support for withdrawal of the stimulated limb.

reflexes contribute to the smooth generation of tension in muscle by regulating muscle stiffness.

The Flexor Withdrawal Reflex. Cutaneous stimulation—such as touch, pressure, heat, cold, or tissue damage—can elicit a **flexor withdrawal reflex**. This reflex consists of a contraction of flexors and a relaxation of extensors in the stimulated limb. The action may be accompanied by a contraction of the extensors on the contralateral side. The axons of cutaneous sensory receptors synapse on interneurons in the dorsal horn. Those interneurons act ipsilaterally to excite the motor neurons of flexor muscles and inhibit those of extensor muscles. Collaterals of interneurons cross the midline to excite contralateral extensor motor neurons and inhibit flexors (Fig. 5.10).

There are two types of flexor withdrawal reflexes: those that result from innocuous stimuli and those that result from potentially injurious stimulation. The first type produces a localized flexor response accompanied by slight or no limb withdrawal; the second type produces widespread flexor contraction throughout the limb and abrupt withdrawal. The function of the first type of reflex is less obvious, but may be a general mechanism for adjusting the movement of a body part when an obstacle is detected by cutaneous sensory input. The function of the second type is protection of the individual. The endangered body part is rapidly removed, and postural support of the opposite side is strengthened if needed (e.g., if the foot is being withdrawn).

Collectively, these reflexes provide for stability and postural support (the myotatic and inverse myotatic) and mobility (flexor withdrawal). The reflexes provide a foundation of automatic responses on which more complicated voluntary movements are built.

The Spinal Cord Can Produce Basic Locomotor Actions

For locomotion, muscle action must occur in the limbs, but the posture of the trunk must also be controlled to provide a foundation from which the limb muscles can act. For example, when a human takes a step forward, not only must the advancing leg flex at the hip and knee, the opposite leg and bilateral truncal muscles must also be properly activated to prevent collapse of the body as weight is shifted from one leg to the other. Responsibility for the different functions that come together in successful locomotion is divided between several levels of the central nervous system.

Studies in experimental animals, mostly cats, have demonstrated that the spinal cord contains the capability for generating basic locomotor movements. This neural circuitry, called a **central pattern generator**, can produce the alternating contraction of limb flexors and extensors that is needed for walking. It has been shown experimentally that application of an excitatory amino acid like glutamate to the spinal cord produces rhythmic action potentials in motor neurons. Each limb has its own pattern generator, and the actions of different limbs are then coordinated. The normal strategy for generating basic locomotion engages central pattern generators and uses both sensory feedback

and efferent impulses from higher motor control centers for the refinement of control.

Spinal Cord Injury Alters Voluntary and Reflex Motor Activity

When the spinal cord of a human or other mammal is severely injured, voluntary and reflex movements are immediately lost caudal to the level of injury. This acute impairment of function is called **spinal shock**. The loss of voluntary motor control is termed **plegia**, and the loss of reflexes is termed **areflexia**. Spinal shock may last from days to months, depending on the severity of cord injury. Reflexes tend to return, as may some degree of voluntary control. As recovery proceeds, myotatic reflexes become hyperactive, as demonstrated by an excessively vigorous response to tapping the muscle tendon with a reflex hammer. Tendon tapping, or even limb repositioning that produces a change in the muscle length, may also provoke **clonus**, a condition characterized by repetitive contraction and relaxation of a muscle in an oscillating fashion every second or so, in response to a single stimulus. Flexor withdrawal reflexes may also reappear and be provoked by lesser stimuli than would be normally required. The acute loss and eventual overactivity of all of these reflexes results from the lack of influence of the neural tracts that descend from higher motor control centers to the motor neurons and associated interneuron pools.

SUPRASPINAL INFLUENCES ON MOTOR CONTROL

Descending signals from the cervical spinal cord, brainstem, and cortex can influence the rate of motor neuron firing and the recruitment of additional motor neurons to increase the speed and force of muscle contraction. The influence of higher motor control centers is illustrated by a walking dog whose right and left limbs show alternating contractions and then change to a running pattern in which both sides contract in synchrony.

The brainstem contains the neural circuitry for initiating locomotion and for controlling posture. The maintenance of posture requires coordinated activity of both axial and limb muscles in response to input from proprioceptors and spatial position sensors, such as the inner ear. Cerebral cortex input through the corticospinal system is necessary for the control of fine individual movements of the distal limbs and digits. Each higher level of the nervous system acts on lower levels to produce appropriate, more refined movements.

The Brainstem Is the Origin of Three Descending Tracts That Influence Movement

Three brainstem nuclear groups give rise to descending motor tracts that influence motor neurons and their associated interneurons. These consist of the **red nucleus**, the **vestibular nuclear complex**, and the **reticular formation** (Fig. 5.11). The other major descending influence on the motor neurons is the corticospinal tract, the only volitional control pathway in the motor system. In most cases, the descending pathways act through synaptic connections on interneurons. The connection is less commonly made directly with motor neurons.

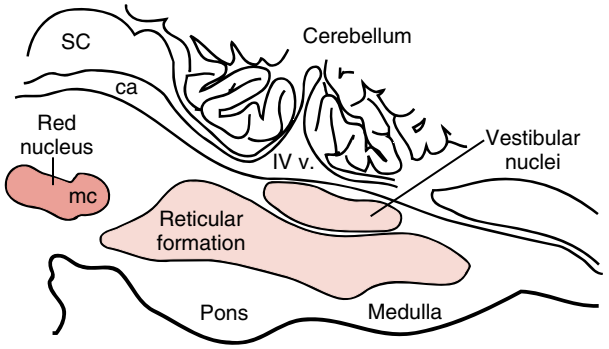

FIGURE 5.11 Brainstem nuclei of descending motor pathways. The magnocellular portion of the red nucleus is the origin of the rubrospinal tract. The lateral vestibular nucleus is the source of the vestibulospinal tract. The reticular formation is the source of two tracts, one from the pontine portion and one from the medulla. Structures illustrated are from the monkey. SC, superior colliculus; ca, cerebral aqueduct; IV v., fourth ventricle; Red nucleus mc, red nucleus magnocellular area.

The Rubrospinal Tract. The red nucleus of the mesencephalon receives major input from both the cerebellum and the cerebral cortical motor areas. Output via the **rubrospinal tract** is directed predominantly to contralateral spinal motor neurons that are involved with movements of the distal limbs. The axons of the rubrospinal tract are located in the lateral spinal white matter, just anterior to the corticospinal tract. Rubrospinal action enhances the function of motor neurons innervating limb flexor muscles while inhibiting extensors. This tract may also influence gamma motor neuron function.

Electrophysiological studies reveal that many rubrospinal neurons are active during locomotion, with more than half showing increased activity during the swing phase of stepping, when the flexors are most active. This system appears to be important for the production of movement, especially in the distal limbs. Experimental lesions that interrupt rubrospinal axons produce deficits in distal limb flexion, with little change in more proximal muscles. In higher animals, the corticospinal tract supersedes some of the function of the rubrospinal tract.

The Vestibulospinal Tract. The vestibular system regulates muscular function for the maintenance of posture in response to changes in the position of the head in space and accelerations of the body. There are four major nuclei in the vestibular complex: the **superior**, **lateral**, **medial**, and **inferior vestibular nuclei**. These nuclei, located in the pons and medulla, receive afferent action potentials from the vestibular portion of the ear, which includes the semicircular canals, the utricle, and the saccule (see Chapter 4). Information about rotatory and linear motions of the head and body are conveyed by this system. The vestibular nuclei are reciprocally connected with the superior colliculus on the dorsal surface of the mesencephalon. Input from the

retina is received there and is utilized in adjusting eye position during movement of the head. Reciprocal connections to the vestibular nuclei are also made with the cerebellum and reticular formation.

The chief output to the spinal cord is the **vestibulospinal tract**, which originates predominantly from the lateral vestibular nucleus. The tract's axons are located in the anterior-lateral white matter and carry excitatory action potentials to ipsilateral extensor motor neuron pools, both alpha and gamma. The extensor motor neurons and their musculature are important in the maintenance of posture. Lesions in the brainstem secondary to stroke or trauma may abnormally enhance the influence of the vestibulospinal tract and produce dramatic clinical manifestations (see Clinical Focus Box 5.1).

The Reticulospinal Tract. The reticular formation in the central gray matter core of the brainstem contains many axon bundles interwoven with cells of various shapes and sizes. A prominent characteristic of reticular formation neurons is that their axons project widely in ascending and descending pathways, making multiple synaptic connections throughout the neuraxis. The medial region of the reticular formation contains large neurons that project upward to the thalamus, as well as downward to the spinal cord. Afferent input to the reticular formation comes from the spinal cord, vestibular nuclei, cerebellum, lateral hypothalamus, globus pallidus, tectum, and sensorimotor cortex.

Two areas of the reticular formation are important in the control of motor neurons. The descending tracts arise from the **nucleus reticularis pontis oralis and nucleus reticularis pontis caudalis** in the pons, and from the **nucleus reticularis gigantocellularis** in the medulla. The pontine reticular area gives rise to the ipsilateral **pontine reticulospinal tract,** whose axons descend in the medial spinal cord white matter. These axons carry excitatory action potentials to interneurons that influence alpha and gamma motor neuron pools of axial muscles. The medullary area gives rise to the **medullary reticulospinal tract,** whose axons descend mostly ipsilateral in the anterior spinal white matter. These axons have inhibitory influences on interneurons that modulate extensor motor neurons.

The Terminations of the Brainstem Motor Tracts Correlate With Their Functions

The vestibulospinal and reticulospinal tracts descend medially in the spinal cord and terminate in the ventromedial part of the intermediate zone, an area in the gray matter containing propriospinal interneurons (Fig. 5.12). There are also some direct connections with motor neurons of the neck and back muscles and the proximal limb muscles. These tracts are the main CNS pathways for maintaining posture and head position during movement.

The rubrospinal tract descends laterally in the spinal cord and terminates mostly on interneurons in the lateral spinal intermediate zone, but it also has some monosynaptic connections directly on motor neurons to muscles of the distal extremities. This tract supplements the medial descending pathways in postural control and the corticospinal tract for independent movements of the extremities.

In accordance with their medial or lateral distributions to spinal motor neurons, the reticulospinal and vestibulospinal tracts are thought to be most important for the control of axial and proximal limb muscles, whereas the rubrospinal (and corticospinal) tracts are most important for the control of distal limb muscles, particularly the flexors.

Sensory and Motor Systems Work Together to Control Posture

The maintenance of an upright posture in humans requires active muscular resistance against gravity. For movement to occur, the initial posture must be altered by flexing some body parts against gravity. Balance must be maintained during movement, which is achieved by postural reflexes initiated by several key sensory systems. Vision, the vestibular system, and the somatosensory system are important for postural reflexes.

CLINICAL FOCUS BOX 5.1

Decerebrate Rigidity

A patient with a history of poorly controlled hypertension, a result of noncompliance with his medication, is brought to the emergency department because of sudden collapse and subsequent unresponsiveness. A neurological examination performed about 30 minutes after onset of the collapse shows no response to verbal stimuli. No spontaneous movements of the limbs are observable. A mildly painful stimulus, compression of the soft tissue of the supraorbital ridge, causes immediate extension of the neck and both arms and legs. This posture relaxes within a few seconds after the stimulation is stopped. After the patient is stabilized medically, he undergoes a magnetic resonance imaging (MRI) study of the brain. The study demonstrates a large area of hemorrhage bilaterally in the upper pons and lower mesencephalon.

The posture this patient demonstrated in response to a noxious stimulus is termed **decerebrate rigidity**. Its presence is associated with lesions of the mesencephalon that isolate the portions of the brainstem below that level from the influence of higher centers. The abnormal posture is a result of extreme activation of the antigravity extensor muscles by the unopposed action of the lateral vestibular nucleus and the vestibulospinal tract. A model of this condition can be produced in experimental animals by a surgical lesion located between the mesencephalon and pons. It can also be shown in experimental animals that a destructive lesion of the lateral vestibular nucleus relieves the rigidity on that side.

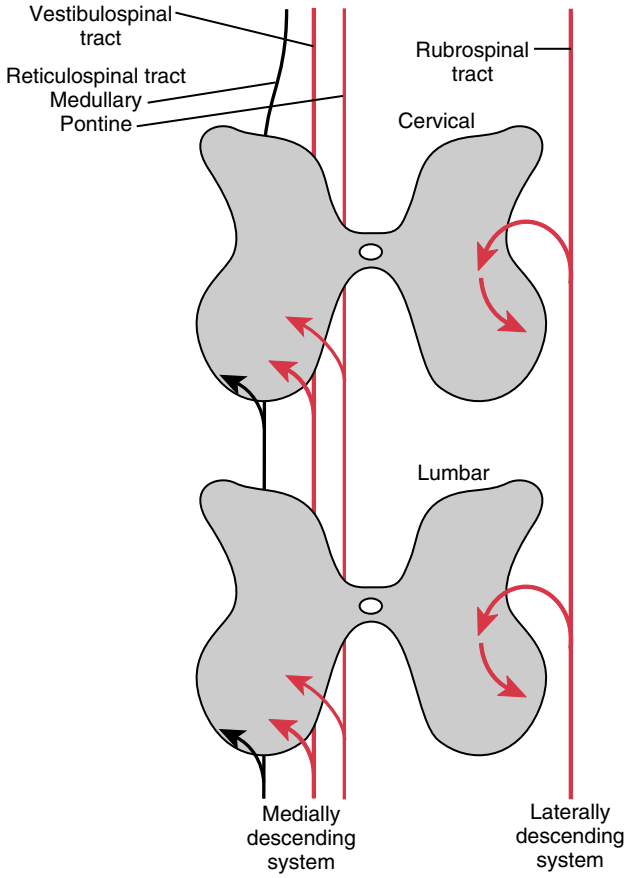

FIGURE 5.12 **Brainstem motor control tracts.** The vestibulospinal and reticulospinal tracts influence motor neurons that control axial and proximal limb muscles. The rubrospinal tract influences motor neurons controlling distal limb muscles. Excitatory pathways are shown in red.

Somatosensory input provides information about the position and movement of one part of the body with respect to others. The vestibular system provides information about the position and movement of the head and neck with respect to the external world. Vision provides both types of information, as well as information about objects in the external world. Visual and vestibular reflexes interact to produce coordinated head and eye movements associated with a shift in gaze. Vestibular reflexes and somatosensory neck reflexes interact to produce reflex changes in limb muscle activity. The quickest of these compensations occurs at about twice the latency of the monosynaptic myotatic reflex. These response types are termed **long loop reflexes**. The extra time reflects the action of other neurons at different anatomic levels of the nervous system.

THE ROLE OF THE CEREBRAL CORTEX IN MOTOR CONTROL

The cerebral cortical areas concerned with motor function exert the highest level of motor control. It is difficult to formulate an unequivocal definition of a **cortical motor area**, but three criteria may be used. An area is said to have a motor function if

- Stimulation using very low current strengths elicits movements.
- Destruction of the area results in a loss of motor function.
- The area has output connections going directly or relatively directly (i.e., with a minimal number of intermediate connections) to the motor neurons.

Some cortical areas fulfill all of these criteria and have exclusively motor functions. Other areas fulfill only some of the criteria yet are involved in movement, particularly volitional movement.

Distinct Cortical Areas Participate in Voluntary Movement

The **primary motor cortex** (MI), Brodmann's area 4, fulfills all three criteria for a motor area (Fig. 5.13). The **supplementary motor cortex** (MII), which also fulfills all three criteria, is rostral and medial to MI in Brodmann's area 6. Other areas that fulfill some of the criteria include the rest of Brodmann's area 6; areas 1, 2, and 3 of the postcentral

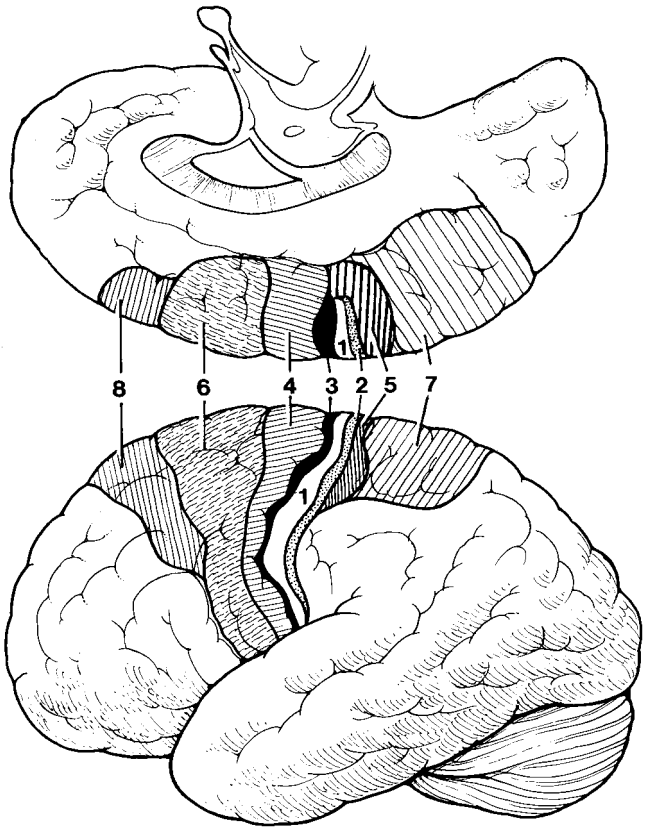

FIGURE 5.13 **Brodmann's cytoarchitectural map of the human cerebral cortex.** Area 4 is the primary motor cortex (MI); area 6 is the premotor cortex and includes the supplementary motor area (MII) on the medial aspect of the hemisphere; area 8 influences voluntary eye movements; areas 1, 2, 3, 5, and 7 have sensory functions but also contribute axons to the corticospinal tract.

gyrus; and areas 5 and 7 of the parietal lobe. All of these areas contribute fibers to the **corticospinal tract,** the efferent motor pathway from the cortex.

The Primary Motor Cortex (MI). This cortical area corresponds to Brodmann's area 4 in the precentral gyrus. Area 4 is structured in six well-defined layers (I to VI), with layer I being closest to the pial surface. Afferent fibers terminate in layers I to V. Thalamic afferent fibers terminate in two layers; those that carry somatosensory information end in layer IV, and those from nonspecific nuclei end in layer I. Cerebellar afferents terminate in layer IV. Efferent axons arise in layers V and VI to descend as the corticospinal tract. Body areas are represented in an orderly manner, as **somatotopic maps**, in the motor and sensory cortical areas (Fig 5.14). Those parts of the body that perform fine movements, such as the digits and the facial muscles, are controlled by a greater number of neurons that occupy more cortical territory than the neurons for the body parts only capable of gross movements.

Low-level electrical stimulation of MI produces twitch-like contraction of a few muscles or, less commonly, a single muscle. Slightly stronger stimuli also produce responses in adjacent muscles. Movements elicited from area 4 have the lowest stimulation thresholds and are the most discrete of any movements elicited by stimulation. Stimulation of MI limb areas produces contralateral movement, while cranial cortical areas may produce bilateral motor responses. Destruction of any part of the primary motor cortex leads to immediate paralysis of the muscles controlled by that area. In humans, some function may return weeks to months later, but the movements lack the fine degree muscle control of the normal state. For example, after a lesion in the arm area of MI, the use of the hand recovers, but the capacity for discrete finger movements does not.

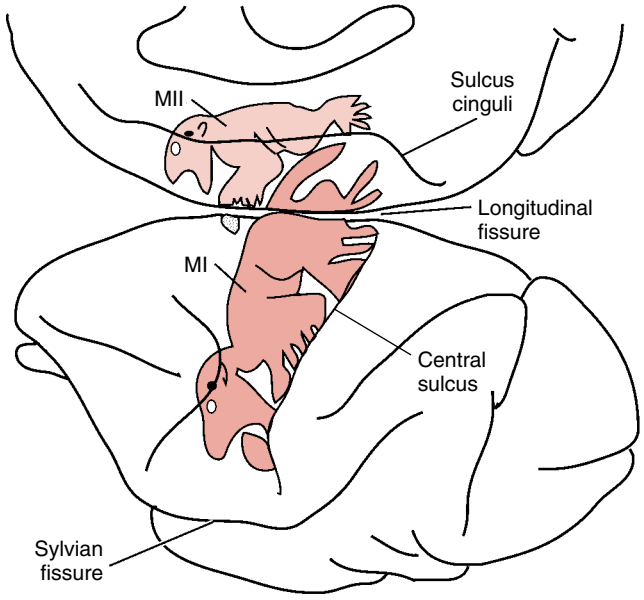

FIGURE 5.14 **A cortical map of motor functions.** Primary motor cortex (MI) and supplementary motor cortex (MII) areas in the monkey brain. MII is on the medial aspect of the hemisphere.

Neurons in MI encode the capability to control muscle force, muscle length, joint movement, and position. The area receives somatosensory input, both cutaneous and proprioceptive, via the ventrobasal thalamus. The cerebellum projects to MI via the red nucleus and ventrolateral thalamus. Other afferent projections come from the nonspecific nuclei of the thalamus, the contralateral motor cortex, and many other ipsilateral cortical areas. There are many axons between the precentral (motor) and postcentral (somatosensory) gyri and many connections to the visual cortical areas. Because of their connections with the somatosensory cortex, the cortical motor neurons can also respond to sensory stimulation. For example, cells innervating a particular muscle may respond to cutaneous stimuli originating in the area of skin that moves when that muscle is active, and they may respond to proprioceptive stimulation from the muscle to which they are related. Many efferent fibers from the primary motor cortex terminate in brain areas that contribute to ascending somatic sensory pathways. Through these connections, the motor cortex can control the flow of somatosensory information to motor control centers.

The close coupling of sensory and motor functions may play a role in two cortically controlled reflexes that were originally described in experimental animals as being important for maintaining normal body support during locomotion—the placing and hopping reactions. The **placing reaction** can be demonstrated in a cat by holding it so that its limbs hang freely. Contact of any part of the animal's foot with the edge of a table provokes immediate placement of the foot on the table surface. The **hopping reaction** is demonstrated by holding an animal so that it stands on one leg. If the body is moved forward, backward, or to the side, the leg hops in the direction of the movement so that the foot is kept directly under the shoulder or hip, stabilizing the body position. Lesions of the contralateral precentral or postcentral gyrus abolish placing. Hopping is abolished by a contralateral lesion of the precentral gyrus.

The Supplementary Motor Cortex (MII). The MII cortical area is located on the medial surface of the hemispheres, above the cingulate sulcus, and rostral to the leg area of the primary motor cortex (see Fig. 5.14). This cortical region within Brodmann's area 6 has no clear cytoarchitectural boundaries; that is, the shapes and sizes of cells and their processes are not obviously compartmentalized, as in the layers of MI.

Electrical stimulation of MII produces movements, but a greater strength of stimulating current is required than for MI. The movements produced by stimulation are also qualitatively different from MI; they last longer, the postures elicited may remain after the stimulation is over, and the movements are less discrete. Bilateral responses are common. MII is reciprocally connected with MI, and receives input from other motor cortical areas. Experimental lesions in MI eliminate the ability of MII stimulation to produce movements.

Current knowledge is insufficient to adequately describe the unique role of MII in higher motor functions. MII is thought to be active in bimanual tasks, in learning and preparing for the execution of skilled movements, and in the control of muscle tone. The mechanisms that underlie

the more complex aspects of movement, such as thinking about and performing skilled movements and using complex sensory information to guide movement, remain incompletely understood.

The Primary Somatosensory Cortex and Superior Parietal Lobe. The **primary somatosensory cortex** (Brodmann's areas 1, 2, and 3) lies on the postcentral gyrus (see Fig. 5.13) and has a role in movement. Electrical stimulation here can produce movement, but thresholds are 2 to 3 times higher than in MI. The somatosensory cortex is reciprocally interconnected with MI in a somatotopic pattern—for example, arm areas of sensory cortex project to arm areas of motor cortex. Efferent fibers from areas 1, 2, and 3 travel in the corticospinal tract and terminate in the dorsal horn areas of the spinal cord.

The **superior parietal lobe** (Brodmann's areas 5 and 7) also has important motor functions. In addition to contributing fibers to the corticospinal tract, it is well connected to the motor areas in the frontal lobe. Lesion studies in animals and humans suggest this area is important for the utilization of complex sensory information in the production of movement.

The Corticospinal Tract Is the Primary Efferent Path From the Cortex

Traditionally, the descending motor tract originating in the cerebral cortex has been called the **pyramidal tract** because it traverses the medullary pyramids on its way to the spinal cord (Fig. 5.15). This path is the **corticospinal tract**. All other descending motor tracts emanating from the brainstem were generally grouped together as the extrapyramidal system. Cells in Brodmann's area 4 (MI) contribute 30% of the corticospinal fibers; area 6 (MII) is the origin of 30% of the fibers; and the parietal lobe, especially Brodmann's areas 1, 2, and 3, supplies 40%. In primates, 10 to 20% of corticospinal fibers ends directly on motor neurons; the others end on interneurons associated with motor neurons.

From the cerebral cortex, the corticospinal tract axons descend through the brain along a path located between the basal ganglia and the thalamus, known as the **internal capsule**. They then continue along the ventral brainstem as the **cerebral peduncles** and on through the pyramids of the medulla. Most of the corticospinal axons cross the midline in the medullary pyramids; thus, the motor cortex in each hemisphere controls the muscles on the contralateral side of the body. After crossing in the medulla, the corticospinal axons descend in the dorsal lateral columns of the spinal cord and terminate in lateral motor pools that control distal muscles of the limbs. A smaller group of axons do not cross in the medulla and descend in the ventral spinal columns. These axons terminate in the motor pools and adjacent intermediate zones that control the axial and proximal musculature.

The corticospinal tract is estimated to contain about 1 million axons at the level of the medullary pyramid. The largest-diameter, heavily myelinated axons are between 9 and 20 μm in diameter, but that population accounts for only a small fraction of the total. Most corticospinal axons are small, 1 to 4 μm in diameter, and half are unmyelinated.

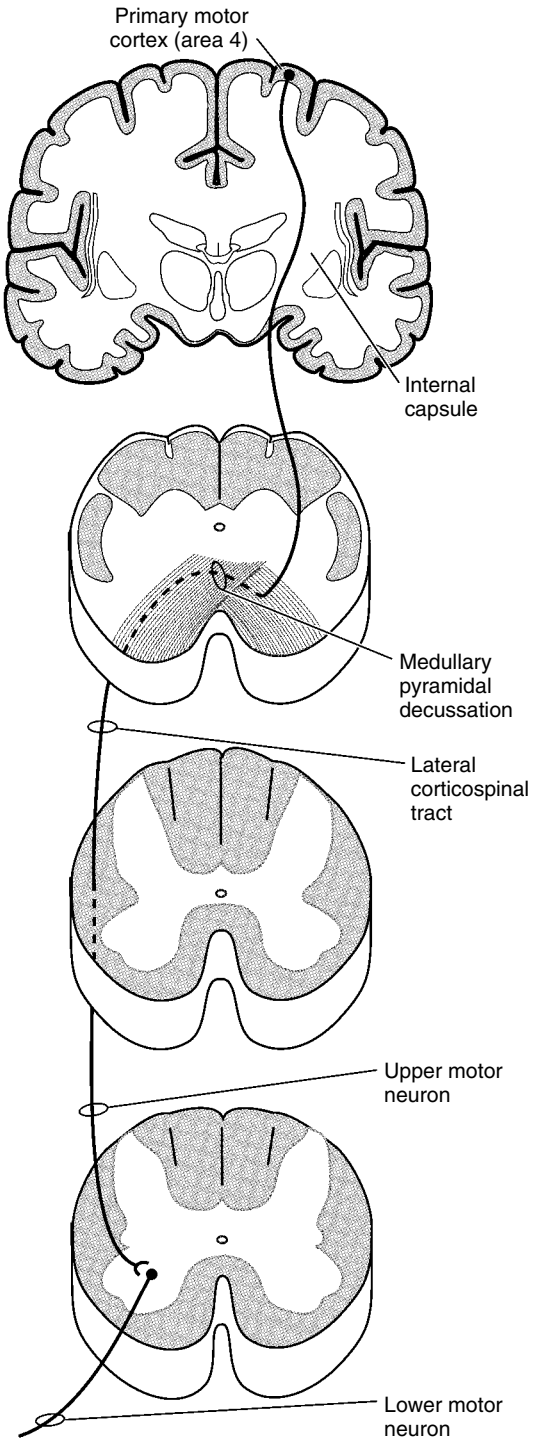

FIGURE 5.15 **The corticospinal tract.** Axons arising from cortical neurons, including the primary motor area, descend through the internal capsule, decussate in the medulla, travel in the lateral area of the spinal cord as the lateral corticospinal tract, and terminate on motor neurons and interneurons in the ventral horn areas of the spinal cord. Note the upper and lower motor neuron designations.

In addition to the direct corticospinal tract, there are other indirect pathways by which cortical fibers influence motor function. Some cortical efferent fibers project to the reticular formation, then to the spinal cord via the reticulospinal tract; others project to the red nucleus, then to the spinal cord via the rubrospinal tract. Despite the fact that these pathways involve intermediate neurons on the way to the cord, volleys relayed through the reticular formation can reach the spinal cord motor circuitry at the same time as, or earlier than, some volleys along the corticospinal tract.

THE BASAL GANGLIA AND MOTOR CONTROL

The **basal ganglia** are a group of subcortical nuclei located primarily in the base of the forebrain, with some in the diencephalon and upper brainstem. The striatum, globus pallidus, subthalamic nucleus, and substantia nigra comprise the basal ganglia. Input is derived from the cerebral cortex and output is directed to the cortical and brainstem areas concerned with movement. Basal ganglia action influences the entire motor system and plays a role in the preparation and execution of coordinated movements.

The forebrain (telencephalic) components of the basal ganglia consist of the **striatum,** which is made up of the **caudate nucleus** and the **putamen**, and the **globus pallidus**. The caudate nucleus and putamen are histologically identical but are separated anatomically by fibers of the anterior limb of the internal capsule. The globus pallidus has two subdivisions: the **external segment** (GPe), adjacent to the medial aspect of the putamen, and the **internal segment** (GPi), medial to the GPe. The other main nuclei of the basal ganglia are the **subthalamic nucleus** in the diencephalon and the **substantia nigra** in the mesencephalon.

The Basal Ganglia Are Extensively Interconnected

Although the circuitry of the basal ganglia appears complex at first glance, it can be simplified into input, output, and internal pathways (Fig. 5.16). Input is derived from the cerebral cortex and is directed to the striatum and the subthalamic nucleus. The predominant nerve cell type in the striatum is termed the **medium spiny neuron,** based on its cell body size and dendritic structure. This type of neuron receives input from all of the cerebral cortex except for the primary visual and auditory areas. The input is roughly somatotopic and is via neurons that use glutamate as the neurotransmitter. The putamen receives the majority of the cortical input from sensorimotor areas. Input to the subthalamus is from the cortical areas concerned with motor function, including eye movement, and is also via glutamate-releasing neurons.

Basal ganglia output is from the internal segment of the globus pallidus (GPi) and one segment of the substantia nigra. The GPi output is directed to ventrolateral and ventral anterior nuclei of the thalamus, which feed back to the cortical motor areas. The output of the GPi is also directed to a region in the upper brainstem termed the **midbrain extrapyramidal area**. This latter area then projects to the neurons of the reticulospinal tract. The substantia nigra output arises from the **pars reticulata** (SNr), which is histologically similar to the GPi. The output is directed to the superior colliculus of the mesencephalon, which is involved in eye movement control. The GPi and SNr output is inhibitory via neurons that use GABA as the neurotransmitter.

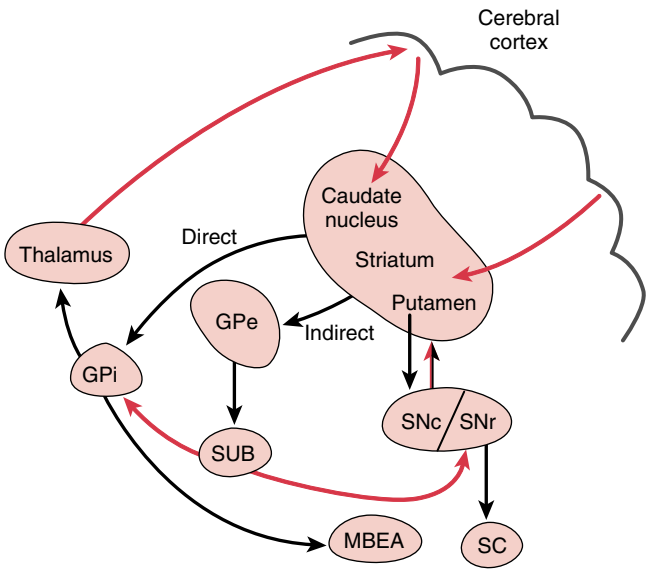

FIGURE 5.16 **Basal ganglia nuclei and circuitry.** The circuit of cerebral cortex to striatum to GPi to thalamus and back to the cortex is the main pathway for basal ganglia influence on motor control. Note the direct and indirect pathways involving the striatum, GPi, GPe, and subthalamic nucleus. GPi output is also directed to the midbrain extrapyramidal area (MBEA). The SNr to SC pathway is important in eye movements. Excitatory pathways are shown in red, inhibitory pathways are in black. GPe and GPi, globus pallidus externa and interna; SUB, subthalamic nucleus; SNc and SNr, substantia nigra pars compacta and pars reticulata; SC, superior colliculus.

The internal pathway circuits link the various nuclei of the basal ganglia. The globus pallidus externa (GPe), the subthalamic nucleus, and the pars compacta region of the substantia nigra (SNc) are the nuclei in these pathways. The GPe receives inhibitory input from the striatum via GABA-releasing neurons. The output of the GPe is also inhibitory via GABA release and is directed to the GPi and the subthalamic nucleus. The subthalamic nucleus output is excitatory and is directed to the GPi and the SNr. This striatum-GPe-subthalamic nucleus-GPi circuit has been termed the **indirect pathway** in contrast to the **direct pathway** of striatum to Gpi (see Fig. 5.16). The SNc receives inhibitory input from the striatum and produces output back to the striatum via dopamine-releasing neurons. The output can be either excitatory or inhibitory depending on the receptor type of the target neurons in the striatum. The action of the SNc may modulate cortical input to the striatum.

The Functions of the Basal Ganglia Are Partially Revealed by Disease

Basal ganglia diseases produce profound motor dysfunction in humans and experimental animals. The disorders can result in reduced motor activity, **hypokinesis**, or abnormally enhanced activity, **hyperkinesis**. Two well-known neuro-

logical conditions that show histological abnormality in basal ganglia structures, Parkinson's disease and Huntington's disease, illustrate the effects of basal ganglia dysfunction. Patients with **Parkinson's disease** show a general slowness of initiation of movement and paucity of movement when in motion. The latter takes the form of reduced arm swing and lack of truncal swagger when walking. These patients also have a resting tremor of the hands, described as "pill rolling." The tremor stops when the hand goes into active motion. At autopsy, patients with Parkinson's disease show a severe loss of dopamine-containing neurons in the SNc region. Patients with **Huntington's disease** have uncontrollable, quick, brief movements of individual limbs. These movements are similar to what a normal individual might show when flicking a fly off a hand or when quickly reaching up to scratch an itchy nose. At autopsy, a severe loss of striatal neurons is found.

The function of the basal ganglia in normal individuals remains unclear. One theory is that the primary action is to inhibit undesirable movements, thereby, allowing desired motions to proceed. Neuronal activity is increased in the appropriate areas of the basal ganglia prior to the actual execution of movement. The basal ganglia act as a brake on undesirable motion by the inhibitory output of the GPi back to the cortex through the thalamus. Enhanced output from the GPi increases this braking effect. The loss of dopamine-releasing neurons in Parkinson's disease is thought to produce this type of result by reducing inhibitory influence on the striatum and, thereby, increasing the excitatory action of the subthalamic nucleus on the GPi through the indirect basal ganglia pathway (see Clinical Focus Box 5.2). Hyperkinetic disorders like Huntington's disease are thought to result from decreased GPi output secondary to the loss of inhibitory influence of the striatum through the direct pathway.

THE CEREBELLUM IN THE CONTROL OF MOVEMENT

The **cerebellum,** or "little brain," lies caudal to the occipital lobe and is attached to the posterior aspect of the brainstem through three paired fiber tracts: the **inferior**, **middle**, and **superior cerebellar peduncles**. Input to the cerebellum comes from peripheral sensory receptors, the brainstem, and the cerebral cortex. The inferior, middle and, to a lesser degree, superior cerebellar peduncles carry the input. The output projections are mainly, if not totally, to other motor control areas of the central nervous system and are mostly carried in the superior cerebellar peduncle. The cerebellum contains three pairs of intrinsic nuclei: the **fastigial**, **interpositus** (interposed), and **dentate**. In some classification schemes, the interposed nucleus is further divided into the **emboliform** and **globose** nuclei.

The Structural Divisions of the Cerebellum Correlate With Function

The cerebellar surface is arranged in multiple, parallel, longitudinal folds termed **folia**. Several deep fissures divide the cerebellum into three main morphological components—the **anterior**, **posterior,** and **flocculonodular lobes,** which also correspond with the functional subdivisions of the cerebellum (Fig. 5.17). The functional divisions are the vestibulocerebellum, the spinocerebellum, and the cerebrocerebellum. These divisions appear in sequence during evo-

CLINICAL FOCUS BOX 5.2

Stereotactic Neurosurgery for Parkinson's disease

Parkinson's disease is a CNS disorder producing a generalized slowness of movement and resting tremor of the hands. Loss of dopamine-producing neurons in the substantia nigra pars compacta is the cause of the condition. Treatment with medications that stimulate an increased production of dopamine by the surviving substantia nigra neurons has revolutionized the management of Parkinson's disease. Unfortunately, the benefit of the medications tends to lessen after 5 to 10 years of treatment. Increasing difficulty in initiating movement and worsening slowness of movement are features of a declining responsiveness to medication. Improved knowledge of basal ganglia circuitry has enabled neurosurgeons to develop surgical procedures to ameliorate some of the effects of the advancing disease.

Degeneration of the dopamine-releasing cells of the substantia nigra reduces excitatory input to the putamen. Inhibitory output of the putamen to the GPe greatly increases via the indirect pathway. This results in decreased inhibitory GPe output to the subthalamic nucleus, which, in turn, acts unrestrained to stimulate the GPi. Stimulation of the GPi enhances its inhibitory influence on the thalamus and results in decreased excitatory drive back to the cerebral cortex.

Stereotactic neurosurgery is a technique in which a small probe can be precisely placed into a target within the brain. Magnetic resonance imaging (MRI) of the brain defines the three-dimensional location of the GPi. The surgical probe is introduced into the brain through a small hole made in the skull and is guided to the target by the surgeon using the MRI coordinates. The correct positioning of the probe into the GPi can be further confirmed by recording the electrical activity of the GPi neurons with an electrode located at the tip of the probe. GPi neurons have a continuous, high frequency firing pattern that, when amplified and presented on a loudspeaker, sounds like heavy rain striking a metal roof. When the target location is reached, the probe is heated to a temperature that destroys a precisely controllable amount of the GPi. The inhibitory outflow of the GPi is reduced and movement improves.

The use of implantable stimulators to modify activity of the basal ganglia nuclei is also being investigated to improve function in patients with Parkinson's disease and other types of movement disorders.

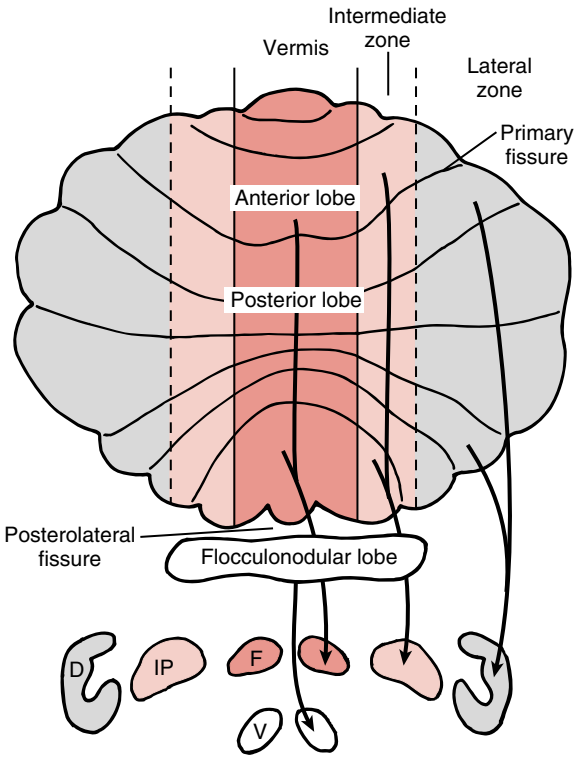

FIGURE 5.17 **The structure of the cerebellum.** The three lobes are shown: anterior, posterior, and flocculonodular. The functional divisions are demarcated by color. The vestibulocerebellum (white) is the flocculonodular lobe and projects to the vestibular (V) nuclei. The spinocerebellum includes the vermis (dark pink) and intermediate zone (pink), which project to the fastigial (F) and interposed (IP) nuclei, respectively. The cerebrocerebellum (gray) projects to the dentate nuclei (D).

lution. The lateral cerebellar hemispheres increase in size along with expansion of the cerebral cortex. The three divisions have similar intrinsic circuitry; thus, the function of each depends on the nature of the output nucleus to which it projects.

The **vestibulocerebellum** is composed of the flocculonodular lobe. It receives input from the vestibular system and visual areas. Output goes to the vestibular nuclei, which can, in a sense, be considered as an additional pair of intrinsic cerebellar nuclei. The vestibulocerebellum functions to control equilibrium and eye movements.

The medially placed **spinocerebellum** consists of the midline **vermis** plus the medial portion of the lateral hemispheres, called the **intermediate zones**. Spinocerebellar pathways carrying somatosensory information terminate in the vermis and intermediate zones in somatotopic arrangements. The auditory, visual, and vestibular systems and sensorimotor cortex also project to this portion of the cerebellum. Output from the vermis is directed to the fastigial nuclei, which project through the inferior cerebellar peduncle to the vestibular nuclei and reticular formation of the pons and medulla. Output from the intermediate zones goes to the interposed nuclei and from there to the red nucleus and, ultimately, to the motor cortex via the ventrolateral nucleus of the thalamus. It is believed that both the fastigial and interposed nuclei contain a complete representation of the muscles of the body. The fastigial output system controls antigravity muscles in posture and locomotion, while the interposed nuclei, perhaps, act on stretch reflexes and other somatosensory reflexes.

The **cerebrocerebellum** occupies the lateral aspects of the cerebellar hemispheres. Input comes exclusively from the cerebral cortex, relayed through the middle cerebellar peduncles of the pons. The cortical areas that are prominent in motor control are the sources for most of this input. Output is directed to the dentate nuclei and from there via the ventrolateral thalamus back to the motor and premotor cortices.

The Intrinsic Circuitry of the Cerebellum Is Very Regular

The cerebellar cortex is composed of five types of neurons arranged into three layers (Fig. 5.18). The molecular layer is the outermost and consists mostly of axons and dendrites plus two types of interneurons, **stellate cells** and **basket cells**. The next layer contains the dramatic **Purkinje cells**, whose dendrites reach upward into the molecular layer in a fan-like array. The Purkinje cells are the only efferent neurons of the cerebellar cortex. Their action is inhibitory via GABA as the neurotransmitter. Deep to the Purkinje cells is the **granular layer**, containing **Golgi cells**, and small local circuit neurons, the **granule cells**. The granule cells are numerous; there are more granule cells in the cerebellum than neurons in the entire cerebral cortex!

Afferent axons to the cerebellar cortex are of two types: mossy fibers and climbing fibers. **Mossy fibers** arise from the spinal cord and brainstem neurons, including those of the pons that receive input from the cerebral

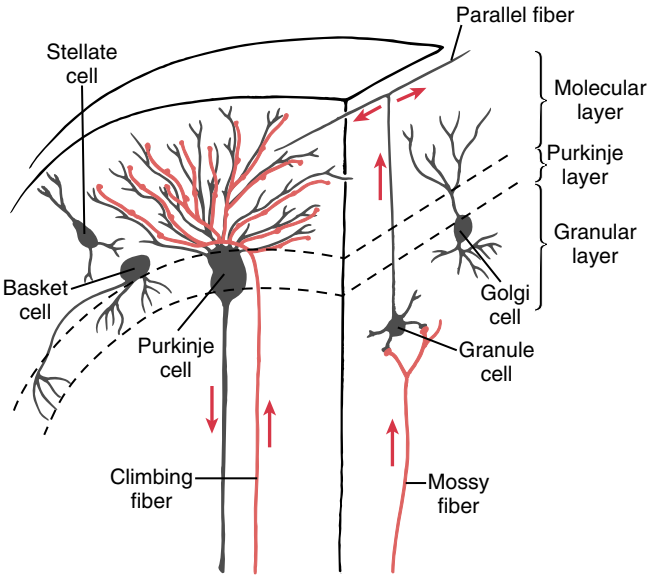

FIGURE 5.18 **Cerebellar circuitry.** The cell types and action potential pathways are shown. Mossy fibers bring afferent input from the spinal cord and the cerebral cortex. Climbing fibers bring afferent input from the inferior olive nucleus in the medulla and synapse directly on the Purkinje cells. The Purkinje cells are the efferent pathways of the cerebellum.

cortex. Mossy fibers make complex multicontact synapses on granule cells. The granule cell axons then ascend to the molecular layer and bifurcate, forming the **parallel fibers**. These travel perpendicular to and synapse with the dendrites of Purkinje cells, providing excitatory input via glutamate. Mossy fibers discharge at high tonic rates, 50 to 100 Hz, which increases further during voluntary movement. When mossy fiber input is of sufficient strength to bring a Purkinje cell to threshold, a single action potential results.

Climbing fibers arise from the **inferior olive,** a nucleus in the medulla. Each climbing fiber synapses directly on the dendrites of a Purkinje cell and exerts a strong excitatory influence. One action potential in a climbing fiber produces a burst of action potentials in the Purkinje cell called a complex spike. Climbing fibers also synapse with basket, Golgi, and stellate interneruons, which then make inhibitory contact with adjacent Purkinje cells. This circuitry allows a climbing fiber to produce excitation in a single Purkinje cell and inhibition in the surrounding ones.

Mossy and climbing fibers also give off excitatory collateral axons to the deep cerebellar nuclei before reaching the cerebellar cortex. The cerebellar cortical output (Purkinje cell efferents) is inhibitory to the cerebellar and vestibular nuclei, but the ultimate output of the cerebellar nuclei is mostly excitatory. A smaller population of neurons of the deep cerebellar nuclei produces inhibitory outflow directed mainly back to the inferior olive.

Lesions Reveal the Function of the Cerebellum

Lesions of the cerebellum produce impairment in the coordinated action of agonists, antagonists, and synergists. This impairment is clinically known as **ataxia**. The control of limb, axial, and cranial muscles may be impaired depending on the site of the cerebellar lesion. Limb ataxia might manifest as the coarse jerking motions of an arm and hand during reaching for an object instead of the expected, smooth actions. This jerking type of motion is also referred to as **action tremor**. The swaying walk of an intoxicated individual is a vivid example of truncal ataxia.

Cerebellar lesions can also produce a reduction in muscle tone, **hypotonia**. This condition is manifest as a notable decrease in the low level of resistance to passive joint movement detectable in normally relaxed individuals. Myotatic reflexes produced by tapping a tendon with a reflex hammer reverberate for several cycles (pendular reflexes) because of impaired damping from the reduced muscle tone. The hypotonia is likely a result of impaired processing of cerebellar afferent action potentials from the muscle spindles and Golgi tendon organs.

While these lesions establish a picture of the absence of cerebellar function, we are left without a firm idea of what the cerebellum does in the normal state. Cerebellar function is sometimes described as comparing the intended with the actual movement and adjusting motor system output in ongoing movements. Other putative functions include a role in learning new motor and even cognitive skills.

REVIEW QUESTIONS

DIRECTIONS: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE lettered answer or completion that is BEST in each case.

1. Which type of motor unit is of prime importance in generating the muscle power necessary for the maintenance of posture?
   (A) Low threshold, fatigue-resistant
   (B) High threshold, fatigable
   (C) Intrafusal, gamma controlled
   (D) High threshold, high force
   (E) Extrafusal, gamma controlled
2. Which type of sensory receptor provides information about the force of muscle contraction?
   (A) Nuclear bag fiber
   (B) Nuclear chain fiber
   (C) Golgi tendon organ
   (D) Bare nerve ending
   (E) Type Ia ending
3. If a patient experiences enlargement of the normally rudimentary central canal of the spinal cord in the midcervical region, which, if any, muscular functions would become abnormal first?
   (A) Finger flexion
   (B) Elbow flexion
   (C) Shoulder abduction
   (D) Truncal extension
   (E) No muscles would become abnormal
4. Tapping the patellar tendon with a reflex hammer produces a brief contraction of the knee extensors. What is the cause of the muscle contraction?
   (A) Elastic rebound of muscle connective tissue
   (B) Golgi tendon organ response
   (C) Muscle spindle activation
   (D) Muscle spindle unloading
   (E) Gamma motor neuron discharge
5. The cyclical flexion and extension motions of a leg during walking result from activity at which level of the nervous system?
   (A) Cerebral cortex
   (B) Cerebellum
   (C) Globus pallidus
   (D) Red nucleus
   (E) Spinal cord
6. Which brainstem-derived descending tract produces action similar to the corticospinal tract?
   (A) Vestibulospinal
   (B) Reticulospinal
   (C) Spinocerebellar
   (D) Rubrospinal
   (E) None
7. What is the location of the primary motor area of the cerebral cortex?
   (A) Upper parietal lobe
   (B) Superior temporal lobe
   (C) Precentral gyrus
   (D) Postcentral gyrus
   (E) Medial aspect of the hemisphere
8. Concurrent flexion of both wrists in response to electrical stimulation is characteristic of which area of the nervous system?
   (A) Postcentral gyrus
   (B) Vestibulospinal tract
   (C) Dentate nucleus
   (D) Primary motor cortex
   (E) Supplementary motor cortex
9. If you could histologically examine the spinal cord of a patient who had experienced a viral illness 10 years before in which only the neurons of the primary motor area of the cerebral cortex were destroyed, what findings would you expect?
   (A) The corticospinal tract would be completely degenerated
   (B) The rubrospinal tract would show an increased number of axons

(continued)

(C) The corticospinal tract would be about one-third depleted of axons
(D) The alpha motor neurons would be atrophic
(E) The corticospinal tract would be normal

10. A disease that produces decreased inhibitory input to the internal segment of the globus pallidus should have what effect on the motor area of the cerebral cortex?
(A) Increased excitatory feedback directly to the cortex
(B) No effect
(C) Decreased excitatory output from the thalamus to the cortex
(D) Increased excitatory output from the putamen to the cortex
(E) Increased excitatory output from the thalamus to the cortex

11. Which cerebellar component would be abnormal in a degenerative disease that affected spinal sensory neurons?
(A) Purkinje cells
(B) Mossy fibers
(C) Parallel fibers
(D) Climbing fibers
(E) Granule cells

SUGGESTED READING

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