

Regulating the Animal Body

Are Pollutants Affecting the Sexual Development of Florida's Alligators?

Alligators are among the most interesting of animals for a biologist to study. Their ecology is closely tied to the environment, and their reptilian biology offers an interesting contrast to that of mammals like ourselves. Studies of alligator development offer powerful general lessons well worthy of our attention.

In no area of biology is this more true than in investigation of alligator sexual development. This importance is not because sexual development in alligators is unusual. It is not. As with all vertebrates, sexual development in alligator males—particularly development of their external sexual organs—is largely dependent on the androgen sex hormone testosterone and its derivatives. In the alligator embryo, these steroid hormones are responsible for the differentiation of the male internal duct system, as well as the formation of the external genitalia. After the alligator's birth, androgen hormones are essential for normal maturation and growth of the juvenile male reproductive system, particularly during puberty.

The strong dependence of a male alligator's sexual development on androgens is not unusual—mammals show the same strong dependence. So why should researchers be interested in alligators? In a nutshell, we humans don't spend our lives sloshing around in an aquatic environment, and alligators do. Florida alligators live in the many lakes that pepper the state, and, living in these lakes, they are exposed all their lives to whatever chemicals happen to be added to the lakewater by chemical spills, industrial wastes, and agricultural runoff.

The androgen-dependent sexual development of alligators provides a sensitive barometer to environmental pollution, because the androgen response can be blocked by a class of pollutant chemicals called endocrine disrupters. When endocrine-disrupting pollutants contaminate Florida lakes, their presence can be detected by its impact on the sexual development of the lakes' resident alligators. Just as the death of coal miners' canaries warn of the buildup of dangerous gas within the shaft of coal mines, so disruption of the sexual development of alligators can warn us of dangerous chemicals in the environment around us.

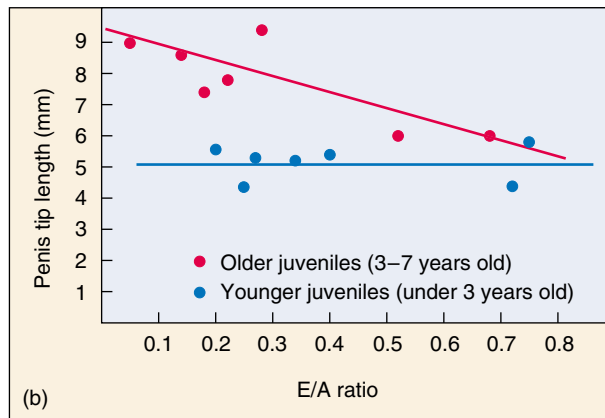
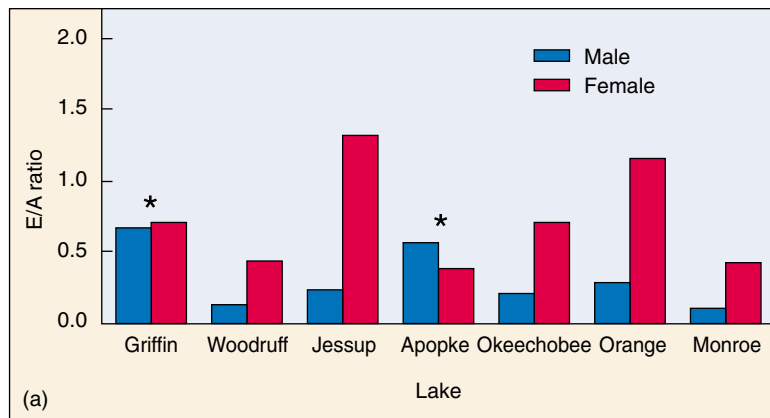


Catching alligators is a job best done at night. Alligators in Florida lakes, like the one shown here in the hands of Professor Guillette, seem to be experiencing developmental abnormalities, perhaps due to pollution of many of Florida's lakes by endocrine-disrupting chemicals.

One of the great joys of biological research is being able to choose research that is fun to do. Few research projects offer the particular joys of studying alligators. With State Game Commission permits, researchers go to lakes in central Florida, wait till after dark, then spend the night on the lake in small boats hand-capturing the animals. As you might guess, researchers mostly choose juvenile individuals. The captured animals are confined in cloth bags until sex can be determined, body measurements made, and blood samples collected, and then released.

For over six years, Louis Guillette of the University of Florida, Gainesville, and his students have been carrying out just this sort of research. Their goal has been to assess the degree to which agricultural and other chemicals have polluted the lakes of central Florida, using as their gauge the disruption of normal sexual development in alligators.

To assess hormonal changes that might be expected to inhibit male sexual development, Guillette's team looked at the relative ratio of androgens (which promote male development) to estrogens (which promote female development) in each captured alligator. Some male endocrine disrupters act like estrogens, while others decrease native androgen levels. In either case, the ratio of estrogen to androgen (the E/A ratio) increases, producing a more estrogenic environment and so retarding male sexual development. Particularly after puberty, the growth of male alligators' external sexual organs is very dependent upon a high-androgen environment. Any pollutant that raises the E/A ratio would be expected to markedly inhibit this development.



Alligator sexual development inhibited by contamination. (a) Ratio of estrogen/androgen (E/A) plasma concentrations in large juvenile alligators 3–7 years old. A relatively larger ratio in males is atypical and indicates an estrogenic hormonal environment, as opposed to the expected androgenic hormonal environment. (b) Sexual development in male alligators, measured by penis length as a function of E/A ratio. In small juveniles under 3 years old, there is no apparent influence. In older juveniles 3–7 years old, there is a pronounced effect, higher E/A ratios retarding sexual development.

The Experiment

Guillette’s team first looked at animals in two lakes and then expanded the research to look at animals from several other lakes. Alligators were initially collected from Lake Woodruff National Wildlife Refuge and from Lake Apopka. Lake Woodruff is a relatively pristine lake with no agricultural or industrial runoff. Lake Apopka, on the other hand, is a large eutrophic lake exposed to various agricultural and municipal contaminants. In 1980, the lake experienced a sulfuric acid spill from a chemical company, and has a history of pesticide contamination by DDT.

Clear comparisons of alligators collected from different lakes required that animals be captured as nearly as possible at the same time, to minimize possible variation due to photoperiod, temperature, and nutrition. This experimental requirement led to truly prodigious feats of alligator catching by the research team. On a single night in 1994, 40 male alligators were hand-captured from Lake Woodruff. The following night, 54 males were captured from Lake Apopka. In a broader study of seven lakes carried out the following year, 528 animals were captured during a 17-day period.

The external genitalia and total body length were measured on captured animals. Body-length is a good indicator of the age of the alligator. Alligators reach puberty at about 3 years of age, and this must be taken into account when making comparisons.

Blood samples were taken from each animal in order to determine the plasma levels of estrogen and testosterone. Investigators measured plasma concentrations of estradiol-17 β and testosterone. By comparing the ratio of the two values, the researchers estimated the E/A ratio, and thus if the internal environment was androgenic or estrogenic.

The Results

In most of the seven lakes studied, female alligators showed

a much higher E/A ratio than males (graph *a* above), a normal result. The exceptions are Lake Griffin and Lake Apopka, the most polluted of the lakes. The larger E/A ratio observed in male alligators caught from these two lakes indicates an estrogenic hormonal environment in these animals rather than the normal androgenic one.

Does this estrogenic environment have an impact on juvenile sexual development? Yes. Researchers observed that postpuberty juvenile males from Lake Apopka and Lake Griffith (where E/A ratios were elevated) exhibited stunted reproductive organs compared to those found in Lake Woodruff and other lakes (graph *b* above).

Prepuberty males did not show this effect, exhibiting the same size external reproductive organs whatever the E/A ratio. This is as you would expect, as organ growth occurs primarily after puberty, in response to androgen hormones released from the testes.

A primary contaminant found in alligators’ eggs in Lake Apopka is *p,p'*-DDE, a major metabolite of DDT. *p,p'*-DDE has been shown to bind to androgen receptors, and functions as an antiandrogen. The presence of *p,p'*-DDE reduces the androgen effect in cells, creating a more estrogenic environment.

The researchers also measured levels of plasma testosterone. The plasma levels of testosterone were significantly reduced in alligators from Lake Apopka compared to the control animals removed from Lake Woodruff. These reduced levels of plasma testosterone from the Lake Apopka alligators also act to reduce the E/A ratio, and so to produce the observed abnormalities in reproductive structures.



To explore this experiment further, go to the Virtual Lab at www.mhhe.com/raven6/vlab14.mhtml

54

The Nervous System

Concept Outline

54.1 The nervous system consists of neurons and supporting cells.

Neuron Organization. Neurons and neuroglia are organized into the central nervous system (the brain and spinal cord) and the peripheral nervous system (sensory and motor neurons).

54.2 Nerve impulses are produced on the axon membrane.

The Resting Membrane Potential. The inside of the membrane is electrically negative in comparison with the outside.

Action Potentials. In response to a stimulus that depolarizes the membrane, voltage-gated channels open, producing a nerve impulse. One action potential stimulates the production of the next along the axon.

54.3 Neurons form junctions called synapses with other cells.

Structure of Synapses. Neurotransmitters diffuse across to the postsynaptic cell and combine with receptor proteins.

Neurotransmitters and Their Functions. Some neurotransmitters cause a depolarization in the postsynaptic membrane; others produce inhibition by hyperpolarization.

54.4 The central nervous system consists of the brain and spinal cord.

The Evolution of the Vertebrate Brain. Vertebrate brains include a forebrain, midbrain, and hindbrain.

The Human Forebrain. The cerebral cortex contains areas specialized for different functions.

The Spinal Cord. Reflex responses and messages to and from the brain are coordinated by the spinal cord.

54.5 The peripheral nervous system consists of sensory and motor neurons.

Components of the Peripheral Nervous System. A spinal nerve contains sensory and motor neurons.

The Autonomic Nervous System. Sympathetic motor neurons arouse the body for fight or flight; parasympathetic motor neurons have antagonistic actions.

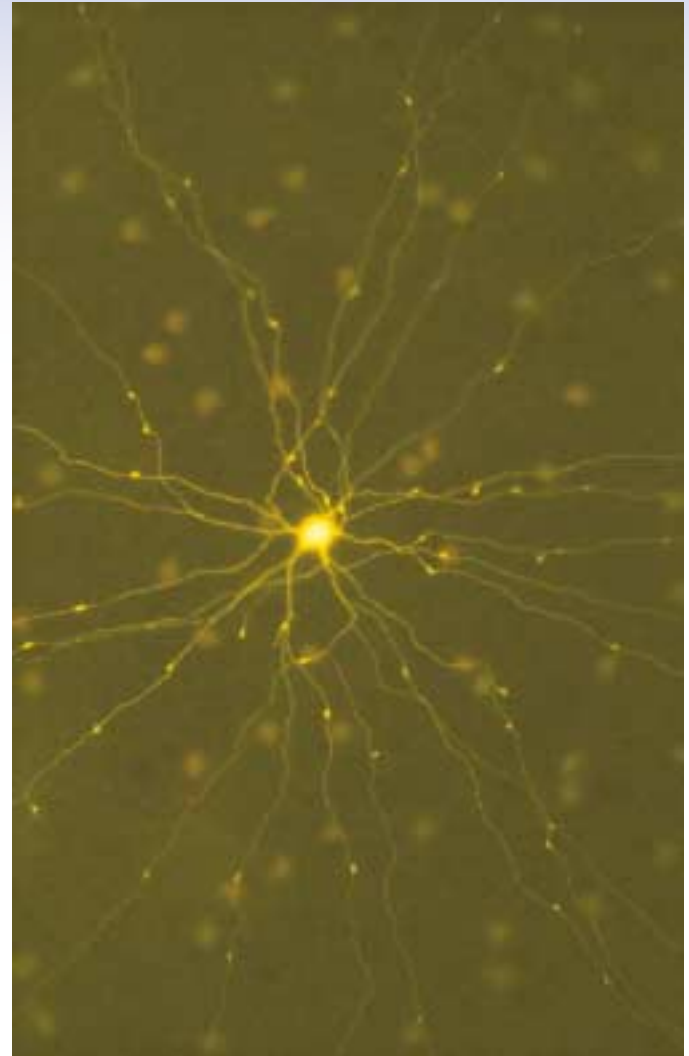


FIGURE 54.1

A neuron in the retina of the eye (500 \times). This neuron has been injected with a fluorescent dye, making its cell body and long dendrites readily apparent.

All animals except sponges use a network of nerve cells to gather information about the body's condition and the external environment, to process and integrate that information, and to issue commands to the body's muscles and glands. Just as telephone cables run from every compartment of a submarine to the conning tower, where the captain controls the ship, so bundles of nerve cells called neurons connect every part of an animal's body to its command and control center, the brain and spinal cord (figure 54.1). The animal body is run just like a submarine, with status information about what is happening in organs and outside the body flowing into the command center, which analyzes the data and issues commands to glands and muscles.

54.1 The nervous system consists of neurons and supporting cells.

Neuron Organization

An animal must be able to respond to environmental stimuli. A fly escapes a swat; the antennae of a crayfish detect food and the crayfish moves toward it. To do this, it must have sensory receptors that can detect the stimulus and motor *effectors* that can respond to it. In most invertebrate phyla and in all vertebrate classes, sensory receptors and motor effectors are linked by way of the nervous system. As described in chapter 49, the nervous system consists of neurons and supporting cells. **Sensory** (or **afferent**) **neurons** carry impulses from sensory receptors to the central nervous system (CNS); **motor** (or **efferent**) **neurons** carry impulses from the CNS to effectors—muscles and glands (figure 54.2).

In addition to sensory and motor neurons, a third type of neuron is present in the nervous systems of most invertebrates and all vertebrates: **association neurons** (or **interneurons**). These neurons are located in the brain and spinal cord of vertebrates, together called the **central nervous system (CNS)**, where they help provide more complex reflexes and higher associative functions, including learning and memory. Sensory neurons carry impulses into the CNS, and motor neurons carry impulses away from the CNS. Together, sensory and motor neurons constitute the **peripheral nervous system (PNS)** of vertebrates. Motor neurons that stimulate skeletal muscles to contract are **somatic motor neurons**, and those that regulate the activity of the smooth muscles, cardiac muscle, and glands are **autonomic motor neurons**. The autonomic motor neurons are further subdivided into the **sympathetic** and **parasympa-**

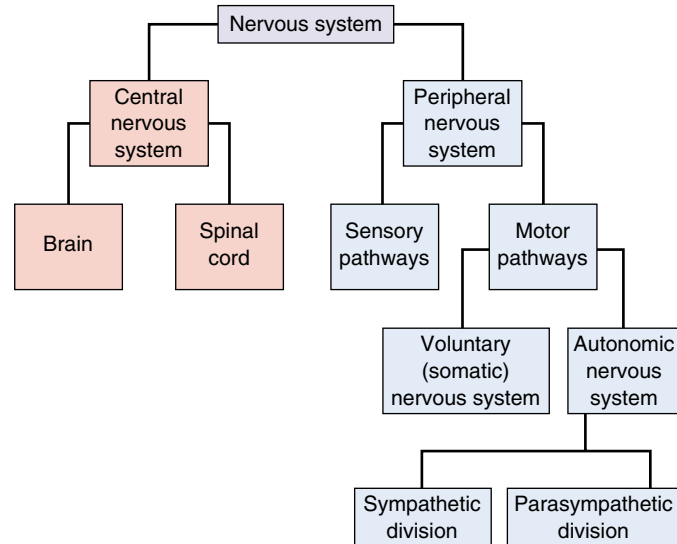


FIGURE 54.3
The divisions of the vertebrate nervous system. The major divisions are the central and peripheral nervous systems.

thetic systems, which act to counterbalance each other (figure 54.3).

Despite their varied appearances, most neurons have the same functional architecture (figure 54.4). The cell body is an enlarged region containing the nucleus. Extending from the cell body are one or more cytoplasmic extensions called **dendrites**. Motor and association neurons possess a profusion of highly branched dendrites, enabling those cells to

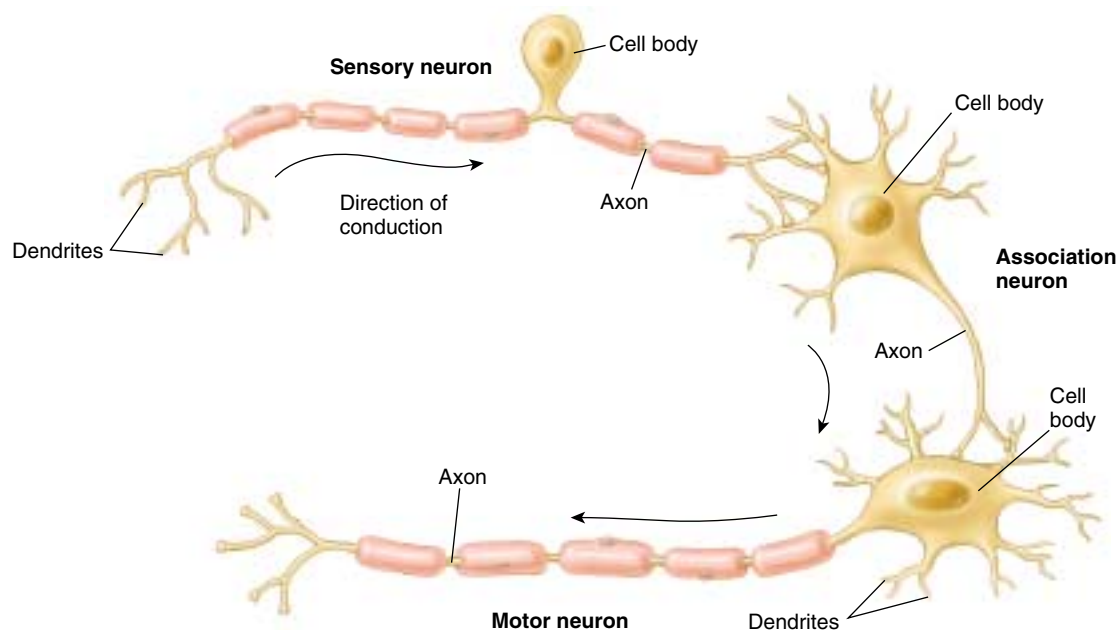


FIGURE 54.2
Three types of neurons. *Sensory neurons* carry information about the environment to the brain and spinal cord. *Association neurons* are found in the brain and spinal cord and often provide links between sensory and motor neurons. *Motor neurons* carry impulses or “commands” to muscles and glands (effectors).

receive information from many different sources simultaneously. Some neurons have extensions from the dendrites called *dendritic spines* that increase the surface area available to receive stimuli. The surface of the cell body integrates the information arriving at its dendrites. If the resulting membrane excitation is sufficient, it triggers impulses that are conducted away from the cell body along an **axon**. Each neuron has a single axon leaving its cell body, although an axon may produce small terminal branches to stimulate a number of cells. An axon can be quite long: the axons controlling the muscles in your feet are more than a meter long, and the axons that extend from the skull to the pelvis in a giraffe are about three meters long!

Neurons are supported both structurally and functionally by **supporting cells**, which are called **neuroglia**. These cells are ten times more numerous than neurons and serve a variety of functions, including supplying the neurons with nutrients, removing wastes from neurons, guiding axon migration, and providing immune functions. Two of the most important kinds of neuroglia in vertebrates are **Schwann cells** and **oligodendrocytes**, which produce **myelin sheaths** that surround the axons of many neurons. Schwann cells produce myelin in the PNS, while oligodendrocytes produce myelin in the CNS. During development, these cells wrap themselves around each axon several times to form the myelin sheath, an insulating covering consisting of multiple layers of membrane (figure 54.5). Axons that have myelin sheaths are said to be myelinated, and those that don't are unmyelinated. In the CNS, myelinated axons form the **white matter**, and the unmyelinated dendrites and cell bodies form the **gray matter**. In the PNS, both myelinated and unmyelinated axons are bundled together, much like wires in a cable, to form **nerves**.

The myelin sheath is interrupted at intervals of 1 to 2 mm by small gaps known as **nodes of Ranvier** (see figure 54.4). The role of the myelin sheath in impulse conduction will be discussed later in this chapter.

Neurons and neuroglia make up the central and peripheral nervous systems in vertebrates. Sensory, motor, and association neurons play different roles in the nervous system, and the neuroglia aid their function, in part by producing myelin sheaths.

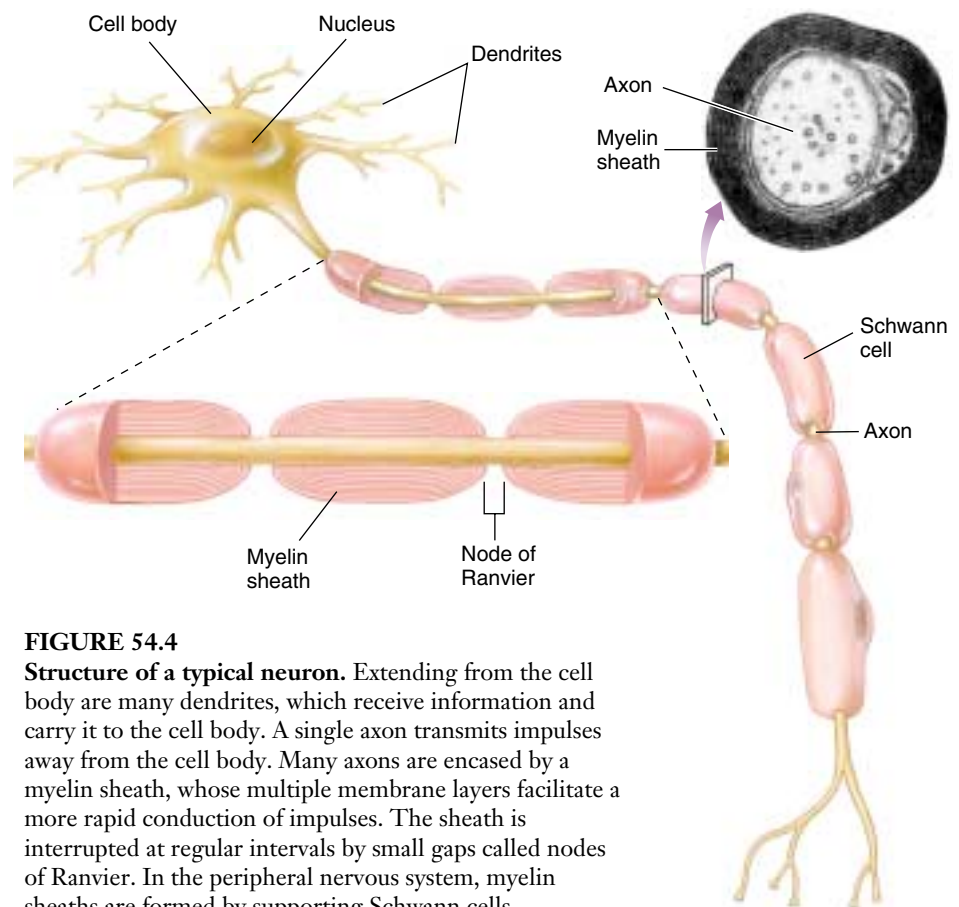


FIGURE 54.4
Structure of a typical neuron. Extending from the cell body are many dendrites, which receive information and carry it to the cell body. A single axon transmits impulses away from the cell body. Many axons are encased by a myelin sheath, whose multiple membrane layers facilitate a more rapid conduction of impulses. The sheath is interrupted at regular intervals by small gaps called nodes of Ranvier. In the peripheral nervous system, myelin sheaths are formed by supporting Schwann cells.

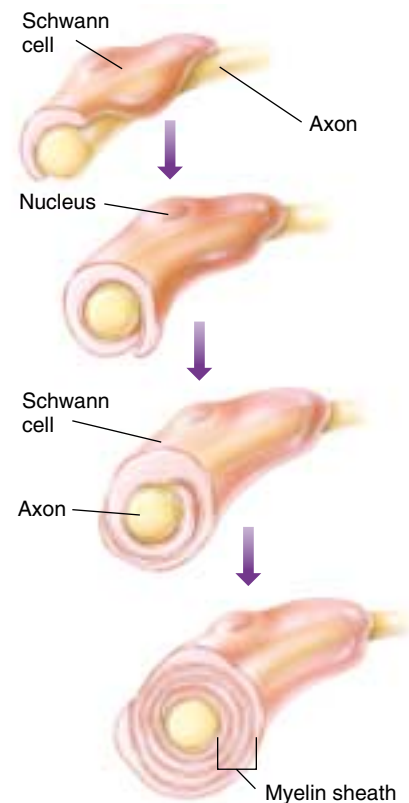


FIGURE 54.5
The formation of the myelin sheath around a peripheral axon. The myelin sheath is formed by successive wrappings of Schwann cell membranes, leaving most of the Schwann cell cytoplasm outside the myelin.

54.2 Nerve impulses are produced on the axon membrane.

The Resting Membrane Potential

Neurons communicate through changes in electrical properties of the plasma membrane that travel from one cell to another. The architecture of the neuron aids the spread of these electrical signals called nerve impulses. To understand how these signals are generated and transmitted within the nervous system, we must first examine some of the electrical properties of plasma membranes.

The battery in a car or a flashlight separates electrical charges between its two poles. There is said to be a *potential difference*, or voltage, between the poles, with one pole being positive and the other negative. Similarly, a potential difference exists across every cell's plasma membrane. The side of the membrane exposed to the cytoplasm is the negative pole, and the side exposed to the extracellular fluid is the positive pole. This potential difference is called the membrane potential.

The inside of the cell is more negatively charged in relation to the outside because of three factors: (1) Large molecules like proteins and nucleic acids that are negatively charged are more abundant inside the cell and cannot diffuse out. These molecules are called *fixed anions*. (2) The sodium-potassium pump brings only two potassium ions (K^+) into the cell for every three sodium ions (Na^+) it pumps out (figure 54.6). In addition to contributing to the electrical potential, this also establishes concentration gradients for Na^+ and K^+ . (3) Ion channels allow more K^+ to diffuse out of the cell than Na^+ to diffuse into the cell. Na^+ and K^+ channels in the plasma membrane have *gates*, portions of the channel protein that open or close the channel's pore. In the axons of neurons and in muscle fibers, the

gates are closed or open depending on the membrane potential. Such channels are therefore known as *voltage-gated ion channels* (figure 54.7).

In most cells, the permeability of ions through the membrane is constant, and the net negativity on the inside of the cell remains constant. The plasma membranes of muscle and neurons, however, are excitable because the permeability of their ion channels can be altered by various stimuli. When a neuron is not being stimulated, it maintains a *resting membrane potential*. A cell is very small, and so its membrane potential is very small. The electrical potential of a car battery is typically 12 volts, but a cell's resting membrane potential is about -70 millivolts (-70 mV or 0.07 volts). The negative sign indicates that the inside of the cell is negative with respect to the outside.

We know that the resting membrane potential is -70 mV because of an unequal distribution of electrical charges across the membrane. But why -70 mV rather than -50 mV or -10 mV? To understand this, we need to remember that there are two forces acting on the ions involved in establishing the resting membrane potential: (1) ions are attracted to ions or molecules of opposite charge; and (2) ions respond to concentration gradients by moving from an area of high concentration to an area of lower concentration.

The positively charged ions, called *cations*, outside the cell are attracted to the negatively charged fixed anions inside the cell. However, the resting plasma membrane is more permeable to K^+ than to other cations, so K^+ enters the cell. Other cations enter the cell, but the leakage of K^+ into the cell has the dominant effect on the resting membrane potential. In addition to the electrical gradient dri-

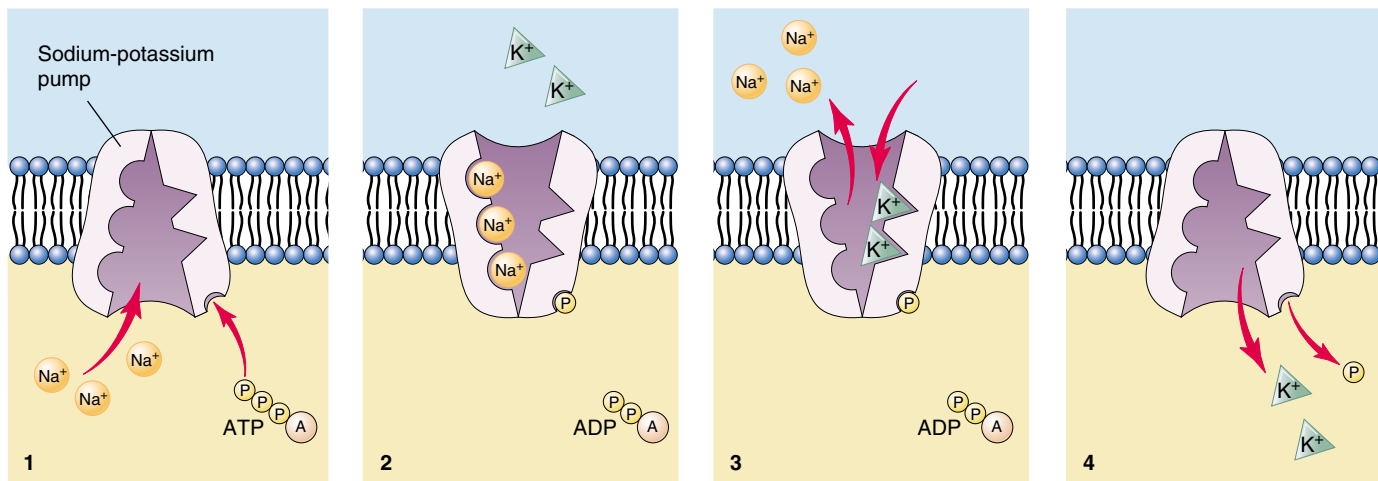


FIGURE 54.6

The sodium-potassium pump. This pump transports three Na^+ to the outside of the cell and simultaneously transports two K^+ to the inside of the cell. This is an active transport carrier requiring the breakdown of ATP.

Table 54.1 The Ionic Composition of Cytoplasm and Extracellular Fluid (ECF)

Ion	Concentration in Cytoplasm (mM)	Concentration in ECF (mM)	Ratio	Equilibrium Potential (mV)
Na ⁺	15	150	10:1	+60
K ⁺	150	5	1:30	-90
Cl ⁻	7	110	15:1	-70

ving K⁺ into the cell, there is also a concentration gradient established by the sodium-potassium pump that is driving K⁺ out of the cell. At a point, these two forces balance each other, and the voltage at which the influx of K⁺ equals the efflux of K⁺ is called the **equilibrium potential** (table 54.1). For potassium, the equilibrium potential is -90 mV. At -80 mV, K⁺ will diffuse out of the cell and at -100 mV K⁺ will diffuse into the cell.

If K⁺ were the only cation involved, the resting membrane potential of the cell would be -90 mV. However, the membrane is also slightly permeable to Na⁺, and its equilibrium potential is +60 mV. The effects of Na⁺ leaking into the cell make the resting membrane potential less negative. With a membrane potential less negative than -90 mV, K⁺ diffuses into the cell, and the combined effect bring the equilibrium potential for the resting cell to -70 mV. The resting membrane potential of a neuron can be seen using a voltmeter and a pair of electrodes, one outside and one inside the cell (figure 54.8)

When a nerve or muscle cell is stimulated, sodium channels become more permeable, and Na⁺ rushes into the cell, down its concentration gradient. This sudden influx of positive charges reduces the negativity on the inside of the cell and causes the cell to *depolarize* (move toward a polarity above that of the resting potential). After a slight delay, potassium channels also become more permeable, and K⁺ flows out of the cell down its concentration gradient. Similarly, the membrane becomes more permeable to Cl⁻, and Cl⁻ flows into the cell. But the effects of Cl⁻ on the membrane potential are far less than those of K⁺. The inside of the cell again becomes more negative and causes the cell to *hyperpolarize* (move its polarity below that of the resting potential).

The resting plasma membrane maintains a potential difference as a result of the uneven distribution of charges, where the inside of the membrane is negatively charged in comparison with the outside (-70 mV). The magnitude, measured in millivolts, of this potential difference primarily reflects the difference in K⁺ concentration.

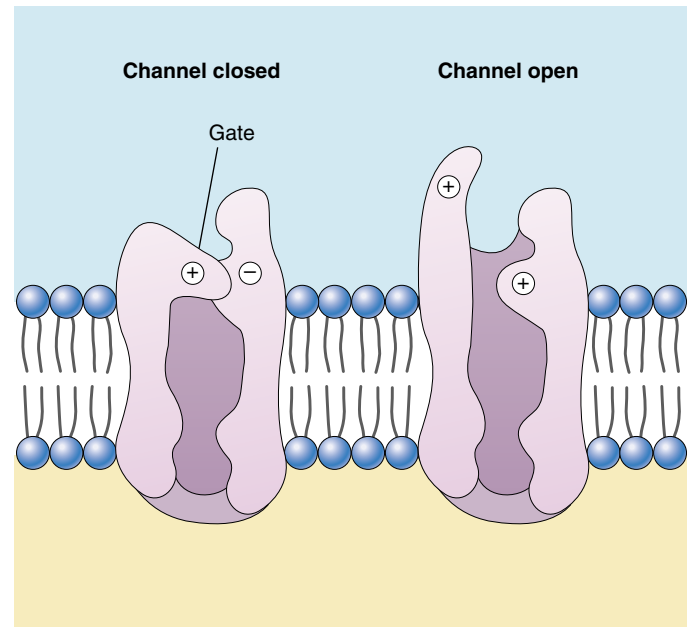


FIGURE 54.7

Voltage-gated ion channels. In neurons and muscle cells, the channels for Na⁺ and K⁺ have gates that are closed at the resting membrane potential but open when a threshold level of depolarization is attained.

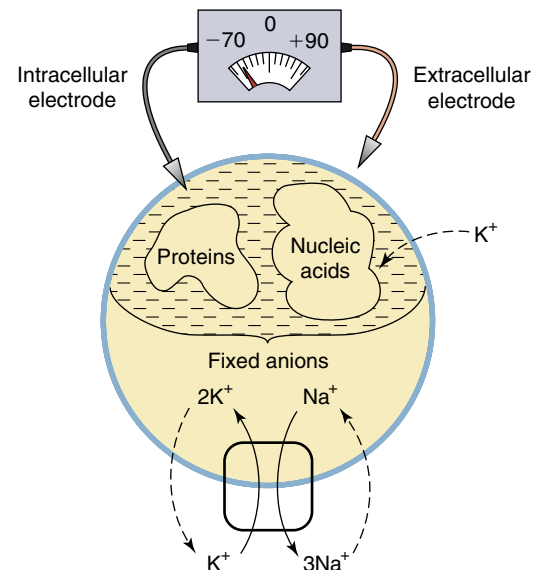


FIGURE 54.8

The establishment of the resting membrane potential. The fixed anions (primarily proteins and nucleic acids) attract cations from the extracellular fluid. If the membrane were only permeable to K⁺, an equilibrium would be established and the membrane potential would be -90 mV. A true resting membrane potential is about -70 mV, because the membrane does allow a low rate of Na⁺ diffusion into the cell. This is not quite sufficiently negative to prevent the outward diffusion of K⁺, so the cell is not at equilibrium and the action of the sodium-potassium pumps is required to maintain stability.

Action Potentials

Generation of Action Potentials

If the plasma membrane is depolarized slightly, an oscilloscope will show a small upward deflection of the line that soon decays back to the resting membrane potential. These small changes in membrane potential are called *graded potentials* because their amplitudes depend on the strength of the stimulus. Graded potentials can be either depolarizing or hyperpolarizing and can add together to amplify or reduce their effects, just as two waves add to make one bigger one when they meet in synchrony or cancel each other out when a trough meets with a crest. The ability of graded potentials to combine is called summation (figure 54.9). Once a particular level of depolarization is reached (about -55 mV in mammalian axons), however, a nerve impulse, or **action potential**, is produced. The level of depolarization needed to produce an action potential is called the *threshold*.

A depolarization that reaches or exceeds the threshold opens both the Na^+ and the K^+ channels, but the Na^+ channels open first. The rapid diffusion of Na^+ into the cell shifts the membrane potential toward the equilibrium potential for Na^+ ($+60$ mV—recall that the positive sign indicates that the membrane reverses polarity as Na^+ rushes in).

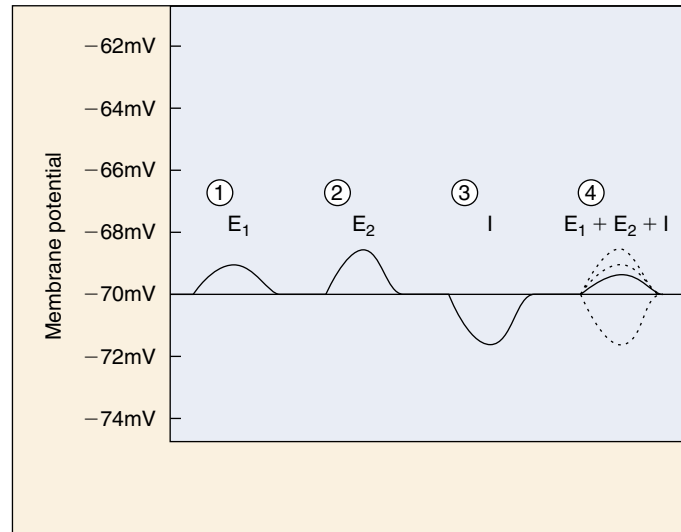


FIGURE 54.9
Graded potentials. (1) A weak excitatory stimulus, E_1 , elicits a smaller depolarization than (2) a stronger stimulus, E_2 . (3) An inhibitory stimulus, I , produces a hyperpolarization. (4) Because graded potentials can summate, if all three stimuli occur very close together, the resulting polarity change will be the algebraic sum of the three changes individually.

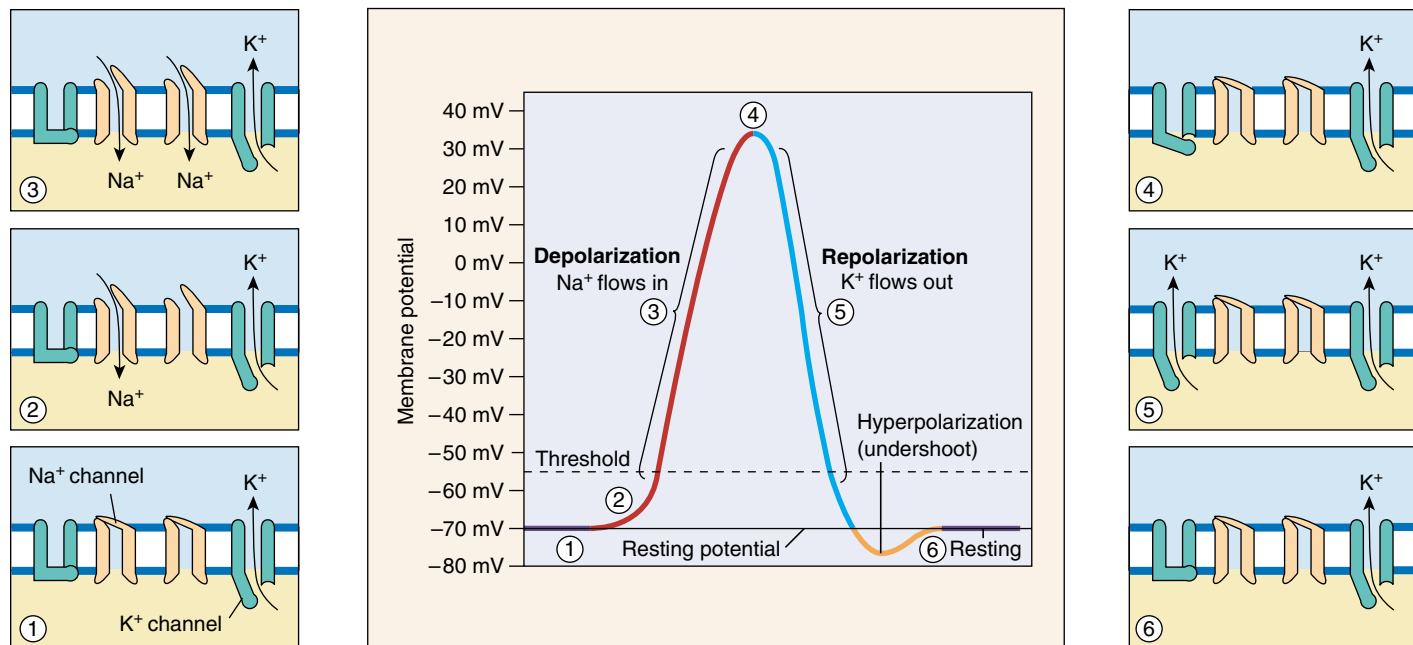


FIGURE 54.10
The action potential. (1) At resting membrane potential, some K^+ channels are open. (2) In response to a stimulus, the cell begins to depolarize, and once the threshold level is reached, an action potential is produced. (3) Rapid depolarization occurs (the rising portion of the spike) because sodium channels open, allowing Na^+ to diffuse into the axon. (4) At the top of the spike, Na^+ channels close, and K^+ channels that were previously closed begin to open. (5) With the K^+ channels open, repolarization occurs because of the diffusion of K^+ out of the axon. (6) An undershoot occurs before the membrane returns to its original resting potential.

When the action potential is recorded on an oscilloscope, this part of the action potential appears as the *rising phase* of a spike (figure 54.10). The membrane potential never quite reaches +60 mV because the Na^+ channels close and, at about the same time, the K^+ channels that were previously closed begin to open. The action potential thus peaks at about +30 mV. Opening the K^+ channels allows K^+ to diffuse out of the cell, repolarizing the plasma membrane. On an oscilloscope, this repolarization of the membrane appears as the *falling phase* of the action potential. In many cases, the repolarization carries the membrane potential to a value slightly more negative than the resting potential for a brief period because K^+ channels remain open, resulting in an *undershoot*. The entire sequence of events in an action potential is over in a few milliseconds.

Action potentials have two distinguishing characteristics. First, they follow an all-or-none law: each depolarization produces either a full action potential, because the voltage-gated Na^+ channels open completely at threshold, or none at all. Secondly, action potentials are always separate events; they cannot add together or interfere with one another as graded potentials can because the membrane enters a brief refractory period after it generates an action potential during which time voltage-gated Na^+ channels cannot reopen.

The production of an action potential results entirely from the passive diffusion of ions. However, at the end of each action potential, the cytoplasm has a little more Na^+ and a little less K^+ than it did at rest. The constant activity of the sodium-potassium pumps compensates for these changes. Thus, although active transport is not required to produce action potentials, it is needed to maintain the ion gradients.

Propagation of Action Potentials

Although we often speak of axons as conducting action potentials (impulses), action potentials do not really travel along an axon—they are events that are reproduced at different points along the axon membrane. This can occur for two reasons: action potentials are stimulated by depolarization, and an action potential can serve as a depolarization stimulus. Each action potential, during its rising phase, reflects a reversal in membrane polarity (from -70 mV to +30 mV) as Na^+ diffuses rapidly into the axon. The positive charges can depolarize the next region of membrane to threshold, so that the next region produces its own action potential (figure 54.11). Meanwhile, the previous region of membrane repolarizes back to the resting membrane potential. This is analogous to people in a stadium performing the “wave”: individuals stay in place as they stand up (depolarize), raise their hands (peak of the action potential), and sit down again (repolarize).

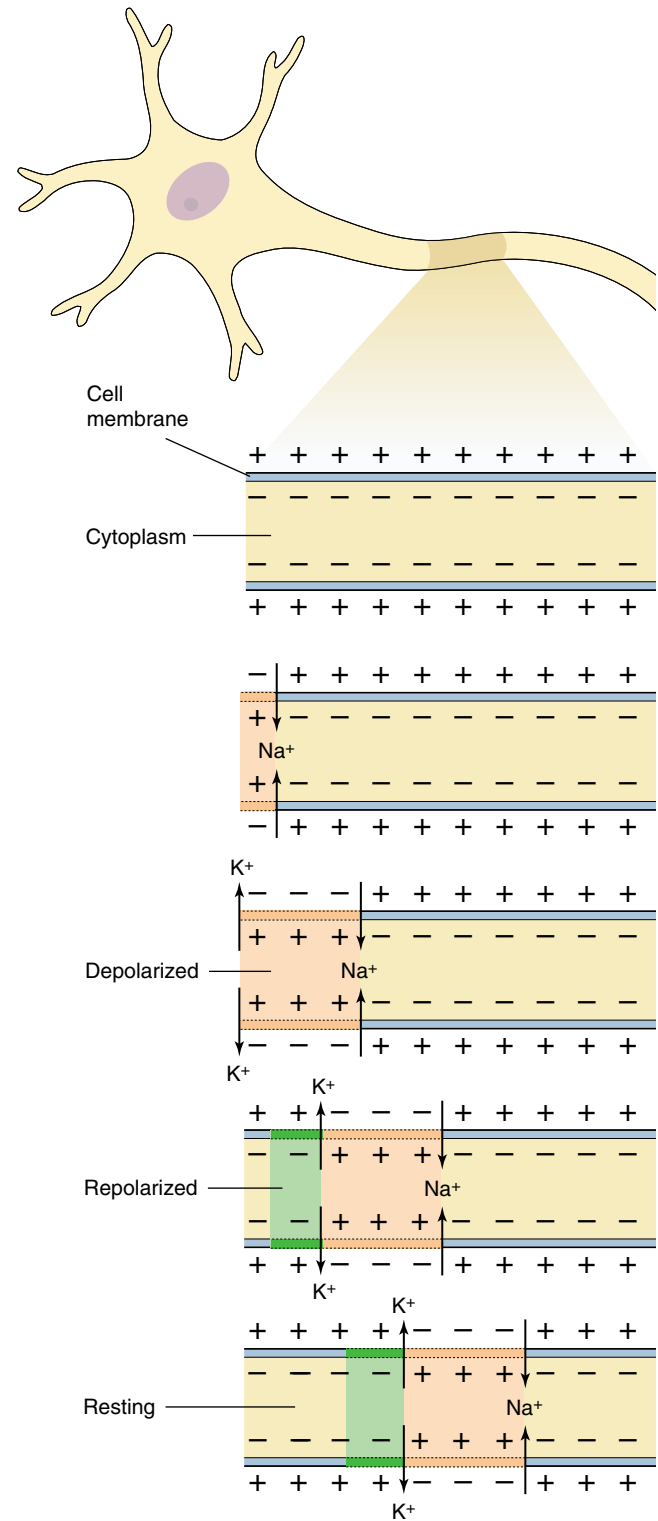


FIGURE 54.11
Propagation of an action potential in an unmyelinated axon.
 When one region produces an action potential and undergoes a reversal of polarity, it serves as a depolarization stimulus for the next region of the axon. In this way, action potentials are regenerated along each small region of the unmyelinated axon membrane.

Saltatory Conduction

Action potentials are conducted without decrement (without decreasing in amplitude); thus, the last action potential at the end of the axon is just as large as the first action potential. The velocity of conduction is greater if the diameter of the axon is large or if the axon is myelinated (table 54.2). Myelinated axons conduct impulses more rapidly than nonmyelinated axons because the action potentials in myelinated axons are only produced at the nodes of Ranvier. One action potential still serves as the depolarization stimulus for the next, but the depolarization at one node must spread to the next before the voltage-gated channels can be opened. The impulses therefore seem to jump from node to node (figure 54.12) in a process called **saltatory conduction** (Latin *saltare*, “to jump”).

To see how saltatory conduction speeds nervous transmission, return for a moment to the “wave” analogy used on the previous page to describe propagation of an action potential. The “wave” moves across the seats of a crowded stadium as fans standing up in one section trigger the next section to stand up in turn. Because the “wave” will skip sections of empty bleachers, it actually progresses around the stadium even faster with more empty sections. The wave doesn’t have to wait for the missing people to stand, simply “jumping” the gaps—just as saltatory conduction jumps the nonconduction “gaps” of myelin between exposed nodes.

The rapid inward diffusion of Na^+ followed by the outward diffusion of K^+ produces a rapid change in the membrane potential called an action potential. Action potentials are all-or-none events and cannot summate. Action potentials are regenerated along an axon as one action potential serves as the depolarization stimulus for the next action potential.

Table 54.2 Conduction Velocities of Some Axons

	Axon Diameter (mm)	Myelin	Conduction Velocity (m/s)
Squid giant axon	500	No	25
Large motor axon to human leg muscle	20	Yes	120
Axon from human skin pressure receptor	10	Yes	50
Axon from human skin temperature receptor	5	Yes	20
Motor axon to human internal organ	1	No	2

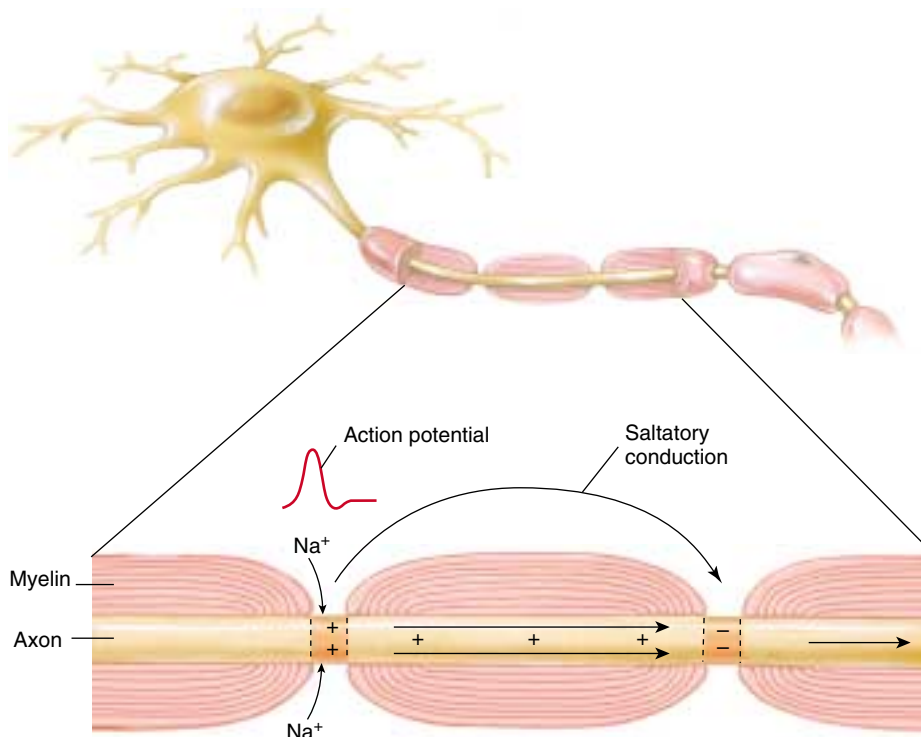


FIGURE 54.12

Saltatory conduction in a myelinated axon. Action potentials are only produced at the nodes of Ranvier in a myelinated axon. One node depolarizes the next node so that the action potentials can skip between nodes. As a result, saltatory (“leaping”) conduction in a myelinated axon is more rapid than conduction in an unmyelinated axon.

54.3 Neurons form junctions called synapses with other cells.

Structure of Synapses

An action potential passing down an axon eventually reaches the end of the axon and all of its branches. These branches may form junctions with the dendrites of other neurons, with muscle cells, or with gland cells. Such intercellular junctions are called **synapses**. The neuron whose axon transmits action potentials to the synapse is the *presynaptic cell*, while the cell on the other side of the synapse is the *postsynaptic cell*. Although the presynaptic and postsynaptic cells may appear to touch when the synapse is seen under a light microscope, examination with an electron microscope reveals that most synapses have a **synaptic cleft**, a narrow space that separates these two cells (figure 54.13).

The end of the presynaptic axon is swollen and contains numerous **synaptic vesicles**, which are each packed with chemicals called **neurotransmitters**. When action potentials arrive at the end of the axon, they stimulate the opening of voltage-gated Ca^{++} channels, causing a rapid inward diffusion of Ca^{++} . This serves as the stimulus for the fusion of the synaptic vesicles membrane with the plasma membrane of the axon, so that the contents of the vesicles can be released by exocytosis (figure 54.14). The higher the frequency of action potentials in the presynaptic axon, the more vesicles will release their contents of neurotransmitters. The neurotransmitters diffuse rapidly to the other side of the cleft and bind to **receptor proteins** in the membrane of the postsynaptic cell. There are different types of neurotransmitters, and different ones act in different ways. We will next consider the action of a few of the important neurotransmitter chemicals.

The presynaptic axon is separated from the postsynaptic cell by a narrow synaptic cleft. Neurotransmitters diffuse across it to transmit a nerve impulse.

FIGURE 54.14

The release of neurotransmitter. Action potentials arriving at the end of an axon trigger the uptake of Ca^{++} , which causes synaptic vesicles to fuse with the plasma membrane and release their neurotransmitters (acetylcholine [ACh] in this case), which diffuse across the synaptic gap and bind to receptors in the postsynaptic membrane.

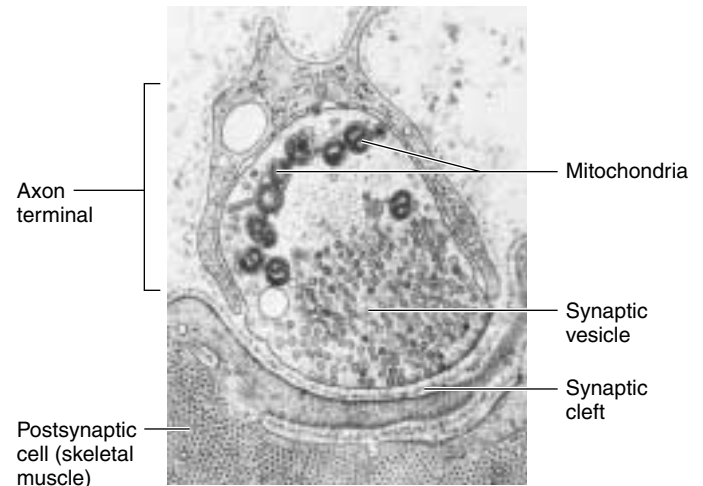
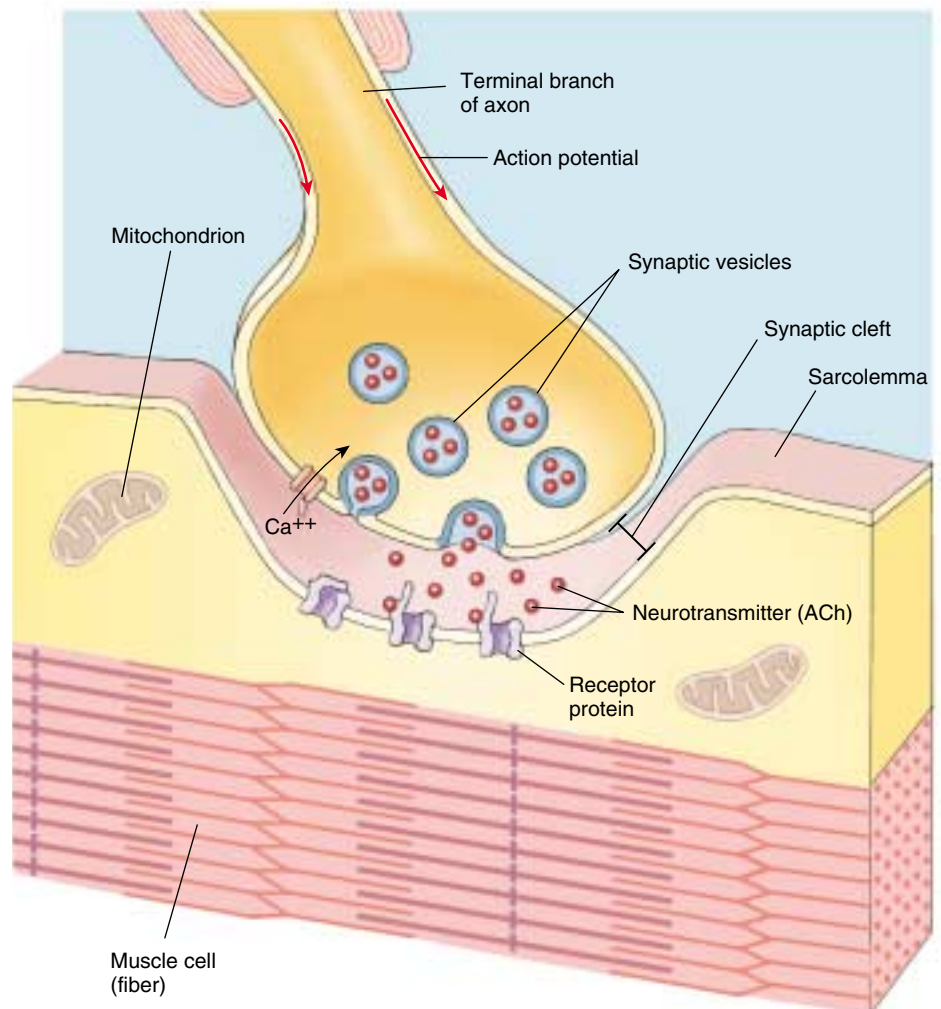


FIGURE 54.13

A synaptic cleft. An electron micrograph showing a neuromuscular synapse.



Neurotransmitters and Their Functions

Acetylcholine was the first neurotransmitter chemical to be discovered and is widely used in the nervous system. Many other neurotransmitter chemicals have been shown to play important roles, however, and ongoing research continues to produce new information about neurotransmitter function.

Acetylcholine

Acetylcholine (ACh) is the neurotransmitter that crosses the synapse between a motor neuron and a muscle fiber. This synapse is called a *neuromuscular junction* (figure 54.15). Acetylcholine binds to its receptor proteins in the postsynaptic membrane and thereby causes ion channels within these proteins to open (figure 54.16). The gates to these ion channels are said to be *chemically gated* because they open in response to ACh, rather than in response to depolarization. The opening of the chemically regulated channels permits Na^+ to diffuse into the postsynaptic cell and K^+ to diffuse out. Although both ions move at the same time, the inward diffusion of Na^+ occurs at a faster rate and has the predominant effect. As a result, that site on the



FIGURE 54.15
Neuromuscular junctions. A light micrograph shows axons branching to make contact with several individual muscle fibers.

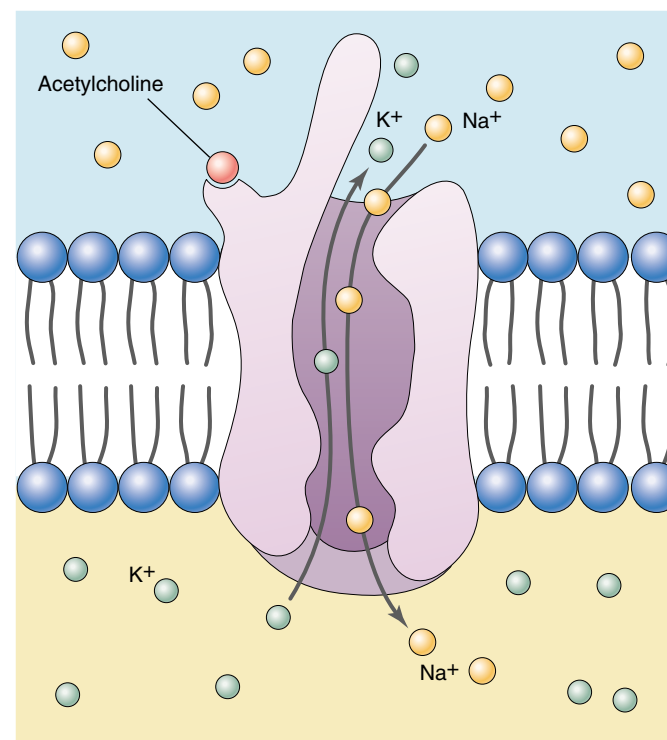
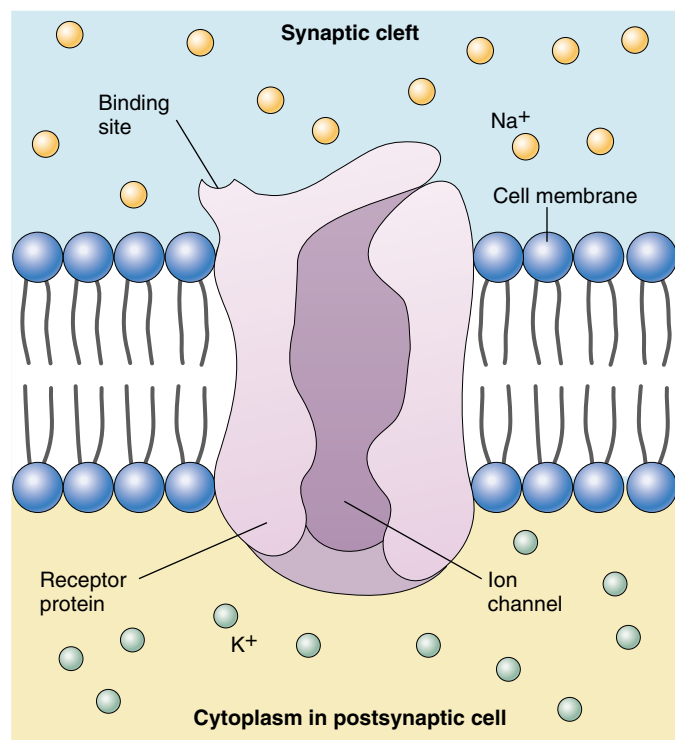


FIGURE 54.16
The binding of ACh to its receptor opens ion channels. The chemically regulated gates to these channels open when the neurotransmitter ACh binds to the receptor.

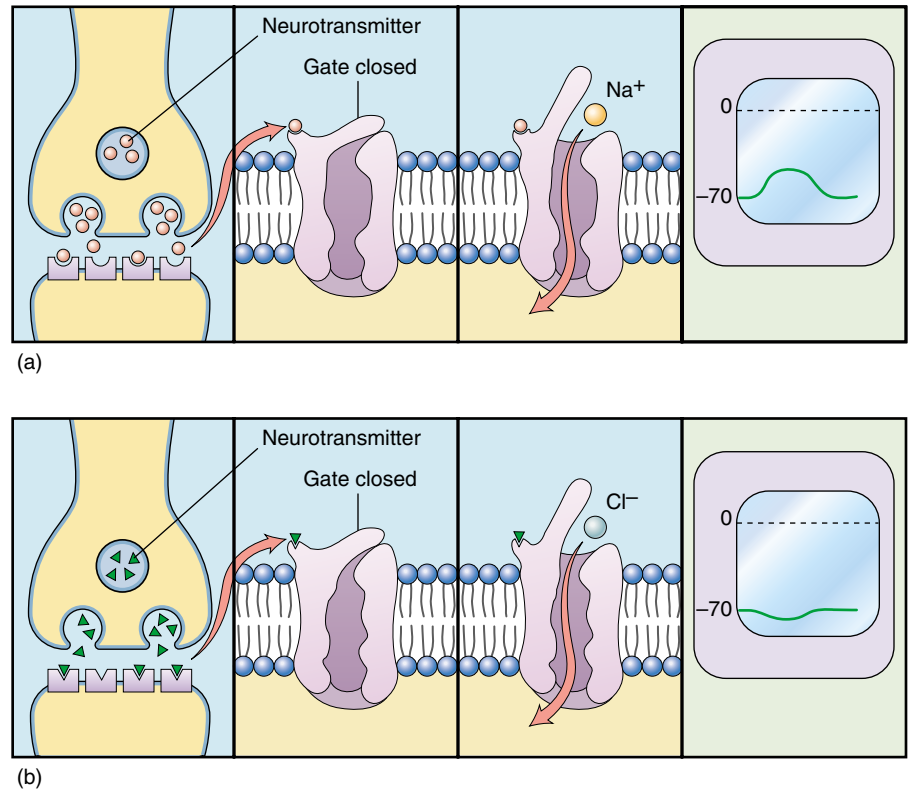


FIGURE 54.17
Different neurotransmitters can have different effects. (a) An excitatory neurotransmitter promotes a depolarization, or excitatory postsynaptic potential (EPSP). (b) An inhibitory neurotransmitter promotes a hyperpolarization, or inhibitory postsynaptic potential (IPSP).

postsynaptic membrane produces a depolarization (figure 54.17a) called an **excitatory postsynaptic potential (EPSP)**. The EPSP can now open the voltage-gated channels for Na⁺ and K⁺ that are responsible for action potentials. Because the postsynaptic cell we are discussing is a skeletal muscle cell, the action potentials it produces stimulate muscle contraction through the mechanisms discussed in chapter 50.

If ACh stimulates muscle contraction, we must be able to eliminate ACh from the synaptic cleft in order to relax our muscles. This illustrates a general principle: molecules such as neurotransmitters and certain hormones must be quickly eliminated after secretion if they are to be effective regulators. In the case of ACh, the elimination is achieved by an enzyme in the postsynaptic membrane called **acetylcholinesterase (AChE)**. This enzyme is one of the fastest known, cleaving ACh into inactive fragments. Nerve gas and the agricultural insecticide parathion are potent inhibitors of AChE and in humans can produce severe spastic paralysis and even death if the respiratory muscles become paralyzed.

Although ACh acts as a neurotransmitter between motor neurons and skeletal muscle cells, many neurons also use ACh as a neurotransmitter at their synapses with other neurons; in these cases, the postsynaptic membrane is generally on the dendrites or cell body of the second neuron. The EPSPs produced must then travel through the dendrites and cell body to the initial segment of the axon, where the first voltage-regulated channels needed for action potentials are located. This is where the first action

potentials will be produced, providing that the EPSP depolarization is above the threshold needed to trigger action potentials.

Glutamate, Glycine, and GABA

Glutamate is the major excitatory neurotransmitter in the vertebrate CNS, producing EPSPs and stimulating action potentials in the postsynaptic neurons. Although normal amounts produce physiological stimulation, excessive stimulation by glutamate has been shown to cause neurodegeneration, as in Huntington's chorea.

Glycine and **GABA** (an acronym for gamma-aminobutyric acid) are inhibitory neurotransmitters. If you remember that action potentials are triggered by a threshold level of depolarization, you will understand why hyperpolarization of the membrane would cause inhibition. These neurotransmitters cause the opening of chemically regulated gated channels for Cl⁻, which has a concentration gradient favoring its diffusion into the neuron. Because Cl⁻ is negatively charged, it makes the inside of the membrane even more negative than it is at rest—from -70 mV to -85 mV, for example (figure 54.17b). This hyperpolarization is called an **inhibitory postsynaptic potential (IPSP)**, and is very important for neural control of body movements and other brain functions. Interestingly, the drug diazepam (Valium) causes its sedative and other effects by enhancing the binding of GABA to its receptors and thereby increasing the effectiveness of GABA at the synapse.

Biogenic Amines

The **biogenic amines** include the hormone epinephrine (adrenaline), together with the neurotransmitters dopamine, norepinephrine, and serotonin. Epinephrine, norepinephrine, and dopamine are derived from the amino acid tyrosine and are included in the subcategory of *catecholamines*. Serotonin is a biogenic amine derived from a different amino acid, tryptophan.

Dopamine is a very important neurotransmitter used in the brain to control body movements and other functions. Degeneration of particular dopamine-releasing neurons produces the resting muscle tremors of Parkinson's disease, and people with this condition are treated with L-dopa (an acronym for dihydroxyphenylalanine), a precursor of dopamine. Additionally, studies suggest that excessive activity of dopamine-releasing neurons in other areas of the brain is associated with schizophrenia. As a result, patients with schizophrenia are sometimes helped by drugs that block the production of dopamine.

Norepinephrine is used by neurons in the brain and also by particular autonomic neurons, where its action as a neurotransmitter complements the action of the hormone epinephrine, secreted by the adrenal gland. The autonomic nervous system will be discussed in a later section of this chapter.

Serotonin is a neurotransmitter involved in the regulation of sleep and is also implicated in various emotional states. Insufficient activity of neurons that release serotonin may be one cause of clinical depression; this is suggested by the fact that antidepressant drugs, particularly fluoxetine (Prozac) and related compounds, specifically block the elimination of serotonin from the synaptic cleft (figure 54.18). The drug lysergic acid diethylamide (LSD) specifically blocks serotonin receptors in a region of the brain stem known as the raphe nuclei.

Other Neurotransmitters

Axons also release various polypeptides, called **neuropeptides**, at synapses. These neuropeptides may have a neurotransmitter function or they may have more subtle, long-term action on the postsynaptic neurons. In the latter case, they are often referred to as **neuromodulators**. A given axon generally releases only one kind of neurotransmitter, but many can release both a neurotransmitter and a neuromodulator.

One important neuropeptide is **substance P**, which is released at synapses in the CNS by sensory neurons activated by painful stimuli. The perception of pain, however, can vary depending on circumstances; an injured football

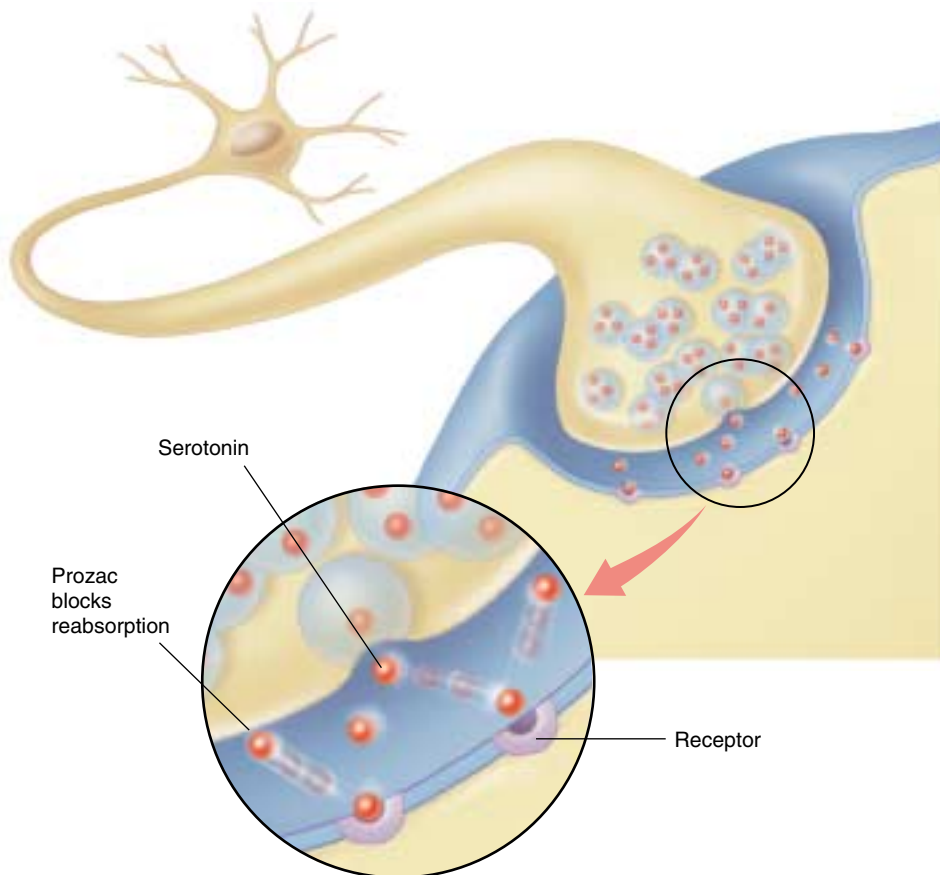
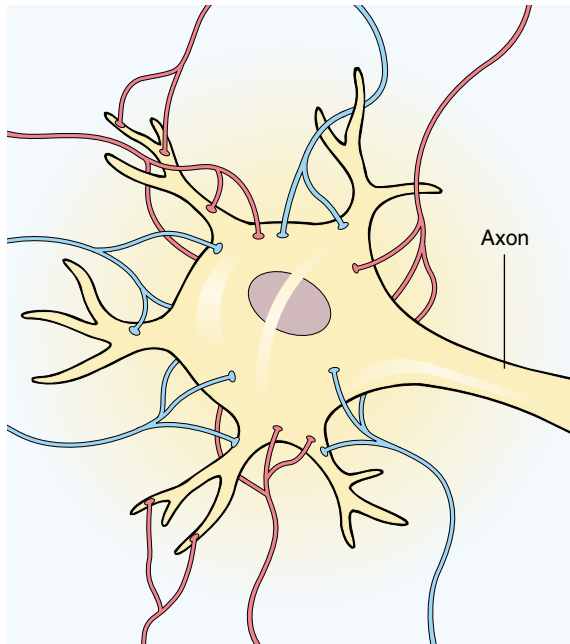
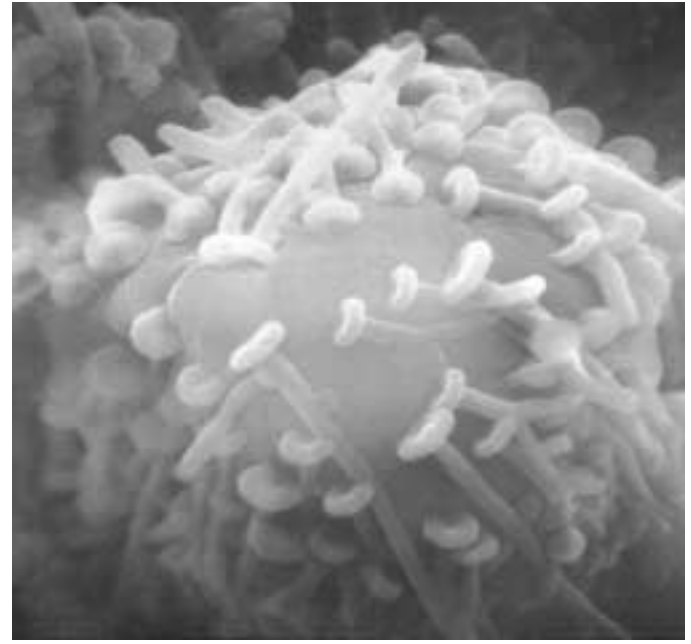


FIGURE 54.18

Serotonin and depression. Depression can result from a shortage of the neurotransmitter serotonin. The antidepressant drug Prozac works by blocking reabsorption of serotonin in the synapse, making up for the shortage.



(a)



(b)

FIGURE 54.19

Integration of EPSPs and IPSPs takes place on the neuronal cell body. (a) The synapses made by some axons are excitatory (blue); the synapses made by other axons are inhibitory (red). The summed influence of all of these inputs determines whether the axonal membrane of the postsynaptic cell will be sufficiently depolarized to produce an action potential. (b) Micrograph of a neuronal cell body with numerous synapses (15,000 \times).

player may not feel the full extent of his trauma, for example, until he's taken out of the game. The intensity with which pain is perceived partly depends on the effects of neuropeptides called **enkephalins** and **endorphins**. Enkephalins are released by axons descending from the brain and inhibit the passage of pain information to the brain. Endorphins are released by neurons in the brain stem and also block the perception of pain. Opium and its derivatives, morphine and heroin, have an analgesic (pain-reducing) effect because they are similar enough in chemical structure to bind to the receptors normally utilized by enkephalins and endorphins. For this reason, the enkephalins and the endorphins are referred to as *endogenous opiates*.

Nitric oxide (NO) is the first gas known to act as a regulatory molecule in the body. Because NO is a gas, it diffuses through membranes so it cannot be stored in vesicles. It is produced as needed from the amino acid arginine. Nitric oxide's actions are very different from those of the more familiar nitrous oxide (N_2O), or laughing gas, sometimes used by dentists. Nitric oxide diffuses out of the presynaptic axon and into neighboring cells by simply passing through the lipid portions of the cell membranes. In the PNS, nitric oxide is released by some neurons that innervate the gastrointestinal tract, penis, respiratory passages, and cerebral blood vessels. These are

autonomic neurons that cause smooth muscle relaxation in their target organs. This can produce, for example, the engorgement of the spongy tissue of the penis with blood, causing erection. The drug sildenafil (Viagra) increases the release of nitric oxide in the penis, prolonging erection. Nitric oxide is also released as a neurotransmitter in the brain, and has been implicated in the processes of learning and memory.

Synaptic Integration

The activity of a postsynaptic neuron in the brain and spinal cord of vertebrates is influenced by different types of input from a number of presynaptic neurons. For example, a single motor neuron in the spinal cord can receive as many as 50,000 synapses from presynaptic axons! Each postsynaptic neuron may receive both excitatory and inhibitory synapses. The EPSPs (depolarizations) and IPSPs (hyperpolarizations) from these synapses interact with each other when they reach the cell body of the neuron. Small EPSPs add together to bring the membrane potential closer to the threshold, while IPSPs subtract from the depolarizing effect of the EPSPs, keeping the membrane potential below the threshold (figure 54.19). This process is called **synaptic integration**.

Neurotransmitters and Drug Addiction

When a cell of your body is exposed to a stimulus that produces a chemically mediated signal for a prolonged period, it tends to lose its ability to respond to the stimulus with its original intensity. (You are familiar with this loss of sensitivity—when you sit in a chair, how long are you aware of the chair?) Nerve cells are particularly prone to this loss of sensitivity. If receptor proteins within synapses are exposed to high levels of neurotransmitter molecules for prolonged periods, that nerve cell often responds by inserting fewer receptor proteins into the membrane. This feedback is a normal function in all neurons, one of several mechanisms that have evolved to make the cell more efficient, in this case, adjusting the number of “tools” (receptor proteins) in the membrane “workshop” to suit the workload.

Cocaine. The drug cocaine causes abnormally large amounts of neurotransmitter to remain in the synapses for long periods of time. Cocaine affects nerve cells in the brain’s pleasure pathways (the so-called limbic system). These cells transmit pleasure messages using the neurotransmitter dopamine. Using radioactively labeled cocaine molecules, investigators found that cocaine binds tightly to the transporter proteins in synaptic clefts. These proteins normally remove the neurotransmitter dopamine after it has acted. Like a game of musical chairs in which all the chairs become occupied, there are no unoccupied carrier proteins available to the dopamine molecules, so the dopamine stays in the cleft, firing the receptors again and again. As new signals arrive, more and more dopamine is added, firing the pleasure pathway more and more often (figure 54.20).

When receptor proteins on limbic system nerve cells are exposed to high levels of dopamine neurotransmitter molecules for prolonged periods of time, the nerve cells “turn down the volume” of the signal by lowering the number of receptor proteins on their surfaces. They respond to the greater number of neurotransmitter molecules by simply reducing the number of targets available for these molecules to hit. The cocaine user is now addicted (figure 54.21). With so few receptors, the user needs the drug to maintain even normal levels of limbic activity.

Is Nicotine an Addictive Drug? Investigators attempting to explore the habit-forming nature of nicotine used what had been learned about cocaine to carry out what seemed a reasonable experiment—they introduced radioactively labeled nicotine into the brain and looked to see what sort of carrier protein it attached itself to. To their great surprise, the nicotine ignored proteins in the synaptic clefts and instead bound directly to a specific receptor on the postsynaptic cell! This was totally unexpected, as nicotine does not normally occur in the brain—why should it have a receptor there?

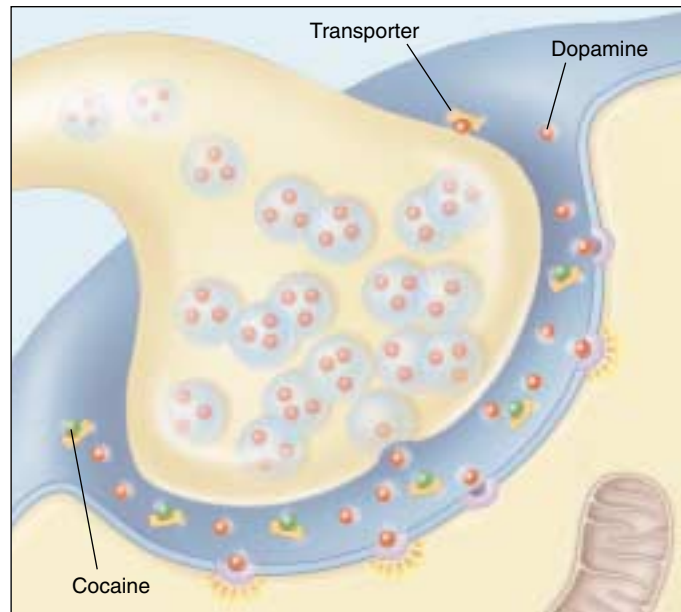


FIGURE 54.20
How cocaine alters events at the synapse. When cocaine binds to the dopamine transporters, the neurotransmitter survives longer in the synapse and continues to stimulate the postsynaptic cell. Cocaine thus acts to intensify pleasurable sensations.

Intensive research followed, and researchers soon learned that the “nicotine receptors” were a class of receptors that normally served to bind the neurotransmitter acetylcholine. There are other types of ACh receptors that don’t respond to nicotine. It was just an accident of nature that nicotine, an obscure chemical from a tobacco plant, was also able to bind to them. What, then, is the normal function of these receptors? The target of considerable research, these receptors turned out to be one of the brain’s most important tools. The brain uses them to coordinate the activities of many other kinds of receptors, acting to “fine tune” the sensitivity of a wide variety of behaviors.

When neurobiologists compare the nerve cells in the brains of smokers to those of nonsmokers, they find changes in both the number of nicotine receptors and in the levels of RNA used to make the receptors. They have found that the brain adjusts to prolonged exposure to nicotine by “turning down the volume” in two ways: (1) by making fewer receptor proteins to which nicotine can bind; and (2) by altering the pattern of *activation* of the nicotine receptors (that is, their sensitivity to neurotransmitter).

It is this second adjustment that is responsible for the profound effect smoking has on the brain’s activities. By overriding the normal system used by the brain to coordinate its many activities, nicotine alters the pattern of release into synaptic clefts of many neurotransmitters, including acetylcholine, dopamine, serotonin, and many others.

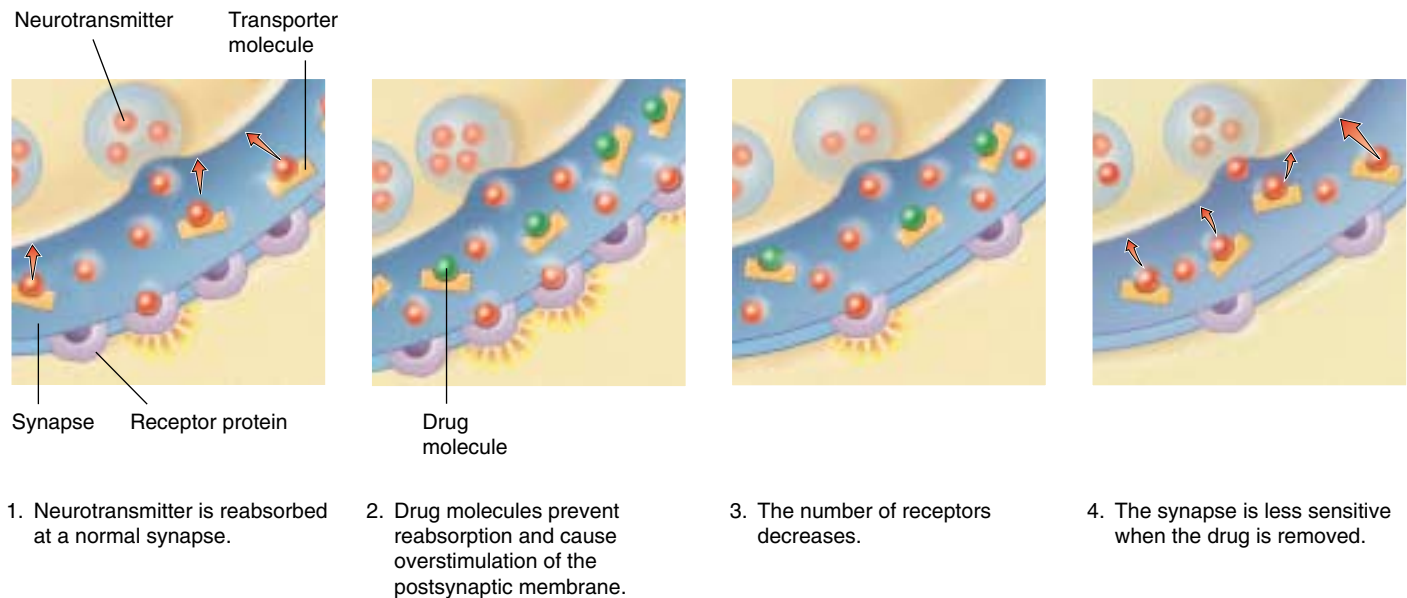


FIGURE 54.21

Drug addiction. (1) In a normal synapse, the neurotransmitter binds to a transporter molecule and is rapidly reabsorbed after it has acted. (2) When a drug molecule binds to the transporters, reabsorption of the neurotransmitter is blocked, and the postsynaptic cell is overstimulated by the increased amount of neurotransmitter left in the synapse. (3) The central nervous system adjusts to the increased firing by producing fewer receptors in the postsynaptic membrane. The result is addiction. (4) When the drug is removed, normal absorption of the neurotransmitter resumes, and the decreased number of receptors creates a less-sensitive nerve pathway. Physiologically, the only way a person can then maintain normal functioning is to continue to take the drug. Only if the drug is removed permanently will the nervous system eventually adjust again and restore the original amount of receptors.

As a result, changes in level of activity occur in a wide variety of nerve pathways within the brain.

Addiction occurs when chronic exposure to nicotine induces the nervous system to adapt physiologically. The brain compensates for the many changes nicotine induces by making other changes. Adjustments are made to the numbers and sensitivities of many kinds of receptors within the brain, restoring an appropriate balance of activity.

Now what happens if you stop smoking? Everything is out of whack! The newly coordinated system *requires* nicotine to achieve an appropriate balance of nerve pathway activities. This is addiction in any sensible use of the term. The body's physiological response is profound and unavoidable. There is no way to prevent addiction to nicotine with willpower, any more than willpower can stop a bullet when playing Russian roulette with a loaded gun. If you smoke cigarettes for a prolonged period, you will become addicted.

What do you do if you are addicted to smoking cigarettes and you want to stop? When use of an addictive drug like nicotine is stopped, the level of signaling will change to levels far from normal. If the drug is not reintroduced, the altered level of signaling will eventually induce the nerve cells to once again make compensatory changes that restore an appropriate balance of activities within the brain. Over time, receptor numbers, their sensitivity, and patterns of release of neurotransmitters all revert to normal, once

again producing normal levels of signaling along the pathways. There is no way to avoid the down side of addiction. The pleasure pathways will not function at normal levels until the number of receptors on the affected nerve cells have time to readjust.

Many people attempt to quit smoking by using patches containing nicotine; the idea is that providing gradually lesser doses of nicotine allows the smoker to be weaned of his or her craving for cigarettes. The patches do reduce the craving for cigarettes—so long as you keep using the patches! Actually, using such patches simply substitutes one (admittedly less dangerous) nicotine source for another. If you are going to quit smoking, there is no way to avoid the necessity of eliminating the drug to which you are addicted. Hard as it is to hear the bad news, there is no easy way out. The only way to quit is to quit.

Acetylcholine stimulates the opening of chemically regulated ion channels, causing a depolarization called an excitatory postsynaptic potential (EPSP). Glycine and GABA are inhibitory neurotransmitters that produce hyperpolarization of the postsynaptic membrane. There are also many other neurotransmitters, including the biogenic amines: dopamine, norepinephrine, and serotonin. The effects of different neurotransmitters are integrated through summation of depolarizations and hyperpolarizations.

54.4 The central nervous system consists of the brain and spinal cord.

The Evolution of the Vertebrate Brain

Sponges are the only major phylum of multicellular animals that lack nerves. The simplest nervous systems occur among cnidarians (figure 54.22): all neurons are similar and are linked to one another in a web, or *nerve net*. There is no associative activity, no control of complex actions, and little coordination. The simplest animals with associative activity in the nervous system are the free-living flatworms, phylum Platyhelminthes. Running down the bodies of these flatworms are two nerve cords; peripheral nerves extend outward to the muscles of the body. The two nerve cords converge at the front end of the body, forming an enlarged mass of nervous tissue that also contains associative neurons with synapses connecting neurons to one another. This primitive “brain” is a rudimentary central nervous system and permits a far more complex control of muscular responses than is possible in cnidarians.

All of the subsequent evolutionary changes in nervous systems can be viewed as a series of elaborations on the characteristics already present in flatworms. For example, earthworms exhibit a central nervous system that is connected to all other parts of the body by peripheral nerves. And, in arthropods, the central coordination of complex response is increasingly localized in the front end of the nerve cord. As this region evolved, it came to contain a progressively larger number of associative interneurons, and to develop tracts, which are highways within the brain that connect associative elements.

Casts of the interior braincases of fossil agnathans, fishes that swam 500 million years ago, have revealed much about the early evolutionary stages of the vertebrate brain. Although small, these brains already had the three divisions that characterize the brains of all contemporary vertebrates: (1) the hindbrain, or rhombencephalon; (2) the midbrain, or mesencephalon; and (3) the forebrain, or prosencephalon (figure 54.23).

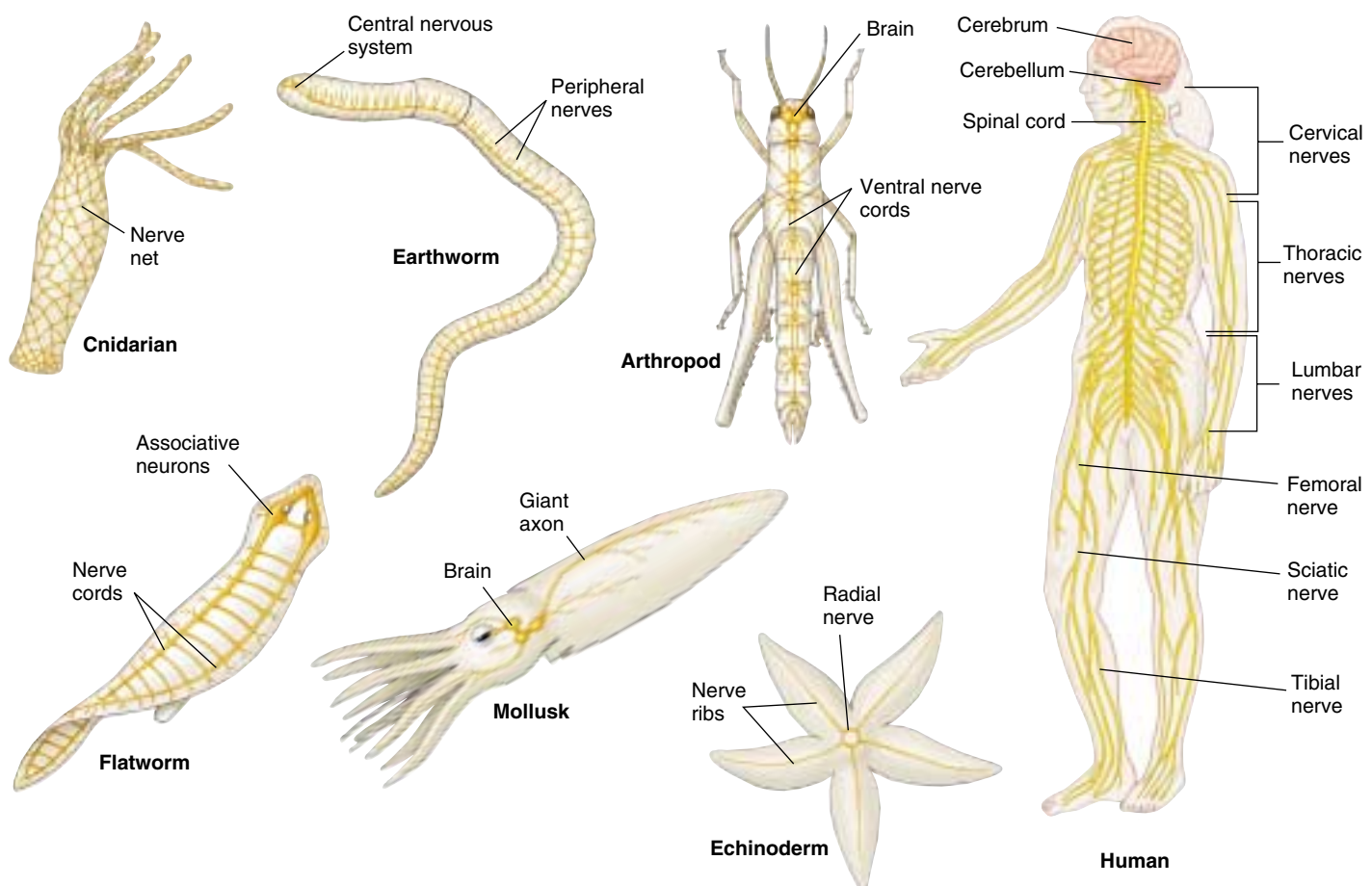


FIGURE 54.22
Evolution of the nervous system. Animals exhibit a progressive elaboration of organized nerve cords and the centralization of complex responses in the front end of the nerve cord.

The hindbrain was the major component of these early brains, as it still is in fishes today. Composed of the *cerebellum*, *pons*, and *medulla oblongata*, the hindbrain may be considered an extension of the spinal cord devoted primarily to coordinating motor reflexes. Tracts containing large numbers of axons run like cables up and down the spinal cord to the hindbrain. The hindbrain, in turn, integrates the many sensory signals coming from the muscles and coordinates the pattern of motor responses.

Much of this coordination is carried on within a small extension of the hindbrain called the cerebellum (“little cerebrum”). In more advanced vertebrates, the cerebellum plays an increasingly important role as a coordinating center for movement and is correspondingly larger than it is in the fishes. In all vertebrates, the cerebellum processes data on the current position and movement of each limb, the state of relaxation or contraction of the muscles involved, and the general position of the body and its relation to the outside world. These data are gathered in the cerebellum, synthesized, and the resulting commands issued to efferent pathways.

In fishes, the remainder of the brain is devoted to the reception and processing of sensory information. The midbrain is composed primarily of the **optic lobes**, which receive and process visual information, while the forebrain is devoted to the processing of *olfactory* (smell) information. The brains of fishes continue growing throughout their lives. This continued growth is in marked contrast to the brains of other classes of vertebrates, which generally complete their development by infancy (figure 54.24). The

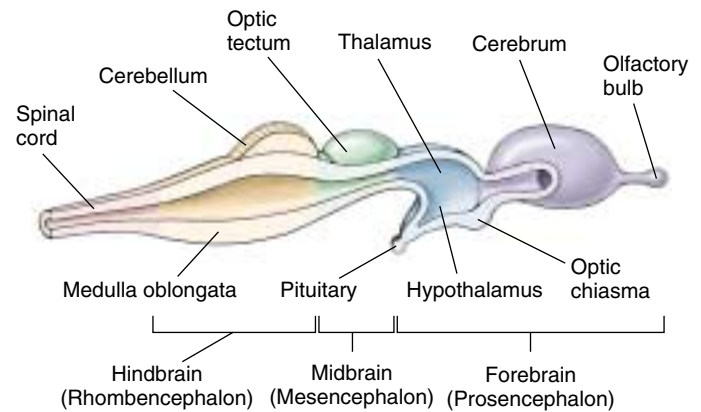


FIGURE 54.23
The basic organization of the vertebrate brain can be seen in the brains of primitive fishes. The brain is divided into three regions that are found in differing proportions in all vertebrates: the hindbrain, which is the largest portion of the brain in fishes; the midbrain, which in fishes is devoted primarily to processing visual information; and the forebrain, which is concerned mainly with olfaction (the sense of smell) in fishes. In terrestrial vertebrates, the forebrain plays a far more dominant role in neural processing than it does in fishes.

human brain continues to develop through early childhood, but no new neurons are produced once development has ceased, except in the tiny hippocampus, which controls which experiences are filed away into long-term memory and which are forgotten.

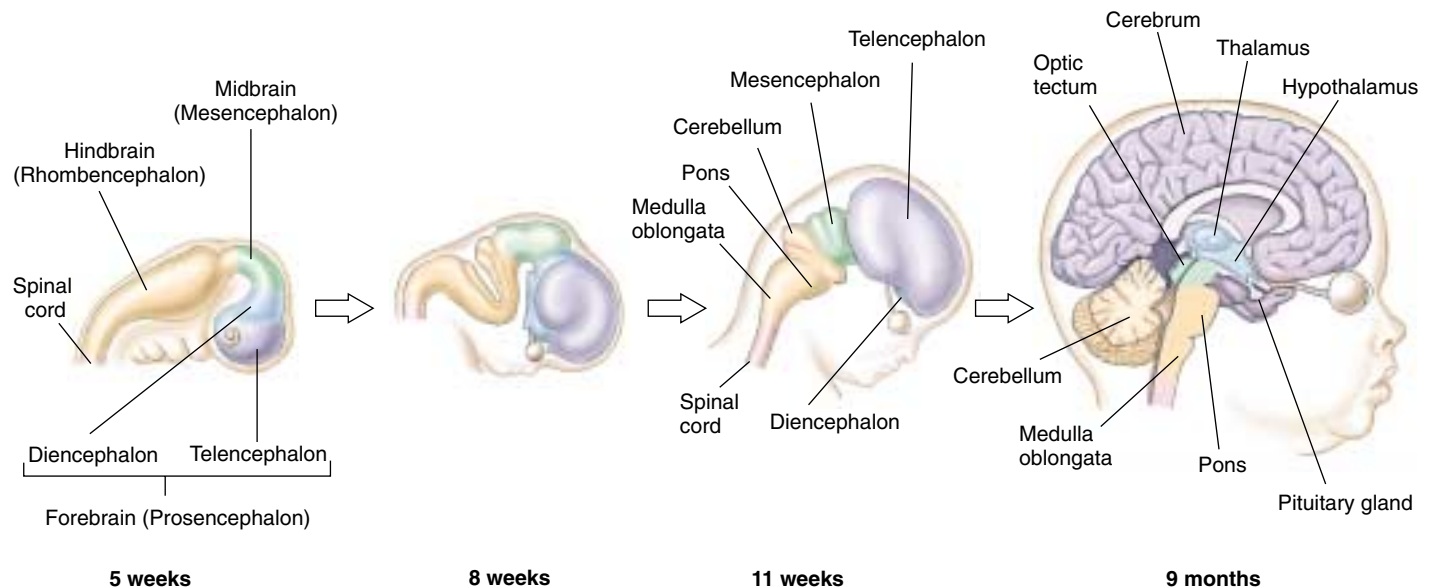


FIGURE 54.24
Development of the brain in humans. The main regions of the brain form during fetal development.

The Dominant Forebrain

Starting with the amphibians and continuing more prominently in the reptiles, processing of sensory information is increasingly centered in the forebrain. This pattern was the dominant evolutionary trend in the further development of the vertebrate brain (figure 54.25).

The forebrain in reptiles, amphibians, birds, and mammals is composed of two elements that have distinct functions. The *diencephalon* (Greek *dia*, “between”) consists of the thalamus and hypothalamus. The **thalamus** is an integrating and relay center between incoming sensory infor-

mation and the cerebrum. The **hypothalamus** participates in basic drives and emotions and controls the secretions of the pituitary gland. The *telencephalon*, or “end brain” (Greek *telos*, “end”), is located at the front of the forebrain and is devoted largely to associative activity. In mammals, the telencephalon is called the **cerebrum**.

The Expansion of the Cerebrum

In examining the relationship between brain mass and body mass among the vertebrates (figure 54.26), you can

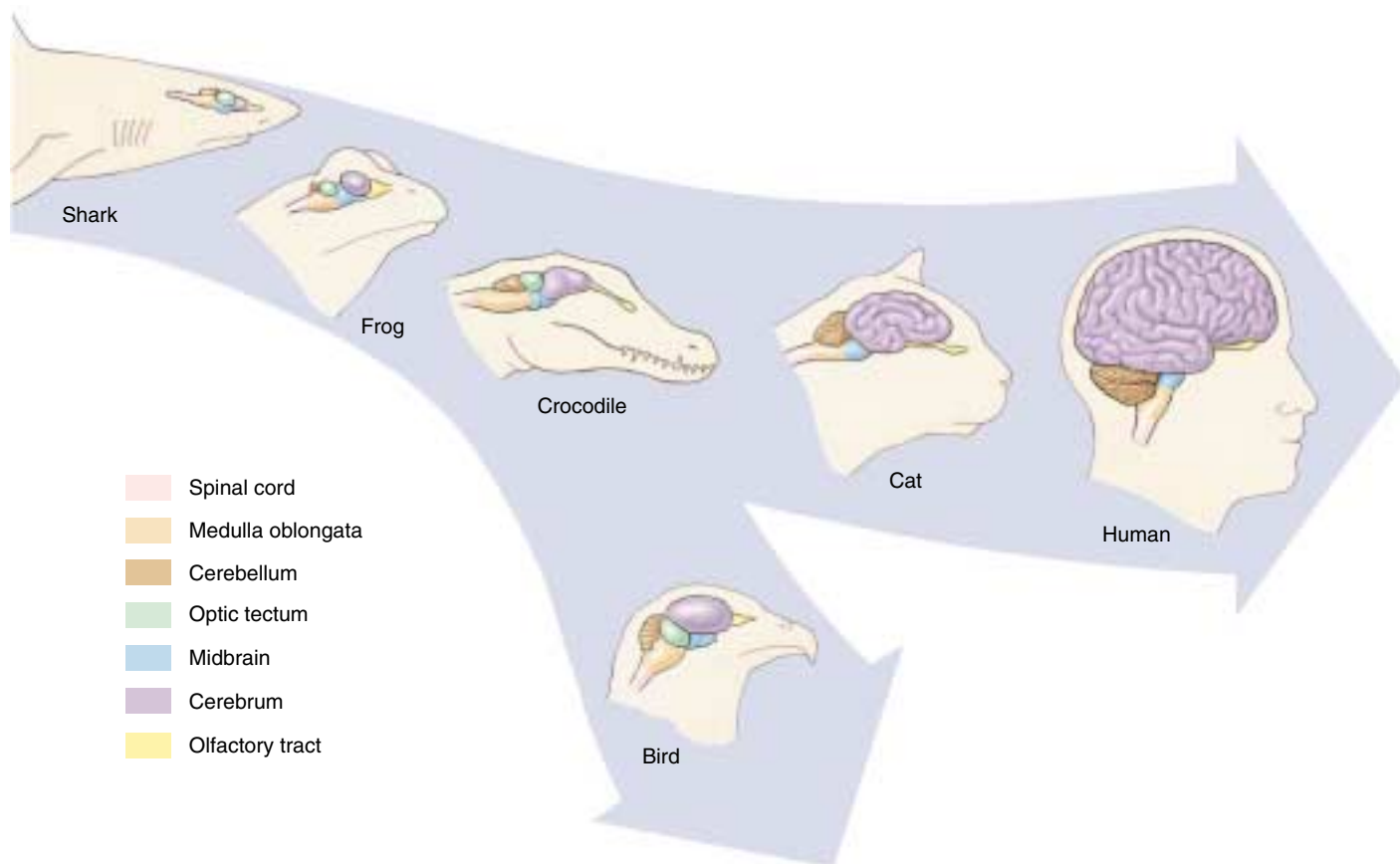


FIGURE 54.25

The evolution of the vertebrate brain involved changes in the relative sizes of different brain regions. In sharks and other fishes, the hindbrain is predominant, and the rest of the brain serves primarily to process sensory information. In amphibians and reptiles, the forebrain is far larger, and it contains a larger cerebrum devoted to associative activity. In birds, which evolved from reptiles, the cerebrum is even more pronounced. In mammals, the cerebrum covers the optic tectum and is the largest portion of the brain. The dominance of the cerebrum is greatest in humans, in whom it envelops much of the rest of the brain.

see a remarkable difference between fishes and reptiles, on the one hand, and birds and mammals, on the other. Mammals have brains that are particularly large relative to their body mass. This is especially true of porpoises and humans; the human brain weighs about 1.4 kilograms. The increase in brain size in the mammals largely reflects the great enlargement of the cerebrum, the dominant part of the mammalian brain. The cerebrum is the center for correlation, association, and learning in the mammalian brain. It receives sensory data from the thalamus and issues motor commands to the spinal cord via descending tracts of axons.

In vertebrates, the central nervous system is composed of the brain and the spinal cord (table 54.3). These two structures are responsible for most of the information processing within the nervous system and consist primarily of interneurons and neuroglia. Ascending tracts carry sensory information to the brain. Descending tracts carry impulses from the brain to the motor neurons and interneurons in the spinal cord that control the muscles of the body.

The vertebrate brain consists of three primary regions: the forebrain, midbrain, and hindbrain. The hindbrain was the principal component of the brain of early vertebrates; it was devoted to the control of motor activity. In vertebrates more advanced than fishes, the processing of information is increasingly centered in the forebrain.

Table 54.3 Subdivisions of the Central Nervous System

Major Subdivision	Function
SPINAL CORD	Spinal reflexes; relays sensory information
HINDBRAIN (rhombencephalon)	
Medulla oblongata	Sensory nuclei; reticular activating system; visceral control
Pons	Reticular activating system; visceral control
Cerebellum	Coordination of movements; balance
MIDBRAIN (Mesencephalon)	Reflexes involving eyes and ears
FOREBRAIN (Prosencephalon)	
Thalamus	Relay station for ascending sensory and descending tracts; visceral control
Hypothalamus	Visceral control; neuroendocrine control
Telencephalon (cerebrum)	
Basal ganglia	Motor control
Corpus callosum	Connects the two hemispheres
Hippocampus (limbic system)	Memory; emotion
Cerebral cortex	Higher functions

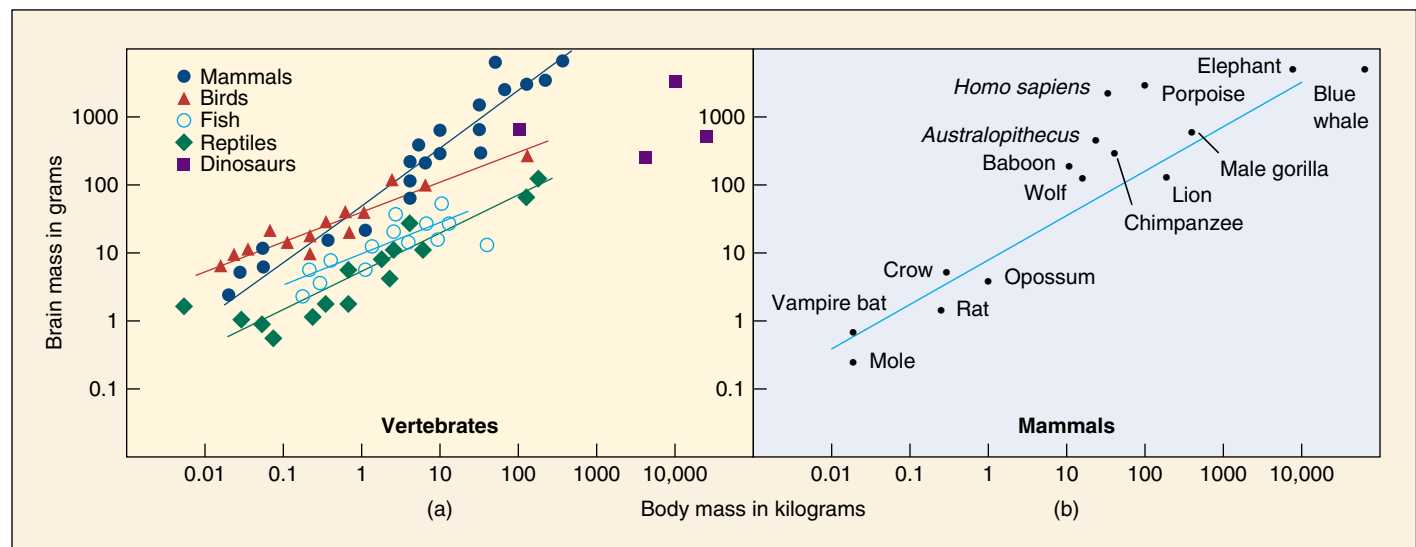


FIGURE 54.26

Brain mass versus body mass. Among most vertebrates, brain mass is a relatively constant proportion of body mass, so that a plot of brain mass versus body mass gives a straight line. (a) However, the proportion of brain mass to body mass is much greater in birds than in reptiles, and it is greater still in mammals. (b) Among mammals, humans have the greatest brain mass per unit of body mass (that is, the farthest perpendicular distance from the plotted line). In second place are the porpoises.

The Human Forebrain

The human cerebrum is so large that it appears to envelop the rest of the brain (figure 54.27). It is split into right and left cerebral hemispheres, which are connected by a tract called the *corpus callosum*. The hemispheres are further divided into the *frontal*, *parietal*, *temporal*, and *occipital lobes*.

Each hemisphere receives sensory input from the opposite, or contralateral, side of the body and exerts motor control primarily over that side. Therefore, a touch on the right hand, for example, is relayed primarily to the left hemisphere, which may then initiate movement of that hand in response to the touch. Damage to one hemisphere due to a stroke often results in a loss of sensation and paralysis on the contralateral side of the body.

Cerebral Cortex

Much of the neural activity of the cerebrum occurs within a layer of gray matter only a few millimeters thick on its outer surface. This layer, called the **cerebral cortex**, is densely packed with nerve cells. In humans, it contains over 10 billion nerve cells, amounting to roughly 10% of all the neurons in the brain. The surface of the cerebral cortex is highly convoluted; this is particularly true in the human brain, where the convolutions increase the surface area of the cortex threefold.

The activities of the cerebral cortex fall into one of three general categories: motor, sensory, and associative. The primary motor cortex lies along the *gyrus* (convolution) on the posterior border of the frontal lobe, just in front of the central *sulcus* (crease) (figure 54.28). Each point on its surface is associated with the movement of a different part of the body (figure 54.29). Just behind the central sulcus, on the anterior edge of the parietal lobe, lies the primary somatosensory cortex. Each point in this area receives input from sensory neurons serving cutaneous and muscle senses in a particular part of the body. Large areas of the motor cortex and primary somatosensory cortex are devoted to the fingers, lips, and tongue because of the need for manual dexterity and speech. The auditory cortex lies within the temporal lobe, and different regions of this cortex deal with different sound frequencies. The visual cortex lies on the occipital lobe, with different sites processing information from different positions on the retina, equivalent to particular points in the visual fields of the eyes.

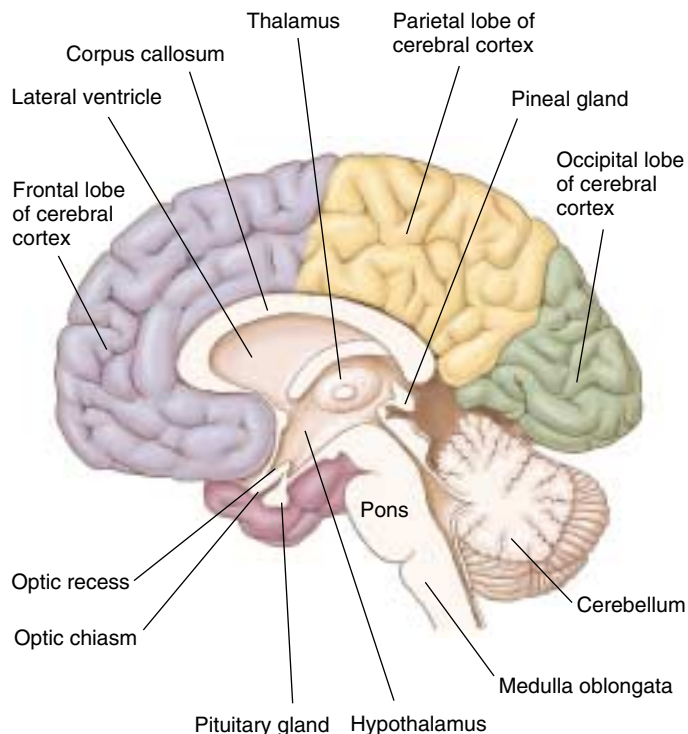


FIGURE 54.27
A section through the human brain. In this sagittal section showing one cerebral hemisphere, the corpus callosum, a fiber tract connecting the two cerebral hemispheres, can be clearly seen.

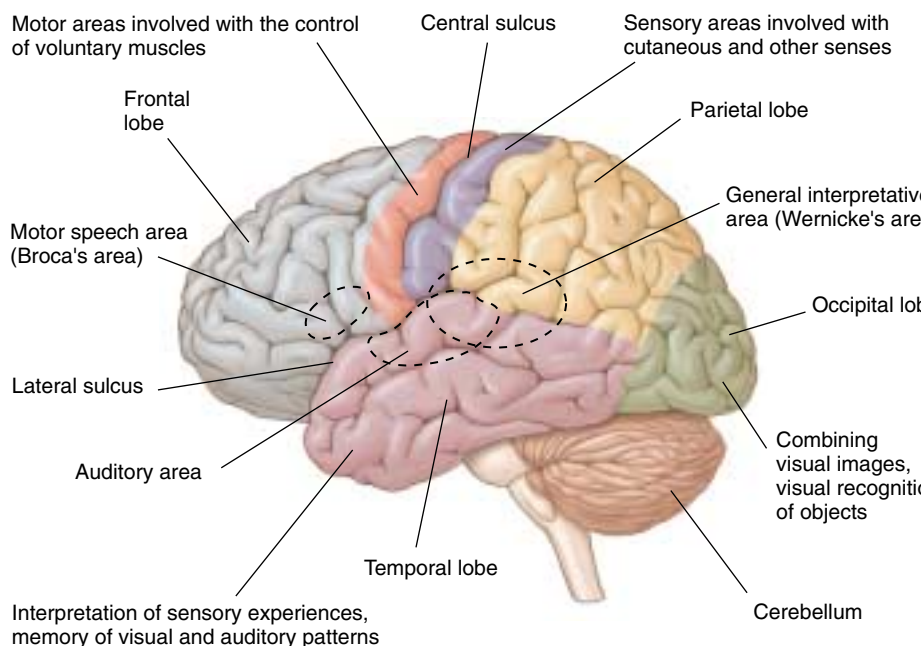


FIGURE 54.28
The lobes of the cerebrum. Some of the known regions of specialization are indicated in this diagram.

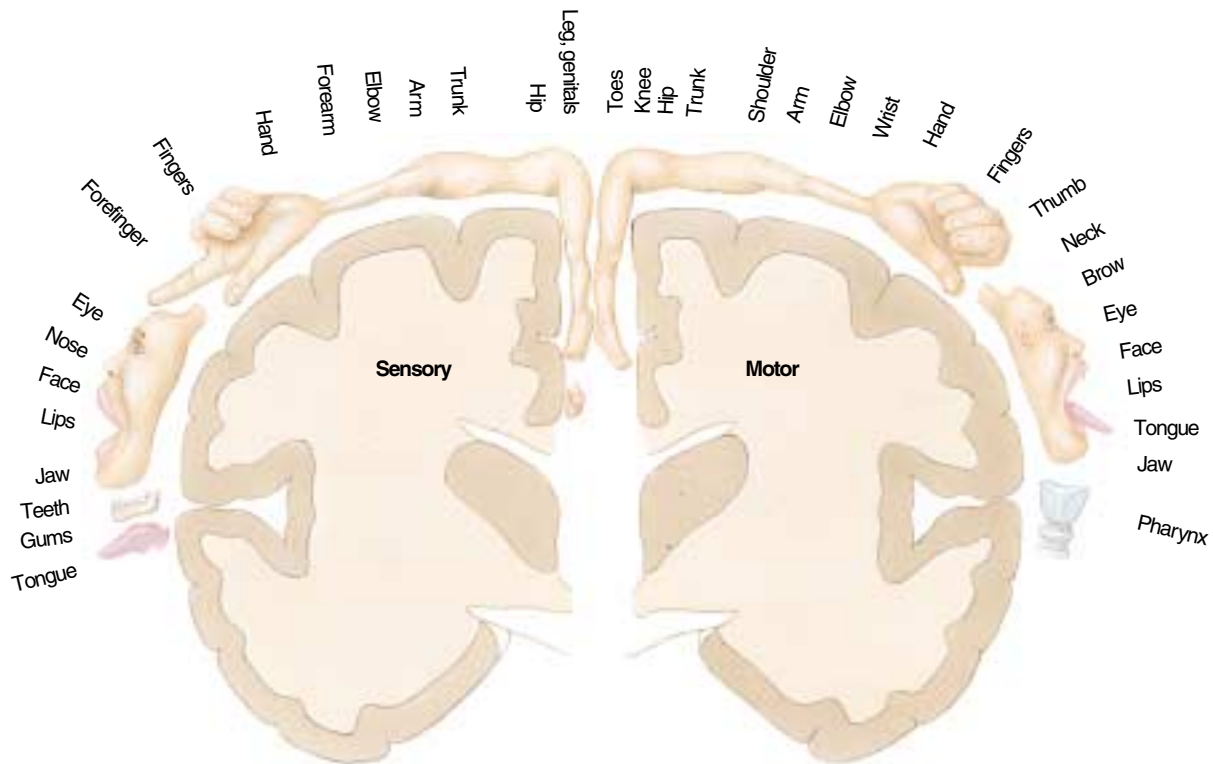


FIGURE 54.29

The primary somatosensory cortex (left) and the primary motor cortex (right). Each of these regions of the cerebral cortex is associated with a different region of the body, as indicated in this stylized map. The areas of the body are drawn in proportion to the amount of cortex dedicated to their sensation or control. For example, the hands have large areas of sensory and motor control, while the pharynx has a considerable area of motor control but little area devoted to the sensations of the pharynx.

The portion of the cerebral cortex that is not occupied by these motor and sensory cortices is referred to as *association cortex*. The site of higher mental activities, the association cortex reaches its greatest extent in primates, especially humans, where it makes up 95% of the surface of the cerebral cortex.

Basal Ganglia

Buried deep within the white matter of the cerebrum are several collections of cell bodies and dendrites that produce islands of gray matter. These aggregates of neuron cell bodies, which are collectively termed the basal ganglia, receive sensory information from ascending tracts and motor commands from the cerebral cortex and cerebellum. Outputs from the basal ganglia are sent down the spinal cord, where they participate in the control of body movements. Damage to specific regions of the basal ganglia can produce the resting tremor of muscles that is characteristic of people with Parkinson's disease.

Thalamus and Hypothalamus

The thalamus is a primary site of sensory integration in the brain. Visual, auditory, and somatosensory information is

sent to the thalamus, where the sensory tracts synapse with association neurons. The sensory information is then relayed via the thalamus to the occipital, temporal, and parietal lobes of the cerebral cortex, respectively. The transfer of each of these types of sensory information is handled by specific aggregations of neuron cell bodies within the thalamus.

The hypothalamus integrates the visceral activities. It helps regulate body temperature, hunger and satiety, thirst, and—along with the limbic system—various emotional states. The hypothalamus also controls the pituitary gland, which in turn regulates many of the other endocrine glands of the body. By means of its interconnections with the cerebral cortex and with control centers in the brain stem (a term used to refer collectively to the midbrain, pons, and medulla oblongata), the hypothalamus helps coordinate the neural and hormonal responses to many internal stimuli and emotions.

The *hippocampus* and *amygdala* are, together with the hypothalamus, the major components of the **limbic system**. This is an evolutionarily ancient group of linked structures deep within the cerebrum that are responsible for emotional responses. The hippocampus is also believed to be important in the formation and recall of memories, a topic we will discuss later.

Language and Other Functions

Arousal and Sleep. The brain stem contains a diffuse collection of neurons referred to as the *reticular formation*. One part of this formation, the reticular activating system, controls consciousness and alertness. All of the sensory pathways feed into this system, which monitors the information coming into the brain and identifies important stimuli. When the reticular activating system has been stimulated to arousal, it increases the level of activity in many parts of the brain. Neural pathways from the reticular formation to the cortex and other brain regions are depressed by anesthetics and barbiturates.

The reticular activating system controls both sleep and the waking state. It is easier to sleep in a dark room than in a lighted one because there are fewer visual stimuli to stimulate the reticular activating system. In addition, activity in this system is reduced by serotonin, a neurotransmitter we previously discussed. Serotonin causes the level of brain activity to fall, bringing on sleep.

Sleep is not the loss of consciousness. Rather, it is an active process whose multiple states can be revealed by recording the electrical activity of the brain in an electroencephalogram (EEG). In a relaxed but awake individual whose eyes are shut, the EEG consists primarily of large, slow waves that occur at a frequency of 8 to 13 hertz (cycles per second). These waves are referred to as *alpha waves*. In an alert subject whose eyes are open, the EEG waves are more rapid (*beta waves* are seen at frequencies of 13 to 30 hertz) and is more desynchronized because multiple sensory inputs are being received, processed, and translated into motor activities.

Theta waves (4 to 7 hertz) and *delta waves* (0.5 to 4 hertz) are seen in various stages of sleep. The first change seen in the EEG with the onset of drowsiness is a slowing and reduction in the overall amplitude of the waves. This slow-wave sleep has several stages but is generally characterized by decreases in arousability, skeletal muscle tone, heart rate, blood pressure, and respiratory rate. During REM sleep (named for the rapid eye movements that occur during this stage), the EEG resembles that of a relaxed, awake individual, and the heart rate, blood pressure, and respiratory rate are all increased. Paradoxically, individuals in REM sleep are difficult to arouse and are more likely to

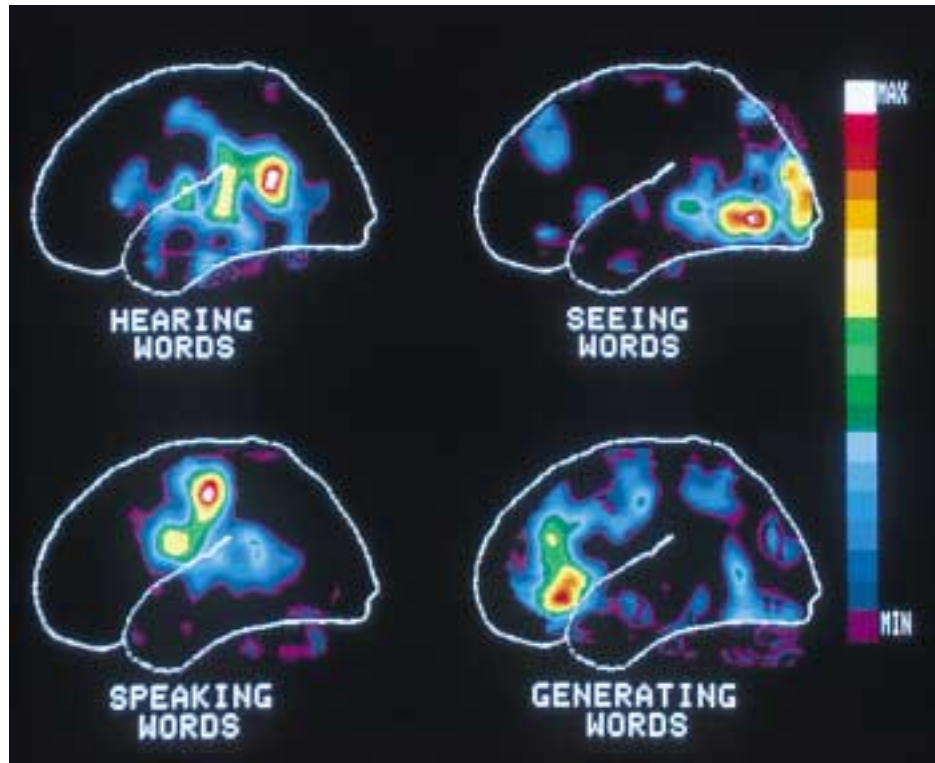


FIGURE 54.30

Different brain regions control various activities. This illustration shows how the brain reacts in human subjects asked to listen to a spoken word, to read that same word silently, to repeat the word out loud, and then to speak a word related to the first. Regions of white, red, and yellow show the greatest activity. Compare this with figure 54.28 to see how regions of the brain are mapped.

awaken spontaneously. Dreaming occurs during REM sleep, and the rapid eye movements resemble the tracking movements made by the eyes when awake, suggesting that dreamers “watch” their dreams.

Language and Spatial Recognition. Although the two cerebral hemispheres seem structurally similar, they are responsible for different activities. The most thoroughly investigated example of this lateralization of function is language. The left hemisphere is the “dominant” hemisphere for language—the hemisphere in which most neural processing related to language is performed—in 90% of right-handed people and nearly two-thirds of left-handed people. There are two language areas in the dominant hemisphere. Wernicke’s area (see figure 54.28), located in the parietal lobe between the primary auditory and visual areas, is important for language comprehension and the formulation of thoughts into speech (figure 54.30). Broca’s area, found near the part of the motor cortex controlling the face, is responsible for the generation of motor output needed for language communication. Damage to these brain areas can

cause language disorders known as *aphasias*. For example, if Wernicke's area is damaged, the person's speech is rapid and fluid but lacks meaning; words are tossed together as in a "word salad."

While the dominant hemisphere for language is adept at sequential reasoning, like that needed to formulate a sentence, the nondominant hemisphere (the right hemisphere in most people) is adept at spatial reasoning, the type of reasoning needed to assemble a puzzle or draw a picture. It is also the hemisphere primarily involved in musical ability—a person with damage to Broca's speech area in the left hemisphere may not be able to speak but may retain the ability to sing! Damage to the nondominant hemisphere may lead to an inability to appreciate spatial relationships and may impair musical activities such as singing. Even more specifically, damage to the inferior temporal cortex in that hemisphere eliminates the capacity to recall faces. Reading, writing, and oral comprehension remain normal, and patients with this disability can still recognize acquaintances by their voices. The nondominant hemisphere is also important for the consolidation of memories of non-verbal experiences.

Memory and Learning. One of the great mysteries of the brain is the basis of memory and learning. There is no one part of the brain in which all aspects of a memory appear to reside. Specific cortical sites cannot be identified for particular memories because relatively extensive cortical damage does not selectively remove memories. Although memory is impaired if portions of the brain, particularly the temporal lobes, are removed, it is not lost entirely. Many memories persist in spite of the damage, and the ability to access them gradually recovers with time. Therefore, investigators who have tried to probe the physical mechanisms underlying memory often have felt that they were grasping at a shadow. Although we still do not have a complete understanding of these mechanisms, we have learned a good deal about the basic processes in which memories are formed.

There appear to be fundamental differences between short-term and long-term memory. Short-term memory is transient, lasting only a few moments. Such memories can readily be erased by the application of an electrical shock, leaving previously stored long-term memories intact. This result suggests that short-term memories are stored electrically in the form of a transient neural excitation. Long-term memory, in contrast, appears to involve structural changes in certain neural connections within the brain. Two parts of the temporal lobes, the hippocampus and the amygdala, are involved in both short-term memory and its consolidation into long-term memory. Damage to these structures impairs the ability to process recent events into long-term memories.

Synapses that are used intensively for a short period of time display more effective synaptic transmission upon subsequent use. This phenomenon is called long-term potentiation (LTP). During LTP, the presynaptic neuron may release increased amounts of neurotransmitter with each action potential, and the postsynaptic neuron may become increasingly sensitive to the neurotransmitter. It is believed that these changes in synaptic transmission may be responsible for some aspects of memory storage.

Mechanism of Alzheimer's Disease Still a Mystery

In the past, little was known about *Alzheimer's disease*, a condition in which the memory and thought processes of the brain become dysfunctional. Drug companies are eager to develop new products for the treatment of Alzheimer's, but they have little concrete evidence to go on. Scientists disagree about the biological nature of the disease and its cause. Two hypotheses have been proposed: one that nerve cells in the brain are killed from the outside in, and the other that the cells are killed from the inside out.

In the first hypothesis, external proteins called β -amyloid peptides kill nerve cells. A mistake in protein processing produces an abnormal form of the peptide, which then forms aggregates, or plaques. The plaques begin to fill in the brain and then damage and kill nerve cells. However, these amyloid plaques have been found in autopsies of people that did not have Alzheimer's disease.

The second hypothesis maintains that the nerve cells are killed by an abnormal form of an internal protein. This protein, called tau (τ), normally functions to maintain protein transport microtubules. Abnormal forms of τ assemble into helical segments that form tangles, which interfere with the normal functioning of the nerve cells. Researchers continue to study whether tangles and plaques are causes or effects of Alzheimer's disease.

Progress has been made in identifying genes that increase the likelihood of developing Alzheimer's and genes that, when mutated, can cause Alzheimer's disease. However, the genes may not reveal much about Alzheimer's as they do not show up in most Alzheimer's patients, and they cause symptoms that start much earlier than when most Alzheimer's patients show symptoms.

The cerebrum is composed of two cerebral hemispheres. Each hemisphere consists of the gray matter of the cerebral cortex overlying white matter and islands of gray matter (nuclei) called the basal ganglia. These areas are involved in the integration of sensory information, control of body movements, and such associative functions as learning and memory.

The Spinal Cord

The spinal cord is a cable of neurons extending from the brain down through the backbone (figure 54.31). It is enclosed and protected by the vertebral column and layers of membranes called *meninges*, which also cover the brain. Inside the spinal cord there are two zones. The inner zone, called gray matter, consists of interneurons and the cell bodies of motor neurons. The outer zone, called white matter, contains the axons and dendrites of nerve cells. Messages from the body and the brain run up and down the spinal cord, an “information highway.”

In addition to relaying messages, the spinal cord also functions in reflexes, the sudden, involuntary movement of muscles. A reflex produces a rapid motor response to a stimulus because the sensory neuron passes its information to a motor neuron in the spinal cord, without higher level processing. One of the most frequently used reflexes in your body is blinking, a reflex that protects your eyes. If anything, such as an insect or a cloud of dust, approaches your eye, the eyelid blinks before you realize what has happened. The reflex occurs before the cerebrum is aware the eye is in danger.

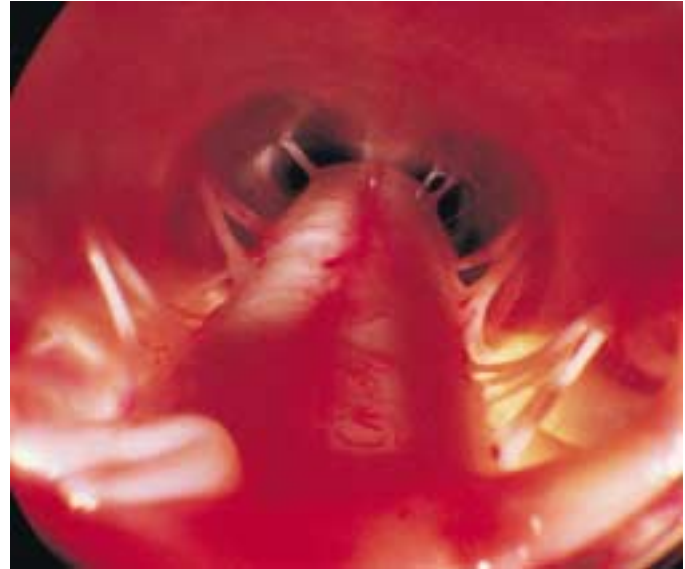


FIGURE 54.31
A view down the human spinal cord. Pairs of spinal nerves can be seen extending from the spinal cord. It is along these nerves, as well as the cranial nerves that arise from the brain, that the central nervous system communicates with the rest of the body.

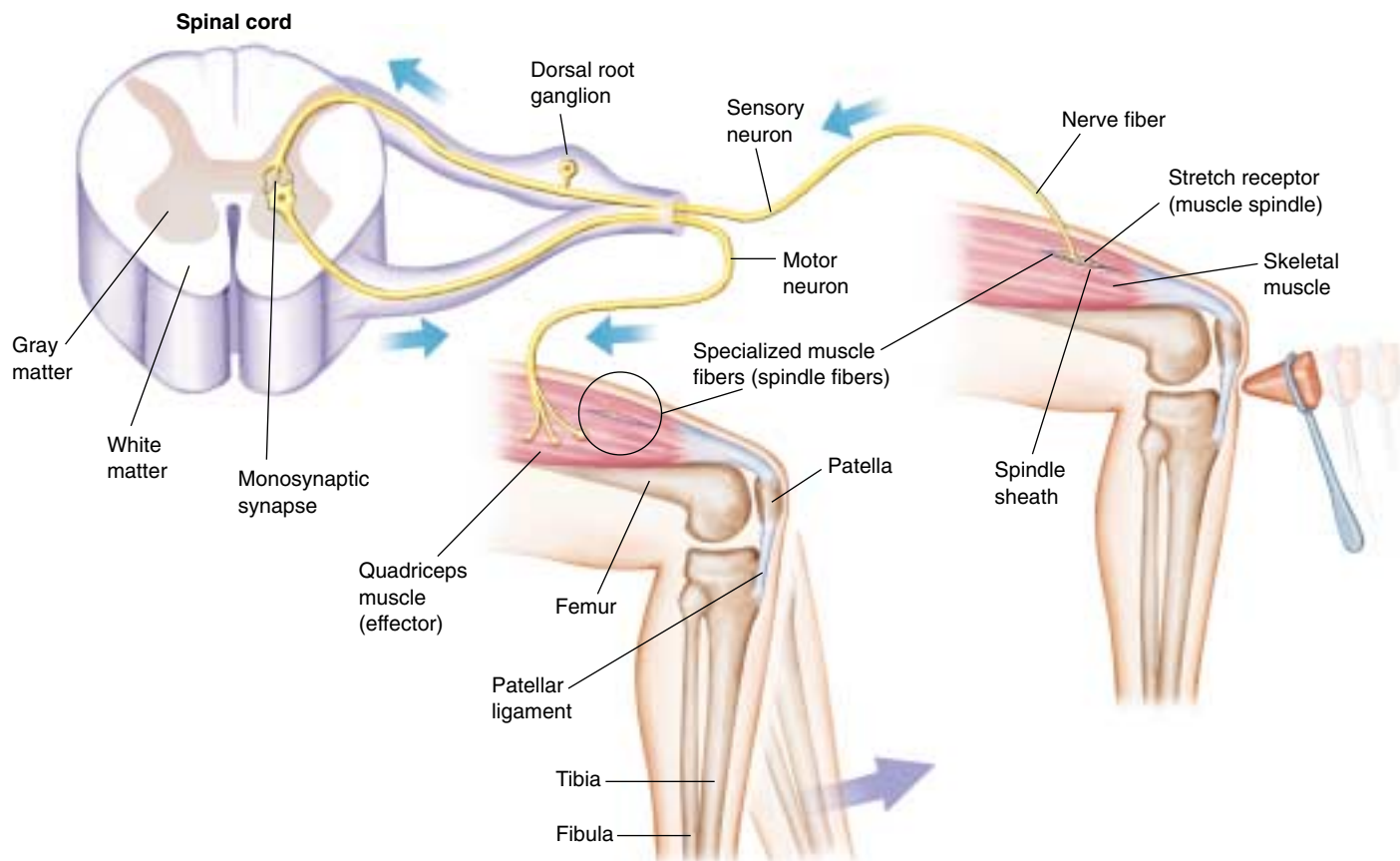


FIGURE 54.32
The knee-jerk reflex. This is the simplest reflex, involving only sensory and motor neurons.

Because they pass information along only a few neurons, reflexes are very fast. Many reflexes never reach the brain. The nerve impulse travels only as far as the spinal cord and then comes right back as a motor response. A few reflexes, like the knee-jerk reflex (figure 54.32), are monosynaptic reflex arcs. In these, the sensory nerve cell makes synaptic contact directly with a motor neuron in the spinal cord whose axon travels directly back to the muscle. The knee-jerk reflex is also an example of a *muscle stretch reflex*. When the muscle is briefly stretched by tapping the patellar ligament with a rubber mallet, the *muscle spindle apparatus* is also stretched. The spindle apparatus is embedded within the muscle, and, like the muscle fibers outside the spindle, is stretched along with the muscle. Stretching of the spindle activates sensory neurons that synapse directly with somatic motor neurons within the spinal cord. As a result, the somatic motor neurons conduct action potentials to the skeletal muscle fibers and stimulate the muscle to contract. This reflex is the simplest in the vertebrate body because only one synapse is crossed in the reflex arc.

Most reflexes in vertebrates, however, involve a single connecting interneuron between the sensory and the motor neuron. The withdrawal of a hand from a hot stove or the blinking of an eye in response to a puff of air involve a relay of information from a sensory neuron through one or more interneurons to a motor neuron. The motor neuron then stimulates the appropriate muscle to contract (figure 54.33).

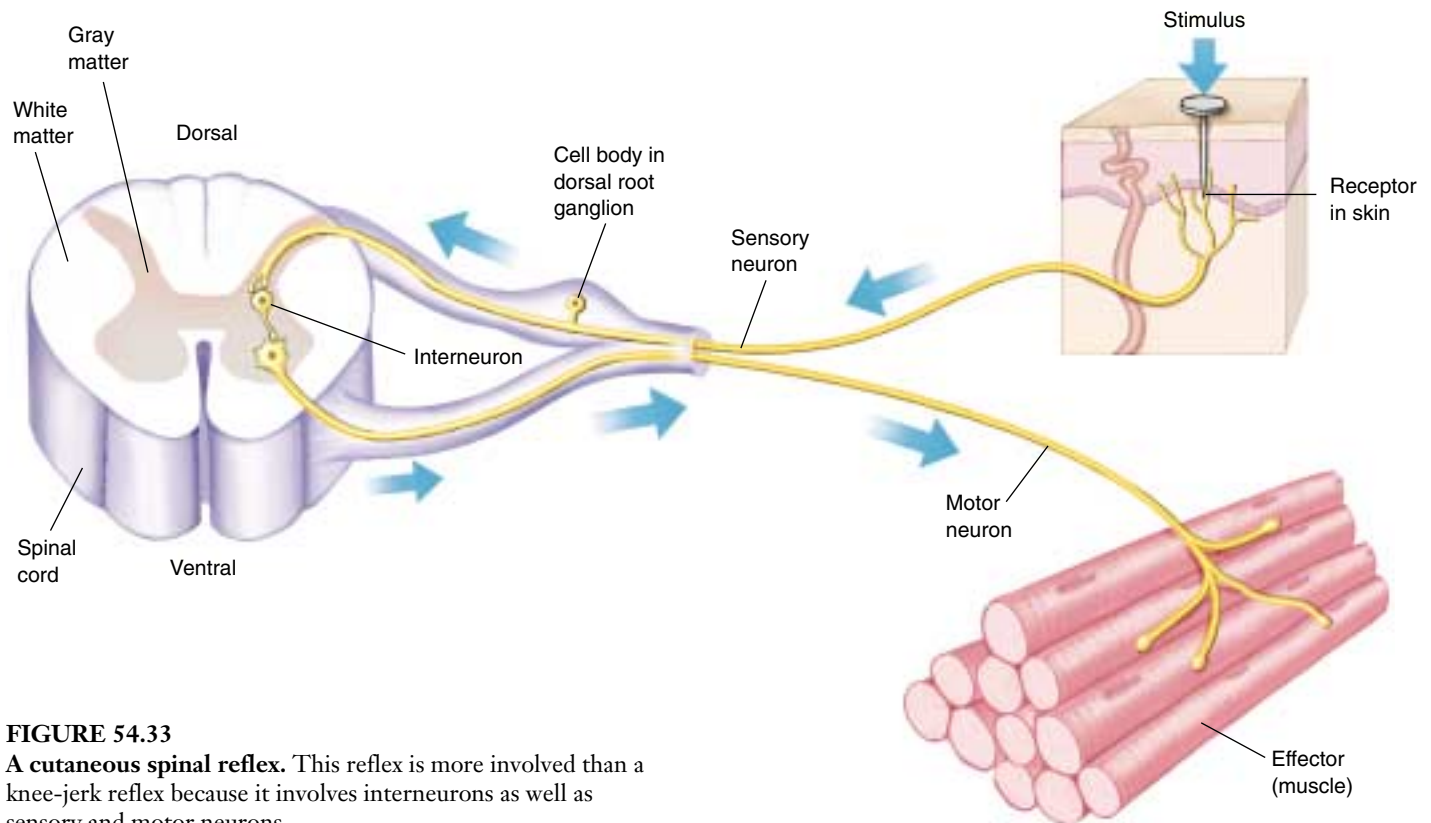


FIGURE 54.33
A cutaneous spinal reflex. This reflex is more involved than a knee-jerk reflex because it involves interneurons as well as sensory and motor neurons.

Spinal Cord Regeneration

In the past, scientists have tried to repair severed spinal cords by installing nerves from another part of the body to bridge the gap and act as guides for the spinal cord to regenerate. But most of these experiments have failed because although axons may regenerate through the implanted nerves, they cannot penetrate the spinal cord tissue once they leave the implant. Also, there is a factor that inhibits nerve growth in the spinal cord. After discovering that fibroblast growth factor stimulates nerve growth, neurobiologists tried gluing on the nerves, from the implant to the spinal cord, with fibrin that had been mixed with the fibroblast growth factor. Three months later, rats with the nerve bridges began to show movement in their lower bodies. In further analyses of the experimental animals, dye tests indicated that the spinal cord nerves had regrown from both sides of the gap. Many scientists are encouraged by the potential to use a similar treatment in human medicine. However, most spinal cord injuries in humans do not involve a completely severed spinal cord; often, nerves are crushed, which results in different tissue damage. Also, while the rats with nerve bridges did regain some locomotory ability, tests indicated that they were barely able to walk or stand.

The spinal cord relays messages to and from the brain and processes some sensory information directly.

54.5 The peripheral nervous system consists of sensory and motor neurons.

Components of the Peripheral Nervous System

The peripheral nervous system consists of nerves and ganglia. Nerves are cablelike collections of axons (figure 54.34), usually containing both sensory and motor neurons. Ganglia are aggregations of neuron cell bodies located outside the central nervous system.

At its origin, a spinal nerve separates into sensory and motor components. The axons of sensory neurons enter the dorsal surface of the spinal cord and form the **dorsal root** of the spinal nerve, whereas motor axons leave from the ventral surface of the spinal nerve and form the **ventral root** of the spinal nerve. The cell bodies of sensory neurons are grouped together outside each level of the spinal cord in the **dorsal root ganglia**. The cell bodies of somatic motor neurons, on the other hand, are located within the spinal cord and so are not located in ganglia.

Somatic motor neurons stimulate skeletal muscles to contract, and autonomic motor neurons innervate involuntary effectors—smooth muscles, cardiac muscle, and glands. A comparison of the somatic and autonomic nervous systems is provided in table 54.4 and each will be discussed in turn. Somatic motor neurons stimulate the skeletal muscles of the body to contract in response to conscious commands and as part of reflexes that do not require conscious control. Conscious control of skeletal muscles is achieved by activation of tracts of axons that descend from the cerebrum to the appropriate level of the spinal cord. Some of these descending axons will stimulate spinal cord motor neurons directly, while others will activate interneurons that in turn stimulate the spinal motor neurons. When a particular muscle is stimulated to contract, however, its antagonist must be inhibited. In order to flex the arm, for example, the flexor muscles must be stimulated while the antagonistic extensor muscle is inhibited (see figure 50.6). Descending motor axons produce this necessary inhibition by causing hyperpolarizations (IPSPs) of the spinal motor neurons that innervate the antagonistic muscles.

A spinal nerve contains sensory neurons that enter the dorsal root and motor neurons that enter the ventral root of the nerve. Somatic motor neurons innervate skeletal muscles and stimulate the muscles to contract.

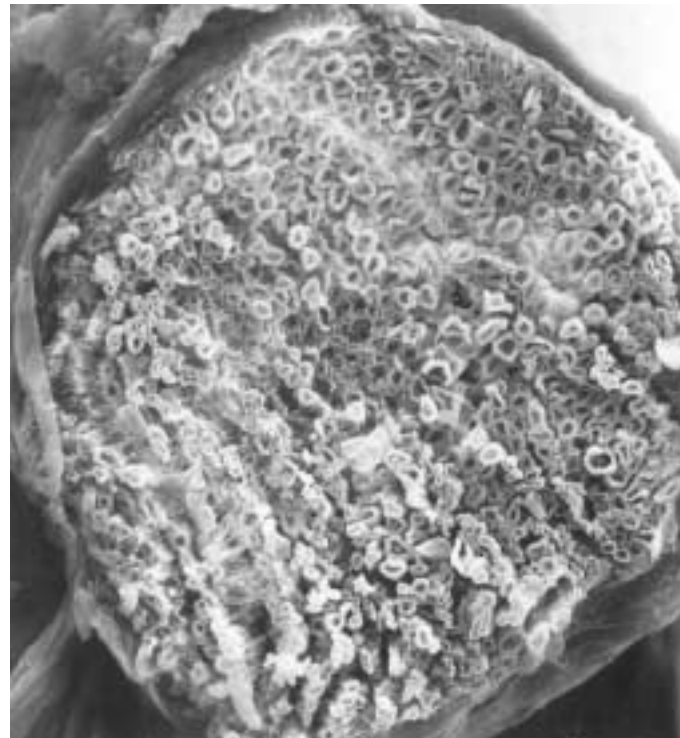


FIGURE 54.34
Nerves in the peripheral nervous system. Photomicrograph (1600×) showing a cross section of a bullfrog nerve. The nerve is a bundle of axons bound together by connective tissue. Many myelinated axons are visible, each looking somewhat like a doughnut.

Table 54.4 Comparison of the Somatic and Autonomic Nervous Systems

Characteristic	Somatic	Autonomic
Effectors	Skeletal muscle	Cardiac muscle Smooth muscle Gastrointestinal tract Blood vessels Airways Exocrine glands
Effect on motor nerves	Excitation	Excitation or inhibition
Innervation of effector cells	Always single	Typically dual
Number of neurons in path to effector	One	Two
Neurotransmitter	Acetylcholine	Acetylcholine Norepinephrine

The Autonomic Nervous System

The autonomic nervous system is composed of the sympathetic and parasympathetic divisions and the medulla oblongata of the hindbrain, which coordinates this system. Though they differ, the sympathetic and parasympathetic divisions share several features. In both, the efferent motor pathway involves two neurons: the first has its cell body in the CNS and sends an axon to an autonomic ganglion, while the second has its cell body in the autonomic ganglion and sends its axon to synapse with a smooth muscle, cardiac muscle, or gland cell (figure 54.35). The first neuron is called a *preganglionic neuron*, and it always releases ACh at its synapse. The second neuron is a *postganglionic neuron*; those in the parasympathetic division release ACh, while those in the sympathetic division release norepinephrine.

In the sympathetic division, the preganglionic neurons originate in the thoracic and lumbar regions of the spinal cord (figure 54.36). Most of the axons from these neurons synapse in two parallel chains of ganglia immediately outside the spinal cord. These structures are usually called the *sympathetic chain* of ganglia. The sympathetic chain contains the cell bodies of postganglionic neurons, and it is the axons from these neurons that innervate the different visceral organs. There are some exceptions to this general pattern, however. Most importantly, the axons of some preganglionic sympathetic neurons pass through the

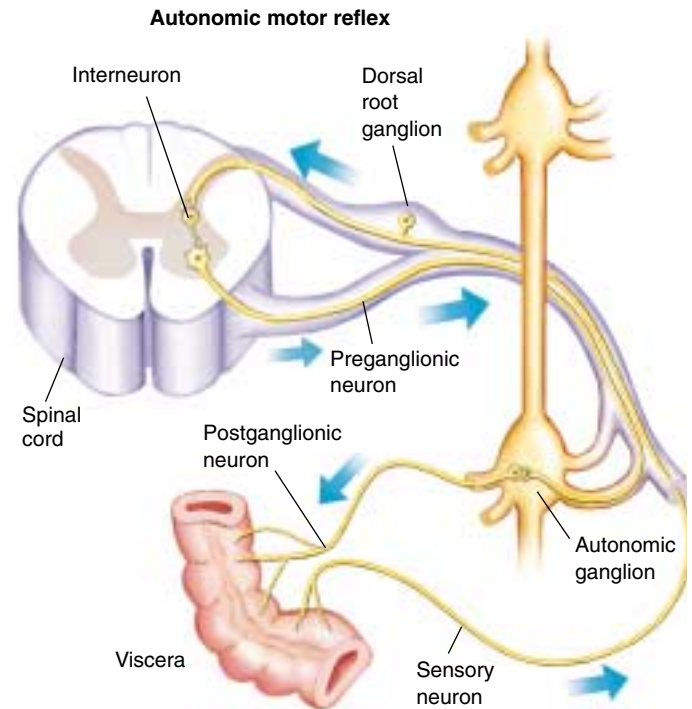


FIGURE 54.35

An autonomic reflex. There are two motor neurons in the efferent pathway. The first, or preganglionic neuron, exits the CNS and synapses at an autonomic ganglion. The second, or postganglionic neuron, exits the ganglion and regulates the visceral effectors (smooth muscle, cardiac muscle, or glands).

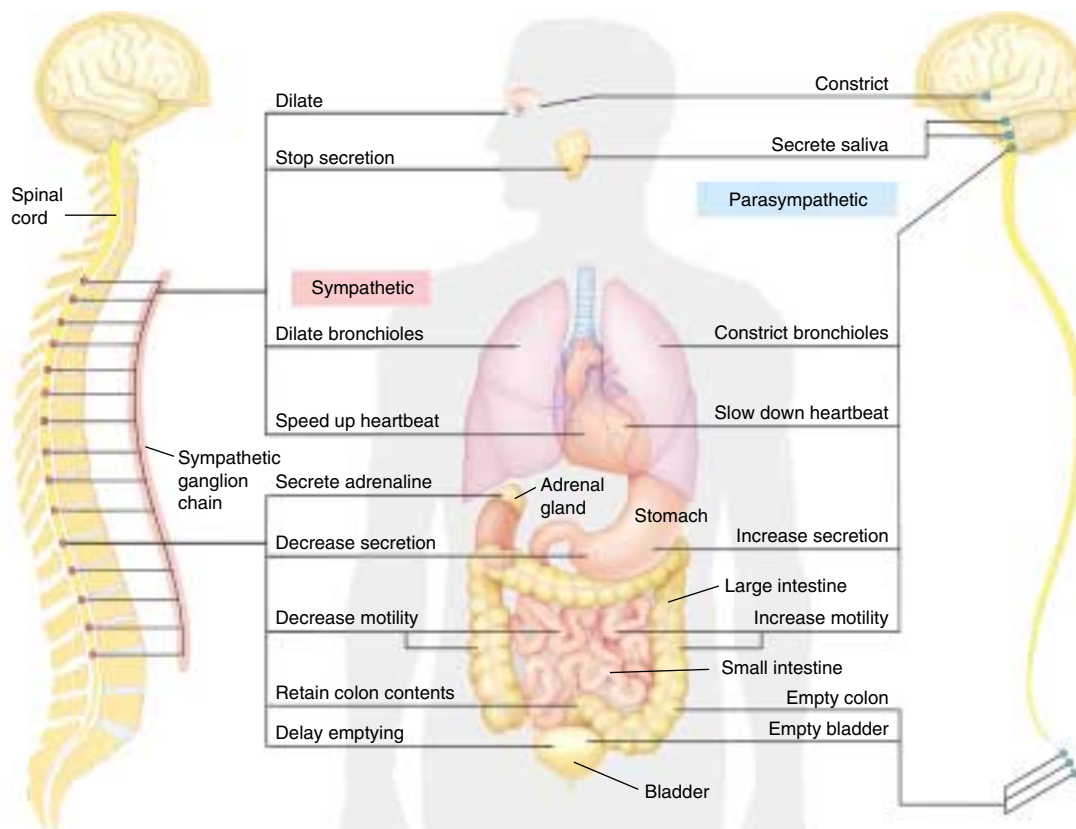


FIGURE 54.36

The sympathetic and parasympathetic divisions of the autonomic nervous system. The preganglionic neurons of the sympathetic division exit the thoracic and lumbar regions of the spinal cord, while those of the parasympathetic division exit the brain and sacral region of the spinal cord. The ganglia of the sympathetic division are located near the spinal cord, while those of the parasympathetic division are located near the organs they innervate. Most of the internal organs are innervated by both divisions.

Table 54.5 Autonomic Innervation of Target Tissues

Target Tissue	Sympathetic Stimulation	Parasympathetic Stimulation
Pupil of eye	Dilation	Constriction
Glands		
Salivary	Vasoconstriction; slight secretion	Vasodilation; copious secretion
Gastric	Inhibition of secretion	Stimulation of gastric activity
Liver	Stimulation of glucose secretion	Inhibition of glucose secretion
Sweat	Sweating	None
Gastrointestinal tract		
Sphincters	Increased tone	Decreased tone
Wall	Decreased tone	Increased motility
Gallbladder	Relaxation	Contraction
Urinary bladder		
Muscle	Relaxation	Contraction
Sphincter	Contraction	Relaxation
Heart muscle	Increased rate and strength	Decreased rate
Lungs	Dilation of bronchioles	Constriction of bronchioles
Blood vessels		
In muscles	Dilation	None
In skin	Constriction	None
In viscera	Constriction	Dilation

sympathetic chain without synapsing and, instead, terminate within the adrenal gland. The adrenal gland consists of an outer part, or cortex, and an inner part, or medulla. The adrenal medulla receives sympathetic nerve innervation and secretes the hormone epinephrine (adrenaline) in response.

When the sympathetic division becomes activated, epinephrine is released into the blood as a hormonal secretion, and norepinephrine is released at the synapses of the postganglionic neurons. Epinephrine and norepinephrine act to prepare the body for fight or flight (figure 54.37). The heart beats faster and stronger, blood glucose concentration increases, blood flow is diverted to the muscles and heart, and the bronchioles dilate (table 54.5).

These responses are antagonized by the parasympathetic division. Preganglionic parasympathetic neurons originate in the brain and sacral regions of the spinal cord. Because of this origin, there cannot be a chain of parasympathetic ganglia analogous to the sympathetic chain. Instead, the preganglionic axons, many of which travel in the vagus (the tenth cranial) nerve, terminate

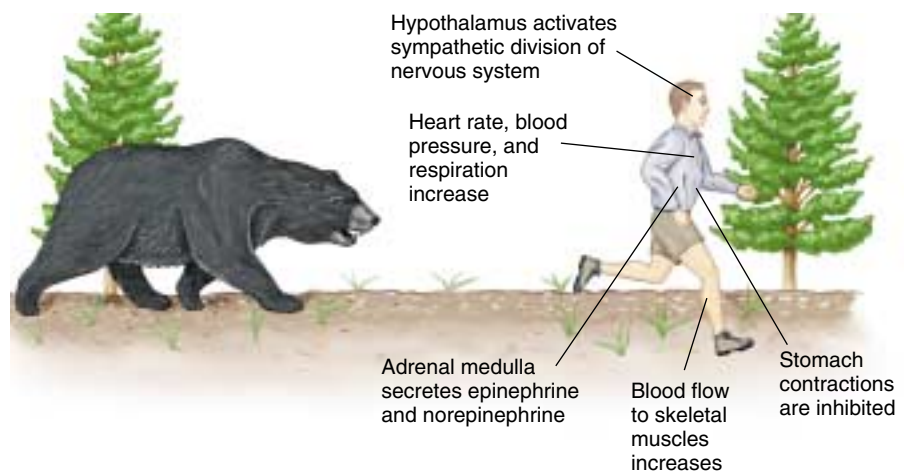


FIGURE 54.37 **The sympathetic division of the nervous system in action.** To prepare the body for fight or flight, the sympathetic division is activated and causes changes in many organs, glands, and body processes.

in ganglia located near or even within the internal organs. The postganglionic neurons then regulate the internal organs by releasing ACh at their synapses. Parasympathetic nerve effects include a slowing of the heart, increased secretions and activities of digestive organs, and so on.

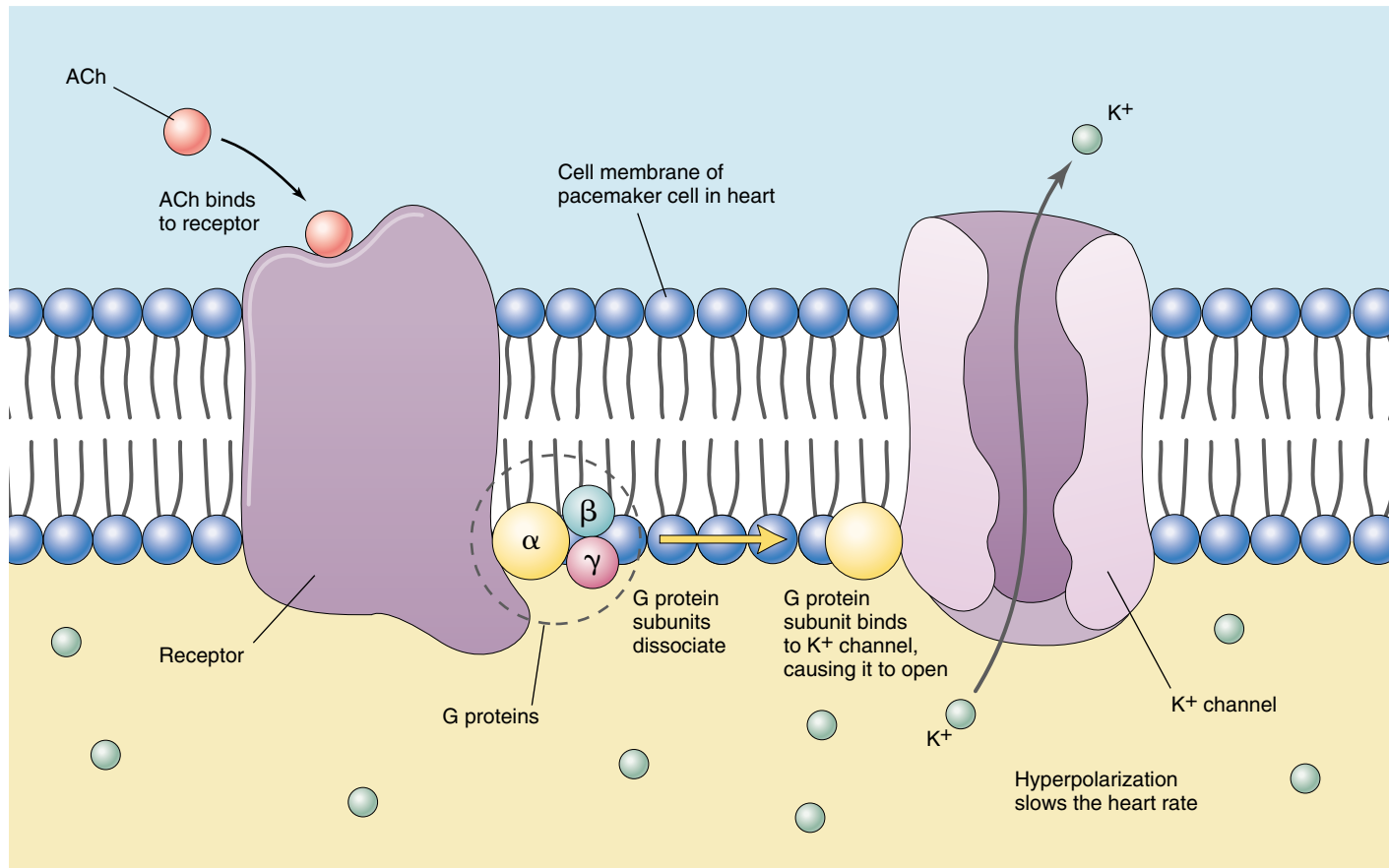


FIGURE 54.38

The parasympathetic effects of ACh require the action of G proteins. The binding of ACh to its receptor causes dissociation of a G protein complex, releasing some components of this complex to move within the membrane and bind to other proteins that form ion channels. The example shown here is the effects of ACh on the heart, where the G protein components cause the opening of potassium channels. This leads to outward diffusion of potassium and hyperpolarization, slowing the heart rate.

G Proteins Mediate Cell Responses to Autonomic Nerves

You might wonder how ACh can slow the heart rate—an inhibitory effect—when it has excitatory effects elsewhere. This inhibitory effect in the pacemaker cells of the heart is produced because ACh causes the opening of potassium channels, leading to the outward diffusion of potassium and thus to hyperpolarization. This and other parasympathetic effects of ACh are produced indirectly, using a group of membrane proteins called **G proteins** (so-called because they are regulated by guanosine diphosphate and guanosine triphosphate [GDP and GTP]). Because the ion channels are located some distance away from the receptor proteins for ACh, the G proteins are needed to serve as connecting links between them.

There are three G protein subunits, designated α , β , and γ , bound together and attached to the receptor protein for ACh. When ACh, released by parasympathetic endings, binds to its receptor, the G protein subunits dissociate (figure 54.38). Specific G protein components move within the

membrane to the potassium channel and cause it to open, producing hyperpolarization and a slowing of the heart. In other organs, the G proteins have different effects that lead to excitation. In this way, for example, the parasympathetic nerves that innervate the stomach can cause increased gastric secretions and contractions.

The sympathetic nerve effects also involve the action of G proteins. Stimulation by norepinephrine from sympathetic nerve endings and epinephrine from the adrenal medulla requires G proteins to activate the target cells. We will describe this in more detail, together with hormone action, in chapter 56.

The sympathetic division of the autonomic system, together with the adrenal medulla, activates the body for fight-or-flight responses, whereas the parasympathetic division generally has antagonistic effects. The actions of parasympathetic nerves are produced by ACh, whereas the actions of sympathetic nerves are produced by norepinephrine.



Summary

Questions

Media Resources

54.1 The nervous system consists of neurons and supporting cells.

- The nervous system is subdivided into the central nervous system (CNS) and peripheral nervous system (PNS).

1. What are the differences and similarities among the three types of neurons?



- Nervous system divisions
- Nervous system cells I
- Nervous system cells II

54.2 Nerve impulses are produced on the axon membrane.

- The resting axon has a membrane potential of -70 mV; the magnitude of this voltage is produced primarily by the distribution of K^+ .
- A depolarization stimulus opens voltage-regulated Na^+ channels and then K^+ channels, producing first the upward phase and then the repolarization phase of the action potential.
- Action potentials are all or none and are conducted without decrease in amplitude because each action potential serves as the stimulus for the production of the next action potential along the axon.

2. Which cation is most concentrated in the cytoplasm of a cell, and which is most concentrated in the extracellular fluid? How are these concentration differences maintained?



- Membrane potential
- Action potential

3. What is a voltage-gated ion channel?



- Activities:
 - Action potential 1
 - Sodium-potassium pump
 - Action potential 2
- Action potential 1
- Membrane potential
- Local potential

4. What happens to the size of an action potential as it is propagated?

54.3 Neurons form junctions called synapses with other cells.

- The presynaptic axon releases neurotransmitter chemicals that diffuse across the synapse and stimulate the production of either a depolarization or a hyperpolarization in the postsynaptic membrane.
- Depolarizations and hyperpolarization can summate in the dendrites and cell bodies of the postsynaptic neuron, allowing integration of information.

5. If a nerve impulse can jump from node to node along a myelinated axon, why can't it jump from the presynaptic cell to the postsynaptic cell across a synaptic cleft?



- Bioethics case study: Smoking bar
- Student Research: Neural development in Moths
- On *Scientific* Articles: Is smoking addictive? Nobel prize 2000

54.4 The central nervous system consists of the brain and spinal cord.

- The vertebrate brain is divided into a forebrain, midbrain, and hindbrain, and these are further subdivided into other brain regions. The cerebral cortex has a primary motor area and a primary somatosensory area, as well as areas devoted to the analysis of vision and hearing and the integration and association of information.
- The spinal cord carries information to and from the brain and coordinates many reflex movements.

6. Where are the basal ganglia located, and what is their function?



- Art activities:
 - Central nervous system
 - Spinal cord anatomy
 - Human brain

7. How are short-term and long-term memory thought to differ in terms of their basic underlying mechanisms?



- Reflex arc

54.5 The peripheral nervous system consists of sensory and motor neurons.

- The sympathetic division is activated during fight-or-flight responses; the parasympathetic division opposes the action of the sympathetic division in most activities.

8. How do the sympathetic and parasympathetic divisions differ in the locations of the ganglionic neurons?



- Art activity: Peripheral nervous system