chapter 1

The Development of Neuropsychology

In Sophocles' (496–406 B.C.) play *Oedipus the King,* Oedipus finds his way blocked by the Sphinx, who threatens to kill him unless he can answer this riddle: "What walks on four legs in the morning, two legs at noon, and three legs in the evening?" Oedipus replies, "A human," and is allowed to pass, because a person crawls as an infant, walks as an adult, and uses a cane when old. The Sphinx's riddle is the riddle of human nature, and as time passes Oedipus comes to understand that it has a deeper meaning: "What *is* a human?" The deeper question in the riddle confounds Oedipus and remains unanswered to this day. The object of this book is to pursue the answer in the place where it should be logically found: the brain.

The term *neuropsychology* in its English version originated quite recently, in part because it represented a new approach to studying the brain. According to Daryl Bruce, it was first used by Canadian physician William Osler in his early-twentieth-century textbook, which was a standard medical reference of the time. It later appeared as a subtitle to Canadian psychologist Donald O. Hebb's 1949 treatise on brain function, *The Organization of Behavior: A Neuropsychological Theory.* Although Hebb neither defined nor used the word in the text itself, he probably intended it to represent a multidisciplinary focus of scientists who believed that an understanding of human brain function was central to understanding human behavior. By 1957, the term had become a recognized designation for a subfield of the neurosciences. Heinrich Kluver, an American investigator into the neural basis of vision, wrote in the preface to his *Behavior Mechanism in Monkeys* that the book would be of interest to neuropsychologists and others. (Kluver had not used the term in the 1933 preface to the same book.) In 1960, it appeared in the title of a widely read collection of writings by American psychologist Karl S. Lashley—*The Neuropsychology of Lashley*—most of which described rat and monkey studies directed toward understanding memory, perception, and motor behavior. Again, *neuropsychology* was neither used nor defined in the text. To the extent that they did use the term, however, these writers, who specialized in the study of basic brain function in animals, were recognizing the emergence of a subdiscipline of investigators who specialized in human research and would find the animal research relevant to understanding human brain function.

Today, we define **neuropsychology** as the study of the relation between human brain function and behavior. Although neuropsychology draws information from many disciplines—for example, anatomy, biology, biophysics, ethology, pharmacology, physiology, physiological psychology, and philosophy—its central focus is the development of a science of human behavior based on the function of the human brain. As such, it is distinct from **neurology,** which is the diagnosis of nervous system injury by physicians who are specialists in nervous system diseases, from **neuroscience,** which is the study of the molecular basis of nervous system function by scientists who mainly use nonhuman animals, and from **psychology,** which is the study of behavior more generally.

Neuropsychology is strongly influenced by two traditional foci of experimental and theoretical investigations into brain function: the **brain hypothesis,** the idea that the brain is the source of behavior; and the **neuron hypothesis,** the idea that the unit of brain structure and function is the neuron. This chapter traces the development of these two ideas. We will see that, although the science is new, its major ideas are not.

The Brain Hypothesis

People knew what the brain looked like long before they had any idea of what it did. Very early in human history, hunters must have noticed that all animals have a brain and that the brains of different animals, including humans, although varying greatly in size, look quite similar. Within the past 2000 years, anatomists began producing drawings of the brain and naming some of its distinctive parts without knowing what function the brain or its parts performed. We will begin this chapter with a description of the brain and some of its major parts and will then consider some major insights into the functions of the brain.

What Is the Brain?

Brain is an Old English word for the tissue that is found within the skull. Figure 1.1 shows a typical human brain as oriented in the skull of an upright human. The brain has two relatively symmetrical halves called **hemispheres,** one on the left side of the body and one on the right. Just as your body is symmetrical, having two arms and two legs, so is the brain. If you make your right hand into a fist and hold it up with the thumb pointing toward the front, the fist can represent the position of the brain's left hemisphere within the skull.

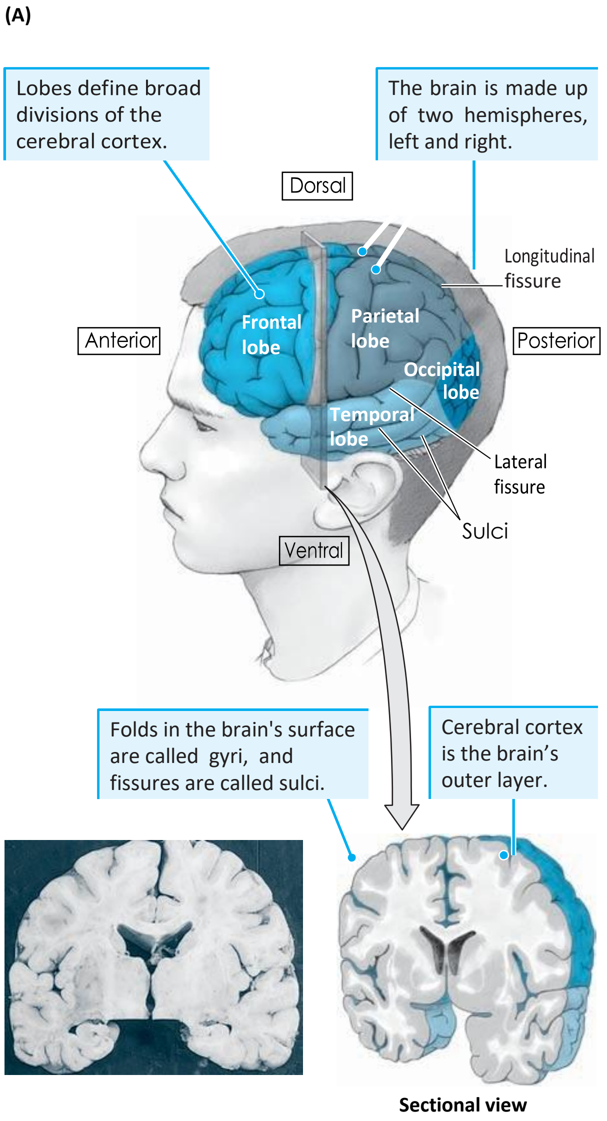
Taken as a whole, the basic plan of the brain is that of a tube filled with fluid, called **cerebrospinal fluid** (CSF). Parts of the covering of the tube have bulged outward and folded, forming the more complicated looking surface structures that initially catch the eye. The most conspicuous outer feature of the brain consists of a crinkled tissue that has expanded from the front of the tube to such an extent that it folds over and covers much of the rest of the brain. This outer layer is known as the **cerebral cortex** (usually referred to as just the cortex). The word *cortex,* which means "bark" in Latin, is aptly chosen both because the cortex's folded appearance resembles the bark of a tree and because its tissue covers most of the rest of the brain, just as bark covers a tree.

The folds of the cortex are called **gyri,** and the creases between them are called **sulci** (*gyrus* is Greek for "circle" and *sulcus* is Greek for "trench"). Some large sulci are called fissures, such as the **longitudinal fissure** that divides the two hemispheres and the **lateral fissure** that divides each hemisphere into halves (in our fist analogy, the lateral fissure is the crease separating the thumb from the other fingers).

The cortex of each hemisphere is divided into four lobes, named after the skull bones beneath which they lie. The **temporal lobe** is located at approximately the same place as the thumb on your upraised fist. The lobe lying immediately above the temporal lobe is called the **frontal lobe** because it is located at the front of the brain. The **parietal lobe** is located behind the frontal lobe, and the **occipital lobe** constitutes the area at the back of each hemisphere.

The cerebral cortex comprises most of the **forebrain,** so named because it develops from the front part of the tube that makes up the embryo's primitive brain. The remaining "tube" underlying the cortex is referred to as the **brainstem.** The brainstem is in turn connected to the **spinal cord,** which descends down the back in the vertebral column. To visualize the relations between these parts of the brain, again imagine your upraised fist: the folded fingers represent the cortex, the hand represents the brainstem, and the arm represents the spinal cord.

This three-part division of the brain is conceptually useful evolutionarily, anatomically, and functionally. Evolutionarily, animals with only spinal cords preceded those with brainstems, which preceded those with forebrains. Likewise, in prenatal development, the spinal cord forms before the brainstem, which forms before the forebrain. Functionally, the forebrain mediates cognitive functions; the brainstem mediates regulatory functions such as eating, drinking, and moving;

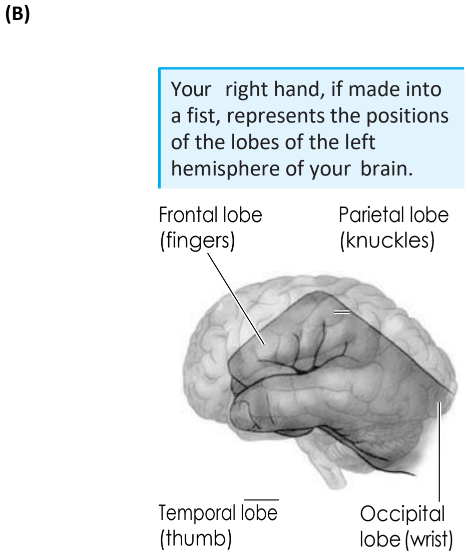


Lobes define broad divisions of the cerebral cortex.

The brain is made up of two hemispheres, left and right.

Folds in the brain's surface are called gyri, and fissures are called sulci.

Cerebral cortex is the brain's outer layer.



Your right hand, if made into a fist, represents the positions of the lobes of the left hemisphere of your brain.

Figure 1.1 (A) This representation of the human brain shows its orientation in the head. The visible part of the intact brain is the cerebral cortex, a thin sheet of tissue folded many times and fitting snugly inside the skull. (B) Your right fist can serve as a guide to the orientation of the brain and its lobes. (Glauberman/Photo Researchers.)

and the spinal cord is responsible for sending commands to the muscles. Neuropsychologists commonly refer to functions of the forebrain as being higher functions because they include thinking, perception, and planning. The regulatory and movement-producing functions of the brainstem and spinal cord are thus sometimes referred to as lower-level functions.

How Is the Brain Related to the Rest of the Nervous System?

The brain and spinal cord in mammals such as ourselves are protected by bones: the skull protects the brain, and the vertebra protect the spinal cord. Because they are both enclosed within this protective covering, the brain and spinal cord together are called the **central nervous system** or CNS. The central nervous system is connected to the rest of the body through **nerve fibers,** some of which carry information away from the CNS and some of which bring information to it. These fibers constitute the **peripheral nervous system,** or PNS.

The fibers that bring information to the CNS are extensively connected to sensory receptors on the body's surface, to internal body organs, and to muscles, enabling the brain to sense what goes on in the world around us and in our body. These fibers are organized into **sensory pathways,** collections of fibers that carry messages for specific sensory systems, such as hearing, vision, and touch. Using information gathered by the various sensory receptors and sent to the brain over these pathways, the brain constructs its current images of the world, its memories of past events, and its expectations about the future. The **motor pathways** are the groups of fibers that connect the brain and spinal cord to the body's muscles. The movements produced by motor pathways include the eye movements that you are using to read this book, the hand movements that you make while turning the pages, and the posture of your body as you read. Motor pathways also influence movements in the muscles of your internal organs, such as the beating of your heart, the contractions of your stomach, and the raising and lowering of your diaphragm, which inflates and deflates your lungs. The pathways that control these organs are a subdivision of the PNS called the **autonomic nervous system.**

The Brain Versus the Heart

Since earliest times, people have puzzled over how behavior is produced. Their conclusions are preserved in the historical records of many different cultures. Among the oldest surviving recorded hypotheses are those of two Greeks, Alcmaeon of Croton (ca. 500 B.C.) and Empedocles of Acragas (ca. 490– 430 B.C.). Alcmaeon located mental processes in the brain and so subscribed to what is now called the *brain hypothesis;* Empedocles located them in the heart and so subscribed to what could be called the *cardiac hypothesis.*

The relative merits of those two hypotheses were debated for the next 2000 years. For example, among Greek philosophers, Plato (427?–347 B.C.) developed the concept of a tripartite soul (nutritive, perceptual, and rational) and placed its rational part in the brain because that was the part of the body closest to the heavens. Aristotle (384–322 B.C.) had a good knowledge of brain structure and realized that, of all animals, humans have the largest brain relative to body size. Nevertheless, he decided that, because the heart is warm and active, it is the source of mental processes, whereas the brain, because it is cool and inert, serves as a radiator to cool the blood (actually, it turns out that the blood cools the brain). He interpreted the large size of the human brain as evidence that our blood is richer and hotter than that of other animals and so requires a larger cooling system.

Early Greek and Roman physicians, such as Hippocrates (ca. 460–377 B.C.) and Galen (A.D. 129–ca. 199), influenced by their clinical experience, described aspects of the brain's anatomy and argued strongly for the brain hypothesis. Before becoming the leading physician in Rome, Galen spent 5 years as a surgeon to gladiators and witnessed some of the behavioral consequences of brain damage. He went to great pains to refute Aristotle, pointing out that not only did brain damage impair behavior but the nerves from the sense organs go to the brain and not to the heart. He also reported on his experiences in attempting to treat wounds to the brain or heart. He noted that pressure on the brain causes cessation of movement and even death, whereas pressure on the heart causes pain but does not arrest voluntary behavior.

Although we now accept the brain hypothesis, the cardiac hypothesis has left its mark on our language. In literature, as in everyday speech, emotion is frequently ascribed to the heart: love is symbolized by an arrow piercing the heart; a person distressed by unrequited love is said to be heartbroken; an unenthusiastic person is described as not putting his or her heart into it; an angry person says, "It makes my blood boil."

Descartes: The Mind–Body Problem

Simply knowing that the brain controls behavior is not enough; the formulation of a complete hypothesis of brain function requires knowing *how* the brain controls behavior. Modern thinking about this question began with René Descartes (1596–1650), a French anatomist and philosopher. Descartes replaced the Platonic concept of a tripartite soul with a single soul that he called the **mind.** Described as nonmaterial and without spatial extent, the mind, as Descartes saw it, was different from the body. The body operated on principles similar to those of a machine, but the mind decided what movements the machine should make. Descartes was impressed by machines made in his time, such as those of certain statues that were on display for public amusement in the water gardens of Paris. When a passerby stopped in front of one particular statue, for example, his or her weight would depress a lever under the sidewalk, causing the statue to move and spray water at the person's face. Descartes proposed that the body is like these machines. It is material and thus clearly has spatial extent, and it responds mechanically and reflexively to events that impinge upon it (Figure 1.2).

Figure 1.2 The concept of a reflex action originated with Descartes. In this very mechanistic depiction of how he thought physical reflexes might work, heat from the flame causes a thread in the nerve to be pulled, releasing ventricular fluid through an opened pore. The fluid flows through the nerve, causing not only the foot to withdraw but also the eyes and head to turn to look at it, the hands to advance, and the whole body to bend to protect it. Descartes applied the reflex concept to behaviors that would today be considered too complex to be reflexive, whereas behavior described as reflexive today was not conceived of by Descartes. (From Descartes, 1664.)

The position that mind and body are separate but can interact is called **dualism,** to indicate that behavior is caused by two things. Descartes's dualism originated what came to be known as the **mind–body problem:** for Descartes, a person is capable of being conscious and rational only because of having a mind, but how can a *nonmaterial* mind produce movements in a *material* body? To understand the problem, consider that, in order for the mind to affect the body, it would have to expend energy, adding new energy to the material world. The creation of new energy would violate a fundamental law of physics. Thus, dualists who argue that the two interact causally cannot explain how. Other dualists avoid this problem by reasoning either that the mind and body function in parallel without interacting or that the body can affect the mind but the mind cannot affect the body. These dualist positions allow for both a body and a mind by sidestepping the problem of violating the laws of physics. Other philosophers called **monists** avoid the mind–body problem by postulating that the mind and body are simply two words for the same thing and both are either material or nonmaterial. Most neuropsychologists are materialists and hold that the terms *mind* and *brain* are two different ways of describing the same object. Clearly, it would be difficult to be a neuropsychologist who is a nonmaterialist, because such a person would believe that there are no physical things to study.

In addition to being a dualist, Descartes ascribed functions to different parts of the brain. He located the site of action of the mind in the **pineal body,** a small structure in the brainstem. His choice of this structure was based on the logic that the pineal body is the only structure in the nervous system not composed of two bilaterally symmetrical halves and moreover that it is located close to the ventricles. His idea was that the mind in the pineal body controlled valves that allowed cerebral spinal fluid to flow from the ventricles through nerves to muscles, filling them and making them move. For Descartes, the cortex was not functioning neural tissue but merely a covering for the pineal body. People later argued against Descartes's hypothesis by pointing out that, when the pineal body was found to be damaged, there were no obvious changes in behavior. Today the pineal body is thought to take part in controlling seasonal rhythms.

In proposing his dualistic theory of brain function, Descartes also proposed that animals did not have minds and so were only machinelike. The inhumane treatment of animals, children, and the mentally ill was justified on the grounds that they did not have minds by some followers of Descartes. For them, an animal did not have a mind, a child developed a mind only when about 7 years of age and able to talk and reason, and the mentally ill had "lost their minds." Misunderstanding Descartes's position, some people still argue that the study of animals cannot be a source of useful insight into human neuropsychology. Descartes himself, however, was not so dogmatic. Although he proposed the idea that animals and humans are different with respect to having a mind, he also suggested that the idea could be tested experimentally. He proposed that the key indications of the presence of a mind are the use of language and reason. He suggested that, if it could be demonstrated that animals could speak or reason, then such demonstration would indicate that they have minds. As we will note later on, some lines of research in modern experimental neuropsychology are directed toward the comparative study of animals and humans with respect to these abilities.

Darwin and Materialism

By the mid–nineteenth century, another theory of the brain and behavior was taking shape. This was the modern perspective of **materialism** — the idea that rational behavior can be fully explained by the working of the nervous system, without any need to refer to a nonmaterial mind. This perspective had its roots in the evolutionary theories of two English naturalists, Alfred Russell Wallace (1823–1913) and Charles Darwin (1809 –1892).

Wallace and Darwin independently arrived at the same conclusion—the idea that all living things are related. Darwin arrived at the idea much earlier than Wallace did but failed to publish his writing at that time. So that both could receive credit for the idea, their papers were presented together before the Linnaean Society of London in July 1858. Darwin elaborated further on the topic in *On the Origin of Species by Means of Natural Selection,* published in 1859.

Both Darwin and Wallace looked carefully at the structures of plants and animals and at animal behavior. Despite the diversity of living organisms, they were struck by the number of similarities and common characteristics. For example, the skeleton, muscles, internal organs, and nervous systems of humans, monkeys, and other mammals are remarkably similar. These observations supported the idea that living things must be related, an idea widely held even before Wallace and Darwin. But more importantly, these same observations led to the idea that the similarities could be explained if all animals evolved from a common ancestor.

Darwin argued that all organisms, both living and extinct, are descended from some unknown ancestor that lived in the remote past. In Darwin's terms, all living things are said to have **common descent.** As the descendants of that original organism spread into various habitats through millions of years, they developed structural and behavioral adaptations that suited them for new ways of life. At the same time, they retained many similar traits that reveal their relatedness to one another. The brain is one such common characteristic found in animal species. It is an adaptation that emerged only once in animal evolution. Consequently, the brains of living animals are similar because they are descendents of that first brain. Furthermore, if animals are related and their brains are related and if all behavior of nonhuman animals is a product of their brains, then all human behavior must also be a product of the brain.

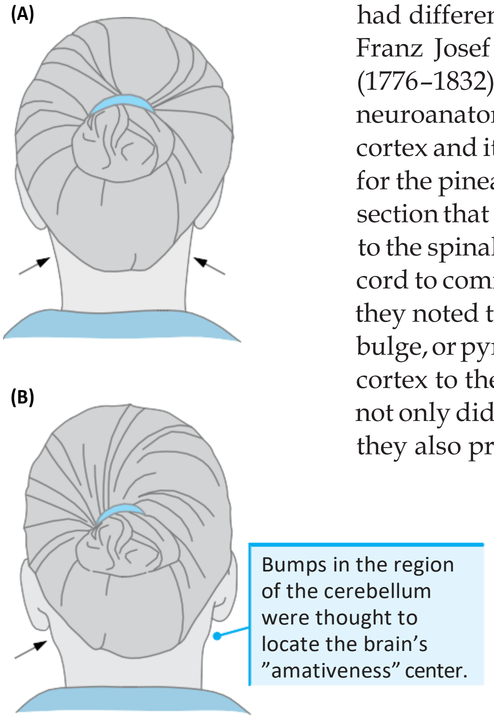
Some people reject the idea that the brain is responsible for behavior, because they think it denies the teaching of their religion that there is a nonmaterial soul that will continue to exist after their bodies die. Others regard the biological explanation of brain and behavior as being neutral with respect to religion. Many behavioral scientists with strong religious beliefs see no contradiction between those beliefs and using the scientific method to examine the relations between the brain and behavior.

Experimental Approaches to Brain Function

Philosophical and theoretical approaches to brain function do not require physical measures of the brain or experimental methods for testing hypotheses. Those methods belong to science. Beginning in the early 1800s, scientists began to test their ideas about brain function by examining and measuring the brain and by developing methods to describe behavior quantitatively (so that researchers could check one another's conclusions). In this section, we will describe a number of influential experimental approaches to the study of brain function and some of the important neuropsychological ideas that resulted from them.

Localization of Function

Philosophers who argue that the mind controls behavior see "the mind" as indivisible. In their view, theories that subdivide brain function cannot possibly be correct. You may have heard statements such as "most people use only 10% of their brains," or "he put his entire mind to the problem." Both sayings suggest that the brain or mind does its work as a unified whole. Nevertheless, most victims of brain damage find that some behavior is lost and some survives, suggesting that different parts of the nervous system have different functions. In the nineteenth century, physiologists perplexed by such observations would often puzzle over the symptoms of brain damage and then speculate about how the observations could be consistent with a holistic notion of the mind.



Bumps in the region of the cerebellum were thought to locate the brain's "amativeness" center.

Figure 1.3 According to phrenologists, depressions (A) and bumps (B) on the skull indicate the size of the underlying area of brain and thus, when correlated with personality traits, indicate the part of the brain controlling the trait. Gall, examining a patient (who because of her behavior became known as "Gall's Passionate Widow"), found a bump at the back of her neck that he thought located the center for "amativeness" in the cerebellum. French physiologist Pierre Flourens refuted this hypothesis by removing a dog's cerebellum to show that the chief purpose of the cerebellum is to coordinate movement. As phrenology (Spurzheim's name for the theory) grew in popularity, bumps and depressions that were not even adjacent to the brain were interpreted as being signs of behavioral and personality traits—as was the case with amativeness. (After Olin, 1910.)

The first general theory to present the idea that different parts of the brain had different functions was the phrenological theory of German anatomist Franz Josef Gall (1758–1828) and his partner Johann Casper Spurzheim (1776–1832). Gall and Spurzheim made a number of important discoveries in neuroanatomy that alone give them a place in history. They proposed that the cortex and its gyri were functioning parts of the brain and not just coverings for the pineal body. They supported their position by showing through dissection that a large pathway called the **pyramidal tract** leads from the cortex to the spinal cord, suggesting that the cortex sends instructions to the spinal cord to command movement of the muscles. As they dissected the pathway they noted that, as it travels along the base of the brainstem, it forms a large bulge, or pyramid, on each side of the brain. Because the tract travels from the cortex to the spinal cord, it is also called the **corticospinal pathway.** Thus, not only did they propose that the cortex was a functioning part of the brain, they also proposed that it produced behavior through the control of other parts of the brain and spinal cord through this pathway. They also recognized that the two symmetrical hemispheres of the brain are connected by another large pathway called the **corpus callosum** and thus could interact with each other.

Gall's behavioral ideas began with an observation made in his youth. He is reported to have been annoyed by students with good memories who achieved excellent marks but did not have an equivalent ability for original thinking. According to his recollection of those days, the students with the best memories had large, protruding eyes. Using this crude observation as a starting point, he developed a general theory of how the brain might produce differences in individual abilities into a theory of brain function called **localization of function.** For example, Gall proposed that a well-developed memory area of the cortex located behind the eyes could cause the eyes to protrude.

Gall and Spurzheim then began to collect instances of individual differences and relate them to other prominent features of the head and skull. They proposed that a bump on the skull indicated a well-developed underlying cortical gyrus and therefore a greater capacity for a particular behavior; a depression in the same area indicated an underdeveloped gyrus and a concomitantly reduced faculty (Figure 1.3). Thus, just as a person with a good memory had protruding eyes, a person who had a high degree of musical ability, artistic talent, sense of color, combativeness, or mathematical skill would have a large bump in other areas of the skull. Figure 1.3B shows where they located the trait of amativeness (sexiness). A person with a bump there would be predicted to have a strong sex drive, whereas a person low in this trait would have a depression in the same region.

Gall and Spurzheim identified a long list of behavioral traits that were borrowed from English or Scottish psychology. Each trait was assigned to a particular part of the skull and, by inference, to the underlying part of the brain. Figure 1.4 shows the resulting map that they devised. Spurzheim called the study of the relation between the skull's surface features and a person's faculties **phrenology** (*phren* is a Greek word for "mind"). The map of the relation between brain functions and the skull surface is called a phrenological map.

Gall and Spurzheim went to considerable effort to gather evidence for their theory. As Gall described it, he devoted himself to observation and waited patiently for nature to bring her results to him. Thus, in developing his idea of the carnivorous instinct, Gall compared the skulls of meat- and plant-eating animals, collecting evidence from more than 50 species, including a description of his own lapdog. His studies of human behavior included accounts of a patricide and a murderer, as well as descriptions of people who delighted in witnessing death or torturing animals or who historically were noted for cruelty and sadism. He also examined the skulls of 25 murderers and even considered evidence from paintings and busts.

Interestingly, Gall placed no emphasis on evidence from cases of brain damage, even though he is credited with giving the first complete account of a case in which left frontal brain damage was followed by loss of the ability to speak. The patient was a soldier who had had a sword pierce his brain through the eye. Note that, on the phrenological map in Figure 1.4, language is located below the eye. Yet Gall felt that this type of finding was not evidence per se but rather confirmation of a finding that was already established by the phrenological evidence.

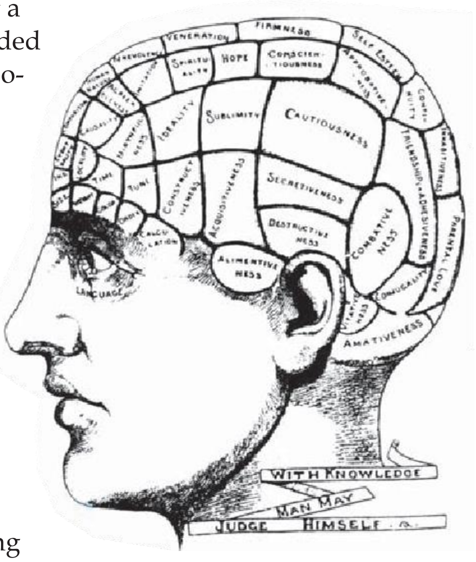


Figure 1.4 Originally, Gall's system identified putative locations for 27 faculties. As the study of phrenology expanded, the number of faculties increased. This drawing shows the location of faculties according to Spurzheim. Language, indicated in the front of the brain (below the eye), actually derived from one of Gall's case studies. A soldier had received a knife wound that penetrated the frontal lobe of his left hemisphere through the eye. The soldier lost the ability to speak. That case represented the first comprehensive report of speech loss following left frontal damage.

Phrenology was seized on by some people as a means of making personality assessments. They developed a method called **cranioscopy,** in which a device was placed around the skull to measure the bumps and depressions there. These measures were then correlated with the phrenological map to determine the person's likely behavioral traits. Cranioscopy invited quackery and thus, indirectly, ridicule by association. Because most of its practitioners produced extremely superficial personality analyses, the entire phrenological endeavor was eventually brought into disrepute. There were other problems intrinsic to the theory. For example, the faculties described in phrenology—characteristics such as faith, self-love, and veneration—are impossible to define and to quantify objectively. The phrenologists also failed to recognize that the superficial features of the skull reveal little about the underlying brain. The outer skull does not mirror even the inner skull, much less the surface features of the cortex.

A historical remnant from the phrenology era is that the lobes of the cortex are named after the bones of the skull; for example, the lobes in the front of the cortex are called frontal lobes and those on the side are called temporal lobes after the respective overlying bones. Additionally, despite the failure of scientific attempts to correlate appearance with various aspects of behavior, it is not uncommon to hear people accord virtues to others on the basis of their physical appearance. Readers might ask themselves how accurate they would be if asked to judge intelligence on the basis of photographs. Social psychologists have found that, when university students are asked to make such judgments, the rule that they apply to the task is, "Beauty equals intelligence." In fairness to Gall, we must note that his science attempted an actual physical measurement. His conclusions were inaccurate in part because he did not test his hypotheses with experiments, a method that was to come into general use only much later.

Recovery of Function

French physiologist Pierre Flourens (1794–1867) is generally credited with the demolition of phrenology. Flourens disagreed with Gall and Spurzheim's correlation of bumps and depressions with behavior, but he did not use argument alone to decide whose ideas were most accurate. He developed the method of controlled laboratory experiments. He was not, however, above using ridicule as well, as the following story from his book *Comparative Psychology* shows:

> The famous physiologist, Magendie, preserved with veneration the brain of Laplace (a famous French mathematician). Spurzheim had the very natural wish to see the brain of a great man. To test the science of the phrenologist, Mr. Magendie showed him, instead of the brain of Laplace, that of an imbecile. Spurzheim, who had already worked up his enthusiasm, admired the brain of the imbecile as he would have admired that of Laplace. (Krech, 1962)

Flourens's experimental method consisted of removing parts of the brains of animals to study the changes produced in their behavior. He removed a small piece of cortex and then observed how the animal behaved and how it recovered from the loss of brain tissue. In essence, he created animal models of humans who had received injury to a part of the brain by a blow to the head or by having the skull pierced by a missile. To search for different functions in the cortex, he varied the location from which he removed brain tissue.

Flourens found that, after he removed pieces of cortex, animals at first moved very little and neglected to eat and drink, but with time they recovered to the point at which they seemed normal. This pattern of loss and recovery held for all his cortex experiments, seeming to refute the idea that different areas of the cortex had specialized functions. He did find that parts of the brainstem had specialized functions. For example, he found that the brainstem is important for breathing, because animals suffocated if it was damaged. He also found that the cerebellum, a part of the brainstem, coordinates locomotion. Gall had proposed that the cerebellum was the location of "amativeness" (see Figure 1.3).

Flourens's experiments furnished neuropsychologists with a number of new ideas. A strict Cartesian, even to the point of dedicating his book to Descartes, Flourens invested the cortex with the properties that Descartes had ascribed to the mind, including the functions of will, reason, and intelligence. Today, we recognize that the cortex is indeed central to most cognitive functions. Another key contribution was the discovery that, after damage to a part of the brain, substantial behavioral recovery could be expected. A central area of investigation in neuropsychology today is the paradox of how a behavior recovers even after the area of the brain thought to be central to the behavior has been damaged. Flourens used these findings to argue, however, that the cortex worked as a whole. For example, recovery from a cortical injury was possible because the remaining cortex could do the same things that the missing cortex had done and so could take over. Flourens's studies were mainly cursory descriptions of changes in the motor behavior of animals, however, and so he has been criticized because he was not really able to adequately test the idea that different regions of the cortex had different functions.

Localization and Lateralization of Language

A now-legendary chain of observations and speculations led to the discovery that really launched the science of neuropsychology, the localization of language. On 21 February 1825, a French physician named Jean Baptiste Bouillaud (1796–1881) read a paper before the Royal Academy of Medicine in France in which he argued from clinical studies that certain functions *are* localized in the neocortex and, specifically, that speech is localized in the frontal lobes, in accordance with Gall's beliefs and opposed to Flourens's beliefs. Observing that acts such as writing, drawing, painting, and fencing are carried out with the right hand, Bouillaud also suggested that the part of the brain that controls them might possibly be the left hemisphere. Physicians had long recognized that damage to a hemisphere of the brain impaired movement of the opposite side of the body. Why, he asked, should people not be left-brained for the movements of speech as well? A few years later, in 1836, Marc Dax read a paper in Montpellier, France, about a series of clinical cases demonstrating that disorders of speech were constantly associated with lesions of the left hemisphere. Dax's manuscript received little attention, however, and was not published until 1865, when it was published by his son.

Although neither Bouillaud's nor Dax's work had much effect when first presented, Ernest Auburtin, Bouillaud's son-in-law, took up Bouillaud's cause. At a meeting of the Anthropological Society of Paris in 1861, he reported the case of a patient who lost the ability to speak when pressure was applied to his exposed frontal lobe. Auburtin also gave the following description of another patient, ending with a promise that other scientists interpreted as a challenge:

> For a long time during my service with M. Bouillaud I studied a patient, named Bache, who had lost his speech but understood everything said to him and replied with signs in a very intelligent manner to all questions put to him. This man, who spent several years at the Bicetre [a Parisian mental asylum], is now at the Hospital for Incurables. I saw him again recently and his disease has progressed; slight paralysis has appeared but his intelligence is still unimpaired, and speech is wholly abolished. Without a doubt this man will soon die. Based on the symptoms that he presents we have diagnosed softening of the anterior lobes. If, at autopsy, these lobes are found to be intact, I shall renounce the ideas that I have just expounded to you. (Stookey,1954)

Paul Broca (1824–1880), founder of the society, attended the meeting and heard Auburtin's challenge. Five days later he received a patient, a Monsieur Leborgne, who had lost his speech and was able to say only "tan" and utter an oath. He had paralysis on the right side of his body but in other respects seemed intelligent and normal. Broca recalled Auburtin's challenge and invited Auburtin to examine Tan, as the patient came to be called. Together they agreed that, if Auburtin was right, Tan should have a frontal lesion. Tan died on 17 April 1861, and the next day Broca submitted his findings to the Anthropological Society (this submission is claimed to be the fastest publication ever made in science). Auburtin was correct, the left frontal lobe was the focus of Tan's lesion. By 1863, Broca had collected eight more cases similar to Tan's and stated:

> Here are eight instances in which the lesion was in the posterior third of the third frontal convolution. This number seems to me to be sufficient to give strong presumptions. And the most remarkable thing is that in all the patients the lesion was on the left side. (Joynt, 1964)

As a result of his studies, Broca located speech in the third convolution (gyrus) of the frontal lobe on the left side of the brain (Figure 1.5). Thus, he accomplished two feats. He demonstrated that language was localized; thus different regions of the cortex could have specialized functions. He also discovered something new: functions could be localized to a side of the brain, a property that is referred to as **lateralization.** Because speech is thought to be central to human consciousness, the left hemisphere is frequently referred to as the dominant hemisphere, to recognize its special role in language. In recognition of Broca's contribution, the anterior speech region of the brain is called **Broca's area,** and the syndrome that results from its damage is called **Broca's aphasia** (from the Greek *a,* for "not," and *phasia,* for "speech").

An interesting footnote to this story is that Broca did not do a very careful examination of Tan's brain. Broca's anatomical analysis was criticized by French anatomist Pierre Marie, who reexamined the brains of Broca's first two patients, Tan and a Monsieur Lelong, 25 years after Broca's death. Marie pointed out in his article titled "The Third Left Frontal Convolution Plays No Particular Role in the Function of Language" that Lelong's brain showed general nonspecific atrophy, common in

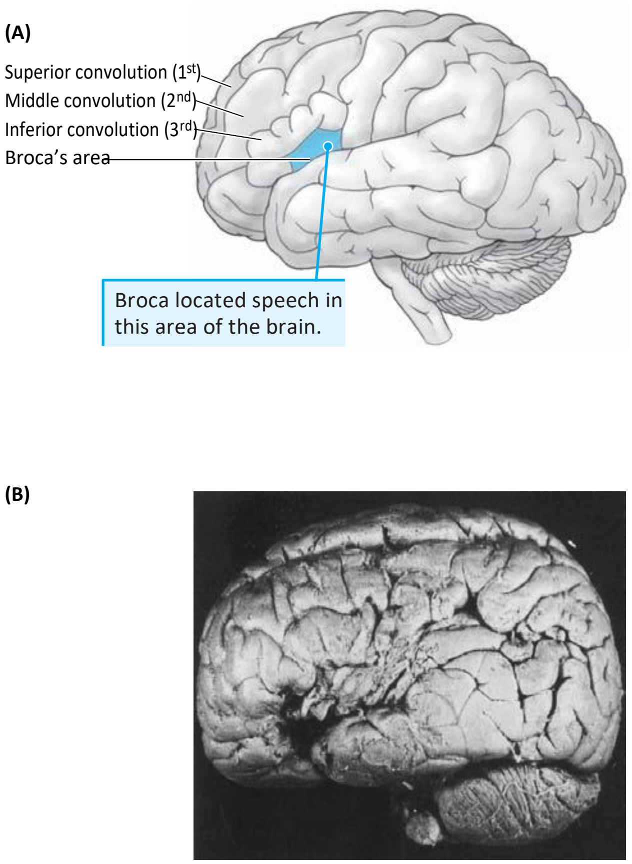


Figure 1.5 (A) A sketch of the lateral view of the left hemisphere of the brain showing the superior, middle, and inferior convolutions (gyri) of the frontal lobes. The convolutions are also referred to as the first, second, and third. Broca's area is located in the posterior third of the inferior convolution. (B) A photograph of the left hemisphere of the brain of Leborgne ("Tan"), Broca's first aphasic patient. (Part B from the Musee Dupuytren; courtesy of Assistance Publique, Hospitaux de Paris.)

senility, and that Tan had additional extensive damage in his posterior cortex that may have accounted for his aphasia. Broca had been aware of Tan's posterior damage but concluded that, whereas the posterior damage contributed to his death, the anterior damage had occurred earlier, producing his aphasia. The question of the extent to which specific functions are localized within the brain is still being explored today, as we shall see.

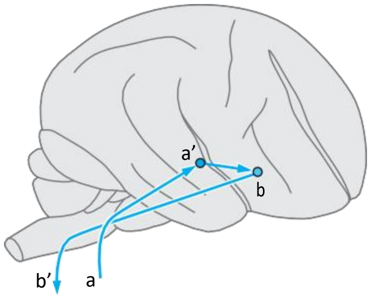
Sequential Programming and Disconnection

Broca's description of aphasia as a condition resulting from left frontal lesions made the following two-part argument: (1) a behavior, such as language, is controlled by a specific brain area; and (2) destroying the area selectively destroys the behavior. People who interpreted Broca's findings in this way are called strict localizationists. Many other scientists began to find that other regions of the brain had localized functions and to interpret their findings in this way. The first notable scientist to dissent was German anatomist Carl Wernicke (1848 –1904). Wernicke was aware that the part of the cortex that receives the sensory pathway, or projection, from the ear—and is thus called the auditory cortex—is located in the temporal lobe, behind Broca's area. He, therefore, suspected a relation between the functioning of hearing and speech, and he described cases of aphasic patients with lesions in this auditory projection area that differed from those described by Broca.

For Wernicke's patients, (1) there was damage in the first temporal gyrus; (2) there was no contralateral paralysis (Broca's aphasia is frequently associated with paralysis of the right arm, as described for Tan); (3) the patients could speak fluently, but what they said was confused and made little sense (Broca's patients could not articulate, but they seemed to understand the meaning of words); and (4) although the patients were able to hear, they could not understand or repeat what was said to them. Wernicke's finding that the temporal lobe also was implicated in language disproved the strict localizationists' view that language was localized to a part of the frontal lobe. Temporal lobe aphasia is sometimes called fluent aphasia, to emphasize that the person can say words. It is more frequently called **Wernicke's aphasia,** however, in honor of Wernicke's description. The region of the temporal lobe associated with the aphasia is called **Wernicke's area.**

Wernicke also provided the first model for how language is organized in the left hemisphere (and the first modern model of brain function). It hypothesizes a programmed sequence of activities in Wernicke's and Broca's language areas (Figure 1.6). Wernicke proposed that auditory information is sent to the temporal lobes from the ear. In Wernicke's area, sounds are turned into sound images or ideas of objects and stored. From Wernicke's area, the ideas can be sent through a pathway called the arcuate fasciculus (from the Latin *arc,* for "bow," and *fasciculus,* for "band of tissue," because the pathway arcs around the lateral fissure as shown in Figure 1.6) to Broca's area, where the representations of speech movements are retained. From Broca's area, instructions are sent to muscles that control movements of the mouth to produce the appropriate sound. If the temporal lobe were damaged, speech movements could still be mediated by Broca's area, but the speech would make no sense, because the person would be unable to monitor the words. Because damage to Broca's area produces loss of speech movements without the loss of sound

(A) Wernicke's model on a chimpanzee brain



(B) Wernicke's model on a human brain

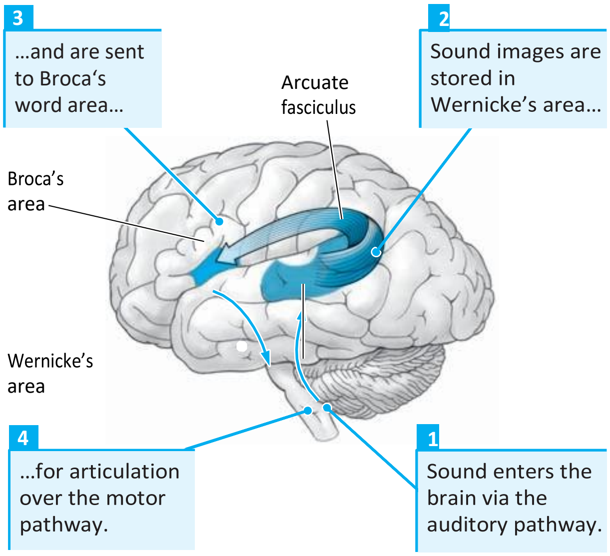


Figure 1.6 (A) Wernicke's 1874 model shows how language is organized in the brain. Sounds enter the brain through the auditory pathway *(a)*. Sound images are stored in Wernicke's area *(a′)* and are sent to Broca's word area *(b)* for articulation through the motor pathway *(b′)*. Lesions along this route *(a-a′-b-b′)* could produce different types of aphasia, depending on their location. Curiously, Wernicke drew all his language models on the right hemisphere and not the left, which is the dominant hemisphere for language, as Wernicke believed. Also curious is that he drew the brain of an ape, which could not speak, as Wernicke knew. (B) Geschwind's model of the neurology of language shows the regions of the cortex involved in human speech. Although the model was a useful summary when published, more recent PET data have shown it to be limited in explanatory value. (Part A after Wernicke, 1874.)

images, Broca's aphasia is not accompanied by a loss of understanding.

Wernicke also predicted a new language disorder, although he never saw such a case. He suggested that, if the arcuate fibers connecting the two speech areas were cut, disconnecting the areas but without inflicting damage on either one, a speech deficit that Wernicke described as **conduction aphasia** would result. In this condition, speech sounds and movements would be retained, as would comprehension, but speech would still be impaired because the person would not be able to judge the sense of the words that he or she heard uttered. Wernicke's prediction was subsequently confirmed. Wernicke's speech model was updated by American neurologist Norman Geschwind in the 1960s and is now sometimes referred to as the Wernicke-Geschwind model.

Wernicke's idea of disconnection was a completely new way of viewing some of the symptoms of brain damage. It proposed that, although different regions of the brain have different functions, they are interdependent in that, to work, they must receive information from one another. Thus, just as cutting a telephone line prevents two people from speaking and so prevents them from performing a complex action such as concluding a business deal, cutting connecting pathways prevents two brain regions from communicating and performing complex functions.

Using this same reasoning, French neurologist Joseph Dejerine (1849–1917) in 1892 described a case in which the loss of the ability to read (alexia, meaning "word blindness," from the Greek *lexia,* for "word") resulted from a disconnection between the visual area of the brain and Wernicke's area. Similarly, Wernicke's student Hugo Liepmann (1863–1925) was able to show that an inability to make sequences of movements (apraxia, from the Greek *praxis,* for "movement") resulted from the disconnection of motor areas from sensory areas. Disconnection is an important idea because it predicts that complex behaviors are built up in assembly-line fashion as information collected by sensory systems enters the brain and travels through different structures before resulting in an overt response of some kind. Furthermore, the disconnection of structures by cutting connecting pathways can result in impairments that resemble those produced by damaging the structures themselves.

Electrophysiological Confirmation of Localization

Although many researchers were excited by the idea of the localization of function, others voiced equally strong objections, largely because they still believed in the indivisibility of the mind. A new approach was developed for using electrical stimulation to study the brain, and it, too, supported the idea of functional localization. This new technique consisted of placing a thin insulated wire, an electrode, onto or into the cortex and passing a small electrical current through the uninsulated tip of the wire, thus exciting the tissue near the electrode tip.

In 1870, Gustav Theodor Fritsch (1838–1929) and Eduard Hitzig (1838–1907) described the new technique in an extraordinary paper, "On the Electrical Excitability of the Cerebrum." Hitzig may have derived the idea of stimulating the cortex from an observation that he made while dressing the head wound of a soldier in the Prussian war: mechanical irritation of the soldier's brain caused twitching in the contralateral limbs. Working in Hitzig's bedroom, the two colleagues performed successful experiments with a rabbit and then a dog in which they showed that stimulating the cortex electrically could produce movements. Furthermore, not only was the neocortex excitable, it was selectively excitable. Stimulation of the frontal lobe produced movements on the opposite side of the body, whereas stimulation of the parietal lobe produced no movement. Stimulation of restricted parts of the frontal lobe elicited movement of particular body parts—for example, neck, forelimb, and hind limb (Figure 1.7)—which suggested that the cortex possesses **topographic representations** of the different parts of the body. Fritsch and Hitzig summarized their interpretation of these findings in the paper's conclusion:

> Furthermore, it may be concluded from the sum of all our experiments that, contrary to the opinions of Flourens and most investigators who followed him, the soul in no case represents a sort of total function of the whole cerebrum, the expression of which might be destroyed by mechanical means in toto, but not in its individual parts. Individual psychological functions, and probably all of them, depend for their entrance into matter or for their formation from it, upon circumscribed centers of the cerebral cortex. (Fritsch and Hitzig, 1960)

The first experiment in which the electrical stimulation of a human cortex was formally reported was performed in 1874 by Roberts Bartholow (1831–1904) in Cincinnati. Mary Rafferty, a patient in his care, had a cranial defect that exposed a part of the cortex in each hemisphere. The following extract is from Bartholow's report:

> Observation 3. *To test faradic reaction of the posterior lobes.* Passed an insulated needle into the left posterior lobe so that the non-insulated portion rested entirely in the substance of the brain. The other insulated needle was placed in contact with the dura mater, within one-fourth of an inch of the first. When the circuit was closed, muscular contraction in the right upper and lower extremities ensued, as in the preceding observations. Faint but visible contraction of the left orbicularis palpebrarum [eyelid], and dilation of the pupils, also ensued. Mary complained of a very strong and unpleasant feeling of tingling in both right extremities, especially in the right arm, which she seized with the opposite hand and rubbed vigorously. Notwithstanding the very evident pain from which she suffered, she smiled as if much amused. (Bartholow, 1874)

Bartholow's publication caused a public outcry and he was forced to leave Cincinnati. Researchers today believe that he probably stimulated the brainstem, not the cortex, because his account says the electrodes were inserted

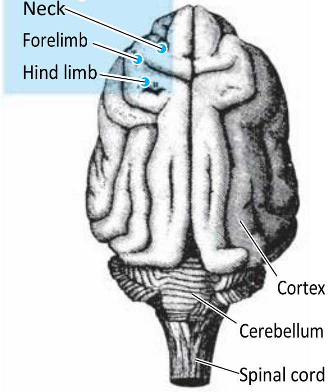

Electrical stimulation of the frontal lobe at various points produced movements on the opposite side of the body.

Figure 1.7 Drawing of the brain of a dog from Fritsch and Hitzig (1870). The areas from which movements of the opposite side of the body were evoked with electrical stimulation are restricted to the frontal cortex. Note that the dog's cortex does not completely cover the brainstem; so the cerebellum can be seen.

about an inch into the brain tissue. The cortex is only a few millimeters thick. Nevertheless, he had demonstrated that the electrical-stimulation technique could be used with a conscious person, who could then report the subjective sensations produced by the stimulation. (The pain that Mary was reported to have suffered was not caused by stimulation of pain receptors in the brain—because there are none—but was probably evoked by a part of the brain that normally receives pain messages from other parts of the body.)

Subsequent research clarified that the movements produced by cortical stimulation were transmitted along a pathway from the cortex to the spinal cord through the pyramidal tract, the pathway that Gall had described nearly a 100 years earlier. David Ferrier (1843–1928), an English physiologist, refined the stimulation technique and duplicated Fritsch and Hitzig's results in many other animals, including primates. The primate studies were especially important because they provided a stepping stone for the construction of similar maps in humans. The technique was adopted by Wilder Penfield (1891–1976) at the Montreal Neurological Institute in Montreal, Canada, for identifying functional areas in human patients who were undergoing elective brain surgery for epilepsy or brain tumors. The maps that he made of a patient's cortex helped guide the surgery.

Hierarchical Organization of the Brain

When Fritsch and Hitzig made their historical discovery that stimulation of restricted parts of the neocortex resulted in specific movement, they concluded that the cortical area evoking a given movement was necessary and sufficient for producing that movement. The experiments performed by Friedrich L. Goltz (1834–1902) in 1892 were intended specifically to test this idea.

Goltz argued that, if a part of the neocortex had a function, then removal of the cortex should lead to a loss of that function. He made large lesions in three dogs, removing the cortex and a good deal of underlying brain tissue, and then studied the dogs for 57 days, 92 days, and 18 months, respectively, until the dogs died. The dog that survived for 18 months was studied in the greatest detail. After the surgery, it was more active than a normal dog. Its periods of sleep and waking were shorter than normal, but it still panted when warm and shivered when cold. It walked well on uneven ground and was able to catch its balance when it slipped. If placed in an abnormal posture, it corrected its position. After hurting a hind limb on one occasion, it trotted on three legs, holding up the injured limb. It was able to orient to touches or pinches on its body and snap at the object that touched it, although its orientations were not very accurate. If offered meat soaked in milk or meat soaked in bitter quinine, it accepted the first and rejected the second. It responded to light and sounds, although its response thresholds were elevated.

In sum, removal of the cortex did not appear to completely eliminate any function, though it seemed to reduce all functions to some extent. This demonstration appeared to be a strong argument against the localization of function and even to cast doubt on the role of the cortex in behavior. We will see, however, that a new theory of brain function was able to resolve the seemingly irreconcilable difference between Fritz and Hitzig's conclusions and Goltz's.

The fundamental disagreement between Goltz and those whom his experiments were intended to contradict was resolved by the **hierarchical organization** concept of brain function proposed by English neurologist John Hughlings-Jackson (1835–1911). Hughlings-Jackson thought of the nervous system as being organized in a number of layers arranged in a functional hierarchy. Each successively higher level would control more complex aspects of behavior but do so through the lower levels. Often Hughlings-Jackson described the nervous system as having three levels: the spinal cord, the brainstem, and the forebrain. But equally often he assigned no particular anatomical area to a given level. He had adopted the theory of hierarchy from philosopher Herbert Spencer's argument that the brain evolved in a series of steps, each of which brought animals the capacity to engage in new behaviors. Spencer in turn derived his idea from Charles Darwin, who had proposed that animals evolved from simple to more complex forms. What Hughlings-Jackson did with Spencer's theory, however, was novel. He suggested that diseases or damage that affected the highest levels would produce *dissolution,* the reverse of evolution: the animals would still have a repertoire of behaviors, but the behaviors would be simpler, more typical of an animal that had not yet evolved the missing brain structure.

If the logic of this argument is followed, it becomes apparent how the results from Goltz's experiments can be reconciled with those of his opponents. Goltz's dogs were "low level" dogs. They were able to walk and to eat but, had food not been presented to them (had they been required to walk to find food), they might have failed to take the necessary action and starved. Under the experimental conditions, the walking did not serve a useful biological function. Hughlings-Jackson's concepts allowed the special role of the cortex in organizing purposeful behavior to be distinguished from the role of lower-level brain areas in supporting the more elementary components of behavior.

Hughlings-Jackson applied his concepts of hierarchical organization to many other areas of behavior, including language and aphasia. It was his view that every part of the brain functions in language, with each part making some special contribution. The relevant question was not where language is localized but what unique contribution is made by each part of the cortex. Hughlings-Jackson was ahead of his time—so much so, in fact, that his ideas are central to the way in which we now think about brain function. We now recognize that functions are localized in one sense but are also distributed over wide areas of the brain in another sense. An expression sometimes used today to encompass Hughlings-Jackson's idea is that behaviors are organized in **distributed systems.**

The Neuron Hypothesis

After the development of the brain hypothesis, that the brain is responsible for all behavior, the second major influence on modern neuropsychology was the development of the neuron hypothesis, the idea that the nervous system is composed of discrete, autonomous units, or neurons, that can interact but are not physically connected. In this section, we will first provide a brief description of the cells of the nervous system, and then we will describe how the neuron hypothesis led to a number of ideas that are central to neuropsychology.

Nervous System Cells

The nervous system is composed of two basic kinds of cells, **neurons** and **glia** (a name that comes from the Greek word for "glue"). The neurons are the functional units that enable us to receive information, process it, and produce actions. The glia help the neurons out, holding them together (some *do* act as glue) and providing other supporting functions. In the human nervous system, there are about 100 billion neurons and perhaps 10 times as many glial cells. (No, no one has counted them all. Scientists have estimated the total number by counting the cells in a small sample of brain tissue and then multiplying by the brain's volume.)

Figure 1.8 shows the three basic parts of a neuron. The neuron's core region is called the **cell body.** Most of a neuron's branching extensions are called **dendrites** (Latin for "branch"), but the main "root" is called the **axon** (Greek for "axle"). Neurons have only one axon, but most have many dendrites. Some small neurons have so many dendrites that they look like garden hedges. The dendrites and axon of the neuron are extensions of the cell body, and their main purpose is to extend the surface area of the cell. The dendrites of a cell can be a number of millimeters long, but the axon can extend as long as a meter, as do those in the pyramidal tract that extend from the cortex to the spinal cord. In the giraffe, these same axons are a number of meters long.

Understanding how billions of cells, many with long, complex extensions, produce behavior is a formidable task, even with the use of the powerful instrumentation available today. Just imagine what the first anatomists with their crude microscopes thought when they first began to make out some of the brain's structural details. But insights into the cellular organization did follow. Through the development of new, more powerful microscopes and techniques for selectively staining tissue, good descriptions of neurons emerged. By applying new electronic inventions to the study of neurons, researchers began to understand how axons conduct information. By studying how neurons interact and by applying a growing body of knowledge from chemistry, they discovered how neurons communicate and how learning takes place.

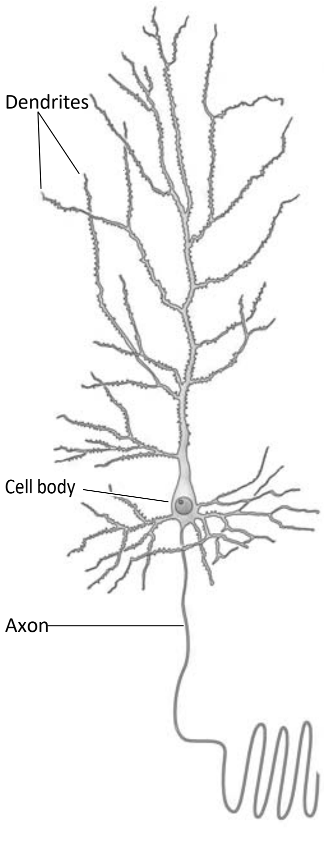


Figure 1.8 The major parts of a neuron include the dendrites, the cell body, and the axon.

The Neuron

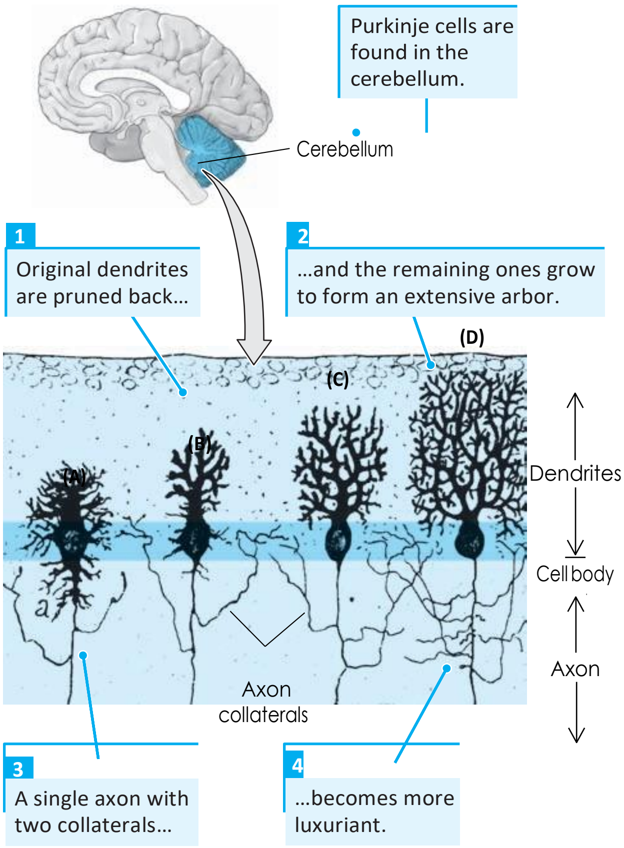
The earliest anatomists who tried to examine the substructure of the nervous system found a gelatinous white substance, almost a goo. Eventually it was discovered that, if brain tissue were placed in alcohol or formaldehyde, water would be drawn out of the tissue, making it firm. Then, if the tissue were cut into thin sections, many different structures could be seen.

Early theories described nerves as hollow, fluid-containing tubes; however, when the first cellular anatomist, Anton van Leeuwenhoek (1632–1723), examined nerves with a primitive microscope, he found no such thing. He did mention the presence of "globules," which may have been cell bodies. As microscopes improved, the various parts of the nerve came into ever sharper focus, eventually leading Theodor Schwann, in 1839, to enunciate the theory that cells are the basic structural units of the nervous system, just as they are for the rest of the body.

An exciting development in visualizing cells was the introduction of staining, which allows different parts of the nervous system to be distinguished. Various dyes used for staining cloth in the German clothing industry were applied to thinly cut tissue with various results: some selectively stained the cell body, some stained the nucleus, and some stained the axons. The most amazing cell stain came from the application of photographic chemicals to nervous system tissue. Italian anatomist Camillo Golgi (1843–1926) in 1875 impregnated tissue with silver nitrate (one of the substances responsible for forming the images in black-and-white photographs) and found that a few cells in their entirety—cell body, dendrites, and axons—became encrusted with silver. This technique allowed the entire neuron and all its processes to be visualized for the first time. Golgi never described how he had been led to his remarkable discovery.

Microscopic examination revealed that the brain was nothing like an amorphous jelly; rather, it had an enormously intricate substructure with components arranged in complex clusters, each interconnected with many other clusters. How did this complex organ work? Was it a net of physically interconnected fibers or a collection of discrete and separate units? If it were an interconnected net, then changes in one part should, by diffusion, produce changes in every other part. Because it would be difficult for a structure thus organized to localize function, a netlike structure would favor a holistic, or "mind," type of brain function and psychology. Alternatively, a structure of discrete units functioning autonomously would favor a psychology characterized by localization of function.

In 1883, Golgi suggested that axons, the longest fibers coming out of the cell body, are interconnected, forming an axonic net. Golgi claimed to have seen connections between cells, and so he did not think that brain functions were localized. This position was opposed by Spanish anatomist Santiago Ramón y Cajal (1852–1934), on the basis of the results of studies in which he used Golgi's own silver-staining technique. Cajal examined the brains of chicks at various ages and produced beautiful drawings of neurons at different stages of growth. He was able to see a neuron develop from a simple cell body with few extensions to a highly complex cell with many extensions (Figure 1.9). He never saw connections from cell to cell. Golgi and Cajal jointly received the Nobel Prize in 1906; each in his acceptance speech argued his position on the organization of neurons, Golgi supporting the nerve net and Cajal supporting the idea of separate cells.



Purkinje cells are found in the cerebellum.

1 Original dendrites are pruned back…

2 …and the remaining ones grow to form an extensive arbor.

3 A single axon with two collaterals…

4 …becomes more luxuriant.

Figure 1.9 Successive phases *(A–D)* in the development of branching in a type of neuron called a Purkinje cell as drawn by Ramón y Cajal (1937).

On the basis of Cajal's work on nerve cells, the expression *neuron hypothesis* has come to describe the idea that neurons are not physically connected through their axons. Images produced by electron microscopes in the twentieth century fully support this hypothesis.

Information Conduction

We have mentioned early views that suggested a hydraulic flow of liquid through nerves into muscles (reminiscent of the way that filling and emptying changes the shape and hardness of a balloon). Such theories have been called **balloonist theories.** Descartes espoused the balloonist hypothesis, arguing that a fluid from the ventricles flows through nerves into muscles to make them move (see Figure 1.2). English physician Francis Glisson (1597–1677) in 1677 made a direct test of the balloon hypothesis by immers- ing a man's arm in water and measuring the change in the water level when the muscles of the arm were contracted. Because the water level did not rise, Glisson concluded that no fluid entered the muscle (bringing no concomitant change in density). Johan Swammerdam (1637–1680) in Holland reached the same conclusion from similar experiments on frogs, but his manuscript lay unpublished for 100 years. (We have asked students in our classes if the water will rise when an immersed muscle is contracted. Many predict that it will.)

The impetus to adopt a theory of electrical conduction in neurons came from an English scientist, Stephen Gray (1666 –1736), who in 1731 attracted considerable attention by demonstrating that the human body could conduct electricity. He showed that, when a rod containing static electricity was brought close to the feet of a boy suspended by a rope, a grass-leaf electroscope (a thin strip of conducting material) placed near the boy's nose would be attracted to the boy's nose. Shortly after, Italian physicist Luigi Galvani (1737–1798) demonstrated that electrical stimulation of a frog's nerve could cause muscle contraction. The idea for this experiment came from his observation that frogs' legs hanging on a metal wire in a market twitched during an electrical storm. In 1886, Joseph Bernstein (1839 –1917) developed the theory that the membrane of a nerve is polarized (has a positive charge on one side and a negative charge on the other) and that an electric potential can be propagated along the membrane by the movements of ions across the membrane. Many of the details of this ionic conduction were worked out by English physiologists Alan Hodgkin (1914 –1988) and Andrew Huxley (1917–), who received the Nobel Prize in physiology in 1963. Their explanation of how neurons conduct information will be more fully described in a later chapter.

As successive findings refuted the hydraulic models of conduction and brought more dynamic electrical models into favor, hydraulic theories of behavior also were critically reassessed. For example, Viennese psychiatrist Sigmund Freud (1856–1939) had originally envisioned the biological basis of his theory of behavior, with its three levels of id, ego, and superego, as being a hydraulic mechanism of some sort. Although conceptually useful for a time, it had no effect on concepts of brain function, because there was no evidence of the brain functioning as a hydraulic system.

Connections Between Neurons As the Basis of Learning

Even though neurons are independent structures, they must influence one another. Charles Scott Sherrington (1857–1952), an English physiologist, examined how nerves connect to muscles and first suggested how the connection is made. He applied an unpleasant stimulation to a dog's paw, measured how long it took the dog to withdraw its foot, and compared that rate with the speed at which messages were known to travel along axons. According to Sherrington's calculations, the dog took 5 milliseconds too long to respond. Sherrington theorized that neurons are connected by junctions, which he called **synapses** (from the Greek word for "clasp"), and that additional time is required for the message to get across the junction. The results of later electron microscopic studies were to confirm that synapses do not quite touch the cells with which they synapse. The general assumption that developed in response to this discovery was that a synapse releases chemicals to influence the adjacent cell. In 1949, on the basis of this principle, Donald Hebb proposed a learning theory stating that, when individual cells are activated at the same time, they grow connecting synapses or strengthen existing ones and thus become a functional unit. He proposed that new or strengthened connections, sometimes called Hebb or plastic synapses, are the structural bases of memory. Just how synapses are formed and change is a vibrant area of research today.

Modern Developments

Given the nineteenth-century advances in knowledge about brain structure and function—the brain and neuron hypotheses, the concept of the special nature of cortical function, and the concepts of localization of function and of disconnection—why was the science of neuropsychology not established by 1900 rather than after 1949, when the word *neuropsychology* first appeared? There are several possible reasons. In the 1920s, some scientists still rejected the classical approach of Broca, Wernicke, and others, arguing that their attempts to correlate behavior with anatomical sites were little more sophisticated than the attempts of the phrenologists. Then two world wars disrupted the progress of science in many countries. In addition, psychologists, who traced their origins to philosophy rather than to biology, were not interested in physiological and anatomical approaches, directing their attention instead to behaviorism, psychophysics, and the psychoanalytical movement.

A number of modern developments have contributed to the emergence of neuropsychology as a distinct scientific discipline: neurosurgery; psychometrics (the science of measuring human mental abilities) and statistical analysis; and technological advances, particularly those that allow a living brain to be imaged.

Neurosurgery

Wilder Penfield and Herbert Jasper, pioneers in brain surgery, have provided a brief but informative history of neurosurgery. They note that anthropologists have found evidence of brain surgery dating to prehistoric times: neolithic

Figure 1.10 (Left) A trephined skull. (Right) In the Zulu Nation of southern Africa, shamans carry a model skull indicating locations at which holes should be made to relieve pressure on the brain in warriors who have received head injuries in battle. (Top, Keith and Betty Collins/Visuals Unlimited, Inc.; Bottom, Obed Zilwa/AP.)

skulls that show postsurgical healing have been found in Europe (Figure 1.10). Similar skulls were left by the early Incas of Peru. It is likely that these early peoples found surgery to have a beneficial effect, perhaps by reducing pressure within the skull when an injured brain began to swell up. Hippocrates gave written directions for **trephining** (cutting a circular hole in the skull) on the side of the head opposite the site of an injury as a means of therapeutic intervention to relieve pressure from a swelling brain. Between the thirteenth and nineteenth centuries, a number of attempts were documented, some of which were quite successful, to relieve various symptoms with surgery.

The modern era in neurosurgery began with the introduction of antisepsis, anesthesia, and the principle of localization of function. In the 1880s, a number of surgeons reported success with operations for the treatment of brain abscesses, tumors, and epilepsy-producing scars. Later, the Horsley-Clarke "stereotaxic device" was developed for holding the head in a fixed position (Figure 1.11). This device immobilizes the head by means of bars placed in the ear canals and under the front teeth. A brain atlas is then used to localize areas in the brain for surgery. Local anesthetic procedures were developed so that the patient could remain awake during surgery and contribute to the success of the operation by providing information about the effects of localized brain stimulation.

The development of neurosurgery as a practical solution to some types of brain abnormality in humans had an enormous influence on neuropsychology. In animal research, the tissue-removal, or lesion, technique had been developed to the point that it became one of the most important sources of information about brain–behavior relations. Research on the human brain, however, was minimal. Most information came from patients with relatively poorly defined lesions—blood-vessel damage that included the brainstem, as well as the cortex, or brain-trauma lesions that were diffuse and irregular. And human patients often lived for years

Figure 1.11 A human patient held in a stereotaxic device for brain surgery. The device allows the precise positioning of electrodes in the head. (Michael English, M.D. / Custom Medical Stock.)

after injury; so histological localization (localization of structures on a microscopic level) was not possible. (Recall Pierre Marie's criticism of Broca's description of Tan's lesion.) Neurosurgery provided a serendipitous solution. The surgical removal of cortical tissue in humans was as localized as the tissue removal in animal experiments. The surgeon would draw a map of the lesion, sometimes after stimulating the surrounding tissue electrically to discover the exact extent of the damages. As a result, good correlations were obtained between focal lesions in the brain and the changes in behavior that resulted from the lesions. Information about behavior obtained from patients who have undergone surgery is very useful for diagnosing the causes of problems in other patients. For example, if tissue removal in the temporal lobes is found to be related to subsequent memory problems, then people who develop memory problems might also have injury or disease of the temporal lobes.

Psychometrics and Statistical Evaluation

The first experiments to measure individual differences in psychological function were made by an astronomer, Friedrich Wilhelm Bessel, in 1796. Bessel had become curious about the dismissal of an assistant at the Greenwich observatory near London for always being a second or so slower than his superior in observing stars and setting clocks. Bessel began a study of reaction time and found quite large variations among people. Individual differences were very much a part of Gall and Spurzheim's phrenology but, unlike their idea of localization of function, this aspect of their research attracted little interest.

The question raised by such observations is, How do we explain individual differences? Charles Darwin's cousin Francis Galton (1822 –1911) maintained a laboratory in London in the 1880s, where he gave subjects three pennies to allow him to measure their physical features, perceptions, and reaction times with the goal of finding individual differences that could explain why some people were superior in ability to others. Galton's elegant innovation was to apply the statistical methods of Adolphe Quetelet (1796–1874), a Belgian statistician, to his results and so rank his subjects on a frequency distribution, the so-called bell-shaped curve (a graphical representation showing that some people perform exceptionally well, some perform exceptionally poorly, and most fall somewhere in between on almost every factor measured). This innovation was essential for the development of modern psychological tests. It seems fitting that Galton's work was directed to describing individual differences, because Darwin's evolutionary theory of natural selection required that individual differences exist. ToGalton's surprise, the perceptual and reaction time differences that he measured did not distinguish between the people he was predisposed to think were average and those he thought were eminent.

French biologist Alfred Binet (1857–1911) came up with a solution to Galton's problem of identifying who would perform poorly on a test. In 1904, the minister of public instruction commissioned Binet to develop tests to identify retarded children so that they could be singled out for special instruction.

In collaboration with Theodore Simon, Binet produced what is now known as the 1905 Binet-Simon scale, designed to evaluate judgment, comprehension, and reason, which Binet thought were essential features of intelligence. The tests were derived empirically by administering questions to 50 normal 3- to 11-year-old children and some mentally retarded children and adults. The scale was revised in 1908; unsatisfactory tests were deleted, new tests were added, and the student population was increased to 300 children aged 3 to 13 years. From the tests, a **mental level** was calculated, a score attained by 80% to 90% of normal children of a particular age. In 1916, Lewis Terman in the United States produced a version of the Stanford-Binet test in which the **intelligence quotient** (IQ)—mental age divided by chronological age times 100—was first used. He set the average intelligence level to equal IQ 100.

Hebb first gave IQ tests to brain-damaged people in Montreal, Canada, in 1940, with the resultant surprising discovery that lesions in the frontal lobes—since Gall's time considered the center of highest intelligence—did not decrease IQ scores. Lesions to other main areas not formerly thought to be implicated in "intelligence" did reduce IQ scores. This counterintuitive finding revealed the utility of such tests for assessing the location of brain damage and effectively created a bond of common interest between neurology and psychology. Many of the clever innovations used for assessing brain function in various patient populations are strongly influenced by intelligence-testing methodology. The tests are brief, easily and objectively scored, and standardized with the use of statistical procedures. In addition, neuropsychologists use the IQ test to assess patients' general level of competence; many other tests that they administer are IQ-like in that they are rapidly administered paper-and-pencil tests. Although certain applications of "mental testing" are liable to criticism, even harsh critics concede that such tests have appropriate uses in neuropsychology. In turn, mental tests are continually being modified in light of new advances in neuropsychology.

Advances in Technology

Because advances in technology have been numerous and because we will consider the most important of them later on, we will not describe individual technological advances here. Instead, we offer Flourens's often-repeated observation that "methods give the results," which was his argument in advocating the experimental method over Gall's anecdotal, merely confirmatory approach. It was repeated by Fritsch and Hitzig when they overthrew Flourens's dogma concerning the mind and the cortex. Progress in science requires advancements in theory and methodology, but it also depends on improvements in technology. In fact, in response to the question of why papers on methods are those most cited in science, one wag declared that you cannot conduct an experiment with a theory. Only through technological advance could the internal structure of neurons be visualized, their electrical activity recorded, and their biochemical activity analyzed and modified. Only through technology can the processes of disease, degeneration, and regeneration in the nervous system be understood. In fact, methodology and results are often so intimately linked that they cannot be dissociated. Technological advances provide new opportunities to review old and well-established ideas, and old and well-established ideas should be thrown into the mill of technological innovation for confirmation or modification.

An important current area of technological advance is brain imaging, of which there are a variety of methods. All of them take advantage of the ability of computers to reconstruct images of the brain. The images describe regional differences in structure or function, electrical activity, cell density, or chemical activity (such as the amount of glucose that a cell is using or the amount of oxygen that it is consuming). Whereas once the neurologist and the psychologist administered time-consuming batteries of tests to patients to locate the site of brain injury, brain-imaging techniques quickly provide a picture of the brain and the injury. The use of such techniques does not mean that neurologists and neuropsychologists are no longer needed. Individual assessments of patients are still required for treatment and research. Moreover, individual brains can be surprisingly different, and so it is difficult to predict what job a given brain region does for a given person.

Brain-imaging methods are important in another way, too. Some imaging techniques can reveal changes in the brain at the very moment a task is being performed or learned or both. The imaging methods thus provide a new and extremely powerful research tool for investigating how the brain produces behavior and changes with experience.

chapter 3

Organization of the Nervous System

To say that the human cerebral cortex is the organ of civilization is to lay a very heavy burden on so small a mass of matter. One is reminded of Darwin's amazement that the wonderfully efficient and diversified behavior of an ant can be carried on with so small a brain, which is "not so large as the quarter of a small pin's head." The complexity of the human brain is as far beyond that of an ant as human conduct is higher than ant's behavior. (C. Juston Herrick, 1926)

The complexity of the human brain and the complexity of human behavior present a major challenge to anyone trying to explain how the one produces the other. The human brain is composed of more than 180 billion cells, more than 80 billion of which are directly engaged in information processing. Each cell receives as many as 15,000 connections from other cells. If there were no order in this complexity, we would have to give up hope of ever understanding how the brain functions. Fortunately, we can obtain some tentative answers about how this machinery works, because it is possible to see a great deal of organization in the way that things are arranged. For example, cells that are close together make most of their connections with one another. Thus, they are like human communities, whose inhabitants share most of their work and engage in social interactions with others who live nearby. Each community of cells also makes connections with more-distant communities through quite large pathways made by their axons. These connections are analogous to the thoroughfares linking human communities.

Although the sizes and shapes of the brains of different people vary, just as their facial features do, the component structures—the communities and main roads of the brain—are common to all human beings. In fact, most of these structures seem to be common to all mammals. About a hundred years ago, anatomist Lorente de Nó examined a mouse brain through a microscope and discovered to his surprise that its fine structure is similar to that of the human brain. Because brain cells are similar in all animals with nervous systems, it is possible to show through experiments that these cells are responsible for behavior. Because the brains of different kinds of animals show structural differences as well as similarities, it is possible to learn about the function of specific brain structures by comparing the behavior of creatures that have those structures with the behavior of creatures that do not. This chapter begins with an overview of the anatomy of the brain and then describes some of its major structures and their function in more detail.

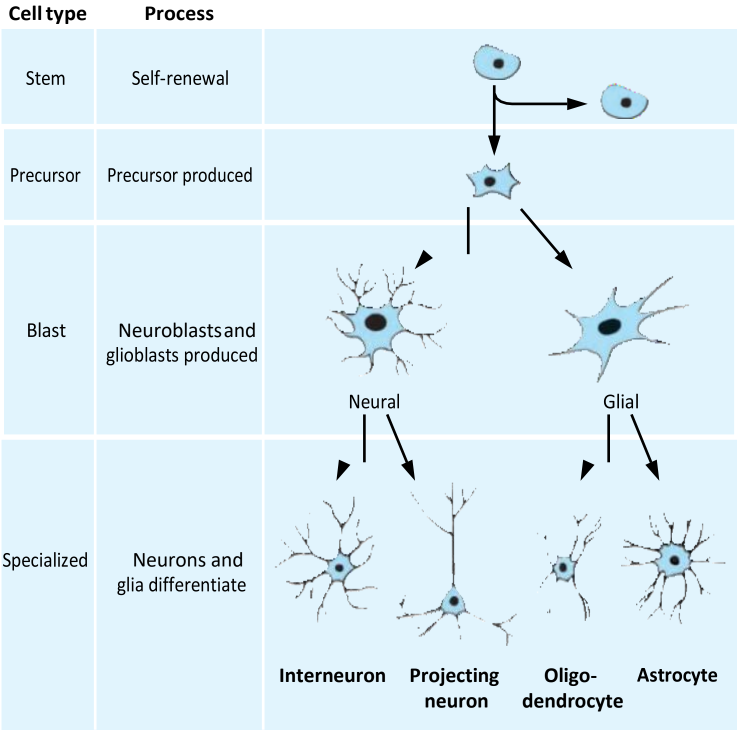
An Overview of the Nervous System

The nervous system is composed of many parts. Individually and in interactions with one another, they are responsible for different aspects of behavior. This section describes the cells of the nervous system and some of the ways in which they are organized to form the different anatomical structures of the brain.

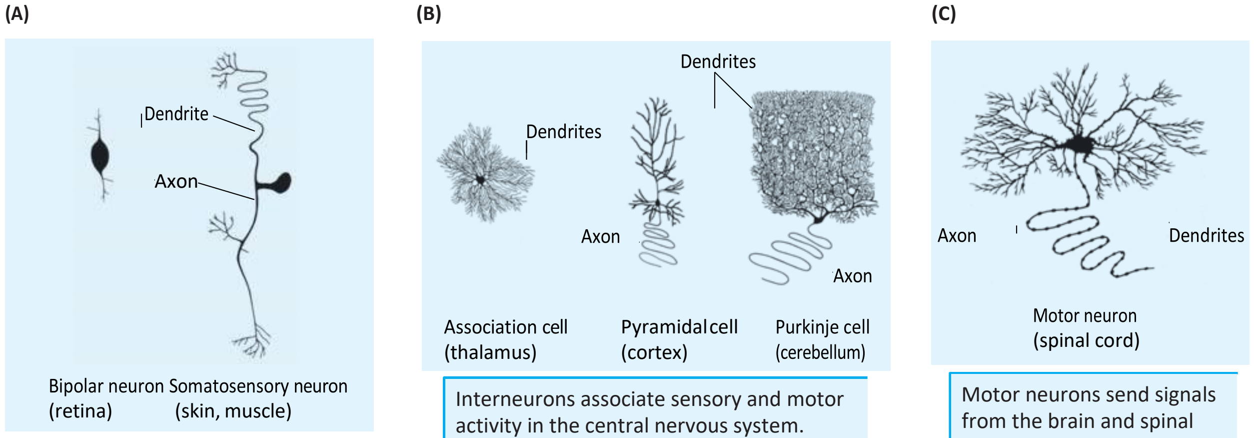
Neurons and Glia

The brain of the embryo has its origin in a single undifferentiated cell called a **stem cell** (also called a germinal cell). Not only do this stem cell and its progeny produce the various specialized kinds of cells that make up the adult brain, but they also produce additional stem cells that persist into adulthood in a brain region called the **ventricular zone,** a region adjacent to the ventricles of the brain, as well as in the retina and spinal cord. A stem cell has an extensive capacity for self-renewal. To initially form a brain, it divides and produces two stem cells, both of which can divide again (Figure 3.1). In the adult, one stem cell dies after each division; so the brain contains a constant number of dividing stem cells. These stem cells serve as a source of new cells for certain parts of the adult brain and so may play a role in brain repair after brain injury.

Figure 3.1 Cells in the brain begin as multipotential stem cells, which become precursor cells, which become blasts, which finally develop into specialized neurons and glia.



In the developing embryo, stem cells give rise to precursor cells, which in turn give rise to primitive types of nervous system cells called **blasts.** Some blasts differentiate into the neurons of the nervous system, whereas others differentiate into the glia. These two basic brain-cell types—neurons and glia—take many forms and make up the entire adult brain. Neuroscientists once thought that the newborn child had all the neurons it would ever possess. Among



Sensory neurons bring information to the central nervous system.

Interneurons associate sensory and motor activity in the central nervous system.

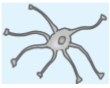
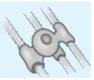
Motor neurons send signals from the brain and spinal cord to muscles.

Figure 3.2 The nervous system is composed of neurons, or nerve cells, each of which is specialized in regard to function. Schematic representations showing the relative sizes and configurations of (A) sensory neurons, (B) neurons in the brain, and (C) motor neurons in the spinal cord.

the most remarkable discoveries of the past few years is that, in fact, new neurons are produced after birth and, in some regions of the brain, continue to be produced into adulthood.

Neurons differ chiefly in overall size and in the complexity of their dendritic processes. Figure 3.2 shows examples of the differences in size and shape that characterize neurons from different parts of the nervous system. Note that the simplest neuron, called a bipolar neuron, consists of a cell body with a dendrite on one side and an axon on the other. Sensory neurons that project from the body's sensory receptors into the spinal cord are modified so that the dendrite and axon are connected, which speeds information conduction because messages do not have to pass through the cell body. Neurons within the brain and spinal cord have many dendrites that branch extensively but, like all neurons, a brain or spinal-cord neuron has only one axon. The architecture of cells differs from region to region in the brain. These differences provide the basis for dividing the brain into different anatomical regions. There are also various types of glial cells, each with a different function; some of them are described in Table 3.1.

Table 3.1 Types of glial cells

Type	Appearance	Features and function
Ependymal cell		Small, ovoid; secretes cerebrospinal fluid (CSF)
Astrocyte		Star shaped, symmetrical; nutritive and support function
Microglial cell		Small, mesodermally derived; defensive function
Oligodendroglial cell		Asymmetrical; forms myelin around axons in brain and spinal cord
Schwann cell		Asymmetrical; wraps around peripheral nerves to form myelin

Gray, White, and Reticular Matter

When a human brain is cut open to reveal its internal structures, some parts appear gray, some white, and some mottled. In general, these visually contrasting parts are described as gray matter, white matter, and reticular matter (Figure 3.3). With respect to our analogy equating brain regions with communities and roads, communities are gray and roads are white.

Gray matter acquires its characteristic gray brown color from the capillary blood vessels and neuronal cell bodies that predominate there. **White matter** consists largely of axons that extend from these cell bodies to form connections with neurons in other brain areas. These axons are covered with an insulating layer of glial cells, which are composed of the same fatty substance (lipid) that gives milk its white appearance. As a result, an area of the nervous system rich in axons covered with glial cells looks white. **Reticular matter** (from the Latin *rete,* meaning "net") contains a mixture of cell bodies and axons, from which it acquires its mottled gray and white, or netlike, appearance.

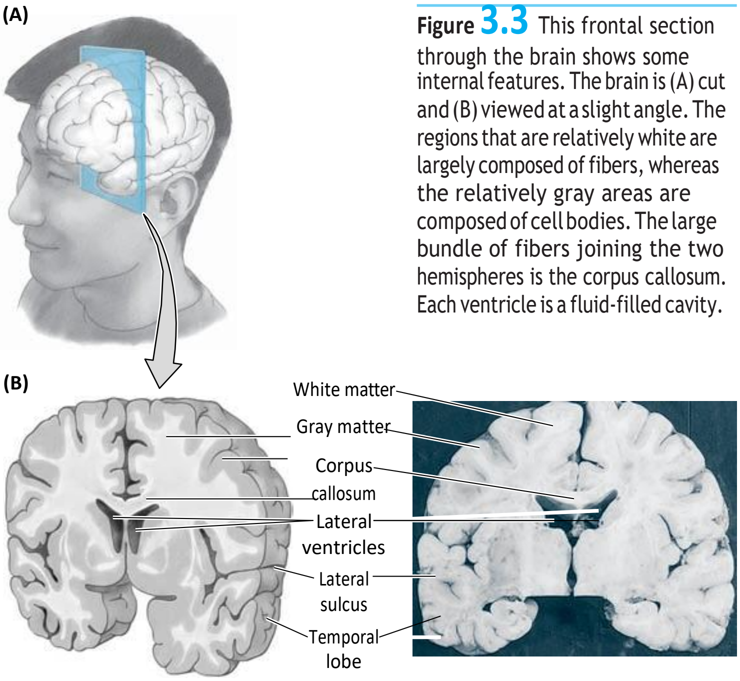


Figure 3.3 This frontal section through the brain shows some internal features. The brain is (A) cut and (B) viewed at a slight angle. The regions that are relatively white are largely composed of fibers, whereas the relatively gray areas are composed of cell bodies. The large bundle of fibers joining the two hemispheres is the corpus callosum. Each ventricle is a fluid-filled cavity.

Nuclei Nerves and Tracts

A large, well-defined group of cell bodies is called a **nucleus** (from the Latin *nux,* meaning "nut") because of its appearance. Some groups of cells are organized linearly, in a row, and are called layers. The ease with which we can visually distinguish these groupings suggests that each nucleus or layer has a particular function, and such is indeed the case. A large collection of axons projecting to or away from a nucleus or layer is called a **tract** (from Old French, meaning "path") or, sometimes, a fiber pathway. Tracts carry information from one place to another within the central nervous system; for example, the corticospinal (pyramidal) tract carries information from the cortex to the spinal cord. The optic tract carries information from the retina of the eye (the retina, strictly speaking, is actually part of the brain) to other visual centers in the brain. Fibers and fiber pathways that enter and leave the central nervous system are called **nerves,** such as the auditory nerve or the vagus nerve, but once they enter the central nervous system they, too, are called tracts. Because cell bodies are gray, nuclei are a distinctive gray; because glial cells make axons appear white, tracts and nerves are a distinctive white. Thus, the nuclei and layers of the brain are its communities, and the tracts are their connecting roadways.

Staining

Because of their respective gray and white coloring, the larger nuclei and tracts of the brain are easy to see in fresh brain tissue or in brain tissue cut into thin sections. The differences in the appearance of smaller nuclei and tracts must be enhanced to make them visible. The technique of staining to differentiate brain tissue consists of placing brain tissue into dyes or certain biochemical agents. Variations in the chemical composition of cells cause them to respond differently to particular coloring agents.

Staining techniques have an important role in neuroscience and are continually being refined. Stains now exist for coloring different parts of a cell, different kinds of cells, cells that contain distinctive proteins or other chemicals, immature or mature cells, sick cells, dead cells, and even cells that have recently played a part in learning some new behavior.

A Wonderland of Nomenclature

To the beginning student, the nomenclature for nuclei and tracts of the nervous system might seem chaotic. It is. Many structures have several names, often used interchangeably. For example, the **precentral gyrus,** which we introduce later in this chapter as the primary motor cortex, is variously referred to as "the primary motor cortex," "area 4," "the motor strip," "the motor homunculus," "Jackson's strip," "area pyramidalis," "the somatomotor strip," "gyrus precentralis," and "M1" (it can be seen in Figure 3.13 under the name "precentral"). This proliferation of terminology corresponds to the long, complex history of the neurosciences. Greek, Latin, and French terminology alternate with English: *mesencephalon* is Greek for "midbrain," *fasciculus opticus* is Latin for "optic tract," and *bouton termineau* is French for "synaptic knob."

The neuroanatomist's imagination has compared brain structures to body anatomy (mammillary bodies), flora (amygdala, or "almond"), fauna (hippocampus, or "sea horse"), and mythology (Ammon's horn). Some terminology is a tribute to early pioneers: the fields of Forel, Rolando's fissure, and Deiters's nucleus. Other terms make use of color: substantia nigra ("black substance"), locus coeruleus ("blue area"), and red nucleus. The longest name for a brain structure is nucleus reticularis tegmenti pontis Bechterewi, affectionately known as NRPT because, as you will observe, scientists have a special fondness for abbreviations. Some labels describe consistency: substantia gelatinosa ("gelatinous substance"); some a lack of knowledge: substantia innominata ("unnamable substance"), zone incerta ("uncertain area"), nucleus ambiguus ("ambiguous nucleus"). Some are based entirely on expediency: cell groups A-1 to A-15 or B1 to B9 (which, incidentally, were named only recently).

We attempt to use consistent and simple terms in this book, but in many cases alternative terms are widely used, and so we have included them where necessary.

Describing Locations in the Brain

Many structures of the brain are labeled according to their locations relative to other structures and landmarks. One convention makes use of seven terms that indicate anatomical direction: *superior* or *dorsal* (above), *lateral* (to the side), *medial* (to the inside), *ventral* (below), *anterior* (in front of), and *posterior* (behind). Thus one structure can be said to lie superior, lateral, medial, ventral, anterior, or posterior to another.

The nervous system is arranged symmetrically, with a left side and a right side. If two structures lie on the same side, they are said to be **ipsilateral;** if they lie on opposite sides, they are said to be **contralateral** to each other; if one lies on each side, they are said to be **bilateral;** that is, there is one in each hemisphere. Moreover, structures that are close to one another are said to be **proximal;** those far from one another are said to be **distal.** Finally, a projection that carries messages toward a given structure is said to be **afferent;** one that carries messages away from the structure is said to be **efferent.**

Approaches to the Study of Anatomy

Neuroanatomists study the structure of the brain by using any of four main conceptual approaches: (1) comparative, (2) developmental, (3) cytoarchitectonic, and (4) functional.

The Comparative Approach

The **comparative approach** examines the brain's evolution from the primitive cord in simple wormlike animals to the large, complex "ravelled knot" in the human head. In addition, it looks for correlations between the increasing complexity of the nervous system and the emergence of new and more complex behaviors in the animals under study. For example, comparing the nervous systems of animals that do not move with those of animals able to swim, crawl, walk, climb, or fly enabled scientists to piece together the story of how neurons and muscles evolved together to produce various movements and behaviors. Such analysis is not necessarily simple. The limbic system, a middle layer in the mammalian brain, first became prominent in the brains of amphibians and reptiles. Is its function to control the new modes of locomotion those animals employ, to orient their travels through a terrestrial rather than an aquatic world, to negotiate the more complex social groups in which they live, or to confer more advanced learning abilities on them than fish seem to enjoy? The answer is uncertain.

The comparative approach has yielded a key piece of information in neuropsychology: a mammal can be distinguished from other animals by its large cortex, and this structure is particularly large in humans. This observation first suggested to neuroscientists that the cortex must have an important function in conferring abilities unique to mammals, especially humans. As a result, the cortex receives proportionately more attention in human neuropsychology than do other structures.

The Developmental Approach

The **developmental approach** (also called the ontogenetic approach) examines the changes in brain structure and size that take place as an individual mammal develops from an egg to an adult.

As each individual organism matures, it passes through the same general phylogenetic stages as its ancestral species did in the course of evolution. This principle has been stated as "ontogeny recapitulates phylogeny" (*ontogeny* is the development of an individual organism, and *phylogeny* is the evolutionary history of a species). Thus, human babies are at first able to make only gross body movements; later they crawl, then walk, and eventually perform highly skilled motions with their hands and mouths. What changes take place in their nervous systems to make each new behavior possible? Like the comparative approach, the developmental approach allows the development and maturation of structures to be correlated with emerging behaviors.

In addition, the developmental approach acquires general information about brain function by studying immature brains as if they were simplified models of the adult brain. Neuropsychologists widely assume, for example, that the neocortex is particularly immature in newborn infants. Thus they believe that, by correlating the development of the neocortex with emerging complex and conscious behavior, they may discover the relations between neocortical structure and function.

Cytoarchitectonic Analysis

Cytoarchitectonic analysis examines the architecture of cells: their differences in structure, size, shape, and connections, as well as their distribution in different parts of the brain. The cytoarchitectonic approach has been used to particular advantage by neuroanatomists to produce various kinds of maps of the brain.

The newest cytoarchitectonic technique analyzes the brain's organization by looking at differences in the cells' biochemical activity. Cellular activity and growth are governed by a cell's nucleus, which releases biochemical "messages" into the cell that initiate the production of whatever new proteins the cell requires. These message molecules can be stained, allowing cells that are undergoing change to be located, mapped, and observed. It is a useful way of identifying cells that may be active in specific processes, such as learning or mediating recovery from brain damage.

Functional Approaches

Functional analysis seeks to discover the roles of the various brain areas, largely by observing changes in behavior that occur after injury or changes in metabolic activity that occur in the course of ongoing behavior. For example, an active brain area will increase its use of oxygen; so, if oxygen use can be detected, active areas of the brain can be distinguished from less-active areas. Various imaging techniques—based on methods for detecting the activity of cells, measuring their uptake of oxygen, recognizing their biochemical changes, and so on—allow the activity of different brain regions to be compared under varying circumstances. These methods have been used to study changes in brain function in the course of development, during movement, in responses to stimuli, and even during thinking. For example, injury to certain brain regions leads to language difficulties. Those same regions are observed to use more oxygen during thinking and speech in normal subjects.

The Origin and Development of the Brain

The developing brain is less complex than the adult brain and provides a clearer picture of the brain's basic three-part structural plan (Figure 3.4). Later, two of the three regions, the front and back components, expand greatly in mammals and become further subdivided, giving five regions in all. Embryologists use rather cumbersome names for the regions of the three-part and five-part brain plans; because some of these names are also used to describe parts of the adult brain, they are given in Figure 3.4.

The three regions of the primitive developing brain are recognizable as a series of three enlargements at the end of the embryonic spinal cord. The adult brain of a fish, amphibian, or reptile is roughly equivalent to this three-part brain: the **prosencephalon** ("front brain") is responsible for olfaction, the **mesencephalon** ("middle brain") is the seat of vision and hearing, and the **rhombencephalon** (hindbrain) controls movement and balance (Figure 3.4A). The spinal cord is considered part of the hindbrain. In mammals (Figure 3.4B), the prosencephalon develops further to form the cerebral hemispheres (the cortex and related structures), which are known collectively as the **telencephalon** ("endbrain"). The remaining part of the old prosencephalon is referred to as the **diencephalon** ("between brain") and includes the hypothalamus. The back part of the brain also develops further. It is subdivided into the **metencephalon** ("across brain," which includes the enlarged cerebellum) and the **myelencephalon** ("spinal brain").

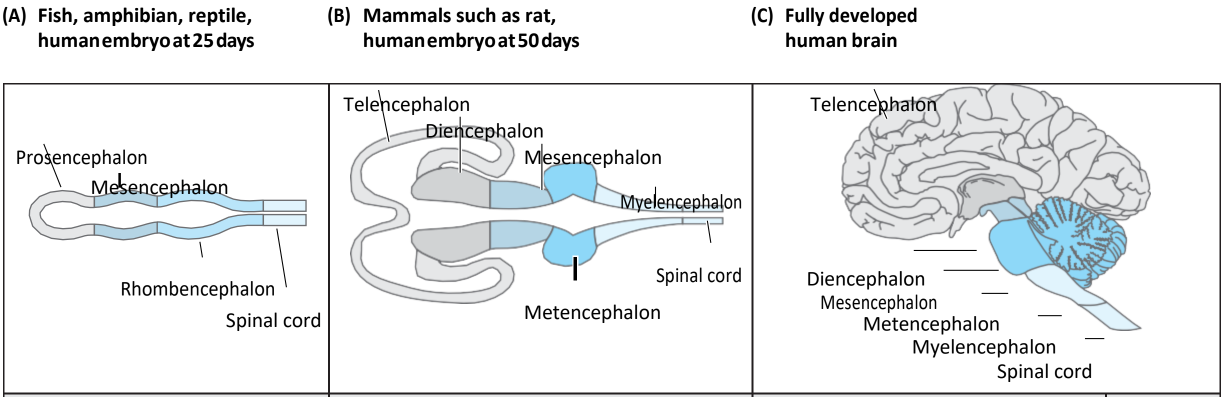


Figure 3.4 Steps in the ontogenic development of the brain. (A) A three-chambered brain. (B) A five-chambered brain. (C) Side view through the center of the human brain.

Prosencephalon (forebrain)	Telencephalon (end brain)	Neocortex, basal ganglia, limbic system olfactory bulb, lateral ventricles	Forebrain
	Diencephalon (between brain)	Thalamus, epithalamus, hypothalamus, pineal body, third ventricle	
Mesencephalon (midbrain)	Mesencephalon	Tectum, tegmentum, cerebral aqueduct	Brainstem
Rhombencephalon (hindbrain)	Metencephalon (across-brain)	Cerebellum, pons, fourth ventricle	
	Myelencephalon (spinal brain)	Medulla oblongata, fourth ventricle	
Spinal cord	Spinal cord	Spinal cord	Spinal cord

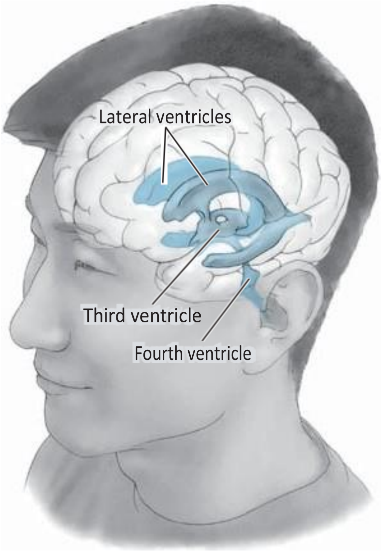


Figure 3.5 There are two lateral cerebral ventricles, one in each hemisphere, and a third and fourth ventricle, each of which lies in the midline of the brain.

The human brain is a more complex mammalian brain, retaining most of the features of other mammalian brains and possessing especially large cerebral hemispheres (Figure 3.4C).

The brain begins as a tube and, even after it folds and matures, its interior remains “hollow.” The four prominent pockets created by the folding of this hollow interior are called **ventricles** (“bladders”) and are numbered 1 through 4 (see Figure 3.4B). The “lateral ventricles” (first and second) form C-shaped lakes underlying the cerebral cortex, whereas the third and fourth ventricles extend into the brainstem (Figure 3.5). All are filled with a fluid—**cerebrospinal fluid,** or CSF—which is produced by ependymal glial cells located adjacent to the ventricles. The CSF flows from the lateral ventricles out through the fourth ventricle and eventually into the circulatory system.

The Spinal Cord

In a very simple animal, such as the earthworm, the body is a tube divided into segments. Within the body is a tube of nerve cells that also is divided into segments. Each segment receives fibers from sensory receptors of the part of the body adjacent to it and sends fibers to the muscles of that part of the body. Each segment functions relatively independently, although fibers interconnect the segments and coordinate their activity. This basic plan also holds for the human body. Let us take a look at our “tube of nerves.”

Spinal-Cord Structure

Figure 3.6 shows the segmental organization of the human body. The segments, called **dermatomes** (meaning “skin cuts”), encircle the spinal column as a stack of rings. Originally, mammalian limbs developed perpendicularly to the spinal cord, but early humans developed an upright posture; so the ring formation in our bodies is distorted into the pattern shown in Figure 3.6. As many as six segments (C4 through T2) can be represented on the arm. If you imagine the person in the drawing standing on all fours, you can see how this pattern makes sense.

There are 30 spinal-cord segments: 8 cervical (C), 12 thoracic (T), 5 lumbar (L), and 5 sacral (S). Each segment is connected by nerve fibers to the body dermatome of the same number, including the organs and musculature

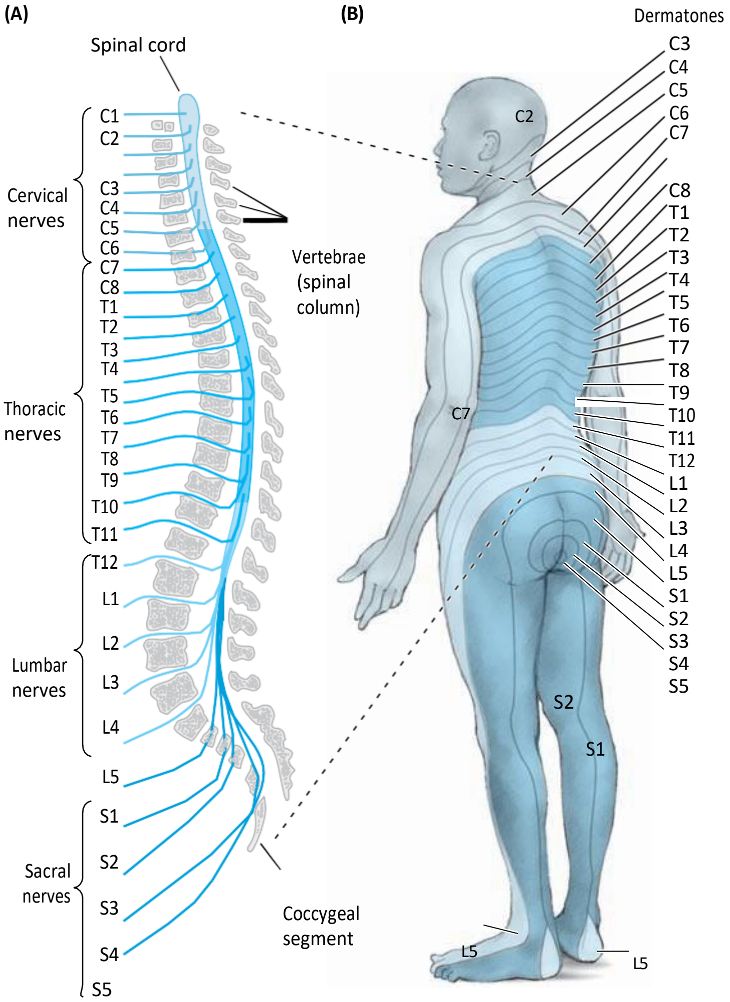


Figure 3.6 (A) The five groups of spinal-cord segments making up the spinal column (cervical, C; thoracic, T; lumbar, L; sacral, S; and coccygeal vertebrae) are shown in this side view. (B) Each spinal segment corresponds to a region of body surface (a dermatome) that is identified by the segment number.

that lie within the dermatome. In the main, the cervical segments control the forelimbs, the thoracic segments control the trunk, and the lumbar segments control the hind limbs.

Figure 3.7 shows a cross section of the spinal cord. Fibers entering the dorsal part of the spinal cord bring information from the sensory receptors of the body. These fibers converge as they enter the spinal cord, forming a strand of fibers referred to as a **dorsal root.** Fibers leaving the ventral part of the spinal cord, carrying information from the spinal cord to the muscles, form a similar strand known as a **ventral root.**

In the spinal cord itself, the outer part consists of white matter or tracts, arranged so that with a few exceptions the dorsally located tracts are motor and the ventrally located tracts are sensory. The tracts carry information to the brain and from the brain. The inner part of the cord consists of gray matter; that is, it is composed largely of cell bodies, which in this case organize movements and give rise to the ventral roots. In cross section, this gray region has the shape of a butterfly.

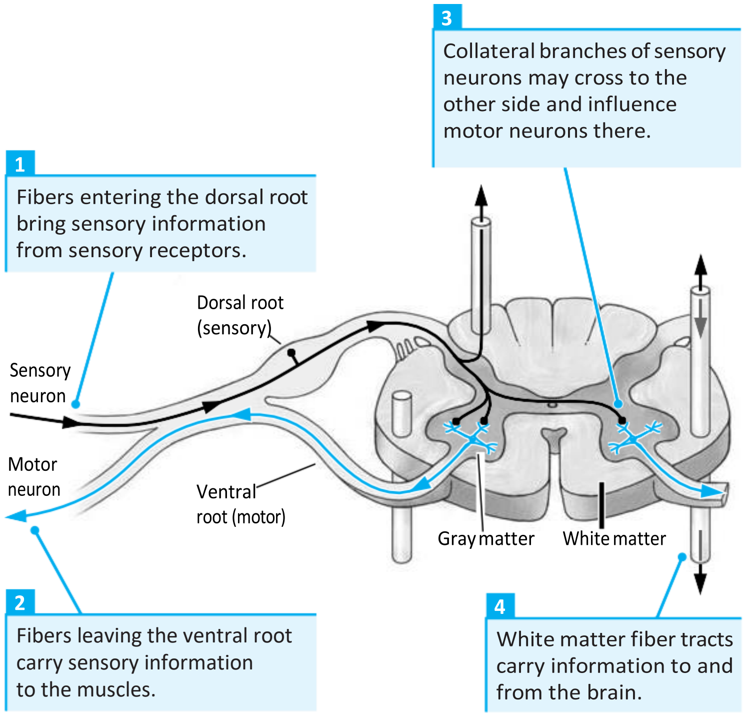


Figure 3.7 A cross section of the spinal cord illustrating a sensory neuron in the dorsal root and a motor neuron in the ventral root. Collateral branches of the sensory fiber cross to the other side of the spinal cord to influence motor neurons on that side and extend to adjacent segments to influence adjacent body parts. The inner regions of the spinal cord consist of cell bodies (gray matter) and the outer regions consist of tracts traveling to and from the brain (white matter).

1 Fibers entering the dorsal root bring sensory information from sensory receptors.

2 Fibers leaving the ventral root carry sensory information to the muscles.

3 Collateral branches of sensory neurons may cross to the other side and influence motor neurons there.

4 White matter fiber tracts carry information to and from the brain.

Spinal-Cord Function

Francois Magendie, a French experimental physiologist, reported in a three-page paper in 1822 that he had succeeded in cutting the dorsal roots of one group of puppies and the ventral roots of another group (the youth of the dogs allowed the different surgeries; in adult dogs, the roots are fused). He found that cutting the dorsal roots caused loss of sensation and cutting the ventral roots caused loss of movement. Eleven years earlier, in 1811, Charles Bell, a Scot, had suggested the opposite functions for each of the roots, basing his conclusions on anatomical information and the results from somewhat inconclusive experiments on rabbits. When Magendie's paper appeared, Bell hotly disputed priority for the discovery, with some success. Today the principle that the dorsal part of the spinal cord is sensory and the ventral part is motor is called the **Bell-Magendie law.** Magendie's experiment has been called the most important ever conducted on the nervous system. It enabled neurologists for the first time to distinguish sensory from motor impairments, as well as to draw general conclusions about the location of neural damage, on the basis of the symptoms displayed by patients. Because of the segmental structure of the spinal cord and the body, rather good inferences can also be made about the location of spinal-cord damage or disease on the basis of changes in sensation or movement in particular body parts. The internal organs, however, although also arranged segmentally, appear not to have their own sensory representation within the spinal cord. Pain in these organs is perceived as coming from the outer parts of the dermatome and so is called **referred pain.** For example, pains in the heart are felt in the shoulder and arm, and kidney pain is felt in the back. Physicians use what is known about the location of referred pains to diagnose problems within the body.

Other major advances in the understanding of spinal-cord function came from the work of Sir Charles Sherrington and his students, who showed that the spinal cord retains many functions even after it has been separated from the brain. Sherrington, a British physiologist, published a summary of this research in 1906, and it had an important influence in the treatment of humans with spinal-cord injury. Persons whose spinal cords are cut so that they no longer have control over their legs are called **paraplegic;** if the cut is higher on the cord so that they cannot use their arms either, they are called **quadriplegic.** Although it was once thought that there was no way to treat such injuries, an understanding of spinal-cord function has led to such huge improvements in treatment that spinal-cord patients today can lead long and active lives.

Sensory information plays a central role in eliciting different kinds of movements organized by the spinal cord. Movements dependent only on spinal-cord function are referred to as reflexes and are specific movements elicited by specific forms of sensory stimulation. There are many kinds of sensory receptors in the body, including receptors for pain, temperature, touch and pressure, and the sensations of muscle and joint movement. The size of fiber coming from each kind of receptor is distinctive; generally, pain and temperature fibers are smaller, and those for touch and muscle sense are larger. The stimulation of pain and temperature receptors in a limb usually produces **flexion** movements—movements that bring the limb inward, toward the body. If the stimulus is mild, only the distal part of the limb flexes in response to it but, with successively stronger stimuli, the size of the movement increases until the whole limb is drawn back. The stimulation of fine touch and muscle receptors in a limb usually produces **extension** movements, which extend the limb outward, away from the body. The **extensor reflex** causes the touched part of the limb to maintain contact with the stimulus; for example, the foot or hand touching a surface will maintain contact with the surface through this reflex. Thus, both withdrawal reflexes and following reflexes, as these reflexes are called, are activated by sensory stimulation. Because each of the senses has its own receptors, fibers, connections, and reflex movements, each can be thought of as an independent sensory system. Furthermore, because the movement produced by each sense is distinct and independent, the senses are thought of as each operating independently of the rest.

In addition to the local connections that they make within the segment of the spinal cord corresponding to their dermatome, pain and tactile receptors communicate with fibers in many other segments of the spinal cord and thus can produce appropriate adjustments in many body parts. For example, when one leg is withdrawn in response to a painful stimulus, the other leg must simultaneously extend to support the body's weight. The spinal cord is capable of producing actions that are more complex than just adjustments of a limb. If the body of an animal that has had its spinal cord sectioned from the brain is held in a sling with its feet touching a conveyor belt, the animal is even capable of walking. Thus, the spinal cord contains all of the connections required for allowing an animal to walk.

Despite the fact that the spinal cord controls both simple and complex behavior, it does depend on the brain, as evidenced by the severe behavioral impairments that follow spinal-cord injury. Because the main effect of spinal-cord injury is to sever connections between the cord and the brain, scientists believe that simply reestablishing these connections can restore function to spinal-cord-injured people. Unfortunately, although the fibers in the spinal tracts do regrow in some vertebrates, such as fish, and in the early stages of development in other animals, they do not regrow in adult mammals. Researchers are experimenting with various approaches to induce regrowth. One approach is based on the idea that new growth is prevented by the presence of certain inhibitory molecules on the tracts of the cord below the cut. The idea under investigation is that, if these inhibitory molecules can in turn be inhibited, fibers will begin to grow across the injured zone. Another line of research is focused on the scarring that accompanies most spinal-cord damage and the possibility that scarring inhibits new growth. Some scientists are conducting experiments in which they attempt to remove the scar, whereas other scientists are attempting to build bridges across the scar over which fibers can grow. All of these approaches have been partly successful in nonhuman animal studies, but they have not been attempted on humans with spinal-cord injury.

The Brainstem

The section of human brain portrayed in Figure 3.8 shows several of the main structures of the brainstem. In general, the brainstem produces more-complex movements than does the spinal cord. In addition to responding to most sensory stimuli in the environment and regulating eating and drinking, body

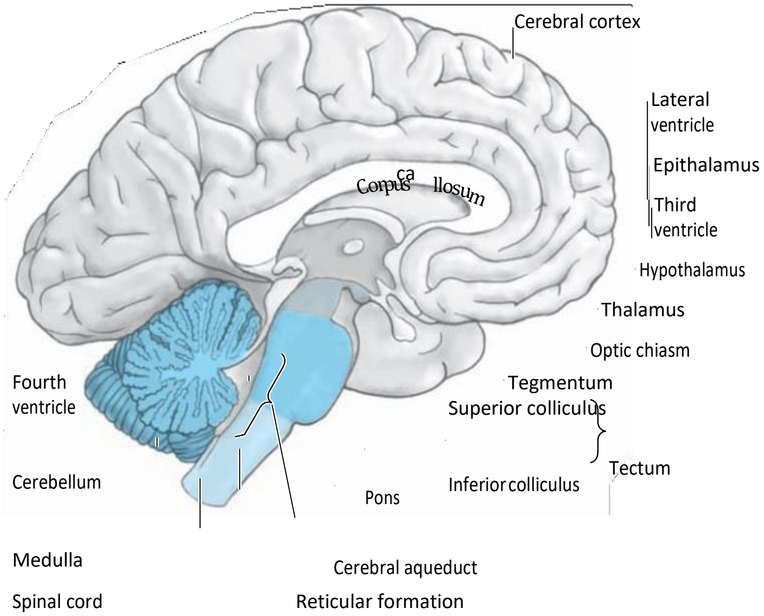


Figure 3.8 Medial view through the center of the brain showing structures of the brainstem.

temperature, sleep and waking, the brain stem can produce the movements of walking and running, grooming, and sexual behavior (all of which are more complex than the reflexive movements produced by the spinal cord). The brains of fish, amphibians, and reptiles are basically equivalent to a mammalian brainstem; in consequence, the behavior of these animals is a good indication of the functions of the brainstem. The brainstem can be subdivided into three parts: the diencephalon, the midbrain, and the hindbrain. Their main structures and functions are summarized next.

Figure 3.9 Relation between thalamic nuclei and various areas of the cortex to which they project. The arrows indicate the sources of input and output from the thalamus: anterior nucleus, A; dorsal medial nucleus, DM; ventral anterior nucleus, VA; ventral lateral nucleus, VL; lateral posterior nucleus, LP; ventral lateral posterior nucleus, VLP; pulvinar, P; lateral geniculate body, LGB; and medial geniculate

The Diencephalon

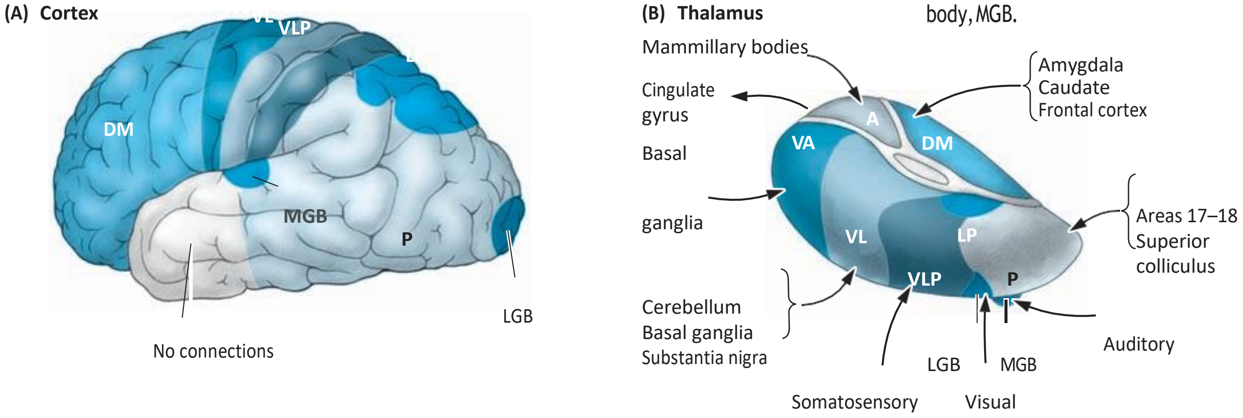
The diencephalon consists of the three thalamic structures: the thalamus ("inner room, or chamber"); the epithalamus ("upper room"); and the hypothalamus ("lower room").

The **thalamus** is composed of a number of nuclei, each of which projects to a specific area of the neocortex, as shown in Figure 3.9. These nuclei route information from three sources to the cortex.

1. One group of nuclei relays information from sensory systems to their appropriate targets. For example, the lateral geniculate body (LGB) receives visual projections; the medial geniculate body (MGB) receives auditory projections; and the ventral-posterior lateral nuclei (VPL) receive touch, pressure, pain, and temperature projections from the body. In turn, these areas project to the visual, auditory, and somatosensory regions of the cortex (see page 64 for more details on the organization of the cortex).
2. Some nuclei relay information between cortical areas. For example, a large area of the posterior cortex sends projections to and receives projections back from the pulvinar nucleus (P).
3. Some of the thalamic nuclei relay information from other forebrain and brainstem regions.

In short, almost all the information that the cortex receives is first relayed through the thalamus.

The function of the **epithalamus** is not well understood, but one of its structures, the **pineal body,** seems to regulate seasonal body rhythms. Recall body, MGB.


(A) Cortex
VL
VLP
DM
MGB
P
LGB
No connections
(B) Thalamus
Mammillary bodies
Cingulate gyrus
Basal ganglia
A
DM
VA
VL
LP
VLP
P
Amygdala
Caudate
Frontal cortex
Areas 17–18
Superior colliculus
Cerebellum
Basal ganglia
Substantia nigra
Somatosensory
LGB
MGB
Visual
Auditory

that Descartes, impressed by the unitary character of the pineal body in comparison with other brain structures, suggested that it is the rendezvous for mind and matter and the source of the cerebral spinal fluid that he believed powers movements.

The **hypothalamus** is composed of about 22 small nuclei, fiber systems that pass through it, and the **pituitary gland.** Although comprising only about 0.3% of the brain's weight, the hypothalamus takes part in nearly all aspects of motivated behavior, including feeding, sexual behavior, sleeping, temperature regulation, emotional behavior, endocrine function, and movement.

The Midbrain

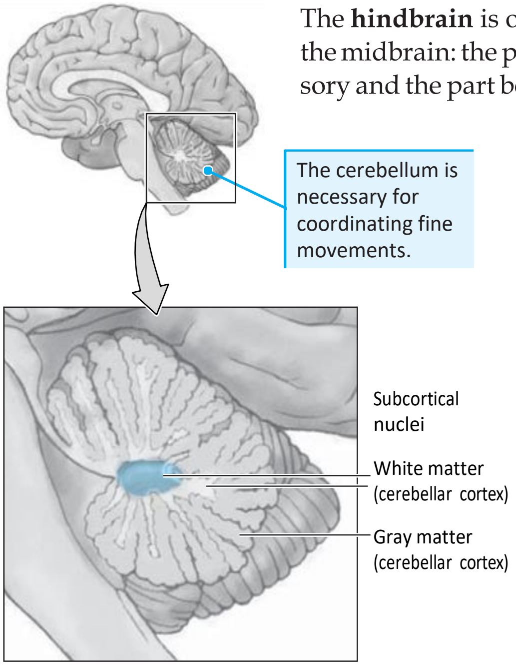
The **midbrain** has two main subdivisions: the **tectum,** or "roof," which is the roof of the third ventricle, and the **tegmentum,** or "floor," which is its floor. The tectum consists primarily of two sets of bilaterally symmetrical nuclei. The **superior colliculi** ("upper hills") are the anterior pair. They receive projections from the retina of the eye, and they mediate many visually related behaviors. The **inferior colliculi** ("lower hills") are the posterior pair. They receive projections from the ear, and they mediate many auditory-related behaviors. A class of behaviors mediated by the colliculi are orienting behaviors. For example, when an owl hears the sound of a moving mouse or a cat sees a moving mouse, each quickly orients its head toward the stimuli. In each case, the movement is enabled by the respective colliculi for vision and audition. The tegmentum contains nuclei for some of the cranial nerves, including a number of motor nuclei. Thus, in the midbrain as in the spinal cord, the dorsal part is sensory and the ventral part is motor.

The Hindbrain

The **hindbrain** is organized in much the same way as the midbrain: the part above the fourth ventricle is sensory and the part below the ventricle is motor. Sensory nuclei of the **vestibular system,** the sensory system governing balance and orientation, lie above the fourth ventricle; beneath this ventricle are more motor nuclei of the cranial nerves.

Perhaps the most distinctive part of the hindbrain is the **cerebellum.** It protrudes above the core of the brainstem, and its surface is gathered into narrow folds, or **folia,** which are like the gyri of the cortex but smaller (Figure 3.10). At the base of the cerebellum are several nuclei, which send connections to other parts of the brain.

Figure 3.10 The cerebellum is necessary for fine coordinated movements. Like the cerebrum, the cerebellum (shown in the detailed cross section) has a cortex, containing gray and white matter and subcortical nuclei.



The cerebellum is necessary for coordinating fine movements.

The cerebellum plays a role in the coordination and learning of skilled movement. Thus, damage to the cerebellum results in equilibrium problems, postural defects, and impairments of skilled motor activity. The parts that receive most of their impulses from the vestibular system (the receptors for balance and movement, located in the middle ear) help to maintain the body's equilibrium, whereas parts receiving impulses mainly from the receptors in the trunk and limbs control postural reflexes and coordinate functionally related groups of muscles.

The core of the brainstem consists of nuclei, including those of the cranial nerves, as well as many bundles of fibers. Fibers from the spinal cord pass through the brainstem on their way to the forebrain; conversely, fibers from the forebrain connect with the brainstem or pass through it on their way to the spinal cord. The brainstem's mixture of nuclei and fibers creates a network referred to as the **reticular formation.**

The reticular formation is more commonly known as the **reticular activating system.** It obtained this designation in 1949 when Moruzzi and Magoun stimulated it electrically in anesthetized cats and found that the stimulation produced a waking pattern of electrical activity in the cats' cortexes. Moruzzi and Magoun concluded that the function of the reticular formation was to control sleeping and waking—that is, to maintain "general arousal" or "consciousness." As a result, the reticular formation came to be known as the reticular *activating* system. Neuroscientists now recognize that the various nuclei within the brainstem serve many functions and that only a few take part in waking and sleeping.

Cranial Nerves

Also leaving or entering the brainstem are the 12 sets of **cranial nerves.** The cranial nerves convey sensory information from the specialized sensory systems of the head, and many have nuclei in the brainstem and send axons to the muscles of the head. For example, movements of the eyes and tongue are produced by cranial nerves. In addition, one of the cranial nerves, the vagus, makes connections with many body organs, including the heart. A knowledge of the organization and function of the cranial nerves is important for making neurological diagnoses. Figure 3.11 illustrates the location of the cranial nerves, and Table 3.2 describes their functions and some of the more common symptoms that arise when they are damaged.

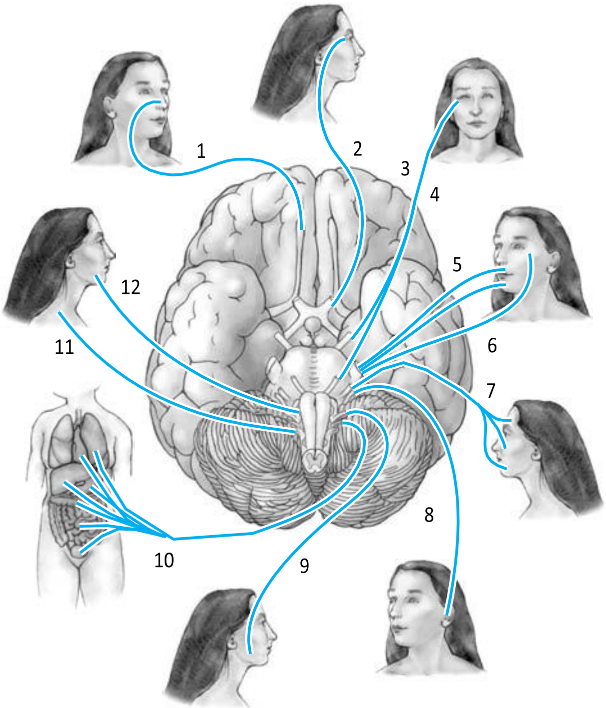


Figure 3.11 Each of the 12 pairs of cranial nerves has a different function. A common device for learning the order of the cranial nerves is, "On old Olympus's towering top, a Finn and German view some hops." The first letter of each word is, in order, the first letter of the name of each nerve.

Table 3.2 The cranial nerves

Number	Name	Functions	Method of examination	Typical symptoms of dysfunction
1	Olfactory	(s) Smell*	Various odors applied to each nostril	Loss of sense of smell (anosmia)
2	Optic	(s) Vision	Visual acuity, map field of vision	Loss of vision (anopsia)
3	Oculomotor	(m) Eye movement*	Reaction to light, lateral movements of eyes, eyelid movement	Double vision (Diplopia), large pupil, uneven dilation of pupils, drooping eyelid (ptosis), deviation of eye outward
4	Trochlear	(m) Eye movement	Upward and downward eye movements	Double vision, defect of downward gaze
5	Trigeminal	(s, m) Masticatory movements	Light touch by cotton baton; pain by pinprick; thermal by hot and cold tubes, corneal reflex by touching cornea; jaw reflex by tapping chin, jaw movements	Decreased sensitivity or numbness of face, brief attacks of severe pain (trigeminal neuralgia); weakness and wasting of facial muscles, asymmetrical chewing
6	Abducens	(m) Eye movement	Lateral movements	Double vision, inward deviation of the eye
7	Facial	(s, m) Facial movement	Facial movements, facial expression, test for taste	Facial paralysis, loss of taste over anterior two-thirds of tongue
8	Auditory vestibular	(s) Hearing	Audiogram for testing hearing; stimulate by rotating patient or by irrigating the ear with hot or cold water (caloric test)	Deafness, sensation of noise in ear (tinnitus); disequilibrium, feeling of disorientation in space
9	Glossopharyngeal	(s, m) Tongue and pharynx	Test for sweet, salt, bitter, and sour tastes on tongue; touch walls of pharynx for pharyngeal or gag reflex	Partial dry mouth, loss of taste (ageusia) over posterior third of tongue, anesthesia and paralysis of upper pharynx
10	Vagus	(s, m) Heart, blood vessels, viscera, movement of larynx and pharynx	Observe palate in phonation, touching palate for palatal reflex	Hoarseness, lower pharyngeal anesthesia and paralysis, indefinite visceral disturbance
11	Spinal accessory	(m) Neck muscles and viscera	Movement, strength, and bulk of neck and shoulder muscles	Wasting of neck with weakened rotation, inability to shrug
12	Hypoglossal	(m) Tongue muscles	Tongue movements, tremor, wasting or wrinkling of tongue	Wasting of tongue with deviation to side of lesion on protrusion

*The letters *s* and *m* refer to sensory and motor function, respectively, of the nerve.

The Cortex

Anatomists use the term *cortex* (from the Latin for "bark," as in a tree's bark) to refer to any outer layer of cells. In neuroscience, the terms *cortex* and *neocortex* (new cortex) are often used interchangeably to refer to the outer part of the forebrain, and so by convention "cortex" refers to "neocortex" unless otherwise indicated. The cortex is the part of the brain that has expanded the most in the course of evolution; it comprises 80% by volume of the human brain.

The human neocortex has an area as large as 2500 cm^2 but a thickness of only 1.5 to 3.0 mm. It consists of four to six layers of cells (gray matter) and is heavily wrinkled. This wrinkling is nature's solution to the problem of confining the huge neocortical surface area within a skull that is still small enough to pass through the birth canal. Just as crumpling a sheet of paper enables it to fit into a smaller box than it could when flat, the folding of the neocortex permits the human brain to fit comfortably within the relatively fixed volume of the skull.

Hemispheres and Lobes

As Figure 3.12 (dorsal view) shows, the cortex consists of two nearly symmetrical **hemispheres,** the left and the right, separated by the **longitudinal fissure.** Each hemisphere is subdivided into four lobes: frontal, parietal, temporal, and occipital. The **frontal lobes** have fixed boundaries: they are bounded posteriorly by the central sulcus, inferiorly by the lateral fissure, and medially by the **cingulate sulcus.** The anterior boundary of the **parietal lobes** is the central sulcus, and their inferior boundary is the lateral fissure. The **temporal lobes** are bounded dorsally by the lateral fissure. On the lateral surface of the brain, there are no definite boundaries between the occipital lobes and the parietal and temporal lobes.

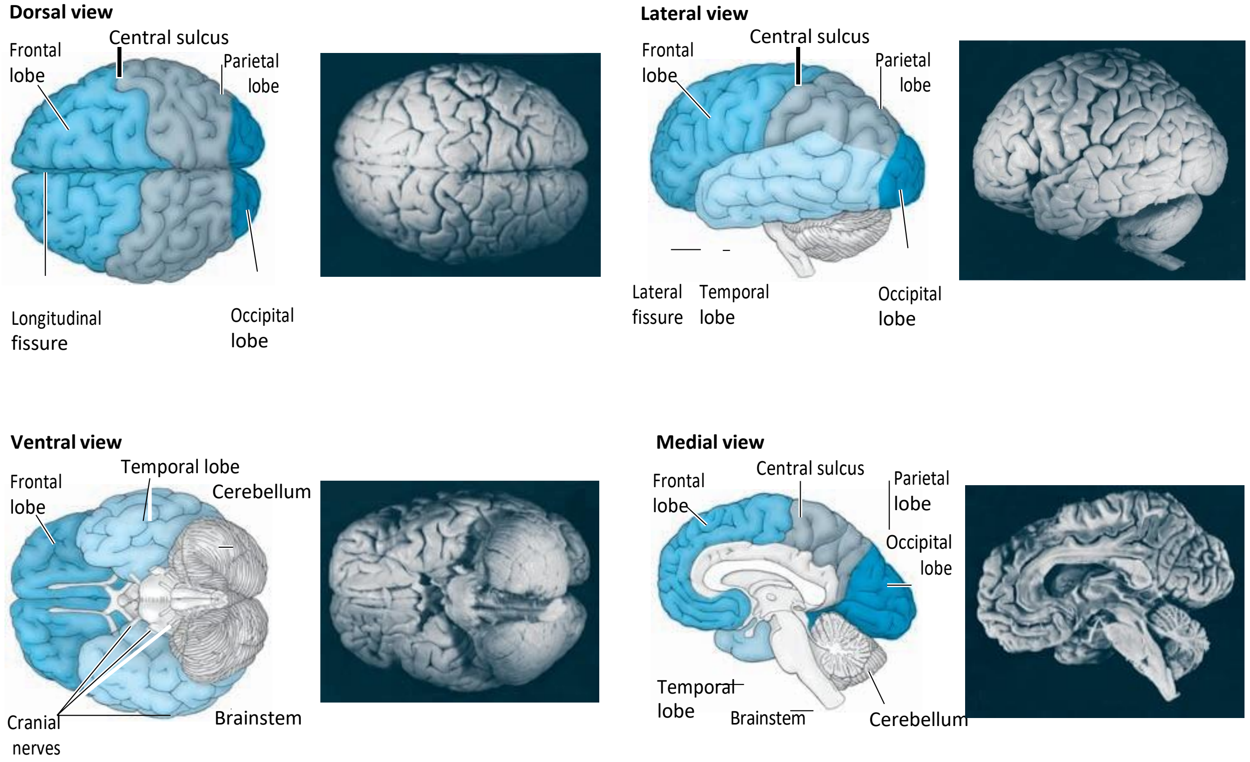


Figure 3.12 In these views of the human brain (from top, dorsal; bottom, ventral; side, lateral; and middle, medial), the locations of the frontal, parietal, occipital, and temporal lobes of the cerebral hemispheres are shown, as are the cerebellum and the three major sulci (the central sulcus, lateral fissure, and longitudinal fissure) of the cerebral hemispheres.

Fissures, Sulci, and Gyri

To review some of the main features of the cortex that were introduced in Chapter 1, the wrinkled surface of the neocortex consists of clefts and ridges. A cleft is called a **fissure** if it extends deeply enough into the brain to indent the ventricles, whereas it is a **sulcus** (plural sulci) if it is shallower. A ridge is called a **gyrus** (plural gyri).

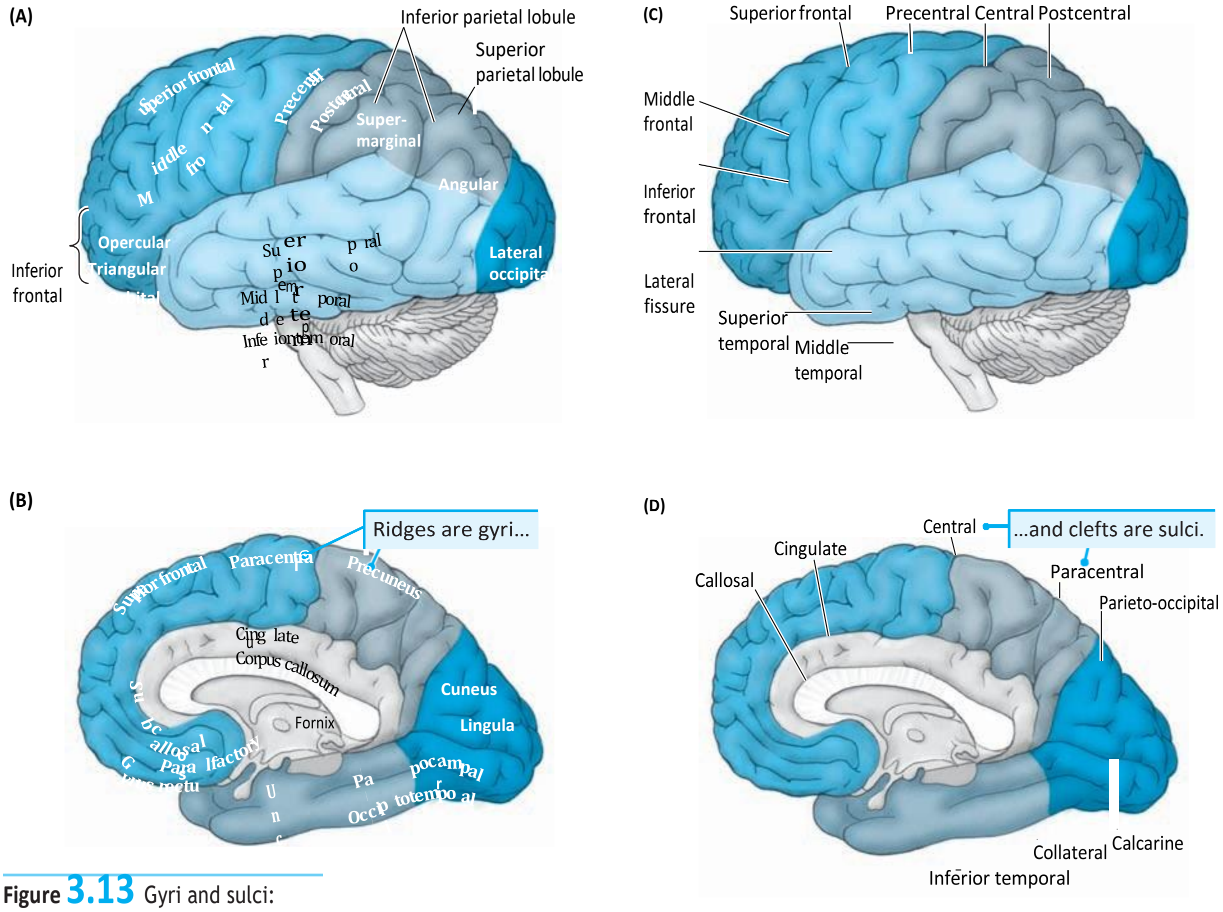


Figure 3.13 Gyri and sulci: lateral (A) and medial (B) views of the gyri; lateral (C) and medial (D) views of the sulci.

Figure 3.13 shows the location of some of the more important fissures, sulci, and gyri of the brain. There is *some* variation in the location of these features on the two sides of a single individual's brain, and *substantial* variation in the location, size, and shape of the gyri and sulci in the brains of different individuals. Adjacent gyri differ in the way that cells are organized within them; the shift from one kind of arrangement to another is usually at the sulcus. There is some evidence that gyri can be associated with specific functions.

As shown in Figure 3.13A, there are four major gyri in the frontal lobe: the superior frontal, middle frontal, inferior frontal, and precentral (which lies in front of the central sulcus). There are five major gyri in the parietal lobe: the superior and inferior lobule (small lobe), the postcentral (lying behind the central sulcus), and the supermarginal and angular (on either side of the lateral fissure). There are three gyri in the temporal lobe: the superior, middle, and inferior. Only the lateral gyrus is evident in the occipital cortex in this lateral view.

The Organization of the Cortex in Relation to Its Inputs and Outputs

Different regions of the neocortex have different functions. Some regions receive information from sensory systems, other regions command movements, and still other regions are the sites of connections between the sensory and the motor areas, enabling them to work in concert. Recall that the inputs are relayed through the thalamic nuclei. The locations of these various inputs and outputs can be represented by a map called a **projection map.** Such a map is constructed by tracing axons from the sensory systems into the brain and tracing axons from the neocortex to the motor systems of the brainstem and spinal cord.

The projection map in Figure 3.14 was constructed in part by following the axons projected by sensory receptors to see where they end in the neocortex and in part by locating the sources in the neocortex of motor axons projected from there to the spinal cord. As Figure 3.14 shows, the projections from the eye can be traced to the occipital lobe, the projections from the ear to the temporal lobe, and the projections from the somatosensory system to the parietal lobe. The olfactory system sends projections to the ventral frontal lobe. The major motor projection to the spinal cord originates in the frontal lobe. These areas that receive projections from structures outside the neocortex or send projections to it are called **primary projection areas.** Note that the lateral view of the brain presented in Figure 3.14 does not represent the entire extent of these primary projection areas, because they also extend down into the gyri and fissures. Much of the auditory zone, for example, is located within the lateral fissure. Nevertheless, the primary projection areas of the neocortex are small relative to the total size of the cortex.

The primary sensory areas send projections into the areas adjacent to them, and the motor areas receive fibers from areas adjacent to them. These adjacent areas, less directly connected with the sensory receptors and motor neurons, are referred to as **secondary areas.** The secondary areas are thought to be more engaged in interpreting perceptions or organizing movements than are the primary areas. The areas that lie between the various secondary areas are referred to as **tertiary areas.** Often referred to as association areas, tertiary areas serve to connect and coordinate the functions of the secondary areas. Tertiary areas mediate complex activities such as language, planning, memory, and attention.

Overall, the neocortex can be conceptualized as consisting of a number of fields: visual, auditory, body senses, and motor. Because vision, audition, and body senses are functions of the posterior cortex, this region of the brain (parietal, temporal, and occipital lobes) is considered to be largely sensory; and, because the motor cortex is located in the frontal neocortex, that lobe is considered to be largely motor. Finally, because each lobe contains one of the primary projection areas, it can roughly be associated with a general function:

Frontal lobes: motor

Parietal lobes: body senses

Temporal lobes: auditory function

Occipital lobes: visual functions

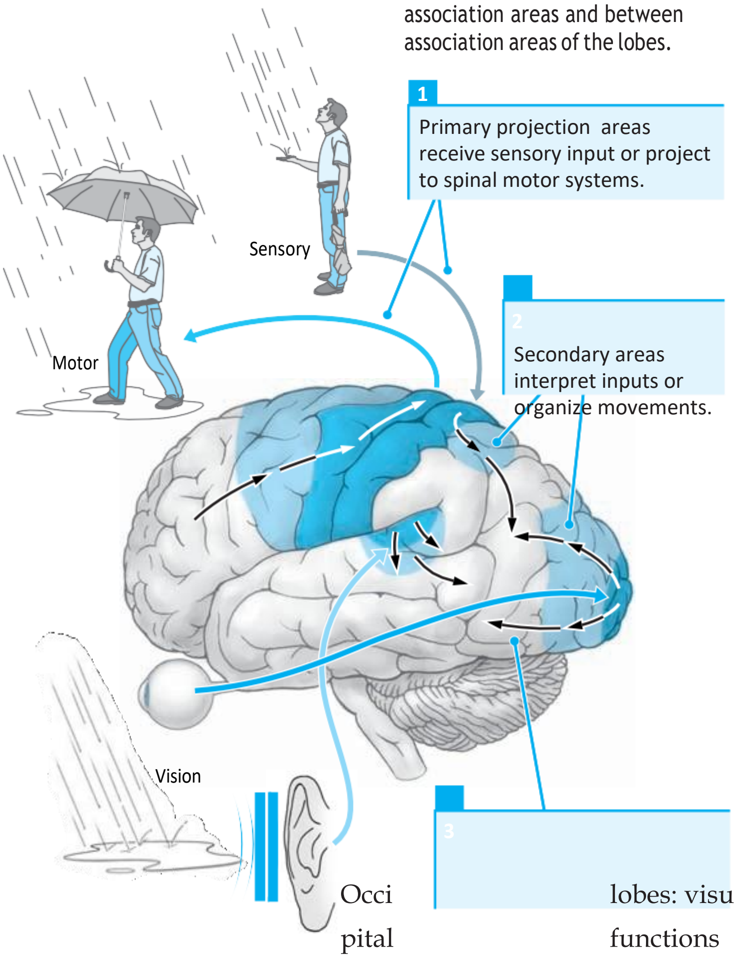


Figure 3.14 A projection map. The darkest shading indicates primary projection areas, which receive input from the sensory systems or project to spinal motor systems. The lighter shading represents secondary areas. The unshaded regions are higher-order association, or tertiary, areas. Arrows indicate that information flows from primary to secondary sensory areas and from secondary motor areas to primary motor areas. Information also flows from secondary to association areas and between association areas of the lobes.

Audition

Plunk!

Association areas (uncolored) modulate information between secondary areas.

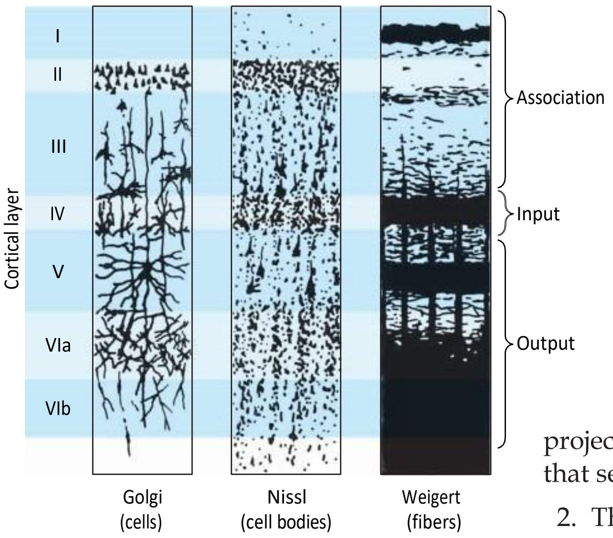


Figure 3.15 The cells of the cortex revealed through the use of three different stains. The Golgi stain penetrates only a few neurons but reveals all of their processes, the Nissl stain highlights only cell bodies, and the Weigert myelin stain reveals the location of axons. Note that these staining procedures highlight the different cell types of the cortex and show that they are organized into a number of layers, each of which contains typical cell types. (After Brodmann, 1909.)

The Organization of the Cells of the Cortex

Examination of the cells of the cortex shows that the cortex can be divided into different areas on the basis of cell organization. Maps of the cortex that are based on cell structure are called cytoarchitectonic maps. The neurons of the neocortex are arranged in about six layers, as shown in Figure 3.15. These six layers can be separated into three groups by function.

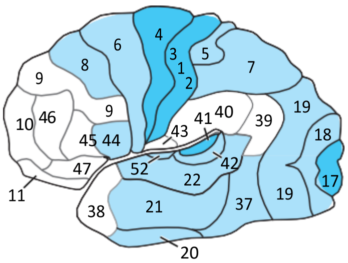
1. The **output cell layers,** layers V and VI, send axons to other brain areas. Both of these layers and the cells of which they are composed are particularly large and distinctive in the motor cortex, which sends projections to the spinal cord. (Large size is typical of cells that send information long distances.)
2. The **input cell layer,** layer IV, receives axons from sensory systems and other cortical areas. This layer features large numbers of small, densely packed cells in the primary areas of vision, somatosensation, audition, and taste-olfaction, which receive large projections from their respective sensory organs.
3. The **association cell layers,** layers I, II, and III, receive input mainly from layer IV and are quite well developed in the secondary and tertiary areas of the cortex.

In short, sensory areas have many layer IV cells, motor areas have many layer V and VI cells, and association areas have many layer I, II, and III cells.

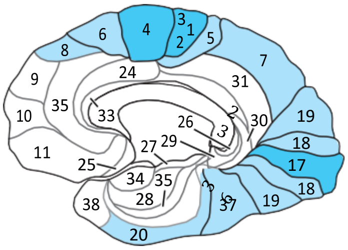
One widely used map of the cortex, known as **Brodmann's map,** is presented in Figure 3.16A. This map represents differences in the density of different kinds of neocortical neurons. In Brodmann's map, the different areas are numbered, but the numbers themselves have no special meaning. To do his

Figure 3.16 (A) Brodmann's areas of the cortex. A few numbers are missing from the original sources of this drawing, including 12 through 16 and 48 through 51. Some areas have histologically distinctive boundaries and are outlined with heavy solid lines; others, such as 6, 18, and 19, have less-distinctive boundaries and are outlined with light solid lines; the remaining areas have no distinct boundaries but gradually merge into one another and are outlined with dotted lines. (B) Functional areas and Brodmann cytoarchitectonic areas. (Part A after Elliott, 1969.)

(A) **Lateral view**



(B) **Medial view**



Function	Map code	Brodmann area
Vision		
primary	■	17
secondary	▨	18, 19, 20, 21, 37
Auditory		
primary	■	41
secondary	▨	22, 42
Body senses		
primary	■	1, 2, 3
secondary	▨	5, 7
Sensory, tertiary	□	7, 22, 37, 39, 40
Motor		
primary	■	4
secondary	▨	6
eye movement	▨	8
speech	▨	44
Motor, tertiary	□	9, 10, 11, 45, 46, 47

analysis, Brodmann divided the brain at the central sulcus and then examined the front and back halves of the brain separately, numbering new conformations of cells as he found them but without following a methodical path over the surface or through the layers. Thus, he found areas 1 and 2 in the posterior section, then switched to the anterior section and found areas 3 and 4, and then switched back again, and then looked somewhere else.

As it turns out, Brodmann's map is very useful because the regions depicted in it correspond quite closely with regions discovered with the use of noncytoarchitectonic techniques. Figure 3.16B summarizes some of the relations between areas on Brodmann's map and areas that have been mapped according to their known functions. For example, area 17 corresponds to the primary visual projection area, whereas areas 18 and 19 correspond to the secondary visual projection areas. Area 4 is the primary motor cortex. Broca's area, an area related to the articulation of words, is area 44. Similar relations exist for other areas and functions.

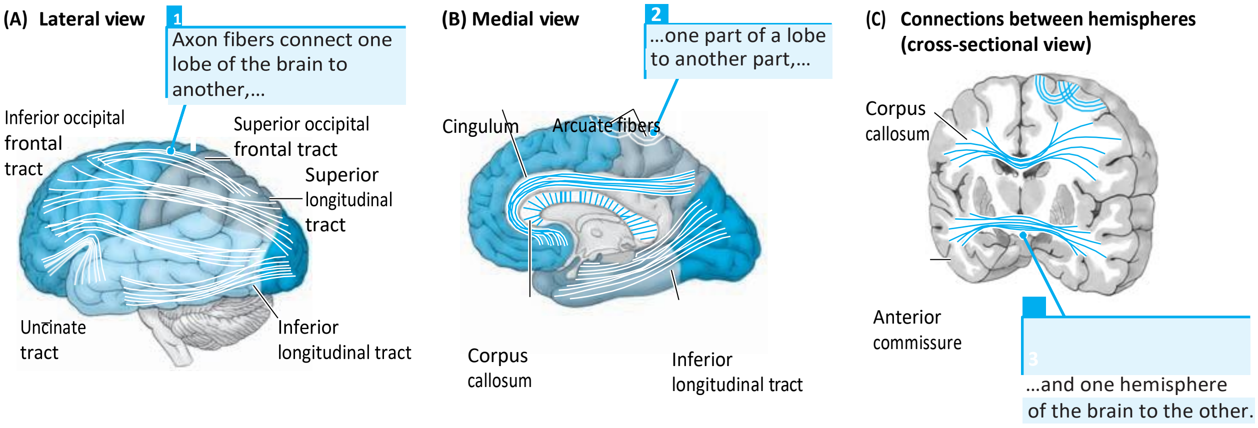
One of the problems with Brodmann's map is that new, more powerful analytical techniques have shown that many Brodmann areas actually consist of two architectonically distinct areas or more. For this reason, the map is continually being updated and now consists of an unwieldy mixture of numbers, letters, and names.

Connections Between Cortical Areas

The various regions of the neocortex are interconnected by three types of axon projections: (1) relatively short connections between one part of a lobe and another, (2) longer connections between one lobe and another, and (3) interhemispheric connections, or **commissures,** between one hemisphere and another. Figure 3.17 shows the locations and names of some of these connections.

Most of the interhemispheric connections link **homotopic** points in the two hemispheres — that is, contralateral points that correspond to one another in the brain's mirror-image structure. Thus, the commissures act as a zipper to link the two sides of the neocortical representation of the world and of the body together. The two main interhemispheric commissures are the corpus callosum and the anterior commissure.

Figure 3.17 Connections between various regions of the cortex.



The cortex also makes other types of connections with itself. Cells in any area, for example, may send axons to cells in a subcortical area such as the thalamus, and the cells there may then send their axons to some other cortical area. These types of relations are more difficult to establish anatomically than are those based on direct connections.

The various connections between regions of the cortex are of considerable functional interest, because damage to a pathway can have consequences as severe as damage to the functional areas connected by the pathway. A glance at Figure 3.17 shows that it is difficult indeed to damage any area of the cortex without damaging one or more of its interconnecting pathways.

The Limbic Lobe and Basal Ganglia

In addition to the neocortex, there are two other main forebrain structures: the limbic system and the basal ganglia. A brief description of the anatomy and function of these regions follows.

The Limbic Lobe

In the course of the evolution of the amphibians and reptiles, a number of three-layer cortical structures that sheath the periphery of the brainstem developed. With the subsequent growth of the neocortex, they became sandwiched between the new brain and the old. Because of the evolutionary origin of these structures, some anatomists have referred to them as the reptilian brain, but the term **limbic lobe** (from the Latin *limbus,* meaning "border" or "hem"), coined by Broca in 1878, is more widely recognized today.

The limbic lobe is also referred to as the **limbic system** (although that may very well be a misnomer, as we soon explain). The limbic lobe consists of a number of interrelated structures, including the **hippocampus** ("sea horse"), **septum** ("partition"), and cingulate ("girdle") gyrus (Figure 3.18). The history of how the limbic "lobe" became the limbic "system" is one of the most interesting chapters in neuroscience.

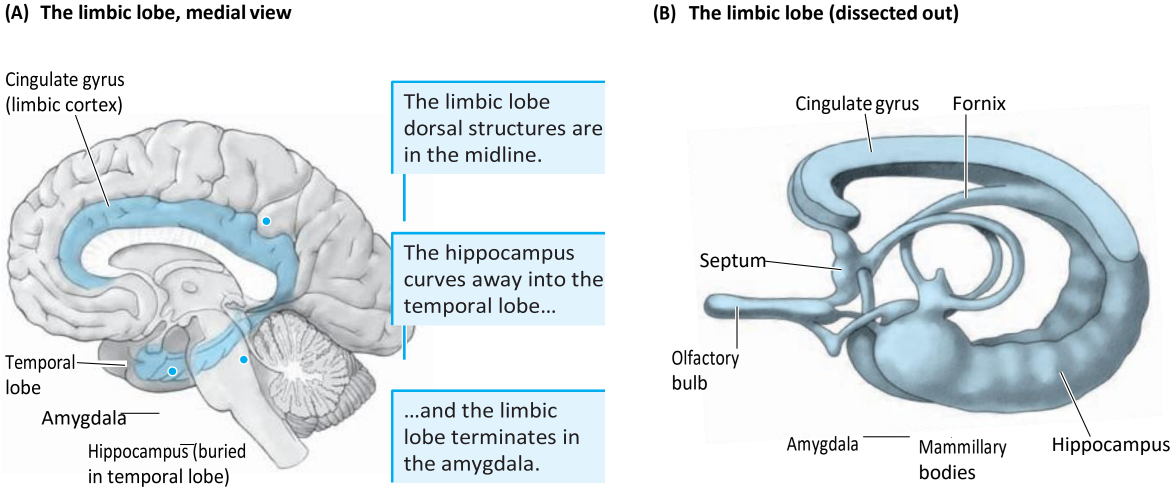


Figure 3.18 (A) This medial view of the right hemisphere illustrates the principal structures of the limbic system, including the cingulate cortex, the hippocampus, and the amygdala. (B) A model of the human limbic system and its major structures. Note: As proposed by Papez, the limbic system forms a circuit in which the hypothalamus (mammillary bodies) connect to the hippocampus through the cingulate gyrus, and the hippocampus connects to the hypothalamus through the fornix. (After Hamilton, 1976.)

(A) The limbic lobe, medial view

The limbic lobe dorsal structures are in the midline.

The hippocampus curves away into the temporal lobe...

...and the limbic lobe terminates in the amygdala.

(B) The limbic lobe (dissected out)

The first theory of limbic function stemmed from the observation that there are connections between the olfactory system and the limbic lobe. On this evidence, anatomists hypothesized that the limbic structures processed olfactory information, and so collectively the structures became known as the **rhinencephalon,** or "smell-brain." Subsequently, a number of experiments demonstrated that some limbic structures had little olfactory function. Then, in 1937, Papez, in what at the time amounted to a scientific tour de force, asked, "Is emotion a magic product, or is it a physiologic process which depends on an anatomic mechanism?" He suggested that emotion, which had no known anatomic substrate, is a product of the limbic lobe, which had no recognized function. He proposed that the emotional brain consists of a circuit in which information flows from the mammillary bodies in the hypothalamus to the anterior thalamic nucleus to the cingulate cortex to the hippocampus and back to the mammillary bodies. Input could enter this circuit from other structures to be elaborated as emotion. For example, an idea ("It is dangerous to walk in the dark") from the neocortex could enter the circuit to be elaborated as fear ("I feel frightened in the dark") and ultimately to influence the hypothalamus to release a hormone that would create the appropriate physical response to the idea and its emotional corollary.

In 1957, Scoville and Milner described the now-famous patient H. M., who had had his medial temporal lobe, including his hippocampus, removed bilaterally as a treatment for epilepsy. His primary deficits were not emotional. He displayed little ability to learn new information, although his presurgery memories were largely intact. Thereafter it was proposed that the limbic system is the memory system of the brain; but, in the years since H. M. was first described, many other regions of the brain also have become recognized as playing a part in memory, diminishing the apparent role of the limbic system in that function. Today, along with evidence that the limbic lobe has some involvement in olfaction, emotion, and memory, most major lines of research also suggest that the limbic system plays a special role in spatial behavior.

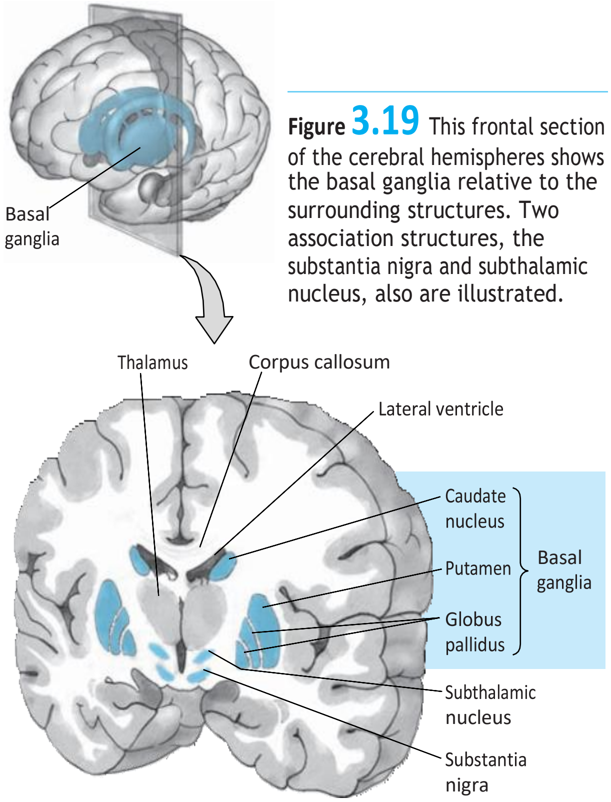


Figure 3.19 This frontal section of the cerebral hemispheres shows the basal ganglia relative to the surrounding structures. Two association structures, the substantia nigra and subthalamic nucleus, also are illustrated.

The Basal Ganglia

The **basal ganglia** ("lower knots," referring to "knots below the cortex") are a collection of nuclei lying mainly beneath the anterior regions of the neocortex (Figure 3.19). They include the **putamen** ("shell"), the **globus pallidus** ("pale globe"), the **caudate nucleus** ("tailed nucleus"), and the **amygdala** ("almond"). These structures form a circuit with the cortex. The caudate nucleus receives projections from all areas of the neocortex and sends its own projections through the putamen and globus pallidus to the thalamus and from there to the motor areas of the cortex. The basal ganglia also have reciprocal connections with the midbrain, especially with a nucleus called the **substantia nigra** ("black area").

The basal ganglia historically have been described as having two functions. First, damage to different parts of the basal ganglia can produce changes in posture, increases or decreases in muscle tone, and abnormal movements such as twitches, jerks, and tremors; so the ganglia are thought to take part in such motor functions as the sequencing of movements into a smoothly executed response, as occurs during talking. Second, the basal ganglia are also thought to support stimulus-response, or habit, learning. For example, a bird that learns after a number of experiences that brightly colored butterflies have a bitter taste would use its basal ganglia to learn the association between taste and color and refrain from eating the insects.

The Crossed Brain

One of the most peculiar features of the organization of the brain is that each of its symmetrical halves responds to sensory stimulation from the contralateral side of the body or sensory world and controls the musculature on the contralateral side of the body (Figure 3.20). The visual system achieves this end by crossing half the fibers of the optic tract and by reversing the image through the lens of the eye. Nearly all the fibers of the motor and somatosensory systems cross. Projections from each ear go to both hemispheres, but there is substantial evidence that auditory excitation from one ear sends a stronger signal to the opposite hemisphere. As a result of this arrangement, numerous crossings, or **decussations,** of sensory and motor fibers are found along the center of the nervous system. Later chapters contain detailed descriptions of some of these crossings, when they are relevant to the discussion of how a given system works. It is sufficient to say here that, because of this arrangement, damage to one side of the brain generally causes sensory and motor impairments not to the same side of the body but to the opposite side.

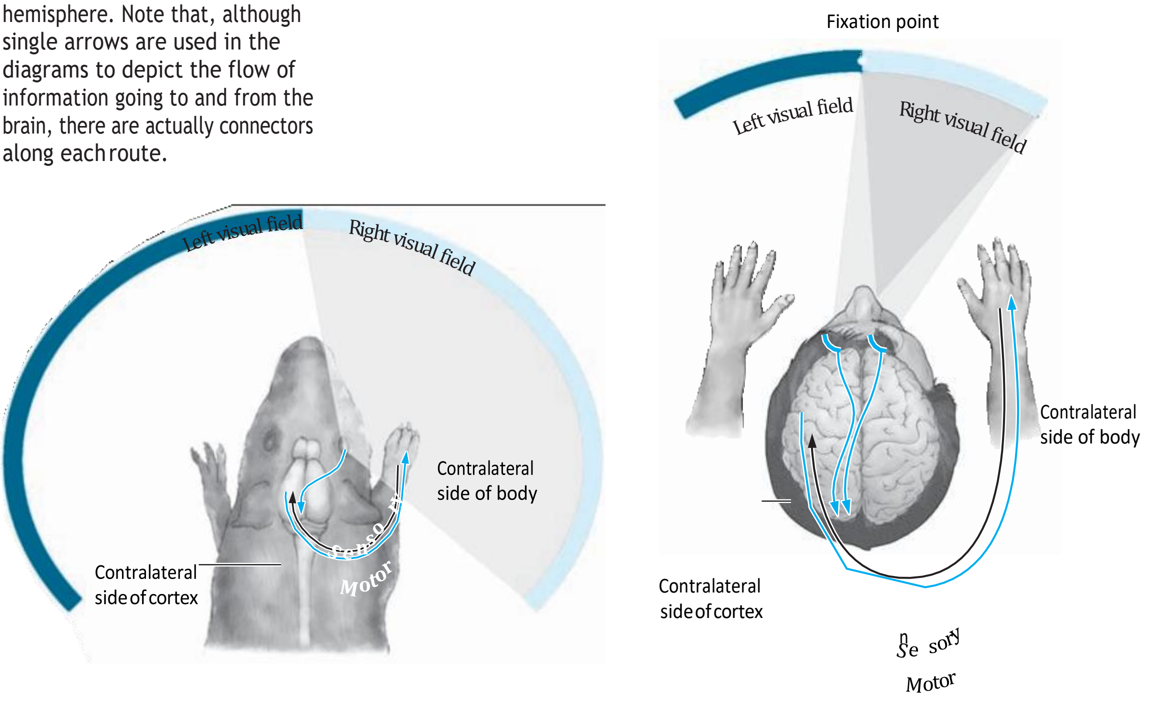


Figure 3.20 (Left) This schematic representation of a rat's brain from a dorsal view shows the projection of visual and somatosensory input to contralateral (opposite-side) areas of the cortex and the projection of the motor cortex to the contralateral side of the body. The eyes of the rat are laterally placed such that most of the input from each eye travels to the opposite hemisphere. (Right) In the human head, the two eyes are frontally placed. As a result, the visual input is split in two, and so input from the right side of the world as seen by both eyes goes to the left hemisphere and input from the left side of the world as seen by both eyes goes to the right hemisphere. The somatosensory input of both rats and humans is completely crossed, and so information coming from the right paw or hand goes to the left hemisphere. Note that, although single arrows are used in the diagrams to depict the flow of information going to and from the brain, there are actually connectors along each route.

Blood Supply

The brain receives its blood supply from two **internal carotid arteries** and two **vertebral arteries;** one of each courses up each side of the neck. The internal carotid arteries enter the skull at the base of the brain, branching off into a number of smaller arteries and two major arteries, the **anterior cerebral artery** and the **middle cerebral artery,** that irrigate the anterior and middle parts of the cortex. The vertebral arteries also enter at the base of the brain but then join together to form the basilar artery. After branching off into several smaller arteries that irrigate the cerebellum, the basilar artery gives rise to the **posterior cerebral artery,** which irrigates the medial temporal lobe and the posterior occipital lobe.

The distribution zones of the anterior, middle, and posterior cerebral arteries are shown in Figure 3.21. Note that, if the hand is placed so that the wrist is on the artery trunk, the extended digits will give an approximate representation of the area of the cortex that is irrigated. These arteries irrigate not only the cortex but also subcortical structures. Thus, a disruption of blood flow to one of these arteries has serious consequences for subcortical as well as cortical structures.

Such a disruption occurs in a condition called **stroke:** an artery becomes blocked by the formation of a blood clot, depriving part of the brain of its blood supply. Within a few minutes of this deprivation,

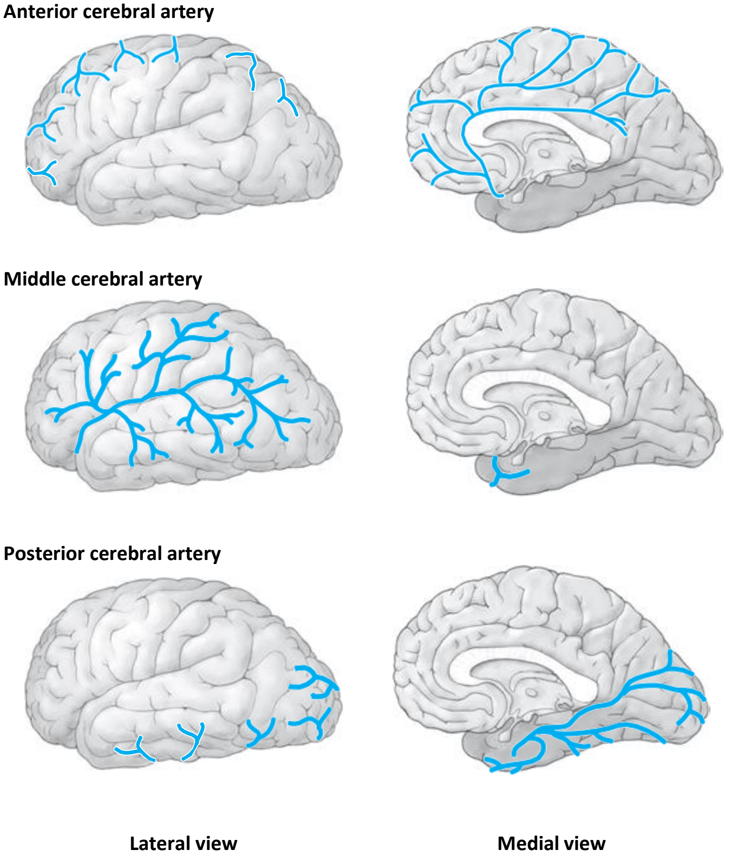


Figure 3.21 Distribution of the major cerebral arteries in the hemispheres: (left) lateral view; (right) medial view. If you align your hand so that your wrist represents the base of the artery, the extended digits will spread over the area of cortex to which blood is distributed by that artery.

the cells in the region begin to die. Sometimes immediate treatment with an anticoagulant can restore the flow of blood within a couple of hours, rescuing significant numbers of cells. The symptoms of stroke vary according to the location of the loss of blood supply. Note in Figure 3.21 that blockade of the anterior cerebral artery results in loss of functions of the medial cortex, which include limbic functions; stroke of the middle cerebral artery results in impairments in motor function; and blockade of the posterior cerebral artery results in loss of visual functions.

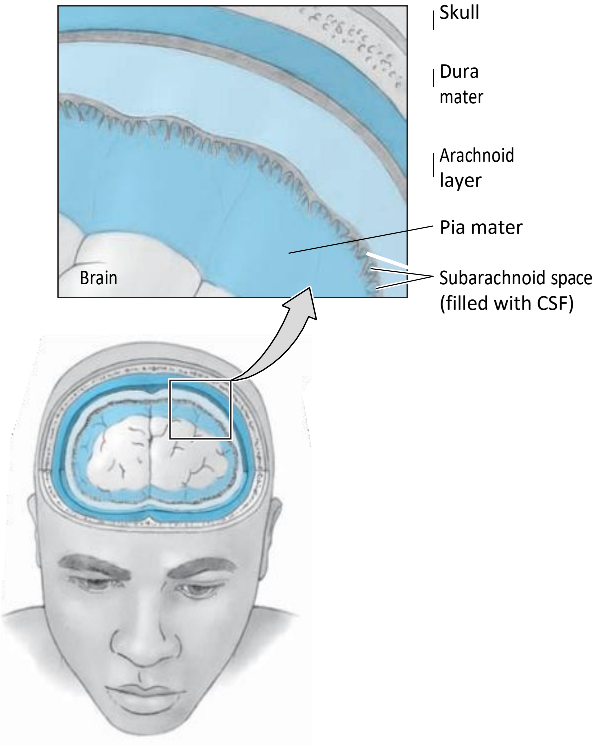
The veins of the brain, through which spent blood returns to the lungs, are classified as external and internal cerebral and cerebellar veins. The venous flow does not follow the course of the major arteries but instead follows a pattern of its own, eventually entering a system of venous sinuses, or cavities, that drain the dura mater (one of the membranes that protect the brain from injury, as described next).

Protection

The brain and spinal cord are supported and protected from injury and infection in four ways (Figure 3.22). First, the brain is enclosed in a thick bone, the **skull,** and the spinal cord is encased in a series of interlocking bony vertebrae. Second, within these bony cases are three membranes: the outer *dura mater* (from the Latin, meaning “hard mother”), a tough double layer of tissue enclosing the brain in a kind of loose sack; the middle *arachnoid membrane* (from the Greek, meaning “resembling a spider’s web”), a very thin sheet of delicate tissue that follows the contours of the brain; and the inner *pia mater* (from the Latin, meaning “soft mother”), which is a moderately tough tissue that clings to the surface of the brain.

Third, the brain is cushioned from shock and sudden changes of pressure by the cerebrospinal fluid, which fills the ventricles inside the brain and circulates around

Figure 3.22 The brain is protected by the skull and a number of thick membranes—the dura, arachnoid, and pia. The subarachnoid space between the arachnoid layer and the pia layer contains cerebral spinal fluid (CSF).



the brain beneath the arachnoid membrane, in the subarachnoid space. This fluid is a colorless solution of sodium chloride and other salts and is secreted continually by a plexus of glial (ependymal) cells that protrudes into each ventricle. The CSF flows from the ventricles, circulates around the brain, and is then absorbed by the venous sinuses of the dura mater. If the outflow is blocked, as occurs in a congenital condition called **hydrocephalus,** the ventricles enlarge in response to CSF pressure and, in turn, dilate the skull. The condition can be ameliorated by draining the ventricles through a tube. Although CSF is not thought to nourish the brain, it may play a role in removing metabolic wastes from the brain.

Fourth, the brain is protected from many chemical substances circulating in the rest of the body by the **blood–brain barrier.** To form this barrier, the cells of the capillaries, the very small blood vessels, form tight junctions with one another, thus preventing many substances from crossing into or out of the capillaries.

Summary

The brain is composed of neurons and glial cells, each of which are present in many forms. The brain is organized into nuclei and tracts, with the nuclei appearing gray and the tracts appearing white to visual inspection. Visualization of brain anatomy in greater detail requires that tissue be stained to highlight differences in the biochemical structures of different groups of nuclei and tracts.

The developing brain first consists of three divisions surrounding a canal filled with cerebrospinal fluid. In adult mammals, increases in the size and complexity of the first and third division produce a brain consisting of five separate divisions. The spinal cord communicates with the body through dorsal roots, which are sensory, and ventral roots, which are motor. The spinal cord is also divided into segments, each representing a dermatome, or segment, of the body. This segmentation and the dorsal-is-sensory and ventral-is-motor