Balance and Control of Movement 4.5

Learning Objectives

- Describe the population code and frequency code for controlling muscle force
- Describe the somatotopic organization of lower motor neurons
- Define what is meant by the motor neuron pool in the spinal cord and its organization by myotome
- Indicate the location of the primary motor cortex, supplementary motor cortex, premotor cortex, and sensory association area
- List the components of the basal ganglia
- Describe the role of the direct pathway in enhancing desired movement
- Describe the role of the indirect pathway in suppressing unwanted movement
- Describe the role of the substantia nigra in balancing the direct and indirect pathways
- List the major inputs into the cerebellum and its function
- Identify the semicircular canals and distinguish them from the utricle and saccule
- Distinguish the perilymph from the endolymph in terms of location and composition
- Identify the information provided by the semicircular canals and the utricle and saccule
- Identify the major features of hair cells and how they respond to deformation of the kinocilium

THE NERVOUS SYSTEM USES A POPULATION CODE AND FREQUENCY CODE TO CONTROL CONTRACTILE FORCE

Large multinucleated cells called muscle fibers make up a skeletal muscle. The overwhelming majority of them are extrafusal fibers that produce force to move or rigidly fix body parts, when antagonistic pairs of muscles are simultaneously activated. As described in Chapter 3.4, the intrafusal fibers report to the CNS on muscle length and its rate of change. The extrafusal fibers differ in size, relative contributions of various subcellular organelles, expression of protein and enzyme isoforms, metabolic capabilities, and contractile properties. Muscle fibers are broadly classified as slow, fast glycolytic or fast oxidative-glycolytic (see Chapter 3.7). Each extrafusal fiber is innervated by a single **α motor neuron**, but each α motor neuron typically innervates a number of muscle fibers. The motor neuron and the set of muscle fibers innervated by it constitute a **motor unit**. Activation of the α motor neuron activates all of the muscle fibers in its motor unit.

Motor neurons that innervate a large number of muscle fibers are larger than those that innervate a small number of muscle fibers. The smaller motor neurons are more easily excitable, probably because they have smaller distances to convey EPSPs to their axon hillocks. During the activation of muscle, the smaller motor units are activated first, and progressively larger motor units are activated until all motor units are **recruited**. This is the **size principle**. The size principle makes subjective sense because delicate movements that require dexterity but little force demand increasing force in the smallest possible increments by recruiting small numbers of muscle fibers. When performing gross motor movements involving lots of force, larger increments of force can be accomplished by recruiting successively larger motor units and more of them. Thus, the contractile force of a muscle can be **graded** (varied more or less continuously from low to high levels), through the recruitment of successively larger proportions of the population of motor neurons. This is the **population code** for encoding the strength of the muscle force. Activation of a larger population of motor neurons activates more muscle fibers and produces more force.

Muscles develop more force upon rapid repetitive stimulation. This wave summation is due to the release of additional activator Ca^{2+} from the sarcoplasmic reticulum before the force from the previous activation has returned to baseline. Thus, repetitive stimulation by the α motor neurons results in a larger force produced over a longer time. For typical movements, muscles must be activated by bursts of activity of their α motor neurons. This is the **frequency code** for varying muscle force.

CONTROL OF MOVEMENT ENTAILS CONTROL OF α MOTONEURON ACTIVITY

Muscular activity is controlled entirely by the activity of the α motor neurons that innervate the muscle. These

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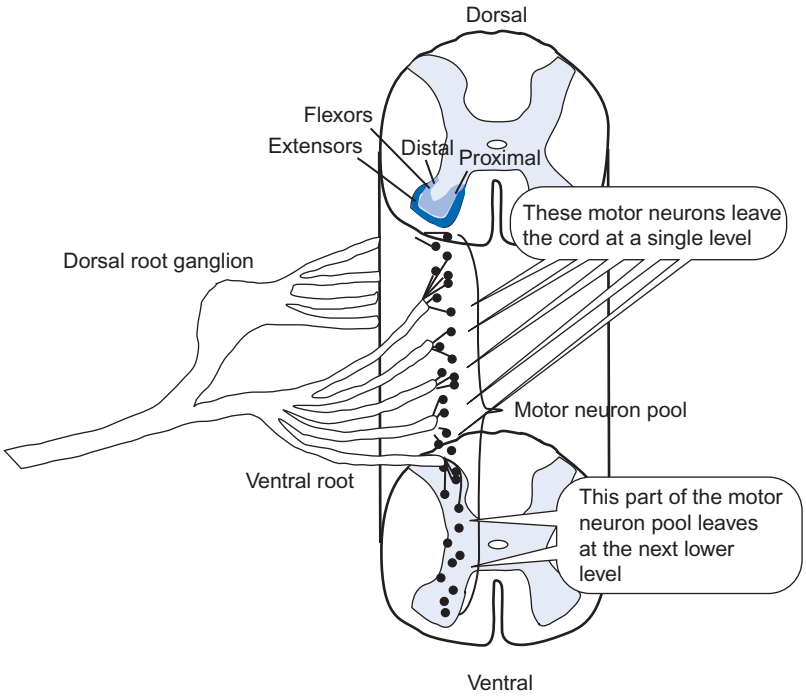

FIGURE 4.5.1 Spatial arrangement of α motor neurons in the spinal cord. The cell bodies of α motor neurons innervating flexor muscles are located in the dorsal part of the ventral horn; those innervating extensor muscles are found more ventrally. Similary, the cell bodies of α motor neurons innervating the muscles of the distal limbs are located laterally, whereas those motor neurons for the proximal muscles are located medially. The motor neurons are not located merely in one spinal segment but are distributed up and down the cord. Groups of these form connections to the ventral root, which joins the dorsal root distal to the dorsal root ganglion. Motor neurons serving specific muscles are grouped together in adjacent spinal segments. These form a **motor neuron pool**. Most motor neurons for a particular muscle leave the cord at a single spinal segment.

cells are called the **lower motor neurons**, to distinguish them from the neurons in the cortex, the **upper motor neurons** that provide the initial drive for the α motor neurons. Some of the control of the α motor neurons resides in the spinal cord, some resides in the motor cortex, and some resides in other structures such as the basal ganglia and in the cerebellum. Most movements are ballistic: muscles are activated in a particular sequence, for short bursts of action potentials, through learned sequences to achieve the desired end. Such coordinated trains of activity are evident in the EMG of muscle, as shown in Figure 3.7.1.

THE CIRCUITRY OF THE SPINAL CORD PROVIDES THE FIRST LAYER IN A HIERARCHY OF MUSCLE CONTROL

The motor neurons in the spinal cord are topographically organized. The cell bodies or somas of the motor neurons lie in the ventral horn of the gray matter of the spinal cord. Their position there is not haphazard. Instead, there is a topographical organization to their arrangement within the cord (see Figure 4.5.1).

THE MOTOR NERVES ARE ORGANIZED BY MYOTOMES

There are thirty pairs of spinal nerves that carry sensory afferents and motor efferents to their targets: There are 8 cervical, 12 thoracic, 5 lumbar, and 5 sacral spinal nerves. Each spinal nerve supplies an embryologically defined **somite** or **body segment**, which is characterized by a **dermatome**, **myotome,** and **sclerotome**. The somatic sensory nerves report on sensory information obtained from a dermatome, the segmental unit of the skin. Each motor nerve innervates a designated area of muscle, called a myotome. These motor nerves exit the spinal cord via the ventral roots, which join the dorsal roots after a short distance, and travel to their targets alongside incoming sensory nerves. Despite this segmental organization, both sensory and motor organization is not absolutely limited to single spinal segments. Instead, motor and sensory innervation often overlaps one or two segments above and below a given spinal segment. Thus, the motor neurons innervating a single muscle are grouped together vertically in adjacent spinal segments, forming a **motor neuron pool**. The spatial arrangement of these is shown in Figure 4.5.1.

SPINAL REFLEXES FORM THE BASIS OF MOTOR CONTROL

The basic wiring of the spinal cord produces reciprocal actions of **synergistic** muscles and **antagonistic** muscles. Synergistic muscles are muscles whose coordinated activity produces a desired result. Flexion of the elbow, for example, requires fixation of the shoulder as well as contraction of the biceps brachii, brachialis, and radiobrachialis. The antagonists are those muscles that work against the desired movement. Typically antagonistic pairs of muscles are reciprocally activated, except when rigid fixation of a joint is desired. Thus, the spinal cord provides circuits which can activate synergists while inhibiting their antagonists, while allowing for coactivation of antagonistic pairs of muscles upon demand by higher centers.

The spinal cord also possesses **locomotor pattern generators**, which are neural circuits that produce or

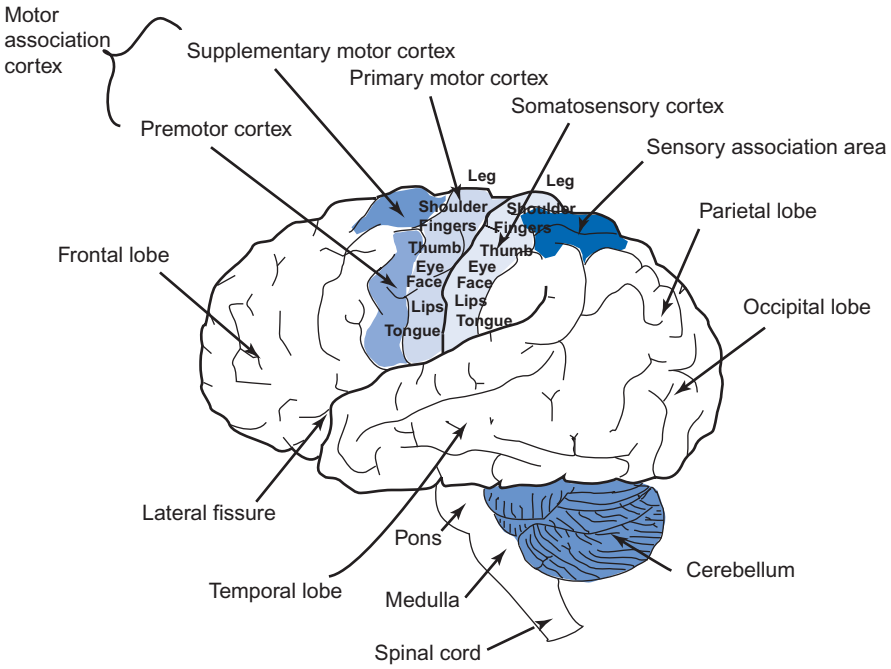

FIGURE 4.5.2 Areas of the cortex involved in motor control. The primary motor cortex has a somatotopic representation that mirrors the somatotopic representation in the somatosensory cortex. The other areas noted (sensory association area; premotor cortex; supplementary motor cortex) have roles in the selection of appropriate muscle programs.

control a particular set of muscles in a defined sequence. Usually the muscles activated by the pattern generator form rhythmic behaviors such as locomotion or breathing. Upon removal of higher inputs by transection of the spinal cord, many animals will exhibit locomotive behaviors upon stimulation of afferent somatosensory nerves. It is not clear how strong the locomotor pattern generators are in humans, but the basic circuitry allowing this behavior remains.

PURPOSEFUL MOVEMENTS ORIGINATE IN THE CEREBRAL CORTEX

The reflexes in the spinal cord form the basic motor plan by which complicated motor movements can be coordinated. However, these circuits are reflexes. As complicated as they might be, they cannot form purposeful movements. Instead, purposeful movements originate in higher brain centers, areas of the cerebral cortex.

THE PRIMARY MOTOR CORTEX HAS A SOMATOTOPIC ORGANIZATION

The **primary motor cortex** is a strip of cortical tissue in the frontal lobe immediately anterior to the central sulcus. It is called the "primary" motor cortex because it is required for the initiation of purposeful movements, and stimulation of areas of this cortex has the lowest threshold for eliciting a motor response. The motor responses that are elicited upon stimulation of the primary motor cortex are organized **somatotopically**: there is a spatial arrangement of motor responses in which adjacent muscles are controlled by adjacent regions of the primary cortex. This somatotopic mapping mirrors that of the somatosensory cortex. In fact, the somatosensory cortex is just on the other side of the central sulcus. These two areas are actually adjacent, being connected by the cortical tissue that follows the contours of the sulcus (the **paracentral lobule**).

The motor cortex is a layered structure, with cells of different overall shape and structure occupying different layers. Layer 5 of the cortex contains giant pyramidal or Betz cells. These cells send processes out over three separate tracts.

A. The **corticobulbar tract** supplies motor commands to cranial nerve motor nuclei of the head and neck
B. The **ventral corticospinal tract** innervates lower motor neurons of the axial and proximal muscles
C. The **lateral corticospinal tract** supplies inputs to lower motor neurons controlling the muscles of the distal extremities. As these muscles control fine movements, this tract is essential for delicate and precise actions of the fingers and hands.

These three tracts also contain fibers from other regions of the cerebrum, including the **motor association cortex**, the **somatosensory cortex**, and the **sensory association area**. These areas, with the somatotopic map of motor function, are illustrated in Figure 4.5.2.

MOTOR ACTIVITY ORIGINATES FROM SENSORY AREAS TOGETHER WITH PREMOTOR AREAS

Although the motor cortex provides an important role in driving the lower motor neurons, which motor neurons are activated and when they are activated is determined elsewhere. Selection of appropriate motor actions depends critically on knowledge of where the

body is in space, where it should go, and how it should get there. Thus, sensory information from the somatosensory cortex and other sensory areas (such as the vestibular apparatus) must be coordinated. One of the major regions for the planning of motor programs is the **motor association cortex**, consisting of the **premotor cortex** and the **supplementary motor cortex**. The supplementary motor cortex is required for bilaterally coordinated movements. Lesions of this area cause **apraxia**, in which simple movements are retained but the affected individual is unable to perform coordinated movements involving both hands, such as tying a shoe or buttoning a shirt.

Sensory information ascends the spinal cord and is relayed in the thalamus to the somatosensory cortex. This information is sent to other areas of the cerebral cortex such as the **sensory association area** in the lateral aspect of the parietal lobe. This area integrates many different sensory modalities to form a kind of neural map of body, visual, and auditory space. Lesions within the sensory association area produce a variety of **neglect syndromes** in which the affected individual appears to lose awareness of body regions or portions of visual or auditory space that are served by the damaged area. Complex movement involving muscles shows specific deficits having to do with only one side of the body or involving near space or distant space, depending on the location of the lesion. These deficits result from incomplete formation of the neural map that forms the target for movement. The movement of the body in real space is planned by its representation in neural space. The sensory association area mingles sensory information to form a neural map of space with the position of the body superimposed on it. Planning of movements requires this mingling of sensory information.

MOTOR CONTROL IS HIERARCHICAL AND SERIAL

The individual connections of neurons controlling motor programs are enormous and cannot be diagrammed or understood in the particulars. Therefore we will approach the overall control systems in terms of block diagrams as shown in Figure 4.5.3. As this figure shows, cortical cells in the sensory association cortex and in the prefrontal region initiate movement by (1) focusing attention and (2) forming a working memory for a motor task. This *working memory* allows us to evaluate the consequences of future actions and to update these plans depending on new sensory information. Outputs from these areas feed into the supplementary motor cortex (see Figure 4.5.2) and the premotor cortex. Somatotopic mapping is present in

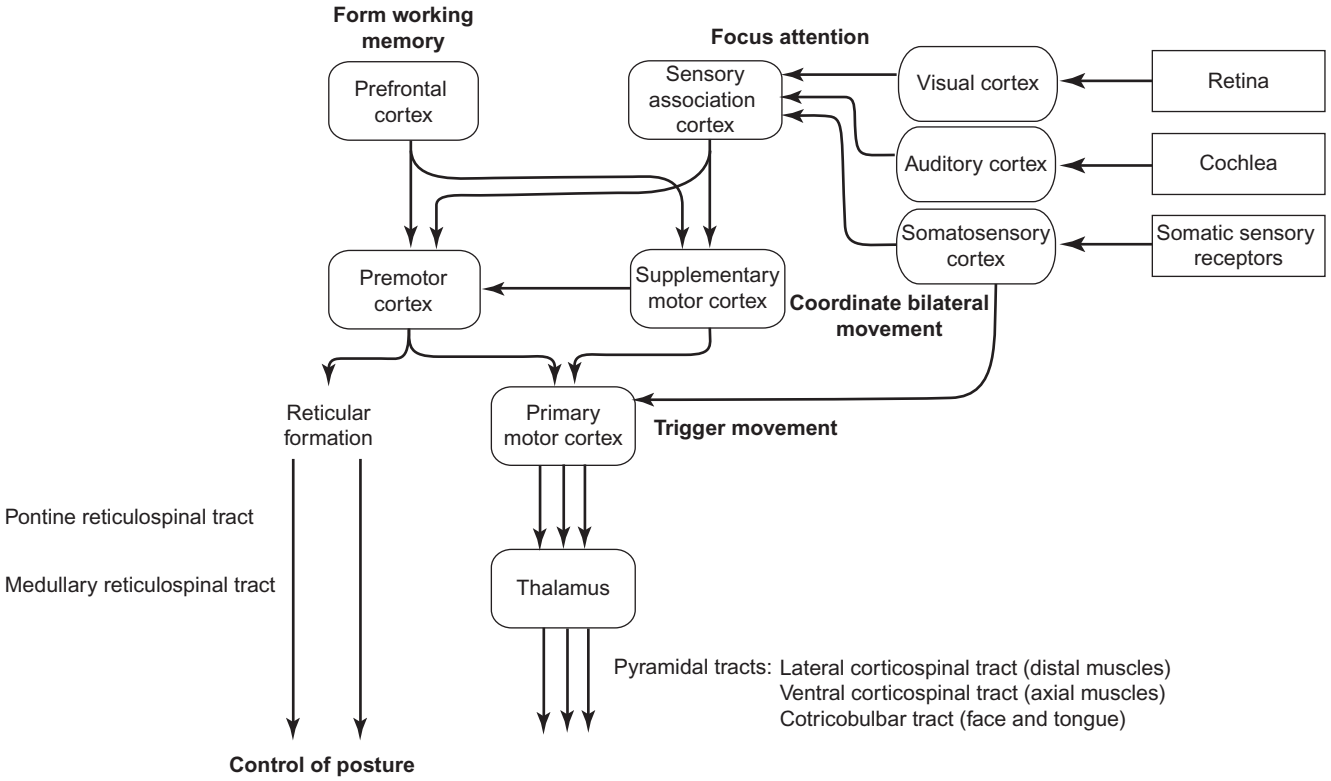

FIGURE 4.5.3 Block diagram for neuronal processing of motor programs. Although lower motor neurons are controlled by cells in the primary motor cortex, voluntary movement is initiated in the prefrontal cortex, which forms a "working memory" that anticipates possible future movements, and in the sensory association cortex that integrates sensory information from a variety of senses and focuses attention on the sensory information relevant to the motor task. This information is forwarded to the next step in the process, which is the formation of a coordinated motor plan involving the premotor cortex and the supplementary motor cortex. When the proper sequence of events is established, the primary motor cortex, containing the upper motor neurons, actually triggers the movement by exciting the proper lower motor neurons through tracts that descend the spinal cord.

the primary motor cortex and in the premotor cortex and the supplementary motor area. The supplementary motor cortex coordinates bilateral movement. Output from the premotor cortex goes to the primary motor cortex and to the reticular formation, whose output is used to orient the body for the motor task at hand. Cells in the primary motor cortex trigger the movement through the pyramidal tracts leading from the motor cortex to the lower motor neurons. Thus information involving motor programs is hierarchical: there is a definite sequence of events from accumulating different sensory information about future actions (where is the baseball?), to thinking about the action, and engaging the appropriate motor program. The goal of training is to shorten the times required for these processes and to make them as automatic as possible. The faster you can identify the curve or the slider, the faster you can adjust the swing of the bat, and the higher the likelihood that you get a piece of that pitch. If you have to think about it, you will strike out.

THE *BASAL GANGLIA* AND *CEREBELLUM* PLAY IMPORTANT ROLES IN MOVEMENT

The basal ganglia and cerebellum compose the major subcortical motor control systems and are critically important for the coordination of movement. The basal ganglia consist of five nuclei (**caudate nucleus**, **putamen**, **globus pallidus**, **subthalamic nucleus**, and **substantia nigra**). They receive widespread inputs from the entire cortex and project back to the cortex over the thalamus. They are important not only for the fine-tuning of motor systems but also have important effects on cognition, mood, and behavior. The **cerebellum**, on the other hand, receives cortical inputs only from the sensory and motor areas but projects to spinal motor areas that do not receive direct basal ganglia connections.

The motor cortex has direct connections to motor neurons in tracts collectively called the **pyramidal system**, named for the pyramid-like structure these tracts form as they pass through the medulla. The basal ganglia constitute part of the **extrapyramidal motor system**, which consists of the pathways from noncortical regions that lead ultimately to the lower motor neurons. The extrapyramidal system also includes output from the cerebellum.

Figure 4.5.4 shows the location of the basal ganglia between the motor cortex and targets in the brain stem and spinal cord. Bundles of fibers that connect sensory information to the cortex (spinocortical tracts and bulbar cortical tracts) and that connect the cortex to lower targets (corticofugal tracts—including the lateral corticospinal tract, the ventral corticospinal tract, and the corticobulbar tract) pass through this region. These bundles of myelinated fibers collectively form a broad band called the **internal capsule**. It penetrates the three basal ganglia (caudate, putamen, and globus pallidus) and the contrast between the myelinated fibers and the ganglia gives the area a striated or striped appearance. For this reason, the caudate, putamen, and globus pallidus are collectively called the **corpus striatum** (literally, *striped body*). The caudate and putamen have similar structures and embryologic origins and are collectively called the **neostriatum**; the globus pallidus consists of two regions, the **internal globus pallidus** and the **external globus pallidus**.

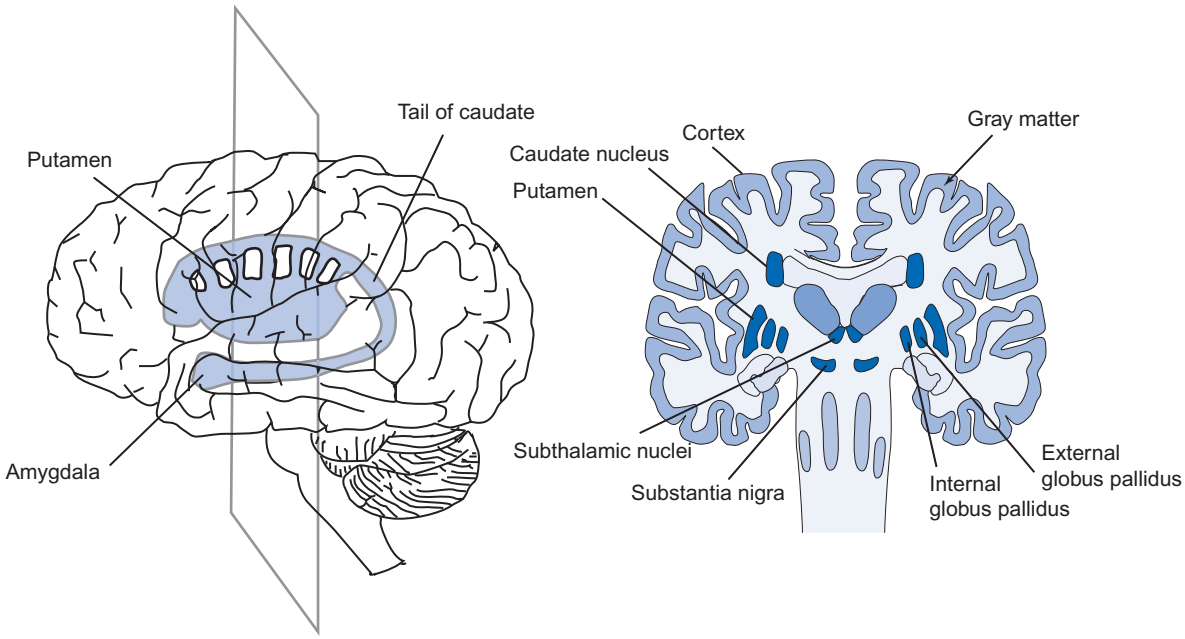

FIGURE 4.5.4 Anatomic arrangement of the basal ganglia. Left, the shape of the caudate and outer aspect of the putamen as seen from the left side. The structures lie internal to the brain and are not visible from its surface. The caudate nucleus follows the line of the lateral ventricles. It is long and thin and its shape resembles a ram's horn. The putamen and globus pallidus are shaped likes lenses and are collectively called the lenticular nucleus.

The basal ganglia scale motor programs for the task at hand and enable automotic performance of practiced motor acts. For example, you can write your name large on a blackboard or you can write your name small on a check. The motor program originates in the cortex but is conditioned by inputs from the basal ganglia and the cerebellum. Part of this conditioning is the scaling factor that determines the size of the movements and their strength. The fine tuning and updating of the motor program is performed by the cerebellum. Thus, the basal ganglia are a side-loop pathway that fine tunes motor instructions as they are being formulated in the premotor area.

The functional connections of the basal ganglia are shown in Figure 4.5.5. The putamen receives inputs from a variety of cortical areas including the somatosensory cortex, sensory association cortex, and prefrontal cortex. The caudate receives input primarily from the prefrontal cortex. Both the putamen and caudate nucleus send fibers to the internal globus pallidus in what is called the **direct pathway**. These connections use GABA as a neurotransmitter and they inhibit activity of the globus pallidus neurons. These neurons in the internal globus pallidus send inhibitory connections to the **ventroanterior** and **ventrolateral nuclei** of the thalamus. These neurons from the globus pallidus are tonically active and therefore they continuously inhibit the excitation of the supplementary motor cortex by the thalamus. Inhibition of the internal globus pallidus therefore removes inhibition of this excitatory pathway. This is referred to as **disinhibition**. Thus activation of the direct pathway is equivalent to exciting the supplementary motor cortex and providing additional neuronal drive for movement.

The **indirect pathway** inhibits the excitatory output of the thalamus to the supplementary association cortex. In this case the cortical input to the neostriatum is sent to the external globus pallidus and then to the subthalamic nucleus, finally sending processes to the internal globus pallidus. As shown in Figure 4.5.5, the connections from the striatum to the external globus pallidus are inhibitory; the connections from the external globus pallidus to the subthalamic nucleus are also inhibitory, whereas the connections from the subthalamic nucleus to the internal globus pallidus are excitatory. Thus activation of this indirect pathway causes activation of the internal globus pallidus, which inhibits the excitatory flow from thalamus to supplementary motor cortex. Activation of the indirect pathway, then, finally inhibits the supplementary motor cortex. **The indirect pathway is inhibitory whereas the direct path is excitatory**.

Inhibition or activation is simply kept track of by multiplying the signs. Activation is given a positive sign, +; inhibition is given a negative sign, −. Inhibition of an inhibitory pathway is $- \times - = +$; thus, inhibition of inhibition, or disinhibition, activates. Following the direct pathway we have − for the connection between neostriatum and internal globus pallidus, − for the connection of internal globus pallidus to thalamus, and + from thalamus to supplementary motor cortex; the whole is $- \times - \times + = +$, or activation. Similarly, the

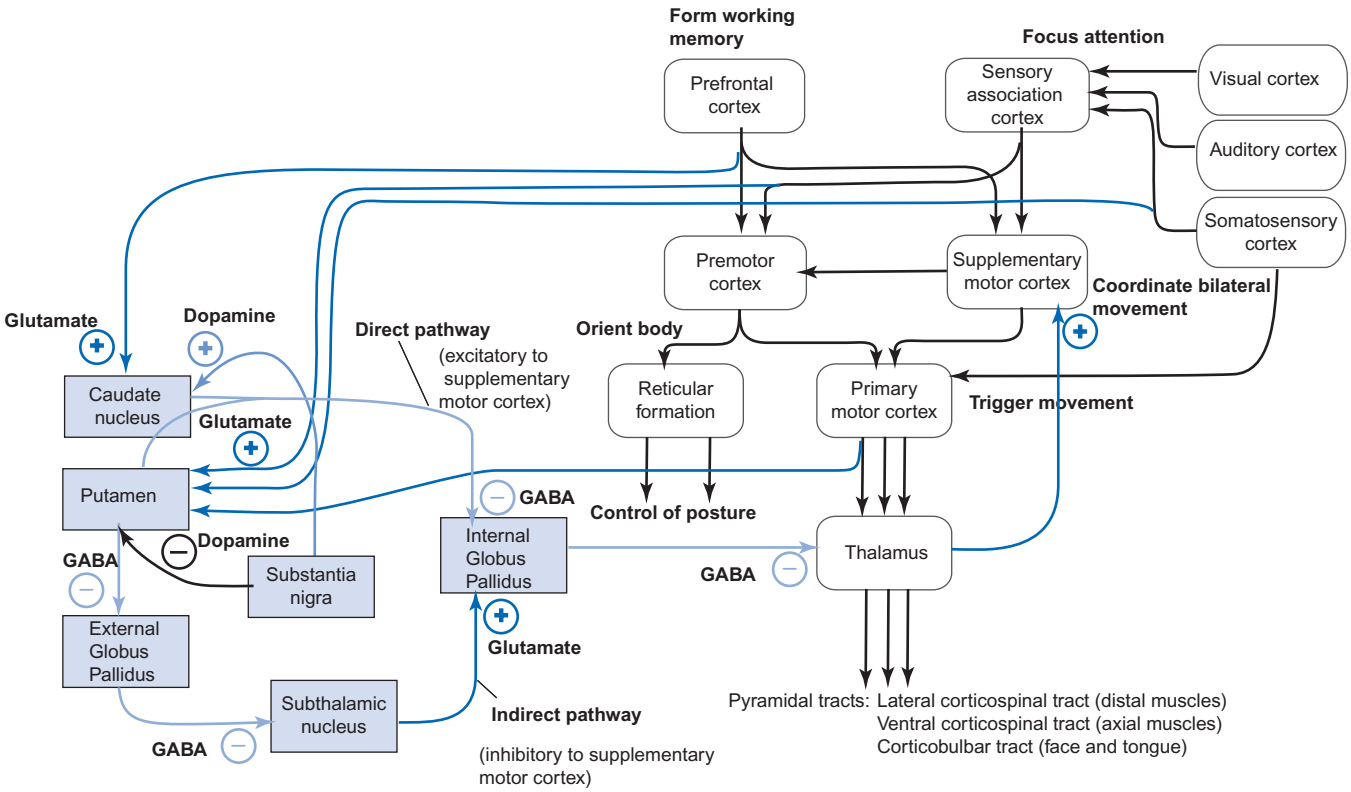

FIGURE 4.5.5 Connections of the basal ganglia and their involvement in strengthening neural drive for motor programs. See text for explanation.

indirect pathway involves − for the connection from neostriatum to external globus pallidus; − for the connection from external globus pallidus to the subthalamic nucleus; + for the connection between subthalamic nucleus and the internal globus pallidus; − for the connection from internal globus pallidus to thalamus; and + for the connection between thalamus and supplementary motor cortex. The final effect is $- \times - \times + \times - \times + = -$. Thus the indirect pathway inhibits excitation of the supplementary motor cortex.

THE *SUBSTANTIA NIGRA* SETS THE BALANCE BETWEEN THE DIRECT AND INDIRECT PATHWAYS

Dopaminergic connections from the **substantia nigra** form the nigrostriatal pathway that connects the substantia nigra to the caudate and putamen. These connections excite the neurons running over the direct, stimulatory pathway, and they inhibit those neurons running over the indirect, inhibitory pathway. Activity of the substantia nigra therefore alters the balance between excitatory (direct pathway) and inhibitory (indirect pathway) motor drive. Activation and inhibition by a single neurotransmitter is possible because of the receptors on the post-synaptic cell (see Chapter 4.2).

THE *CEREBELLUM* MAINTAINS MOVEMENT ACCURACY

Persons whose cerebellum is damaged exhibit abnormal movements marked by a loss of motor coordination, and lack of smooth sequences of motor programs. The lack of coordination is called **cerebellar ataxia**. Part of this coordination includes the integration of the sense of balance, which originates from receptors in the **vestibular apparatus**. The clumsiness, loss of equilibrium and inability to target motor tasks in inebriated persons derives largely from depression of cerebellar function. The cerebellum also is critically important in learning motor skills. The point of practicing motor skills, from athletics to playing a musical instrument or typing, is to make the sequence of motions automatic. During these activities we voluntarily engage an entire muscle program without having to think about each action. If we had to think about each part of the complicated program separately, we could not perform it rapidly or smoothly. The block diagram of some of the cerebellar connections is shown in Figure 4.5.6.

When we engage a motor program, commands pass from the primary motor cortex down the pyramidal tracts to the lower motor neurons in the spinal cord. At the same time, a duplicate of these commands is sent to the cerebellum through relay nuclei in the pons. These nuclei send projections called **mossy fibers** to the cerebellar cortex where they synapse on **granule cells** (see Figures 4.5.7 and 4.5.8). Excitatory input to these granule cells is directed to **parallel fibers** that make contact with **Purkinje cells**, which form the major output of the cerebellar cortex. Purkinje cells receive as many as 200,000 synapses from parallel fibers. The small EPSPs generated by these connections summate temporally and spatially to produce Purkinje cell action potentials, but because of their large number of contacts the granule cells drive Purkinje cells with a tonic level of 50 to 100 action potentials per second. The excitatory drive of the granule cells is modulated by interneurons, **stellate cells** and **basket cells**, which are excited by parallel fibers but inhibit the Purkinje cells. **Golgi cells** are other interneurons in the cerebellar cortex that receive input from the parallel fibers and feed back to inhibit the granule cells.

Sensory information from the spinal cord, brain stem, and cerebral cortex passes through the **inferior olivary complex** in the medulla which sends processes that synapse directly on the primary output cells of the cerebellar cortex, the **Purkinje cells**. Because of their vine-like appearance, these processes are called **climbing fibers**. The climbing fibers form strong connections that make large EPSPs on the Purkinje cells.

The mossy fibers from the pontine nuclei bring in a duplicate copy of the motor program. At the same time, sensory information about the movement that was actually made enters the cerebellum through the climbing fibers. Both are processed in the cerebellar cortex. This mingling of the motor programs and sensory information about what the body actually did allows us to make adjustments to the motor program so that when we activate it, the body will do what we want.

The Purkinje cells form the major output of the cerebellar cortex. Fibers connect to the **dentate nucleus**, which relays output to the red nucleus and the thalamus. The red nucleus in turn projects to spinal motor neurons through the rubrospinal tract, and the thalamus projects back to the premotor and primary motor cortex. Purkinje cells also send projections to two deep cerebellar nuclei, the **fastigial nucleus** and the **interposed nucleus**, which send information to the spinal cord through three paths:

A. through the reticular formation and the reticulospinal tract;
B. indirectly through the red nucleus and the rubrospinal tract;
C. directly to spinal motor neurons.

THE SENSE OF BALANCE ORIGINATES IN *HAIR CELLS* IN THE *VESTIBULAR APPARATUS*

Each inner ear contains a **vestibular apparatus,** also called the **labyrinth,** that consists of three mutually orthogonal semicircular canals. The canals are encased in the **bony labyrinth** of the temporal bone. The three semicircular canals are the **posterior, anterior**, and **horizontal canals**. The canals are filled with **endolymph**, a special fluid that is extracellular but nevertheless is high in K^+. They are surrounded by **perilymph**, a fluid similar in composition to the cerebrospinal fluid, or CSF. The posterior and anterior canals are oriented

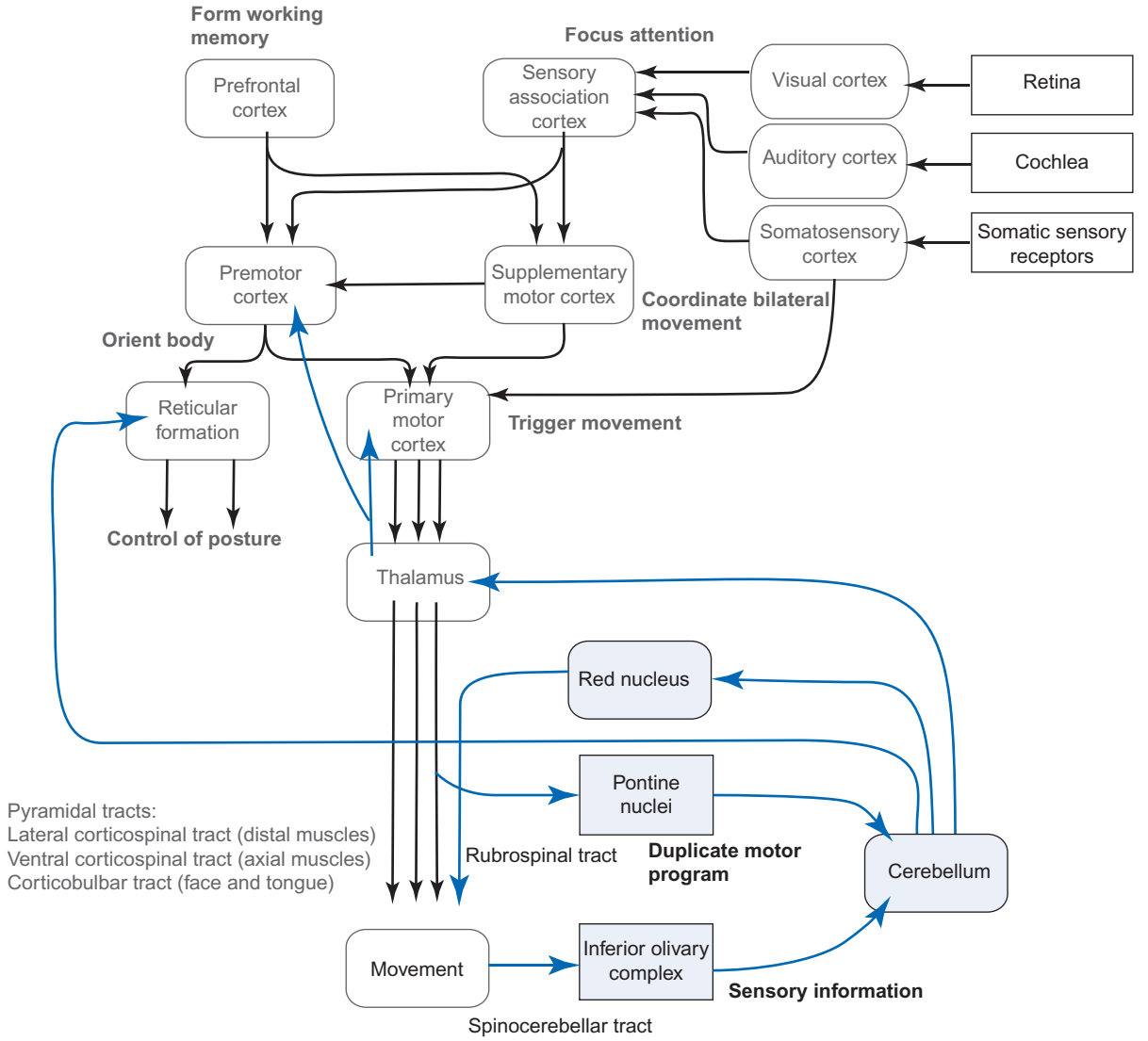

FIGURE 4.5.6 Block diagram of connections between the cerebellum and other centers involved with the coordination of muscle movement.

vertically when the head is held upright. In addition, each vestibular apparatus contains two chambers, the **utricle** and **saccule**, that contain a field of **hair cells** that provide information about the position of the head relative to gravity. The utricle is horizontal whereas the saccule is oriented vertically (see Figure 4.5.9). The three canals are continuous with each other and with the utricle and saccule, as well as the **cochlea**, that part of the inner ear that is devoted to hearing (see Chapter 4.6).

Each semicircular canal forms an enlarged region, the **ampulla**, near its junction with the utricle. Each ampulla contains a sensory epithelium that consists of a ridge of columnar hair cells. The hair cells are embedded in a gelatinous mass called the **cupola**. The cupola extends to the opposite wall of the ampulla. The entire structure is called the **ampullary crest**. The "hairs" on these cells are not true hairs, nor are they true **cilia** because they do not contain the 9 + 2 arrangement of microtubules that characterize true cilia, nor do they possess propulsive power. Because of their cilia-like appearance, the "hairs" of these mechanosensitive cells are called **stereocilia**. The hair cells have some 50 to 100 sterocilia and one **kinocilium**. The kinocilium is the longest "hair" and it defines a polarity of the hair cell. The stereocilia become progressively shorter as their distance from the kinocilium increases. The axis of the hair cell is defined by the line of sterocilia that point toward the kinocilium.

Electron micrographs reveal thin connections, called **tip links**, between the tips of neighboring stereocilia. These are believed to connect to K^+ channels on the surfaces of the stereocilia. Bending of the stereocilia modulates the conductance to K^+ ions and alters the membrane potential. The surface of the hair cells faces the endolymph which contains higher $[K^+]$ than the intracellular fluid, so opening a K^+ channel causes influx of K^+, rather than the efflux that would occur with most cells that face the low $[K^+]$ of the extracellular fluid. Movement of the kinocilium away from the stereocilia

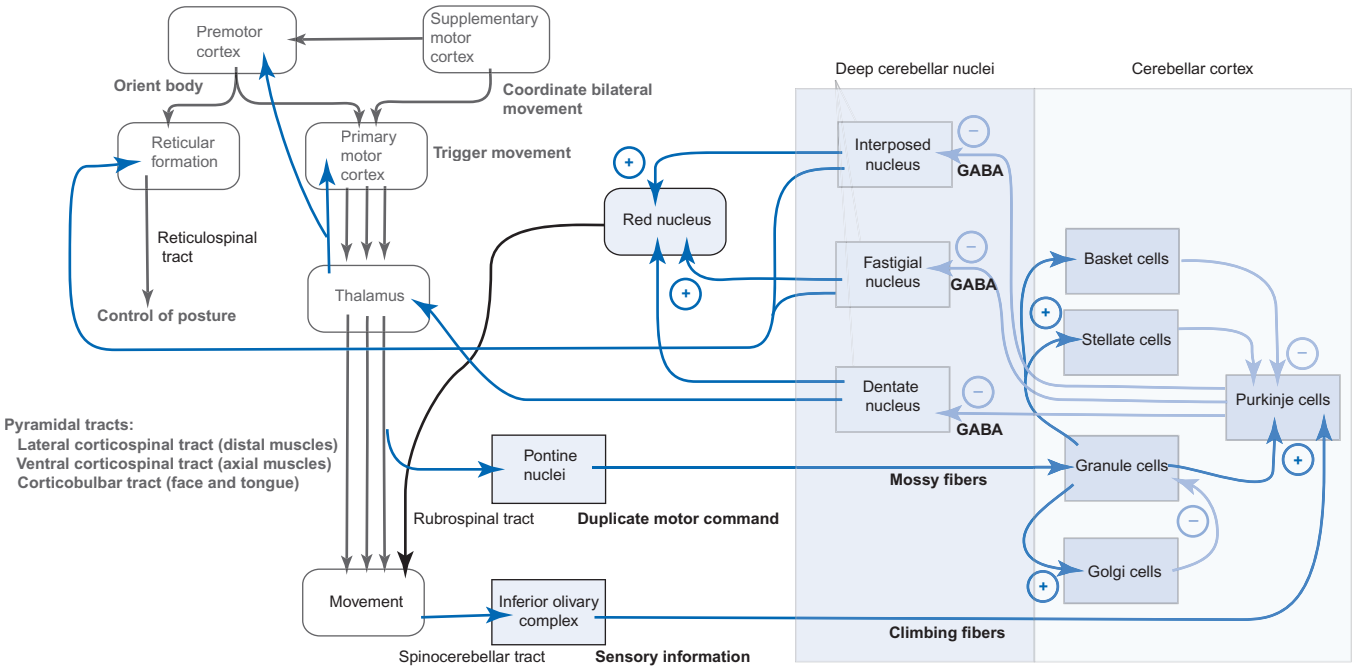

FIGURE 4.5.7 Block diagram of connections within the cortex and deep nuclei of the cerebellum. Duplicate motor commands enter the cerebellum on mossy fibers from the pontine nuclei. These synapse on granule cells that form parallel fibers that make excitatory synapses on Purkinje cells. The parallel fibers also synapse on stellate cells and basket cells that inhibit Purkinje cells. This inhibition sharpens the excitatory drive by lateral inhibition. Granule cells also synapse on Golgi cells that feed back to inhibit the granule cells. Purkinje cells project to the dentate, fastigial, and interposed nuclei. The dentate nucleus projects to the thalamus and to the red nucleus. The fastigial and interposed nuclei project to the reticular formation and to the red nucleus. The red nucleus sends activating processes down the cord on the rubrospinal tract. The reticular formation sends fibers to control muscles of posture on the reticulospinal tract. The thalamus sends processes to the premotor cortex and the primary motor cortex to adjust for inaccuracies in the desired motor act. Sensory information enters the cerebellum from the inferior olivary complex over climbing fibers that have strong connections to the Purkinje cells. In this way, motor information over the mossy fibers can be compared to sensory information over the climbing fibers, and motor tasks can be refined and conditioned.

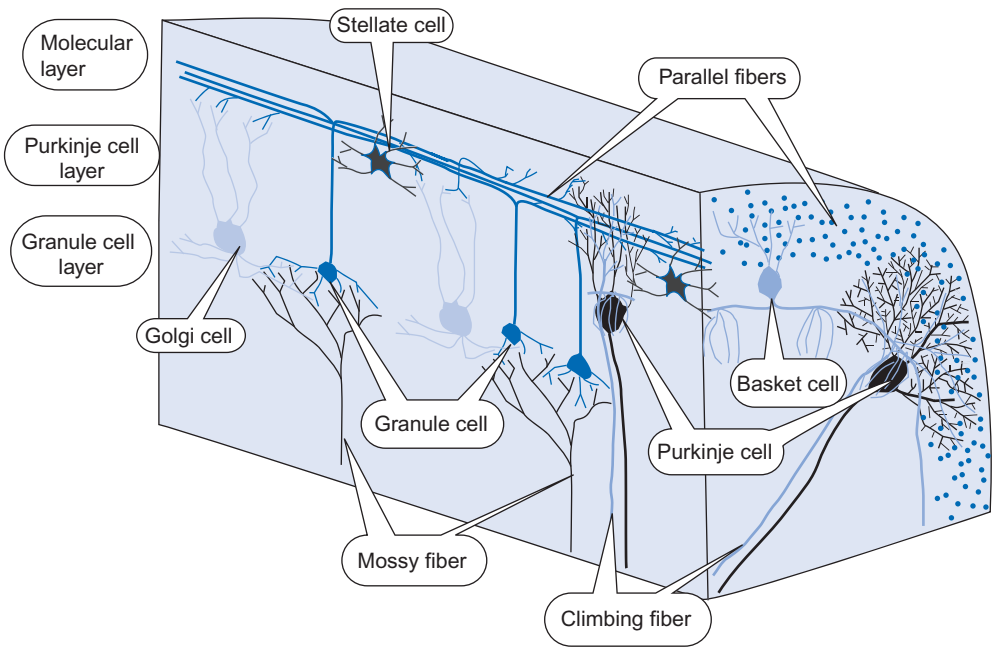

FIGURE 4.5.8 Schematic diagram of the cytoarchitecture of the cerebellar cortex. The mossy fibers synapse on granule cells whose axons divide to form two parallel fibers that synapse on Golgi cells that feed back onto granule cells, inhibiting them. They also make many synapses on Purkinje cells, whose dendritic fields form a fan whose long axis is perpendicular to the parallel fibers. Basket cells are excited by parallel fibers and inhibit Purkinje cells. Their processes are perpendicular to the parallel fibers. Stellate cells provide lateral inhibition of Purkinje cells. Climbing fibers bring in sensory information and form strong excitatory connections with just a few Purkinje cells. (Source: *Modified from L.R. Johnson (ed.)* "Essential Medical Physiology", *Lipincott-Raven, Philadelphia (1998).*)

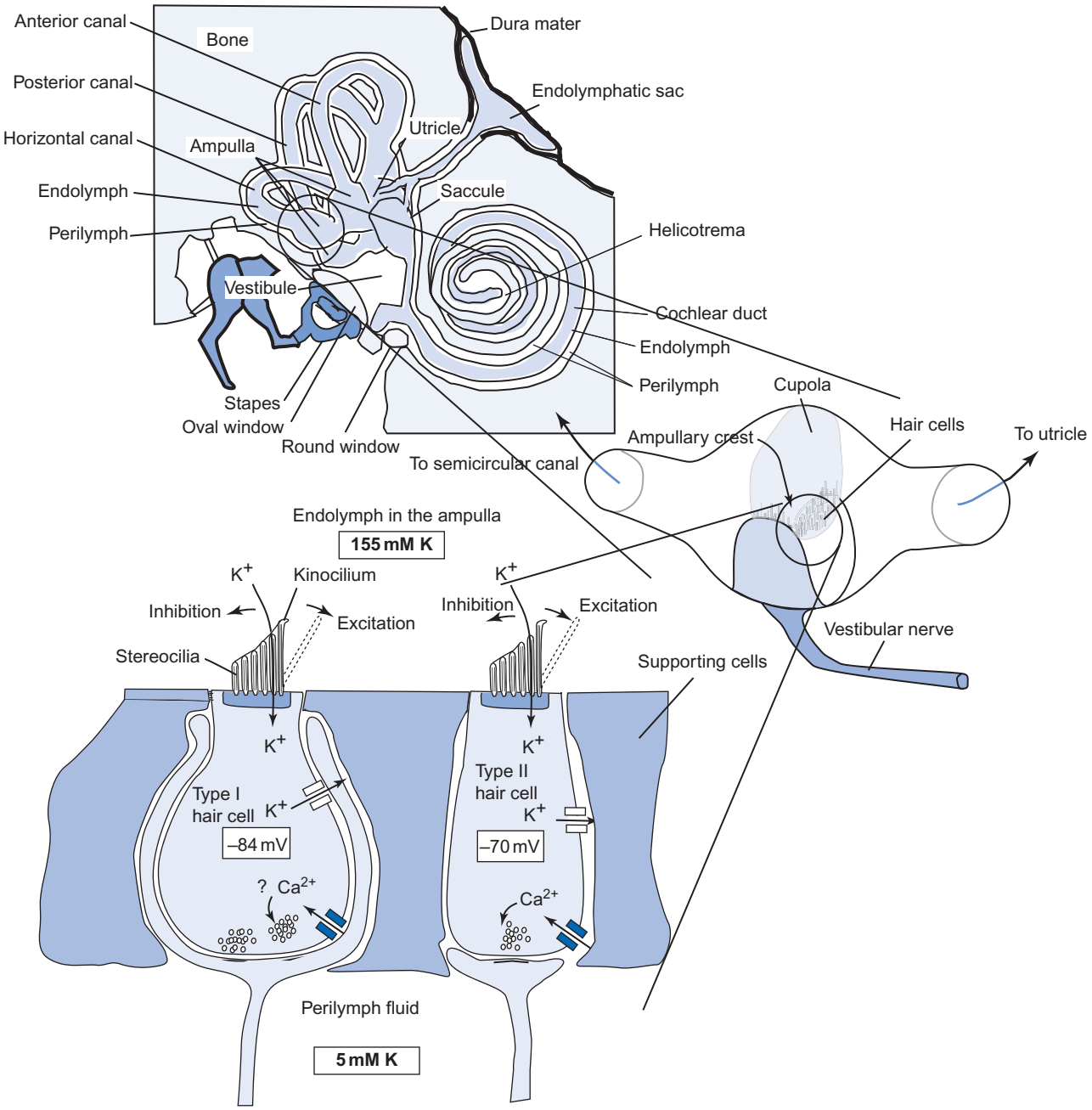

FIGURE 4.5.9 Structure of the vestibular apparatus. Hair cells in three semicircular canals provide dynamic sensation of movement of the head. The hair cells reside in an enlarged part of the canal called the ampulla. Three mutually perpendicular canals provide information that allows computation of the final vector of movement. The semicircular canals form part of the labyrinth that is surrounded by temporal bone (osseous labyrinth). The fluid within the labyrinth is endolymph, a special fluid that contains higher [K^+] than the intracellular fluid, so that opening of K^+ channels on the surface membrane produces an inward K^+ flux and depolarization of the cell. The hair cells are located on a ridge called the ampullary crest within the ampulla. A gelatinous mass called the cupola extends from the base of the hair cells to the opposite wall of the ampulla. Movement of the endolymph relative to the hair cells results in deformation of the "hairs" and changes in the membrane potential that results in neurotransmission to afferent sensory nerves that closely appose the hair cells' membrane. Static response to gravity originates from hair cells in the utricle and saccule.

produces excitation (it stretches the tip link) and movement toward the stereocilia inhibits the cell. There are two types of hair cells. Type I has a resting E_m of -84 mV and type II has a resting E_m of -70 mV. In type I cells the afferent sensory nerve nearly surrounds the hair cell and leaves a tiny microdomain between the two cells. The response of the afferent nerve cells may be related to ionic changes in this microdomain. Type I cells respond to stereocilia deformation with large receptor potentials, whereas the response of type II cells is smaller and shows **rectification**: the response is much greater to deformation toward the kinocilium than it is to deformation away from it. In type II cells, depolarization increases the conductance to Ca^{2+} along

its basal-lateral membrane. The local [Ca^{2+}] in this region causes vesicles containing neurotransmitter to fuse with the basal-lateral membrane, which in turn activates the sensory afferent neuron that innervates the hair cells (Figure 4.5.9).

ROTATION OF THE HEAD GIVES OPPOSITE SIGNALS FROM THE TWO VESTIBULAR APPARATUSES

Because the semicircular canals and the hair cells are rigidly attached to the head, they rotate with the head and initially sweep through the stationary endolymph. The endolymph does not immediately move, because of its inertia and lack of rigid attachment to the skeleton. Thus, rotation to the right entails a relative motion of the endolymph to the left. The labyrinth in the right ear is a mirror image of the one in the left, and the axes of the hair cells are also mirror images. The direction of endolymph movement will be to the left in both ears. Thus, the relative motion of the endolymph will be in the direction of the hair cell axis in one ear, and opposite in the other. Movement of the endolymph in the direction of the axis (toward the kinocilium) excites the cell, whereas movement opposite to the axis (away from the kinocilium) inhibits the cell. The hair cells in one ear respond with increased firing frequency upon rotation of the head, while the hair cells in the other ear respond with decreased firing frequency. This situation is shown schematically in Figure 4.5.10. The firing of hair cells in the three orthogonal semicircular canals informs the central nervous system about rotational acceleration in three dimensions.

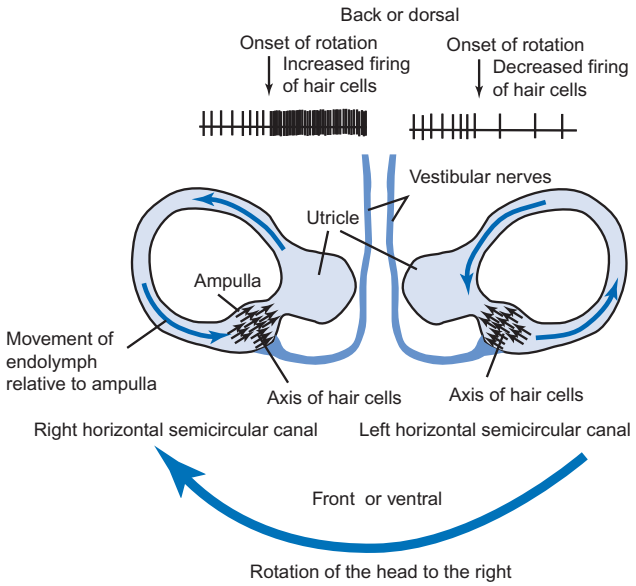

FIGURE 4.5.10 Response of hair cells in the horizontal semicircular canal to rotation of the erect head. Cross-sections of the horizontal semicircular canal are shown, as viewed from above. The nose faces the bottom of the page. Rotation of the head to the right, indicated by the arrow at the bottom of the figure, sweeps the ampullary crest through endolymph which resists the movement because of the fluid's inertia. Thus there is a relative movement of the endolymph to the left across the ampullary crest in both right and left inner ear. The hair cells, however, have mirror image orientations in the two inner ears, so that in the right ear the endolymph deforms the stereocilia toward the kinocilium whereas in the left ear (to the right in the figure) the deformation of the stereocilia is away from the kinocilium. Since movement toward the kinocilium is excitatory, the right ampulla increases its firing rate while the left ampulla decreases its firing rate.

THE UTRICLES AND SACCULES CONTAIN HAIR CELLS THAT RESPOND TO STATIC FORCES OF GRAVITY

The bilateral utricles and saccules contain specialized epithelia that is analogous to the ampullary crest. Each of these regions is called a **macula**. The macula in the utricle and saccule contains an array of hair cells whose stereocilia project into the **otolithic membrane**, a gelatinous mass that contains tiny crystals of calcium carbonate, called **otoliths** (literally, "ear stones"). When the head is held erect, the macula in the utricles is oriented in the horizontal plane whereas the macula in the saccule is oriented vertically. Gravity pulls on the dense otoliths, which deform the gelatinous mass and subsequently press on the stereocilia and influence the firing rate of the hair cells. Since gravity pulls constantly, the hair cells in the utricle and saccule provide tonic information about the orientation of the head.

THE AFFERENT SENSORY NEURONS FROM THE VESTIBULAR APPARATUS PROJECT TO THE VESTIBULAR NUCLEI IN THE MEDULLA

Sensory neurons from the vestibular apparatus joins the auditory sensory afferents to form **cranial nerve VIII**, the vestibular and auditory nerve. This nerve enters the central nervous system near the junction of the pons and the medulla. The vestibular sensory afferents synapse on neurons found in the vestibular nuclei in the lateral medulla. Four recognized areas make up the vestibular nuclei: the lateral vestibular nuclei have an inferior and a superior nucleus, and the medial vestibular nuclei also are divided into superior and inferior portions. Information in these nuclei travel down the cord in the **lateral vestibulospinal tract** to provide excitation for maintaining body posture. The medial and superior vestibular nuclei receive inputs primarily from the semicircular canals. They send processes onto three pairs of nuclei that control eye movement. The motor outputs of these three pairs of nuclei travel in cranial nerves **III (oculomotor)**, **IV (trochlear)**, and **VI (abducens)**. This pathway enables the reflex movement of the eyes to the left when the head rotates to the right. Because of this reflex, rapid movement of the head back and forth does not produce as blurred an image of the hand compared to rapid movement of the hand back and forth.

SUMMARY

The lower motor neurons provide the final common pathway by which muscles are activated. The sequence

Clinical Applications: Parkinsonism

In 1817 James Parkinson, an English physician, wrote a book entitled "An Essay on the Shaking Palsy" in which he described the disorder that is now known as **Parkinson's disease**. People with Parkinsonism exhibit rhythmic tremor at rest with lessened muscular power, rigidity, difficulty in initiating movements (**akinesia**) and slowness in executing movements **(bradykinesia**). More complex motor programs show the largest deficits. Patients with this disease cannot execute simultaneous or sequential motor tasks, indicating that the deficit lies in the activation of motor plans for complex motor tasks. Patients also cannot execute normal rapid movements. When thrown off balance, such a patient falls before righting reflexes can be activated.

Parkinson's disease is caused by damage to the projections of the substantia nigra to the neostriatum. These projections use dopamine as a neurotransmitter. The loss of these projections removes activation of the direct pathway that stimulates the supplementary motor cortex, and removes inhibition of the indirect pathway that inhibits the supplementary motor cortex through its action on the thalamus. This lack of dopaminergic stimulation removes the excitatory boost that is necessary for a critical level of activity in the supplementary motor cortex, and the result is tentative movement and reduced muscle recruitment.

Oral administration of L-DOPA (L-dihydroxy phenyl alanine, a precursor for dopamine synthesis; see Chapter 4.2) increases dopamine synthesis in the remaining substantia nigra cells. This temporarily relieves symptoms, but it does not postpone or mitigate further loss of dopaminergic cells in the nigrostriatal pathway. Parkinson's disease affects about 1% of the population over age 50.

of activation of particular lower motor neurons, their frequency of firing and duration of the train of action potentials determines the movement of the torso, limb or digits. Purposeful movement requires coordinated activation and inhibition of synergistic muscles and antagonistic muscles. Activation of the population of motor neurons that make up the pool supplying any given muscle determines the strength of contraction. Much of the basic pattern of these movements is provided by spinal reflexes, but purposeful movement itself originates in the cortex and is coordinated and modulated by the basal ganglia and cerebellum.

The primary motor cortex is a strip of cortex lying rostral to the central sulcus. Stimulation of this region has the lowest threshold for eliciting a motor response. Areas of the musculature map onto this primary motor cortex so that the leg is controlled by areas lying beside the longitudinal fissure, the arm is controlled by areas lateral to the fissure, and the facial muscles are controlled by areas further lateral. This somatotopic mapping mirrors the somatotopic sensory projection of the body. The somatosensory map and somatomotor map are connected through cortex lining the central sulcus. Although neurons in this primary motor cortex drive lower motor neurons most strongly, the primary motor cortex does not initiate motor commands. Rather, they execute them. Motor commands begin by comparing one's position in the world to the position one wants to be. The sensory association cortex receives sensory input from a variety of sources and integrates the information to form a neural map of the real world and the body's position in it. Motor plans originate in the prefrontal cortex, which forms its plans based on the output of the sensory association area. The prefrontal cortex forwards a "working memory" of the movement to the premotor cortex and supplementary motor cortex which prepares the body for movement by positioning the axis of the body and engaging the primary motor cortex.

The basal ganglia consists of a set of structures, the caudate nucleus, putamen, external and internal globus pallidi, the subthalamic nucleus, and the substantia nigra. These modulate movement by providing an excitatory boost to desired movement and inhibiting undesired movements. The direct pathway excites the supplementary motor cortex and the indirect pathway inhibits it. The substantia nigra sets the balance between the indirect and direct pathways.

The cerebellum receives a duplicate of the motor commands over the mossy fibers arising from pontine nuclei. Simultaneously, sensory fibers from the inferior olivary nucleus reach the cerebellum over climbing fibers. This mingling of motor commands and sensory information allows the cerebellum to condition movement to match its intended target.

Hair cells in special structures of the inner ear detect the static pull of gravity and the acceleration of the head. These hair cells have stereocilia that respond to movement. Hair cells in the utricle and saccule detect static gravity while hair cells in the ampulla of the three semicircular canals detect acceleration. These cells are bathed in endolymph, which is distinctive because of its high $[K^+]$. Opening of K^+ channels on the apical membrane of the hair cells depolarizes the cells, causing them to release neurotransmitters to afferent sensory neurons adjacent to the hair cells. This occurs when the endolymph moves relative to the hair cells during acceleration. This sensory information is carried over cranial nerve VIII to the vestibular nuclei in the medulla, which sends information down the cord to maintain posture and to centers that control eye movement.

REVIEW QUESTIONS

1. What neurons directly control muscle contraction? Where are the cell bodies of these neurons?
2. What is a motor unit? How is muscle contraction graded?
3. What is the primary motor cortex? Where is the sensory association area? Where is the premotor cortex and the supplementary motor cortex? What is the somatotopic mapping of motor control?
4. What role does the spinal cord play in control of movement?
5. What happens when there is damage to the sensory association area?
6. Name the basal ganglia. What is the major input to the caudate nucleus? To the putamen?
7. What is the direct pathway? Does it promote or inhibit wanted effort? How does it do this?
8. What is the indirect pathway? Does it promote or inhibit wanted effort?
9. What role does the substantia nigra play in the control of movement by the basal ganglia? What disease is association with dysfunction of the substantia nigra?
10. What information is carried by the mossy fibers? The climbing fibers? What happens when cerebellar function is compromised?
11. What is the endolymph? What is the perilymph? How do hair cells detect acceleration? Where is the information processed in the CNS?