

Chapter 4: The Neuroanatomical Bases by Which Neural Circuits Mediate Behavior

Introduction

THE HUMAN BRAIN carries out actions in ways no current computer can begin to approach. Merely to see—to look onto the world and recognize a face or facial expression—entails amazing computational achievements. Indeed, all our perceptual abilities—seeing, hearing, smelling, tasting, and touching—are analytical triumphs. Similarly, all of our voluntary actions are triumphs of engineering. Sensation and movement, while wondrous in their own right, pale in comparison to complex cognitive behaviors such as forming memories or understanding social conventions.

The brain accomplishes these computational feats because its nerve cells are wired together in very precise functional circuits. The brain is hierarchically organized such that information processed at one level is passed to higher-level circuits for more complex and refined processing. In essence, the brain is a network of networks. Different brain areas work in an integrated fashion to accomplish purposeful behavior.

In this chapter, we outline the neuroanatomical organization of some of the circuits that enable the brain to process sensory input and produce motor output. We focus on touch as a sensory modality because the somatosensory system is particularly well understood and because touch clearly illustrates the interaction of sensory processing circuits at several levels, from the spinal cord to the cerebral cortex. Our purpose here is to illustrate the basic principles of how circuits control behavior. In the next chapter, we consider the functional properties of these circuits, including the computations by which they process information. In subsequent chapters, we consider in more detail the anatomy and function of the various sensory modalities and how sensory input regulates movement.

Finally, we provide a preview of the brain circuits that are instrumental in producing the memories of our daily lives, called explicit memory (see [Chapters 52 and 54](#)). We do this to make the point that while many of the neurons in the memory circuits are similar to those in the sensory and motor circuits, not all are. Moreover, the organization of the pathways between circuits is different in the memory system than it is in the motor and sensory systems. This highlights a basic neurobiological tenet that different circuits of the brain have evolved an organization to most efficiently carry out specific functions.

Comprehending the functional organization of the brain might at first seem daunting. But as we saw in the previous chapter, the organization of the brain is simplified by three anatomical considerations. First, there are relatively few types of neurons. Each of the many thousands of spinal motor neurons or millions of neocortical pyramidal cells has a similar anatomical structure and serves a similar function. Second, neurons in the brain and spinal cord are clustered in functional groups called nuclei or discrete areas of the cerebral cortex, which form networks or functional systems. Third, the discrete areas of the cerebral cortex are specialized for sensory, motor, or associative functions such as memory.

Local Circuits Carry Out Specific Neural Computations That Are Coordinated to Mediate Complex Behaviors

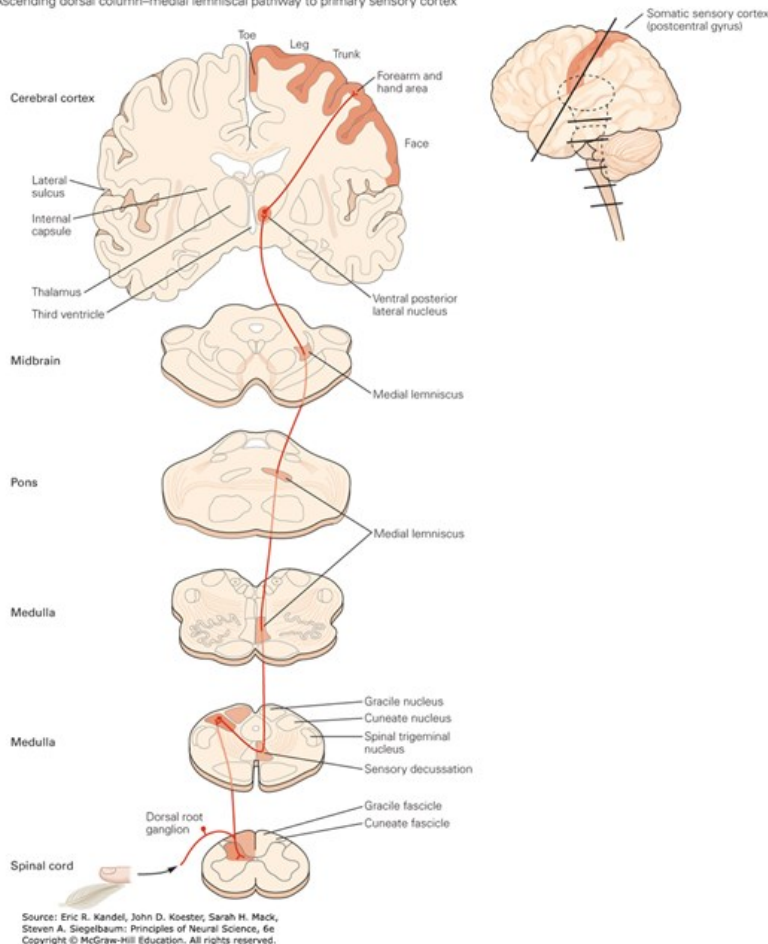
Neurons are interconnected to form functional circuits. Within the spinal cord, for example, simple reflex circuits receive sensory information from stretch receptors and send output to various muscle groups. For more complex behavioral functions, different stages of information processing are carried out in networks in different regions of the nervous system. Connections between neurons within the nervous system can be of different lengths.

Within a brain region, local connections, which may be excitatory or inhibitory, integrate many of the neurons into functional networks. Such local networks may then provide outputs to one or more other brain regions through longer projections. Many of these longer pathways have names. For example, projections from the lateral geniculate nucleus of the thalamus to the visual cortex are called the optic radiations. Connections from the neocortex—the region of the cerebral cortex nearest the surface of the brain—of one side of the brain to the other side of the brain form the corpus callosum. Information carried by these long pathways integrates the output of many local circuits ([Figure 4-1](#)).

Figure 4-1

The dorsal column–medial lemniscal pathway is the major afferent pathway for somatosensory information. Somatosensory information enters the central nervous system through the dorsal root ganglion cells. The flow of information ultimately leads to the somatosensory cortex. Fibers that relay information from different parts of the body maintain an orderly relationship to each other and form a neural map of the body surface in their pattern of termination at each synaptic relay.

Ascending dorsal column–medial lemniscal pathway to primary sensory cortex



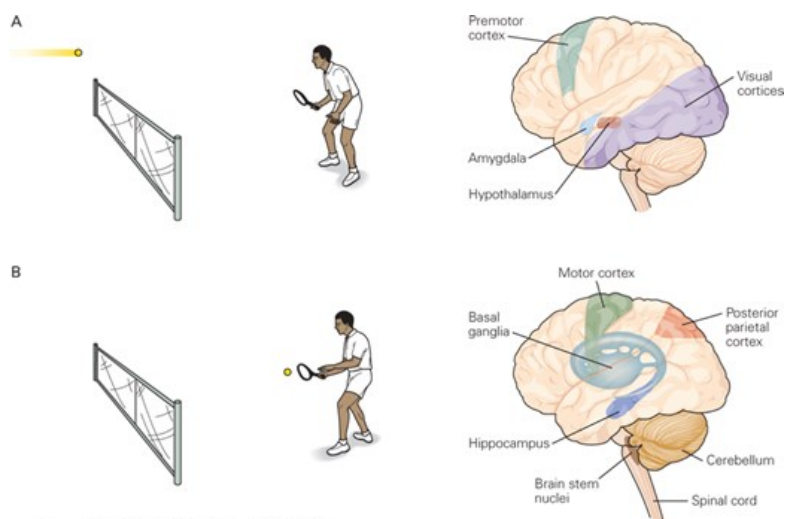
Consider the simple act of hitting a tennis ball (Figure 4-2). Visual information about the motion of the approaching ball is analyzed in the visual system, which is itself a hierarchically organized system extending from the retina to the lateral geniculate nucleus of the thalamus to dozens of cortical areas in the occipital and temporal lobes (Chapter 21). This information is combined in the motor cortex with proprioceptive information about the position of the arms, legs, and trunk to calculate the movement necessary to intercept the ball. Once the swing is initiated, many minor adjustments of the motor program are made by other brain regions dedicated to movement, such as the cerebellum, based on a steady stream of sensory information about the trajectory of the approaching ball and the position of the arm.

Figure 4-2

A simple behavior is mediated by many parts of the brain.

- A.** A tennis player watching an approaching ball uses the visual cortex to judge the size, direction, and velocity of the ball. The premotor cortex develops a motor program to return the ball. The amygdala acts in conjunction with other brain regions to adjust the heart rate, respiration, and other homeostatic mechanisms and also activates the hypothalamus to motivate the player to hit well.
- B.** To execute the shot, the player must use all of the structures illustrated in part A as well as others. The motor cortex sends signals to the spinal cord that activate and inhibit many muscles in the arms and legs. The basal ganglia become involved in initiating motor patterns and perhaps recalling

learned movements to hit the ball properly. The cerebellum adjusts movements based on proprioceptive information from peripheral sensory receptors. The posterior parietal cortex provides the player with a sense of where his body is located in space and where his racket arm is located with respect to his body. Brain stem neurons regulate heart rate, respiration, and arousal throughout the movement. The hippocampus is not involved in hitting the ball but is involved in storing the memory of the return so that the player can brag about it later.



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Like most motor behaviors, hitting a tennis ball is not hardwired into brain circuits but requires learning and memory. The memory for motor tasks, termed procedural or implicit memory, requires modifications to circuits in motor cortex, the basal ganglia, and the cerebellum. Finally, this entire act is accessible to consciousness and may elicit conscious recall of past similar experiences, termed explicit memory, and emotions. Explicit memory depends on circuits in the hippocampus (Chapters 52 and 54), whereas emotions are regulated by the amygdala (Chapters 42 and 53) and portions of the orbitofrontal, cingulate, and insular cortices. Of course, as the swing is being executed, the brain is also engaged in coordinating the player's heart rate, respiration, and other homeostatic functions through equally complex networks.

Sensory Information Circuits Are Illustrated in the Somatosensory System

Complex behaviors, such as differentiating the motor acts required to grasp a ball versus a book, require the integrated action of several nuclei and cortical regions. Information is processed in the brain in a hierarchical fashion. Thus, information about a stimulus is conveyed through a succession of subcortical and then cortical regions; at each level of processing, the information becomes increasingly more complex.

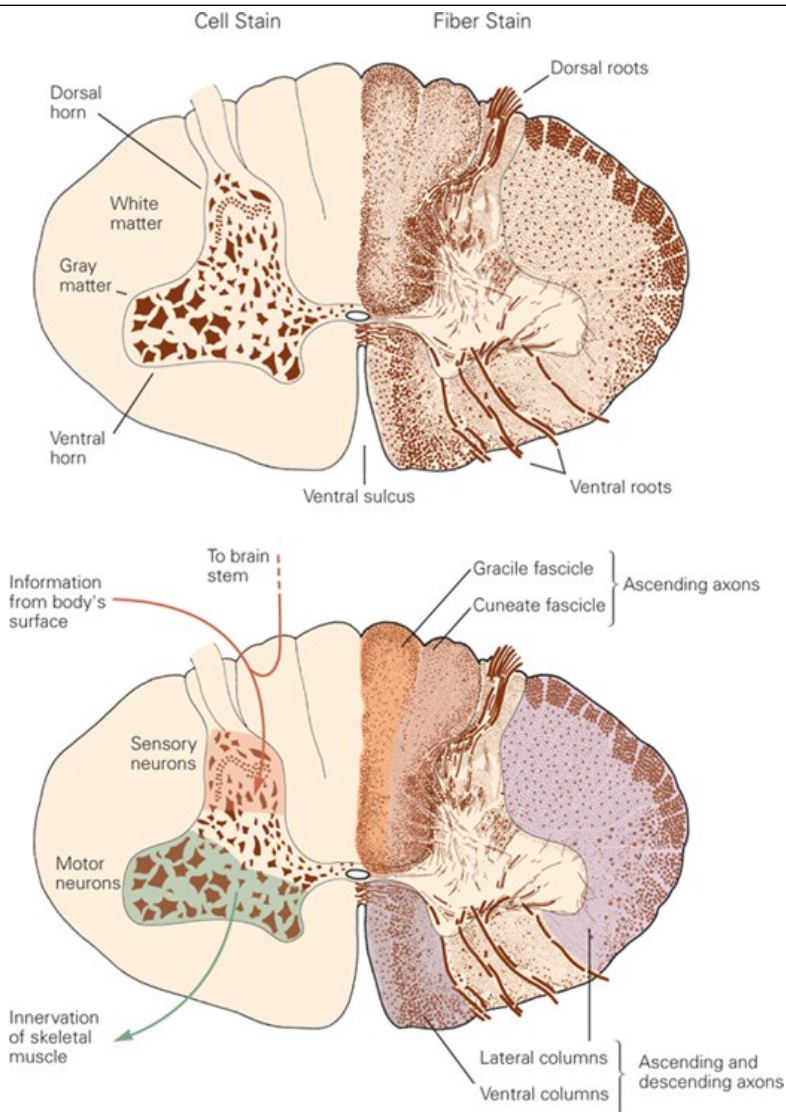
In addition, different types of information, even within a single sensory modality, are processed in several anatomically discrete pathways. In the somatosensory system, a light touch and a painful pin prick to the same area of skin are mediated by different sensory receptors in the skin that connect to distinct pathways in the brain. The system for fine touch, pressure, and proprioception is called the epicritic system, whereas the system for pain and temperature is called the protopathic system.

Somatosensory Information From the Trunk and Limbs Is Conveyed to the Spinal Cord

All forms of somatosensory information from the trunk and limbs enter the spinal cord, which has a core H-shaped region of gray matter where neuronal cell bodies are located. The gray matter is surrounded by white matter formed by myelinated axons that make up both short and long connections. The gray matter on each side of the cord is divided into dorsal (or posterior) and ventral (or anterior) horns (Figure 4-3).

Figure 4-3

The major anatomical features of the spinal cord. The ventral horn (green) contains large motor neurons, whereas the dorsal horn (orange) contains smaller neurons. Fibers of the gracile fascicle carry somatosensory information from the lower limbs, whereas fibers of the cuneate fascicle carry somatosensory information from the upper body. Fiber bundles of the lateral and ventral columns include both ascending and descending fiber bundles.



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The dorsal horn contains groups of secondary sensory neurons (sensory nuclei) whose dendrites receive stimulus information from primary sensory neurons that innervate the body's skin, muscles, and joints. The ventral horn contains groups of motor neurons (motor nuclei) whose axons exit the spinal cord and innervate skeletal muscles. The spinal cord has circuits that mediate behaviors ranging from the stretch reflex to coordination of limb movements.

As we discussed in Chapter 3, when considering the knee-jerk reflex, interneurons of various types in the gray matter regulate the output of the spinal cord motor neurons (see Figure 3-5). Some of these interneurons are excitatory, whereas others are inhibitory. These interneurons modulate both sensory information flowing toward the brain and motor commands descending from the brain to the spinal motor neurons. Motor neurons can also adjust the output of other motor neurons via the interneurons. These circuits will be considered in more detail when we discuss the spinal cord in Chapter 32.

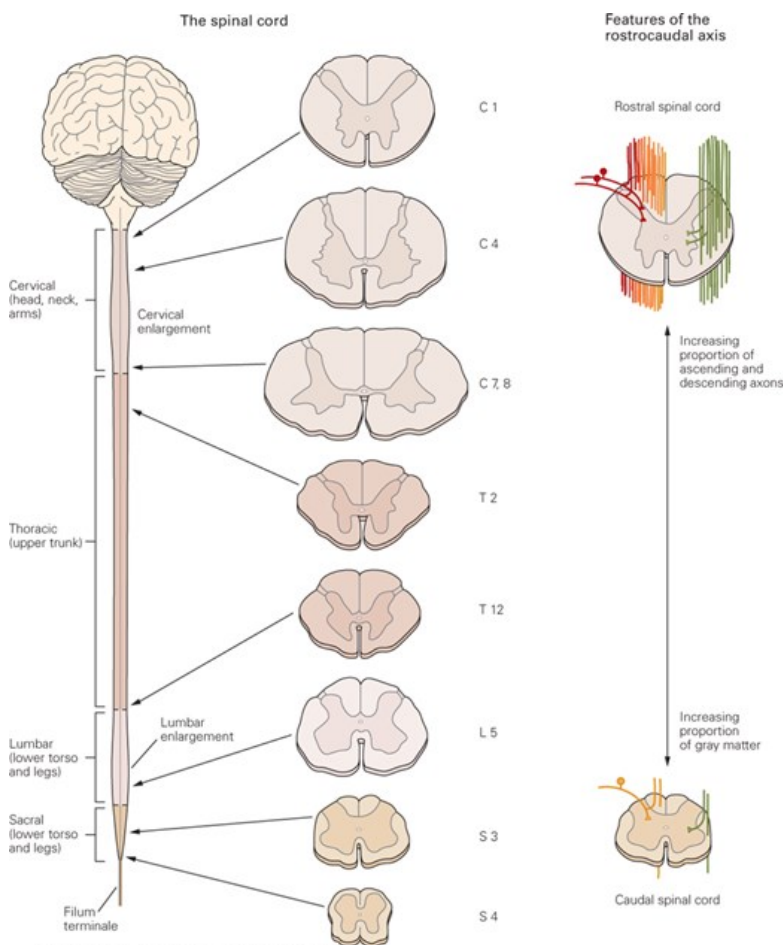
The white matter surrounding the gray matter contains bundles of ascending and descending axons that are divided into dorsal, lateral, and ventral columns. The dorsal columns, which lie between the two dorsal horns of the gray matter, contain only ascending axons that carry somatosensory information to the brain stem (Figure 4-1). The lateral columns include both ascending and descending axons from the brain stem and neocortex that innervate spinal interneurons and motor neurons (Figure 4-3). This demonstrates a general principle about central nervous system connections. Processing tends to be hierarchical: Projections from a lower to a higher processing region are said to be feedforward, while descending projections can modulate spinal reflexes and are considered to be feedback. The motif in which region A projects to region B and, in turn, also receives return

projections from B, is recapitulated throughout the nervous system. The ventral columns also include ascending and descending axons. The ascending somatosensory axons in the lateral and ventral columns constitute parallel pathways that convey information about pain and thermal sensation to higher levels of the central nervous system. The descending axons control axial muscles and posture.

The spinal cord is divided along its length into four major regions: cervical, thoracic, lumbar, and sacral (Figure 4–4). Connections arising from these regions are segregated according to the embryological somites from which muscles, bones, and other components of the body develop (Chapter 45). Axons projecting from the spinal cord to body structures that develop at the same segmental level join with axons entering the spinal cord in the intervertebral foramen to form spinal nerves. Spinal nerves at the cervical level are involved with sensory perception and motor function of the back of the head, neck, and arms; nerves at the thoracic level innervate the upper trunk; lumbar and sacral spinal nerves innervate the lower trunk, back, and legs.

Figure 4–4

The internal and external appearances of the spinal cord vary at different levels. The proportion of gray matter (the H-shaped area within the spinal cord) to white matter is greater at sacral levels than at cervical levels. At sacral levels, very few incoming sensory axons have joined the spinal cord, whereas most of the motor axons have already terminated at higher levels of the spinal cord. The cross-sectional enlargements at the lumbar and cervical levels are regions where the large number of fibers innervating the limbs enter or leave the spinal cord.



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Each of the four regions of the spinal cord contains multiple segments corresponding approximately to the different vertebrae in each region; there are 8 cervical segments, 12 thoracic segments, 5 lumbar segments, and 5 sacral segments. The actual substance of the mature spinal cord does not look segmented, but the segments of the four spinal regions are nonetheless defined by the number and location of the dorsal and ventral roots that enter or exit the spinal cord. The spinal cord varies in size and shape along its rostrocaudal axis because of two organizational features.

First, relatively few sensory axons enter the cord at the sacral level. The number of sensory axons entering the cord increases at progressively higher levels (lumbar, thoracic, and cervical). Conversely, most descending axons from the brain terminate at cervical levels, with progressively fewer descending to lower levels of the spinal cord. Thus, the number of fibers in the white matter is highest at cervical levels (where there are the highest numbers of both ascending and descending fibers) and lowest at sacral levels. As a result, sacral levels of the spinal cord have much less white matter than gray matter, whereas the cervical cord has more white matter than gray matter (Figure 4-4).

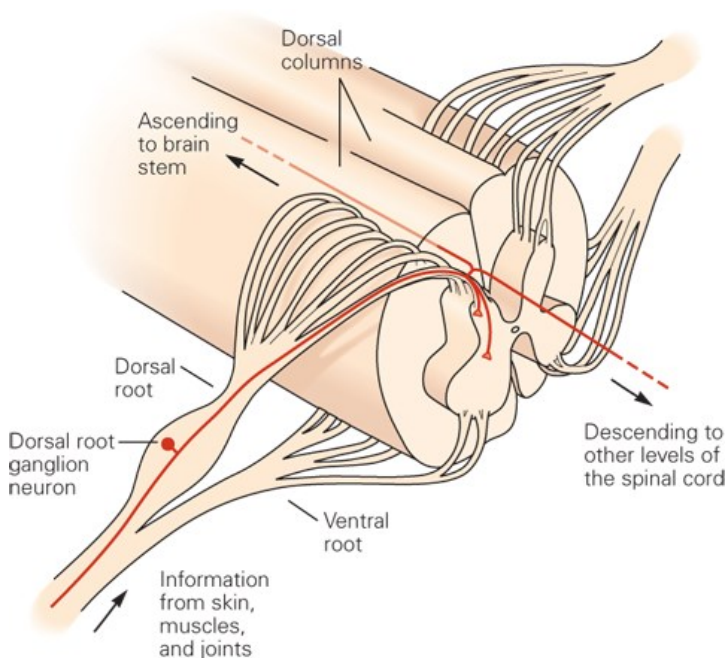
The second organizational feature is variation in the size of the ventral and dorsal horns. The ventral horn is larger at the levels where the motor nerves innervate the arms and legs. The number of ventral motor neurons dedicated to a body region roughly parallels the dexterity of movements of that region. Thus, a larger number of motor neurons is needed to innervate the greater number of muscles and to regulate the greater complexity of movement in the limbs as compared with the trunk. Likewise, the dorsal horn is larger where sensory nerves from the limbs enter the cord. Limbs have a greater density of sensory receptors to mediate finer tactile discrimination and thus send more sensory fibers to the cord. These regions of the cord are known as the lumbosacral and cervical enlargements (Figure 4-4).

The Primary Sensory Neurons of the Trunk and Limbs Are Clustered in the Dorsal Root Ganglia

The sensory neurons that convey information from the skin, muscles, and joints of the limbs and trunk to the spinal cord are clustered together in dorsal root ganglia within the vertebral column, immediately adjacent to the spinal cord (Figure 4-5). These neurons are pseudo-unipolar in shape; they have a bifurcated axon with central and peripheral branches. The peripheral branch innervates the skin, muscle, or other tissue as a free nerve ending or in association with specialized receptors for sensing touch, proprioception (stretch receptors), pain, and temperature.

Figure 4-5

Dorsal root ganglia and spinal nerve roots. The cell bodies of neurons that bring sensory information from the skin, muscles, and joints lie in the dorsal root ganglia, clusters of cells that lie adjacent to the spinal cord. The axons of these neurons are bifurcated into peripheral and central branches. The central branch enters the dorsal portion of the spinal cord.



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The somatosensory system and its pathways from receptors to perception are more fully described in Chapters 17, 18, 19, 20. Suffice it to say at this point that there are essentially two somatosensory pathways from the periphery that carry either touch and stretch (epicritic system) or pain and temperature (protopathic system). Epicritic fibers travel in the posterior column–medial lemniscal system (Figure 4-6). The centrally directed axons from neurons in the dorsal root ganglion ascend in the dorsal (or posterior) column white matter and terminate in the gracile nucleus or cuneate nucleus of the medulla. The centrally directed axons of the pain and temperature pathway form the spinothalamic pathway. They terminate within the

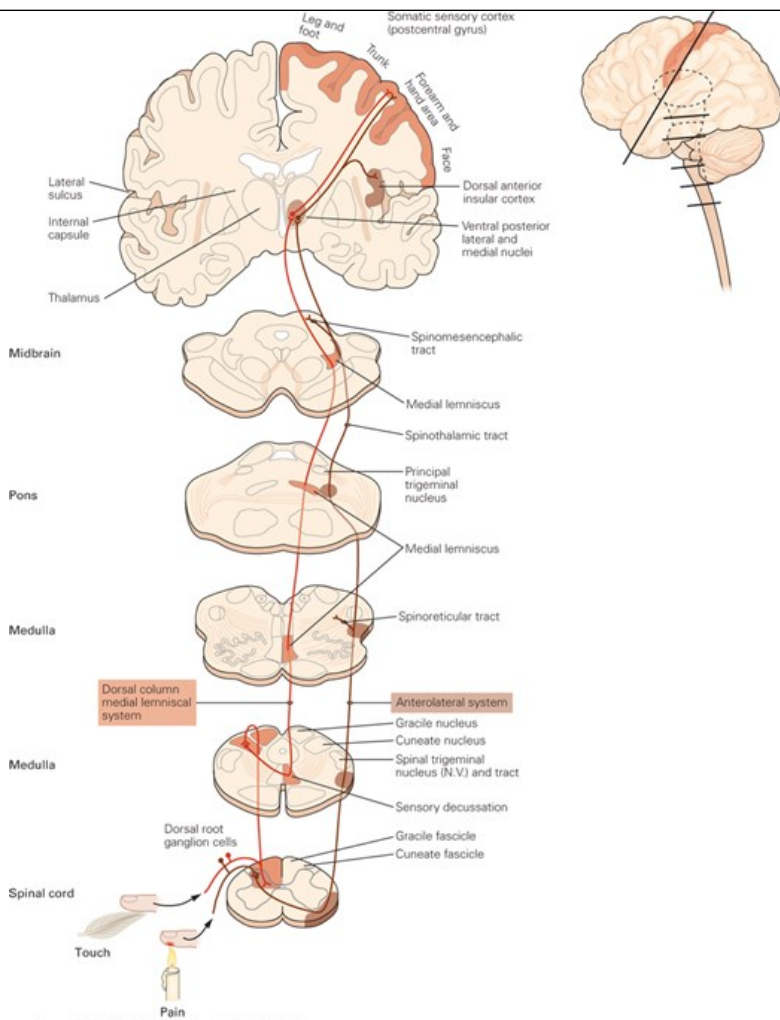
gray matter of the dorsal horn of the spinal cord. Second-order neurons cross to the other side of the spinal cord and ascend in the anterior and lateral spinothalamic tracts (Figure 4-6). Both pathways ultimately terminate in the thalamus, which sends projections to the primary somatosensory area of the cerebral cortex. In the next section, we focus on the epicritic system.

Figure 4-6

Somatosensory information from the limbs and trunk is conveyed to the thalamus and cerebral cortex by two ascending pathways. Brain slices along the neuraxis from the spinal cord to the cerebrum illustrate the anatomy of the two principal pathways conveying somatosensory information to the cerebral cortex. The two pathways are separated until they reach the pons, where they are juxtaposed.

Dorsal column–medial lemniscal system (orange). Touch and limb proprioception signals are conveyed to the spinal cord and brain stem by large-diameter myelinated nerve fibers and transmitted to the thalamus in this system. In the spinal cord, the fibers for touch and proprioception divide, one branch going to the ipsilateral spinal gray matter and the other ascending in the ipsilateral dorsal column to the medulla. The second-order fibers from neurons in the dorsal column nuclei cross the midline in the medulla and ascend in the contralateral medial lemniscus toward the thalamus, where they terminate in the lateral and medial ventral posterior nuclei. Thalamic neurons in these nuclei convey tactile and proprioceptive information to the primary somatosensory cortex.

Anterolateral system (brown). Pain, itch, temperature, and visceral information is conveyed to the spinal cord by small-diameter myelinated and unmyelinated fibers that terminate in the ipsilateral dorsal horn. This information is conveyed across the midline by neurons within the spinal cord and transmitted to the brain stem and the thalamus in the contralateral anterolateral system. Anterolateral fibers terminating in the brain stem compose the spinoreticular and spinomesencephalic tracts; the remaining anterolateral fibers form the spinothalamic tract.



The local and ascending branches from touch and proprioceptive sensory neurons provide two functional pathways for somatosensory information entering the spinal cord from dorsal root ganglion cells. The local branches can activate local reflex circuits that modulate motor output, while the ascending branches carry information into the brain, where this information is further processed in the thalamus and cerebral cortex.

The Terminals of Central Axons of Dorsal Root Ganglion Neurons in the Spinal Cord Produce a Map of the Body Surface

The manner in which the central axons of the dorsal root ganglion cells terminate in the spinal cord forms a neural map of the body surface. This orderly somatotopic distribution of inputs from different portions of the body surface is maintained throughout the entire ascending somatosensory pathway. This arrangement illustrates another important principle of neural organization. Neurons that make up neural circuits at any particular level are often connected in a systematic fashion and appear similar from individual to individual. Similarly, fiber bundles that connect different processing regions at different levels of the nervous system are also arranged in a highly organized and stereotypical fashion.

Axons that enter the cord in the sacral region ascend in the dorsal column near the midline, whereas those that enter at successively higher levels ascend at progressively more lateral positions within the dorsal columns. Thus, in the cervical cord, where axons from all portions of the body have already entered, sensory fibers from the lower body are located medially in the dorsal column, while fibers from the trunk, arm and shoulder, and finally the neck occupy progressively more lateral areas. In the cervical spinal cord, the axons forming the dorsal columns are divided into two bundles: a medially situated gracile fascicle and a more laterally situated cuneate fascicle (Figure 4-1).

Each Somatic Submodality Is Processed in a Distinct Subsystem From the Periphery to the Brain

The submodalities of somatic sensation—touch, pain, temperature, and position sense—are processed in the brain through different pathways that end in different brain regions. We illustrate the specificity of these parallel pathways by the path of information for the submodality of touch.

The primary afferent fibers that carry information about touch enter the ipsilateral dorsal column and ascend to the medulla. Fibers from the lower body run in the gracile fascicle and terminate in the gracile nucleus, whereas fibers from the upper body run in the cuneate fascicle and terminate in the cuneate nucleus. Neurons in the gracile and cuneate nuclei give rise to axons that cross to the other side of the brain and ascend to the thalamus in a long fiber bundle called the medial lemniscus (Figure 4–1).

As in the dorsal columns of the spinal cord, the fibers of the medial lemniscus are arranged somatotopically. Because the fibers carrying sensory information cross the midline to the other side of the brain, the right side of the brain receives sensory information from the left side of the body, and vice versa. The fibers of the medial lemniscus end in a specific subdivision of the thalamus called the ventral posterior lateral nucleus (Figure 4–1). There the fibers maintain their somatotopic organization such that those carrying information from the lower body end laterally and those carrying information from the upper body end medially.

The Thalamus Is an Essential Link Between Sensory Receptors and the Cerebral Cortex

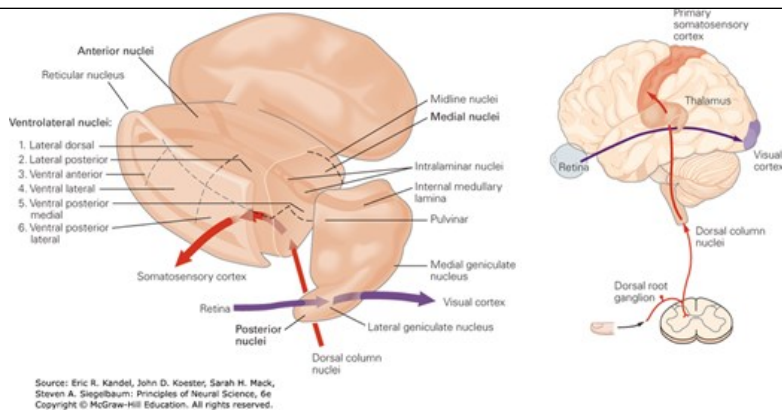
The thalamus is an egg-shaped structure that constitutes the dorsal portion of the diencephalon. It contains a class of excitatory neurons called thalamic relay cells that convey sensory input to the primary sensory areas of the cerebral cortex. However, the thalamus is not merely a relay. It acts as a gatekeeper for information to the cerebral cortex, preventing or enhancing the passage of specific information depending on the behavioral state of the organism.

The cerebral cortex has feedback projections that terminate, in part, in a special portion of the thalamus called the thalamic reticular nucleus. This nucleus forms a thin sheet around the thalamus and is made up almost totally of inhibitory neurons that synapse onto the relay cells. It does not project to the neocortex at all. In addition to receiving feedback projections from the neocortex, the reticular nucleus receives input from axons leaving the thalamus en route to the neocortex, enabling the thalamus to modulate the response of its relay cells to incoming sensory information.

The thalamus is a good example of a brain region made up of several well-defined nuclei. As many as 50 thalamic nuclei have been identified (Figure 4–7). Some nuclei receive information specific to a sensory modality and project to a specific area of the neocortex. For example, cells in the ventral posterior lateral nucleus (where the medial lemniscus terminates) process somatosensory information, and their axons project to the primary somatosensory cortex (Figures 4–1 and 4–7). Projections from the retinal ganglion cells terminate in another portion of the thalamus called the lateral geniculate nucleus (Figure 4–7). Neurons in this nucleus project in turn to the visual cortex. Other portions of the thalamus participate in motor functions, transmitting information from the cerebellum and basal ganglia to the motor regions of the frontal lobe. Axons from cells of the thalamus that project to the neocortex travel in the corona radiata, a large fiber bundle that carries most of the axons running to and from the cerebral hemispheres. Through its connections with the frontal lobe and hippocampus, the thalamus may play a role in cognitive functions, such as memory. Some nuclei that may play a role in attention project diffusely to large but distinctly different regions of cortex.

Figure 4–7

The major subdivisions of the thalamus. The thalamus is the critical relay for the flow of sensory information from peripheral receptors to the neocortex. Somatosensory information is conveyed from dorsal root ganglia to the ventral posterior lateral nucleus and from there to the primary somatosensory cortex. Likewise, visual information from the retina reaches the lateral geniculate nucleus, from which it is conveyed to the primary visual cortex in the occipital lobe. Each of the sensory systems, except olfaction, has a similar processing step within a distinct region of the thalamus.



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The nuclei of the thalamus are most commonly classified into four groups—anterior, medial, ventrolateral, and posterior—with respect to the internal medullary lamina, a sheet-like bundle of fibers that runs the rostrocaudal length of the thalamus (Figure 4–7). Thus, the medial group of nuclei is located medial to the internal medullary lamina, whereas the ventrolateral and posterior groups are located lateral to it. At the rostral pole of the thalamus, the internal medullary lamina splits and surrounds the anterior group. The caudal pole of the thalamus is occupied by the posterior group, dominated by the pulvinar nucleus. Groups of neurons are also located within the fibers of the internal medullary lamina and are collectively referred to as the intralaminar nuclei.

The *anterior group* receives its major input from the mammillary nuclei of the hypothalamus and from the presubiculum of the hippocampal formation. The role of the anterior group is uncertain, but because of its connections, it is thought to be related to memory and emotion. The anterior group is mainly interconnected with regions of the cingulate and frontal cortices.

The *medial group* consists mainly of the mediodorsal nucleus. This large thalamic nucleus has three subdivisions, each of which is connected to a particular portion of the frontal cortex. The nucleus receives inputs from portions of the basal ganglia, the amygdala, and midbrain and has been implicated in memory and emotional processing.

The nuclei of the *ventrolateral group* are named according to their positions within the thalamus. The ventral anterior and ventral lateral nuclei are important for motor control and carry information from the basal ganglia and cerebellum to the motor cortex. The ventral posterior nuclei convey somatosensory information to the neocortex. The ventroposterior lateral nucleus conveys information from the spinal cord tracts, as described earlier. The ventroposterior medial nucleus conveys information from the face, which enters the brain stem mainly through the trigeminal nerve (cranial nerve V).

The *posterior group* includes the medial and lateral geniculate nuclei, the lateral posterior nucleus, and the pulvinar. The medial geniculate nucleus is a component of the auditory system and is organized tonotopically based on the sound frequency information carried by its inputs; it conveys auditory information to the primary auditory cortex in the superior temporal gyrus of the temporal lobe. The lateral geniculate nucleus receives information from the retina and conveys it to the primary visual cortex in the occipital lobe. Compared to rodents, the pulvinar is enlarged disproportionately in the primate brain, especially in the human brain, and its development seems to parallel the enlargement of the association regions of the parietal, occipital, and temporal cortices. It has been divided into at least three subdivisions and is extensively interconnected with widespread regions of the parietal, temporal, and occipital lobes, as well as with the superior colliculus and other nuclei of the brain stem related to vision.

As noted previously, the thalamus not only projects to the neocortex (feedforward connections) but also receives extensive return inputs back from the neocortex (feedback connections). For example, in the lateral geniculate nucleus, the number of synapses formed by axons from the feedback projection from the visual cortex is actually greater than the number of synapses that the lateral geniculate nucleus receives from the retina! This feedback is thought to play an important modulatory role in the processing of sensory information, although the exact function is not yet understood. Although this feedback is mainly from cortical neurons that are activated by both eyes, the neurons in the lateral geniculate nucleus are responsive to only one or the other eye. The implication is that they are primarily driven by input from the retina (which is from different eyes in different layers), not the feedback from the cortex, despite its numerical advantage. Most nuclei of the thalamus receive a similarly prominent return projection from the cerebral cortex, and the significance of these projections is one of the unsolved mysteries of neuroscience.

The thalamic nuclei described thus far are called the *relay (or specific) nuclei* because they have a specific and selective relationship with a particular portion of the neocortex. Other thalamic nuclei, called *nonspecific nuclei*, project to several cortical and subcortical regions. These nuclei are located

either on the midline of the thalamus (the midline nuclei) or within the internal medullary lamina (the intralaminar nuclei). The largest of the midline nuclei are the paraventricular, paratenial, and reuniens nuclei; the largest of the intralaminar cell groups is the centromedian nucleus. The intralaminar nuclei project to medial temporal lobe structures, such as the amygdala and hippocampus, but also send projections to portions of the basal ganglia. These nuclei receive inputs from a variety of sources in the spinal cord, brain stem, and cerebellum and are thought to mediate cortical arousal.

The thalamus is an important step in the hierarchy of sensory processing, not a passive relay station where information is simply passed on to the neocortex. It is a complex brain region where substantial information processing takes place (Figure 4–1). To give but one example, the output of somatosensory information from the ventral posterior lateral nucleus is subject to four types of processing: (1) local processing within the nucleus; (2) modulation by brain stem inputs, such as from the noradrenergic and serotonergic systems; (3) inhibitory input from the reticular nucleus; and (4) modulatory feedback from the neocortex.

Sensory Information Processing Culminates in the Cerebral Cortex

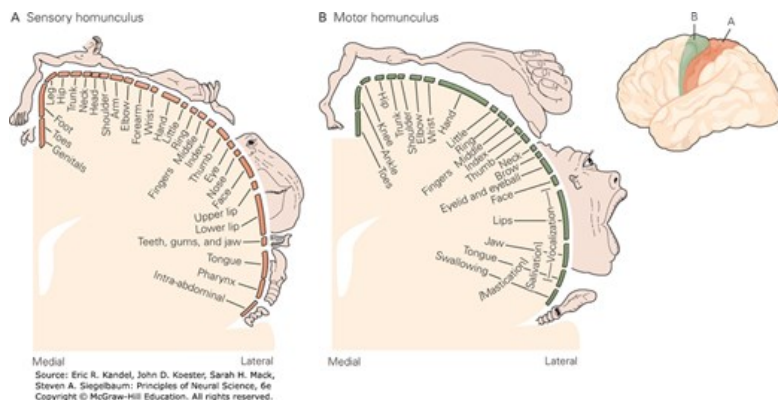
Somatosensory information from the ventral posterior lateral nucleus is conveyed mainly to the primary somatosensory cortex (Figure 4–1). The neurons here are exquisitely sensitive to tactile stimulation of the skin surface. The somatosensory cortex, like earlier stages in tactile sensory processing, is somatotopically organized (Figure 4–8).

Figure 4–8

Homunculi illustrate the relative amounts of cortical area dedicated to sensory and motor innervation of individual parts of the body. The entire body surface is represented in an orderly array of somatosensory inputs in the cortex. (From Penfield and Rasmussen 1950. Reproduced by permission of the Osler Library of the History of Medicine, McGill University.)

A. The area of cortex dedicated to processing sensory information from a particular part of the body is not proportional to the mass of the body part but instead reflects the density of sensory receptors in that part. Thus, sensory input from the lips and hands occupies more area of cortex than, say, that from the elbow.

B. Output from the motor cortex is organized in similar fashion. The amount of cortical surface dedicated to a part of the body is related to the degree of motor control of that part. Thus, in humans, much of the motor cortex is dedicated to controlling the muscles of the fingers and the muscles related to speech.



When the neurosurgeon Wilder Penfield stimulated the surface of the somatosensory cortex in patients undergoing brain surgery in the late 1940s and early 1950s, he found that sensation from the lower limbs is mediated by neurons located near the midline of the brain, whereas sensations from the upper body, hands and fingers, face, lips, and tongue are mediated by neurons located laterally. Penfield found that, although all parts of the body are represented in the cortex somatotopically, the amount of surface area of cortex devoted to each body part is not proportional to its mass. Instead, it is proportional to the fineness of discrimination in the body part, which in turn is related to the density of innervation of sensory fibers (Chapter 19). Thus, the area of cortex devoted to the fingers is larger than that for the arms. Likewise, the representation of the lips and tongue occupies more cortical surface than that of the remainder of the face (Figure 4–8). As we shall see in Chapter 53, the amount of cortex devoted to a particular body part is not fixed but can be modified by experience, as seen in concert violinists, where there is an expansion of the region of somatosensory cortex devoted

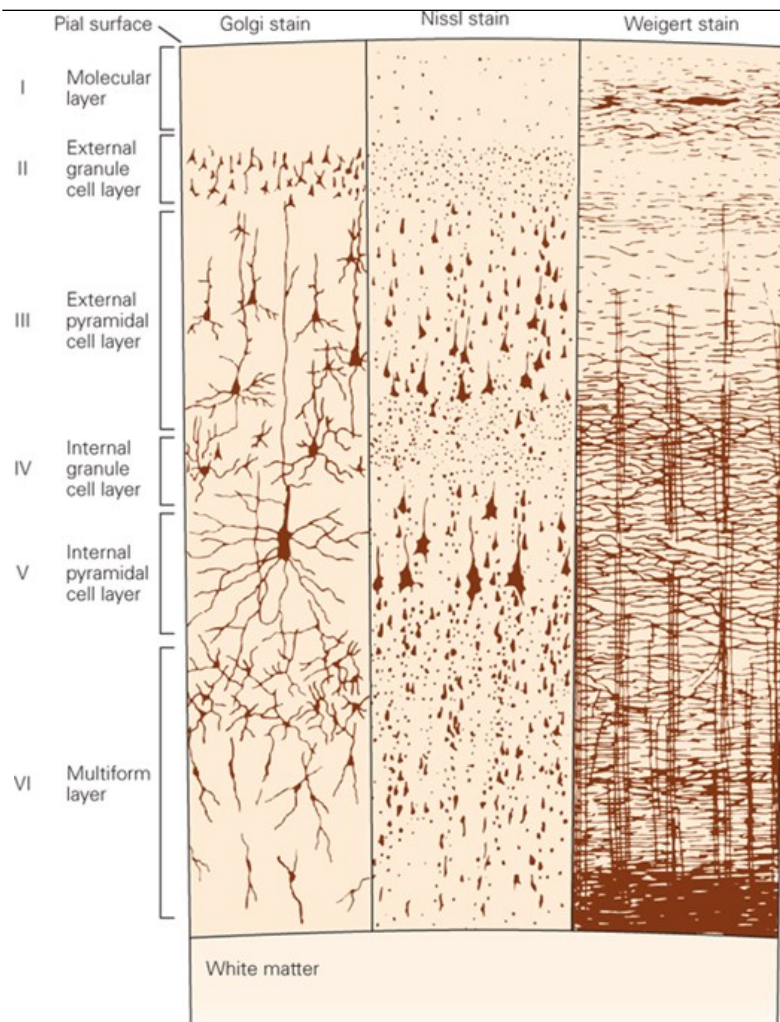
to the fingers of the hand used to finger the strings. This illustrates an important aspect of brain circuitry: It is capable of plastic changes in response to use or disuse. Such changes are important for various forms of learning, including the ability to recover function after a stroke.

The region of cerebral cortex nearest the surface of the brain is organized in layers and columns, an arrangement that increases its computational efficiency. The cortex has undergone dramatic expansion in evolution. The more recent neocortex comprises most of the cortex of mammals. In larger brains of primates and cetaceans, the neocortical surface is a sheet that is folded with deep wrinkles, thus allowing for three times more cortical surface to be packed into an only modestly enlarged head. Indeed, approximately two-thirds of the neocortex is along the deep wrinkles of the cortex, termed sulci. The remainder of neocortex is at the external folds of the sheet, termed gyri. The neocortex receives inputs from the thalamus, other cortical regions on both sides of the brain, and other subcortical structures. Its output is directed to other regions of the cortex, basal ganglia, thalamus, pontine nuclei, and spinal cord.

These complex input–output relationships are efficiently organized in the orderly layering of cortical neurons; each layer contains different inputs and outputs. Many regions of the neocortex, in particular the primary sensory areas, contain six layers, numbered from the outer surface of the brain to the white matter (Figure 4–9).

Figure 4–9

The neurons of the neocortex are arranged in distinctive layers. The appearance of the neocortex depends on what is used to stain it. The Golgi stain (*left*) reveals a subset of neuronal cell bodies, axons, and dendritic trees. The Nissl method (*middle*) shows cell bodies and proximal dendrites. The Weigert stain (*right*) reveals the pattern of myelinated fibers. (Reproduced, with permission, from Heimer 1994.)



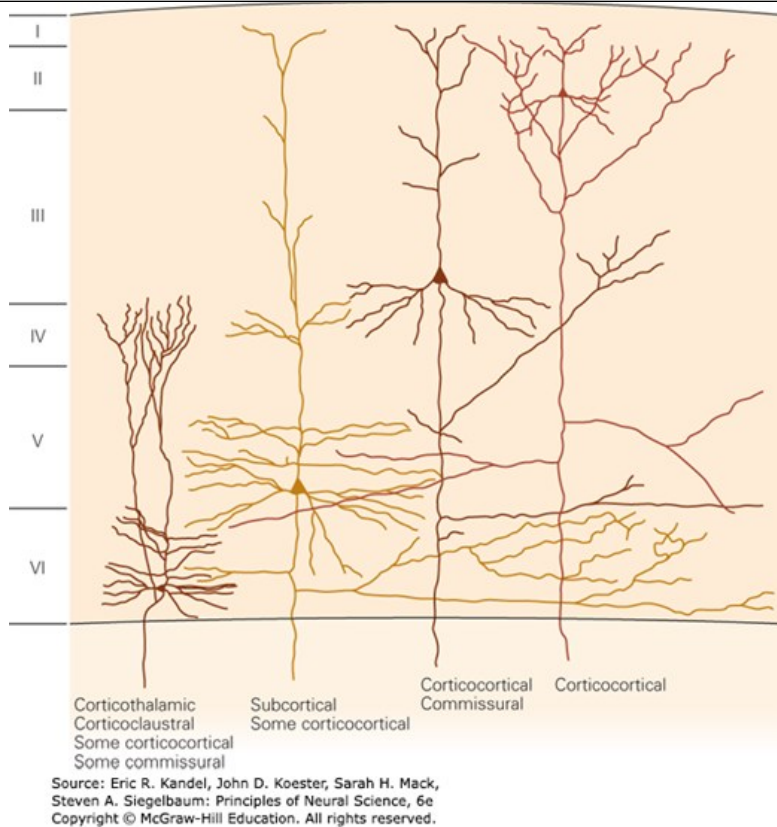
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Layer I, the molecular layer, is occupied by the dendrites of cells located in deeper layers and axons that travel through this layer to make connections in other areas of the cortex.

Layers II and III contain mainly small pyramidal shaped cells. Layer II, the external granular cell layer, is one of two layers that contain small spherical neurons. Layer III is called the external pyramidal cell layer (an internal pyramidal cell layer lies at a deeper level). The neurons located deeper in layer III are typically larger than those located more superficially. The axons of pyramidal neurons in layers II and III project locally to other neurons within the same cortical area as well as to other cortical areas, thereby mediating intracortical communication (Figure 4-10).

Figure 4-10

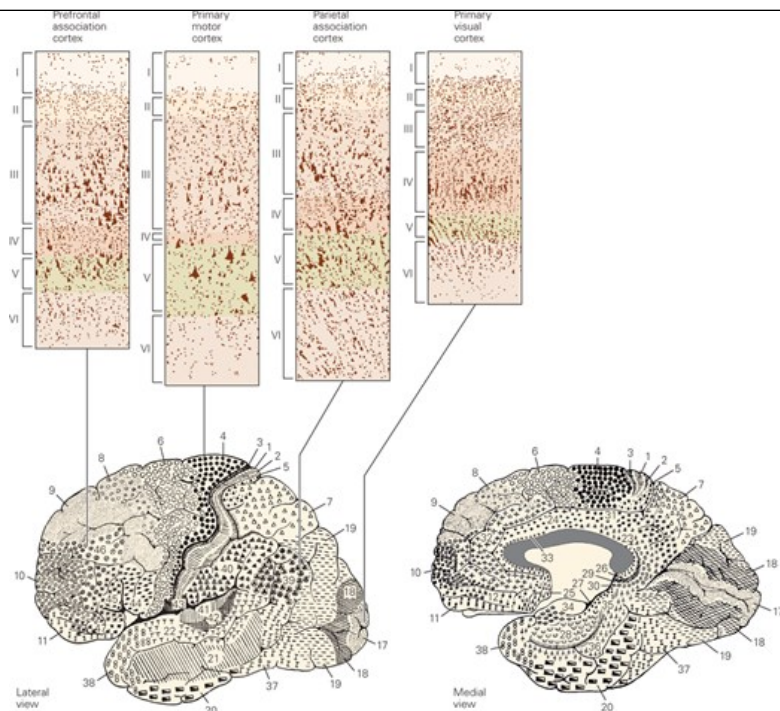
Neurons in different layers of neocortex project to different parts of the brain. Projections to all other parts of the neocortex, the so-called corticocortical or associational connections, arise primarily from neurons in layers II and III. Projections to subcortical regions arise mainly from layers V and VI. (Reproduced, with permission, from Jones 1986.)



Layer IV contains a large number of small spherical neurons and thus is called the internal granular cell layer. It is the main recipient of sensory input from the thalamus and is most prominent in primary sensory areas. For example, the region of the occipital cortex that functions as the primary visual cortex has an extremely prominent layer IV. Layer IV in this region is so heavily populated by neurons and so complex that it is typically divided into three sublayers. Areas with a prominent layer IV are called granular cortex. In contrast, the precentral gyrus, the site of the primary motor cortex, has essentially no layer IV and is thus part of the so-called agranular frontal cortex. These two cortical areas are among the easiest to identify in histological sections (Figure 4–11).

Figure 4–11

The extent of each cell layer of the neocortex varies throughout the cortex. Sensory areas of cortex, such as the primary visual cortex, tend to have a very prominent internal granular cell layer (layer IV), the site of sensory input. Motor areas of cortex, such as the primary motor cortex, have a very meager layer IV but prominent output layers, such as layer V. These differences led Korbinian Brodmann and others working at the turn of the 20th century to divide the cortex into various cytoarchitectonic regions. Brodmann's 1909 subdivision shown here is a classic analysis but was based on a single human brain. (Reproduced, with permission, from Martin 2012.)



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Layer V, the internal pyramidal cell layer, contains mainly pyramidally shaped cells that are typically larger than those in layer III. Pyramidal neurons in this layer give rise to the major output pathways of the cortex, projecting to other cortical areas and to subcortical structures (Figure 4–9).

The neurons in layer VI are fairly heterogeneous in shape, so this layer is called the polymorphic or multiform layer. It blends into the white matter that forms the deep limit of the cortex and carries axons to and from areas of cortex.

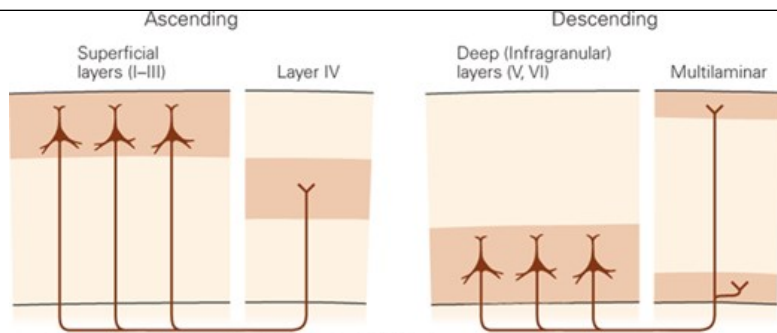
The thickness of individual layers and the details of their functional organization vary throughout the cortex. An early student of the cerebral cortex, Korbinian Brodmann, used the relative prominence of the layers above and below layer IV, cell size, and packing characteristics to distinguish different areas of the neocortex. Based on such cytoarchitectonic differences, in 1909, Brodmann divided the cerebral cortex into 47 regions (Figure 4–11).

Although Brodmann’s demarcation coincides in part with information on localized functions in the neocortex, the cytoarchitectonic method alone does not capture the subtlety or variety of function of all the distinct regions of the cortex. For example, Brodmann identified five regions (areas 17–21) as being concerned with visual function in the monkey. In contrast, modern connective neuroanatomy and electrophysiology have identified more than 35 functionally distinct cortical regions within the five regions recognized by Brodmann.

Within the neocortex, information passes from one synaptic relay to another using feedforward and feedback connections. In the visual system, for example, feedforward projections from the primary visual cortex to secondary and tertiary visual areas originate mainly in layer III and terminate mainly in layer IV of the target cortical area. In contrast, feedback projections to earlier stages of processing originate from cells in layers V and VI and terminate in layers I, II, and VI (Figure 4–12).

Figure 4–12

Ascending and descending cortical pathways are distinguished by the organization of their origins and terminations within the cortical layers. Ascending or feedforward pathways generally originate in superficial layers of the cortex and invariably terminate in layer IV. Descending or feedback pathways generally originate from deep layers and terminate in layers I and VI. (Adapted, with permission, from Felleman and Van Essen 1991.)



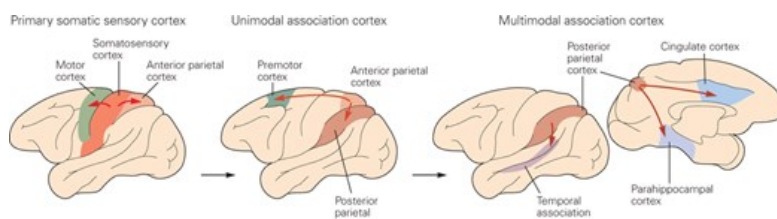
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The cerebral cortex is organized functionally into columns of cells that extend from the white matter to the surface of the cortex. (This columnar organization is not particularly evident in standard histological preparations and was first discovered in electrophysiological studies.) Each column is about one-third of a millimeter in diameter. The cells in each column form a computational module with a highly specialized function. Neurons within a column tend to have very similar response properties, presumably because they form a local processing network. The larger the area of cortex dedicated to a function, the greater the number of computational columns that are dedicated to that function (Chapter 23). The highly discriminative sense of touch in the fingers is a result of many cortical columns in the large area of cortex dedicated to processing somatosensory information from the hand.

Beyond the identification of the cortical column, a second major insight from the early electrophysiological studies was that the somatosensory cortex contains not one but several somatotopic maps of the body surface. The primary somatosensory cortex (anterior parietal cortex) has four complete maps of the skin, one each in Brodmann areas 3a, 3b, 1, and 2. The thalamus sends, in parallel, a lot of deep receptor information (eg, from muscles) to area 3a and most of its cutaneous information to areas 3b and 1. Area 2 receives input from these thalamorecipient cortical areas and may be responsible for our integrated perception of three-dimensional solid objects, termed stereognosis. Neurons in the primary somatosensory cortex project to neurons in adjacent areas, and these neurons in turn project to other adjacent cortical regions (Figure 4–13). At higher levels in the hierarchy of cortical connections, somatosensory information is used in motor control, eye–hand coordination, and memory related to touch.

Figure 4–13

The processing of sensory information in the cerebral cortex begins with primary sensory areas, continues in unimodal association areas, and is further elaborated in multimodal association areas. Sensory systems also communicate with portions of the motor cortex. For example, the primary somatosensory cortex projects to the motor area in the frontal lobe and to the somatosensory association area in the parietal cortex. The somatosensory association area, in turn, projects to higher-order somatosensory association areas and to the premotor cortex. Information from different sensory systems converges in the multimodal association areas, which include the parahippocampal, temporal association, and cingulate cortices.



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The cortical areas involved in the early stages of sensory processing are concerned primarily with a single sensory modality. Such regions are called primary sensory or unimodal (sensory) association areas. Information from the unimodal association areas converges on multimodal association areas of the cortex concerned with combining sensory modalities (Figure 4–13). These multimodal association areas, which are heavily interconnected with the hippocampus, appear to be particularly important for two functions: (1) the production of a unified percept and (2) the representation of the percept in memory (we will return to this at the end of this chapter).

Thus, from the mechanical pressure on a receptor in the skin to the perception that a finger has been touched by a friend shaking your hand, somatosensory information is processed in a series of increasingly more complex circuits (networks) from the dorsal root ganglia to the

somatosensory cortex, to unimodal association areas, and finally to multimodal association areas. One of the primary purposes of somatosensory information is to guide directed movement. As one might imagine, there is a close linkage between the somatosensory and motor functions of the cortex.

Voluntary Movement Is Mediated by Direct Connections Between the Cortex and Spinal Cord

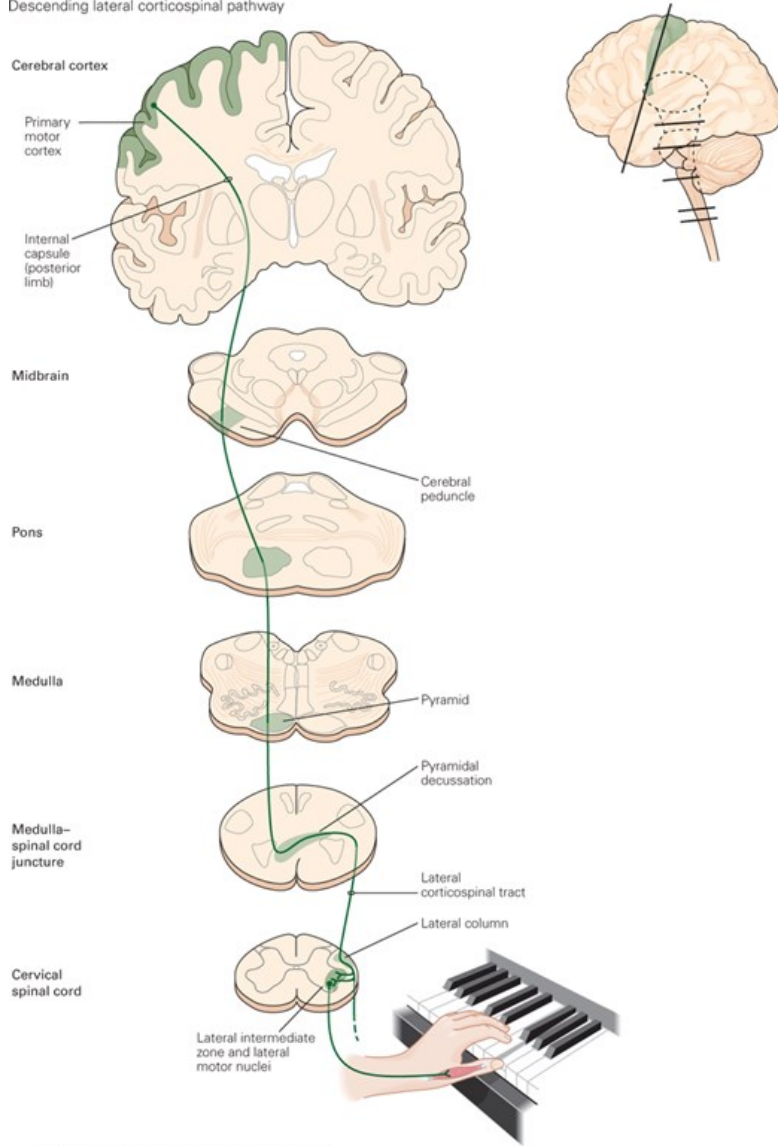
As we shall see in [Chapters 25](#) and [30](#), a major function of the perceptual systems is to provide the sensory information necessary for the actions mediated by the motor systems. The primary motor cortex is organized somatotopically like the somatosensory cortex ([Figure 4–8B](#)). Specific regions of the motor cortex influence the activity of specific muscle groups ([Chapter 34](#)).

The axons of neurons in layer V of the primary motor cortex provide the major output of the neocortex to control movement. Some layer V neurons influence movement directly through projections in the corticospinal tract to motor neurons in the ventral horn of the spinal cord. Others influence motor control by synapsing onto motor output nuclei in the medulla or onto striatal neurons in the basal ganglia. The human corticospinal tract consists of approximately one million axons, of which approximately 40% originate in the motor cortex. These axons descend through the subcortical white matter, the internal capsule, and the cerebral peduncle in the midbrain ([Figure 4–14](#)). In the medulla, the fibers form prominent protuberances on the ventral surface called the medullary pyramids, and thus the entire projection is sometimes called the pyramidal tract.

Figure 4–14

A significant number of fibers in the corticospinal tract originate in the primary motor cortex and terminate in the ventral horn of the spinal cord. The same axons are, at various points in their projections, part of the internal capsule, the cerebral peduncle, the medullary pyramid, and the lateral corticospinal tract.

Descending lateral corticospinal pathway



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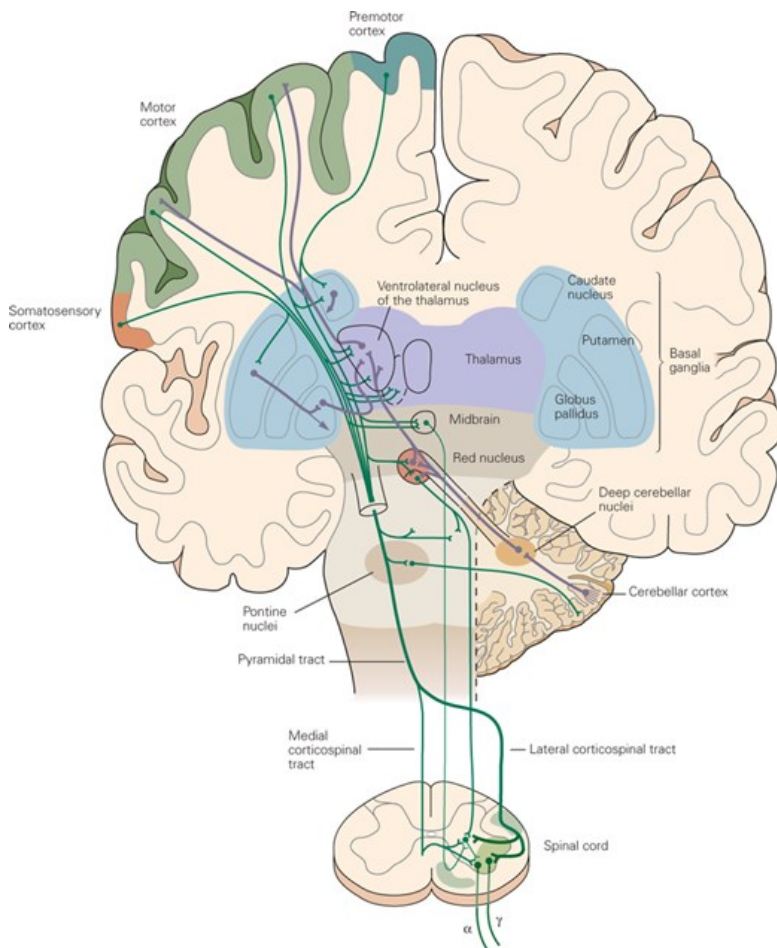
Like the ascending somatosensory system, the descending corticospinal tract crosses to the opposite side of the spinal cord. Most of the corticospinal fibers cross the midline in the medulla at a location known as the pyramidal decussation. However, approximately 10% of the fibers do not cross until they reach the level of the spinal cord at which they will terminate. The corticospinal fibers make monosynaptic connections with motor neurons, connections that are particularly important for individuated finger movements. They also form synapses with both excitatory and inhibitory interneurons in the spinal cord, connections that are important for coordinating larger groups of muscles in behaviors such as reaching and walking.

The motor information carried in the corticospinal tract is significantly modulated by both sensory information and information from other motor regions. A continuous stream of tactile, visual, and proprioceptive information is needed to make voluntary movement both accurate and properly sequenced. In addition, the output of the motor cortex is under the substantial influence of other motor regions of the brain, including the cerebellum and basal ganglia, structures that are essential for smoothly executed movements. These two subcortical regions, which are described in detail in [Chapters 37](#) and [38](#), provide feedback essential for the smooth execution of skilled movements and thus are also important for the improvement in motor skills through practice ([Figure 4–15](#)).

Figure 4–15

Voluntary movement requires coordination of all components of the motor system. The principal components are the motor cortex, basal

ganglia, thalamus, midbrain, cerebellum, and spinal cord. The principal descending projections are shown in **green**; feedback projections and local connections are shown in **purple**. All of this processing is incorporated in the inputs to the motor neurons of the ventral horn of the spinal cord, the so-called “final common pathway” that innervates muscle and elicits movements. (This figure is a composite view made from sections of the brain taken at different angles.)



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Modulatory Systems in the Brain Influence Motivation, Emotion, and Memory

Some areas of the brain are neither purely sensory nor purely motor, but instead modulate specific sensory or motor functions. Modulatory systems are often involved in behaviors that respond to a primary need such as hunger, thirst, or sleep. For example, sensory and modulatory systems in the hypothalamus determine blood glucose levels (Chapter 41). When blood sugar drops below a certain critical level, we feel hunger. To satisfy hunger, modulatory systems in the brain focus vision, hearing, and smell on stimuli that are relevant to feeding.

Distinct modulatory systems within the brain stem modulate attention and arousal (Chapter 40). Small nuclei in the brain stem contain neurons that synthesize and release the modulatory neurotransmitter **norepinephrine** (the locus coeruleus) and serotonin (the dorsal raphe nucleus). Such neurons set the general arousal level of an animal through their widespread connections with forebrain structures. A group of cholinergic modulatory neurons, the basal nucleus of Meynert, is involved in arousal or attention (Chapter 40). This nucleus is located beneath the basal ganglia in the basal forebrain portion of the telencephalon. The axons of its neurons project to essentially all portions of the neocortex.

If a predator finds potential prey, a variety of cortical and subcortical systems determine whether the prey is edible. Once food is recognized, other cortical and subcortical systems initiate a comprehensive voluntary motor program to bring the animal into contact with the prey, capture it and place it in the mouth, and chew and swallow.

Finally, the physiological satisfaction the animal experiences in eating reinforces the behaviors that led to the successful predation. A group of dopaminergic neurons in the midbrain are important for monitoring reinforcements and rewards. The power of the dopaminergic modulatory systems has been demonstrated by experiments in which electrodes were implanted into the reward regions of rats and the animals were freely allowed to press a lever to electrically stimulate their brains. They preferred this self-stimulation to obtaining food or water, engaging in sexual behavior, or any other naturally rewarding activity. The role of the dopaminergic modulatory system in learning through reinforcement of exploratory behavior is described in [Chapter 38](#).

How the brain's modulatory systems, concerned with reward, attention and motivation, interact with the sensory and motor systems is one of the most interesting questions in neuroscience, one that is also fundamental to our understanding of learning and memory storage ([Chapter 40](#)).

The Peripheral Nervous System Is Anatomically Distinct From the Central Nervous System

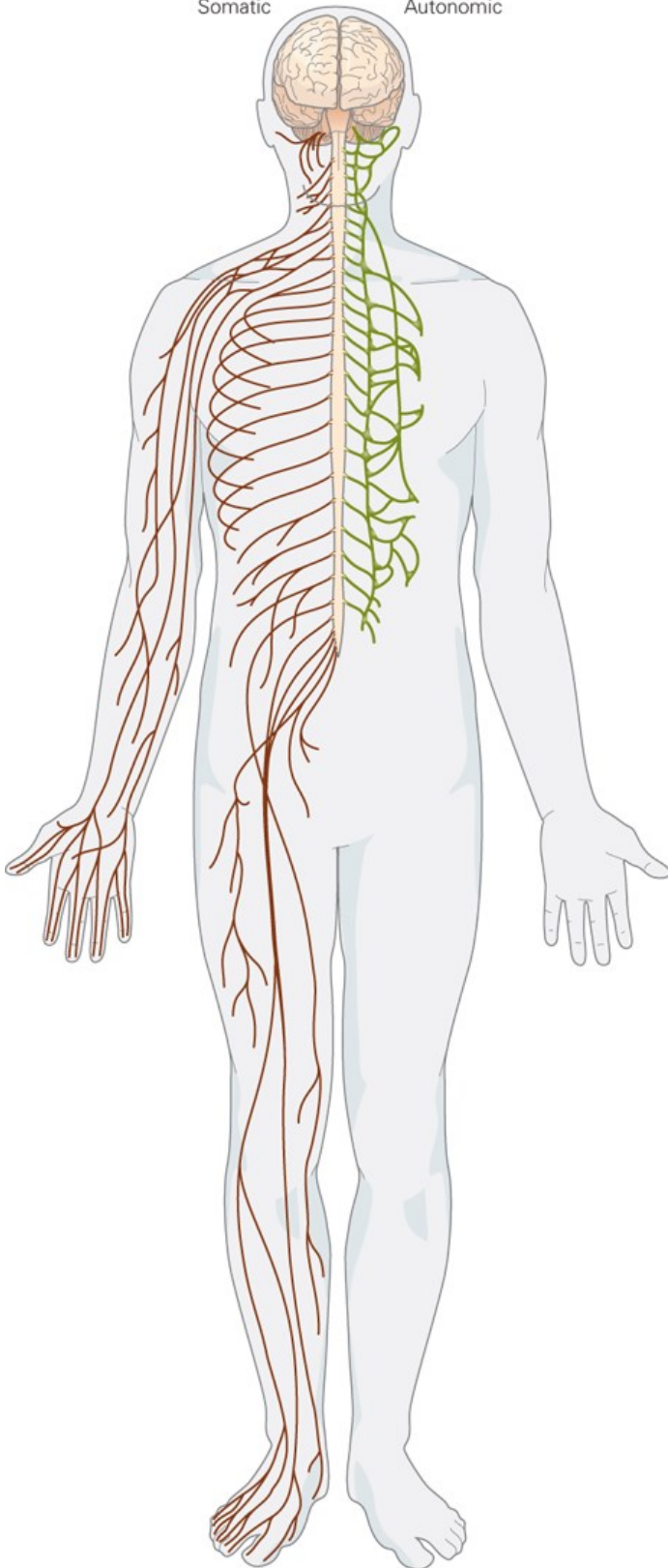
The peripheral nervous system supplies the central nervous system with a continuous stream of information about both the external environment and the internal environment of the body. It has somatic and autonomic divisions ([Figure 4–16](#)).

Figure 4–16

The peripheral nervous system has somatic and autonomic divisions. The somatic division carries information from the skin to the brain and from the brain to muscles. The autonomic division regulates involuntary functions, including activity of the heart and smooth muscles in the gut and glands.

Peripheral Nervous System

Somatic Autonomic



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The *somatic division* includes the sensory neurons that receive information from the skin, muscles, and joints. The cell bodies of these sensory neurons lie in the dorsal root ganglia and cranial ganglia. Receptors associated with these cells provide information about muscle and limb position and about touch and pressure at the body surface. In Part IV (Perception), we shall see how remarkably specialized these receptors are in transducing one or another type of physical energy (eg, deep pressure or heat) into the electrical signals used by the nervous system. In Part V (Movement), we shall see that sensory receptors in the muscles and joints are crucial to shaping coherent movement of the body.

The *autonomic division* of the peripheral nervous system mediates visceral sensation as well as motor control of the viscera, vascular system, and exocrine glands. It consists of the sympathetic, parasympathetic, and enteric systems. The sympathetic system participates in the body's response to stress, whereas the parasympathetic system acts to conserve body resources and restore homeostasis. The enteric nervous system, with neuronal cell bodies located in or adjacent to the viscera, controls the function of smooth muscle and secretions of the gut. The functional organization of the autonomic nervous system is described in [Chapter 41](#) and its role in emotion and motivation in [Chapter 42](#).

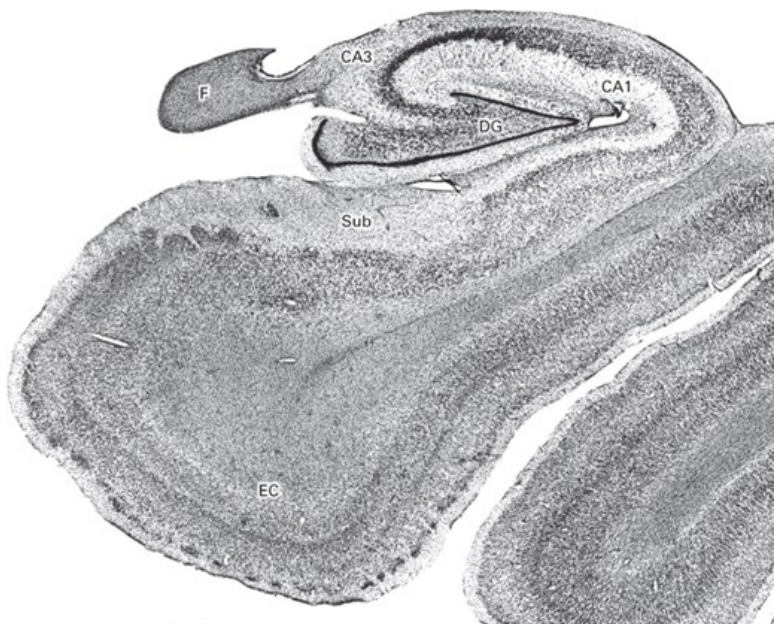
Memory Is a Complex Behavior Mediated by Structures Distinct From Those That Carry Out Sensation or Movement

Research over the past 50 years has provided a sophisticated view of memory systems in the brain. We now know that different forms of memory (eg, fear memory versus skill memory) are mediated by different brain regions. Here we contrast the organization of the system responsible for coding and storing our experiences of other individuals, places, facts, and episodes, a process called explicit memory.

We know that a structure called the hippocampus (or more properly the hippocampal formation, since it is several cortical regions) is a key component of a medial temporal lobe memory system that encodes and stores memories of our lives ([Figure 4-17](#)). This understanding is based largely on the analysis of the famous patient Henry Molaison (referred to as HM by the scientists who studied him during his life), who in the early 1950s had bilateral temporal lobe surgery to reduce his life-threatening epilepsy. In contrast to the six-layered neocortex, the hippocampus, along with olfactory cortex (piriform cortex), is a three-layered cortical structure referred to as archicortex, one of the phylogenetically older areas of cortex.

Figure 4-17

Coronal section of the human hippocampal formation stained by the Nissl methods to demonstrate cell bodies. The main cytoarchitectonic fields are shown in this section of the human hippocampal formation. (Abbreviations: CA3 and CA1, subdivisions of the hippocampus; DG, dentate gyrus; EC, entorhinal cortex; F, fimbria; Sub, subiculum.)



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The reason we briefly describe the hippocampal formation in this chapter is to emphasize that not all brain circuits are alike. In fact, whether one talks

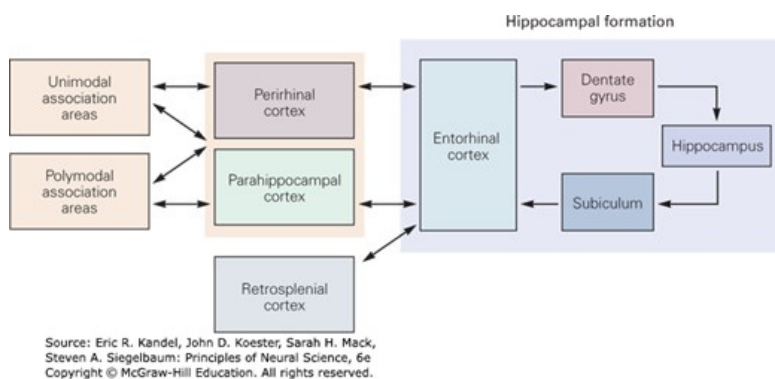
about the olfactory bulb, where the sense of smell begins to be processed, or the cerebellum, where fine motor movements are refined, the general principle is that the structure of a circuit is specific to the function that it mediates. And the hippocampal circuit is as different from the circuits that mediate sensory perception or motor movement as one could imagine. Hippocampal circuitry of the brain will be dealt with in much more detail in later chapters. [Chapter 5](#) introduces the idea that the hippocampus encodes information about an animal's spatial location in its environment and that the encoding of explicit memory (including spatial memory) requires plastic changes in synaptic function. [Chapters 52](#) and [54](#) explore human memory function and the cellular and molecular bases of explicit memory and spatial representation, respectively.

The Hippocampal System Is Interconnected With the Highest-Level Polysensory Cortical Regions

Sensory systems are hierarchical and process progressively more complex stimuli at higher levels, particularly of the neocortex. Moreover, from the highest levels of each modality, circuits connect with polysensory cortical regions located at various places around the cortex, where information from many sensory modalities converges onto single neurons. The hippocampal system receives most of its input, the raw material with which it makes memories, from a few specific polysensory regions. These include the perirhinal and parahippocampal cortices, located in the medial temporal lobe, as well as the retrosplenial cortex, located in the caudal portion of the cingulate gyrus. These polysensory regions converge on the entry structure to the hippocampal system, the entorhinal cortex ([Figure 4-18](#)). The polysensory information that enters the entorhinal cortex can be thought of as providing summaries of immediate experience.

Figure 4-18

Hierarchical organization of connections to the hippocampal formation. The hippocampal formation receives highly processed sensory information, primarily through the entorhinal cortex, from multimodal association regions such as the perirhinal, parahippocampal, and retrosplenial cortices.



The Hippocampal Formation Comprises Several Different but Highly Integrated Circuits

The hippocampal formation is made up of a number of distinct cortical regions that are simpler in organization than the neocortex—at least they have fewer layers. The regions include the dentate gyrus, hippocampus, subiculum, and entorhinal cortex. Each of these regions is made up of subregions containing many neuronal cell types. The simplest subregion of the hippocampal formation is the dentate gyrus, which has a single principal neuron called the granule cell. The subregions of the hippocampus termed CA1, CA2, and CA3, consist of a single layer of pyramidal cells whose dendrites extend above and below the cell body layer and receive inputs from several regions. The subiculum (divided into subiculum, presubiculum and parasubiculum) is another region made up largely of pyramidal cells. Finally, the most complex part of the hippocampal formation is the entorhinal cortex, which has multiple layers but still has an organization distinctly different from the neocortex. For example, it lacks a layer IV and has a much more prominent layer II.

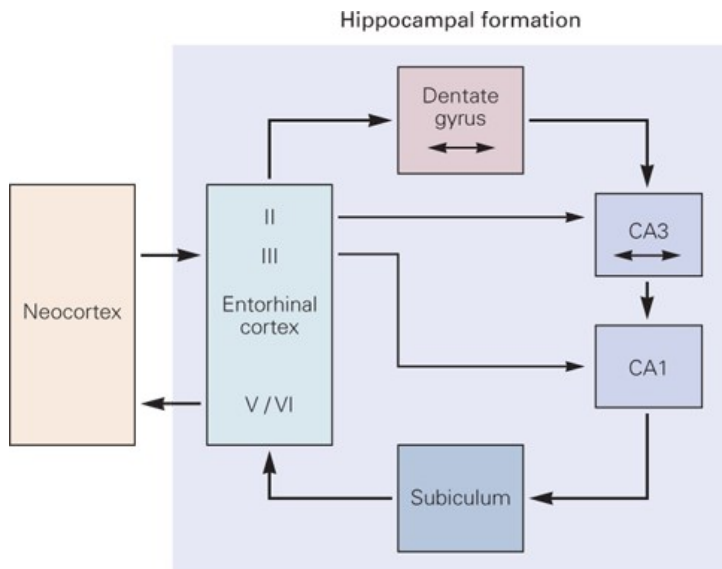
The Hippocampal Formation Is Made Up Mainly of Unidirectional Connections

Here we describe the fundamental circuitry of the hippocampal formation. The circuitry is described in more detail in [Chapter 54](#). The simplified version of the hippocampal circuit shown in [Figure 4-19](#) emphasizes its stepwise serial processing of multimodal sensory information, with each hippocampal region contributing to the formation of explicit memories. This serial processing implies that damage to any one of the components of this system would lead to memory impairment. And, in fact, another famous patient, known by the initials R.B., did suffer profound memory

impairment due to loss of cells in the CA1 region after an ischemic episode.

Figure 4–19

Simplified diagram on internal connections within the hippocampal formation. The circuit begins from cells in layer II of the entorhinal cortex to the dentate gyrus, which then projects to the CA3 region of the hippocampus. The CA3 portion of the hippocampus projects to CA1, and CA1 then projects to the subiculum. The hippocampal circuit is closed when the subiculum projects to the deep layers of the entorhinal cortex. Not shown are the feedback pathways from entorhinal cortex to the same multimodal areas from which it receives sensory information.



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As it turns out, while the hippocampal formation is essential for the initial formation of memories of our lives, these memories are ultimately stored elsewhere in the brain. In patients such as HM, in whom the entorhinal cortex and much of the rest of the hippocampal system was removed, memories prior to the surgery were largely intact. Thus, to achieve creation and long-term storage of the memories of our lives, the hippocampus and entorhinal cortex must communicate with circuits in the cerebral cortex. Where and precisely how that happens remain a mystery.

Highlights

1. Individual neurons are not able to carry out behavior. They must be incorporated into circuits that comprise different types of neurons that are interconnected by excitatory, inhibitory, and modulatory connections.
2. Sensory and motor information is processed in the brain in a variety of discrete brain regions that are active simultaneously.
3. A functional pathway is formed by the serial connection of identifiable brain regions, and each brain region's circuits process more complex or specific information than the preceding brain region.
4. The sensations of touch and pain are mediated by pathways that run between different circuits in the spinal cord, brain stem, thalamus, and neocortex.
5. All sensory and motor systems follow the pattern of hierarchical and reciprocal processing of information, whereas the hippocampal memory system is organized largely for serial processing of very complex, polysensory information. A general principle is that circuits in the brain have an organizational structure that is suited for the functions that they are carrying out.
6. Contrary to an intuitive analysis of our personal experience, perceptions are not precise copies of the world around us. Sensation is an abstraction, not a replication, of reality. The brain's circuits construct an internal representation of external physical events after first analyzing various features of those events. When we hold an object in the hand, the shape, movement, and texture of the object are simultaneously analyzed in different brain

regions according to the brain's own rules, and the results are integrated in a conscious experience.

7. How sensation is integrated in a conscious experience—the *binding problem*—and how conscious experience emerges from the brain's analysis of incoming sensory information are two of the most intriguing questions in cognitive neuroscience (Chapter 56). An even more complex issue is how these conscious impressions are encoded into memories that are stored for decades.

David G. Amaral

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