9 Organization of Motor Function

LEARNING OBJECTIVES

Upon completion of this chapter, the student should be able to answer the following questions:

1. What is a motor neuron, and how are α and γ motor neurons different?
2. What is a motor unit? How does the "size principle" apply to the orderly recruitment of motor units?
3. What is a reflex, and why are reflexes useful for clinical and scientific understanding?
4. What information about the state of the muscle is sensed by the muscle spindles, and what afferent fibers convey this information to the central nervous system (CNS)?
5. How do γ motor neurons modulate the responses of the muscle spindle?
6. What are the pathways and functions of the basic spinal reflexes?
7. What is a central pattern generator, and what types of movements can it be used for?
8. What distinguishes the pathways of the medial and lateral descending pathways in motor control?
9. What is decerebrate rigidity, and what are its implications for the control of muscle tone?
10. What distinguishes the cortical motor areas from each other?
11. What motor parameters are coded for in the activity of neurons in motor cortex?
12. How does the organization of the mossy and olivocerebellar (climbing) fiber afferent systems to the cerebellum differ in their origins, topography, and synaptic connections.
13. What is the geometric relationship between the major cellular elements of the cerebellar cortex?
14. What are simple and complex spikes in Purkinje neurons?
15. What are the direct and indirect pathways in the basal ganglia, and how does their activity influence movement?
16. How is the balance of activity between the direct and indirect pathways altered in Parkinson disease and Huntington's disease?
17. How do the vestibulo-ocular and optokinetic reflexes act to stabilize gaze? How do they complement each other?
18. What are the roles of saccades and smooth pursuit movements in visual tracking?
19. What is nystagmus, and what types of sensory stimulation can drive nystagmus in a normal individual?
20. What is the somatotopic organization of the different CNS regions involved in motor control.

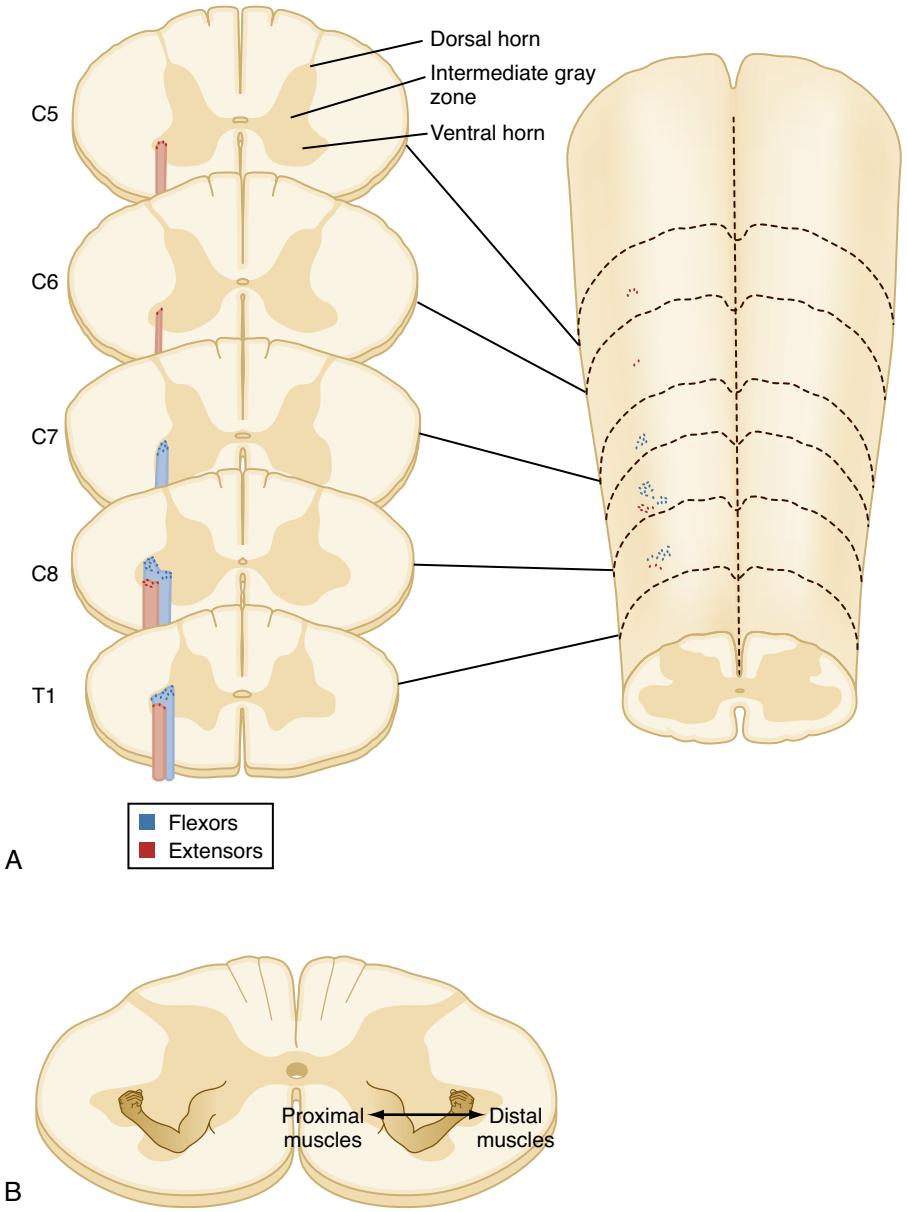
Movements are the major way in which humans interact with the world. Most activities—including running, reaching, eating, talking, writing, and reading—ultimately involve motor acts. Motor control is a major task of the central nervous system (CNS). It can be defined as the generation of signals to coordinate contraction of the musculature of the body and head, either to maintain a posture or to make a movement (transition between two postures). Not surprisingly, a large amount of the CNS is devoted to motor control.

Because large amounts of the nervous system are involved in motor control, damage or diseases of the nervous system frequently disrupt aspects of motor function. Conversely, particular motor symptoms help determine the location of the damaged or malfunctioning region—assessment of motor function has proven to be an important, noninvasive clinical tool.

In this chapter, each major CNS area involved in motor control is described, starting with the spinal cord and continuing with the brainstem, cerebral cortex, cerebellum, and basal ganglia. Eye movements are discussed at the end of the chapter because of their importance and the specialized circuits involved in their generation. Each CNS area is described separately; however, CNS regions do not function in isolation, and most movements result from the coordinated action of multiple brain regions. For example, even spinal reflexes, which are mediated by local circuits in the spinal cord, can be modified by descending motor commands, and virtually all voluntary movements, which arise from cerebral activity, are ultimately generated by activation of the spinal cord circuitry, or analogous brainstem nuclei for muscles in the head and face.

Principles of Spinal Cord Organization

The spinal cord has a cylindrical shape in which the white matter is located superficially and the gray matter is found deep to the white matter shell. The gray matter forms a continuous column that runs the length of the cord. However, the nerve roots that enter and exit the spinal cord bundle



• **Fig. 9.1** Musculotopic organization of motor neurons in the ventral horn of the spinal cord. **A,** Schematic view of the cervicothoracic spinal cord and associated cross-sections, showing the locations of motor neurons that innervate a flexor *(blue dots)* and an extensor *(red dots).* **B,** Spinal cord cross-section, with locations of different muscles represented by a drawing of the arm. (Redrawn from Purves D, Augustine G, Fitzpatrick D, et al, eds. *Neuroscience.* 3rd ed. Sunderland, MA: Sinauer; 2004.)

into discrete nerves, which form the basis for naming the specific levels ("segments") of the spinal cord (8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal). When viewed in cross-section, the gray matter column typically has an "H" or butterfly shape. The "butterfly wings" are divided into dorsal and ventral horns that are separated by an intermediate zone (Fig. 9.1) (at some spinal cord levels, a small lateral horn is also present; see Chapter 11). As discussed previously (Chapter 7), the dorsal horn is the major recipient of incoming sensory information and the main source of ascending sensory pathways (e.g., the spinothalamic tract; see spinothalamic tract, Chapter 7). The ventral horn is where motor neurons reside, and thus it has primarily a motor function. Correspondingly, it is the main target of descending motor pathways from the brain. Motor neurons comprising the ventral horn of the spinal cord, and motor neurons of the cranial nerve nuclei, have similar characteristics and organizational principles for controlling muscles of the body, and muscles of the head and neck, respectively.

Somatic Motor Neurons

A motor neuron is a neuron that projects to muscle cells. Because motor neurons represent the only route for CNS activity to control muscle activity, motor neurons have been termed the **final common pathway.** There are somatic

motor neurons, which activate skeletal muscle, and autonomic motor neurons, which innervate smooth muscle and glands, and act largely unconsciously. In this chapter, the term *motor neuron* refers only to somatic motor neurons; autonomic motor neurons are discussed in Chapter 11. The two main classes of somatic motor neurons that innervate the skeletal (striated) muscles of the body are distinguished on the basis of their axonal diameters: α and γ **motor neurons.**

α Motor Neurons

The α motor neurons are large, multipolar neurons that range in size up to 70 μm in diameter (see Fig. 4.10*A*). Their axons leave the spinal cord through the ventral roots, and the brainstem via several cranial nerves, where they are distributed to the appropriate skeletal muscles via peripheral nerves. The α motor neuron axon also projects to other neurons by giving off collateral axons before leaving the CNS. The main axon terminates by synapsing onto the extrafusal muscle fibers. These synapses are called *neuromuscular junctions* (NMJs) or *end plates.* Extrafusal fibers are large muscle fibers that make up the bulk of a skeletal muscle and generate its contractile force (a muscle also contains intrafusal fibers whose functions are detailed later in this chapter; also see Chapter 12).

A key functional aspect of the motor neuron projection pattern from the CNS is that each neuron's axon innervates only one muscle, but it branches to innervate multiple fibers within that muscle. Moreover, each extrafusal muscle fiber in mammals is supplied by only one α motor neuron, and thus a **motor unit** can be defined as an α motor neuron and all of the skeletal muscle fibers that its axon supplies. The motor unit can be regarded as the basic unit of movement because firing of an α motor neuron under normal circumstances leads to activation and contraction of all of the muscle fibers of that particular motor unit. As described previously (Chapter 6), the safety factor of the NMJ is greater than 1, so each action potential in the motor neuron axon triggers an action potential in every muscle fiber of the motor unit.

An important principle is that the average size of the motor unit (i.e., the number of muscle fibers innervated by an axon) varies between muscles, depending on how fine a control of the muscle is required. For finely controlled muscles, such as the eye muscles, an α motor neuron may supply only a few muscle fibers, whereas in a proximal limb muscle, such as the quadriceps femoris, a single α motor neuron may innervate thousands of muscle fibers.

The muscle fibers that belong to a given motor unit are called a *muscle unit.* All the muscle fibers in a muscle unit are of the same histochemical type (i.e., they are all either slow-twitch [type I] or fast-twitch [type IIA or IIB] fibers). For an in-depth description of muscle fiber types, see Chapter 12. Of importance in this chapter is that a number of physiological properties are correlated with this histochemical classification scheme. In particular, slow-twitch fibers, which contract and relax slowly, as implied by their name, also generate low-force levels but essentially never fatigue. In contrast, the fast-twitch fiber contract and relax rapidly, generate higher levels of force, and fatigue at varying rates.

The first motor units to be activated in many cases, either by voluntary effort or during reflex action or just to maintain posture, are those with the smallest motor axons. These motor units contain slow-twitch fibers and thus generate the smallest contractile force, allowing the initial contraction to be finely graded. These units tend to be active much of the time, if not continuously, and so their lack of fatigability makes good functional sense.

As more motor units are recruited for a motor act, motor neurons with progressively larger axons become involved, and these axons synapse onto the fast-twitch fibers, thereby generating progressively larger amounts of tension. The most powerful such motor units are typically recruited only for tasks requiring large amounts of force (e.g., sprinting, jumping, and lifting a heavy weight), tasks that people can perform for only for short periods of time.

The orderly recruitment of motor units helps the CNS generate a large range of forces and also maintain relatively precise control at the different force levels. This recruitment pattern is called the **size principle** because the motor units are recruited in order of motor neuron axon size. The size principle depends on the property of small motor neurons being activated more easily than are large motor neurons. Recall that if an excitatory synapse is active, it opens channels in the postsynaptic membrane and causes an excitatory postsynaptic current (EPSC). The same-size EPSC generates a larger potential change at the initial segment of an axon of a small motor neuron than it does at a larger motor neuron, simply as a consequence of Ohm's law (V = IR), and due to the smaller motor neurons having higher membrane resistance than larger motor neurons. Because excitatory postsynaptic potentials (EPSPs) in the CNS are small and need to summate to reach threshold for triggering spikes, as the level of synaptic activation rises from zero, the resulting depolarization will reach spiking threshold in smaller motor neurons sooner. As the size principle is usually obeyed, this assumption generally appears to hold; however, there can be exceptions, and in these cases, the descending motor pathways presumably must provide differing levels of synaptic drive to the different-sized motor neurons.

γ Motor Neurons

The γ motor neurons are smaller than α motor neurons; they have a soma diameter of about 35 μm. The γ motor neurons that project to a particular muscle are located in the same regions of the ventral horn as the α motor neurons that supply that muscle. γ Motor neurons do not supply extrafusal muscle fibers; instead, they synapse on specialized striated muscle fibers called **intrafusal muscle fibers,** which traverse receptors called *muscle spindles* that are embedded in skeletal muscles. The function of γ motor neurons is to regulate the sensitivity of these receptors (discussed later).

IN THE CLINIC

A clinically useful way to monitor the activity of motor units is **electromyography.** An electrode is placed within a skeletal muscle to record the summed action potentials of the skeletal muscle fibers of a muscle unit. If no spontaneous activity is noted, the patient is asked to contract the muscle voluntarily to increase the activity of motor units in the muscle. As the force of voluntary contraction increases, more motor units are recruited. In addition to the recruitment of more motor neurons, contractile strength increases with increases in the rate of discharge of the active α motor neurons. Electromyography is used for various purposes. For example, the conduction velocity of motor axons can be estimated as the difference in latency of motor unit potentials when a peripheral nerve is stimulated at two sites separated by a known distance. Another use is to observe fibrillation potentials that occur when muscle fibers are denervated. Fibrillation potentials are spontaneously occurring action potentials in single muscle fibers. These spontaneous potentials contrast with motor unit potentials, which are larger and have a longer duration because they represent the action potentials in a set of muscle fibers that belong to a motor unit.

Topographic Organization of Motor Neurons in the Ventral Horn

The spatial distribution of motor neurons in the spinal cord are topographically organized. A given skeletal muscle in the body is supplied by a group of α motor neurons, called a **motor nucleus,** located in the ventral horn. Each such motor nucleus takes the form of a rostrocaudally running column that can span several spinal cord levels (see Fig. 9.1*A*). Motor neurons that supply the axial musculature collectively form a column of neurons that extends the length of the spinal cord. In the cervical and lumbosacral enlargements, these neurons are located in the most medial part of the ventral horn; at other levels, they form the entire ventral horn. The motor neurons innervating the limb muscles are in the cervical and lumbosacral enlargements, where they form columns that are lateral to those for the axial muscles. Motor neurons to muscles of the distal part of the limb are located most laterally, whereas those that innervate more proximal muscles are located more medially (see Fig. 9.1*B*). Also, motor neurons to flexors are dorsal to those that innervate extensors. Note that the α and γ motor neurons to a given muscle are found intermixed within the same motor neuron column.

The interneurons that connect with the motor neurons in the enlargements are also similarly topographically organized. In general, interneurons that supply the limb muscles are located mainly in the lateral parts of the deep dorsal horn and the intermediate region between the dorsal and ventral horns. Those that supply the axial muscles, however, are located in the medial part of the ventral horn. All of these interneurons receive synaptic connections from primary afferent fibers and from the axons of pathways that descend from the brain, and thus they are part of both spinal reflex arcs and descending motor control pathways.

An important aspect of interneuronal systems is that the laterally placed interneurons project ipsilaterally to motor neurons that supply the distal or the proximal limb muscles, whereas the medial interneurons project bilaterally. This arrangement of the lateral interneurons allows the limbs to be controlled independently. In contrast, the bilateral arrangement of the medial interneurons allows bilateral coordination of motor neurons controlling the axial muscles providing postural support to the trunk and neck.

Spinal Reflexes

Although motor neurons are the final common pathway from the CNS to muscles, and thus shape how neuronal activity is transformed into muscular contraction, each motor neuron directly acts on only a single muscle. Normal movements (or postures), however, are rarely, if ever, caused by the isolated contraction of an individual muscle. Rather, they reflect the coordinated activity of large groups of muscles. For example, elbow flexion involves an initial burst of activity in flexor muscles, such as the biceps, and in relaxation of extensor muscles, such as the triceps. This activity is then succeeded by a burst of activity of the triceps and then a second burst of activity in the biceps to stop the flexion movement at the desired position. Additionally, other muscles are also activated during the elbow flexion to maintain overall balance and posture.

As the elbow flexion example shows, different roles are played by each muscle during a movement: (1) The muscle that initiates, and is the prime cause of the movement, is called the *agonist.* (2) Muscles that act similarly to the agonist are called *synergist*. (3) Muscles whose activity opposes the action of the agonist are *antagonists.* (4) Lastly, muscles can act as *fixators* to immobilize a joint and in postural roles. The relationship these various muscle actions may have to each other also depends on the specific movement being performed. For example, during elbow flexion, the triceps acts an antagonist to the biceps. In contrast, during supination of the forearm without rotation occurring about the elbow, the biceps (which also acts to supinate the forearm) is again an agonist, but the role of the triceps is that of an elbow fixator.

Motor control requires flexibly linking (and unlinking) the activity of groups of motor neurons that connect to different muscles. The circuits of the spinal cord are a major mechanism used by the CNS for this aspect of motor control. Indeed, descending pathways from the brain target primarily the interneurons of the spinal cord, although there are some descending axons that synapse directly onto motor neurons.

Spinal cord circuitry has several levels of organization. The most basic is the segmental level: that is, a circuit that is largely confined to a single or several neighboring segments and that is repeated again at many levels. The basic spinal reflexes covered below (i.e., the myotatic, inverse myotatic,

and flexion reflexes) are mediated by such circuits. Superimposed on this segmental organization is the propriospinal system, which is a series of neurons whose axons run up and down the spinal cord to interconnect the different levels of the cord. This system allows the coordination of activity at different spinal levels, which is important for behavior involving both the forelimbs and the hind limbs, such as locomotion. Finally, there are descending motor pathways that interact with these spinal circuits. These motor pathways carry signals related to voluntary movement, but they are also important for the more automatically (or nonconsciously) controlled aspects of motor function, such as the setting of muscle tone (the resting resistance of muscles to changes in length).

Spinal cord circuits are thus involved in all movements made by the body, but they have been most extensively studied with the use of reflexes. A **reflex** is a fast, predictable, involuntary, and stereotyped response to an eliciting stimulus. Because of these properties, spinal reflexes have been used to identify and classify spinal cord neurons, determine their connectivity, and study their response properties—knowledge of spinal reflexes is essential for understanding spinal cord function.

The basic circuit that underlies a reflex is called a **reflex arc.** A reflex arc can be divided into three parts: (1) an afferent limb (sensory receptors and axons) that carries information to the CNS, (2) a central component (synapses and interneurons within the CNS), and (3) an efferent limb (motor neurons) that causes the motor response. For example, tapping the patellar tendon with a reflex hammer causes a brief stretching of the quadriceps muscle (stimulus), which in turn activates sensory receptors (group Ia fibers in muscle spindles); activation of sensory receptors then send an excitatory signal to the spinal cord (central processing) to activate motor neurons that project back to the quadriceps to elicit a contraction and consequent kick (stereotyped response). The person feels the kicking motion, but it is involuntary, and the person has no sense of having generated it. In sum, this relatively simple reflex shows the afferent limb (activation of muscle spindles by a stimulus), the central processing of this reflex arc (the synapse from the group Ia afferent fibers onto the motor neurons), and the response (the leg kick). Many reflexes are more complex and can involve multiple types of interneurons.

It is the predictable linking of stimulus and response that makes reflexes useful tools both for clinicians and for neuroscientists trying to understand spinal cord function. However, one danger to avoid is thinking that a particular neuron's function is solely participation in a particular reflex, because these same neurons are the targets of descending motor pathways and are involved in generating voluntary movement. Indeed, many of these neurons are active even when the afferent leg of their reflex arc is silent. One such example is the interneurons of the flexion reflex arc that are also part of the central pattern generator for locomotion.

In the next several sections, three well-known spinal reflexes are discussed in detail because they illustrate important aspects of spinal cord circuitry and function and because of their behavioral and clinical importance. However, many additional reflexes mediated by spinal circuits exist (e.g., see micturition reflex; Fig. 11.3).

The Myotatic or Stretch Reflex

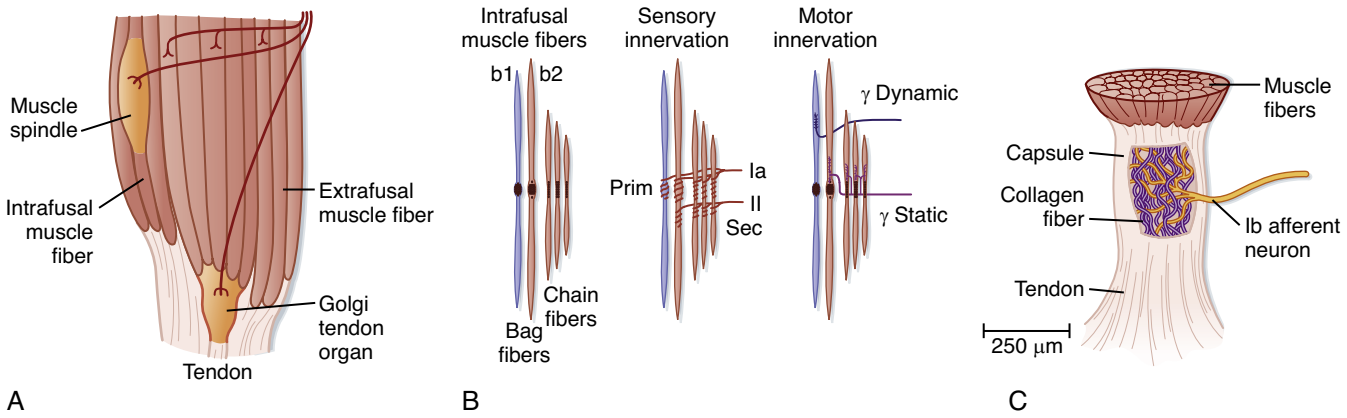
The stretch reflex, as implied by its name, is a group of motor responses elicited by stretch of a muscle. The knee jerk reflex described previously is a well-known example. The stretch reflex is crucial for the maintenance of posture and helps overcome unexpected impediments during a voluntary movement. Changes in the stretch reflex are involved in actions commanded by the brain, and pathological alterations in this reflex are important signs of neurological disease. The phasic stretch reflex occurs in response to rapid, transient stretches of the muscle, such as those elicited by a physician's use of a reflex hammer or by an unexpected impediment to an ongoing movement. The tonic stretch reflex occurs in response to a slower or steady stretch applied to the muscle. The receptor responsible for initiating a stretch reflex is the muscle spindle. Muscle spindles are found in almost all skeletal muscles and are particularly concentrated in muscles that exert fine motor control (e.g., the small muscles of the hand and eye). This reflex circuit is a universal mechanism for helping regulate muscle activity.

Structure of the Muscle Spindle

As its name implies, a muscle spindle is a spindle or fusiform-shaped organ composed of a bundle of specialized muscle fibers richly innervated both by sensory axons and by motor axons (Fig. 9.2). A muscle spindle is about 100 μm in diameter and up to 10 mm long. The innervated part of the muscle spindle is encased in a connective tissue capsule. Muscle spindles lie between regular muscle fibers and are typically located near the tendinous insertion of the muscle. The ends of the spindle are attached to the connective tissue within the muscle (endomysium). The key point is that muscle spindles are connected in parallel with the regular muscle fibers and thus are able to sense changes in the length of the muscle.

The muscle fibers within the spindle are called **intrafusal fibers,** to distinguish them from the regular or extrafusal fibers that make up the bulk of the muscle. Individual intrafusal fibers are much narrower than extrafusal fibers and do not run the length of the muscle. They are also too weak to contribute significantly to muscle tension or to cause changes in the overall length of the muscle directly by their contraction.

Morphologically, two types of intrafusal muscle fibers are found within muscle spindles: **nuclear bag** and **nuclear chain fibers** (see Fig. 9.2*B*). These names are derived from the arrangement of nuclei in the fibers. (Muscle fibers are formed by the fusion of many individual myoblasts during development; thus mature muscle cells are multinucleate.) Nuclear bag fibers are larger than nuclear chain fibers, and their nuclei are bunched together like a bag of oranges in the central, or equatorial, region of the fiber. In nuclear chain fibers, the



• **Fig. 9.2** Muscle proprioceptors. Skeletal muscles contain sensory receptors embedded within the muscle (spindles) and within their tendons (Golgi tendon organs). **A,** Schematic view of a muscle, showing the arrangement of a spindle in parallel with extrafusal muscle fibers and a tendon organ in series with muscle fibers. **B,** Structure and innervation (motor and sensory) of a muscle spindle. **C,** Structure and innervation of a tendon organ.

nuclei are arranged in a row. Functionally, nuclear bag fibers are divided into two types: bag1 and bag2. As detailed later, bag2 fibers are functionally similar to chain fibers.

The neural innervation of an intrafusal fiber differs significantly from that of an extrafusal fiber, which is innervated by a single motor neuron. Intrafusal fibers are receive both sensory and motor innervation. The sensory innervation typically includes a single group Ia afferent fiber and a variable number of group II afferent fibers (see Fig. 9.2*B*). Group Ia fibers belong to the class of sensory nerve fibers with the largest diameters and conduct at 80 to 120 m/second; group II fibers are intermediate in size and conduct at 35 to 75 m/second. A group Ia afferent fiber forms a spiral-shaped termination, referred to as a *primary ending,* on each of the intrafusal muscle fibers in the spindle. Primary endings are found on both types of nuclear bag fibers and on nuclear chain fibers. The group II afferent fiber forms a secondary type ending on nuclear chain and bag2 fibers, but not on bag1 fibers. The primary and secondary endings have mechanosensitive channels that are sensitive to the level of tension on the intrafusal muscle fiber.

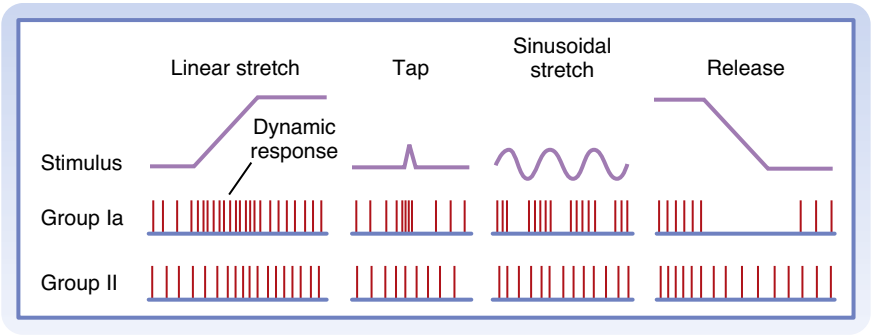
The motor supply to a muscle spindle consists of two types of γ motor axons (see Fig. 9.2*B*). Dynamic γ motor axons end on nuclear bag1 fibers, and static γ motor axons end on nuclear chain and bag2 fibers.

Muscle Spindles Detect Changes in Muscle Length

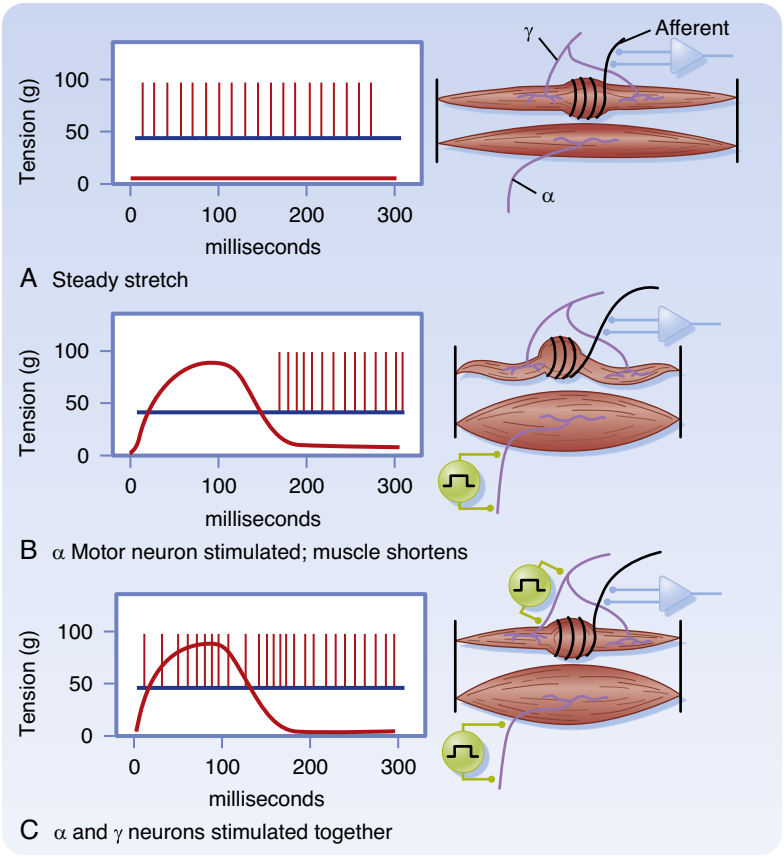
Muscle spindles respond to changes in muscle length because they lie in parallel with the extrafusal fibers, and therefore are stretched or shortened along with the extrafusal fibers. Because intrafusal fibers, like all muscle fibers, display spring-like properties, a change in their length changes the tension that they are under, and this change is sensed by mechanoreceptors of the group Ia and group II spindle afferent fibers. The nonselective cation channel Piezo2 has been identified as the principal transduction channel that allows spindle sensory afferent fibers to sense changes in mechanical stress that occur when a muscle changes length.

Fig. 9.3 shows the changes in activity of the afferent fibers of a muscle spindle when the muscle is stretched. It is clear that group Ia and group II fibers respond differently to stretch. Group Ia fibers are sensitive both to the amount of muscle stretch and to its rate, whereas group II fibers respond chiefly to the amount of stretch. Thus, when a muscle is stretched to a new, longer length, group II firing increases in proportion to the amount of stretch (see Fig. 9.3, *left*), and when the muscle is allowed to shorten, its firing rate decreases proportionately (see Fig. 9.3, *right*). Group Ia fibers show this same **static-type response,** and thus under steady-state conditions (i.e., constant muscle length), their firing rate reflects the amount of muscle stretch, similar to that of group II fibers.

While muscle length is changing, group Ia firing reflects the rate of stretch or shortening that the muscle is undergoing. Its activity overshoots during muscle stretch and undershoots (and possibly ceases) during muscle shortening. These are called dynamic responses. This dynamic sensitivity also means that the activity of group Ia fibers is much more sensitive to transient and oscillatory stretches, such as shown in the middle diagrams of Fig. 9.3. In particular, the tap profile is what occurs when a reflex hammer is used to hit the muscle tendon leading to a brief stretching of the attached muscle. The change in muscle length is too brief for significant changes in group II firing to occur, but because the magnitude of the rate of change (slopes of the tap profile) is so high with this stimulus, large dynamic responses are elicited in the group Ia fibers. Thus, the functionality of reflex arcs involving group Ia afferent fibers is being assessed when a reflex hammer is used to tap on tendons. More importantly, the behavior of this reponse provides information about the source of potential motor dysfunction (e.g., CNS or PNS; see section later in this chapter, "Motor Deficits Caused by Lesions of Descending Motor Pathways").



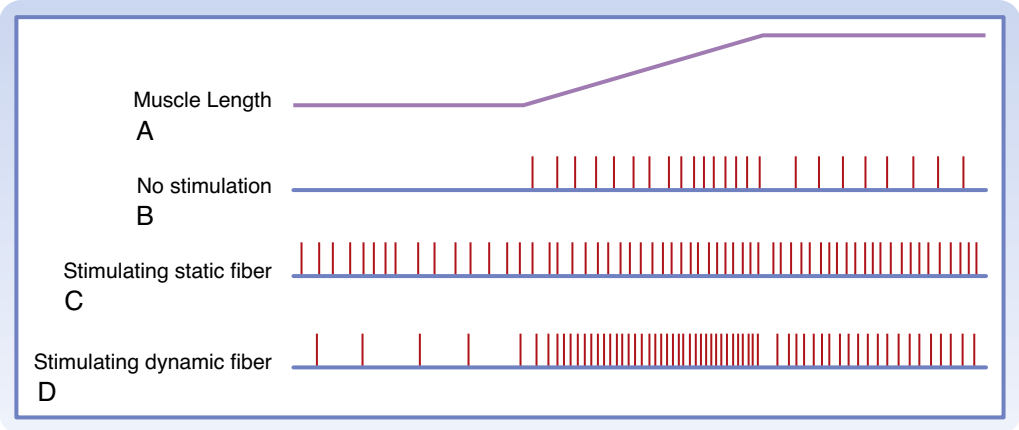
• **Fig. 9.3** Responses of a primary ending (group Ia) and a secondary ending (group II) to changes in muscle length. Note the difference in dynamic and static responsiveness of these endings. The waveforms at the *top* represent the changes in muscle length. The *middle and bottom rows* show the discharges of a group Ia fiber and a group II fiber, respectively, during the various changes in muscle length.



• **Fig. 9.4** The activity of γ motor neurons can counteract the effects of unloading on the discharge of a muscle spindle afferent fiber. **A,** The activity of a muscle spindle afferent fiber during steady stretch. **B,** Stimulation of α motor neuron at 0 millisecond causes contraction of the extrafusal fibers, which leads to muscle shortening and increased muscle tension but unloading of the tension across the muscle spindle, which in turn induces the afferent fiber to stop firing. Upon relaxation, the muscle returns to its original length, and tension is restored on the intrafusal fibers, causing the return of activity in the group Ia afferent fiber. **C,** Coactivation of α and γ motor neurons causes shortening of both extrafusal and intrafusal fibers. Thus there is no unloading of the spindle, and the afferent fiber maintains its spontaneous activity. (Redrawn from Kuffler SW, Nicholls JG. *From Neuron to Brain.* Sunderland, MA: Sinauer; 1976.)

γ Motor Neurons Adjust the Sensitivity of the Spindle

Up to this point, we have described only how muscle spindles behave when there are no changes in γ motor neuron activity. The efferent innervation of muscle spindles is extremely important, however, because it determines the sensitivity of muscle spindles to stretch. For example, in Fig. 9.4*A*, the activity of a muscle spindle afferent fiber is shown during a steady stretch. If only the extrafusal muscle fibers were to contract (this can be done experimentally by selective stimulation of α motor neurons; see Fig. 9.4*B*), the



• **Fig. 9.5** Effects of static and dynamic γ motor neurons on the responses of a primary ending to muscle stretch. **A,** The time course of the stretch. **B,** The discharge of group Ia fibers in the absence of γ motor neuron activity. **C,** Stimulation of a static γ motor axon. **D,** Stimulation of a dynamic γ motor axon. (Redrawn from Crowe A, Matthews PBC. *J Physiol* 1964;174:109.)

muscle spindle would be unloaded by the resultant shortening of the muscle. If this happens, the muscle spindle afferent fiber may stop discharging and become insensitive to further decreases in muscle length. However, the unloading of the spindle can be prevented if α and γ motor neurons are stimulated simultaneously. Such combined stimulation causes the intrafusal muscle fibers of the spindle to shorten along with the extrafusal muscle fibers, maintaining the baseline tension on the equatorial portion of the intrafusal fibers (see Fig. 9.4*C*).

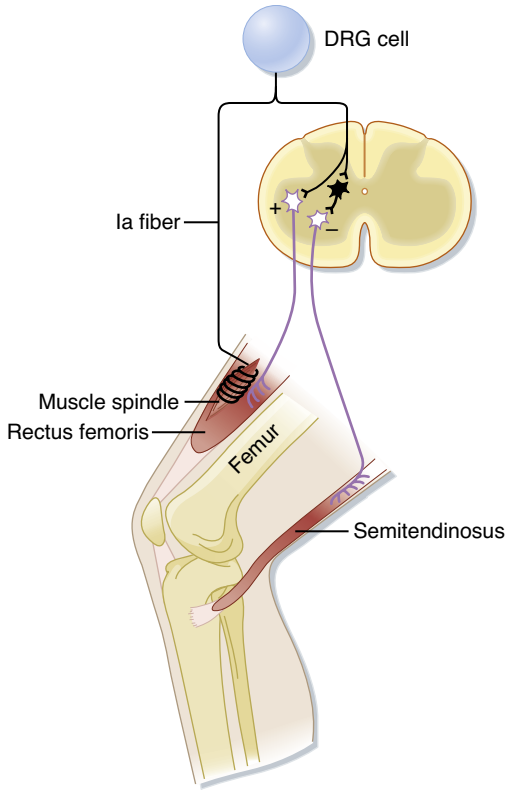
Note that only the two polar regions of the intrafusal muscle contract; the equatorial region, where the nuclei are located, does not contract because it has little contractile protein. Nevertheless, when the polar regions contract, the equatorial region elongates and regains its sensitivity. Conversely, when a muscle relaxes (α motor neuron activity drops) and thus elongates (if its ends are being pulled), a concurrent decrease in γ motor neuron activity allows the intrafusal fibers to relax (and thus elongate) as well, and thereby prevent the tension on the central portion of the intrafusal fiber from reaching a level at which firing of the afferent fibers is saturated. Thus, the γ motor neuron system allows the muscle spindle to operate over a wide range of muscle lengths while retaining high sensitivity to small changes in length.

For voluntary movements, descending motor commands from the brain typically activate α and γ motor neurons simultaneously, presumably to maintain spindle sensitivity, as just described. This has two important functions: First, by maintaining the muscle spindle's sensitivity as the muscle changes length, the spindle remains capable of sensing, and signaling to the CNS, any disturbances to the ongoing movement that cause an unexpected stretch of the muscle, and this in turn allows the CNS to initiate both reflex (see next section) and voluntary corrections. Second, if the spindle were to become unloaded during the movement, this would oppose the intended movement by decreasing the excitatory drive, via the group Ia reflex arc (see next section), to the α motor neurons driving the agonist muscles.

As mentioned earlier, there are two types of γ motor neurons: dynamic and static (see Fig. 9.2). This allows the CNS to have very precise control over the sensitivity of the muscle spindle. Dynamic γ motor axons end on nuclear bag1 fibers, and static γ motor axons synapse on nuclear chain and bag2 fibers. When a dynamic γ motor neuron is activated, the response of the group Ia afferent fiber is enhanced, but the activity of the group II afferent fibers is unchanged; when a static γ motor neuron discharges, the responsiveness of the group II afferent fibers and the static responsiveness of the group Ia afferent fibers are increased. The effects of stimulating the static and dynamic fibers on a group Ia afferent fiber's response to stretch are illustrated in Fig. 9.5. Descending pathways can preferentially influence dynamic or static γ motor neurons and thereby alter the nature of reflex activity in the spinal cord and also, presumably, the functioning of the muscle spindle during voluntary movements.

The Phasic (or Ia) Stretch Reflex

The reflex arc responsible for the phasic stretch reflex is depicted in Fig. 9.6; the rectus femoris muscle serves as an example. A rapid stretch of the rectus femoris muscle strongly activates the group Ia fibers of the muscle spindles, which then convey this signal into the spinal cord. In the spinal cord, each group Ia afferent fiber branches many times to form excitatory synapses directly (monosynaptically) on virtually all α motor neurons that supply the same (also known as the *homonymous*) muscle and with many α motor neurons that innervate synergists, such as the vastus intermedius muscle in this case, which also acts to extend the leg at the knee. If the excitation is powerful enough, the motor neurons discharge and cause a contraction of the muscle. Note that the group Ia fibers do not contact the γ motor neurons, possibly to avoid a positive-feedback loop situation. This selective targeting of α motor neurons is exceptional in that most other reflex and descending pathways target both α and γ motor neurons.



• **Fig. 9.6** Reflex arc of the stretch reflex. The pathway back to the rectus femoris in this arc contains a single synapse within the central nervous system; hence, it is a monosynaptic reflex. The interneuron, shown in *black,* is a group Ia inhibitory interneuron. *DRG*, Dorsal root ganglion.

Other branches of group Ia fibers end on a variety of interneurons; however, one type, the reciprocal Ia inhibitory interneuron (the black neuron in Fig. 9.6), is particularly important with regard to the stretch reflex. These interneurons are identifiable because they are the only inhibitory interneurons that receive input from both the group Ia afferent fibers and Renshaw cells (see Fig. 9.12). They end on α motor neurons that innervate the antagonist muscles—in this case, the hamstring muscles, including the semitendinosus muscle—which act to flex the knee. Other branches of the group Ia afferent fibers synapse with yet other neurons that originate ascending pathways that provide various parts of the brain (particularly the cerebellum and cerebral cortex) with information about the state of the muscle.

The organization of the stretch reflex arc guarantees that one set of α motor neurons is activated and the opposing set is inhibited. This arrangement is known as **reciprocal innervation.** Although many reflexes involve such reciprocal innervation, this type of innervation is not the only possible organization of a motor control system; descending motor pathways can override such patterns.

The stretch reflex is quite powerful, in large part because of its monosynaptic nature. The power of this reflex also derives from the optimal convergence and divergence that exist in this pathway, which is not apparent from the circuit diagrams, such as Fig. 9.6, that are typically used to illustrate reflex pathways. That is, each group Ia fiber contacts virtually all homonymous α motor neurons, and each such α motor neuron receives input from every spindle in that muscle. Although its monosynaptic nature makes the group Ia reflex rapid and powerful, it also means that there is relatively little opportunity for direct control of activity flow through its reflex arc. The CNS overcomes this problem by controlling muscle spindle sensitivity via the γ motor neuron system, as described previously.

The Tonic Stretch Reflex

The tonic stretch reflex can be elicited by passive bending of a joint. This reflex circuit includes both group Ia and group II afferent fibers from muscle spindles. Group II fibers make monosynaptic excitatory connections with α motor neurons, but they also excite them through disynaptic and polysynaptic pathways. Normally, there is ongoing activity in the group Ia and group II afferent fibers that helps maintain a baseline rate of firing of α motor neurons; therefore, the tonic stretch reflex contributes to muscle tone. Its activity also contributes to the ability to maintain a posture. For example, if the knee of a soldier standing at attention begins to flex because of fatigue, the quadriceps muscle is stretched, a tonic stretch reflex is elicited, and the quadriceps contracts more, thereby opposing the flexion and restoring the posture (note also that contracting the leg muscles mitigates pooling of the blood in the legs and possible orthostatic hypotension—fainting).

The foregoing discussion suggests that stretch reflexes can act like a negative-feedback system to control muscle length. By following the stretch reflex arc, it is possible to see that changes in its activity act to oppose changes in muscle length from a particular equilibrium point. For example, if the muscle's length is increased, there will be an increase in firing by group Ia and group II fibers, which excites homonymous α motor neurons and leads to contraction of the muscle and reversal of the stretch. Similarly, passive shortening of the muscle unloads the spindles and leads to a decrease in the excitatory drive to the motor neurons and thus relaxation of the muscle. So how are humans able to rotate their joints? It is partly because the γ motor neurons are coactivated during a movement and thereby shift the equilibrium point of the spindle and partly because the gain or strength of the reflex is low enough that other input to the motor neuron can override the stretch reflex.

Inverse Myotatic or Group Ib Reflex

The inverse myotatic reflex acts to oppose changes in the level of force in the muscle. Just as the stretch reflex can be thought of as a feedback system to regulate muscle length, the inverse myotatic, or group Ib, reflex can be thought of as a feedback system to help maintain force levels in a muscle. With the upper part of the leg as an example, the group Ib reflex arc is depicted in Fig. 9.7.

The arc starts with the Golgi tendon organ receptor, which senses the tension in the muscle. Golgi tendon organs are located at the junction of the tendon and the muscle fibers and thus lie in series with the muscle fibers, in contrast to the parallel arrangement of the muscle spindles (see Fig. 9.2). Golgi tendon organs have a diameter of about

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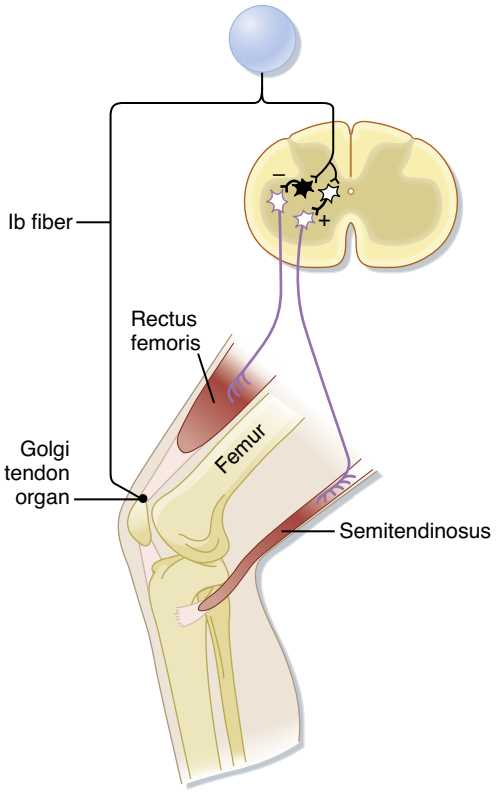
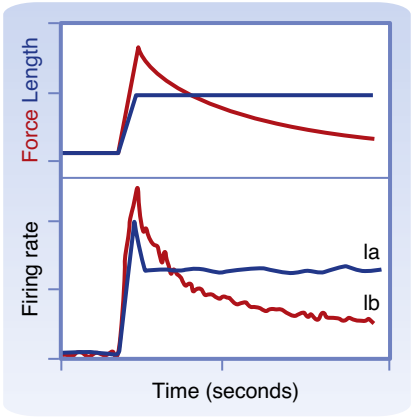
Hyperactive stretch reflexes can lead to tremors and clonus, which are types of involuntary rhythmic movements. Although the negative-feedback action of the stretch reflex can help stabilize the limb at a particular position, if an external perturbation to the limb occurs, the conduction delay between the initiating stimulus (muscle stretch) and the response (muscle contraction) can cause the stretch reflex circuit to be a source of instability that leads to rhythmic movements. Specifically, clonus is elicited by a sustained stretch of a muscle in a person who has spinal cord damage. Normally, an imposed sustained stretch on a muscle elicits an increase in group Ia and group II fiber activity, which after a delay causes a contraction in the muscle that opposes the stretch but does not completely return the muscle to its initial length because the gain of the stretch reflex is much less than 1.[a]

This partial compensation, in turn, leads to a decrease in group Ia and group II fiber activity, which causes the limb to lengthen again, but not fully. This lengthening once again increases group Ia and group II fiber activity, and so on. The delay is essential in setting up this oscillation because it causes the feedback signal to continue even after the muscle has compensated and thus results in an overcompensation that leads to the next overcorrection. However, because the reflex gain is normally much less than 1, this oscillation normally dies out quickly (the overcompensations decrease in amplitude rapidly), and the muscle comes to rest at an intermediate length. In contrast, when descending motor pathways are damaged, the resulting changes in spinal cord connectivity and increases in neuronal excitability result in a hyperactive reflex (which is equivalent to raising the gain of the stretch reflex close to 1). In this case, the successive overcompensations are much larger, and an overt but transient oscillation can be observed (clonus). If the gain equals 1, the clonus does not die out but rather persists for as long as the initial stretch stimulus is maintained.

[a]In general, *gain* of a system is defined as its output for a given input. In this case, the input to the system is the imposed stretch, and the output is movement caused by the stretch reflex–evoked contraction



• **Fig. 9.7** Reflex arc of the inverse myotatic reflex. The interneurons include both excitatory *(white)* and inhibitory *(black)* interneurons. This is an example of a disynaptic reflex.

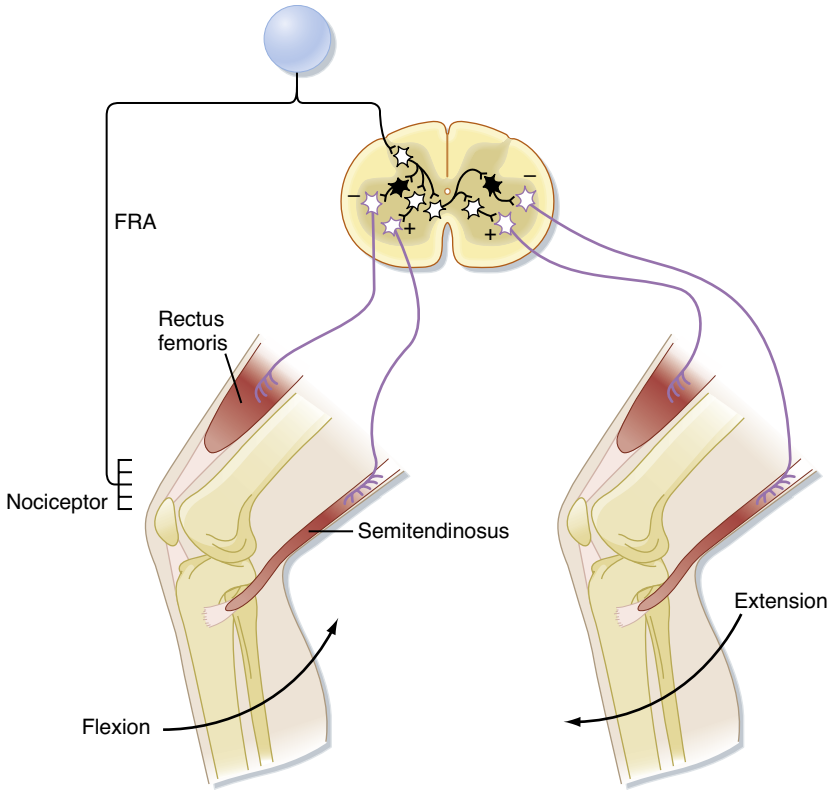


• **Fig. 9.8** Changes in group Ia and group Ib firing rates when muscle is stretched to a new length. After a transient burst, the firing rate of the group Ia fiber remains constant at a new higher level that is proportional to the increase in length (compare *blue lines in upper and lower graphs*). In contrast, the group Ib fiber shows an initial rapid increase in firing followed by a slow decrease back toward its original level *(lower graph, red line)* and has a firing profile that matches the tension level in the muscle caused by the stretch *(upper graph, red line).*

100 μm and a length of about 1 mm. A Golgi tendon organ is innervated by the terminals of group Ib afferent fibers. These terminals wrap about bundles of collagen fibers in the tendon of a muscle (or in tendinous inscriptions within the muscle).

Because of their in-series relationship to the muscle, Golgi tendon organs can be activated either by muscle stretch or by muscle contraction. In both cases, the actual stimulus sensed by the Golgi tendon organ is the force that develops in the tendon to which it is linked. For stretch, the response is due to the spring-like nature of the muscle, with the force on the muscle ("spring") being proportional to how much it is stretched (based on Hooke's law).

To distinguish between the responsiveness of the muscle spindles and Golgi tendon organs, the firing patterns of group Ia and group Ib fibers can be compared when a muscle is stretched and then held at a longer length (Fig. 9.8). The firing rate of the group Ia fibers maintains its increase until the stretch is reversed. In contrast, the group Ib fiber shows an initial large increase in firing, reflecting the increased tension on the muscle caused by the stretch, but then shows a gradual return toward its initial firing rate as the tension on the muscle is lowered because of cross-bridge recycling and the resultant lengthening of the sarcomeres. Therefore, Golgi tendon organs signal force, whereas spindles signal muscle length. Further evidence of this distinction is that



• **Fig. 9.9** The reflex arc of the flexion reflex. *Black* interneurons are inhibitory, and *white* ones are excitatory. *FRA*, Flexion reflex afferent fiber.

group Ib firing is correlated with force level during isometric contraction even though muscle length and therefore group Ia activity are unchanged.

The group Ib afferent fibers branch as they enter the spinal cord and end on interneurons. There are no monosynaptic connections to α motor neurons. Rather, the group Ib afferent fibers synapse onto two classes of interneurons: interneurons that inhibit α motor neurons that supply the homonymous muscle (in this case the rectus femoris muscle) and excitatory interneurons that activate α motor neurons to the antagonist (the semitendinosus muscle). Because there are two synapses in series in the CNS, this is a disynaptic reflex arc. Because of these connections, group Ib fiber activity should have the opposite action of the group Ia stretch reflex during passive stretch of the muscle, which explains the group Ib reflex's other name, the inverse myotatic reflex.

Functionally, however, the two reflex arcs can act synergistically, as the following example shows. Recall that the Golgi tendon organs monitor force levels across the tendon that they supply. If during maintained posture (such as standing at attention) knee extensors (such as the rectus femoris muscle) begin to fatigue, the force pulling on the patellar tendon declines. The decline in force reduces the activity of Golgi tendon organs in this tendon. Because the group Ib reflex normally inhibits the α motor neurons to the rectus femoris muscle, reduced activity of the Golgi tendon organs enhances the excitability of (i.e., disinhibits) the α motor neurons and thereby helps reverse the decrease in force caused by the fatigue. Simultaneously, bending of the knee stretches the knee extensors and activates the afferent fibers from the muscle spindles, which then excite the same α motor neurons. The coordinated action of afferent fibers from both the muscle spindle and Golgi tendon organ help oppose the decrease in contraction of the rectus femoris muscle due to fatigue and thereby work together to maintain the standing posture.

Flexion Reflexes and Locomotion

The flexion reflex starts with activation of one or more of a variety of sensory receptors, including nociceptors, whose signals can be carried to the spinal cord via a variety of afferent fibers, including group II and group III fibers, collectively called the **flexion reflex afferent (FRA)** fibers. In flexion reflexes, afferent volleys (1) cause excitatory interneurons to activate the α motor neurons that supply the flexor muscles in the ipsilateral limb and (2) cause inhibitory interneurons to inhibit the α motor neurons that supply the antagonistic extensor muscles (Fig. 9.9). This pattern of activity causes one or more joints in the stimulated limb to flex. In addition, commissural interneurons evoke the opposite pattern of activity in the contralateral side of the spinal cord (see Fig. 9.9), which results in extension of the opposite limb, the **crossed extension reflex.** For lower limbs in humans (or for both forelimbs and hind limbs in quadrupeds), the crossed extension part of the reflex helps in maintaining balance by enabling the contralateral limb to

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After damage to the descending motor pathways, hyperactive stretch reflexes may result in spasticity, in which there is large resistance to passive rotation of the limbs. In this condition, it may be possible to demonstrate what is called the **clasp-knife reflex.** When spasticity is present, attempts to rotate a limb about a joint initially meet high resistance. However, if the applied force is increased, there comes a point at which the resistance suddenly dissipates and the limb rotates easily. This change in resistance is caused by reflex inhibition. The group Ib reflex arc suggests that rising activity in this pathway could underlie the sudden release of resistance, and indeed, the clasp-knife reflex was once attributed to the activation of Golgi tendon organs when these receptors were thought to have a high threshold to muscle stretch. However, the tendon organs have since been shown to be activated at very low levels of force and are no longer thought to cause the clasp-knife reflex. It is now thought that this reflex is caused by the activation of other high-threshold muscle receptors that supply the fascia around the muscle. Signals from these receptors cause the activation of interneurons that lead to inhibition of the homonymous motor neurons.

be able to support the additional load that is transferred to it when the flexed limb is lifted.

Because flexion typically brings the affected limb in closer to the body and away from a painful stimulus, flexion reflexes are a type of withdrawal reflex. In Fig. 9.9, the neural circuit of the flexion reflex is shown for neurons that affect only the knee joint. Actually, however, considerable divergence of the primary afferent and interneuronal pathways occurs in the flexion reflex. In fact, all the major joints of a limb (e.g., hip, knee, and ankle) may be involved in a strong flexor withdrawal reflex. Details of the flexor withdrawal reflex vary, depending on the nature and location of the stimulus.

The interneurons subserving flexion reflexes also appear to be part of the **central pattern generator (CPG)** for generating locomotion, demonstrating how reflex circuits are used for multiple purposes. A CPG is a set of neurons and circuits capable of generating the rhythmic activity that underlies motor acts, even in the absence of sensory input. For example, activation of the FRA interneurons leads to a pattern of flexor excitation and extensor inhibition on one side, and the converse pattern on the opposite side; alternating activation of FRA interneurons on each side of the spinal cord leads to a stepping pattern. That is, walking motion could result from alternately activating the FRA interneurons on each side. Note that such a rhythmic activity pattern in the FRA circuits need not be dependent on activity from the FRA fibers themselves (e.g., they could be activated by descending pathways from the brain).

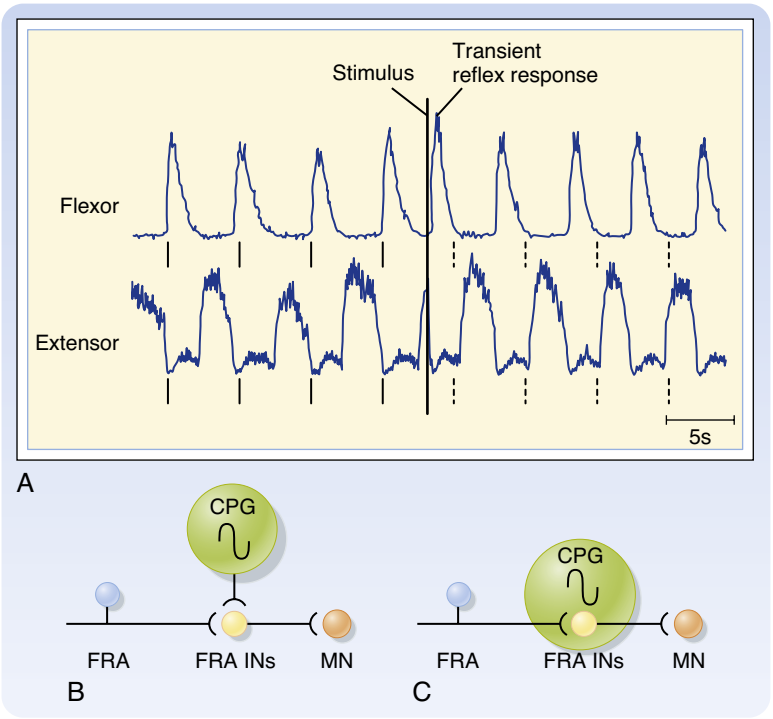
To show that these circuits are actually involved in generating the locomotion rhythm, spinal cord preparations were made that showed spontaneous locomotion (i.e., if the brainstem is transected and weight is supported, the spinal cord circuits can generate activity that causes the limbs to perform a normal locomotion sequence). In one such preparation, the electromyographic signals from the flexors and extensors of a limb were recorded, and the FRA fibers then stimulated to demonstrate the effect on locomotion rhythm (Fig. 9.10). Before any stimulus, a spontaneous alternating pattern of flexor and extensor electromyographic (EMG) activity exists. If the FRA fibers were not involved in the locomotion circuit, or at least were not a critical part of the circuits responsible for generating the rhythm (see Fig. 9.10*B*), the stimulus would be expected to produce only a transient response (i.e., a single burst in the flexor EMG record and brief inhibition of activity in the extensor EMG record) but to have no long-term effect on ongoing EMG pattern. Such a transient response is observed (see Fig. 9.10*A;* EMG records just after the stimulus). However, the stimulus also causes a permanent, approximately 180-degree phase shift in locomotor rhythm, as can be shown by comparing the times of contractions before and after the stimulus. The dashed vertical lines indicate the times at which a flexor EMG response would be expected if the stimulus had produced no phase shift from the EMG activity pattern. Before the stimulus, each vertical line is aligned with the onset of a flexor EMG burst, whereas after the stimulus, each vertical line occurs at the end of the flexor burst. Therefore, the stimulus affected the locomotor CPG itself, and the FRA interneurons are a critical part of this CPG (see Fig. 9.10*C*).

A second important point illustrated by this experiment is that the locomotion CPG (and CPGs in general) can be influenced by strong afferent fiber activity. The afferent fiber's influence ensures that the pattern generator adapts to changes in the terrain as locomotion proceeds. Such changes may occur rapidly during running, and locomotion must then be adjusted to ensure proper coordination.

Determining Spinal Cord Organization Through the Use of Reflexes

Convergence and divergence are important aspects of reflex pathways and of neuronal circuits in general. Several examples of these phenomena have been described in the previous discussion of the reflexes. Reflexes can be used to identify and characterize these phenomena in the spinal cord. For example, convergent input can be demonstrated through the phenomenon of **spatial facilitation,** which is illustrated in Fig. 9.11.

In this example, a monosynaptic reflex is elicited by electrical stimulation of the group Ia fibers in each of two nerves (see Fig. 9.11*A*). The reflex response is characterized by a recording of the discharges of α motor axons from the appropriate ventral root (as a compound action potential). When nerve A is stimulated, a small compound action potential is recorded as reflex A. Similarly, when nerve B is stimulated, reflex B is recorded. Fig. 9.11*B* depicts the motor neurons contained within the motor nucleus. The



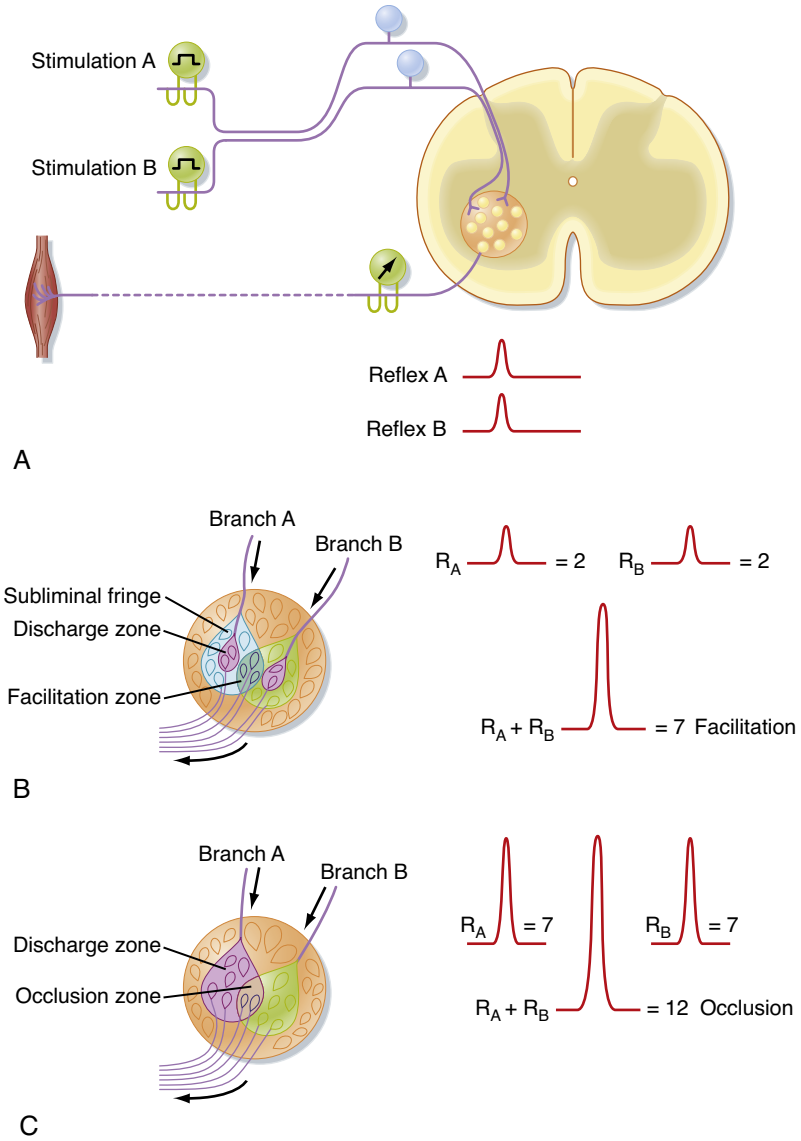
• **Fig. 9.10** Phase reset of locomotion rhythm by flexion reflex afferent *(FRA)* fiber stimulation helps identify neuronal components of the underlying central pattern generator *(CPG)*. **A,** EMG records from knee flexor and extensor muscles. Note the rhythmic alternating pattern before application of the stimulus. The *solid vertical lines* below each trace indicate the times at which flexor contraction is initiated. The *dashed vertical lines* indicate the times at which flexor contraction would have been initiated if the stimulus caused no lasting effect on the rhythmic pattern. **B** and **C,** Two possible models for the CPG underlying the locomotor rhythm depicted in **A. B,** The FRA interneurons *(INs)* in the CPG are not shown. **C,** The FRA interneurons are shown. The data shown in **A** support the model shown in **C.** *MN*, Motoneuron. (Data from Hultborn H, Conway B, Gossard J, et al. *Ann N Y Acad Sci* 1998;860:70.)

α motor neurons in the discharge zones are activated above threshold when each nerve branch is stimulated separately. Thus, a distinct pair of α motor neurons spike when each nerve is stimulated alone. In addition, each of these motor neuron pairs is surrounded by a subliminal fringe of eight additional motor neurons that are excited but not sufficiently to trigger spikes. When the two nerves are stimulated at the same time, a much larger reflex discharge is recorded (compare R_A and R_B with $R_A + R_B$ recordings at the right of Fig. 9.11*B*). As the figure demonstrates, this reflex represents the discharge of seven α motor neurons: the four that spiked after the singular stimulation of each nerve (two per nerve) and three additional α motor neurons (located in the facilitation zone) that are made to discharge only when the two nerves are stimulated simultaneously because they lie in the subliminal fringe for both nerves.

A similar effect could be elicited by repetitive stimulation of one of the nerves, provided that the stimuli occur close enough together that some of the excitatory effect of the first volley still persists after the second volley arrives. This effect is called **temporal summation.** Both spatial summation and temporal summation depend on the properties of the EPSPs evoked in α motor neurons by the group Ia afferent fibers (see Fig. 6.8).

Convergence can also lead to inhibitory interactions between stimuli, a phenomenon called **occlusion.** If a volley in one of the two nerves in Fig. 9.11 reaches the motor nucleus at a time when the motor neurons are highly excitable, the reflex discharge is relatively large (see Fig. 9.11*C*). A similar volley in the other nerve might also produce a large reflex response. However, when the two nerves are excited simultaneously, the reflex can be less than the sum of the two independently evoked reflexes if the neurons reaching threshold to activation of either of the two nerves alone overlap significantly. In this case, each afferent nerve activates 7 α motor neurons, but the volleys in the two nerves together cause only 12 α motor neurons to discharge because two motor neurons lie in the individual discharge zones of both afferent nerves.

The phenomena of spatial and temporal summation and occlusion can also be used to demonstrate interactions between spinal cord neurons and the various reflex circuits. To start, a monosynaptic reflex discharge can be evoked by stimulation of the group Ia afferent fibers in a muscle nerve. This is a test of the reflex excitability of a population of α motor neurons. The discharges of either extensor or flexor α motor neurons can be recorded if the proper muscle nerve to be stimulated is chosen. Other kinds of afferent fibers are then stimulated

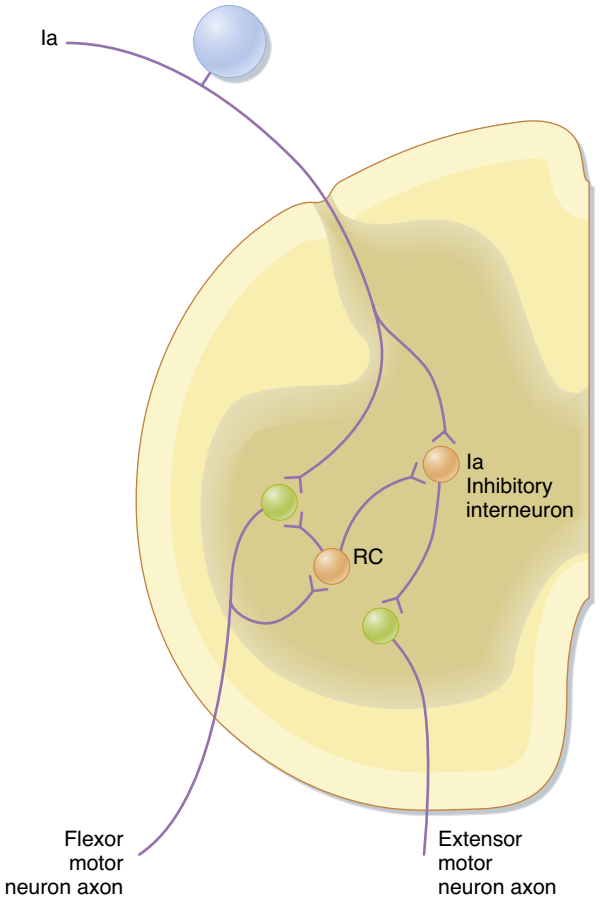


• **Fig. 9.11** Spatial facilitation. **A,** Arrangement for using electrically evoked afferent volleys and recordings from motor axons in a ventral root to study reflexes. **B,** Experiment in which combined stimulation of afferent fibers in two muscle nerves resulted in spatial summation (R_A *and* R_B). The discharge zones *(pink areas)* enclose α motor neurons that are activated above threshold when each nerve branch is stimulated separately. In **C,** the combined volleys caused occlusion. (Redrawn from Eyzaguirre C, Fidone SJ. *Physiology of the Nervous System.* 2nd ed. Chicago: Mosby–Year Book; 1975.)

along with the homonymous group Ia afferent fibers from the muscle to demonstrate whether the response to the group Ia stimulation changes. For example, stimulation of group Ia afferent fibers in the nerve to the antagonist muscles produces inhibition of the response to the homonymous group Ia stimulation (which is mediated by the reciprocal group Ia inhibitory interneuron described previously).

As another example, if the small afferent fibers of a cutaneous nerve are stimulated to evoke a flexion reflex, the responses to group Ia stimulation of the α motor neurons that innervate the extensor muscles are inhibited (and those of α motor neurons that innervate flexor muscles are potentiated).

As a final example, stimulation of a ventral root causes inhibition of group Ia responses and inhibits the reciprocal group Ia inhibition. Because the ventral root contains only motor neuron axons, this result implies the presence of axon collaterals that excite inhibitory interneurons that feed back onto the same motor neuron population (Fig. 9.12). These interneurons are named **Renshaw cells**. Because ventral root stimulation also inhibits the group Ia inhibition of antagonist motor neurons, but no other classes of interneurons, the reciprocal group Ia interneurons are uniquely inhibited by ventral root stimulation (and activated by group Ia stimulation).



• **Fig. 9.12** Renshaw cell *(RC)* connections with motor neurons and group Ia inhibitory interneurons. The circuits shown mediate group Ia reciprocal inhibition of antagonist muscles (in this case, an extensor) and inhibition of this reciprocal inhibition by Renshaw cells. Note that equivalent numbers of Renshaw cells and group Ia inhibitory interneurons are associated with extensor motor neurons and group Ia input from spindles in extensor muscles, but they are not shown for simplicity. *Orange cells* are inhibitory, and *blue* and *green cells* are excitatory.

Descending Motor Pathways

Classification of Descending Motor Pathways

Descending motor pathways were traditionally subdivided into **pyramidal** and **extrapyramidal pathways.** This terminology reflects a clinical dichotomy between pyramidal tract disease and extrapyramidal disease. In pyramidal tract disease, the **corticospinal** (pyramidal) tract is interrupted. The signs of this disease were originally attributed to the loss of function of the pyramidal tract (so named because the corticospinal tract passes through the pyramids of the medulla). However, in many cases of pyramidal tract disease, the functions of other pathways are also altered, and most signs of pyramidal tract disease (see the later section "Motor Deficits Caused by Lesions of Descending Motor Pathways") are apparently not caused solely by loss of the corticospinal tract, but also reflect damage to additional motor pathways (sometimes called the *extra*pyramidal system).

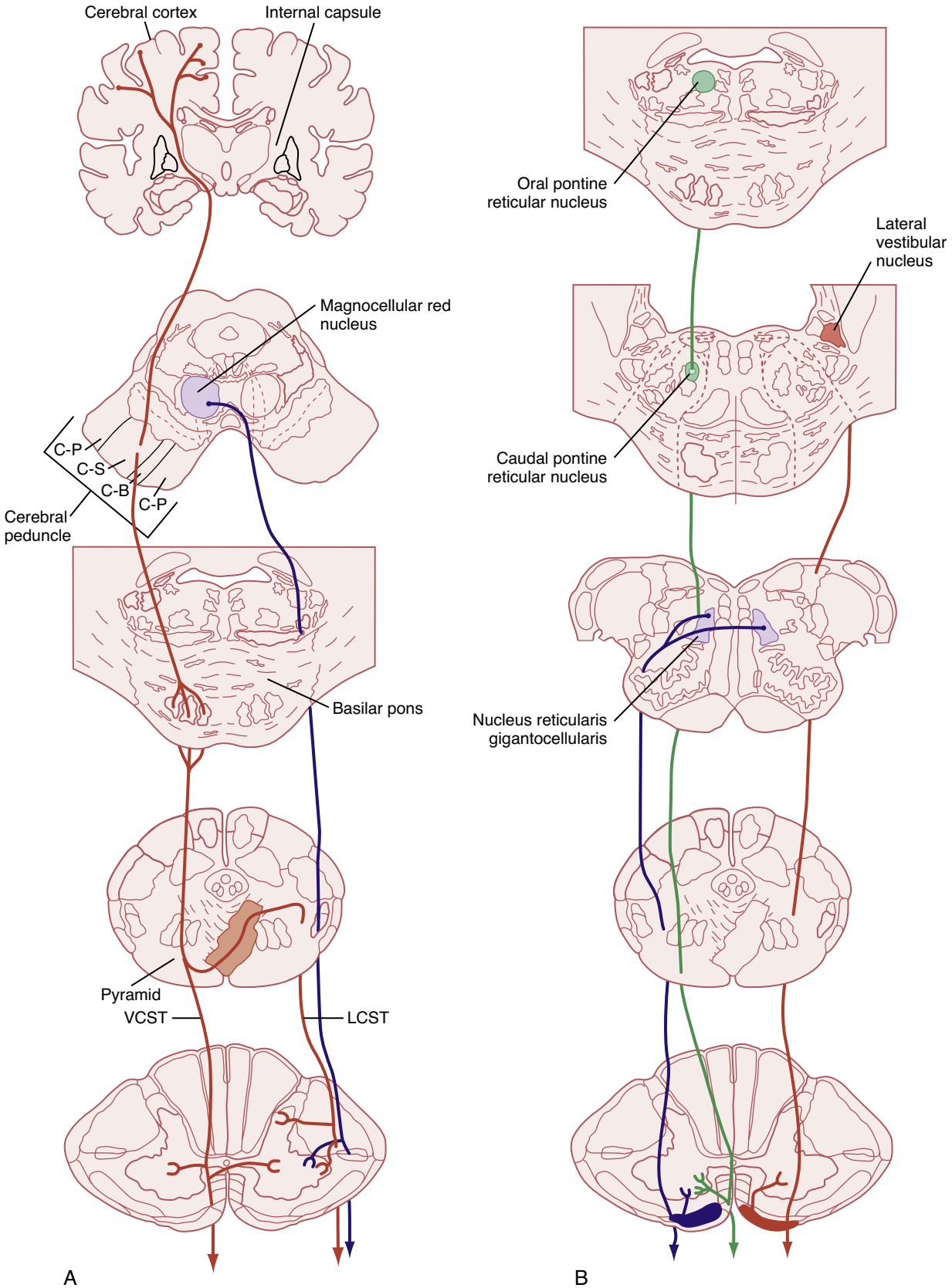
Another way of classifying the motor pathways is based on their sites of termination in the spinal cord and their roles in the control of movement and posture. The **lateral pathways** terminate in the lateral portions of the spinal cord's gray matter (Fig. 9.13). The lateral pathways can excite motor neurons directly, although interneurons are their main target. They influence reflex arcs that control fine movement of the distal ends of limbs, as well as, those that activate supporting musculature in the proximal ends of limbs. The **medial pathways** end in the medial ventral horn on the medial group of interneurons (see Fig. 9.13). These interneurons connect bilaterally with motor neurons that control the axial musculature for balance and posture. They also contribute to the control of some proximal limb muscles. In this book, the terms *lateral* and *medial* are used to classify the descending motor pathways. However, this terminology is not accurate, partly because motor neuron cell bodies in localized columns, have large motor neuron dendritic trees that typically span most of the ventral horn. As a consequence, any motor neuron can potentially receive input from so-called medial or lateral system pathways.

The Lateral System

Lateral Corticospinal and Corticobulbar Tracts

The corticospinal and corticobulbar tracts originate from a wide region of the cerebral cortex. This region includes the primary motor, premotor, supplementary, and cingulate motor areas of the frontal lobe and the somatosensory cortex of the parietal lobe. The cells of origin of these tracts include both large and small pyramidal neurons of layer V of the cortex, including the **giant pyramidal cells of Betz.** Although Betz cells are a defining feature of the primary motor cortex, they represent a small minority (<5%) of the neurons that contribute to these tracts, in part because they are found only in the primary motor cortex, and even there they represent a minority of the neurons contributing to the tracts. These tracts leave the cortex and enter the internal capsule, then traverse the midbrain in the cerebral peduncle, pass through the basilar pons, and emerge to form the pyramids on the ventral surface of the medulla (see Fig. 9.13*A*). The corticobulbar axons leave the tract as it descends in the brainstem and terminate in the motor nuclei of the various cranial nerves. The corticospinal fibers continue caudally, and in the most caudal region of the medulla, about 85% of them cross to the opposite side. They then descend in the contralateral lateral funiculus as the lateral corticospinal tract. The lateral corticospinal axons terminate at all spinal cord levels, primarily on interneurons, but also on motor neurons. The remaining uncrossed axons continue caudally in the ventral funiculus on the same side as the ventral corticospinal tract, which belongs to the medial system. Many of these fibers ultimately decussate (cross) at the spinal cord level at which they terminate.

The lateral corticospinal tract is a relatively minor tract in lower mammals but is quantitatively and functionally very



• **Fig. 9.13** Descending motor pathways. Major pathways connecting the cortical and brainstem motor areas to the spinal cord are shown. **A,** Lateral system pathways, corticospinal *(red)* and rubrospinal *(blue)* pathways. Note that the ventral corticospinal pathway is part of the medial system but is shown in **A** for simplicity. **B,** Medial system pathways, medullary *(blue)* and pontine *(green)* reticulospinal and lateral vestibulospinal *(red)* pathways. C-B, Corticobulbar; C-P, corticopontine; C-S, corticospinal; LCST, lateral corticospinal tract; VCST, ventral corticospinal tract.

important in primates, particularly in humans, in which it contains more than 1 million axons. This number still represents a relatively small proportion of the outflow from the cortex because there are approximately 20 million axons in the cerebral peduncles. Nevertheless, the corticospinal pathway is critical for the fine independent control of finger movement, inasmuch as isolated lesions of the corticospinal tract typically lead to a permanent loss of this ability, even though other movement abilities are often recovered with such lesions. Indeed, in primates, corticospinal synapses directly onto motor neurons are particularly prevalent for the motor neurons controlling finger muscles and are probably the basis of the ability to make independent, finely controlled finger movements.

The corticobulbar tract, the name for the tract that projects from the cortex to the brainstem cranial nerve motor nuclei, has subdivisions that are comparable with the lateral and ventral corticospinal tracts. For example, part of the corticobulbar tract ends contralaterally in the portion of the facial nucleus that supplies muscles of the lower part of the face and in the hypoglossal nucleus. This component of the corticobulbar tract is organized like the lateral corticospinal tract. The remainder of the corticobulbar tract ends bilaterally, including bilateral innervation of both sides of the upper face (forehead). This particular arrangement of input to the lower and upper face can have important clinical implications if, for example, only lower face muscles on one side are disrupted versus disruption of both upper and lower face muscles on one side.

Rubrospinal Tract

The rubrospinal tract, which plays a more prominent role in nonprimates than primates, originates in the magnocellular portion of the red nucleus, which is located in the midbrain tegmentum. These fibers decussate in the midbrain, descend through the pons and medulla, and then take up a position just ventral to the lateral corticospinal tract in the spinal cord. They preferentially affect motor neurons controlling distal musculature, as do the corticospinal fibers. Red nucleus neurons receive input from the cerebellum and from the motor cortex, which allows for integration of activity from these two motor systems.

The Medial System

The ventral corticospinal tract (also called, anterior corticospinal tract), and much of the corticobulbar tract, can be regarded as medial system pathways. These tracts end on the medial group of interneurons in the spinal cord and on equivalent neurons in the brainstem. The axial muscles are controlled by these pathways. These muscles often contract bilaterally to provide postural support or some other bilateral function, such as swallowing or wrinkling of the brow.

Other medial system pathways originate in the brainstem. These include the pontine and medullary reticulospinal tracts, the lateral and medial vestibulospinal tracts, and the tectospinal tract.

Pontine and Medullary Reticulospinal Tracts

Neurons in the medial area of the rectiular formation of the pons give rise to the pontine reticulospinal tract. The tract descends in the ventral funiculus and ends on the ipsilateral medial group of interneurons. Its function is to excite motor neurons controlling the proximal extensor muscles that support posture.

The medullary reticulospinal tracts arise from neurons of the medial medulla, particularly those of the gigantocellularis reticular nucleus. The tracts descend bilaterally in the ventral lateral funiculus, and they end mainly on interneurons associated with cell groups of medial motor neurons. The function of the pathway is mainly inhibitory.

Lateral and Medial Vestibulospinal Tracts

The lateral vestibulospinal tract originates in the lateral vestibular nucleus (also known as *Deiter's nucleus*), is located around the medulla and pons junction. This tract descends ipsilaterally through the ventral funiculus of the spinal cord and ends on interneurons associated with the medial motor neuron groups. The lateral vestibulospinal tract excites motor neurons that supply extensor muscles of the proximal part of the limb that are important for postural control. In addition, this pathway inhibits flexor motor neurons by exciting the reciprocal group Ia interneurons that receive group Ia input from extensor muscles, which in turn inhibit flexor motor neurons. The excitatory input to the lateral vestibular nucleus is from both the semicircular canals and the otolith organs, whereas the inhibitory input is from the Purkinje neurons of the anterior vermis region of the cerebellar cortex. An important function of the lateral vestibulospinal tract is to assist in postural adjustments after angular and linear accelerations of the head.

The medial vestibulospinal tract originates from the medial vestibular nucleus. This tract descends in the ventral funiculus of the spinal cord to the cervical and midthoracic levels, and it ends on the medial group of interneurons. Sensory input to the medial vestibular nucleus from the labyrinth is chiefly from the semicircular canals. This pathway thus mediates adjustments in head position in response to angular acceleration of the head.

The Tectospinal Tract

The tectospinal tract originates in the deep layers of the superior colliculus in the midbrain (the area where the superior colliculi and inferior colliculi are located is known as the *tectum*). The axons cross to the contralateral side, just below the periaqueductal gray matter. They then descend in the ventral funiculus of the spinal cord to terminate on the medial group of interneurons in the upper cervical spinal cord. The tectospinal tract regulates head movement in response to visual, auditory, and somatic stimuli.

Monoaminergic Pathways

In addition to the lateral and medial systems, less specifically organized systems descend from the brainstem to the

spinal cord. These include several pathways in which monoamines serve as neurotransmitters.

The locus coeruleus and the nucleus subcoeruleus are nuclei located in the rostral pons, and they are composed of norepinephrine-containing neurons. These nuclei project widely throughout the CNS, and their projection to the spinal cord travels in the lateral funiculus. Their terminals are on interneurons and motor neurons. The dominant effect of the pathway is inhibitory.

The raphe nuclei of the medulla also project widely throughout the CNS and give rise to several raphe-spinal pathways. With regard to motor function, the ventral horn projection may enhance motor activity.

In general, the monoaminergic pathways act to alter the responsiveness of spinal cord circuits, including the reflex arcs. In this way, they induce widespread changes in excitability, rather than, eliciting discrete movements or specific changes in behavior.

Motor Deficits Caused by Lesions of Descending Motor Pathways

Motor impairment in humans may result from damage to efferent cerebral cortical fibers passing within the internal capsule. This might happen following a stroke to the blood supply to the internal capsule. The resulting disorder is often termed a **pyramidal tract syndrome** or **upper motor neuron disease,** although these names are misnomers. Motor changes characteristic of this disorder include: (1) increased phasic and tonic stretch reflexes (spasticity); (2) weakness, usually of the distal muscles, especially the finger muscles; (3) pathological reflexes, including the **sign of Babinski** (dorsiflexion of the big toe and fanning of the other toes when the sole of the foot is stroked); and (4) a reduction in superficial reflexes, such as the abdominal and cremasteric reflexes. Of importance is that if only the corticospinal tract is interrupted, as can occur with a lesion of the medullary pyramid, most of these signs are much reduced or absent. In this situation, the most prominent deficits are weakness of the contralateral distal muscles, especially those of the fingers, and a Babinski sign. Spasticity does not occur; instead, muscle tone may actually decrease. Evidently, the presence of spasticity requires the disordered function of other pathways, such as the reticulospinal tracts, as would occur after loss of the descending cortical influence to the brainstem nuclei of origin of these tracts.

The effects of interruption of the medial system pathways are quite different from those produced by corticospinal tract lesions. The main deficits associated with medial system interruption are an initial reduction in the tone of postural muscles and loss of righting reflexes. Long-term effects include locomotor impairment and frequent falling. However, manual manipulation of objects is perfectly normal.

The Decerebrate Preparation

The decerebrate preparation has been useful for experimentally investigating how various descending pathways interact with the spinal cord circuitry. Surgical decerebration is achieved either by transection of the midbrain, often at an intercollicular level, or by occlusion of the blood vessels feeding this area. In the latter case, a lesion also occurs in the anterior vermis of the cerebellum, an important distinction. With the intercollicular transection, some descending pathways, such as those originating in the cerebral cortex, are interrupted, whereas others, such as those originating in the brainstem, remain intact.

Remember, however, that the corticospinal tract is only one component of the cortical descending fibers. Many other cortical fibers project to locations throughout the brainstem, including the nuclei of origin for the medial descending pathways. Loss of these cortical control systems results in altered activity in the intact descending pathways. As a result, affected animals show hypertonia and suppression of some spinal reflexes, such as the flexion reflex, and exaggeration of others, such as the stretch reflex; this condition is called **decerebrate rigidity.** Decerebrate animals maintain a posture that has been called **exaggerated standing.** Human patients with brainstem damage may also develop a decerebrate state that has many of the same reflex features as animal preparations.

Loss of descending control of the reticular formation results in increased activity in the pontine reticulospinal pathway and decreased activity in the medullary reticulospinal pathway. Such increase and decrease in activity, respectively, produce increased excitation and decreased inhibition (disinhibition) of the motor neurons, which explains the observed rigidity. Interestingly, this hypertonia can be relieved by cutting the dorsal roots, which indicates that the reticulospinal tracts have a major effect on γ motor neurons. This is because γ motor neuron activity alters muscle stiffness by increasing muscle spindle sensitivity and thereby causes increased activity in the group Ia and group II afferent fibers, which travel through the dorsal roots into the spinal cord in order to innervate the α motor neurons.

When vessel occlusion is used to generate the decerebrate state, the lateral vestibulospinal tract becomes hyperactive because of damage to Purkinje neurons in the anterior vermis of the cerebellum, which provide the major inhibitory projection to the lateral vestibular nucleus. This hypertonia is actually not lost after transection of the dorsal roots, which implies that the lateral vestibulospinal tract is acting to a significant extent directly on α motor neurons (either monosynaptically or via interneurons).

Brainstem Control of Posture and Movement

The importance of motor control pathways that originate in the brainstem is evident from observations of the extensor hypertonus and increased phasic stretch reflexes that occur in decerebrate animals. Particular brainstem systems have been identified as influencing posture and locomotion. Brainstem circuits are also critically involved in the control

of eye movement; these circuits are discussed in a separate section at the end of the chapter.

Postural Reflexes

Several reflex mechanisms are evoked when the head is moved or the neck is bent. There are three types of postural reflexes: vestibular reflexes, tonic neck reflexes, and righting reflexes. The sensory receptors responsible for these reflexes include the vestibular apparatus (see Chapter 8), which is stimulated by head movement, and stretch receptors in the neck.

The **vestibular reflexes** constitute one class of postural reflex. Rotation of the head activates hair cells of the semicircular canals (see Chapter 8). In addition to generating eye movement, the sensory input to the vestibular nuclei results in postural adjustments. Such adjustments are mediated by commands transmitted to the spinal cord through the lateral and medial vestibulospinal tracts and the reticulospinal tracts. The lateral vestibulospinal tract activates extensor muscles that support posture. For instance, if the head is rotated to the left, postural support is increased on the left side. This increased support prevents the person from falling to the left as the head rotation continues. A person who has any disease that eliminates labyrinthine function in the left ear tends to fall to the left. Conversely, a person with a disease that irritates (stimulates) the left labyrinth tends to fall to the right. The medial vestibulospinal tract causes contractions of neck muscles that oppose the induced movement **(vestibulocollic reflex).**

Tilting the head also changes the linear acceleration on individual hair cells of the otolith organs of the vestibular apparatus. The resulting changes in hair cell activity can produce eye movement and postural adjustment. For example, when a quadruped, such as a cat, tilts the head and body forward (without bending the neck and consequently without evoking the tonic neck reflexes), the result is extension of the forelimbs and flexion of the hind limbs. This vestibular action tends to restore the body toward its original orientation. Conversely, if the quadruped tilts the head and body backward (without bending the neck), the forelimbs flex and the hind limbs extend. Otolithic organs also contribute to the **vestibular placing reaction.** If an animal, such as a cat, is dropped, stimulation of the utricles leads to extension of the forelimbs in preparation for landing.

The **tonic neck reflexes** are another type of positional reflex. These reflexes are activated by the muscle spindles found in neck muscles. These muscles contain the largest concentration of muscle spindles of any muscle in the body. If the neck is bent (without tilting of the head), the neck muscle spindles evoke tonic neck reflexes without interference from the vestibular system. When the neck is extended, the forelimbs extend and the hind limbs flex. The opposite effects occur when the neck is flexed. Note that these effects are opposite to those evoked by the vestibular system. Furthermore, if the neck is bent to the left, the extensor muscles in the limbs on the left contract more, and the flexor muscles in the limbs on the right side relax.

The third class of postural reflex is the **righting reflexes.** These reflexes tend to restore an altered position of the head and body toward normal. The receptors responsible for righting reflexes include the vestibular apparatus, the neck stretch receptors, and mechanoreceptors of the body wall.

Brainstem Control of Locomotion

The spinal cord contains neural circuits that serve as **central pattern generators** for locomotion, as discussed earlier. These CPG circuits produce very regular rhythmic output that characterizes stereotyped behavior, such as walking. The irregularities of real-world environments, however, often require modification of this stereotyped output (e.g., if you are walking and see a hole in the floor where you are about to step, you can extend the forward swing of your leg past the hole onto solid ground beyond it).

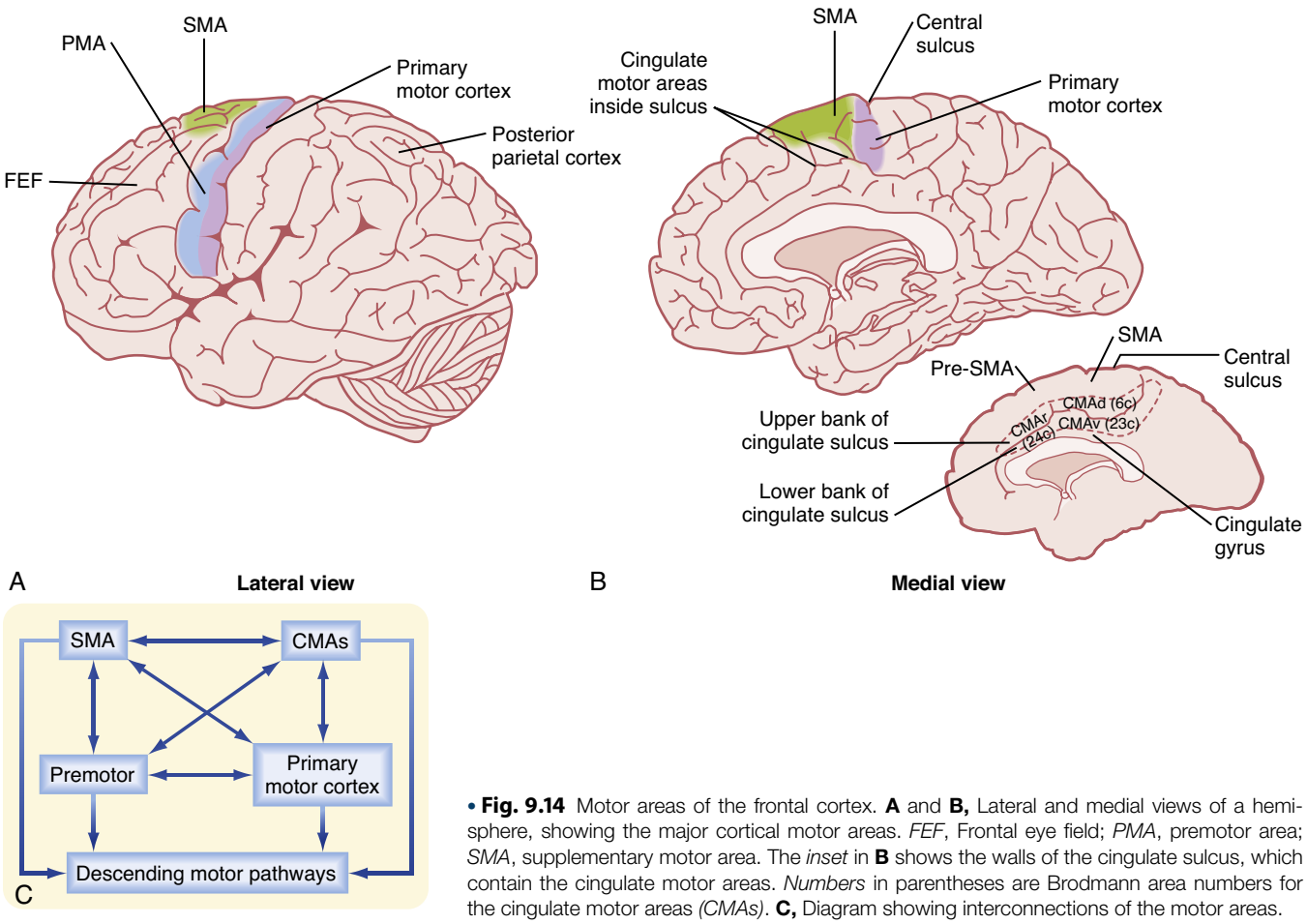
Such modifications can be the result of sensory input to the spinal cord, as shown in Fig. 9.10, in which stimulation of FRA fibers in a peripheral nerve caused a phase shift in the locomotor pattern. They can also be the result of descending commands along the motor pathways discussed earlier. In this case, sensory data (e.g., visual) can be used by the brain to make anticipatory modifications in CPG activity so that potential obstacles can be avoided. In addition, people can voluntarily control activation, or shutdown, of the CPG (i.e., deciding consciously when to start and stop walking). Such voluntary regulation of spinal CPGs originates in the cerebral cortex; however, much of the cortical influence on locomotion appears to be mediated via projections to brainstem regions known as *locomotor regions.* A locomotor region can be defined as a brain area that, when stimulated, leads to sustained locomotion.

There are several such locomotor regions in the brainstem, and they are located at different levels ranging from the subthalamus to the medulla and are connected with each other. The best known is the **midbrain locomotor region,** which is thought to organize commands to initiate locomotion. It is located in the midbrain at the level of the inferior colliculus. Voluntary activity that originates in the motor cortex can trigger locomotion by the action of corticobulbar fibers projecting to the midbrain locomotor region. The commands are relayed through the reticular formation and then to the spinal cord via the reticulospinal tracts.

Motor Control by the Cerebral Cortex

Thus far in this chapter, emphasis has been on reflexes and relatively automatic types of movement. We now discuss the neural basis for more complex, goal-directed voluntary movement. Such movement often varies when repeated and is frequently initiated as a result of cognitive processes, rather than in direct response to an external stimulus, and thus requires the participation of motor areas of the cerebral cortex.

First, consider what is necessary to generate a voluntary movement. For example, to make a reaching movement



• **Fig. 9.14** Motor areas of the frontal cortex. **A** and **B,** Lateral and medial views of a hemisphere, showing the major cortical motor areas. *FEF*, Frontal eye field; *PMA*, premotor area; *SMA*, supplementary motor area. The *inset* in **B** shows the walls of the cingulate sulcus, which contain the cingulate motor areas. *Numbers* in parentheses are Brodmann area numbers for the cingulate motor areas *(CMAs)*. **C,** Diagram showing interconnections of the motor areas.

with your arm, you must first identify the target (or goal) and locate it in external space. Next, a limb trajectory must be determined on the basis of an internal representation of your arm and, in particular, your hand in relation to the target. Finally, a set of forces necessary to generate the desired trajectory must be computed. This process is often thought of as a series of transformations between coordinate systems. For example, the location of a visually identified target is measured in a retinotopic space, but its location is perceived in an external or world space (i.e., the position of a nonmoving target is perceived as stable, even when the eye, and thus the target's image on the retina, changes). Next, calculation of a trajectory would involve a body- or hand-centered system, and finally forces must ultimately be computed in a muscle-based reference frame.

These steps form a linear sequence, and traditionally it was thought that a hierarchy of motor areas carried out the successive steps. For example, the target of the movement was thought to be identified by pooling of sensory information in the **posterior parietal cerebral cortex** (Fig. 9.14*A*). This information would then be transmitted to the supplementary motor and premotor areas, where a motor plan would be developed and then forwarded to the primary motor cortex, whose activity would be related to the final execution stage (e.g., generation of appropriate force levels). The motor cortex would then transmit commands, via the descending pathways discussed earlier, to the spinal cord and brainstem motor nuclei.

Although there is significant evidence in support of this hierarchical view of the generation of voluntary movement by the cortical motor system, more recent data suggest that the various motor areas communicate via a parallel distributed network rather than a strict hierarchy (see Fig. 9.14*C*). For example, each cortical motor area makes its own significant contribution to the descending motor pathways; the primary motor cortex contributes only approximately half the fibers in the corticospinal tract that arise from the frontal lobe. Moreover, the various motor areas are all bidirectionally connected to each other, and results of the single-unit recording studies described later suggest that each of the areas plays a role in several of the stages of planning and executing a movement. This debate forms one of the themes of the following discussion because in its various guises, the distributed network versus hierarchical organization debate has been ongoing for decades and will probably continue for some time.

Cortical Motor Areas

The motor areas in the cerebral cortex were originally defined on the basis of experiments in which electrical stimuli applied to the cortex evoked discrete, contralateral movement. Movement, however, can also be evoked when other

cortical areas are stimulated more intensely. Based on these observations, motor areas are defined as those from which movement can be evoked by the lowest stimulus intensity. In addition to these stimulation studies, the results of electrophysiological recordings and anatomical experiments, the results of modern imaging studies in humans, and observations following lesions indicate that many "motor" areas of the cerebral cortex are involved, including: the **primary motor cortex** in the precentral gyrus, the **premotor area** just rostral to the primary motor cortex, the **supplementary motor cortex** on the medial aspect of the hemisphere, and three **cingulate motor areas** located on the walls of the cingulate sulcus in the frontal lobe (see Fig. 9.14). There are also cortical regions in other lobes whose activity is related specifically to eye movement (see the section "Eye Movement").

Somatotopic Organization of Cortical Motor Areas

Primary Motor Cortex

The primary motor cortex (or just motor cortex) can be defined as the region of cortex from which movements are elicited with the least amount of electrical stimulation. It is essentially congruent with the Brodmann cytoarchitectonic area 4 (see Fig. 10.3). In humans it is located on the parts of the precentral gyrus that form the rostral wall of the central sulcus and the caudal half of the apex of the gyrus. On the basis of initial mapping studies, which were done with surface stimulation, the motor cortex was described as having a topographic organization that parallels that of the somatosensory cortex. The face, body, and upper limb were represented on the lateral surface with the face located inferiorly, near the lateral fissure, the torso most superiorly, and the lower extremity mostly on the medial aspect of the hemisphere. This somatotopic organization is often represented as a figurine or in a graphic form called a **motor homunculus** (Fig. 9.15*B*). The distortion of the various body parts in the homunculus indicates approximately how much of the cortex is devoted to their motor control. This simple homunculus fits well with traditional conceptions of the motor cortex being the final cortical stage and acting as a relay for sending motor commands to the spinal cord.

Beginning in the 1960s and 1970s, mapping studies began using microelectrodes inserted to the deep, or output, layers of the cortex to apply stimuli. With this technique, called **intracortical microstimulation,** much lower stimulus intensities could be used to evoke movements and thus allowed higher-resolution mapping of the motor cortex, thereby revealing a much more complex topography than was previously imagined (see Fig. 9.15*C*). Movement about each joint was found to be evoked by many noncontiguous columns throughout wide regions of the motor cortex, demonstrating that cell columns related to movement about a particular joint are interspersed among columns that control movement about many other joints. In sum, the motor cortex may have large subdivisions corresponding to a limb or the head, but within each such area there is a complex intermingling of cell columns that control the muscles within that body part.

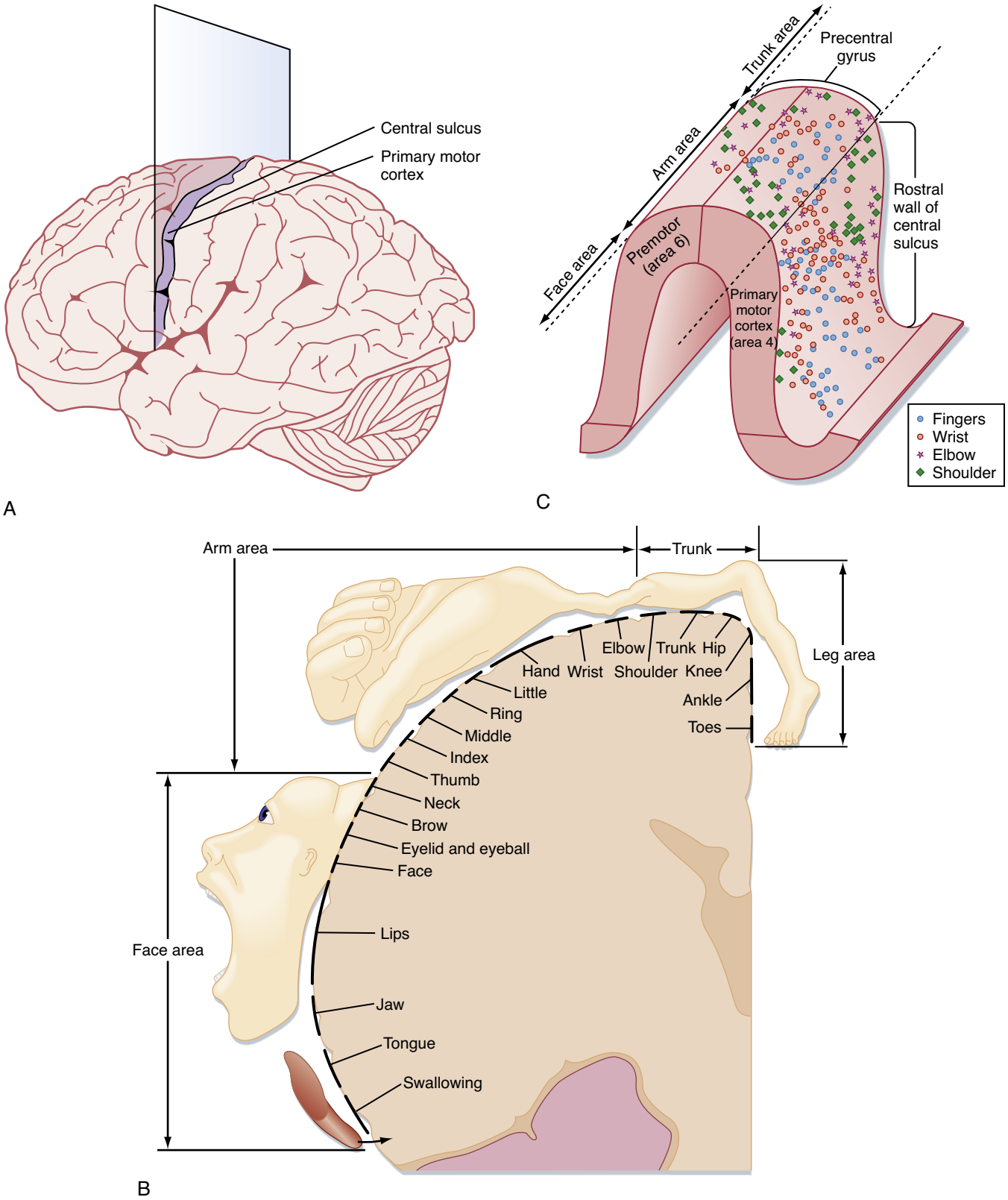
Such mixing of cell columns makes functional sense because most movement requires the coordinated action of muscles throughout a limb, and most connectivity in the cortex is localized (i.e., axon collaterals that connect different cell columns are primarily confined to a 1- to 3-mm region surrounding the column from which they originate). When multiple cell columns that control movement about a joint are present and intermixed with columns controlling movement about other joints, multi-joint movement can occur in a coordinated manner.

Although the topographic map of the motor cortex is in part anatomically determined by the topography of the corticospinal pathway, it is also a dynamic map. Axon collaterals link the different cell columns, so that activity in one column could potentially lead to movement about multiple joints. In fact, this can happen, but these intercolumnar connections are modulated by inhibitory interneurons that transmit or secrete GABA. This was shown by locally blocking GABA with a pharmacological antagonist in one region of the motor cortex, then stimulating the neighboring region. Before the block, stimuli evoked contractions of one set of muscles, but once inhibition was blocked, contractions were also evoked in muscles controlled by the region that was no longer inhibited (Fig. 9.16). Functional connections between cell columns can be controlled on a millisecond time scale, and depending on their state, the motor cortex map can be radically changed. Longer-term plastic changes are also known to occur; for example, the use (or disuse) of a body part can affect the size of its somatotopic representation.

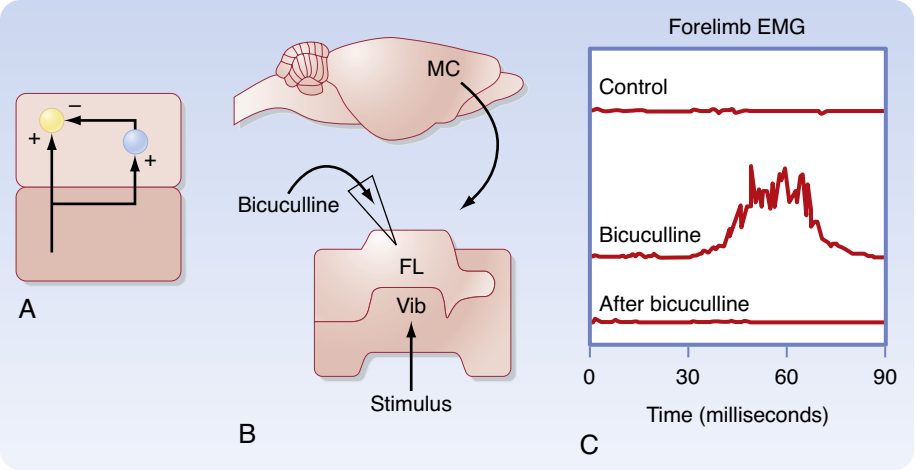
Supplementary Motor Area

The supplementary motor area (SMA) is located mainly on the medial surface of the hemisphere, just anterior to the primary motor cortex, and corresponds to the medial portion of Brodmann area 6 (see Fig. 9.14). It is subdivided into two regions: the more posterior part is referred to as the *SMA proper* (or just *SMA*), and the anterior portion is called the *pre-SMA.* The SMA proper is similar to the other motor areas already listed: it contains a complete somatotopic map, it contributes to the corticospinal tract, and it is interconnected with the other motor areas. In contrast, the pre-SMA is not strongly connected with the other motor areas and spinal cord, but rather is connected to the prefrontal cortex.

The results of stimulation studies show that, as in the motor cortex, there is a complete somatotopic map in the SMA. Stimulation of the SMA can evoke isolated movement about single joints, similar to that after stimulation of the motor cortex, but stimulation must be of higher intensity and longer duration; moreover, the evoked movements are often more complex than those evoked by stimulation of the motor cortex. However, longer-duration stimulation of the primary motor cortex can also evoke complex,



• **Fig. 9.15** Traditional and modern views of motor cortex musculotopic organization. **A,** Lateral view of the cerebrum, showing a plane of section through the precentral gyrus (primary motor cortex) that corresponds to the section shown in **B. B,** Classic view of motor cortex musculotopy ("muscular homunculus"). **C,** Modern view of motor cortex organization in which each body part is represented multiple times across several discrete regions.



• **Fig. 9.16** Dynamic nature of a motor cortex musculotopic map. Inhibitory GABAergic interneurons play an important role in shaping motor responses to stimulation of each region of the motor cortex. **A,** Schematic view of excitatory connections between two regions of primary motor cortex and local inhibitory neurons within a single region. **B,** Schematic view of a rat brain, indicating motor cortex *(MC)* regions where electrical stimuli were applied to evoke movements (Vib region) and bicuculline was applied to block GABAergic synapses (in the FL region). *FL*, Forelimb; *Vib*, vibrissa. **C,** Forelimb EMG records showing response to stimulation of the Vib region before and during the application of bicuculline and after it was washed out. Note that Vib stimulation evoked vibrissae movement in all conditions but evoked forelimb movement only when inhibitory interneurons in FL were blocked. (Data from Jacobs K, Donoghue J. *Science* 1991;251:944.)

apparently purposeful movement sequences, and so the distinction is not absolute. In addition, stimulation of the SMA can produce vocalization or complex postural movements, but it can also have the opposite result: namely, a temporary arrest of movement or speech. Removal of the supplementary motor cortex retards movement of the opposite extremities and may result in forced grasping movements with the contralateral hand.

Premotor Area

This area lies rostral to the primary motor cortex and is contained in Brodmann area 6 on the lateral surface of the brain (see Fig. 9.14). It can be distinguished from the primary motor cortex by the higher stimulus intensities needed to evoke movement. The premotor area has been divided into two functionally distinct subdivisions: dorsal and ventral. Like the motor cortex, both subdivisions are somatotopically organized and both contribute to the corticospinal tract. The dorsal division (PMd) contains a relatively complete map representing the leg, trunk, arm, and face. In contrast, the somatotopic map of the ventral division (PMv) is mostly limited to the arm and face, with only a small leg representation. Thus, the PMv appears to be specialized for control of upper limb and head movement. A second difference between the subdivisions is that the PMd contains a large representation of the proximal muscles, whereas the PMv has a large representation of the distal muscles.

Cingulate Motor Areas

These motor areas are located within the cingulate sulcus at approximately the same anterior-posterior level as the SMA. There are three cingulate motor areas (dorsal, ventral, and rostral; see Fig. 9.14*B*). Each contains a somatotopic map and contributes to the corticospinal tract. Microstimulation in these areas evokes movement similar to that evoked by motor cortex stimulation, except that, again, higher stimulus intensities are needed. Single-cell recordings during movements have shown that the spontaneous activity of neurons in the cingulate motor areas is related to the preparation and execution of movements.

Connections of the Cortical Motor Areas

The motor areas of the cortex receive input from a number of sources, cortical and subcortical; however, the largest source of synapses in an area is the area itself: specifically, the local intrinsic connections. Moreover, all the motor areas described earlier are bidirectionally connected to each other with high topographic specificity (see Fig. 9.14*C*). For example, the arm regions of the primary motor cortex and the cingulate motor areas project to each other. Ascending pathways relay sensory information to the thalamus. This information can reach the motor cortex directly from the thalamus or indirectly by way of the somatosensory cortex. Both somatosensory information and visual information are conveyed to the motor areas from the posterior parietal cortex. The motor areas of the cortex also receive information through circuits that interconnect them with the other major brain regions involved in motor control: namely, the cerebellum and basal ganglia. These two structures project to distinct parts of the thalamus (the ventral lateral and ventral anterior nuclei), which then project to the cortical motor areas.

The output of the cortical motor areas to the spinal cord and brainstem is conducted through several descending pathways. These pathways include not only direct projections through the corticospinal and corticobulbar tracts (to the cranial nerve nuclei) but also indirect projections to the red nucleus and various nuclei in the reticular formation (see section in the chapter, "Descending Motor Pathways"). Control of head and neck muscles is mediated by projections to the various cranial nerve nuclei. The motor regions also project to the cerebellum and basal ganglia, thus completing neuroanatomical loops with these structures. The major connection to the cerebellum is via the corticopontine projections to the basilar pontine nuclei, which in turn project to the cerebellum. In addition, the cortical motor areas project, mostly via disynaptic pathways that synapse in the midbrain, to the inferior olivary nucleus, another important neural area that projects to the cerebellum. The cortical motor regions project directly to the striatum of the basal ganglia. Finally, there are major projections to the thalamus by which the cortex regulates thalamic function.

Activity of Motor Cortex Neurons

The role of individual motor cortex neurons in the control of movement has been extensively investigated in trained monkeys. In these experiments, discharges from a neuron in the primary motor cortex are recorded during the execution of a previously learned simple movement, such as wrist flexion, made immediately in response to a sensory cue (Fig. 9.17). Motor cortex neurons were found to change their firing rates before initiation of the movement, and the onset of this change was correlated with the reaction time (i.e., the time from the cue to onset of the movement). Moreover, in this task, the change in firing of motor cortex neurons was often correlated with the contractile force of the muscle that generates the movement and with the rate of change in force rather than with the position of the joint. These findings suggest that these neurons are involved in the final stages of planning and executing movements, which is consistent with the hierarchical view of the cortical motor areas.

However, even in these early experiments, the firing rates of some motor cortex neurons appeared to relate to earlier planning stages. Moreover, even when a monkey was trained to withhold the movement for a certain period after the cue, the firing rates of motor cortex neurons still changed despite the absence of any movement. Such "set-related" activity has been amply confirmed in a variety of other tasks and suggests that motor cortex activity may be involved in the earlier planning stages along with activity in other motor areas of the cortex. It also suggests the possibility that other, perhaps subcortical, systems may be needed to generate a trigger signal for the initiation of movement.

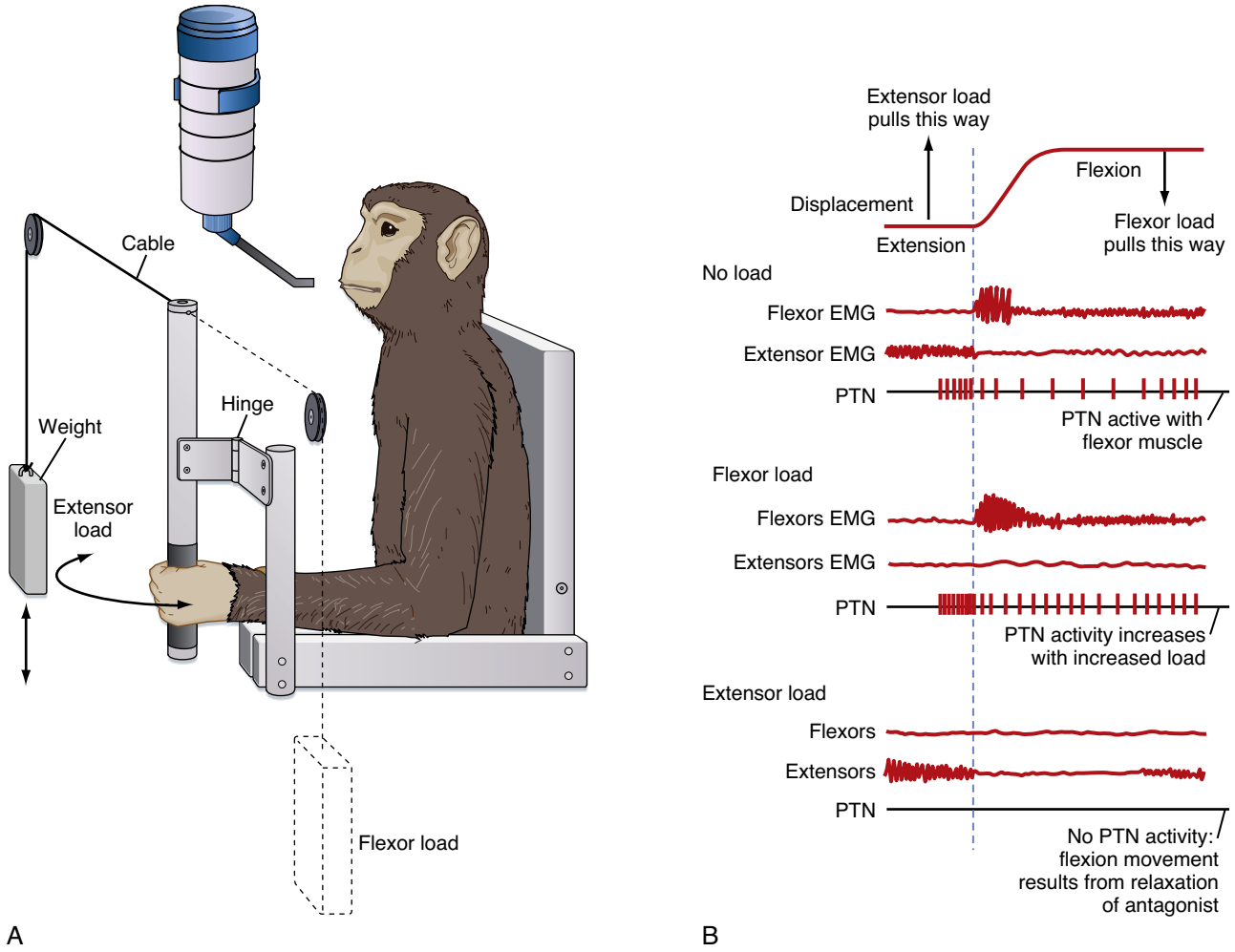
In subsequent studies, researchers have used tasks in which animals were trained to move a manipulandum (a device with a handle to hold and a small circle on the end) to capture lighted targets on a surface in front of them (Fig. 9.18*A*). These experiments demonstrated that neurons in the arm region of the motor cortex show changes in their firing rates in response to movement in many different directions, and thus can be described as broadly tuned (see Fig. 9.18*B*). That is, a neuron that showed a maximal increase for movement in one particular direction, called its preferred direction, would also show somewhat smaller increases, or even decreases, for movement in other directions (see Fig. 9.18*C*). Moreover, the preferred directions of the different neurons were uniformly distributed across all 360 degrees of possible movement directions.

These results implied that a particular neuron is probably involved in most arm movements, but they also raised the issue of how precise movements can be made with such broadly tuned neurons. It was suggested that although changes in the activity of individual neurons could not precisely predict or specify the direction of the upcoming movement, the net activity of the population of neurons can determine the movement. To test this idea, models were made in which the activity of each neuron is represented as a vector (see Fig. 9.18*D*). The direction of each neuron vector is determined by the preferred direction of the neuron, and the magnitude of the vector for a particular movement is proportional to the firing rate of the neuron during the time preceding the movement. The individual neuron vectors (see Fig. 9.18*D,* black lines) from hundreds of neurons can then be vectorially summed to get a resultant or population vector (see Fig. 9.18*D,* red lines) that accurately predicts the upcoming movement.

One of the difficulties in assessing the relationship between firing of cortical neurons and various movement parameters, such as force, velocity, displacement, and target location, is that these parameters are normally correlated with each other. Therefore, variations of the tasks described earlier have been used to decorrelate these various parameters (e.g., using weights to vary the force needed to make a movement without changing the displacement, as illustrated in Fig. 9.17*A,* or rotating the starting position of the wrist so that different muscles are required to generate the same trajectory in external space). The results of these experiments showed that the activity of motor cortex neurons may be related to each of the various motor planning stages. Furthermore, the activity of a single neuron may be correlated with one parameter initially, then switch as the time for onset of movement approaches.

Activity in Other Cortical Motor Areas

Activity in the premotor and supplementary motor areas is in many ways similar to that in the primary motor cortex. Neurons in these areas show activity related to upcoming movement, and the activity is correlated with movement parameters, such as displacement, force, and target location, just as primary motor cortex activity can be, which is consistent with the distributed network view of the cortical motor areas. There appear, however, to be differences between the areas as well, although these differences may be more



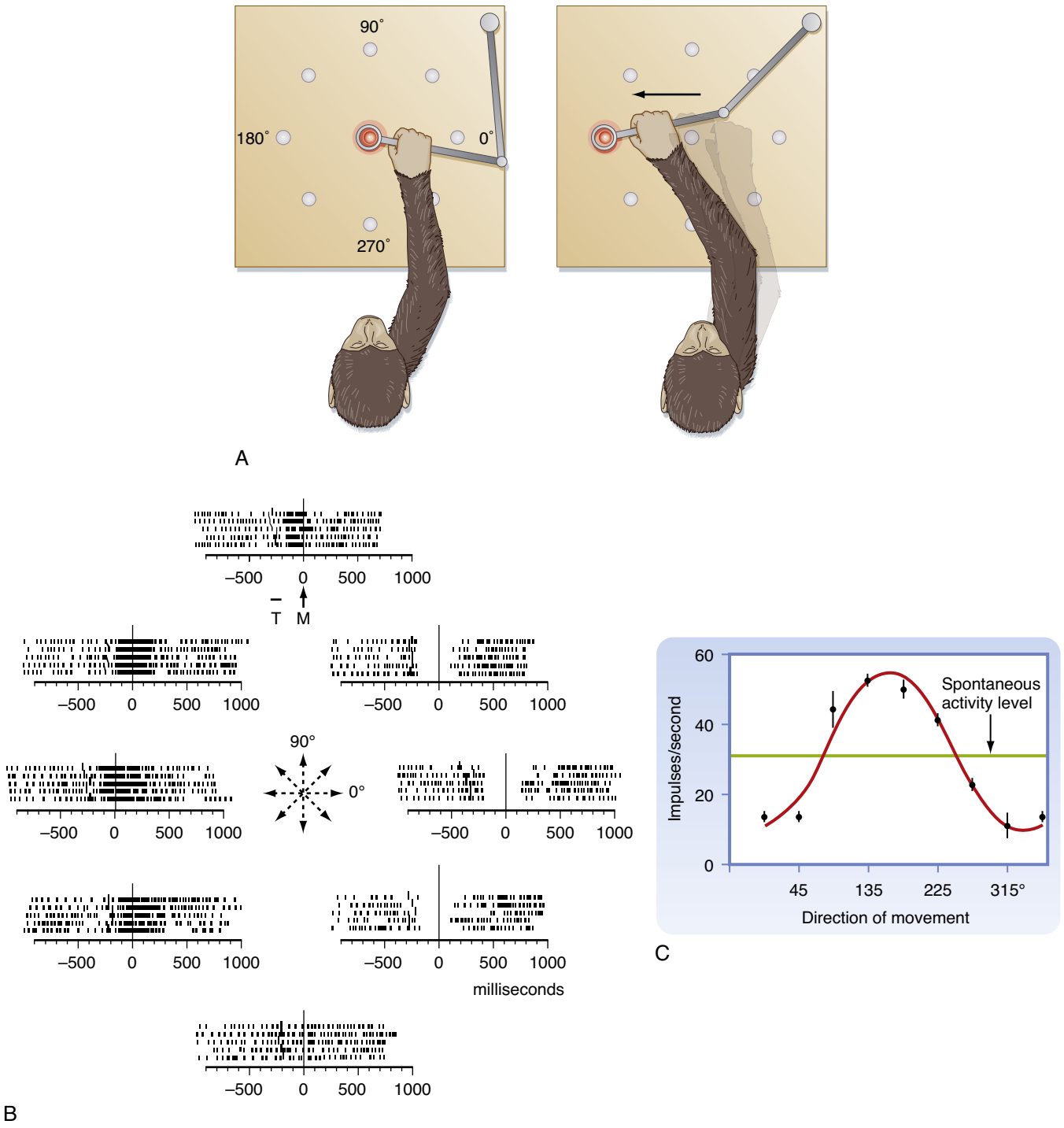
• **Fig. 9.17 A,** Experimental arrangement for recording from a corticospinal neuron while a monkey performs trained wrist movements. A stimulation electrode is used to elicit antidromic spikes that are used to identify the motor cortex neuron specifically as a pyramidal tract neuron. Stimuli are not applied while the monkey is performing movements. **B,** The pyramidal tract neuron *(PTN)* discharges before the onset of movement or EMG activity when flexors need to generate force (no load and flexor load conditions). Moreover, the firing rate is correlated with the level of flexor force that is needed. In the extensor load condition, flexors do not need to contract to generate movement, and thus there is no activity in this PTN. The *top trace* shows wrist movement, which is identical for all three experimental conditions. Thus this cell's activity involves encoding force magnitude and direction, but not displacement. (Figure based on work of Evarts and colleagues. Comment to editors: This figure is based on the seminal work of EV Evarts; specifically, EV Evarts, *Relation of Pyramidal Tract Activity to Force Exerted During Voluntary Movement,* J Neurophysiol, 1968, 31 (1):14-27. A similar figure to this one appears in the textbook, Principles of Neural Science, 5th edition, Kandel et al, Figure 37-12.)

quantitative than qualitative. For example, the percentage of neurons in the premotor and supplementary motor areas that show activity related to earlier motor planning stages is higher than that of such neurons in the primary motor cortex. In addition, the premotor and supplementary motor areas can be distinguished from each other by the apparently greater involvement of the premotor area in movements made to external cues (such as in the task shown in Fig. 9.18) and the greater involvement of the supplementary motor area in movements made in response to internal cues (i.e., self-initiated). Research has also revealed that each of these areas is functionally heterogeneous and can therefore be further subdivided; however, such details are beyond the scope of this discussion.

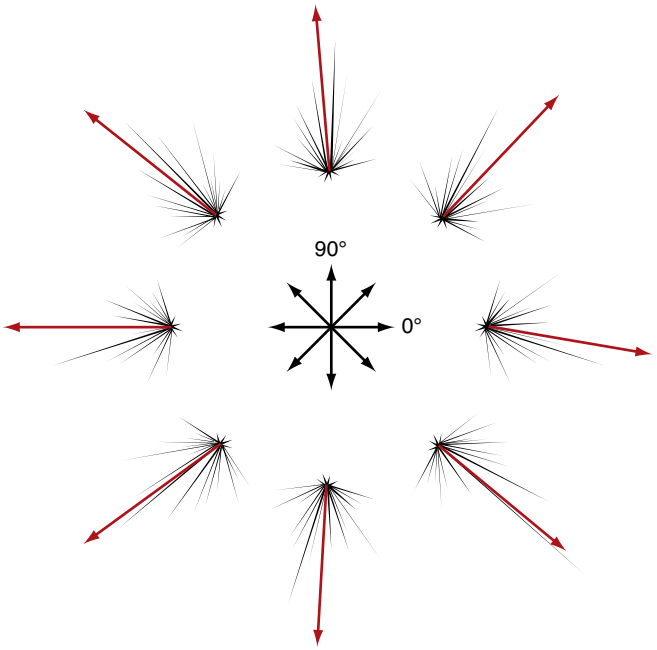
Motor Control by the Cerebellum

Overview of the Role of the Cerebellum in Motor Control

In the early 1900s scientists showed that damage to the cerebellum leads to deficits in motor coordination. That is, damage or loss of the cerebellum does not lead to paralysis, loss of sensation, or an inability to understand the nature of a task; rather, it leads to an inability to perform smooth, coordinated movements. Despite these early findings, it has been challenging defining the precise role(s) of the cerebellum in movement, although, paradoxically, we have relatively detailed knowledge of its deceptively simple anatomic



• **Fig. 9.18** **A,** Experimental setup in which a monkey holds onto the arm of the apparatus and captures light spots with the distal end of the arm. The monkey first captures the central light spot and then captures whichever of the surrounding targets that becomes illuminated. **B,** Raster plots showing the activity of one motor cortex cell during movement in eight different directions. *T* indicates the time at which the target light turns on, whereas *M* indicates the time at the onset of movement, which is at the center of each raster. Each mark on a raster represents a spike of a motor cortex cell, and each row of marks shows the cell's activity during one trial. **C,** Cosine function was fit to the firing level as a function of the direction of movement. The *horizontal bar* indicates the average spontaneous firing rate in the absence of an upcoming movement. Note that for most directions, the activity in the periods just before and during movement changed significantly from baseline.



D

• **Fig. 9.18 cont'd D,** Vector model of population activity in the motor cortex. *Black lines* represent individual cell vectors. When all of them are summed for a particular direction of movement, the resulting population vector *(red)* points in essentially the direction of the upcoming movement. (**B** and **C,** Modified from Georgopoulos AP, JF Kalaska, R Caminiti, JT Massey. *J Neurosci.* 1982;2:1527. **D,** Modified from Georgopoulos AP, JF Kalaska, R Caminiti, JT Massey. In: Massion J, Paillard J, Schultz W, Wiesendanger M, eds. *Experimental Brain Research Series,* vol. 7: *Neuronal Coding of Motor Performance.* Berlin: Springer-Verlag; 1983.)

and physiological. The cerebellum plays a critical role in the learning and execution of both voluntary and certain reflex movements. In this section, the behavioral effects of damaging the cerebellum are considered, followed by a description of its connectivity, both intrinsic and with the rest of the CNS, and then finally a discussion of its activity.

Behavioral Consequences of Cerebellar Damage

Damage to one side of the cerebellum impairs motor function on the ipsilateral side of the body. This reflects a double crossing of most cerebellum-related output before motor commands reach motor neurons in the spinal cord. The first crossing occurs in the cerebellar efferent pathway projecting to the contralateral thalamus, and from the thalamus to the ipsilateral motor cortex. The second crossing takes place in the descending motor pathway from the motor cortex, since ~85% of its axons cross in the lower medulla as part of the pyramidal decussation. In summary, the cerebellum projects to the contralateral motor cortex, via the thalamus, and the corticospinal pathway re-crosses the midline in the lower medulla.

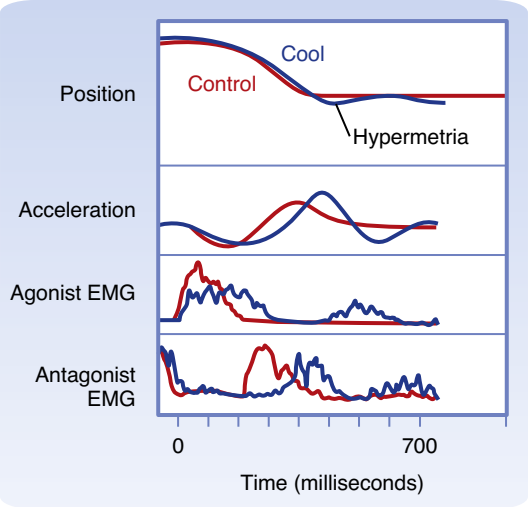
The specific motor deficits that result from cerebellar lesions depend on which functional component of the cerebellum is most affected. If the flocculonodular lobe is damaged, the motor disorders resemble those produced by a lesion of the vestibular apparatus; such disorders include difficulty in balance and in gait and often nystagmus. If the vermis is affected, the motor disturbance affects the trunk, and if the intermediate region or hemisphere is involved, motor disorders occur in the limbs. The part of the limbs affected depends on the site of damage; hemispheric lesions affect the distal muscles more than paravermal lesions do.

Types of motor dysfunction in cerebellar disease include disorders of coordination, equilibrium, and muscle tone. This lack of coordination is called **ataxia** and is often manifested as an awkward gait, or with **dysmetria,** a condition in which errors in the direction and force of movement prevent a limb from being moved smoothly to a desired position. Ataxia may also be manifested as **dysdiadochokinesia,** in which rapid alternating of supination and pronation of the hand is difficult to execute. When more complicated movement is attempted, **decomposition of movement** occurs, in which the movement is accomplished in a series of discrete steps rather than as a smooth sequence. An **intention tremor** appears when the subject is asked to touch a target; the affected hand (or foot) develops a tremor that increases in magnitude as the target is approached. When equilibrium is disturbed, impaired balance may be seen, and the individual tends to fall toward the affected side and may walk with a wide-based stance (gait ataxia). Speech may be slow and slurred; such a defect is called **scanning speech.** Muscle tone may be diminished **(hypotonia),** except for lesions of the anterior vermis (see earlier section on decerebrate rigidity); the diminished tone may be associated with a **pendular knee jerk.** This can be demonstrated by eliciting a phasic stretch reflex of the quadriceps muscle by striking the patellar tendon. The leg continues to swing back and forth because of the hypotonia, in contrast to the highly damped oscillation in a normal person.

These disorders reflect, in part, abnormal timing of muscle contractions. When assessed with EMG, normal limb movements involve precisely timed bursts of activity in both agonist and antagonist muscles. There is an initial agonist burst followed by a burst in the antagonist and, finally, a second agonist burst. With cerebellar damage, the relative timing of these bursts is abnormal (Fig. 9.19).

Cerebellar Organization

The cerebellum ("little brain") is located in the posterior fossa of the cranium, just below the occipital lobe, and is connected to the brainstem via three cerebellar peduncles (superior, middle, and inferior). From the outer surface, only the cortex is visible. Deep to the cortex is the white matter of the cerebellum, and buried within the white matter are the four deep cerebellar nuclei: proceeding medially to laterally, the fastigial, globose, emboliform, and dentate nuclei. The middle two nuclei are often grouped together and referred to as the *interpositus nucleus.* For the most part, cerebellar afferent fibers to the cortex and nuclei enter the



• **Fig. 9.19** Disruption of cerebellar activity alters the timing of EMG responses during movement. The cerebellar nuclei were cooled to block their functioning temporarily while monkeys performed movements about their elbow. Loss of cerebellar activity disrupts the relative timing of agonist and antagonist EMG bursts. This leads to abnormal acceleration of the limb and a movement trajectory that overshoots the target position (hypermetria). (Data from Flament D, Hore J. *J Neurophysiol* 1986;55:1221.)

cerebellum via the inferior and middle peduncles, and efferent fibers from the cerebellar nuclei leave via the superior peduncle.

The cerebellar cortex is subdivided into three rostrocaudally arranged lobes: the **anterior lobe,** the **posterior lobe,** and the **flocculonodular lobe** (Fig. 9.20*A*). The cerebellar lobes are separated by two major fissures, the **primary fissure** and the **posterolateral fissure,** and each lobe is made up of one or more **lobules.** Each lobule of the cerebellar cortex is composed of a series of transverse folds called **folia.**

The cerebellar cortex has also been divided into longitudinal compartments (see Fig. 9.20*B*, *C*). Initially, the cerebellar cortex was divided into three such compartments: the vermis, which lies on the midline; the paravermis, which lies adjacent to both sides of the vermis; and the lateral hemispheres. These regions have now been subdivided into many further compartments on the basis of **myeloarchitectonics** (patterns of axonal bundles in the white matter) and the expression patterns of specific molecules, such as aldolase C. Although the functional significance of these compartments is not fully known, the topography of cerebellar afferent fibers, particularly the olivocerebellar system, is precisely aligned with them, and the receptive field properties of cerebellar Purkinje neurons also tend to follow this organizational scheme.

Cerebellar Cortex

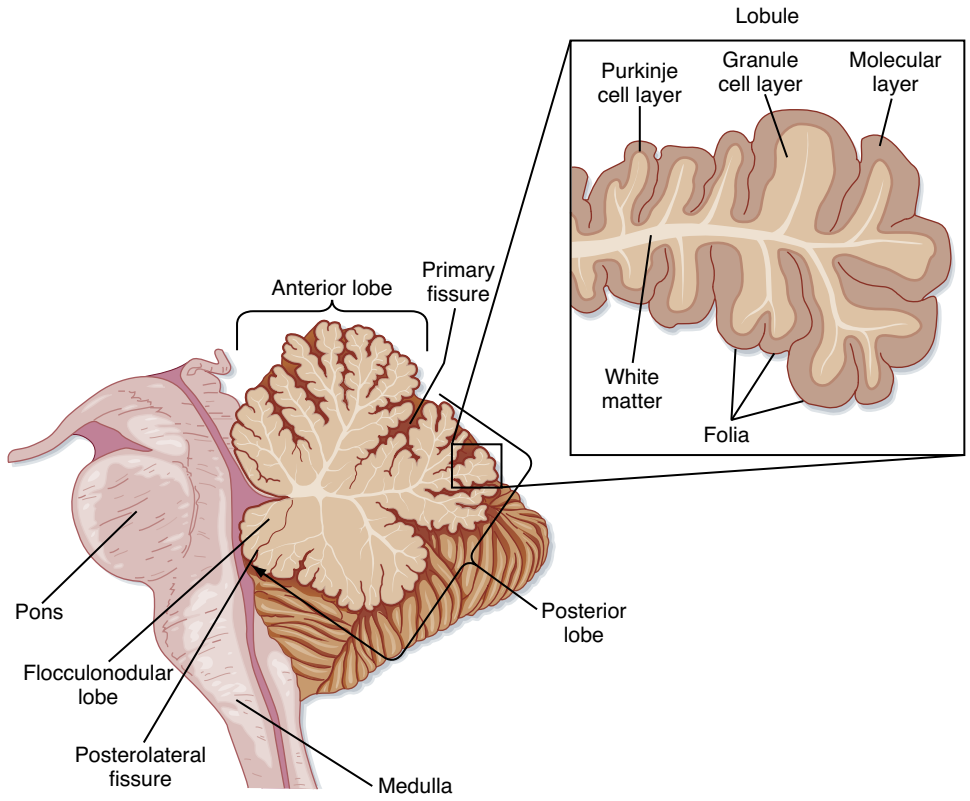
Afferent Systems

There are two major classes of cerebellar afferent systems: mossy fibers and **olivocerebellar fibers. Mossy fibers** are named for their distinctive appearance in the cerebellar cortex: as a mossy fiber courses through the granule layer, on occasion it swells and sends out a bunch of short twisted branchlets. These entities are called *rosettes* and are points of synaptic contact between these fibers and neurons in the granule cell layer. Mossy fibers arise from many sources, including the spinal cord (the spinocerebellar pathways), dorsal column nuclei, trigeminal nucleus, nuclei in the reticular formation, primary vestibular afferent fibers, vestibular nuclei, cerebellar nuclei, and the basilar pontine nuclei. The details of specific mossy fiber projection patterns are beyond the scope of this chapter; however, several general points are worth noting:

1. Mossy fibers are excitatory.
2. They convey exteroceptive and proprioceptive information from the body and head and form at least two somatotopic maps of the body across the cerebellar cortex. However, like those of the motor cortex, these maps are fractured in the sense that contiguous body regions are not necessarily represented on contiguous areas of the cerebellar cortex; rather, the maps are complicated mosaics.
3. Mossy fibers conveying vestibular information are restricted to the flocculonodular lobe and regions of the vermis. As a result, the flocculonodular lobe and regions of the vermis are sometimes referred to as the *vestibulocerebellum.* However, these same regions also receive a variety of other information (e.g., visual, neck, oculomotor), and so their function is not exclusively vestibular.
4. The largest sources of mossy fibers are the basilar pontine nuclei, which serve to relay information from areas throughout much of the cerebral cortex.
5. Mossy fibers enter the cerebellum via all three cerebellar peduncles and provide collateral fibers to the cerebellar nuclei before heading up to the cortex. In sum, via the mossy fiber system, the cerebellum receives a wide variety of sensory information, as well as descending motor-related and cognitive-related activity.

In contrast to the diverse origins of mossy fibers, olivocerebellar fibers all originate from a single nucleus, the inferior olivary nucleus, located in the rostral medulla, just dorsal and lateral to the pyramids. Almost all the olivary neurons are projection neurons whose axons leave the nucleus without giving off collaterals and then cross the brainstem to enter the cerebellum primarily via the inferior cerebellar peduncle. Like mossy fibers, olivocerebellar axons are excitatory and send collaterals to the cerebellar nuclei as they ascend through the cerebellar white matter to the cortex. In the cerebellar cortex, olivocerebellar axons may synapse with basket, stellate, and Golgi cells, but they form a special synaptic arrangement with Purkinje neurons. Each Purkinje neuron receives input from only a single climbing fiber, which "climbs" up its proximal dendrites and makes hundreds of excitatory synapses. (The terminal portion of the olivocerebellar axon is referred to as a climbing fiber.) Conversely, each olivary axon branches to form about 10 to 15 climbing fibers.

The inferior olivary nucleus is a distinctive brain region for several reasons. As already noted, its neurons are virtually all projection cells, and so there is little local chemical



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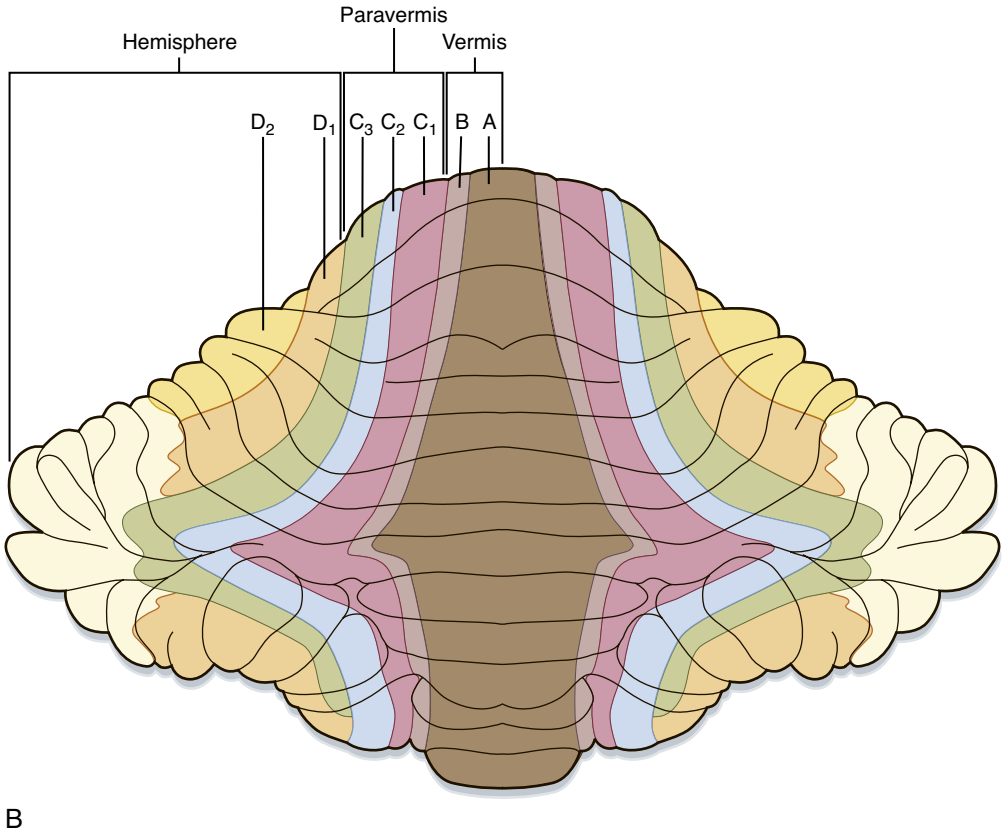
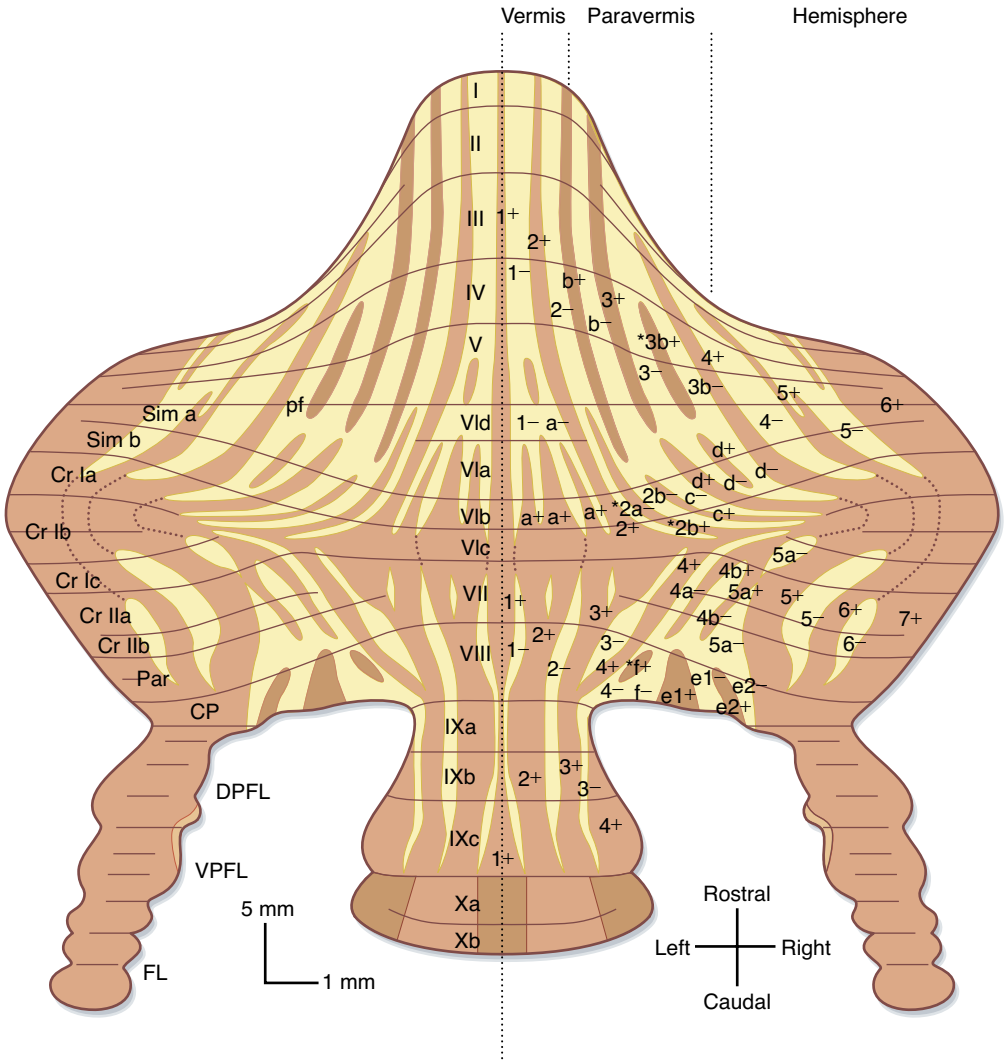


B

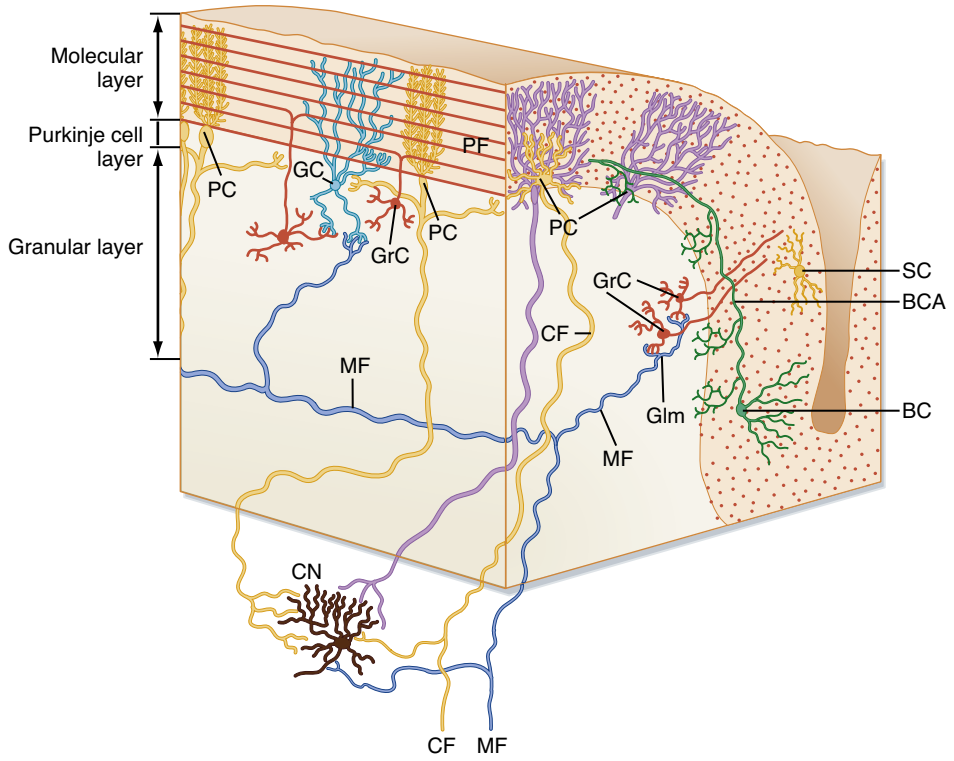
• **Fig. 9.20** Anatomic divisions of the cerebellum. **A,** Schematic midsagittal view of the folding of the cortex into lobe, lobules, and folia. **B,** Schematic view of an unfolded ferret cerebellar cortex to illustrate earlier compartmentation schemes for subdividing the cerebellar cortex into three (vermis, paravermis, and hemisphere) and then seven longitudinally running zones *(A, B, C_1, C_2, C_3, D_1, D_2)*. The *light yellow* portion of each hemisphere indicates an area for which no data were available.



C

• **Fig. 9.20 cont'd** **C,** Schematic view of an unfolded rat cerebellum, showing its subdivision into more than 20 compartments, according to staining for molecular markers: in this case, zebrin II (aldolase C). *Letters and numbers on the right half* of the cerebellum indicate the zebrin compartment number. *Roman numerals down the center* indicate cerebellar lobules. *Names on left hemisphere* indicate names of cerebellar lobules. *CP*, Copula pyramis; *Cr*, crus; *DPFL*, dorsal paraflocculus; *FL*, flocculus; *Par*, paramedian; *pf*, primary fissure; *Sim*, simplex; *VPFL*, ventral paraflocculus. (**B,** Modified from Voogd J. In: Llinás RR, ed. *Neurobiology of Cerebellar Evolution and Development.* Chicago: American Medical Association; 1969. **C,** Courtesy of Dr. Izumi Sugihara.)

synaptic interaction between the cells. Instead, olivary neurons are electrically coupled to each other by gap junctions. In fact, the inferior olivary nucleus has the highest density of neuronal gap junctions in the CNS. This allows olivary neurons to have synchronized activity that is transmitted to the cerebellum. Afferent fibers to the inferior olivary nucleus may be divided into two main classes: those transmitting excitatory input, which arises from many regions throughout the CNS; and those transmitting inhibitory GABAergic input from the cerebellar nuclei and a few brainstem nuclei. Although these afferent fibers can modulate the firing rates of olivary neurons (as is typical in most brain regions), the membrane properties of olivary neurons limit this modulation to a range of a few hertz and endow these neurons with the potential to be intrinsic oscillators. Instead of just modulating firing rates, olivary afferent activity also acts to modify the effectiveness of the electrical coupling between olivary neurons and thus changes the patterns of synchronous activity delivered to the cerebellum. Afferent activity may also modulate expression of the oscillatory potential of olivary neurons. Thus, the inferior olivary nucleus appears to be organized to generate patterns of synchronous activity across the cerebellar cortex. The functional significance of these patterns remains controversial. One hypothesis is that they provide a gating signal for synchronizing motor commands to various muscle combinations.



• **Fig. 9.21** Three-dimensional view of the cerebellar cortex, showing some of the cerebellar neurons. The cut face at the *left* is along the long axis of the folium; the cut face at the *right* is at right angles to the long axis. *BC*, Basket cell; *BCA*, basket cell axon; *CF*, climbing (olivocerebellar) fiber; *CN*, cerebellar nuclear cell; *GC*, Golgi cell; *Glm*, glomerulus; *GrC*, granule cell; *MF*, mossy fiber; *PC*, Purkinje cell; *PF*, parallel fiber; *SC*, stellate cell.

Cellular Elements and Efferent Fibers of the Cerebellar Cortex

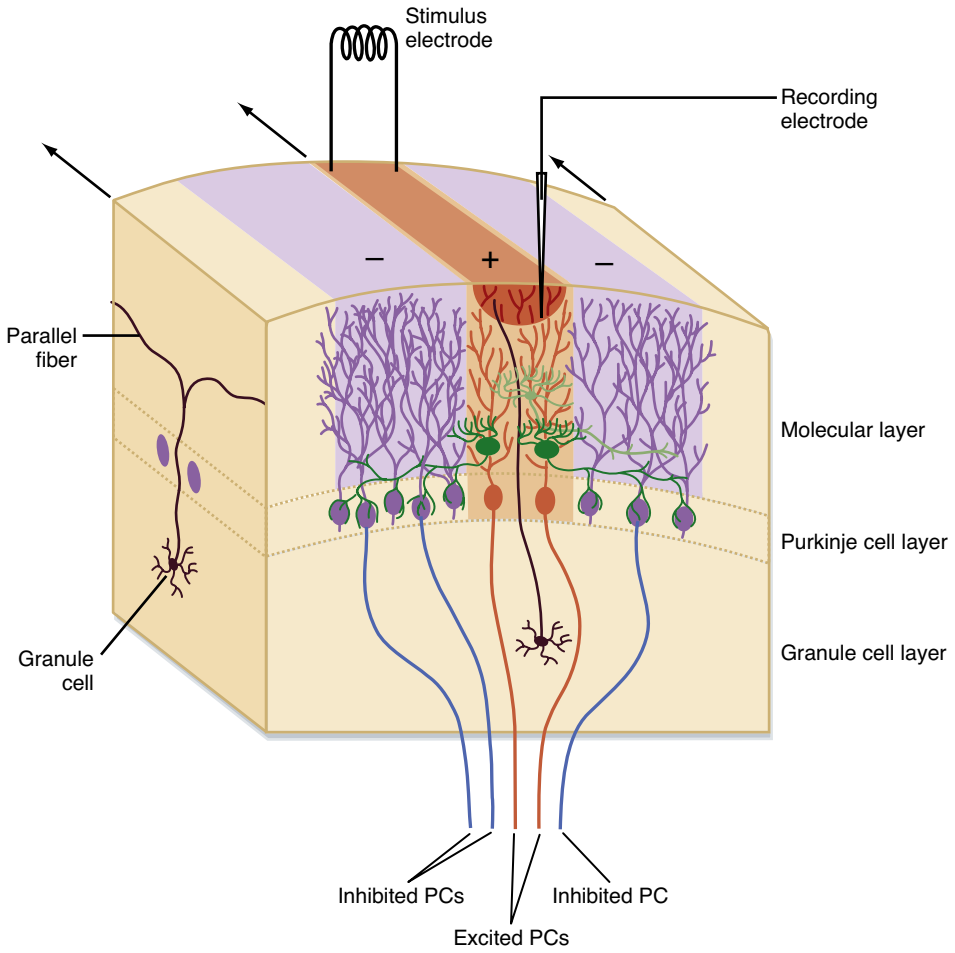
Despite its enormous expansion throughout vertebrate evolution, the basic anatomical organization of the cerebellar cortex has remained nearly invariant. The circuitry is also among the most regular and stereotyped of any brain region. The cerebellar cortex contains eight different neuronal types: Purkinje cells, Golgi cells, granule cells, Lugaro cells, basket cells, stellate cells, unipolar brush cells, and candelabrum cells. These neurons are found in all regions of the cerebellar cortex, with the exception of unipolar brush cells, which are limited mainly to cerebellar areas receiving vestibular input. These eight neuron types are distributed among the three layers that make up the cerebellar cortex of higher vertebrates (Fig. 9.21). The outer or superficial layer is the **molecular layer; stellate** and **basket cells** are found there. The deepest layer is the **granule cell layer;** this layer has the highest cellular density in the CNS and contains granule, **Golgi,** and **unipolar brush cells.** Separating the molecular and granule cell layers is the **Purkinje cell layer,** formed by Purkinje neuron somata, which are arranged as a one-cell-thick sheet of cells. **Candelabrum cells** are also located in this layer. **Lugaro cells** are situated slightly deeper at the upper border of the granule cell layer.

The sole efferent projection from the cerebellar cortex originates with Purkinje neurons, which are inhibitory because their presynaptic terminals release GABA. Purkinje neurons also have local projections. The remaining seven cell types are exclusively local interneurons. Of these, the stellate, basket, Golgi, Lugaro, and candelabrum cells are also GABAergic, inhibitory interneurons, whereas the granule and unipolar brush cells are glutamatergic, excitatory interneurons.

Microcircuitry of the Cerebellar Cortex

The dendrites, axons, and patterns of synaptic connections of most neurons within the cerebellar cortex are organized with regard to the transverse (short) and longitudinal (long) axes of the folium (Fig. 9.21). In the vermis, where the folia run perpendicular to the sagittal plane, these axes lie in the sagittal and coronal planes, respectively. In the hemispheres, where the folia are oriented at various angles with regard to the sagittal plane, this correspondence is lost, and the local axes of the folia must then serve as the reference axes.

The Purkinje neuron dendritic tree is the largest in the CNS. It extends from the Purkinje cell layer through the molecular layer to the surface of the cerebellar cortex and for several hundred microns along the transverse axis of the folium, and only for only 30 to 40 μm in the longitudinal direction giving it a flat appearance. It looks like a flat tree that lies in a plane parallel to the transverse axis of the folium. Accordingly, a set of Purkinje dendritic trees can be thought of as a stack of pancakes, with the stack running along the longitudinal axis of the folium.



• **Fig. 9.22** Functional connectivity of the cerebellar cortex. Because of the geometric organization of the cerebellar cortical circuits, the functional connectivity of the cellular elements can be determined electrophysiologically. The figure depicts a classic paradigm in which stimulation of the cerebellar cortex activates a beam of parallel fibers *(orange).* Recordings from the stellate and basket cells *(green cells)* and Purkinje cells (PCs; *orange cells*) in line with this beam show that they are excited by the parallel fibers. In contrast, Purkinje cells flanking the beam receive only inhibition *(purple areas)* as a result of the perpendicular spatial relationship of the parallel fibers and the stellate and basket cell axons.

The dendritic trees of the molecular layer interneurons (stellate and basket cells) are oriented in a manner similar to that of the Purkinje cell dendritic tree, although they are much less extensive. The axons of stellate and basket cells run transversely across the folium and form synapses with Purkinje neurons. Stellate and basket cells synapse onto Purkinje dendrites. In addition, basket cells make synapses on the Purkinje soma and form a basket-like structure around the base of the soma, which gives the basket cell its name.

Granule cells are small neurons with four to five short unbranched dendrites, each ending in a claw-like expansion that synapses with a mossy fiber rosette and with terminals from Golgi cell axons in a complex arrangement known as a *glomerulus.* The axons of granule cells ascend through the Purkinje cell layer to the molecular layer, where they bifurcate and form parallel fibers. The parallel fibers run parallel to the cerebellar surface along the longitudinal axis of the folium (perpendicular to the planes of the Purkinje, stellate, and basket cell dendritic trees) and form excitatory synapses with the dendrites of the Purkinje, Golgi, stellate, and basket cells.

The orthogonal relationship between the parallel fibers and the dendritic trees of the Purkinje cells and molecular layer interneurons (basket and stellate cells) has significant functional consequences. This arrangement allows maximal convergence and divergence to occur. A single parallel fiber, which can be up to 6 mm long, passes through more than 100 Purkinje cell dendritic trees (and also interneuron dendrites); however, it only makes one or two synapses with any particular cell because it crosses through the short dimension of the flat dendritic tree. Conversely, a given Purkinje dendrite receives synapses from on the order of 100,000 parallel fibers. Thus, a beam of parallel fibers can be excited experimentally, which excites a row of Purkinje cells and interneurons that are in line with this beam (Fig. 9.22). In addition, because the axons of the interneurons run perpendicular to the parallel fibers, this beam of excitation is flanked by inhibition. Although this classic electrophysiological

experiment clearly demonstrates the functional connectivity of the cerebellar cortex, whether such beams of excitation occur physiology has not been resolved.

The Golgi cells are inhibitory interneurons in the granule cell layer. The geometric organization of their axonal and dendritic arbors is an exception to the orthogonal and planar organization of the cortex in that their dendrites and axons carve out approximately conical territories: like two cones, tip to tip, in which the soma is at the point where the two cone tips meet. The dendritic tree forms the upper cone, which often extends into the molecular layer, and the axon forms the lower one. Golgi cells are excited by mossy and olivocerebellar fibers and by granule cell axons (parallel fibers) and inhibited by basket, stellate, and Purkinje cell axon collaterals. They in turn inhibit granule cells, so Golgi cells participate in both feedback (when excited by parallel fibers) and feedforward (when excited by mossy fibers) inhibitory loops that control activity in the mossy fiber–parallel fiber pathway to the Purkinje cell.

Lugaro cells have fusiform somata from which emerge two relatively unbranched dendrites, one from each side, that run along the transverse axis of the folium for several hundred microns, usually just under the Purkinje cell layer. Purkinje cell axon collaterals provide the main input to these neurons, and granule cell axons add minor input. The axon terminates mainly in the molecular layer on basket, stellate, and possibly Purkinje neurons. These neurons appear to sample the activity of Purkinje neurons and provide both positive-feedback signals (they inhibit the interneurons that inhibit Purkinje neurons) and negative-feedback signals (they directly inhibit the Purkinje neurons).

Unipolar brush cells have only a single dendrite that ends as a tight bunch of branchlets that resemble a brush. These cells receive excitatory input from mossy fibers and inhibitory input from Golgi cells. It is thought that they synapse with granule and Golgi cells, which would make these cells an excitatory feedforward link in the mossy fiber–parallel fiber pathway.

Candelabrum cells are GABAergic cells located in the Purkinje layer. Their dendrites and axons terminate in the molecular layer, where the axonal arborization pattern resembles a candelabrum.

Cerebellar Nuclei

The deep cerebellar nuclei are the main targets of the cerebellar cortex. This projection is topographically organized in such a way that each longitudinal strip of cortex targets a specific region of the cerebellar nuclei. The gross pattern is that the vermis projects to the fastigial and vestibular nuclei, the paravermal region projects to the interpositus, and the lateral hemisphere projects to the dentate nucleus.

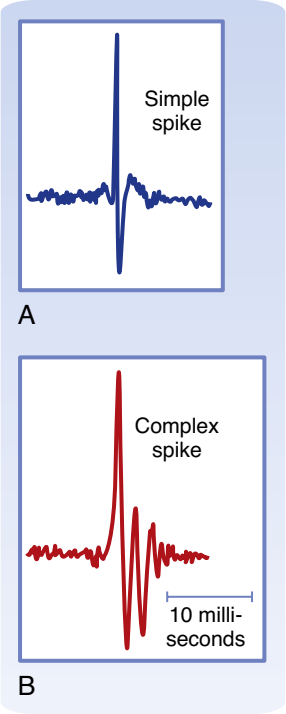
The deep cerebellar nuclear neurons in turn provide the output from the cerebellum to the rest of the brain (with the primary exception of Purkinje neurons that project directly to the vestibular nuclei). In discussing the output of the deep cerebellar nuclei, it is useful to group the nuclear cells according to whether they are GABAergic, because the GABAergic cells project back to the inferior olivary nucleus and form a negative-feedback loop to one of the cerebellum's principal afferent sources. Of importance is that GABAergic cells project to the specific part of the inferior olivary nucleus from which they receive input and from which their overlying longitudinal strip of cortex receives climbing fibers. Thus, the cerebellar cortex, cerebellar nuclei, and inferior olivary nucleus are functionally organized as a series of closed loops. The non-GABAergic, excitatory nuclear cells project to a variety of targets from the spinal cord to the thalamus. In general, each nucleus gives rise to crossed ascending and descending projections that leave the cerebellum via the superior cerebellar peduncle. The fastigial nucleus also gives rise to significant uncrossed fibers, as well as a second crossed projection called the *uncinate gyrus,* or *hook bundle,* that leaves via the inferior cerebellar peduncle.

Although there are differences in the specific targets of each nucleus, in general, the ascending cerebellar projections target midbrain structures, such as the red nucleus and superior colliculus, and the ventral lateral nucleus of the thalamus, which connects to the primary motor cortex and thereby links the cerebellum to motor areas of the cerebrum. (The cerebral motor areas are likewise linked to the cerebellum by multiple pathways, including ones that relay in the basilar pons and inferior olivary nucleus.) It should also be mentioned that ascending cerebellar projections, particularly from the dentate nucleus of the cerebellum, also target nonmotor regions of the cerebrum, particularly in the frontal lobe. The descending fibers target mainly the basilar pontine nuclei, inferior olivary nucleus, and several reticular nuclei. Lastly, a small cerebellospinal pathway arises principally from the fastigial nucleus. The fastigial nucleus has significant projections to the vestibular nuclei.

Activity of Purkinje Cells in the Cerebellar Cortex in the Context of Motor Coordination

Mossy fiber input to the cerebellar cortex, via their excitation of granule cells, causes a Purkinje neuron to discharge single action potentials, referred to as *simple spikes* (Fig. 9.23). The spontaneous simple spike firing rate of a Purkinje neuron typically is between 20 and 100 Hz, but can be modulated over a much wider range (from 0 to >200 Hz), depending on the relative balance of excitation from parallel fiber input and inhibition from cerebellar cortex interneurons. This activity reflects the state of the cerebellar cortex. Interestingly, evidence from studies performed in the early 2000s indicates that the spontaneous levels of simple spike activity vary systematically across the cerebellar cortex: firing rates in zebrin-negative regions average twice those of the zebrin-positive regions. The full significance of this discovery is not known, but it suggests that despite the anatomical uniformity of the cerebellar cortical circuits, they might be functionally quite distinct.

In contrast, a climbing fiber discharge causes a high-frequency burst of action potentials, called a *complex spike*



• **Fig. 9.23** Responses of a Purkinje cell to excitatory input, recorded extracellularly. **A,** Granule cells, via their ascending axons and parallel fibers, excite Purkinje cells and trigger simple spikes. **B,** Climbing fiber activity leads to high-frequency (≈500-Hz) bursts of spikes known as *complex spikes* in Purkinje cells. Note that the spikes following the initial one are smaller and referred to as spikelets.

(see Fig. 9.23), in an all-or-none manner because of the massive excitation that is provided by the single climbing fiber synapsing on a Purkinje neuron. This excitation is so powerful that there is essentially a one-to-one relationship between climbing fiber discharge and a complex spike, enabling complex spikes to override what is happening at the cortex level and reflect the state of the inferior olivary nucleus. The average firing rate of a spontaneous complex spike is only about 1 Hz.

Because the climbing fibers generate complex spikes at such a low frequency, they do not substantially change the average firing rates of Purkinje cells, and as a consequence, it is commonly argued that they have no direct role in shaping the output of the cerebellar cortex and are not involved in ongoing motor control. Instead, it is commonly thought that their function is to alter the responsiveness of Purkinje neurons to parallel fiber input. In particular, under certain circumstances, complex spike activity contributes to a prolonged depression in synaptic efficacy of parallel fibers, termed *long-term depression* **(LTD).** LTD at parallel fiber synapses is believed to be the biological basis for motor learning. According to the prevailing hypothesis, the parallel fiber system, and hence simple spikes, are involved in generating ongoing movement, and when there is a mismatch between the intended and actual movement, this error activates the complex spikes in the inferior olivary nucleus, whose projections converge on the same Purkinje neurons, leading to LTD of the active parallel fiber synapses. Changes in synaptic strength result in long-term changes in modulation of motor output. If this change results in a properly executed movement, activation of the inferior olivary nucleus does not occur, and the motor program is unchanged, but if there is still an error, the olivocerebellar system triggers additional complex spikes that cause further changes in synaptic efficacy, and so on. In essence, this interplay in cerebellar circuits provides the biological unpinning for "practice makes perfect."

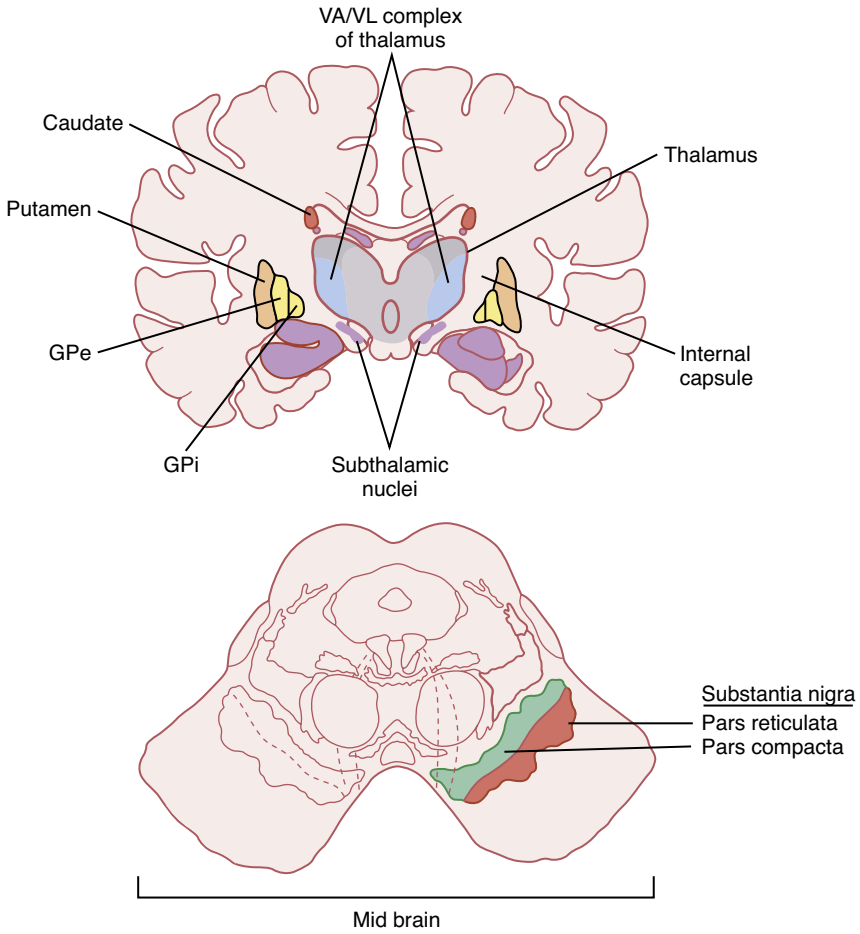
An alternative view is that the olivocerebellar system is directly involved in motor control (note that this does not preclude a role in motor learning, as well) and, in particular, helps in the timing of motor commands. This view follows from the types of motor deficits observed in cerebellar damage and accounts for the special properties of the inferior olivary nucleus mentioned earlier: namely, that it can generate rhythmic, synchronous complex spike discharges across populations of Purkinje cells. These complex spikes would then produce synchronized inhibitory postsynaptic currents (IPSPs) on cerebellar nuclear neurons as a result of the convergence present in the Purkinje axon projecting to the cerebellar deep nuclei. Because of the membrane properties of cerebellar nuclear neurons, these synchronized IPSPs could have a qualitatively different effect on deep nuclei cell firing than would the IPSPs caused by simple spikes, which are more numerous, but largely asynchronous. Specifically, they could trigger large, precisely timed changes in the nuclear cell activity that would then be transmitted to other motor systems as a gating signal. In fact, voluntary movements appear to be composed of a series of periodic accelerations that reflect a central oscillatory process. Determining whether this happens—olivocerebellar system control of the timing of motor commands—is still to be determined.

Motor Control by the Basal Ganglia

The basal ganglia are a collection of structures deep in the cerebrum. Like the cerebellum, a major function of the basal ganglia is to regulate motor activity, which we will focus on in this section. It is worth noting, first, that they, like the cerebellum, also contribute to affective and cognitive functions. To understand basal ganglia function in motor control, the following discussion is organized around two major themes: (1) the reciprocal connections between basal ganglia and the cerebral cortex, and (2) that there are two functionally distinct pathways through the basal ganglia: the *direct pathway* and *indirect pathway*.

Organization of the Basal Ganglia and Related Nuclei

The motor component of the basal ganglia is composed of a group of subcortical nuclei that includes **dorsal striatum** (the **caudate nucleus** and the **putamen**), the



• **Fig. 9.24** Components of basal ganglia and other closely associated brain regions. The main components of the basal ganglia are the caudate nucleus, putamen, globus pallidus, and substantia nigra pars reticulata. Major portions of the basal ganglia connect with motor areas in the frontal cortex, via the ventral anterior and ventral lateral thalamic nuclei, and with the superior colliculus. Input from the substantia nigra pars compacta is critical for normal basal ganglia function. *GPe*, External segment of globus pallidus; *GPi*, internal segment of globus pallidus.

globus pallidus, the **substantia nigra**, and the **subthalamic nucleus**. (Fig. 9.24). The term **striatum,** derived from the striated appearance of these nuclei, refers only striations produced by the fiber bundles formed by the anterior limb of the internal capsule as it separates the caudate nucleus and putamen. The globus pallidus typically has two parts: an **external segment** and an **internal segment.** The combination of putamen and globus pallidus is often referred to as the **lentiform nucleus.** The **subthalamic nucleus** is part of the diencephalon, and the **substantia nigra** is located in the midbrain (see Fig. 9.24). The substantia nigra ("black substance") derives its name from its content of melanin pigment. Many of the neurons in the **pars compacta** of this nucleus contain melanin, a by-product of dopamine synthesis. The other subdivision of the substantia nigra is the **pars reticulata.**

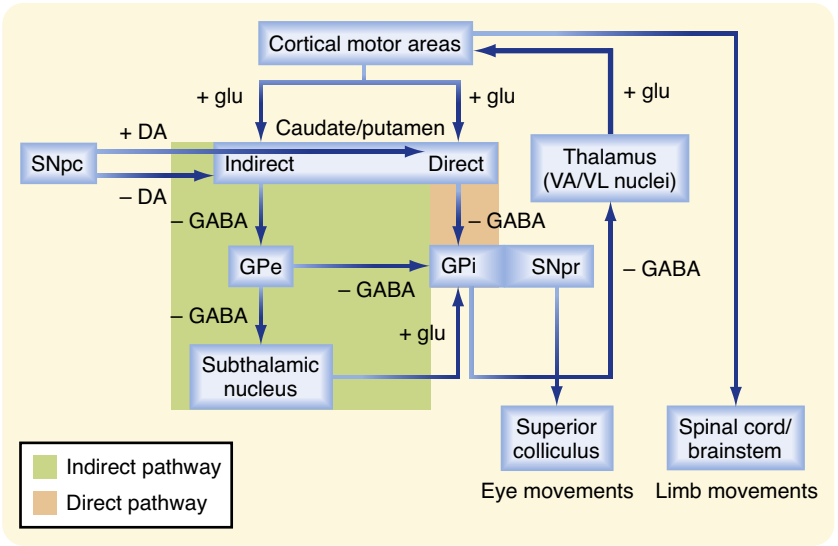
The basal ganglia primarily communicates with two thalamic nuclei, the **ventral anterior (VA)** and **ventral lateral (VL) nuclei,** and to a lesser degree with the **intralaminar nuclei** (or intralaminar complex) (see Fig. 9.24).

Connections and Operation of the Basal Ganglia

With the exception of the primary visual and auditory cortices, most regions of the cerebral cortex project topographically to the striatum. The corticostriatal projection arises predominantly from excitatory glutamatergic neurons in layer V of the cortex. The striatum then influences excitability of the VA and VL thalamic nucleic via the direct and indirect pathways (Fig. 9.25*A*). The thalamic neurons, in turn, excite neurons of the cerebral cortex, thereby forming closed loops with most of the cortex (i.e., cortex → basal ganglia → thalamus → cortex). Several distinct loops have been identified on the basis of cortical regions and function (motor and cognitive); the focus here will be on the motor-related loops as a model for basal ganglia operation (see Fig. 9.25*A*).

Direct Pathway

The overall action of the direct pathway through the basal ganglia to thalamus, and ultimately the motor areas of the



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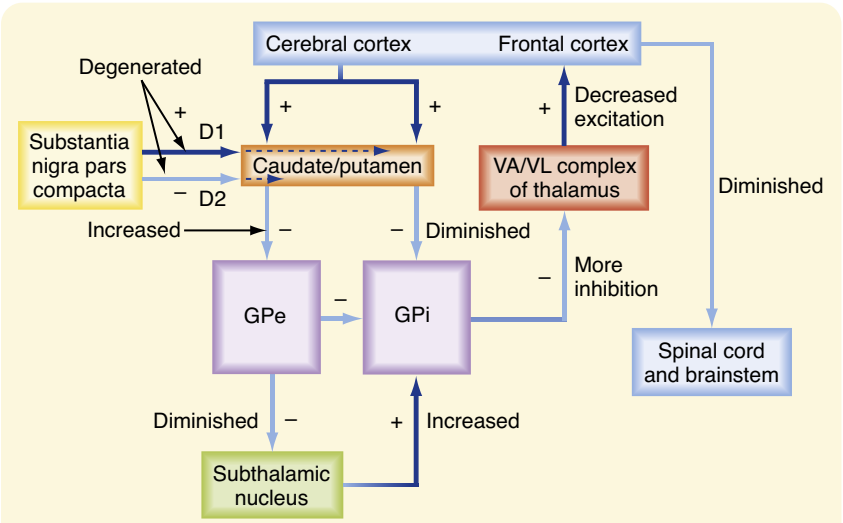
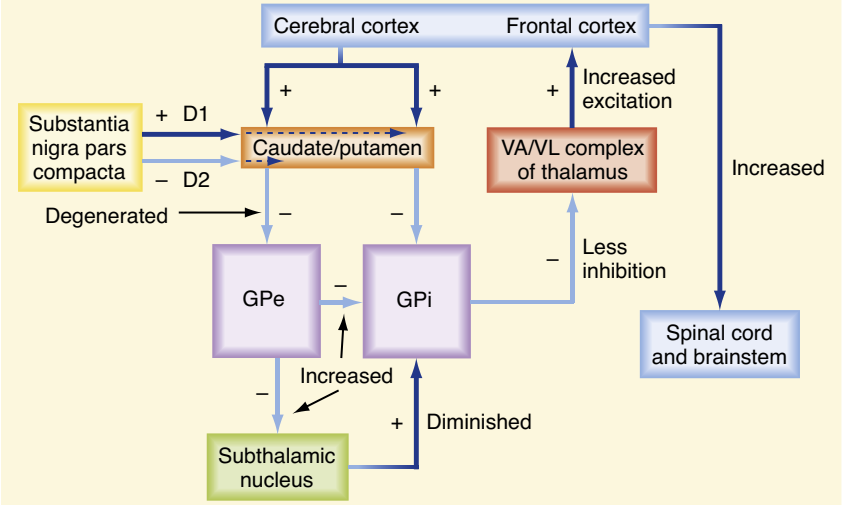


B Parkinson's disease (hypokinetic)



C Huntington's disease (hyperkinetic)

• **Fig. 9.25** Functional connectivity of the basal ganglia for motor control. **A,** Connections between various basal ganglia components and other associated motor areas. The excitatory cortical input to the caudate and putamen influences output from the GPi and the substantia nigra pars reticulata *(SNpr)* via a direct and an indirect pathway. The two inhibitory steps in the indirect pathway mean that activity through this pathway has an effect on basal ganglia output to the thalamus and superior colliculus opposite to that of the direct pathway. Dopamine *(DA)* is a neuromodulator that acts on D_1 and D_2 receptors on striatal neurons that participate in the direct and indirect pathways, respectively. **B,** Changes in activity flow that occur in Parkinson's disease, in which the substantia nigra pars compacta *(SNpc)* degenerates. **C,** Changes in activity flow in Huntington disease, in which inhibitory control of the GPe is lost. *Plus symbols* (+) and *minus symbols* (–), respectively, indicate the excitatory or inhibitory nature of a synaptic connection. glu, Glutamate; *GPe*, external globus pallidus; *GPi*, internal globus pallidus; *VA/VL*, ventral anterior/ventral lateral nuclei of the thalamus.

cortex, is to enhance motor activity. In the direct pathway, the striatum projects to the internal segment of the globus pallidus (GPi). This projection is inhibitory, and the main transmitter is GABA. The GPi projects to the VA and VL nuclei of the thalamus. These connections also function with GABA and are inhibitory. The VA and VL nuclei send excitatory connections to the prefrontal, premotor, and supplementary motor cortex. This input to the cortex influences motor planning, and also affects the discharge of corticospinal and corticobulbar neurons.

The direct pathway appears to function as follows: neurons in the striatum have little background activity, but during movement they are activated by input from the cortex. In contrast, neurons in the GPi have a high level of background activity. When the striatum is activated, its inhibitory projections to the GP decrease the activity of GPi neurons. The GPi neurons are inhibitory and they normally provide tonic inhibition of neurons in the VA and VL nuclei of the thalamus. Therefore, activation of the striatum inhibits GPi leading to **disinhibition** of neurons of the VA and VL nuclei. When disinhibited, the VA/VL neurons increase their firing rates, exciting their target neurons in the motor areas of the cerebral cortex. Because the motor areas evoke movement by activating α and γ motor neurons in the spinal cord and brainstem, the basal ganglia can regulate movement by enhancing the activity of neurons in the motor cortex.

Indirect Pathway

The overall effect of the indirect pathway is to reduce the activity of neurons in motor areas of the cerebral cortex. The indirect pathway involves inhibitory connections from the striatum to the external segment of the globus pallidus (GPe), which in turn sends an inhibitory projection to the subthalamic nucleus, which sends an excitatory projection to GPi (see Fig. 9.25*A*).

In this pathway, GPe neurons are inhibited by the inhibitory, GABAergic projection of the striatum. The GPe also is GABAergic, so its projection to the subthalamic nucleus is inhibitory. Therefore, striatal inhibition of the GPe results in the disinhibition of neurons of the subthalamic nucleus, which then excite neurons in the GPi by releasing glutamate. As a consequence of increased excitation of GPi, there is greater inhibition of VA and VL thalamic nuclei via the GPi GABAergic projection. The activity of the thalamic neurons consequently decreases, as does the activity of the cortical neurons that they influence.

The direct and indirect pathways, thus, have opposing actions; an increase in the activity of either one of these pathways might lead to an imbalance in motor control. Such imbalances, which are typical of basal ganglion diseases, may alter the motor output of the cortex.

Actions of Neurons in the Pars Compacta of the Substantia Nigra on the Striatum

Dopamine is the neurotransmitter produced by neurons of the substantia nigra pars compacta. In the nigrostriatal pathway, release of dopamine has an overall excitatory action on the direct pathway and an inhibitory action on the indirect pathway. This is, however, a modulatory effect; dopamine is causing its action not by triggering spikes directly, but rather by altering the striatal cells' response to other transmitters. The different actions on the direct and indirect pathways result from the expression of different types of dopamine receptors (D_1 and D_2) by the medium spiny projection cells of the striatum that contribute to the direct and indirect pathways. D_1 receptors are found on striatal cells in the direct pathway, whereas D_2 receptors are found on striatal cells that participate in the indirect pathway. The overall consequence of dopamine release in both cases is facilitation of activity in VA and VL, and ultimately increased activation of the motor areas of the cerebral cortex.

Subdivision of the Striatum Into Striosomes and Matrix

On the basis of the associated neurotransmitters, the striatum has been subdivided into zones called **striosomes** (also called patches) and **matrix.** The cortical projections related to motor control end in the matrix area. The limbic system projects to the striosomes. Striosomes are thought to synapse in the pars compacta of the substantia nigra and to influence the dopaminergic nigrostriatal pathway.

Role of the Basal Ganglia in Motor Control

The basal ganglia influence the cortical motor areas. Therefore, the basal ganglia have an important influence on the lateral corticospinal system of motor pathways. Such an influence is consistent with some of the movement disorders observed in diseases of the basal ganglia. The basal ganglia also regulate the medial motor pathways, because diseases of the basal ganglia can also affect the posture and tone of proximal muscles.

The deficits seen in the various basal ganglia diseases include abnormal movement **(dyskinesia),** increased muscle tone **(cogwheel rigidity),** and slowness in initiating movement **(bradykinesia).** Abnormal movement includes tremor, **athetosis, chorea, ballism,** and **dystonia.** The **tremor** of basal ganglion disease is a 3-Hz "pill-rolling" tremor that occurs when the limb is at rest. Athetosis consists of slow, writhing movement of the distal parts of the limbs, whereas chorea is characterized by rapid, flicking movement of the extremities and facial muscles. Ballism

is associated with flailing movement of the limbs (ballistic movement). Finally, dystonic movements are slow involuntary movements that may cause distorted body postures.

Parkinson disease is a disorder characterized by tremor, rigidity, and bradykinesia. This disease is caused by degeneration of neurons in the pars compacta of the substantia nigra, and consequently, the loss of dopamine in the striatum. Neurons of the locus coeruleus and the raphe nuclei, as well as other monoaminergic nuclei, are also lost. The loss of dopamine diminishes the activity of the direct pathway and increases the activity of the indirect pathway (see Fig. 9.25*B*). The net effect is an increase in the activity of GPi neurons and greater inhibition of neurons in the VA and VL nuclei. Decreased VA and VL excitation results in less activation of motor cortex areas, and difficulty initiating movement and slowed movement (bradykinesia).

Before the dopaminergic neurons are completely lost, administration of levodopa can relieve some of the motor deficits in Parkinson disease. Levodopa is a precursor of dopamine, and it can cross the blood-brain barrier. Additional therapies have been developed to mitigate some of the devastating symptoms of Parkinson disease by decreasing basal ganglia inhibition of VA and VL. For example, an electrode implanted in GPi or the subthalamic nucleus can be used to inhibit those sites and thereby reduce inhibition of VA and VL. Although it is known as Deep Brain Stimulation (DBS), which might imply activation, DBS typically suppresses activity in the local area of the electrode placement.

Another basal ganglia disturbance is Huntington disease, which results from a genetic defect that involves an autosomal dominant gene. This defect first leads to the preferential loss of striatal median spiny GABAergic neurons of the indirect pathway that project to GPe and cholinergic neurons, and subsequently, median spiny neurons of the direct pathway (long-term, there is also degeneration of the cerebral cortex, with resultant dementia). Loss of inhibition of the GPe leads to diminished activity of neurons in the subthalamic nucleus and consequent (see Fig. 9.25*C*) reduced activation of GPi. This leads to disinhibition of the VA and VL nuclei and greater activation of the motor cortex. The resulting enhancement of activity in neurons in the motor areas of the cerebral cortex leads to the choreiform movements associated with Huntington disease. The rigidity in Parkinson disease may in a sense be the opposite of chorea because overtreatment of patients with Parkinson disease with levodopa can result in chorea.

Hemiballism is typically caused by damage to the subthalamic nucleus on one side of the brain. In this disorder, involuntary, violent flailing movements of the limbs may occur on the side of the body contralateral to the lesion. Because the subthalamic nucleus excites neurons of the GPi, a lesion of the subthalamic nucleus reduces activity of these GPi neurons, and as a consequence there is less inhibition of VA and VL nuclei of the thalamus, and greater activity of neurons in the motor cortex and uncontrolled movement.

In all these basal ganglia disorders, motor dysfunction is contralateral to the damaged component. This is understandable because the main final output of the basal ganglia to the body is mediated by the corticospinal tract, most of which crosses in the medulla.

Eye Movement

Eye movement has a number of features that distinguish it from other motor behavior. In comparison with the movement that limbs, with their multiple joints and muscles, can perform, eye movement is relatively simple, but very fast. For example, each eye is controlled by only three agonist-antagonist muscle pairs: the medial and lateral recti, the superior and inferior recti, and the superior and inferior oblique muscles. These muscles allow the eye to rotate about three axes. Assuming that the head is in an upright position, the axes are the vertical axis, a horizontal axis that runs left to right, and the torsional axis (which is directed along the axis of sight). The medial and lateral recti control movement about the vertical axis; the other four muscles generate movement about the horizontal and torsional axes. Another simplifying feature is that there are no external loads for which to be compensated. Furthermore, eye movement appears to be separable into a few distinct types, with each type being controlled by its own specialized circuitry. Moreover, deficits in eye movement provide important clinical clues for noninvasive diagnosis of neurological problems. We first review the different eye movement types and then discuss the neural circuitry underlying their generation.

Types of Eye Movement

Vestibulo-ocular Reflex

Eye movement probably first evolved to hold the image of the external world still. In contrast, limb movements evolved to generate changes in the position of the limb with regard to the external world. The reason is that visual acuity degrades rapidly when there is eye movement in relation to the external world (i.e., the visual scene slips across the retina). A major cause of such slippage is movement of the head. The vestibulo-ocular reflex (VOR) is the primary mechanism by which head movement is compensated in order to maintain stability of the visual scene on the retina.

To maintain a stable visual scene on the retina, the VOR produces movements of the eyes that are equal and opposite to the movement of the head. This reflex is initiated by stimulation of the hair cells in the vestibular system (see Chapter 8). Recall that the vestibular organs are sensitive to head acceleration, not visual cues, and thus the VOR occurs in both the light and dark. Functionally, it is what is called an *open-loop system* in that it generates an output (eye movement) in response to a stimulus (head acceleration), but its immediate behavior is not regulated by feedback about the success or failure of its output. It is worth noting, however, that in the light at least, any failure by the VOR to match eye and head rotation results in what is called *retinal slip* (i.e., slip of the visual image across the retina), and this error signal can be fed back to the VOR circuits by other

neuronal pathways, and over time can lead to adjustments in the strength of the VOR to eliminate the error.

The head can move in six different ways, often referred to as *six degrees of freedom:* three translational and three rotational. To compensate for these different types of movement, there are both translational and angular VORs, as well as separate subsystems for handling movement about different directions (e.g., rotation about a vertical or a horizontal axis).

Optokinetic Reflex

The optokinetic reflex (OKR) is a second mechanism by which the CNS stabilizes the visual scene on the retina, and it often works in conjunction with the VOR. Whereas the VOR is activated only by head motion, the OKR is activated by movement of the visual scene, whether caused by motion of the scene itself or by head motion. Specifically, the sensory stimulus for this reflex is slip of the visual scene on the retina as detected by motion-sensitive retinal ganglion cells. An example of the former occurs when you are sitting in a train and a train on the adjacent track begins moving: Your eyes rotate to keep the image of the neighboring car stable. This often leads to a sensation that you are moving (this is not entirely surprising because OKR circuits feed into the same circuits as used by the vestibular system).

The OKR can work in conjunction with the VOR to stabilize the visual image and is particularly important for maintaining a stable image when head movements are slow because the VOR works poorly in these conditions.

Saccades

In animals whose eyes have a fovea, it becomes particularly advantageous to be able to move the eye in relation to the world (i.e., the main visual scene) so that objects of importance can be focused onto the area with the highest resolution, the fovea. Two classes of eye movement underlie this ability: saccadic and smooth pursuit. Very rapid discrete movements that bring a particular region of the visual world onto the fovea are called *saccades.* For example, to read this sentence, you are making a series of saccades to bring successive words onto your fovea to be read. However, even in animals that lack a fovea, the eyes make saccades, and thus saccades may also be used to rapidly scan the visual environment.

Saccades are extremely rapid eye movements. In humans, eye velocity during a saccade can reach 800 degrees/second, in comparison with movement velocity of less than 10 degrees/second generated in response to typical VOR and OKR stimuli (velocities of up to ≈120 degrees/second can be produced by OKR stimuli in humans; however, they are still much slower than the maximal saccade velocities). Saccades can be voluntary or reflexive. Moreover, although they are usually made in response to visual targets, they can also be made toward auditory or other sensory cues, in the dark, or toward memorized targets.

Interestingly, visual processing appears to be suppressed just before and during saccades, particularly in the magnocellular visual pathway that is concerned with visual motion. This phenomenon is known as *saccadic suppression* and may function to prevent sensations of sudden, rapid movement of the visual world that would result during a saccade in the absence of such suppression. The mechanisms underlying saccadic suppression are not fully known, but in areas of the cortex related to visual processing, the responsiveness of the cells to visual stimuli is reduced and altered during saccades.

Smooth Pursuit

Once a saccade has brought a moving object of interest onto the fovea, the smooth pursuit system allows one to keep it stable on the fovea, despite its continued motion. This ability appears to be limited to primates and allows prolonged continuous observation of a moving object. Note that in some respects, smooth pursuit might seem similar to the OKR; in fact, there may not be an absolute difference because as the target size grows, the distinction between target and background is lost; however, for small moving targets, smooth pursuit requires suppression of the OKR. You can see the effect of this suppression by moving your finger back and forth in front of this text while tracking it with your eyes. Your finger will be in focus, but the words on this page will be part of the background scene and will become illegible as they slip along your retina.

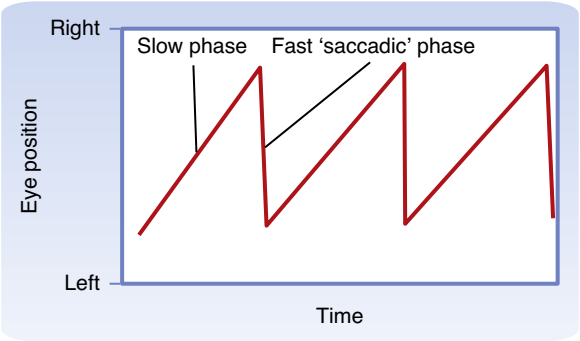
Nystagmus

When there is a prolonged OKR or VOR stimulus (e.g., if you keep turning in one direction), these reflexes will initially counterrotate the eyes in an attempt to maintain a stable image on the retina, as described earlier. However, with a prolonged stimulus, the eyes will reach their mechanical limit, no further compensation will be possible, and the image will begin to slip on the retina. To avoid this situation, a fast saccade-like movement of the eyes occurs in the opposite direction, essentially resetting the eyes to begin viewing the visual scene again. Then the slow OKR- or VOR-induced counterrotation will start anew. This alternation of slow and fast movement in opposite directions is nystagmus and can be recorded on a nystagmogram (Fig. 9.26). Thus, nystagmus can be defined as oscillatory or rhythmic movements of the eye in which there is a fast phase and a slow phase. The nystagmus is named according to the direction of the fast phase because the fast phase is more easily observed.

In addition to being induced physiologically by VOR or OKR stimuli, nystagmus can result from damage to the vestibular circuits, either in the periphery (e.g., cranial nerve VIII) or centrally (e.g., vestibular nuclei), and can be an informative diagnostic symptom.

Vergence

Conjugate eye movement is movement of both eyes in the same direction and in an equal amount. Such coordination allows a target to be maintained on both foveae during eye movement and is necessary to maintain binocular vision



• **Fig. 9.26** Nystagmogram showing eye movements that occur during nystagmus. The plot shows a left nystagmus because the fast phase is directed toward the left (downward on the graph).

without diplopia (double vision). However, when objects are close (<30 m), maintaining a target on both foveae requires nonidentical movements of the two eyes. Such disjunctive, or vergence, movements are also necessary for fixation of both eyes on objects that are approaching or receding. Stimuli that trigger vergence movements are diplopia and blurry images. It should be noted that when tracking an approaching object in addition to convergence movements, the lens accommodates for near vision, and pupillary constriction occurs.

Neural Circuitry and Activity Underlying Eye Movement

Motor Neurons of the Extraocular Muscles

Three cranial nerve nuclei supply the extraocular muscles: oculomotor, trochlear, and abducens nuclei. These three nuclei are sometimes referred to collectively as the *extraocular motor nuclei;* however, the context (the specific nucleus or all three) should be clear. Motor neurons for the ipsilateral medial and inferior recti, ipsilateral inferior oblique, and contralateral superior rectus muscles reside in the oculomotor nucleus; those for the contralateral superior oblique muscle reside in the trochlear nucleus; and those for the ipsilateral lateral rectus muscle are located in the abducens nucleus. These motor neurons form some of the smallest motor units (1:10 nerve-to-muscle ratio), which is consistent with the very fine control needed for precise eye movement.

An important point regarding motor neurons innervating the extraocular muscles is that most have spontaneous activity when the eye is in the primary position (looking straight ahead), and their firing rate is correlated with eye position and velocity. This spontaneous activity allows the antagonist muscle pairs to act in a push-pull manner, which increases the responsiveness of the system. That is, as motor neurons innervating one muscle are activated and cause increased contraction, those innervating its antagonist are inhibited, which leads to relaxation.

In addition to motor neurons, the abducens nuclei have internuclear neurons. These neurons project, via the medial longitudinal fasciculus (MLF), to medial rectus motor neurons in the contralateral oculomotor nucleus. As described later, this projection facilitates the coordinated action of the medial and lateral recti muscles that is needed for conjugate movements, such as those that occur in the VOR.

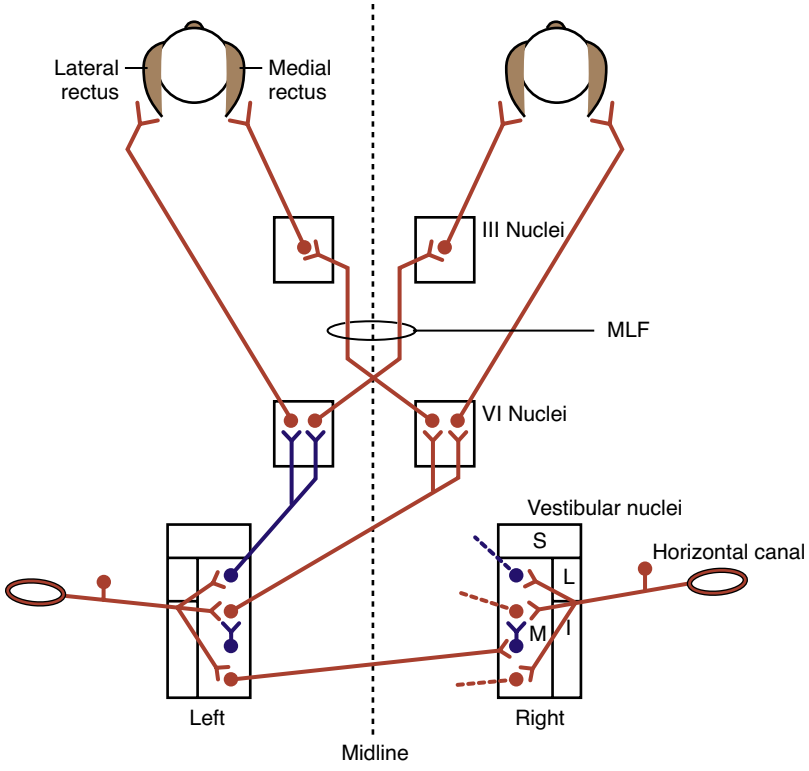
Circuits Underlying the Vestibulo-ocular Reflex

The VOR acts to counter head motion by causing rotation of the eyes in the opposite direction. There are separate circuits for rotational and translational movement of the head. The sensors for the former are hair cells in the semicircular canals and for the latter, hair cells in the otoliths (the utricle and saccule). The circuits for the angular VOR are more straightforward (but still complex), and this section focuses on these pathways to illustrate how this reflex works. Vestibular afferent fibers project to vestibular nuclei; the vestibular nuclei, in turn, project to various oculomotor nuclei; and motor neurons in the oculomotor nuclei give rise to axons that innervate the extraocular muscles.

With regard to the angular VOR pathways, the pathway for generating horizontal eye movement originates in the horizontal canals, and the analogous one for vertical movement originates in the anterior and posterior canals. Fig. 9.27*A* shows the basic circuit for the horizontal VOR. Note that only the major central circuits originating in the left horizontal canal and vestibular nuclei are shown; however, mirror image pathways arise from the right canal and vestibular nuclei. Vestibular afferent fibers involved in the horizontal VOR pathway synapse primarily in the medial vestibular nucleus, which projects to the abducens nucleus bilaterally; inhibitory neurons project ipsilaterally, and excitatory ones project contralaterally. Control of the medial rectus muscle is achieved by abducens internuclear neurons that project from the abducens to the part of the oculomotor nucleus controlling the medial rectus muscle. Note the double decussation of this pathway results in aligning of the responses of functional synergists (e.g., the left medial rectus with the right lateral rectus).

The vertical VOR pathway involves primarily the superior vestibular nucleus, which has direct bilateral projections to the oculomotor nucleus.

Consider what happens in the horizontal canal pathway when there is head rotation to the left, as shown in Fig. 9.27*B.* Leftward head rotation would cause the visual image to slip to the right. However, compensation by the VOR would be triggered by depolarization of the hair cells of the left canal in response to the angular acceleration (see Fig. 8.27). The depolarized hair cells cause increased activity in the left vestibular afferent fibers and thereby excite neurons of the left medial vestibular nucleus. These include excitatory vestibular neurons that project to the contralateral abducens nucleus and synapse with both motor neurons and internuclear neurons. Excitation of the motor neurons leads to contraction of the right lateral rectus muscle and rotation of the right eye to the right, whereas excitation of the internuclear neurons of the right abducens nucleus leads



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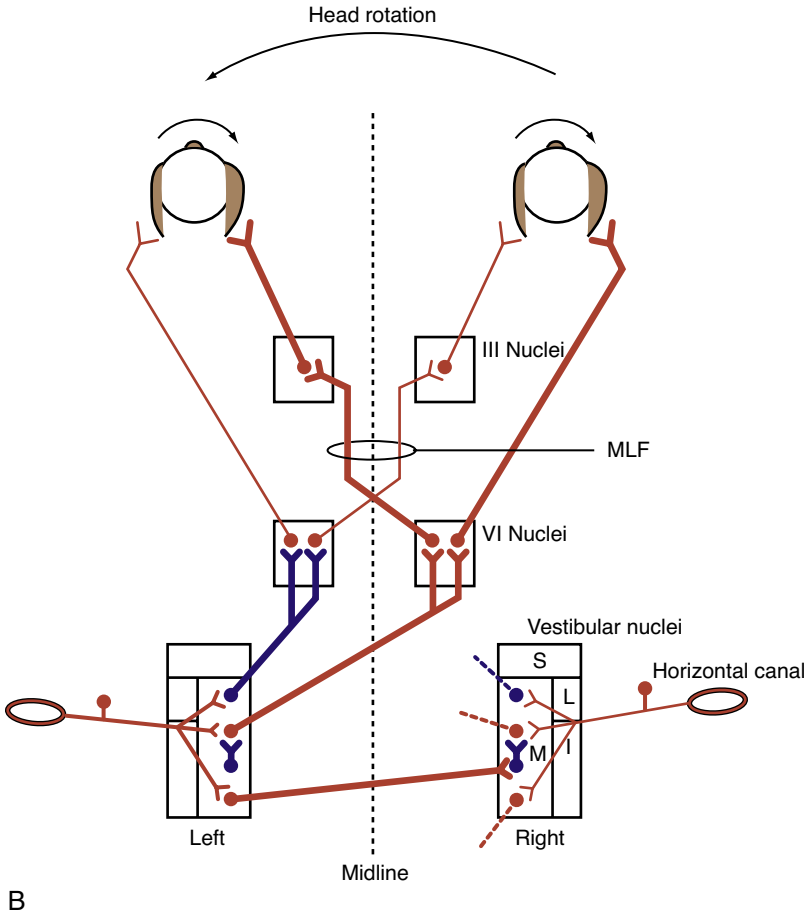


B

• **Fig. 9.27** Circuits underlying the horizontal vestibulo-ocular reflex (VOR). **A,** The vestibular nuclei receive excitatory input from the afferent fibers of the horizontal canal and project to the abducens (cranial nerve VI) nucleus. This nucleus innervates the lateral rectus muscle and projects to the contralateral oculomotor (cranial nerve III) nucleus, which controls the medial rectus muscle. Excitatory neurons are shown in *red;* inhibitory ones, in *blue.* Note that only the major pathways originating in the left vestibular nuclei are shown. For clarity, only the beginnings of mirror image pathways from the right vestibular nuclei are shown *(dotted lines).* **B,** Flow of activity in the VOR circuitry induced by leftward head rotation. Increased axonal thickness indicates increased activity; thinner axons indicate decreased activity in comparison with levels at rest **(A).** Note that leftward rotation causes both an increase in activity of the left vestibular afferent fibers and a decrease in activity of the right ones. *I*, inferior; *L*, lateral; *M*, medial; *MLF*, Medial longitudinal fasciculus; *S*, superior; *VI*, vestibular nuclei.

to excitation of the medial rectus motor neurons in the left oculomotor nucleus, thus causing the left eye to rotate to the right as well.

Along the pathway starting with the inhibitory vestibular neurons that project from the left medial vestibular nucleus to the ipsilateral abducens nucleus, the activity of these cells leads to inhibition of motor neurons to the left lateral rectus muscle and motor neurons to the right medial rectus muscle (the latter via internuclear neurons to the right oculomotor nucleus). Consequently, these muscles relax, thereby facilitating rotation of the eyes to the right. Thus, the eye is being pulled by the increased tension of one set of muscles and "pushed" by the release of tension in the antagonist set of muscles.

Note again that the mirror image pathways originating from the right canal have been left out of Fig. 9.27 for clarity, but the changes in activity through them with leftward head rotation would be exactly the opposite, and thus they would function synergistically with those that are shown. In summary, leftward head rotation hyperpolarizes the hair cells of the right canal, thereby leading to a decrease in right vestibular afferent activity and dis-facilitation of the right vestibular nuclear neurons.

Now, consider the commissural fibers that connect the two medial vestibular nuclei are excitatory, but end on local inhibitory interneurons of the contralateral vestibular nucleus to inhibit projection neurons of that nucleus. This pathway reinforces the actions of the contralateral vestibular afferent fibers on their target vestibular nuclear neurons. In this example, commissural cells in the left vestibular nucleus are activated and cause active inhibition of the right medial vestibular nuclei projection neurons, which reinforces the dis-facilitation caused by the decrease in right afferent activity. In fact, this commissural pathway is sufficiently powerful to modulate the activity of the contralateral vestibular nuclei even after unilateral labyrinthectomy, which destroys the direct vestibular afferent input to these nuclei.

Of importance is that superimposed on the brainstem circuits is the cerebellum. Parts of the vermis and flocculonodular lobe receive primary vestibular afferent fibers or secondary vestibular afferent fibers (axons of the vestibular nuclear neurons), or both, and in turn project back to the vestibular nuclei directly and via a disynaptic pathway involving the fastigial nucleus. The exact role of these cerebellar circuits in generating the VOR is much debated, but they are critical inasmuch as damage to them leads to abnormal eye movement, such as spontaneous nystagmus, and other symptoms of vestibular dysfunction.

Circuits Underlying the Optokinetic Reflex

The stimulus eliciting the OKR is visual (retinal slip), so photoreceptors are the start of the reflex arc. Key brainstem centers for this reflex lie in the tegmentum and pretectal region of the rostral midbrain. They are the nucleus of the optic tract (NOT) and a group of nuclei collectively known as the accessory optic nuclei (AON). Direction-selective, motion-sensitive retinal ganglion cells are a major afferent source carrying visual information to these nuclei. In addition, input comes from primary and higher order visual cortical areas in the occipital and temporal lobes. These latter afferent sources are particularly important in primates and humans. Cells of the NOT and AON have large receptive fields, and their responses are selective for the direction and speed of movement of the visual scene. Of interest is that the preferred directions of movement of the NOT/AON cells correspond closely to motion caused by rotation about axes perpendicular to the semicircular canals, thereby facilitating coordination of the VOR and OKR to produce stable retinal images.

The efferent connections of these nuclei are numerous and complex and not fully understood. There are polysynaptic pathways to the oculomotor and abducens nuclei and monosynaptic input to the vestibular nuclei, which allow interaction with the VOR. There are projections to various precerebellar nuclei, including the inferior olivary nucleus and basilar pontine nuclei. These pathways then loop through the flocculus and back to the vestibular nuclei. In sum, via several pathways operating in parallel, activity ultimately arrives at the various oculomotor nuclei whose motor neurons are activated, and proper counterrotation of the eyes results.

Circuits Underlying Saccades

Saccades are generated in response to activity in the superior colliculus or the cerebral cortex (frontal eye fields [FEF] and posterior parietal areas). Activity in the superior colliculus is related to computation of the direction and amplitude of the saccade. Indeed, the deep layers of the superior colliculus contain a topographic motor map of saccade locations. From the superior colliculus, information is forwarded to distinct sites for control of horizontal and vertical saccades, referred to as the *horizontal* and *vertical gaze centers,*

IN THE CLINIC

When a labyrinth is irritated in one ear, such that occurs with **Meniere's disease,** or when a labyrinth not functional, as may happen as a result of head trauma or disease of the labyrinth, the signals transmitted through the VOR pathways from the two sides become unbalanced. This, in turn, can lead to pathological nystagmus. For example, irritation of the labyrinth of the left ear can increase the discharge of afferent fibers that supply the left horizontal semicircular duct. The signal produced resembles that normally generated when the head is rotated to the left. Because the stimulus is ongoing, a left nystagmus results, with a slow phase to the right (caused by the VOR pathway) and a fast phase to the left. Destruction of the labyrinth in the right ear produces effects similar to those induced by irritation of the left labyrinth. Interestingly, the nystagmus is temporary, which shows the ability of these circuits to adapt over time.

IN THE CLINIC

Clinical testing of labyrinthine function is done either by rotating the patient in a Bárány chair to activate the labyrinths in both ears or by introducing cold or warm water into the external auditory canal of one ear **(caloric test).** When a person is rotated in a Bárány chair, nystagmus develops during the rotation. The direction of the fast phase of the nystagmus is in the same direction as the rotation. When the rotation of the chair is halted, nystagmus in the opposite direction develops (postrotatory nystagmus) because stopping a rotation has the same effect as accelerating in the opposite direction.

The caloric test is more useful because it can distinguish between malfunction of the labyrinths on the two sides. The neck is bent backward about 60 degrees so that the two horizontal canals are essentially vertical. If warm water is introduced into the left ear, the endolymph in the outer portion of the loop of the left semicircular canal tends to rise as the specific gravity of the endolymph decreases because of heating. This sets up a convection flow of endolymph, and as a result, the kinocilia of the left ampullary crest hair cells are deflected toward the utricle, as if the head had rotated to the left; the discharge of the afferent fibers that supply this canal increases; and nystagmus occurs with the fast phase toward the left. The nystagmus produces a sensation that the environment is spinning to the right, and the person tends to fall to the right. The opposite effects are produced if cold water is placed in the ear. A mnemonic expression that can help in remembering the direction of the nystagmus in the caloric test is *COWS* ("cold opposite, warm same"). In other words, cold water in one ear results in a fast phase of nystagmus toward the opposite side, and warm water causes a fast phase toward the same side.

respectively. The horizontal gaze center consists of neurons in the paramedian pontine reticular formation (PPFR), in the vicinity of the abducens nucleus (Fig. 9.28*A*). The vertical gaze center is located in the reticular formation of the midbrain: specifically, the rostral interstitial nucleus of the medial longitudinal fasciculus and the interstitial nucleus of Cajal. Because the circuitry and operation of the horizontal gaze center are better understood than those of the vertical gaze center, it is discussed here in detail. However, cells showing analogous activity patterns have been described in the vertical gaze center.

Fig. 9.28*A* is an overview of the neural circuitry by which saccades are generated, and Fig. 9.28*B* shows the activity of certain types of neurons found in the gaze center that are responsible for horizontal saccades. Each horizontal gaze center has excitatory burst neurons (EBN) that project to motor neurons in the ipsilateral abducens nucleus and to the internuclear neurons (which excites medial rectus motor neurons in the contralateral oculomotor nucleus). It also has inhibitory burst neurons (IBN) that inhibit the contralateral abducens. These burst neurons are capable of extremely high bursts of spikes (up to 1000 Hz). Moreover, the gaze center has neurons showing tonic activity and burst-tonic activity.

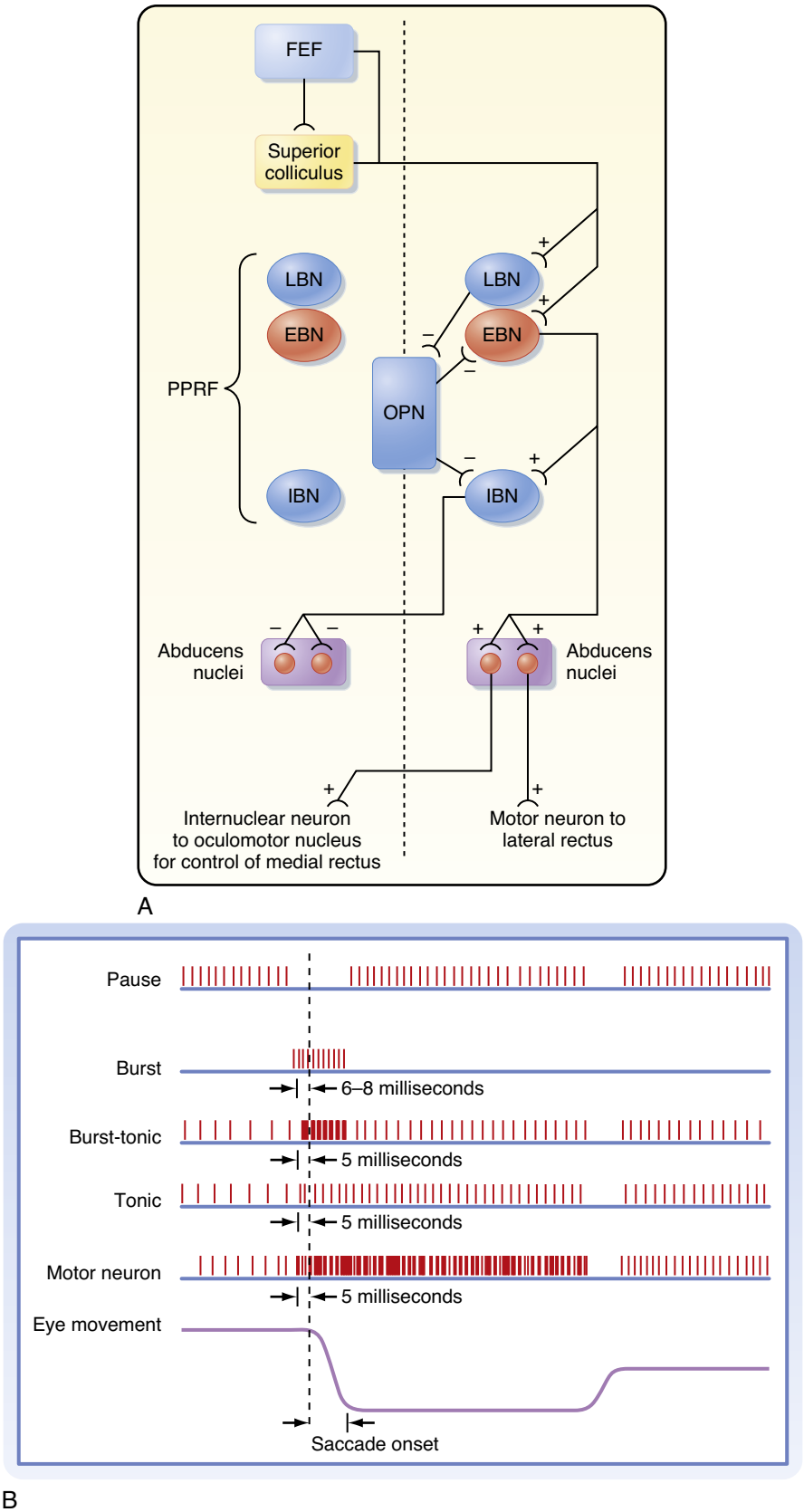
Normally, both inhibitory and excitatory burst neurons are inhibited by omnipause neurons located in the nucleus of the dorsal raphe. When a saccade is to be made, activity from the frontal eye fields or the superior colliculus, or both, leads to inhibition of the omnipause cells and excitation of the burst cells on the contralateral side. The resulting high-frequency bursts in the excitatory burst neurons provide a powerful drive to motor neurons of the ipsilateral lateral rectus and contralateral medial rectus muscles (see Fig. 9.28*A*); at the same time, inhibitory burst neurons enable relaxation of the antagonists. The initial bursts of these neurons allow strong contraction of the appropriate extraocular muscles, which overcomes the viscosity of the extraocular muscle and enables rapid movement to occur.

Circuits Underlying Smooth Pursuit

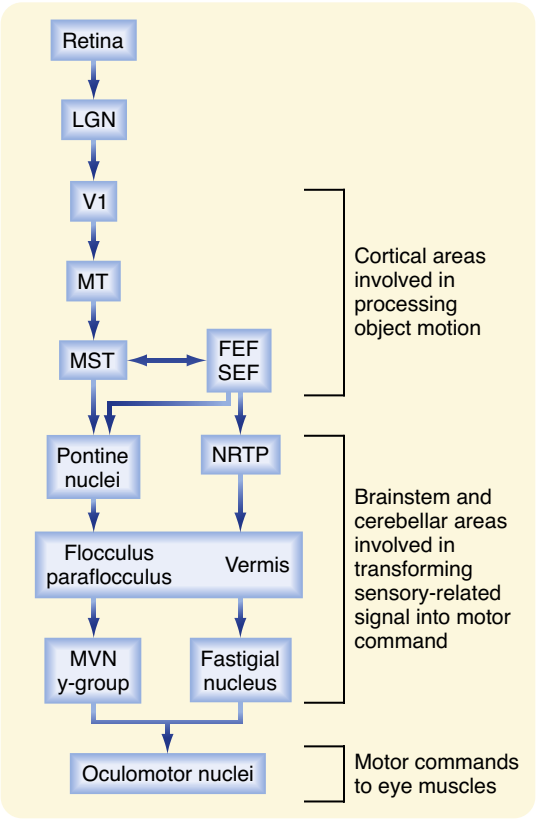
Smooth pursuit involves tracking a moving target with the eyes (Fig. 9.29). Visual information about target velocity is processed in a series of cortical areas, including the visual cortex in the occipital lobe, several temporal lobe areas, and the frontal eye fields. In the past, the frontal eye fields were thought to be related only to control of saccades, but more recent evidence has shown that there are distinct regions within the frontal eye fields dedicated to either saccade production or smooth pursuit. Indeed, there may be two distinct cortical networks, each specialized for one of these types of eye movement. Cortical activity from multiple cortical areas is fed to the cerebellum via parts of the pontine nuclei and nucleus reticularis tegmenti pontis. Specific areas in the cerebellum—namely, parts of the posterior lobe vermis, the flocculus, and the paraflocculus—receive this input, and they in turn project to the vestibular nuclei. From the vestibular nuclei, activity can then be forwarded to the oculomotor, abducens, and trochlear nuclei, as was described for the VOR earlier.

Circuits Underlying Vergence

The neural circuits underlying vergence movements are not well known. There are premotor neurons (neurons that feed onto motor neurons) located in the brainstem areas surrounding the various oculomotor nuclei. In some cortical visual areas and the frontal eye fields, there are neurons whose activity is related to the disparity of the image on the two retinas or to the variation of the image during vergence movements. How vergence signals in these cortical areas feed into the brainstem premotor neurons is not clear. The cerebellum also appears to play a role in vergence movements because cerebellar lesions impair this type of eye movement. Note that lesions of the medial longitudinal fasciculus that result in a loss of the VOR do not compromise vergence.



• **Fig. 9.28** Horizontal saccade pathways. **A,** Circuit diagram of the major pathways. *EBN*, Excitatory burst neuron; *FEF*, frontal eye field; *IBN*, inhibitory burst neuron; *LBN*, long lead burst neuron; *OPN*, omnipause neuron; *PPRF*, paramedian pontine reticular formation. **B,** Firing patterns of some of the neurons involved in making saccades. Excitation of burst neurons of the right horizontal gaze center causes abducens motor neurons on the right and medial rectus motor neurons on the left to be activated. The ascending pathway to the oculomotor nucleus is through the medial longitudinal fasciculus. The left horizontal gaze center is simultaneously inhibited.



• **Fig. 9.29** Smooth pursuit pathways. The stimulus for smooth pursuit eye movement is a moving visual target. This causes activity to flow through the circuitry diagramed in the figure and leads to maintenance of the fovea on the target. *FEF*, Frontal eye field; *LGN*, lateral geniculate nucleus; *MST and MT*, higher order visual association areas; *MVN*, medial vestibular nucleus; *NRTP*, nucleus reticularis tegmenti pontis; *SEF*, supplementary eye field; *V1*, primary visual cortex.

Key Points

1. The extrafusal skeletal muscle fibers are innervated by α motor neurons. A motor unit consists of a single α motor neuron and all the muscle fibers with which it synapses. Motor unit size varies greatly among muscles; small motor units allow finer control of muscle force.
2. The size principle refers to the orderly recruitment of α motor neurons according to their size, from smallest to largest. Because smaller motor neurons connect to weaker motor units, the relative fineness of motor control is similar for weak and strong contractions.
3. A reflex is a simple, stereotyped motor response to a stimulus. A reflex arc includes the afferent fibers, interneurons, and motor neurons responsible for the reflex.
4. Muscle spindles are complex sensory receptors found in skeletal muscle. They lie parallel to extrafusal muscle fibers, and they contain nuclear bag and nuclear chain intrafusal muscle fibers. By being in parallel to the main muscle, the spindle can detect changes in muscle length.
5. Group Ia afferent fibers form primary endings on nuclear bag1, bag2, and chain fibers, and group II fibers form secondary endings on nuclear chain and bag2 fibers.
6. Primary endings demonstrate both static and dynamic responses that signal muscle length and rate of change in muscle length. Secondary endings demonstrate only static responses and signal only muscle length.
7. The intrafusal muscle fibers associated with muscle spindles are innervated by γ motor neurons. Contraction of intrafusal fibers does not directly cause significant changes in muscle tension or length; however, when the level of tension in these fibers is adjusted, γ motor neurons influence the sensitivity of the muscle spindle to stretch.
8. Golgi tendon organs are located in the tendons of muscles and are thus arranged in series with the muscle. They are supplied by group Ib afferent fibers. Their in-series relationship means that tendon organs can detect the force level generated by the muscle, whether it is due to passive stretch or to active contraction of the muscle.
9. The phasic stretch (or myotatic) reflex includes (1) a monosynaptic excitatory pathway from group Ia afferent fibers in muscle spindles to α motor neurons that supply the same and synergistic muscles and (2) a disynaptic inhibitory pathway to antagonistic motor neurons.
10. The inverse myotatic reflex is evoked by Golgi tendon organs. Afferent volleys in group Ib fibers from a given muscle cause disynaptic inhibition of α motor neurons

to the same muscle, and they excite α motor neurons to antagonist muscles.

11. The flexion reflex is an important protective response because it acts to withdraw a limb from damaging stimuli. The reflex is evoked by volleys in afferent fibers that supply various receptors, particularly nociceptors. Via polysynaptic pathways, these volleys cause excitation of flexor motor neurons and inhibition of extensor motor neurons ipsilaterally. Concurrently, the opposite pattern of action (inhibition of flexor and excitation of extensor motor neurons) occurs contralaterally and is referred to as the *crossed extension reflex.*
12. Descending pathways can be subdivided into (1) a lateral system, which ends on motor neurons to limb muscles and on the lateral group of interneurons, and (2) a medial system, which ends on the medial group of interneurons.
13. The lateral system includes the lateral corticospinal tract and part of the corticobulbar tract. These pathways influence the contralateral motor neurons that supply the musculature of the limbs, especially of the digits, and the muscles of the lower part of the face and the tongue.
14. The medial system includes the ventral corticospinal, lateral and medial vestibulospinal, reticulospinal, and tectospinal tracts. These pathways affect mainly posture and provide the motor background for movement of the limbs and digits.
15. Locomotion is triggered by commands relayed through the midbrain locomotor center. However, central pattern generators formed by spinal cord circuits and influenced by afferent input provide for the detailed organization of locomotor activity.
16. Voluntary movements depend on interactions among motor areas of the cerebral cortex, the cerebellum, and the basal ganglia.
17. Motor areas of the cerebral cortex are arranged as a parallel distributed network, in which each contributes to the various descending motor pathways. The areas primarily involved in body and head movement include the primary motor cortex, the premotor area, the supplementary motor cortex, and the cingulate motor areas. The frontal eye fields are important for eye movement and help initiate voluntary saccades.
18. Individual corticospinal neurons discharge before voluntary contractions of related muscles occur. The discharges are typically related to contractile force rather than to joint position. However, the activity of an individual neuron may encode different parameters of a movement at different times in relation to the execution of that movement.
19. The population activity of motor cortex neurons can be used to predict the direction of upcoming movements.
20. The cerebellum influences the rate, range, force, and direction of movements. It also influences muscle tone and posture, as well as eye movement and balance.
21. The intrinsic circuitry of the cerebellum is remarkably uniform. Differences in function of different parts of the cerebellum arise largely as a result of differing afferent sources and efferent targets.
22. Anatomical and physiological techniques have shown that the cerebellar cortex may be divided into many functionally distinct, longitudinally running compartments.
23. Most of the input to the cerebellum is through pathways that end as mossy fibers. Mossy fibers excite granule cells, which in turn can evoke single action potentials, called *simple spikes,* in Purkinje cells, whose axons form the only output pathway from the cerebellar cortex.
24. The projections of the inferior olivary nucleus to the cerebellum end as climbing fibers and are the only source of them. Each Purkinje cell receives massive input from just one climbing fiber. As a result, each climbing fiber discharge produces a high-frequency burst of several action potentials, known as a *complex spike,* in the Purkinje cell.
25. Although complex spike activity is relatively rare in comparison to simple spike activity, complex spikes are precisely synchronized across populations of Purkinje cells, and because of the convergence of these cells onto cerebellar nuclear neurons, this synchronization may allow complex spike activity to significantly affect cerebellar output. Synchronization of complex spikes is the result of electrical coupling of inferior olivary neurons by gap junctions.
26. The basal ganglia include several deep telencephalic nuclei (including the caudate nucleus, putamen, and globus pallidus). The basal ganglia interact with the cerebral cortex, subthalamic nucleus, substantia nigra, and thalamus.
27. Activity transmitted from the cerebral cortex through the basal ganglia can either facilitate or inhibit the thalamic neurons that project to motor areas of the cortex, depending on the balance between direct and indirect basal ganglia pathways. When there is an imbalance of these two pathways, hyperkinetic or hypokinetic disorders occur.
28. Some types of eye movement help stabilize the view of the visual world. This is critical because visual acuity drops dramatically when the visual world moves, or slips, across the retina. Vestibulo-ocular and optokinetic movements help stabilize the visual world on the retina by compensating for movement of the head or external world (or both). Smooth pursuit movements allow tracking of a visual target so that it remains centered on the foveae.
29. Saccades act to move a specific part of the visual scene to the fovea, the retinal area of highest acuity, for detailed inspection.
30. There are specialized circuits and areas in the brainstem for control of vertical and horizontal eye movements. These areas are used both by the cortex (when voluntary eye movements are made) and by the sensory input that initiates reflexive eye movement.