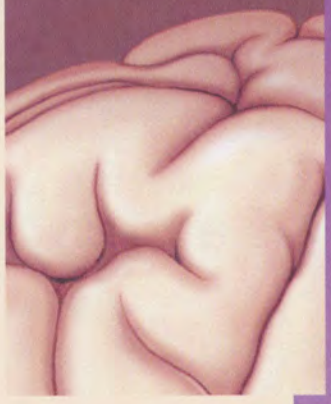
CHAPTER

7

The Structure of the Nervous System



▼ INTRODUCTION

In previous chapters, we saw how individual neurons function and communicate. Now we are ready to assemble them into a nervous system that sees, hears, feels, moves, remembers, and dreams. Just as an understanding of neuronal structure is necessary for understanding neuronal function, we must understand nervous system structure in order to understand brain function.

Neuroanatomy has challenged generations of students—and for good reason: The human brain is extremely complicated. However, our brain is merely a variation on a plan that is common to the brains of all mammals (Figure 7.1). The human brain appears complicated because it is distorted as a result of the selective growth of some parts within the confines of the skull. But once the basic mammalian plan is understood, these specializations of the human brain become transparent.

We begin by introducing the general organization of the mammalian brain and the terms used to describe it. Then we take a look at how the three-dimensional structure of the brain arises during embryological and fetal development. Following the course of development makes it easier to understand how the parts of the adult brain fit together. Finally, we explore the cerebral neocortex, a structure that is unique to mammals and proportionately the largest in humans. An Illustrated Guide to Human Neuroanatomy follows the chapter as an appendix.

The neuroanatomy presented in this chapter provides the canvas on which we will paint the sensory and motor systems in Chapters 8–14. Because you will encounter a lot of new terms, self-quizzes within the chapter provide an opportunity for review.

▼ GROSS ORGANIZATION OF THE MAMMALIAN NERVOUS SYSTEM

The nervous system of all mammals has two divisions: the central nervous system (CNS) and the peripheral nervous system (PNS). In this section, we identify some of the important components of the CNS and the PNS. We also discuss the membranes that surround the brain and the fluid-filled ventricles within the brain. We then explore some new methods of examining the structure of the living brain. But first, we need to review some anatomical terminology.

Anatomical References

Getting to know your way around the brain is like getting to know your way around a city. To describe your location in the city, you would use points of reference such as north, south, east, and west, up and down. The same is true for the brain, except that the terms—called *anatomical references*—are different.

Consider the nervous system of a rat (Figure 7.2a). We begin with the rat, because it is a simplified version that has all the general features of mammalian nervous system organization. In the head lies the brain, and the spinal cord runs down inside the backbone toward the tail. The direction, or anatomical reference, pointing toward the rat's nose is known as **anterior** or **rostral** (from the Latin for "beak"). The direction pointing toward the rat's tail is **posterior** or **caudal** (from the Latin for "tail"). The direction pointing up is **dorsal** (from the Latin for "back"), and the direction pointing down is **ventral** (from the Latin for "belly"). Thus, the rat

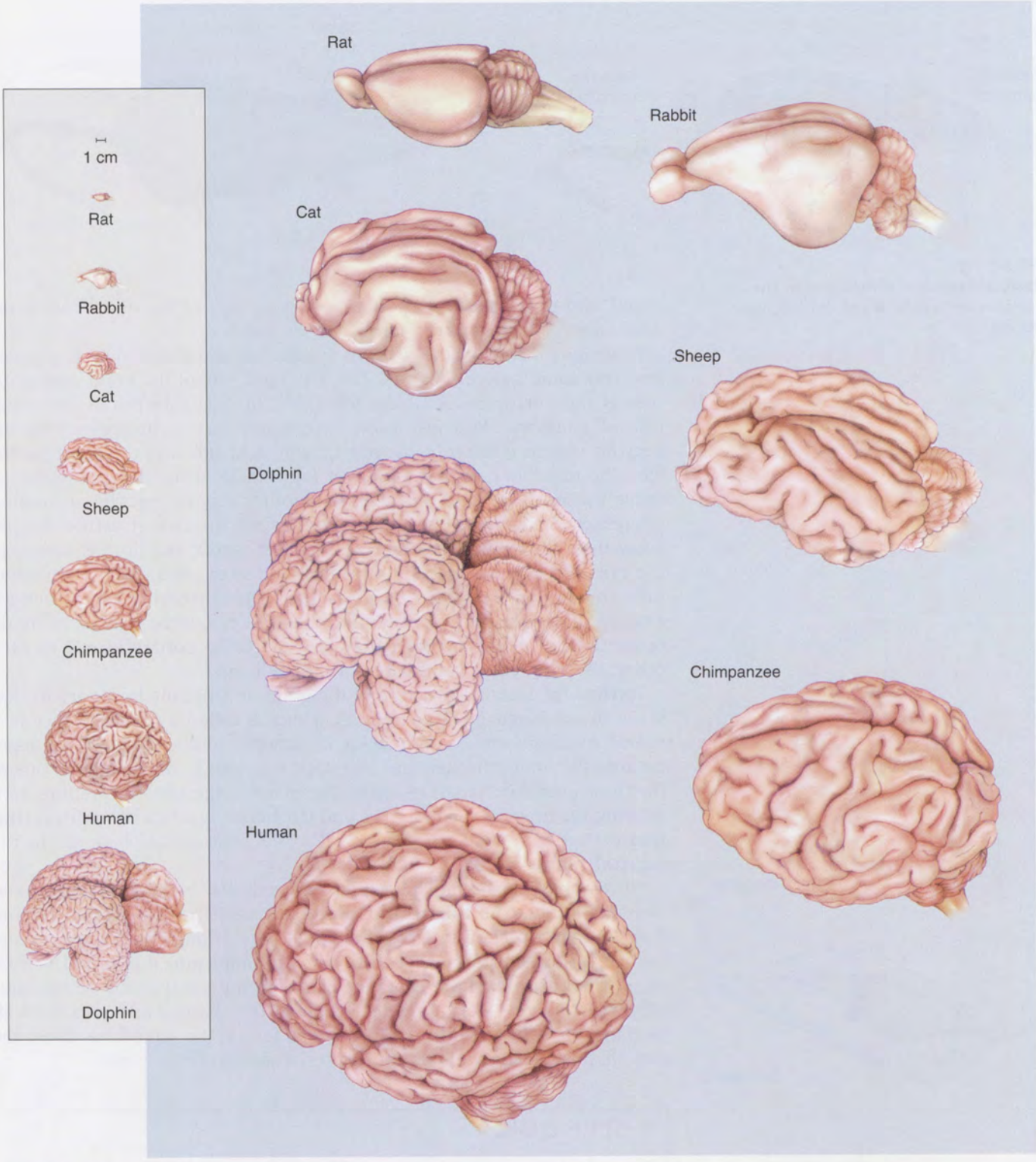


FIGURE 7.1
Mammalian brains. Despite differences in complexity, the brains of all these species have many features in common. The brains have been drawn to appear approximately the same size; their relative sizes are shown in the inset on the left.

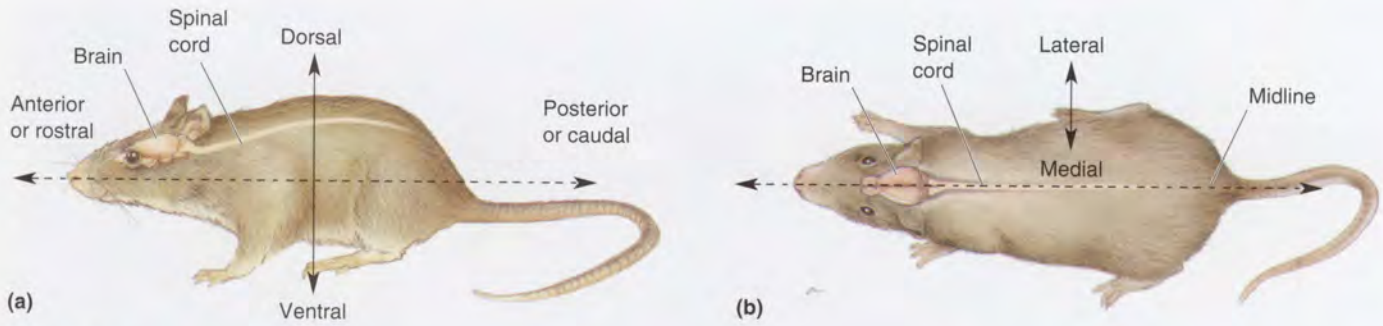


FIGURE 7.2
Basic anatomical references in the nervous system of a rat. (a) Side view. **(b)** Top view.

spinal cord runs anterior to posterior. The top side of the spinal cord is the dorsal side, and the bottom side is the ventral side.

If we look down on the nervous system, we see that it may be divided into two equal halves (Figure 7.2b). The right side of the brain and spinal cord is the mirror image of the left side. This characteristic is known as *bilateral symmetry*. With just a few exceptions, most structures within the nervous system come in pairs, one on the right side and the other on the left. The invisible line running down the middle of the nervous system is called the **midline**, and this gives us another way to describe anatomical references. Structures closer to the midline are **medial**; structures farther away from the midline are **lateral**. In other words, the nose is medial to the eyes, the eyes are medial to the ears, and so on. In addition, two structures that are on the same side are said to be **ipsilateral** to each other; for example, the right ear is ipsilateral to the right eye. If the structures are on opposite sides of the midline, they are said to be **contralateral** to each other; the right ear is contralateral to the left ear.

To view the internal structure of the brain, it is usually necessary to slice it up. In the language of anatomists, a slice is called a *section*; to slice is *to section*. Although one could imagine an infinite number of ways we might cut into the brain, the standard approach is to make cuts parallel to one of the three *anatomical planes of section*. The plane of the section resulting from splitting the brain into equal right and left halves is called the **midsagittal plane** (Figure 7.3a). Sections parallel to the midsagittal plane are in the **sagittal plane**.

The two other anatomical planes are perpendicular to the sagittal plane and to one another. The **horizontal plane** is parallel to the ground (Figure 7.3b). A single section in this plane could pass through both the eyes and the ears. Thus, horizontal sections split the brain into dorsal and ventral parts. The **coronal plane** is perpendicular to the ground and to the sagittal plane (Figure 7.3c). A single section in this plane could pass through both eyes or both ears, but not through all four at the same time. Thus, the coronal plane splits the brain into anterior and posterior parts.

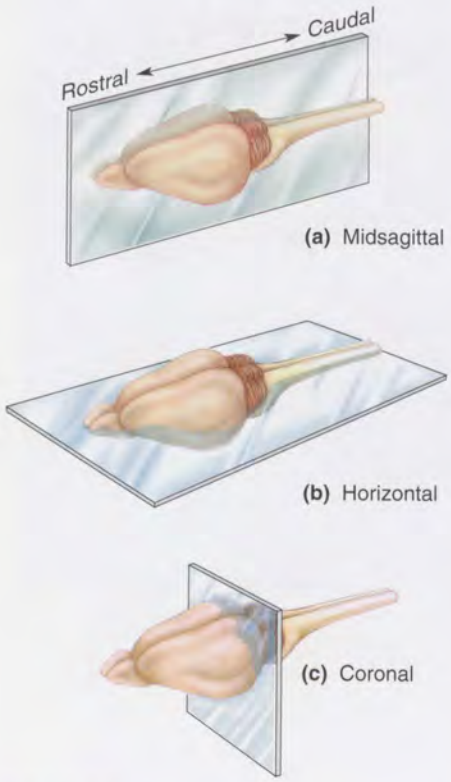


FIGURE 7.3
Anatomical planes of section.

▼ SELF-QUIZ

Take a few moments right now and be sure you understand the meaning of these terms:

anterior	ventral	contralateral
rostral	midline	midsagittal plane
posterior	medial	sagittal plane
caudal	lateral	horizontal plane
dorsal	ipsilateral	coronal plane

The Central Nervous System

The **central nervous system** (**CNS**) consists of the parts of the nervous system that are encased in bone: the **brain** and the **spinal cord**. The brain lies entirely within the skull. A side view of the rat brain reveals three parts that are common to all mammals: the cerebrum, the cerebellum, and the brain stem (Figure 7.4a).

The Cerebrum. The rostral-most and largest part of the brain is the **cerebrum**. Figure 7.4b shows the rat cerebrum as it appears when viewed from above. Notice that it is clearly split down the middle into two **cerebral hemispheres**, separated by the deep *sagittal fissure*. In general, the *right* cerebral hemisphere receives sensations from, and controls movements of, the *left* side of the body. Similarly, the *left* cerebral hemisphere is concerned with sensations and movements on the *right* side of the body.

The Cerebellum. Lying behind the cerebrum is the **cerebellum** (the word is derived from the Latin for "little brain"). While the cerebellum is in fact dwarfed by the large cerebrum, it actually contains as many neurons as both cerebral hemispheres combined. The cerebellum is primarily a movement control center that has extensive connections with the cerebrum and the spinal cord. In contrast to the cerebral hemispheres, the left side of the cerebellum is concerned with movements of the left side of the body, and the right side of the cerebellum is concerned with movements of the right side.

The Brain Stem. The remaining part of the brain is the brain stem, best observed in a midsagittal view of the brain (Figure 7.4c). The **brain stem** forms the stalk from which the cerebral hemispheres and the cerebellum sprout. The brain stem is a complex nexus of fibers and cells that in part serves to relay information from the cerebrum to the spinal cord and cerebellum, and vice versa. However, the brain stem is also the site where vital functions are regulated, such as breathing, consciousness, and the control of body temperature. Indeed, while the brain stem is considered the most primitive part of the mammalian brain, it is also the most important to life. One can survive damage to the cerebrum and cerebellum, but damage to the brain stem usually means rapid death.

The Spinal Cord. The spinal cord is encased in the bony vertebral column and is attached to the brain stem. The spinal cord is the major conduit of

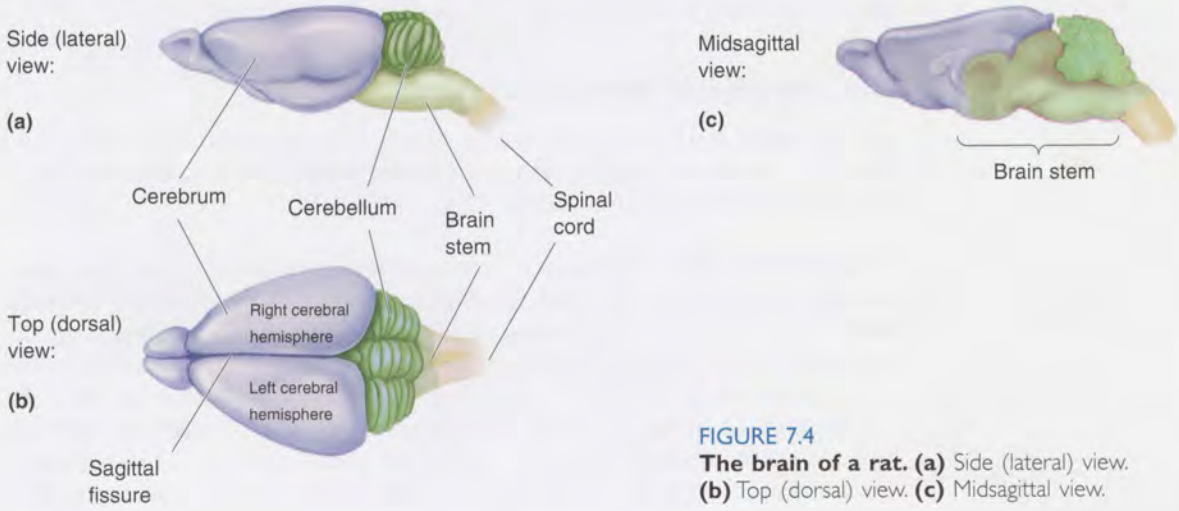


FIGURE 7.4
The brain of a rat. (a) Side (lateral) view. **(b)** Top (dorsal) view. **(c)** Midsagittal view.

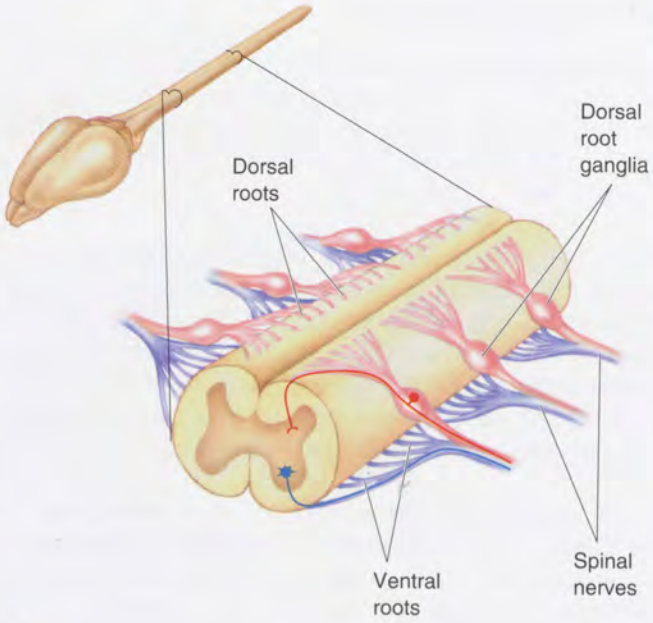


FIGURE 7.5
The spinal cord. The spinal cord runs inside the vertebral column. Axons enter and exit the spinal cord via the dorsal and ventral roots, respectively. These roots come together to form the spinal nerves that course through the body.

information from the skin, joints, and muscles of the body to the brain, and vice versa. A transection of the spinal cord results in anesthesia (lack of feeling) in the skin and paralysis of the muscles in parts of the body caudal to the cut. Paralysis in this case does not mean that the muscles cannot function but that they cannot be controlled by the brain.

The spinal cord communicates with the body via the **spinal nerves**, which are part of the peripheral nervous system (discussed below). Spinal nerves exit the spinal cord through notches between each vertebra of the vertebral column. Each spinal nerve attaches to the spinal cord by means of two branches, the **dorsal root** and the **ventral root** (Figure 7.5). Recall from Chapter 1 that François Magendie showed that the dorsal root contains axons bringing information *into* the spinal cord, such as those that signal the accidental entry of a thumbtack into your foot (see Figure 3.1). Charles Bell showed that the ventral root contains axons carrying information *away from* the spinal cord—for example, to the muscles that jerk your foot away in response to the pain of the thumbtack.

The Peripheral Nervous System

All the parts of the nervous system other than the brain and spinal cord comprise the **peripheral nervous system (PNS)**. The PNS has two parts: the somatic PNS and the visceral PNS.

The Somatic PNS. All the spinal nerves that innervate the skin, the joints, and the muscles that are under voluntary control are part of the **somatic PNS**. The somatic motor axons, which command muscle contraction, derive from motor neurons in the ventral spinal cord. The cell bodies of the motor neurons lie within the CNS, but their axons are mostly in the PNS.

The somatic sensory axons, which innervate and collect information from the skin, muscles, and joints, enter the spinal cord via the dorsal roots. The cell bodies of these neurons lie outside the spinal cord in clusters called

dorsal root ganglia. There is a dorsal root ganglion for each spinal nerve (see Figure 7.5).

The Visceral PNS. The **visceral PNS**, also called the involuntary, vegetative, or **autonomic nervous system** (**ANS**), consists of the neurons that innervate the internal organs, blood vessels, and glands. Visceral sensory axons bring information about visceral function to the CNS, such as the pressure and oxygen content of the blood in the arteries. Visceral motor fibers command the contraction and relaxation of muscles that form the walls of the intestines and the blood vessels (called smooth muscles), the rate of cardiac muscle contraction, and the secretory function of various glands. For example, the visceral PNS controls blood pressure by regulating the heart rate and the diameter of the blood vessels.

We will return to the structure and function of the ANS in Chapter 15. For now, remember that when one speaks of an emotional reaction that is beyond voluntary control—like "butterflies in the stomach" or blushing—it usually is mediated by the visceral PNS (the ANS).

Afferent and Efferent Axons. Our discussion of the PNS is a good place to introduce two terms that are used to describe axons in the nervous system. Derived from the Latin, **afferent** ("carry to") and **efferent** ("carry from") indicate whether the axons are transporting information *toward* or *away from* a particular point. Consider the axons in the PNS relative to a point of reference in the CNS. The somatic or visceral sensory axons bringing information *into* the CNS are afferents. The axons that emerge *from* the CNS to innervate the muscles and glands are efferents.

The Cranial Nerves

In addition to the nerves that arise from the spinal cord and innervate the body, there are 12 pairs of **cranial nerves** that arise from the brain stem and innervate (mostly) the head. Each cranial nerve has a name and a number associated with it (originally numbered by Galen, about 1800 years ago, from anterior to posterior). Some of the cranial nerves are part of the CNS, others are part of the somatic PNS, and still others are part of the visceral PNS. Many cranial nerves contain a complex mixture of axons that perform different functions. The cranial nerves and their various functions are summarized in the chapter appendix.

The Meninges

The CNS, that part of the nervous system encased in the skull and vertebral column, does not come in direct contact with the overlying bone. It is protected by three membranes collectively called the **meninges** (singular: meninx), from the Greek for "covering." The three membranes are the dura mater, the arachnoid membrane, and the pia mater (Figure 7.6).

The outermost covering is the **dura mater**, from the Latin words meaning "hard mother," an accurate description of the dura's leatherlike consistency. The dura forms a tough, inelastic bag that surrounds the brain and spinal cord. Just under the dura lies the **arachnoid membrane** (from the Greek for "spider"). This meningeal layer has an appearance and a consistency resembling a spider web. While there normally is no space between the dura and the arachnoid, if the blood vessels passing through the dura are ruptured, blood can collect here and form what is called a *subdural hematoma*. The buildup of fluid in this subdural space can disrupt brain function by

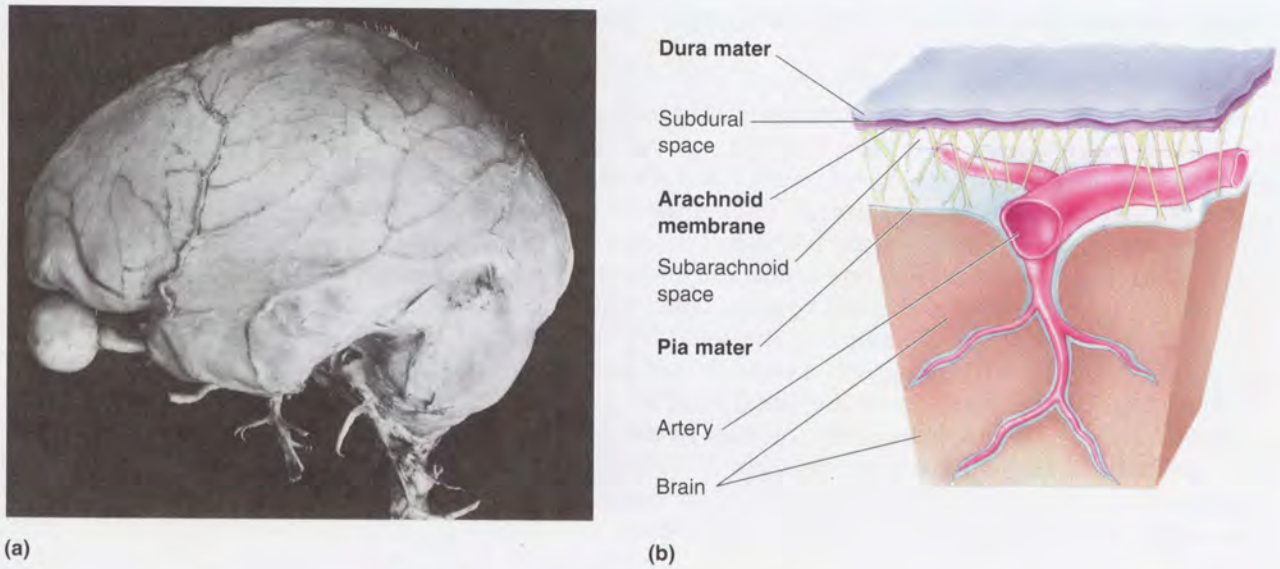


FIGURE 7.6
The meninges. (a) The skull has been removed to show the tough outer meningeal membrane, the dura mater. (Source: Gluhbegoric and Williams, 1980.) **(b)** Illustrated in cross section, the three meningeal layers protecting the brain and spinal cord are the dura mater, the arachnoid membrane, and the pia mater.

compressing parts of the CNS. The disorder is treated by drilling a hole in the skull and draining the blood.

The **pia mater**, the "gentle mother," is a thin membrane that adheres closely to the surface of the brain. Along the pia run many blood vessels that ultimately dive into the substance of the underlying brain. The pia is separated from the arachnoid by a fluid-filled space. This *subarachnoid space* is filled with salty clear liquid called **cerebrospinal fluid** (**CSF**). Thus, in a sense, the brain floats inside the head in this thin layer of CSF.

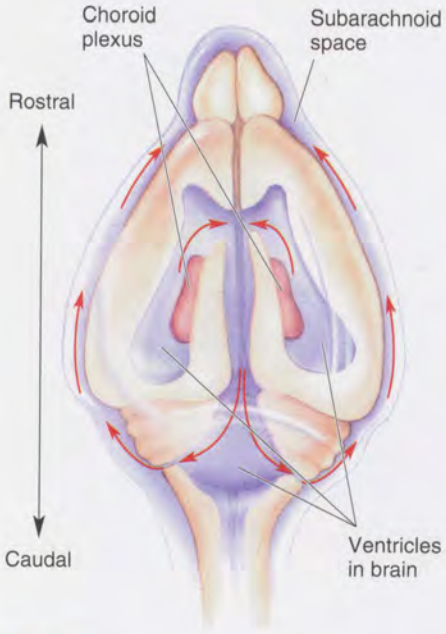


FIGURE 7.7
The ventricular system in a rat brain. CSF is produced in the ventricles of the paired cerebral hemispheres and flows through a series of unpaired ventricles at the core of the brain stem. CSF escapes into the subarachnoid space via small apertures near the base of the cerebellum. In the subarachnoid space, CSF is absorbed into the blood.

The Ventricular System

In Chapter 1, we noted that the brain is hollow. The fluid-filled caverns and canals inside the brain constitute the **ventricular system**. The fluid that runs in this system is CSF, the same as the fluid in the subarachnoid space. CSF is produced by a special tissue, called the choroid plexus, in the ventricles of the cerebral hemispheres. CSF flows from the paired ventricles of the cerebrum to a series of connected, unpaired cavities at the core of the brain stem (Figure 7.7). CSF exits the ventricular system and enters the subarachnoid space by way of small openings, or apertures, located near where the cerebellum attaches to the brain stem. In the subarachnoid space, CSF is absorbed by the blood vessels at special structures called arachnoid villi. If the normal flow of CSF is disrupted, brain damage can result (Box 7.1).

We will return to fill in some details about the ventricular system in a moment. As we will see, understanding the organization of the ventricular system holds the key to understanding how the mammalian brain is organized.

Imaging the Living Brain

For centuries, anatomists have investigated the structure of the brain by removing it from the head, sectioning it in various planes, staining the

Box 7.1 OF SPECIAL INTEREST

Water on the Brain

If the flow of CSF from the choroid plexus through the ventricular system to the subarachnoid space is impaired, the fluid will back up and cause a swelling of the ventricles. This condition is called *hydrocephalus*, meaning "water head."

Occasionally, babies are born with hydrocephalus. However, because the skull is soft and not completely formed, the head will expand in response to the increased intracranial fluid, sparing the brain from damage. Often, this condition goes unnoticed until the size of the head reaches enormous proportions.

In adults, hydrocephalus is a much more serious situation because the skull cannot expand, and intracranial pressure increases as a result. The soft brain tissue is then compressed, impairing function and leading to death if left untreated. Typically, this "obstructive" hydrocephalus is also accompanied by severe headache, caused by the distention of nerve endings in the meninges. Treatment consists of inserting a tube into the swollen ventricle and draining off the excess fluid (Figure A).

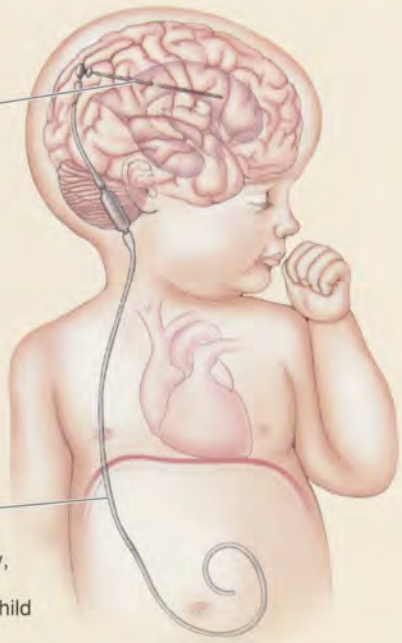


FIGURE A

sections, and examining the stained sections. Much has been learned by this approach, but there are some limitations. Most obviously, the brain removed from the head is dead. This, to say the least, limits the usefulness of this method for examining the brain, and for diagnosing neurological disorders, in living individuals. Neuroanatomy has been revolutionized by the introduction of exciting new methods that enable one to produce images of the living brain. Here we briefly introduce them.

Computed Tomography. Some types of electromagnetic radiation, like X-rays, penetrate the body and are absorbed by various "radiopaque" tissues. Thus, using X-ray-sensitive film, one can make two-dimensional images of the shadows formed by the radiopaque structures within the body. This technique works well for the bones of the skull, but not for the brain. The brain is a complex three-dimensional volume of slight and varying radiopacity, so little information can be gleaned from a single two-dimensional X-ray image.

An ingenious solution, called *computed tomography* (*CT*), was developed by Godfrey Hounsfields and Allan Cormack, who shared the Nobel Prize in 1979. The goal of CT is to generate an image of a slice of brain. (The word *tomography* is derived from the Greek for "cut.") To accomplish this, an X-ray source is rotated around the head within the plane of the desired cross section. On the other side of the head, in the trajectory of the X-ray beam, are sensitive electronic sensors of X-irradiation. The information about relative radiopacity obtained with different "viewing" angles is fed to a computer

that executes a mathematical algorithm on the data. The end result is a digital reconstruction of the position and amount of radiopaque material within the plane of the slice. CT scans noninvasively revealed, for the first time, the gross organization of gray and white matter, and the position of the ventricles, in the living brain.

Magnetic Resonance Imaging. While still used widely, CT is gradually being replaced by a newer imaging method, called *magnetic resonance imaging (MRI)*. The advantages of MRI are that it yields a much more detailed map of the brain than CT, it does not require X-irradiation, and images of brain slices can be made in any plane desired. MRI uses information about how hydrogen atoms in the brain respond to perturbations of a strong magnetic field (Box 7.2). The electromagnetic signals emitted by the atoms are detected by an array of sensors around the head and fed to a powerful computer that constructs a map of the brain. The information from an MRI scan can be used to build a strikingly detailed image of the whole brain.

Functional Brain Imaging. CT and MRI are extremely valuable for detecting structural changes in the living brain, such as brain swelling after a head injury and brain tumors. Nonetheless, much of what goes on in the brain—healthy or diseased—is chemical and electrical in nature, and not observable by simple inspection of the brain's anatomy. Amazingly, however, even these secrets are beginning to yield to the newest imaging techniques.

The two "functional imaging" techniques now in widespread use are *positron emission tomography (PET)* and *functional magnetic resonance imaging (fMRI)*. While the technical details differ, both methods detect changes in regional blood flow and metabolism within the brain (Box 7.3). The basic principle is simple. Neurons that are active demand more glucose and oxygen. The brain vasculature responds to neural activity by directing more blood to the active regions. Thus, by detecting changes in blood flow, PET and fMRI reveal the regions of brain that are most active under different circumstances.

The advent of imaging techniques has offered neuroscientists the extraordinary opportunity of peering into the living, thinking brain. As you can imagine, however, even the most sophisticated brain images are useless unless you know what you are looking at. Next, let's take a closer look at how the brain is organized.

▼ SELF-QUIZ

Take a few moments right now, and be sure you understand the meaning of these terms:

central nervous system (CNS)
brain
spinal cord
cerebrum
cerebral hemispheres
cerebellum
brain stem
spinal nerve
dorsal root
ventral root
peripheral nervous system (PNS)
somatic PNS
dorsal root ganglia
visceral PNS
autonomic nervous system (ANS)
afferent
efferent
cranial nerve
meninges
dura mater
arachnoid membrane
pia mater
cerebrospinal fluid (CSF)
ventricular system

Box 7.2 BRAIN FOOD

Magnetic Resonance Imaging

Magnetic resonance imaging (*MRI*) is a general technique that can be used for determining the amount of certain atoms at different locations in the body. It has become an important tool in neuroscience because it can be used noninvasively to obtain a detailed picture of the nervous system, particularly the brain.

In the most common form of MRI, the hydrogen atoms are quantified—for instance, those located in water or fat in the brain. An important fact of physics is that when a hydrogen atom is put in a magnetic field, its nucleus (which consists of a single proton) can exist in either of two states: a high-energy state or a low-energy state. Because hydrogen atoms are abundant in the brain, there are many protons in each state.

The key to MRI is making the protons jump from one state to the other. Energy is added to the protons by passing an electromagnetic wave (i.e., a radio signal) through the head while it is positioned between the poles of a large magnet. When the radio signal is set at just the right frequency, the protons in the low-energy state will absorb energy from the signal and hop to the high-energy state. The frequency at which the protons absorb energy is called the resonant frequency (hence the name magnetic resonance). When the radio signal is turned off, some of the protons fall back down to the low-energy state, thereby emitting a radio signal of their own at a particular frequency. This signal can be picked up by a radio receiver. The stronger the signal, the more hydrogen atoms between the poles of the magnet.

If we used the procedure described above, we would simply get a measurement of the total amount of hydrogen in the head. However, it is possible to measure hydrogen amounts at a fine spatial scale by taking advantage of the fact that the frequency at which protons emit energy is proportional to the size of the magnetic field. In the MRI machines used in hospitals, the magnetic fields vary from one side of the magnet to the other. This gives a spatial code to the radio waves emitted by the protons: High-frequency signals come from hydrogen atoms near the strong side of the magnet, and low-frequency signals come from the weak side of the magnet.

The last step in the MRI process is to orient the gradient of the magnet at many different angles relative to the head and measure the amount of hydrogen. It takes about 15 minutes to make all the measurements for a typical brain scan. A sophisticated computer program is then used to make a single image from the measurements, resulting in a picture of the distribution of hydrogen atoms in the head.

Figure A is an MRI image of a lateral view of the brain in a living human. In Figure B, another MRI image, a slice has been made in the brain. Notice how clearly you can see the white and gray matter. This differentiation makes it possible to see the effects of demyelinating diseases on white matter in the brain. MRI images also reveal lesions in the brain because tumors and inflammation generally increase the amount of extracellular water.

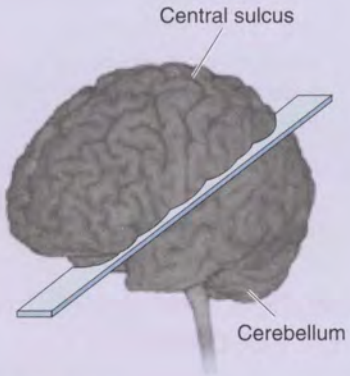


FIGURE A

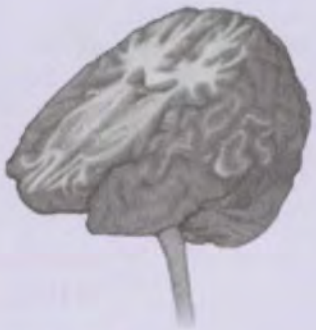


FIGURE B

Box 7.3 BRAIN FOOD

Functional Imaging of Brain Activity: PET and fMRI

Until recently, "mind reading" has been beyond the reach of science. However, with the introduction of *positron emission tomography (PET)* and *functional magnetic resonance imaging (fMRI)*, it is now possible to observe and measure changes in brain activity associated with the planning and execution of specific tasks.

PET imaging was developed in the 1970s by two groups of physicists, one at Washington University led by M. M. Ter-Pogossian and M. E. Phelps, and a second at UCLA led by Z. H. Cho. The basic procedure is very simple. A radioactive solution containing atoms that emit positrons (positively charged electrons) is introduced into the bloodstream. Positrons, emitted wherever the blood goes, interact with electrons to produce photons of electromagnetic radiation. The locations of the positron-emitting atoms are found by detectors that pick up the photons.

One powerful application of PET is the measurement of metabolic activity in the brain. In a technique developed by Louis Sokoloff and his colleagues at the National Institute of Mental Health, a positron-emitting isotope of fluorine or oxygen is attached to 2-deoxyglucose (2-DG). This radioactive 2-DG is injected into the bloodstream, and it travels to the brain. Metabolically active neurons, which normally use glucose, also take up the 2-DG. The 2-DG is phosphorylated by enzymes inside the neuron, and this modification prevents the 2-DG from leaving. Thus, the amount of radioactive 2-DG accumulated in a neuron, and the number of positron emissions, indicate the level of neuronal metabolic activity.

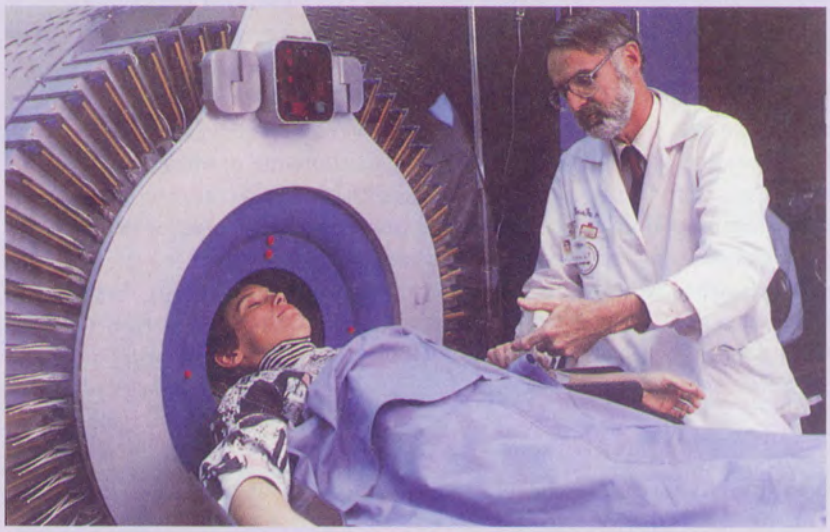
In a typical PET application, a person's head is placed in an apparatus surrounded by detectors (Figure A). Using computer algorithms, the photons (resulting from positron emissions) reaching each of the detectors are recorded. With this information, levels of activity for populations of neurons at various sites in the brain can be calculated. Compiling these measurements produces an image of the brain activity pattern. The researcher monitors brain activity while the subject performs a task, such as moving a finger or reading aloud. Different tasks "light up" different brain areas. In order to obtain a picture of the activity induced by a particular behavioral or thought task, a subtraction technique is used. Even in the absence of any sensory stimulation, the PET image will contain a great deal of brain activity. To create an image of the brain activity resulting from a specific task, such as a person looking at a picture, this background activity is subtracted out (Figure B).

Although PET imaging has proven to be a valuable technique, it has significant limitations. Because the spatial resolution is only 5–10 mm^3, the images show the activity of many thousands of cells. Also, a single PET brain scan may take one to many minutes to obtain. This, along with concerns about radiation exposure, limits the number of obtainable scans from one person in a reasonable time period. Thus, the work of S. Ogawa at Bell Labs, showing that MRI techniques could be used to measure local changes in blood oxygen levels that result from brain activity, was an important advance.

The fMRI method takes advantage of the fact that oxyhemoglobin (the oxygenated form of hemoglobin in the blood) has a different magnetic resonance than deoxyhemoglobin (hemoglobin that has donated its oxygen). More active regions of the brain receive more blood, and this blood donates more of its oxygen. Functional MRI detects the locations of increased neural activity by measuring the ratio of oxyhemoglobin to deoxyhemoglobin. It has emerged as the method of choice for functional brain imaging because the scans can be made rapidly (50 msec), they have good spatial resolution (3 mm^3), and they are completely noninvasive.

▼ UNDERSTANDING CNS STRUCTURE THROUGH DEVELOPMENT

The entire CNS is derived from the walls of a fluid-filled tube that is formed at an early stage in embryonic development. The tube itself becomes the adult ventricular system. Thus, by examining how this tube changes during the course of fetal development, we can understand how the brain is organized and how the different parts fit together. In this section, we focus on development as a way to understand the structural organization of the brain. In Chapter 23, we will revisit the topic of development to see how neurons are born, how they find their way to their final locations in the



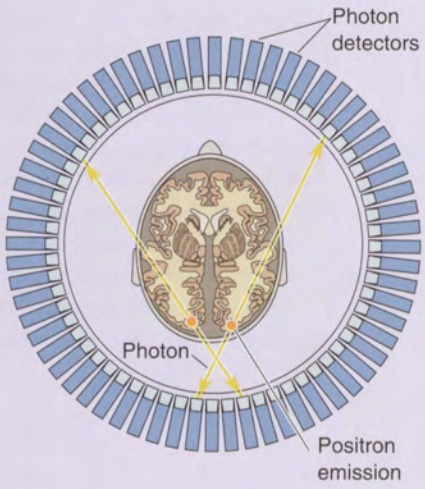


FIGURE A
The PET procedure. (Source: Posner and Raichle, 1994, p. 61.)

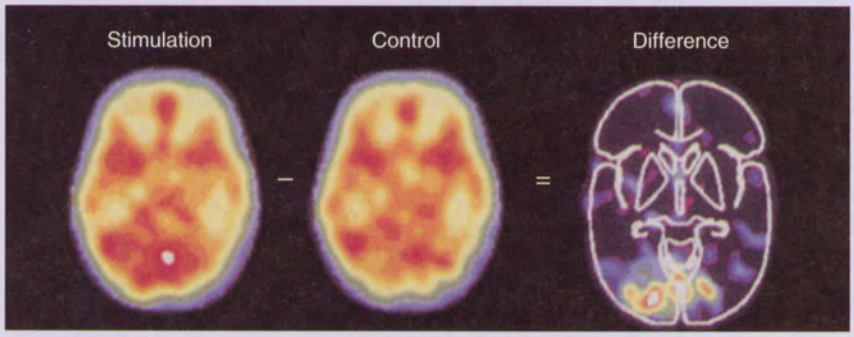


FIGURE B
A PET image. (Source: Posner and Raichle, 1994, p. 65.)

CNS, and how they make the appropriate synaptic connections with one another.

As you work your way through this section, and through the rest of the book, you will encounter many different names used by anatomists to refer to groups of related neurons and axons. Some common names for describing collections of neurons and axons are given in Tables 7.1 and 7.2. Take a few moments to familiarize yourself with these new terms before continuing.

Anatomy by itself can be pretty dry. It really comes alive only after the functions of different structures are understood. The remainder of this book

Table 7.1 Collections of Neurons

NAME	DESCRIPTION AND EXAMPLE
Gray matter	A generic term for a collection of neuronal cell bodies in the CNS. When a freshly dissected brain is cut open, neurons appear gray.
Cortex	Any collection of neurons that form a thin sheet, usually at the brain's surface. *Cortex* is Latin for "bark." Example: *cerebral cortex*, the sheet of neurons found just under the surface of the cerebrum.
Nucleus	A clearly distinguishable mass of neurons, usually deep in the brain (not to be confused with the nucleus of a cell). *Nucleus* is from the Latin word for "nut." Example: *lateral geniculate nucleus*, a cell group in the brain stem that relays information from the eye to the cerebral cortex.
Substantia	A group of related neurons deep within the brain, but usually with less distinct borders than those of nuclei. Example: *substantia nigra* (from the Latin for "black substance"), a brain stem cell group involved in the control of voluntary movement.
Locus (plural: loci)	A small, well-defined group of cells. Example: *locus coeruleus* (Latin for "blue spot"), a brain stem cell group involved in the control of wakefulness and behavioral arousal.
Ganglion (plural: ganglia)	A collection of neurons in the PNS. *Ganglion* is from the Greek for "knot." Example: the *dorsal root ganglia*, which contain the cells bodies of sensory axons entering the spinal cord via the dorsal roots. Only one cell group in the CNS goes by this name: the *basal ganglia*, which are structures lying deep within the cerebrum that control movement.

is devoted to explaining the functional organization of the nervous system. However, we have punctuated this section with a preview of some structure-function relationships to provide you with a general sense of how the different parts contribute, individually and collectively, to the function of the CNS.

Formation of the Neural Tube

The embryo begins as a flat disk with three distinct layers of cells called endoderm, mesoderm, and ectoderm. The *endoderm* ultimately gives rise to the lining of many of the internal organs (viscera). From the *mesoderm* arise the bones of the skeleton and the muscles. The nervous system and the skin derive entirely from the *ectoderm*.

Our focus is on changes in the part of the ectoderm that gives rise to the nervous system: the *neural plate*. At this early stage (about 17 days from

Table 7.2 Collections of Axons

NAME	DESCRIPTION AND EXAMPLE
Nerve	A bundle of axons in the PNS. Only one collection of CNS axons is called a nerve: the *optic nerve*.
White matter	A generic term for a collection of CNS axons. When a freshly dissected brain is cut open, axons appear white.
Tract	A collection of CNS axons having a common site of origin and a common destination. Example: *corticospinal tract*, which originates in the cerebral cortex and ends in the spinal cord.
Bundle	A collection of axons that run together but do not necessarily have the same origin and destination. Example: *medial forebrain bundle*, which connects cells scattered within the cerebrum and brain stem.
Capsule	A collection of axons that connect the cerebrum with the brain stem. Example: *internal capsule*, which connects the brain stem with the cerebral cortex.
Commissure	Any collection of axons that connect one side of the brain with the other side.
Lemniscus	A tract that meanders through the brain like a ribbon. Example: *medial lemniscus*, which brings touch information from the spinal cord through the brain stem.

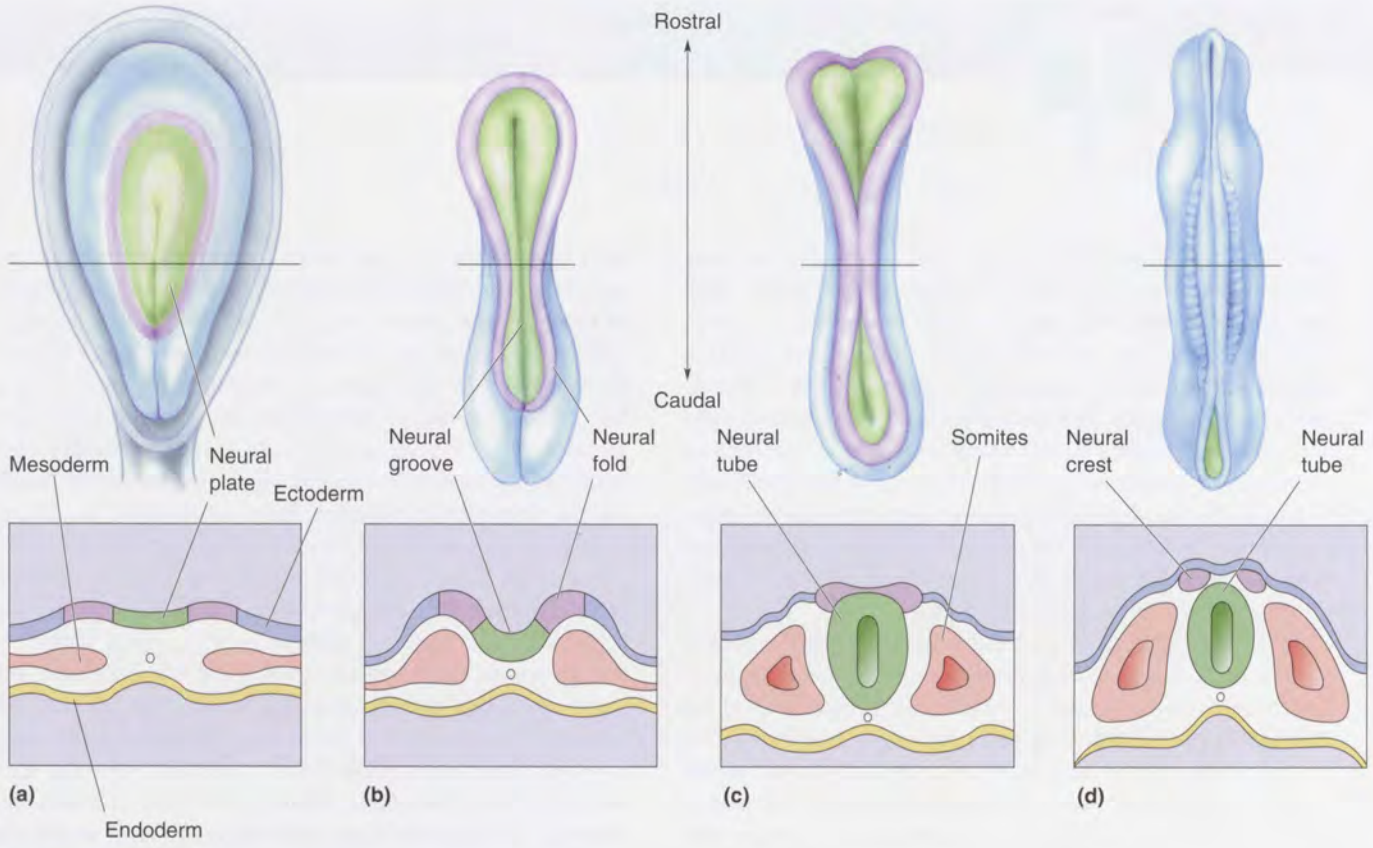


FIGURE 7.8
Formation of the neural tube and neural crest. These schematic illustrations follow the early development of the nervous system in the embryo. The drawings above are dorsal views of the embryo; those below are cross sections. **(a)** The primitive embryonic CNS begins as a thin sheet of ectoderm. **(b)** The first important step in the development of the nervous system is the formation of the neural groove. **(c)** The walls of the groove, called neural folds, come together and fuse, forming the neural tube. **(d)** The bits of neural ectoderm that are pinched off when the tube rolls up is called the neural crest, from which the PNS will develop. The somites are mesoderm that will give rise to much of the skeletal system and the muscles.

conception in humans), the brain consists only of a flat sheet of cells (Figure 7.8a). The next event of interest is the formation of a groove in the neural plate that runs rostral to caudal, called the *neural groove* (Figure 7.8b). The walls of the groove are called *neural folds*, which subsequently move together and fuse dorsally, forming the **neural tube** (Figure 7.8c). *The entire central nervous system develops from the walls of the neural tube.* As the neural folds come together, some neural ectoderm is pinched off and comes to lie just lateral to the neural tube. This tissue is called the **neural crest** (Figure 7.8d). *All neurons with cell bodies in the peripheral nervous system derive from the neural crest.*

The neural crest develops in close association with the underlying mesoderm. The mesoderm at this stage in development forms prominent bulges on either side of the neural tube called *somites*. From these somites, the 33 individual vertebrae of the spinal column and the related skeletal muscles will develop. The nerves that innervate these skeletal muscles are therefore called *somatic* motor nerves.

The process by which the neural plate becomes the neural tube is called **neurulation**. Neurulation occurs very early in embryonic development, about 22 days after conception in humans. A common birth defect is the

Box 7.4 OF SPECIAL INTEREST

Nutrition and the Neural Tube

Neural tube formation is a crucial event in the development of the nervous system. It occurs early—only 3 weeks after conception—when the mother may be unaware she is pregnant. Failure of the neural tube to close correctly is a common birth defect, occurring in approximately 1 out of every 500 live births. A recent discovery of enormous public health importance is that many neural tube defects can be traced to a deficiency of the vitamin *folic acid* (or *folate*) in the maternal diet during the weeks immediately after conception. It has been estimated that dietary supplementation of folic acid during this period could reduce the incidence of neural tube defects by 90%.

Formation of the neural tube is a complex process (Figure A). It depends on a precise sequence of changes in the three-dimensional shape of individual cells, as well as on changes in the adhesion of each cell to its neighbors. The timing of neurulation also must be coordinated with simultaneous changes in non-neural ectoderm and the mesoderm. At the molecular level, successful neurulation depends on specific sequences of gene expression that are controlled, in part, by the position and local chemical environment of the cell. It is not surprising that this process is highly sensitive to chemicals, or chemical deficiencies, in the maternal circulation.

The fusion of the neural folds to form the neural tube occurs first in the middle, then anteriorly and posteriorly (Figure B). Failure of the anterior neural tube to close results in *anencephaly*, a condition characterized by degeneration of the forebrain and skull that is always fatal. Failure of the posterior neural tube to close results in a condition called *spina bifida*. In its most severe form, spina bifida is characterized by the failure of the posterior spinal cord to form from the neural plate (*bifida* is from the Latin word meaning "cleft in two parts"). Less severe forms are characterized by defects in the meninges and vertebrae overlying the posterior spinal cord. Spina bifida, while usually not fatal, does require extensive and costly medical care.

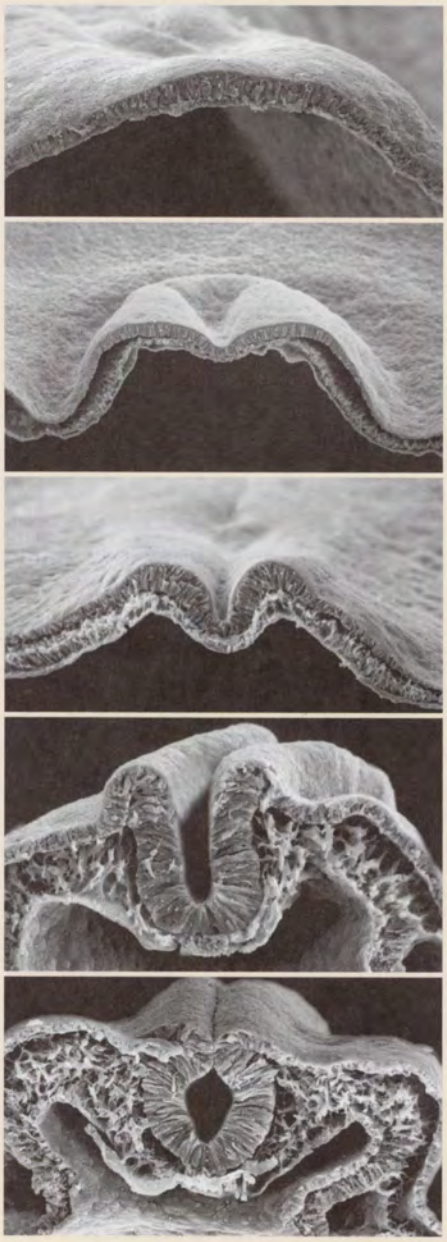
Folic acid plays an essential role in a number of metabolic pathways, including the biosynthesis of DNA, which naturally must occur during development as cells divide. Although we do not precisely understand why folic acid deficiency increases the incidence of neural tube defects, one can easily imagine how it could alter the complex choreography of neurulation. The name is derived from the Latin word for "leaf," reflecting the fact that folic acid was first isolated from spinach leaves. Besides green leafy vegetables, good dietary sources of folic acid are liver, yeast, eggs, beans, and oranges. Many breakfast cereals are now fortified with folic acid. Nonetheless, the folic acid intake of the average American is only half of what is recommended to prevent birth defects (0.4 mg/day). The U.S. Centers for Disease Control and Prevention recommends that women take multivitamins containing 0.4 mg of folic acid before planning pregnancy.

FIGURE A ▶
Scanning electron micrographs of neurulation. (Source: Smith and Schoenwolf, 1997.)

failure of appropriate closure of the neural tube. Fortunately, recent research suggests that most cases of neural tube defects can be avoided by ensuring proper maternal nutrition during this period (Box 7.4).

Three Primary Brain Vesicles

The process by which structures become more complex and functionally specialized during development is called **differentiation**. The first step in the differentiation of the brain is the development, at the rostral end of the



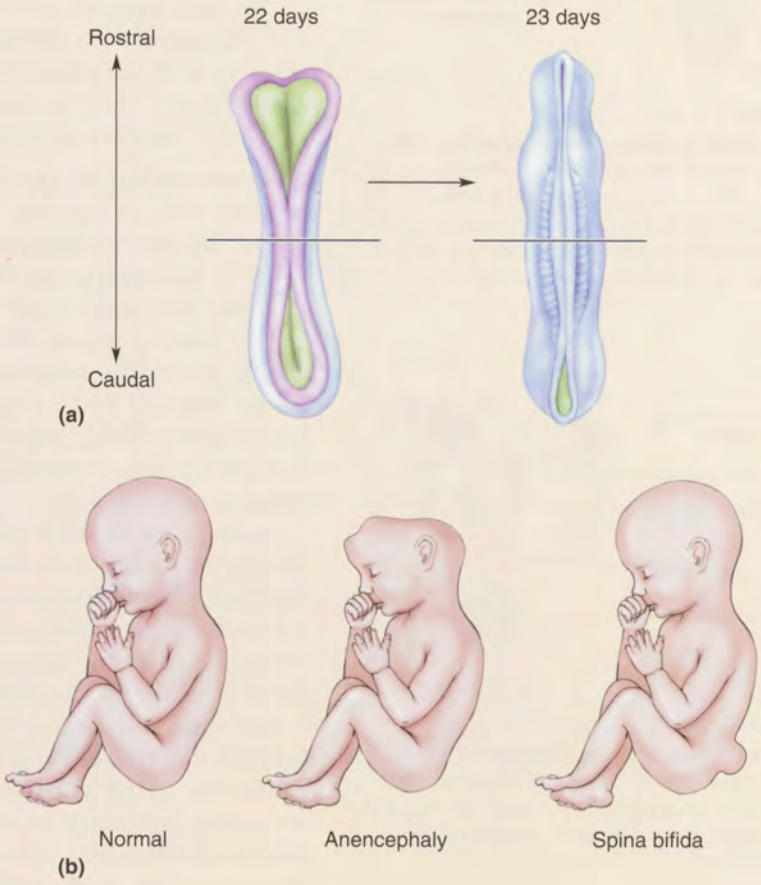


FIGURE B
(a) Neural tube closure. **(b)** Neural tube defects.

neural tube, of three swellings called the primary vesicles (Figure 7.9). *The entire brain derives from the three primary vesicles of the neural tube.*

The rostral-most vesicle is called the *prosencephalon*. *Pro* is Greek for "before"; *encephalon* is derived from the Greek for "brain." Thus, the prosencephalon is also called the **forebrain**. Behind the prosencephalon lies another vesicle called the *mesencephalon*, or **midbrain**. Caudal to this is the third primary vesicle, the *rhombencephalon*, or **hindbrain**. The rhombencephalon connects with the caudal neural tube, which gives rise to the spinal cord.

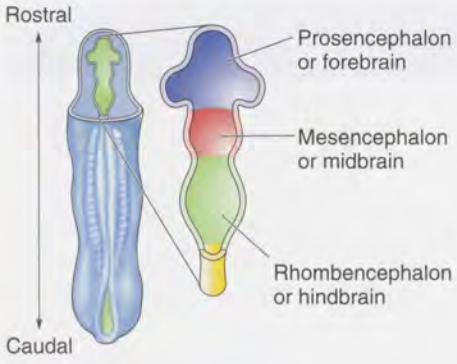


FIGURE 7.9
The three primary brain vesicles. The rostral end of the neural tube differentiates to form the three vesicles that will give rise to the entire brain. This view is from above, and the vesicles have been cut horizontally so that we can see the inside of the neural tube.

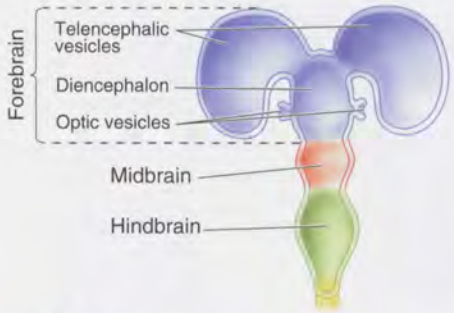


FIGURE 7.10
The secondary brain vesicles of the forebrain. The forebrain differentiates into the paired telencephalic and optic vesicles, and the diencephalon. The optic vesicles develop into the eyes.

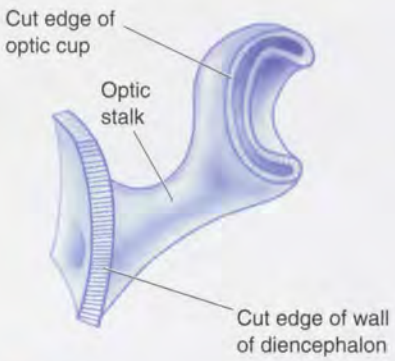


FIGURE 7.11
Early development of the eye. The optic vesicle differentiates into the optic stalk and the optic cup. The optic stalk will become the optic nerve, and the optic cup will become the retina.

Differentiation of the Forebrain

The next important developments occur in the forebrain, where secondary vesicles sprout off on both sides of the prosencephalon. The secondary vesicles are the *optic vesicles* and the *telencephalic vesicles*. The unpaired structure that remains after the secondary vesicles have sprouted off is called the **diencephalon**, or "between brain" (Figure 7.10). Thus, the forebrain at this stage consists of the two optic vesicles, the two telencephalic vesicles, and the diencephalon.

The optic vesicles grow and invaginate (fold in) to form the optic stalks and the optic cups, which will ultimately become the *optic nerves* and the two *retinas* in the adult (Figure 7.11). The important point is that the retina at the back of the eye, and the optic nerve connecting the eye to the diencephalon, are part of the brain, not the PNS.

Differentiation of the Telencephalon and Diencephalon. The telencephalic vesicles together form the **telencephalon**, or "endbrain," consisting of the two cerebral hemispheres. The telencephalon continues to develop in four ways: (1) The telencephalic vesicles grow posteriorly so that they lie over and lateral to the diencephalon (Figure 7.12a). (2) Another pair of vesicles sprout off the ventral surfaces of the cerebral hemispheres, giving rise to the **olfactory bulbs** and related structures that participate in the sense of smell (Figure 7.12b). (3) The cells of the walls of the telencephalon divide and differentiate into various structures. (4) White matter systems develop, carrying axons to and from the neurons of the telencephalon.

Figure 7.13 shows a coronal section through the primitive mammalian forebrain, to illustrate how the different parts of the telencephalon and diencephalon differentiate and fit together. Notice that the two cerebral hemispheres lie above and on either side of the diencephalon, and that the ventral-medial surfaces of the hemispheres have fused with the lateral surfaces of the diencephalon (Figure 7.13a).

The fluid-filled spaces within the cerebral hemispheres are called the **lateral ventricles**, and the space at the center of the diencephalon is called the **third ventricle** (Figure 7.13b). The paired lateral ventricles are a key landmark in the adult brain: Whenever you see paired fluid-filled ventricles in a brain section, you know that the tissue surrounding them is in the telencephalon. The elongated, slitlike appearance of the third ventricle in cross section is also a useful feature for identifying the diencephalon.

Notice in Figure 7.13 that the walls of the telencephalic vesicles appear swollen due to the proliferation of neurons. These neurons form two different types of gray matter in the telencephalon: the **cerebral cortex** and the **basal telencephalon**. Likewise, the diencephalon differentiates into two structures: the **thalamus** and the **hypothalamus** (Figure 7.13c). The thalamus, nestled deep inside the forebrain, gets its name from the Greek word for "inner chamber."

The neurons of the developing forebrain extend axons to communicate with other parts of the nervous system. These axons bundle together to form three major white matter systems: the cortical white matter, the corpus callosum, and the internal capsule (Figure 7.13d). The **cortical white matter** contains all the axons that run to and from the neurons in the cerebral cortex. The **corpus callosum** is continuous with the cortical white matter and forms an axonal bridge that links cortical neurons of the two cerebral hemispheres. The cortical white matter is also continuous with the **internal capsule**, which links the cortex with the brain stem, particularly the thalamus.

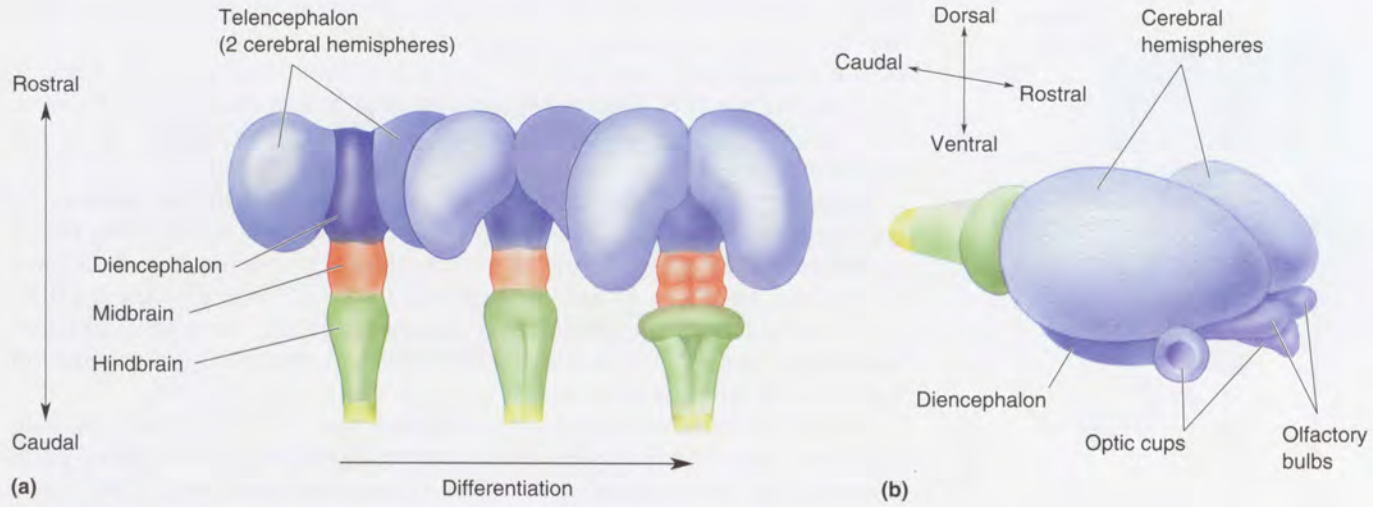


FIGURE 7.12
Differentiation of the telencephalon. (a) As development proceeds, the cerebral hemispheres swell and grow posteriorly and laterally to envelop the diencephalon. **(b)** The olfactory bulbs sprout off the ventral surfaces of each telencephalic vesicle.

Forebrain Structure-Function Relationships. The forebrain is the seat of perceptions, conscious awareness, cognition, and voluntary action. All this depends on extensive interconnections with the sensory and motor neurons of the brain stem and spinal cord.

Arguably the most important structure in the forebrain is the cerebral cortex. As we will see later in this chapter, the cortex is the brain structure that has expanded the most over the course of human evolution. Cortical neurons receive sensory information, form perceptions of the outside world, and command voluntary movements.

Neurons in the olfactory bulbs receive information from cells that sense chemicals in the nose (odors) and relay this information caudally to a part

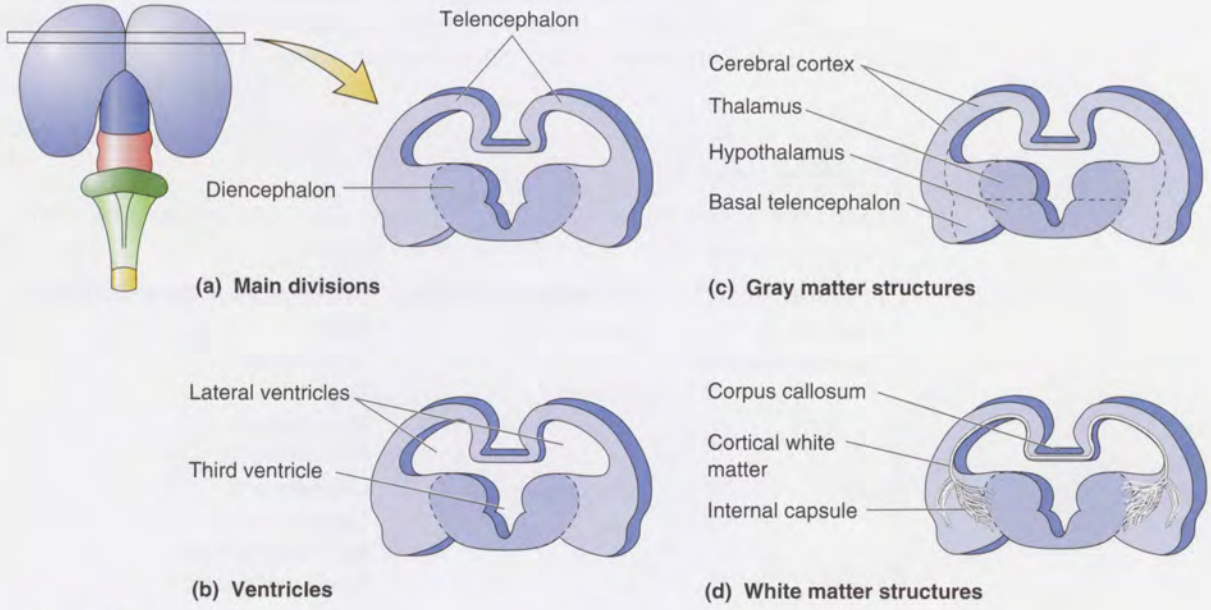


FIGURE 7.13
Structural features of the forebrain.

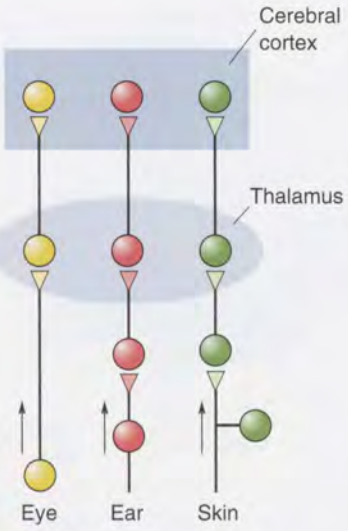


FIGURE 7.14
The thalamus: gateway to the cerebral cortex. The sensory pathways from the eye, ear, and skin all relay in the thalamus before terminating in the cerebral cortex. The arrows indicate the direction of information flow.

of the cerebral cortex for further analysis. Information from the eyes, ears, and skin is also brought to the cerebral cortex for analysis. However, each of the sensory pathways serving vision, audition (hearing), and somatic sensation relays (i.e., synapses upon neurons) in the thalamus en route to the cortex. Thus, the thalamus is often referred to as the gateway to the cerebral cortex (Figure 7.14).

Thalamic neurons send axons to the cortex via the internal capsule. As a general rule, the axons of each internal capsule carry information to the cortex about the contralateral side of the body. Therefore, if a thumbtack entered the *right* foot, it would be relayed to the *left* cortex by the *left* thalamus via axons in the *left* internal capsule. But how does the right foot know what the left foot is doing? One important way is by communication between the hemispheres via the axons in the corpus callosum.

Cortical neurons also send axons through the internal capsule, back to the brain stem. Some cortical axons course all the way to the spinal cord, forming the corticospinal tract. This is one important way cortex can command voluntary movement. Another way is by communicating with neurons in the basal ganglia, a collection of cells in the basal telencephalon. The term *basal* is used to describe structures deep in the brain, and the basal ganglia lie deep within the cerebrum. The functions of the basal ganglia are poorly understood, but it is known that damage to these structures disrupts the ability to initiate voluntary movement. Other structures, contributing to other brain functions, are also present in the basal telencephalon. For example, in Chapter 18 we'll discuss a structure called the amygdala that is involved in fear and emotion.

Although the hypothalamus lies just under the thalamus, functionally it is more closely related to certain telencephalic structures, like the amygdala. The hypothalamus performs many primitive functions and therefore has not changed much over the course of mammalian evolution. "Primitive" does not mean unimportant or uninteresting, however. The hypothalamus controls the visceral (autonomic) nervous system, which regulates bodily functions in response to the needs of the organism. For example, when you are faced with a threatening situation, the hypothalamus orchestrates the body's visceral fight-or-flight response. Hypothalamic commands to the ANS will lead to (among other things) an increase in the heart rate, increased blood flow to the muscles for escape, and even the standing of your hair on end. Conversely, when you're relaxing after Sunday brunch, the

▼ SELF-QUIZ

Listed below are derivatives of the forebrain that we have discussed. Be sure you know what each of these terms means.

PRIMARY VESICLE	SECONDARY VESICLE	SOME ADULT DERIVATIVES
Forebrain (prosencephalon)	Optic vesicle	Retina
		Optic nerve
	Thalamus (diencephalon)	Dorsal thalamus
		Hypothalamus
		Third ventricle
	Telencephalon	Olfactory bulb
		Cerebral cortex
		Basal telencephalon
		Corpus callosum
		Cortical white matter
		Internal capsule

hypothalamus ensures that the brain is well-nourished via commands to the ANS, which will increase peristalsis (movement of material through the gastrointestinal tract) and redirect blood to your digestive system. The hypothalamus also plays a key role in motivating animals to find food, drink, and sex in response to their needs. Aside from its connections to the ANS, the hypothalamus also directs bodily responses via connections with the pituitary gland located below the diencephalon. This gland communicates to many parts of the body by releasing hormones into the bloodstream.

Differentiation of the Midbrain

Unlike the forebrain, the midbrain differentiates relatively little during subsequent brain development (Figure 7.15). The dorsal surface of the mesencephalic vesicle becomes a structure called the **tectum** (Latin for "roof"). The floor of the midbrain becomes the **tegmentum**. The CSF-filled space in between constricts into a narrow channel called the **cerebral aqueduct**. The aqueduct connects rostrally with the third ventricle of the diencephalon. Because it is small and circular in cross section, the cerebral aqueduct is a good landmark for identifying the midbrain.

Midbrain Structure-Function Relationships. For such a seemingly simple structure, the functions of the midbrain are remarkably diverse. Besides serving as a conduit for information passing from the spinal cord to the forebrain and vice versa, the midbrain contains neurons that contribute to sensory systems, the control of movement, and several other functions.

The midbrain contains axons descending from the cerebral cortex to the brain stem and the spinal cord. For example, the corticospinal tract courses through the midbrain en route to the spinal cord. Damage to this tract in the midbrain on one side produces a loss of voluntary control of movement on the opposite side of the body.

The tectum differentiates into two structures: the superior colliculus and the inferior colliculus. The *superior colliculus* receives direct input from the eye, so it is also called the optic tectum. One function of the optic tectum is to control eye movements, which it does via synaptic connections with the motor neurons that innervate the eye muscles. Some of the axons that

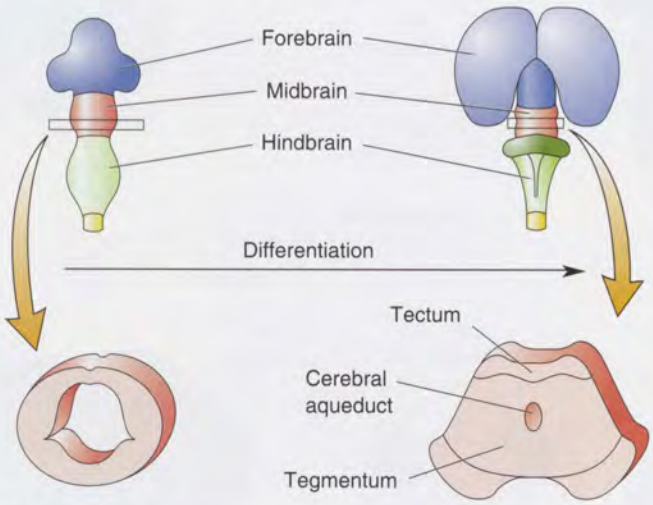


FIGURE 7.15
Differentiation of the midbrain. The midbrain differentiates into the tectum and the tegmentum. The CSF-filled space at the core of the midbrain is the cerebral aqueduct. (Drawings are not to scale.)

supply the eye muscles originate in the midbrain, bundling together to form cranial nerves III and IV (see the chapter appendix).

The *inferior colliculus* also receives sensory information, but from the ear instead of the eye. The inferior colliculus serves as an important relay station for auditory information en route to the thalamus.

The tegmentum is one of the most colorful regions of the brain because it contains both the substantia nigra (the black substance) and the red nucleus. These two cell groups are involved in the control of voluntary movement. Other cell groups scattered in the midbrain have axons that project widely throughout much of the CNS and function to regulate consciousness, mood, pleasure, and pain.

Differentiation of the Hindbrain

The hindbrain differentiates into three important structures: the cerebellum, the **pons**, and the **medulla oblongata**—also called, simply, the **medulla**. The cerebellum and pons develop from the rostral half of the hindbrain (called the metencephalon); the medulla develops from the caudal half (called the myelencephalon). The CSF-filled tube becomes the **fourth ventricle**, which is continuous with the cerebral aqueduct of the midbrain.

At the three-vesicle stage, the rostral hindbrain in cross section is a simple tube. In subsequent weeks, the tissue along the dorsal-lateral wall of the tube, called the rhombic lip, grows dorsally and medially until it fuses with its twin on the other side. The resulting flap of brain tissue grows into the cerebellum. The ventral wall of the tube differentiates and swells to form the pons (Figure 7.16).

Less dramatic changes occur during the differentiation of the caudal half of the hindbrain into the medulla. The ventral and lateral walls of this region swell, leaving the roof covered only with a thin layer of non-neuronal ependymal cells (Figure 7.17). Along the ventral surface of each side of the medulla runs a major white matter system. Cut in cross section, these

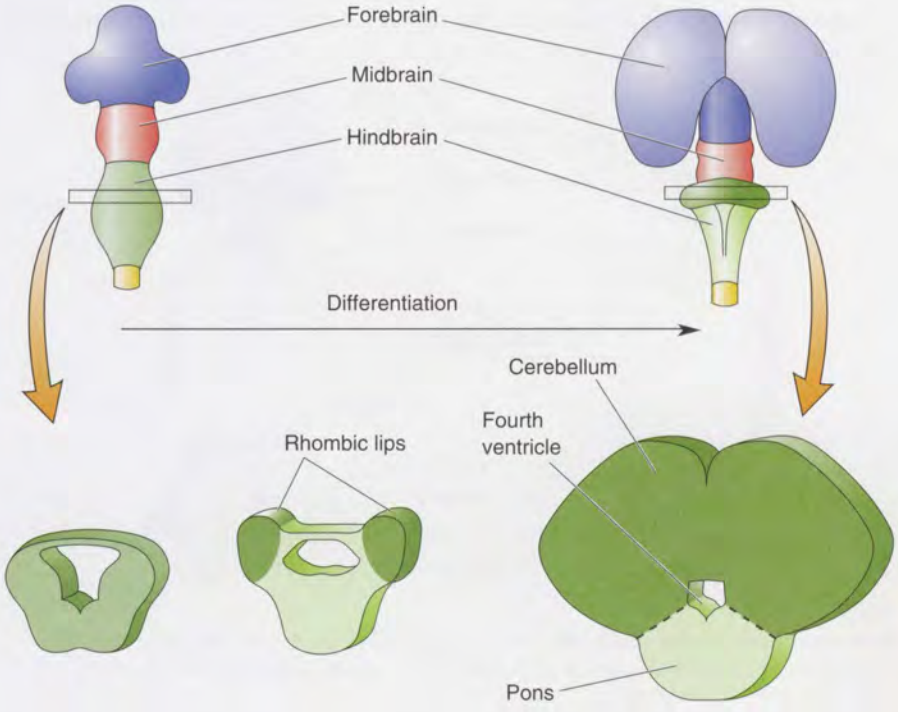


FIGURE 7.16
Differentiation of the rostral hindbrain. The rostral hindbrain differentiates into the cerebellum and pons. The cerebellum is formed by the growth and fusion of the rhombic lips. The CSF-filled space at the core of the hindbrain is the fourth ventricle. (Drawings are not to scale.)

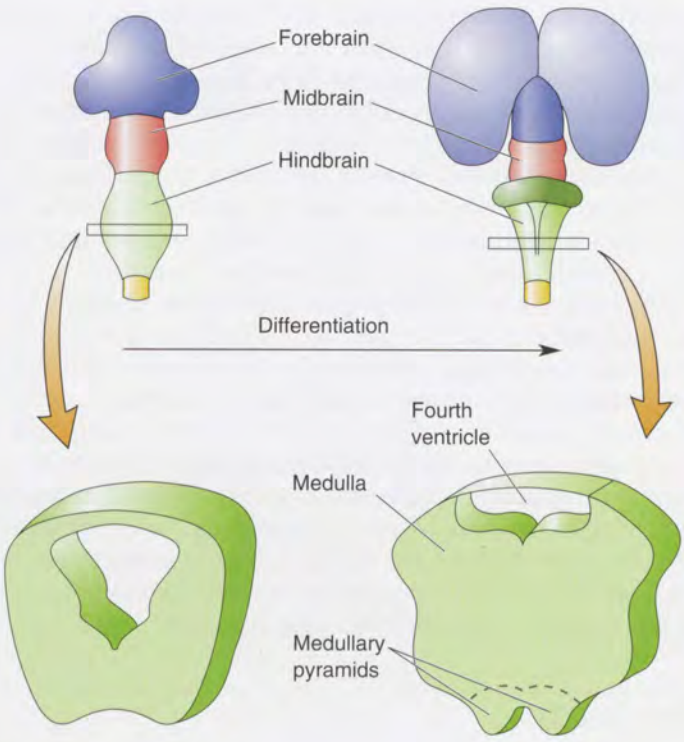


FIGURE 7.17
Differentiation of the caudal hindbrain. The caudal hindbrain differentiates into the medulla. The medullary pyramids are bundles of axons coursing caudally toward the spinal cord. The CSF-filled space at the core of the medulla is the fourth ventricle. (Drawings are not to scale.)

bundles of axons appear somewhat triangular in shape, explaining why they are called the *medullary pyramids*.

Hindbrain Structure-Function Relationships. Like the midbrain, the hindbrain is an important conduit for information passing from the forebrain to the spinal cord, and vice versa. In addition, neurons of the hindbrain contribute to the processing of sensory information, the control of voluntary movement, and regulation of the ANS.

The cerebellum, the "little brain," is an important movement control center. It receives massive axonal inputs from the spinal cord and the pons. The spinal cord inputs provide information about the body's position in space. The inputs from the pons relay information from the cerebral cortex, specifying the goals of intended movements. The cerebellum compares these types of information and calculates the sequences of muscle contractions that are required to achieve the movement goals. Damage to the cerebellum results in uncoordinated and inaccurate movements.

Of the descending axons passing through the midbrain, more than 90%—about 20 million axons in the human—synapse on neurons in the pons. The pontine cells relay all this information to the cerebellum on the opposite site. Thus, the pons serves as a massive switchboard connecting the cerebral cortex to the cerebellum. (The word *pons* is from the Latin word for "bridge.") The pons bulges out from the ventral surface of the brain stem to accommodate all this circuitry.

The axons that do not terminate in the pons continue caudally and enter the medullary pyramids. Most of these axons originate in the cerebral cortex and are part of the corticospinal tract. Thus, "pyramidal tract" is often

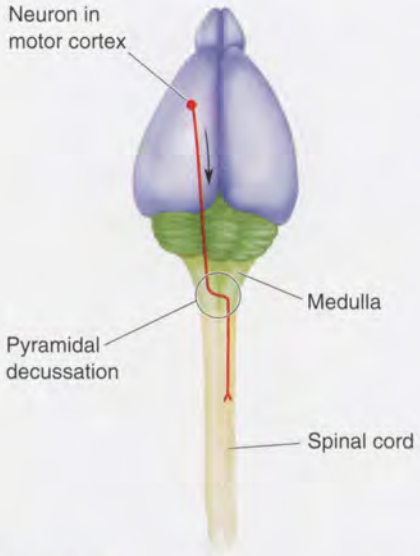


FIGURE 7.18
The pyramidal decussation. The corticospinal tract crosses from one side to the other in the medulla.

used as a synonym for corticospinal tract. Near where the medulla joins with the spinal cord, each pyramidal tract crosses from one side of the midline to the other. A crossing of axons from one side to the other is known as a *decussation*, and this one is called the *pyramidal decussation*. The crossing of axons in the medulla explains why the cortex of one side of the brain controls movements on the opposite side of the body (Figure 7.18).

In addition to the white matter systems passing through, the medulla contains neurons that perform many different sensory and motor functions. For example, the axons of the auditory nerves, bringing auditory information from the ears, synapse on cells in the cochlear nuclei of the medulla. The cochlear nuclei project axons to a number of different structures, including the tectum of the midbrain (inferior colliculus, discussed above). Damage to the cochlear nuclei leads to deafness.

Other sensory functions of the medulla include touch and taste. The medulla contains neurons that relay somatic sensory information from the spinal cord to the thalamus. Destruction of the cells leads to anesthesia (loss of feeling). Other neurons relay gustatory (taste) information from the tongue to the thalamus. And among the motor neurons in the medulla are cells that control the tongue muscles via cranial nerve XII. (So think of the medulla the next time you stick out your tongue!)

▼ SELF-QUIZ

Listed below are derivatives of the midbrain and hindbrain that we have discussed. Be sure you know what each of these terms means.

PRIMARY VESICLE	SOME ADULT DERIVATIVES
Midbrain (mesencephalon)	Tectum
	Tegmentum
	Cerebral aqueduct
Hindbrain (rhombencephalon)	Cerebellum
	Pons
	Fourth ventricle
	Medulla

Differentiation of the Spinal Cord

As shown in Figure 7.19, the transformation of the caudal neural tube into the spinal cord is straightforward compared to the differentiation of the brain. With the expansion of the tissue in the walls, the cavity of the tube constricts to form the tiny CSF-filled **spinal canal**.

Cut in cross section, the gray matter of the spinal cord (where the neurons are) has the appearance of a butterfly. The upper part of the butterfly's wing is the **dorsal horn**, and the lower part is the **ventral horn**. The gray matter between the dorsal and ventral horns is called the *intermediate zone*. Everything else is white matter, consisting of columns of axons that run up and down the spinal cord. Thus, the bundles of axons running along the dorsal surface of the cord are called the *dorsal columns*, the bundles of axons lateral to the spinal gray matter on each side are called the *lateral columns*, and the bundles on the ventral surface are called the *ventral columns*.

Spinal Cord Structure-Function Relationships. As a general rule, dorsal horn cells receive sensory inputs from the dorsal root fibers, ventral horn cells project axons into the ventral roots that innervate muscles, and intermediate zone cells are interneurons that shape motor outputs in response to sensory inputs and descending commands from the brain.

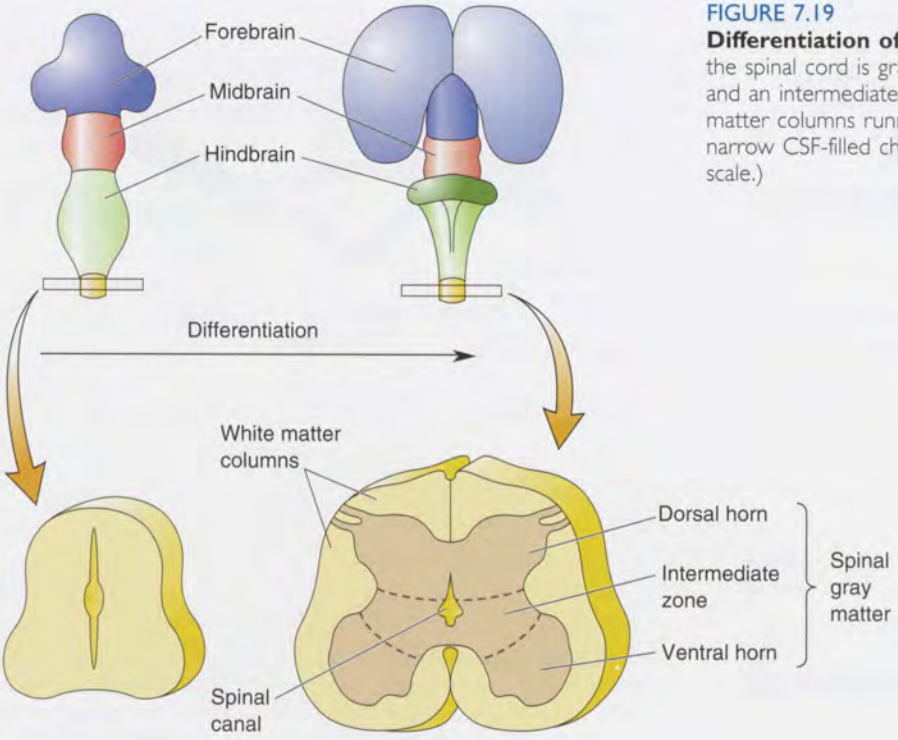


FIGURE 7.19
Differentiation of the spinal cord. The butterfly-shaped core of the spinal cord is gray matter, divisible into dorsal and ventral horns, and an intermediate zone. Surrounding the gray matter are white matter columns running rostrocaudally, up and down the cord. The narrow CSF-filled channel is the spinal canal. (Drawings are not to scale.)

The large dorsal column contains axons that carry somatic sensory (touch) information up the spinal cord toward the brain. It's like a superhighway that speeds information from the ipsilateral side of the body up to nuclei in the medulla. The postsynaptic neurons in the medulla give rise to axons that decussate and ascend to the thalamus on the contralateral side. This crossing of axons in the medulla explains why touching the left side of the body is sensed by the right side of the brain.

The lateral column contains the axons of the descending corticospinal tract, which also cross from one side to the other in the medulla. These axons innervate the neurons of the intermediate zone and ventral horn and communicate the signals that control voluntary movement.

There are at least a half-dozen tracts that run in the columns of each side of the spinal cord. Most are one-way and bring information to or from the brain. Thus, the spinal cord is the major conduit of information from the skin, joints, and muscles to the brain, and vice versa. However, the spinal cord is also much more than that. The neurons of the spinal gray matter begin the analysis of sensory information, play a critical role in coordinating movements, and orchestrate simple reflexes (such as jerking away your foot from a thumbtack).

Putting the Pieces Together

We have discussed the development of different parts of the CNS: the telencephalon, diencephalon, midbrain, hindbrain, and spinal cord. Now let's put all the individual pieces together to make a whole central nervous system.

Figure 7.20 is a highly schematic illustration that captures the basic organizational plan of the CNS of all mammals, including humans. The paired hemispheres of the telencephalon surround the lateral ventricles. Dorsal to the lateral ventricles, at the surface of the brain, lies the cortex. Ventral and lateral to the lateral ventricles lies the basal telencephalon. The lateral ventricles are continuous with the third ventricle of the diencephalon.

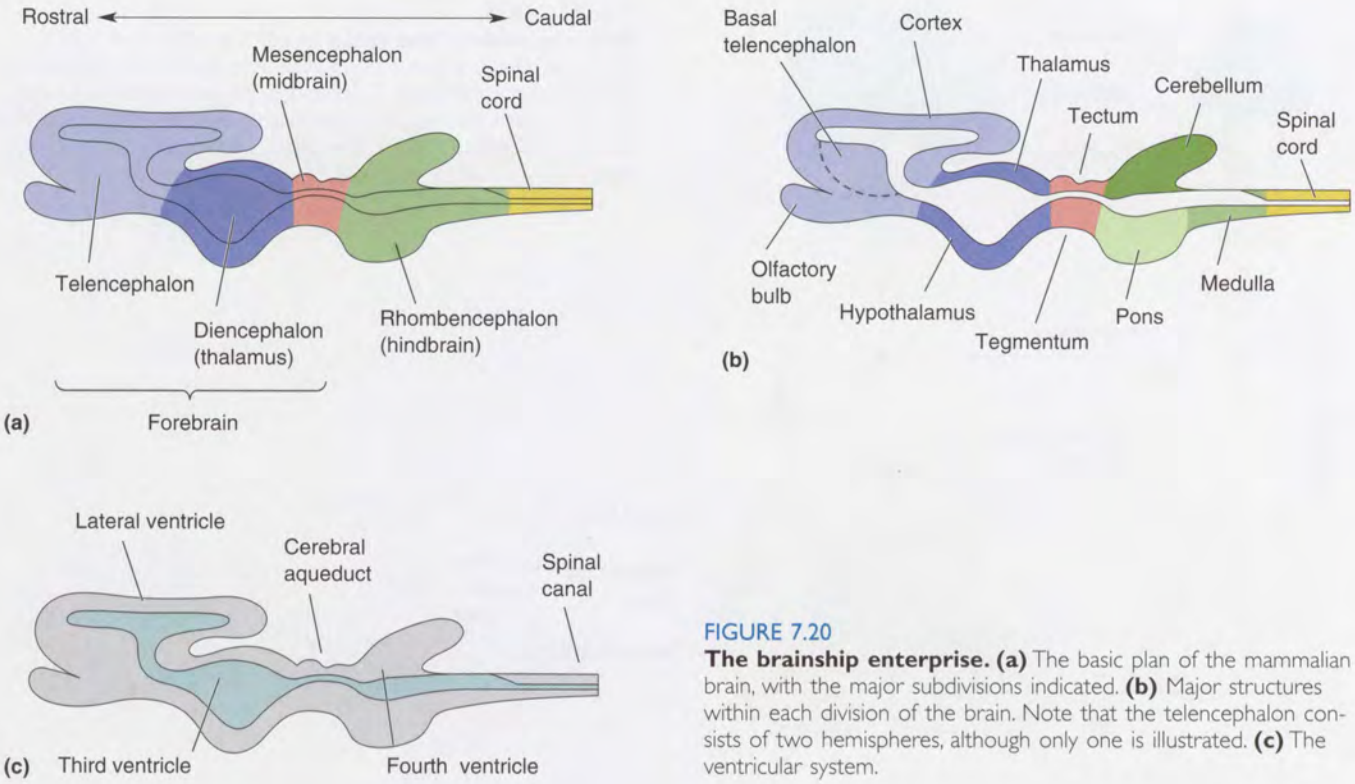


FIGURE 7.20
The brainship enterprise. (a) The basic plan of the mammalian brain, with the major subdivisions indicated. **(b)** Major structures within each division of the brain. Note that the telencephalon consists of two hemispheres, although only one is illustrated. **(c)** The ventricular system.

Surrounding this ventricle are the thalamus and the hypothalamus. The third ventricle is coninuous with the cerebral aqueduct. Dosal to the aqueduct is the tectum. Ventral to the aqueduct is the midbrain tegmentum. The aqueduct connects with the fourth ventricle that lies at the core of the hindbrain. Dorsal to the fourth ventricle sprouts the cerebellum. Ventral to the fourth ventricle lie the pons and the medulla.

You should see by now that finding your way around the brain is easy if you can identify which parts of the ventricular system are in the neighborhood (Table 7.3). Even in the complicated human brain, the ventricular system holds the key to understanding brain structure.

Special Features of the Human CNS

So far, we've explored the basic plan of the CNS as it applies to all mammals. Figure 7.21 compares the brains of the rat and the human. You can

Table 7.3 **The Ventricular System of the Brain**

COMPONENT	RELATED BRAIN STRUCTURES
Lateral ventricles	Cerebral cortex Basal telencephalon
Third ventricle	Thalamus Hypothalamus
Cerebral aqueduct	Tectum Midbrain tegmentum
Fourth ventricle	Cerebellum Pons Medulla

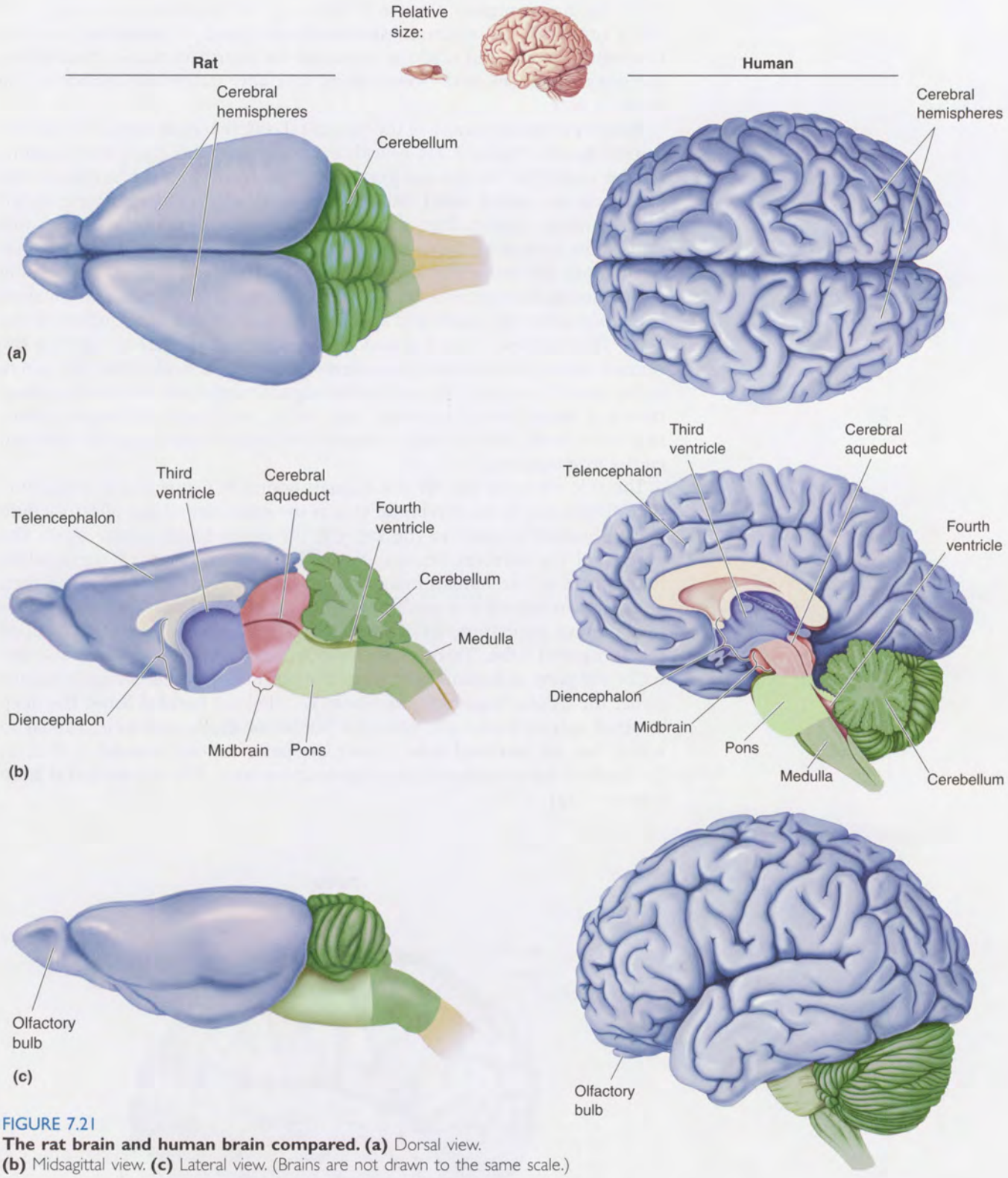


FIGURE 7.21
The rat brain and human brain compared. (a) Dorsal view. **(b)** Midsagittal view. **(c)** Lateral view. (Brains are not drawn to the same scale.)

see immediately that there are indeed many similarities, but also some obvious differences.

Let's start by reviewing the similarities. The dorsal view of both brains reveals the paired hemispheres of the telencephalon (Figure 7.21a). A midsagittal view of the two brains shows the telencephalon extending rostrally

from the diencephalon (Figure 7.21b). The diencephalon surrounds the third ventricle, the midbrain surrounds the cerebral aqueduct, and the cerebellum, pons, and medulla surround the fourth ventricle. Notice how the pons swells below the cerebellum, and how structurally elaborate the cerebellum is.

Now let's consider some of the structural differences between the rat and human brains. Figure 7.21a reveals a striking one: the many convolutions on the surface of the human cerebrum. The grooves in the surface of the cerebrum are called **sulci** (singular: sulcus), and the bumps are called **gyri** (singular: gyrus). Remember, the thin sheet of neurons that lies just under the surface of the cerebrum is the cerebral cortex. Sulci and gyri result from the tremendous expansion of the surface area of the cerebral cortex during human fetal development. The adult human cortex, measuring about 1100 cm^2, must fold and wrinkle to fit within the confines of the skull. This increase in cortical surface area is one of the "distortions" of the human brain. Clinical and experimental evidence indicates that the cortex is the seat of uniquely human reasoning and cognition. Without cerebral cortex, a person would be blind, deaf, mute, and unable to initiate voluntary movement. We will take a closer look at the structure of the cerebral cortex in a moment.

The side views of the rat and human brains in Figure 7.21c reveal further differences in the forebrain. One is the small size of the olfactory bulb in the human relative to the rat. On the other hand, notice again the growth of the cerebral hemisphere in the human. See how the cerebral hemisphere of the human brain arcs posteriorly, ventrolaterally, and then anteriorly to resemble a ram's horn. The tip of the "horn" lies right under the temporal bone (temple) of the skull, so this portion of the brain is called the **temporal lobe**. Three other lobes (named after skull bones) also describe the parts of human cerebrum. The portion of the cerebrum lying just under the frontal bone of the forehead is called the **frontal lobe**. The deep **central sulcus** marks the posterior border of the frontal lobe, caudal to which lies the **parietal lobe**, under the parietal bone. Caudal to that, at the back of the cerebrum under the occipital bone, lies the **occipital lobe** (Figure 7.22).

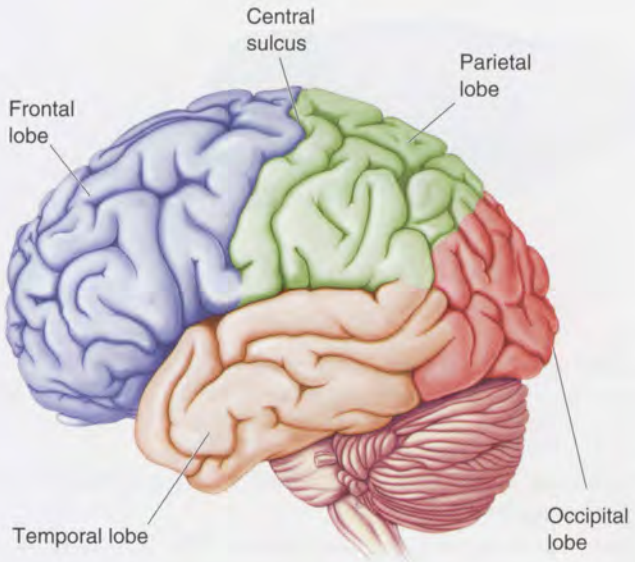


FIGURE 7.22
The lobes of the human cerebrum.

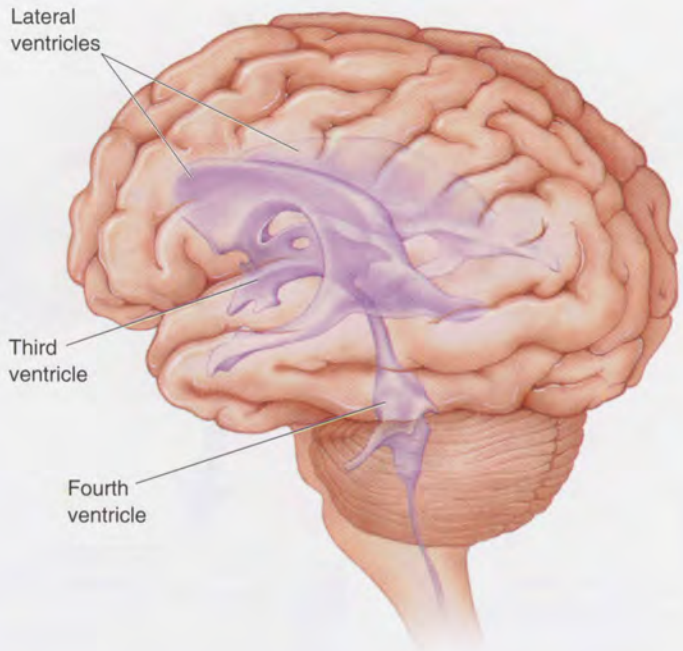


FIGURE 7.23
The human ventricular system. Although the ventricles are distorted by the growth of the brain, the basic relationships of the ventricles to the surrounding brain are the same as those illustrated in Figure 7.20c.

It is important to realize that, despite the disproportionate growth of the cerebrum, the human brain still follows the basic mammalian brain plan laid out during embryonic development. Again, the ventricles are key. Although the ventricular system is distorted, particularly by the growth of the temporal lobes, the relationships that relate the brain to the different ventricles still hold (Figure 7.23).

▼ A GUIDE TO THE CEREBRAL CORTEX

Considering its prominence in the human brain, the cerebral cortex deserves further description. As we will see repeatedly in subsequent chapters, the systems in the brain that govern the processing of sensations, perceptions, voluntary movement, learning, speech, and cognition all converge in this remarkable organ.

Types of Cerebral Cortex

Cerebral cortex in the brain of all vertebrate animals has several common features, as shown in Figure 7.24. First, the cell bodies of cortical neurons are always arranged in layers, or sheets, that usually lie parallel to the surface of the brain. Second, the layer of neurons closest to the surface (the most superficial cell layer) is separated from the pia mater by a zone that lacks neurons; it is called the molecular layer, or simply *layer I*. Third, at least one cell layer contains pyramidal cells that emit large dendrites, called *apical dendrites*, that extend up to layer I, where they form multiple branches. Thus, we can say that the cerebral cortex has a characteristic cytoarchitecture that distinguishes it, for example, from the nuclei of the basal telencephalon or the thalamus.

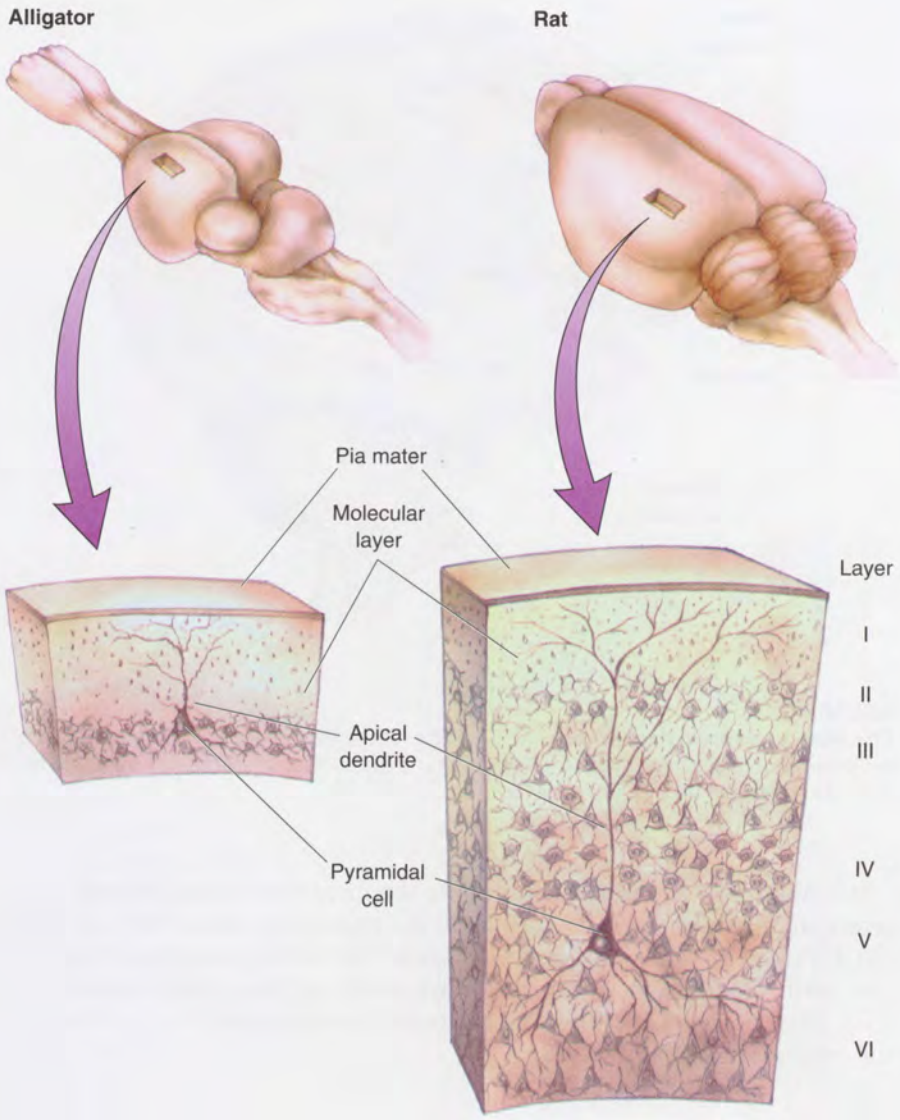


FIGURE 7.24
General features of the cerebral cortex. On the left is the structure of cortex in an alligator; on the right, a rat. In both species, the cortex lies just under the pia matter of the cerebral hemisphere, contains a molecular layer, and has pyramidal cells arranged in layers.

Figure 7.25 shows a Nissl-stained coronal section through the caudal telencephalon of a rat brain. You don't need to be Cajal to see that different types of cortex can also be discerned based on cytoarchitecture. Medial to the lateral ventricle is a piece of cortex that is folded onto itself in a peculiar shape. This structure is called the **hippocampus**, which, despite its bends, has only a single cell layer. (The term is from the Greek for "seahorse.") Connected to the hippocampus ventrally and laterally is another type of cortex that has only two cell layers. It is called the **olfactory cortex**, because it is continuous with the olfactory bulb, which sits farther anterior. The olfactory cortex is separated by a sulcus, called the *rhinal fissure*, from another more elaborate type of cortex that has many cell layers. This remaining cortex is called **neocortex**. Unlike the hippocampus and olfactory cortex, *neocortex is found only in mammals*. Thus, when we said previously that the cerebral cortex has expanded over the course of human evolution, we really meant that the neocortex has expanded. Similarly, when we said that the thalamus is the gateway to the cortex, we meant that it is the gateway to the neocortex. Most neuroscientists are such neocortical chauvinists (ourselves included) that the term cortex, if left unqualified, is usually intended to refer to the cerebral neocortex.

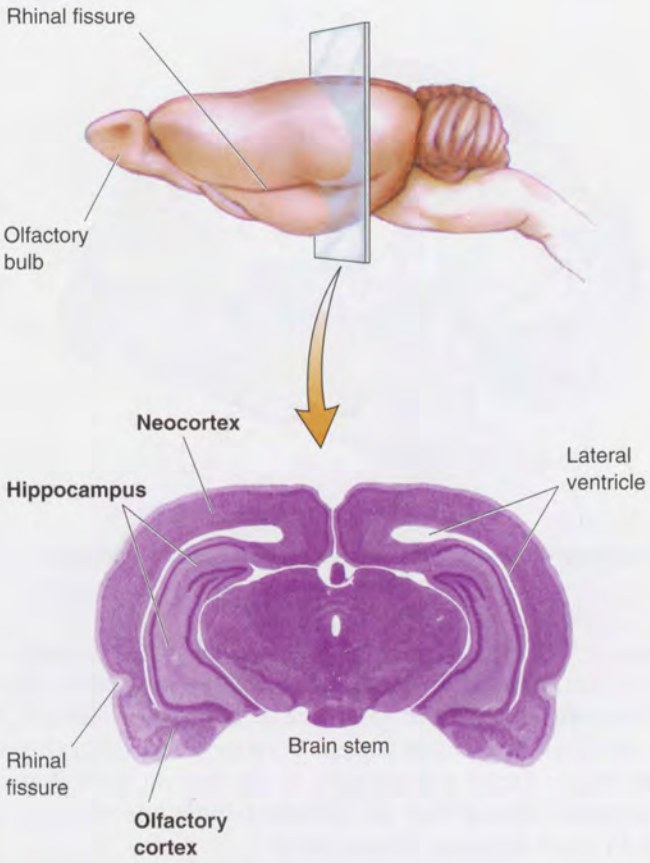


FIGURE 7.25
Three types of cortex in a mammal. In this section of a rat brain, the lateral ventricles lie between the neocortex and the hippocampus on each side. The ventricles are not obvious because they are very long and thin in this region. Below the telencephalon lies the brain stem. What region of brain stem is this, based on the appearance of the fluid-filled space at its core?

In Chapter 8, we will discuss the olfactory cortex in the context of the sense of smell. Further discussion of the hippocampus is reserved until later in this book, when we will explore its role in the limbic system (Chapter 18) and in memory and learning (Chapters 24 and 25). The neocortex will figure prominently in our discussions of vision, audition, somatic sensation, and the control of voluntary movement in Part II, so let's examine its structure in more detail.

Areas of Neocortex

Just as cytoarchitecture can be used to distinguish the cerebral cortex from the basal telencephalon, and the neocortex from the olfactory cortex, it can be used to divide the neocortex up into different zones. This is precisely what the famous German neuroanatomist Korbinian Brodmann did at the beginning of the twentieth century. He constructed a **cytoarchitectural map** of the neocortex (Figure 7.26). In this map, each area of cortex having a common cytoarchitecture is given a number. Thus, we have "area 17" at the tip of the occipital lobe, "area 4" just anterior to the central sulcus in the frontal lobe, and so on.

What Brodmann guessed, but could not show, was that cortical areas that look different perform different functions. We now have evidence that this is

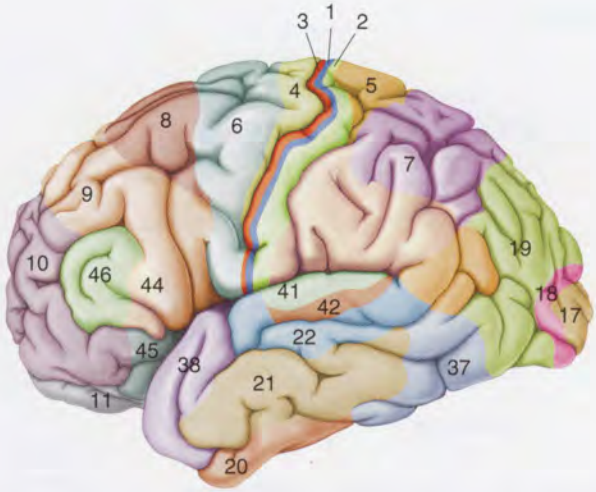


FIGURE 7.26
Brodmann's cytoarchitectural map of the human cerebral cortex.

true. For instance, we can say that area 17 is visual cortex because it receives signals from a nucleus of the thalamus that is connected to the retina at the back of the eye. Indeed, without area 17, a human is blind. Similarly, we can say that area 4 is motor cortex, because neurons in this area project axons directly to the motor neurons of the ventral horn that command muscles to contract. Notice that the different functions of these two areas are specified by their different connections.

Neocortical Evolution and Structure-Function Relationships. A problem that has fascinated neuroscientists since the time of Brodmann is how neocortex has changed over the course of mammalian evolution. The brain is a soft tissue, so there is not a fossil record of the cortex of our early mammalian ancestors. Nonetheless, considerable insight can be gained by comparing the cortex of different living species (see Figure 7.1). The surface area of the cortex varies tremendously among species; for example, a comparison of mouse, monkey, and human cortex reveals differences in size on the order of 1:100:1000. On the other hand, there is little difference in the thickness of the neocortex in different mammals, varying by no more than a factor of two. Thus, we can conclude that the amount of cortex has changed over the course of evolution, but not in its basic structure.

Brodmann proposed that neocortex expanded by the insertion of new areas. Leah Krubitzer at the University of California, Davis, has addressed this issue by studying the structure and function of different cortical areas in many different species (Box 7.5). Her research suggests that the primordial neocortex consisted mainly of three types of cortex—cortex that also exists to some degree in all living species. The first type consists of *primary sensory areas*, which are first to receive signals from the ascending sensory pathways. For example, area 17 is designated as primary visual cortex, or V1, because it receives input from the eyes via a direct path: retina to thalamus to cortex. The second type of neocortex consists of *secondary sensory areas*, so designated because of their heavy interconnections with the primary sensory areas. The third type of cortex consists of *motor areas*, which are intimately involved with the control of voluntary movement. These cortical areas receive inputs from thalamic nuclei that relay information from the basal telencephalon and the cerebellum, and they send

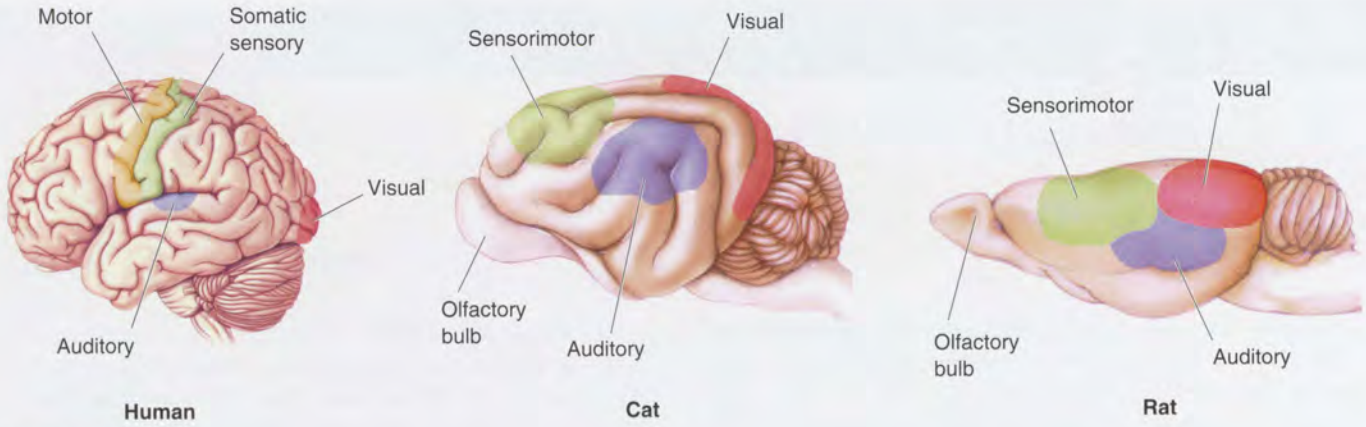


FIGURE 7.27
A lateral view of the cerebral cortex in three species. Notice the expansion of the human cortex that is neither strictly primary sensory nor strictly motor.

outputs to motor control neurons in the brain stem and spinal cord. For example, because cortical area 4 sends outputs directly to motor neurons in the ventral horn of the spinal cord, it is designated primary motor cortex, or M1. Krubitzer's analysis suggests that the common mammalian ancestor had on the order of about 20 different areas that could be assigned to these three categories.

Figure 7.27 shows views of the brain of a rat, a cat, and a human, with the primary sensory and motor areas identified. It is plain to see that when we speak of the expansion of the cortex in mammalian evolution, what has expanded is the region that lies in between these areas. Research by Jon Kaas at Vanderbilt University and others has shown that much of the "in-between" cortex reflects expansion of the number of secondary sensory areas devoted to the analysis of sensory information. For example, in primates that depend heavily on vision, such as humans, the number of secondary visual areas has been estimated to be between 20 and 40. However, even after we have assigned primary sensory, motor, and secondary sensory functions to large regions of cortex, a considerable amount of area remains in the human brain, particularly in the frontal and temporal lobes. These are the *association areas* of cortex. Association cortex is a more recent development, a noteworthy characteristic of the primate brain. The emergence of the "mind"—our unique ability to interpret behavior (our own and that of others) in terms of unobservable mental states, such as desires, intentions, and beliefs—correlates best with the expansion of the frontal cortex. Indeed, as we will see in Chapter 18, lesions of the frontal cortex can profoundly alter an individual's personality.

▼ CONCLUDING REMARKS

Although we have covered a lot of new ground in this chapter, we have only scratched the surface of neuroanatomy. Clearly, the brain deserves its status as the most complex piece of matter in the universe. What we have presented here is a shell, or scaffold, of the nervous system and some of its contents.

Understanding neuroanatomy is necessary for understanding how the brain works. This statement is just as true for an undergraduate first-time neuroscience student as it is for a neurologist or a neurosurgeon. In fact,

Box 7.5 PATH OF DISCOVERY

Evolution of My Brain

by Leah Krubitzer

How does evolution build a complex brain? How did some mammals, like humans, come to posses a brain with so many parts? Can I make one myself?

Let me assure you, this mad scientist did not hatch from an egg into a fully formed intellectual with questions in hand. My journey is probably not unlike your own. My direction was based on decisions made with little or no information, on taking roads that were somewhat off the beaten path and, most importantly, on a burning desire to find something I could be passionate about, something I could create, something that would help me make sense of the world.

I attended Pennsylvania State University as an undergraduate, a decision based primarily on the fact that I liked their football team. Like most undergraduates, I was faced with the dilemma of deciding what I was going to do with the rest of my life. My initial decision, prompted by meeting someone I thought was interesting at a wedding, after having consumed several glasses of champagne, was to major in speech pathology. By the time I realized that I was not a clinical sort of girl, that it was ridiculous to even consider helping others utter coherent sentences when I could barely do the same myself, and that I was simply not prepared to wear pantyhose every day for the rest of my life, it was too late. Upon graduation, although I did not know exactly what I wanted to do, I was sure I did not want to be a speech pathologist.

I decided to attend graduate school, mainly to postpone having to make the next big decision about my future. To my good fortune, at Vanderbilt University I met Jon Kaas, one of the forerunners in studies of brain evolution in primates. Since that day, my life has never been the same. I had finally found something that inspired me. It was in Jon's laboratory that I learned to critically think about how the neocortex might work and to interpret data in light of brain evolution. I immersed myself in the brain and allowed my thinking about evolution to become completely intertwined with my thoughts on every aspect of life, both scientific and personal. Science consumed me, and it was glorious. During this time, I also had a glimmer of an idea that there were underlying principles of brain construction that dictated how brains were made. While I did not know what these rules were, I was convinced that in order to understand them, one must consider the brain from an evolutionary perspective. Ironically, however, scientists who worked on brain evolution were becoming increasingly rare by 1988. New technologies such as single unit recordings in awake monkeys were all the rage in systems neuroscience, and these types of techniques, and the questions they addressed, seemed to eclipse the comparative approach to understanding brain evolution. As a result, most neuroscientists were not particularly interested in how brains evolved. Shocking, but true.

I pulled my head out of the clouds for a brief period and accepted a post-doctoral position at MIT to polish my pedigree with some cutting-edge technology. I was at the top of the heap, had quite a few publications for a new graduate student, had the world on a string—and was com-

neuroanatomy has taken on a new relevance with the advent of methods of imaging the living brain (Figure 7.28).

An Illustrated Guide to Human Neuroanatomy appears as an appendix to this chapter. Use the Guide as an atlas to locate various structures of interest. Labeling exercises are also provided to help you learn the names of the parts of the nervous system you will encounter in this book.

In Part II, Sensory and Motor Systems, the anatomy presented in Chapter 7 and its appendix will come alive, as we explore how the brain goes about the tasks of smelling, seeing, hearing, sensing touch, and moving.

pletely miserable. Although I knew this was a path I should follow for all of the obvious reasons, my heart wasn't in it. I made a major decision. I surrendered my position at MIT, followed my heart, and moved to Australia so that I could work on monotremes, such as the duck-billed platypus (Figure A) and spiny anteater. My reasoning was that if I wanted to study how the mammalian neocortex became really complex, the place to start was with the brain of an animal that diverged very early in mammalian evolution and still retained reptilian characteristics, such as egg-laying. I thought that perhaps the monotreme neocortex would better reflect that of the ancestral neocortex of all mammals, and I could have a better starting point for understanding how a basic plan was modified in different lineages.

It was there, in collaboration with Mike Calford and Jack Pettigew, that I really came to understand the evolution of the neocortex at a much deeper level. We worked on a number of amazing mammals, including monotremes, marsupials, and even large megachirpteran bats. I began to have an appreciation for the whole animal and its behaviors, rather than just the brain. In my mind, this work was critically important, and I spent far greater than an allotted two-year post-doc period in Australia. I remained there for more than 6 years.

Around 1994, the Australian government changed, and it became increasingly difficult to get funding to study brain evolution. Luckily, a new Center for Neuroscience at the University of California, Davis, had an opening for an evolutionary neurobiologist. I flew to Davis, gave a talk, and got the job. At U.C. Davis (1995 to the present), we began in earnest to test our theories of cortical evolution by manipulating the nervous system in developing animals, in an attempt to apply the rules of brain construction I envisioned from my work in Australia. Fortunately, recent advances in molecular developmental neurobiology have led to a resurgence of interest in brain evolution. Our goal is to mimic the evolutionary process to make new cortical areas, and then to determine how these changes result in alterations in behavior. This is a tall order, but a girl has got to have a dream.

FIGURE A
A duck-billed platypus.

KEY TERMS

Gross Organization of the Mammalian Nervous System

anterior (p. 168)
rostral (p. 168)
posterior (p. 168)
caudal (p. 168)
dorsal (p. 168)
ventral (p. 168)
midline (p. 170)
medial (p. 170)
lateral (p. 170)
ipsilateral (p. 170)
contralateral (p. 170)
midsagittal plane (p. 170)
sagittal plane (p. 170)
horizontal plane (p. 170)
coronal plane (p. 170)
central nervous system (CNS) (p. 171)
brain (p. 171)
spinal cord (p. 171)
cerebrum (p. 171)
cerebral hemispheres (p. 171)
cerebellum (p. 171)

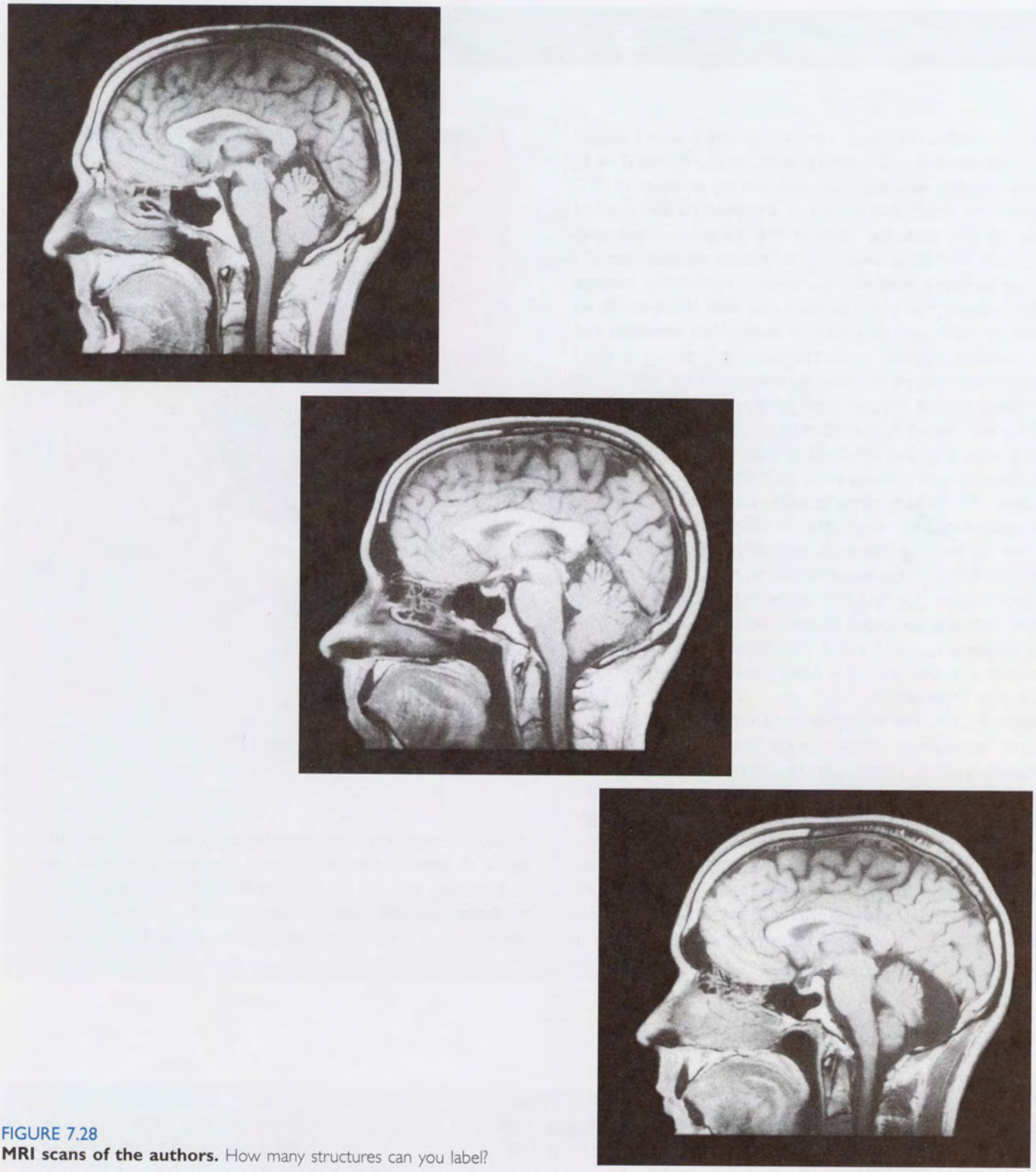


FIGURE 7.28
MRI scans of the authors. How many structures can you label?

brain stem (p. 171)
spinal nerve (p. 172)
dorsal root (p. 172)
ventral root (p. 172)
peripheral nervous system (PNS) (p. 172)
somatic PNS (p. 172)
dorsal root ganglion (p. 173)
visceral PNS (p. 173)
autonomic nervous system (ANS) (p. 173)
afferent (p. 173)
efferent (p. 173)
cranial nerve (p. 173)
meninges (p. 173)
dura mater (p. 173)
arachnoid membrane (p. 173)
pia mater (p. 174)
cerebrospinal fluid (CSF) (p. 174)
ventricular system (p. 174)

Understanding CNS Structure Through Development

gray matter (p. 180)
cortex (p. 180)
nucleus (p. 180)
substantia (p. 180)
locus (p. 180)
ganglion (p. 180)
nerve (p. 180)
white matter (p. 180)
tract (p. 180)
bundle (p. 180)
capsule (p. 180)
commissure (p. 180)
lemniscus (p. 180)
neural tube (p. 181)
neural crest (p. 181)
neurulation (p. 181)
differentiation (p. 182)
forebrain (p. 183)
midbrain (p. 183)
hindbrain (p. 183)
diencephalon (p. 184)
telencephalon (p. 184)
olfactory bulb (p. 184)
lateral ventricle (p. 184)
third ventricle (p. 184)
cerebral cortex (p. 184)
basal telencephalon (p. 184)
thalamus (p. 184)
hypothalamus (p. 184)
cortical white matter (p. 184)
corpus callosum (p. 184)
internal capsule (p. 184)
tectum (p. 187)
tegmentum (p. 187)
cerebral aqueduct (p. 187)
pons (p. 188)
medulla oblongata (medulla) (p. 188)
fourth ventricle (p. 188)
spinal canal (p. 190)
dorsal horn (p. 190)
ventral horn (p. 190)
sulcus (p. 194)
gyrus (p. 194)
temporal lobe (p. 194)
frontal lobe (p. 194)
central sulcus (p. 194)
parietal lobe (p. 194)
occipital lobe (p. 194)

A Guide to the Cerebral Cortex

hippocampus (p. 196)
olfactory cortex (p. 196)
neocortex (p. 196)
cytoarchitectural map (p. 197)

REVIEW QUESTIONS

1. Are the dorsal root ganglia in the central or peripheral nervous system?
2. Is the myelin sheath of optic nerve axons provided by Schwann cells or oligodendroglia? Why?
3. Imagine that you are a neurosurgeon, about to remove a tumor lodged deep inside the brain. The top of the skull has been removed. What now lies between you and the brain? Which layer(s) must be cut before you reach the CSF?
4. What is the fate of tissue derived from the embryonic neural tube? Neural crest?
5. Name the three main parts of the hindbrain. Which of these are also part of the brain stem?
6. Where is CSF produced? What path does it take before it is absorbed into the bloodstream? Name the parts of the CNS it will pass through in its voyage from brain to blood.
7. What are three features that characterize the structure of cerebral cortex?

FURTHER READING

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