Chapter 9: The Central Nervous System

Second Year Pharmacy Students

Chapter 5: The Nervous System

Part 1A

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Faculty of Pharmacy

Al-Azhar University of Gaza

5th Year Pharmacy Students

1st Semester 2020/2021

The Nervous System

■ The way humans act and react **depends on** complex, organized, discrete neuronal processing.

■ Many of basic life-supporting neuronal patterns (such as those controlling respiration and circulation) are **similar** in **all** individuals, but, there must be subtle differences in neuronal integration between people. For example, someone who is a math wizard and someone who struggles with long division.

The Nervous System

- Some of the differences in nervous system are genetically endowed; However, the rest due to environmental encounters and experiences.

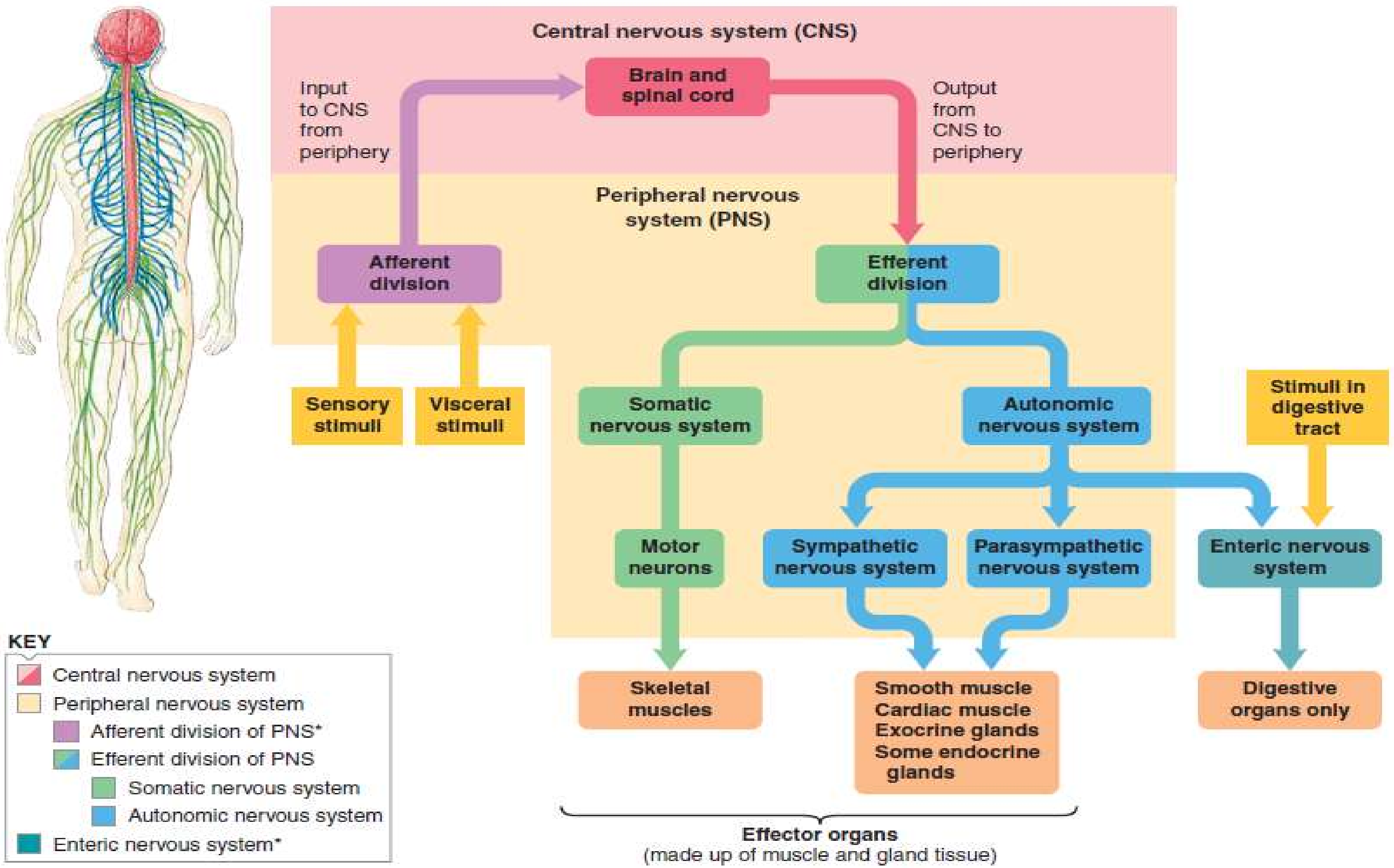
- When the immature nervous system **develops** according to its genetic plan, an over abundance of neurons and synapses is formed, depending on external stimuli and the extent these pathways are used, some are retained, firmly established and even enhanced, whereas others are eliminated.

■ For e.g., **amblyopia** (lazy eye), in which the weaker of the 2 eyes is **not** used for vision. A lazy eye that **does not** get appropriate visual stimulation during a sensitive developmental period will almost completely and permanently **lose** the power of vision. The functionally blind eye **itself** is completely normal; the defect **lies** in the lost neuronal connections in the brain's visual pathways. However, if the weak eye is forced to work by **covering** the stronger eye during the sensitive developmental period, the weaker eye will **retain** full vision.

The Nervous System

■ The maturation of the nervous system involves instances of “use it or lose it”. Once the nervous system has matured, ongoing modifications s**till** occur as we continue to learn from our unique set of experiences. For example, the act of reading this slide is somehow **altering** the neuronal activity of your brain as you (as it is hoped) **tuck** the information **away** in your memory.

The Nervous System



● **FIGURE 5-1 Organization of the nervous system.** *The afferent division of the PNS and enteric nervous system are not shown in the human figure. Afferent fibers travel within the same nerves as efferent fibers but in the opposite direction. The enteric nervous system lies entirely within the wall of the digestive tract.

The Nervous System

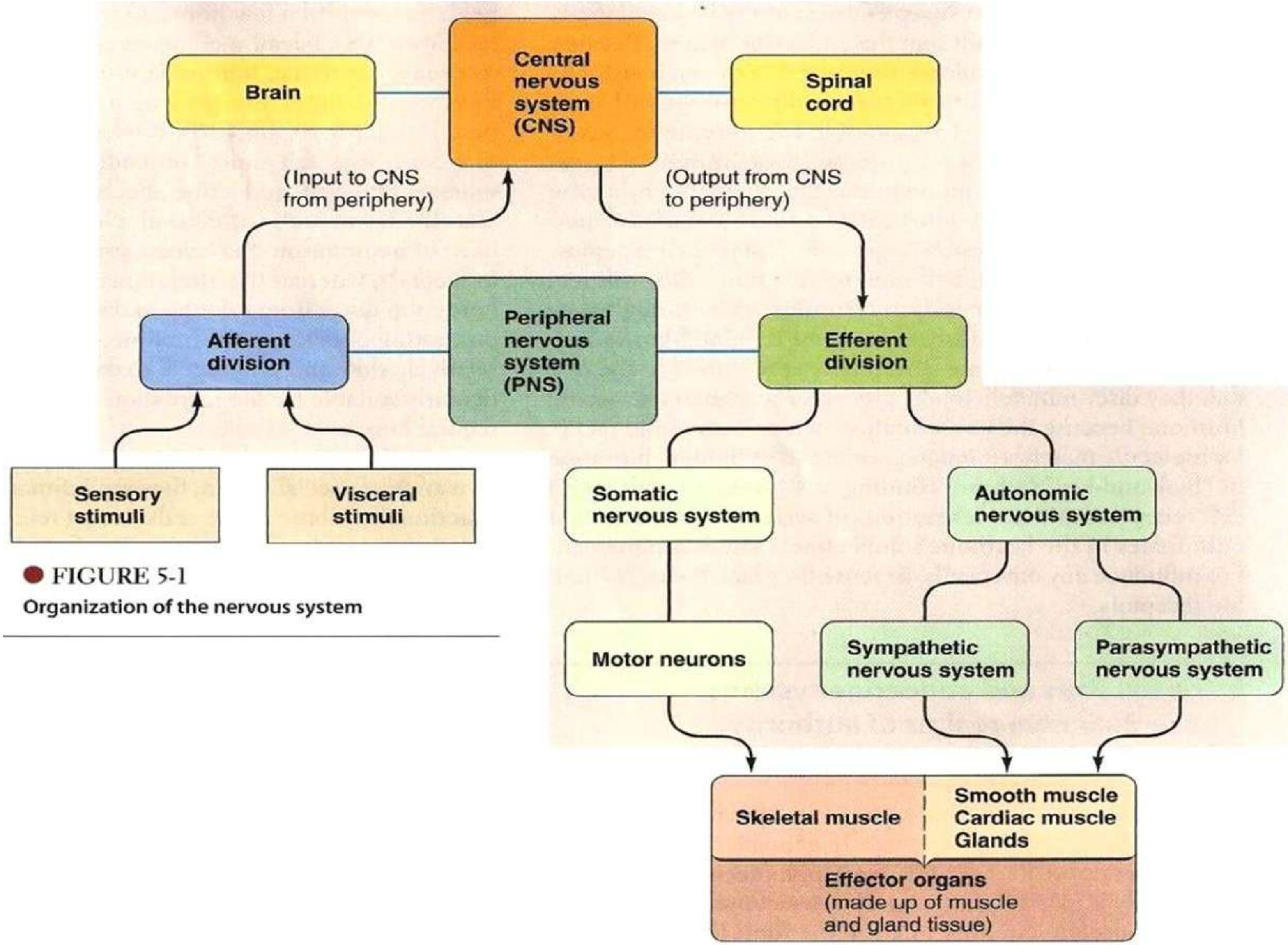


FIGURE 5-1

Organization of the nervous system

■ **Organization of the Nervous System:**

■ The nervous system is organized into the central nervous system (CNS) and the peripheral nervous system (PNS):

■ The nervous system is organized into the **CNS**, consisting of the brain and spinal cord, and the **PNS**, consisting of nerve fibers that carry information between the CNS and other parts of the body (the periphery).

■ The PNS is further subdivided into **afferent** and **efferent** divisions.

The Nervous System

(1) The **afferent** division carries information to the CNS, apprising it of the external environment and providing status reports on internal activities being regulated by the nervous system.

■ Instructions from the CNS are transmitted **via** the **efferent** division to **effector organs**, the muscles or glands that carry out the orders to bring about the desired effect.

The Nervous System

(2) The **efferent** nervous system is divided into the **somatic** nervous system, which consists of the fibers of the motor neurons that **supply** the **skeletal muscles**; and the **autonomic** nervous system, which consists of fibers that **innervate** smooth muscle, cardiac muscle, and glands.

■ The **autonomic** nervous system is further subdivided into the **sympathetic** nervous system and the **parasympathetic** nervous system, **both** of which **innervate** most of the organs **supplied** by the **autonomic** system.

The Nervous System

■ **The 3 functional classes of neurons are afferent neurons, efferent neurons, and interneurons:**

■ 3 functional classes of neurons make up the nervous system: afferent neurons, efferent neurons, and interneurons.

(1) The **afferent** division of the **PNS** consists of **afferent** neurons, which are shaped **differently** from efferent neurons and interneurons. At its peripheral ending, **afferent** neuron has a **sensory receptor** that **generates** action potentials in response to a particular type of stimulus.

■ The **afferent** neuron cell body (which is devoid of dendrites and presynaptic inputs) is located **adjacent** to the spinal cord.

■ **A long** peripheral axon (the afferent fiber), extends from the receptor to the cell body, and **a short** central axon **passes** from the cell body into the spinal cord.

■ Action potentials are initiated at the receptor end of the peripheral axon in response to a stimulus and are propagated along the peripheral axon and central axon **toward** the spinal cord.

■ The **terminals** of the **central** axon **diverge** and **synapse** with other neurons within the spinal cord, thus disseminating information about the stimulus.

■ Afferent neurons **lie primarily within the PNS system**. **Only** a small portion of their central axon endings **projects** into the spinal cord to **relay** signals from the periphery to the CNS.

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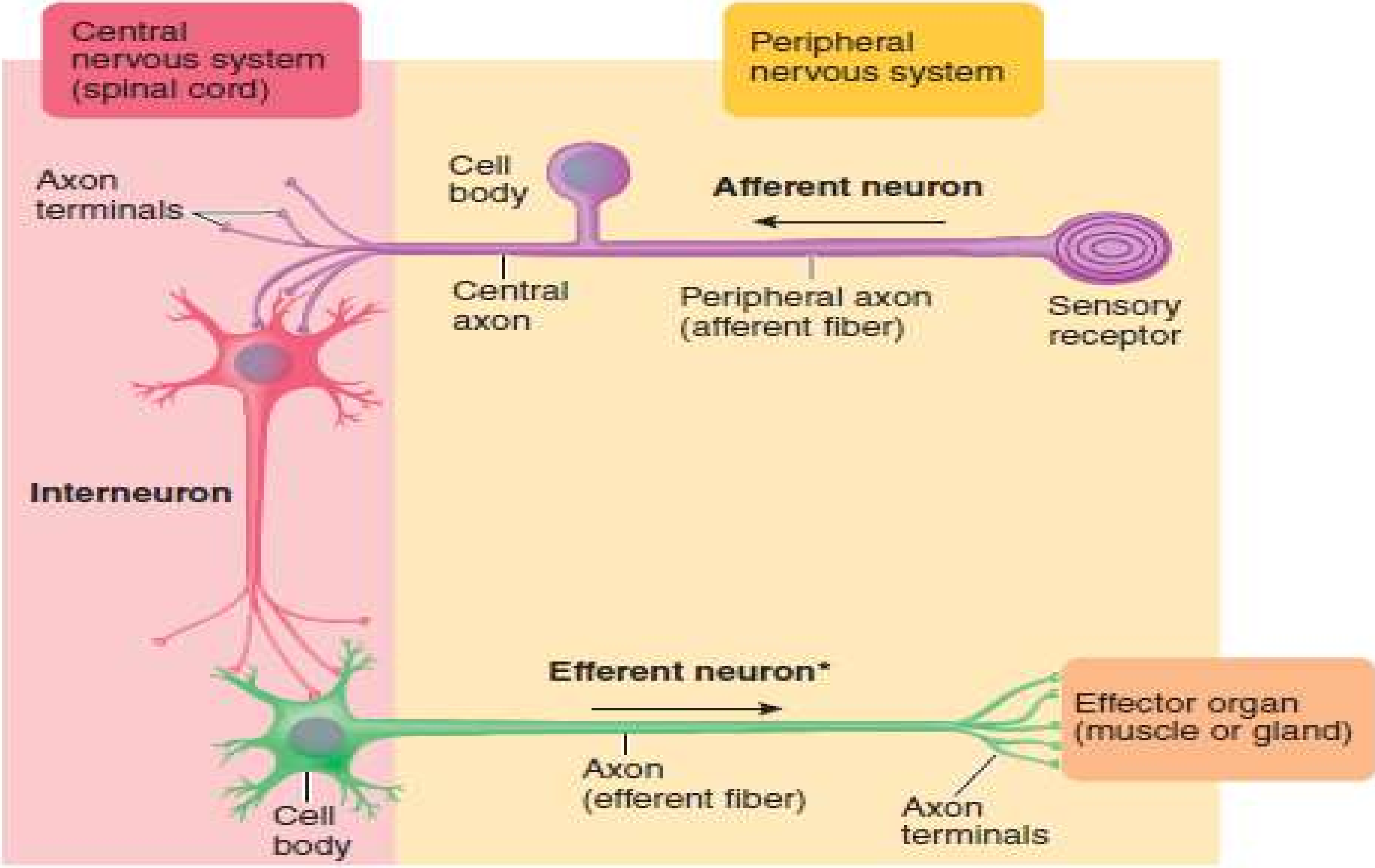
The Nervous System



● **FIGURE 5-2 Structure and location of the three functional classes of neurons.** *Efferent autonomic nerve pathways consist of a two-neuron chain between the CNS and the effector organ.

(2) Efferent neurons also **lie** primarily in the **PNS**. Efferent neuron cell bodies **originate** in the CNS, where many centrally located presynaptic inputs **converge** on them to influence their outputs to the effector organs. Efferent axons (efferent fibers) **leave** the CNS to course their way to the muscles or glands they innervate, **conveying** their integrated output for the effector organs to **put into** effect. (An autonomic nerve pathway consists of two-neuron chain between the CNS and the effector organ).

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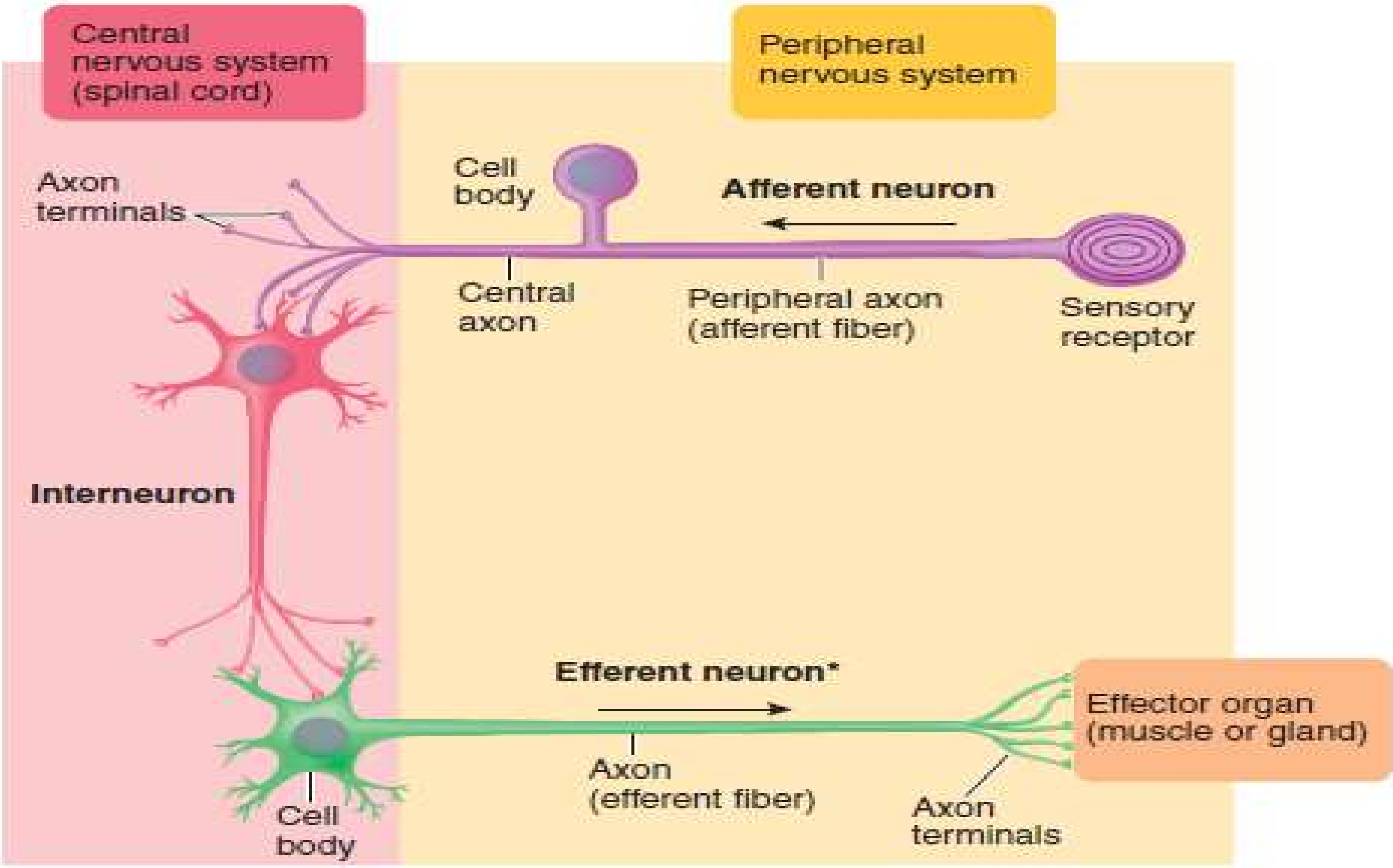
The Nervous System



● **FIGURE 5-2 Structure and location of the three functional classes of neurons.** *Efferent autonomic nerve pathways consist of a two-neuron chain between the CNS and the effector organ.

(3) About 99% of **all** neurons are **interneurons**, which **lie entirely** within the CNS. The human CNS has more than 100 billion interneurons! Interneurons **lie** between the afferent and efferent neurons and are important in integrating peripheral responses to peripheral information. For example, on receiving information through afferent neurons that you are touching a hot object, appropriate interneurons **signal** efferent neurons that transmit to your hand and arm muscles the message: “Pull the hand away from the hot object!”

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The Nervous System

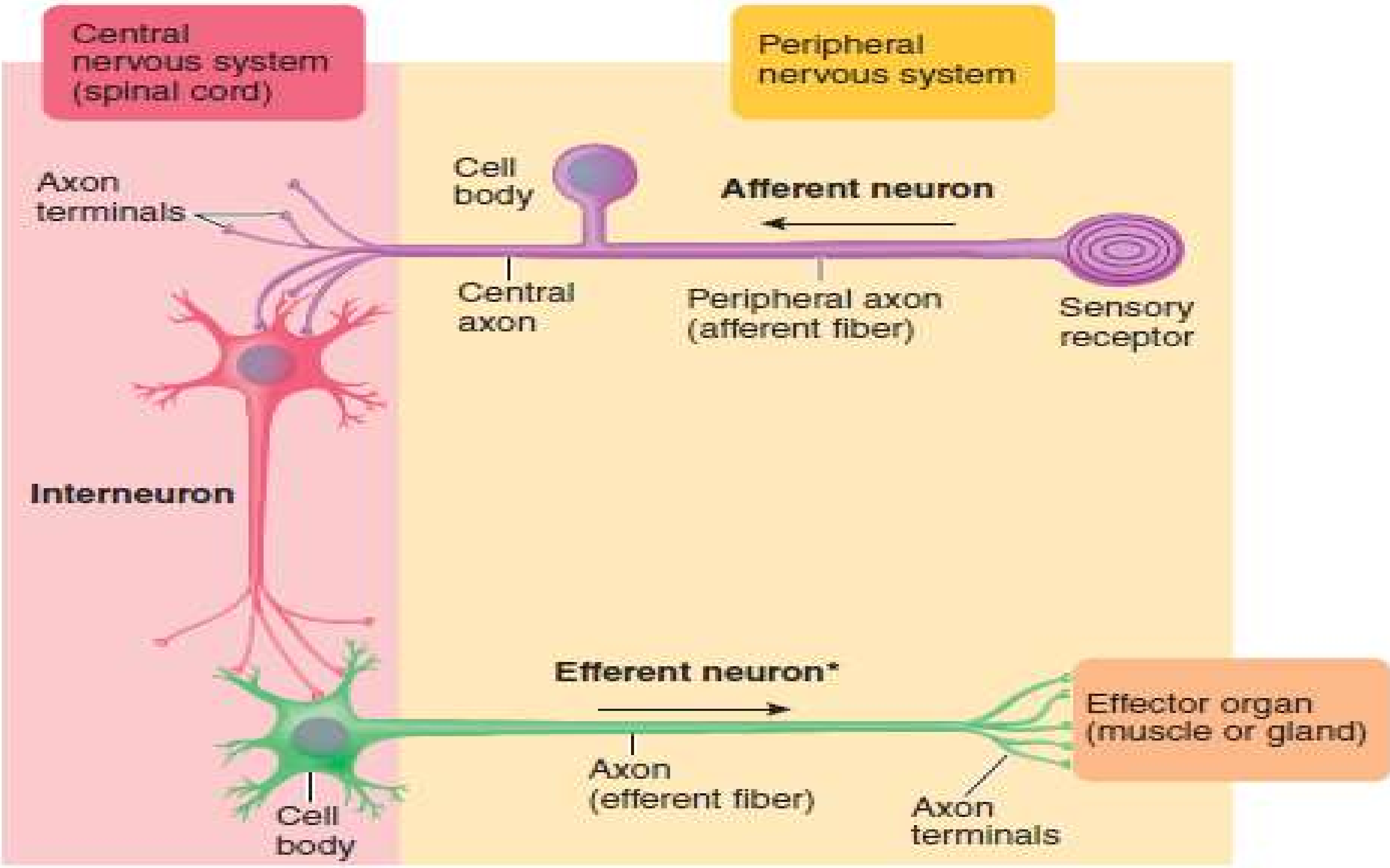

FIGURE 5-2 Structure and location of the three functional classes of neurons. *Efferent autonomic nerve pathways consist of a two-neuron chain between the CNS and the effector organ.

■ The more complex the required action, the greater is the number of interneurons interposed between the afferent message and efferent response.

■ In addition, interconnections between interneurons **themselves** are responsible for the abstract phenomena associated with the “mind”, such as thoughts, emotions, memory, creativity, intellect, and motivation. These activities are the least understood functions of the nervous system.

The End

Chapter 5 Part 1A

☻☻☻

Chapter 5: The Nervous System
Second Year Pharmacy Students
Part 2A

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1st Semester 2020/2021

The Nervous System

■ **Protection and Nourishment of the brain:**

■ Glial cells support the interneurons physically, metabolically, and functionally:

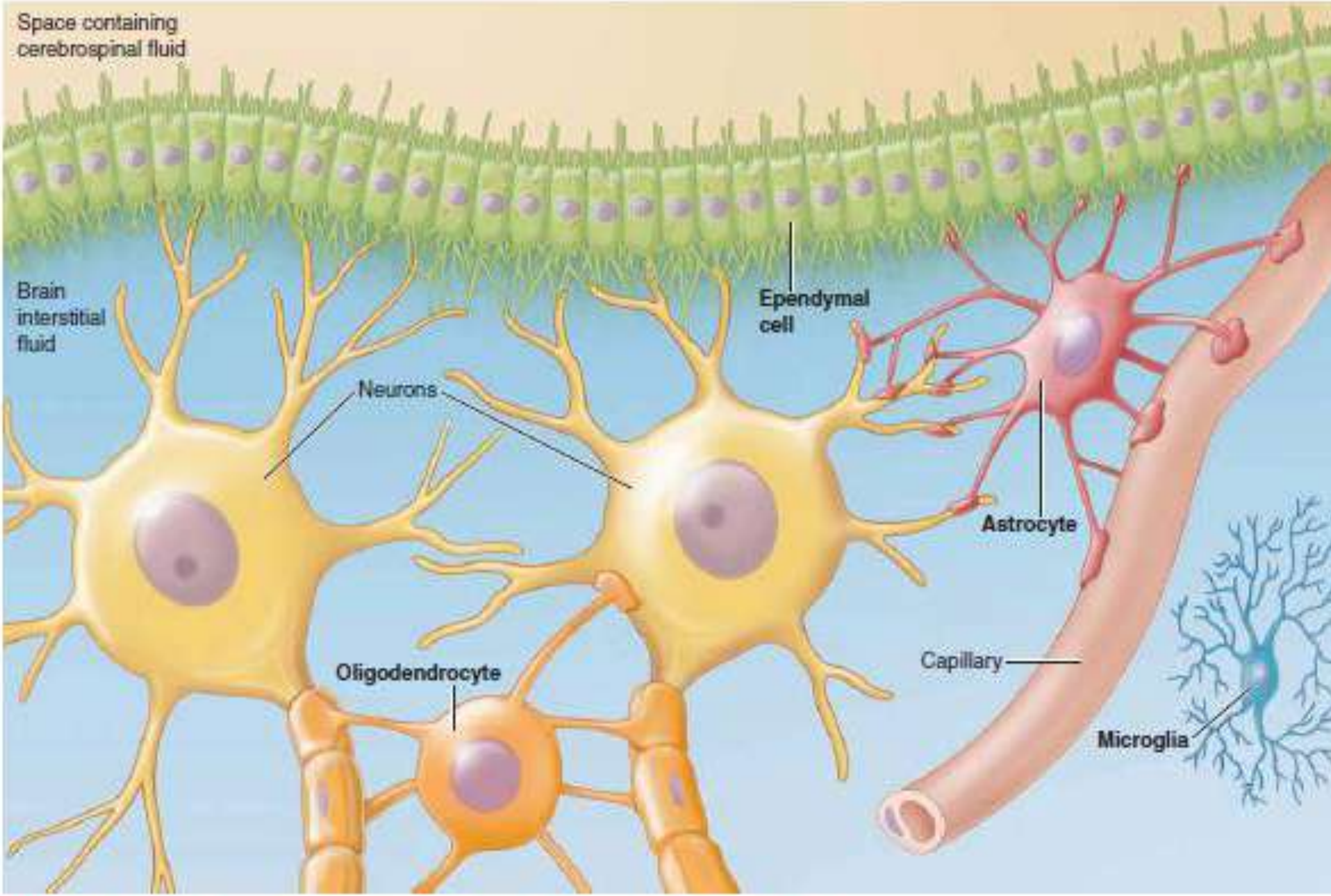
■ About 90% of the cells within the CNS are **not** neurons but glial cells (or neuroglia). Despite their large numbers, glial cells occupy **only** about half the volume of the brain, because they **do not** branch as extensively as neurons do. **Unlike** neurons, glial cells **do not initiate** or **conduct** nerve impulses. However, they communicate with neurons and among themselves by means of chemical signals.

■ Glial cells **serve** as the connective tissue of the CNS and, as such, help support the neurons **both** physically and metabolically.

■ They homeostatically **maintain** the composition of the specialized extracellular environment surrounding the neurons within the narrow limits optimal for normal neuronal function. Furthermore, they **modulate** synaptic function and are considered nearly as important as neurons to learning and memory.

The Nervous System

- There are **4 major types** of glial cells in the CNS: **astrocytes, oligodendrocytes, microglia**, and **ependymal cells**, each having **specific roles** (see the table in the next slide).



● **FIGURE 5-3 Glial cells of the central nervous system.** The glial cells include the astrocytes, oligodendrocytes, microglia, and ependymal cells.

TABLE 5-1 Functions of Glial Cells

Type of Glial Cell	Functions
Astrocytes	Physically support neurons in proper spatial relationships
	Serve as a scaffold during fetal brain development
	Induce formation of blood–brain barrier
	Help transfer nutrients to neurons
	Form neural scar tissue
	Take up and degrade released neurotransmitters
	Take up excess K^+ to help maintain proper brain-ECF ion concentration and normal neural excitability
	Enhance synapse formation and strengthen synaptic transmission via chemical signaling with neurons
	Communicate by chemical means with neurons and among themselves
Oligodendrocytes	Form myelin sheaths in CNS
Microglia	Play a role in defense of brain as phagocytic scavengers
	Release nerve growth factor
Ependymal Cells	Line internal cavities of brain and spinal cord
	Contribute to formation of cerebrospinal fluid
	Serve as neural stem cells with the potential to form new neurons and glial cells

■ **The delicate central nervous tissue is well protected:**

■ Central nervous tissue is **very delicate**, and **irreplaceable**, makes it necessary that this tissue be well protected. **4 major features** help protect the CNS from injury:

1. It is enclosed by hard, bony structures. The cranium (skull) encases the brain, and the vertebral column surrounds the spinal cord.

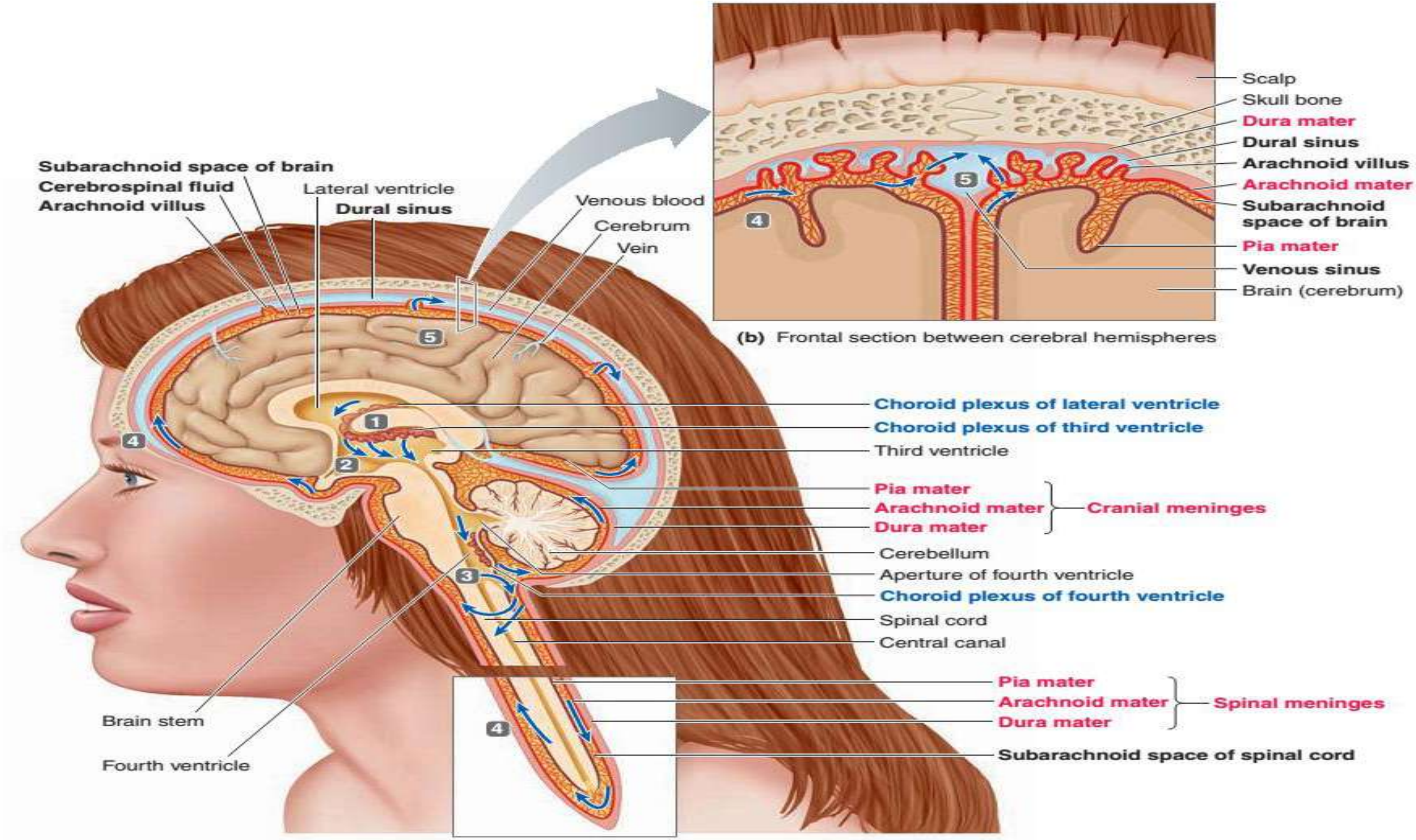
2. Three protective and nourishing membranes, **the meninges**, lie between the bony covering and the nervous tissue.

3. The brain "**floats**" in a special cushioning fluid, the **cerebrospinal fluid** (CSF).

4. **A highly selective blood–brain barrier** (BBB) **limits** access of blood-borne materials into the vulnerable brain tissue.

■ **Three meningeal membranes wrap, protect, and nourish the central nervous system:**

■ Three membranes, **the meninges**, **wrap** the CNS. From the outermost to the innermost layer they are the **dura mater**, the **arachnoid mater**, and the **pia mater.**



(b) Frontal section between cerebral hemispheres

(a) Sagittal section of brain and spinal cord

Cerebrospinal fluid

1 is produced by the choroid plexuses,

2 circulates throughout the ventricles,

3 exits the fourth ventricle at the base of the brain,

4 flows in the subarachnoid space between the meningeal layers, and

5 is finally reabsorbed from the subarachnoid space into the venous blood across the arachnoid villi.

■ The brain floats in its own special cerebrospinal fluid (CSF):

■ CSF surrounds and cushions the brain and spinal cord. The CSF has about the same density as the brain itself, so the brain **floats** or is **suspended** in this special fluid environment. The major function of CSF is to serve as **a shock-absorbing fluid** to prevent the brain from bumping against the interior of the hard skull when the head is subjected to sudden, jarring movements.

■ The CSF plays an important role in the exchange of materials between the neural cells and the interstitial fluid surrounding the brain. **Only** the brain interstitial fluid (not the blood or CSF) comes into direct contact with the neurons and glial cells.

■ Materials are exchanged freely between the CSF and brain interstitial fluid, whereas **only** limited exchange occurs between the blood and brain interstitial fluid. Thus, the composition of the CSF must be carefully regulated.

■ Because the brain interstitial fluid directly bathes the neural cells, its composition is critical. The composition of the brain interstitial fluid is influenced **more** by changes in the composition of the CSF than by alterations in the blood.

■ **The composition** of **CSF differs** from that of **blood** (e.g., CSF is **lower** in K^+ and slightly higher in Na^+) so the brain interstitial fluid an ideal environment for movement of these ions down concentration gradients.

■ The **biggest difference** is the presence of **plasma proteins** in the blood but almost **no** proteins normally present in the CSF. Plasma proteins **cannot exit** the brain capillaries to leave the blood during formation of CSF.

■ The pressure of CSF is about 10 mm Hg. Reduction of this pressure by removal of even a few milliliters of CSF during a spinal tap (lumbar puncture) for laboratory analysis may produce **severe headaches.**

■ The entire CSF volume of about 125-150 ml is **replaced** more than **3 times a day.**

■ When there is a defect in CSF formation, circulation, and reabsorption, excess CSF **accumulates**, **hydrocephalus** (“water on the brain”) occurs. The resulting increase in CSF pressure can lead to brain damage and mental retardation if untreated.

Chapter 5: The Central Nervous System
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Part 2B

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5th Year Pharmacy Students

1st Semester 2020/2021

■ **A highly selective blood–brain barrier (BBB) regulates exchanges between the blood and brain:**

■ The brain is carefully protected from harmful changes in the blood by **a highly selective BBB**. Throughout the body, materials can be exchanged between the blood and interstitial fluid **only** across the walls of capillaries (the smallest blood vessels). **Unlike** the free exchange across capillaries **elsewhere**, **only** selected, carefully regulated exchanges can be made across the BBB.

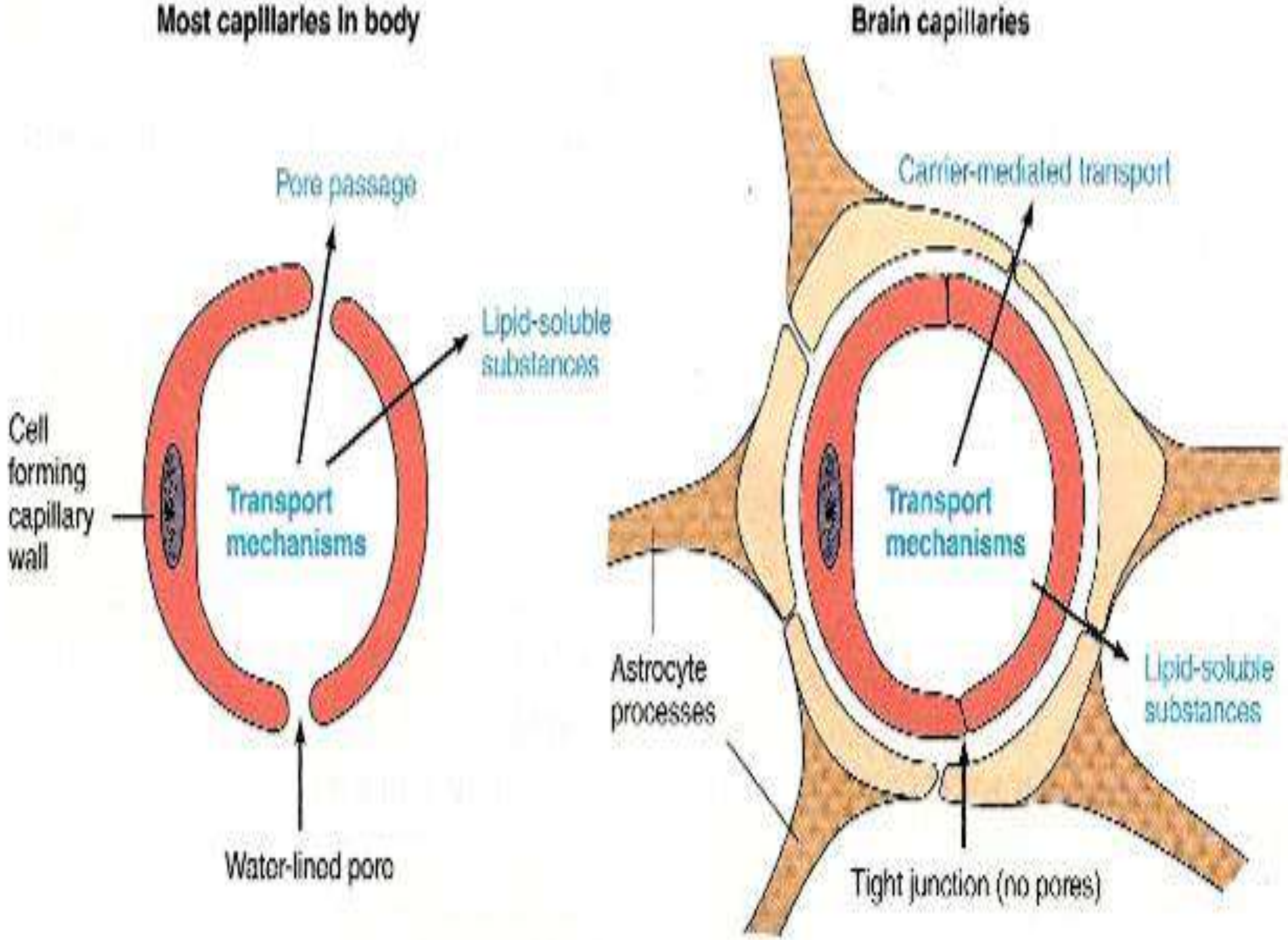
■ For example, even if the K^+ level in the blood is **doubled**, little change occurs in the K^+ concentration of the fluid bathing the central neurons. This is beneficial because alterations in interstitial fluid K^+ would be detrimental to neuronal function.

■ The BBB has both **anatomic** and **physiologic** features:

■ **Capillary walls** throughout the body are formed by a single layer of cells.

■ Usually, **all** blood plasma components (except the large plasma proteins) can be freely exchanged between the blood and the interstitial fluid through holes (pores) between the cells of the capillary wall.

■ In brain capillaries, however, the cells are **joined** by **tight junctions**, which completely seal the capillary wall so that **nothing** can be exchanged across the wall by passing between the cells. The **only** possible exchanges are through the capillary cells themselves.



Capillaries in cross section

■ **Lipid-soluble** substances (e.g., O_2, CO_2, alcohol, and hormones) **penetrate** these cells **easily** by dissolving in their lipid plasma membrane.

■ **Small water** molecules also diffuse through easily, by passing between the phospholipid molecules of the plasma membrane, or through aquaporins (water channels).

■ **All other** substances **exchanged** between the blood and brain interstitial fluid (including such essential materials as glucose, amino acids, and ions) are **transported** by **highly selective membrane-bound carriers.**

■ Thus, **transport** across **brain capillary walls** between **the wall-forming cells** is **prevented** anatomically and **transport through** the cells is **restricted physiologically.**
Together, these mechanisms constitute the BBB.

■ By **strictly** limiting **exchange** between the blood and brain, the BBB:

(1) Protects the delicate brain from chemical fluctuations in the blood.

(2) Minimizes the possibility that potentially harmful blood-borne substances might reach the central neural tissue.

(3) It **prevents** certain circulating hormones that could also act as neurotransmitters from reaching the brain, where they could produce uncontrolled nervous activity.

■ On the **negative side**, the BBB **limits** the use of drugs for the treatment of brain and spinal cord disorders because many drugs are **unable** to **penetrate** this barrier.

■ Brain capillaries are surrounded by **astrocytes**, which at one time were erroneously thought to be **physically** responsible for the BBB. Now, it is known that astrocytes play 2 roles in the BBB:

(1) They signal the cells **forming** the brain capillaries to “get tight.” Capillary cells **do not** have an inherent ability to **form** tight junctions; they do so **only** at the command of a signal within their neural environment.

(2) Astrocytes **participate** in the cross-cellular transport of some substances, such as K^+.

■ **The brain depends on constant delivery of oxygen and glucose by the blood:**

■ Even though many substances in the blood **never** actually come in contact with the brain tissue, the brain is **more** dependent than any other tissue on a constant blood supply.

■ **Unlike** most tissues (which can resort to anaerobic metabolism to produce ATP in the absence of O_2 for at least short periods), the brain **cannot** produce ATP **without** O_2.

■ It was discovered that an **O_2-binding protein**, (i.e., neuroglobin), in the brain. This molecule (which is similar to hemoglobin, the O_2-carrying protein in red blood cells), is thought to play **a key role** in O_2 handling in the brain, although its exact function remains to be determined.

■ Also, in contrast to most tissues (which can use other sources of fuel for energy production in lieu of glucose), the brain **normally** uses **only** glucose but **does not store** any of it.

■ Because of its high rate of demand for ATP, under resting conditions the brain uses 20% of the O_2 and 50% of the glucose consumed in the body. So, the brain depends on a continuous, adequate blood supply of O_2 and glucose. Although it constitutes only 2% of body weight, the brain receives 15% of the blood pumped out by the heart. **(**Instead of using glucose during starvation, the brain can resort to using ketone bodies produced by the liver, but this alternate nutrient source also must be delivered by the blood to the brain**).**

■ Brain damage results if the brain is deprived of its O_2 supply for **more than** 4-5 minutes, or, if its glucose supply is cut off for **more than** 10-15 minutes. The most common cause of inadequate blood supply to the brain is a stroke.

Chapter 5: The Central Nervous System

Second Year Pharmacy Students

Part 3A

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Al-Azhar University of Gaza

First Semester 2020/2021

The Central Nervous System

■ Overview of the Central Nervous System:

■ The CNS consists of the brain and spinal cord. The estimated 100 billion neurons in the brain are assembled into complex networks that enable you to:

(1) subconsciously regulate the internal environment.

(2) experience emotions.

(3) voluntarily control our movements.

(4) perceive (be consciously aware of) our own body and our surroundings, and

(5) engage in other higher cognitive processes such as thought and memory.

The Central Nervous System

- No part of the brain acts in isolation from other brain regions, Why? Because:

(1) Networks of neurons are anatomically linked by synapses.

(2) Neurons throughout the brain communicate extensively with each other by electrical and chemical means.

- However, neurons that work together to ultimately accomplish a given function tend to be organized within a discrete location. Therefore, even though the brain operates as a whole, it is organized into different regions.

The Central Nervous System

- The parts of the brain can be grouped in various ways based on anatomic distinctions, functional specialization, and evolutionary development.
- The following grouping will be used: The order in which these components are listed generally represents both their anatomic location (from bottom to top) and their complexity and sophistication of function (from the least specialized, oldest level to the newest, most specialized level):

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The Central Nervous System

1. Brain stem

2. Cerebellum

3. Forebrain

a. Diencephalon

(1) Hypothalamus

(2) Thalamus

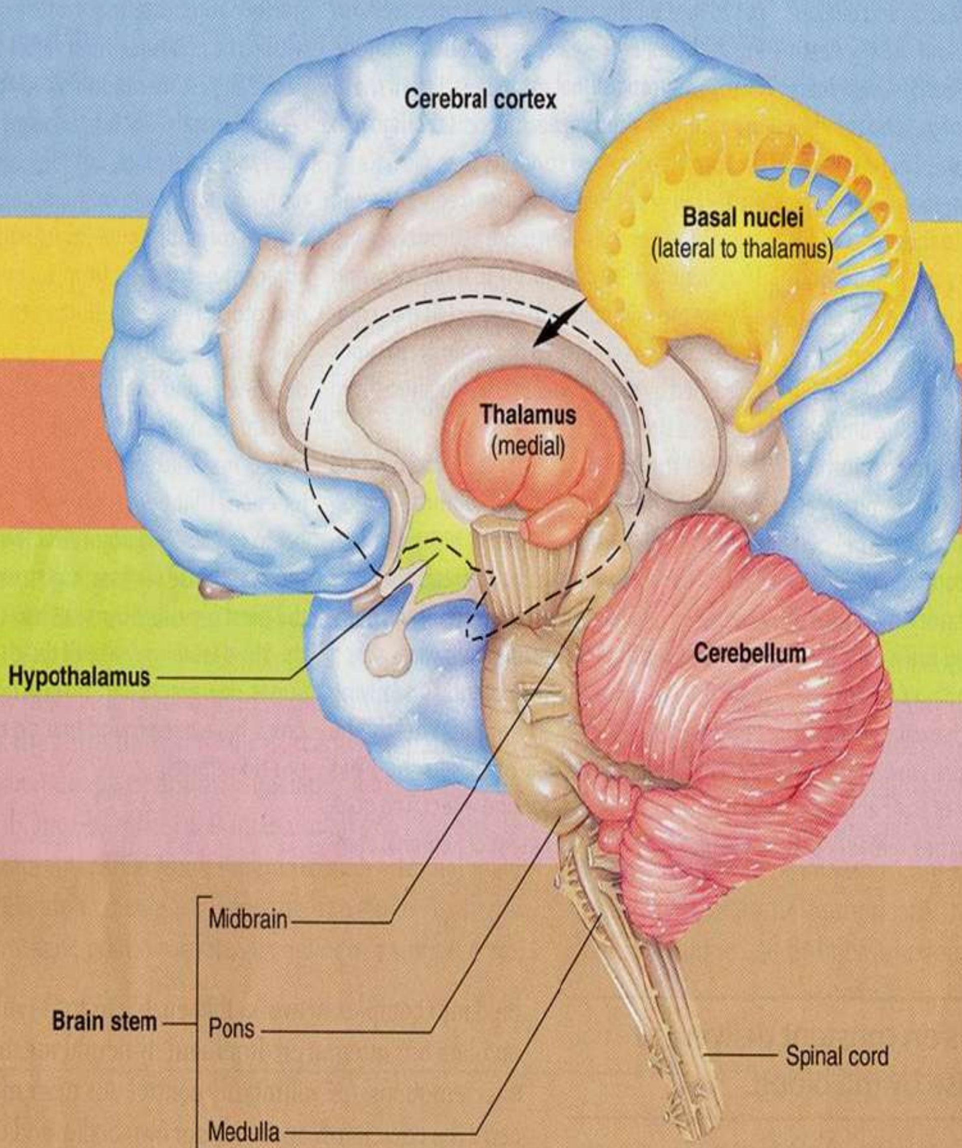
b. Cerebrum

(1) Basal nuclei

(2) Cerebral cortex

▲ TABLE 5-3

Overview of Structures and Functions of the Major Components of the Brain



Brain Componen	Major Functions
Cerebral cortex	1. Sensory perception 2. Voluntary control of movement 3. Language 4. Personality traits 5. Sophisticated mental events, such as thinking, memory, decision making, creativity, and self-consciousness
Basal nuclei	1. Inhibition of muscle tone 2. Coordination of slow, sustained movements 3. Suppression of useless patterns of movement
Thalamus	1. Relay station for all synaptic input 2. Crude awareness of sensation 3. Some degree of consciousness 4. Role in motor control
Hypothalamus	1. Regulation of many homeostatic functions, such as temperature control, thirst, urine output, and food intake 2. Important link between nervous and endocrine systems 3. Extensive involvement with emotion and basic behavioral patterns
Cerebellum	1. Maintenance of balance 2. Enhancement of muscle tone 3. Coordination and planning of skilled voluntary muscle activity
Brain stem (midbrain, pons, and medulla)	1. Origin of majority of peripheral cranial nerves 2. Cardiovascular, respiratory, and digestive control centers 3. Regulation of muscle reflexes involved with equilibrium and posture 4. Reception and integration of all synaptic input from spinal cord; arousal and activation of cerebral cortex 5. Role in sleep–wake cycle

TABLE 5-2 **Overview of Structures and Functions of the Major Components of the Brain**

Brain Component

Cerebral cortex

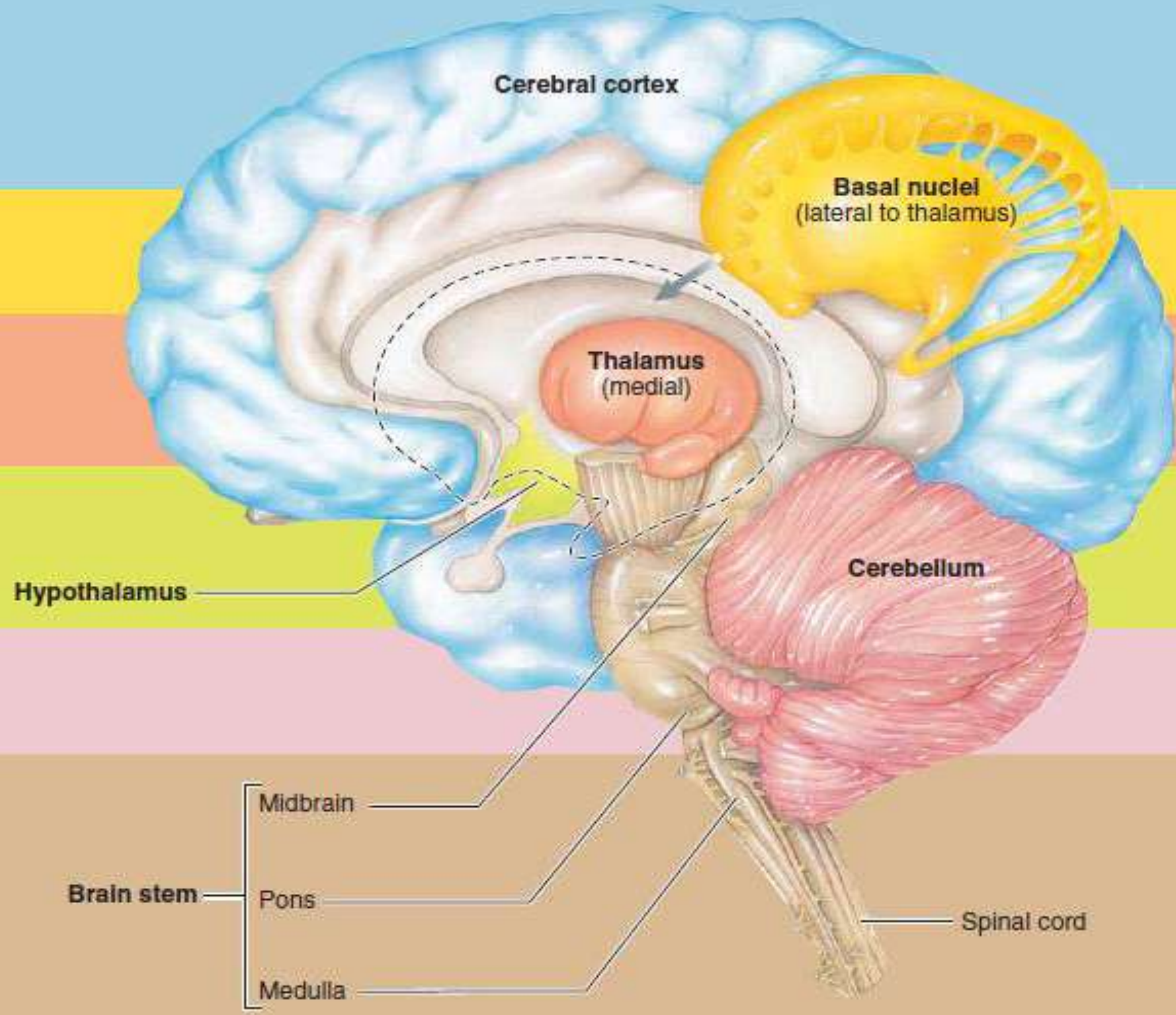
Basal nuclei

Thalamus

Hypothalamus

Cerebellum

Brain stem



Major Functions

1. Sensory perception
2. Voluntary control of movement
3. Language
4. Personality traits
5. Sophisticated mental events, such as thinking, memory, decision making, creativity, and self-consciousness

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2. Cardiovascular, respiratory, and digestive control centers
3. Regulation of muscle reflexes involved with equilibrium and posture
4. Reception and integration of all synaptic input from spinal cord; arousal and activation of cerebral cortex
5. Role in sleep–wake cycle

The Central Nervous System

- The cerebrum, by far the largest portion of the human brain, is divided into two halves: the right and left cerebral hemispheres. They are connected to each other by the corpus callosum (a thick band consisting of an estimated 300 million neuronal axons that connect the two hemispheres), is the body's "information superhighway".
- The two hemispheres communicate and cooperate with each other by means of constant information exchange through this neural connection.

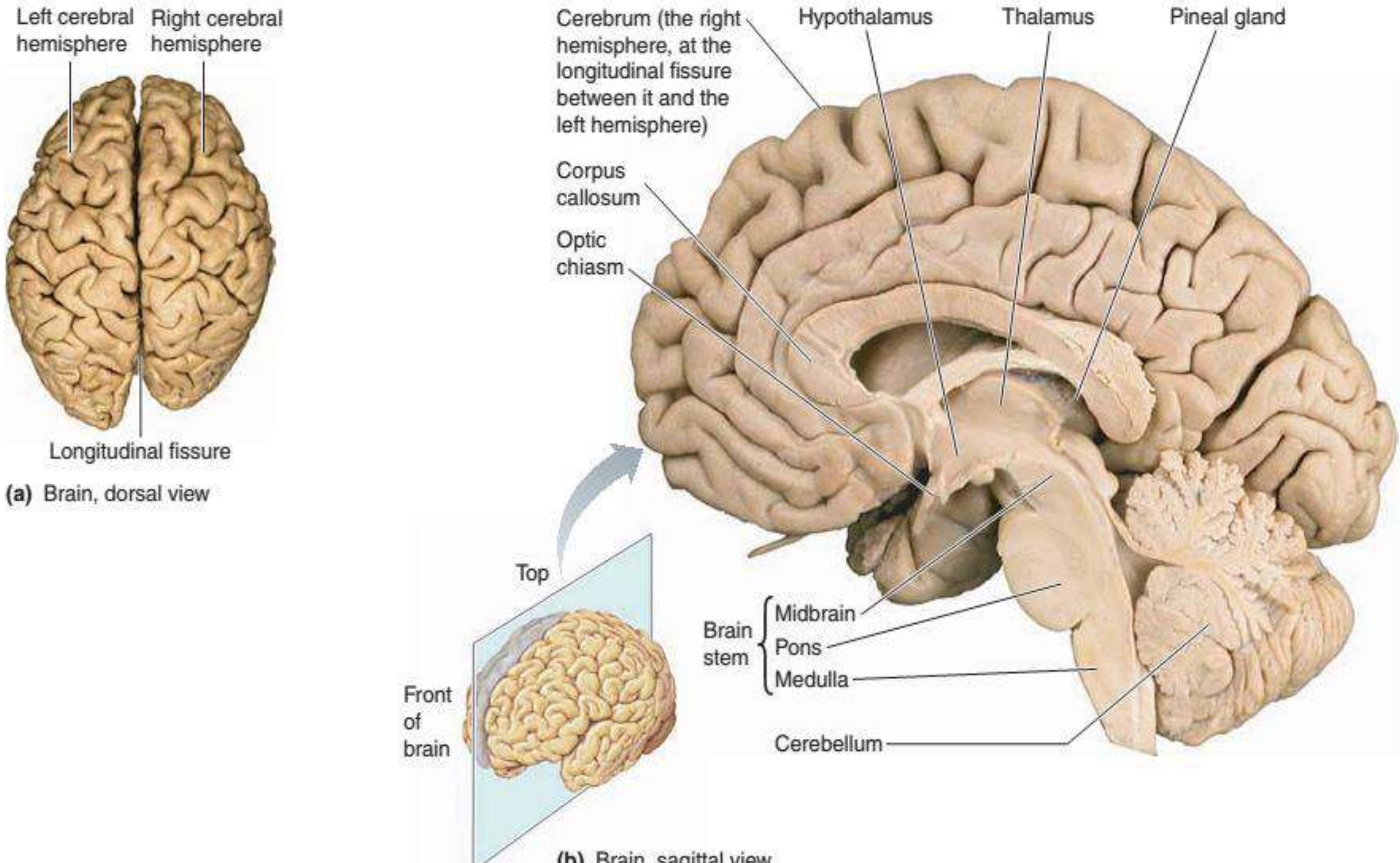


FIGURE 5-7 Brain of a human cadaver. (a) Dorsal view looking down on the top of the brain. Note that the deep longitudinal fissure divides the cerebrum into the right and left cerebral hemispheres. (b) Sagittal view of the right half of the brain. All major brain regions are visible from this midline interior view. The corpus callosum serves as a neural bridge between the two cerebral hemispheres.

- **The cerebral cortex is an outer shell of gray matter covering an inner core of white matter:**

- Each hemisphere is composed of a thin outer shell of gray matter, the cerebral cortex, covering a thick central core of white matter.

- Several other masses of gray matter that collectively constitute the basal nuclei are located deep within the white matter.

The Central Nervous System

- Throughout the entire CNS, gray matter consists predominantly of densely packaged neuronal cell bodies and their dendrites as well as most glial cells.
- Bundles (or tracts) of myelinated nerve fibers (axons) constitute the white matter.
- Integration of neural input and initiation of neural output take place at synapses within the gray matter.

■ The fiber tracts in the white matter transmit signals from one part of the cerebral cortex to another, or , between the cortex and other regions of the CNS. Such communication between different areas of the cortex and other regions of the CNS facilitates integration of their activity. This integration is essential for even a relatively simple task such as picking a flower.

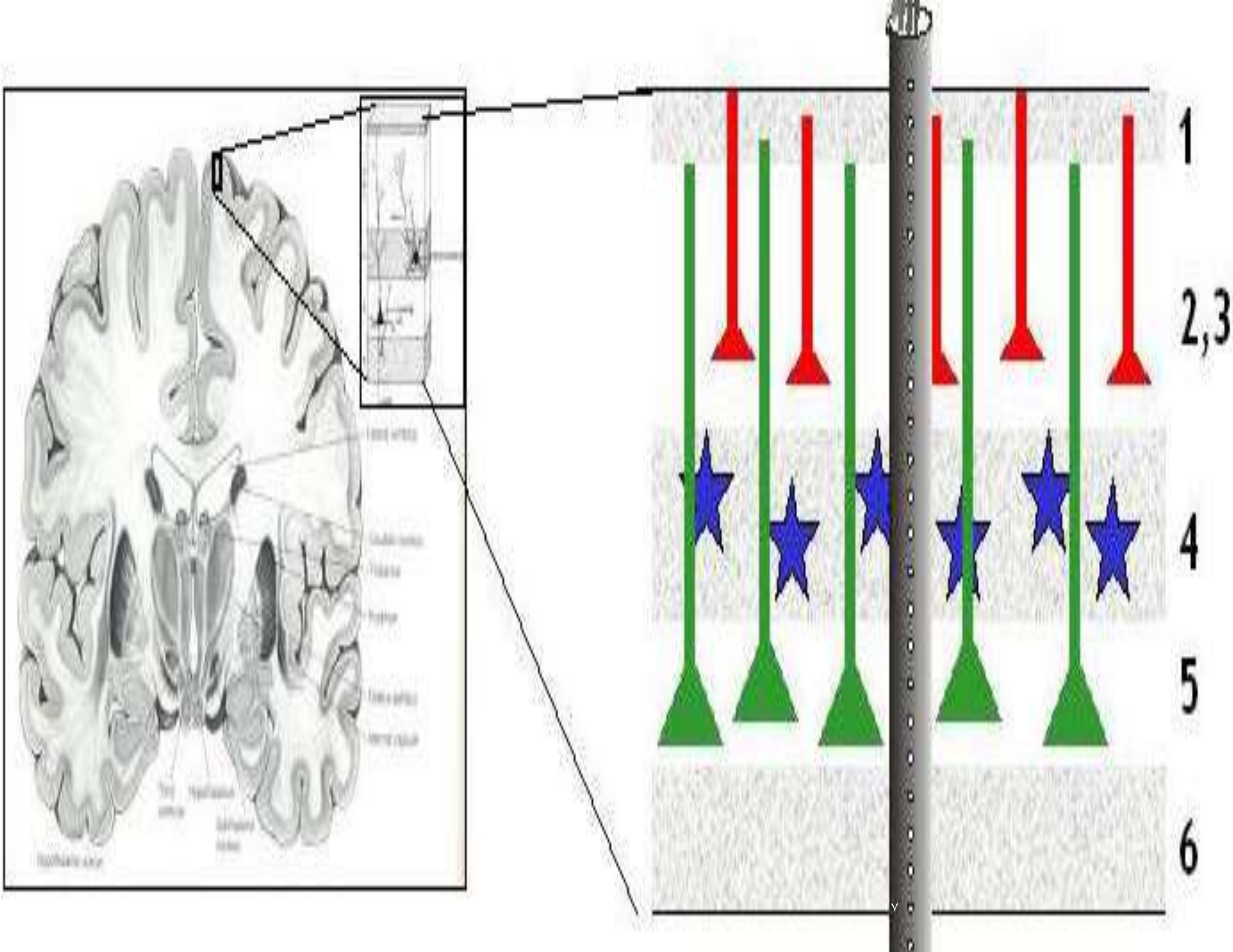
■ **The cerebral cortex is organized into layers and functional columns:**

■ The cerebral cortex is organized into 6 well-defined layers based on varying distributions of several distinctive cell types.

■ These layers are organized into functional vertical columns that extend perpendicularly about 2 mm from the cortical surface down through the thickness of the cortex to the underlying white matter.

- The functional differences between various areas of the cortex result from different layering patterns within the columns and from different input–output connections.
- For example, those regions of the cortex responsible for sensory perception have an expanded layer 4 (a layer rich in stellate cells, whose neurons are responsible for initial processing of sensory input to the cortex).

- In contrast, cortical areas that control output to skeletal muscles have a thickened layer 5 (which contains an abundance of large neurons known as pyramidal cells, which send fibers down the spinal cord from the cortex to terminate on efferent motor neurons that innervate skeletal muscles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Chapter 5: The Central Nervous System
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Part 3B

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First Semester 2020/2021

■ **The four pairs of lobes in the cerebral cortex are specialized for different activities:**

■ The anatomic landmarks used in cortical mapping are specific deep folds that divide each half of the cortex into four major lobes: the occipital, temporal, parietal, and frontal lobes.

■ The occipital lobes, located posteriorly (at the back of the head), carry out the initial processing of visual input.

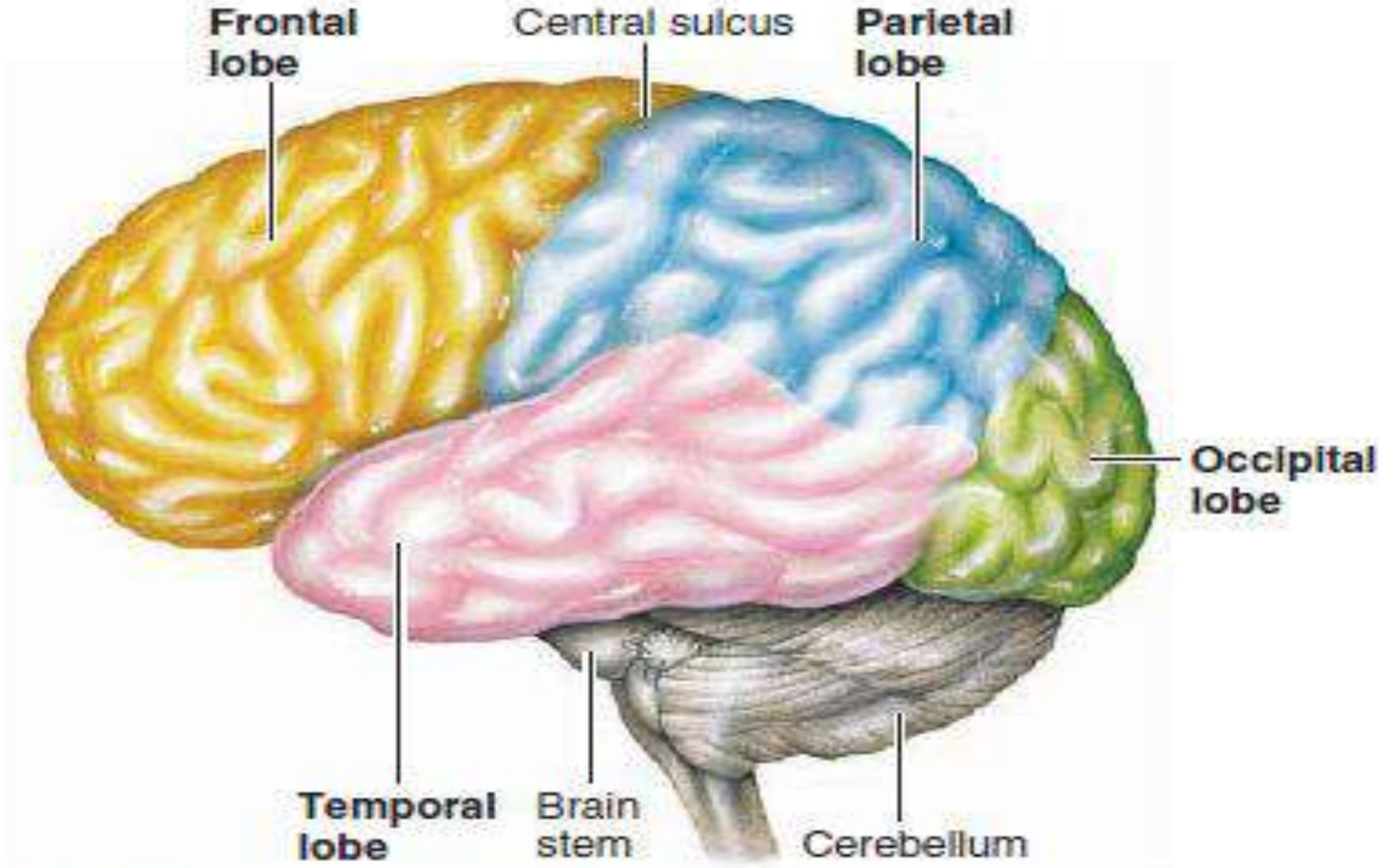
■ Auditory (sound) sensation is initially received by the temporal lobes, located laterally (on the sides of the head).

The Central Nervous System

- The parietal lobes and frontal lobes, located on the top of the head, are separated by a deep infolding, the central sulcus. The parietal lobes lie to the rear of the central sulcus on each side, and the frontal lobes lie in front of the central sulcus.
- The parietal lobes are primarily responsible for receiving and processing sensory input.
- The frontal lobes are responsible for 3 main functions:

(1) voluntary motor activity.

(2) speaking ability. (3) elaboration of thought.



● **FIGURE 5-8 Cortical lobes.** Each half of the cerebral cortex is divided into the occipital, temporal, parietal, and frontal lobes, as depicted in this lateral view of the brain.

The Central Nervous System

■ The **parietal lobes** accomplish **somatosensory processing**:

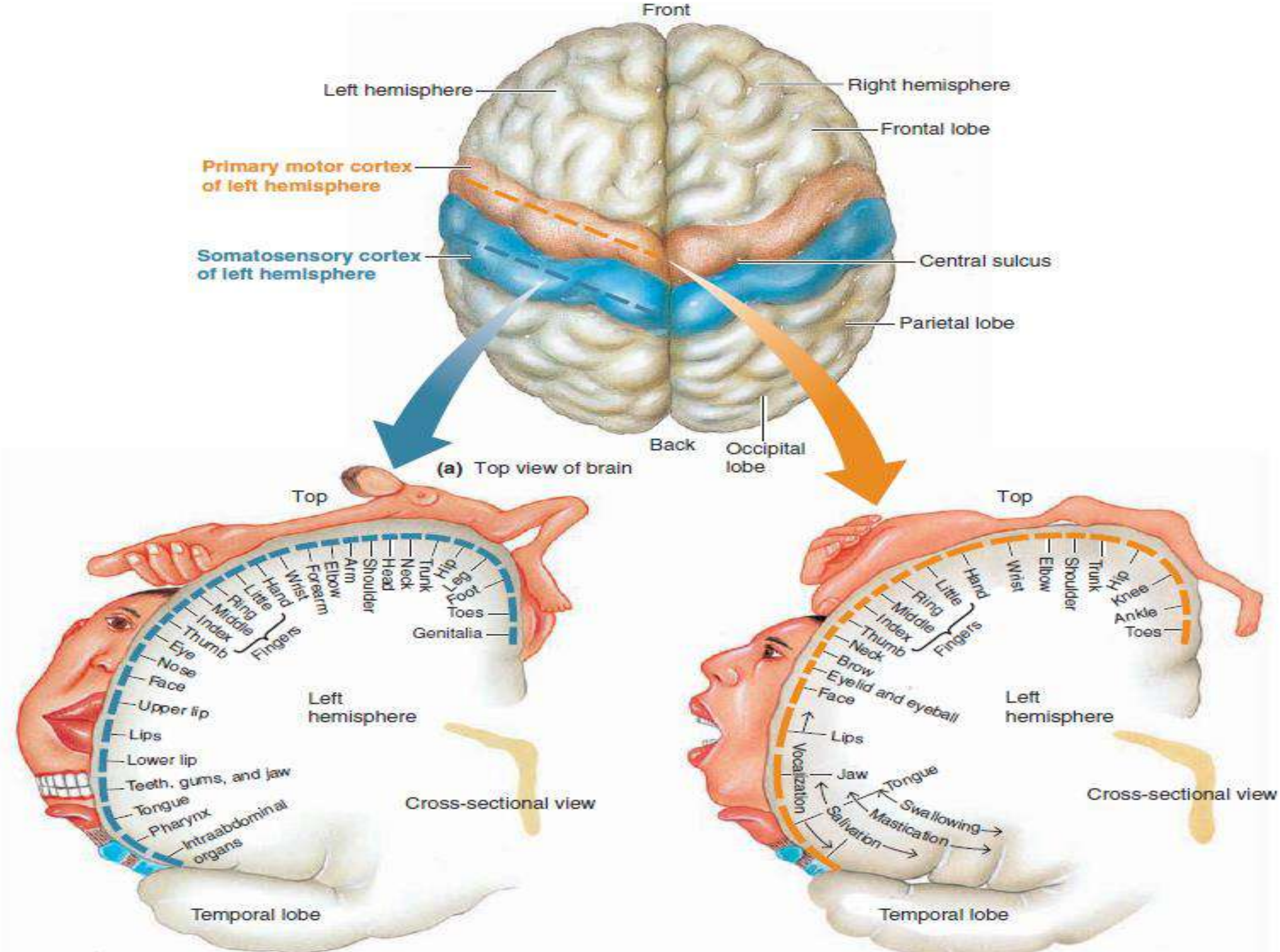
■ Sensations from the surface of the body (e.g., touch, pressure, heat, cold, and pain) are collectively known as somesthetic sensations (somesthetic means “body feelings”).

■ Within the CNS, this information is projected (transmitted along specific neural pathways to higher brain levels) to the somatosensory cortex (which is located in the front portion of each parietal lobe immediately behind the central sulcus), and is the site for initial cortical processing and perception of both somesthetic and proprioceptive (is the awareness of body position) input.

- Each region within the somatosensory cortex receives somesthetic and proprioceptive input from a specific area of the body.

- Note that on this so-called “sensory homunculus” (homunculus means “little man”), the body is represented upside down on the somatosensory cortex, and the different parts of the body are not equally represented. The size of each body part in this homunculus indicates the relative proportion of the somatosensory cortex devoted to that area.

- The exaggerated size of the face, tongue, hands, and genitalia indicates the high degree of sensory perception associated with these body parts.

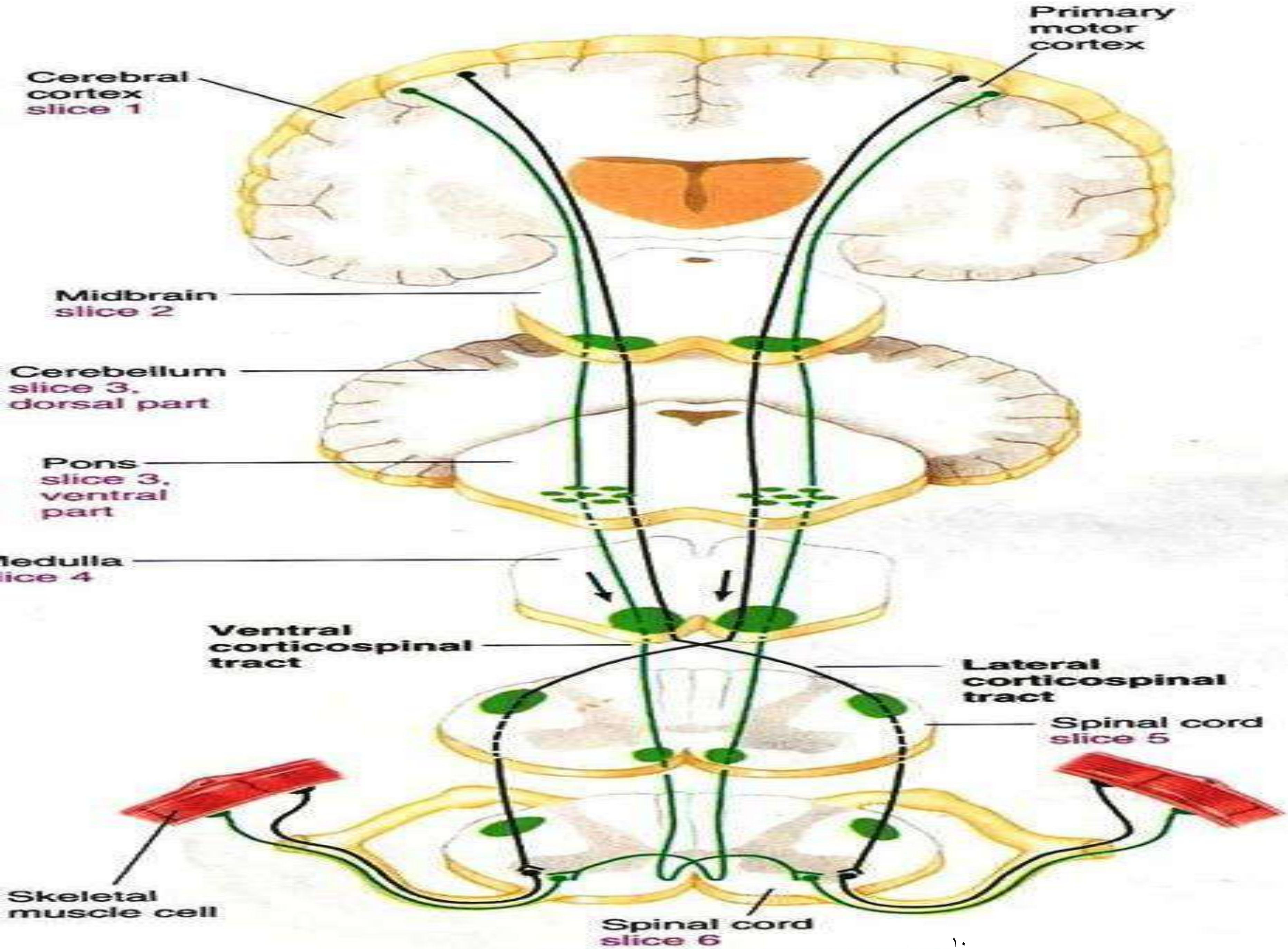


(a) Top view of brain

(b) Sensory homunculus

(c) Motor homunculus

- The somatosensory cortex on each side of the brain receives sensory input from the opposite side of the body, WHY?? Because most of the ascending (afferent) pathways that carry sensory information up the spinal cord cross over to the opposite side before eventually terminating in the cortex.
- Thus, damage to the somatosensory cortex in the left hemisphere produces sensory deficits on the right side of the body, whereas sensory losses on the left side of the body are associated with damage to the right half of the cortex.



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(c) Descending tracts

The Central Nervous System

■ Simple awareness of touch, pressure, temperature, or pain is detected by the thalamus (a lower level of the brain). The thalamus makes you aware that something hot versus something cold is touching your body. But thalamus does not tell you where or of what intensity, but the somatosensory cortex goes beyond mere recognition of sensations to fuller sensory perception. The somatosensory cortex localizes the source of sensory input and perceives the level of intensity of the stimulus.

The Central Nervous System

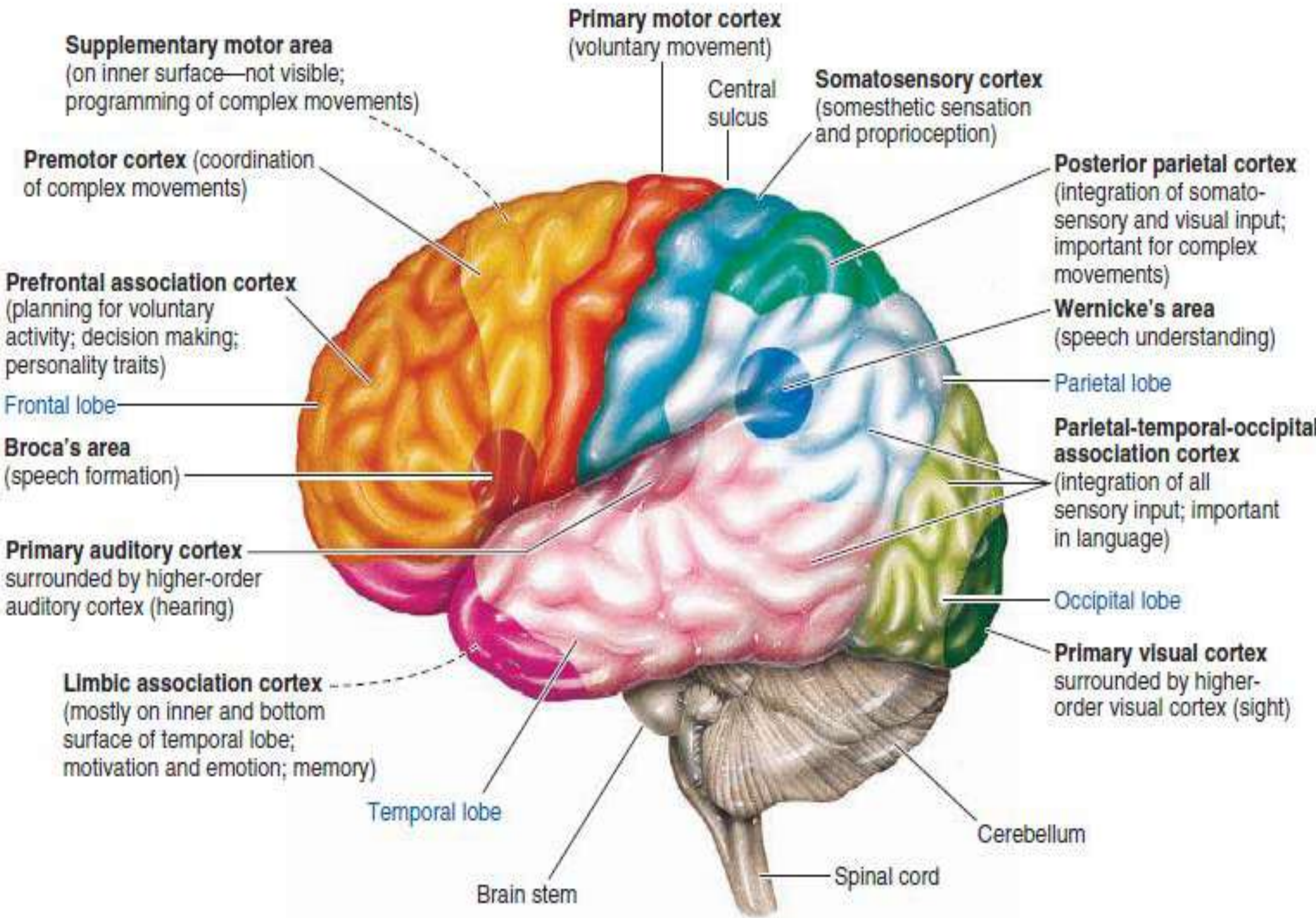
- It also is capable of spatial discrimination, so it can discern shapes of objects being held and can distinguish subtle differences in similar objects that come into contact with the skin.
- The somatosensory cortex, in turn, projects this sensory input via white matter fibers to adjacent higher sensory areas for even further elaboration, analysis, and integration of sensory information.

- These higher areas are important in perceiving complex patterns of somatosensory stimulation, for example, simultaneous appreciation of the texture, firmness, temperature, shape, position, and location of an object you are holding.

■ The **primary motor cortex** located in the **frontal lobes controls the skeletal muscles:**

■ The area in the rear portion of the frontal lobe immediately in front of the central sulcus and next to the somatosensory cortex is the primary motor cortex, which confers voluntary control over movement produced by skeletal muscles.

■ As in sensory processing, the motor cortex on each side of the brain primarily controls muscles on the opposite side of the body.



(a) Regions of the cerebral cortex responsible for various functions

- Neuronal tracts originating in the motor cortex of the left hemisphere cross over before passing down the spinal cord to terminate on efferent motor neurons that trigger skeletal muscle contraction on the right side of the body.
- Accordingly, damage to the motor cortex on the left side of the brain produces paralysis on the right side of the body, and the converse is also true.
- Stimulation of different areas of the primary motor cortex brings about movement in different regions of the body.

- Like the sensory homunculus for the somatosensory cortex, the motor homunculus, which depicts the location and relative amount of motor cortex devoted to output to the muscles of each body part, is distorted (upside down).
- Note that the fingers, thumbs, and muscles important in speech (especially those of the lips and tongue), are grossly exaggerated, indicating the fine degree of motor control these body parts have.

- Compare this to how little brain tissue is devoted to the trunk, arms, and lower extremities, which are not capable of such complex movements.
- Thus, the extent of representation in the motor cortex is proportional to the precision and complexity of motor skills required of the respective part.

Chapter 5: The Central Nervous System

Second Year Pharmacy Students

Part 4A

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5th Year Pharmacy Students

1st Semester 2020/2021

■ **The higher motor areas are also important in motor control:**

■ The motor cortex is not the only region of the brain involved with motor control:

(1) Lower brain regions and spinal cord control involuntary skeletal muscle activity, e.g. posture maintenance. Some of these same regions also play an important role in monitoring and coordinating voluntary motor activity that the primary motor cortex has set in motion.

(2) Although fibers originating from the motor cortex can activate motor neurons to bring about muscle contraction, motor cortex itself does not initiate voluntary movement.

■ The motor cortex is activated by a widespread pattern of neuronal discharge, the “readiness potential”, which occurs about 750 msec before specific electrical activity is detectable in the motor cortex.

Cerebral Cortex

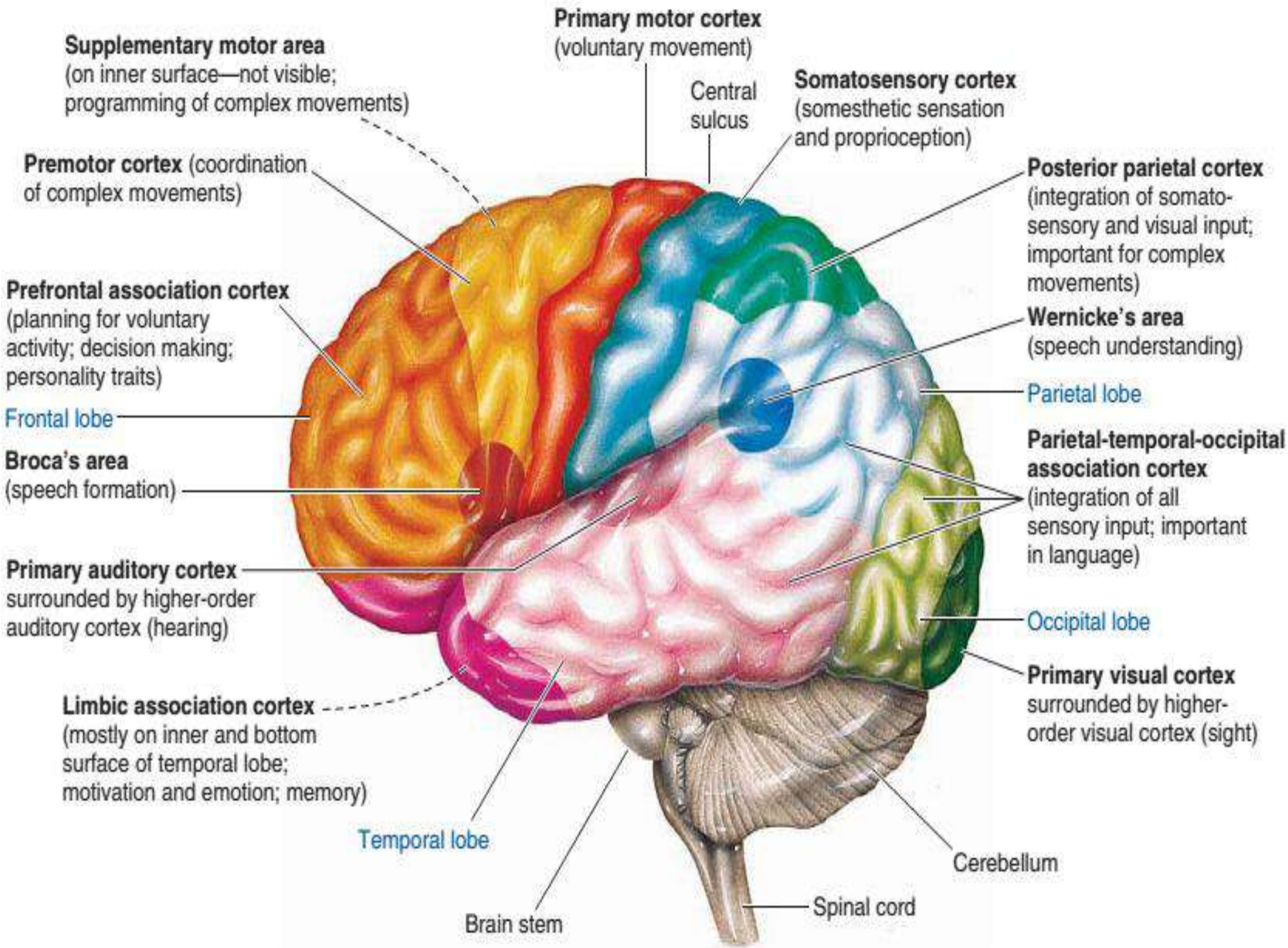
- 3 higher motor areas of the cortex are involved in this voluntary decision-making period. These higher areas, which all command the primary motor cortex, include the supplementary motor area, the premotor cortex, and the posterior parietal cortex. These three higher motor areas of the cortex, as well as the cerebellum carry out different, related functions that are all important in programming and coordinating complex movements that involve simultaneous contraction of many muscles.

Cerebral Cortex

- When either of these higher motor areas is damaged, the person cannot process complex sensory information to accomplish purposeful movement in a spatial context; for example, the person cannot successfully manipulate eating utensils.

Cerebral Cortex

- When either of these higher motor areas is damaged, the person cannot process complex sensory information to accomplish purposeful movement in a spatial context; for example, the person cannot successfully manipulate eating utensils.



(a) Regions of the cerebral cortex responsible for various functions

Cerebral Cortex

■ **Different regions of the cortex control different aspects of language:**

■ In the vast majority of people the areas of the brain responsible for language ability are found in only one hemisphere, the left hemisphere.

■ Language involves the integration of 2 distinct capabilities: **expression** (speaking ability) and **comprehension**, each of which is related to a specific area of the cortex.

■ The primary areas of cortical specialization for language are: Broca’s area and Wernicke’s area.

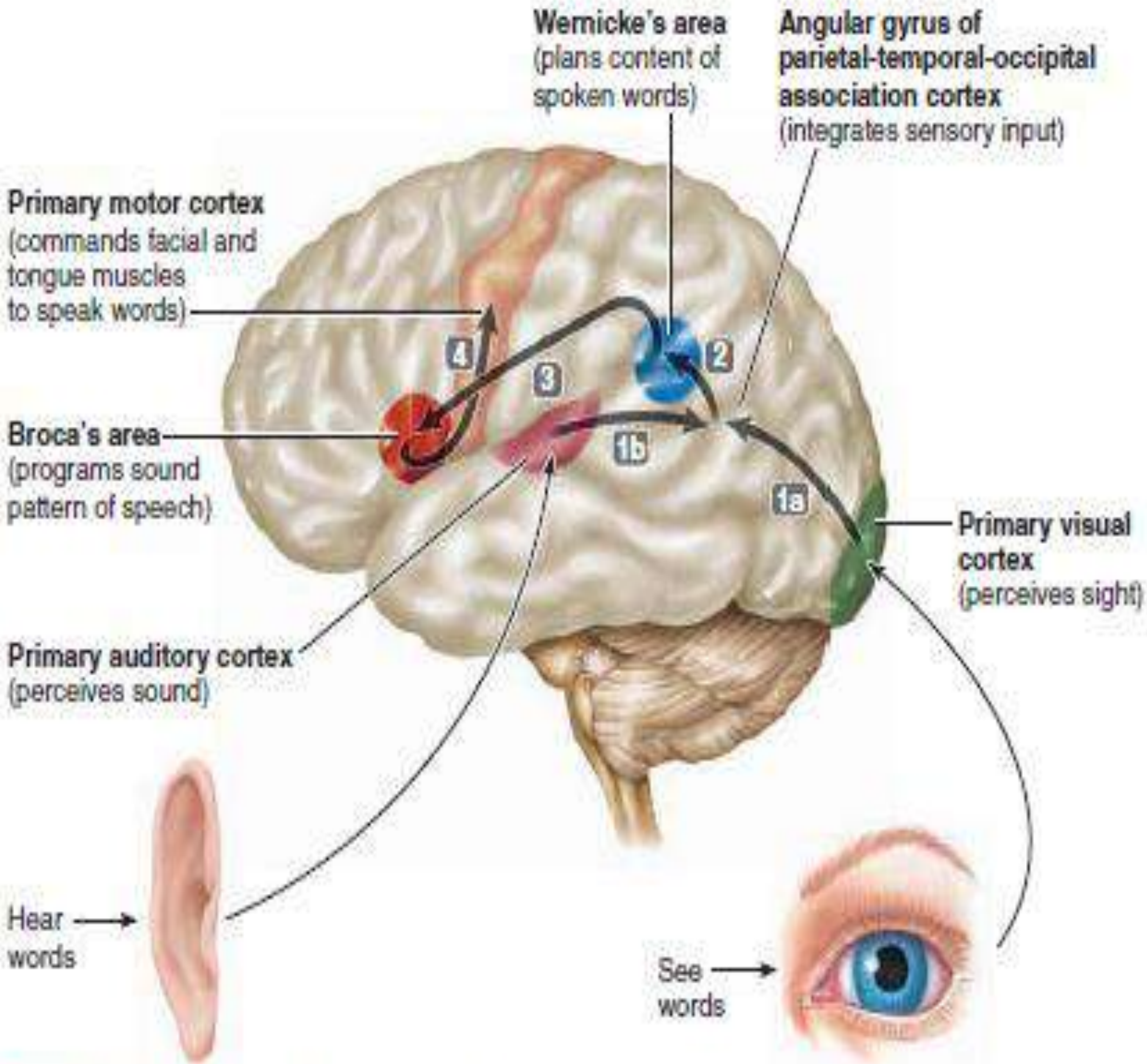
■ **Role of Broca's area and Wernick's area:**

(1) Broca's area, which governs speaking ability, is located in the left frontal lobe in close association with the motor areas of the cortex that control the muscles necessary for articulation.

(2) Wernicke's area, which is concerned with language comprehension, is located in the left cortex at the juncture of the parietal, temporal, and occipital lobes. It plays a critical role in understanding both spoken and written messages.

Cerebral Cortex

- It is also responsible for formulating coherent patterns of speech that are transferred via a bundle of fibers to Broca's area, which in turn controls articulation of this speech. Wernicke's area receives input from: (1) the visual cortex in the occipital lobe (reading comprehension and in describing objects seen), (2) the auditory cortex in the temporal lobe (understanding spoken words), and (3) the somatosensory cortex (the ability to read Braille). Precise interconnecting pathways between these localized cortical areas are involved in the various aspects of speech.



● **FIGURE 5-11 Cortical pathway for speaking a word seen or heard.** The arrows and numbered steps describe the pathway used to speak about something seen or heard. Similarly, appropriate muscles of the hand can be commanded to write the desired words.

1a To speak about something seen, the brain transfers the visual information from the primary visual cortex to the angular gyrus of the parietal-temporal-occipital association cortex, which integrates inputs such as sight, sound, and touch.

1b To speak about something heard, the brain transfers the auditory information from the primary auditory cortex to the angular gyrus.

2 The information is transferred to Wernicke's area, where the choice and sequence of words to be spoken are formulated.

3 This language command is then transmitted to Broca's area, which translates the message into a programmed sound pattern.

4 This sound program is conveyed to the precise areas of the primary motor cortex that activate the appropriate facial and tongue muscles for causing the desired words to be spoken.

Chapter 5: The Central Nervous System
Second Year Pharmacy Students
Part 4B

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Cerebral Cortex

■ The association areas of the cortex (the cortical association areas) are involved in many higher functions:

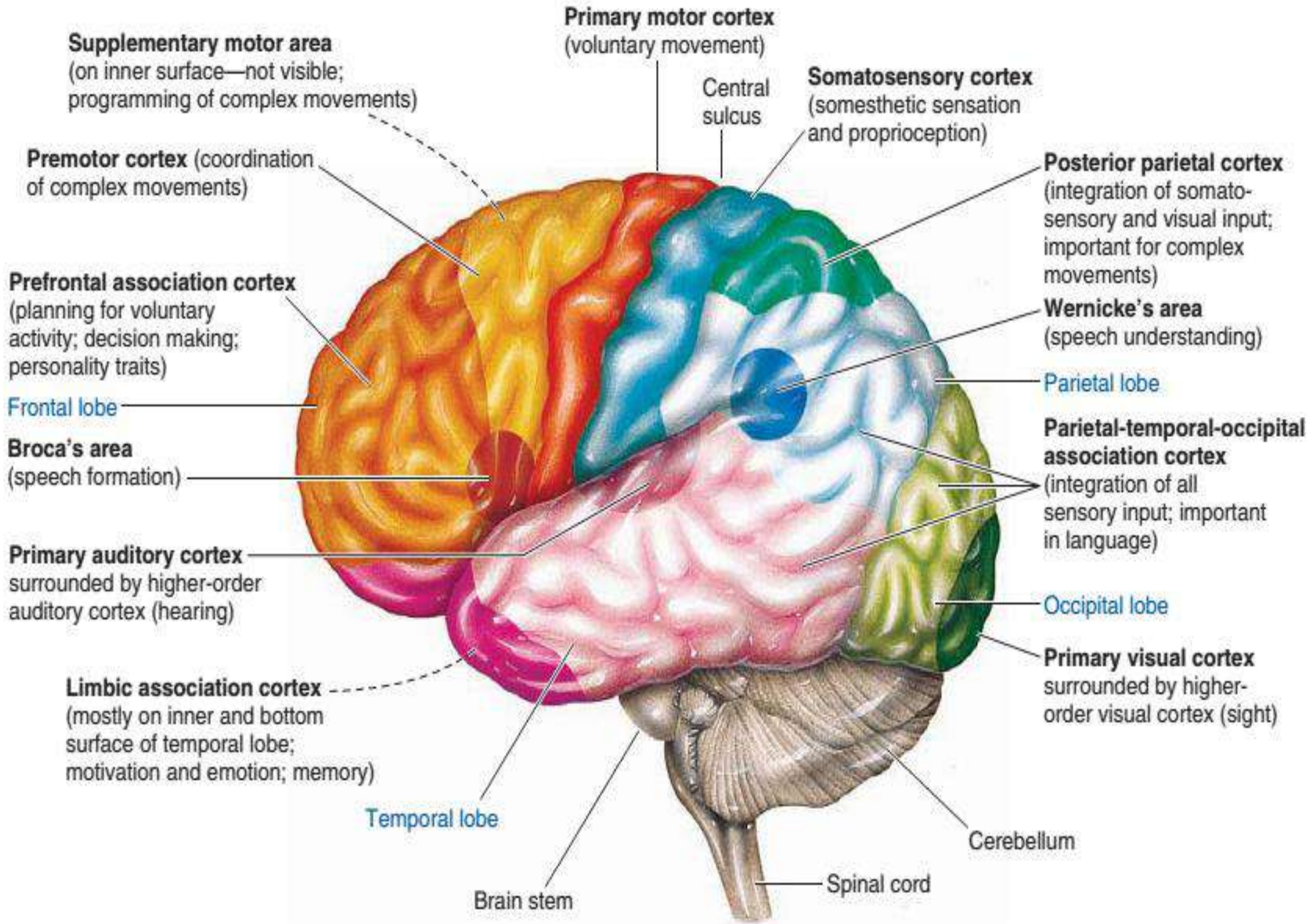
■ The motor, sensory, and language areas account for only about half of the total cerebral cortex.

■ The remaining areas, called **association areas**, are involved in higher functions. There are three association areas:

(1) the prefrontal association cortex.

(2) the parietal-temporal-occipital association cortex, and

(3) the limbic association cortex.



(a) Regions of the cerebral cortex responsible for various functions

Cerebral Cortex

(1) The prefrontal association cortex:

■ This is the part of the brain that "brainstorms" (or thinks).

■ Specifically, the functions attributed to this region are:

(1) planning for voluntary activity. (2) decision making.

(3) creativity. (4) personality traits.

■ Stimulating the prefrontal cortex does not produce any observable effects, but deficits in this area change personality and social behavior.

Cerebral Cortex

(2) The parietal-temporal-occipital association cortex: lies at the interface of the 3 lobes. In this strategic location, it pools and integrates somatic, auditory, and visual sensations projected from these 3 lobes for complex perceptual processing, so it enables us to “get the complete picture” of the relationship of various parts of our body with the external world.

Cerebral Cortex

(3) The limbic association cortex: is located on the bottom and adjoining inner portion of each temporal lobe. This area is concerned primarily with motivation and emotion and is extensively involved in memory.

■ The cortical association areas are all interconnected by bundles of fibers within the cerebral white matter. Collectively, the association areas integrate diverse information for purposeful action.

Cerebral Cortex

■ The cerebral hemispheres have some degree of specialization:

(1) The left hemisphere is also most commonly the dominant hemisphere for fine motor control. Thus, most people are right-handed, because the left side of the brain controls the right side of the body.

■ The left cerebral hemisphere excels in logical, analytic, sequential, and verbal tasks, such as math, language forms, and philosophy, and process information in fine-details (e.g. thinkers).

Cerebral Cortex

(2) The right cerebral hemisphere excels in non-language skills, especially spatial perception and artistic and musical talents. It views the world in a big-picture (e.g. creators).

■ An electroencephalogram (EEG) is a record of postsynaptic activity in cortical neurons:

■ Extracellular current flow arising from electrical activity within the cerebral cortex can be detected by placing recording electrodes on the scalp to produce a graphic record known as an electroencephalogram, or EEG.

Cerebral Cortex

- These "brain waves" are not due to action potential, but instead represent the momentary collective postsynaptic potential activity (that is, EPSPs and IPSPs) in the cell bodies and dendrites located in the cortical layers under the recording electrode.
- Electrical activity can always be recorded from the living brain, even during sleep and unconscious states, but the waveforms vary, depending of the degree of activity of the cerebral cortex.

Cerebral Cortex

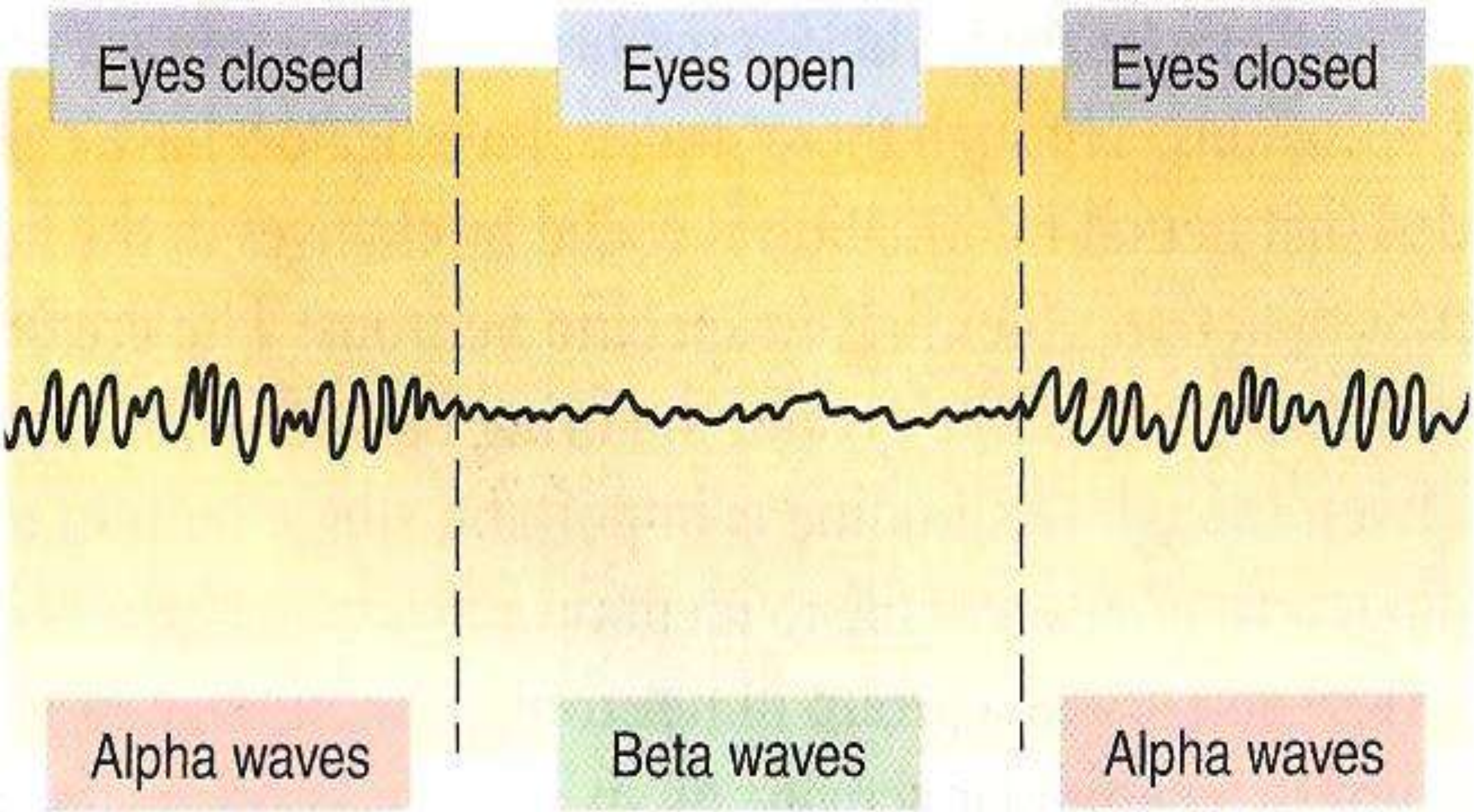
■ Often the waveforms appear irregular, but sometimes distinct patterns in the wave's amplitude and frequency can be observed. For example, the EEG waveform recorded over the occipital cortex changes markedly in response to simply opening and closing the eyes.

■ **The EEG has 3 major uses:** (1) Often used as a clinical tool in the diagnosis of cerebral dysfunction, e.g., epilepsy.

(2) Used in the legal determination of brain death. (3) Used to distinguish various stages of sleep.

FIGURE 5-15

Replacement of an alpha rhythm on an EEG with a beta rhythm when the eyes are opened



Chapter 5: The Central Nervous System
Second Year Pharmacy Students
Part 5A

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First Semester 2020/2021

■ **The limbic system**

■ The limbic system is not a separate structure but a ring of forebrain structures that surround the brain stem and are interconnected by complex neuron pathways. It includes portions of each of the following: the lobes of the cerebral cortex (especially the limbic association cortex), the basal nuclei, the thalamus, and the hypothalamus. This complex interacting network is associated with emotions, basic survival and socio-sexual behavioral patterns, motivation, and learning.

■ Reward and Punishment centers:

■ Certain regions of the limbic system have been designated as “reward” and “punishment” centers, because stimulation in these respective areas gives rise to pleasant (gratifying) or unpleasant sensations.

■ Reward centers are found most abundantly in regions involved in mediating the highly motivated behavioral activities of eating, drinking, and sexual activity.

The Central Nervous System

■ Learning and Memory

■ The limbic system and higher cortex are involved in learning and memory.

■ **Learning** is the acquisition of knowledge as a result of experiences:

■ Learning is the acquisition of knowledge or skills as a consequence of experience, instruction, or both. It is believed that rewards and punishments are integral parts of many types of learning.

- If an animal is rewarded on responding in a particular way to a stimulus, the likelihood increases that the animal will respond in the same way again to the same stimulus as a consequence of this experience. Conversely, if a particular response is accompanied by punishment, the animal is less likely to repeat the same response to the same stimulus. When behavioral responses that give rise to pleasure are reinforced or those accompanied by punishment are avoided, learning has taken place. An example is "housebreaking a puppy".

The Central Nervous System

■ Thus, learning is a change in behavior that occurs as a result of experiences.

■ Learning highly depends on the organism's interaction with its environment. The only limits to the effects that environmental influences can have on learning are the biological constraints imposed by species-specific and individual genetic endowments.

- **Memory** is laid down in stages:
- Memory is the storage of acquired knowledge for later recall.
- Learning and memory form the basis by which individuals adapt their behavior to their particular external circumstances. Without these mechanisms, it would be impossible for individuals to plan for successful interactions and to intentionally avoid predictably disagreeable circumstances.
- The neural change responsible for retention or storage of knowledge is known as the memory trace.

The Central Nervous System

■ Storage of acquired information is accomplished in at least two stages: short-term memory and long-term memory.

■ Short-term memory lasts for seconds to hours, whereas long-term memory is retained for days to years.

■ The process of transferring and fixing short-term memory traces into long-term memory stores is known as consolidation.

■ working memory (so-called "the erasable blackboard of the mind"), temporarily holds and interrelates various pieces of information relevant to a current mental task.

The Central Nervous System

■ This integrative function is crucial to your ability to reason, plan, and make judgments. In short, it enables people to string thoughts together in a logical sequence and plan for future action.

BLE 5-3 Comparison of Short-Term and Long-Term Memory

cteristic	Short-Term Memory	Long-Term Memory
of Storage after Acquisition v Information	Immediate	Later; must be transferred from short-term long-term memory through consolidation hanced by practice or recycling of informa through short-term mode
ion	Lasts for seconds to hours	Retained for days to years
ity of Storage	Limited	Very large
val Time (remembering)	Rapid retrieval	Slower retrieval, except for thoroughly in- grained memories, which are rapidly retri
ity to Retrieve (forgetting)	Permanently forgotten; memory fades quickly unless consolidated into long-term memory	Usually only transiently unable to access; tively stable memory trace
anism of Storage	Involves transient modifications in functions of preexisting synapses, such as altering amount of neu-rotransmitter released	Involves relatively permanent functional o structural changes between existing neuro such as formation of new synapses; synthe of new proteins plays a key role

The Central Nervous System

- Memory traces are present in multiple regions of the brain:
- What parts of the brain are responsible for memory? ”Where”?
- There is no single “memory center” in the brain. Instead, the neurons involved in memory traces are widely distributed throughout the subcortical and cortical regions of the brain. The regions of the brain most extensively implicated in memory include: the hippocampus and associated structures of the medial temporal lobes, the limbic system, the cerebellum, the prefrontal cortex, and other areas of the cerebral cortex.

Chapter 5: The Central Nervous System
Second Year Pharmacy Students
Part 5B

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First Semester 2020/2021

The Central Nervous System

■ The **brain stem** is a vital link between the spinal cord and higher brain regions:

■ All incoming (sensory information to the brain) and outgoing fibers (carrying command signals from the brain for efferent output) passing between the periphery and higher brain centers must pass through the brain stem for important processing. Thus, the brain stem is a connecting link between the rest of the brain and the spinal cord.

■ **Sleep is an active process consisting of alternating periods of slow-wave and paradoxical sleep:**

■ The **sleep–wake cycle** is a normal cyclic variation in awareness of surroundings. In contrast to being awake, sleeping people are not consciously aware of the external world, but they do have inward conscious experiences such as dreams. Furthermore, they can be aroused by external stimuli, such as an alarm going off.

■ Sleep is an active process, not just the absence of wakefulness. The brain's overall level of activity is not reduced during sleep. During certain stages of sleep, O_2 uptake by the brain is even increased above normal waking levels.

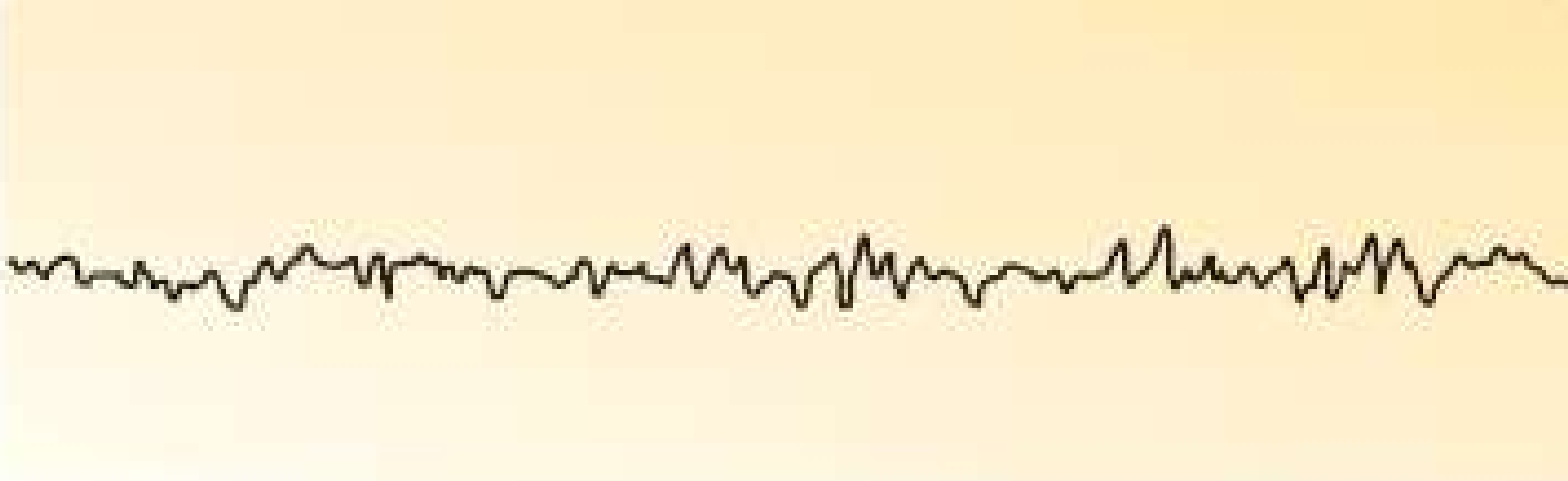
■ There are 2 types of sleep characterized by **different EEG patterns** and **different behaviors**: Slow-wave sleep "SWS" ,and, Paradoxical, or, "REM" (Rapid Eye Movement) sleep.

■ **EEG patterns during sleep:**

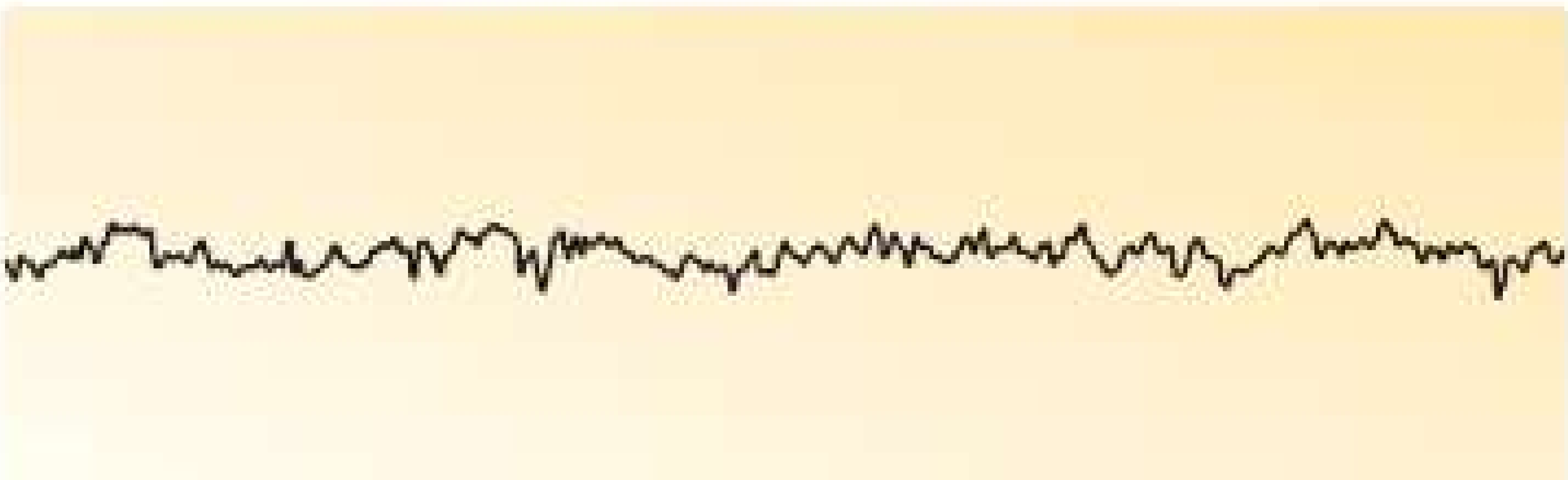
■ Slow-wave sleep occurs in 4 stages: each displaying progressively slower EEG waves of higher amplitude (hence, “slow-wave” sleep).

Slow-wave sleep, stage 4

- At the onset of sleep, you move from the light sleep of stage 1 to the deep sleep of stage 4 of slow-wave sleep during a period of 30 to 45 minutes; then you reverse through the same stages in the same amount of time. A 10- to 15-minute episode of paradoxical sleep punctuates the end of each slow-wave sleep cycle. Paradoxically, your EEG pattern during this time abruptly becomes similar to that of an awake, alert individual, even though you are still asleep (hence, “paradoxical” sleep). After the paradoxical episode, the stages of slow-wave sleep repeat.



Paradoxical sleep



Awake, eyes open

- A person cyclically alternates between the two types of sleep throughout the night. Brief periods of wakefulness occasionally occur.
- Most stage 4 deep sleep occurs during the first several hours of sleep, with REM sleep occupying an increasingly greater share of sleep time as morning approaches. Because of the resemblance of this graphic representation of the cyclical sleep pattern to a city skyline, the pattern of sleep is sometimes referred to as “sleep architecture”.

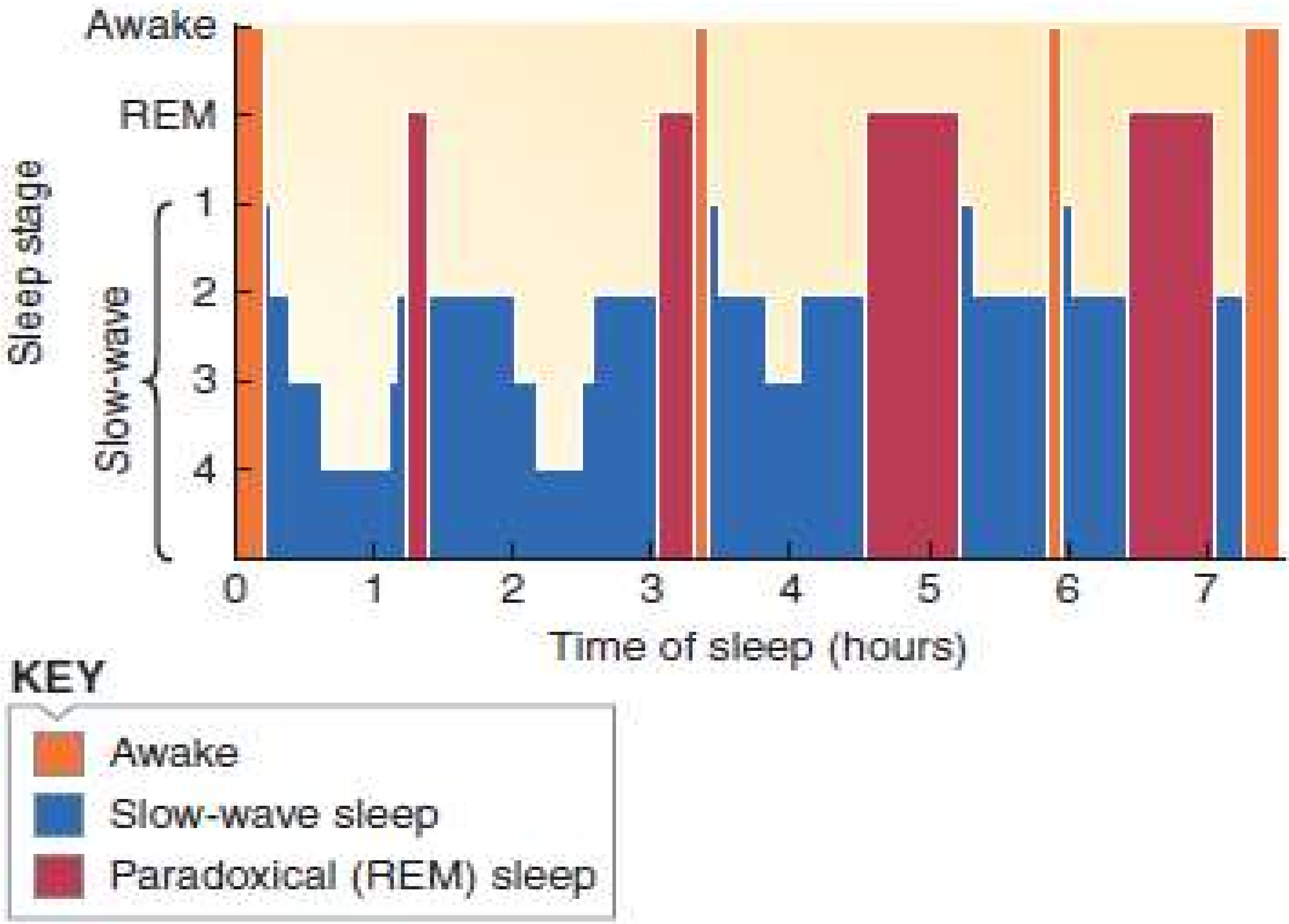


FIGURE 5-23 Typical cyclical sleep pattern in a young adult.

■ In a normal sleep cycle, you always pass through slow-wave sleep before entering paradoxical sleep. Paradoxical sleep occupies 20% of total sleeping time throughout adolescence and most of adulthood. Infants spend considerably more time in paradoxical sleep. In contrast, paradoxical as well as deep stage 4 slow-wave sleep declines in the elderly. People who require less total sleeping time than normal spend more time in paradoxical and deep stage 4 slow-wave sleep and less time in the lighter stages of slow-wave sleep.

■ Behavioral patterns during sleeping:

(1) Behavioral patterns accompanying Slow-wave sleep(SWS):

■ It is difficult to pinpoint exactly when an individual drifts from drowsiness into SWS. In SWS, the person still has considerable muscle tone and frequently shifts body position. Only minor reductions in respiratory rate, heart rate, and blood pressure occur. During this time the sleeper can be easily awakened and rarely dreams. The mental activity associated with SWS is less visual than dreaming.

■ It is more conceptual and plausible, like an extension of waking-time thoughts concerned with everyday events, and it is less likely to be recalled. The major exception is nightmares, which occur during stages 3 and 4. People who walk and talk in their sleep do so during SWS.

(2) Behavioral patterns accompanying paradoxical sleep(REM):

■ The behavioral pattern accompanying paradoxical sleep is marked by abrupt inhibition of muscle tone throughout the body.

■ The muscles are completely relaxed, with no movement taking place except in the eye muscles. Paradoxical sleep is characterized by rapid eye movements, hence the alternative name, REM sleep. Heart rate and respiratory rate become irregular, and blood pressure may fluctuate. Another characteristic of REM sleep is dreaming. The rapid eye movements are not related to “watching” the dream imagery. The eye movements are driven in a locked, oscillating pattern uninfluenced by dream content.

■ Brain imaging of volunteers during REM sleep shows heightened activity in the higher-level visual processing areas and limbic system (the seat of emotions), coupled with reduced activity in the prefrontal cortex (the seat of reasoning). This pattern of activity lays the groundwork for the characteristics of dreaming: internally generated visual imagery reflecting activation of the person’s “emotional memory bank” with little guidance or interpretation from the complex thinking areas.

TABLE 5-4 Comparison of Slow-Wave and Paradoxical Sleep

	TYPE OF SLEEP	
Characteristic	**Slow-Wave Sleep**	**Paradoxical Sleep**
EEG	Displays slow waves	Similar to EEG of alert, awake
Motor Activity	Considerable muscle tone; frequent shifting	Abrupt inhibition of muscle to movement
Heart Rate, Respiratory Rate, Blood Pressure	Minor reductions	Irregular
Dreaming	Rare (mental activity is extension of waking-time thoughts)	Common
Arousal	Sleeper easily awakened	Sleeper hard to arouse but apt up spontaneously
Percentage of Sleeping Time	80%	20%
Other Important Characteristics	Has four stages; sleeper must pass through this type of sleep first	Rapid eye movements

- The normal cycle can easily be interrupted, with the arousal system more readily overriding the sleep systems than vice versa; that is, it is easier to stay awake when you are sleepy than to fall asleep when you are wide awake. The arousal system can be activated by afferent sensory input (for example, a person has difficulty falling asleep when it is noisy) or by input descending to the brain stem from higher brain regions.

- Intense concentration or strong emotional states, such as anxiety or excitement, can keep a person from falling asleep, just as motor activity (such as getting up and walking around) can arouse a drowsy person.