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Introduction to Nerves and the Nervous System

Learning Objectives

Upon completion of this chapter, you will be able to:

- 1. Label the parts of a neuron and describe the functions of each part.
- 2. Describe an action potential, including the roles of the various electrolytes involved in the action potential.
- 3. Explain what a neurotransmitter is, including its origins and functions at the synapse.
- 4. Describe the function of the cerebral cortex, cerebellum, hypothalamus, thalamus, midbrain, pituitary gland, medulla, spinal cord, and reticular activating system.
- 5. Discuss what is known about learning and the impact of emotion on the learning process.

Glossary of Key Terms

- action potential: sudden change in electrical charge of a nerve cell membrane; the electrical signal by which neurons send information
- afferent: neurons or groups of neurons that bring information to the central nervous system; sensory nerve
- axon: long projection from a neuron that carries information from one nerve to another nerve or effector
- dendrite: short projection on a neuron that transmits information

depolarization: opening of the sodium channels in a nerve membrane to allow the influx of positive sodium ions, reversing the membrane charge from negative to positive

- effector cell: cell stimulated by a nerve; may be a muscle, a gland, or another nerve cell
- efferent: neurons or groups of neurons that carry information from the central nervous system to an effector; motor neurons are efferent
- engram: short-term memory made up of a reverberating electrical circuit of action potentials
- forebrain: upper level of the brain; consists of the two cerebral hemispheres, where thinking and coordination of sensory and motor activity occur

ganglia: a group of nerve bodies

hindbrain: most primitive area of the brain, the brainstem; consists of the pons and medulla, which control basic, vital functions and arousal, and the cerebellum, which controls motor functions that regulate balance

- limbic system: area in the midbrain that is rich in epinephrine, norepinephrine, and serotonin and seems to control emotions
- midbrain: the middle area of the brain; it consists of the hypothalamus and thalamus and includes the limbic system

neuron: structural unit of the nervous system

- neurotransmitter: chemical produced by a nerve and released when the nerve is stimulated; reacts with a specific receptor site to cause a reaction
- repolarization: return of a membrane to a resting state, with more sodium ions outside the membrane and a relatively negative charge inside the membrane
- Schwann cell: insulating cell found on nerve axons; allows "leaping" electrical conduction to speed the transmission of information and prevent tiring of the neuron
- soma: cell body of a neuron; contains the nucleus, cytoplasm, and various granules
- synapse: junction between a nerve and an effector; consists of the presynaptic nerve ending, a space called the synaptic cleft, and the postsynaptic cell

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he nervous system is responsible for controlling the functions of the human body, analyzing incoming stimuli, and integrating internal and external responses. The nervous system is composed of the central nervous system (CNS; the brain and spinal cord) and the peripheral nervous system (PNS). The PNS is composed of sensory receptors that bring information into the CNS and motor nerves that carry information away from the CNS to facilitate response to stimuli. The autonomic nervous system, which is discussed in Chapter 29, uses components of the CNS and PNS to regulate automatic or unconscious responses to stimuli. $\prod_{i=1}^n$

The structural unit of the nervous system is the nerve cell, or **neuron.** The billions of nerve cells that make up the nervous system are organized to allow movement realization of various sensations; response to internal and external stimuli; and learning, thinking, and emotion. The mechanisms that are involved in all of these processes are not clearly understood. The actions of drugs that are used to affect the functioning of the nerves and the responses that these drugs cause throughout the nervous system provide some of the current theories about the workings of the nervous system.

PHYSIOLOGY OF THE NERVOUS SYSTEM.

The nervous system operates through the use of electrical impulses and chemical messengers to transmit information throughout the body and to respond to internal and external stimuli. The properties and functions of the neuron provide the basis for all nervous system function.

Neurons

As noted previously, the neuron is the structural unit of the nervous system. The human body contains about 14 billion neurons. About 10 billion of these are located in the brain, and the remainder make up the spinal cord and PNS.

Neurons have several distinctive cellular features (Figure 19.1). Each neuron is made up of a cell body, or **soma,** which contains the cell nucleus, cytoplasm, and various granules and other particles. Short, branch-like projections that cover most of the surface of a neuron are known as **dendrites.** These structures, which provide increased surface area for the neuron, bring information into the neuron from other neurons.

One end of the nerve body extends into a long process that does not branch out until the very end of the process. This elongated process is called the nerve **axon,** and it emerges from the soma at the axon hillock, a slightly enlarged area of the soma from which the axon emerges. The axon of a nerve can be extremely tiny, or it can extend for several feet. The axon carries information from a nerve to be transmitted to **effector** cells—cells stimulated by a nerve, which may include a muscle, gland, or another nerve. This transmission occurs at the end of the axon, where the axon branches out in what is called the axon terminal.

The axons of many nerves are packed closely together in the nervous system and look like cable or fiber tracts. **Afferent** fibers are nerve axons that run from peripheral receptors into the CNS. In contrast, **efferent** fibers are nerve axons that carry nerve impulses from the CNS to the periphery to stimulate muscles or glands. (An easy way to remember the difference between afferent and efferent is to recall that efferent fibers exit from the CNS.)

It is currently thought that neurons are unable to reproduce; so, if nerves are destroyed, they are lost. If dendrites and axons are lost, nerves regenerate those structures; however, for this regeneration to occur, the soma and the axon hillock must remain intact. For a clinical example, consider a person who has closed a car door on his or her finger. Sensation and movement may be lost or limited for a certain period, but because the nerve bodies for most of the nerves in the hand are located in **ganglia** (groups of nerve bodies) in the wrist, they are able to regenerate the damaged axon or dendrites. Over time, sensation and full movement should return.

Research on possible ways to stimulate the reproduction of nerves is under way. Although scientists have used nerve growth factor with fetal cell implants to stimulate some nerve growth, it is currently assumed that nerves are unable to reproduce.

Action Potential

Nerves send messages by conducting electrical impulses called **action potentials.**

● FIGURE 19.1 The neuron, functional unit of the nervous system.

Nerve membranes, which are capable of conducting action potentials along the entire membrane, send messages to nearby neurons or to effector cells that may be located inches to feet away via this electrical communication system. Like all cell membranes, nerve membranes have various channels or pores that control the movement of substances into and out of the cell. Some of these channels allow the movement of sodium, potassium, and calcium. When cells are at rest, their membranes are impermeable to sodium. However, the membranes are permeable to potassium ions.

The sodium–potassium pump that is active in the membranes of neurons is responsible for this property of the membrane. This system pumps sodium ions out of the cell and potassium ions into the cell. At rest, more sodium ions are outside the cell membrane, and more potassium ions are inside. Electrically, the inside of the cell is relatively negative compared with the outside of the membrane, which establishes an electrical potential along the nerve membrane. When nerves are at rest, this is referred to as the resting membrane potential of the nerve.

Stimulation of a neuron causes **depolarization** of the nerve, which means that the sodium channels open in response to the stimulus, and sodium ions rush into the cell, following the established concentration gradient. If an electrical monitoring device is attached to the nerve at this point, a positive rush of ions is recorded. The electrical charge on the inside of the membrane changes from relatively negative to relatively positive. This sudden reversal of membrane potential, called the action potential (Figure 19.2), lasts less than a microsecond. Using the sodium–potassium pump, the cell then returns that section of membrane to the resting membrane potential, a process called **repolarization.** The action potential generated at one point along a nerve membrane stimulates the generation of an action potential in adjacent portions of the cell membrane, and the stimulus travels the length of the cell membrane.

Nerves can respond to stimuli several hundred times per second, but for a given stimulus to cause an action potential, it must have sufficient strength and must occur when the nerve membrane is able to respond—that is, when it has repolarized. A nerve cannot be stimulated again while it is depolarized. The balance of sodium and potassium across the cell membrane must be re-established.

Nerves require energy (i.e., oxygen and glucose) and the correct balance of the electrolytes sodium and potassium to maintain normal action potentials and transmit information into and out of the nervous system. If an individual has anoxia or hypoglycemia, the nerves might not be able to maintain the sodium–potassium pump, and that individual may become severely irritable or too stable (not responsive to stimuli).

Long nerves are myelinated: they have a myelin sheath that speeds electrical conduction and protects the nerves from the fatigue that results from frequent formation of action potentials. Even though many of the tightly packed nerves in the brain do not need to travel far to stimulate another nerve,

● FIGURE 19.2 The action potential. **A.** A segment of an axon showing that, at rest, the inside of the membrane is relatively negatively charged and the outside is positively charged. A pair of electrodes placed as shown would record a potential difference of about –70 mV; this is the resting membrane potential. **B.** An action potential of about 1 msec that would be recorded if the axon shown in panel A were brought to threshold. At the peak of the action potential, the charge on the membrane reverses polarity.

they are myelinated. The effect of this myelination is not understood.

Myelinated nerves have **Schwann cells,** which are located at specific intervals along nerve axons and are very resistant to electrical stimulation (Figure 19.1). The Schwann cells wrap themselves around the axon in jellyroll fashion (Figure 19.3). Between the Schwann cells are areas of uncovered nerve membrane called the nodes of Ranvier. So-called "leaping" nerve conduction occurs along these exposed nerve fibers. An action potential excites one section of nerve membrane, and the electrical impulse then "skips" from one node to the next, generating an action potential. Because the membrane is forming fewer action potentials, the speed of conduction is much faster and the nerve is protected from being exhausted or using up energy to form multiple action potentials. This node-to-node mode of conduction is termed *saltatory* or leaping *conduction* (Figure 19.1)*.*

B

● FIGURE 19.3 Formation of a myelin sheath. **A.** Schwann cells wrap around the axon, creating a myelin coating. **B**. The outermost layer of the Schwann cell forms the neurilemma. Spaces between the cells are the nodes of Ranvier.

If the Schwann cells become enlarged or swollen and block the nodes of Ranvier, which is what occurs in the neuromuscular disease multiple sclerosis, conduction does not occur because the electrical impulse has a limited firing range. A stimulus may simply be "lost" along the nerve. Believed to be an autoimmune disorder that attacks Schwann cells and leads to swelling and scarring of these cells, multiple sclerosis is characterized by a progressive loss of nerve response and muscle function.

Nerve Synapse

When the electrical action potential reaches the end of an axon, the electrical impulse comes to a halt. At this point the stimulus no longer travels at the speed of electricity. The transmission of information between two nerves or between a nerve and a gland or muscle is chemical. Nerves communicate with other nerves or effectors at the nerve **synapse** (Figure 19.4). The synapse is made up of a presynaptic nerve, the synaptic cleft, and the postsynaptic effector cell. The nerve axon, called the presynaptic nerve, releases a chemical called a **neurotransmitter** into the synaptic cleft, and the neurotransmitter reacts with a very specific receptor site on the postsynaptic cell to cause a reaction.

Neurotransmitters

Neurotransmitters stimulate postsynaptic cells either by exciting or by inhibiting them. The reaction that occurs when a neurotransmitter stimulates a receptor site depends on the specific neurotransmitter that it releases and the receptor site it activates. A nerve may produce only one type of neurotransmitter, using building blocks such as tyrosine or choline from the extracellular fluid, often absorbed from dietary sources. The neurotransmitter, packaged into vesicles, moves to the terminal membrane of the axon, and when the nerve is stimulated, the vesicles contract and push the neurotransmitter into the synaptic cleft. The calcium channels in the nerve membrane are open during the action potential, and the presence of calcium causes the contraction. When the cell repolarizes, calcium leaves the cell, and the contraction stops. Once released into the synaptic cleft, the neurotransmitter reacts with very specific receptor sites to cause a reaction.

To return the effector cell to a resting state so that it can be stimulated again, if needed, neurotransmitters must be inactivated. Neurotransmitters may be either reabsorbed by the presynaptic nerve in a process called reuptake (a recycling effort by the nerve to reuse the materials and save resources) or broken down by enzymes in the area (e.g., monoamine oxidase breaks down the neurotransmitter norepinephrine; the enzyme acetylcholinesterase breaks down the neurotransmitter acetylcholine). Several neurotransmitters have been identified. As research continues, other neurotransmitters may be discovered, and the actions of known neurotransmitters will be better understood.

The following are selected neurotransmitters:

- *Acetylcholine*, which communicates between nerves and muscles, is also important as the preganglionic neurotransmitter throughout the autonomic nervous system and as the postganglionic neurotransmitter in the parasympathetic nervous system and in several pathways in the brain.
- *Norepinephrine* and *epinephrine* are catecholamines, which are released by nerves in the sympathetic branch of the autonomic nervous system and are classified as hormones when they are released from cells in the adrenal medulla. These neurotransmitters also occur in high levels in particular areas of the brain, such as the limbic system.
- *Dopamine*, which is found in high concentrations in certain areas of the brain, is involved in the coordination of impulses and responses, both motor and intellectual.
- *Gamma-aminobutyric acid (GABA),* which is found in the brain, inhibits nerve activity and is important in preventing overexcitability or stimulation such as seizure activity.
- *Serotonin*, which is also found in the limbic system, is important in arousal and sleep, as well as in preventing depression and promoting motivation.

Many of the drugs that affect the nervous system involve altering the activity of the nerve synapse. These drugs have

● FIGURE 19.4 The sequence of events in synaptic transmission: **(1)** Synthesis of the neurotransmitter; **(2)** uptake of the neurotransmitter into storage vesicles; **(3)** release of the neurotransmitter by an action potential in the presynaptic nerve; **(4)** diffusion of the neurotransmitter across the synaptic cleft; **(5)** combination of the neurotransmitter with a receptor; **(6)** a sequence of events leading to activation of second messengers within the postsynaptic nerve; **(7)** change in permeability of the postsynaptic membrane to one or more ions, causing **(8a)** an inhibitory postsynaptic potential or **(8b)** an excitatory postsynaptic potential. Characteristic responses of the postsynaptic cell are as follows: **(9a)** The gland secretes hormones; **(9b)** the muscle cells have an action potential; and **(10)** the muscle contracts. The action of the neurotransmitter is terminated by one or more of the following processes. **(A)** inactivation by an enzyme; **(B)** diffusion out of the synaptic cleft and removal by the vascular system; and **(C)** reuptake into the presynaptic nerve followed by storage in a synaptic vesicle or deactivation by an enzyme.

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several functions, including blocking the reuptake of neurotransmitters so that they are present in the synapse in greater quantities and cause more stimulation of receptor sites; blocking receptor sites so that the neurotransmitter cannot stimulate the receptor site; blocking the enzymes that break down neurotransmitters to cause an increase in neurotransmitter concentration in the synapse; stimulating specific receptor sites when the neurotransmitter is not available; and causing the presynaptic nerve to release greater amounts of the neurotransmitter.

KEY POINTS

- ◆ The nervous system controls the body, analyzes external stimuli, and integrates internal and external responses to stimuli.
- ➧ The neuron, comprising a cell body, dendrites and an axon, is the functional unit of the nervous system. Dendrites route information to the nerve, and axons take the information away.
- ➧ Nerves transmit information by way of action potentials. An action potential is a sudden change in membrane charge from negative to positive that is triggered when stimulation of a nerve opens sodium channels and allows positive sodium ions to flow into the cell.
- ➧ When sodium ions flow into a nerve, the nerve membrane depolarizes. Mechanically, this is recorded as a flow of positive electrical charges. Repolarization immediately follows, with the sodium–potassium pump in the cell membrane pumping sodium and potassium ions out of the cell, leaving the inside of the membrane relatively negative to the outside.
- ♦ At the end of the axon, neurons communicate with chemicals called neurotransmitters, which are produced by the nerve. Neurotransmitters are released into the synapse when the nerve is stimulated; they react with a very specific receptor site to cause a reaction and are immediately broken down or removed from the synapse.

CENTRAL NERVOUS SYSTEM

The CNS consists of the brain and the spinal cord, the two parts of the body that contain the vast majority of nerves. The bones of the vertebrae protect the spinal cord; and the bones of the skull, which are corrugated much like an egg carton and serve to absorb impact, protect the brain (Figure 19.5). In addition, the meninges, which are membranes that cover the nerves in the brain and spine, furnish further protection.

The blood–brain barrier, a functioning boundary, also plays a defensive role. It keeps toxins, proteins, and other large structures out of the brain and prevents their contact with the sensitive and fragile neurons. The blood–brain barrier represents a therapeutic challenge to drug treatment of brain-related disorders because a large percentage of drugs

● FIGURE 19.5 Bony and membranous protection of the brain.

are carried bound to plasma proteins and are unable to cross into the brain. When a patient is suffering from a brain infection, antibiotics cannot cross into the brain until the infection is so severe that the blood–brain barrier can no longer function.

The brain has a unique blood supply to protect the neurons from lack of oxygen and glucose. Two arteries—the carotids—branch off the aortic arch and go up into each side of the brain at the front of the head, and two other arteries the vertebrals—enter the back of the brain to become the basilar arteries. These arteries all deliver blood to a common vessel at the bottom of the brain called the circle of Willis, which distributes the blood to the brain as it is needed (Figure 19.6). The role of the circle of Willis becomes apparent when an individual has an occluded carotid artery. Although the passage of blood through one of the carotid arteries may be negligible, the areas of the brain on that side will still have a full blood supply because of the blood sent to those areas via the circle of Willis.

Anatomy of the Brain

The brain has three major divisions: the hindbrain, the midbrain, and the forebrain (Figure 19.7).

The **hindbrain,** which runs from the top of the spinal cord into the midbrain, is the most primitive area of the brain and contains the brainstem, where the pons and medulla oblongata are located. These areas of the brain control basic, vital functions, such as the respiratory centers, which control breathing; the cardiovascular centers, which regulate blood

● FIGURE 19.6 The protective blood supply of the brain: the carotid, vertebral, and basilar arteries join to form the circle of Willis.

pressure; the chemoreceptor trigger zone and emetic zone, which control vomiting; the swallowing center, which coordinates the complex swallowing reflex; and the reticular activating system (RAS), which controls arousal and awareness of stimuli and contains the sleep center. The RAS filters the billions of incoming messages, selecting only the most significant for response. When levels of serotonin become high in the RAS, the system shuts down, and sleep occurs. The medulla absorbs serotonin from the RAS; when the levels are low enough, consciousness or arousal results.

The cranial nerves (see Figure 19.7), which also emerge from the hindbrain, involve *specific* senses (sight, smell, hearing, balance, taste) and some muscle activity of the head and neck (e.g., chewing, eye movement). The cerebellum—a part of the brain that looks like a skein of yarn and lies behind the other parts of the hindbrain—coordinates the motor function that regulates posture, balance, and voluntary muscle activity.

The **midbrain** contains the thalamus, the hypothalamus, and the limbic system (see Figure 19.7). The thalamus sends direct information into the cerebrum to transfer sensations, such as cold, heat, pain, touch, and muscle sense. The hypothalamus, which is poorly protected by the blood–brain barrier, acts as a major sensor for activities in the body. Areas of the hypothalamus are responsible for temperature control, water balance, appetite, and fluid balance. In addition, the hypothalamus plays a central role in the endocrine system and in the autonomic nervous system.

The **limbic system** is an area of the brain that contains high levels of three neurotransmitters: epinephrine, norepinephrine, and serotonin. Stimulation of this area, which

● FIGURE 19.7 Anatomy of the brain. **A.** A view of the underside of the brain. **B.** The medial or midsagittal view of the brain.

appears to be responsible for the expression of emotions, may lead to anger, pleasure, motivation, stress, and so on. This part of the brain seems to be largely responsible for the "human" aspect of brain function. Drug therapy aimed at alleviating emotional disorders such as depression and anxiety often involves attempting to alter the levels of epinephrine, norepinephrine, and serotonin.

The **forebrain** is made up of two cerebral hemispheres joined together by an area called the corpus callosum. These two hemispheres contain the sensory neurons, which receive nerve impulses, and the motor neurons, which send them. They also contain areas that coordinate speech and communication and seem to be the area where learning takes place (see Figure 19.7). Different areas of the brain appear to be responsible for receiving and sending information to specific areas of the body. When the brain is viewed at autopsy, it looks homogeneous, but scientists have mapped the general areas that are responsible for sensory response, motor function, and other functions (see Figure 19.8). In conjunction with the cerebellum, groups of ganglia or nerve cell bodies called the basal ganglia, located at the bottom of the brain, make up the extrapyramidal motor system. This system coordinates motor activity for unconscious activities such as posture and gait.

Frontal lobe Parietal lobe Temporal lobe Occipital lobe

● FIGURE 19.8 Functional areas of the brain. **A.** Topographical organization of functions of control and interpretation in the cerebral cortex. **B.** Areas of the brain that control specific areas of the body. Size indicates relative distribution of control.

Anatomy of the Spinal Cord

The spinal cord is made up of 31 pairs of spinal nerves. Each spinal nerve has two components or roots. These mixed nerve parts include a sensory fiber (called the dorsal root) and a motor fiber (called the ventral root). The spinal sensory fibers bring information into the CNS from the periphery. The motor fibers cause movement or reaction.

Functions of the Central Nervous System

The brain is responsible for coordinating reactions to the constantly changing external and internal environment. In all animals, the function of this organ is essentially the same. The human component involving emotions, learning, and conscious response takes the human nervous system beyond a simple reflex system and complicates the responses seen to any stimulus.

Sensory Functions

Millions of sensory impulses are constantly streaming into the CNS from peripheral receptors. Many of these impulses go directly to specific areas of the brain designated to deal with input from particular areas of the body or from the senses. The responses that occur as a result of these stimuli can be altered by efferent neurons that respond to emotions through the limbic system, to learned responses stored in the cerebral cortex, or to autonomic input mediated through the hypothalamus.

The intricacies of the human brain can change the response to a sensation depending on the situation. People may react differently to the same stimulus. For example, if an individual drops a can on his or her foot, the physiological response is one of pain and a stimulation of the sympathetic

branch of the autonomic nervous system. If the person is alone or in a very comfortable environment (e.g., fixing dinner at home), he or she may scream, swear, or jump around. However, if that person is in the company of other people (e.g., a cooking teacher working with a class), he or she may be much more dignified and quiet, even though the physiological effect on the body is the same.

Motor Functions

The sensory nerves that enter the brain react with related motor nerves to cause a reaction mediated by muscles or glands. The motor impulses that leave the cortex are further regulated or coordinated by the pyramidal system, which coordinates voluntary movement, and the extrapyramidal system, which coordinates unconscious motor activity that regulates control of position and posture. For example, some drugs may interfere with the extrapyramidal system and cause tremors, shuffling gait, and lack of posture and position stability. Motor fibers from the cortex cross to the other side of the spinal cord before emerging to interact with peripheral effectors. In this way, motor stimuli coming from the right side of the brain affect motor activity on the left side of the body. For example, an area of the left cortex may send an impulse down to the spinal cord that reacts with an interneuron, crosses to the other side of the spinal cord, and causes a finger on the right hand to twitch.

Intellectual and Emotional Functions

The way that the cerebral cortex uses sensory information is not clearly understood, but research has demonstrated that the two hemispheres of the brain process information in different ways. The right side of the brain is the more artistic

side, concerned with forms and shapes, and the left side is more analytical, concerned with names, numbers, and processes. Why the two hemispheres are different and how they develop differently is not known.

When learning takes place, distinct layers of the cerebral cortex are affected, and an actual membrane change occurs in a neuron to store information in the brain permanently. Learning begins as an electrical circuit called an **engram,** a reverberating circuit of action potentials that eventually becomes a long-term, permanent memory in the presence of the proper neurotransmitters and hormones. Scientists do not understand exactly how this happens, but it is known that the nerve requires oxygen, glucose, and sleep to process an engram into a permanent memory, and during that processing structural changes occur to the cells involved in the engram. This reverberating circuit is responsible for short-term memory. When patients have a decreased blood supply to the brain, short-term memory may be lost, and they are not able to remember new things. Because they are unable to remember new things, the brain falls back on long-term, permanent memory for daily functioning. For example, a patient may be introduced to a nurse and have no recollection of the nurse 2 hours later and yet be able to recall the events of several years ago vividly.

Several substances appear to affect learning. Antidiuretic hormone (ADH), which is released during reactions to stress, is one such substance. Although too much stress prevents learning, feeling slightly stressed may increase a person's ability to learn. A patient who is a little nervous about upcoming surgery, for example, seems to display a better mastery of facts about the surgery and postoperative procedures than a patient who is very stressed and scared or one who appears to show no interest or concern. Oxytocin is another substance that seems to increase actual learning. Because childbirth is the only known time that oxytocin levels increase, the significance of this is not understood. Nurses who work with maternity patients should know that women in labor will very likely remember the smallest details about the whole experience and should use whatever opportunity is made available to do teaching.

In addition, the limbic system appears to play an important role in how a person learns and reacts to stimuli. The emotions associated with a memory as well as with the present have an impact on stimulus response. The placebo effect is a documented effect of the mind on drug therapy: If a person perceives that a drug will be effective, it is much more likely to actually be effective. This effect, which uses the actions of the cerebrum and the limbic system, can have a tremendous impact on drug response. Events that are perceived as stressful by some patients may be seen as positive by other patients.

KEY POINTS

➧ The CNS consists of the brain and spinal cord, which are protected by bone and meninges. To ensure blood flow to the brain if a vessel should become damaged, the brain also has a protective blood supply moderated by the circle of Willis.

- ➧ The hindbrain, the most primitive area of the brain, contains the centers that control basic, vital functions. The pons, the medulla, and the reticular activating system (RAS), which regulates arousal and awareness, are all located in the hindbrain. The cerebellum, which helps to coordinate motor activity, is found at the back of the hindbrain.
- ➧ The midbrain consists of the hypothalamus, the thalamus, and the limbic system. The limbic system is responsible for the expression of emotion, and the thalamus and hypothalamus coordinate internal and external responses and direct information into the cerebral cortex.
- ➧ The cerebral cortex consists of two hemispheres, which regulate the communication between sensory and motor neurons and are the sites of thinking and learning.

CLINICAL SIGNIFICANCE OF DRUGS THAT ACT ON THE NERVOUS SYSTEM

The features of the human nervous system, including the complexities of the human brain, sometimes make it difficult to predict the exact reaction of a particular patient to a given drug. When a drug is used to affect the nervous system, the occurrence of many systemic effects is always a possibility because the nervous system affects the entire body. The chapters in this section address the individual classes of drugs used to treat disorders of the nervous system, including their adverse effects. An understanding of the actions of specific drugs makes it easier to anticipate what therapeutic and adverse effects might occur. In addition, nurses should consider all of the learned, cultural, and emotional aspects of the patient's situation in an attempt to provide optimal therapeutic benefit and minimal adverse effects.

CHAPTER SUMMARY

- Although nerves do not reproduce, they can regenerate injured parts if the soma and axon hillock remain intact.
- Efferent nerves take information out of the CNS to effector sites; afferent nerves are sensory nerves that take information into the CNS.
- When the transmission of action potentials reaches the axon terminal, it causes the release of chemicals called neurotransmitters, which cross the synaptic cleft to stimulate an effector cell, which can be another nerve, a muscle, or a gland.
- A neurotransmitter must be produced by a nerve (each nerve can produce only one kind); it must be released into the synapse when the nerve is stimulated; it must react with a very specific receptor site to cause a reaction; and it must be immediately broken down or removed from the synapse so that the cell can be ready to be stimulated again.
- Much of the drug therapy in the nervous system involves receptor sites and the release or reuptake and breakdown of neurotransmitters.

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- The CNS consists of the brain and spinal cord, which are protected by bone and meninges. To ensure blood flow to the brain if a vessel should become damaged, the brain also has a protective blood supply moderated by the circle of Willis.
- The hindbrain, the most primitive area of the brain, contains the centers that control basic, vital functions. The pons, the medulla, and the reticular activating system (RAS), which regulates arousal and awareness, are all located in the hindbrain. The cerebellum, which helps to coordinate motor activity, is found at the back of the hindbrain.
- The midbrain consists of the hypothalamus, the thalamus, and the limbic system. The limbic system is responsible for the expression of emotion, and the thalamus and hypothalamus coordinate internal and external responses and direct information into the cerebral cortex.
- The cerebral cortex consists of two hemispheres, which regulate the communication between sensory and motor neurons and are the sites of thinking and learning.
- The mechanisms of learning and processing learned information are not understood. Emotion-related factors influence the human brain, which handles stimuli and responses in complex ways.
- Much remains to be learned about the human brain and how drugs influence it. The actions of many drugs that have known effects on human behavior are not understood.

Health care providers and patients may want to consult the following internet source:

http://www.InnerBody.com

Review of the organization and actions of the nervous system.

http://www.NationalGeographic.com

Interactive view of the nervous system at work.

CHECK YOUR UNDERSTANDING M

Answers to the questions in this chapter can be found in Answers to Check Your Understanding Questions on the CD-Rom in the front of the book.

MULTIPLE CHOICE

Select the best answer to the following.

- **1.** The cerebellum
	- a. initiates voluntary muscle movement.
	- b. helps regulate the tone of skeletal muscles.
	- c. if destroyed, would result in the loss of all voluntary skeletal activity.
	- d. contains the centers responsible for the regulation of body temperature.
- **2.** At those regions of the nerve membrane where myelin is present, there is
	- a. low resistance to electrical current.
	- b. high resistance to electrical current.
	- c. high conductance of electrical current.
	- d. energy loss for the cell.

3. The nerve synapse

- a. is not resistant to electrical current.
- b. cannot become exhausted.
- c. has a synaptic cleft.
- d. transfers information at the speed of electricity.
- **4.** Which of the following could result in the initiation of an action potential?
	- a. Depolarizing the membrane
	- b. Decreasing the extracellular potassium concentration
	- c. Increasing the activity of the sodium–potassium active transport system
	- d. Stimulating the nerve with a threshold electrical stimulus during the absolute refractory period of the membrane
- **5.** Neurotransmitters are
	- a. produced in the muscle to communicate with nerves.
	- b. the chemicals used to stimulate or suppress effectors at the nerve synapse.
	- c. usually found in the diet.
	- d. nonspecific in their action on various nerves.
- **6.** The limbic system is an area of the brain that
	- a. is responsible for coordination of movement.
	- b. is responsible for the special senses.
	- c. is responsible for the expression of emotions.
	- d. controls sleep.
- **7.** The most primitive area of the brain, the brainstem, contains areas responsible for
	- a. vomiting, swallowing, respiration, arousal, and sleep. b. learning.
	- c. motivation and memory.
	- d. taste, sight, hearing, and balance.
- **8.** A clinical indication of poor blood supply to the brain, particularly to the higher levels where learning takes place, would be
	- a. loss of long-term memory.
	- b. loss of short-term memory.
	- c. loss of coordinated movement.
	- d. insomnia.

MULTIPLE RESPONSE

Select all that apply.

- **1.** In explaining the importance of a constant blood supply to the brain, the nurse would tell the student which of the following?
	- a. Energy is needed to maintain nerve membranes and cannot be produced without oxygen.
	- b. Carbon dioxide must constantly be removed to maintain the proper pH.
- c. Little glucose is stored in nerve cells, so a constant supply is needed.
- d. The brain needs a constant supply of insulin and thyroid hormone.
- e. The brain swells easily and needs the blood supply to reduce swelling.
- f. Circulating aldosterone levels maintain the fluid balance in the brain.
- **2.** The blood–brain barrier could be described by which of the following?
	- a. It is produced by the cells that make up the meninges.
	- b. It is regulated by the microglia in the CNS.
	- c. It is weaker in certain parts of the brain.
	- d. It is uniform in its permeability throughout the CNS.
	- e. It is an anatomical structure that can be punctured.
	- f. It is more likely to block the entry of proteins into the CNS.

BIBLIOGRAPHY AND REFERENCES

- Fox, S. (1991). *Perspectives on human biology.* Dubuque, IA: Wm. C. Brown.
- Ganong, W. (2003). *Review of medical physiology* (21st ed.). Norwalk, CT: Appleton & Lange.
- Gilman, A., Hardman, J. G., & Limbird, L. E. (Eds.). (2006). *Goodman and Gilman's the pharmacological basis of therapeutics* (11th ed.). New York: McGraw-Hill.
- Guyton, A., & Hall, J. (2007). *Textbook of medical physiology* (11th ed.). Philadelphia: W. B. Saunders.
- Karch, A. M. (2009). *2010 Lippincott's nursing drug guide.* Philadelphia: Lippincott Williams & Wilkins.
- Noback, C., Strominger, N. L., Demarest, R. J., Ruggiero, D. A. (2005). *The human nervous system: Structure and function* (6th ed.). Totowa, NJ: Humana Press.
- Parpura, V., & Hayden, P. (2008). *Astrocytes in the physiology of the nervous system.* New York: Springer.
- Porth, C. M. (2008). *Pathophysiology: Concepts of altered health states* (8th ed.). Philadelphia: Lippincott Williams & Wilkins.
- Thibodeau, G., & Patton, K (2006). *Anthony's textbook of anatomy and physiology* (18th ed.). St. Louis, MO: Mosby.