CHAPTER

2

The Nervous System

Chapter Outline

- Cells in the Nervous System
- The Nervous System
- Cerebral Blood Flow and Cerebrospinal Fluid
- Genes and the Physiological Processes of Cells
- From Actions to Effects: Advances in Therapeutic Use of CRISPR Genetic Technology

Learning Objectives

- Explain the components and functions of cells in the nervous system
- Identify the features and functions of structures and systems in the nervous system
- Describe the function of genes and their impact on cells

The study of psychoactive drugs requires knowledge about how drugs act on the nervous system. This chapter provides a basic overview of the nervous system, with an emphasis on cells and structures important for psychoactive drug effects.

Cells in the Nervous System

Each structure of the brain contains a dense ensemble of neurons and glial cells. **Neurons** are specialized cells in the nervous system that control behavior, convey sensory information, and signal movement. Neurons communicate by receiving and transmitting information to neurons and glial cells in the nervous system via chemicals called *neurotransmitters* (covered in Chapter 3). **Glial cells** support the function of neurons. General estimates give the brain approximately 86 billion neurons and just as many non-neuronal cells, including glial cells (Herculano-Houzel, 2012).

Neurons
Specialized cells in the nervous system that control behavior, convey sensory information, and signal movement

Glial cells (or glia cells)
Cells that support the function of neurons

Neurons

Neurons comprise dense communication networks in the brain. These networks support the function of individual brain structures and facilitate communication between structures. Like other cells in the body, neurons have basic characteristics such as a membrane, nucleus, ribosomes, and an endoplasmic reticulum (**Figure 2.1**), yet they have many unique characteristics for cellular communication.

Neurons have four major components: a soma, dendrites, axon, and axon terminal (**Figure 2.2**). The soma is the body of the neuron. It also contains the nucleus, which holds DNA. Overall, components within the soma support a neuron's basic physiological processes.

FIGURE 2.1 **Soma of a Neuron**

The soma of a neuron contains the same basic components that other cells of the body have.

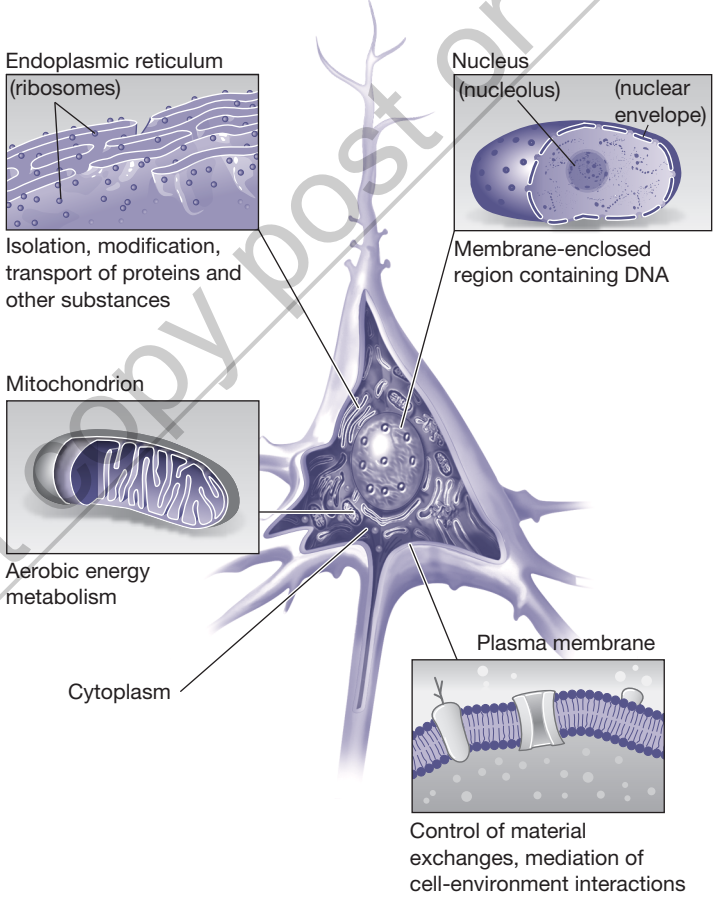
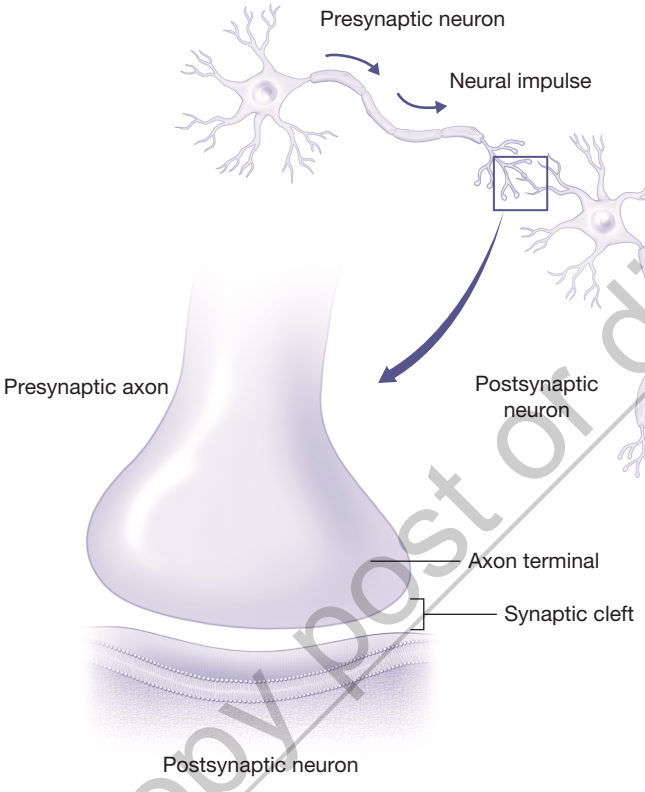


FIGURE 2.2 Major Components of a Neuron

The four major components of a neuron are the soma, dendrites, an axon, and an axon terminal. Dendrites receive information, and axons send information.



Generally, a neuron has many dendrites that branch off from the soma. The **dendrites** of a neuron receive information from other neurons. Small stems called *dendritic spines* grow along the length of dendritic branches. The membranes of dendrites and dendritic spines contain proteins called *receptors* that neurotransmitters can activate. When activated, receptors cause changes in the functioning of the neuron.

Dendrites
Parts of a neuron that receive information from other neurons

Axons release neurotransmitters for signalling with other neurons. Most neurons have only one axon, which branches from the soma, usually opposite from the dendrites. An axon begins at a part of the soma called the *axon hillock* and ends with multiple branches containing axon terminals.[1] These branches are called *axon collaterals*. An axon terminal contains and releases neurotransmitters near a part of a dendrite called a *postsynaptic terminal*. The postsynaptic terminal contains

Axons
Part of a neuron that releases neurotransmitters for signalling with other neurons

[1]Also referred to as *presynaptic terminals*.

receptors for neurotransmitters. The small space between the axon terminal and postsynaptic terminal is called the *synaptic cleft*. The term **synapse** refers to the components that comprise this connection—the axon terminal, the postsynaptic terminal, and the synaptic cleft.

Synapse
Components that make up a connection between neurons that includes an axon terminal, postsynaptic terminal, and synaptic cleft

Neuroscientists use different terms to describe the location of a neuron and the direction of its axon. The term **interneuron** describes a neuron with the soma and axon found within the same structure (**Figure 2.3**). An *afferent* neuron has an axon *going to* another structure. **Sensory neurons**, which convey sensory information via axons to the central nervous system, are considered afferent neurons. An *efferent* neuron has an axon *coming from* a structure. **Motor neurons** (or **motoneurons**), which convey motor information via axons from the central nervous system, are considered efferent neurons (Figure 2.3). Thus, the terms *afferent* and *efferent* can refer to any structure being studied. For example, the thalamus, a structure that routes sensory information to different parts of the cerebral cortex, has both types of neurons: afferent neurons send axons *to* the thalamus, and efferent neurons send axons *from* the thalamus.

Interneuron
Neuron with the soma and axon found within the same structure

Sensory neuron
Neuron that conveys sensory information via axons to the central nervous system

Motor neuron (or motoneuron)
Neuron that conveys motor information via axons from the central nervous system

Glial Cells

Glial cells consist of three different types: (1) oligodendrocytes, (2) astrocytes, and (3) microglial cells (**Figure 2.4**). **Oligodendrocytes** extend their membranes around axons to form a material called *myelin*. Myelin is found in segments along the length of an axon, and myelin serves to facilitate the movement of electrical impulses down an axon (more on this in Chapter 3). A single oligodendrocyte can provide myelin for multiple neurons and for multiple segments of an axon. *Schwann cells* are like oligodendrocytes, but they are found in the peripheral nervous system and they extend themselves around an axon to form only a single segment of myelin. Motor dysregulation, paralysis, and other symptoms of multiple sclerosis result from degeneration of myelin sheaths surrounding axons in the nervous system.

Oligodendrocyte
Glial cell that forms a material called myelin around the axons of neurons

Astrocytes play a role in forming the blood–brain barrier, facilitating neuronal function, and responding to injury. Astrocytes form the blood–brain barrier (discussed in Chapter 5) by forcing endothelial cells to fit tightly together. Astrocytes support neuronal function through acting at synapses during neurotransmission, which we consider in Chapter 3.

Astrocyte
Glial cell that plays a role in forming the blood-brain barrier, facilitating neuronal function, and responding to injury

Microglial cells remove normal cellular waste and serve as immune cells in the central nervous system. Two types of microglial cells exist: M1 and M2. M1 microglial cells release chemicals that promote inflammation and can damage the blood–brain barrier, whereas M2 microglial cells release chemicals that reduce inflammation and promote the growth and development of cells. Inflammation caused by M1 microglial weakens the blood–brain barrier, allowing in cells that can damage neurons. The potential for inflammation-induced damage to neurons to contribute to mental and neurological disorders provides an important reason to study microglial cells (Nakagawa & Chiba, 2015).

Microglial cell
Glial cell that removes normal cellular waste and serves as an immune cell in the central nervous system

FIGURE 2.3 Motor Neurons, Sensory Neurons, and Interneurons

Motor neurons convey movement information to muscles in the body, and sensory neurons convey sensory information to the central nervous system (CNS). Relative to the central nervous system, motor neurons are efferent neurons (going away from the CNS), and sensory neurons are afferent neurons (going to the CNS). Interneurons have the soma, dendrites, and axon all contained within the same structure.

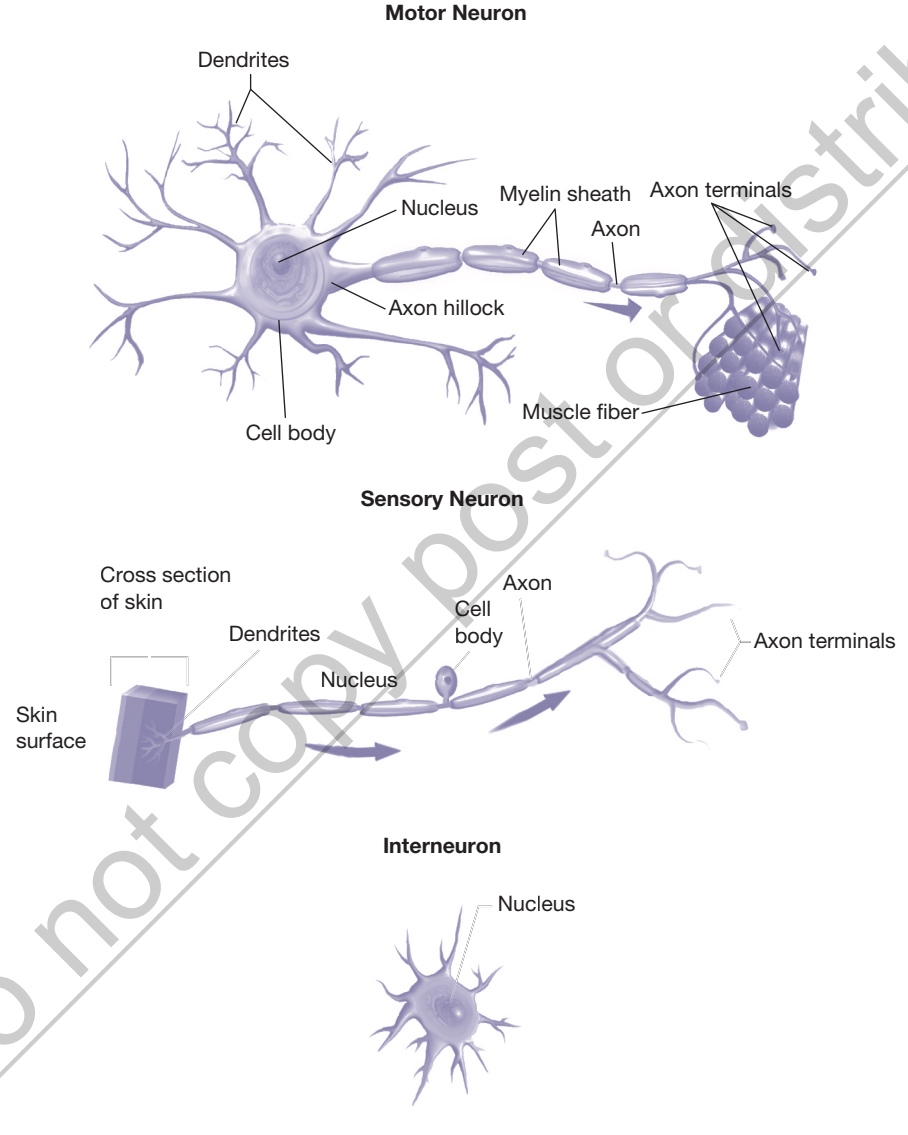
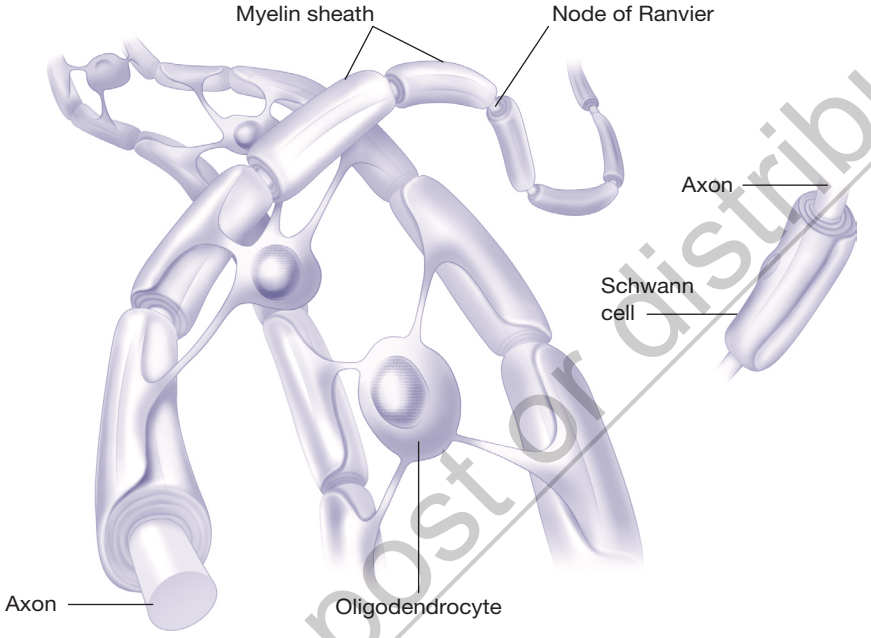


FIGURE 2.4 Glial Cells

Glial cells support neuronal functioning. Oligodendrocytes and Schwann cells provide myelin sheathing for axons. Astrocytes form the blood–brain barrier, break down certain neurotransmitters, and respond to injury in the nervous system. Microglial cells remove cellular waste.



STOP & CHECK

1. What are the two types of cells found in the brain?
2. _____ receive information from other neurons, and _____ send information to other axons.
3. Sensory neurons are also called _____ neurons because axons go to the central nervous system.
4. Which types of glial cells provide myelin sheathing for axons?

1. Neurons and glial cells **2.** Dendrites, axons **3.** afferent **4.** Oligodendrocytes produce myelin sheathing around axons in the central nervous system, and Schwann cells produce myelin sheathing around axons outside of the central nervous system.

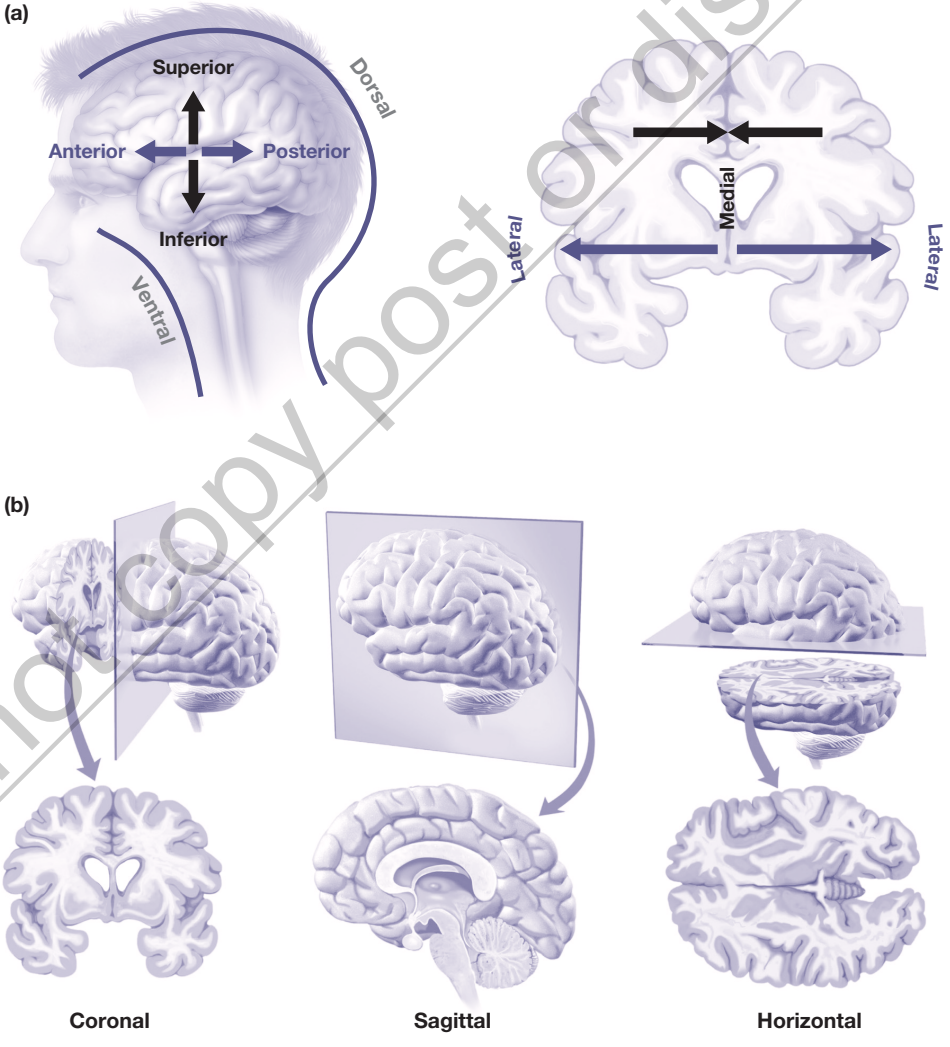
The Nervous System

Learning the basic terms used to describe where nervous system structures are located is an important first step for studying the brain. Standard terms describe

the location of structures in the nervous system. For example, we refer to the front portion of the brain as *anterior* and the back portion of the brain as *posterior*. The bottom of the brain, the side that faces toward the stomach, is referred to as the *ventral* side, and the top of the brain is referred to as the *dorsal* side. We refer to structures near the sides of the brain as *lateral*; structures near the middle of the brain are described as *medial*. **Figure 2.5** presents these and other terms that describe structures in the brain.

FIGURE 2.5 The Human Brain

The human brain can be dissected in coronal (i.e., frontal), sagittal, and horizontal sections. We use special terms to describe the location of structures in the brain. See text for further details.



Looking at structures inside the brain may be accomplished through any of three basic types of dissection planes. Slicing the brain from anterior to posterior produces a *coronal* (or *frontal*) section. We produce horizontal sections by slicing the brain from dorsal to ventral, and sagittal sections provide lateral views of the brain. Dissection planes provide different perspectives of a structure.

The Peripheral Nervous System

The nervous system consists of two systems: (1) the peripheral nervous system and (2) the central nervous system (CNS). Much of what we discuss in this book pertains to the central nervous system, which consists of the brain and spinal cord. Drugs also have many effects on the peripheral nervous system, which contains two subsystems called the *somatic nervous system* and *autonomic nervous system* (**Figure 2.6**).

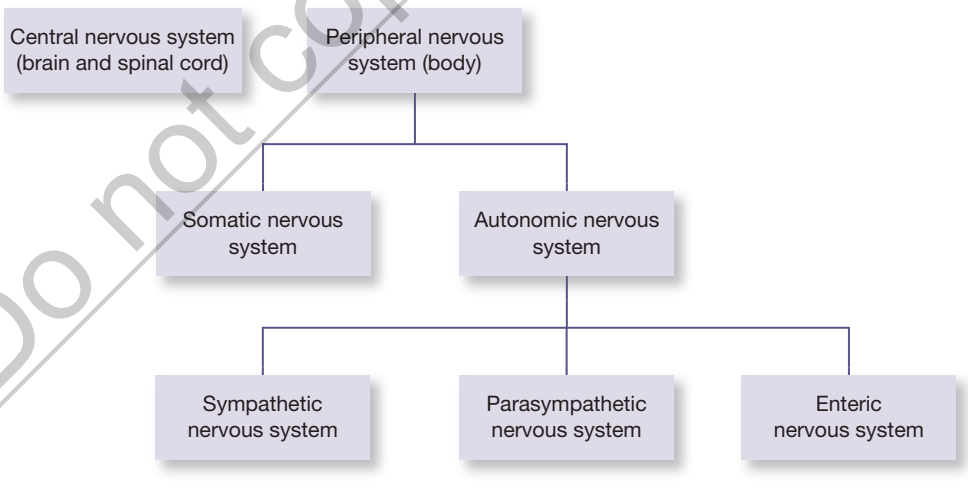
Somatic nervous system
System responsible for delivering voluntary motor signals from the central nervous system to muscles throughout the body and for conveying sensory information from the body to the central nervous system

The Somatic Nervous System: Delivering Motor Signals to Muscles and Sensory Signals to the Spinal Cord

The **somatic nervous system** is responsible for delivering voluntary motor signals from the CNS to muscles and for conveying sensory information from the body to the CNS. Thus, the somatic nervous system is made up of motor neurons and sensory neurons. Sensory neurons send information to the dorsal part of the spinal cord (through the *dorsal root* to the *dorsal horn*), whereas motor signals are sent

FIGURE 2.6 The Peripheral Nervous System

The peripheral nervous system contains the somatic nervous system and the autonomic nervous system. The autonomic nervous system consists of the sympathetic nervous system, the parasympathetic nervous system, and the enteric nervous system.



to muscles from the ventral part of the spinal cord (from the *ventral horn* to the *ventral root*) (**Figure 2.7**). The point where a motor neuron meets a muscle fiber is called the *neuromuscular junction*. Muscles contract when motor neurons release the neurotransmitter acetylcholine at neuromuscular junctions.

Autonomic nervous system System that controls involuntary movements for vital functions, such as heartbeat, breathing, swallowing, and digestion

Sympathetic nervous system Subsystem of the autonomic nervous system that prepares the body for rigorous activity by increasing heartbeat, inhibiting digestion, and opening airways, among many other involuntary functions

The Autonomic Nervous System: Controlling Vital Functions

Whereas the somatic nervous system produces voluntary movement, the **autonomic nervous system** controls involuntary movements for functions such as heartbeat, breathing, swallowing, digestion, and sweating by controlling heart muscle, smooth muscle, and exocrine glands. Exocrine glands secrete substances through a duct, such as sweat, saliva, and tears. The autonomic nervous system consists of three systems: (1) the sympathetic nervous system, (2) the parasympathetic nervous system, and (3) the enteric nervous system (**Figure 2.8**). The **sympathetic nervous system** prepares the body for rigorous activity by increasing heartbeat, inhibiting digestion, and opening airways, among many other involuntary functions. The **parasympathetic nervous system** is dominant during relaxed states and decreases heartbeat, stimulates digestion, and closes airways. The **enteric nervous system** controls digestion via communication within its system and with the central nervous system (Furness, 2007).

Both the sympathetic and parasympathetic nervous systems contain ganglia (singular *ganglion*). *Ganglia* are clusters of neuron cell bodies for neurons in the sympathetic and parasympathetic nervous systems. A ganglion fully contains a

FIGURE 2.7 Spinal Cord

Sensory neurons send information to the dorsal part of the spinal cord, whereas motor signals are sent to muscles from the ventral part of the spinal cord. Gray matter appears in the middle portion of the spinal cord forming an H shape. White matter appears in the outermost portions of the spinal cord.

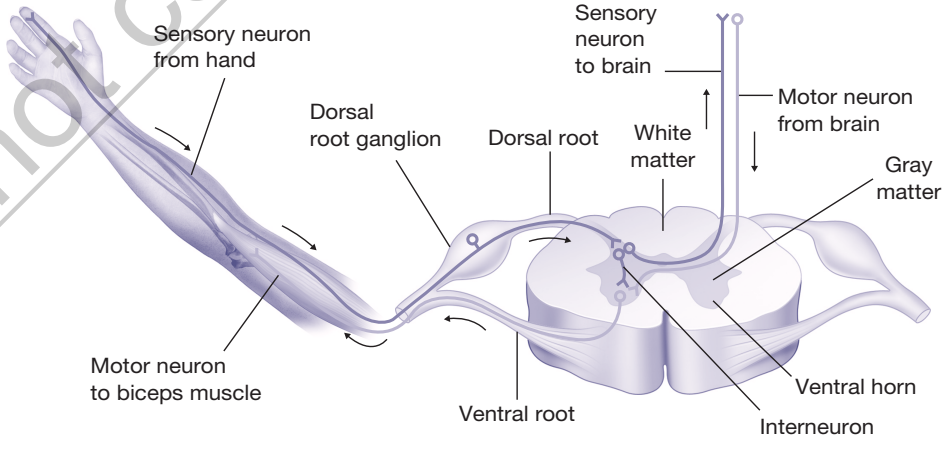
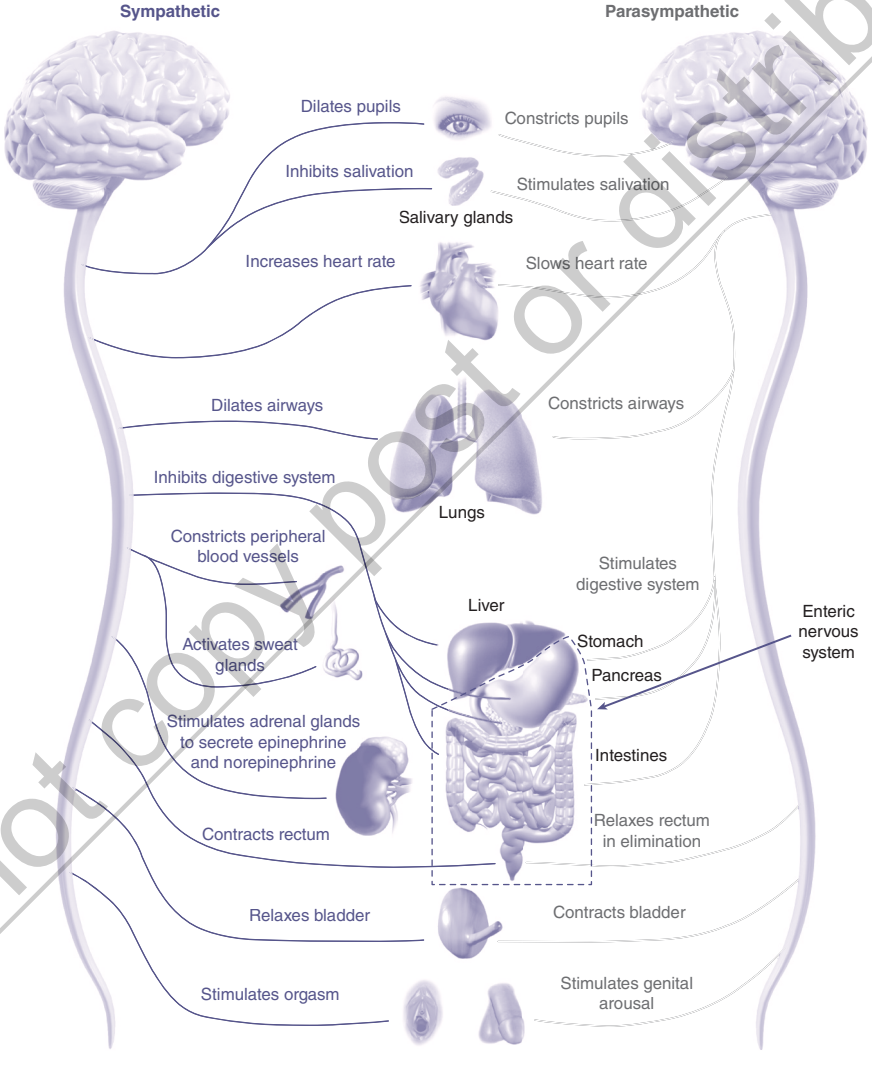


FIGURE 2.8 Autonomic Nervous System

The autonomic nervous system is made up of the sympathetic nervous system, the parasympathetic nervous system, and the enteric nervous system. The sympathetic nervous system enhances the activity of organs in the body and the parasympathetic nervous system diminishes the activity of these same organs. The activation of each system occurs by preganglionic neurons releasing acetylcholine in ganglia, which binds to receptors on postganglionic neurons. The enteric nervous system controls digestion, and it carries out independent functions as well as responding to information from the central nervous system.



neuron's soma and dendrite, while a neuron's axon extends from the ganglion to a muscle or gland. We call this a *postganglionic* neuron because its axon comes after the ganglion and goes to a muscle or gland. A neuron that instead sends an axon from the spinal cord to a ganglion is referred to as a *preganglionic* neuron.

Preganglionic neurons control sympathetic and parasympathetic nervous system neurons by releasing the neurotransmitter acetylcholine at synapses for postganglionic neurons. Through the process of neurotransmission (discussed in Chapter 3) acetylcholine makes these postganglionic neurons more active. Axons for the activated postganglionic neurons then release neurotransmitters at their axon terminals. This leads target muscles or glands to have increased (for sympathetic nervous system neurons) or decreased (for parasympathetic nervous system neurons) activity.

Parasympathetic nervous system Subsystem of the autonomic system that is dominant during relaxed states, including decreases in heartbeat, stimulation of digestion, and the closing of airways

The enteric nervous system consists of 200-600 million neurons found within the gastrointestinal tract, with thousands of ganglia located throughout the system. While this system communicates with the central nervous system, the enteric nervous system handles many of its functions independently—this makes the system unique from the other systems in the peripheral nervous system. As discussed in Chapter 3, the nature of afferent communication to the central nervous system creates a number of intriguing research questions concerning bacteria that live in the gut and the chemical messengers released from these bacteria (Furness, 2007).

Enteric nervous system Subsystem of the autonomic system that controls digestion via communication within its system and with the central nervous system

STOP & CHECK

1. Brain sections produced by slicing the brain from anterior to posterior are referred to as _____ sections.
2. The somatic nervous system delivers movement signals to muscles by releasing acetylcholine at _____.
3. The _____ system controls vital functions such as breathing and heartbeat.

1. coronal 2. neuromuscular junctions 3. autonomic

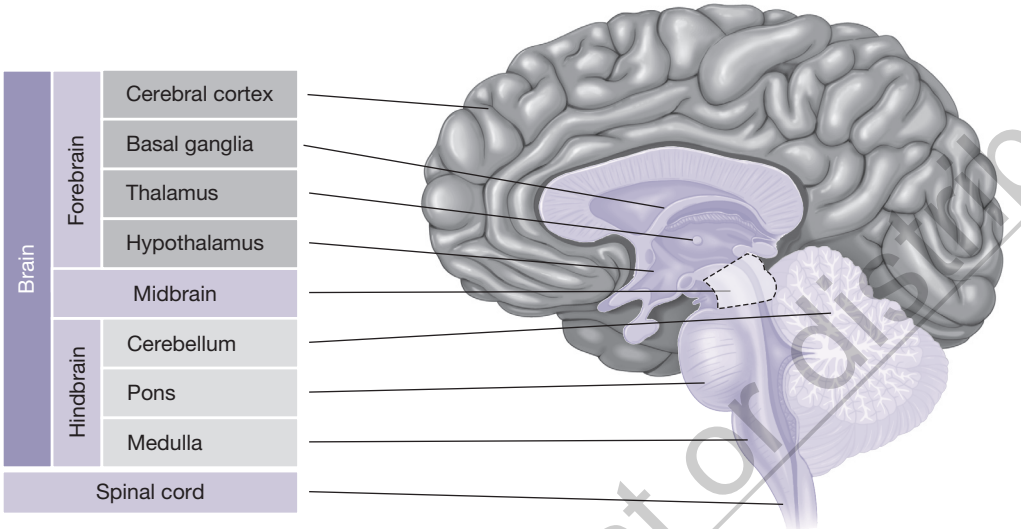
The Central Nervous System

The brain and spinal cord make up the central nervous system (**Figure 2.9**). The surface of the brain—the **cerebral cortex**—has hills called *gyri* (singular *gyrus*) and valleys called *sulci* (singular *sulcus*). The base of the brain, where the spinal cord meets, is called the *brain stem*. Above the brain stem sits a structure called the *cerebellum*. The brain is divided into two hemispheres, left and right. Structures found in one hemisphere have a matching structure in the other hemisphere.

Cerebral cortex The surface of the brain; comprising gyri and sulci

FIGURE 2.9 **Regions of the Brain**

The brain is divided into three different divisions or regions called the *hindbrain, midbrain*, and *forebrain*.



The brain has three different divisions called the *hindbrain, midbrain*, and *forebrain,* also shown in Figure 2.9. The hindbrain consists mostly of the brain stem, and it begins where the spinal cord meets the brain stem at a structure called the *medulla*. The midbrain comprises a region between the hindbrain and forebrain; it includes the *inferior colliculus*, which plays a role in auditory processing, and the *superior colliculus*, which directs eye movement. The forebrain includes the rest of the brain and contains the cerebral cortex and structures beneath the cerebral cortex, such as the *corpus callosum, basal ganglia, thalamus*, and *hypothalamus*.

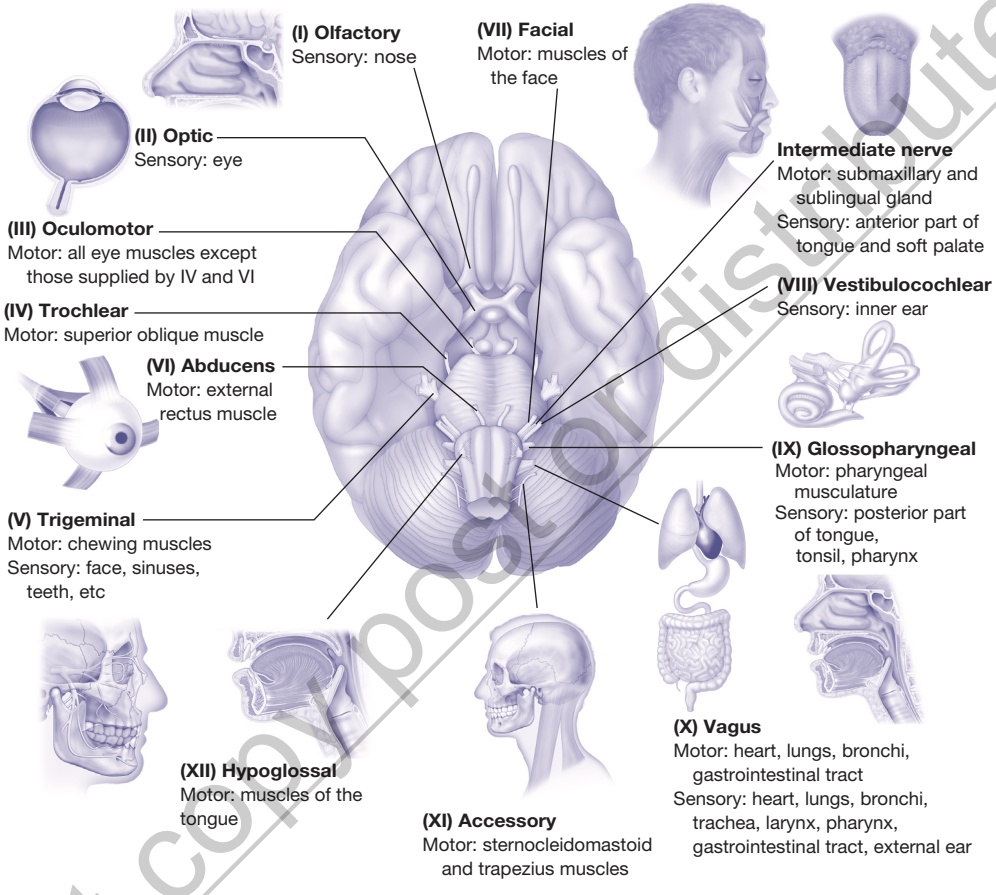
The Medulla and Hypothalamus: Controlling Unlearned Behaviors

Medulla
Structure that controls the autonomic nervous system and is situated where the spinal cord meets the hindbrain

We previously discussed the autonomic system, which maintains vital functions in the body. The autonomic nervous system is controlled by the medulla (**Figure 2.10**). As already described, the **medulla** rests where the spinal cord meets the hindbrain. In fact, from the surface, the medulla looks like a thicker section of spinal cord. Through controlling the autonomic nervous system, the medulla controls basic autonomic functions such as breathing, heart rate, and vomiting. Many of the cranial nerves also come from the medulla. These nerves are devoted to movement and sensations of the head (**Figure 2.10**). There are 12 cranial nerves, each noted by its number and name.

FIGURE 2.10 Ventral Surface of the Brain

The ventral side of the brain reveals many features, including the structures in the brain stem and all 12 of the cranial nerves.



Source: Encyclopaedia Britannica/Contributor/Universal Images Group/Getty.

The vagus nerve (roman numeral X) differs from the functions of the other cranial nerves because it controls and receives sensory information from various internal organs in the body, including the heart, liver, and intestines. The vagus nerve serves as a primary line of intercommunication between the enteric nervous system and the central nervous system. Mostly afferent axons (again, going to the central nervous system) make up the vagus nerve, and in the brain, the vagus nerve sends input to a hindbrain structure called the *nucleus of the solitary tract*. Outputs from the nucleus of the solitary tract reach the medulla (in the hindbrain) and many structures in the forebrain, including the hypothalamus, thalamus, amygdala, and cerebral cortex (Schachter & Saper, 1998).

Given that the vagus nerve is accessible outside of the brain and that it interacts with numerous systems in the brain, clinical researchers have explored *vagal nerve stimulation* as a therapeutic strategy. Vagal nerve stimulation occurs through surgically installing an electrical pulse generator in the chest and connecting it to wire wrapped around a portion of the vagus nerve in the throat. The procedure is FDA approved in the United States for reducing seizures in epilepsy and for treatment-resistant depression (i.e., depression not improved by psychotherapy or antidepressant drugs) (O'Reardon, Cristancho, & Peshek, 2006; Schachter & Saper, 1998).

Damaging the medulla can be life threatening, and suppressing its functioning can be just as dangerous. Narcotics and central nervous system depressants suppress medullary functions, which can be fatal at high-enough doses. Moreover, mixing two or more CNS depressants at otherwise safe amounts can produce combined suppressant effects on medullary functions.

Hypothalamus
Structure found in the forebrain that maintains important physiological conditions, in part by motivating an organism's behavior

The **hypothalamus**, a structure found in the forebrain, maintains important physiological conditions (**Figure 2.11**). The hypothalamus maintains many physiological processes by motivating an organism's behavior. When the body requires food, for example, the hypothalamus elicits feelings of hunger. Similarly, the hypothalamus elicits thirst when we become dehydrated. Other processes the hypothalamus regulates include body temperature, sleep, and motivation for sexual activity.

The hypothalamus controls the *pituitary gland*, which sits on the ventral surface of the brain. The pituitary gland releases many hormones into the bloodstream, affecting organ functions in the body. These effects include water absorption into the kidneys, growth, thyroid function, and reproductive functions. The hypothalamus also controls the *pineal gland*, another forebrain structure that is responsible for the release of *melatonin*, a sleep-regulating hormone.

STOP & CHECK

1. The central nervous system contains the brain and _____.
2. What is the primary structure in the brain for controlling autonomic functions?
3. How does the hypothalamus alter hormone levels in the body?

1. spinal cord 2. The medulla 3. The hypothalamus controls the pituitary gland, which releases many hormones throughout the body.

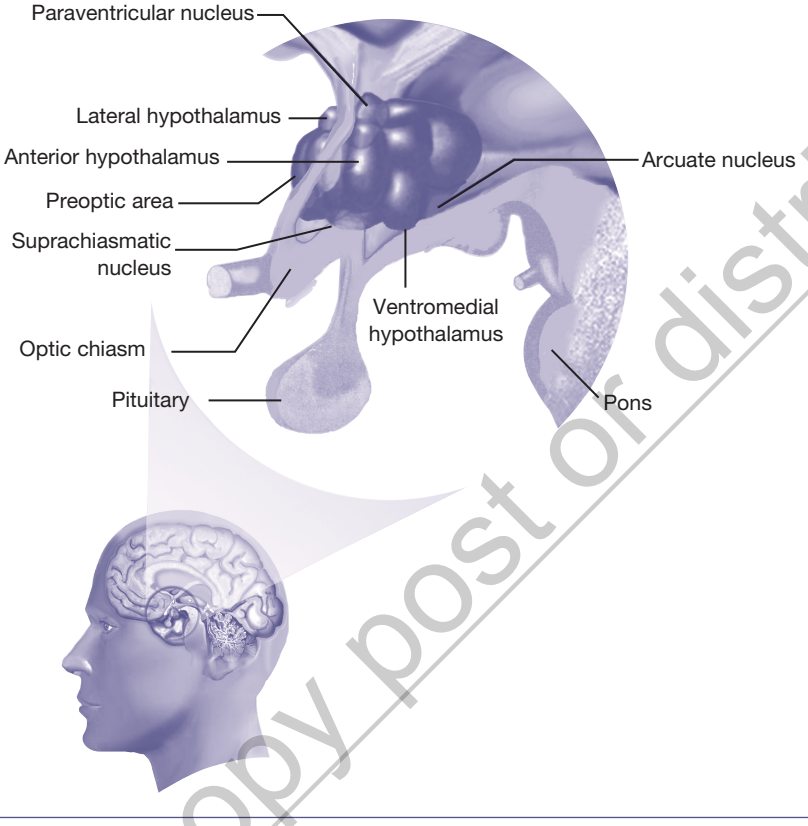
The Limbic System: Controlling Emotional Behaviors

Limbic system
Series of structures that together appear to form a ring around the thalamus and hypothalamus

The **limbic system** consists of a series of structures that together form a ring around the thalamus and hypothalamus. These limbic system structures include the *cingulate gyrus, hippocampus, amygdala,* and *olfactory bulb* (**Figure 2.12**). Many structures within the limbic system control emotional behavior. The amygdala, for

FIGURE 2.11 The Hypothalamus

The hypothalamus plays an important role in homeostasis, partly by eliciting motivation for various physiological activities such as eating and drinking.



example, facilitates fear and aggression. Many drugs that reduce anxiety decrease the activity of neurons in the amygdala.

The **nucleus accumbens** rests adjacent and anterior to the amygdala and facilitates rewarding effects. For this reason, we refer to the nucleus accumbens as the brain's *reward center*. The nucleus accumbens belongs to a network of other structures referred to as the *reward circuit*. Chapter 5 presents more information on the brain's reward circuitry and the role this circuitry plays in the rewarding effects of abused substances.

Nucleus accumbens Limbic system structure that facilitates rewarding effects

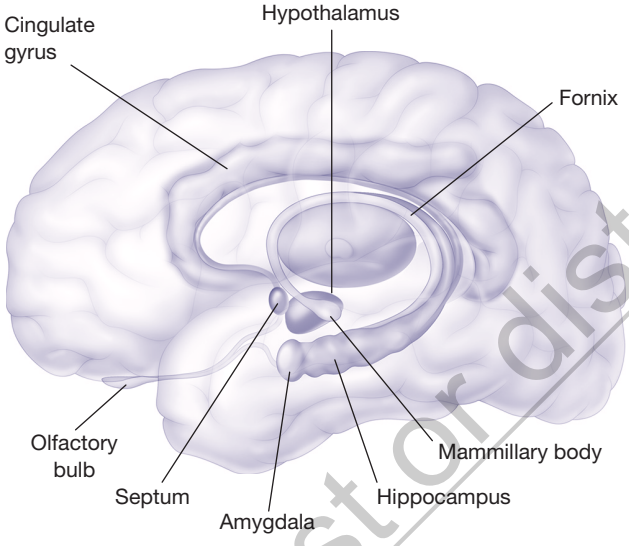
The Cerebral Cortex: Processing Sensory Information, Controlling Cognitive Functions, and Eliciting Movement

Four lobes divide the cerebral cortex (**Figure 2.13**). The **occipital lobe** is the most posterior portion of the cerebral cortex and processes visual information. The

Occipital lobe Region of the cerebral cortex important for processing visual information

FIGURE 2.12 The Limbic System

The limbic system generally is important for emotion, although the hippocampus also plays an important role in long-term memory.



Source: Carolina Hrejsa/Body Scientific Intl.

Temporal lobe
Region of the cerebral cortex important for processing auditory information and supporting language comprehension and production

Parietal lobe
Region of the cerebral cortex important for processing touch information

Frontal lobe
Region of the cerebral cortex important for decision making and movement

Prefrontal cortex
Most anterior part of the frontal cortex; an integration area for all types of sensory input; initiates movements

Thalamus
Forebrain structure that routes sensory information from the body to the appropriate lobes

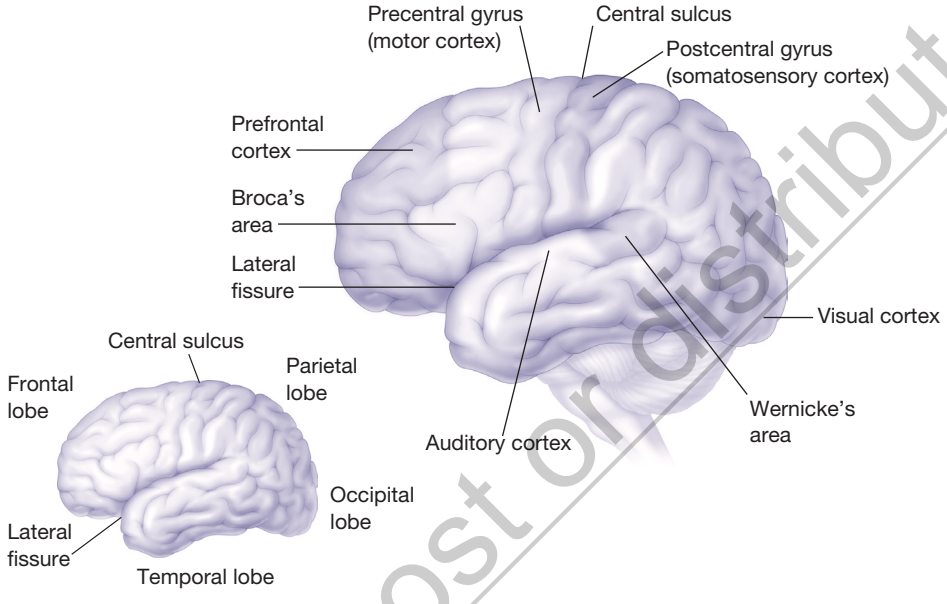
temporal lobe is anterior to the occipital lobe and below the parietal lobe. The temporal lobe processes auditory information and supports language comprehension and production. This area of the cerebral cortex also processes certain aspects of vision, including shape and color analysis. The **parietal lobe** is anterior to the occipital lobe and above the temporal lobe and includes the *somatosensory cortex*, the structure responsible for processing touch information from the body. The parietal lobe also analyzes visual information that contains movement.

The **frontal lobe**, which is at the anterior of the brain, supports decision making and movement. The frontal lobe contains the motor cortex. The most anterior part of the frontal lobe is called the **prefrontal cortex** and is an integration area for all types of sensory input and where the signal to produce movement occurs. Prefrontal cortical function also supports short-term memory and attention.

The **thalamus** routes sensory information from the body to the appropriate lobes. For example, visual information is sent from the eyes through the thalamus and to the occipital lobe, whereas auditory information is sent from the ears through the thalamus and to the temporal lobe. Olfactory information, however, is sent directly to the prefrontal cortex. After processing, all sensory information integrates in the prefrontal cortex.

FIGURE 2.13 Lobes of the Cerebral Cortex

Each lobe of the cerebral cortex processes different types of sensory information. The prefrontal cortex, within the frontal lobe, is an integration center for all types of sensory information.



STOP & CHECK

1. What are the primary functions of the amygdala and nucleus accumbens?
2. Which lobe analyzes sound, including language?
3. What role does the thalamus play in processing sensory information?

1. The amygdala elicits feelings of fear, anxiety, and aggression, whereas the nucleus accumbens elicits rewarding effects. 2. Temporal lobe 3. The thalamus routes sensory information to the appropriate lobes of the cerebral cortex.

The Frontal Lobe and Basal Ganglia: Controlling Voluntary Movement

After the prefrontal cortex signals a movement to occur, the **motor cortex** sends movement signals to the body via neurons (in this case, referred to as *tracts*) that cross from one hemisphere to the opposite side of the body to the limbs, hands, and feet. Tracts sent to the middle parts of the body, for posture and balance, have far fewer neurons crossing to the opposite side of the body.

Motor cortex Part of the frontal lobe that sends movement signals to the body

Basal ganglia
Forebrain structure that aids in the stabilization of movement

The **basal ganglia** act to stabilize voluntary movements (**Figure 2.14**). The basal ganglia, also called the *striatum*, have three major substructures: the *caudate nucleus*, the *putamen*, and the *globus pallidus*. The term *ganglia* used for this structure comes from early anatomical studies that considered these to be distinct structures, but modern physiologists consider the basal ganglia as a single structure (Lanciego, Luquin, & Obeso, 2012). The *substantia nigra* aids in regulating activity in the basal ganglia. The primary symptoms of Parkinson's disease, a disorder characterized by muscle rigidity, tremor, and resistance to voluntary movement, occurs from the destruction of substantia nigra neurons that go to the basal ganglia. Many of the first drugs to treat schizophrenia, called *antipsychotic drugs*, disrupt these neurons, leading to Parkinson-like symptoms called *extrapyramidal side effects*.

Pons
A hindbrain structure that elicits startle reflexes

Cerebellum
A hindbrain structure that facilitates balance and the timing of movements

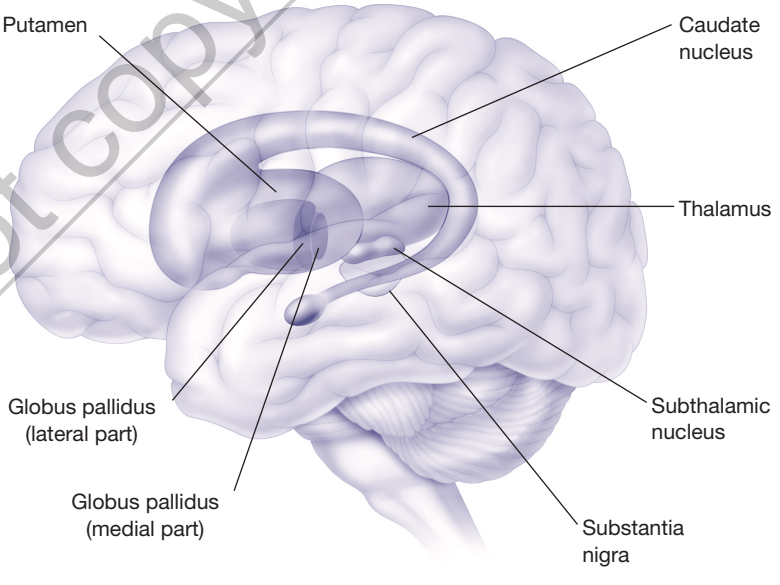
Some other components of the overall motor system must be noted. The **pons**, a structure located just above the medulla in the hindbrain, elicits startle reflexes. The **cerebellum** facilitates balance and the timing of movements.

Learning and Memory Processes in the Brain

Psychologists characterize short- and long-term memories in different ways. Most consider short-term memory as working memory. *Working memory* consists of short-term verbal or nonverbal memories employed when carrying out a task. In essence, we are "working" with memory. *Long-term memory* (or *reference memory*),

FIGURE 2.14 Basal Ganglia

The basal ganglia, which include the globus pallidus, putamen, and caudate nucleus, regulate movement signals sent from the motor cortex.



consists of stored verbal and nonverbal information. Long-term memories include information that we can declare, such as the capital of the United States, or information we can demonstrate, such as how to swing a golf club.

The prefrontal cortex facilitates working memory function. Recall that information from all sensory modalities integrates in the prefrontal cortex. The prefrontal cortex uses this information to control behavior when engaging in a task.

Long-term memory formation and retrieval requires the **hippocampus**. The hippocampus then sends information to the prefrontal cortex, possibly for use during working memory function. Damage to the hippocampus in Alzheimer's disease may account for impairments in long-term memory. Long-term motor memories, also referred to as *procedural memories*, may depend on the basal ganglia. Procedural memories include such things as riding a bicycle or tying a shoelace.

Hippocampus
A forebrain structure in the limbic system important for long-term memory

Other parts of the brain indirectly aid memory formation by keeping the brain active. Many of these parts are found in the **reticular activating system**, which includes the *reticular formation*, *tegmentum*, *thalamus*, and *hypothalamus*. The activity within these structures ultimately supports arousal in the cerebral cortex. Another structure important for cortical arousal is the basal forebrain area. Drugs that increase cortical arousal include psychostimulant drugs; drugs that depress cortical arousal include benzodiazepines, barbiturates, and alcohol.

Reticular activating system
System of structures that support arousal in the cerebral cortex

STOP & CHECK

1. Which part of the cerebral cortex sends movement signals to the body?
2. What parts of the brain are damaged in Parkinson's disease?
3. Which structures are linked to working memory and long-term memory, respectively?

1. The motor cortex **2.** Parkinson's disease arises from damage to neurons that begin in the substantia nigra and end in the basal ganglia. **3.** The prefrontal cortex is particularly important for working memory, whereas the hippocampus is important for long-term memory.

Cerebral Blood Flow and Cerebrospinal Fluid

Proper blood flow throughout the brain, called **cerebral blood flow**, is critical for neuron and glial cell function. Highly active brain areas require increased blood flow. When you are working hard on a task such as an exam, your prefrontal cortex is very active. Blood flow increases to the prefrontal cortex to sustain this activity. Blood flow changes throughout the brain when blood capillaries dilate and contract. Highly active cells release a chemical called *nitric oxide* that dilates blood capillaries, which in turn delivers more oxygen.

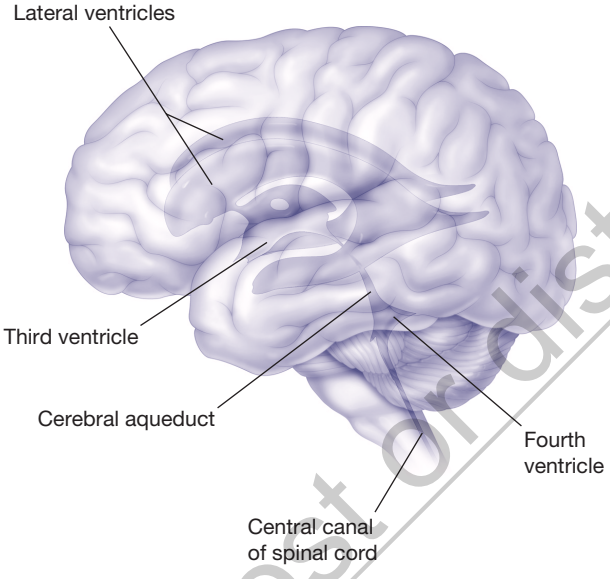
Cerebral blood flow
Blood flow throughout the brain

Cerebrospinal fluid is a clear fluid that surrounds cells in the brain. Cerebrospinal fluid provides a medium through which nutrients, a sugar called *glucose*, hormones, and other chemicals access brain cells (**Figure 2.15**). In addition to surrounding cells in the brain, cerebrospinal fluid fills many spaces and canals in the

Cerebrospinal fluid
Fluid that surrounds cells in the brain

FIGURE 2.15 Brain Ventricles

The ventricles are filled with cerebrospinal fluid. The third and fourth ventricles are connected by the cerebral aqueduct. Within the spinal cord, the central canal is filled with cerebrospinal fluid.



brain. The central canal of the spinal cord is filled with cerebrospinal fluid, and there is a smaller canal-like structure in the brain called the *cerebral aqueduct*. The cerebral aqueduct is surrounded by a small layer of tissue called **periaqueductal gray**. The brain also contains cerebrospinal fluid-filled cavities called **ventricles**.

Periaqueductal gray Small layer of tissue that surrounds the cerebral aqueduct

Ventricles Cerebrospinal fluid-filled cavities in the brain

Cerebrospinal fluid is also found in the *meninges* that surround the brain. Cerebrospinal fluid forms in a layer of the meninges called the *subarachnoid space*. By filling this space, cerebrospinal fluid forms a protective cushion around the brain, protecting it from injury. Cerebrospinal fluid serves as the medium through which drug molecules travel upon crossing into the brain from the blood-brain barrier.

STOP & CHECK

1. How might thinking be affected if the brain had poor cerebral blood flow?
2. The meninges protect the brain from injury because they contain a clear fluid called _____.

1. Since cells in the brain require oxygen to meet increased energy demands, thinking would certainly be compromised from poor flow. **2.** cerebrospinal fluid

Genes and the Physiological Processes of Cells

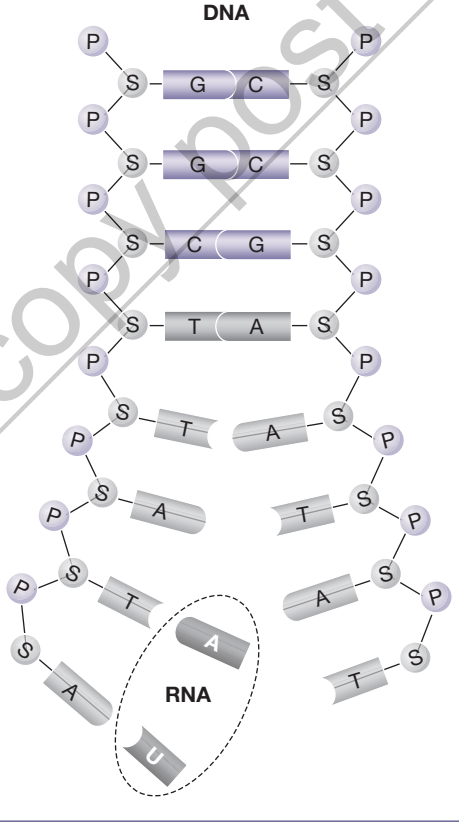
The blueprints for a cell and its functions reside within the cell's nucleus. The nucleus of every cell for humans contains 46 chromosomes. A child inherits 23 chromosomes from each parent. Two of the 46 chromosomes consist of X and Y chromosomes, which determine an individual's sex. If both of these sex chromosomes are X's, then an individual is genetically female. However, if one of these sex chromosomes is a Y, then the individual is genetically male. All of the other chromosomes are called *autosomal chromosomes*.

Each chromosome contains a strand of *deoxyribonucleic acid* (DNA), which contains the specific coding instructions for the basic functions of cells called **genes**. Genes are encoded with the traits we have (**Figure 2.16**). Within this role, genes contain information to synthesize new proteins. Researchers can alter genetic information in animals to study the nervous system (**Box 2.1**).

Gene
Segment of DNA encoded with the traits expressed in an organism

FIGURE 2.16 DNA and RNA

When a gene is activated, a specific DNA segment is unraveled and transcribed onto ribonucleic acid (RNA), which may then leave the nucleus and carry the transcribed information to ribosomes that synthesize proteins as instructed.



BOX 2.1

GENETICALLY MODIFIED ORGANISMS

Genetic technologies allow researchers to characterize the role genes play in behavior and physiological functions. These advances led to the creation of genetically modified invertebrate and vertebrate organisms. For vertebrates, most genetic modification research uses mice, although the development of CRISPR technology (discussed in this chapter's *From Actions to Effects* section) makes the use of genetic modification in other species more feasible.

The genetic modification process starts by injecting genetic material into a pregnant mouse. After the mouse has a litter, researchers test the *genotype*, or genetic makeup, of each mouse pup to identify those with the targeted genetic change. Genetically modified mice fall largely into two categories: transgenic animals and knock-out animals. A *transgenic animal* has either altered genes or additional genetic information. For example, researchers alter amyloid precursor protein genes in transgenic mice to cause production of amyloid plaques, a key neurobiological characteristic found in Alzheimer's disease. A *knock-out animal* fails to express traits from a particular gene; in essence, the gene is "knocked out."

Scientists use a notation system to describe different genotypes for knock-out animals. A heterozygous genotype is noted by a "–/+," with the "–" sign indicating the removed or deactivated gene on one chromosome and the "+" indicating the unaffected gene on the other chromosome. A "+/+" notation, indicating unaffected genes on both chromosomes, describes a nongenetically modified animal, also referred to as a *wildtype*. Animals with a homozygous genotype for a certain trait are noted with a "–/–," indicating a deactivated gene on each chromosome.

For example, serotonin transporter "–/–" knock-out mice exhibit greater levels of the neurotransmitter serotonin in the synaptic cleft and show anxious behavior (Holmes, Li, Murphy, Gold, & Crawley, 2003). The "–/–" describes the deactivation of the serotonin transporter gene on both chromosomes. Thus, these mice completely lack serotonin transporters (serotonin transporters are discussed in Chapter 3). A *phenotype* describes the physiological or behavioral changes caused by a genetic alteration. In this example, enhanced serotonin levels and increased anxiety describe the physiological and behavioral phenotypes for a serotonin transporter knock-out mouse.

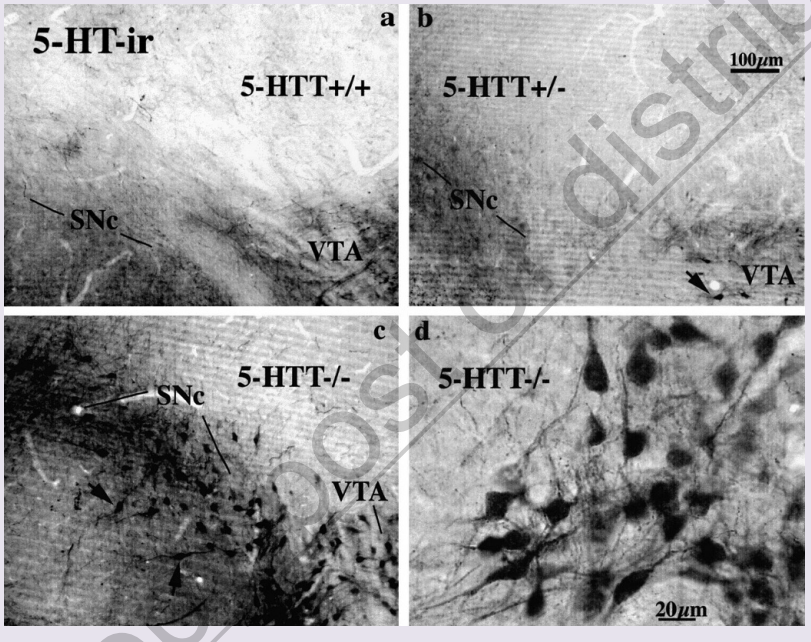
Although transgenic and knock-out data provide important links between genetics and physiological and behavioral activity, scientists keep in mind that genetic alterations may cause unexpected changes during neurodevelopment. In fact, a study by Zhou, Lesch, and Murphy (2002) demonstrated a unique and unexpected consequence of knocking out the serotonin transporter.

In this study, researchers compared serotonin levels in serotonin transporter knock-out mice and confirmed that greater serotonin levels occurred at serotonin synapses, as described previously. However, these researchers also discovered serotonin neurotransmitters inside of neurons that produce the neurotransmitter dopamine. Exploring further, the team found that dopamine transporters had adapted to allow entry of serotonin into dopamine neurons (Zhou et al., 2002). Thus, instead of having mice with an altered serotonin system, they unintentionally produced mice that also had an altered dopamine system (**Box 2.1 Figure 1**).

For these caveats and other reasons, researchers seek to refine and develop new approaches for developing genetically modified organisms. In a variation of the knock-out mouse, researchers have developed *conditional knock-out mice* that have normally functioning genes until a researcher administers a type of enzyme that deactivates a gene. Thus, these mice develop normally but still allow researchers to assess the effects of gene deactivation on some physiological or behavior characteristic. During a study, researchers might wait until mice reach an adult age before administering the enzyme. This technology also allows researchers to specify a particular part of the body to alter the gene, such as a structure within the central nervous system. These and other genetic modification procedures have important implications for understanding the nervous system and for characterizing drug actions and their effects.

BOX 2.1 FIGURE 1 **Serotonin Transporters on Dopamine Neurons**

Few neurons reveal the neurotransmitter serotonin in the dopamine-rich ventral tegmental area and substantia nigra in wildtype mice (top panel, a). However, in serotonin transporter knock-out mice (bottom panel, c & d), many dopamine neurons contain serotonin. These findings suggest that removal of serotonin transporters led to the nervous system adapting to the loss of serotonin by using dopamine neurons for synthesizing serotonin instead. VTA = ventral tegmental area; 5-HT = serotonin; 5-HTT = serotonin transporter; ir = immunoreactive; the labeling technique used to identify serotonin; SNc = substantia nigra. From Zhou et al. (2002).



Source: Dr. Feng Zhou/Brain Research/Elsevier.

Although genes contain codes to express certain traits such as eye color or production of a particular enzyme, the coding sequence for genes may not be precisely the same from individual to individual. We term these differences *polymorphisms*. A **polymorphism** is a difference in the encoding of a gene compared to the most common sequence in a population. Polymorphisms are common, and determining what type of polymorphism an individual has can aid greatly in understanding a person's response to drug effects. For example, some polymorphisms lead to greater production of certain types of enzymes in the liver. For these individuals, the extra enzymes may break down a drug before it produces any substantial effects.

Activating genes leads to the copying of genetic information, a process referred to as *gene transcription*. A **transcription factor** consists of a substance that increases or decreases gene transcription. During gene transcription, the coding sequence of

Polymorphism A difference in the encoding of a gene compared to the most common sequence in a population

Transcription factor Substance that increases or decreases gene transcription

a gene copies onto ribonucleic acid (RNA). The type of RNA used to trigger protein synthesis is called *messenger RNA* because it leaves the nucleus and binds to ribosomes in the cell. Ribosomes produce the type of protein specified in the message. Gene transcription is one of many areas studied in the field of **epigenetics**, the study of mechanisms of gene expression not involving alterations to DNA sequences. Future drug therapies may target epigenetic mechanisms for treating neurological or mental disorders (Arango, 2015).

Epigenetics
Mechanisms of gene expression not involving alterations to DNA sequences

Neurogenetics
How genes support the function of neurons

The field of **neurogenetics** aims to understand how genes support the function of neurons. In doing so, this field also studies how gene mutations, alterations in the DNA sequence for genes, cause neurological disorders, such as Huntington's disease and Alzheimer's disease. For example, neurogenetics studies revealed a mutation in the Huntington gene that leads to the destruction of neurons and subsequently a host of motor and cognitive disturbances in Huntington's disease. The disease is inheritable and ultimately fatal.

We refer to a *Mendelian disease* as one occurring from a single gene mutation inheritable to offspring. Genetic tests arising from neurogenetic studies provide a means for identifying the risk of contracting a Mendelian disease. For example, one can be tested for a mutated Huntington gene that has near 100 percent accuracy before the disease's symptoms occur. Other genetic diseases occur from different types of gene mutations. Sometimes, a mutation occurs as a repeating pattern of nucleotides, the chemical building blocks of DNA, or through an error in replicating or repairing a gene, resulting in *gene duplication*. Many of these diseases can be traced to mutations in multiple genes. For example, *cerebellar ataxia* is a disorder marked by coordination and balance deficits that derives from mutations in over 30 different genes (Jayadev, Smith, & Bird, 2011).

STOP & CHECK

1. How many chromosomes does a human cell contain?
2. A _____ is a protein that activates a gene.
3. Genetic code is copied onto _____, which delivers the code to ribosomes outside the nucleus.

1. 46 2. transcription factor 3. messenger RNA

From Actions to Effects: Advances in Therapeutic Use of CRISPR Genetic Technology

Patients suffering from diseases derived from genetic mutations may benefit from emerging genetic technologies to correct or counteract the effects from these mutations. Such efforts require precision genetic alterations, and for this reason, therapeutic genetic strategies increasingly involve the use of CRISPR technology.

CRISPR (pronounced "crisper") is an acronym for *clustered regularly interspaced short palindromic repeats*, referring to sections of DNA that fit this characterization. That is, patterns of DNA are repeated in multiple copies. "Palindromic" refers to a sequence of nucleic acids in one strand of DNA bound to nucleic acids in a matching but opposite order on the second strand of DNA. Spacer DNA refers to noncoding segments of DNA (i.e., DNA that doesn't lead to the production of proteins). Thus, interspaced refers to noncoding DNA that separates the repeated patterns of DNA.

Generally, reference to CRISPR technology includes the use of a protein that can sever bounds in a DNA sequence associated with a particular CRISPR segment. The current leading strategy for therapeutic genetic editing is *Cas9* (CRISPR-associated protein 9). The Cas9 enzyme includes a DNA sequence that will selectively bind to a short sequence of RNA that is copying the genetic code from a specific pattern of DNA linked to a specific CRISPR sequence. This selective targeting is a step up from previous strategies that held the likelihood of affecting genes unrelated to the therapeutic goals of the genetic manipulation. Thus, lacking specificity in genetic editing can cause more harm than good.

At the present time, CRISPR-Cas9 treatments have received fast-track status for review by the U.S. Food and Drug Administration. Recently, the results from a patient with sickle cell disease enrolled in CRISPR-Cas9 clinical trial were aired on CBS's "60 Minutes" (LaPook, 2019). Sickle cell disease caused the patient to experience severe sharp pain throughout her body due to a miscoding of the gene for the hemoglobin protein that caused what should be doughnut-shaped red blood cells to be cells shaped instead like a sickle. The researchers extracted stem cells from the patient's bone marrow and then introduced corrected gene sequences using CRISPR-Cas9. The stem cells were reintroduced into bone marrow and then developed into normal stem cells.

Researchers also use CRISPR-Cas9 approaches to genetically modify animals for the purpose of mimicking human diseases or disorders. In one such study, Horie and colleagues (2018) used CRISPR-Cas9 to prevent the synthesis of the hormone oxytocin in prairie voles. Oxytocin facilitates sociability, among other functions, and prairie voles are well characterized as social animals that are monogamous with mates and raise their pups together. Thus, the researchers sought to determine how the elimination of oxytocin production might affect social attachment among these animals. The researchers measured anxiety, parenting behaviors, sociability toward a familiar vole versus a novel vole, and repetitive behavior. Without oxytocin, voles appeared normal in regard to anxiety and parenting behavior. However, the affected voles did not show a preference between a familiar vole and a novel vole. Moreover, the voles engaged in repetitive behavior. At the conclusion of their report, the authors suggested that the prevention of oxytocin production in the animals led to behaviors—lack of recognition of a familiar vole, repetitive behavior—that appeared in some ways like autism spectrum disorder in humans.

Overall, CRISPR technology holds promise for novel genetic therapies in humans. Further, CRISPR offers innovative approaches for behavioral neuroscience research.

STOP & CHECK

1. What is the advantage of using CRISPR for genetic therapy in humans?
2. For preclinical research, how does the ability to use genetic manipulation in other species, aside from mice (see Box 2.1), aid in neuroscience research?

1. Genetic manipulation can lead to a host of unintended gene mutations, and thus serious adverse effects, unless high precision can be used for the genetic procedures. CRISPR-Cas9 may meet this "high precision" requirement and, for this reason, is the most promising genetic therapy tool to date.
2. While enormous discoveries about the brain and medical advances have come from mice, this species is not always the best to use for the objectives of the study. In the study about prairie voles presented in this section, researchers desired to closely study prosocial behaviors using genetic manipulation. The voles, they found, exhibited a number of social behaviors found in humans, and therefore, the voles (instead of mice) would provide information that would be more useful to translating their findings to humans.

CHAPTER SUMMARY

The cells in the central nervous system consist of glial cells and neurons. Neurons consist of dendrites, a soma, an axon, and an axon terminal. Signals from other neurons are received through dendrites, and the message is sent to other neurons from the axon terminal. Glial cells play an important role in supporting the function of neurons.

The nervous system consists of the peripheral nervous system and the central nervous system. The peripheral nervous system consists of the somatic nervous system—for sensory and motor signals—and the autonomic nervous system—for vital functions. The autonomic nervous system consists of the sympathetic, parasympathetic, and enteric nervous systems.

The central nervous system consists of the brain and spinal cord. We divide the brain into subdivisions called the *hindbrain*, *midbrain*, and *forebrain*. The forebrain division is the largest and encompasses the four cortical lobes in the brain called the *occipital lobe* (for vision), the *parietal lobe* (mainly for processing touch information), the *temporal lobe* (for audition and language), and the *frontal lobe* (for cognition and movement). The limbic system consists of the amygdala, hippocampus, cingulate gyrus, thalamus, and hypothalamus. Together these limbic system structures play an important role in emotion. With the exception of olfactory information, which goes directly to the prefrontal cortex, sensory information is received from the head and body and routed through the thalamus to the appropriate lobe for processing. The prefrontal cortex is the most anterior portion of the frontal lobe and the integration center for all sensory information. Motor signals are sent down to the body beginning in the primary motor cortex. The basal ganglia help to regulate voluntary movements.

The cells in the brain receive important sugars and nutrients from the cerebrospinal fluid surrounding these cells and oxygen from blood vessels. Cerebrospinal fluid exists throughout the central nervous system through the central canal in the spinal

cord and through a network of ventricles and the cerebral aqueduct in the brain. Cerebral blood flow increases in active parts of the brain.

The basic functions and development of cells are directed by genes, which are segments of DNA. Molecules that activate genes are called *transcription factors*. Gene activation causes a copy of the gene to be imprinted on RNA. RNA directs the production of protein synthesis through ribosomes found outside of the cell's nucleus.

KEY TERMS

Neurons 29
Glial cells (or glia cells) 29
Dendrites 31
Axons 31
Synapse 32
Interneuron 32
Sensory neurons 32
Motor neurons 32
Oligodendrocytes 32
Astrocytes 32
Microglial cells 32
Somatic nervous system 36
Autonomic nervous system 37
Sympathetic nervous system 37
Parasympathetic nervous system 37
Enteric nervous system 37
Cerebral cortex 39
Medulla 40
Hypothalamus 42
Limbic system 42
Nucleus accumbens 43
Occipital lobe 43
Temporal lobe 44
Parietal lobe 44
Frontal lobe 44
Prefrontal cortex 44
Thalamus 44
Motor cortex 45
Basal ganglia 46
Pons 46
Cerebellum 46
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