The nervous system is made up of three types of organs: the brain, the spinal cord, and nerves (Fig. 6.1). The brain and the spinal cord are referred to as the central nervous system (CNS) because they are along the midline of the body. The nerves constitute the peripheral nervous system (PNS), extending from the brain and spinal cord to the farthest reaches of the body. The functions of the brain, spinal cord, and nerves are performed by the highly specialized nerve cells (i.e., neurons) they contain.

**MAIN FUNCTIONS FOR HOMEOSTASIS**

The overall goal of the nervous system is to regulate the operations of parts of the body to make sure they contribute to homeostasis and a satisfactory quality of life. The nervous system regulates muscles and glands directly by sending impulses to those structures. Among the glands controlled by the nervous system are the sweat glands and salivary glands. This system regulates other parts of the body indirectly by adjusting the amounts of hormones produced by some of the endocrine glands.

**Monitoring**

The nervous system performs six main functions to carry out its overall goal. Three operations stem from the three steps in negative feedback systems: monitoring, communicating, and adjusting. Many of the neurons in the brain and nerves monitor conditions in and around the body. These neurons do very little if conditions are proper and fairly stable. However, they are affected by harmful conditions and are sensitive to any change in conditions. When conditions are unfavorable for the cells or when there is a change (a stimulus), the neurons respond by starting messages (nerve impulses) within themselves.

**Communicating**

The initiation of impulses by neurons leads to the second main function: communicating. The neurons carry impulses to other parts of the nervous system, where they are passed on to other neurons, which pass them to still other neurons, and so on. Thus, many parts of the nervous system are informed that a change has occurred. They are
also informed of the nature of the change, its extent, and where it is happening. For example, if an insect bites a person, that person feels that something is happening. He or she also knows that it is a bite rather than something soft brushing against the skin, has a sense of the severity of the bite, and knows where to scratch or hit to remove the insect.

**Stimulating**

Communicating leads to the third function: stimulating. In the case of an insect bite, the nervous system activates muscles in the arms to remove the source of irritation. Note that the nervous system does not actually perform the adjustment, which is the third step in negative feedback. It only stimulates other parts of the body to do so.

These three functions can activate responses to promote beneficial changes as well as eliminate harmful ones. For example, when neurons in the stomach sense that it is empty and brain neurons detect that the nutrient level in the blood is low, a person feels hungry. If other neurons detect the sound of someone cooking in the kitchen while still others detect dinner aromas, the nervous system will activate muscles so that the hungry person will go to the kitchen and obtain nourishment. When the stomach has become full and blood nutrient levels begin to rise, other neurons initiate a negative response, causing the person to stop eating.

**Coordinating**

Making adjustments often requires the contributions of many parts of the body, and the nervous system must stimulate them so that they all work in harmony. At the same time, parts of the body that can interfere with achieving the desired outcome must be inhibited from acting. The nervous system provides these stimulations and inhibitions through its fourth main function: coordinating. For example, to walk to the kitchen, a person must activate some muscles while inhibiting others in order to step forward with one foot at a time.

**Remembering**

When a person must adjust to a new situation, it may take quite a while for all the necessary impulses to reach their destinations, especially when the situation is complicated and the proper response requires the coordinated stimulation of many structures. Furthermore, sometimes mistakes are made and the wrong response occurs. This is when remembering, the fifth main function of the nervous system, becomes helpful.

By remembering, the nervous system stores information about past experiences that includes the recollection of a situation, the responses that were made, and the degree of success that was provided by each response. Then, when faced with the same situation, a person can avoid trial and error by remembering what to do. This procedure saves time and prevents costly mistakes. Simple examples include remembering the way home after traveling the route a few times and
remembering the answers to test questions using information that was studied many times.

The benefits of remembering are used on an unconscious level as well. For example, when one is practicing an activity such as walking, playing an instrument, or riding a bicycle, the nervous system remembers the sequences of muscle contractions that resulted in failure or success. With enough practice, one need only consciously start the activity. One can then continue to perform well without thinking about the activity because, like a recording, the nervous system plays the rest of the program of successful commands for the muscles.

Memory also recalls situations that led to favorable or unfavorable outcomes. When the nervous system recognizes the presence of such situations, it will alert a person to proceed or take evasive action. This is why an experienced child will reach out for candy but back away from fire.

Thinking

Remembering tends to provide the same type of successful response every time a person is in the same circumstance. The more successful the same response is in the same situation, the faster and more accurately that response will occur. However, remembering does little when a person is faced with a new situation. That person must try to find the correct response by trial and error or by mentally imagining different responses and the results they might cause. Creating mental images of new courses of action and their possible outcomes is the sixth main function of the nervous system: thinking.

Thinking depends on memory to provide initial mental images and information. In thinking, a person intelligently rearranges the remembered images and information to create new images that have not been experienced before. Many alternatives can be mentally explored in a few seconds without actually trying any of them. People are thinking when they make plans, solve problems by analysis, and create mental images of things that do not occur naturally. Thinking provides the variety of acting that many people believe separates humans from other living things.

Thinking allows people to decide the best response to a new situation quickly, accurately, and without having to risk the consequences of untested attempts. It can even produce new responses to situations that have been created by people. For example, this is how people return to the Earth from a trip to the moon.

NEURONS

Components

All the billions of neurons in the nervous system have three basic parts. The nerve cell body contains the nucleus of the cell along with cytoplasm and organelles (e.g., mitochondria and ribosomes) (Fig. 6.2). The nerve cell body supplies the other two parts of the neuron with the materials and energy they need. It can also pick up messages from other neurons.

One or more extensions called dendrites project from the nerve cell body. Each dendrite can branch up to several hundred times. Like nerve cell bodies, dendrites can pick up messages from other nerve cells. They are also the parts of the sensory cells that monitor conditions. A dendrite being activated by another neuron or by a stimulus starts nerve impulses that travel along the dendrite to the nerve cell body, which passes the impulses to the third part of the neuron: the axon.

Each neuron has only one axon, which extends out from the nerve cell body. Each axon may have up to several hundred branches (axon collaterals). The impulses that are passed to the axon travel the entire length of each of its branches. Each branch then passes the impulses to another structure. Axons can pass impulses to other neurons, muscle cells, and gland cells, although all the branches from one neuron's axon can go to only one of these types of cells.

Operations

Reception All neurons perform three main functions. Reception involves having impulses generated in response to environmental conditions or messages from other neurons. Dendrites and nerve cell bodies are the parts that usually perform reception (Fig. 6.3).

Conduction The second function—conduction—refers to the movement of impulses along the neuron to the end of the axon (Fig. 6.3). Conduction in longer dendrites and axons occurs through a special mechanism called an action potential.
FIGURE 6.2 Neuron structure.
This mechanism involves several activities of the neuron cell membrane that carefully control the inward and outward movement of ions, especially sodium and potassium ions.

Transmission Once impulses have been conducted to the end of the axon, they are passed to the next structure by the third neuron function: transmission. The place where transmission occurs between neurons is called a synapse. Transmission to muscle cells occurs at neuromuscular junctions, and transmission to gland cells takes place at neuroglandular junctions. The process of transmission is essentially the same in all three cases (Fig. 6.3).

At a synapse, when an action potential reaches the end of an axon, it causes small packets (synaptic vesicles) at the end of the axon terminal to burst like blisters. These packets contain a chemical called a neurotransmitter, which is then released into the small space (synaptic cleft) between the neurons. Most neurons can release only one type of neurotransmitter. The neurotransmitter diffuses to the dendrite or cell body of the next neuron, where it attaches to receptor molecules on the cell membrane. Each type of receptor molecule is designed to bind to only one type of neurotransmitter.

Once enough neurotransmitter has been bound to the receptor molecules, the receiving neuron responds. Depending on the type of neurotransmitter and the type of neuron, the receiving neuron will be stimulated to perform reception and start its own impulses or will be inhibited from acting. The nervous system uses stimulatory transmissions to start or speed up an activity; it uses inhibitory transmissions to slow down, stop, or avoid an activity. A neurotransmitter continues to have its effect on the next cell until it is eliminated or counteracted. Neurotransmitters can be counteracted when antagonistic neurotransmitters are sent into the synapse.

Although a few synapses involve one neuron transmitting to one other neuron, synapses often have many neurons converging to transmit messages to a single neuron. The amount and length of the response by the receiving neuron depend on the balance between the amount of stimulatory and inhibitory neurotransmitters it receives at any moment from the many neurons connected to it. Thus, by changing the combinations of neurotransmitters at synapses, the nervous system can provide exquisitely precise adjustments to its impulses and the resulting body activities. The effect of such an interplay of stimulatory and inhibitory transmitters is experienced, for example, by a person whose hands are being burned by a hot beverage but who puts down the cup slowly and carefully to avoid spilling the beverage.

The branching of axons allows for divergence. Thus, impulses in one neuron can spread to many muscle cells, gland cells, or neurons. One can experience the effects of divergence when hearing a frightening sound or noticing a flirtatious glance. The heart pounds, the breathing increases, the stomach tightens, and the legs may become weak and shaky.
Another important function of synapses is to keep order in the nervous system. Since messages can pass only from axons to the next neuron, synapses ensure that impulses move through the system only in the correct direction.

NEUROGLIA

The CNS contains neuroglia cells, which provide a variety of services for the neurons (e.g., support and defense). These cells do not perform reception or conduct or transmit nerve impulses. One type makes a material called myelin, which forms a coating on CNS axons. The myelin coating on an axon resembles beads on a string. It causes impulses to travel faster by making them jump along the neuron (Fig. 6.2). Since myelin is white, it causes the regions that contain it to become white in appearance; these areas are referred to as the white matter of the brain and spinal cord.

The areas of the CNS that do not have myelin possess the pinkish gray color of plain neurons; these regions constitute the gray matter. The gray matter is important because it contains the synapses. All the complicated nervous system functions, including coordination, remembering, and thinking, require these synapses.

SCHWANN CELLS

Neurons in the PNS are assisted by Schwann cells. These cells produce myelin on dendrites and axons; this myelin is structurally and functionally similar to CNS myelin (Fig. 6.2).

NERVOUS SYSTEM ORGANIZATION

Central Nervous System

Recall that there are two main subdivisions of the nervous system—the central nervous system and the peripheral nervous system—and that the two parts of the CNS are the brain and the spinal cord. The neurons in different regions of these two organs are specialized to contribute to one or more of the main functions of the nervous system. For example, certain areas of gray matter in the brain monitor conditions such as temperature and the level of CO₂; others start impulses that stimulate muscles to contract, and still other areas are for remembering. Myelinated axons in the white matter allow regions of gray matter to communicate with each other.

Peripheral Nervous System

Sensory Portion The sensory portion of the peripheral nervous system contains sensory neurons, which monitor body conditions outside the brain and spinal cord. They also monitor conditions on the surface of the body and in its surroundings. Each type of sensory neuron is designed to monitor only one type of condition. For example, one kind responds to changes in temperature, while another is activated by pressure. Those in the nose and on the tongue respond to chemicals.

Most sensory neurons are long thin cells that extend through nerves from the regions they monitor to the brain or spinal cord. For example, sensory neurons from the fingertips extend through nerves in the arm all the way up to the middle of the back, where they enter the spinal cord. Once a sensory neuron performs reception in response to a condition, it carries impulses to communicate information about that condition to the brain or spinal cord.

Sensory neurons that do not have myelin release two substances (i.e., calcitonin gene-related peptides, substance P) at sites of wound injury. The combined effects are providing adequate inflammation while promoting healing.

Motor Portion The motor portion of the PNS consists of motor neurons that control the activities of muscles and glands. Somatic motor neurons control muscles that are attached to bones. Usually there is voluntary control of these muscles, although sometimes the nervous system causes them to contract involuntarily.

Somatic motor neurons extend from the brain and spinal cord, through nerves, to muscles they control. For example, the motor neurons that enter and stimulate the muscles in the lower leg begin in the spinal cord just below the middle of the back.

Other motor neurons make up the autonomic portion of the PNS. Autonomic motor neurons control many of the functions of the integumentary, circulatory, respiratory, digestive, urinary, and reproductive systems by regulating many glands and also muscles that are usually not under voluntary control. The sweat glands and sali-
vary glands, for example, are under autonomic control. Muscles under autonomic control include the heart and the smooth muscle in the walls of blood vessels, the bronchi, the stomach, and the urinary bladder.

Autonomic motor neurons are of two types: sympathetic and parasympathetic. Though a few structures (e.g., sweat glands, skin vessels) are controlled by only one type of autonomic motor neuron, most receive both sympathetic and parasympathetic motor neurons. In places where both types are present, one type of autonomic motor neuron stimulates the structure and the other type inhibits it. By balancing the amount of stimulation and inhibition, the autonomic nervous system can precisely control the speed and strength of activity of a structure. For example, sympathetic motor neurons increase the rate and strength of the heartbeat while parasympathetic motor neurons decrease them. By automatically adjusting the ratio between sympathetic and parasympathetic impulses, the autonomic nervous system varies the rate and strength of the heartbeat as the amount of blood flow needed by the body fluctuates.

NERVOUS SYSTEM PATHWAYS

Reflexes

The individual components of the nervous system work together to regulate the operations of parts of the body in order to maintain homeostasis. The simplest level of regulation involves a reflex, which is an involuntary response to a stimulus. Reflexes that use somatic neurons include blinking when something moves close to the eyes, coughing when something gets caught in the throat, and withdrawing from something that is painful. All activities controlled by autonomic neurons are reflex responses.

Many reflexes are built into the nervous system as it develops before birth. Others are acquired reflexes which develop when a person repeats the response every time a certain stimulus occurs. These reflexes involve the use of unconscious remembering.

A reflex occurs in basically the same way every time a particular stimulus occurs because the nervous system pathway that causes it is firmly established. Sensory neurons detect the stimulus and communicate through synapses with specific neurons in the CNS, and the CNS neurons quickly communicate with specific motor neurons. In a few reflex pathways, such as the one for the knee jerk, sensory neurons synapse directly with motor neurons. In either case the motor neurons complete the pathway by sending impulses to a muscle or gland, causing it to make the response.

Note that reflex pathways involve monitoring, communicating, and stimulating (or inhibiting). In many reflexes the adjustment caused by the response prevents or reverses the situation created by the stimulus. For example, the cough reflex removes material that enters the airways. These reflexes therefore are negative feedback systems that help maintain homeostasis. The responses produced by other reflexes contribute to homeostasis by improving conditions for the body. For example, the sight and smell of appetizing food cause a reflex that increases the secretion of saliva, which will be useful when the person begins to eat because it makes swallowing easier.

Some reflexes simultaneously use sensory impulses from several types of sense organs, such as the eyes, ears, skin receptors, and proprioceptors. Proprioceptors detect motion and tension in muscles and at joints. Some reflexes require a considerable amount of coordination by both brain and spinal cord interneurons and synapses. Some are influenced by voluntary motor impulses or by higher brain activities such as emotions and thinking, which send modifying impulses into the reflex synapses.

Reflex Pathways The specific parts and activities in a reflex pathway must be understood to appreciate the effects of aging on reflexes. The withdrawal reflex that occurs when a sharp object jabs the bottom of the foot provides a good example (Fig. 6.4).

When sensory neurons in the skin of the left foot detect the intense pressure caused by stepping on a sharp object, their dendrites carry out (1) reception. This causes the dendrites to (2) conduct impulses up through the nerve in the leg. These impulses reach and enter the gray matter in the back of the spinal cord via the sensory neuron axons, which (3) transmit them through synapses to other neurons in the spinal cord gray matter. Since these next neurons extend from one neuron to another, they are called interneurons. The interneurons (4) transmit the impulses to somatic motor neurons in the front part of the gray
matter of the spinal cord. The impulses are then (5) conducted down the motor axons in the nerves in the left leg to certain muscles in the thigh and calf. Neurotransmitters from the motor axons (6) stimulate these muscles to contract, causing the response of lifting the foot and thus relieving the intense pressure and protecting the foot from harm.

Proper reflex responses may require coordination in addition to monitoring, communicating, stimulating, and unconscious remembering. For example, to prevent loss of balance when lifting the foot, cooperation by a second reflex must occur. Branches of the sensory axons transmit impulses to other interneurons that cross over to the right side of the spinal cord. These crossing interneurons (7) transmit the impulses to other somatic motor neurons in the right side of the gray matter. Impulses in these motor neurons are (8) conducted down the nerves in the right leg. The impulses cause certain muscles in the right leg to contract, resulting in a straightening of the right leg at the same time that the left leg is bending and lifting the foot off the object. In this way, the right leg supports the weight of the body so that the person does not fall down.

**FIGURE 6.4** Reflex pathways involving skeletal muscles.
Another aspect of coordination is shown by the withdrawal reflex. As the interneurons stimulate motor neurons to the muscles that will make the appropriate actions occur, the interneurons send (9) inhibitory impulses to motor neurons controlling leg muscles that would interfere with the proper movements. This prevents antagonism among the muscles.

The reflex pathway for the withdrawal reflex is a fairly simple one. Other reflex pathways may involve interneurons that extend up or down the spinal cord or through several areas of the brain. Countless synapses may become involved before the impulses are finally transmitted to the motor neurons. Autonomic reflexes are further complicated by the synapses in the PNS. This increased complexity permits more coordination and modulation in responses. However, more complicated reflex pathways operate in essentially the same manner as simple reflex pathways.

**Conscious Sensation**

Though a reflex is completely involuntary and requires no conscious awareness, a person may feel the stimulus. For example, a person feels a sharp object jabbing the foot because the sensory neurons may synapse with other interneurons extending up to the brain. These other neurons help form the **conscious sensory pathways** in the nervous system.

Information from perceived sensations is used to initiate and adjust voluntary actions so that people can respond properly to conditions in their bodies and the world around them. These sensations provide information necessary for learning. Finally, conscious sensation provides much of the enjoyment that makes life worthwhile.

All conscious sensory pathways begin in the same way as do reflex pathways. That is, sensory neurons that have carried out reception conduct impulses into the CNS (Fig. 6.5). Sensory neurons that monitor regions below the head extend into the spinal cord, while those which monitor the head region pass into the brain. Once in the CNS, sensory impulses are passed to interneurons extending into the gray matter of the brain.

Impulses in each type of sensory neuron and from each part of the body are directed by synapses to the part of the brain designed to monitor that type of stimulus from that region. For example, impulses from the eyes are sent to vision centers, while impulses from the auditory parts of the ears are sent to hearing centers. The impulses are interpreted as perceived sensations when they reach the appropriate areas of the **cerebral cortex**, a layer of gray matter on the surface of the **cerebral hemispheres**. The **postcentral gyrus** is a raised area of the cortex on each cerebral hemisphere that is concerned mostly with conscious sensations from the integumentary, muscle, and skeletal systems (Fig. 6.5). Other
FIGURE 6.6 A somatic (voluntary) motor pathway.

Voluntary Movements

In many situations a person voluntarily chooses to move or not move in response to stimuli. One can also choose the type and degree of motion to make. For example, if someone calls, a person can choose to answer or not answer. If that person answers, the response may include a variety of motions or sounds. If the response is vocal, the sounds produced may be loud or soft, enunciated quickly or slowly, and projected with different inflections.

In addition to deciding whether to move in response to conscious stimuli, one can decide whether to take action on the basis of internal thought processes. Again, the type and degree of motion are usually up to the individual. Thus, one need not be called in order to decide to move or say something. A person may spontaneously decide to start a conversation or simply to sing.

Voluntary movements allow a person to take what he or she judges to be an appropriate action to optimize conditions in a given situation. Unlike reflex responses, voluntary movements allow freedom to select among many options rather than forcing a person to respond in a particular way.

Whether voluntary motion is initiated by stimuli or by thought processes in the brain, the nervous system pathway causing the motion is the same. It is called the somatic motor pathway because it controls voluntary muscles. The somatic motor pathway begins in a band of the cerebral cortex running down the side of each cerebral hemisphere. Each band is called a precentral gyrus (Fig. 6.6).

Each region of a precentral gyrus is designed to control the voluntary muscles in one area of the body. To move, a person (1) starts impulses from the area of the precentral gyrus that controls the muscles for the part of the body to be moved. Impulses from the precentral gyrus begin to (2) travel down the brain through white matter. As the impulses descend, they pass through areas of gray matter, where they are modified as they move through the gray matter synapses. In this way, the motion is performed at exactly the speed, strength, and distance chosen. Several important areas of gray matter that modify the motor impulses are called the (3) basal ganglia, located regions of the cortex are used for the special senses, such as vision, hearing, and smell.
inside the cerebral hemispheres. In general, the basal ganglia dampen motor impulses so that motions are not exaggerated.

Descending motor impulses are also channeled through the gray matter of the (4) cerebellum, which lies behind and below the cerebral hemispheres. Its gray matter forms a wrinkled coating called the (5) cerebellar cortex. The synapses in the cerebellar cortex modify the impulses so that the resulting motion starts and stops smoothly, at the proper time, and within the desired distance. The cerebellar cortex also adds impulses to ensure that all muscles that can assist in the motion are stimulated appropriately. The additional impulses activate muscles that move in the same direction and muscles that hold other parts of the body still or prevent loss of balance. At the same time the cerebellar cortex blocks impulses that would cause muscle contractions antagonistic to the desired action.

The cerebellar cortex continues to work throughout the time during which the desired action is occurring. It monitors the motion that is occurring and, if the motion is not exactly what was intended, provides impulses to muscles that can correct the error. With practice, the cerebellar cortex improves its ability to adjust the action, leading to increasing skill at performing that action. Similar control activities occur in the part of the cerebral cortex in front of the precentral gyrus.

Other synapses in the descending somatic motor pathways modify impulses to a lesser degree. Finally, the impulses reach (6) synapses to the dendrites and cell bodies of the somatic motor neurons. These synapses are the last places where the impulses can be modified. Once within the somatic motor neurons, the impulses leave the CNS and travel along the (7) motor axons in the nerves.

Upon arriving at the ends of the motor axons, the impulses cause the (8) release of the neurotransmitter acetylcholine. Like neurotransmitters in synapses, acetylcholine binds to the receptor molecules on the cell membranes of muscle cells. Once enough acetylcholine is bound, the muscle cells initiate the steps that lead to contraction, producing the desired action. Enzymes from the muscle cells then destroy the acetylcholine, and the cells relax until the next nerve impulses arrive.

The brain improves the efficiency of this process by sending some impulses to somatic motor neurons just before the person attempts a motion. Some of these anticipatory impulses are sent to motor neurons controlling the muscles that will contract, making them more sensitive to the main impulses telling the muscle to contract. The result is that when the motion should occur, the correct muscle moves faster and stronger while muscles that oppose its motion are inactivated.

Higher-Level Functions

The nervous system is also involved in activities that produce conscious remembering, thinking, interpretations, emotions, and personality traits. All these higher-level functions take place in the brain.

The neuron pathways that produce these activities are poorly understood. There seem to be complicated interactions among several areas of the brain for each activity. Also, each activity seems to influence and interact with the others. However, many of the areas of the brain that are involved with these higher-level functions have been identified, and some of the details of their operations have been discovered.

AGE CHANGES IN SENSORY FUNCTIONING

Age changes that affect the sensory neurons are important because by providing monitoring and communication, these neurons initiate reflexes and start or influence many voluntary actions, memories, thoughts, and emotions. Therefore, alterations in sensory functioning can affect homeostasis and the quality of life.

Aging causes a gradual decline in sensory functioning as a result of a reduction in the numbers of several types of sensory neurons, a decline in the functioning of the remaining sensory neurons, and changes within the CNS. The following section concentrates on changes in PNS sensory neurons other than those involved in vision, hearing, and other inner ear functions.

Skin Receptors

In the skin there is little change in either the number of sensory neurons for touch that are associated with hairs or the number of pain receptors. However, touch receptors called Meissner's corpuscles, which are not associated with hairs, and pressure receptors called pacinian corpuscles
decrease in number and become structurally distorted. In addition, the capsule in each pacinian corpuscle becomes thicker. Further reductions in sensations from the skin seem to result from a weakening of the action potentials that conduct impulses to the CNS. Alterations in action potentials may be due to age changes in neuron cell membranes or thickening of the myelin that surrounds many sensory neurons.

The age changes in Meissner’s corpuscles and pacinian corpuscles lead to a decreased ability to (1) notice that something is touching or pressing on the skin, (2) identify the place where touch or pressure is occurring, (3) distinguish between being touched by one object and being touched by more than one at the same time, and (4) identify objects by touching them. In addition, some skin sensory neurons require more time to respond to stimuli; this may contribute to the declining ability to feel vibrations, particularly those with higher frequencies. An age-related increase in impulse speed in some sensory neurons may partially compensate for these changes.

In addition to the effects of age changes on sensory neurons, the monitoring of conditions in and on the skin may be altered by changes in the thickness of the skin and the subcutaneous layer; the quality and distribution of hair; the ability of the CNS gray matter to respond to and interpret impulses from sensory neurons; and psychological status. Because of these factors, the effects of aging on the perception of temperature and pain are ambiguous.

Decreases in the ability to detect, locate, and identify objects touching or pressing on the skin result in decreases in the ability to respond to those objects. As a consequence, harmful objects may be encountered more frequently, more severely, and for longer periods. There is also a decline in the ability to perform precise actions that depend on good sensory input, such as moving the lips when forming words and manipulating small objects with the fingers. Reductions in skills may lead to problems in certain professions and loss of satisfaction with hobbies. Furthermore, reduced sensation means reduced pleasure from favorable physical contact, and this can have psychological and social consequences. Since sensory neurons associated with pain release substances that promote wound healing, age-related decreases in these neurons or in processing impulses from them may contribute to the age-related slowing of healing.

Sense of Smell

Aging causes decreases in the number of sensory neurons for smell. These neurons are called olfactory neurons and are high in the nasal cavities. Aging also causes deterioration of the pathways that carry olfactory impulses through the brain. All these changes cause a decline in the ability to detect and identify aromas. The degree of change is difficult to measure, however, because of the influence of changes in other brain functions (e.g., memory, emotional state) and of previous experiences. Furthermore, the degree of change seems to be highly variable among individuals.

Since much of what is commonly referred to as flavor is actually aroma, age changes in the sense of smell reduce the pleasure derived from eating and can contribute to malnutrition. Reduced olfaction also means a reduced ability to detect harmful aromas such as toxic fumes and dangerous gases. Finally, a declining ability to notice offensive odors can lead to socially embarrassing situations.

Sense of Taste

The sense of taste accounts for only four of the sensations that many people call flavors; all other flavors are due to the sense of smell. The four taste flavors are salt, sweet, sour, and bitter. Aging seems to cause slight decreases only in the ability to detect salty and bitter substances. The amount of change is highly variable among individuals, and the ability to detect salt declines the most. Even in the oldest individuals, the threshold levels for these four taste sensations are well below the levels in ordinary foods. The threshold for a stimulus is the lowest level of that stimulus which causes a response. If the threshold for tastes approaches the values found in foods, adding more of the ingredient that produces the flavor can compensate for this age change. Therefore, unlike the sense of smell, age changes in the sensory neurons for taste normally do not have a significant effect on food selection or diet. Of course this may not be true for persons with medical problems such as high blood pressure because these individuals may be on restricted diets that prohibit the use of flavorings such as salt. It may also be untrue for individuals who smoke because smoking greatly reduces taste sensations.
A main reason for the small age change in the sense of taste may be the lifelong ability of these sensory neurons to reproduce rapidly and thus replace taste receptors lost to aging or injury (e.g., from hot foods).

**Other Sensory Neurons**

Other types of sensory neurons that seem to have reduced functioning because of aging include those which monitor blood pressure in arteries; materials in the throat; thirst; amount of urine in the urinary bladder; amount of material in the rectum (the end of the large intestine); and positions, tensions, and lengths of the joint structures, muscles, and tendons. Additional decrements in these sensory functions may derive from changes in the ability of the organs being monitored to stretch and from alterations in the ability of the CNS to respond to sensory impulses.

Corresponding outcomes from these decreases in sensory functioning include high blood pressure; dehydration; swallowing and choking problems; urinary incontinence; constipation or bowel incontinence; and reduced control and coordination of voluntary movements.

**AGE CHANGES IN SOMATIC MOTOR FUNCTIONING**

**Somatic Motor Neurons**

Important age changes in somatic motor neurons involve their numbers, action potentials, and transmission sites. The first two changes are similar to those we have noted in sensory neurons.

**Number** There is a decrease in the number of motor neurons, and this reduces the number of cells that can be stimulated in a muscle. Therefore, the maximum strength of contraction that muscles can produce declines. In the lumbar region of the spinal cord, which controls muscles in the lower half of the body, as many as 50 percent of the somatic motor neurons are lost by age 60. Muscle cells that lose their motor neurons degenerate completely because they are no longer stimulated.

The resulting decrease in muscle strength can be minimized by increasing the strength of contraction provided by muscle cells that retain their motor neurons. This effect can be achieved on a short-term basis by increasing the amount of stimulation by the surviving motor neurons. However, using this strategy puts extra strain on the stimulated muscle cells. It also can produce the feeling that one must work harder to perform a strenuous activity which formerly was not difficult. Over the long term much of the strength of each muscle can be retained through programs of physical training and ordinary activities that require very strong muscle contractions.

**Action Potentials** The second age change in motor neurons is a slight decrease in the speed of action potentials in their axons. The amount of slowing is different in different neurons. The changes in speeds caused by aging increase the original differences in speed found among young neurons. As a result, when an aging muscle is supposed to contract, the burst of impulses sent to it by the motor neurons arrives over an increasingly long period. Therefore, the contractions of muscle cells are spread out over a longer period.

Slower action potentials in motor neurons may result from age changes in motor neuron cell membranes, myelin, or blood vessels within the nerves. Aging causes some myelin in peripheral nerves to separate from its axons. Damaged myelin is removed by macrophages, and its replacement occurs more slowly with age. Age changes in blood vessels were described in Chap. 4. These changes reduce blood flow in the nerves and therefore decrease the supply of nutrients and the elimination of wastes.

Alterations in muscle contraction resulting from slower action potentials and the spreading of muscle cell contractions include slower contraction, lower peak strength of contraction, and slower relaxation. Age-related decreases in anticipatory impulses increase these changes. All these alterations reduce the maximum amount of strength a muscle can produce when it performs very quick movements.

**Neuromuscular Transmission** The third age change is a substantial decrease in the speed of transmission from motor neurons to muscle cells. This decline may be from the formation of irregularities at the ends of aging motor axons. Slower transmission results in further delay in starting a motion.

All three age changes mean that activities that require strong and/or fast actions cannot be
performed as well. This can have a significant impact on individuals whose careers or recreational activities depend on such actions. For other people, modifying or changing strategies to achieve their goals can help compensate for the slow decline in strength and speed.

AGE CHANGES IN AUTONOMIC MOTOR FUNCTIONING

Aging of the autonomic motor neurons has not been as well studied as aging of other parts of the nervous system because of difficulties in distinguishing such changes from other age-related changes. Therefore, little can be said with confidence about the effects of aging on autonomic motor neurons. However, some aspects of the aging of these neurons are coming to light. In general, aging seems to have little effect on their ability to regulate body functions under normal conditions. This is due in part to overall slow loss of sympathetic motor neurons in the spinal cord (i.e., 5 percent to 8 percent per decade). Additionally, sympathetic motor neurons compensate for some age changes by modifying their dendrites and axons throughout life. However, when conditions become unfavorable, the autonomic neurons controlling certain structures have difficulty causing adequate adjustments to preserve homeostasis.

Autonomic Motor Neurons

An apparently inadequate autonomic response occurs when older people stand up or remain standing for long periods. Normally, sympathetic neurons prevent a substantial drop in blood pressure by stimulating the heart and causing constriction of many blood vessels. The ability of the sympathetic neurons to cause these adjustments decreases in many people. The resulting low blood pressure when one is in an upright position—orthostatic hypotension—can cause dizziness, light-headedness, and fainting. This is a major cause of falls and physical injury (e.g., fractures). Orthostatic hypotension does not occur in all older individuals, and some cases result from abnormalities in the circulatory system.

Aging of autonomic neurons can lead to elevated blood pressure as well as low blood pressure. Normally, parasympathetic impulses slow and weaken the heartbeat to keep blood pressure down while a person is at rest, when a person ends vigorous physical activity, and during each inspiration. Aging causes this parasympathetic function to decline and therefore diminishes the ability of these neurons to prevent blood pressure from exceeding the proper levels.

Age changes in autonomic neurons may also contribute to a decrease in the ability to adjust to extremes in temperature. Normally, sympathetic impulses cause blood vessels in the skin to constrict when a person is getting cold; this helps stabilize body temperature by reducing the rate of heat loss. With increasing age, there is a decrease in such constriction. Thus, older individuals are at greater risk of developing hypothermia. This age change may be due largely to age changes in blood vessels.

Another age change that may be due in part to aging of autonomic neurons involves erection of the penis. Normally, erection occurs when parasympathetic neurons cause dilation of blood vessels in the penis during sexual arousal, increasing blood flow into the penis and causing it to enlarge and become stiffer. With advancing age, these processes occur more slowly and to a lesser degree. These age-related changes may be due to reduced parasympathetic functioning or to age changes or disease in penile vessels. Parasympathetic control of other blood vessels is not changed by aging.

Another age change believed to result from aging of autonomic nerves is a decrease in the responsiveness of the pupil. Normally, sympathetic nerves stimulate muscles in the iris that cause dilation of the pupil and parasympathetic nerves stimulate muscles in the iris that cause constriction of the pupil. Balancing these autonomic influences results in letting enough light enter the eye for vision while preventing the entry of excess light, which can hinder vision and damage the eye. With advancing age, there is a decrease in the amount of pupillary dilation and slower constriction of the pupil, which reduces adaptation by the eye. Both changes may be caused by changes in the autonomic neurons or in the iris.

Finally, there is a decrease in the number of neurons controlling the movements of the esophagus during swallowing. Normally, when solids or liquids enter the esophagus from the throat, these materials are pushed down to the stomach by a wave of muscular contraction in the esophagus. The contraction is initiated by the swallowing reflex and is coordinated by a group of motor neu-
rons (Auerbach’s plexus) in the esophagus. With aging, the number of neurons in Auerbach’s plexus decreases. Swallowing becomes more difficult because the wave of contraction starts later, is weaker, and is less well coordinated. Sometimes the esophagus fails to empty completely, resulting in considerable discomfort.

**Sympathetic Neurotransmitters**

Sympathetic functioning is also affected by changes at neuromuscular and neuroglandular junctions. Sympathetic neurons become especially active when conditions become unfavorable and homeostasis is threatened or when such a threat is suspected or anticipated. The effects of sympathetic activity include increases in heart functioning, blood pressure, and perspiration as well as dilation of the airways. At the same time, sympathetic neurons inhibit certain activities, including digestion, urine production, and the functioning of the reproductive organs. Overall, these effects are adaptive and beneficial because they channel more of the body’s energies into actions that help the individual overcome or escape danger. The combination of effects caused by the sympathetic neurons is often referred to as the **fight-or-flight response**, which is part of the body’s reaction to stress.

Most sympathetic motor neurons use norepinephrine as a neurotransmitter at neuromuscular and neuroglandular junctions. At the direction of sympathetic neurons, norepinephrine is also produced and secreted into the blood by a gland called the **adrenal medulla** (Chap. 14). Norepinephrine from the adrenal medulla increases the intensity and duration of the effects of sympathetic norepinephrine.

Aging affects blood levels of norepinephrine in three ways:

1. The concentration of norepinephrine in the blood of resting individuals rises.
2. When a stressful situation is encountered, the level of norepinephrine increases faster.
3. Once the stress has passed, the level of circulating norepinephrine returns to its resting concentration more slowly.

There seem to be two reasons for the higher levels of norepinephrine in older individuals. One may be the stiffening of arteries (Chap. 4). The other seems to be a compensatory response for an age-related decline in the effectiveness of norepinephrine in some organs. This decline may be due to age changes in receptor molecules (e.g., lungs) or in reactions within cells (e.g., heart).

In conclusion, although the effects of age changes in autonomic neurons are not unimportant, such changes are few compared with the number of autonomic functions that seem to be unaffected by aging. Autonomic neurons can provide proper regulatory impulses to most of the structures they control regardless of age or the degree of stress placed on the body.

**AGE CHANGES IN REFLEXES**

Since aging causes many detrimental changes in sensory and motor neurons as well as in myelin, it produces deleterious effects on the reflexes that use these structures. Some of these effects were mentioned in the sections on sensory, somatic, and autonomic neurons. The decrease in number and the decline in sensitivity of certain sensory neurons mean that more stimulation is required to start many reflexes. It takes more time for the response to begin because reception takes longer and action potentials are weaker and slower. Changes in action potentials, together with decreases in the number of motor neurons and the effectiveness of certain neurotransmitters, cause the response to be weaker and of longer duration.

Age changes in the structures that surround the sensory neurons, such as the skin and blood vessels, further alter reflexes by preventing sensory neurons from properly detecting stimuli. Reflex responses are also reduced by age changes in the glands and muscles producing the responses and in the skeletal system.

Reflexes also seem to be detrimentally affected by age changes in the CNS. It has been observed that the more complicated the pathway in the CNS, the more dramatic the effect of aging on reflexes. In addition to reflexes occurring more slowly and weakly, there is a decline in the amount of coordination provided by the CNS in complicated reflex responses. Reflex contraction of large muscles is a good example.

The simplest muscle reflexes in the body are those which help maintain posture. These **stretch reflexes** or **deep tendon reflexes** use few synapses and no interneurons. A stretch reflex is initiated when a muscle is stretched, as occurs when a person’s posture begins to change because of slumping, an external force causes a joint to bend,
or an object hits a tendon. When the impulses in the reflex pathway reach the muscle that has been stretched, it contracts to restore the body to its original posture. The knee-jerk reflex is an example of a stretch reflex. Such simple reflexes become weaker but only slightly slower with age. The degree of weakening in different individuals is highly variable. The degree ranges from virtually no change in the strength of the response to essentially total loss of the response. However, many cases of very weak or absent stretch reflex responses result not from aging but from abnormal or disease conditions such as traumatic injury, atherosclerosis, arthritis, and diabetes mellitus.

In contrast to stretch reflexes, reflexes that maintain balance while one is standing in place require the proper timing of a sequence of many muscle contractions. Keeping one’s balance while there is movement of either the body or the surface on which a person is standing requires an even more complicated series of muscle contractions. Though the same sensory and motor neurons involved in stretch reflexes may be used, many interneurons and synapses in various parts of the brain and spinal cord are involved in these pathways. Sensory inputs from the eyes, ears, and skin may assist in these reflexes.

Complex reflexes such as those which maintain balance show a substantially greater slowing with age than do simple muscle reflexes. Aging also causes disturbances in the coordination required for such reflexes. For example, there is a change in the sequence in which the muscle contractions occur during these reflexes and an increase in the number of antagonistic muscle contractions. In comparison to simple reflexes, some of the additional slowing and much of the decline in coordination seen in complex reflexes seem to be due to age changes in the synapses and interneurons in the CNS.

Interestingly, some age changes in the CNS seem to involve adjustments in reflex pathways that compensate for diminished sensory functioning, muscle strength, skeletal system functioning, and confidence in one’s ability to maintain balance. This can be observed in the age change in gait. Part of walking involves voluntary activity, but many of the muscles used for walking are controlled by acquired reflexes. Older individuals walk with smaller steps, at a slower pace and with the feet more widely spread. Such a gait minimizes the risk of losing one’s balance. Gradually modifying voluntary actions and reflexes to walk in this manner seems to reduce the demands on the muscles, joints, and reflexes needed to maintain balance.

In summary, reflexes undergo several age changes. They require more stimulation to be activated, and it takes longer for a response to begin. The response is weaker, takes longer to occur, and shows less coordination. These changes are caused by alterations in both the PNS and the CNS. With more complicated reflexes, aging of the CNS makes a larger contribution to alterations in reflexes than do age changes in the PNS. As aging diminishes the functioning of reflexes, it reduces their ability to provide automatic, fast, and accurate responses to changes in internal and external conditions and therefore to maintain homeostasis.

AGE CHANGES IN CONSCIOUS SENSATION AND VOLUNTARY MOVEMENTS

As with reflexes, aging affects conscious sensation and voluntary movements because of age changes in sensory neurons, motor neurons, myelin, and CNS neurons and synapses. Since conscious sensation and voluntary movement use even more CNS synapses and interneurons than are used in reflexes, age changes in the CNS have a greater impact on these activities.

The results of PNS and CNS age changes on conscious sensation include a declining ability to detect, recognize, and determine levels of stimuli. These decrements make selecting and performing appropriate voluntary actions more difficult, inhibit learning, and diminish enjoyment from experiences.

The ability to maintain homeostasis and the quality of life is decreased further because aging of nerve pathways used for voluntary movements causes such movements to become slower, weaker, less accurate, and less well coordinated. Since these changes occur gradually, individuals are able to make adjustments in their activities and minimize the undesirable effects.

AGE CHANGES IN THE CNS

Correlations between the alterations in reflexes, conscious sensation, and voluntary movements and age changes in the structure and functioning of the CNS are not well understood. The reasons
for this ambiguity include (1) the necessity of studying brains obtained from autopsies, which have undergone variable degrees of postmortem changes, (2) the difficulty in determining how much, if any, disease was present in the brain or in other organs, and (3) the paucity of psychological or behavioral information about the people whose brains are studied. However, as these correlations become clear, it may become possible to influence the decreases in nervous system functioning caused by aging.

**Spinal Cord**

In the white matter, there is an age-related decrease in the motor neurons, especially of motor neurons that control somatic motor functions. These neurons carry anticipatory impulses and main impulses from the brain to lower somatic motor neurons in spinal cord gray matter. Within the gray matter, the average loss of motor neurons is approximately 25 percent during adulthood and into very old age. The rate is highly variable, and may be two to three times higher in some individuals. There seems to be a preferential loss of somatic motor neurons. This corresponds with the loss of motor units in muscles (see Chapter 8).

**Brain**

**Dimensions**

Many studies report that there is a decrease in the size and weight of the brain as age increases. The fluid-filled cavities inside the brain enlarge, the raised ridges (gyri) on the surface shrink, and the grooves (sulci) between the gyri become wider (Fig. 6.7).

How much of the age-related shrinkage of the brain is due to aging and how much is due to diseases such as atherosclerosis has not been determined. One reason for the overall shrinkage may be a decrease in the number of neurons in several areas of the brain. The cause of this neuron death is not known, and there is no indication that what is considered to be a normal amount of overall shrinkage has any effect on brain functioning.

**Numbers of Neurons**

Some parts of the brain show a substantial decline in the number of neurons, and this may affect specific functions. In the cerebrum, these parts include areas that control voluntary movements, areas for vision and hearing, and possibly areas involved in other conscious sensations. Other parts of the cerebral cortex seem to lose few if any neurons. The cerebellar cortex, which coordinates muscle movements and controls many complicated muscle reflexes, and the basal ganglia, which are also involved in modifying muscle actions, lose many neurons.

The regions of the brain other than the cerebral hemispheres and the cerebellum are referred to as the brain stem. The only regions of the brainstem that seem to lose neurons because of aging are the nucleus of Meynert, which produces acetylcholine for short-term memory, and the locus coeruleus, which produces norepinephrine and helps regulate sleep.

It has been suggested that neuron losses in these areas contribute to age-related detrimental changes in the functions to which they contribute: voluntary movements, conscious sensation, muscle reflexes, memory, and sleep. However, there is no conclusive evidence that localized loss of brain neurons caused by aging has any effect on the functions performed by the areas that incur neuron loss.

One reason why neuron loss may have no effect is that the remaining brain neurons can branch and produce many new synapses. The new neuron pathways created by the new synapses may compensate for the decrease in neurons.

**FIGURE 6.7** Structure of the brain.
Second, there may initially be many more neurons in the brain than are needed, and these additional neurons may constitute a reserve capacity. Third, the loss of neurons may actually improve the brain by eliminating neurons that are not used or have made errors. The brain may be able to recognize and eliminate unused or undesirable neuron pathways and thus improve its efficiency. This process may constitute part of the development of wisdom.

Neuron Structure and Functioning  Many neurons remaining in the aging brain undergo several age changes. For example, the cell membranes of brain neurons become less fluid and stiffer. These changes may contribute to age-related alterations in brain functioning by altering reception, conduction, and transmission. Second, internal membranes (e.g., endoplasmic reticulum) become irregular in structure, and many neurons have an accumulation of lipofuscin. The effects of abnormal amounts of lipofuscin are not known.

A third change in brain neurons is the formation of neurofibrillar tangles. Normally, neurons contain long thin structures called neurofibrils. These structures are present in the cell bodies and extend down the axons. Neurofibrils seem to be important in the movement of neurotransmitters from their sites of production to the ends of the axon. The formation of tangled neurofibrils may mean that not enough neurotransmitter is reaching the end of the axon; this could result in a decrease in or an elimination of transmission by neurons with neurofibrillar tangles. The result would be a decrease in the functioning of synapses.

Synapses  Because most research on changes in brain synapses has been directed toward alterations caused by disease, the effects of aging are not well understood. For example, there may be dozens or even hundreds of different neurotransmitters in the brain, and much confusion and contradictory information exist about age changes in these. All that can be said at this point is that aging seems to cause decreases in some neurotransmitters in some areas of the brain. There are few or no cases where the amount of a neurotransmitter increases with aging.

Information about age changes in the number of synapses in various brain areas is also incomplete. It is known that the number of synapses in an area may increase or decrease depending on how much use is made of that area. Neurons that are heavily used increase their number of synapses by growing new axon branches or new dendrites and dendrite branches (dendritic spines). The ability of neurons to do this decreases with age. There is also evidence that at least in some areas, neurons that get little use reduce their number of dendrites or dendritic spines and thus decrease the number of synapses in those areas of the brain.

The interpretation of information about changes in the number of synapses is complicated because the effectiveness of synapses depends not only on their numbers but also on changes in their neurotransmitters and in the exact neuron pathways that are gained or lost. For example, many inefficient synapses may be replaced by a few efficient ones, resulting in an improvement rather than a decline in functional capacity.

Adding to the confusion is the fact that synapses undergo age changes in structure as well as number. For example, though there is a decrease in the number of synapses in the precentral gyrus, the remaining synapses become broader. This may mean that these synapses work better and therefore compensate for those which are lost.

Perhaps the best-known age change in synaptic structure is the buildup of the protein called amyloid. A mass of amyloid in a synapse is called a plaque. As with other age changes, different amounts of plaques develop in different areas of the brain. It is believed that plaques decrease the functioning of synapses. Normally, however, a person does not form enough plaques to alter brain functioning to a detectable degree.

AGING OF OTHER BRAIN FUNCTIONS

Memory  The process of consciously remembering information is referred to as memory. Memory is a very complicated process that is not well understood. Though certain areas of the brain, such as the hippocampus, are especially important, many areas in the cerebral cortex and other brain regions act cooperatively to provide memory.

Memory can be divided into two broad types short-term memory and long-term memory. Information that is stored in short-term memory is re-
tained for brief periods (seconds or minutes). The brain may be temporarily storing this information by continuously repeating the impulses containing the information, and the information is forgotten as soon as the impulses fade away. The information is also easily forgotten if a person is distracted by different information that sends other impulses through the neurons.

It is possible to increase the time information is stored in short-term memory by keeping the impulses going. This can be done by repeating the stimulus over and over, just as a person can keep a wheel spinning by giving it a push now and then. This technique is used when people remember a telephone number for a short period by repeating it until the number is dialed.

Long-term memory can store information for many years. For example, remembering an incident from childhood requires the use of long-term memory. Apparently, information is stored in long-term memory when impulses produce physical changes in the neurons processing the information. The more times impulses about an incident pass through the neurons, the greater the chances that they will cause the physical changes. This is why a person studies material over and over to remember it for a test.

Two types of changes are believed to occur in neurons that store information in long-term memory. In one case, new molecules are produced in the neurons. Alternatively or additionally, the synapses in the nerve pathway are altered. In either case the impulses for the information travel much more easily. Then a small stimulus can trigger the neurons to produce the same impulses, resulting in the person consciously remembering the information.

Memory can also be classified according to the types of information stored. Incidental memory involves remembering information or skills that were self-taught. Procedural memory involves recalling how to perform a process or series of steps. Both types may include explicit memory and implicit memory. Explicit memory (declarative memory) involves remembering specific facts that a person tried to learn so they could be remembered. Implicit memory involves remembering specific facts that a person did not try intentionally to learn so they could be remembered. For example, a person may be unaware of learning procedures, processes, motor skills, or vocabulary by experience. Episodic memory involves recalling the times and places events happened. The events are mentally separated and oriented correctly regarding their proper time, sequence, and locations of occurrence. Working memory involves holding information at or close to the level of consciousness so it can be used in cognitive processing, such as solving a problem or planning a complex activity.

Age Changes in Memory Aging causes a decline in short-term memory in most people. The rate of decline varies highly between individuals. This may be due in part to differences in the rate of age changes within the nervous system, but it is caused by other factors to a greater degree. These factors include differences in general health, diet, presence of specific diseases, past patterns of mental activity, motivation, and diverse psychological, social, and economic parameters. So many features affect memory that it is impossible to predict which changes have occurred or will occur in a particular individual.

On the average, the decline in short-term memory is gradual and slow until approximately age 60 and then becomes ever more rapid, especially after age 70. However, the total amount of loss in memory functioning in a normal individual is relatively slight regardless of age. In many cases changes in memory can be noticed only in carefully controlled experimental situations and because people develop compensatory strategies, such age changes usually do not affect ordinary activities significantly.

The greatest decline in short-term memory occurs for information that is presented quickly and verbally. Information about completely unfamiliar things also becomes much harder to remember. Older people have more difficulty recalling information than simply recognizing it. For example, questions that require an older person to supply the answer are harder than those which require the person to select the correct answer from among several incorrect ones. To help elderly people remember, information should be presented slowly, in an organized manner, using relevant and concrete examples and visual aids. People are better able to recall information when cues such as notes and mnemonic devices are used and when they are allotted additional time to study and respond. It is also helpful to make adjustments to compensate for deficits in vision and hearing.
The reasons for the decline in short-term memory are not understood but may include age changes in the number of neurons, the number or structure of synapses, and the amounts of different neurotransmitters present in memory pathways.

Long-term memory seems to be largely unaffected or to improve as people get older.

Age changes in incidental memory and procedural memory depend upon whether they use explicit memory or implicit memory. Explicit memory decreases with aging, especially when the facts have to be learned quickly or they must be remembered quickly. Aging has much less effect on explicit memory when more time is used to learn or to remember facts. Implicit memory shows little decline when elders unknowingly experience or are given prompts related to the passed information, such as being placed in a familiar setting. Implicit memory shows the greatest age-related decline when a person tries intentionally to remember. Because of different age-related changes in these two types of memory, elders largely keep ability to perform even complex procedures they have practiced, but they may have difficulty explaining how to carry them out. Episodic memory also decreases with age. Failure of episodic memory results in erroneously remembering widely separate events as having occurred together or being unable to connect related events.

Working memory decreases with aging. Therefore, while the ability to remember specific information does not decline much, the ability to use multiple pieces of information in complex cognitive activity declines significantly. This may result from age-related reductions in effectively selecting, retrieving, and processing information consciously.

Elders can increase their memory functions through educational and training programs about memory. Memory training programs may emphasize specific memory techniques. Examples of such techniques include using written notes; mentally repeating information often; organizing material into large meaningful blocks rather than many unrelated details; making up sentences or words where letters (e.g., first letter in each word, letters of the words) stand for the items being remembered; mentally picturing information, images, or processes; putting information into a story, rhyme or song; sketching pictures or diagrams; finding experiences in life that are relevant or related to the information. Factors that help learning include studying when energy levels are high, but not after eating a large meal; avoiding large quantities of aspartame artificial sweetener (e.g., diet beverages); avoiding distractions when learning; getting restful REM sleep.

Other memory training programs take less direct approaches. Sometimes using cognitive restructuring to promote positive expectations in memory performance produces greater and more lasting beneficial effects on memory. This may result from using practical techniques in only similar situations, while cognitive restructuring techniques are often used in diverse situations.

Knowledge of the associations between memory and aging is important for improving outcomes from training programs for elders. For example, modifying job training programs to accommodate age changes in memory becomes more important as the numbers and ages of older workers increase.

Thinking

Like memory, thinking occurs entirely within the brain, but it is an even more complicated and less well understood process. Thinking includes problem solving, planning, and other activities that may be called intelligence. Intelligence may be divided into two categories. Crystallized intelligence involves using cognitive skills with familiar learned activities. Fluid intelligence involves using cognitive skills in new situations. Examples of fluid intelligence include learning novel problem solving, motor activities, or reasoning. It involves more flexibility in dealing with situations. No attempt will be made here to explain how the brain performs thinking.

Age Changes in Thinking  As with age changes in short-term memory, there is on the average a slow and gradual decline in thinking to approximately age 60; the rate of decline increases more each year after that, especially after age 70. Note
however, that the loss of thinking ability is relatively slight regardless of age and that changes can be noticed only through careful testing. The small amount of change, coupled with the use of compensatory strategies, usually means that there is not a significant effect on ordinary normal activities. There is much variability among individuals in regard to age-related changes in thinking because of variations in aging of the nervous system and differences in other factors that affect thinking. As a result, no one can anticipate how aging will affect an individual’s ability to think. Some individuals show no changes in thinking, and up to 10 percent of older people show an increase in thinking ability. This increase seems to be due to continued use of thinking, ongoing education, or good economic status. Among those whose thinking declines with aging, thinking becomes slower and changing one’s train of thought becomes more difficult.

Aging has little effect on crystallized intelligence, and many people show age-related increases. Fluid intelligence usually shows age-related decreases. Men show earlier decline in crystallized intelligence; women show earlier decline in fluid intelligence. Deterioration in the ability to solve problems and make decisions quickly and accurately is most evident when these processes require the consideration of many factors.

Vocabulary and Conversation

Language functions rely heavily upon memory and intelligence. There is little or no age-related change in knowing the meanings of words, though vocabulary may increase throughout life. Age-related changes in conversation include using more short and simple sentences; sentence fragments; pronouns and less specific terms; vague adjectives; vague references to time and place. Working vocabulary, ability to find the right word, and adherence to one topic decline. These changes increase as background distractions increase (e.g., noise, motion). Comprehension of conversations decreases as the content of a conversation becomes more complex; more disjointed; more novel; faster; and with increased distractions. These age-related changes usually do not prevent elders from carrying on meaningful conversations. The changes seem to result from age-related changes in memory and in cognition, including changes in methods of processing verbal information.

Supporting Memory and Intelligence

Factors that reduce age-related decreases in memory and intelligence and often improve these functions include good health; exercise; past and continuing education; activities requiring complex mental functions; self-determination and self-direction; and a sense of self-efficacy. Estrogen therapy in postmenopausal women improves some aspects of memory and cognition including short-term verbal memory, abstract reasoning, logical thinking, and overall cognitive functioning. Using proper prevention, intervention, and cognitive training programs for elders help to sustain and improve memory and intelligence as age increases.

Personality

Personality includes many facets, including levels of anxiety, depression, self-consciousness, vulnerability, impulsiveness, hostility, warmth, assertiveness, gregariousness, and emotions.

Age Changes in Personality Personality undergoes changes up to about 30 years of age, after which most of its aspects are extremely stable. However, major upsetting events in a person’s life, such as a major illness, may significantly alter one’s personality.

Personality greatly influences the choices made throughout life, particularly in matters related to education, exercise, diet, and health care. All these parameters influence the length and quality of life. Also, personality is a major determinant of an individual’s ability to adapt to changing circumstances. Since personality becomes stable, the nature of its contribution to the ability to adjust remains about the same throughout life. Therefore, knowledge of personality can be useful in predicting an individual’s future ability to adapt to the new life situations that develop with aging.
Sleep

The effects of aging on sleep are of great interest. One reason for this is the perception that older individuals are sleepier during the day. Second, there is evidence that compared with wakeful (daytime) values, body functions are different during sleep and at night. To fully understand aging, the body must be studied in the sleeping as well as the wakeful state.

Age Changes in Sleep  As people get older, several changes in sleep usually occur. Complaints about sleep difficulties rise from 15 percent among young adults to almost 40 percent among elders. With aging, more time is needed to fall asleep, there are more awakenings during the night, and wakeful periods are longer. Reasons for the increased number of awakenings include a higher incidence of indigestion, pain (e.g., arthritis), rhythmic leg movements, sleep apnea, and circulatory problems (e.g., irregular heartbeat). Some individuals have more awakenings because a decline in the capacity of the urinary bladder requires them to void urine more often. The rise in the level of norepinephrine may also contribute since norepinephrine increases alertness. The increase in awakenings is greater in men than in women. Even though sleep becomes more fragmented, the total amount of time spent asleep in each 24-hour period remains about the same because more time is spent in bed as age increases.

Changes occur in the type of sleep as well as in its continuity. While there is increasing variability among people as they get older, there is an average increase in the time spent in stage 1 sleep, the least restful of the five types. The existence and significance of age changes in amounts of stage 2 and stage 3 sleep are uncertain.

While asleep, people switch between stage 4 sleep and rapid eye movement (REM) sleep every 80 to 100 minutes. These are the most restful stages of sleep. There is an age-related decline in the amounts of time spent in stage 4 sleep and REM sleep, although the decrease in REM sleep becomes substantial only in very old age.

It is difficult to determine how much or which of the changes in sleep are due to aging of the brain and which are due to other age-related factors, such as having diseases, taking more medication, being past menopause, having different daily routines because of retirement, having more freedom for daytime napping, and experiencing altered social situations such as death of a spouse or a move to a different home or institution.

Sleep can be improved by keeping to a schedule; adhering to bedtime routine; creating an environment conducive to sleep (e.g., quiet, dark); exercise; treating medical problems and sleep apnea; entraining circadian rhythms with bright light therapy; biofeedback training; and mental relaxation techniques. Things to avoid include daytime naps; stimulants (e.g., caffeine) late in the day; strenuous activity shortly before bed; using the bed and bedroom for work, worrying, or solving problems; medications that adversely affect sleep (e.g., diuretics at bedtime); and chronic use of sedatives, hypnotics, and other sleep inducers.

The effects of age-related changes in sleep include a reduction in the quality of sleep and alterations in the time when it occurs during each 24-hour period. These effects probably explain why more people feel sleepy during the day as they get older. However, this is not a normal part of aging. When daytime sleepiness interferes with regular activities, it should be considered abnormal and warrants further diagnosis. The presence of age-related increases in abnormal sleepiness has contributed to the stereotype of the older person who nods or falls asleep at inappropriate times.

Biorhythms

Many activities in the body show regular cyclic fluctuations or biorhythms. One of these is a daily biorhythm that repeats itself approximately every 24 hours. It is aptly called the circadian rhythm, meaning "approximately daily rhythm." Perhaps the most obvious manifestation is the cycle of sleeping and being awake. Another well-known biorhythm is the menstrual cycle in women, which recurs approximately every 28 days. Faster cycles include the cardiac cycle and the breathing cycle. People also exhibit annual rhythms that accompany seasons of the year.

In the body, the circadian rhythm is controlled primarily by the brain. When light entering the eyes causes impulses to be sent to the brain, many of the impulses reach a brain area called the suprachiasmatic nucleus (SCN). The SCN is in the hypothalamus, located between the basal ganglia...
Impulses from the SCN travel an indirect route to the **pineal gland** of the brain. The pineal gland is in the crevice between the cerebral hemisphere and the cerebellum (Fig. 6.7, Fig. 14.1). The pineal gland secretes the hormone **melatonin**. When less light enters the eyes, more impulses travel from the SCN to the pineal, causing more melatonin secretion. More light entering the eyes causes the opposite effect. Both the intensity and wavelengths of light influence its effects on melatonin secretion.

Since usually more light enters the eyes during the day and light decreases during the evening, remaining very low during the night, melatonin secretion increases during the evening and remains low during the day. Melatonin influences many bodily functions including the SCN, and it produces some manifestations of the circadian rhythm. However, even with no light entering the eyes, the SCN causes melatonin to be secreted in a circadian rhythm. The SCN is the main regulator of the body's circadian rhythm. The circadian rhythm is influenced by other factors including environmental cues, physical activity, and eating.

Body circadian rhythms include sleep: wakefulness; stages of sleep; lowering of body temperature, blood pressure, and urine production at night; and oscillations in blood levels of many substances including hormones (e.g., melatonin, glucocorticoids, growth hormone, testosterone, estrogen, progesterone). Oscillations of these hormones cause manifestations of the circadian rhythm (see Chap. 14). The importance of maintaining normal circadian rhythms is evident when they are disrupted. Examples include "jet lag," working night shifts, or having sleep: wakefulness cycles disrupted by environmental irregularities (e.g., nighttime noise).

Aging causes changes in circadian rhythms. Many changes begin during the third decade and increase after that through old age. In general, manifestations of the circadian rhythm have lower peak intensities. Examples include difficulty falling asleep; poorer sleep quality; more urine production at night; and lower peak hormone levels. The circadian rhythm tends to shorten, and most manifestations begin up to one hour earlier in the 24-hour day. However, phase shifts are unequal, and some manifestations of the circadian rhythm occur later rather than earlier. The result is an age-related loss of synchrony among manifestations of the circadian rhythm. Perhaps the most obvious troublesome consequence is the age-related deterioration of the sleep: wakefulness cycle accompanied by deterioration of sleep quality.

Age changes in circadian rhythms may be due to a combination of age changes in the brain and the eyes. Weak or disrupted circadian rhythms can be brought toward normal by regulating exposure to bright light, by voluntarily regulating routines (e.g., physical activity), and by carefully timed melatonin supplementation.

In general, there are only small age changes in seasonal rhythms. Exceptions include levels of clinically important substances in the blood (e.g., creatinine, urea, urate, blood proteins).

Understanding and accounting for age-related changes in circadian rhythms and seasonal rhythms are important because circadian rhythms influence patient evaluations and effects of medications. The changes should also be considered in research studies so that measurements are taken at proper times of the 24-hour day.

**CONCLUSION**

In spite of age changes, the normal nervous system can help maintain homeostasis and sustain a satisfactory quality of life for many decades. However, as with other body systems, the comfort derived from these conclusions may diminish when one considers the frequency and effects of nervous system diseases that increase with age.

**DISEASES OF THE NERVOUS SYSTEM**

**Strokes**

Strokes are the third leading cause of death among people over age 65, accounting for approximately 9 percent of all these deaths. Beginning at a rate of less than 6 percent at age 65, the percentage of deaths from strokes rises steadily as age increases, surpassing 12 percent for those over age 85.

Heart disease accounts for 4.5 times as many deaths, and cancer, which is the second leading cause of death among the elderly, accounts for more than twice as many deaths among people above age 65. While the death rate from cancer has remained stable for many years, the death rates from strokes and heart disease have declined...
steadily since about 1960. These declines are probably due in large part to better prevention of atherosclerosis and better diagnosis and treatment of strokes and heart disease.

Many people who have a stroke survive. Therefore, not only the percentage of deaths but also the overall incidence of strokes increases with age, especially after age 65. About 4.5 percent of those between 65 and 75 years of age have a stroke, and the rate among those over age 75 is about 7.3 percent. Strokes occur more frequently in men than in women and much more frequently in blacks than in whites. Those who survive are often left with serious lifelong disabilities.

Causes and Types To understand how and why strokes occur, some additional information about the brain must be understood. Most of these facts are also true of the heart.

Brain neurons are always very active and therefore need a constant supply of energy. This energy is obtained by breaking down glucose in processes that consume oxygen and thereby prevent the formation of lactic acid and other harmful waste products. Flowing blood delivers the glucose and oxygen to the brain. If the supply of glucose or oxygen drops, the brain neurons will be injured or killed. A low oxygen supply for a few seconds will cause the neurons to malfunction, and a very low oxygen supply for several minutes can result in neuron death. The brain can adjust the amount of blood flow it receives by signaling the heart to adjust cardiac output, directing blood vessels throughout the body to adjust blood pressure, and constricting or dilating its own blood vessels.

Blood being pumped to the brain by the left ventricle passes first through part of the aorta and then through the arteries (carotid and vertebral arteries) that lead up the neck and into the skull (Fig. 6.8). Blood can be felt pulsing through the carotid arteries on either side of the neck. Branches from these ascending arteries carry blood over the brain’s surface and deep into the brain.

Strokes occur when blood flow to and through the brain is disrupted. Because of the sudden and devastating effects on the brain, the victim may appear to have been struck with a heavy blow, hence the name “stroke.” Since strokes affect the brain and are almost always caused by abnormalities in the blood vessels or heart, they are also called cerebrovascular accidents (CVAs).

The most common circulatory system problem resulting in strokes is atherosclerosis. As in all arteries, atherosclerosis in brain arteries reduces blood flow by causing them to become narrow, rough, and stiff. Recall that roughness leads to thrombus and embolus formation, blocking blood flow, and that stiffness prevents an artery from dilating when necessary. Blood flow to the brain can also be reduced by emboli formed on a myocardial infarction that causes roughness of the inner lining of the heart. Additional causes of blocked brain arteries include emboli or pieces of plaque that break free from the wall of an artery leading to the brain. Coronary artery disease may decrease blood flow by reducing heart functioning. Since all these strokes prevent adequate blood flow in the brain, they are called ischemic strokes. Ischemia means inadequate blood flow, and about 80 percent of all strokes are ischemic strokes.

Thrombus formation, narrowing, and stiffening in brain arteries develop gradually, and there is some time for enzymes in the blood to dissolve some of the thrombus and for blood vessels to compensate for the reduced flow by dilating. Sometimes this restores blood flow sufficiently so that even though neurons are injured, they survive. Additional neuron injury occurs when blood flow is restored because the increase in O₂ combined with injured cells causes an increase in free radical production and damage. Injured neurons can repair themselves and regain their normal functions.

Ischemic strokes from emboli tend to produce greater injury and more neuron death because they cause blood flow to be stopped suddenly and completely. Even if the blocked artery dilates, the embolus is likely to slide farther along until it gets stuck at the next narrowing. Furthermore, since a rough spot in the heart or in an artery may continue to produce emboli, many brain regions may be affected and many strokes can occur in succession.

After a stroke, the neurons that were killed are not replaced since neurons cannot reproduce. However, the remaining neurons may form new dendrites and synapses to compensate for the dead neurons. The surviving neurons may be trained to take on some of the jobs previously performed by the killed neurons.

Atherosclerosis of brain arteries also causes strokes in another way. Arteries weakened by ath-
Erosclerosis can rupture and bleed, causing hemorrhagic strokes. These constitute the remaining 20 percent of all strokes. Since they are often associated with high blood pressure, hemorrhagic strokes are also referred to as hypertensive hemorrhagic strokes.

When an artery in the brain ruptures, the region it supplies no longer receives adequate blood flow because some of the blood is leaking. Neurons near the site of the rupture are injured as blood sprays on them and pushes them apart and aside. The hemoglobin that leaks out of the red blood cells further injures these neurons. Part of the injury is from free radicals produced in the presence of iron in hemoglobin.

Hemorrhagic strokes cause additional brain damage because as more blood leaks from the artery, it increases the pressure inside the skull. This condition begins to damage neurons in all parts of the brain. The pressure also tends to compress vessels, reducing blood flow to many parts of the brain. If the blood pushes the brain far out of position, more neurons will be torn and crushed and more blood vessels will be squeezed shut.
Pressure within the skull increases further when inflammation in the injured areas causes the brain to swell, and all areas of the brain can be injured. If the brain regions controlling the heart, respiration, or blood pressure are affected, the victim’s life is severely threatened.

Since hemorrhagic strokes can injure many parts of the brain, they are more serious than ischemic strokes and are much more likely to cause death. About 80 percent of all hemorrhagic strokes in people with high blood pressure are fatal.

**Signs and Symptoms** Malfunctioning of the brain starts as soon as a stroke begins. Depending on which regions are injured and the severity of the damage, the malfunctions are apparent as any of a wide variety of signs and symptoms. Some more common ones are tingling, numbness, and muscle weakness or paralysis in one or more parts of the body. These alterations often occur on only one side of the body. Other frequently encountered changes include loss of balance or muscle coordination, altered vision, difficulty speaking, mental confusion, and diminished or lost consciousness.

Sometimes the signs and symptoms disappear in a few seconds or hours. Strokes of this type are called *transient ischemic attacks (TIAs)* because they result from a brief decline in blood flow and the injured neurons recover quickly. TIAs frequently occur over and over in exactly the same way because a thrombus forms in the same place in a brain artery. Though TIAs may appear to be unimportant, they are often followed by more serious strokes.

The signs and symptoms of other strokes last for days or weeks and subside very gradually, if at all. Strokes of this type are referred to as *reversible ischemic neurological deficits (RINDs)* because the brain is able to regain some of its functions.

The third type of stroke is called a *completed stroke* because the signs and symptoms develop quickly and show no improvement.

**Treatments** The best way to reduce the effects of strokes is prevention. Since most strokes result from atherosclerosis, this entails reducing the risk factors for atherosclerosis. This process should begin as soon as possible and continue throughout one’s life (Chap. 4).

Other ways of reducing the risk of a stroke in individuals of advanced age include reducing high blood pressure, treating blood disorders, and avoiding exhaustion. When a person seems to be having a stroke, medical attention should be obtained immediately to minimize possible complications.

Treatments for strokes involve reducing the risk of having another stroke and may include medications or surgery. During and after medical treatment, steps should be taken to provide psychological and social support for the stroke patient and the members of his or her family. Physical therapy and rehabilitation often help the patient improve or compensate for functions detrimentally affected by the stroke.

Many stroke patients are disabled for the rest of their lives. The disabilities not only adversely affect their ability to care for their physical needs but also may impinge heavily on their self-image, mental health, interactions with others, and ability to support themselves economically. The cost of treatments and care may add substantially to the economic difficulties.

**Dementia**

*Dementia* is a broad category of diseases, all of which involve a serious decline in memory accompanied by a major decline in at least one other mental function. Three other criteria must be met before a person can be said to have dementia. First, the person must be affected to such an extent that he or she has significant difficulty carrying out normal activities and interacting with other people. Second, these difficulties must be present on a continuing and long-term basis rather than sporadically. Third, they must be caused by an identifiable physical abnormality or at least must not be caused by an identifiable mental illness such as depression. Functions that are often reduced in patients with dementia include abstract thinking; speaking, reading, and writing; making judgments; solving problems; identifying common objects; and performing simple voluntary tasks.

The number and rate of cases of dementia are increasing because the number of older people and the proportion of the population made up of older people are growing. In addition, since better diagnostic tests are being developed and the social stigma attached to the diagnosis of demen-
Dementia is declining, more cases are being identified and reported. However, incidence rates and death rates are only estimates because of difficulty with diagnosis and other diseases can mask the presence of dementia. Also, dementias contribute to other causes of death, leaving cases of dementia unreported as the cause of death.

The incidence of dementia increases with the age of a population. The incidence rate rises exponentially, meaning the greater the age, the faster the rate of incidence rises. Very few cases occur in people below age 60, and less than 2 percent of all people between the ages of 60 and 65 have dementia. The percentages approximately double for every five years above age 65, so that more than 30 percent of those over age 85 suffer from dementia to some degree. Overall, between 16 and 24 percent of the population over age 65 suffer from mild dementia and up to 8 percent of those over age 65 have severe dementia. Among those over age 65, the number of people with dementia is greater than the number who have strokes. For adults, the death rate from dementias approximately doubles with each decade of life until age 90, when the death rate begins to plateau.

There are more than 60 different types of dementia. Some forms are reversible, including dementia caused by medications; drugs; alcohol; anemia; malnutrition; CNS infection; malfunction of the thyroid gland or adrenal glands; and malfunction of organs such as the liver and kidneys. Some forms of dementia are irreversible, including the forms associated with Alzheimer’s disease and Parkinson’s disease and those caused by strokes, heart failure, repeated head injury, AIDS, and Huntington’s disease.

Some individuals have more than one type of dementia. Others have dementia along with nervous system disorders such as delirium and depression. As a result, a definitive diagnosis of dementia is quite difficult to obtain. At present, cases can be diagnosed with about 90 percent accuracies.

The many causes of dementia occur as follows: 10 percent to 20 percent from atherosclerosis or, occasionally, another circulatory system disease; at least 55 percent from Alzheimer’s disease; 8 percent from Parkinson’s disease; 4 percent from head trauma; 12 percent from a mixture of these causes; and 6 percent from other causes. Approximately 70 percent of cases after age 60 are caused by Alzheimer’s disease.

**Multi-Infarct Dementia**

Dementia caused by circulatory disease is often called *multi-infarct dementia* because it results from having many areas of the brain die from inadequate blood flow. Free radicals also cause damage. The amount of infarction usually increases over an extended period because the victim has one stroke after another or because arteries remain nearly completely blocked. Therefore, multi-infarct dementia becomes progressively worse. Sometimes one large stroke will leave the patient with dementia. Since almost all cases of multi-infarct dementia result from atherosclerosis, taking steps to prevent atherosclerosis reduces the risk of multi-infarct dementia.

**Alzheimer’s Disease**

*Alzheimer’s disease* (*AD*) is named for Alois Alzheimer, who first described the disease in 1907. The rate of occurrence of Alzheimer’s disease doubles every five years after age 60 up to age 90. The earliest cases occur at about age 40. However, less than 1 percent of those under age 65 have AD, compared with up to 20 percent of those over age 80. Overall, 10 percent to 15 percent of people over age 64 have Alzheimer’s disease, and it affects approximately 50 percent of those over age 84. Alzheimer’s disease occurs more frequently in women compared with men.

There are now four million people with AD. The number is expected to reach nine million by AD 2040. Alzheimer’s disease is now the fourth leading cause of death in the U.S., causing 100,000 deaths per year. AD is becoming more important, as death rates from cardiovascular disease and strokes continue to decline, the elder population continues to increase, and the proportion of very elderly people increases. Older statistical tables do not list AD as a major cause of death among older people because widespread and accurate diagnosis of AD has occurred only in recent years. By AD 2020, costs from AD are expected to exceed costs from heart disease and cancer. Costs come from physicians, health care providers, social workers and in-home care givers; diagnostic procedures and medications; hospitalizations and nursing homes; special apparatus, diets, and living accommodations; and loss of income and productivity. These costs bear on families, insurance companies, and society as a whole. Non-economic
costs include social costs (e.g., disrupted family life, isolation, increased conflicts) and personal costs (e.g., stress, fatigue, psychological detriments such as depression and anger, reduced quality of life). These costs increase synergistically as the disease progresses and as other disorders develop.

Types Alzheimer’s disease can be subdivided into two types. One type is early onset AD or familial AD (FAD). Onset occurs before age 65, usually during the sixth decade of life. The second is late onset AD or senile dementia of the Alzheimer’s type (SDAT), with onset usually after age 60. SDAT, also called sporadic Alzheimer’s disease, is the most common form of AD.

Causes Though the causes of most AD cases are not known, as many as 50 percent are probably caused by genetic abnormalities since AD tends to run in families. Other factors must be involved because when one identical twin develops AD, the other may not develop the disease (see Genetics of AD, below). A main difficulty in finding causes of AD is that no animals are known to develop AD or conditions very similar to AD. Therefore, research is limited.

Some scientists propose that AD is not a disease but is part of normal aging. They point out that all aging brains develop the same physical changes found in brains from AD victims, though to a lesser degree. Perhaps like other age changes, AD develops in everyone, though at different rates. They suggest that if people lived long enough, everyone might eventually develop AD.

Though the causes of some forms of AD remain unknown, risk factors have been identified. The greatest risk factor is increasing age. Other risk factors include having relatives with AD; suffering head trauma (e.g., boxing); being exposed to aluminum; having high blood cholesterol; having low education; and for women, being postmenopausal. Factors that seem to reduce the risk for AD include education; taking anti-inflammatory medications (e.g., steroids, ibuprofen); smoking; and for postmenopausal women, taking estrogen supplements.

Effects The effects of Alzheimer’s disease develop in a steady and fairly predictable sequence. At first there is a decrease in short-term memory. Because the change is gradual and resembles the normal decrease, it is not uncommon for normal individuals to fear that they have Alzheimer’s disease when the ability to remember begins to decline. Conversely, individuals with Alzheimer’s disease may attribute their memory impairment to aging.

With AD, however, memory function declines to such an extent that affected individuals have considerable difficulty performing ordinary daily activities such as preparing food, dressing, and shopping. Patients with AD become disoriented with respect to location and have trouble learning new information. Early in the disease some patients begin to have trouble with language skills such as speaking. Perhaps because of fear of some of these changes or because of the disease itself, personality changes such as irritability, hostility, and agitation may appear. Often affected individuals tend to withdraw from social contact.

As AD progresses, loss of short-term memory becomes severe enough to dramatically decrease the ability to learn information or new skills, solve problems, and perform the ordinary tasks of daily living or working. Abstract thinking and making judgments become increasingly impaired. Language functions such as speaking, reading, and writing decline. Affected individuals become easily disoriented not only in terms of where they are but also with regard to time and date. Confusion occurs easily and frequently. Many patients wander away from home and become lost. Long-term memory, including recognizing familiar people, may also diminish.

Major personality changes that commonly accompany these more advanced effects of Alzheimer’s disease may include high levels of agitation, paranoia, hostility, and aggressiveness. These patients may have verbal and physical outbursts of anger or other emotions. They may strike out violently. These changes make cooperation and acceptable interactions with others difficult. For many people, social withdrawal becomes more intense.

By this stage affected individuals require a great deal of care. They need to be bathed, dressed, and fed. Their behavior must be monitored so that they do not engage in destructive actions or wander off. Eventually the care must extend for 24 hours a day. The changes in personality and behavioral traits caused by AD make providing such care emotionally draining on family members. Families that cannot provide ad-
Equate care are faced with the financial burden of paying others to provide it. All these problems intensify as the disease progresses.

In the most advanced stages of Alzheimer’s disease patients lose essentially all memory and intelligence capabilities. Performing any task and talking with others become impossible. Apparently, there is a complete loss of awareness of one’s surroundings. Bladder and bowel incontinence develop. The nervous system seems to forget how to stimulate muscles so that walking, eating, and other voluntary motions dwindle and finally cease. Curiously, long-lasting muscle spasms may occur. The victim becomes bedridden and paralyzed. The final result of Alzheimer’s disease is death, which is caused by complications from immobilization. The complications may include infections of the skin and respiratory systems, thrombus and embolus formation, malnutrition, and respiratory failure.

Though this sequence of events occurs in most patients with Alzheimer’s disease, individual cases vary considerably. For example, changes in personality may be the first noticeable indication that something is wrong. In other cases, problems with speaking may occur early in the disease or not until most of the other effects have developed.

There is also much variation in the time that passes from the diagnosis of AD until death occurs; this period may range from 2 to 20 years. The average length of time from diagnosis to death is eight years. More rapidly progressing and serious cases are correlated with an earlier age of onset. Alzheimer’s disease almost always progresses at a steady rate. There is never a period of improvement.

Diagnosis Diagnosing Alzheimer’s disease by observing changes in behavior is difficult until the disease has progressed into more advanced stages because at first these changes seem to be normal fluctuations. Only specific tests can detect early abnormalities in mental status. Repeating tests every few years to detect changes associated with AD may help detect AD at earlier stages.

Making a definitive diagnosis of Alzheimer’s disease remains difficult even after the recognition of abnormal behaviors because similar behavioral changes can be caused by many other factors (e.g., medications, depression, altered social situations) and by other diseases of the nervous system or other systems. Furthermore, the simultaneous presence of other types of dementia can mask the presence of AD. Researchers continue developing other diagnostic procedures including tests at the chemical, genetic, and cellular through system levels. Being able to detect and diagnose AD earlier could lead to developing effective treatments.

Eventually, after all other possible causes of the behavioral signs and symptoms have been ruled out, a clinical diagnosis of Alzheimer’s disease can be made with an accuracy of over 90 percent. Only an autopsy examination of the brain can determine conclusively that a person had Alzheimer’s disease.

Changes in the Brain A brain from an Alzheimer’s patient can be identified because it has two characteristics: an excessive number of senile plaques and neurofibrillar tangles. A third important finding is a low level of the neurotransmitter acetylcholine. These features are especially prevalent in brain areas involved in memory. The functioning of synapses in these areas may be hampered because the neurons produce inadequate neurotransmitters; the tangles may prevent enough neurotransmitters from reaching the ends of the axons; and the plaques may block transmission at synapses.

Plaques and Tangles Senile plaques (SPs) are round microscopic masses having various mixtures and densities of materials. They are at or near synapses. SPs usually contain a protein called beta-amyloid (β-A), dead neurons and neuroglia cells, pieces of synapses, and fibrous material called neurofibrillar tangles (NTs). Neurofibrillar tangles are composed of one or two protein fibers twisted into a helix. Much of the protein is tau protein (τ-protein). NTs also contain other materials including enzymes, inflammatory molecules, β-A, a lipoprotein called apolipoprotein E (APOE), and carbohydrate/protein complexes. NTs also form in neuron cell bodies, axons, and dendrites.

SPs and NTs appear first in the hippocampus region, which is near the center and bottom of the cerebral hemispheres. The hippocampus has a major role in memory functions. Later, SPs and NTs appear in wider areas near the bottom of the hemispheres. Later still they appear in upper regions of the cerebral cortex. Eventually, all regions of the cerebral cortex develop SPs and NTs. Neu-
ron connections to the nucleus of Meynert also develop many SPs and NTs, and SPs form in the cerebellum. The final distribution of SPs and NTs in brain areas corresponds to the sequence in which they appear. Areas showing SPs and NTs first develop the highest densities of them.

As SPs and NTs form, neurons are damaged and die, and synapses are destroyed. Scientists do not know if SPs and NTs form and then cause damage to neurons or if neurons damage occurs first, causing SPs and NTs to develop. Neurons that interconnect other neurons (i.e., association neurons) are affected much more than sensory neurons and motor neurons.

As AD progresses, brain vessels also change. Small vessels accumulate much β-A in their middle layer. Vessels become twisted, shrunken and broken, which reduces blood flow in the brain. The cerebral hemispheres shrink dramatically. Some scientists believe that reduction in blood flow causes the SPs, NTs and other neuronal and synaptic changes in the AD brain.

**Beta-amyloid** Many cells in the body produce *amyloid protein*. There are more than 10 types of amyloid protein. The type called β-amyloid (β-A) is found in AD. Its function is unknown. Beta-amyloid may be produced by neurons and by blood vessels. It is produced when an enzyme breaks a protein called *amyloid precursor protein* (APP), which extends across cell membranes. Breaking normal APP produces a small amount of soluble short β-A. In AD, APP is abnormal. When it is broken by enzymes, much abnormal long β-A is produced and released from the cell membrane.

The abnormal “sticky” β-A binds easily to APOE and to τ-protein, forming many SPs quickly. The abnormal β-A increases free radicals, inflammation, cell membrane damage, and neuron apoptosis. Excess glycation of proteins also occurs. All these processes seem to promote each other synergistically. Finally, APP itself binds to τ-protein and to APOE, suggesting that it can contribute to the formation of NTs and SPs.

The causes, method of formation, sources of β-A and NTs, and sequence in which materials are deposited are unknown.

**Tau Protein** Brain cells produce other proteins called *tau proteins* (τ-proteins). Their functions are unknown, though they seem to promote microtubule formation. The brain contains at least six types of τ-protein, and their proportions vary from childhood through adulthood. Abnormal modifications of τ-proteins (e.g., glycation, adding phosphate groups) cause τ-proteins to help form NTs.

**APOE** Many cells produce apolipoprotein E (e.g., brain, liver, adrenals). Most brain APOE comes from neuroglia cells and macrophages. Though neurons do not produce APOE, it enters them. APOE helps move cholesterol and other lipoproteins from cell to cell and through cell membranes. APOE also seems to help in neuron development and repair.

Brain APOE has different forms including APOE-e3 and APOE-e4. APOE-e4 seems to promote the formation of SPs and NTs. The mechanisms are not clear, but they may involve disruption of neuron membranes; formation of free radicals; excess accumulation of β-A; and the formation of abnormal microtubules in neurons. Interactions between the β-A and the abnormal microtubules seem to result in SPs and NTs.

**Presenilins** The last groups of brain proteins to mention are the presenilins. Two important forms of presenilin in the brain are *presenilin-1 (PS-1)* and *presenilin-2 (PS-2)*, which are membrane proteins. Their functions are unknown.

In summary, AD may be caused by or promoted by abnormal protein formation; chronic inflammation; inadequate blood flow; free radical damage from brain proteins, metal ions, damaged endothelium, or neurotransmitters; decreased FR defenses; mitochondrial malfunctioning; reduced insulin sensitivity; immune responses; or abnormal apoptosis of neurons. Regardless of the causes or mechanisms, the results are the same; too many SPs, too many NTs, too much neuron death, and too much loss of synapses.

**Genetics of AD** There are several genes that promote different types of AD. Though these genes are in different chromosomal locations, have effects at different ages, and may act by different mechanisms, they all produce the same outcomes in the brain and the same manifestations of AD. Some genes that promote or modify AD have not been identified. One or more of these genes may contribute to a form of AD that begins after age 70. These latter genes may be on chromosomes 12 or 3.
Three genes for one type of familial Alzheimer’s disease (FAD) are on chromosomes 21. The mutated forms of the genes cause the production of abnormal “sticky” β-amyloid, resulting in 7 percent of AD cases and 25 percent of FAD cases. Age of onset is between ages 45 and 65, with most cases developing before age 60. The mutations are present in approximately 19 families. An individual with only one copy of one of the mutated genes has a 100 percent chance of developing AD because each mutated gene is a dominant gene.

Certain forms of a gene on chromosome 19 promote SDAT. The gene has three forms (i.e., three alleles), each of which contains the genetic information for producing APOE-ε. One form codes for APOE-ε4, one form for APOE-ε3, and one for APOE-ε2. Since a person has two copies of chromosome 19, each person has two of these genes. The pair of genes may be in any combination (i.e., ε4:ε4, ε4:ε3, ε4:ε2, ε3:ε3, ε3:ε2, ε2:ε2). In the general population, the genes are found in the proportion ε4:ε3:ε2:14:78:8.

The genes are codominant, meaning that each produces its form of APOE-ε regardless of which other forms of the gene are present. Having two ε4 genes provides the highest risk from APOE genes and makes the AD occur at earlier ages. The risk for developing AD is eight times higher in people with two ε4 genes than in people with two ε2 genes. However, people with two ε4 genes do not always get AD.

The different combinations of APOE-ε genes provide decreasing risk of getting AD and increasing average age of onset in the order ε4:ε4 (age 68), ε4:ε3 (age 71), ε3:ε3 (age 74). Still, age of onset shows great variability with any of these combinations. Very few people with even one ε2 gene develop AD.

The APOE-ε gene influences other problems. Having an ε4 gene increases the age-related decline in cognitive functions even if AD does not develop. The ε4 gene also promotes amyloid formation in blood vessels, so people with the ε4 gene are at higher risk for developing atherosclerosis. Having an ε2 gene reduces the risk of atherosclerosis.

Chromosome 14 has the gene for PS-1, and chromosome 1 has the gene for PS-2. Nearly 50 percent of FAD cases are associated either with mutations in the APP gene on chromosome 21 or a presenilin gene. Nearly 70 percent of cases of FAD are associated with mutations in the PS genes. Mutations in either presenilin gene increase the risk of developing AD, apparently because abnormal PS-1 and abnormal PS-2 increase the production of “sticky” β-A.

The PS-1 mutation is known to occur in nearly 50 families. The PS-2 mutation is known to occur in descendants from certain German families (i.e., Volga Germans). For people with the PS-1 mutation, average age of onset is in the fifth decade, but cases develop as early as age 30. The PS-1 mutation also promotes late onset SDAT. For people with the PS-2 mutation, the average age of onset is higher than with the PS-1 mutation, but onset may occur before age 30.

Treatments There are no effective treatments to slow, stop, or reverse the effects of Alzheimer’s disease. Therapies being investigated include antioxidant supplements; anti-inflammatory drugs; medications that increase brain acetylcholine (e.g., tacrine); medications that slow atherosclerosis or reduce blood clotting; and for women, estrogen supplements. Until effective treatments are found, all that can be done is reduce the signs and symptoms and maintain as much functioning as possible. In the early stages of the disease memory aids such as notes and verbal reminders help. Various medications can alleviate the behavioral and psychological problems. Maintaining social contacts and providing emotional support for the patient and his or her families are important components in a complete treatment program.

As the disease progresses, outside help from support groups and social agencies is usually required. Day care centers can relieve the burden of full-time care by family members. Attention must be paid to preventing complications such as malnutrition and infections. Finally, full-time institutionalization may be necessary.

Parkinson’s Disease

Though the incidence of Parkinson’s disease is less than half that of strokes or Alzheimer’s disease, it remains a leading disease of the nervous system among older Americans. Its rate of occurrence is extremely low before age 50, but the rate increases gradually after that until about age 75; after that age it diminishes steadily. About 2 percent of those over age 50 will develop Parkinson’s disease. This disease occurs with equal frequency in men and in women and among people of different races.
Human Aging: Biological Perspectives

Causes  The cause of true, or primary, Parkinson's disease is unknown, and it does not tend to run in families. Scientists suspect the involvement of free radicals and reduced blood flow. Many cases of what appear to be Parkinson's disease actually result from abnormalities such as CNS infections, atherosclerosis, brain tumors or other brain diseases, head injury, toxins, and medications. These cases are called secondary parkinsonism.

Effects  The development of Parkinson's disease is shown primarily by changes in the control of muscle contractions. These changes usually occur in the same sequence. At first, ongoing movements of the fingers and hands occur. The movements of the fingers give the appearance that the victim is rolling pills between the fingers.

Tremors of the hand, arm, and leg muscles often develop next. The movements are rhythmic, with alternating contractions between muscles that bend the joints and muscles that straighten them. Four to eight contractions occur each second. The tremors are greatest when the person is awake but resting. They diminish during voluntary movements and stop when the patient falls asleep.

Further progress of the disease causes muscle stiffness and difficulty moving rapidly and smoothly. As control of muscle contraction diminishes further, the patient may find it impossible to complete a motion once it has been started. For example, a person who is walking may suddenly stop in the middle of taking a step. Ordinary motions occur ever more slowly. Performing ordinary tasks and job-related activities becomes difficult or impossible.

As normal contractions of muscles continue to diminish, facial expressions disappear. The voice becomes soft and loses inflection. Weaker, slower, and fewer contractions of leg, trunk, and arm muscles cause walking to occur more slowly and with shuffling of the feet, a stooped posture, and little swinging of the arms. Muscle contractions for swallowing and breathing also weaken and slow.

Declining muscle control and muscle activity causes drooling. Constipation is not uncommon because patients are less active and have weaker contraction of the abdominal muscles that normally help with bowel movements.

Gradually, coordination of muscles declines to such an extent that the person has trouble with balance. Not only do these patients tend to fall more frequently, they make little or no effort to slow or stop themselves as they are falling.

Parkinson's disease often produces effects other than those involving control of muscles. During the night patients tend to wake up and have difficulty going back to sleep. They become restless and begin to wander about. Because of declining muscle coordination and balance, they are at great risk of physical injury from falls. The interrupted sleep also causes these patients to be sleepy during the day.

Psychological changes may begin at any stage in the disease. Many patients experience depression, loss of interest in activities, and other mood changes. These psychological alterations seem to be caused partly by the disease itself and partly by the awareness of its effects. Reductions in very short-term memory are common. Parkinson's disease causes dementia in over 15 percent of patients.

While the sequence of changes caused by Parkinson's disease is fairly regular and progresses steadily, the rate of change varies greatly from one person to another. A few cases reach extreme conditions in as few as five years, although most cases progress more slowly, so that severe disability is delayed for many years.

Nervous System Changes  The mechanism by which Parkinson's disease affects muscle control is fairly clear. Recall that impulses controlling voluntary movements are modified as they descend through the somatic motor pathway. Some areas of modification are in the basal ganglia inside the cerebral hemispheres (Fig. 6.7). The normal impulse modifications occurring in the basal ganglia actually result from the interplay among several neurotransmitters in the basal ganglia. Acetylcholine tends to increase the impulses and thus increases muscle contractions. Dopamine (DOPA) and another neurotransmitter (gamma-aminobutyric acid) tend to dampen the impulses and the movements they cause.

In Parkinson's disease a major decline in the amount of DOPA in the basal ganglia creates an imbalance among the antagonistic transmitters. This imbalance causes impulses and the muscle contractions they produce to become excessive and uncontrolled. Hence, muscle contractions occur. Neurotransmitter imbalances also cause the other effects of this disease.

Diagnosis  Parkinson's disease is accompanied by a decrease in certain CNS chemicals that are
used by the brain to manufacture dopamine. Dopamine is a neurotransmitter that is present in inadequate amounts in patients with Parkinson's disease. Because this and the other effects of the disease are somewhat different from those of other diseases and the effects develop in a fairly regular sequence, Parkinson's disease can be diagnosed accurately.

**Treatments** There is no cure for Parkinson's disease and no way to slow its progress. However, its effects can be greatly diminished by administering levodopa because this chemical boosts brain production of DOPA. Dosages must be carefully monitored and adjusted during the disease to minimize adverse side effects such as increased uncontrolled movements. Since increasing the level of DOPA seems to be so important, attempts have been made to implant into the brains of Parkinson's disease patients tissues that produce DOPA. Pieces of adrenal medulla and pieces of brain regions from aborted human fetuses have been used. Transplants of adrenal medulla have not yet produced satisfactory results. However, experiments using fetal brain tissue have resulted in dramatic and long-term improvements in muscle control in individuals having severe cases of Parkinson's disease. As the controversial and experimental techniques employing fetal brain tissue improve and become more standardized, they may gain widespread acceptance and use.

Other medications can relieve certain signs and symptoms sometimes. However, the specific types and amounts of substances used to treat Parkinson's disease vary from case to case because individuals have such varied responses to these medications and because their responses change as the disease progresses.

Besides medications, treatment of Parkinson's disease should include physical therapy to help sustain the movements used in ordinary and occupational tasks. Speech therapy and psychological support are also important components of a treatment plan.

**Dementia with Lewy Bodies**

*Dementia with Lewy bodies* is a newly classified type of age-related dementia. It has been identified in nearly 20 percent of the brains from people who died after developing any dementia. Lewy bodies are round masses of clumped microfilaments in neurons. They occur in all areas of the brain. This type of dementia also shows amyloid deposits.