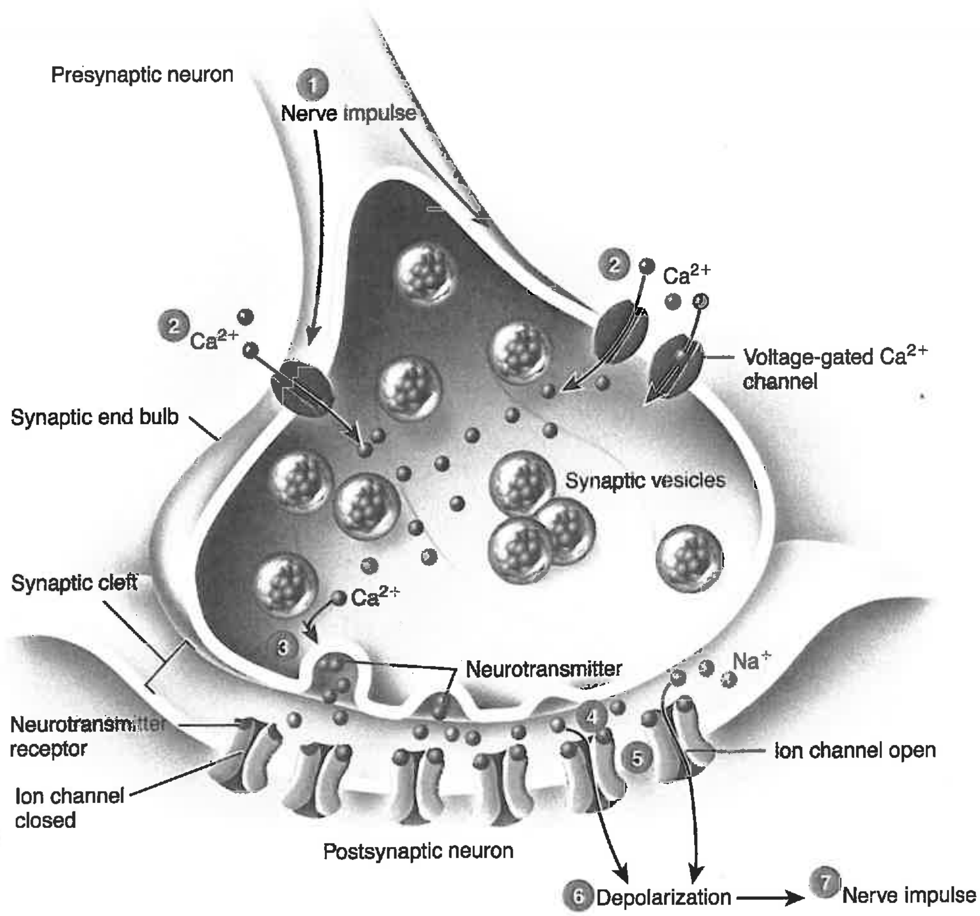
Events at a Synapse

Although the presynaptic and postsynaptic neurons are in close proximity at a synapse, their plasma membranes do not touch. They are separated by the ***synaptic cleft***, a tiny space filled with interstitial fluid. Because nerve impulses cannot conduct across the synaptic cleft, an alternate, indirect form of communication occurs across this space. A typical synapse operates as follows (Figure 9.7):

1. A nerve impulse arrives at a synaptic end bulb of a presynaptic axon.
2. The depolarizing phase of the nerve impulse opens *voltage-gated Ca^{2+} channels*, which are present in the membrane of synaptic end bulbs. Because calcium ions are more concentrated in the interstitial fluid, Ca^{2+} flows into the synaptic end bulb through the opened channels.
3. An increase in the concentration of Ca^{2+} inside the synaptic end bulb triggers exocytosis of some of the synaptic vesicles, which releases thousands of neurotransmitter molecules into the synaptic cleft.
4. The neurotransmitter molecules diffuse across the synaptic cleft and bind to ***neurotransmitter receptors*** in the postsynaptic neuron's plasma membrane.
5. Binding of neurotransmitter molecules opens ion channels, which allows certain ions to flow across the membrane.
6. As ions flow through the opened channels, the voltage across the membrane changes. Depending on which ions

Figure 9.7 Synaptic transmission at a chemical synapse. Exocytosis of synaptic vesicles from a presynaptic neuron releases neurotransmitter molecules, which bind to receptors in the plasma membrane of the postsynaptic neuron.

At a chemical synapse, a presynaptic electrical signal (nerve impulse) is converted into a chemical signal (neurotransmitter release). The chemical signal is then converted back into an electrical signal (depolarization or hyperpolarization) in the postsynaptic cell.



What causes the voltage-gated Ca^{2+} channels in synaptic end bulbs to open?

Focus on Wellness

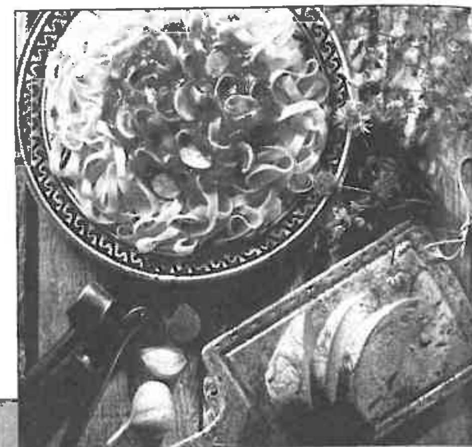
Neurotransmitters—Why Food Affects Mood

Everyone who has enjoyed the soothing relaxation of a good meal has experienced the effect of food on mood. Neurons manufacture neurotransmitters from chemicals that come from food, so you could say that the story of the food–mood link begins with digestion. Many neurotransmitters are made from amino acids, which are the basic building blocks of proteins. Amino acids are made available when your body digests the protein in the food you eat. For example, the neurotransmitter serotonin is made from the amino acid tryptophan, and both dopamine and norepinephrine are synthesized from the amino acid tyrosine.

Mind-altering Food?

Regulation of neurotransmitter levels in the brain is quite complicated and depends not only on the availability of amino acid (and other) precursors, but also on competition of these precursors for entry into the brain. Consider serotonin, one of the neurotransmitters that appears to have an important effect on mood. Serotonin leads to feelings of relaxation and sleepiness.

Although serotonin is manufactured from the amino acid tryptophan, protein foods do not lead to higher levels of tryptophan in the blood or brain. This is because, after a high-protein meal, tryptophan must compete with more than 20 other amino acids for entry into the central nervous system, so its concentration in the brain remains relatively low. On the other hand, consumption of carbohydrate-rich foods, such as bread, pasta, potatoes, or sweets, is associated with an increase in the synthesis and release of serotonin in the brain. The result: Carbohydrates help us feel relaxed and sleepy.



▶ **Think It Over . . .**

▶ *Why might consuming a high-protein diet for several days lead to cravings for carbohydrate-rich foods?*

the channels admit, the voltage change may be a depolarization or a hyperpolarization.

7 If a depolarization occurs in the postsynaptic neuron and reaches threshold, then it triggers one or more nerve impulses.

At most synapses, only *one-way information transfer* can occur—from a presynaptic neuron to a postsynaptic neuron or to an effector, such as a muscle fiber or a gland cell. For example, synaptic transmission at a neuromuscular junction (NMJ) proceeds from a somatic motor neuron to a skeletal muscle fiber (but not in the opposite direction). Only synaptic end bulbs of presynaptic neurons can release neurotransmitters, and only the postsynaptic neuron's membrane has the correct receptor proteins to recognize and bind that neurotransmitter. As a result, nerve impulses move along their pathways in one direction.

When a postsynaptic neuron depolarizes, the effect is excitatory: If threshold is reached, one or more nerve impulses occur. By contrast, hyperpolarization has an inhibitory effect on the postsynaptic neuron: As the membrane potential moves farther away from threshold, nerve impulses are less likely to arise. A typical neuron in the CNS receives input from 1000 to 10,000 synapses. Some of this input is excitatory and some is inhibitory. The sum of all the excitatory and inhibitory effects at any given time determines whether one or more impulses will occur in the postsynaptic neuron.

A neurotransmitter affects the postsynaptic neuron, muscle fiber, or gland cell as long as it remains bound to its receptors. Thus, removal of the neurotransmitter is essential for normal synaptic function. Neurotransmitter is removed in three ways. (1) Some of the released neurotransmitter molecules diffuse away from the synaptic cleft. Once a neurotransmitter molecule is out of reach of its receptors, it can no longer exert an effect. (2) Some neurotransmitters are destroyed by enzymes. (3) Many neurotransmitters are actively transported back into the neuron that released them (reuptake). Others are transported into neighboring neuroglia (uptake).

Several therapeutically important drugs selectively block reuptake of specific neurotransmitters. For example, the drug fluoxetine (Prozac®) is a **selective serotonin reuptake inhibitor (SSRI)**. By blocking reuptake of serotonin, Prozac prolongs the activity of this neurotransmitter at synapses in the brain. SSRIs provide relief for those suffering from some forms of depression.

Neurotransmitters

About 100 substances are either known or suspected neurotransmitters. Most neurotransmitters are synthesized and loaded into synaptic vesicles in the synaptic end bulbs, close to their site of release. One of the best-studied neurotransmitters is ***acetylcholine (ACh)***, which is released by many PNS neurons and by some CNS neurons. ACh is an excitatory neurotransmitter at some synapses, such as the neuromuscular junction. It is also known to be an inhibitory neurotransmitter at other synapses. For example, parasympathetic neurons slow heart rate by releasing ACh at inhibitory synapses.

Several amino acids are neurotransmitters in the CNS. ***Glutamate*** and ***aspartate*** have powerful excitatory effects. Two other amino acids, ***gamma aminobutyric*** (GAM-ma am-i-nō-bū-TIR-ik) ***acid (GABA)*** and ***glycine***, are important inhibitory neurotransmitters. Antianxiety drugs such as diazepam (Valium®) enhance the action of GABA.

Some neurotransmitters are modified amino acids. These include norepinephrine, dopamine, and serotonin. ***Norepinephrine (NE)*** plays roles in arousal (awakening from deep sleep), dreaming, and regulating mood. Brain neurons containing the neurotransmitter ***dopamine (DA)*** are active during emotional responses, addictive behaviors, and pleasurable experiences. In addition, dopamine-releasing neurons help regulate skeletal muscle tone and some aspects of movement due to contraction of skeletal muscles. One form of schizophrenia is due to accumulation of excess dopamine. ***Serotonin*** is thought to be involved in sensory perception, temperature regulation, control of mood, appetite, and the onset of sleep.

Neurotransmitters consisting of amino acids linked by peptide bonds are called ***neuropeptides*** (noor-ō-PEP-tīds). The ***endorphins*** (en-DOR-fins) are neuropeptides that are the body's natural painkillers. Acupuncture may produce analgesia (loss of pain sensation) by increasing the release of endorphins. They have also been linked to improved memory and learning and to feelings of pleasure or euphoria.

An important newcomer to the ranks of recognized neurotransmitters is the simple gas ***nitric oxide (NO)***, which is different from all previously known neurotransmitters because it is not synthesized in advance and packaged into synaptic vesicles. Rather, it is formed on demand, diffuses out of cells that produce it and into neighboring cells, and acts immediately. Some research suggests that NO plays a role in learning and memory.

Substances naturally present in the body as well as drugs and toxins can **modify the effects of neurotransmitters** in several ways. Cocaine produces euphoria—intensely pleasurable feelings—by blocking reuptake of dopamine. This action allows dopamine to linger longer in synaptic clefts, producing excessive stimulation of certain brain regions. Isoproterenol (Isuprel®) can be used to dilate the airways during an asthma attack because it binds to and activates receptors for norepinephrine. Zyprexa®, a drug prescribed for schizophrenia, is effective because it binds to and blocks receptors for serotonin and dopamine.

CHECKPOINT

9. How are neurotransmitters removed after they are released from synaptic vesicles?

COMMON DISORDERS

Multiple Sclerosis

Multiple sclerosis (MS) is a disease that causes progressive destruction of myelin sheaths of neurons in the CNS. It afflicts about 2 million people worldwide and affects females twice as often as males. The condition's name describes the anatomical pathology: In *multiple* regions, the myelin sheaths deteriorate to *scleroses*, which are hardened scars or plaques. The destruction of myelin sheaths slows and then short-circuits conduction of nerve impulses.

The most common form of the condition is relapsing-remitting MS, which usually appears in early adulthood. The first symptoms may include a feeling of heaviness or weakness in the muscles, abnormal sensations, or double vision. An attack is followed by a period of remission during which the symptoms temporarily disappear. One attack follows another over the years. The result is a progressive loss of function interspersed with remission periods, during which symptoms abate.

MS is an autoimmune disease—the body's own immune system spearheads the attack. Although the trigger of MS is unknown, both genetic susceptibility and exposure to some environmental factor (perhaps a herpes virus) appear to contribute. Many patients with relapsing-remitting MS are treated with injections of beta interferon. This treatment lengthens the time between relapses, decreases the severity of relapses, and slows formation of new lesions in some cases. Unfortunately, not all MS patients can tolerate beta interferon, and therapy becomes less effective as the disease progresses.

Epilepsy

Epilepsy is a disorder characterized by short, recurrent, periodic attacks of motor, sensory, or psychological malfunction, although it almost never affects intelligence. The attacks, called *epileptic seizures*, afflict about 1% of the world's population. They are initiated by abnormal, synchronous electrical discharges from millions of neurons in the brain. As a result, lights, noise, or smells may be sensed when the eyes, ears, and nose have not been stimulated. In addition, the skeletal muscles of a person having a seizure may contract involuntarily. *Partial seizures* begin in a small focus on one side of the brain and produce milder symptoms; *generalized seizures* involve larger areas on both sides of the brain and loss of consciousness.

Epilepsy has many causes, including brain damage at birth (the most common cause); metabolic disturbances such as insufficient glucose or oxygen in the blood; infections; toxins; loss of blood or low blood pressure; head injuries; and tumors and abscesses of the brain. However, most epileptic seizures have no demonstrable cause.

Epileptic seizures often can be eliminated or alleviated by antiepileptic drugs, such as phenytoin, carbamazepine, and valproate sodium. An implantable device that stimulates the vagus (X) nerve also has produced dramatic results in reducing seizures in some patients whose epilepsy was not well-controlled by drugs.

MEDICAL TERMINOLOGY AND CONDITIONS

Demyelination (dē-mī-e-li-NĀ-shun) Loss or destruction of myelin sheaths around axons in the CNS or PNS.

Guillain-Barré Syndrome (GBS) (gē-an ba-RĀ) A demyelinating disorder in which macrophages remove myelin from PNS axons. It is a common cause of sudden paralysis and may result from the immune system's response to a bacterial infection. Most patients recover completely or partially, but about 15% remain paralyzed.

Neuropathy (noo-ROP-a-thē; *neuro-* = a nerve; *-pathy* = disease) Any disorder that affects the nervous system, but particularly a disorder of a cranial or spinal nerve.

STUDY OUTLINE

Overview of the Nervous System (p. 226)

1. Components of the nervous system include the brain, 12 pairs of cranial nerves and their branches, the spinal cord, 31 pairs of spinal nerves and their branches, sensory receptors, ganglia, and enteric plexuses.
2. Three basic functions of the nervous system are detecting stimuli (sensory function); analyzing, integrating, and storing sensory information (integrative function); and responding to integrative decisions (motor function).
3. Sensory (afferent) neurons provide input to the CNS; motor (efferent) neurons carry output from the CNS to effectors.
4. The two main subsystems of the nervous system are (1) the central nervous system (CNS), the brain and spinal cord, and (2) the peripheral nervous system (PNS), all nervous tissues outside the brain and spinal cord.
5. The PNS also is subdivided into the somatic nervous system (SNS), autonomic nervous system (ANS), and enteric nervous system (ENS).
6. The SNS consists of (1) sensory neurons that conduct impulses from somatic and special sense receptors to the CNS, and (2) motor neurons from the CNS to skeletal muscles.
7. The ANS contains (1) sensory neurons from visceral organs and (2) motor neurons in two divisions, sympathetic and parasympathetic, that convey impulses from the CNS to smooth muscle tissue, cardiac muscle tissue, and glands.
8. The ENS consists of neurons in two enteric plexuses that extend the length of the gastrointestinal (GI) tract; it monitors sensory changes and controls operation of the GI tract.

Histology of Nervous Tissue (p. 228)

1. Nervous tissue consists of two types of cells: neurons and neuroglia. Neurons are specialized for nerve impulse conduction and provide most of the unique functions of the nervous system, such as sensing, thinking, remembering, controlling muscle activity, and regulating glandular secretions. Neuroglia support, nourish, and protect the neurons and maintain homeostasis in the interstitial fluid that bathes neurons.
2. Most neurons have three parts. The dendrites are the main receiving or input region. Integration occurs in the cell body. The output part typically is a single axon, which conducts nerve impulses toward another neuron, a muscle fiber, or a gland cell.
3. Two types of neuroglia produce myelin sheaths: oligodendrocytes myelinate axons in the CNS, and Schwann cells myelinate axons in the PNS.
4. White matter primarily contains myelinated axons; gray matter contains neuronal cell bodies, dendrites, axon terminals, unmyelinated axons, and neuroglia.
5. In the spinal cord, gray matter forms an H-shaped inner core that is surrounded by white matter. In the brain, a thin, superficial shell of gray matter covers the cerebrum and cerebellum.
6. Neuroglia include astrocytes, oligodendrocytes, microglia, ependymal cells, Schwann cells, and satellite cells (see Table 9.1 on page 231).

Action Potentials (p. 230)

1. Neurons communicate with one another using nerve action potentials, also called nerve impulses.
2. Generation of action potentials depends on the existence of a resting membrane potential and the presence of voltage-gated channels for Na^+ and K^+.
3. A typical value for the resting membrane potential (difference in electrical charge across the plasma membrane) is −70 mV. A cell that exhibits a membrane potential is polarized.

4. The resting membrane potential arises due to an unequal distribution of ions on either side of the plasma membrane and a higher membrane permeability to K^+ than to Na^+. The level of K^+ is higher inside and the level of Na^+ is higher outside, a situation that is maintained by sodium-potassium pumps.
5. The ability of muscle fibers and neurons to respond to a stimulus and convert it into action potentials is called excitability.
6. During an action potential, voltage-gated Na^+ and K^+ channels open in sequence. Opening of voltage-gated Na^+ channels results in depolarization, the loss and then reversal of membrane polarization (from -70 mV to $+30$ mV). Then, opening of voltage-gated K^+ channels allows repolarization, recovery of the membrane potential to the resting level.
7. According to the all-or-none principle, if a stimulus is strong enough to generate an action potential, the impulse generated is of a constant size.
8. During the refractory period, another action potential cannot be generated.
9. Nerve impulse conduction that occurs as a step-by-step process along an unmyelinated axon is called continuous conduction. In saltatory conduction, a nerve impulse "leaps" from one node of Ranvier to the next along a myelinated axon.
10. Axons with larger diameters conduct impulses faster than those with smaller diameters; myelinated axons conduct impulses faster than unmyelinated axons.

Synaptic Transmission (p. 234)

1. Neurons communicate with other neurons and with effectors at synapses in a series of events known as synaptic transmission.
2. At a synapse, a neurotransmitter is released from a presynaptic neuron into the synaptic cleft and then binds to receptors on the postsynaptic plasma membrane.
3. An excitatory neurotransmitter depolarizes the postsynaptic neuron's membrane, brings the membrane potential closer to threshold, and increases the chance that one or more action potentials will arise. An inhibitory neurotransmitter hyperpolarizes the membrane of the postsynaptic neuron, thereby inhibiting action potential generation.
4. Neurotransmitter is removed in three ways: diffusion, enzymatic destruction, and reuptake by neurons or neuroglia.
5. Important neurotransmitters include acetylcholine, glutamate, aspartate, gamma amino butyric acid (GABA), glycine, norepinephrine, dopamine, serotonin, neuropeptides, and nitric oxide.

SELF-QUIZ

1. Which of the following are incorrectly matched?
   a. central nervous system: composed of the brain and spinal cord
   b. somatic nervous system: includes motor neurons to skeletal muscles
   c. sympathetic nervous system: includes motor neurons to skeletal, smooth, and cardiac muscles
   d. peripheral nervous system: includes cranial and spinal nerves
   e. autonomic nervous system: includes parasympathetic and sympathetic divisions
2. The portion of the nervous system that regulates the gastrointestinal (GI) tract is the
   a. somatic nervous system b. sympathetic division c. integrative division d. central nervous system e. enteric nervous system
3. Damage to dendrites would interfere with a neuron's ability to
   a. receive input b. make proteins c. conduct nerve impulses to another neuron d. release neurotransmitters e. form myelin
4. The type of cell that produces myelin sheaths around axons in the CNS is the
   a. astrocyte b. myelinocyte c. Schwann cell d. oligodendrocyte e. microglia
5. A bundle of axons in the CNS is
   a. a tract b. a nucleus c. a mixed nerve d. a ganglion e. an enteric plexus
6. Which of the following is NOT true concerning the repair of nervous tissue?
   a. If the cell body is not damaged, neurons in the PNS may be able to repair themselves.
   b. In the CNS, myelin inhibits neuronal regeneration.
   c. Injury to the CNS is usually permanent.
   d. Active Schwann cells contribute to the repair process in the PNS
   e. A regeneration tube forms across the injured area of a CNS neuron that undergoes repair.
7. In a resting neuron
   a. there is a high concentration of K^+ outside the cell
   b. negatively charged ions move freely through the plasma membrane
   c. the sodium-potassium pumps help maintain the low concentration of Na^+ inside the cell
   d. the outside surface of the plasma membrane has a negative charge
   e. the plasma membrane is highly permeable to Na^+
8. The depolarizing phase of a nerve impulse is caused by a
   a. rush of Na^+ into the neuron
   b. rush of Na^+ out of the neuron
   c. rush of K^+ into the neuron
   d. rush of K^+ out of the neuron
   e. pumping of K^+ into the neuron

9. If a stimulus is strong enough to generate an action potential, the impulse generated is of a constant size. A stronger stimulus cannot generate a larger impulse. This is known as
   a. the principle of polarization–depolarization
   b. saltatory conduction
   c. the all-or-none principle
   d. the principle of reflex action
   e. the absolute refractory period

10. Place the following events in the correct order of occurrence:
   1. Voltage-gated Na^+ channels open and permit Na^+ to rush inside the neuron.
   2. The Na^+/K^+ pump restores the ions to their original sites.
   3. A stimulus of threshold strength is applied to the neuron.
   4. The membrane polarization changes from negative (−55 mV) to positive (+30 mV).
   5. Voltage-gated K^+ channels open, and K^+ flows out of the neurons.

   a. 4, 1, 2, 3, 5 b. 4, 3, 1, 2, 5 c. 3, 1, 4, 2, 5
   d. 5, 3, 1, 4, 2 e. 3, 1, 4, 5, 2

11. Saltatory conduction occurs
   a. in unmyelinated axons
   b. at the nodes of Ranvier
   c. in the smallest diameter axons
   d. in skeletal muscle fibers
   e. in cardiac muscle fibers

12. The speed of nerve impulse conduction is increased by
   a. cold b. a very strong stimulus c. small diameter of the axon d. myelination e. astrocytes

13. For a signal to be transmitted by means of a chemical synapse from a presynaptic neuron to a postsynaptic neuron,
   a. the presynaptic neuron must be touching the postsynaptic neuron
   b. the postsynaptic neuron must contain neurotransmitter receptors
   c. there must be gap junctions present between the two neurons
   d. the postsynaptic neuron needs to release neurotransmitters from its synaptic vesicles
   e. the neurons must be myelinated

14. What would happen at the postsynaptic neuron if the total inhibitory effects of the neurotransmitters were greater than the total excitatory effects?
   a. A nerve impulse would be generated.
   b. It would be easier to generate a nerve impulse when the next stimulus was received.
   c. The nerve impulse would be rerouted to another neuron.
   d. No nerve impulse would be generated.
   e. The neurotransmitter would be broken down more quickly.

15. Match the following neurotransmitters with their descriptions.

___ a. inhibitory amino acid in the CNS	A. serotonin
___ b. a gaseous neurotransmitter that is not packaged into synaptic vesicles	B. acetylcholine
___ c. excitatory amino acid in the CNS	C. endorphins
___ d. body's natural painkillers	D. GABA
___ e. helps regulate mood	E. nitric oxide
___ f. neurotransmitter that activates skeletal muscle fibers	F. glutamate

16. Match the following.

___ a. the portion of a neuron containing the nucleus	A. synaptic end bulb
___ b. rounded structure at the distal end of an axon terminal	B. motor neuron
___ c. highly branched, input part of a neuron	C. sensory neuron
___ d. sac in which neurotransmitter is stored	D. dendrite
___ e. neuron located entirely within the CNS	E. interneuron
___ f. long, cylindrical process that conducts impulses toward another neuron	F. nucleus
___ g. produces myelin sheath in PNS	G. myelin sheath
___ h. unmyelinated gap in the myelin sheath	H. Schwann cell
___ i. substance that increases the speed of nerve impulse conduction	I. cell body
___ j. neuron that conveys information from a receptor to the CNS	J. node of Ranvier
___ k. neuron that conveys information from the CNS to an effector	K. ganglion
___ l. bundle of many axons in the PNS	L. nerve
___ m. bundle of many axons in the CNS	M. neurotransmitter
___ n. group of cell bodies in the PNS	N. tract
___ o. group of cell bodies in the CNS	O. synaptic vesicle
___ p. substance used for communication at chemical synapses	P. axon

CRITICAL THINKING APPLICATIONS

1. The buzzing of the alarm clock awoke Rodrigo. He stretched, yawned, and started to salivate as he smelled the brewing coffee. List the divisions of the nervous system that are involved in each of these activities.

2. Angelina just figured out that her A & P class actually starts at 10:00 A.M. and not at 10:15, which has been her arrival time since the beginning of the term. One of the other students remarks that Angelina's "gray matter is pretty thin." Should Angelina thank him?

3. Sarah really looks forward to the great feeling she has after going for a nice long run on the weekends. By the end of her run, she doesn't even feel the pain in her sore feet. Sarah read in a magazine that some kind of natural brain chemical was responsible for the "runner's high" that she feels. Are there such chemicals in Sarah's brain?

4. The pediatrician was trying to educate the anxious new parents of a six-month-old baby. "No, don't worry about him not walking yet. The myelination of the baby's nervous system is not finished yet." Explain what the pediatrician means by this reassurance.

ANSWERS TO FIGURE QUESTIONS

9.1 The total number of cranial and spinal nerves in your body is $(12 \times 2) + (31 \times 2) = 86$.

9.2 Sensory or afferent neurons carry input to the CNS. Motor or efferent neurons carry output from the CNS.

9.3 The axon conducts nerve impulses and transmits the message to another neuron or effector cell by releasing a neurotransmitter at its axon terminals.

9.4 A typical value for the resting membrane potential in a neuron is -70 mV.

9.5 Voltage-gated Na^+ channels are open during the depolarizing phase, and voltage-gated K^+ channels are open during the repolarizing phase of an action potential.

9.6 The two main factors that influence conduction speed of a nerve impulse are the axon diameter (larger axons conduct impulses more rapidly) and the presence or absence of a myelin sheath (myelinated axons conduct more rapidly than unmyelinated axons).

9.7 The depolarizing phase of the action potential opens the voltage-gated Ca^{2+} channels in synaptic end bulbs.