2

Neuroanatomy

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OBJECTIVES

After reading this chapter, the student will be able to:

1. Differentiate between the central and peripheral nervous systems.
2. Identify significant structures within the nervous system.
3. Understand primary functions of structures within the nervous system.
4. Describe the vascular supply to the brain.
5. Discuss components of the cervical, brachial, and lumbosacral plexuses.

INTRODUCTION

The purpose of this chapter is to provide the student with a review of neuroanatomy. Basic structures within the nervous system are described and their functions discussed. This information is important to physical therapists and physical therapist assistants who treat patients with neurologic dysfunction because it assists clinicians with identifying clinical signs and symptoms. In addition, it allows the clinician to develop an appreciation of the patient's prognosis and potential functional outcome. It is, however, outside the scope of this text to provide a comprehensive discussion of neuroanatomy. The reader is encouraged to review neuroscience and neuroanatomy texts for a more in-depth discussion of these concepts.

OVERVIEW OF THE NERVOUS SYSTEM

Individuals are able to perceive sensory experiences, to initiate movement, and to perform cognitive tasks as a result of a functioning nervous system. To function properly, nervous systems have to solve two very different problems. On the one hand, nervous systems must be able to reliably communicate with the rest of the body to accurately convey sensory and motor signals. However, nervous systems must also be flexible enough to change over time to learn and solve problems. Our nervous system is able to balance reliability and flexibility through several divisions of labor.

The nervous system is divided into two parts: the flexible *central nervous system* (CNS) and the reliable *peripheral nervous system* (PNS). The CNS is the site of information integration and is composed of the *brain* and *spinal cord*. The PNS is designed to provide robust communication between the CNS and body and comprises all of the components outside the cranium and spine. Physiologically, the PNS is divided into the *somatic nervous system* and the *autonomic nervous system* (ANS). The ANS is further subdivided into sympathetic and parasympathetic components. Fig. 2.1 illustrates the major components of the CNS. Before we discuss the functions of these nervous system divisions, we will review the cellular makeup of nervous tissue and the specializations that allow for rapid communication.

CELLULAR COMPONENTS OF THE NERVOUS SYSTEM

The nervous system is a highly organized communication system comprising more than 100 billion nerve cells. *Nerve cells* allow us to properly navigate our world by communicating with sensory and motor structures throughout the body. For example, sensations, such as touch, proprioception, pain, and temperature, are transmitted from the periphery as *electrochemical impulses* to the CNS through sensory tracts. Once information is processed within the CNS, it is relayed as new electrochemical impulses to peripheral structures through motor tracts. A *tract* is a group of nerve fibers that are similar in origin, destination, and function. In this section, we will review the basic types of nerve cells and how they participate in the electrochemical signaling of tracts.

Types of Nerve Cells

There are two basic types of nerve cells: neurons and neuroglia. *Neurons* are specialized for communication through their ability to generate rapid electrochemical signals. *Neuroglia* are diverse support cells that facilitate neuron function and survival. Although it is increasingly clear that neuroglia can also play an active role in electrochemical signaling, this

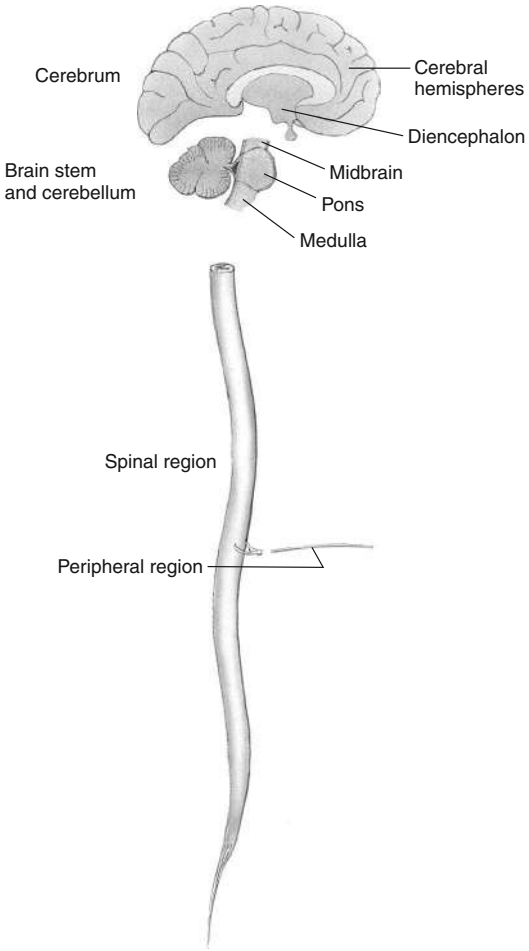

Fig. 2.1 Lateral view of the regions of the nervous system. Regions are listed on the left, and subdivisions are listed on the right. (From Lundy-Ekman L: *Neuroscience: fundamentals for rehabilitation,* ed 4, St. Louis, 2013, Elsevier.)

topic is beyond the scope of this chapter (Halassa et al., 2007).

Neurons are sometimes divided into the three following categories: (1) afferent neurons, (2) interneurons, and (3) efferent neurons. Afferent neurons project toward a given structure (i.e., they arrive), efferent neurons project away from a given structure (i.e., they exit), and interneurons relay signals between two neurons. Although these may sound like clear divisions, a single neuron can actually be all three types. For example, all neurons in the cortex are interneurons. Interneurons in layer five of the cortex that make up the corticospinal tract project their axons to the spinal cord, acting as cortical efferents and spinal afferents. To avoid this confusion, we suggest you use the following function categories: (1) *motor neurons*, which convey output from the CNS to the muscles, and (2) *sensory neurons*, which detect environmental or bodily stimuli and relay it to the CNS. All other neurons should simply be called neurons (or interneurons, if you prefer). It should be noted that there is no strict naming convention for neurons. In fact, the same layer five cortical neurons mentioned earlier that make up the corticospinal tract are called upper motor neurons, even though they do not innervate muscles.

Neuroglia are nonneuronal supporting cells that provide critical services for neurons. Different types of neuroglia (astrocytes, oligodendrocytes, microglia, and ependymal cells) have been identified in the CNS. Fig. 2.2 depicts the types of neuroglia. *Astrocytes* are responsible for maintaining the capillary endothelium and as such provide a vascular link to neurons. Additionally, astrocytes contribute to the metabolism of the CNS, regulate extracellular concentrations of ions and neurotransmitters, and proliferate after an injury to create a glial scar (Fitzgerald et al., 2012). *Oligodendrocytes* wrap myelin sheaths around axons, forming the white matter of the CNS. Nonmyelinating oligodendrocytes (*satellite oligodendrocytes*) associate with the cell bodies of neurons and appear to regulate ion concentrations, similar to astrocytes. *Microglia* are known as the phagocytes of the CNS. They engulf and digest pathogens and assist with nervous system repair after injury. *Ependymal cells*, which line the ventricular system, produce and circulate cerebrospinal fluid (Fitzgerald et al., 2012).

Neuroglia in the PNS fulfill similar functions as in the CNS. *Satellite cells* buffer extracellular ion concentrations around neuronal cell bodies. The major neuroglial cell of the PNS is the *Schwann cell*, which is further divided into different functional classes. Myelinating Schwann cells ensheath axons in myelin, similar to oligodendrocytes. Nonmyelinating Schwann cells outnumber myelinating Schwann cells ~4:1 and have similar functions to astrocytes, as they contact vasculature and participate in ion buffering. Terminal Schwann cells help maintain the neuromuscular junction (Ko and Robitaille, 2015).

Neuron Structures

As depicted in Fig. 2.3, a typical neuron consists of dendrites, a cell body, and an axon. *Dendrites* are responsible for transducing extracellular physical or chemical input into an intracellular signal. Most commonly, a dendrite produces electrical currents, which are transferred to the cell body for processing. Neurons have variable morphologies, differing in size, number of dendrites, and degree of dendrite branching (Fig. 2.4). Neurons with no true dendrite are *unipolar* or *pseudounipolar*, neurons with a single dendrite are *bipolar*, and neurons with multiple dendrites are called *multipolar*. The number and arrangement of dendrites is related to the function of the neuron. For example, somatosensory neurons are pseudounipolar, allowing for linear communication of sensory stimuli. However, multipolar Purkinje cells in the cerebellum have elaborate dendrites, allowing them to integrate a large number of inputs and allow for motor learning. As mentioned earlier, nervous system function requires both reliable and flexible signaling.

The *cell body* or *soma* is composed of a nucleus and a number of different cellular organelles. The cell body is responsible for synthesizing proteins and supporting functional activities of the neuron, such as transmitting electrochemical impulses and repairing cells. The fact that the cell body is responsible

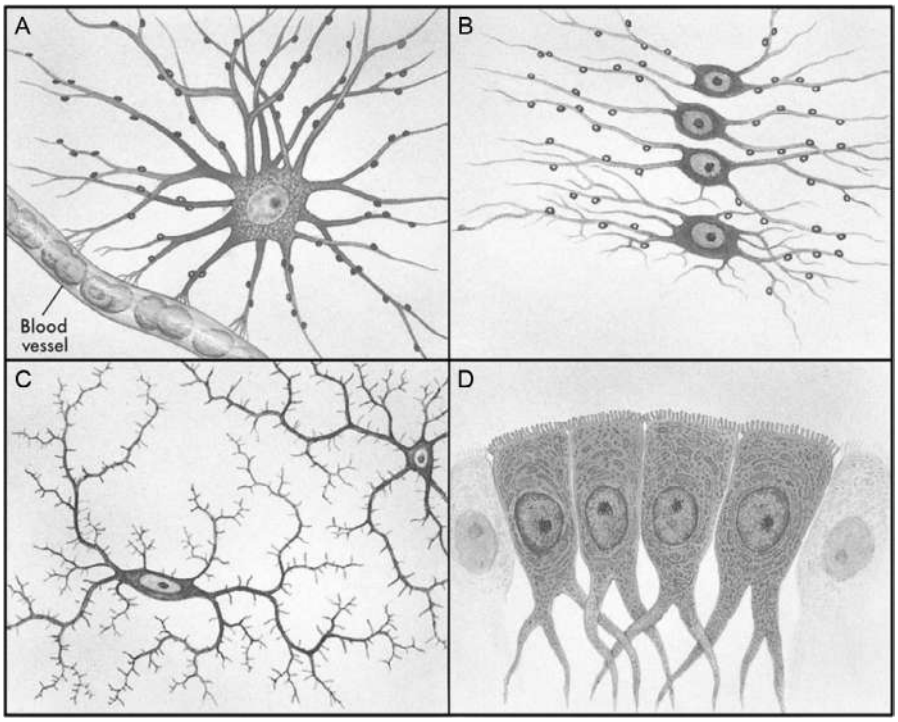

Fig. 2.2 The four types of neuroglia cells: **(A)** astrocytes, **(B)** oligodendrocytes, **(C)** microglia, and **(D)** ependymal cells. (From Copstead LEC, Banasik JL: *Pathophysiology: biological and behavioral perspectives,* ed 2, Philadelphia, 2000, WB Saunders.)

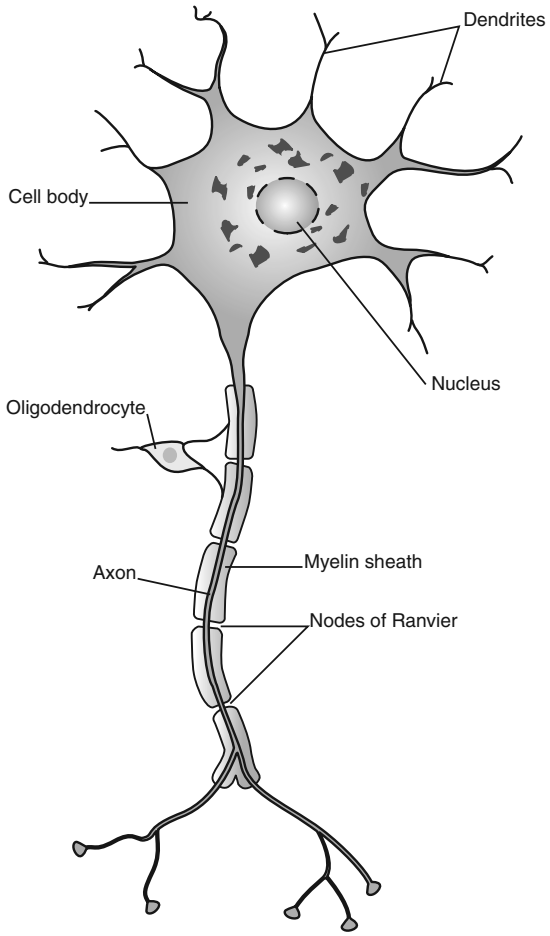

Fig. 2.3 Diagram of a neuron.

for protein synthesis explains why axons degrade distally to the site of injury—they are unable to produce protein and survive. Cell bodies of neurons with similar functions are often grouped together to form *nuclei* in the CNS and *ganglia* in the PNS.

The *axon* is the message-sending component of neurons. Axons extend from the cell body and contact target cells that can include muscle cells, glands, or other neurons. Neurons communicate with target cells by conducting electrical signals called *action potentials* down their axon. Action potentials stimulate the release of chemical signals called *neurotransmitters* that bind to receptors on target cells to elicit a response. All nerve signaling pathways involve this alternating pattern of electrical signaling within neurons, and chemical signaling between a neuron and a target cell.

Electrical Conduction Within Neurons

Electrical signaling occurs through the movement of ions across the membrane. Ions can only cross the membrane through proteins called *ion channels*. In some axons, electrical conduction is facilitated by *myelin*, a lipid/protein that encases and insulates the axon.

Myelin in the CNS and PNS have some important distinctions. Myelin produced by oligodendrocytes in the CNS is more compact, which is an advantage because space is limited by the skull. Myelin produced by Schwann cells in the PNS is less compact, providing additional protection for peripheral nerves. PNS myelin also allows for axon regrowth, whereas CNS myelin appears to prevent axon regrowth

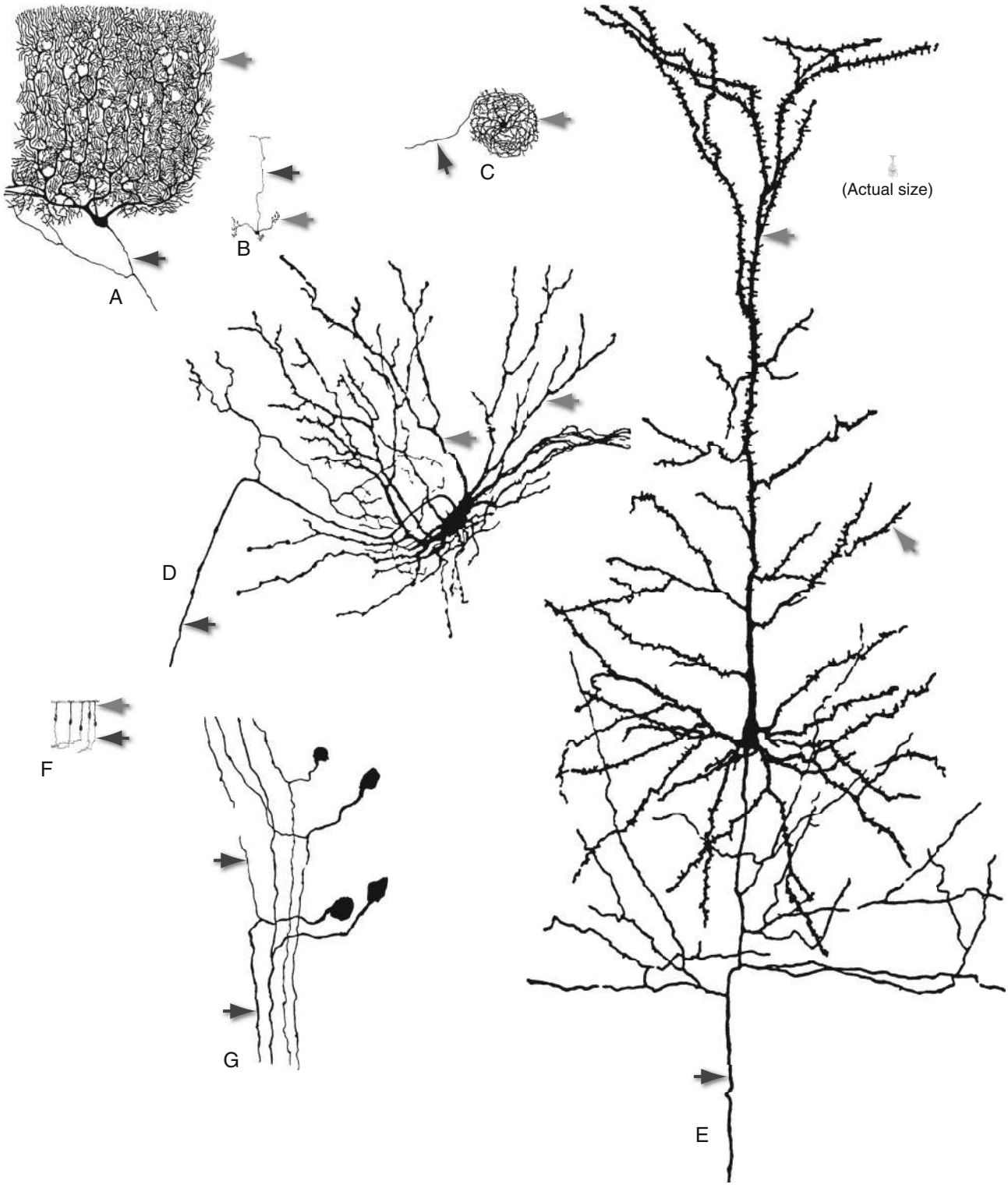

Fig. 2.4 Morphologies of different types of neurons. All neurons are drawn to roughly the same scale to illustrate the diversity of cell size. Drawings are based on Golgi stains. The dendrites and axons are labeled with green and blue arrows, respectively. All neurons have a single axon but can vary in terms of dendrite number and branching. Multipolar neurons **(A-E)** have multiple dendrites emerging from their cell body. Bipolar neurons **(F)** have a single dendrite. Unipolar and pseudounipolar neurons **(G)** have no true dendrites. **(A)** Purkinje cell from the cerebellar cortex; **(B)** granule cell from the cerebellar cortex; **(C)** projection neuron from the inferior olivary nucleus; **(D)** spinal cord motor neuron; **(E)** large pyramidal neuron from the cerebral cortex (the inset shows the actual size); **(F)** olfactory receptor neurons; **(G)** dorsal root ganglion cells. (From Vanderah T, Gould DJ: *Nolte's the human brain e-book: an introduction to its functional anatomy, Philadelphia,* 2015, Elsevier Health Sciences, Fig. 1.4, p. 5.)

TABLE 2.1 Conduction Velocities in Different Axon Types

Group Name	Diameter (μm)	Myelinated	Conduction Velocity (m/s)	Information Transmitted
Group I (Aα)	13–20	Yes	70–120	Motor signals
Group II (Aβ)	6–12	Yes	40–70	Touch sensation
Group III (Aδ)	1–5	Yes	12–36	First pain
Group IV (C)	0.2–1.5	No	0.5–2	Second pain

following injury. This difference in myelin may explain the limited recovery in spinal cord injuries compared with peripheral nerve injuries.

Myelin increases the efficiency of action potential conduction down the axon in two important ways: (1) increased conduction velocity, and (2) decreased metabolic expenditure. Myelinated axons conduct action potentials more rapidly than unmyelinated axons (Table 2.1). Myelination increases conduction velocity by insulating the axon. Myelinated regions of the axon are devoid of ion channels, which prevents electrical charge from leaking out of the axon. The myelin sheath also prevents the charge within the axon from being stored at the membrane, allowing it to more rapidly flow within the axon. As a result of this, there is a noticeable delay (approximately 0.5 to 1 second) of our perception of tactile sensation conveyed by myelinated fibers, and painful sensation conveyed by unmyelinated fibers.

The myelin sheath surrounding the axon is not continuous; it contains interruptions or spaces within the myelin called the *nodes of Ranvier* (or, more simply, nodes). Nodes are only 2 μm in length and contain ion channels that restore the action potential as it travels along the axon. However, myelinated regions (or *internodes*) each span 0.3 to 2 mm in length and are devoid of ion channels. The lack of ion channels in internodes causes action potentials to "leap" from node to node in a process called *saltatory conduction* (*saltare* means "to leap" in Latin). Saltatory conduction is much faster than active conduction that takes place in unmyelinated axons, which contain ion channels along their entire length (Fig. 2.5).

The second advantage of myelin arises from the fact that over 99% of the axon length is myelinated, and thus ion impermeable. Myelinated axons conduct far fewer ions across the membrane than unmyelinated axons. Because of this, myelinated axons have fewer ions to pump back across the membrane, which reduces the adenosine triphosphate (ATP) cost of each action potential. The importance of this concept is illustrated by demyelinating states. For example, multiple sclerosis is a neurodegenerative disorder caused by the autoimmune destruction of oligodendrocytes. Early on, the loss of myelin impairs action potential conduction. Over time, demyelinated neurons must continue to spend higher amounts of ATP for each action potential. The production of additional ATP leads to the production of free radicals, which damage macromolecules and are generally toxic to cells. Thus myelination helps keep neurons alive.

Synapses

The site of contact between the axon and its target cell is called a *synapse*. Synapses are the site at which electrical signals within the axon (i.e., action potentials) are translated into a chemical signal that creates some effect on the target cell. These chemical messages are called *neurotransmitters*. After neurotransmitters are released from the axon, they diffuse across the 20 nm space between the axon and the target cell. This space is called the *synaptic cleft*. After crossing the synaptic cleft, neurotransmitters bind to *receptors* and create some change in the function of the target cell. Neurotransmitter receptors may cause long-lived changes in cell function by altering gene expression in the target cell. More commonly, neurotransmitter receptors are ion channels that create fast electrical events to cause some short-term effect. For example, motor neurons cause muscles to contract, whereas interneurons alter the electrical activity of a neighboring neuron, perhaps stimulating an action potential and another round of neurotransmitter release.

Neurotransmitters

Neurotransmitters are chemicals that are released from neurons to communicate with target cells. An in-depth discussion of neurotransmitters is beyond the scope of this text. We will, however, discuss some common neurotransmitters because of their relationship to CNS disease. Furthermore, many of the pharmacologic interventions available to patients with CNS pathology act by facilitating or inhibiting neurotransmitter activity.

Common neurotransmitters include acetylcholine, glutamate, γ-aminobutyric acid, dopamine, serotonin, and norepinephrine. Acetylcholine conveys information in the PNS and is the neurotransmitter used by lower motor neurons that synapse onto skeletal muscle fibers (Lundy-Ekman, 2018). Acetylcholine also plays a role in regulating heart rate and other autonomic functions. Glutamate is an excitatory neurotransmitter used widely throughout the CNS. Excessive glutamate release is thought to contribute to neuron destruction after an injury to the CNS—this is discussed further in the last section of this chapter. γ-Aminobutyric acid is the major inhibitory neurotransmitter of the brain, and glycine is the major inhibitory neurotransmitter of the spinal cord. Dopamine influences motor activity, motivation, general arousal, and cognition. Serotonin plays a role in "mood, behavior, and inhibits pain" (Dvorak and Mansfield, 2013). Norepinephrine is used by the sympathetic nervous systems and produces the

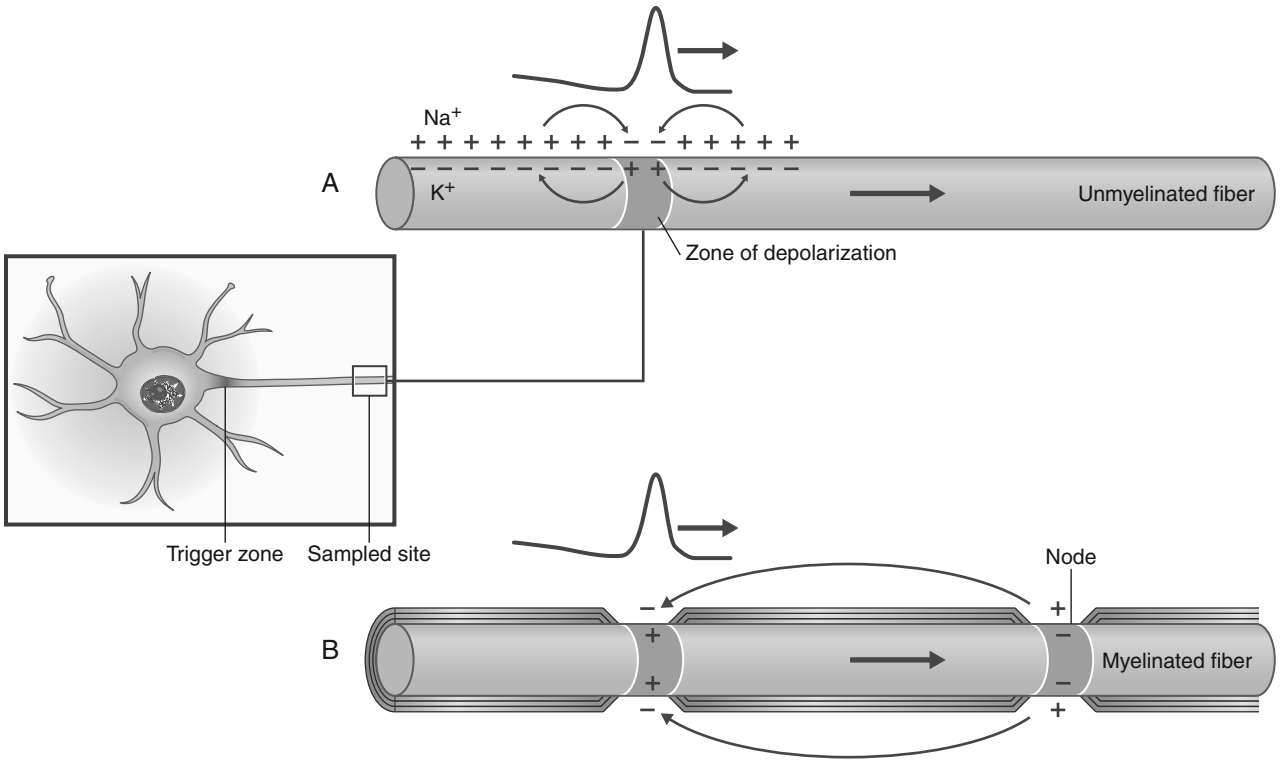

Fig. 2.5 Action potential propagation along axons. Current flow along the axons of active neurons. At rest, neurons have a negative charge at their membrane (represented as "–" signs and a light pink color inside the axon). As the action potential moves down the axon, it creates areas of positive charge (represented as "+" signs and a darker pink color inside the axon). Unmyelinated axons **(A)** move ions across the membrane along the entire length of the axon. Myelinated axons **(B)** only move ions across the membrane at nodes, allowing for more rapid saltatory conduction. (From Mtui E, Gruener G, Dockery P: *Fitzgerald's clinical neuroanatomy and neuroscience e-book*, Philadelphia, 2015, Elsevier Health Sciences, Fig. 7.12, p. 83.)

"fight-or-flight response" to stress (Fitzgerald et al., 2012; Lundy-Ekman, 2018).

ANATOMIC COMPONENTS OF THE CENTRAL NERVOUS SYSTEM

The CNS comprises the brain and spinal cord. The brain consists of the cerebrum, the thalamic complex, the brainstem, and the cerebellum. We will cover each of these major divisions of the CNS from top to bottom. Before we cover the CNS, we must first discuss the protective structures that house it.

Supportive and Protective Structures

The CNS is protected by a number of different structures and substances to minimize the possibility of injury (Fig. 2.6). First, the brain and spinal cord are surrounded by bony skull and vertebral column, which provide mechanical protection against injury. Immediately below the skull and within the vertebrae, we find three layers of membranes called the *meninges*, which provide additional protection.

The outermost layer is the *dura mater*. The dura is a thick, fibrous connective tissue membrane that adheres to the skull. The dural covering has two distinct projections: the falx cerebri, which separates the cerebral hemispheres, and the tentorium cerebelli, which provides a separation between the posterior

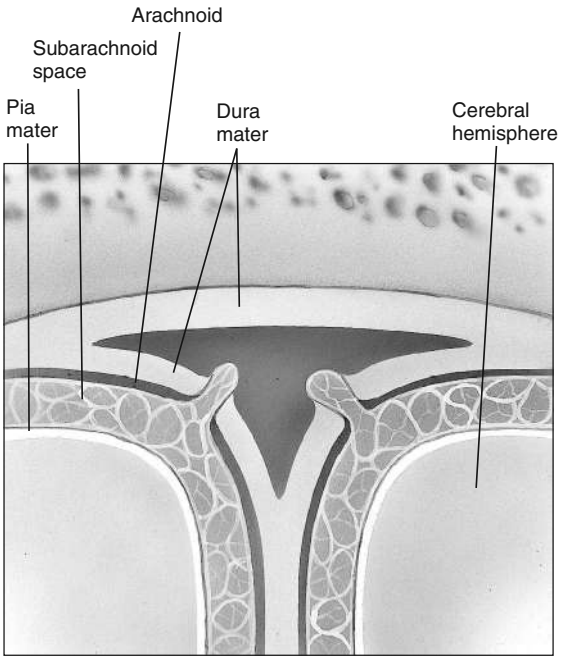

Fig. 2.6 Coronal section through the skull, meninges, and cerebral hemispheres. The section shows the midline structures near the top of the skull. The three layers of meninges, the superior sagittal sinus, and arachnoid granulations are indicated. (From Lundy-Ekman L: *Neuroscience: fundamentals for rehabilitation,* ed 4, St. Louis, 2013, Elsevier.)

cerebral hemispheres and the cerebellum. The area between the dura mater and the skull is a potential space known as the *epidural space*. The epidural space is called a potential space because it only exists in the case of injury. Assuming we don't have any cranial bleeding, the epidural space should not be visible. The next or middle layer is the *arachnoid mater*. Another potential space lies between the dura and the arachnoid—the *subdural space*. Below the arachnoid mater, we find our first bona fide space: the *subarachnoid space*, which contains the cerebral arteries. The subarachnoid space is filled with cerebrospinal fluid, which allows it to act as a cushion for the CNS. The third layer is the *pia mater*. This is the innermost layer and adheres to the brain and spinal cord. The pia mater is delicate and fairly permeable compared with the other layers. For the most part, the meninges are continuous with the connective tissues found in peripheral nerves. The dura mater forms the epineurium and the arachnoid mater forms the perineurium.

The Cerebral Cortex

The surface of the cerebrum or cerebral cortex is composed of depressions *(sulci)* and ridges *(gyri)*. These convolutions increase the surface area of the cerebrum (and thus increases the number of cortical neurons) without requiring an increase in the size of the brain. The outer surface of the cerebrum is composed of gray matter approximately 2 to 4 mm thick, whereas the inner surface is composed of white matter fiber tracts (Fitzgerald et al., 2012).

Lobes of the Cerebrum

The cerebrum is divided into four lobes—frontal, parietal, temporal, and occipital—each having unique functions, as shown in Fig. 2.7, *A*. The hemispheres of the brain, although apparent mirror images of one another, have specialized functions as well. This sidedness of brain function is called hemispheric specialization or lateralization.

Frontal lobe. The *frontal lobe* contains the *primary motor cortex* (PMC). The frontal lobe is responsible for voluntary control of complex motor activities. In addition to its motor responsibilities, the frontal lobe also exhibits a strong influence over cognitive functions, including judgment, attention, awareness, abstract thinking, mood, and aggression. The principal motor region responsible for speech (the Broca area) is located within the frontal lobe, near the primary motor regions that control the lips, tongue, and larynx.

Parietal lobe. The *parietal lobe* contains the primary somatosensory cortex. Incoming sensory information is processed within this lobe and meaning is provided to the stimuli. Perception is the process of attaching meaning to sensory information and requires interaction between the brain, body, and the individual's environment (Lundy-Ekman, 2018). Much of our perceptual learning requires a functioning parietal lobe. Specific body regions are assigned locations within the parietal lobe for this interpretation. This mapping is known as the sensory homunculus (Fig. 2.7, *B*).

Temporal lobe. The *temporal lobe* contains the primary auditory cortex. The primary auditory cortex decodes pitch and volume of sounds. The meaning of sounds is distinguished in other cortical regions. One particularly important region is the Wernicke area, which ascribes meaning to particular sounds (i.e., words). The temporal lobe is also involved in declarative memory function (i.e., factual memories), as it houses important memory-relevant structures such as the amygdala and hippocampus.

Occipital lobe. The *occipital lobe* contains the primary visual cortex. The eyes take in visual signals concerning objects in the visual field and relay that information to the thalamus before finally reaching the primary visual cortex. Like the primary auditory cortex, the primary visual cortex distinguishes fine details of an image (e.g., line angles). The meaning of these fine details are determined in downstream association regions. The visual association cortex is extensive and is located throughout the cerebral hemispheres along two main streams. The dorsal stream includes regions in the parietal lobes and determines object location. The ventral stream includes regions in the temporal lobes and determines object identity.

Primary versus Association Cortex

Primary cortices deal with granular details, whereas association cortices create meaning from these details. For example, neurons in the primary visual cortex are responsive to very specific visual stimuli, such as the angle of a line, whereas visual association cortices will construct objects (e.g., an octagon) and ascribe meaning to these objects (e.g., a stop sign). An excellent example of an association cortex for the physical therapist is the *parietoinsular vestibular cortex*. The parietoinsular vestibular cortex constructs our sense of balance based on input from the somatosensory cortex (*What is our body position?*), visual cortex (*Is anything around us moving?*), and vestibular system (*Is our body moving?)*. Association areas are responsible for all higher-order functions of the CNS, including personality, intelligence, memory, and consciousness. Fig. 2.7, *C* depicts association areas within the cerebral hemispheres.

Motor Areas of the Cerebral Cortex

The PMC, located in the frontal lobe, is primarily responsible for contralateral voluntary control of the upper and lower extremity and facial movements. Thus a greater proportion of the total surface area of this region is devoted to neurons that control these body parts. It is important to understand that although neurons in the PMC do control specific body parts, they do not map to specific muscles. Instead, PMC neurons are organized around movements, whereas lower motor neurons in the spinal cord are organized around muscles. Other motor areas include the *premotor area* and *supplementary motor area* (SMA). Both of these regions project directly to the spinal cord and to the PMC. The premotor area is involved in well-patterned, bilateral movements and appears to direct our movements based more on external cues (i.e., sensory information). The SMA is involved with eye control and appears to create sequences of movements based more on internal cues (i.e., learned information).

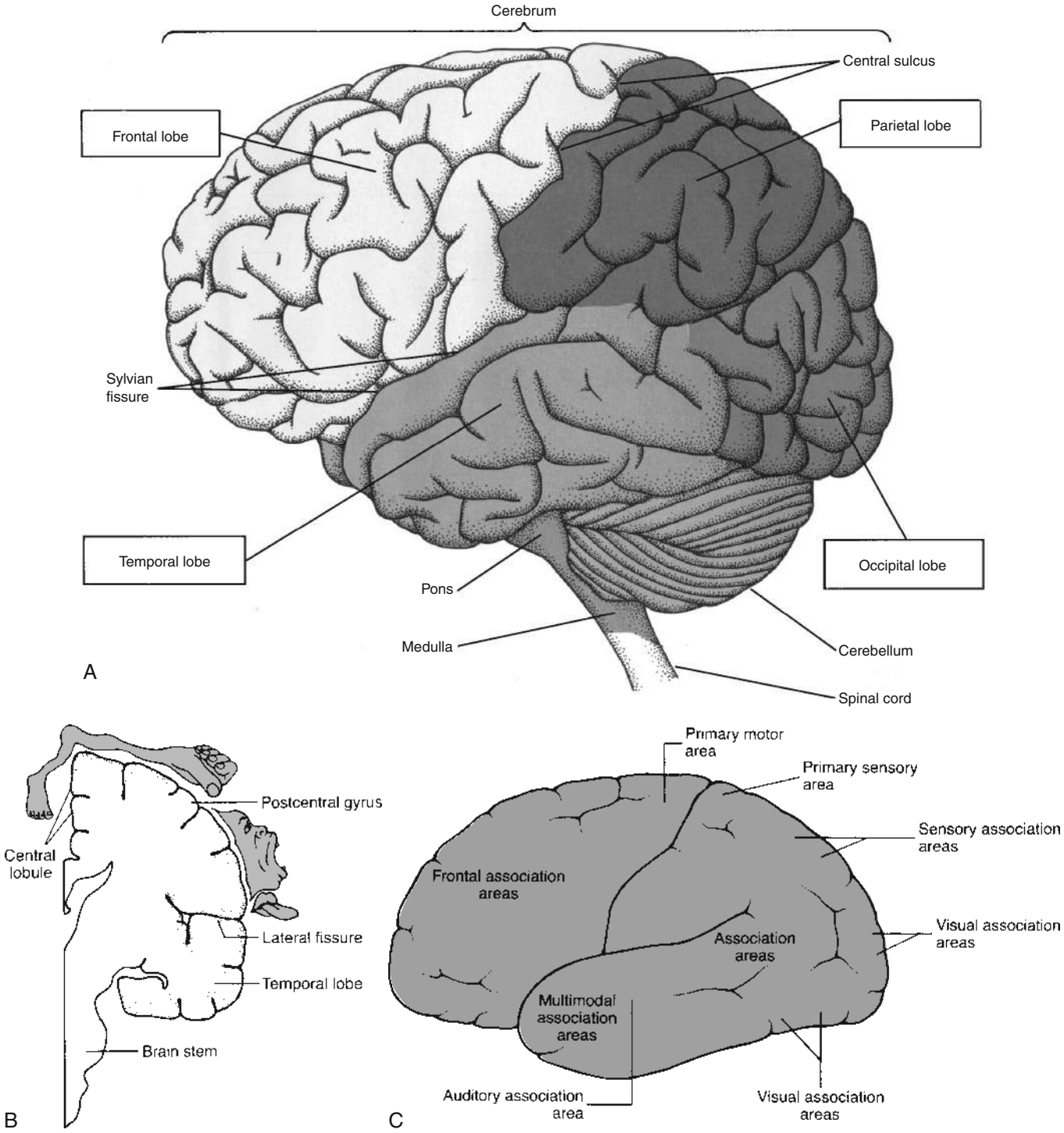

Fig. 2.7 The brain. **(A)** Left lateral view of the brain, showing the principal divisions of the brain and the four major lobes of the cerebrum. **(B)** Sensory homunculus. **(C)** Primary and association sensory and motor areas of the brain. (A, from Guyton AC: *Basic neuroscience: anatomy and physiology*, ed 2, Philadelphia, 1991, WB Saunders; B and C, from Cech D, Martin S: *Functional movement development across the life span,* ed 3, St. Louis, 2012, Elsevier.)

Hemispheric Specialization

The cerebrum can be further divided into the right and left *cerebral hemispheres*. Gross anatomic differences have been demonstrated within the hemispheres. The hemisphere that is responsible for language is considered the dominant hemisphere. Approximately 95% of the population, including all right-handed individuals, are left-hemisphere dominant. Even in individuals who are left-hand dominant, the left hemisphere is the primary speech center in about 50% of these people (Geschwind and Levitsky, 1968; Gilman and Newman, 2003; Guyton, 1991). Table 2.2 lists primary functions of both the dominant and nondominant cerebral