## THE COGNITIVE NEUROSCIENTIST'S TOOLKIT Navigating the Brain

For anatomists, the head is merely an appendage to the body, so the terms that are used to describe the orientation of the head and its brain are in relation to the body. Confusion arises due to differences in how the head and body are arranged in animals that walk on four legs versus humans, who are upright. Let's first picture the body of the cutest kind of dog, an Australian shepherd, looking off to the left of the page (Figure 1, top). The front end is the rostral end, meaning "nose." The opposite end is the caudal end, the "tail." Along his back is the dorsal surface, just like the dorsal fin is on the back of a shark. The bottom surface along the dog's belly is the ventral surface. We can refer to the dog's nervous system by using the same coordinates (Figure 1, bottom). The part of the brain toward the front is the rostral end (toward the frontal lobes); the posterior end is the caudal end (toward the occipital lobe). Along the top of his head is the dorsal surface, and the bottom surface of the brain is the ventral surface.

We humans are atypical animals because we stand upright and, therefore, tilt our heads forward in order to be parallel with the ground. Thus, the dorsal surface of the body and brain are now at right angles to each other (Figure 2). Luckily, we have a cerebral cortex that can understand this. In humans, we also use the terms *superior* and *inferior* to refer to the top and bottom of the brain, respectively.

Similarly, along with the terms *rostral*, which still means "toward the frontal pole," and *caudal*, which still means "toward the occipital pole," *anterior* and *posterior* are also used to refer to the front and back of the brain, respectively.





When we consider the spinal cord, the coordinate systems align with the body axis. Thus, in the spinal cord, *rostral* means "toward the brain," just as it does in the dog.

Throughout this book, pictures of brain slices usually will be in one of three planes (Figure 3). If we slice it from nose to tail, that is a *sagittal* section. When that slice is directly through the middle, it is a *midsagittal* or *medial* section. If it is off to the side, it is a *lateral* section. If sliced from top to bottom, separating the front of the brain from the back, we have made a *coronal* section. If we slice in a plane that separates dorsal from ventral, that is known as either an *axial*, *transverse*, or *horizontal* section.



FIGURE 1 A dog brain in relation to the body.

FIGURE 3 Three orthogonal planes through the brain.

## HOW THE BRAIN WORKS The Chambers of the Mind

Scientists have understood for many decades that neurons in the brain are functional units, and that how they are interconnected yields specific circuits for the support of particular behaviors. Centuries ago, early anatomists, believing that the head contained the seat of behavior, examined the brain to see where the conscious self (soul, if you wish) was located. They found a likely candidate: Some chambers in the brain seemed to be empty (except for some fluid) and thus were possible containers for higher functions. These chambers are called *ventricles* (Figure 1). What is the function of these chambers within the brain?

The brain weighs a considerable amount but has little or no structural support; there is no skeletal system for the brain. To overcome this potential difficulty, the brain is immersed in a fluid called *cerebrospinal fluid* (CSF). This fluid allows the brain to float to help offset the pressure that would be present if the brain were merely sitting on the base of the skull. CSF also reduces shock to the brain and spinal cord during rapid accelerations or decelerations, such as when we fall or are struck on the head.

The ventricles inside the brain are continuous with the CSF surrounding the brain. The largest of these chambers are the lateral ventricles, which are connected to the third ventricle in the brain's midline. The cerebral aqueduct joins the third to the fourth ventricle in the brainstem below the cerebellum. The CSF is produced in the lateral ventricles and in the third ventricle by the choroid plexus, an outpouching of blood vessels from the ventricular wall. Hence, CSF is similar to blood, being formed from an ultrafiltrate of blood plasma; essentially, CSF is a clear fluid containing proteins, glucose, and ions, especially potassium, sodium, and chloride. It slowly circulates from the lateral and third ventricles through the cerebral aqueduct to the fourth ventricle and on to the subarachnoid space surrounding the brain, to be reabsorbed by the arachnoid villi in the sagittal sinus (the large venous system located between the two hemispheres on the dorsal surface; not shown).



FIGURE 1 Ventricles of the human brain. (left) Midsagital section showing the medial surface of the left hemisphere. (right) Transparent brain showing the ventricular system in 3D view.

white matter tracts. The more centrally located gray matter, consisting of neuronal bodies, resembles a butterfly with two separate sections or horns: the *dorsal horn* and *ventral horn*. The ventral horn contains the large motor neurons that project to muscles. The dorsal horn contains sensory neurons and interneurons. The interneurons project to motor neurons on the same (*ipsilateral*) and opposite (*contralateral*) sides of the spinal cord to aid in the coordination of limb movements. The gray matter surrounds the *central canal*, which is an anatomical extension of the ventricles in the brain and contains cerebrospinal fluid.



FIGURE 2.20 Gross anatomy of a brain showing brain stem. (a) Midsagittal section through the head, showing the brainstem, cerebellum, and spinal cord. (b) Highresolution structural MRI obtained with a 4-tesla scanner, showing the same plane of section as in (a).

## The Brainstem: Medulla, Pons, Cerebellum, and Midbrain

We usually think of the **brainstem** as having three main parts: the medulla (myelencephalon), the pons and cerebellum (metencephalon), and the midbrain (mesencephalon). These three sections form the central nervous system between the spinal cord and the diencephalon. Though the brainstem is rather small compared to the vast bulk of the forebrain (Figures 2.20 and 2.21), it plays a starring role in the brain. It contains groups of motor and sensory nuclei, nuclei of widespread modulatory neurotransmitter systems, and white matter tracts of ascending sensory information and descending motor signals.

Damage to the brainstem is life threatening, largely because brainstem nuclei control respiration and global states of consciousness such as sleep and wakefulness. The medulla, pons, and cerebellum make up the hindbrain, which we look at next.

**Meclulla** The brainstem's most caudal portion is the **medulla**, which is continuous with the spinal cord (Figure 2.21). The medulla is essential for life. It houses the cell bodies of many of the 12 cranial nerves, providing sensory and motor innervations to the face, neck, abdomen, and throat (including taste) as well as the motor nuclei that innervate the heart. The medulla controls vital functions such as respiration, heart rate, and arousal. All of the ascending somatosensory information entering from the spinal cord passes through the medulla via two bilateral nuclear groups, the *gracile* and *cuneate nuclei*. These projection systems continue through the brainstem

to synapse in the thalamus en route to the somatosensory cortex. Another interesting feature of the medulla is that the corticospinal motor axons, tightly packed in a pyramid-shaped bundle (called the *pyramidal tract*), cross here to form the *pyramidal decussation*. Thus, the motor neurons originating in the right hemisphere cross to control muscles on the left side of the body, and vice versa. Functionally, the medulla is a relay station for sensory and motor information between the body and brain; it is the crossroads for most of the body's motor fibers;



FIGURE 2.21 Lateral view of the brainstem showing the thalamus, pons, medulla, midbrain, and spinal cord. Anterior in the brain is at the top, and the spinal cord is toward the bottom in this left lateral view. The cerebellum is removed in this drawing.

it controls several autonomic functions, including the essential reflexes that determine respiration, heart rate, blood pressure, and digestive and vomiting responses.

**Pons** The **pons**, Latin for "bridge," is so named because it is the main connection between the brain and the cerebellum. Sitting anterior to the medulla, the pons is made up of a vast system of fiber tracts interspersed with nuclei (Figure 2.21). Many of the cranial nerves synapse in the pons; these include the sensory and motor nuclei from the face and mouth and the visuomotor nuclei controlling some of the extraocular muscles. Thus, the pons is important for some eye movements as well as those of the face and mouth. In addition, some auditory information is channeled through another pontine structure, the superior olive. This level of the brainstem contains a large portion of the reticular formation that modulates arousal. Interestingly, the pons is also responsible for generating rapid eye movement (REM) sleep.

**Cerebellum** The **cerebellum** (literally, "small cerebrum" or "little brain"), which clings to the brainstem at the level of the pons, is home to most of the brain's neurons (see Figures 2.20 and 2.22). Visually, the surface of the cerebellum appears to be covered with thinly spaced, parallel grooves; but in reality, it is a continuous layer of tightly folded neural tissue (like an accordion). It forms the roof of the fourth ventricle and sits on the cerebellar *peduncles* (meaning "feet"), which are massive input and output fiber tracts of the cerebellum (see Figure 2.21).





Anterior in the brain is at the top, and the spinal cord is toward the bottom (not shown). This dorsal view of the cerebellum shows the underlying deep nuclei in a see-through projection.

The cerebellum has several gross subdivisions, including the cerebellar cortex, four pairs of deep nuclei, and the internal white matter (Figure 2.22). In this way, the cerebellum resembles the forebrain's cerebral hemispheres.

Most of the fibers arriving at the cerebellum project to the cerebellar cortex, conveying information about motor outputs and sensory inputs describing body position. Inputs from vestibular projections involved in balance, as well as auditory and visual inputs, also project to the cerebellum from the brainstem. The output from the cerebellum originates in the deep nuclei. Ascending outputs travel to the thalamus and then to the motor and premotor cortex. Other outputs project to nuclei of the brainstem, where they impinge on descending projections to the spinal cord.

The cerebellum is critical for maintaining posture, walking, and performing coordinated movements. It does not directly control movements; instead, it integrates information about the body, such as its size and speed, with motor commands. Then, it modifies motor outflow to effect smooth, coordinated movements. It is because of the cerebellum that Yo-Yo Ma can play the cello and the Harlem Globetrotters can dunk a ball with such panache. If your cerebellum is damaged, your movements will be uncoordinated and halting, and you may not be able to maintain balance. In Chapter 8, we look more closely at the cerebellum's role in motor control. In the 1990s, it was discovered that the cerebellum is involved with more than motor functions. It has been implicated in aspects of cognitive processing including language, attention, learning, and mental imagery.

Midbrain The mesencephalon, or midbrain, lies superior to the pons and can be seen only in a medial view. It surrounds the cerebral aqueduct, which connects the third and fourth ventricles. Its dorsal portion consists of the tectum (meaning "roof"), and its ventral portion is the tegmentum ("covering"). Large fiber tracts course through the ventral regions from the forebrain to the spinal cord, cerebellum, and other parts of the brainstem. The midbrain also contains some of the cranial nerve ganglia and two other important structures: the superior and inferior colliculi (Figure 2.23). The superior colliculus plays a role in perceiving objects in the periphery and orienting our gaze directly toward them, bringing them into sharper view. The inferior colliculus is used for locating and orienting toward auditory stimuli. Another structure, the red nucleus, is involved in certain aspects of motor coordination. It helps a baby crawl or coordinates the swing of your arms as you walk. Much of the midbrain is occupied by the mesencephalic reticular formation, a rostral continuation of the pontine and medullary reticular formation.



FIGURE 2.23 Anatomy of the midbrain. The dorsal surface of the brainstem is shown with the cerebral cortex and cerebellum removed.

## **TAKE-HOME MESSAGES**

- The spinal cord conducts the final motor signals to the muscles, and it relays sensory information from the body's peripheral receptors to the brain.
- The brainstem's neurons carry out many sensory and motor processes, including visuomotor, auditory, and vestibular functions as well as sensation and motor control of the face, mouth, throat, respiratory system, and heart.
- The brainstem houses fibers that pass from the cortex to the spinal cord and cerebellum, and sensory fibers that run from spinal levels to the thalamus and then to the cortex.

- Many neurochemical systems have nuclei in the brainstem that project widely to the cerebral cortex, limbic system, thalamus, and hypothalamus.
- The cerebellum integrates information about the body and motor commands and modifies motor outflow to effect smooth, coordinated movements.

# The Diencephalon: Thalamus and Hypothalamus

After leaving the brainstem, we arrive at the diencephalon, which is made up of the **thalamus** and **hypothalamus**. These subcortical structures are composed of groups of nuclei with interconnections to widespread brain areas.

**Thalamus** Almost smack dab in the center of the brain and perched on top of the brainstem (at the rostral end; see Figure 2.21), the thalamus is the larger of the diencephalon structures. The thalamus is divided into two parts—one in the right hemisphere and one in the left—that straddle the third ventricle. In most people, the two parts are connected by a bridge of gray matter called the *massa intermedia* (see Figure 2.23). Above the thalamus are the fornix and corpus callosum; beside it is the *internal capsule*, containing ascending and descending axons running between the cerebral cortex and the medulla and spinal cord.

The thalamus has been referred to as the "gateway to the cortex" because, except for some olfactory inputs, all of the sensory modalities make synaptic relays in the thalamus before continuing to the primary cortical sensory receiving areas (Figure 2.24). The thalamus is involved in relaying primary sensory information. It also receives inputs from the basal ganglia, cerebellum, neocortex, and medial temporal lobe and sends projections back to these structures to create circuits involved in many different functions. It also relays



FIGURE 2.24 The thalamus, showing inputs and outputs and major subdivisions. The various subdivisions of the thalamus serve different sensory systems and participate in various cortical-subcortical circuits. The posterior portion of the thalamus (lower right) is cut away in cross section and separated from the rest of the thalamus to reveal the internal organization of the thalamic nuclei (upper left). most of the motor information that is on its way to the spinal cord. Thus, the thalamus, a veritable Grand Central Station of the brain, is considered a relay center where neurons from one part of the brain synapse on neurons that travel to another region. In the thalamus, information can be reorganized and shuttled, like in a train station switching yard, according to the connection patterns formed by the neurons.

The thalamus is divided into several nuclei that act as specific relays for incoming sensory information (Figure 2.24). The lateral geniculate nucleus receives information from the ganglion cells of the retina and sends axons to the primary visual cortex. Similarly, the medial geniculate nucleus receives information from the inner ear, via other brainstem nuclei in the ascending auditory pathway, and sends axons to the primary auditory cortex. Somatosensory information projects via the ventral posterior (medial and lateral) nuclei of the thalamus to the primary somatosensory cortex. Sensory relay nuclei of the thalamus not only project axons to the cortex but also receive heavy descending projections back from the same cortical area that they contact. Located at the posterior pole of the thalamus is the pulvinar nucleus, which is involved in attention and in integrative functions involving multiple cortical areas.

**Hypothalamus** The main link between the nervous system and the endocrine system is the hypothalamus, which is the main site for hormone production and control. Easily located, it lies on the floor of the third ventricle (see Figure 2.20a). The two bumps seen on the ventral surface of the brain, the *mammillary bodies*, belong to the small collection of nuclei and fiber tracks contained in the hypothalamus (Figure 2.25). It receives inputs from the limbic system structures and other brain areas. One of its jobs is to control circadian rhythms (light–dark cycles) with inputs from the mesencephalic reticular formation, amygdala, and the retina. Extending from the hypothalamus are major projections to the prefrontal cortex, amygdala, spinal cord, and pituitary gland. The pituitary gland is attached to the base of the hypothalamus.

The hypothalamus controls the functions necessary for maintaining the normal state of the body (homeostasis). It sends out signals that drive behavior to alleviate such feelings as thirst, hunger, and fatigue, and it controls body temperature and circadian cycles. You would not want to be in the broiling hot desert without your hypothalamus. It accomplishes much of this work through the endocrine system and via control of the **pituitary gland**.

The hypothalamus produces hormones, as well as factors that regulate hormone production in other parts of the brain. For example, hypothalamic neurons send axonal projections to the *median eminence*, an area bordering the pituitary gland. There it releases peptides (releasing factors) into the circulatory system of the



FIGURE 2.25 Midsagittal view of the hypothalamus. Various nuclear groups are shown diagrammatically. The hypothalamus is the floor of the third ventricle, and, as the name suggests, it sits below the thalamus. Anterior is to the left in this drawing.

anterior pituitary gland. These in turn trigger (or inhibit) the release of a variety of hormones from the anterior pituitary into the bloodstream, such as growth hormone, thyroid-stimulating hormone, adrenocorticotropic hormone, and the gonadotropic hormones.

Hypothalamic neurons in the anteromedial region, including the *supraoptic nucleus* and *paraventricular nuclei*, send axonal projections into the posterior pituitary gland. There they stimulate the gland to release the hormones vasopressin and oxytocin into the blood to regulate water retention in the kidneys, milk production, and uterine contractility, among other functions. Circulating peptide hormones in the bloodstream can also act on distant sites and influence a wide range of behaviors, from the fightor-flight response to maternal bonding. The hypothalamus can itself be stimulated by hormones circulating in the blood that were produced in other regions of the body.

## **TAKE-HOME MESSAGES**

- The thalamus is the relay station for almost all sensory information.
- The hypothalamus is important for the autonomic nervous system and endocrine system. It controls functions necessary for the maintenance of homeostasis. It is also involved in control of the pituitary gland.
- The pituitary gland releases hormones into the bloodstream where they can circulate to influence other tissues and organs (e.g., gonads).

## The Telencephalon: Limbic System, Basal Ganglia, and Cerebral Cortex

Toward the front of and evolutionarily newer than the diencephalon, the telencephalon develops into the cerebrum, which includes the cerebral cortex, the limbic system, and the basal ganglia. Compared to the diencephalon, the anatomy (and functions) of the forebrain above the thalamus are less straightforward. Instead of a rather linear stacking of structures, it forms a clump of structures found deep within the cerebral hemispheres nestled over and around the diencephalon. In the 17th century, Thomas Willis observed that the brainstem appeared to sport a cortical border encircling it and named it the cerebri limbus (in Latin, limbus means "border"). For better or for worse, in a move that began to tie the area with specific functioning, Paul Broca in 1878 renamed it the grand lobe limbique and suggested that it was a primary player in olfaction.

**Limbic System** The "classical" limbic lobe (Figure 2.26) is made up of the *cingulate gyrus* (a band of cerebral cortex that extends above the corpus callosum in the anterior–posterior direction and spans both the frontal and parietal lobes), the hypothalamus, anterior thalamic nuclei, and the **hippocampus**, an area located on the

ventromedial aspect of the temporal lobe. In the 1930s James Papez (pronounced "payps") first suggested the idea that these structures were organized into a system for emotional behavior, which led to the use of the term Papez circuit. It was named the limbic system by Paul MacLean in 1952 when he suggested the addition of more brain areas, such as the amygdala and prefrontal cortex. Note that the limbic system is neither anatomically nor functionally organized to the degree that other systems are in the brain. In fact, some researchers feel that the limbic system is sufficiently nebulous that the concept should be discarded or reevaluated. The classical limbic system, as noted earlier, has been extended to include the **amygdala**, a group of neurons anterior to the hippocampus, along with the orbitofrontal cortex and parts of the basal ganglia (see Figure 2.26). Sometimes the medial dorsal nucleus of the thalamus is also included. The organization and role of the limbic system are described in more detail in Chapter 10.

**Basal Ganglia** The **basal ganglia** are a collection of nuclei bilaterally located deep in the brain beneath the anterior portion of the lateral ventricles, near the thalamus (Figure 2.27). These subcortical nuclei, the *caudate nucleus*, *putamen*, *globus pallidus*, *subthalmic nucleus*, and *substantia nigra*, are extensively interconnected. The caudate nucleus together with the putamen is



### FIGURE 2.26 The human limbic system.

(a) Anatomy of the limbic system. (b) Major connections of the limbic system, shown diagrammatically in a medial view of the right hemisphere. The figure zooms in on the region in purple in (a). The basal ganglia are not represented in this figure, nor is the medial dorsal nucleus of the thalamus. More detail is shown here than needs to be committed to memory, but this figure provides a reference that will come in handy in later chapters.





## FIGURE 2.27 Coronal and transparent views of the brain showing the basal ganglia.

(a) Cross sections through the brain at two anterior-posterior levels (as indicated), showing the basal ganglia. The inset shows a transparent brain with the basal ganglia in 3D in blue. (b) Corresponding high-resolution, structural MRI (4-tesla scanner) taken at approximately the same level as the more posterior drawing in (a). This image also shows the brainstem as well as the skull and scalp, which are not shown in (a).

known as the striatum. The basal ganglia receive inputs from sensory and motor areas, and the striatum receives extensive feedback projections from the thalamus. A comprehensive understanding of how these deep brain nuclei function remains elusive. They are involved in a variety of crucial brain functions including action selection, action gating, motor preparation, timing, fatigue, and task switching (Cameron et al., 2009). Notably, the basal ganglia have many dopamine receptors. The dopamine signal appears to represent the error between predicted future reward and actual reward (Shultz et al., 1997), and plays a crucial role in motivation and learning. The basal ganglia may also play a big role in reward-based learning and goal-oriented behavior. One summary of basal ganglia function proposes that it combines an organism's sensory and motor context with reward information and passes this integrated information to the motor and prefrontal cortex for a decision (Chakravarthy et al., 2009).

## **TAKE-HOME MESSAGES**

- The limbic system includes subcortical and cortical structures that are interconnected and play a role in emotion.
- The basal ganglia are involved in a variety of crucial brain functions, including action selection, action gating, reward-based learning, motor preparation, timing, task switching, and more.

## The Cerebral Cortex

The crowning glory of the cerebrum is its outermost tissue, the cerebral cortex. It is made up of large sheets of (mostly) layered neurons, draped and folded over the two symmetrical hemispheres like frosting on a cake. It sits over the top of the core structures that we have been discussing, including parts of the limbic system and basal ganglia, and surrounds the structures of the diencephalon. The term cortex means "bark," as in tree bark, and in higher mammals and humans it contains many infoldings, or convolutions (Figure 2.28). The infoldings of the cortical sheet are called sulci (the crevices) and gyri (the crowns of the folded tissue that one observes when viewing the surface).

The folds of the human cortex serve several functions. First, they enable more cortical surface to be packed into the skull. If the human cortex were smoothed out to resemble that of the rat, for example, humans would need to have very large heads. The total surface area of the human cerebral cortex is about 2,200 to 2,400 cm<sup>2</sup>, but because of extensive folding, about two thirds of this area is confined within the depths of the sulci. Second, having a highly folded cortex brings neurons into closer threedimensional relationships to one another, reducing axonal distance and hence neuronal conduction time between different areas. This savings occurs because the axons that make long-distance corticocortical connections run under the cortex through the white matter and do not follow the foldings of the cortical surface in their paths to



## FIGURE 2.28 The human cerebral cortex.

Lateral view of the left hemisphere (a) and dorsal view of the brain (b) in humans. The major features of the cortex include the four cortical lobes and various key gyri. Gyri are separated by sulci and result from the folding of the cerebral cortex that occurs during development of the nervous system, to achieve economies of size and functionality.



#### FIGURE 2.29 Cerebral cortex and white matter tracts.

(a) Horizontal section through the cerebral hemispheres at the level indicated at upper left. White matter is composed of myelinated axons, and gray matter is composed primarily of neurons. This diagram shows that the gray matter on the surface of the cerebral hemispheres forms a continuous sheet that is heavily folded. (b) High-resolution structural MRI in a similar plane of section in a living human. This T2 image was obtained on a 4-tesla scanner (a high-magnetic-field scanner). Note that on T2 images, the white matter appears darker than the gray matter, but this is due to the imaging technique, not the actual appearance.

distant cortical areas. Third, by folding, the cortex brings some nearby regions closer together; for example, the opposing layers of cortex in each gyrus are in closer linear proximity than they would be if the gyri were flattened.

The cortex ranges from 1.5 to 4.5 mm in thickness, but in most regions it is approximately 3 mm thick. The cortex contains the cell bodies of neurons, their dendrites, and some of their axons. In addition, the cortex includes axons and axon terminals of neurons projecting to the cortex from other brain regions, such as the subcortical thalamus. The cortex also contains blood vessels. Because the cerebral cortex has such a high density of cell bodies, it appears grayish in relation to underlying regions that are composed primarily of the axons that connect the neurons of the cerebral cortex to other locations in the brain. These appear slightly paler or even white (Figure 2.29) because of their lipid sheaths (myelin). As described earlier, for this reason anatomists used the terms *gray matter* and *white matter* when referring to areas of cell bodies and axon tracts, respectively.

## Dividing the Cortex Anatomically

The cerebral hemispheres have four main divisions, or lobes, that are best seen in a lateral view: the **frontal**, **parietal**, **temporal**, and **occipital lobes** (Figure 2.30).

These names are derived from names given to the overlying skull bones; for example, the temporal lobe lies underneath the temporal bone. The skull bones themselves are named for their locations. The temporal bone lies under the temple, where the passage of time can be



FIGURE 2.30 The four lobes of the cerebral cortex.

This is a lateral view of the left hemisphere showing the four major lobes of the brain, and some of the major landmarks that separate them.