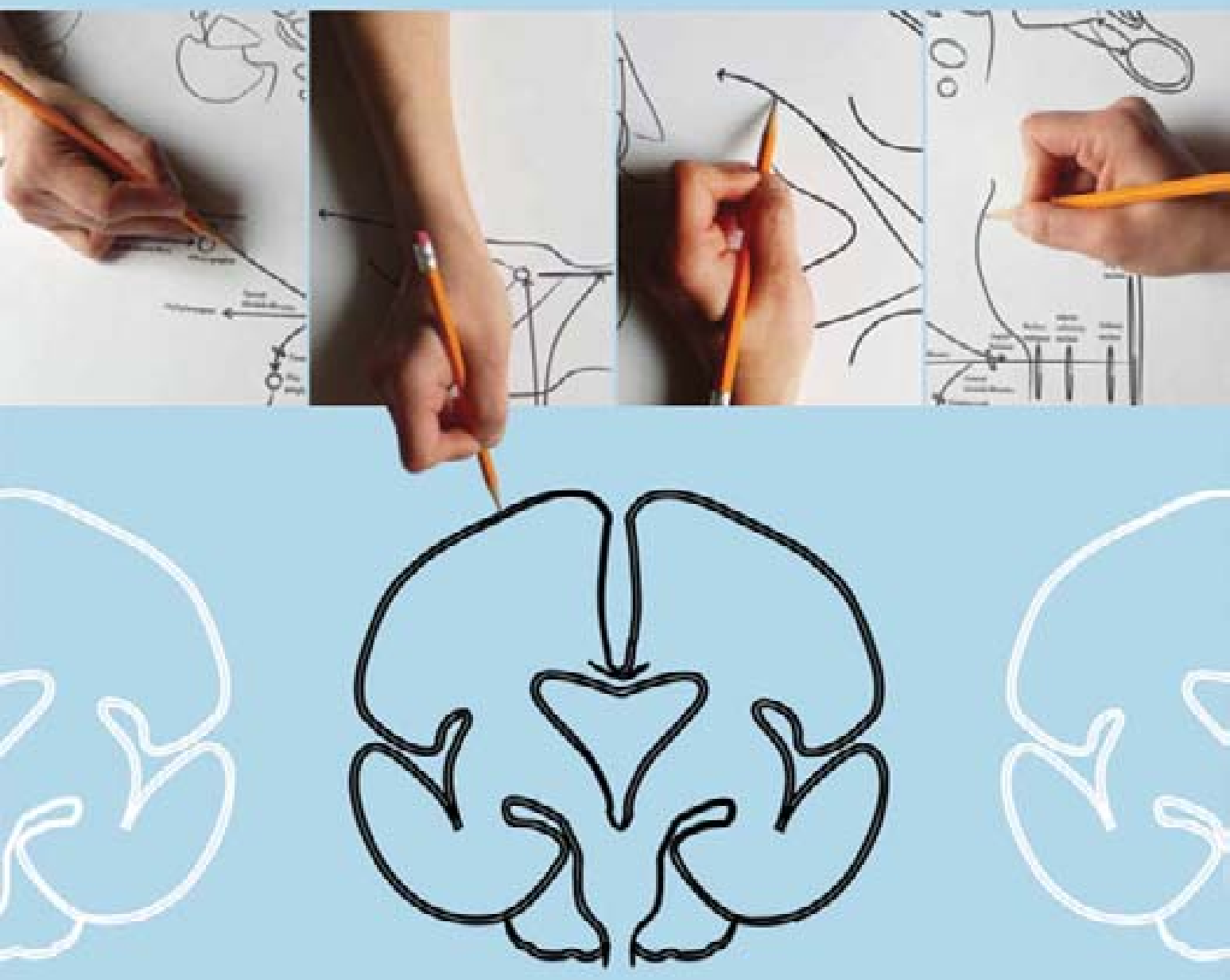
NEUROANATOMY

draw it to know it



ADAM FISCH

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This book is dedicated in loving memory
to my younger brother, David,
whose humility and enthusiasm for
learning remain a source of inspiration.

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Neuroanatomy is a nightmare for most medical students. The complex array of nuclei, ganglia, tracts, lobes, Brodmann areas and cortical layers seem to the uninitiated as the height of useless trivia. My own memory of my neuroanatomy class in medical school is vivid. Our professor, a Ph.D. neuroanatomist, ordered each member of the class to buy a set of colored pencils; the kind you had in third grade. Each color was coded for particular structures (red for the caudate, green for the putamen, yellow for the claustrum and burnt sienna for the globus pallidus). At our senior play, which poked fun at our professors, a beleaguered medical student was asked to name the components of the basal ganglia. Without knowing what the structures even were or did, he responded "red, green, yellow, and burnt sienna." Almost forty years later, this remains a class joke. Except for the handful of us who went into neurology, neurosurgery and psychiatry, the basal ganglia to the rest of my class is just a fading joke from the distant past.

And yet, no one can practice even rudimentary neurology without some basic understanding of the neuroanatomy. Non-neurologists in particular, many of whom see large numbers of patients with neurological complaints, have no hope of sorting out common problems such as headache, dizziness, tiredness, fatigue, sleep disorders, numbness and tingling and pain, without a reasonable grasp of how the nervous system is organized. Despite all of the marvelous advances in neuroscience, genetics and neuroimaging, the actual practice of neurology, whether it is done by a neurologist or a non-neurologist involves localizing the problem. The nervous system is just too complicated to skip this step. Without an organized approach based on a reasonable understanding of functional neuroanatomy, clinical neurology becomes incomprehensible.

In his wonderful book, *Neuroanatomy: Draw It to Know It*, neurologist Adam Fisch applies my old neuroanatomy professor's colored pencil idea in a manner that actually works, and it's fun! Over the course of 39 chapters, most of the clinically important neuroanatomically important subjects are covered, ranging through the overall organization of the nervous system, the coverings of the brain, the peripheral nervous system, the spinal cord, the brainstem, the cerebellum and the cerebral cortex. It is clear that the book was written by an experienced neurologist, as the topics are organized in a fashion that illuminates the principle of anatomical-pathophysiological correlation, which is the tool with which neurologists approach clinical problems.

This book should be of great interest to all neurologists, neurosurgeons, neurology residents and students of neurology. Others who see patients with neurological complaints, such as internists, emergency physicians and obstetrician-gynecologists should also review their neuroanatomy if they wish to provide excellent care to their patients. As any

experienced teacher knows, one only really knows a subject when one can teach it oneself. By drawing the anatomy, the reader of this book literally teaches the subject to himself. By making it clinically relevant, the information learned in this manner is likely to stick. Adam Fisch has done us all a great service by rekindling the enjoyment in learning the relevant, elegant anatomy of the nervous system.

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MY NEUROANATOMY MENTOR, the late Dr. William DeMyer, often remarked, "if you can't draw it, you don't know it." His teaching method was straightforward: to learn the structures and fiber pathways of the nervous system, draw and re-draw them, and when you think you know them well, draw them some more. This book tries to emulate his approach. It is written in an instructive rather than a didactic manner so that we use the material to learn it.

The analogy is simple: if you want to become a table expert, put one together. Invariably, you will screw the legs on backwards and hammer on the top upside down first, but how else will you learn about the washers and wing-nuts, bolts and fillets that fasten one together? How else will you understand what makes a table strong or learn its weak points and the ways to improve upon one? Reading about tables will never teach you: you have to put one together, yourself.

With this book, we will trace nerve pathways down our limbs, demonstrate eye movements and vestibular directionality with our hands, palpate sensory distributions and muscle patterns across our face and body, imagine cognitive sensory deficits, and rigorously draw and re-draw the structures and pathways of the nervous system until they become second nature.

The text is comprehensive but pearls of neuroanatomy are highlighted for those who are short on time. Anatomic and radiographic images accompany the figures to clarify what the drawings cannot. Synonymous terms are listed to mitigate confusion; inter-textual discrepancies are brought to attention; and historical and current contexts for the anatomical structures are discussed. In short, this book provides the tools you need to learn neuroanatomy in a practical and complete way so that you can use it at the bedside.

I apologize to readers who are unable to perform exercises in this book due to physical impairments. If you have trouble imagining them, please write to me and I will gladly try to find alternative exercises for you.

Neuroanatomy is hardly simple but it should always be fun, so let's enjoy this trip through the nervous system and every trip back through it.

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TO TRY TO ACKNOWLEDGE all of the people I ought to would be impossible and self-defeating so I will only mention a few.

The foremost is Susan Pioli who, along with my uncle, Bruce, championed this book from the start. Without her enthusiasm for this project, it never would have been done. I'd also like to thank my editor, Craig Panner, and his editorial assistant, David D'Addona, as well as the book's production manager, Jennifer Bossert; they, along with many others at Oxford University Press, steered this book to completion with remarkable vision.

I am grateful to the faculty and staff in the Departments of Anatomy and Neurology at Indiana University and Washington University in St. Louis and to Robert J. Schwartzman of Drexel University School of Medicine for all they taught me about neuroanatomy and clinical neurology during my neurology training. Special thanks are owed to Mohammed Al-Lozi, Joseph Black, Kelly Brown, William DeMyer, Adriana Escandon, Stephen Duntley, Mark Jacquin, David Holtzman, William Landau, Abdullah Nassief, Robert Pascuzzi, Beth Ward, Thomas Woolsey, and Allyson Zazulia.

I'd also like to thank Denny Fiske, Paul Lysy, and Michael Schwartz for their help generating the muscle testing photographs, and Tammie Benzinger and Robert Cargile in the Department of Neuroradiology at Washington University in St. Louis for their help creating the diffusion tensor images.

I owe special thanks to my family for all of their encouragement during this process.

Most of all, though, I owe my wife, Kate, all of my love and gratitude for allowing the cat and me to devote our mornings, nights, and weekends to writing and illustrating this book. We look forward to being a part of your life, again.

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Organization of the Nervous System

THROUGHOUT THIS BOOK, we will learn the anatomy of the nervous system in detail, but first, in this chapter, let's march briskly through the nervous system to form a broad perspective on it.

Draw a coronal section through the brain. From outside to inside, label the *meninges*, *cortex*, *subcortical white matter*, *basal ganglia*, *thalamus*, and *ventricular system*. In general, the meninges protect and vascularize the nervous system; the cortex is the gray matter, highly cellular outer layer of the brain; the subcortical white matter carries impulses within the brain and ushers them to and from remote nervous system regions; the basal ganglia are involved in motor and behavioral functions; the thalamus receives and modifies sensory impulses, which it projects throughout the brain; and the ventricular system assists the meninges in their task of nourishing and supporting the rest of the nervous system.

Below the brain, draw the brainstem; it is a funnel-shaped structure with a bulbous out-pouching in the middle. From superior to inferior, show the brainstem comprises the *midbrain*, *pons*, and *medulla*. The brainstem is requisite for human life; it contains neuronal pools essential for survival and is the major thoroughfare for fibers passing between the brain and spinal cord.

On the lateral aspects of the brainstem, draw the leafy hemispheres of the *cerebellum*. The cerebellum is pivotal in motor coordination skills as well as non-motor behavioral functions, such as learning.

Next, draw the long, thin *spinal cord* with its cervical and lumbosacral enlargements.Draw the dorsal nerve root off the posterior spinal cord, which carries sensory fibers, and attach a *dorsal root ganglion* onto it; sensory cell bodies lie within the dorsal root ganglion. Now, draw the *ventral nerve root* from the anterior surface of the spinal cord; it carries motor fibers. Show the nerve roots form a mixed spinal nerve, and indicate it exits the spinal canal through a neural foramen.

Mixed spinal nerves often intertwine into plexuses, which complicate the localization of peripheral nerve injuries. Within the upper extremity, show there are two different plexuses: the *cervical* and *brachial plexuses*. Then, below them, indicate the *thoracic nerves* remain unmixed. Next, show the lumbosacral roots form the *lumbosacral plexus*, and specifically indicate the lower lumbosacral roots form the *cauda equina* before they exit the spinal canal.

At the tip of a representative thoracic peripheral nerve, draw a *neuromuscular junction synapse* and attach *muscle fibers* to it. *Muscles* and *neuromuscle junctions* are commonly affected parts of the peripheral nervous system as are the sensory receptors that exist at the tips of peripheral nerves.

Lastly, include the peripheral autonomic nervous system, which we represent here with one of the two sympathetic *paravertebral chains* that flank the spinal cord. Prevertebral sympathetic ganglia and parasympathetic ganglia also constitute the peripheral autonomic nervous system. The peripheral autonomic nervous system most notably executes cardiopulmonary and gastrointestinal functions.

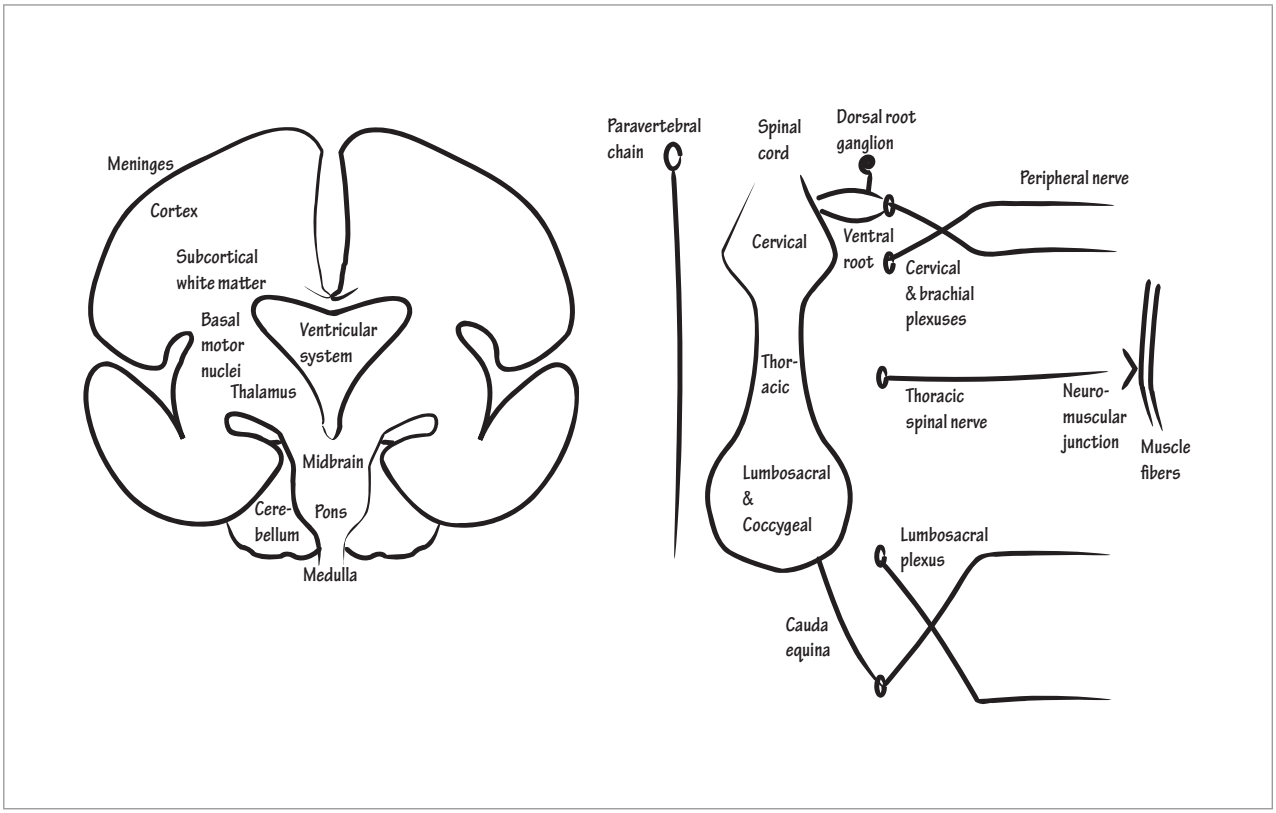

Figure 1-1 Overview of nervous system anatomy

Orientational Terminology

THE NERVOUS SYSTEM has several orientational planes that even experienced neurologists find challenging. Take the time to learn them now, as this knowledge is requisite to understanding the remainder of the book. If you try to skip this chapter, you will invariably find yourself hopelessly disoriented later.

At the top of the page, draw intersecting horizontal and vertical lines. Along the horizontal line, label left as *anterior* and right as *posterior*. Label the top of the vertical line as *superior* and the bottom as *inferior*. The two superior–inferior and anterior–posterior orientational axes are consistent throughout the nervous system; that is, top is always superior and bottom is always inferior, and front is always anterior and behind is always posterior. We are not so lucky with the dorsal–ventral and rostral–caudal orientational axes we will soon introduce because of the rotation of the neuraxis during embryogenesis.

Next, let's draw a *sagittal* (aka longitudinal) section through the oblong cerebral hemisphere. The sagittal plane runs from anterior to posterior and the sagittal suture, which runs from the front to the back of the skull, is a good example of this plane of orientation. Label the top of the cerebral hemisphere as *dorsal* and the bottom as *ventral*. To remind yourself that dorsal is on top and ventral is on bottom, remember the *dorsal* fin of a shark is on its back whereas its underbelly is *ventral*. Label the anterior portion of the hemisphere as *rostral* and the posterior portion as *caudal*. Rostral is related to the word "beak" and caudal is related to the word "tail."

Within the cerebral hemispheres, which orientational terms are synonymous? *Superior* is synonymous with *dorsal*, *inferior* with *ventral*, *anterior* with *rostral*, and *posterior* with *caudal*.

Next, include a sagittal section of the brainstem at a −80° angle to the cerebral hemispheres (i.e., almost in perpendicular to it). During early embryogenesis, both the cerebral hemispheres and brainstem lie along the same orientational plane. However, as human forebrains develop, they undergo an 80° flexion that results in the so-called "cephalic flexure" at the junction between the brainstem and the cerebral hemispheres. Thus, the plane of the brainstem is −80° to that of the cerebral hemispheres. Let's explore how this affects the orientation of the dorsal-ventral and rostral-caudal axes of the brainstem; remember, the superior–inferior and anterior–posterior axes are unchanged throughout the nervous system. Label behind the brainstem as *dorsal* and in front of it as *ventral*. Then, label the top of the brainstem as *rostral* and the bottom as *caudal*. Now, within the brainstem, which orientational terms are most similar? Indicate *superior* is most similar with *rostral*, *inferior* with *caudal*, *anterior* with *ventral*, and *posterior* with *dorsal*.

Next, draw a *coronal* (i.e., frontal) section through the brain. Coronal relates to the word "crown." Imagine the blooming cerebral hemispheres sit like a crown on top of the neuraxis. Indicate the top of the brain is *dorsal* (*superior*) and the bottom is *ventral* (*inferior*).

Now, let's introduce two more planes of orientation: lateral–medial and right–left. Label the outside edges of the hemispheres as *lateral* and the midline as *medial*. Then, label the left-hand side as *radiographic right* and *anatomic left* and the right-hand side as *radiographic left* and *anatomic right*. These planes refer to the standardized ways

radiographic images and anatomic sections are viewed. Coronal radiographic sections are viewed head-on and anatomic sections are viewed from behind.

Lastly, draw an *axial* (aka horizontal) section through the brain. Although the superior–inferior and anterior–posterior axes do not change within the nervous system, they will alter as our perspective changes because we will be drawing three-dimensional structures on a two-dimensional page. In axial section, the top of the page is the front of the brain and the bottom is the back. Label the front of the section as *rostral* (*anterior*) and the back as *caudal* (*posterior*). Label the left side of the section as *radiographic right* and *anatomic left* and the right side as *radiographic left* and *anatomic right*. Radiographic axial images are viewed from below (i.e., as if the patient's feet are coming out at you) whereas anatomic axial images are viewed from above (i.e., as if the patient's head is coming up at you). Label the center of the cerebral hemispheres as *medial* and their periphery as *lateral*.

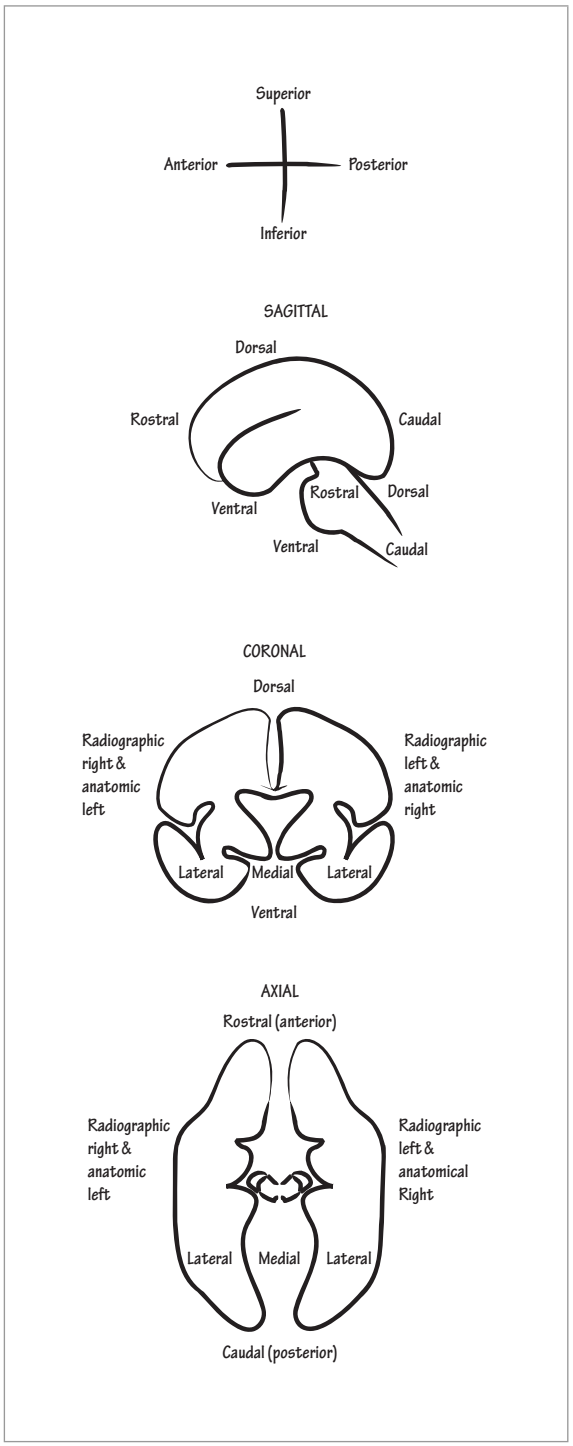

Figure 2-1 Orientational planes

Meninges and Ventricular System

THE VENTRICULAR SYSTEM runs through the center of the nervous system and the choroid plexus that lines it produces cerebrospinal fluid, which suspends and nourishes the brain and spinal cord.The meninges cover the nervous system and are layered in the following manner: the pia mater is the innermost layer; the arachnoid mater overlies it; and the dura mater is the thick outer-covering of the nervous system. Fluid enters the subarachnoid space and then is reabsorbed into the venous sinuses within the dura mater.

There is approximately 120 mL of cerebrospinal fluid in the nervous system at any one time, and it is formed and reabsorbed at a rate of 0.33 mL/min. Clinicians often withdraw cerebrospinal fluid from the nervous system through a procedure called a lumbar puncture, discussed later in the "Structure of the Spinal Cord and Spinal Canal" chapter. Depending on the purpose of the procedure, the amount of fluid withdrawn during a lumbar puncture ranges from just a few milliliters to as much as 40 mL; however, in a typical lumbar puncture roughly 12 mL of fluid is withdrawn. What percent of the cerebrospinal fluid in the nervous system is this? Ten percent. And how quickly is it replaced? In about half-an-hour (or, more exactly, in 36 min).

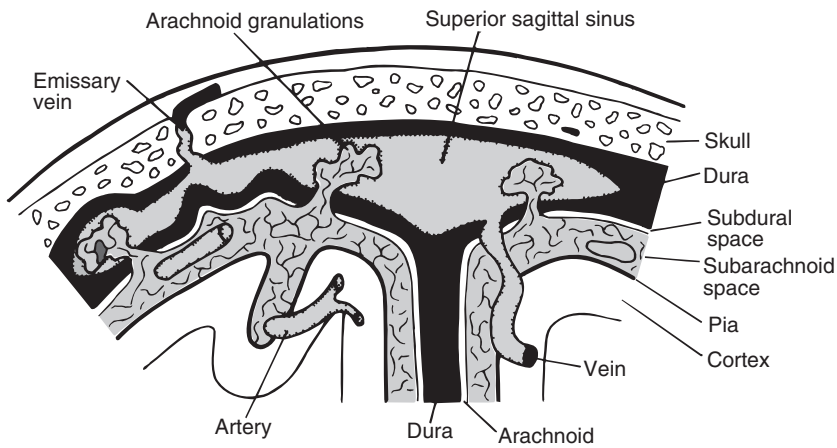

Photo 3-1 Intracranial meninges
With permission From Brodal, P. *The Central Nervous System: Structure and Function*. 3rd ed. New York: Oxford University Press, 2004.

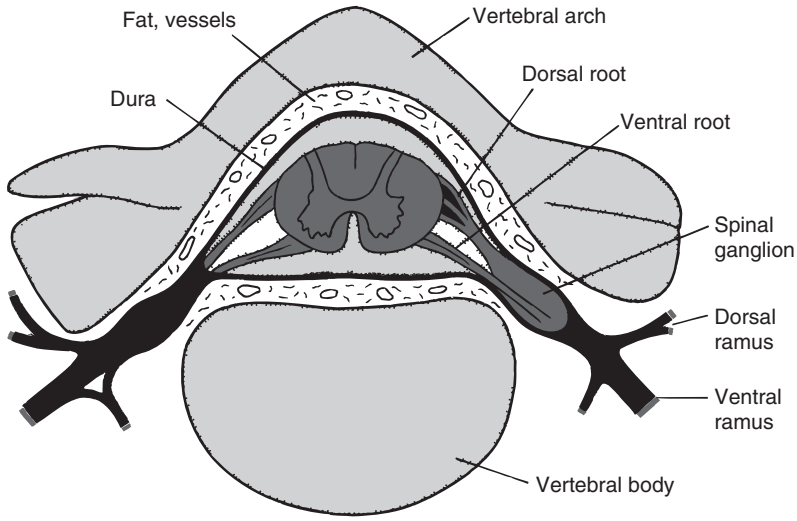

Photo 3-2 Intraspinal meninges

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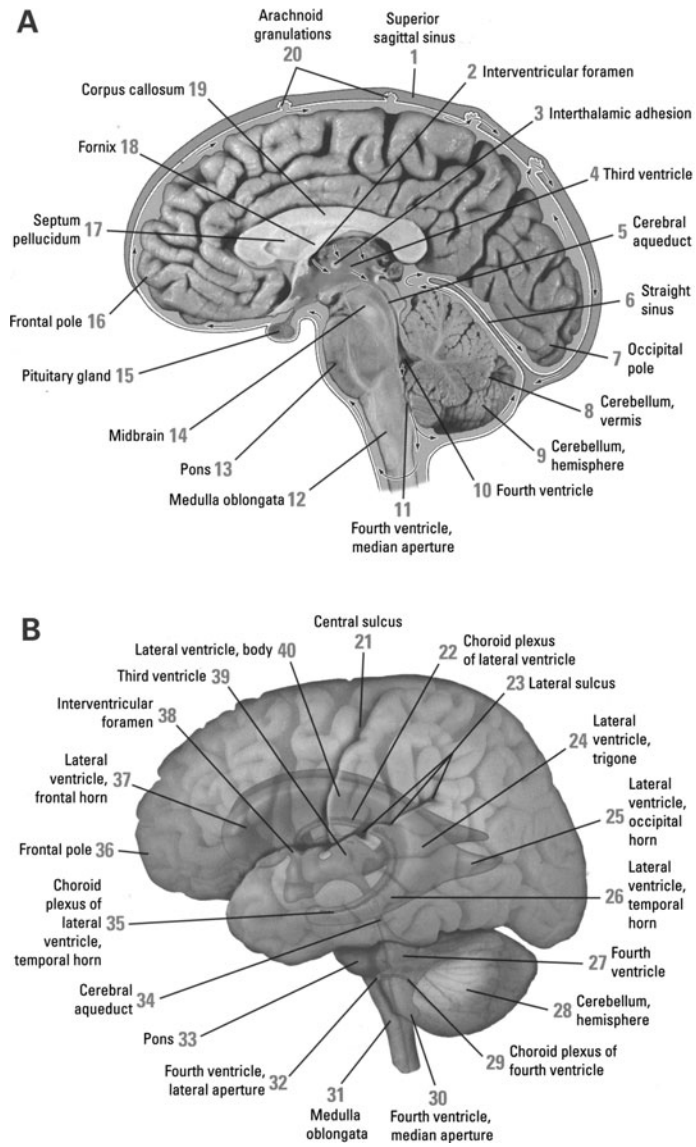


Photo 3-3 Flow pattern of cerebrospinal fluid & Anatomy of the ventricular system

From Woolsey, T. A., J. Hanaway, and M. H. Gado. *The Brain Atlas: A Visual Guide to the Human Central Nervous System*. 3rd ed. Hoboken, NJ: Wiley, 2008. Reproduced with permission of John Wiley & Sons Inc.

First, we will establish the different cerebrospinal fluid spaces and meningeal layers and then we will address the flow pattern of cerebrospinal fluid. Each cerebrospinal fluid space has intracranial and intraspinal divisions and we will account for their differences. After we complete this diagram, we will address the folding and contour of ventricular system, as it will help us understand the shape of many other intracerebral structures.

Draw a coronal diagram of the central nervous system. Start with the intracranial division of the ventricular system. In the center of the brain, draw its T-shaped portion. Label the lateral arms of the "T" as the *lateral ventricles* and the caudal extension as the *third ventricle*. The hypothalamus, an important central autonomic nervous system structure, surrounds the third ventricle.

Next, draw the narrow *cerebral aqueduct* (aka the *aqueduct of Sylvius*), which extends from the bottom of the third ventricle into the diamond-shaped *fourth ventricle*, which you should draw, now. The area postrema sits at the base of the fourth ventricle. It is one of the circumventricular organ interfaces between the blood and cerebrospinal fluid. Normally, there is a barrier to the diffusion of large molecules between the blood vessels and the cerebrospinal fluid, the so-called blood–brain barrier. Circumventricular organs lack this blood–brain barrier so they are sensitive to toxins and other large molecules. The area postrema, specifically, is an important chemoreceptor trigger zone. Direct activation of the area postrema produces vomiting, often without the sensation of nausea. We will discuss the area postrema further in the "Brainstem" chapter.

Now, draw the ventricular extension from the fourth ventricle into the spinal division of the nervous system: the *central canal*, which runs the length of the spinal cord. After the second decade of life, the central canal progressively narrows and obliterates; by middle adulthood, it is mostly nonfunctional. When this happens, how is cerebrospinal fluid delivered to the spinal canal?

In midline, draw the *foramen of Magendie* (aka the *median aperture*) and at both lateral aspects of the fourth ventricle, draw the *foramina of Luschka* (aka the *lateral apertures*). Note that a good mnemonic for the foramen of Magendie and the foramina of Luschka is that the first letter of their names corresponds to the first letter of their locations: Magendie-midline and Luschka-lateral. Cerebrospinal fluid flows from the fourth ventricle into the subarachnoid space through these foramina and, in this manner, is able to reach the spinal cord after the central canal obliterates. We will diagram the complete flow pattern of cerebrospinal fluid after we draw the meninges.

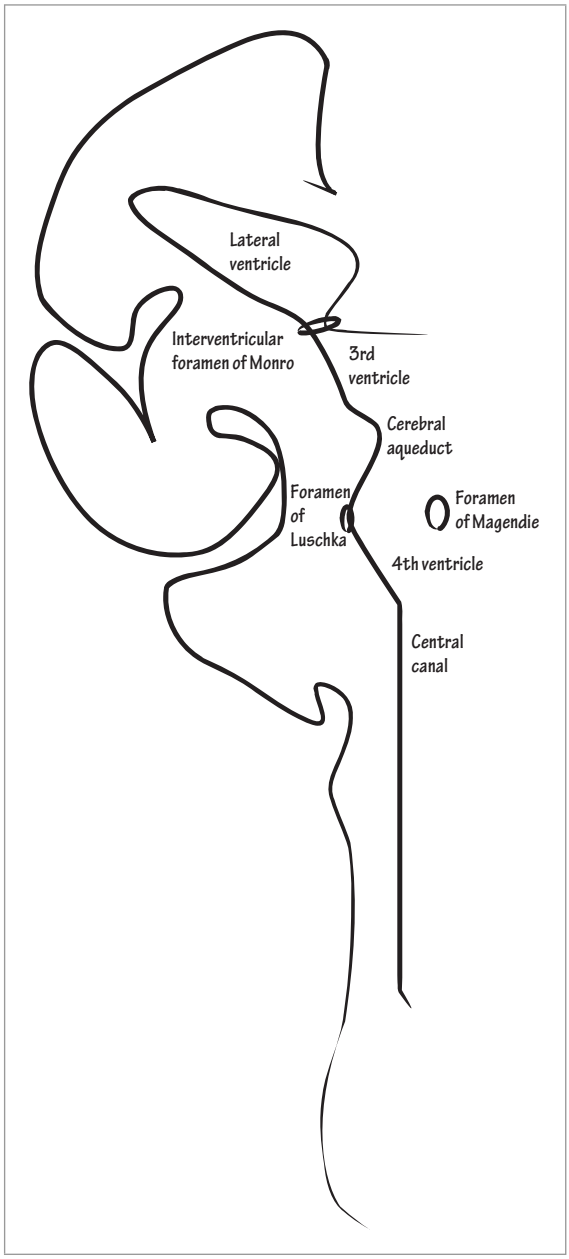


Figure 3-1 Coronal view of ventricular system

The meninges form a membranous covering composed of fibroblasts and extracellular connective tissue. The variability in meningeal tissue composition at different depths creates a three-layered structure, which is, from outside to inside, the dura mater, arachnoid mater, and pia mater. Let's first draw the outermost meningeal layer, the *dura mater* (aka *pachymeninges*, *pachymeninx*), which means "thick membrane." Intracranially, draw the dura as directly lining the inner-surface of the skull, but within the spinal column, show that space exists between the dura and the overlying vertebrae.

We commonly discuss the dura as a single layer, but it comprises heterogenous tissue that can be further subdivided into two or three different sublayers. These different sublayers help us understand the cerebrospinal fluid spaces that collect outside of, within, and beneath the dura as the epidural, intradural, and subdural spaces, respectively. The three dural sublayers, from outside to inside, are the periosteal, meningeal, and dural border cell sublayers.

Intracranially, draw the outer, *periosteal dural sublayer* lining the inner-surface of the *skull*. Within the spinal canal, however, show that a true *epidural space* separates the dura from the overlying *vertebral column*. It is easy, then, to imagine how a spinal epidural abscess can form within this true epidural space or how anesthesia can be injected into it. But how do epidural processes take place intracranially, if no true intracranial epidural space exists? For instance, how does an intracranial epidural hematoma, a common clinical condition, arise?

Several arteries run through the dura that are susceptible to rupture. When they tear, their high-pressure forces shear the periosteal dural layer from the overlying skull and create an epidural space filled with blood; this is called an epidural hematoma. The classic example of an intracranial epidural hematoma occurs from trauma to the temporal bone. The fractured bone severs the underlying middle meningeal artery and its high arterial pressure rips the periosteal dural layer away from the skull, which allows blood to pool between the dura and cranium.

Draw the *meningeal dural sublayer*. Between the two cerebral hemispheres bilateral meningeal dura sublayer reflections form the *falx cerebri* (aka *interhemispheric fissure*); venous sinuses form within these dural reflections, as we will soon draw. Increased intracranial pressure occasionally forces brain tissue from one hemisphere underneath the falx to the other side, called *subfalcine herniation* (beneath the falx herniation).

Next, indicate that the meningeal dural sublayer also forms the tentorium cerebelli, which overlies the cerebellum. The tentorium cerebelli divides the cranial vault into a supratentorial compartment (aka the combined anterior and middle cranial fossae) and an infratentorial compartment (aka the posterior cranial fossa). The supratentorial compartment contains the cerebrum and the infratentorial compartment holds the cerebellum and brainstem. We will draw the anterior, middle, and posterior cranial fossae in the "Skull Base" chapter.

To complete our discussion of herniation syndromes, increased supratentorial intracranial pressure also causes central herniation wherein the midline brain structures are forced down through the tentorium cerebelli, and uncal herniation occurs when a medial temporal lobe (its uncus) extends over the tentorium and down into the infratentorial compartment.

Within the dural reflections (i.e., the falx cerebri and tentorium cerebelli), *venous sinuses* exist as separations between the outer, periosteal dura and inner, meningeal dura sublayers. Draw the *superior sagittal* venous sinus within the falx cerebri and the *transverse sinuses* within the tentorium cerebelli. Venous sinuses are important in fluid absorption as we will later show. We will draw the entire venous sinus system at the end of this chapter.

Dural reflections do not exist in the spinal column, so the spinal column is without venous sinuses.

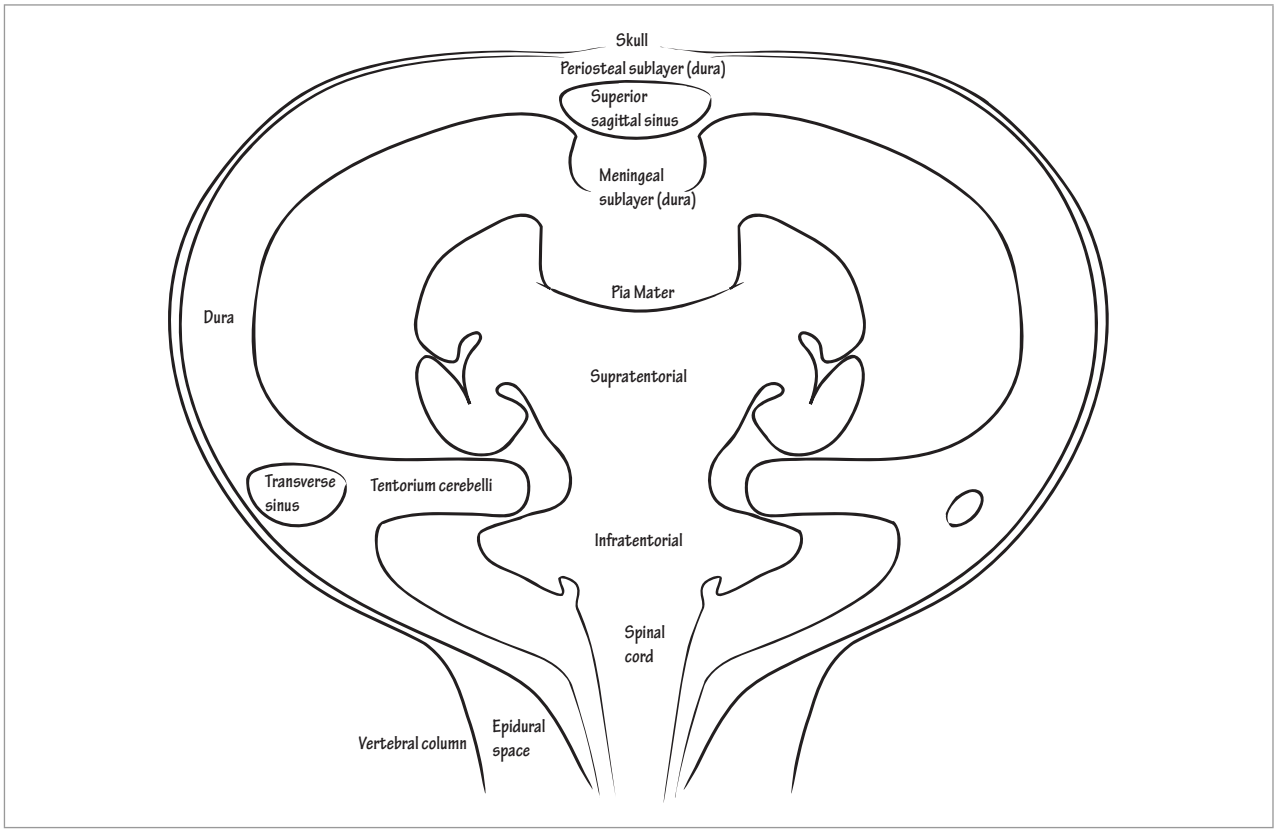


Figure 3-2 Meninges (incomplete)

We have discussed the cerebrospinal fluid spaces outside of and within the dura. Now, we will draw the subdural space. In order to do so, first draw the next innermost meningeal layer, the arachnoid mater. Then, show that a potential space exists between the dura and the underlying arachnoid layer called the *subdural space*. However, indicate that this space is actually filled with the loosely arranged *dural border cell sublayer*. Pathologic bleeding into the border cell sublayer creates a subdural fluid space; otherwise, no true space actually exists.

Although rupture of high-pressure arteries running through the dura mater is required to cause epidural hematoma, shearing of low-pressure bridging veins is all that is necessary to create a subdural hematoma. The classic cause of a subdural hematoma is blunt trauma. Bleeding occurs because of the rapid shift of the cerebral hemispheres within the cranium. The cerebellum is tethered within the posterior fossa by the tentorium cerebelli, but the cerebral hemispheres are free to move. Sudden shift of the cerebral hemispheres in combination with vein friability (most commonly in older adults) leads to subdural hematoma.

Indicate the *pia mater* immediately surrounds the *brain* and *spinal cord*; it is the delicate innermost layer of the meninges and is in direct contact with the underlying brain and spinal cord parenchyma. The pia mater also joins the ependymal lining of the inner surface of the ventricular system, and together, the pia mater and ependymal layer form choroid plexus, which produces cerebrospinal fluid.

Next, label the space above the pia mater and underneath the arachnoid mater as the *subarachnoid space*; note that it is a true (actual) space.

The subarachnoid system is a collection of many different spaces—its basal cisterns comprise numerous named spaces, which will be specified in a separate diagram. Here, intracranially, simply label the subarachnoid space around the fourth ventricle as the *basal cisterns*. The subarachnoid space at the caudal end of the spinal canal is the lumbar cistern; it is the site of fluid extraction during a lumbar puncture.

To recap, beneath the dural border cell sublayer lies the arachnoid layer and beneath it is the pia mater. The subarachnoid cerebrospinal fluid space lies between the arachnoid layer and pia mater.

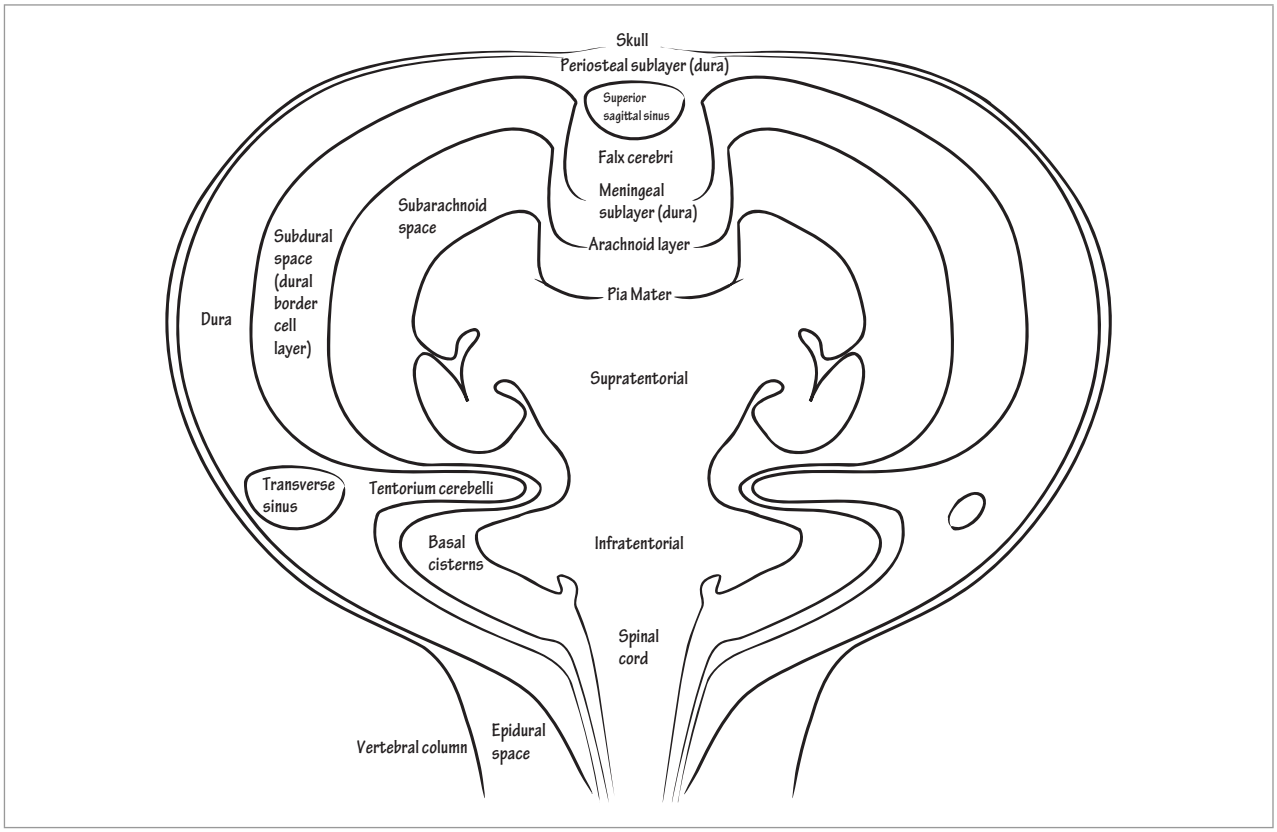


Figure 3-3 Meninges (complete)

Clinicians often need to distinguish an epidural from a subdural hematoma on radiographic imaging. In epidural hematoma, blood collects between the periosteal dura and skull; it has the ability to either continue to rip apart the firm attachment between them and form a long, thin layer of blood underneath the cranium or push aside the relatively spongy brain parenchyma. Which offers less resistance? The brain tissue. So the epidural hematoma forms a biconvex lens-shaped fluid collection with one side of the convexity displacing brain matter and the other layering against the cranium.

Now, think about a subdural hematoma in which blood forms between the inner border cell sublayer and the underlying arachnoid layer. Will venous blood displace the loose subdural cell sublayer or will it push against the more resistant brain tissue? Since the venous blood flow pressure is low, blood will layer within the border cell sublayer. Subdural hematomas form a crescent with its concavity along the brain's surface.

You should remember that these rules are not perfect; that is, a lot depends on how quickly the subdural blood fills the space. Use the following method to determine whether the blood represents epidural or subdural hematoma. Observe whether the hematoma respects the dural reflections or the cranial sutures.Which hematoma type will layer across the dural reflections and which will not? Epidural hematomas cross the dural folds (i.e., the falx cerebri or the tentorium cerebelli) because these hematomas form outside the periosteal sublayer. Subdural hematomas, on the other hand, pool at the site of the reflections and are unable to
cross them.

Next, what are the cranial sutures and do epidural or subdural hematomas cross them? While a discussion of the cranial sutures is most fitting in the "Skull Base" chapter, it is most clinically relevant to our discussion of the accumulation pattern of hematomas, so we will take the time now to learn about the cranial sutures. The bones of the skull come together during childhood but jagged defects, called cranial sutures, remain, which ossify throughout adulthood. The names of the skull bones reflect the lobes of the brain they overlie. The frontal bone comprises the anterior–superior portion of the skull and covers the frontal lobes (it is undivided, except posteriorly); bilateral parietal bones cover the parietal lobes; and an occipital bone covers the occiput. The coronal suture separates the frontal bone from the parietal bones, the sagittal suture separates the bilateral parietal bones, and the lambdoid suture separates the parietal bones from the occipital bone.

The next time you are able to palpate an infant's head, feel over the anterior one-third of his/her skull for the anterior fontanelle, a normal opening in the skull also known as the "soft spot"; it closes during the third year of life. It is a defect between the posterior frontal bone and the anterior parietal bones. In infants, cerebrospinal fluid is sometimes drawn directly from this anterior fontanelle.

Cranial deformities occur if premature closure of the cranial sutures occurs. Generalized premature closure of the sutures results in microcephaly (an abnormally small head and underdeveloped brain), but isolated premature closure of the different sutures also occurs and results in different forms of skull deformity. On the contrary, accumulation of excessive cerebrospinal fluid causes ventricular enlargement, called hydrocephalus. If this occurs before the ossification of the sutures, the skull bones will separate and the patient's head will enlarge. For a more detailed explanation of skull suture anatomy, refer to a textbook on head anatomy.

But, now, let's return to our question whether epidural hematomas or subdural hematomas cross cranial sutures. Epidural hematomas layer between the periosteal dura and the skull so the blood is interrupted at suture lines. On the contrary, subdural hematomas fill the deep dural border sublayer and are unaffected by the cranial sutures.

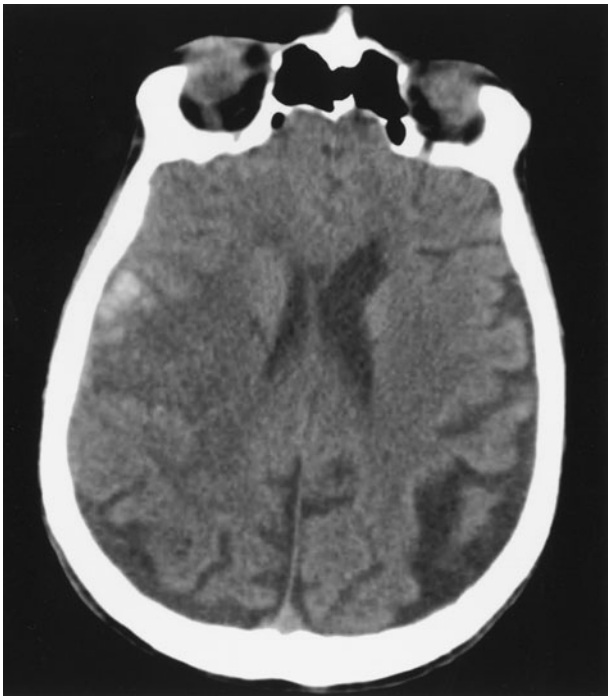


Photo 3-4 Subdural hematoma on the left side of image (right hemisphere)

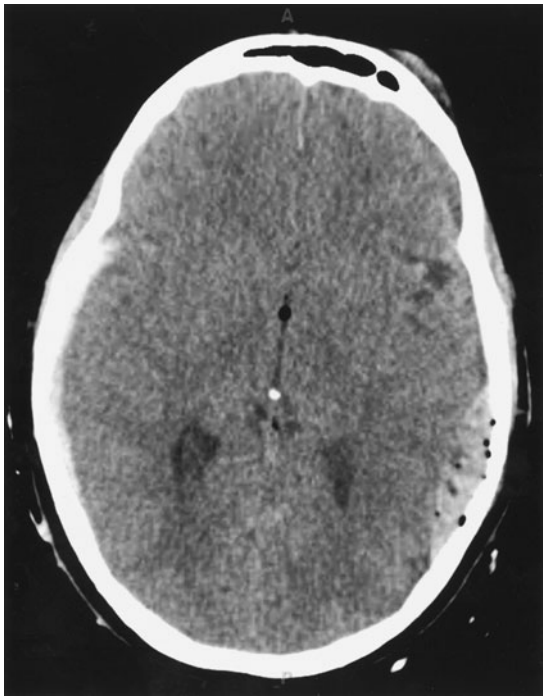


Photo 3-5 Subdural hematoma on left side of image (right hemisphere) and epidural hematoma on right side of image (left hemisphere)

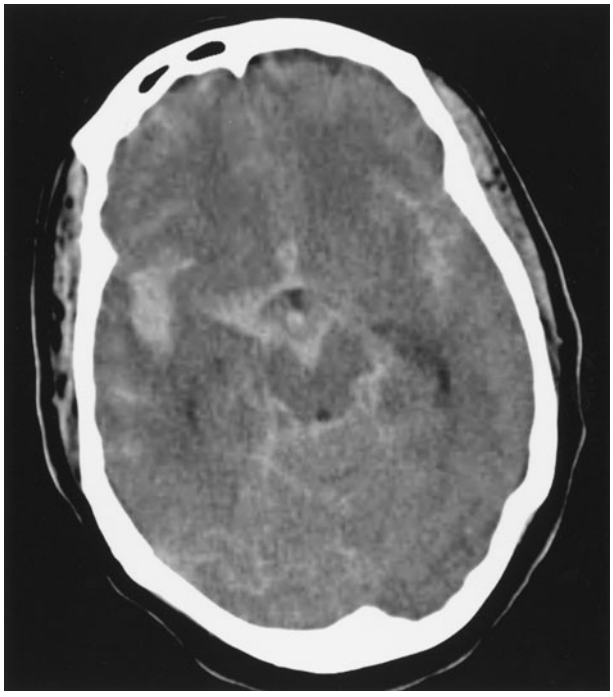


Photo 3-6 Subarachnoid hemorrhage

Now, let's draw our cerebrospinal fluid flow diagram. As mentioned, pia mater and the ependymal lining of the ventricular system form choroid plexus, which produces cerebrospinal fluid. Tela choroidea lines the third and fourth ventricles and suspends the choroid plexus in those spaces. Draw some representative *choroid plexus* lining the ventricular system. Show cerebrospinal fluid pass from the lateral ventricles through one interventricular foramen into the third ventricle. Indicate it descends from the third ventricle through the cerebral aqueduct into the fourth ventricle and down the central canal of the spinal cord, but as mentioned, the central canal is obliterated by middle adulthood.

Next, show fluid empty from the fourth ventricle into the subarachnoid space through the foramen of Magendie, in midline, and the foramina of Luschka, laterally. Draw it flow into the spinal canal to bathe the spinal cord and rostrally into the cranial vault to bathe the rest of the brain. It is then reabsorbed through the venous sinuses, which are the separations between the outer periosteal and the inner meningeal dural layers. Draw an *arachnoid villus* extending from the *subarachniod space* through the *subdural* space into a venous sinus. Show cerebrospinal fluid pass from the subarachnoid space into the *arachnoid villus* and empty into the venous sinus. Meningiomas are tumors of the meninges that arise from arachnoid cells found in the arachnoid villi. Are they more likely to be found intracranially or in the spinal canal? Remember venous sinuses exist only in the cranium; thus ninety percent of meningiomas arise intracranially and they most commonly grow parasagittally, near the superior sagittal sinus.

Now we have completed our diagram of the cerebrospinal fluid flow pattern and are ready to draw the ventricular system, venous system, and the basal cisterns of the subarachnoid system, separately.

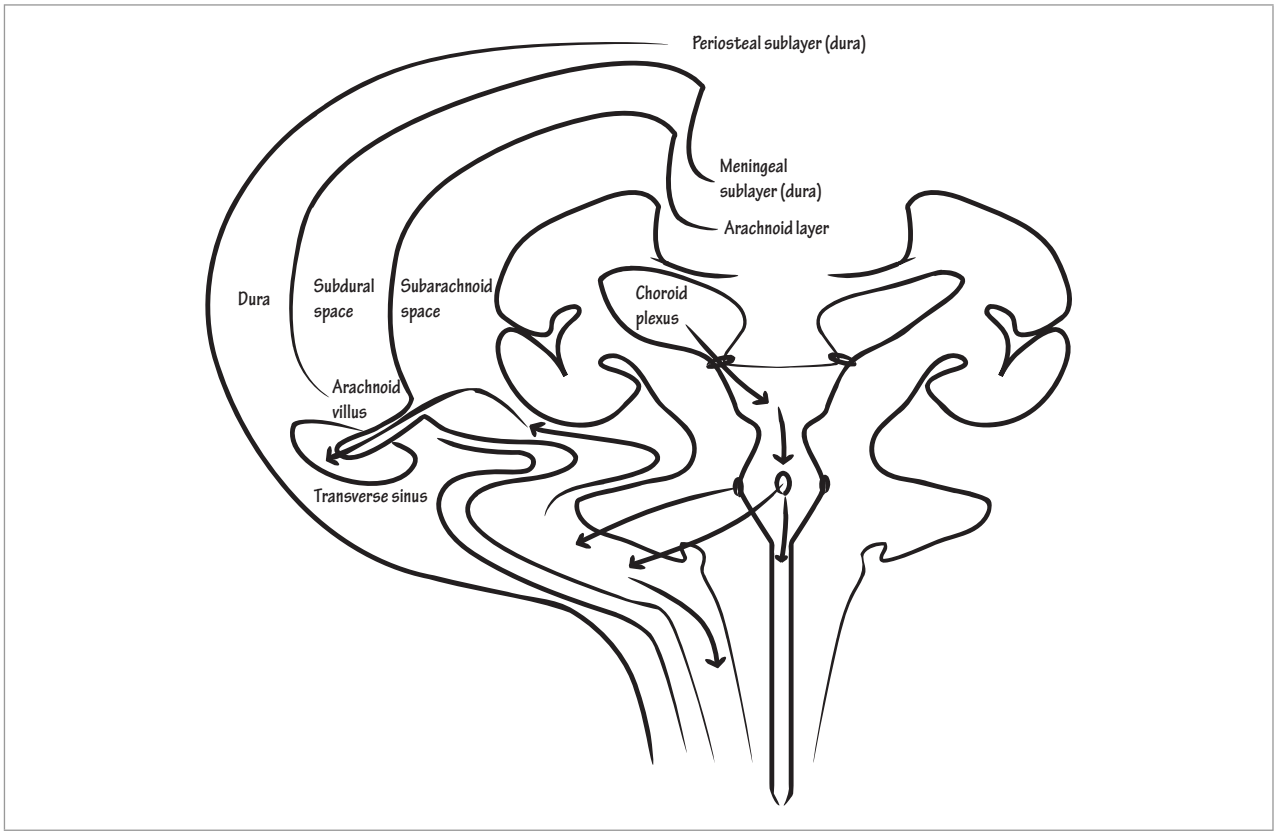


Figure 3-4 Cerebrospinal fluid flow diagram

Let's begin with the three-dimensional C-shaped morphometry of the intracranial ventricular system. Its shape is similar to that of the cerebral hemispheres, the striatum (the caudate–putamen combination), the fornix–hippocampus system, and the stria terminalis–amygdala system. During embryogenesis, all of these structures undergo a backward, downward, and forward migration along with the lateral ventricles; let's learn this migration to understand their common shape.

To demonstrate this migration, create a coronal view of the developing brain with your hands in the following manner. Hold your arms in front of you, flexed at the elbows with your forearm undersurfaces together. Extend your wrists so you could set a plate on your palms. Your hyper-extended palms represent the flat surface of the brain when it first forms. During early development, there is *inrolling* of the walls of the hemispheres. Curl your fingertips over to demonstrate it. Show them combine into a heart shape; this represents the early shape of the ventricles. Then continue to curl your fingers in so they touch your palms, which forms the bilateral *lateral ventricles* and the small midline *third ventricle*.

Next, initiate the backward, downward, and forward evagination. Bring your forearms *back* together toward your chest, then fan your elbows apart as you bring your hands *downward*, and then extend your forearms at the elbows as you reach your arms *forward*. This is the backward, downward, and forward evagination of the ventricular system; the other cerebral structures we mentioned follow the same pattern.

Now, let's draw the ventricular system in a sagittal section to make sense of this demonstration. First, draw the body of the *lateral ventricles* (frontal, occipital, and temporal horns); show it is C-shaped and has a posterior tail. Next, label the individual horns of the lateral ventricles. Label the superior–anterior region as the *frontal horn* (aka *anterior horn*), the posterior tail as the *occipital horn* (aka *posterior horn*), and the inferior–anterior region as the *temporal horn* (aka *inferior horn*). The frontal horns of the lateral ventricles in the anterior–superior cerebrum take shape during the origination of the ventricular system, the occipital horns in the posterior–superior cerebrum are created during the backward rotation of the ventricular system, and the temporal horns in the anterior–inferior cerebrum form during the downward and forward migration of the ventricular system.

Label the region where the three horns come together as the *atrium*; show it empty into the triangular-shaped *third ventricle*, which lies in between the anterior and inferior horns. Indicate the massa intermedia (aka the interthalamic adhesion) extends through the third ventricle. Then, show the narrow *cerebral aqueduct* drop down from the third ventricle into the fin-shaped *fourth ventricle*. Draw the *foramen of Magendie* coming out of the midline of the fourth ventricle, the *foramen of Luschka* coming off to the side, and the *obex* extending down from the bottom. At the obex, the cerebrospinal fluid channel becomes the *central canal*.

Off to the side, draw a sagittal section of the triangular-shaped fourth ventricle. Show how large it actually is in comparison to the cerebral aqueduct and central canal that feed and empty it. Draw its anterior border, the *floor*, as a straight line. Then draw the superior–posterior border as the *superior medullary velum* (aka *anterior medullary velum*) and then the inferior–posterior border as the *inferior medullary velum* (aka *posterior medullary velum*). Medulloblastoma tumors evolve from the superior medullary velum of the fourth ventricle.

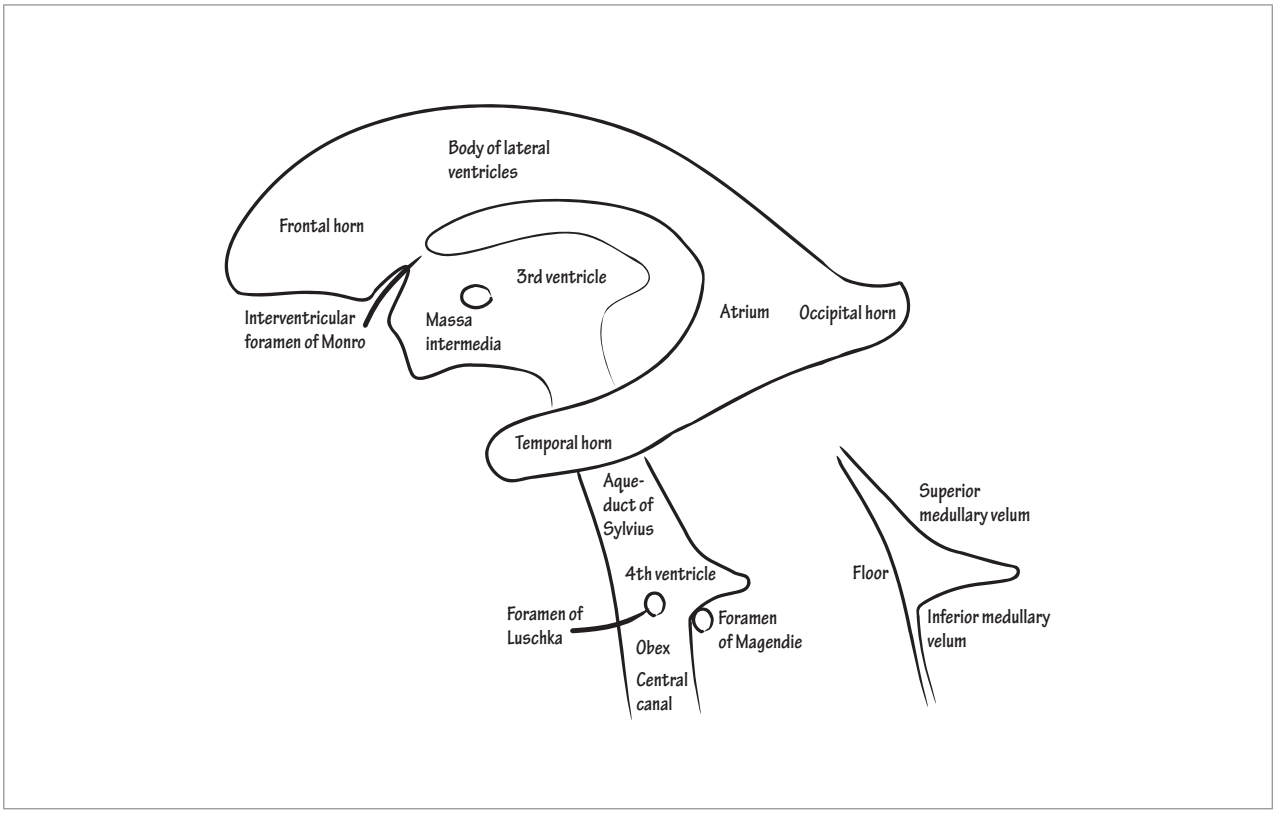


Figure 3-5 Sagittal view of ventricular system

Now, let's draw the dural venous system. The dural venous sinus system is one division of cerebral venous vasculature; the other division is the cerebral veins, which divide into superficial, deep (aka internal), and posterior fossa veins. The superficial cortical veins run along sulci on the surface of the brain and drain into venous sinuses. The superficial cerebral veins we will draw here are: on the surface of the brain, a representative superficial cortical vein, and in the center of the brain, the vein of Galen (aka the great cerebral vein) and the basal vein of Rosenthal. The deep cerebral veins underlie the ventricular ependyma. The single deep cerebral vein that we will draw here is called the internal cerebral vein and is an anterior extension of the vein of Galen.

Let's draw a sagittal section of the venous system. Neurologists commonly view the venous system from this perspective radiographically when venous occlusion is in question. Venous occlusion presents with a myriad of symptoms with variable severity. Sometimes the symptoms are as mild as simple headaches and othertimes they are severe enough to produce confusion, stupor, or even coma, along with paralysis and other focal neurologic deficits. Along the superior convexity of the brain, draw the *superior sagittal sinus*. Draw an unnamed *superficial cortical vein* connected to it. Next, where the superior sagittal sinus drops to the occiput, label the *sinus confluence* (aka torcular Herophili). Show that coming out of the page in both directions are horizontally mediated sinuses—the *transverse sinuses*. Indicate the transverse sinuses drop into the *sigmoid sinuses*, which empty into the jugular veins.

The aforementioned veins are the most prominent in the venous system and typically when venous occlusion comes to clinical attention, one of the larger venous components is affected. Interestingly, it is common for one of the transverse sinuses to be much smaller than the other without perceivable clinical consequences and it is sometimes difficult to know whether this is the cause of the patient's symptoms.

Next, draw the *straight* sinus along an antero-superior diagonal from the sinus confluence. Then, attach the *inferior sagittal sinus*; it follows the curvature of the superior sagittal sinus and runs just above the corpus callosum.

Now, show the *vein of Galen* (aka the *great cerebral vein*) loop down from the straight sinus and then come back up to run above the cerebellum. Indicate its antero-inferior extensions are the bilateral *basal veins of Rosenthal*, which wrap around the midbrain, and its antero-superior extension is the *internal cerebral vein*, which drains the thalamic region.

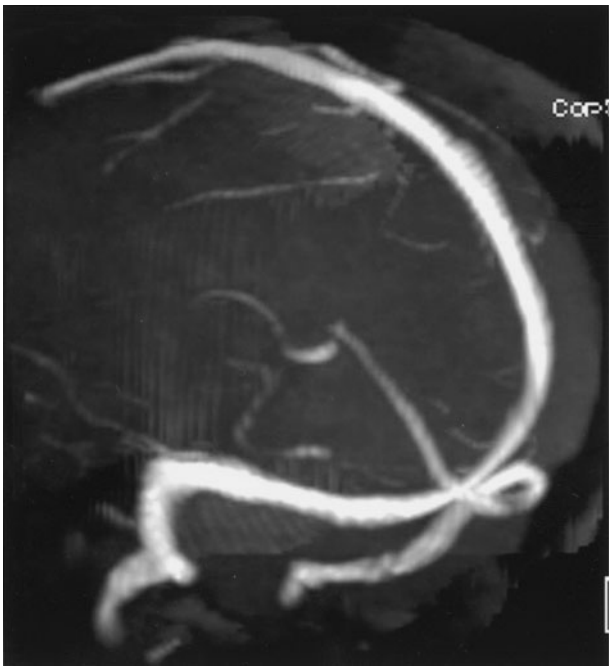


Photo 3-7 Oblique magnetic resonance venous image

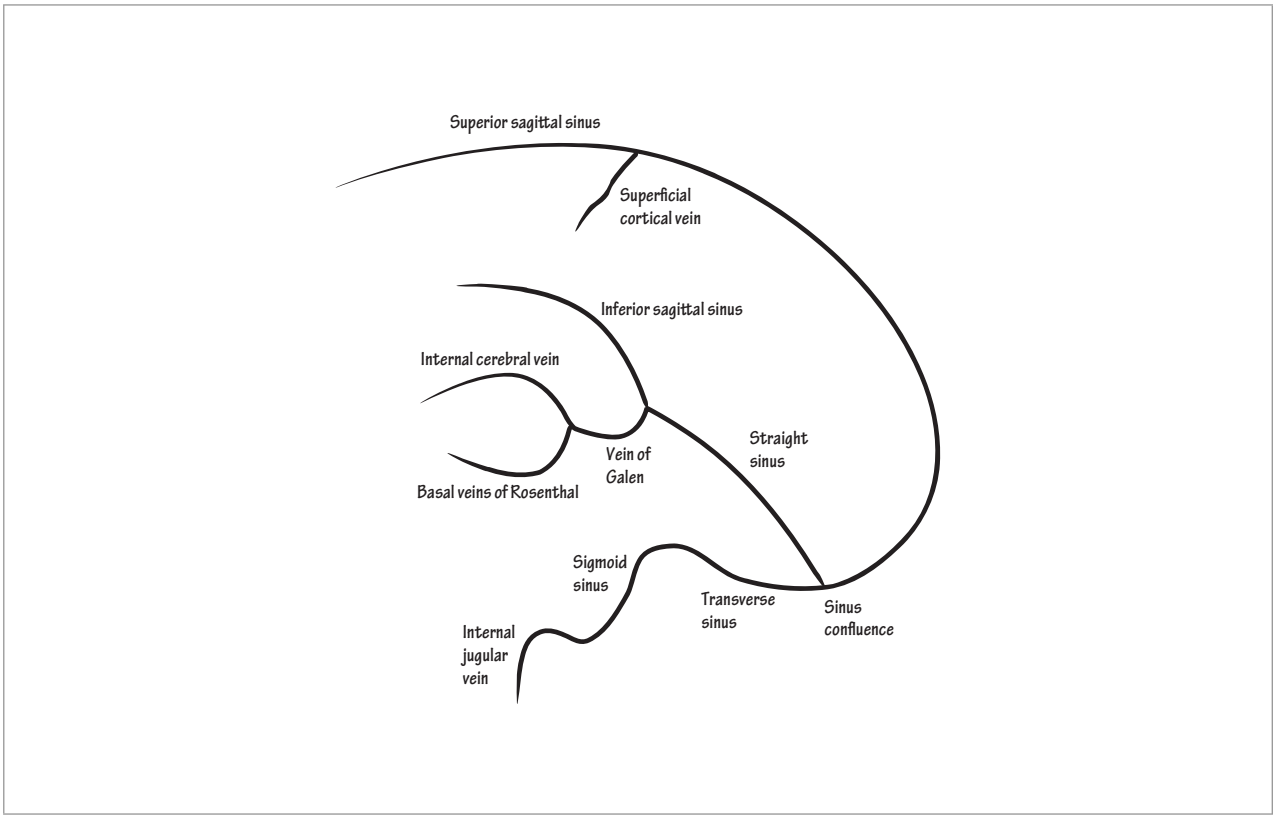


Figure 3-6 Cerebral venous system

The basal cisterns are the most important area of the brain to review on radiographic imaging; these cisterns lie at the base of the skull, and it is extremely important to know whether they are patent. Obliteration of the basal cisterns suggests brainstem swelling or compression, which is often deadly. Clinicians rarely parse the basal cisterns into their individual spaces, which may explain why the individual named cisterns are only variably included in anatomy texts. We address them here because if we can't name them, we won't look for them, and they are too important to miss. The names of the individual cisterns are derived from their locations, which will help us learn them.

To diagram the *basal cisterns*, draw a mid-sagittal section through the brain. Show the basal frontal lobe, brainstem, cerebellum, and quadrigeminal plate. Also include the massa intermedia of the thalamus; it is an important demarcation point of the cistern of velum interpositum. Lastly, include an outline of the skull underlying these brain structures; be sure to show the sella turcica, which is the skull depression in which the pituitary body sits.

In the posterior basal frontal area, label the *cistern of the lamina terminalis*. The lamina terminalis is the anterior border of the hypothalamus; it separates the hypothalamus from the frontal lobe. Then, label the space surrounding the optic chiasm as the *suprasellar cistern*; it is called the suprasellar cistern because it lies above the sella turcica. The suprasellar cistern is also known as the chiasmatic cistern because the optic chiasm lies within it. In front of the midbrain, label the *interpeduncular cistern*; its name comes from its position between the two midbrain cerebral peduncles, which carry descending motor fibers from the cortex.

Lateral to the midbrain, label the *ambient cistern*. The uncus of the temporal lobe descends into this cistern during uncal herniation (aka medial temporal lobe herniation). Directly behind the midbrain, label the *quadrigeminal cistern*, named by its proximity to the quadrigeminal plate. Pineal tumors extend through this cistern and disrupt the quadrigeminal plate. Farther posterior, above the cerebellum, label the *superior cerebellar cistern*. Behind the massa intermedia and above the quadrigeminal cistern, label the *cistern of velum interpositum*. It is best seen on axial imaging where it lies above the third ventricle and between the posterior thalami.

Drop down to the level of the pons. In front of the pons, label the *prepontine cistern* and to its side, label the *cerebellopontine cistern*. Nerve fibers from cranial nerves 5, 7, and 8 traverse the cerebellopontine cistern. Next, drop down to the level of the medulla. What do you think the cistern in front of the medulla is called? Label it as the *premedullary cistern* (aka *medullary cistern*) and just underneath the cerebellopontine cistern, label the *lateral cerebellomedullary cistern*. Nerve fibers from cranial nerves 9, 10, and 11 traverse the cerebellomedullary cistern. Then, underneath the cerebellum, label the *cisterna magna* (aka *dorsal cerebellomedullary cistern*). A cisternal puncture involves fluid removal from the dorsal cerebellomedullary cistern, and it is done when a lumbar puncture can't be performed.

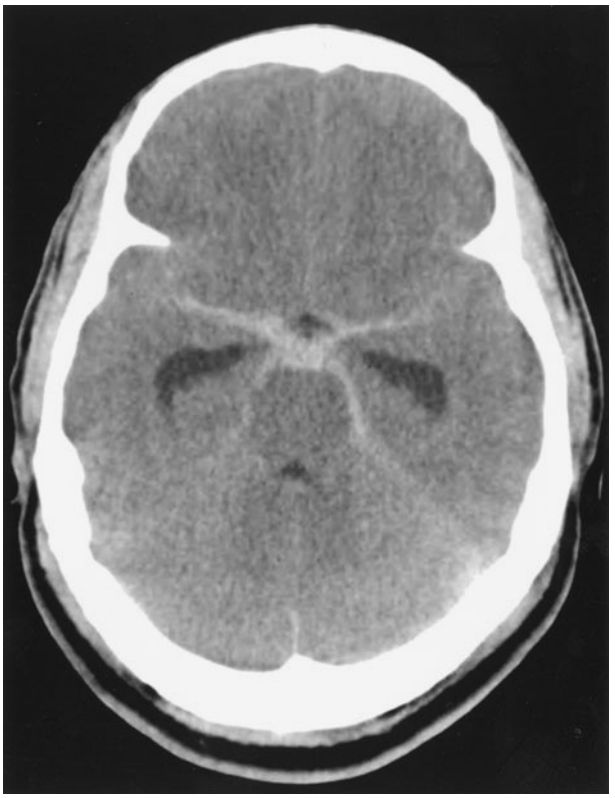


Photo 3-8 Subarachnoid hemorrhage filling the basilar cisterns ("star sign")

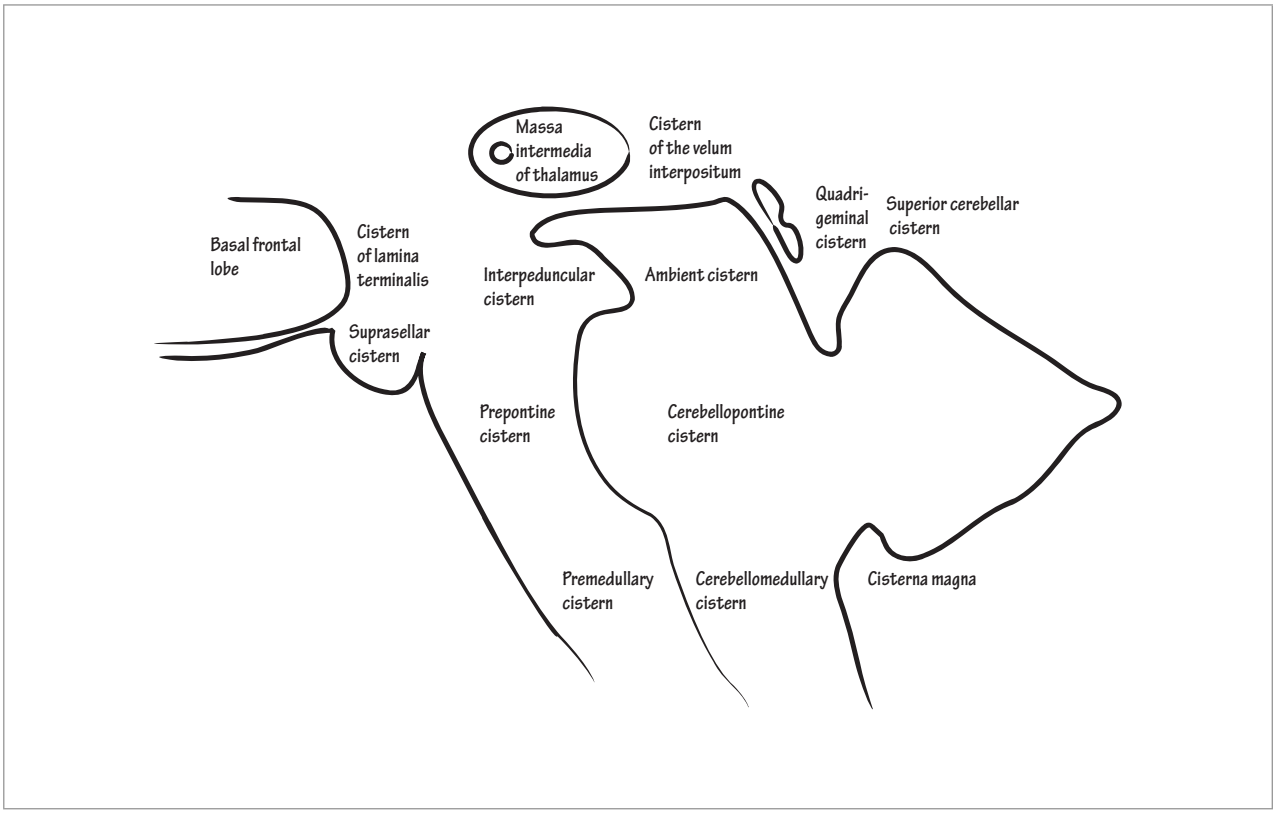


Figure 3-7 Sagittal view of basal cisterns

Nerve Roots and Rami

THE ANATOMY OF THE NERVE roots and rami appears deceptively simple, and you may be tempted to skip this chapter. Resist this urge. Certain of its details directly affect our evaluation of neuromuscular disorders and are important to our interpretation of neurophysiologic studies (nerve conduction studies and electromyography).

Let's begin with an axial cross section through the spinal cord and the surrounding vertebra. Show a *ventral root* (aka *anterior root* or *motor root*) emerge from the *anterior horn cell* in the ventral horn of the spinal cord gray matter and exit ventrally. Next, show a *dorsal root* (aka *posterior root* or *sensory root*) enter the spinal cord through the *dorsal funiculus* (aka *dorsolateral fasciculus of Lissauer*) and terminate in the dorsal horn of the gray matter. Show these nerves pass laterally through the spinal canal toward the intervertebral foramen. In the intervertebral foramen, attach the *dorsal root ganglion* to the posterior nerve root. The dorsal root ganglion houses the cell bodies of sensory nerves. It is called pseudounipolar or bipolar because it has two distinct axons, central and peripheral.

Next, show the anterior and posterior roots join one another just distal to the intervertebral foramen to form a *spinal nerve*. Show the spinal nerve continue a short distance before it separates into *dorsal* and *ventral rami* (aka posterior and anterior rami).

Dorsal rami innervate the paraspinal muscles and also provide sensory coverage to the back of the head and posterior trunk. Ventral rami also provide *both* motor and sensory innervation but to a far more widespread group of muscles and sensory areas. They cover sensation to the angle of the mandible, anterior trunk, and upper and lower limbs. The trigeminal nerve covers sensation to the face. While the dorsal rami remain as separated fibers, the ventral rami intercommunicate in several different plexuses (cervical, brachial, and lumbosacral), which we will draw separately. Note that it is common, although technically wrong, to refer to the proximal components of the brachial and lumbosacral plexuses as nerve roots (we even do so in this book). In actuality, the proximal plexus segments comprise only the ventral rami of mixed spinal nerves—the dorsal rami do not contribute to the plexuses. Let's review: nerve roots form spinal nerves, which then divide into anterior and posterior rami, and the anterior rami comprise the different plexuses.

We will draw the interwoven cervical, brachial and lumbosacral plexuses in separate chapters. Here, in our diagram, we will draw a representative thoracic nerve. Thoracic nerves course individually within their intercostal space in the chest wall and do not anastomose with other nerves. Continue the anterior ramus laterally along the chest wall and show it form an *intercostal nerve*.

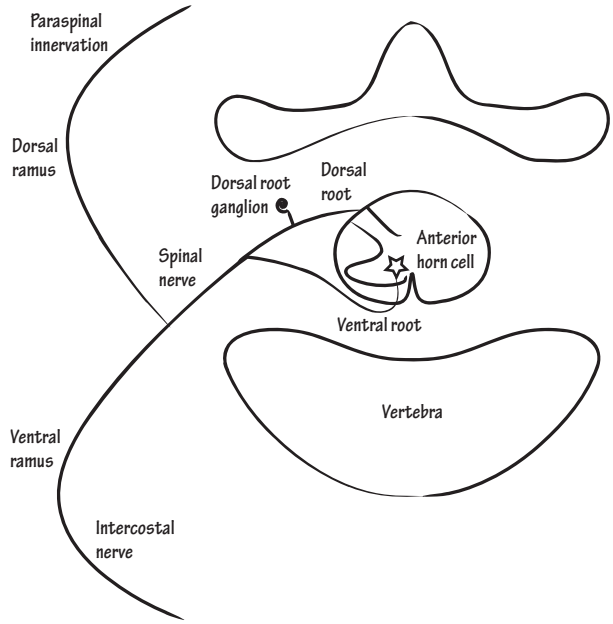


Figure 4-1 Nerve roots and rami

Now, turn your attention to where the rami split. First, along the ventral ramus, attach the *white ramus*. Then, more proximally, just past the takeoff of the dorsal ramus, attach the *gray ramus*. Indicate the gray and white rami meet in a *paravertebral sympathetic ganglion*. Sympathetic ganglia form two long chains that flank the vertebral column from the cervico–medullary junction, superiorly, to the coccyx, inferiorly. Sympathetic cell bodies originate in the intermediolateral cell column of the intermediate horn of the spinal cord gray matter from T1–L2 and project to the paravertebral sympathetic chains.

Indicate the impulse travels along the ventral ramus past the gray ramus to the white ramus, so named because it is myelinated. It travels up the white ramus to the paravertebral sympathetic ganglion and then down the gray ramus, which is unmyelinated, back to the ventral ramus and disseminates along either the dorsal or ventral rami. As we will show in the "Peripheral Autonomic Nervous System" chapter, nerve fibers from the white ramus synapse in the sympathetic ganglion either at their level of entry or ascend or descend before forming a synapse, or they pass through the ganglion along with a splanchnic nerve (which then innervates prevertebral ganglia).

When cell bodies die, their axons undergo Wallerian degeneration, which means the axons attached to the cell bodies also die. What happens to the motor and sensory nerves when there is disease proximal to the dorsal root ganglion that affects the motor neuron and sensory roots? The proximal transmission of sensory information is interrupted as is the motor signaling. But only the motor axon undergoes Wallerian degeneration. The distal sensory axon remains intact because it is attached to the dorsal root ganglion, which survives. This principle has important electrophysiologic implications and is used to help localize disease.

Alternatively, a clinical process that affects only the dorsal root ganglion produces peripheral sensory nerve disease without motor involvement. This occurs in dorsal root ganglionopathy (aka sensory neuronopathy) and is often due to paraneoplastic disease such as the anti-Hu antibody syndrome associated with limbic encephalitis.

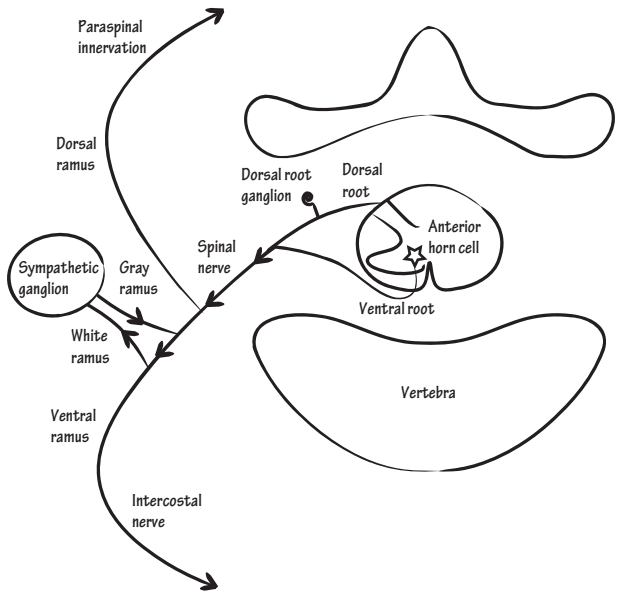


Figure 4-2 Nerve roots and rami with sympathetic ganglion

Brachial Plexus

EVERY MEDICAL STUDENT memorizes and promptly forgets the brachial plexus. Even the majority of neurology residents only cram it into memory before board exams and then actively forget it afterward. For physicians who use it daily in the electromyography suite, however, it is a grail. The brachial plexus is fundamental to the peripheral nervous system exam. Without it, we are able to memorize the major muscle groups and their innervation patterns but the nuance of the exam escapes us. Let's learn the brachial plexus well, here, so that even if we forget its details, they will be accessible to us when we need them.

Although we avoid using abbreviations throughout this book, in the peripheral nervous system chapters we will use "C" for cervical, "T" for thoracic, "L" for lumbar, "S" for sacral, and "Co" for coccygeal, for simplicity.

Our page is oriented so that left is proximal, right is distal, up is superior, and down is inferior. First, draw three horizontal lines in parallel; we will eventually divide each of these lines into the different segments of the brachial plexus. From proximal to distal, the segments of the brachial plexus are the ventral rami (of C5–T1), the trunks (upper, middle, and lower), the divisions (anterior and posterior), the cords (lateral, posterior, and medial), and the terminal branches (the musculocutaneous, radial, median, and ulnar nerves).

At their proximal ends, label the horizontal lines, from top to bottom as *upper trunk*, *middle trunk*, and *lower trunk*. Next, attach the ventral rami that form each of them. Show the ventral rami of C5 and C6 form the upper trunk. The anatomical site where this occurs is called Erb's point and an upper trunk injury is commonly referred to as an Erb's palsy. Indicate the ventral ramus of C7 makes up the middle trunk and the ventral rami of C8 and T1 derive the lower trunk. Second-order sympathetic fibers exit the spinal cord at the level of T1; so a C8–T1 spinal root avulsion will cause both deficits of the brachial plexus and disruption of sympathetic fibers to the face, called Horner's syndrome. This syndrome is discussed in detail in the "Peripheral Autonomic Nervous System" chapter, but briefly, it causes enophthalmosis, ptosis and miosis and, variably, facial anhidrosis.

While the brachial plexus is typically formed from the ventral rami of C5–T1, it also has two important anatomical anomalies, which we will indicate. Attach the C4 ventral ramus directly to C5 and the T2 ventral ramus directly to T1. In a *prefixed plexus*, C4 contributes significantly to the plexus and T1 contributes minimally (the plexus is shifted up one level), whereas in a *postfixed plexus*, T2 contributes significantly and C5 contributes minimally (the plexus is shifted down one level).

Now, let's move distally. The trunks divide into anterior and posterior divisions, which then join divisions of other trunks to form cords. The simplest way to learn the divisions is to recognize that the posterior divisions join together to form the posterior cord whereas the anterior divisions form the lateral and medial cords. With that in mind, just distal to the trunk segments, label the lines from top to bottom as follows (specify both the division and the trunk): *anterior division* (*upper trunk*), *posterior division* (*middle trunk*), and *anterior division* (*lower trunk*). Next, we will add in the posterior division (upper trunk), the anterior division (middle trunk), and the posterior division (lower trunk).

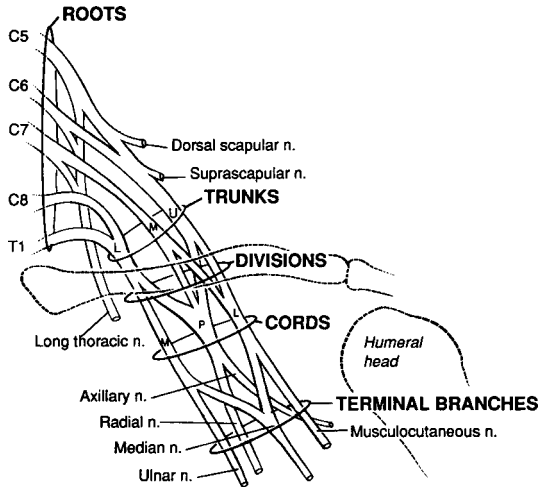


Photo 5-1 The brachial plexus

With permission From Mendell, J. R., J. T. Kissel, and D. R. Cornblath. *Diagnosis and Management of Peripheral Nerve Disorders*, Contemporary Neurology Series. Oxford: Oxford University Press, 2001.

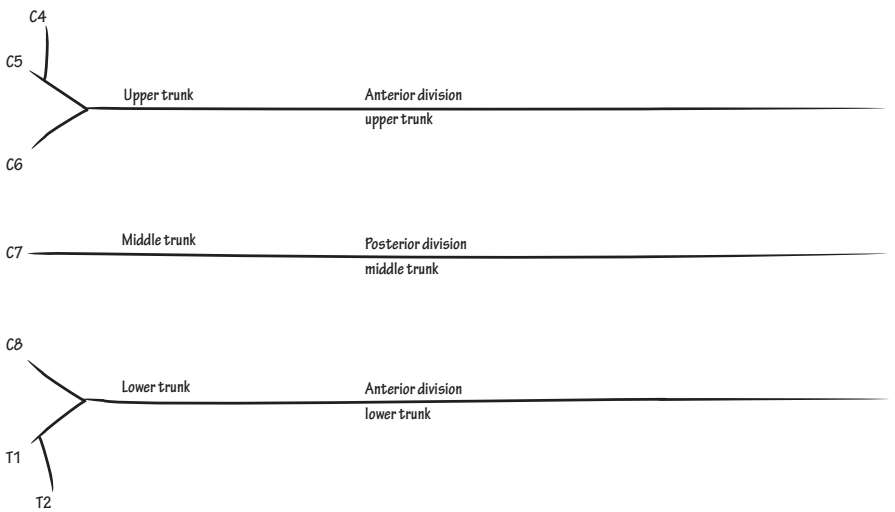


Figure 5-1 Brachial plexus: roots, trunks, incomplete divisions

Show the *posterior division* (*upper trunk*) join the posterior division of the middle trunk. Next, indicate the *posterior division* (*lower trunk*) joins the posterior division of the middle trunk. Where the posterior divisions of the upper, middle, and lower trunks meet, label the line as the *posterior cord*.

Next, show the *anterior division* (*middle trunk*) join the anterior division of the upper trunk and where the middle and upper trunks meet, label the line the *lateral cord*. Then, at the bottom, where the anterior division of the lower trunk ends, label the *medial cord*. This completes the anterior rami, trunks, divisions, and cords of the brachial plexus.

Anatomically, the divisions of the brachial plexus lie at the level of the clavicle, within the shoulder. The trunks and spinal rami are proximal, so they are supraclavicular, and run in between the anterior and middle scalene muscles in the scalene groove, alongside the subclavian artery. The cords are distal to the divisions, so they are infraclavicular and are named based on their anatomical relationship to the axillary artery (lateral, posterior, and medial). If you raise your shoulder and press down into the cavity just behind your clavicle, into the posterior cervical triangle, you can palpate the actual brachial plexus. Refer to the "Cervical Plexus" chapter for a detailed description of the anatomy of the posterior cervical triangle.

Now, let's draw the last segment of the brachial plexus—the major terminal branches: the median nerve, musculocutaneous nerve, ulnar nerve, and radial nerve. Let's first get the most difficult branch out of the way. Draw a diagonal line from the distal edge of the lateral cord across the posterior cord, and join it with a diagonal line from the distal edge of the medial cord. Where these lines come together, draw a line that extends distally and label it the *median nerve*. Now, just distal to the branch point for the median nerve from the medial cord, label the bottom line the *ulnar nerve*. Finally, just distal to the posterior cord, label the *radial nerve*.

We will discuss the median, ulnar, and radial nerves in detail in Chapters 6–8, respectively, but let's introduce the motor innervation and sensory coverage of these nerves here. The median nerve primarily comprises sensory nerves from the C6, C7 roots of the lateral cord and motor nerves from the C8, T1 roots of the medial cord. We will learn in Chapter 13 why its C6, C7 sensory supply is to the lateral portion of the upper limb (with the arm in supination, lateral is the thumb side of the arm). Its primary C8, T1 motor supply tells us that its motor pattern is mostly in the distal portion of the upper limb. The median nerve does have C6, C7 pronation innervation to the forearm, however. The C8, T1 roots of the medial cord supply the ulnar nerve. Again, its motor innervation is to the distal upper limb and its C8, T1 sensory coverage is specifically to the *medial* portion of the hand. The C5–C8 roots of the posterior cord supply the radial nerve. Its sensory coverage and motor innervation involve the extensor surface of the upper limb.

Now, just distal to the lateral cord, label the *musculocutaneous nerve*. The C5, C6 roots supply it and it innervates the *biceps brachii*. Flex your arm at the elbow to demonstrate the action of the biceps muscle.

This completes the ventral rami, trunks, divisions, cords, and terminal branches of the brachial plexus, but to complete the brachial plexus, we still need to draw the other terminal branches that sprout from the rami, trunks, and cords.

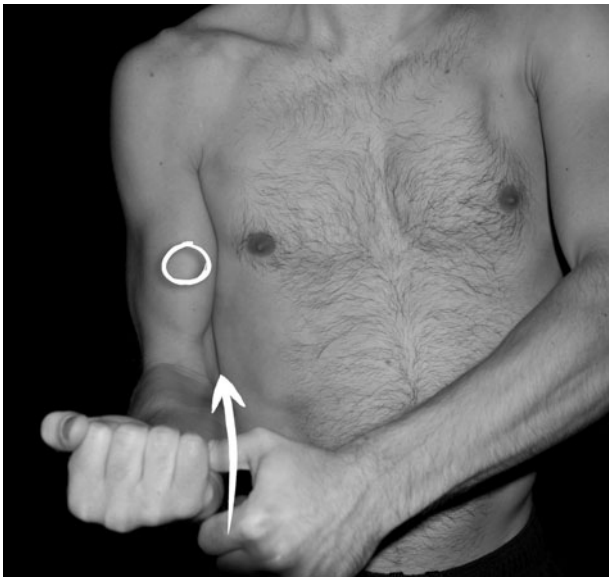


Photo 5-2 Biceps brachii

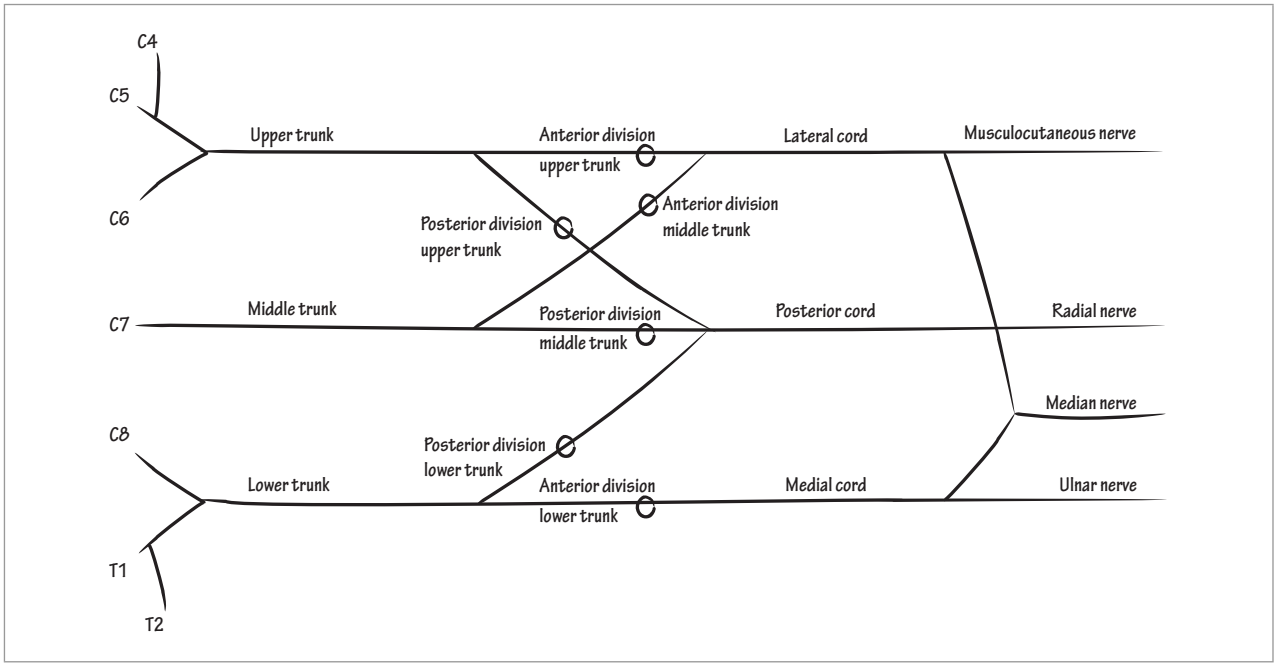


Figure 5-2 Brachial plexus: roots, trunks, divisions, and incomplete nerve branches

Before we complete our diagram, let's address a few things we will leave out of it. C5 contributes to the phrenic nerve, which we will study in the "Cervical Plexus" chapter. We remember the ventral rami that form the phrenic nerve with the mnemonic "C3, C4, C5 keep the diaphragm alive." We leave out the phrenic nerve here and we also purposely leave out the branches from the C5–C8 roots that innervate the longus colli and scalene muscles.

From the C5 ventral ramus, draw the origins of the *long thoracic nerve*. Show it also receive contributions from the rami of C6 and C7 as it passes inferiorly. This nerve innervates the *serratus anterior muscle*, which pulls the scapula forward and abducts it (moves it

outward). Next, show the *dorsal scapular nerve* originate from C5 and innervate the *rhomboid muscles*, which pull the scapula in the opposite direction of the serratus anterior muscle; they pull it toward midline and rotate it downward. Injury to either of these two muscles or to the trapezius muscle, which we discuss in the "Cervical Plexus" chapter, results in different forms of scapular winging.

Scapular winging occurs in many peripheral nervous system diseases but when it occurs in association with weakness of facial, humeral, and peroneal distribution muscles and spares the deltoid, it is likely from *fascio-scapulo-humeral disease*. And when it occurs in association with weakness of the proximal upper and lower extremities instead, it is commonly due to a recessive form of limb–girdle muscular dystrophy.

Next, show the *suprascapular nerve* originate from the upper trunk and innervate the *supraspinatus* and *infraspinatus muscles*. The supraspinatus muscle is responsible for the first 20 to 30 degrees of arm abduction when the arm is extended at the elbow, and the infraspinatus muscle is responsible for external rotation of the arm when it is flexed at the elbow. We will leave out the other nerve that originates off the upper trunk, the *subclavius nerve*, because it is unable to be examined clinically or electrodiagnostically.

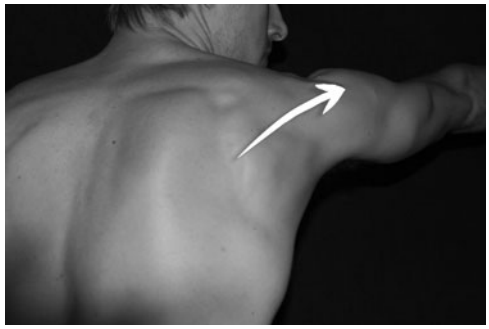


Photo 5-3 Serratus anterior

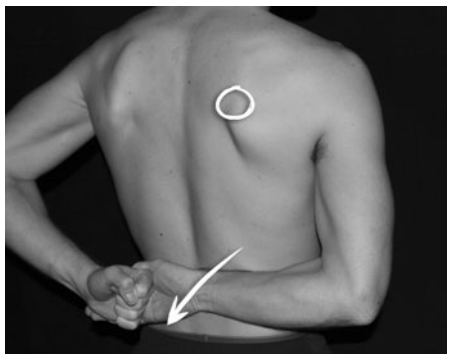


Photo 5-4 Rhomboid muscles

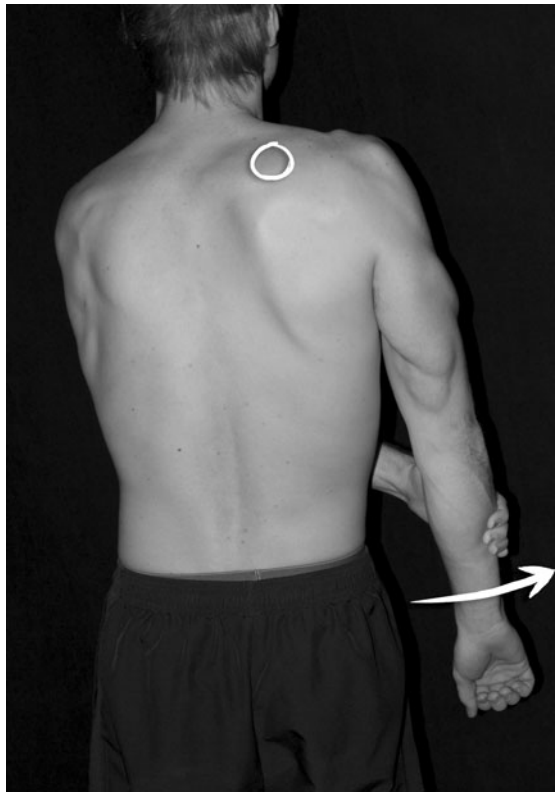


Photo 5-5 Supraspinatus

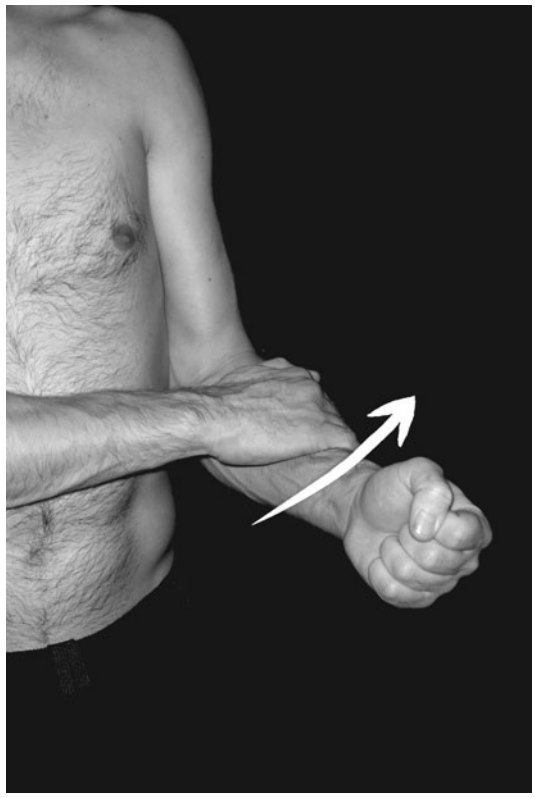


Photo 5-6 Infraspinatus

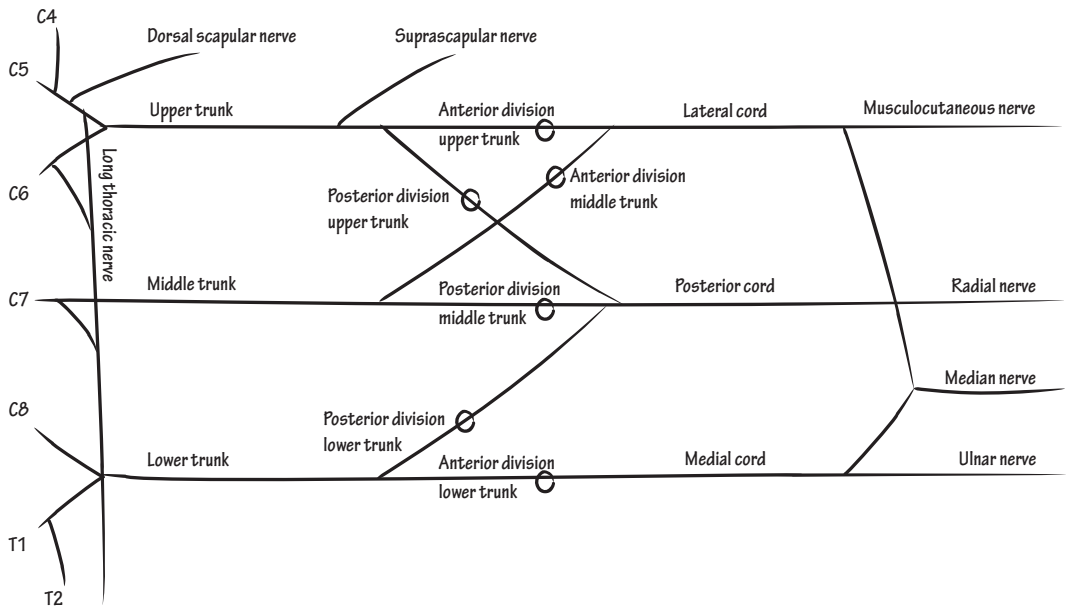


Figure 5-3 Brachial plexus: roots, trunks, divisions, incomplete nerve branches

Moving distally, indicate the *lateral pectoral nerve* originates from the lateral cord and innervates the *clavicular head of pectoralis major*, which adducts and internally rotates the arm. Then, draw three branches, from proximal to distal, off the posterior cord: the *upper subscapular*, *thoracodorsal*, and *lower subscapular nerves*, which innervate the subscapularis, latissimus dorsi, and teres minor muscles, respectively. All three of these muscles adduct and internally rotate the arm, and are able to be isolated and tested through appropriate positioning techniques.

Distal to these three nerves, off the posterior cord, draw the *axillary nerve*, which innervates the *deltoid muscle*. Whereas the supraspinatus muscle is responsible for the first 20 to 30 degrees of arm abduction, the deltoid muscle is responsible for the latter 70 to 80 degrees. Mild traction on the brachial plexus often places tremendous stress on the axillary nerve because it is fixed as it passes through the quadrangular space, and therefore, it is easily stretched. The muscle bellies of teres minor (superiorly), teres major (inferiorly), the lateral head of the triceps (laterally), and the long head of the triceps (medially) form the quadrangular space.

Finally, draw the three nerves, from proximal to distal, that originate from the medial cord: the *medial pectoral nerve*, the *medial brachial cutaneous nerve*, and the *medial antebrachial cutaneous nerve*. The medial pectoral nerve (not shown in figure) originates from the medial cord and innervates the *sternal head of the pectoralis major muscle*. The sternal head of the pectoralis muscle provides the last 30 degrees of arm adduction, which distinguishes it from the clavicular head of the pectoralis major. The medial pectoral nerve also innervates the *pectoralis minor muscle*, which is unable to be isolated and tested. The medial brachial cutaneous and medial antebrachial cutaneous nerves are sensory nerves that cover the medial aspect of the upper arm and forearm, respectively. The medial antebrachial cutaneous nerve is often tested electrodiagnostically to help distinguish between injury to the medial cord and injury to the ulnar nerve. In ulnar nerve injuries, sensation in the medial forearm remains intact because this area is covered by the medial antebrachial cutaneous nerve, which originates from the medial cord.

This completes our diagram of the brachial plexus. Note that no nerves stem from the division segments of the plexus; they only originate from the rami, trunks, and cords. Next, we will draw the median, ulnar, and radial nerves in further detail.

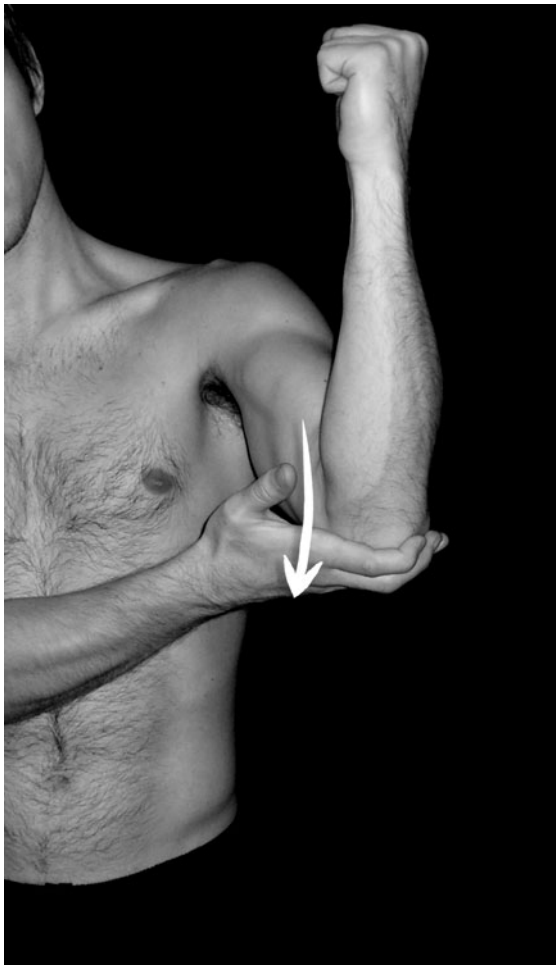


Photo 5-7 Clavicular head of pectoralis major

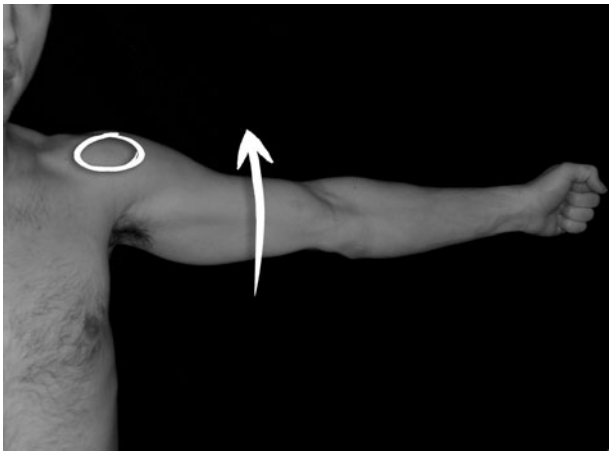


Photo 5-8 Deltoid muscle

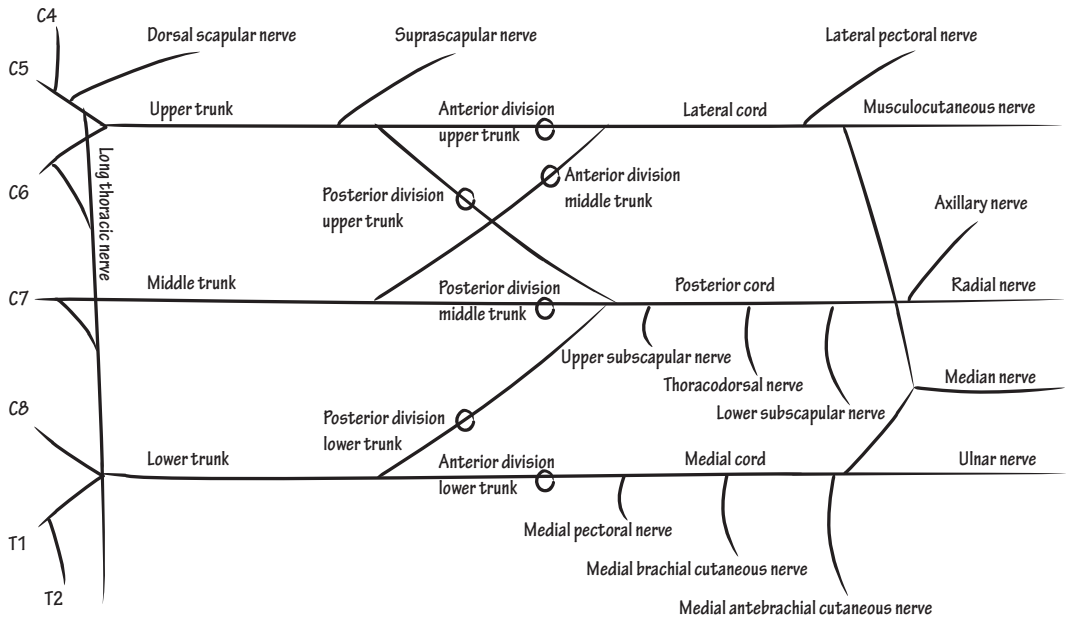


Figure 5-4 Complete brachial plexus

Median Nerve

THE LATERAL AND MEDIAL CORDS of the brachial plexus form the median nerve and the C6 to T1 nerve roots supply it. The lateral cord C6 and C7 fibers are primarily sensory and the medial cord C8 and T1 fibers are mostly motor. Briefly, the median nerve provides pronation of the forearm, radius (lateral)-deviated wrist flexion, and thumb abduction out of the plane of the palm, and it is the primary flexor and extensor of digits two and three. The median nerve also provides sensory coverage to the thenar eminence (ball of the thumb) and the entire palmar surface and dorsal tips of the lateral three and a half digits. In anatomical position, the arm is in supination so "the lateral three and a half digits" refer to the thumb, index finger, middle finger, and lateral half of the ring finger.

To trace the course of the median nerve down your arm, approximate where the lateral and medial cords of the brachial plexus join to form the median nerve by palpating deep to the pectoralis major muscle a few fingerbreadths below your clavicle. Next, feel your pulsating brachial artery between your biceps and triceps muscles in your proximal upper arm. The median nerve travels just lateral to the brachial artery in a neurovascular bundle; trace its course down the midline of your upper arm.

The median nerve is sometimes compressed at the distal end of the humerus by the ligament of Struthers, a ligamentous band present in roughly 1% of the population. The ligament of Struthers connects the antero-medial distal humerus to the medial epicondyle, the bony prominence you should palpate, now, on the antero-medial aspect of your elbow at the distal tip of the humerus. If you palpate posterior to the medial epicondyle, you will feel another bony prominence—the olecranon of the ulna. The ulnar nerve runs in the ulnar groove between these bony protrusions. The median nerve, however, crosses the elbow just lateral to the medial epicondyle in the antecubital fossa, which is just in front of the biceps tendon.

Next, with your arm still supinated, trace the path of the median nerve through the antecubital fossa and down the midline of your forearm. In the proximal forearm, the median nerve often becomes entrapped between the heads of the pronator teres (PT) muscle. Pronate your forearm to palpate the contracting pronator teres muscle belly in the midline of your antecubital fossa.

Distally, the median nerve passes through the carpal tunnel in the wrist—an incredibly common entrapment site. To approximate where along the wrist the median nerve runs, gently flex and radially (laterally) deviate your wrist. Two tendons will become palpable and even visible—palmaris longus (PL) (in midline) and flexor carpi radialis (FCR) (lateral to it). However, 15% of people do not have a palmaris longus muscle. The median nerve runs deep between these tendons. Tap over the nerve to reproduce symptoms of median nerve entrapment at the carpal tunnel. A positive Tinel's sign refers to the physical examination sign of elicitation of symptoms of nerve entrapment when you tap over the nerve.

Now, let's diagram the clinically relevant segments of the median nerve. Divide the page into five sections from left to right, proximal to distal, and label them as follows: *nerve roots* and *brachial plexus*, *upper arm*, *forearm*, and *hand*. At the left side of the page, underneath the brachial plexus segment, show the

branches of the lateral and medial cords anastomose to form the median nerve. Indicate the nerve roots from the *lateral cord* are *C6* and *C7* (*mostly sensory*) and the *medial cord* roots are *C8* and *T1* (*mostly motor*).

Next, continue the line through the upper arm segment to the forearm. The median does not innervate any of the muscles of the upper arm or provide any of its sensory coverage.

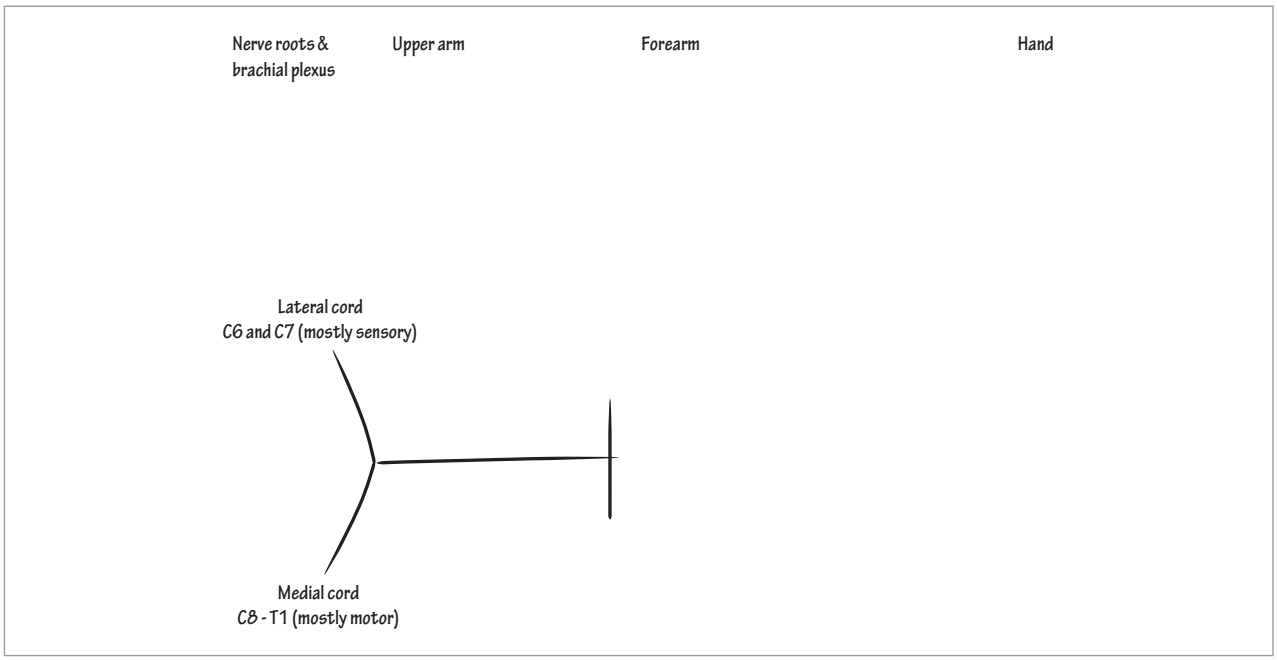


Figure 6-1 Incomplete median nerve

One-third of the way down the forearm, draw the *anterior interosseous nerve* branch. It innervates the *deep forearm muscle group* (*C7–T1*), which comprises *flexor pollicus longus* (*FPL*), *pronator quadratus* (*PQ*), and *flexor digitorum profundus 2 and 3* (*FDP 2 and 3*). Flex the distal interphalangeal (DIP) joint of your thumb against resistance to demonstrate the action of flexor pollicus longus. This muscle is referred to as the "long" flexor of the thumb because the flexor pollicus longus tendon has to travel past the metacarpal–phalangeal joint to the interphalangeal joint, whereas the flexor pollicus brevis tendon (discussed later) stops at the metacarpal–phalangeal joint.

Next, it is classically taught that you use pronator quadratus to pronate your forearm with it in flexion at the elbow and pronator teres, a member of the *superficial* forearm muscle group, to pronate your forearm with it in extension at the elbow, but this is still debated.

Lastly, flex the distal interphalangeal joints of your 2nd and 3rd digits to demonstrate the action of flexor digitorum profundus 2 and 3. The ulnar nerve, as we will soon demonstrate, provides distal interphalangeal joint flexion of digits 4 and 5.

In short, the anterior interosseous group innervates the deep muscles of the forearm, which provide distal interphalangeal joint flexion of the thumb and the 2nd and 3rd digits, and pronation of the forearm when it is flexed at the elbow.

Now, complete the path of the median nerve through the forearm and label the *superficial forearm muscle group* (*C6, C7*), which comprises *flexor carpi radialis* (*FCR*), *pronator teres* (*PT*), *palmaris longus* (*PL*), and *flexor digitorum sublimis* (*FDS*) (aka *flexor digitorum superficialis*). Flex your wrist in a radial direction to demonstrate the action of flexor carpi radialis. Flexor carpi ulnaris is an ulnar-innervated muscle; it provides ulnar-directed wrist flexion (toward the body) and will be discussed further in the "ulnar nerve" chapter.

To demonstrate the action of pronator teres, as mentioned above, extend your forearm at the elbow and pronate it against resistance. Next, flex your wrist in midline and the palmaris longus tendon will pop out just proximal to the wrist, but as mentioned, 15% of people do not have this muscle. Palmaris longus corrugates the skin over the wrist. On the contrary, palmaris brevis, which is ulnar-innervated, corrugates the skin of the hypothenar eminence (the ball of the little finger).

Lastly, flex digits 2 through 5 at their proximal interphalangeal joints to demonstrate the role of flexor digitorum sublimis. Remember, flexor digitorum profundus of the *deep* forearm group provides *distal* interphalangeal joint flexion.

In summary, the superficial forearm muscle group provides forearm pronation in elbow extension, radially deviated wrist flexion, and proximal interphalangeal joint flexion of digits 2 to 5.

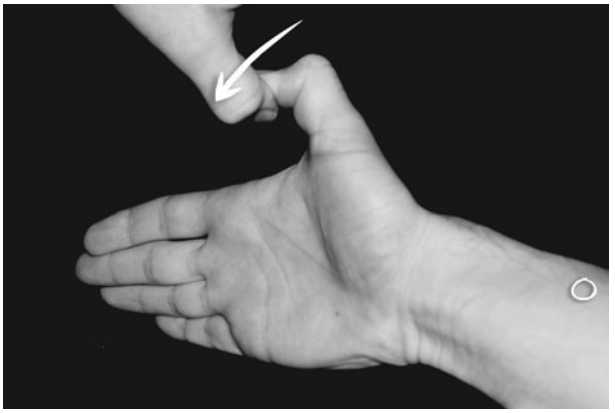


Photo 6-1 Flexor pollicis longus

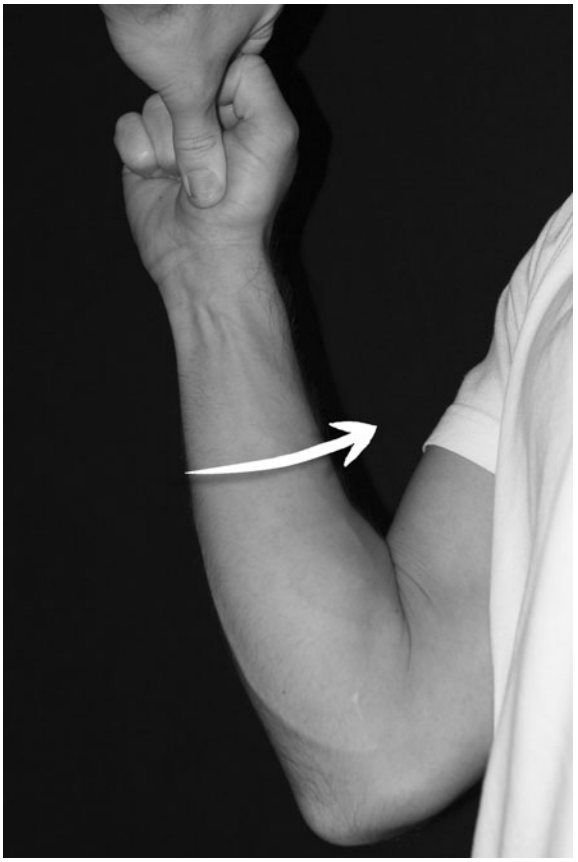


Photo 6-2 Pronator quadratus

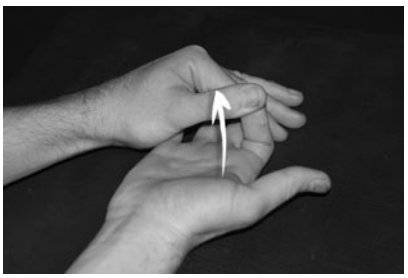


Photo 6-3 Flexor digitorum profundus 2 & 3

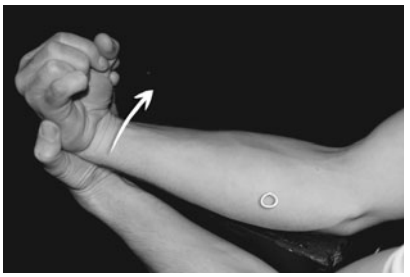


Photo 6-4 Flexor carpi radialis

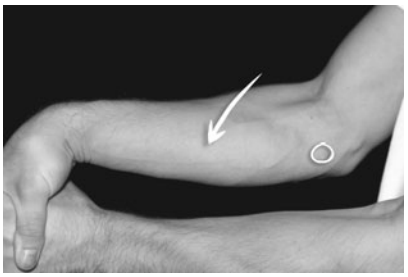


Photo 6-5 Pronator teres

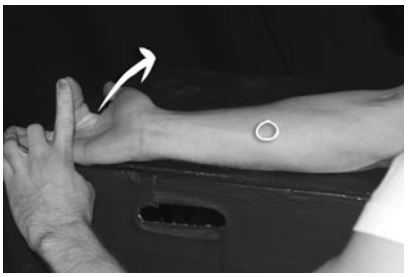


Photo 6-6 Flexor digitorum sublimis

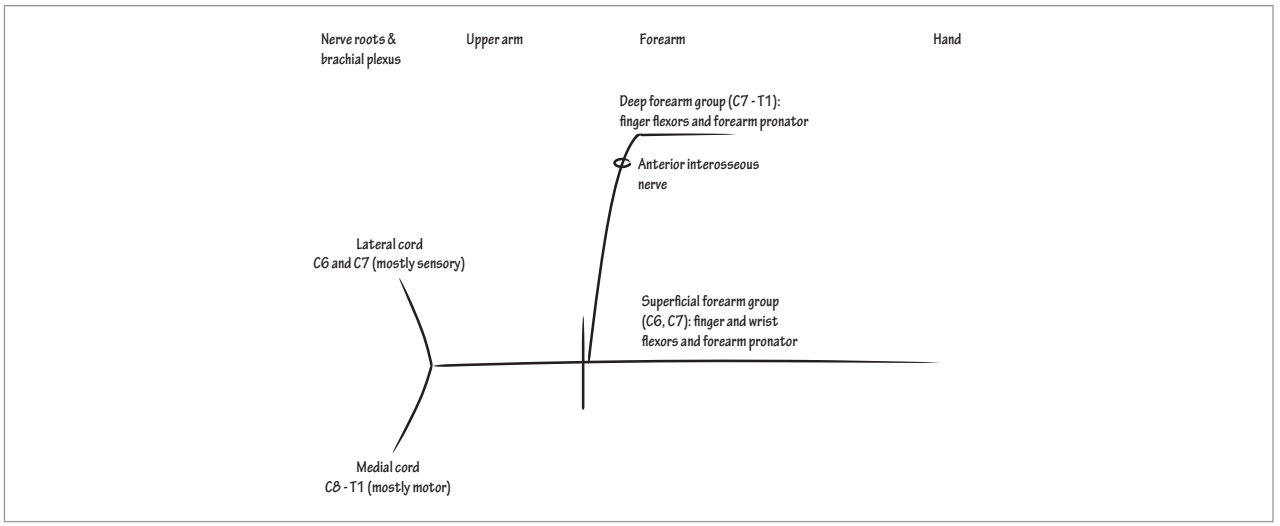


Figure 6-2 Incomplete median nerve

Next, at the distal end of the forearm segment of the median nerve, draw the *palmar cutaneous nerve* sensory branch. Note, its take-off is proximal to where the median nerve passes through the carpal tunnel in the wrist, as this will be discussed later.

Now, draw the median nerve as it passes into the hand. The *recurrent motor branch of the thumb* originates in the proximal hand. It supplies the median-innervated *thenar group* (*C8*, *T1*), which comprises *abductor pollicus brevis* (*APB*), *opponens pollicus* (*OP*), and *flexor pollicus brevis* (*FPB*). Abductor pollicus brevis is an important but often misunderstood muscle. To demonstrate the action of this muscle, place the back of your hand down on a flat surface and raise your thumb toward the ceiling. Abductor pollicus brevis provides for thumb abduction perpendicular to the plane of the palm. In contradistinction, the radially-innervated abductor pollicus longus abducts the thumb in the plane of the palm.

Next, stretch your thumb across your palm and touch the tip of your little finger to demonstrate the action of the opponens pollicis muscle. While the median nerve provides thumb opposition, the ulnar nerve provides opposition of the little finger.

To demonstrate the action of flexor pollicus brevis, which provides flexion of the thumb at the metacarpal–phalangeal joint, flex your thumb against your palm. The ulnar nerve also contributes to the innervation of this muscle. As discussed in the anterior interosseous-innervated deep forearm muscle group section, flexor pollicus *longus* provides flexion of the thumb at the distal interphalangeal joint.

The most distal motor group the median nerve innervates is the *terminal motor group*, which comprises the *first* and *second lumbricals*. To demonstrate the action of these muscles, extend the proximal interphalangeal joints of your index and middle fingers against resistance while you flex the index and middle fingers at the metacarpal–phalangeal joints.

To recap the role of the median nerve in the hand, it innervates muscles of the recurrent motor branch and terminal motor group. The recurrent motor branch of the thumb provides thumb abduction perpendicular to the plane of the palm, thumb opposition to the little finger, and thumb flexion across the palm. The terminal motor group innervates the 1st and 2nd lumbricals, which provide extension of the index and middle fingers at the proximal interphalangeal joints.

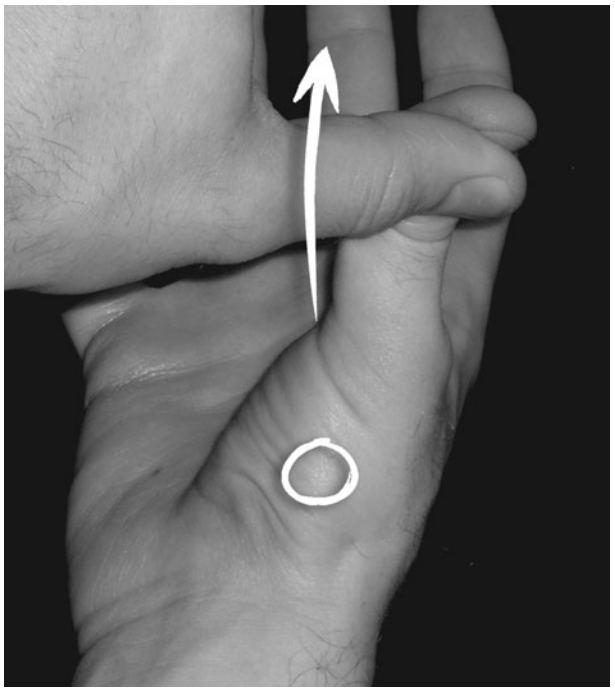


Photo 6-7 Abductor pollicus brevis

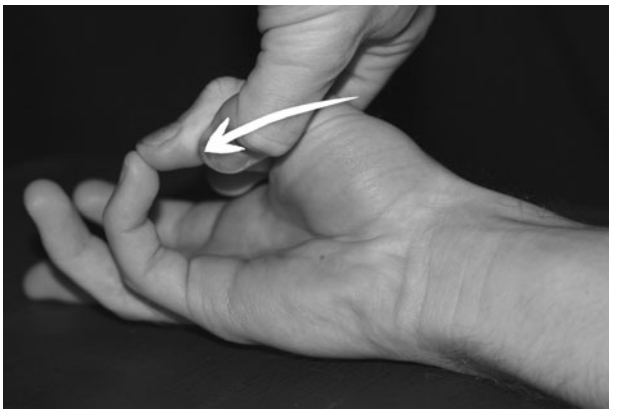


Photo 6-8 Opponens pollicus

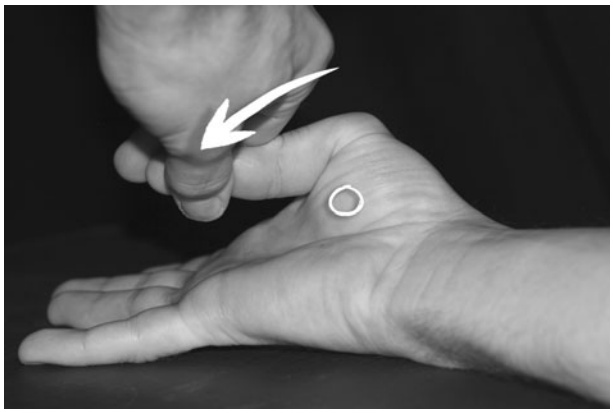


Photo 6-9 Flexor pollicus brevis

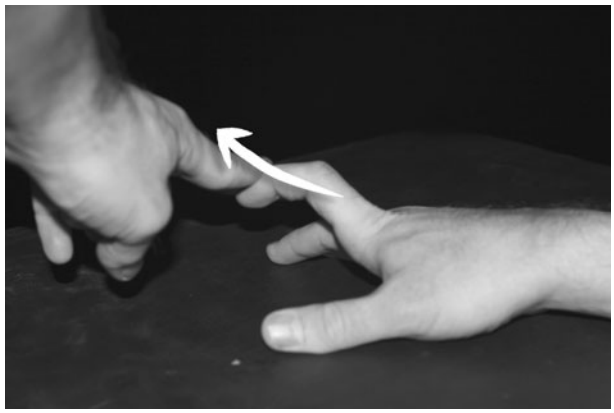


Photo 6-10 Second lumbrical

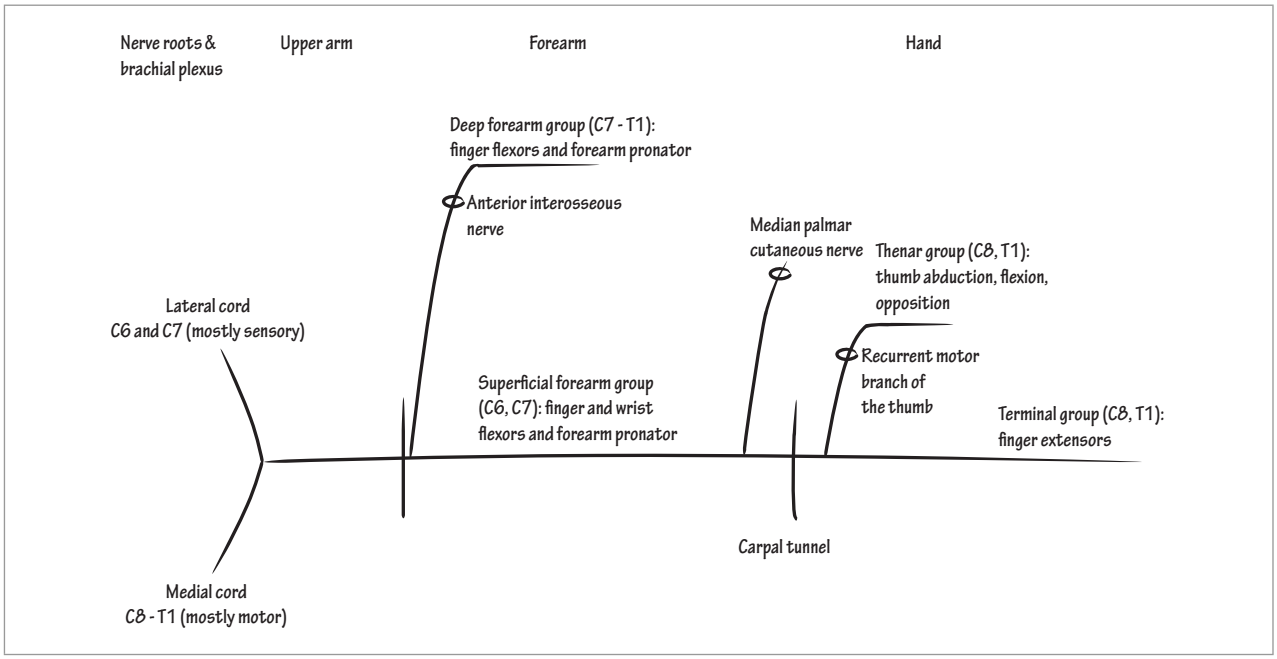


Figure 6-3 Complete median nerve

We have now completed the diagram for motor innervation of the median nerve. On a separate sheet of paper, trace your hands palm-up and palm-down so that we will be able to map the ventral and dorsal sensory coverage of the median nerve. On the palm-up tracing (i.e., ventral side), square off a section on the ball of the thumb to indicate the sensory coverage of the *palmar cutaneous nerve*. Remember, as discussed earlier, the take-off of this sensory nerve branch is proximal to the entry of the median nerve into the carpal tunnel and, therefore, carpal tunnel entrapment of the median nerve does not affect it. In this same drawing, draw a line down the middle of the fourth digit and continue it to the wrist. To indicate the *primary sensory coverage of the median nerve*, shade everything lateral to the lateral ring finger except for the ball of the thumb (lateral half of the ring finger, middle and index fingers, and the thumb). This coverage is specifically named the *radial and ulnar divisions of the median nerve*. Show the median dorsal sensory coverage of the dorsal tips of the thumb, index and middle fingers, and lateral half of the ring finger on the palm-down tracing.

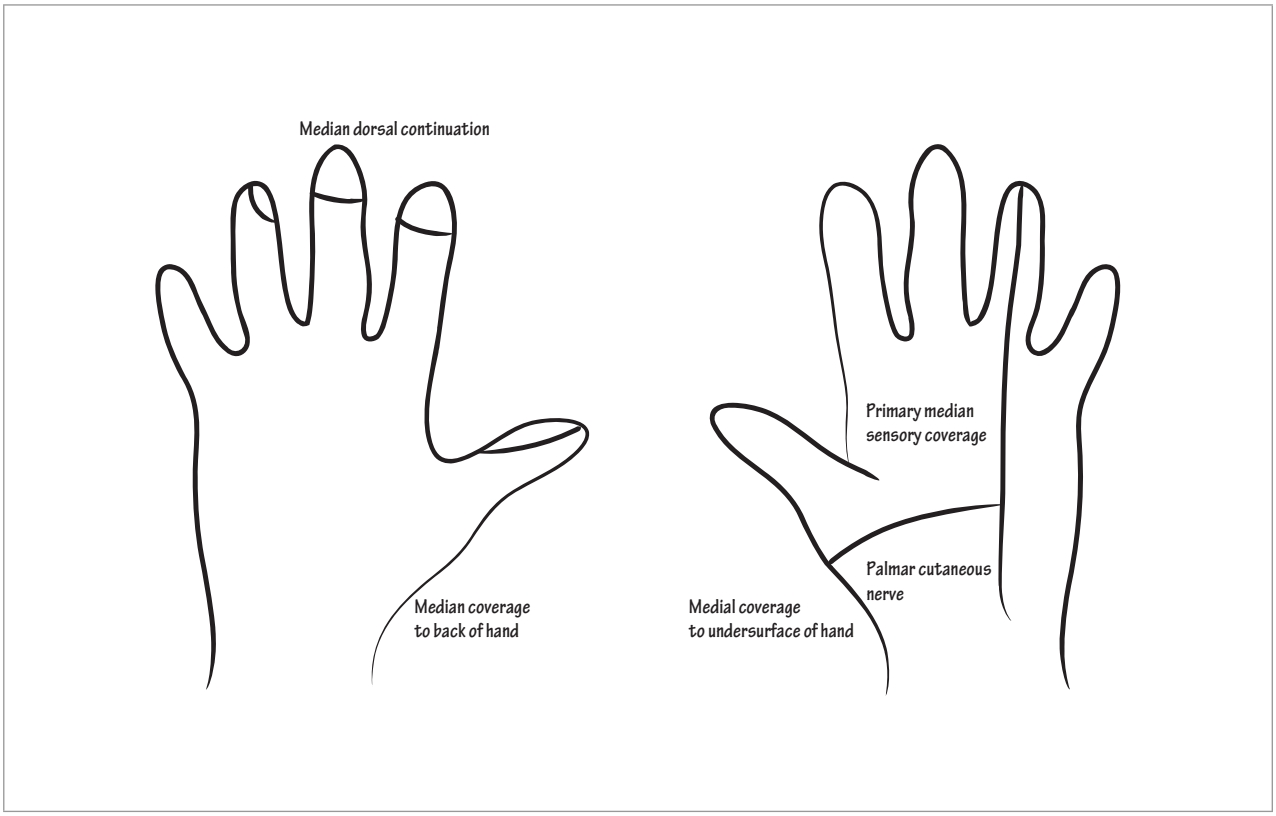


Figure 6-4 Median sensory coverage

Ulnar Nerve

THE C7–T1 NERVE ROOTS of the medial cord of the brachial plexus supply the ulnar nerve. It provides ulnar (medial)-deviated wrist flexion, thumb adduction, finger spread and closure, and the primary flexor and extensor movements of the fourth and fifth digits. The ulnar nerve provides sensory coverage to the palmar and dorsal aspects of the medial third of the hand, medial half of the ring finger, and little finger. Just proximal to the formation of the ulnar nerve, the medial cord supplies the *medial cutaneous nerve of the arm* (aka *medial brachial cutaneous nerve*) and the *medial cutaneous nerve of the forearm* (aka *medial antebrachial cutaneous nerve*), which provide sensory coverage to the medial upper arm and forearm, respectively.

To trace the course of the ulnar nerve in your own upper extremity, first find its origination site deep to the pectoralis major muscle a few fingerbreadths below the clavicle. Then try to palpate the pulsating brachial artery in the neurovascular bundle of your proximal upper arm between the biceps and triceps muscles as you did for the median nerve. While the median nerve lies just lateral to the brachial artery, the ulnar nerve lies just medial to it (remember medial is toward the body with the arm in supination). And while the median nerve continues down the midline of the upper arm within the neurovascular bundle, the ulnar nerve, instead, passes deep to the triceps muscle and tracks down the medial aspect of the upper arm. Trace its path down the ventral side of the medial upper arm and through the ulnar groove in the elbow (aka postcondylar groove) into the forearm. The medial epicondyle of the humerus and the olecranon of the ulna form the ulnar groove. These structures are the bony prominences on the medial side of the elbow that you palpated in our discussion of the median nerve. The olecranon of the ulna sits on the back of your arm; the medial epicondyle lies above it.

Flex and extend your elbow. If you feel the cord-like ulnar nerve snap in and out of the groove, you are in the minority of people who lack a significant aponeurosis covering. Aponeurotic tissue over the ulnar nerve protects it against external trauma but causes compression of the nerve, itself, with repeated elbow flexion and extension. The ulnar groove is the first of two significant compression sites of the ulnar nerve at the elbow. The second is just distal to the ulnar groove in the proximal forearm along the antero-medial ulna in the cubital tunnel. In the cubital tunnel, the ulnar nerve passes underneath a fibrous web that connects the two heads of the flexor carpi ulnaris (FCU) muscle.

Continue to trace the ulnar nerve down your forearm along the antero-medial ulna and across your medial wrist. While the median nerve crosses the wrist through midline in the carpal tunnel, the ulnar nerve, instead, crosses through the medially situated Guyon's canal (aka Guyon's tunnel). It enters the canal lateral to the pisiform bone, the bony prominence you can palpate on the ventro-medial aspect of your wrist. Tap over the nerve just lateral to the pisiform bone to reproduce symptoms of ulnar nerve entrapment at the wrist as you did with the carpal tunnel for the median nerve.

Begin the ulnar nerve diagram like that for the median nerve. Label the top of the page from left to right as follows: nerve roots and brachial plexus, upper arm, forearm, and hand. Indicate the ulnar

nerve is formed from the *medial cord* of the brachial plexus, which the *C8–T1* roots of the lower trunk supply. The C8–T1 nerve roots supply all of the ulnar-innervated nerves so we do not have to further specify the nerve root supply of the different groups. Occasionally, the ulnar nerve is also supplied by C7 through an uncommon anatomic variation where the lateral cord connects to the ulnar nerve but this is unnecessary for us to include in our diagram.

Along the medial cord, include the *medial cutaneous nerve to the arm* (aka *medial brachial cutaneous nerve*) and the medial cutaneous nerve to the forearm (aka *medial antebrachial cutaneous nerve*); they provide sensory coverage to the undersurface of the arm and forearm, respectively.

Like the median nerve, the ulnar nerve lacks motor innervation or sensory coverage to the upper arm, so continue your line directly through it to the forearm.

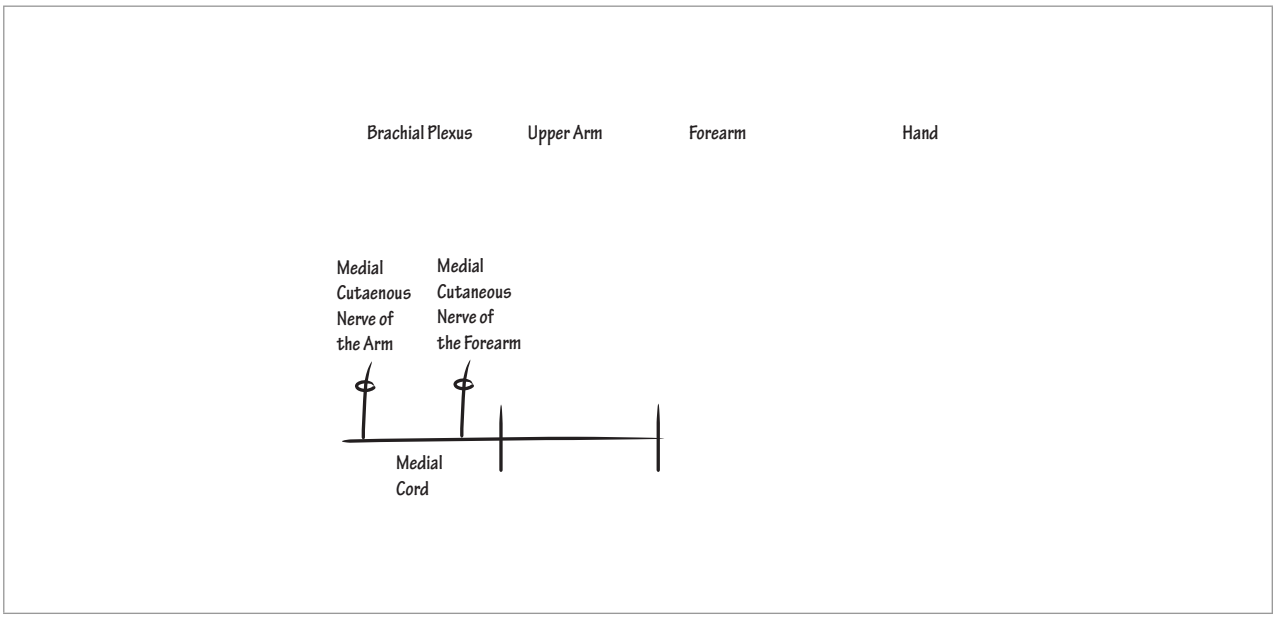


Figure 7-1 Incomplete ulnar nerve

In the forearm, label the *ulnar forearm muscle group*; it comprises *flexor carpi ulnaris* (*FCU*) and *flexor digitorum profundus 4 and 5* (*FDP 4 and 5*). With your arm supinated, flex and angle your wrist in the direction of the ulna (in adduction) to demonstrate the action of flexor carpi ulnaris. Flexor carpi ulnaris provides ulnar-deviated wrist flexion, whereas the median-innervated flexor carpi radialis provides radial-deviated wrist flexion. Next, flex your fourth and fifth digits at their distal interphalangeal joints while immobilizing their proximal interphalangeal joints to demonstrate the action of flexor digitorum profundus 4 and 5. This action is analogous to that which the median-innervated flexor digitorum profundus provides for digits 2 and 3.

To recap, the ulnar forearm muscle group provides ulnar-deviated wrist flexion and 4th and 5th digit flexion at the distal interphalangeal joints.

Similar to the median nerve, which gives off the palmar cutaneous sensory nerve before it enters the carpal tunnel, the ulnar nerve produces two sensory nerves before it crosses through Guyon's canal and passes into the hand: the *palmar ulnar cutaneous nerve* and the *dorsal ulnar cutaneous nerve*. We will map their sensory coverage once we complete our diagram of the motor groups of the ulnar nerve.

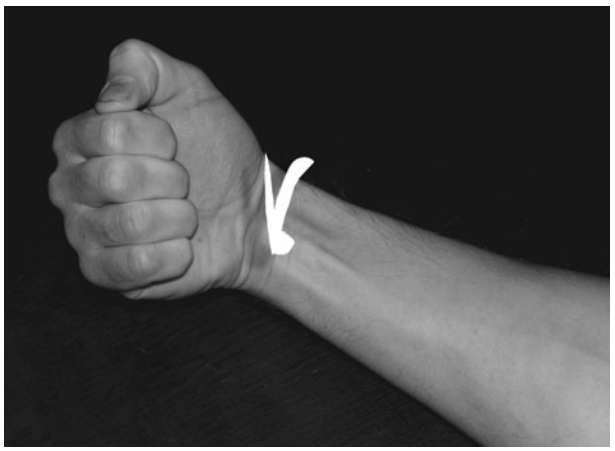


Photo 7-1 Flexor carpi ulnaris

As the ulnar nerve enters the hand, show it divide into the *superficial sensory* and *deep motor divisions*. The superficial sensory division is mostly a sensory nerve, but indicate it also provides motor innervation to *palmaris brevis*. Forcibly spread out your fifth digit and contract your hypothenar eminence to demonstrate the action of palmaris brevis; it causes skin corrugation of the hypothenar eminence. Recall that when the median-innervated palmaris longus muscle activates during wrist flexion, its tendon appears in midline and the skin over the wrist corrugates.

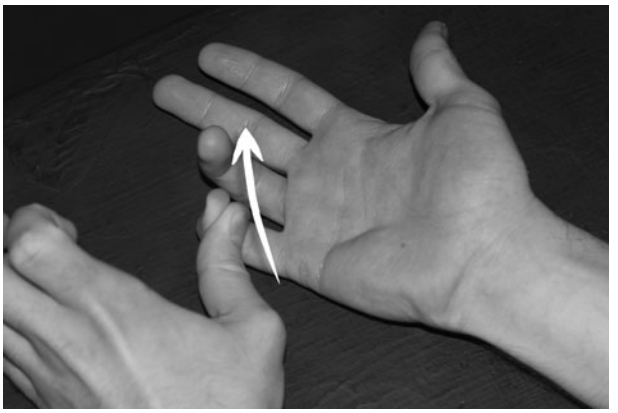


Photo 7-2 Flexor digitorum profundus 4 & 5

Photo 7-3 Palmaris brevis muscle

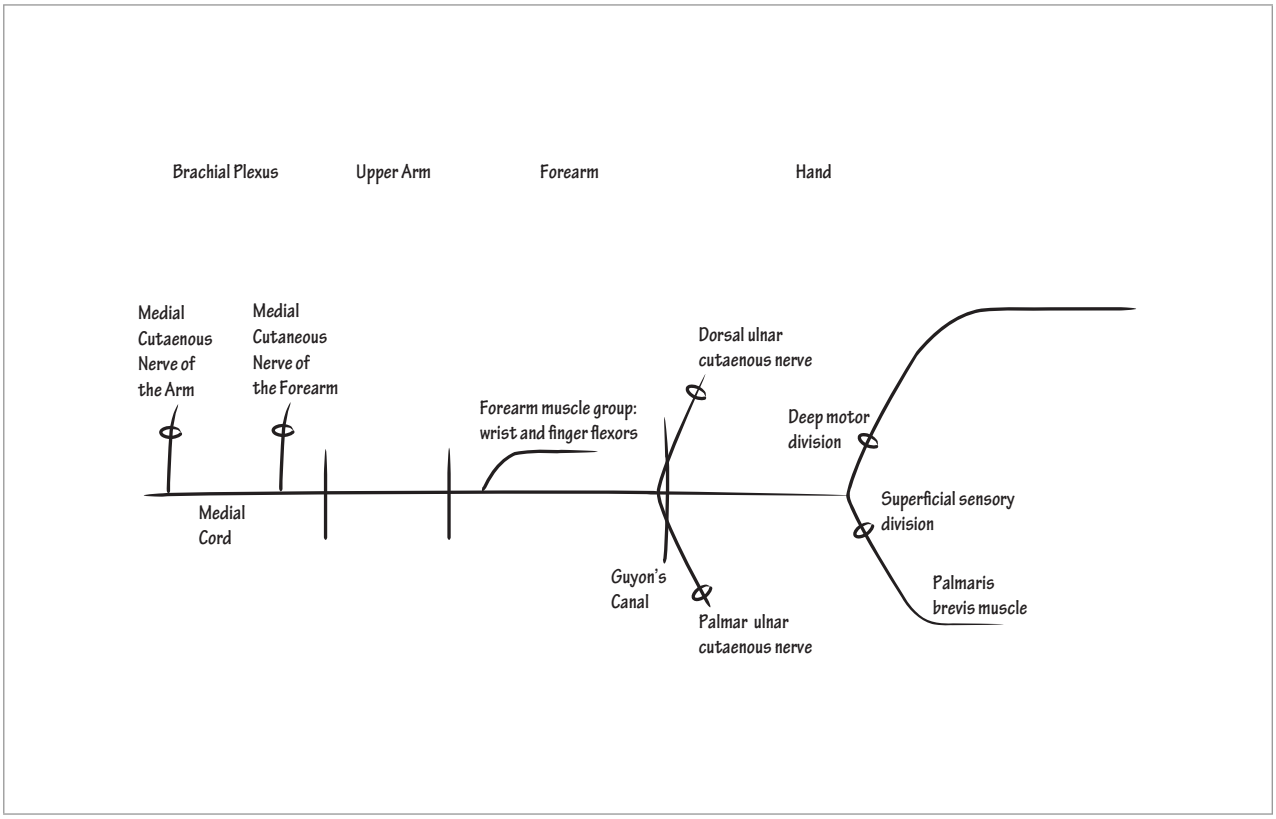


Figure 7-2 Incomplete ulnar nerve

Now, let's address the deep ulnar motor division; indicate that it splits into two different branches that course in opposite directions, one superiorly and the other inferiorly. Indicate the inferior branch innervates the muscles of *hypothenar muscle group*, which comprises *abductor digiti minimi* (*ADM*), *flexor digiti minimi* (*FDM*), and *opponens digiti minimi* (*ODM*). Demonstrate the actions of each of these muscles in succession: spread out your little finger in the plane of your palm to demonstrate abductor digiti minimi, flex your little finger against your palm to demonstrate flexor digiti minimi, and then oppose your little finger against your thumb to demonstrate opponens digiti minimi. The fourth lumbrical muscle, which we will soon discuss, also contributes to flexion of the fifth digit, so fifth digit flexion is not purely due to flexor digiti minimi.

In short, the superficial sensory branch and inferior division of the deep motor branch of the ulnar nerve supply the hypothenar muscles after they pass through Guyon's tunnel. They corrugate the skin over the hypothenar eminence, spread out and flex digit 5, and oppose it against the thumb.

Now, let's address the branch of the deep motor division of the ulnar nerve that courses superiorly. The first muscle group it innervates is the *hand intrinsic muscle group*, which consists of the *lumbricals 3 and 4* (*L3 and 4*), *dorsal interossei* (*DI*), and *palmar interossei* (*PI*) muscles. To demonstrate the action of lumbricals 3 and 4, extend the proximal interphalangeal joints of digits 4 and 5 against resistance with your hand palm down. To mimic the *claw hand* or *benediction posture* that results from lumbrical 3 and 4 weakness, keep your wrist and metacarpal-phalangeal joints extended but flex digits 4 and 5 at the proximal interphalangeal joints.

To use your dorsal interossei muscles, simply spread your fingers widely apart against resistance. And to use your palmar interossei muscles, bring them back together against resistance. Only digits 2, 4, and 5 have interosseous muscles. To mimic third palmar interosseous muscle weakness, called *Wartenberg sign*, let your fifth digit passively abduct (spread out).

In short, the hand intrinsic muscle group provides finger spread and closure and digit 4 and 5 proximal interphalangeal joint extension.

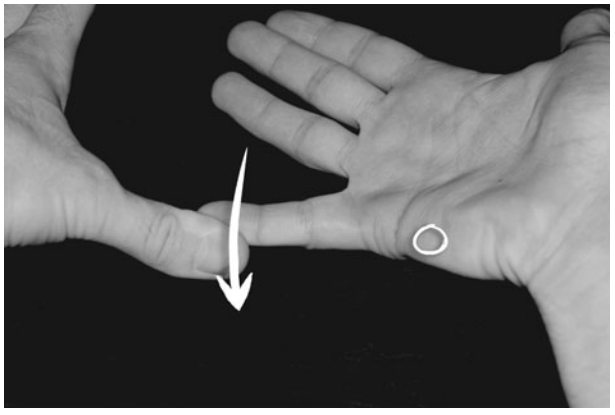


Photo 7-4 Abductor digiti minimi muscle

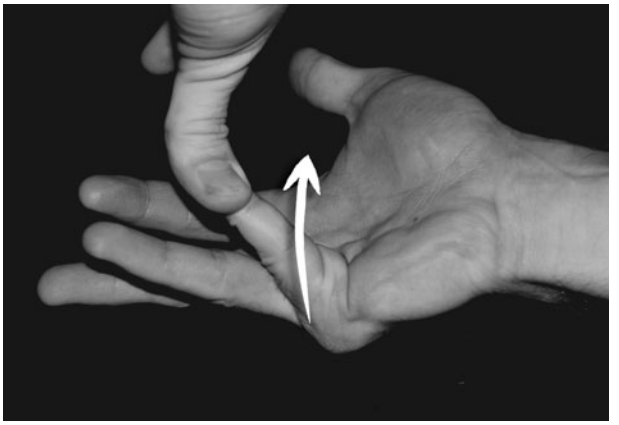


Photo 7-5 Flexor digiti minimi muscle

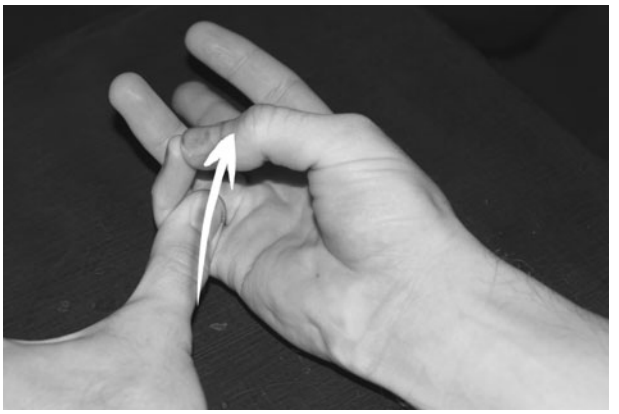


Photo 7-6 Opponens digiti minimi muscle

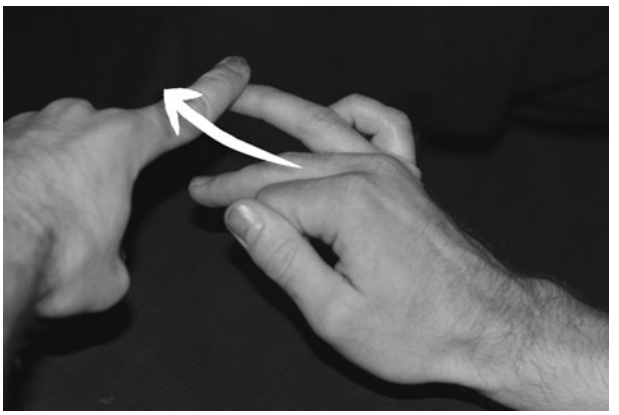


Photo 7-7 Lumbrical muscles 3 & 4

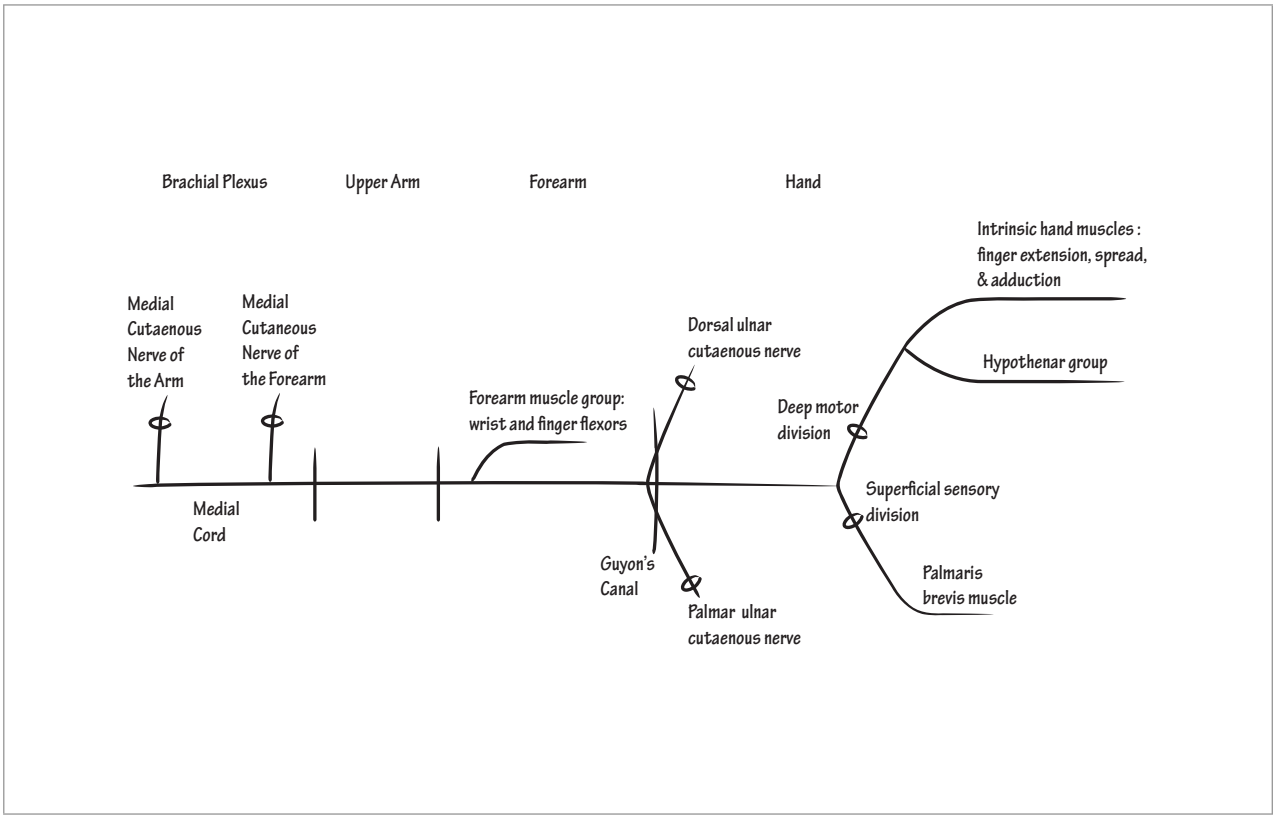


Figure 7-3 Incomplete ulnar nerve

The last ulnar-innervated muscle group we need to include is the ulnar-innervated *thenar group*, which comprises the *flexor pollicis brevis* (*FPB*) and *adductor pollicis* (*AP*) muscles. Both the median and ulnar nerves innervate the flexor pollicis brevis muscle. To review its action, flex your thumb across your palm against resistance.

Next, to demonstrate the action of adductor pollicis, straighten your thumb and tighten it against the side of your palm. This movement opposes the radially-innervated abductor pollicis longus action, which abducts the thumb in the plane of the palm. Recall, the median nerve innervates abductor pollicis brevis, which abducts the thumb in perpendicular to the plane of the palm. We are able to test all three nerves with just the thumb.

There are two variations of a physical exam sign called *Froment's sign*, which distinguishes ulnar-innervated adductor pollicis longus weakness from median nerve (anterior interosseous branch) flexor pollicis longus weakness. One variation is the *okay* sign. Make an okay sign with the distal tips of your index finger and thumb. If the volar pads rather than the fingertips touch (i.e., if the thumb remains extended at the interphalangeal joint), then there is flexor pollicis longus weakness. The other variation of the test is to hold a piece of paper between your thumb and the side of your index finger and try to prevent it from being pulled out of your grasp. The adductor pollicis should do the work, so if you rely on flexion of the thumb at the interphalangeal joint (i.e., if it flexes), the adductor pollicis muscle is weak.

To recap, the ulnar-innervated thenar group contributes to flexion of the thumb across the palm and tightens the thumb against the side of the palm.

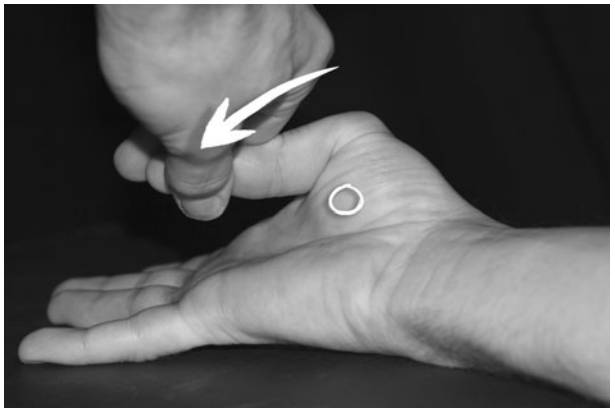


Photo 7-8 Flexor pollicis brevis muscle

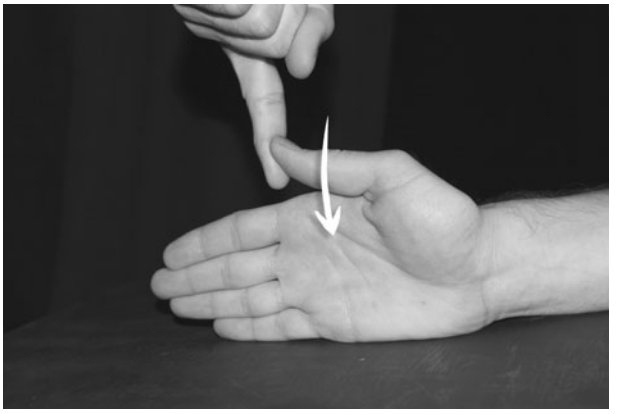


Photo 7-9 Adductor pollicis muscle

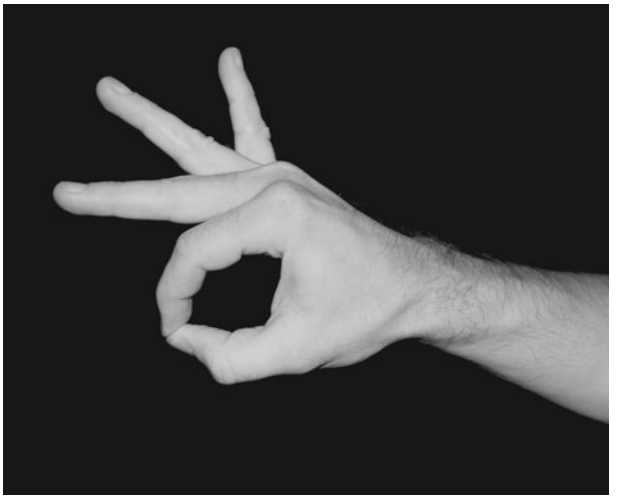


Photo 7-10 Okay sign

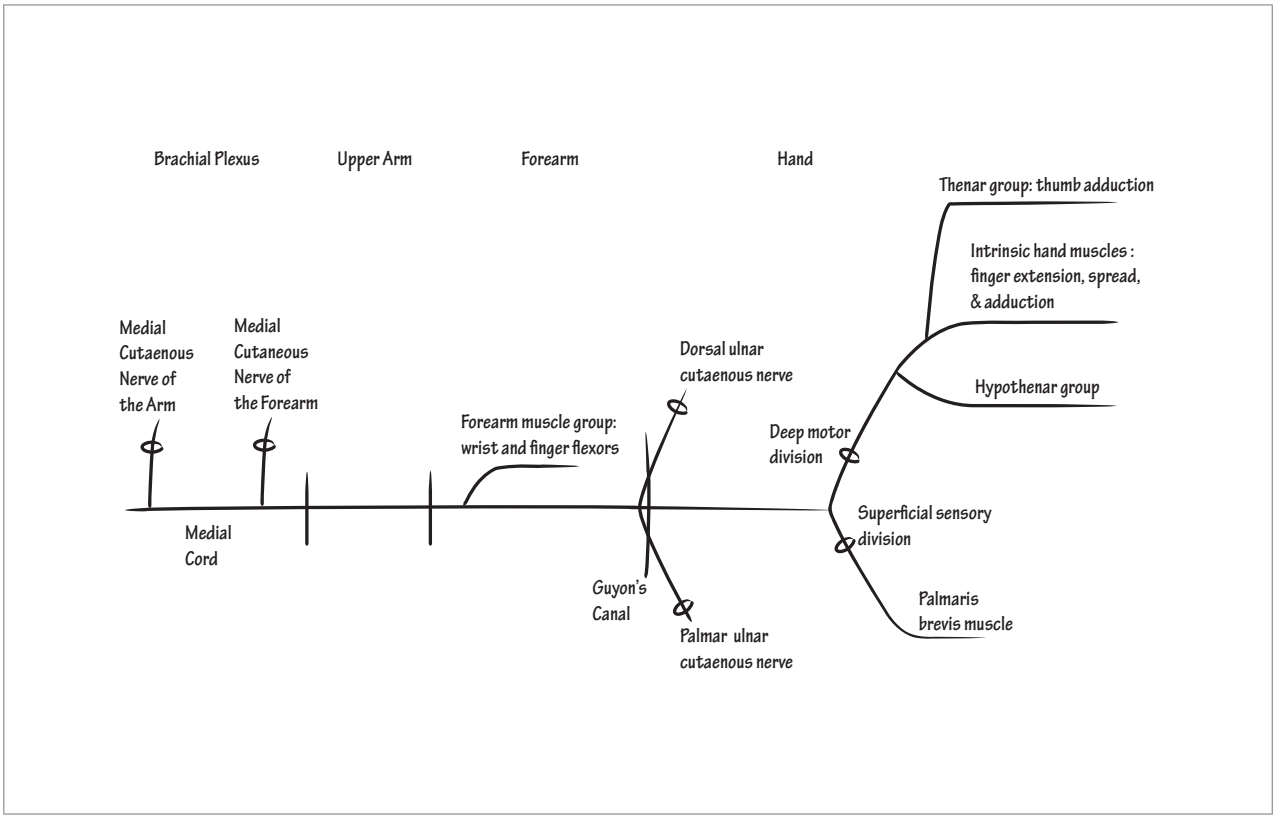


Figure 7-4 Complete ulnar nerve

Now, let's turn our attention to the sensory coverage of the ulnar nerve. To do so, trace your hand palm up and down as you did with the median nerve. We will show the ulnar nerve provides sensory coverage to the medial one-third of the hand: specifically, the medial one-half of the fourth digit, the entire fifth digit, and the medial one-third of the ventral palm and dorsal hand. This is nearly all you need to know about the sensory innervation of the ulnar nerve. However, also remember that both the dorsal ulnar cutaneous nerve and the palmar ulnar cutaneous nerve branch from the ulnar nerve before it passes through Guyon's canal, whereas the superficial sensory division of the ulnar nerve originates after the ulnar nerve passes through Guyon's canal. A lesion within Guyon's canal will affect the superficial sensory division, but the dorsal ulnar cutaneous and palmar ulnar cutaneous nerves will be unaffected.

Now, let's draw the sensory maps. On the palm-up tracing, show the *palmar ulnar cutaneous nerve* covers the hypothenar eminence (similar to the palmar median cutaneous nerve, which covers the thenar eminence) and the *superficial sensory division of the ulnar nerve* covers the remaining ulnar distribution—the medial half of the fourth digit and the fifth digit back to the hypothenar eminence.

Next, on the palm-down tracing, show the *dorsal ulnar cutaneous nerve* covers the medial one-third of the dorsal surface of the hand, including the medial half of the fourth digit and fifth digit. Technically, the superficial sensory division continues to the dorsal tips of the digits, but we leave this out for simplicity.

Now that we have drawn the typical innervation patterns of the median and ulnar nerves, it is worth mentioning a couple of important anatomical variants. The first is the *Martin-Gruber* anastomosis, which is a connection between either the median nerve or the anterior interosseous nerve in the forearm and the ulnar nerve. The second is the *Riche-Cannieu* anastomosis, which is a connection between the median nerve branch to the thenar muscle group and the ulnar nerve deep motor division, which supplies the hypothenar group, the thenar group, and the intrinsic hand muscles. These connections allow for crosstalk between the nerves. Roughly 15% of the population has one of these anastomoses; keep them in mind when the exam findings fail to make sense.

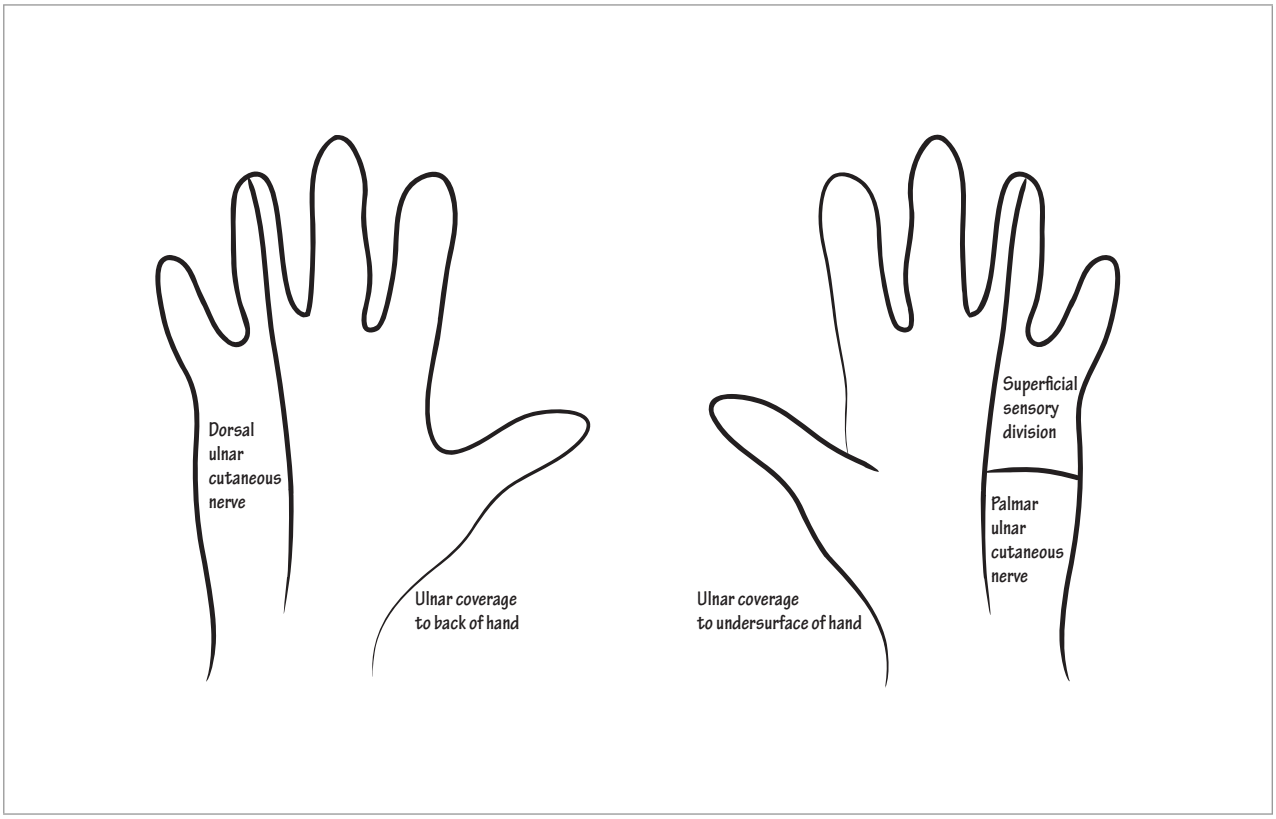


Figure 7-5 Ulnar sensory coverage

Radial Nerve

THE RADIAL NERVE originates from the posterior cord of the brachial plexus and the C5–C8 nerve roots supply it. It provides forearm extension and supination, wrist extension, abduction of the thumb in the plane of the palm, and extension of the digits at their metacarpal–phalangeal joints. Simply put, it is the primary extensor innervator in the upper extremity. From a sensory standpoint, the radial nerve is responsible for coverage of the midline posterior arm and forearm and the dorsal surface of the lateral half of the hand and proximal lateral three and a half digits (remember, in anatomic position, the arm is supinated and the thumb is directed away from the body so the lateral three digits are the thumb, index and middle fingers, and lateral half of the ring finger). The median nerve covers the dorsal tips and ventral surfaces of those digits.

To understand the course of the radial nerve, first palpate its origination at the termination of the posterior cord deep to the pectoralis major muscle, a few fingerbreadths below the clavicle. An injury to the radial nerve, here, as from underarm compression from crutches, will cause total radial nerve palsy. The axillary nerve-innervated deltoid and thoracodorsal nerve-innervated latissimus dorsi muscles will be unaffected because they originate from the posterior cord proximal to the radial nerve.

The radial nerve originates in close proximity to the median and ulnar nerves in the anterior aspect of the upper arm. It quickly passes posteriorly and winds itself around the back of the humerus in the spiral groove. Hold your arm out to the side and palpate its course posteriorly through the triceps and then trace it around the humerus in the spiral groove.

Before entering the spiral groove, the radial nerve gives off the posterior cutaneous nerve of the arm, which provides sensory coverage to the posterior aspect of the forearm. Within the spiral groove, the radial nerve passes between the medial and lateral heads of the triceps. An injury in the spiral groove, such as in Saturday night palsy, affects muscles distal to the triceps but spares the triceps and the posterior cutaneous nerve of the arm because the branches to the triceps and the posterior cutaneous nerve of the arm originate proximal to the spiral groove.

Continue to trace the course of the radial nerve down the remainder of the posterior aspect of your upper arm and across your elbow. As the radial nerve enters the forearm, it divides into two different nerves. One of these nerves is the posterior interosseous nerve, which primarily innervates motor extensors of the wrist, thumb, and digits. The other is the superficial radial sensory nerve, which provides sensory coverage to the dorsal surface of the lateral half of the hand and proximal lateral three and a half digits. Trace the posterior interosseous and superficial radial sensory nerves down the posterior aspect of your forearm and continue the superficial radial nerve across your wrist to the dorsolateral half of your hand.

Begin the diagram of the radial nerve as we did for the median and ulnar nerves. Across the top of the page, label: nerve roots & brachial plexus, upper arm, forearm, and hand. Under the brachial plexus, label the *posterior cord* and indicate it is derived from the *C5–8 nerve roots*. Indicate the *axillary nerve* (*C5*, *C6*) originates from the posterior cord and innervates the *deltoid muscle*. Abduct your arm to demonstrate its action.

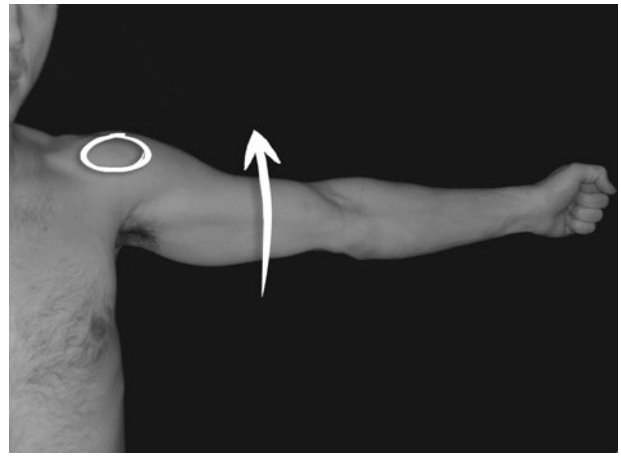


Photo 8-1 Deltoid muscle

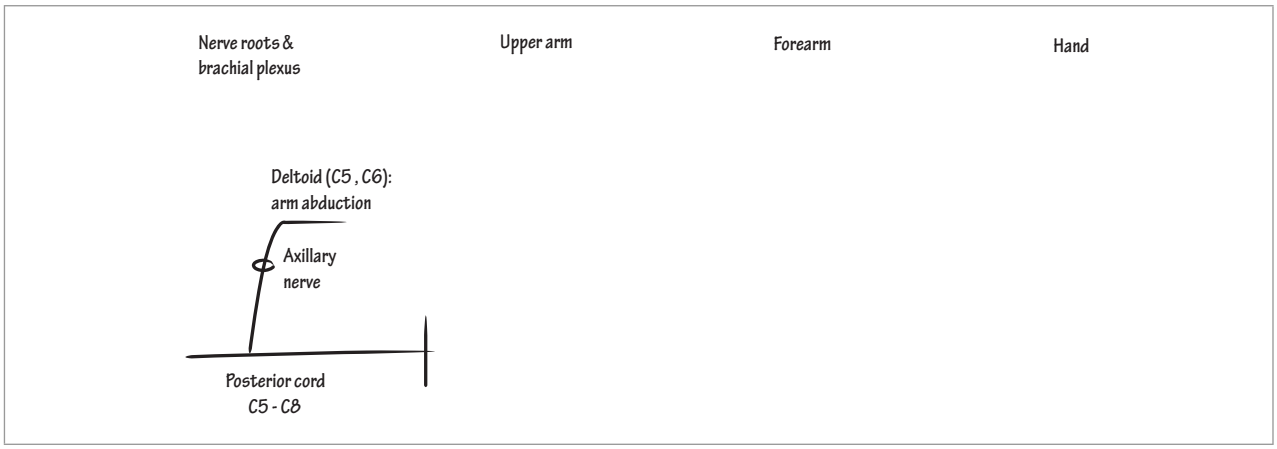


Figure 8-1 Incomplete radial nerve

Now, continue the line into the upper arm. Unlike the median and ulnar nerves, the radial nerve has a few important motor and sensory branches in the upper arm. First, let's show the motor branch. Along the radial nerve, label the *triceps muscle* (*C6–C8*). To demonstrate the action of the triceps muscle, extend your forearm at the elbow against resistance. This muscle has the opposite action of the musculocutaneous-innervated biceps brachialis muscle, which provides elbow flexion.

Next, let's show its proximal sensory branches. Indicate the *posterior cutaneous nerve* to the arm originates proximal to the origination of the triceps and the *lower lateral cutaneous nerve to the arm* originates distal to the triceps but proximal to the spiral groove. These nerves cover the midline posterior arm and forearm and anterior upper arm.

Where the upper arm and forearm meet, label the *lateral epicondyle group* (*C5–C8*), which comprises *brachioradialis* (*C5*, *C6*) (*BR*), *brachialis* (*B*), and *extensor carpi radialis longus* and *brevis* (*ECRL and B*). These muscles attach at the distal upper arm and proximal forearm. To demonstrate the action of brachioradialis, hold your arm at your side, thumb up (in a position midway between pronation and supination), and flex it against resistance. Brachioradialis is one of three forearm flexors. The others are the musculocutaneous nerve-innervated biceps brachii: to demonstrate it, flex your forearm with it supinated; and the musculocutaneous- and radial-innervated *brachialis* muscle, which provides forearm flexion in any position. Now, extend and drive your wrist radially against resistance to demonstrate the action of the extensor carpi radialis longus and brevis muscles. We will soon demonstrate the action of the posterior interosseous nerve innervated extensor carpi ulnaris, which extends and drives the wrist toward the ulna.

To recap, the lateral epicondyle group provides forearm flexion and wrist extension with radial deviation.

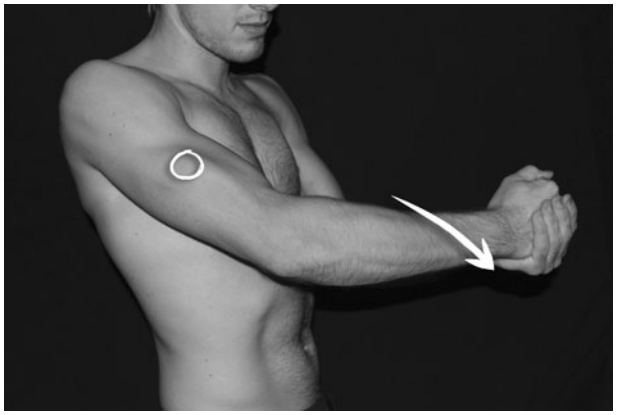


Photo 8-2 Triceps muscle

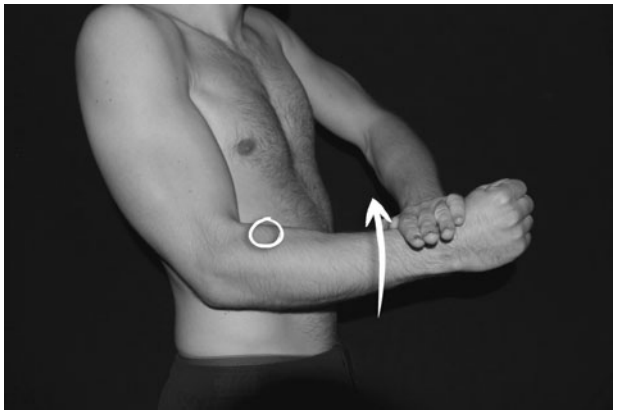


Photo 8-3 Brachioradialis muscle

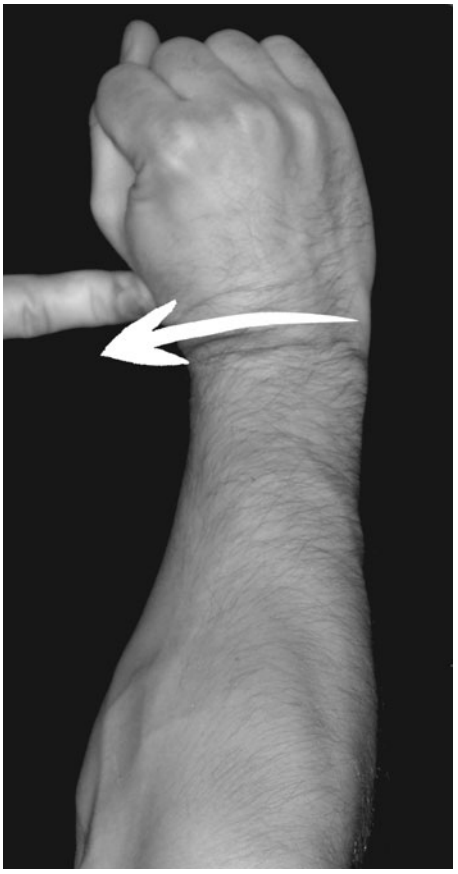


Photo 8-4 Extensor carpi radialis longus muscle

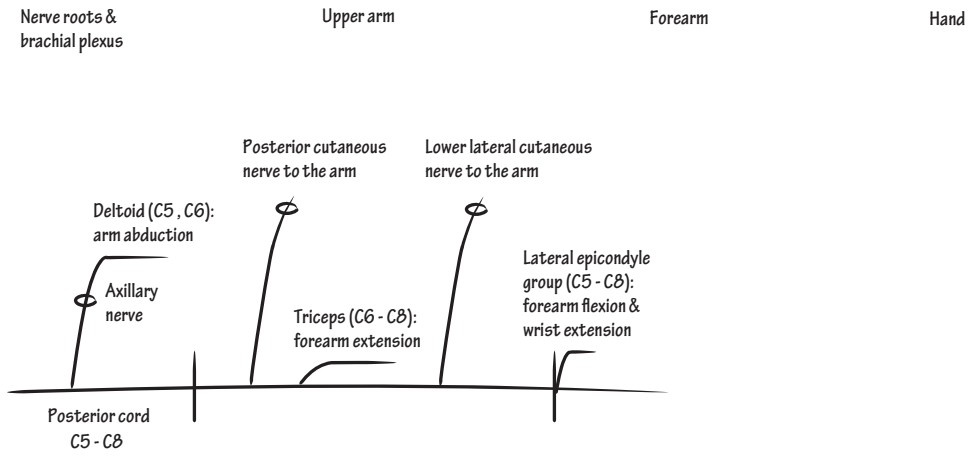


Figure 8-2 Incomplete radial nerve

Now, split the radial nerve into the posterior interosseus nerve and the superficial radial sensory nerve. In the proximal segment of the posterior interosseus nerve, indicate the *supinator* (*C6*, *C7*) (*S*). To demonstrate its action, simply rotate your forearm outward against resistance. Remember, in contradistinction, the median nerve innervated pronator teres is the primary pronator of the forearm, and is part of the superficial median forearm group. Indicate that the next, more distal muscle group the posterior interosseus nerve innervates is the *superficial extensor group* (*C7*, *C8*), which comprises *extensor carpi ulnaris* (*ECU*) and *extensor digitorum communis* (*ECU*).

To demonstrate the action of extensor carpi ulnaris, as mentioned above, extend and bend the wrist toward the ulna; this is the opposite movement of the extensor carpi radialis, which provides wrist extension and radial deviation. To demonstrate the action of extensor digitorum communis, extend the third and fourth digits at their metacarpal–phalangeal joints. The word *communis* is Latin for "common," which helps us remember that the extensor digitorum communis helps extend the second and fifth digits, as well; they have additional innervation from *extensor indicis* and *extensor digiti minimi*, respectively.

In short, the posterior interosseous nerve supplies the supinator muscle and the superficial extensor group; together they generate forearm supination, wrist extension with ulnar-deviation, and extension of the second through fifth digits at the metacarpal phalangeal joints through the extensor digitorum communis (with help from the extensor digitorum indicis and extensor digiti minimi).

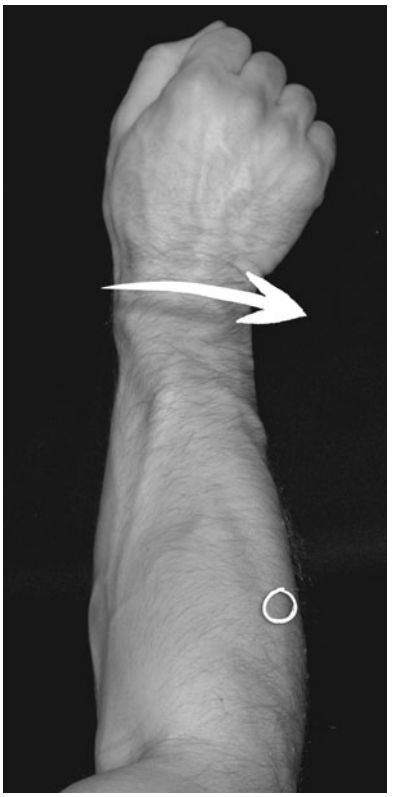


Photo 8-6 Extensor carpi ulnaris muscle

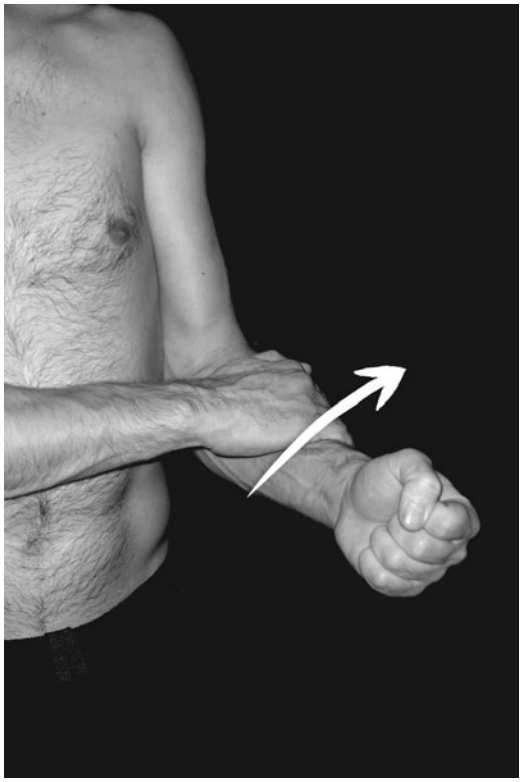


Photo 8-5 Supinator muscle

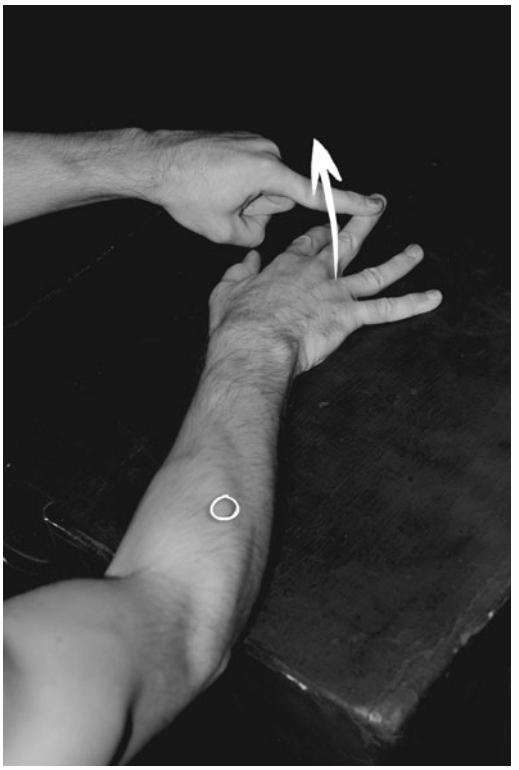


Photo 8-7 Extensor digitorum communis muscle

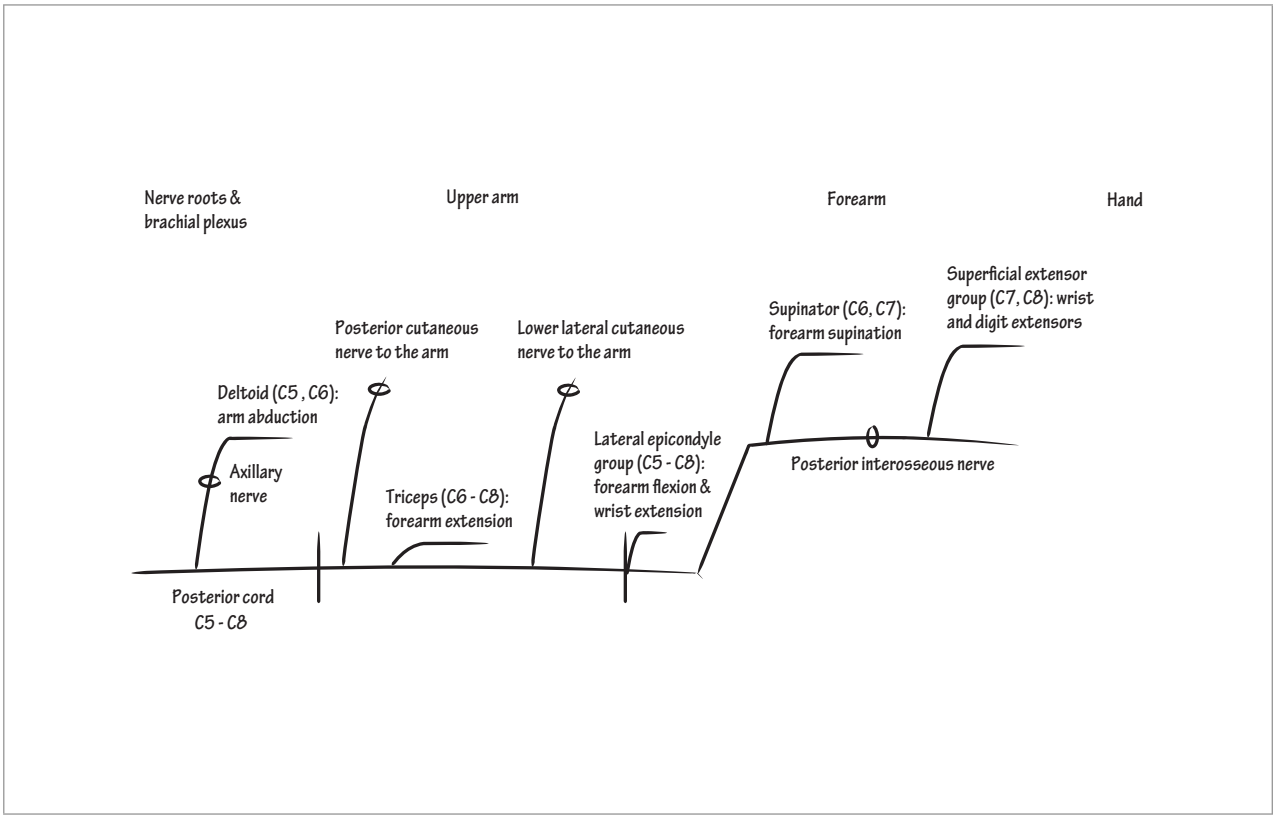


Figure 8-3 Incomplete radial nerve

Next, label the posterior interosseous innervation to the *deep extensor group* (*C7*, *C8*), which comprises *abductor pollicus longus*, *extensor pollicus longus*, and *extensor pollicus brevis*. At this point you may already be able to demonstrate the actions of these muscles without reading anymore. We have already demonstrated the action of abductor pollicus longus in the "Median Nerve" and "Ulnar Nerve" chapters in our discussion of the abductor pollicis brevis and adductor pollicis longus muscles. To remind you, the median nerve innervates abductor pollicus brevis, which provides abduction of the thumb in perpendicular to the plane of the palm, and the ulnar nerve innervates adductor pollicus, which brings the thumb against the lateral edge of the palm. Now, demonstrate that abductor pollicus longus abducts the thumb in the plane of the palm.

Regarding extensor pollicus longus and extensor pollicis brevus, the extensor pollicus brevus tendon is the shorter of the two tendons and attaches to the most proximal joint, the metacarpal phalangeal joint; extend your thumb at the metacarpal phalangeal joint to demonstrate its action. The extensor pollicus longus tendon is the longer of the two tendons and attaches to the proximal interphalangeal joint; extend the proximal interphalangeal joint of your thumb against resistance to demonstrate its action.

To recap, the deep extensor group provides abduction of the thumb in the plane of the palm and extension of the thumb at both the metacarpal and proximal interphalangeal joints.

Now, draw the *superficial sensory radial nerve* through the forearm segment and into the hand. Trace your hand with your palm down. Show the *superficial sensory radial nerve* covers the lateral two-thirds of the dorsum of the hand, the proximal thumb, proximal second and third digits, and proximal lateral one-half of the fourth digit.

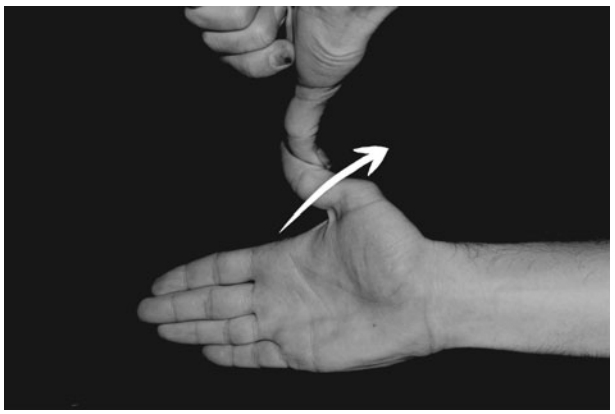


Photo 8-8 Abductor pollicus longus muscle

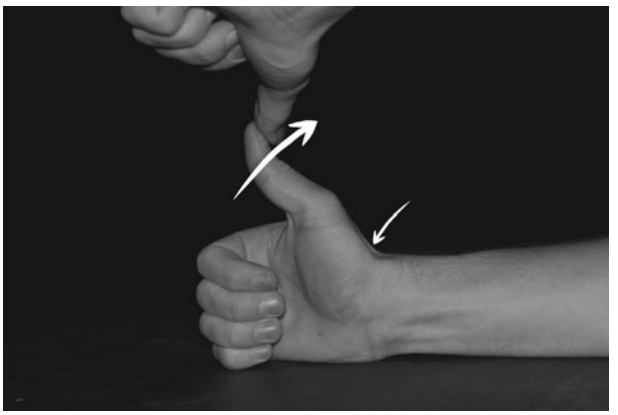


Photo 8-9 Extensor pollicus longus muscle

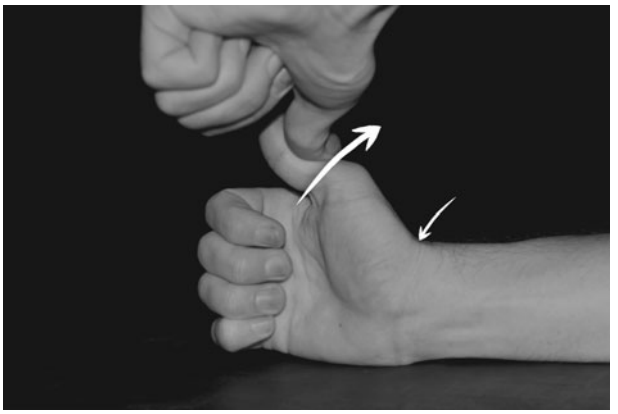


Photo 8-10 Extensor pollicus brevis muscle

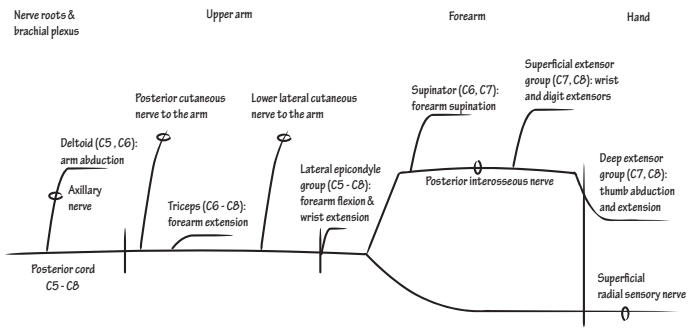


Figure 8-4 Complete radial nerve

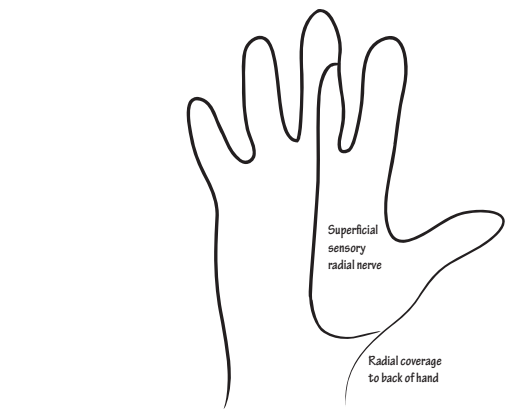


Figure 8-5 Sensory coverage of the radial nerve

Lumbosacral Plexus

THE VENTRAL RAMI of the L1–S4 spinal nerves form the lumbosacral plexus; nine spinal nerves contribute, which makes it a challenge to untangle. Fortunately, though, there are fewer anastomoses in the lumbosacral plexus than in the brachial plexus, so it is easier to understand. Whereas in the brachial plexus there are roots, trunks, divisions, cords, and nerve segments, in the lumbosacral plexus we are limited to roots and nerve segments.

Label the top of the page from left to right as follows: pelvis and hip, thigh, leg, and foot. In this diagram, left is proximal, right is distal, up is superior, and down is inferior. Now, let's draw the nerves of the lumbosacral plexus. We will draw them as horizontal lines that begin from their spinal root and travel varying distances throughout the lower limb.

Begin with the *sciatic nerve*, which the *L4–S3* ventral rami derive. Show it pass through the pelvis and hip and through the posterior thigh. In the distal thigh, indicate the sciatic nerve branches into two separate nerves drawn in parallel: the *peroneal* and *tibial nerves*. These nerves continue through the leg into the foot. During its course, the peroneal nerve wraps around the fibular head into the anterior lower leg, whereas the tibial nerve continues through the posterior lower leg. We will detail these nerves in the following chapter; they supply the entire lower leg and are extremely important. Here, let's focus on the proximal portion of their anatomy where the peroneal and tibial nerves are bundled together within the sciatic nerve.

Within the sciatic nerve, the peroneal and tibial nerves remain as two separate nerves bundled together within a common epineurium, which is the connective tissue that surrounds the nerve bundle. Now, show the ventral rami of *L4–S2* form the peroneal nerve and the ventral rami of *L4–S3* form the tibial nerve. Their spinal nerve supply is identical except that the tibial nerve additionally receives innervation from S3. To remember this, consider the tibial nerve travels a farther distance than the peroneal nerve (it extends underneath the foot) and so it requires additional innervation from a lower spinal segment.

One complicating feature of the lumbosacral plexus is that the majority of its ventral rami separate into anterior and posterior divisions. The separation is clinically irrelevant so if you want to skip ahead, do so; we pause to discuss it here, though, so that we don't confuse these anterior and posterior divisions with the anterior and posterior rami. In order to understand the difference, let's review the anatomy of the spinal nerve roots and rami. The anterior and posterior nerve roots leave the spinal cord and anastomose in the intervertebral foramen as a spinal nerve, which then divides into anterior (aka ventral) and posterior (aka dorsal) rami. Only in the lumbosacral plexus do the anterior rami again divide into anterior and posterior divisions. It is the posterior divisions of L4–S2 that derive the peroneal nerve and the anterior divisions of L4–S3 that form the tibial nerve.

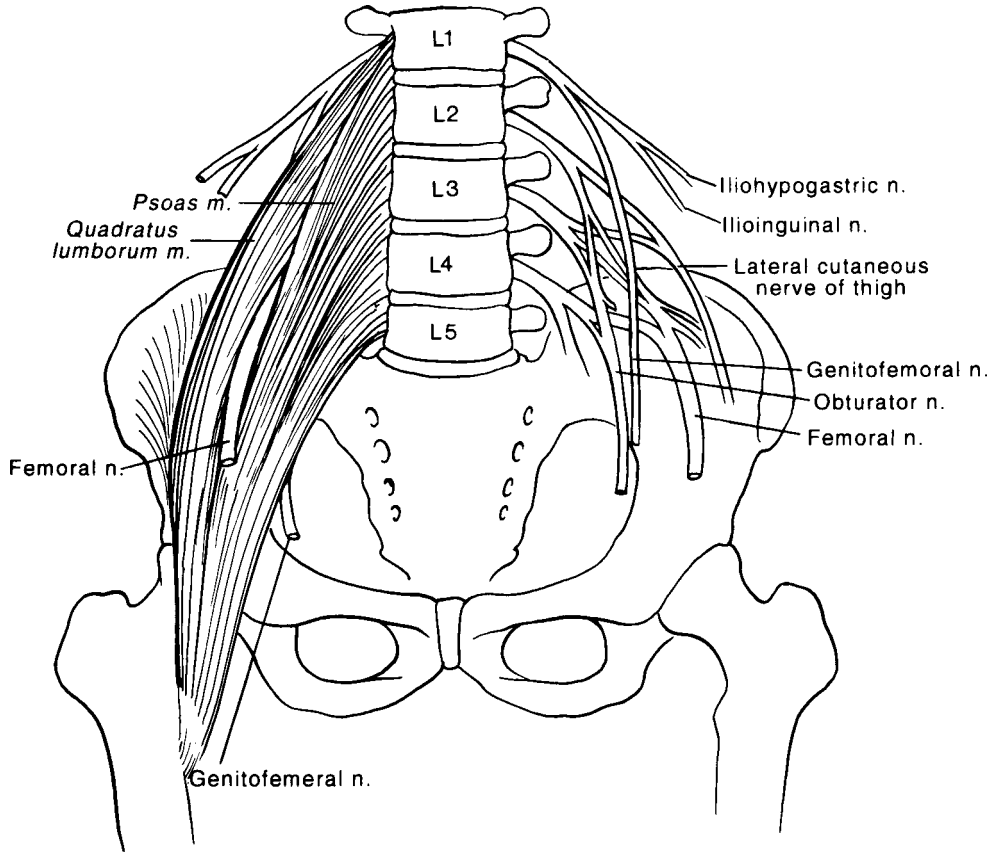


Photo 9-1 The lumbar plexus
With permission from Mendell, J. R., J. T. Kissel, and D. R. Cornblath. *Diagnosis and Management of Peripheral Nerve Disorders*, Contemporary Neurology Series. Oxford: Oxford University Press, 2001.

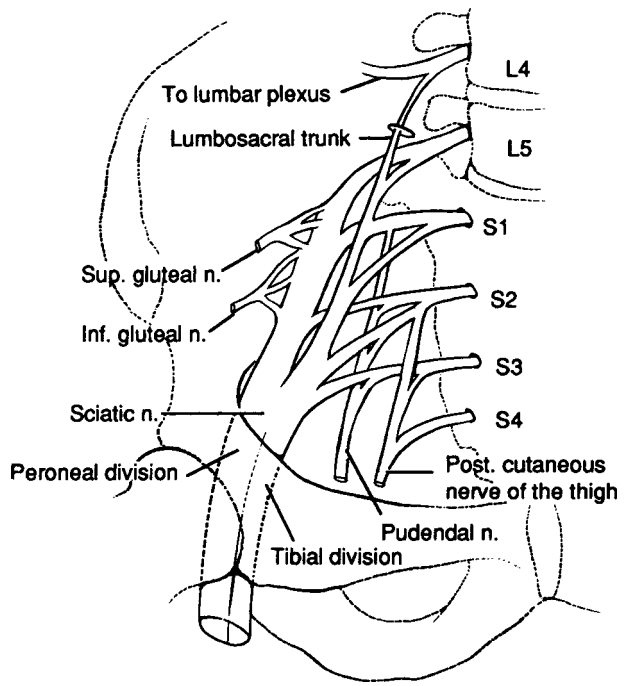


Photo 9-2 The sacral plexus
With permission from Mendell, J. R., J. T. Kissel, and D. R. Cornblath. *Diagnosis and Management of Peripheral Nerve Disorders*, Contemporary Neurology Series. Oxford: Oxford University Press, 2001.

At the same level as the sciatic nerve, draw the *inferior gluteal nerve*, derived from *L5–S2*. Show it terminate in the pelvis and hip. The inferior gluteal nerve innervates *gluteus maximus*, which provides hip extension. One level above it, draw the *superior gluteal nerve*, derived from *L4–S1*; indicate it also terminates in the pelvis and hip. The superior gluteal nerve innervates *gluteus medius*, which provides hip abduction. Palpate the gluteus medius nerve *superiorly*, at the wing of the ilium (along the lateral hip; activate the muscle to feel it), and palpate the gluteus maximus *inferiorly*, down the buttock. This will remind you that the superior gluteal nerve innervates gluteus medius and the inferior gluteal nerve innervates gluteus maximus.

Both the superior and inferior gluteal nerves exit the pelvis through the greater sciatic foramen along with, most notably, the sciatic nerve, posterior femoral cutaneous nerve, and pudendal nerve. The gluteal nerves pass above the pyriformis muscle and the sciatic nerve passes either directly through or inferior to the pyriformis muscle. Debate exists about the role of the pryriformis muscle in sciatic nerve injury.

Now move up in the diagram and draw two lines close together in parallel to represent the *femoral* and *obturator nerves*; indicate the ventral rami of *L2–L4* form these spinal nerves. They comprise the major nerves of the anterior thigh. As with the sciatic nerve, the anterior rami divide into clinically unimportant anterior and posterior divisions; the anterior divisions of the ventral rami of L2–L4 supply the obturator nerve and the posterior divisions supply the femoral nerve.

If weakness is present in a femoral nerve distribution, test obturator-innervated muscles to distinguish femoral neuropathy from more proximal disease that involves both the femoral and obturator nerves (i.e., L2–L4 plexopathy, root, or motor neuron disease). The obturator nerve innervates the *adductor muscles of the thigh*: *adductor longus* and *adductor magnus*. Bring your thighs together to activate them.

The sciatic nerve supplements innervation to adductor magnus, so on needle electromyography, adductor longus is preferentially tested because it is purely an obturator-innervated muscle.

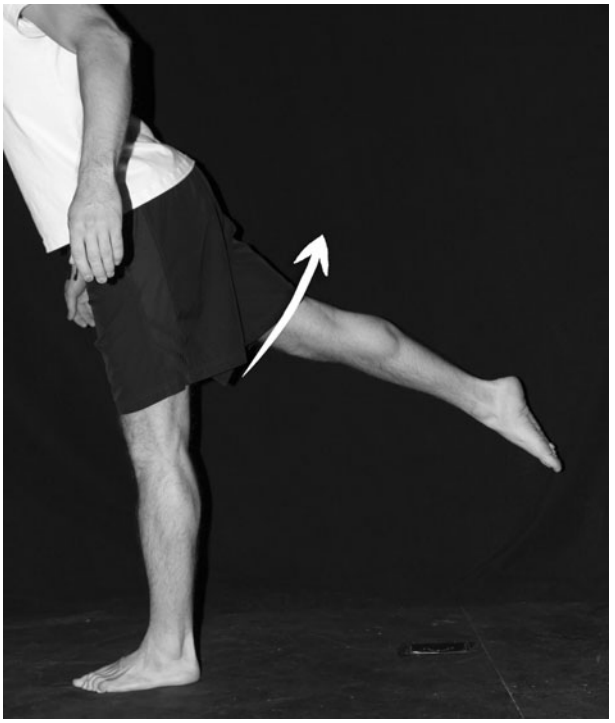


Photo 9-3 Gluteus maximus muscle

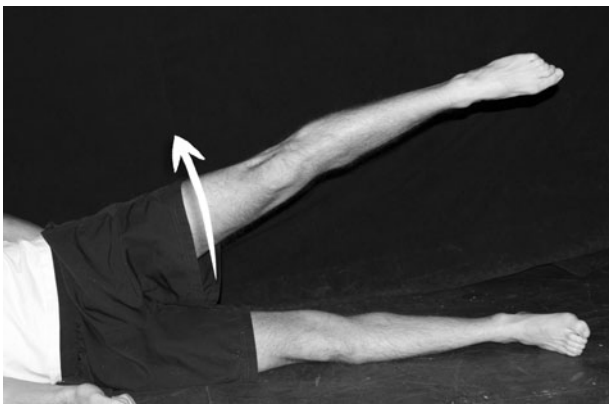


Photo 9-4 Gluteus medius muscle

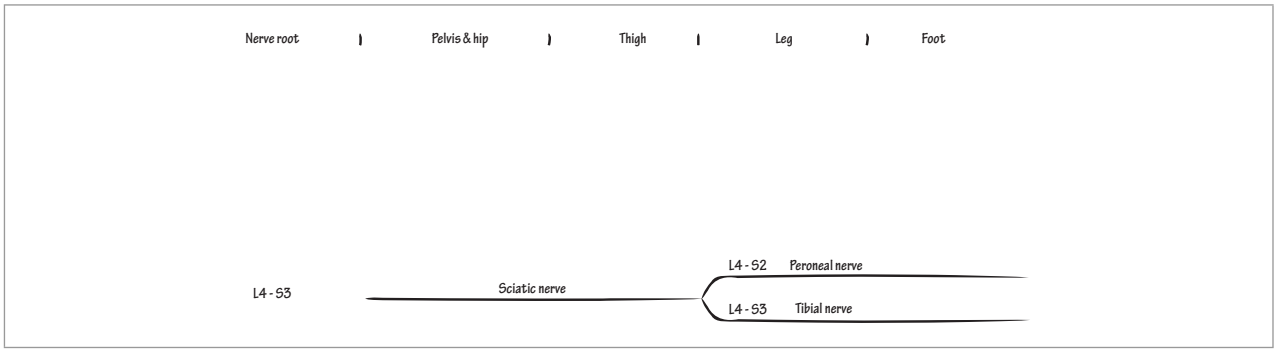


Figure 9-1 Incomplete lumbosacral plexus

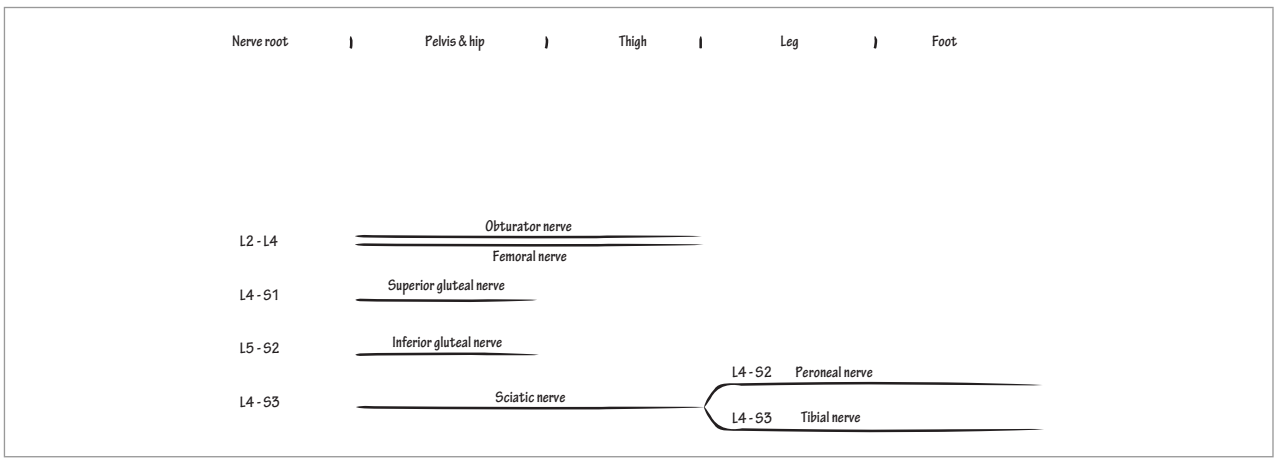


Figure 9-2 Incomplete lumbosacral plexus

Now, let's conclude the lumbosacral plexus. Above the femoral and obturator nerves, draw the *lateral femoral cutaneous nerve*, which extends into the thigh. Show the *L2* and *L3* spinal nerves supply it. Injury to this nerve is common where it courses beneath the inguinal ligament near the anterior-superior iliac spine; this causes tingling on the anterior-lateral aspect of the thigh. Think of a long holster on a tool-belt to remember this sensory distribution; we will draw it in the "Sensory Maps of the Body" chapter.

Above the lateral femoral cutaneous nerve of the thigh, draw the *genitofemoral nerve*, which terminates in the pelvis and hip. Indicate the *L1–L2* spinal nerves supply it. The genitofemoral nerve passes through psoas major and, proximal to the inguinal ligament, it divides into femoral and genital branches. The femoral branch covers sensation from the femoral triangle in the anterior thigh and the genital branch covers the cremaster muscle and scrotum/labia.

Draw a pair of lines at the top of the diagram that terminate in the pelvis and hip. Label the top one as the *iliohypogastric nerve* and the bottom one as the *ilioinguinal nerve* and show the *T12 and L1* ventral rami supply them. Note that T12 is not actually a part of the lumbosacral plexus, but just like with the brachial plexus, a pre- and postfixed lumbosacral plexus can occur. A prefixed lumbosacral plexus receives a large contribution from T12 and a small contribution from S4 and a postfixed lumbosacral plexus receives a large supply from S4 and a small supply from L1. Normally, S4 supplies only the pudendal nerve. The iliohypogastric nerve travels superior to the ilioinguinal nerve as they both course around the pelvic crest and through the abdominal musculature (transversus abdominis and external and internal oblique muscles) and terminate in the pubic and inguinal areas. Specifically, the iliohypogastric nerve carries sensory information from the upper-lateral gluteal region and suprapubic area, and the ilioinguinal nerve provides sensory coverage to the inguinal ligament, superior-medial portion of the thigh, and mons pubis.

Now, go back beneath the sciatic nerve and draw the *posterior femoral cutaneous nerve* (aka *posterior cutaneous nerve of the thigh*), which extends through the posterior thigh into the posterior upper leg. Indicate the ventral rami of *S1–S3* form it. This nerve is commonly referred to as the "lesser sciatic nerve" because it travels medial to the sciatic nerve in the buttock region and then courses superficially.

Lastly, at the bottom, draw the *pudendal nerve*, which terminates in the pelvis and hip. Show *S4* primarily supplies it but *S2* and *S3* also contribute to it. The pudendal nerve has three branches: the inferior rectal nerve, the perineal nerve, and the dorsal nerve to the penis or clitoris. These nerve branches innervate the sphincters of the bladder and rectum and provide sensory information from the anus and genitalia. The pudendal nerve is sometimes damaged along with the gluteal nerves, sciatic nerve, and the posterior femoral cutaneous nerve where they all exit the pelvis together through the greater sciatic foramen.

For reference, the nerves that pass through the greater sciatic foramen are the gluteal nerves, sciatic nerve, posterior femoral cutaneous nerve, and the nerves to the obturator internus and quadratus femoris muscles.

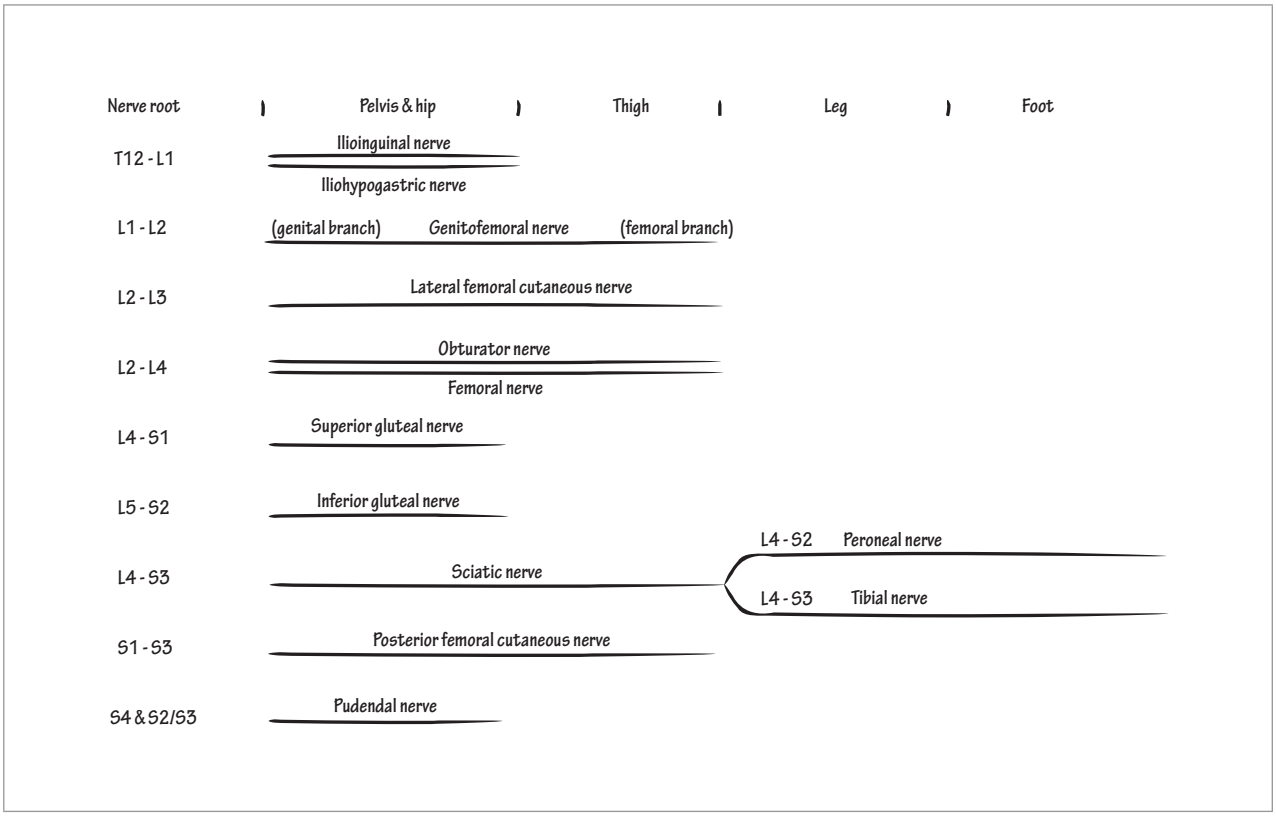


Figure 9-3 Complete lumbosacral plexus

Sciatic Nerve

THE L4–S3 NERVE roots form the sciatic nerve, which comprises both the peroneal and tibial nerves. The sciatic nerve is responsible for knee flexion and the actions of the lower extremity. As well, it provides sensory coverage to the posterior thigh, most of the lower leg, and the foot.

Now, trace the course of your sciatic nerve. Palpate the gluteus maximus muscle's midpoint where the sciatic nerve leaves the greater sciatic foramen and then trace its course down the midline of your posterior thigh. The posterior femoral cutaneous nerve travels alongside the sciatic nerve through the thigh and provides sensory coverage to the posterior leg. Just proximal to the patellar fossa, the peroneal and tibial nerves unbundle from the sciatic nerve. First, trace the tibial nerve straight down the back of your leg and along the bottom of your foot. Next, return to the patellar fossa and trace the common peroneal nerve around the lateral aspect of the leg (i.e., around the head of the fibula) into the anterior leg. The common peroneal nerve further divides into deep and superficial branches. Trace the deep peroneal nerve anteriorly across your leg and down the palpable midline long bone (the tibia) and then over the dorsum of your foot. Next, starting back from the common peroneal nerve division, trace the superficial peroneal nerve a short distance down the lateral aspect of your lower leg. This completes the course of the sciatic nerve.

Cross your legs; this is a common cause of *foot drop* for reasons we are now able to understand. In this position, the peroneal nerve from the top leg is squeezed between its own fibular head and the patella from the opposite leg.

To draw the sciatic nerve from proximal to distal, label the top portion of the page from left to right as: lumbosacral plexus nerve roots, buttock and thigh, lower leg, and foot. Indicate *L4–S3* form the sciatic nerve (L4–S2 contribute to both the peroneal and tibial nerves and S3 supplements only the tibial nerve). Next, draw the *posterior femoral cutaneous nerve* (aka *posterior cutaneous nerve of thigh*), which is supplied by *S1–S3*. Extend this line through the buttock and thigh; the posterior femoral cutaneous nerve covers sensation from the midline posterior thigh.

Now, continue the sciatic nerve through the buttock and thigh and label its motor innervation to the *hamstrings (L5–S2)* muscle group, which consists of the *medial hamstrings (the semitendinous* and *semimembranous muscles)* and the *long* and *short heads of the biceps femoris*. To demonstrate the action of the hamstrings muscles, flex your leg at the knee against resistance. The tibial component of the sciatic nerve innervates all of the hamstrings muscles except the short head of the biceps femoris, which the peroneal nerve innervates. The clinical relevance of this differential innervation pattern is minor because all of the different heads of the hamstring muscles provide knee flexion but it is important to know when performing electromyography to localize neuromuscular disease. Next, show the sciatic nerve supplies *adductor magnus*, which is primarily innervated by the obturator nerve. Bring your knees together to demonstrate its action.

In short, the sciatic nerve in the buttock and thigh provides flexion of the leg at the knee and contributes to thigh adduction.

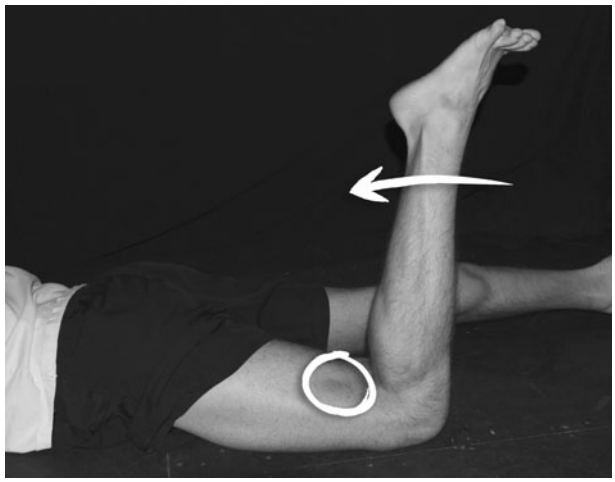


Photo 10-1 Hamstring muscle

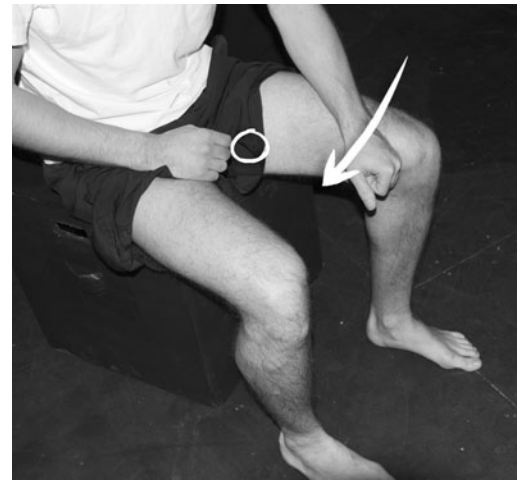


Photo 10-2 Adductor muscles

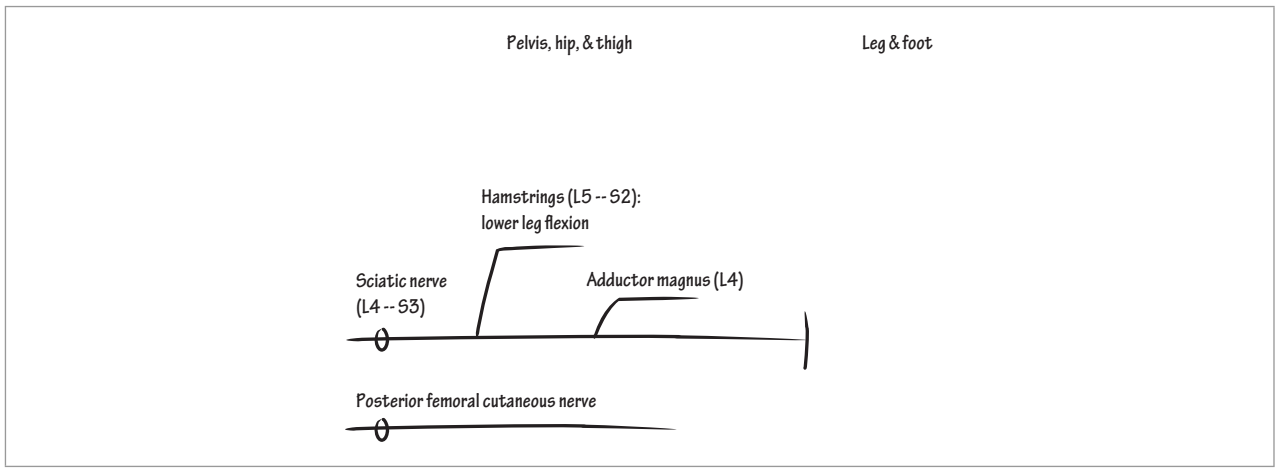


Figure 10-1 Incomplete sciatic nerve

Now, show the sciatic nerve unbundle into the *common peroneal* and *tibial nerves* proximal to the patellar fossa. Indicate that branches from both nerves join to form the *sural nerve*. Next, show the peroneal nerve enter the lower leg segment. As it wraps around the fibular head in the lateral leg, it again divides. Draw it branch into the *deep peroneal* and *superficial peroneal nerves*. Show the deep peroneal nerve pass through the lower leg and indicate it innervates the *anterior compartment lower leg muscles*, which are *tibialis anterior (TA), extensor hallicus longus (EHL), extensor digitorum longus (EDL)*, and *extensor digitorum brevis*. Dorsiflex your foot (i.e., angle it up) to demonstrate the action of tibialis anterior. Dorsiflex your great toe and then your remaining digits to demonstrate the actions of extensor hallicus longus and extensor digitorum longus, respectively.

The last muscle of the anterior compartment flexors is extensor digitorum brevis; its action is difficult to distinguish from that of extensor digitorum longus. Wiggle your toes and palpate the contracting and relaxing extensor digitorum brevis muscle belly on the lateral dorsum of the foot. Extensor digitorum longus provides distal joint extension, whereas extensor digitorum brevis provides extension at the proximal metatarsal phalangeal joint. A helpful clinical pearl is that extensor digitorum brevis weakness is never from muscle disease, rather it occurs from nerve or neuronal pathology. Bear in mind, however, it is absent or weak in 15% of normal patients.

Next, show the superficial peroneal nerve extend midway into the lower leg. Indicate it innervates the *peroneus muscles*, which are *peroneus longus (PL), peroneus brevis (PB)*, and *peroneus terius (PT)*. Evert your foot to demonstrate the peroneus muscle group action. Block the outside of the foot or it will be difficult to perform this action.

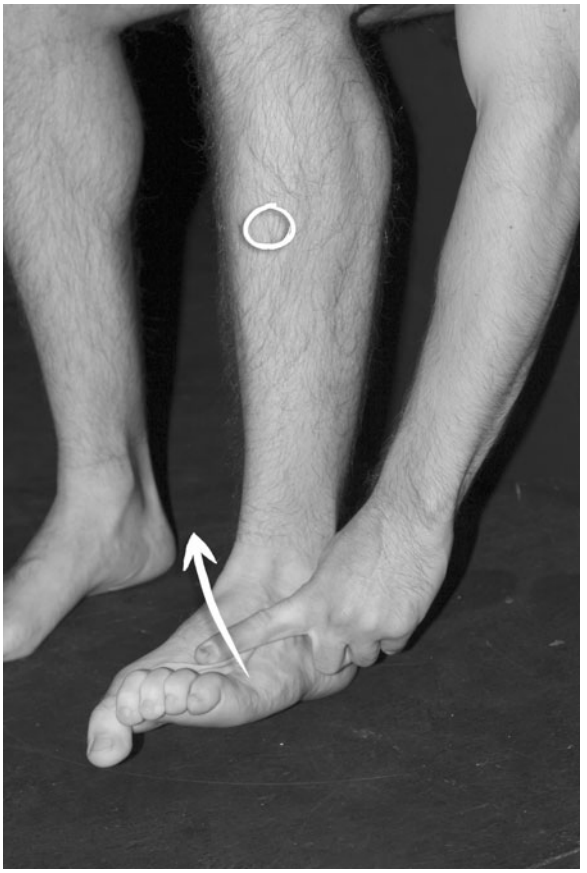


Photo 10-3 Tibialis anterior muscle

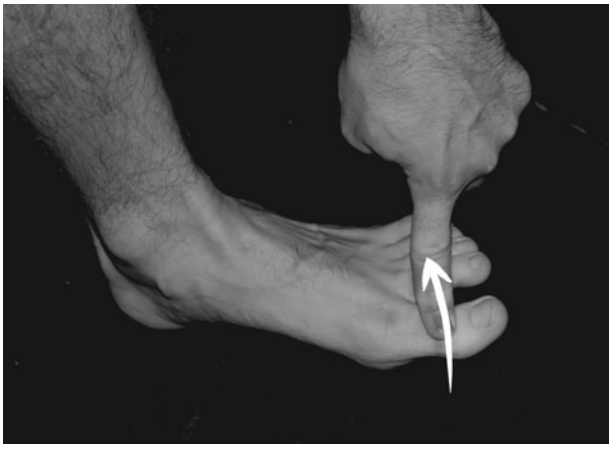


Photo 10-4 Extensor hallucis longus muscle

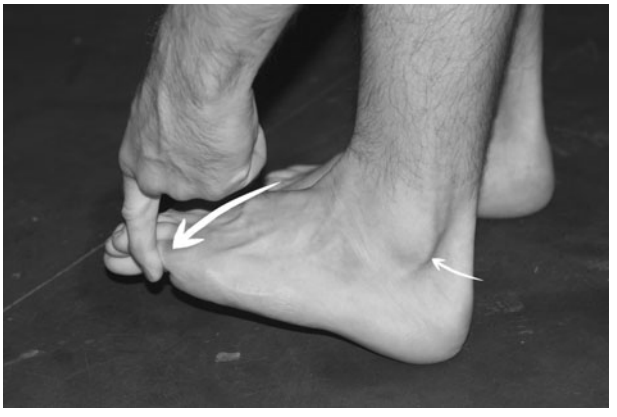


Photo 10-5 Peroneus muscles

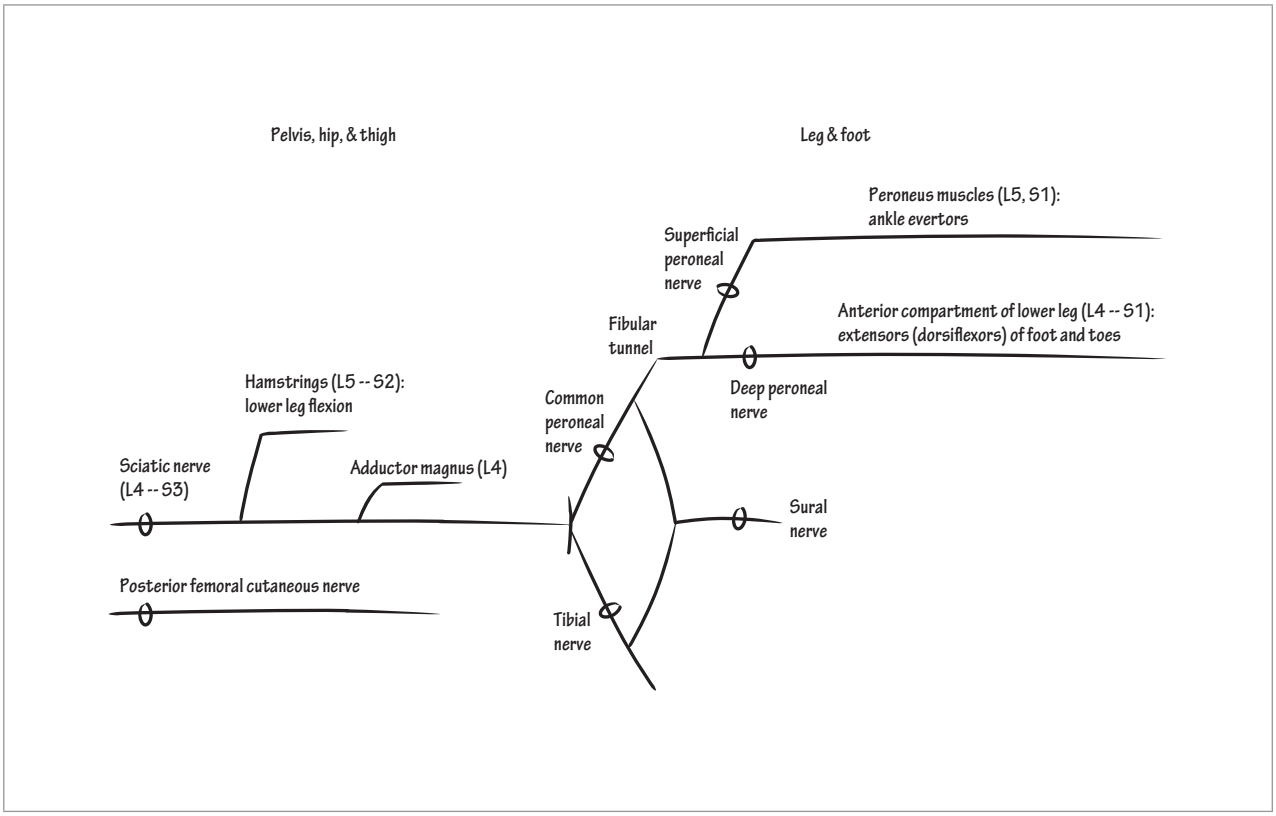


Figure 10-2 Incomplete sciatic nerve

Now, let's draw the tibial nerve; show it pass through the lower leg. Indicate it innervates the *posterior compartment lower leg muscles*, which are the *gastrocnemius (G), soleus (S), tibialis posterior (TP)*, and the *toe flexors (flexor hallicus longus* and *flexor digitorum longus*). Flexor digitorum brevis is innervated by the more distal medial plantar branch. Extend your leg at the knee and flex it at the ankle (i.e., step on the gas) to demonstrate the action of the gastrocnemius muscle. The soleus flexes the foot at the ankle when the knee is in flexion, whereas the gastrocnemius does so when the knee is extended. Next, invert your foot (i.e., angle it inward) to demonstrate the action of tibialis posterior. Similar to the peroneus action of evertion, invertion is best performed against resistance.

Curl your toes against resistance to demonstrate the action of the toe flexors. When you activate your toe flexors, you flex your toes at both their proximal and distal joints. You are probably able to discern from the nomenclature that flexor hallicus longus flexes the great toe; flexor digitorum longus flexes the rest of the toes at their distal joint; and flexor digitorum brevis, which the medial plantar nerve innervates, flexes the rest of the toes at their proximal joint.

Now, continue the tibial nerve to just proximal to the foot. Draw a branch for the *medial calcaneal* sensory nerve. The sensory set-up for the medial calcaneal nerve is similar to that for the median and ulnar nerves. The palmar cutaneous median nerve branches proximal to the carpal tunnel and the proximal ulnar cutaneous nerves branch prior to Guyon's tunnel. These proximal median and ulnar nerve cutaneous branches provide sensory coverage to the proximal hand, and similarly, the medial calcaneal nerve provides sensory coverage to the proximal foot. We will sketch the sensory coverage of the foot later.

Next, continue the tibial nerve into the foot and indicate it branches into *medial* and *lateral plantar nerves*. Indicate these nerves innervate the *intrinsic foot muscles*, which are *abductor hallicus, flexor digitorum brevis, quadratus plantae, abductor digiti minimi pedis*, and *adductor hallicus*. Demonstrate the action of the intrinsic foot muscles in two different ways: (1) cup your foot and (2) spread out your toes. There is little clinical utility in distinguishing the specific actions of the individual intrinsic foot muscles.

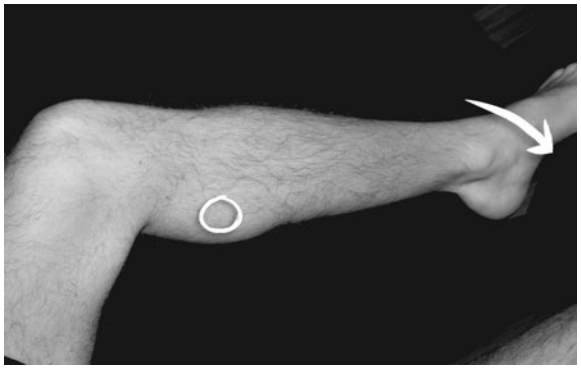


Photo 10-6 Gastrocnemius muscle

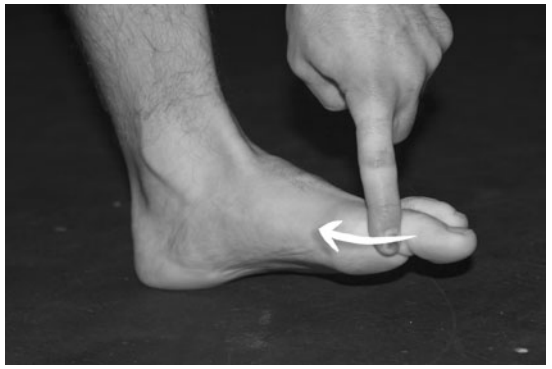


Photo 10-7 Tibialis posterior muscle

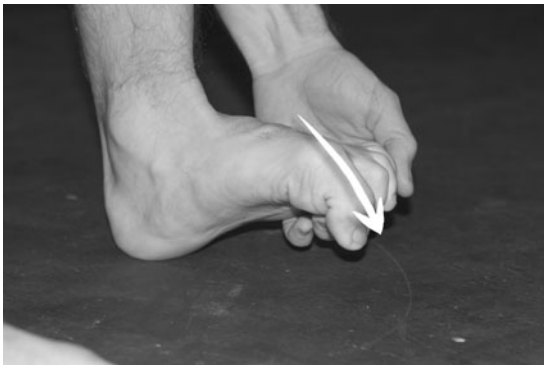


Photo 10-8 Toe flexor muscles

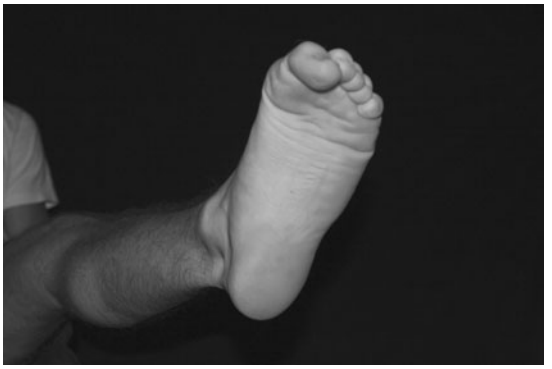


Photo 10-9 Intrinsic foot muscles

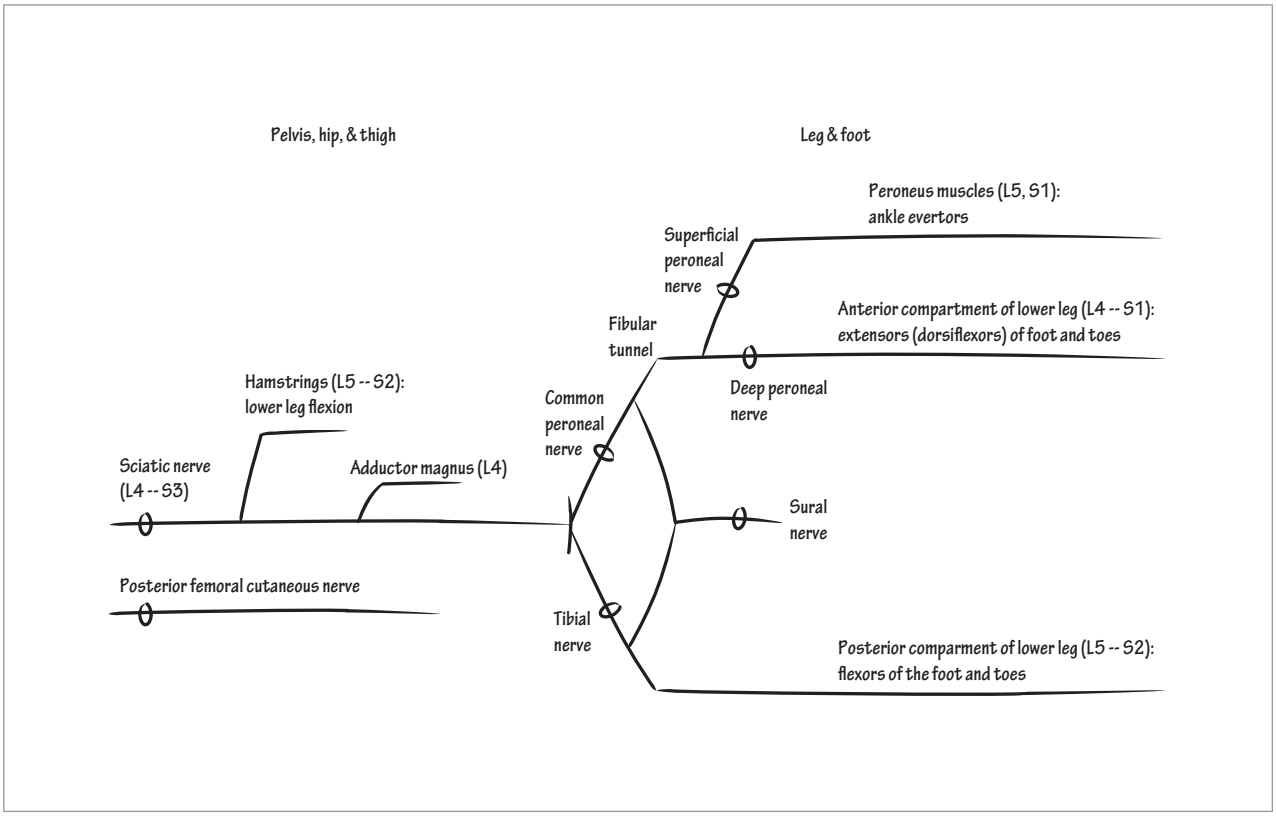


Figure 10-3 Complete sciatic nerve

Now, let's sketch the sensory coverage of the feet. Trace your feet. Label one as the dorsal surface (top) of the foot and the other as the ventral surface (bottom). For clinical purposes, it is probably sufficient to just know that the peroneal nerve provides sensory coverage to the dorsum of the foot; the superficial division provides almost all of the peroneal nerve coverage except for the webbing between the great toe and second digit, which the deep peroneal division provides; and the tibial nerve provides sensory coverage to the ventral surface of the foot.

However, there is additional division within the sensory coverage of the foot and we will explain it here. There are several similarities between the sensory coverage of the ventral surface of the foot and that of the ventral surface of the hand. One similarity has already been discussed: the medial calcaneal nerve separates from the tibial nerve before it passes into the foot and provides sensory coverage to the proximal portion of the foot. Go ahead, now, and indicate the *medial calcaneal nerve* coverage to the heel.

Next, just as the sensory coverage of the fourth finger is split between the ulnar nerve medially and the median nerve laterally (with the hand supinated), the sensory coverage of the ventral surface of the foot is split at the fourth digit, as well. On the ventral surface of the foot, draw a line down the center of the fourth digit and along the foot to the heel. Indicate the *medial plantar nerve* provides sensory coverage to the medial aspect of the fourth digit, first three digits, and the medial foot distal to the heel; and the *lateral plantar nerve* provides sensory coverage to the lateral fourth digit, fifth digit, and the lateral foot distal to the heel.

Finally, return to the tracing of the dorsal surface of the foot. Indicate the *superficial peroneal nerve* covers all of it except the webbing between the great toe and second digit, which the *deep peroneal nerve* covers.

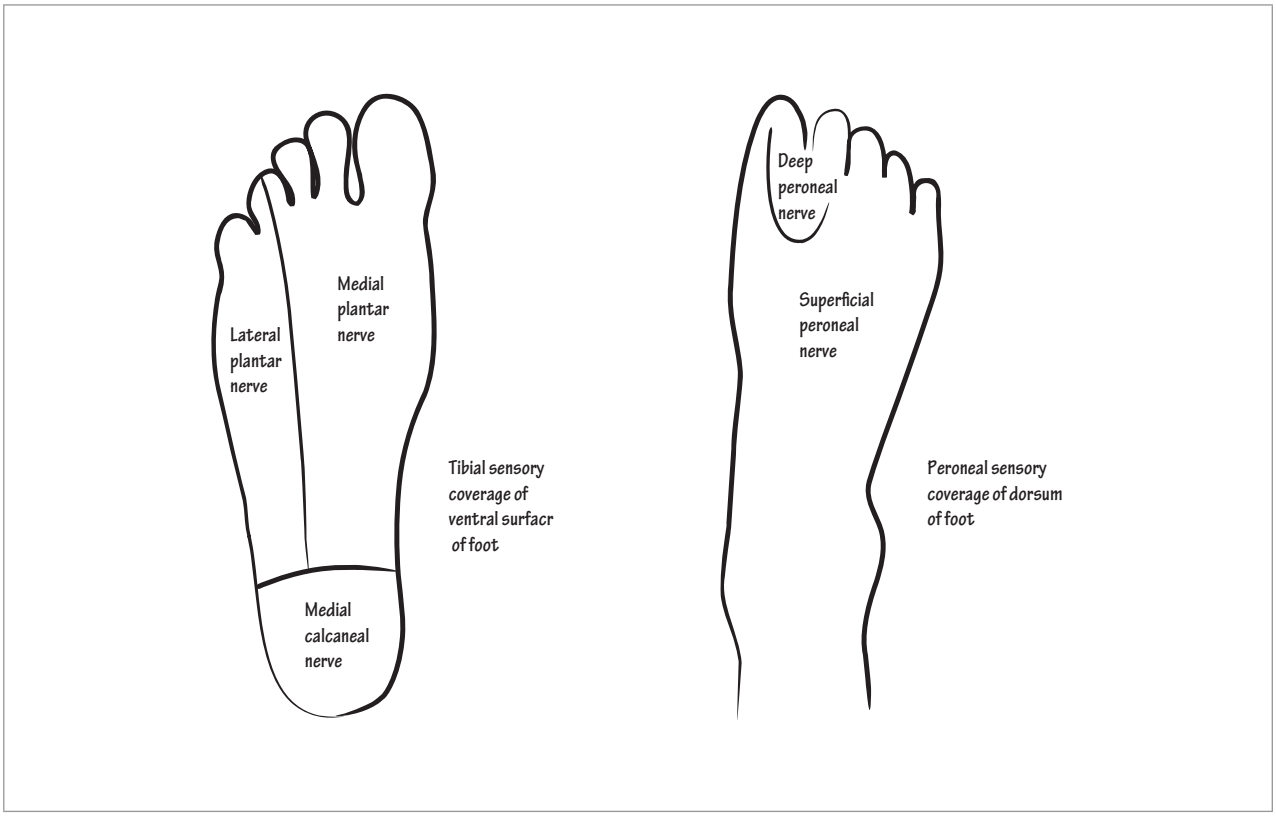


Figure 10-4 Sensory coverage to the ventral and dorsal surfaces of the foot

Femoral Nerve

THE L2–L4 NERVE roots supply the femoral and obturator nerves. The femoral nerve provides thigh flexion and lower leg extension and the obturator nerve provides thigh adduction. Together, they provide sensory coverage to the anterior thigh and medial lower leg.

To trace the course of the femoral nerve, lie flat and raise your leg off the ground. You activate the iliopsoas muscle, innervated by the femoral nerve, when you flex your thigh at the hip. Palpate this superficial muscle just distal to the inguinal ligament. Next, inch your fingers medially until you reach your pulsating femoral artery in the femoral groove. Within the femoral groove, from lateral to medial, lie the femoral nerve, artery, vein, and lymph tissue. Remember the order of this series with the acronym "NAVL," which stands for nerve, artery, vein, and lymph; and runs from outside to inside. The order of these neurovascular structures is noteworthy because when we cannulate the femoral vein for central intravenous access, we need to know these landmarks.

Now, trace the femoral nerve inferomedially toward the medial aspect of your patella. All of its motor branches lie proximal to the patella. Its long-reaching saphenous sensory branch, however, travels within the subsartorial canal and then within the adductor canal (aka Hunter's canal) in the anteromedial thigh. Continue to trace down the medial aspect of your lower leg to the instep of your foot to complete the course of the saphenous nerve.

Next, trace the course of the obturator nerve from the medial aspect of the inguinal nerve a short distance down the medial aspect of your thigh.

For our femoral nerve diagram, label across the top of the page from left to right, from proximal to distal: pelvis, thigh, lower leg, and foot. Under the pelvis segment, indicate the *L2–L4* nerve roots form the femoral nerve. Then, continue the femoral nerve through the pelvis and into the thigh. Where the pelvis and thigh meet, at the inguinal ligament, indicate the femoral nerve innervates the *iliopsoas muscle*. Proximally, in the abdomen and pelvis, the iliopsoas has three distinct heads: *psoas minor, psoas major*, and *iliacus*. When they cross into the thigh, these muscles combine to form the *iliopsoas muscle*. Flex your thigh at the hip to demonstrate the action of iliopsoas.

Next, continue the femoral nerve through the thigh. Indicate it innervates the *sartorius* and *quadriceps muscles*. The quadriceps comprises four distinct muscles: *rectus femoris*, *vastus lateralis*, *vastus intermedialis*, and *vastus medialis*. The sartorius performs a combination of thigh abduction, flexion, and external rotation. Cross one leg over the other, and run your heel up and down your opposite shin to demonstrate the action of the sartorius muscle. Then, extend your lower leg against resistance to demonstrate the action of your quadriceps muscle. Quadriceps weakness presents with difficulty walking *down*stairs whereas iliopsoas weakness presents with difficulty climbing *upstairs* or in rising from a low chair. The most common pattern of weakness in muscle diseases involves the iliopsoas and other proximal lower extremity girdle muscles along with the proximal upper extremity muscles (the deltoid and humeral muscles). This distribution is referred to as a

limb-girdle pattern. When isolated quadriceps and wrist flexor weakness are found in an older adult, it is almost always due to inclusion body myositis—a specific type of inflammatory muscle disease.

The femoral nerve also innervates the *pectinus muscle* but it can't be isolated and tested clinically. The femoral nerve continues into the lower leg as the *saphenous* branch, which is a sensory nerve.

Photo 11-1 Iliopsoas muscle

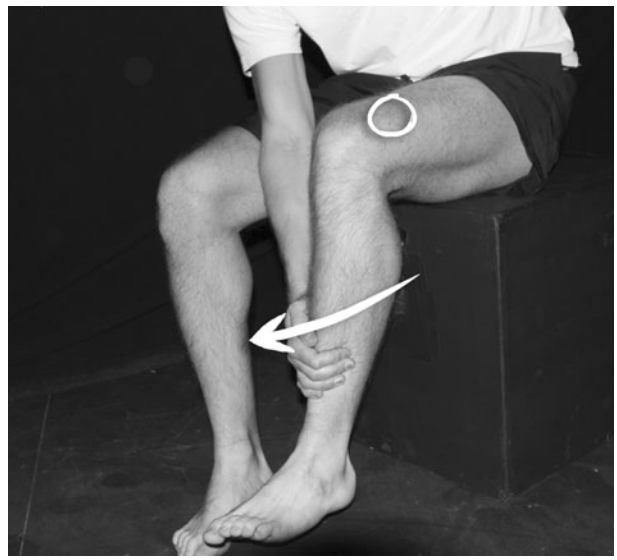


Photo 11-2 Quadriceps muscles

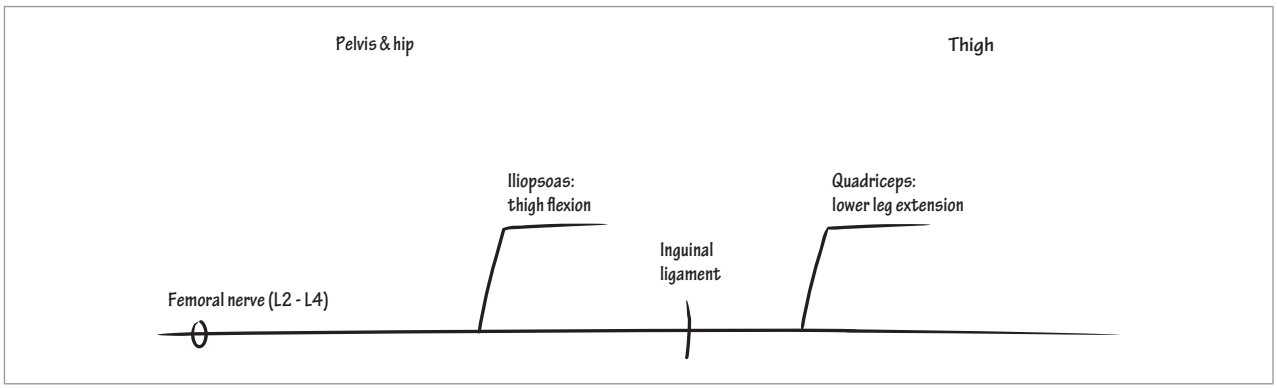


Figure 11-1 Femoral nerve

Cervical Plexus

THE CERVICAL PLEXUS is formed from the ventral rami of the C1–C4 spinal nerves and provides motor and sensory coverage to the head and neck and also helps activate the diaphragm. Cervical roots exit their respective cervical foramina underneath the sternocleidomastoid muscle and emerge into the anterior and posterior cervical triangles. We will group the motor nerves that emanate from the cervical plexus based on whether they enter the anterior or posterior cervical triangle, so let's first demonstrate the anatomical boundaries of these triangles.

When you turn your head, you activate the sternocleidomastoid muscle opposite the direction of your head turn; turn your head, now. Palpate the sternocleidomastoid insertion onto the anterior portion of the clavicle. The anterior cervical triangle lies in front of the sternocleidomastoid muscle: the sternocleidomastoid is its postero-lateral border. Feel your laryngeal prominence and palpate the midline structures of your neck; these structures comprise the medial border of the anterior triangle. Lastly, feel along your mandible; it is the upper border of the anterior triangle.

Now, on the same side of your neck, raise and rotate forward your shoulder using your trapezius muscle. Palpate your trapezius along the back of your shoulder and neck; the posterior cervical triangle lies in between it and the sternocleidomastoid muscle. Roll your fingers over your clavicle to appreciate the depth of the posterior cervical triangle.

From anterior to posterior, the floor of the posterior cervical triangle comprises the scalene muscles (anterior, middle, and posterior); the levator scapulae muscle; and the splenius capitis muscle. In between the anterior and middle scalene muscles is the scalene groove (aka scalene triangle), which contains the subclavian artery and the proximal portion of the brachial plexus.

Now, let's draw the anatomical structures related to the cervical plexus. Make the left side anterior, the right side posterior, the top superior, and the bottom inferior. Draw the *clavicle* as a horizontal line along the bottom of the page. Next, draw the vertically oriented *trapezius muscle* in the posterior portion of the diagram. Then, draw the *inferior attachment* of the *sternocleidomastoid muscle* to the anterior clavicle and its *superior attachment* to the mastoid bone of the cranium, just in front of the upper trapezius muscle. We draw these attachments, only, and leave out the sternocleidomastoid muscle belly because it overlies the cervical plexus.

In the midline of the page, draw seven small foramina in a vertical column to represent, from top to bottom: the *jugular foramen*, the *hypoglossal canal*, and the exit foramina of *C1*, *C2*, *C3*, *C4*, and *C5*. As mentioned before, the cervical plexus is formed from the ventral rami of spinal nerves C1–C4, but here we include the jugular foramen and the hypoglossal canal, and also C5, because they comprise important related anatomical structures.

We begin our diagram with the sensory nerves of the cervical plexus, all of which emerge from behind the sternocleidomastoid muscle and travel into the posterior cervical triangle. First, draw an *anastomosis* between the ventral rami of spinal nerves *C2* and *C3*. Three nerves are formed from this connection: the lesser occipital, greater auricular, and transverse cervical nerves (the greater occipital nerve is formed from the *dorsal* ramus of C2). First, show the *lesser occipital nerve* ascend to the superior pole of the pinna and lateral portion of the head. Next, indicate

the *greater auricular nerve* ascends to the inferior pole of the pinna and the angle of the mandible. Then, show the *transverse cervical nerve* (aka the *anterior cutaneous nerve of the neck*) pass anteriorly to the anterior and antero-lateral neck.

Now, draw an *anastomosis* between the ventral rami of spinal nerves *C3* and *C4*. The *supraclavicular nerve* descends to the clavicle and covers sensation from the shoulder, postero-lateral neck, and upper chest. We leave out of our diagram the minor C3 and C4 sensory branches to the trapezius muscle.

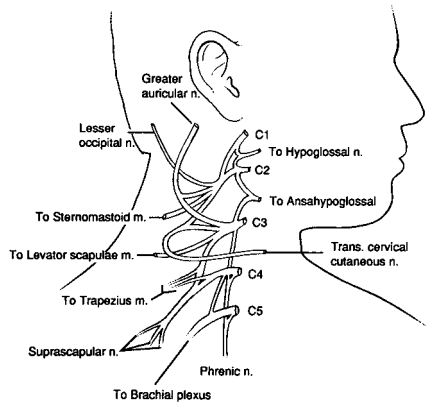


Photo 12-1 Cervical plexus
With permission from Mendell, J. R., J. T. Kissel, and D. R. Cornblath, *Diagnosis and Management of Peripheral Nerve Disorders*, Contemporary Neurology Series. Oxford: Oxford University Press, 2001.

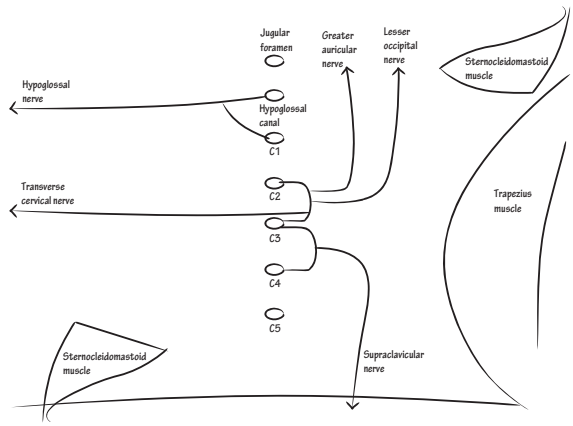


Figure 12-1 Cervical plexus: sensory component

Now, let's draw the motor nerves of the cervical plexus. For this, we begin with the nerves that enter the anterior cervical triangle. The most important motor nerve derived from the cervical plexus is the *phrenic nerve*. Show it originate from the C3 and C4 cervical plexus spinal nerves and the C5 brachial plexus spinal nerve. Indicate it descends through the thoracic cavity to the diaphragm.

Next, draw the *hypoglossal nerve* as it exits the hypoglossal canal and innervates the musculature of the floor of the mouth. It is primarily constituted by cranial nerve 12; however, for completeness, show C1 fibers also supply it. Thus, although cranial nerve 12 is the primary innervator of the floor of the mouth, C1, via the hypoglossal nerve, also helps supply it.

Draw a separate branch from *C1* that descends and connects with the *C2* and *C3 branches* and loops anteriorly in the *ansa cervicalis*. This nerve bundle provides motor innervation to the *hyoid musculature of the neck* and then travels back up to join the hypoglossal nerve. The upper hyoid musculature (geniohyoid and thyrohyoid) receive their motor innervation from C1 via the hypoglossal nerve; and the lower hyoid musculature (sternohyoid, sternothyroid, and omohyoid) receive their motor innervation from C2 and C3 via the ansa cervicalis. Deep motor branches of the cervical plexus also exist in the anterior cervical triangle: C1 and C2 branches innervate the rectus capitus muscle; C1–C3 branches innervate the longus capitus muscle; and C2–C4 branches innervate the longus colli and intertransverse muscles.

Now, let's draw the motor nerves from the cervical plexus in the posterior cervical triangle. The ventral rami of C1–C4 form cranial nerve 11, the *spinal accessory nerve*. The C1–C4 fiber bundle ascends the spinal canal, passes through the foramen magnum to enter the cranium, and then exits the jugular foramen as cranial nerve 11, the spinal accessory nerve. Indicate this nerve innervates the sternocleidomastoid muscle, which turns the head, and then show the spinal accessory nerve cross the floor of the posterior cervical triangle to innervate the trapezius muscle, which elevates the shoulder. We previously demonstrated the action of both of these muscles. When the spinal accessory nerve is injured, the trapezius is paralyzed, which causes the shoulder to drop. This places traction on the brachial plexus (because it lies within the posterior cervical triangle), and so, in this manner, injury to the cervical plexus can secondarily cause injury to the brachial plexus.

The C3 and C4 roots provide deep motor branches that enter the posterior cervical triangle and innervate the levator scapulae and the anterior and middle scalene muscles, but we leave them out of our diagram for simplicity.

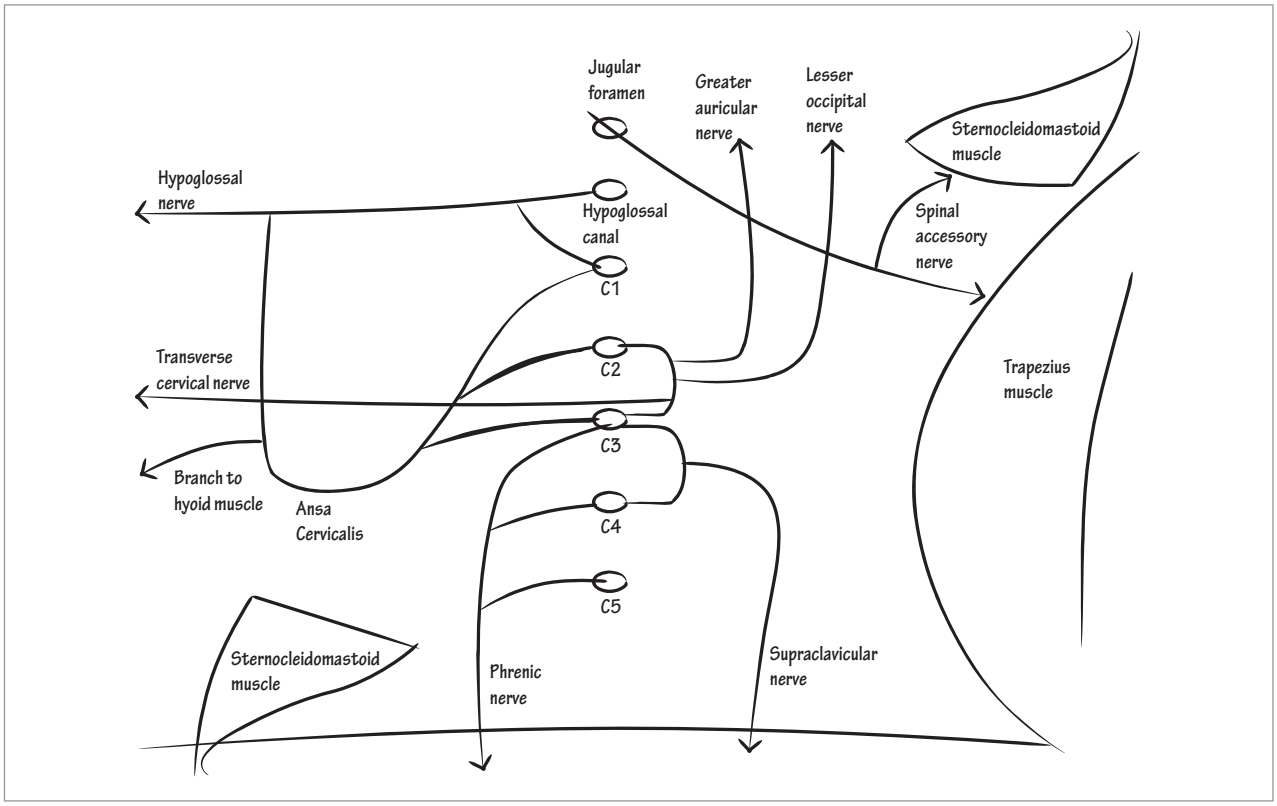


Figure 12-2 Complete cervical plexus: motor and sensory components

Sensory Maps of the Body

The 1953 edition of Woodhall and Haymaker's book, *Peripheral Nerve Injuries*, contains two separate sensory maps: one based on Keegan and Garrett's 1948 work and the other based on sensory maps from O. Foerster's 1933 *Brain* publication. Now, no neurologist is clear about which map to follow. Both maps work well, though, so we will use elements of both of them in this chapter. We also include Keegan and Garrett's 1948 dermatomal maps for reference, here.

First, let's draw sensory maps of the trunk and anterior extremities. On one side of the figure, we will indicate the territories of the cutaneous nerves and on the other side, we will draw a dermatomal map. For the cutaneous nerve map, we will divide the body into its torso, arm, and leg. Our goal is not to draw the complete map of all known cutaneous nerves, as this would be unmanageable, but rather to indicate the most important cutaneous nerve distributions. First, draw the torso. Show the *supraclavicular nerve* covers the upper shoulder and the *axillary nerve* covers the area below it. Then, indicate the *anterior and lateral cutaneous rami of the thoracic nerves* cover the medial and lateral areas of the trunk, respectively. Note, these nerves are often referred to as "intercostal nerves." Anterior cutaneous rami exist at each spinal level and are individually named in reference to the nerve root that supplies them.

Next, indicate the *inguinal nerves* cover the inguinal region. The inguinal nerves are, from superior to inferior: the iliohypogastric, ilioinguinal, and genitofemoral nerves. Their names are derived from their discrete anatomical positions.

Now, draw the anterior upper extremity. Indicate the *lateral cutaneous nerve of the arm* (a radial nerve branch) and the *lateral cutaneous nerve of the forearm* (a musculocutaneous nerve branch) cover the lateral arm and forearm, respectively. Then, indicate the *medial cutaneous nerve of the arm* and the *medial cutaneous nerve of the forearm*, both of which are branches of the medial cord of the brachial plexus, cover the medial arm and forearm, respectively. The intercostobrachial nerves also cover the medial half of the anterior forearm, but we exclude them for simplicity. Many texts substitute the word "arm" with the Latin term "brachi" and the word "forearm" with the Latin term "antebrachi." Thus, the term "cutaneous nerves of the arm" becomes the "brachial cutaneous nerves" and the term "cutaneous nerves of the forearm" becomes "antebrachial cutaneous nerves."

Now, draw the anterior lower extremity. Show the *lateral femoral cutaneous nerve* (aka *lateral cutaneous nerve of the thigh*) covers the lateral aspect of the thigh and the *anterior branches of the femoral nerve* (aka *intermediate and medial cutaneous nerves*) cover the medial and anterior thigh. Both of them branch from the femoral nerve. Also, show the *obturator nerve* covers a small patch on the medial aspect of the thigh. Next, indicate the *saphenous nerve*, a sensory extension of the femoral nerve, covers the medial aspect of the lower leg to the instep of the foot. Then, show the *superficial peroneal nerve* covers the lower lateral aspect of the lower leg. In the posterior lower extremity section of this chapter, we draw the sural nerve. It is formed from branches of both the common peroneal and tibial nerves, and it covers the ankle. In

the "Sciatic Nerve" chapter, we showed the deep peroneal nerve covers the webbing between the great toe and second digit. The common peroneal nerve supplies the lateral cutaneous nerve of the calf (aka lateral sural cutaneous nerve), which covers the upper lateral aspect of the lower leg, but we exclude it, here, for simplicity.

Now turn your attention to the other half of the figure. First, show *C7* covers the middle finger, *C8* covers the medial hand, and *C6* covers the lateral hand. Then divide the upper extremity into an upper arm and a forearm, and split them down the middle into medial and lateral compartments. Show C6 covers the lateral forearm (in addition to the lateral hand) and *C5* covers the upper lateral arm. Then, show *T1* covers the medial forearm and *T2* covers the medial upper arm.

Next, show *T4* covers the band across nipple line, *T10* covers the umbilicus, and *L1* covers the inguinal region.

Now, to show the sensory coverage of the lower extremity, divide it into four compartments from superior lateral to inferior medial using three sloping lines. Label them *L2*, *L3*, *L4*, and *L5*, respectively. Then, label the lateral ankle *S1*.

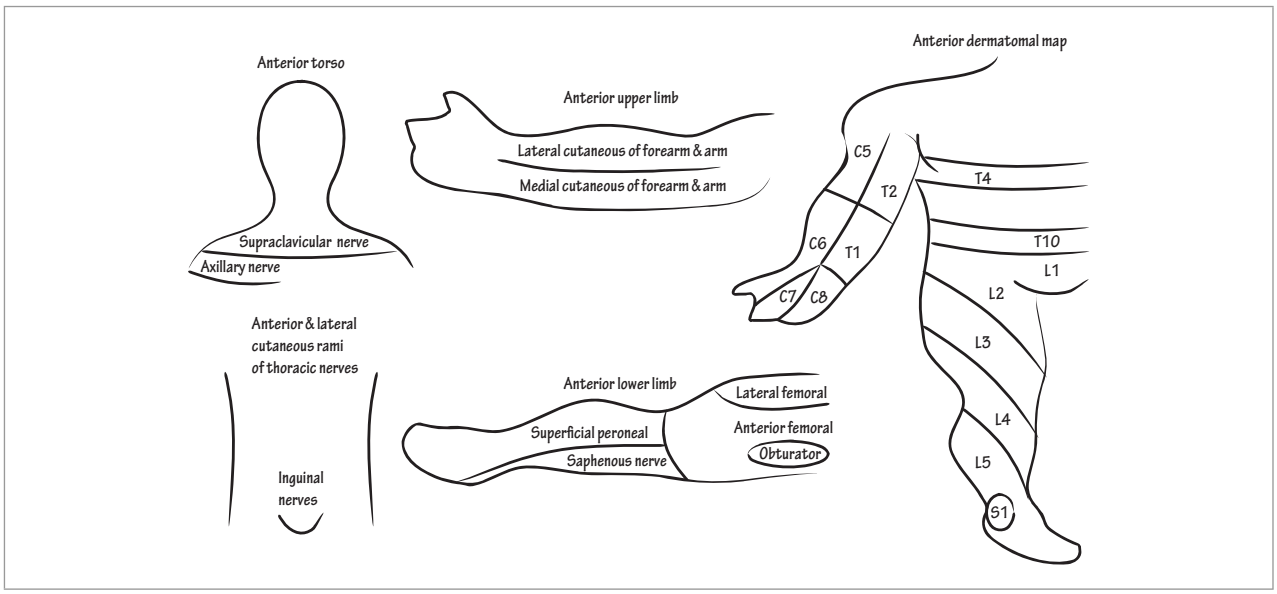


Figure 13-1 Anterior maps

Now, let's label the peripheral nerves of the back and posterior surfaces of the upper and lower extremities. They are quite similar to the nerves of the trunk and the anterior surface extremities.

First, let's draw the sensory coverage of the posterior torso. Show the *supraclavicular nerve* covers the posterior shoulder region and the *axillary nerve* covers the lateral region beneath it. The greater occipital nerve, derived from *C2*, covers the posterior scalp. Then, show the *posterior cutaneous rami* cover from the upper back to the buttock. Posterior cutaneous rami exist at each spinal level and, like the anterior rami, are individually named in reference to the nerve root that supplies them.

In the anterior diagram, we divided the upper extremity into lateral and medial halves and separated the nerves to the arm from those to the forearm. The posterior upper extremity has *three* divisions from lateral to medial, instead; yet, the only difference is the addition of the upper arm and forearm posterior cutaneous nerves, which the radial nerve innervates. Otherwise, the sensory coverage is the same. Label the lateral posterior upper extremity with the *lateral cutaneous nerves of the forearm and arm* and the midline posterior upper extremity with the *posterior cutaneous nerves of the forearm and arm*; the radial nerve supplies both the lateral and posterior nerve groups (except for the lateral cutaneous nerve to the forearm, which the musculocutaneous nerve supplies). Then, label the medial posterior upper extremity with the *medial cutaneous nerves of the forearm and arm*, which the medial cord supplies.

Next, show the *posterior femoral cutaneous nerve* (aka *posterior cutaneous nerve of the thigh*), which is unrelated to the femoral nerve, itself, covers the midline back of the thigh, and the *sural* nerve covers the lateral lower leg and lateral foot. The sural nerve is formed from branches of both the peroneal and tibial nerves.

Lastly, let's create a posterior surface dermatomal map. We begin with the anus; label it *S5*. For simplicity, we exclude the coccyx, which is present within the center of S5. Show *S4* encircle S5 and show *S3* encircle S4. Then, show *S2* encircle S3 superiorly and extend down the medial leg. Next, show *S1* extend down the lateral leg.

Now, show that the dermatomal sensory coverage of the posterior arms is the same as that of the anterior arms. Indicate *C5* covers the upper outer arm, *C6* the outer forearm and lateral hand, *C7* the middle finger and midline forearm, *C8* the medial hand, *T1* the inner forearm, and *T2* the inner upper arm.

Show *C2* covers the back of the head. The trigeminal nerve covers the face and a small portion of the upper back of the head but C2 covers the rest. Show *C3* and *C4* cover the posterior neck and *T2–L2* covers the upper back down to the buttocks.

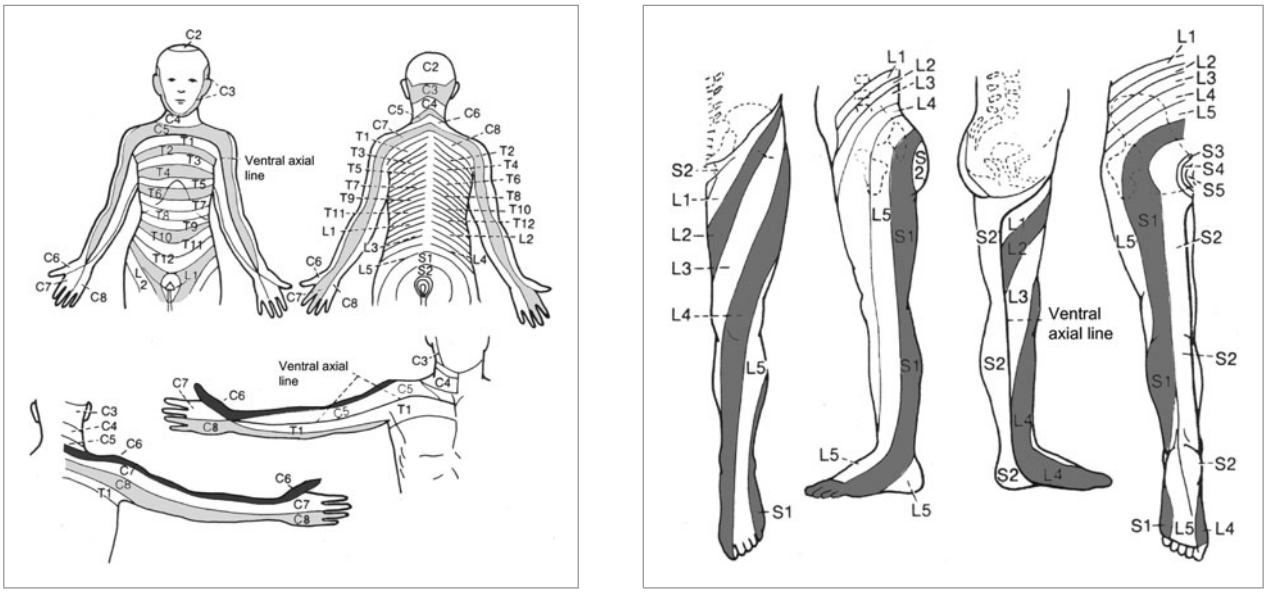


Photo 13-1 Reproduction of Keegan and Garrett's dermatomal maps from 1948
With permission from Brodal, P. *The Central Nervous System: Structure and Function*. 3rd ed. Oxford and New York: Oxford University Press, 2004. Modified from Anat Rec 101:430, 433, *1948*. Reprinted with permission of John Wiley & Sons, Inc.

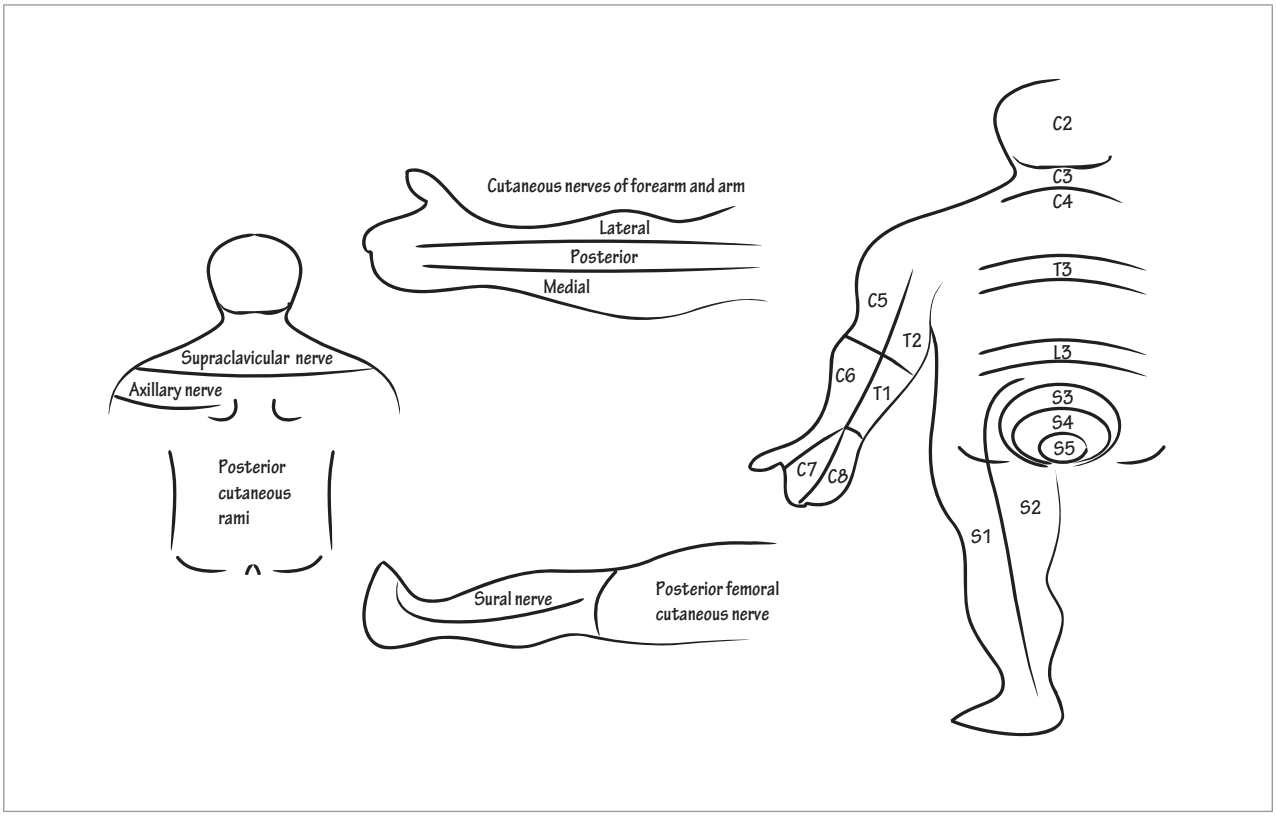


Figure 13-2 Posterior maps

Peripheral Autonomic Nervous System

The peripheral autonomic nervous system comprises the craniosacral parasympathetic, thoracolumbar sympathetic, and enteric nervous systems. In this chapter, we will focus on the parasympathetic and sympathetic systems and we will briefly discuss the enteric nervous system at the end.

Both the parasympathetic and sympathetic systems include preganglionic neurons, ganglion relay cells, postganglionic neurons, and effector tissues. The sympathetic and parasympathetic systems produce opposing actions on overlapping visceral tissues. In general, the parasympathetic nervous system drives the body towards a resting state and the sympathetic nervous system generates a "fight or flight" response. Gap junctions in autonomic tissues produce electrical cellular coupling so a small release of neurotransmitter produces widespread effects. However, neither system is "all or none": both act selectively as well as non-selectively.

In our first diagram, we will arrange the origination sites, ganglia, and effector tissues of the parasympathetic nervous system. First, draw an outline of one side of the brainstem and sacral spinal cord. Label the brainstem as the *cranial component* and the sacral spinal cord as the *sacral component*. Next, draw the cranial and sacral origination sites. In the midbrain, indicate the *nucleus of cranial nerve 3*—the *Edinger-Westphal nucleus*; in the pons, draw the nucleus of *cranial nerve 7*—the *superior salivatory nucleus*; and in the medulla, label the nuclei of *cranial nerves 9* and *10* as the *inferior salivatory nucleus* and the *dorsal motor nucleus of the vagus*, respectively. Note that nucleus ambiguus also contributes minor visceromotor (autonomic motor) fibers to cranial nerve 10 with specific effects on the heart, but we exclude it here for simplicity.

Refer to the "Cranial and Spinal Nerves Overview" chapter for details about the position of the nuclei within the brainstem; however, we provide a brief explanation here. In regards to their medial-lateral position, the parasympathetic visceromotor cells lie medially because they are motor nuclei, but not in midline because the midline is reserved for somatomotor nuclei (cranial nerves 3, 4, 6, 12, and 11). In regards to their anterior-posterior position, they reside in the posterior one-third of the brainstem (along with the rest of the cranial nerves).

Now, indicate the sacral nuclei of the parasympathetic craniosacral system are the *intermediolateral cell column nuclei* that span from *sacral levels 2–4*. These nuclei reside in lamina 7 in the intermediate gray matter horn of the spinal cord, which we will discuss in the "Structure of the Spinal Cord and Spinal Canal" chapter.

Next, let's indicate the parasympathetic ganglia sites. We refer to the ganglia as "relay sites" to underscore their primary function, which is the transfer of information from the pre- to the postganglionic neurons; however, they also perform some signal processing, as well. The ganglia targets of the parasympathetic fibers lie far from their origination nuclei and near to their target organs. Indicate cranial nerve 3 relays in the *ciliary ganglion*, cranial nerve 7 relays in both the *pterygopalatine* (aka *sphenopalatine*) and *submandibular ganglia*, cranial

nerve 9 relays in the *otic ganglion*, and cranial nerve 10 relays in the walls of its target organs in the *thoracoabdominal cavity*, which we will list shortly. The visceromotor cell axons from sacral levels 2–4 pass through the sacral plexus and then travel as pelvic splanchnic nerves before they relay in the ganglia of their *target organs in the abdomen and pelvis*. Draw arrows from the nuclei to their ganglia.

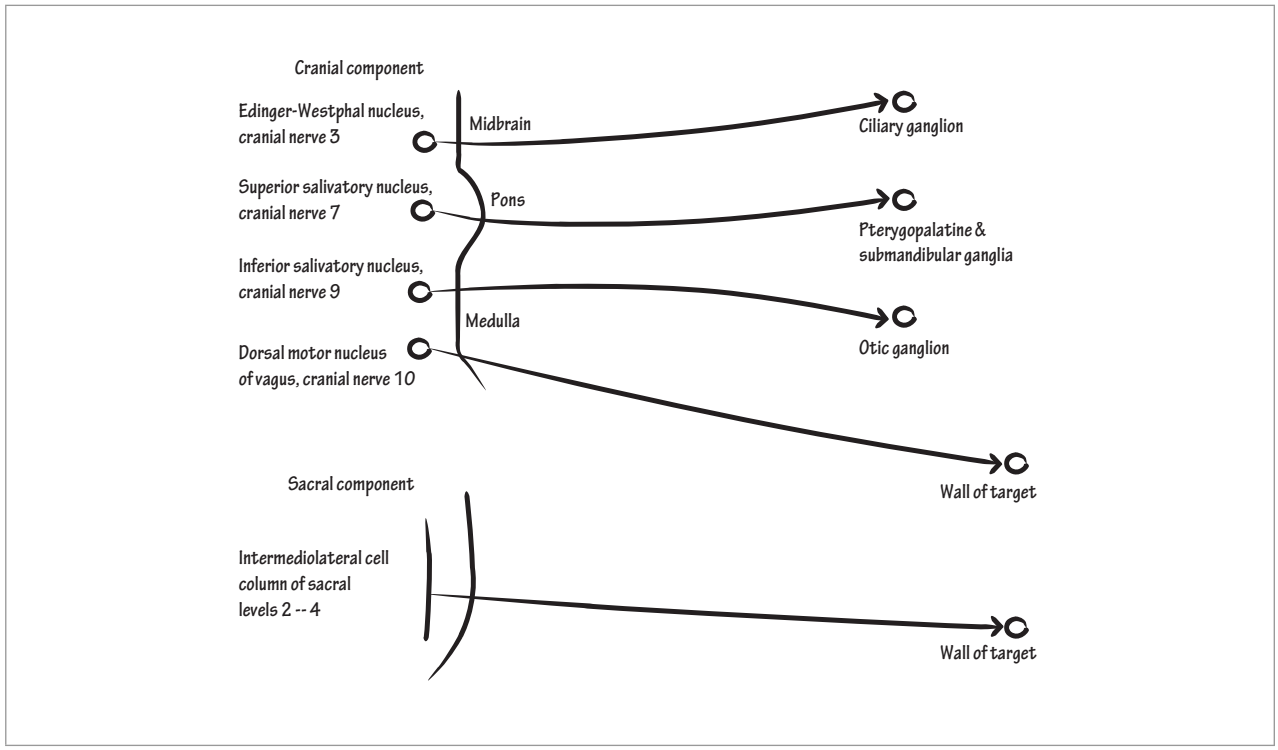


Figure 14-1 Incomplete parasympathetic nervous system

Now, we will address the termination sites of the parasympathetic system and discuss their functional effect. First, indicate the postganglionic parasympathetic fibers from the ciliary ganglion terminate in the *ciliary body*, which provides lens thickening, and in the *pupillary constrictors*, which as their name indicates cause pupillary constriction.

Next, show the postganglionic parasympathetic fibers from the pterygopalatine ganglion terminate in the *nasal* and *lacrimal glands*, the fibers from the submandibular ganglion terminate in the *submandibular* and *sublingual glands*, and the fibers from the otic ganglion terminate in the *parotid gland*. All three postganglionic parasympathetic fiber groups cause glandular secretion.

Now, list the thoracoabdominal target organs of cranial nerve 10, the vagus nerve. Simply put, these target organs constitute the whole of the *thoracoabdominal viscera minus the abdominal hindgut derivatives*; indicate this in the diagram. A comprehensive list of the cranial nerve 10 thoracoabdominal targets is the *heart*, *thoracic vasculature*, *respiratory system*, *esophagus*, *foregut derivatives* (stomach, superior duodenum, liver and gallbladder, and pancreas), and *midgut derivatives* (from the inferior duodenum through the first two-thirds of the transverse colon). The sacral component of the parasympathetic system innervates the abdominal hindgut derivatives, as we will label next. In short, cranial nerve 10 produces heart rate depression, bronchial constriction, increased blood flow to the gut, and increased gut peristalsis and secretion.

Now, indicate in your diagram the sacral parasympathetic system innervates the *pelvic viscera plus the abdominal hindgut derivatives*. A comprehensive list of these targets is the *abdominal hindgut derivatives* (*distal 1/3 of the transverse colon* and *descending colon*), *pelvic hindgut derivatives* (*sigmoid colon* and *rectum*), *bladder*, and *reproductive organs*. Sacral parasympathetic activation increases blood flow to the gut, increases gut peristalsis and secretion, provides urinary bladder detrusor muscle tone (shown in Figure 14-6), and penile or clitoral erection. Draw arrows from the ganglia to their effector tissues.

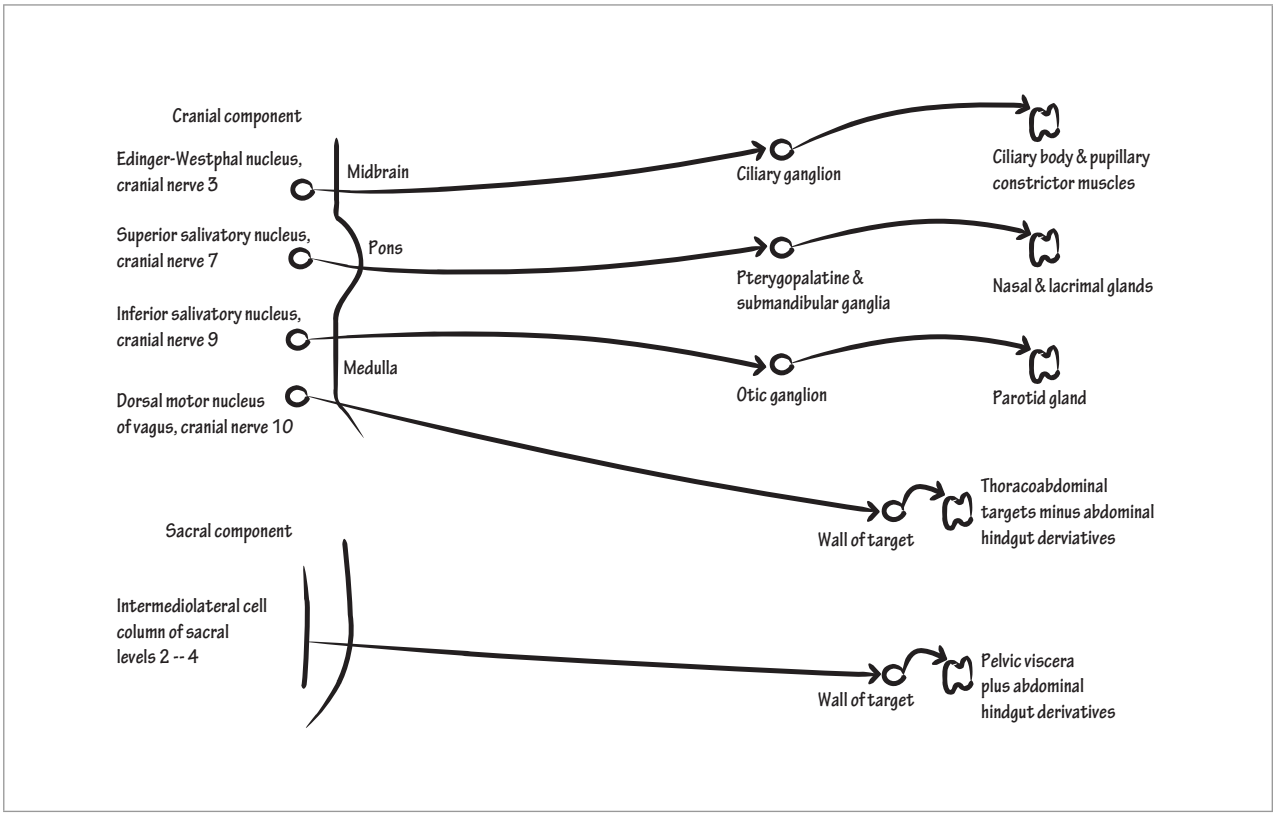


Figure 14-2 Complete parasympathetic nervous system

Now, let's arrange the peripheral sympathetic nervous system. Indicate the sympathetic nervous system originates in the *intermediolateral cell column of the spinal cord* from *T1 to L2*. Next, draw the *paravertebral chain* (aka *sympathetic chain* or *sympathetic ganglia*). It resembles a string of pearls, lies just lateral to the vertebral column, and extends vertically from the cervical to the sacral spinal canal (even though its spinal cells of origin are confined to the thoracic and lumbar levels). The paravertebral chain contains *3 cervical, 10 thoracic, 3–5 lumbar*, and *3–5 sacral ganglia* on each side and a single *coccygeal ganglion* shared by both paravertebral chains. The somatotopy of these ganglia is fairly broad. Fibers from rostral intermediolateral cells of the spinal cord synapse in rostral ganglia and fibers from caudal intermediolateral cells synapse in caudal ganglia. Of the 24 sympathetic ganglia, only 3 are clinically worth specifying: the *superior cervical ganglion*, which sits at the top of the chain; the *middle cervical ganglion*, which lies beneath it; and the *stellate ganglion*, which is a combination of the *inferior cervical* and the *first thoracic ganglia*. Show the postganglionic fibers from the superior cervical ganglion terminate in the *head and neck* (the *C1–C4* dermatomal level). Then, indicate the postganglionic fibers from the middle cervical and stellate ganglia terminate in the *arm*.

In Horner's syndrome, sympathetic innervation to one-half of the face is disrupted. What, then, do you imagine is the clinical presentation of this syndrome? The sympathetic system generates pupillary dilation and eye widening and also vasoconstriction in the blood vessels of the skin and sweat glands. Thus, Horner's syndrome presents with (1) narrowing of the palpebral fissure, which is superior eyelid droop and inferior eyelid raise from loss of sympathetic tone to the superior and inferior tarsal muscles; (2) pupillary constriction from loss of innervation to the pupillary dilator muscles; (3) vasodilation of the face (aka facial flushing) from loss of blood vessel vasoconstriction in the skin; and (4) facial anhidrosis, which is loss of sweat production on the side of the face, best appreciated by facial palpation. This important clinical syndrome can occur with lesions anywhere within the pathway of sympathetic innervation to the face. It most commonly points to either a brainstem lesion, a paravertebral mass, specifically a tumor at the apex of the lung (e.g., a Pancoast tumor), or a carotid dissection, as we will discuss further in the next couple of paragraphs.

Let's address the general anatomy of sympathetic innervation to the face since Horner's syndrome is so important. We will discuss the specific constituents of the supraspinal pathways (e.g., the hypothalamospinal pathway) in the "Hypothalamus" chapter; however, let's consider them here under the general heading of "supraspinal pathways." Draw descending *supraspinal input* through the brainstem to the *intermediolateral cell column* of the spinal cord. Rostral midline brainstem or lateral caudal brainstem lesions, such as lateral medullary syndrome (aka Wallenberg's syndrome), cause unilateral sympathetic nervous system disruption.

Within the intermediate horn of the spinal cord at the C8–T1 level is the *ciliospinal center of Budge*. Draw a representative preganglionic fiber exit the spinal cord from the ciliospinal center of Budge and ascend the sympathetic chain to the superior cervical ganglion. Paravertebral masses, such as apical lung tumors, specifically Pancoast tumors, potentially interrupt these exiting preganglionic sympathetic fibers. The T2–T4 fibers carry sympathetic innervation for facial sweating so if the lesion remains above T2–T4, facial sweating will be unaffected.

Now, draw a representative postganglionic sympathetic fiber from the superior cervical ganglion. These fibers envelop and ascend the *common carotid artery*. Next, continue the representative fiber up the *internal carotid artery* into the cranium. A dissection of either the common or internal carotid artery will cause Horner's syndrome.

Here, we will address the differential innervation of facial sweating; skip ahead, if you like. Fibers that ascend the internal carotid artery provide medial forehead facial sweating, whereas the fibers for facial sweating from the rest of the face travel along the external carotid artery (we exclude it from the diagram for simplicity). If the internal carotid artery, alone, is affected, then loss of sweating only occurs on the medial forehead. Otherwise, if the sympathetic fibers are disrupted proximal to the bifurcation of the common carotid artery, or along both the internal and external carotid arteries, then loss of sweating occurs over the entire ipsilateral face.

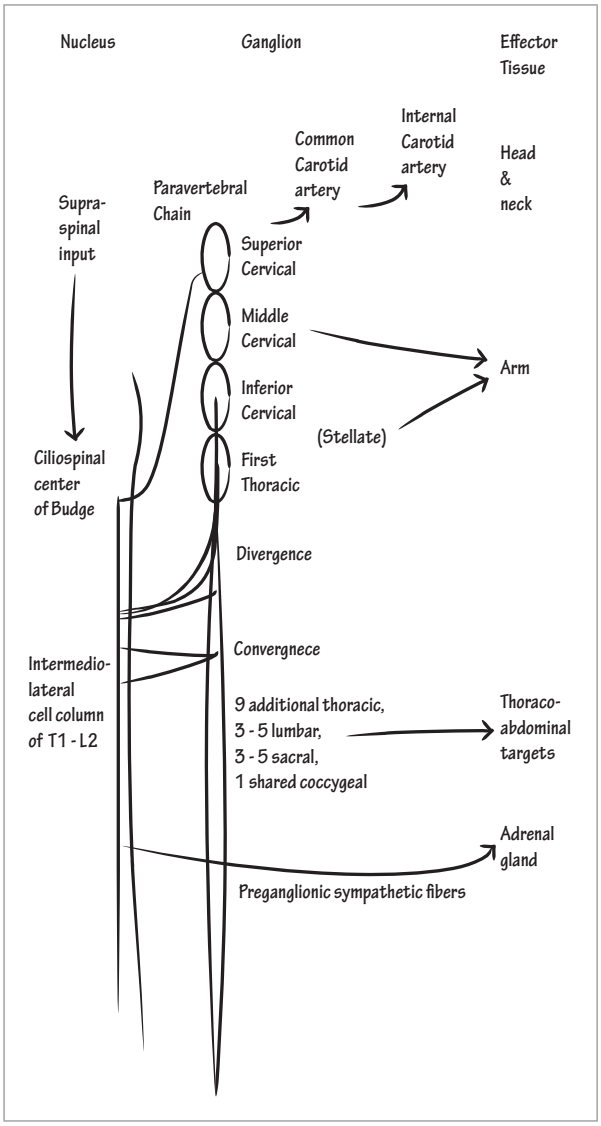


Figure 14-3 Incomplete sympathetic nervous system

Within the sympathetic system, both divergence and convergence of preganglionic sympathetic fibers occur. *Divergence* is the multi-level synapses of different preganglionic fibers originating from the same spinal level: preganglionic fibers synapse in ganglia at their level of origin or at levels above or below along the sympathetic chain. Draw an example, now. In contrast, *convergence* is the confluence of fibers from different preganglionic levels; show an example of this in our diagram.

Now, draw a representative postganglionic midthoracic fiber. Thoracic postganglionic sympathetic fibers either join a spinal nerve or project alone to thoracic targets, as cervical or thoracic cardiac or pulmonary nerves, for instance.

Move down the rostro–caudal axis. Certain preganglionic sympathetic fibers circumvent the paravertebral ganglia and synapse directly in the adrenal gland; show one example, now. Note, the adrenal medulla is derived from neural crest cells and it mainly releases epinephrine, which is part of the same class of neurotransmitters that postganglionic sympathetic neurons release.

Next, draw the four prevertebral ganglia, which span from the level of the lower thoracic to the sacral vertebral column. Show four representative *splanchnic nerves* leave the spinal cord, pass through the sympathetic chain, and synapse in the prevertebral ganglia. Label the prevertebral ganglia, from superior to inferior, as the *celiac*, *aorticorenal*, *superior mesenteric*, and *inferior mesenteric ganglia*. In Figure 14-6, we draw the autonomic innervation to and from the bladder, which provides an example of the anatomy of this region. Each of the prevertebral ganglia is associated with a branch of the aorta and bears its name. In gross anatomy, we learn the names of these aortic branches well; let's refresh our memories as we go along, now. Indicate the celiac ganglion innervates the *spleen* and *foregut derivatives*; the aorticorenal ganglion innervates the *renal vessels*; the superior mesenteric ganglion innervates the *midgut derivatives*; and the inferior mesenteric ganglion innervates the *hindgut derivatives*, *urinary, and reproductive organs*. These are the target organs of the parasympathetic branches of the vagus nerve and the S2–S4 sacral spinal cord intermediolateral cell column, which underscores the point made at the beginning of this chapter that most visceral targets receive opposing parasympathetic and sympathetic innervation. Those targets that receive only sympathetic innervation are the blood vessels to skeletal muscle and skin, sweat glands, and hair follicles.

In the next diagram, Figure 14-5, we will draw simplified versions of the parasympathetic and sympathetic systems to compare their neuroanatomy and neurobiology.

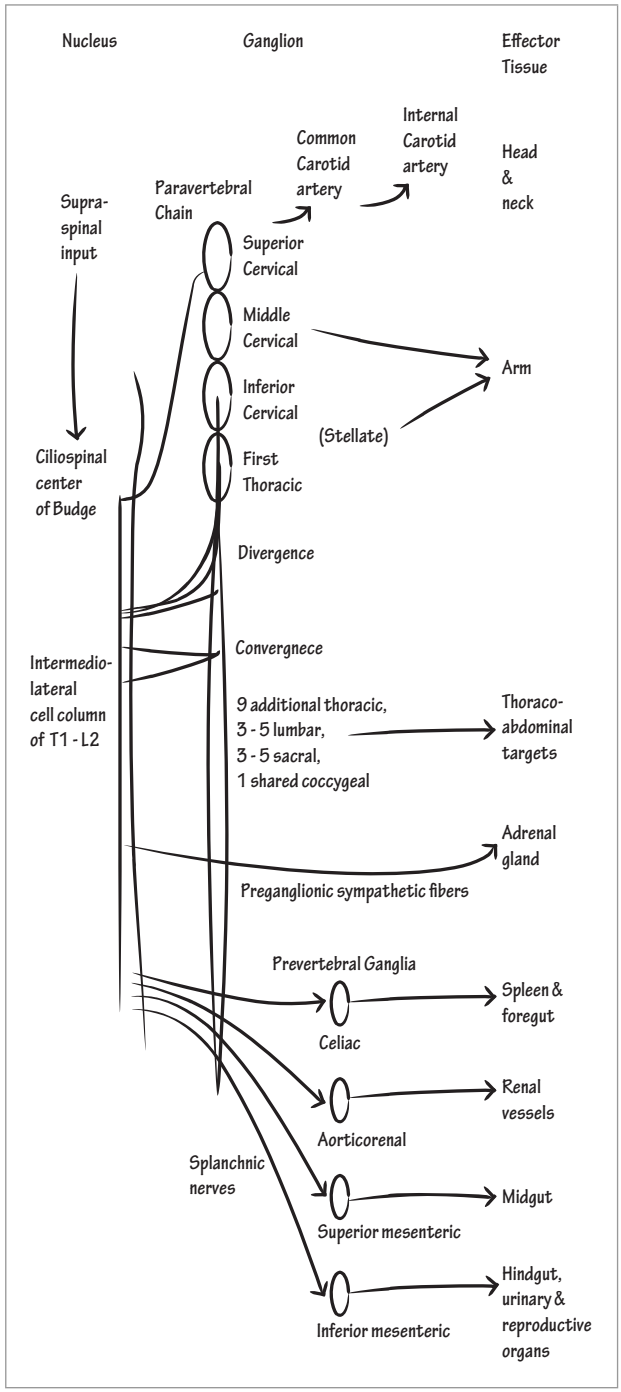


Figure 14-4 Complete sympathetic nervous system

Draw representative *preganglionic neurons* for both the parasympathetic and sympathetic systems and indicate that both release *acetylcholine*. Next, in the parasympathetic arrangement, show a long axon synapse on a ganglion within its effector tissue—cranial nerve and sacral parsympathetic ganglia lie either very close to or at the site of their target organ. Then, draw a short sympathetic axon to a nearby peripheral ganglion; sympathetic axons are short and synapse either in the paravertebral chain or one of the prevertebral ganglia. Preganglionic sympathetic fibers to the adrenal gland are the exception; they travel the long distance to make their primary synapse in the adrenal gland, itself.

Draw a postganglionic neuron in each arrangement. Indicate the postganglionic parasympathetic fiber projects from just outside or just inside the wall of the target organ to its *effector site*, whereas, the postganglionic sympathetic fiber travels the long distance to its *target organ*. Indicate all postganglionic *parasympathetic* fibers release *acetylcholine* and all postganglionic *sympathetic* fibers release *norepinephrine* except the postganglionic *sympathetic* fibers to sweat glands, which release *acetylcholine*. The preganglionic sympathetic fibers to the adrenal gland stimulate the release of a different adrenergic neurotransmitter type, epinephrine, which assists in the "fight or flight" response.

Neuropeptides are also released from both the pre- and postganglionic nerve terminals; generally, less importance is given to the neuropeptides of the peripheral autonomic nervous system, skip ahead, if you like. Indicate the preganglionic sympathetic fibers release *enkephalin* and *substance P* and the postganglionic sympathetic fibers release *neuropeptide Y*. Then, indicate the postganglionic parasympathetic fibers release *vasoactive intestinal peptide*. As a class, neuropeptides play a role in the potentiation of pain; they are large molecules with long-lasting effects. Neurotransmitters, in contrast, are small molecules with transient effects.

The interaction between neuropeptide pain potentiation and the sympathetic nervous system is best understood in the context of the clinical syndrome of complex regional pain syndrome (aka *reflex sympathetic dystrophy*). Patients with this disorder suffer from abnormal pain production and dystrophic sympathetic skin response. In particular, patients complain of hypersensitivity to mild noxious stimuli or abnormal perception of pain from otherwise normal stimuli (e.g., pain when the bedsheets touch their legs). Remember, sympathetic fibers innervate blood vessels in skeletal muscle and skin, sweat glands, and hair fibers, and indeed, these patients manifest with venous mottling, abnormal sweating patterns, and abnormal hair growth or hair loss. The pathophysiology of this disorder is still under investigation; however, the intermingling of efferent sympathetic motor fibers with afferent sensory fibers is believed to be important. Surgical or pharmacologic disruption of the sympathetic tracts is often used to treat complex regional pain syndrome.

Autonomic nerves also have afferent fibers; they comprise a large proportion of the parasympathetic nerve fibers but are only sparsely found within sympathetic nerves. Parasympathetic afferents mostly carry non-noxious stimuli (physiologic information). On the contrary, sympathetic afferents predominately carry noxious information. Both parasympathetic and sympathetic afferent fibers project to the intermediolateral cell column at the level of their visceromotor efferent counterparts. The fibers ascend the spinal cord as part of the anterolateral system, either as part of the direct spinothalamic tract or as one of the indirect spinothalamic pathways.

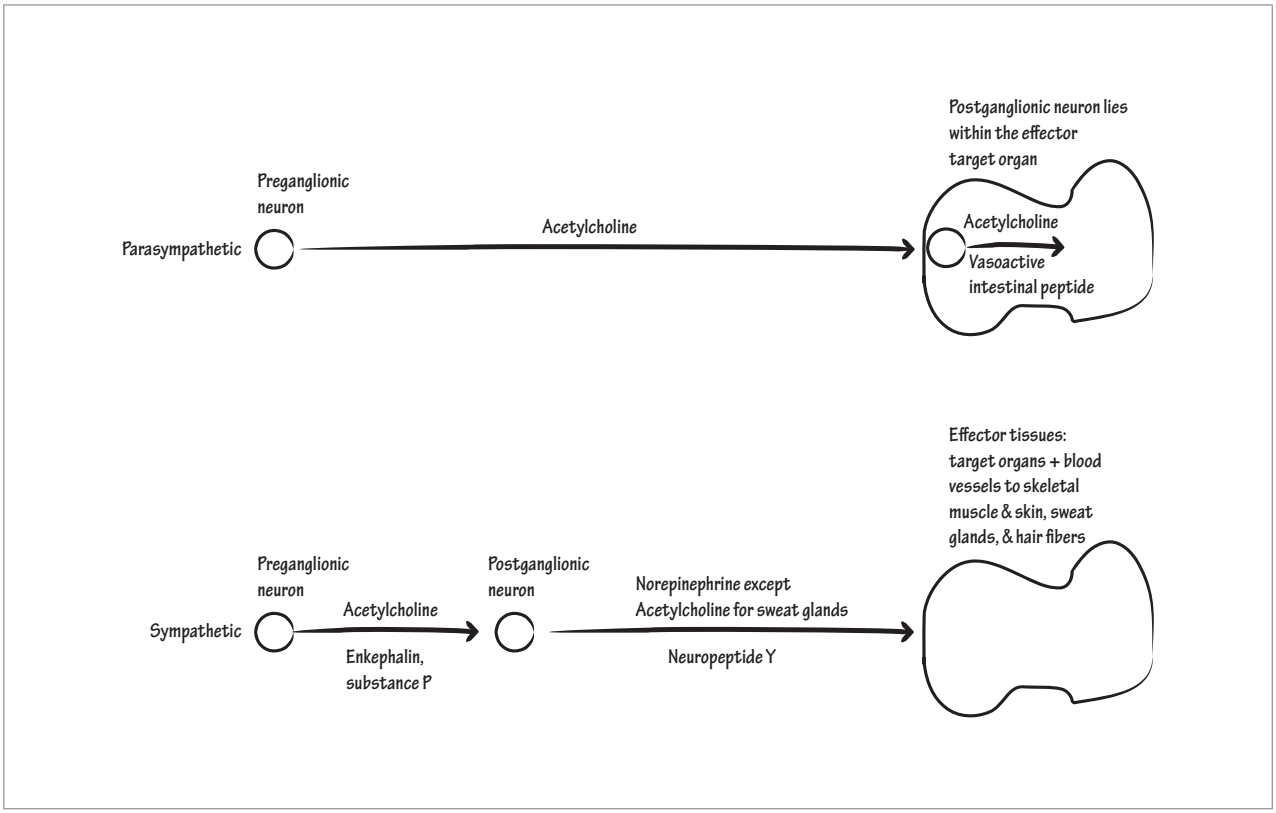


Figure 14-5 Sympathetic and parasympathetic peripheral autonomic nervous system arrangements

Parasympathetic afferents have a complicated, but important, role in the maintenance of homeostasis, level of arousal, and response to physiologic stress. They terminate in cortical regions, such as the parietal operculum, and more midline areas, such as the midbrain and hypothalamus. In a moment, we will demonstrate how sacral parasympathetic information is passed to efferent fibers and how it generates a spinal reflex.

Sympathetic viscerosensory afferents cause referred pain, whereby internal organs manifest with body surface pain. Since Sir Henry Head wrote about this subject in the early 1900s, many accounts of the dermatomal distribution of visceral pain have been published; however, the pathophysiologic mechanism underlying visceral pain remains unclear. It results either from direct intermingling of sympathetic and somatic afferent fibers or from indirect somatic fiber sensitization. Also, it occurs either peripherally (i.e., in the peripheral nerves) or centrally (i.e., in the spinal cord). Regardless of the exact pathophysiologic mechanism, it is clear that visceral organs refer pain to their related somatic dermatomal distributions.

Using this rule, let's work out the somatotopic map of referred pain for the diaphragm and then the heart. First, what is the autonomic innervation of the diaphragm? (Hint: "they keep the diaphragm alive!" . . . C3, C4, C5). Cervical levels 3–5 innervate the diaphragm. And where do you feel pain from your diaphragm? In your neck and upper shoulder, which is the dermatomal distribution of these cervical levels. Next, let's figure out the visceral map for the heart. Where do you feel pain from your heart? On the left-side of the chest and down the inside of the left arm. What innervates the left-side of the heart? The T1–T5 spinal nerves, which distribute along the left-side of the chest and the inside of the left arm. Notably, cardiac pain does not extend into the fingers; they are supplied by the C6–8 dermatomal levels.

Now, let's draw the bladder system to introduce the viscerosensory system and show how the parasympathetic and sympathetic motor systems interact during micturition (aka urination). First, draw a *bladder* and its *urethra*; label the bladder wall as the *detrusor muscle*. Next, indicate a *viscerosensory afferent* impulse from the bladder wall to the autonomic nervous system center in the spinal cord. Indicate the impulse stimulates the *S2–S4 parasympathetic efferents*, which cause the bladder wall to contract. However, as you can imagine, these parasympathetic efferents require regulation; otherwise your bladder would automatically empty whenever it filled.

Indicate *preganglionic sympathetic efferents* from *L1–L2* synapse in the *inferior mesenteric ganglion*. Then, show *postganglionic symapthetic fibers* from the ganglion inhibit both the parasympathetic efferent constrictors as well as the bladder wall, itself. The sympathetic fiber system also stimulates the internal urinary sphincter to prevent leakage of urine. It has the same functional effect as does relaxation of the detrusor muscle, therefore, we leave it out of our diagram. Next, indicate *S2–S4 somatic efferents* control the *external urethral sphincter*. The external urethral sphincter, like the internal urethral sphincter, is tonically contracted to prevent leakage of urine; however, it is under conscious control. How do we inhibit it and the sympathetic fibers in order to urinate? With supraspinal inhibition; show descending *supraspinal inhibition* onto the sympathetic and somatic spinal cord centers, now.

What happens when supraspinal pathways for autonomic and somatic innervation of the bladder are interrupted? Depending on the site of the lesion, either bladder distension isn't felt and it empties on its own, so-called hypotonic bladder incontinence, or the urethra becomes secondarily hypertonic and the bladder is unable to empty, so-called bladder spasticity. In patients with spinal cord injuries, always address the necessity for bladder catheterization (i.e., urethral tube placement for automatic bladder emptying) to prevent bladder rupture.

In the above system, the pelvic nerve carries the parasympathetic fibers, the hypogastric nerve carries the postganglionic sympathetic fibers, and the pudendal nerve carries the somatic fibers.

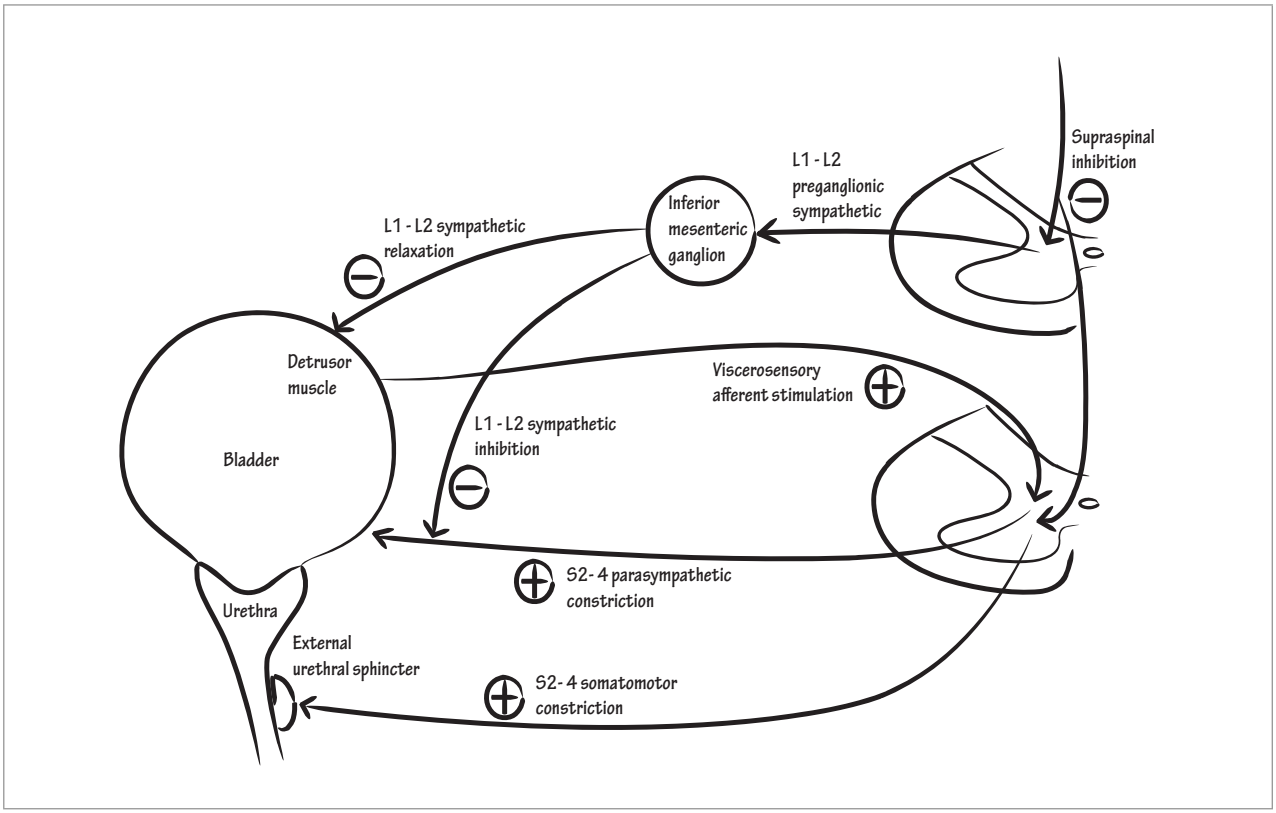


Figure 14-6 Bladder innervation

Now, we will draw the baro- and chemoreceptor reflexes. Chemoreceptors respond to certain blood properties, such as arterial oxygen and carbon dioxide levels, blood acidity, temperature, and the presence of pharmacologic agents; whereas, baroreceptors respond to changes in arterial blood pressure. We test the integrity of the baroreceptor reflex in clinical neurology to understand the pathophysiology of different autonomic disorders. When the baroreceptor reflex fails, blood pressure drops precipitously upon standing. This causes a drop in cerebral perfusion pressure, which manifests as lightheadedness and, if severe, syncope (aka loss of consciousness). The mean arterial pressure is given by

Mean arterial pressure = diastolic pressure + 1/3 pulse pressure
where the pulse pressure = systolic pressure − diastolic pressure.

When the mean arterial pressure drops below 40 millimeters of mercury (mmHg), we almost invariably lose consciousness. When going from a lying to an upright sitting or standing position, a sustained drop in systolic blood pressure of 20 mmHg or a sustained drop in diastolic blood pressure of 10 mmHg is called *orthostatic hypotension*. The duration of a "sustained drop" is commonly considered to be 2 minutes for reasons we will discuss shortly. Orthostatic hypotension can occur because the baroreceptors fail; autonomic fibers to or from blood vessels fail; blood pressure processing in the central nervous system fails; or because there is insufficient blood volume to maintain blood pressure despite an intact autonomic nervous system. One way of distinguishing a dysfunctional autonomic nervous system from lack of blood volume is by assessing the heart rate response to a drop in blood pressure. When blood pressure falls, if the autonomic nervous system is intact, the heart rate will increase. With a sustained drop in blood pressure, a 15-beat compensatory increase in heart rate ought to occur. If not, then the autonomic nervous system is defective.

Another way to test the autonomic nervous system is to assess the cardiac output response to changes in circulating blood volume; there are two simple ways to do so at the bedside. Feel your pulse, now, and get a good sense of your heart rate. Take a deep breath and hold it. Wait 5 or 6 seconds. What happened to your heart rate? It sped up. Why? When you inhale deeply, you open up lung tissue and shunt blood into the lung capillaries, which reduces your effective circulating blood volume (aka stroke volume). Cardiac output is stroke volume multiplied by heart rate. Therefore, to compensate for a decreased stroke volume, you *increased your heart rate* (typically by 8 beats per minute).

What happens when you perform a *valsalva maneuver* or forcibly exhale with your mouth closed? Venous blood is unable to return to your heart; this again reduces your effective circulating blood volume and the result is the same—the heart rate increases. If your cardiac output is unable to compensate sufficiently, you pass out. Micturition syncope is an example of an inability to compensate for a drop in effective circulating blood volume.

What is another way to compensate for a decreased stroke volume other than by increasing your heart rate? What happens when you stand up and blood pools in your veins? Your heart rate increases, initially. But you also need a longer term solution. Once you have been standing for a full minute, T5 sympathetic splanchnic fibers command the abdominal vessels to shunt 1.5 units of blood from your abdomen into your peripheral vasculature, which bolsters your circulating blood volume. This is why when you test orthostatic blood pressure, you must wait at least 2 minutes in between measuring supine and standing blood pressure so as to allow this response to take effect; otherwise you will not be accurately assessing the integrity of the autonomic nervous system. Instead, you will be only detecting the natural blood pressure drop that occurs when blood pools in the veins. Some clinicians argue you should wait even longer.

Now that we have discussed the clinical relevance of the baroreceptor reflex, let's diagram the joint baro- and chemoreceptor reflexes. First, draw the *carotid body* and *aortic arch chemoreceptors*, as well as the *carotid sinus* and *aortic arch baroreceptors*. Show that the afferent fibers from these structures travel via parasympathetic fibers of *cranial nerve 9* (the *glossopharyngeal nerve*) and *cranial nerve 10* (the *vagus nerve*). Their target ganglia have superior and inferior divisions. Indicate the afferent ganglia for these viscerosensory fibers are the *inferior ganglia*. The superior divisions of these respective ganglia are relay stations for *somato*sensory afferent fibers (i.e., from pharyngeal tissues). The way to remember this (although not a perfect rule) is that visceral fibers come from below the level of the ganglia and somatosensory fibers come from above it; hence,

visceral fibers synapse in the inferior division and somatosensory fibers synapse in the superior division.

Next, draw an axial cross-section through the medulla. Indicate the fibers from the inferior ganglia of the glossopharyngeal and vagus nuclei project to the *solitary tract nucleus* in the posterior one-third of the brainstem.

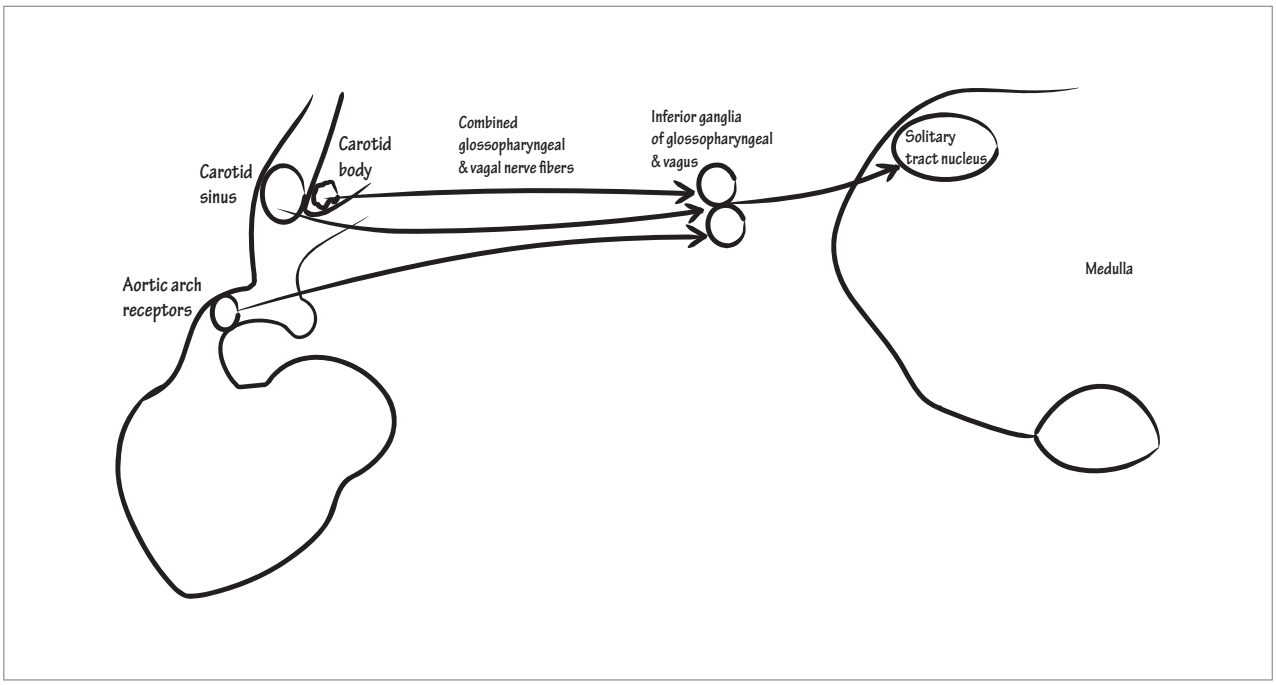


Figure 14-7 Incomplete baroreceptor and chemoreceptor reflex

Now, draw the *dorsal motor nucleus of the vagus nerve* medial to the solitary nucleus and also label the *anterolateral portion of the medulla*. The dorsal motor nucleus of the vagus sends *parasympathetic* visceromotor fibers to the heart, whereas the antero-lateral portion of the medulla is a supraspinal center that influences the *sympathetic* visceromotor fibers to the heart. Show the solitary tract nucleus project to the dorsal motor nucleus of the vagus nerve and also to the anterolateral medulla to communicate afferent carotid and aortic chemo- and baroreceptor information. Nucleus ambiguus performs minor visceromotor functions similar to that of the dorsal motor nucleus of the vagus; however, it is primarily a somatomotor nucleus so we leave it out of the drawing.

Where should the preganglionic parasympathetic fibers from the dorsal motor nucleus of the vagus project? Do parasympathetic ganglia lie close to or far from their target organ? They lie close to or within the organ, itself. Indicate the parasympathetic ganglion for the vagal nerve fibers is within the *wall of the heart*. Draw *preganglionic parasympathetic efferent fibers* that project to the ganglion, and then draw *postganglionic parasympathetic projection fibers* that project deep into the heart.

Next, turn your attention to the sympathetic anterolateral portion of the medulla. Show the anterolateral medullary supraspinal input descends the spinal cord to the *thoracic intermediolateral cell column* of the spinal cord. Then, show a representative cardiac thoracic nerve projection from this cell column to the *paravertebral chain ganglia*, and then show a *postganglionic sympathetic projection* to the heart.

What effect does this pathway have on the heart? The dorsal vagal fibers provide parasympathetic *vasodepressor* effects, which *decrease* both the heart rate and blood pressure, and the anterolateral medullary fibers provide sympathetic *vasopressor* effects, which *increase* both the heart rate and blood pressure.

The digestive tract is under the influence of the central nervous system through the parasympathetic and sympathetic pathways; however, it also contains its own autonomic system called the enteric nervous system (aka intrinsic nervous system of the gut). The enteric nervous system comprises numerous neurons distributed in myenteric and submoucosal plexuses that communicate motor, sensory, and other visceral information. The enteric nervous system and the pacemaker-like smooth muscle cells of the digestive system wall (the interstitial cells of Cajal) generate and propagate patterns of depolarization that result in waves of peristaltic muscle contraction. Food ingestion triggers this peristaltic reflex, which propels food through the digestive tract, and the enteric neural circuits adjust intestinal blood flow and secretomotor activity for absorption.

Notably, psychopharmacologic drugs often affect the neurotransmitters and neuromodulators of the enteric nervous system. For instance, acetylcholine is an important peristaltic promoter, so cholinesterase inhibitors, which increase circulating levels of acetylcholine, promote gastrointestinal activity and can result in loose stools. In contrast, tricyclic antidepressants contain anticholinergic properties that can cause constipation.

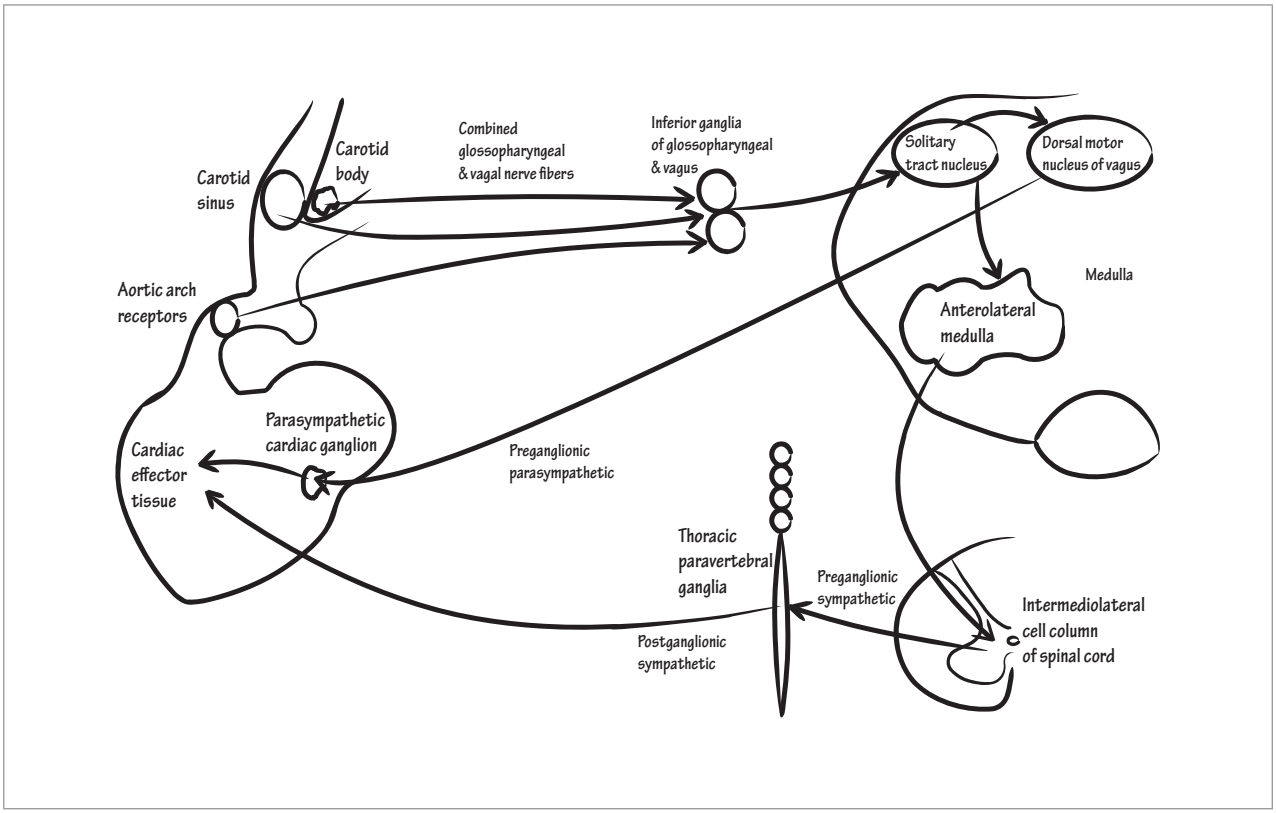


Figure 14-8 Complete baroreceptor and chemoreceptor reflex

Structure of the Spinal Cord and Spinal Canal

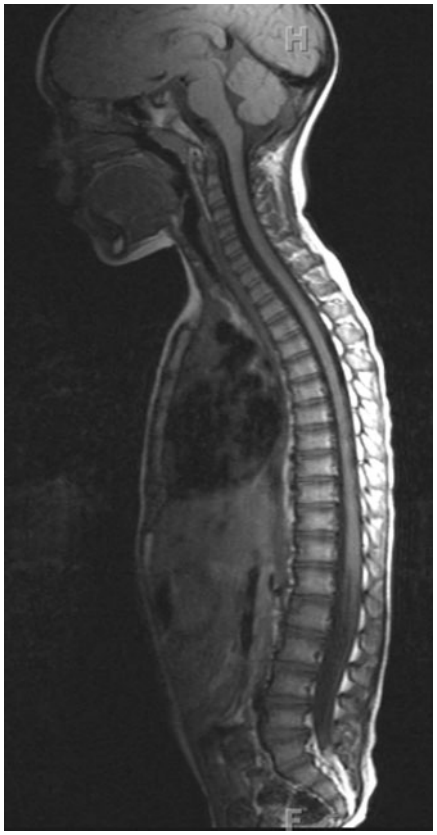


Photo 15-1 Complete spine

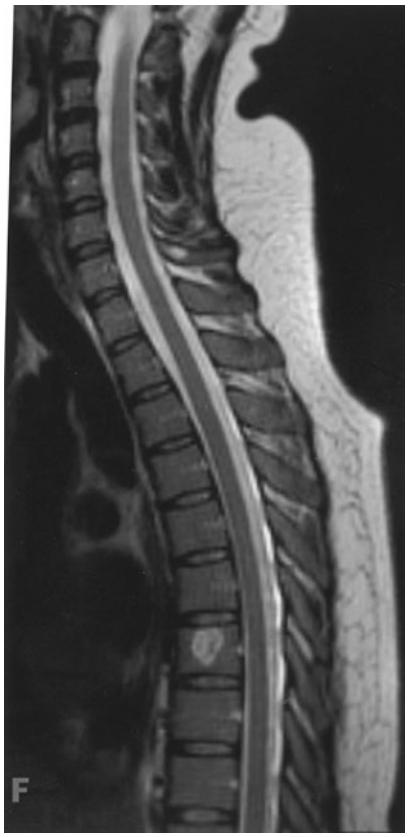


Photo 15-2 Cervical and thoracic spine: the hemangioma (the bright round lesion) found in the body of T7 is also seen in Photo 15-3 and is a useful orientational landmark in this patient

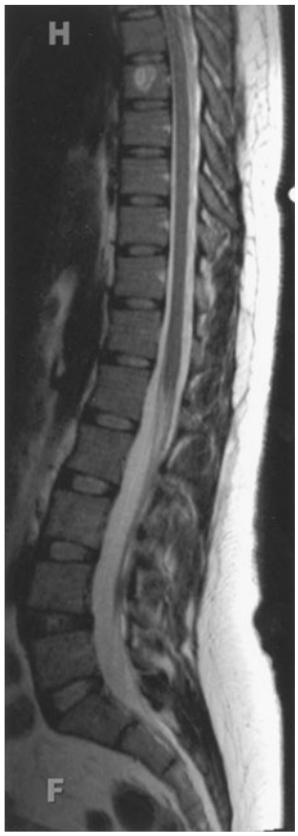


Photo 15-3 Lumbosacral spine

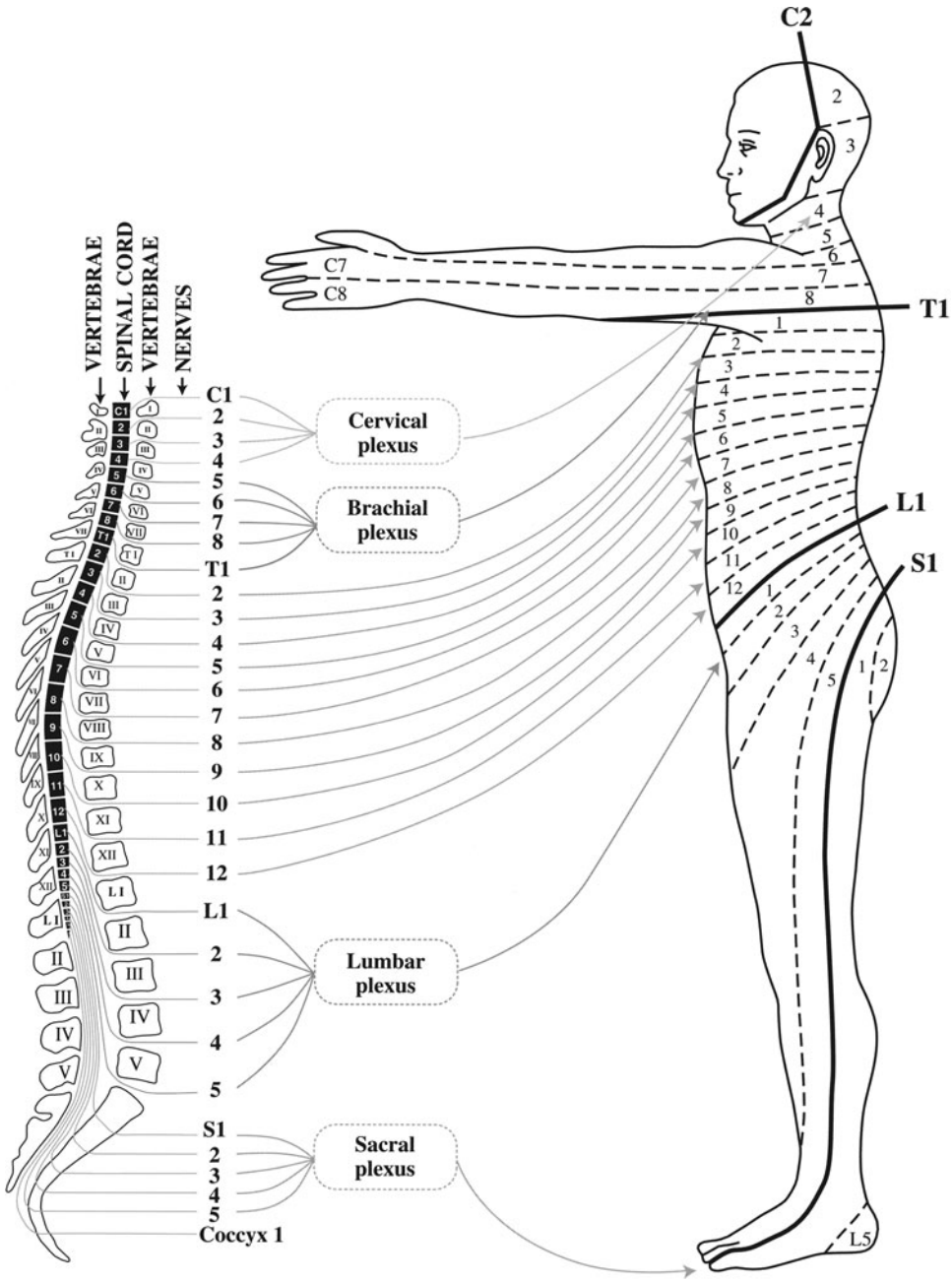


Photo 15-4 Segmental organization of the spinal cord, vertebral column, nerve roots, plexuses and thoracic nerves, and cutaneous dermatomes

With permission from Altman, J., and S. A. Bayer. *Development of the Human Spinal Cord: An Interpretation Based on Experimental Studies in Animals*. Oxford and New York: Oxford University Press, 2001.

THE SPINAL CORD is the gateway between the brain and the periphery; it carries and modulates transmissions between them and generates impulses of its own. The spinal canal protects and supports the spinal cord; therefore, it is important to know the anatomy of the spinal canal as well as that of the spinal cord. In this chapter, we will draw the relevant structures of the spinal canal and discuss their rostro–caudal regional characteristics.

Another name for the spinal cord is the *medulla spinalis*. If you want to understand the origin of this name, read on; otherwise, skip ahead. The brainstem is similar to the spinal cord in appearance and function. The lower one-third of the brainstem is called the medulla, which is short for medulla oblongata. *Medulla* simply means "marrow," and both the spinal cord and brainstem share a similar medullar histological appearance. *Oblongata* refers to the oblong shape of the lower brainstem, and *spinalis* refers to the location of the spinal cord within the spinal canal. From these origins, we get "medulla oblongata" for the lower one-third of the brainstem and "medulla spinalis" for the spinal cord. The lowermost section of the spinal cord is called the "conus medullaris" due to its conical shape.

We begin our diagram of the spinal canal with a sagittal section through the spinal cord and brainstem. Draw the cervical segment of the spinal cord angling anteriorly, the thoracic segment angling posteriorly, and the lumbosacral segment angling anteriorly, again.

Next, we will draw an outline of the vertebral bodies of the spinal cord. There are 7 cervical, 12 thoracic, 5 lumbar, and 5 sacral vertebral bodies, as well as 1 coccyx. The shape of the spinal canal is more challenging to draw than that of the spinal cord; however, it is worth learning, especially for reading spinal imaging. First, consider that the spinal cord ends at the level of the L1–L2 vertebral bodies. Thus, in any axial (aka horizontal) segment, the spinal cord level is lower than the vertebral column, and the vertical difference between the spinal and vertebral levels increases as you descend the spinal canal. Instead of drawing the curvature of the spinal canal with a continuous line, as we did for the spinal cord, it will be easiest to simply draw the superior-most and inferior-most vertebral bodies in each segment of the vertebral column. Then, at the end, we will be set to show the passage of the spinal nerves through the vertebral bodies, which is a clinically important anatomical subject matter.

In the upper canal, the vertebral column follows the spinal cord curvature: it moves anteriorly in the cervical segment and posteriorly in the upper thoracic segment. But it bends back anteriorly in the lower thoracic segment. Why should this be? In order to accommodate the lumbosacral spinal cord, which also bends anteriorly. Next, show the vertebral column angles posteriorly, again, in its lower lumbar segment. Then, draw the sacral vertebral column with an even sharper posterior angle. This hyperflexion of the sacral column helps demarcate the clinically important L5–S1 junction, which is a common site of nerve root compression. Finally, draw the coccygeal bodies curving back anteriorly.

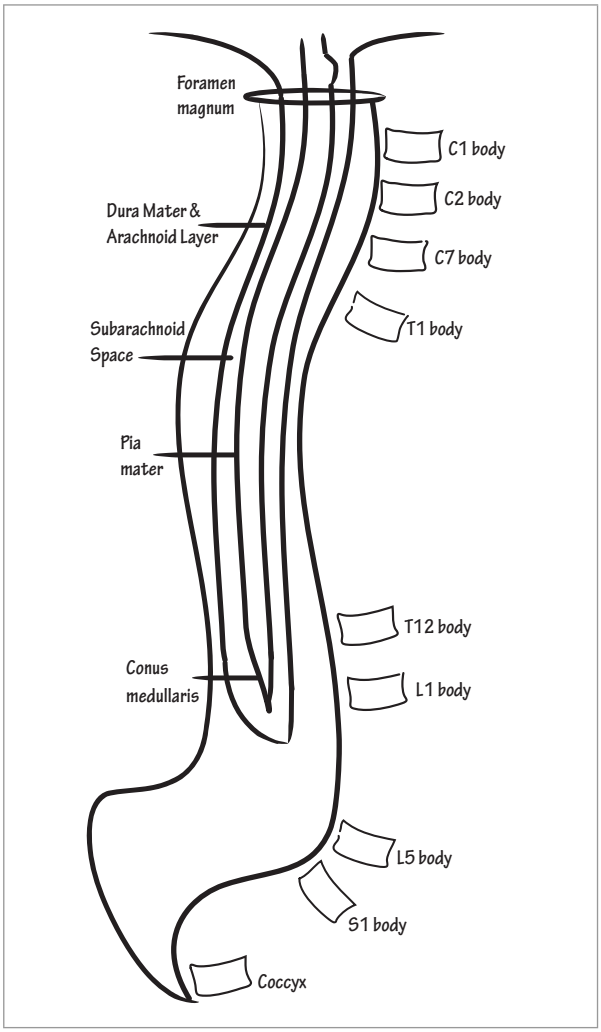


Figure 15-1 Incomplete spinal canal

A pair of motor and sensory roots exit the spinal cord separately and combine within an intervertebral neural foramen to form a spinal nerve. The intervertebral neural foramina are formed from vertebral notches in vertebrae. The superior vertebral notch of one vertebra forms the lower margin of the intervertebral foramen and the inferior vertebral notch of the vertebra above it forms the upper margin of the intervertebral foramen. Vertebrae comprise a body, anteriorly, two pedicles that extend posteriorly from the back of the body, two laminae that connect to the posterior ends of the pedicles, and transverse and spinous processes that connect to the laminae. Refer to a skeletal anatomy text for further detail. Certain nerves pass above the vertebrae and others pass below it; thus, the numbering arrangement for the nerves and bodies is confusing. There are 8 numbered cervical spinal nerves but only 7 cervical vertebrae; all the rest of the segments (thoracic, lumbar, sacral, and coccygeal) have equivalent nerves and bodies. Show the first cervical spinal nerve, C1, exit below the skull (beneath the *foramen magnum*) and above the first cervical vertebra. Then, illustrate C2 exits above its vertebra, and so on. Show C7 exit above the C7 vertebra, which is the lowermost cervical vertebra. So where does C8 go? C8 exits underneath the C7 vertebra and above the T1 vertebra. Where, then, must the T1 nerve exit? Below the T1 vertebra because the space above it is filled with the exiting C8 nerve.

Draw out the exit course of the superior-most and inferior-most spinal nerves for each vertebral segment and you will notice that only the cervical nerves exit above their bodies. C8 and all the nerves below it exit below their respective vertebrae. Pay attention to the lumbosacral roots, as they have a particularly extensive intraspinal column course before they exit the caudal aspect of the vertebral column.

Now, label the collection of nerve fibers that traverse the caudal spinal canal as the *cauda equina*, which is the Latin term for "tail of the horse." The anatomically related, threadlike fibrous tissue that extends from the distal tip of the spinal cord through the caudal spinal canal is the filum terminale. Label the most distal, bulbous region of the spinal cord as the *conus medullaris*.

Next, let's label the meningeal coverings of the spinal canal. Label the surface of the spinal cord, itself, as covered with *pia mater*. Then, draw the *dura mater* and underlying *arachnoid mater*. Show there is plenty of separation between these meningeal coverings and the underlying spinal cord and also space between the dura and the overlying veretebrae. Indicate the naturally occurring space between the arachnoid and pia mater layers is called the *subarachnoid space*.

To collect cerebrospinal fluid, clinicians insert a needle into the lumbar cistern, which is inside the dura, below the spinal cord. Feel for your iliac crests (the tops of your hips); they correlate to the L3–L4 spinal level. When you perform a spinal tap, insert the spinal needle into the back at that level. In a normal spine, the spinal cord ends at L1–L2, so at L3 and below, it is safe from puncture. Sometimes the spinal cord is pathologically tethered to the base of a vertebral body and stretches below the L1–L2 level. In these cases, cerebrospinal fluid may need to be withdrawn from the cisterna magna at the base of the brain.

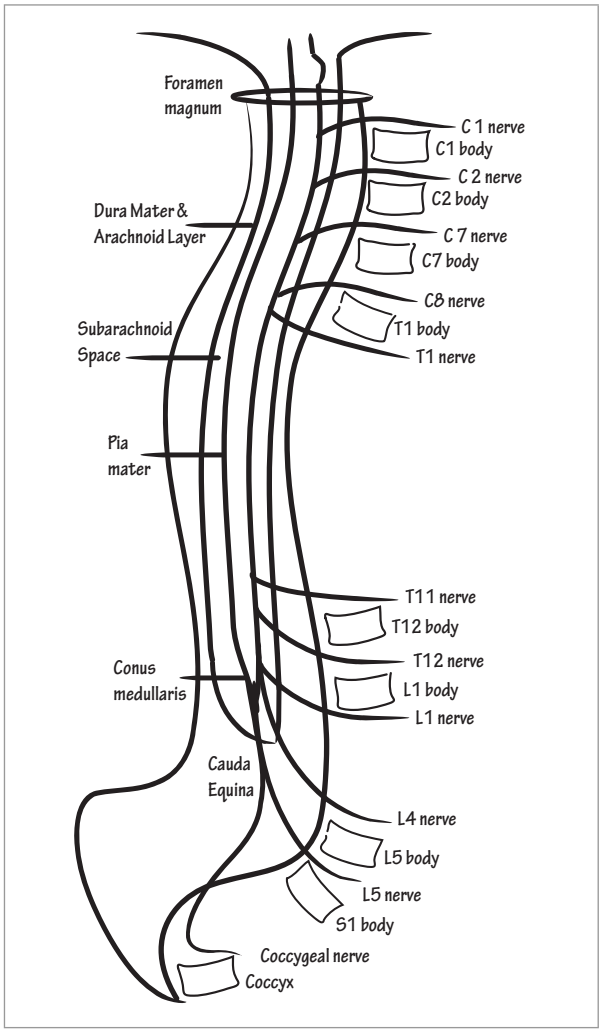


Figure 15-2 Complete spinal canal

Spinal Cord

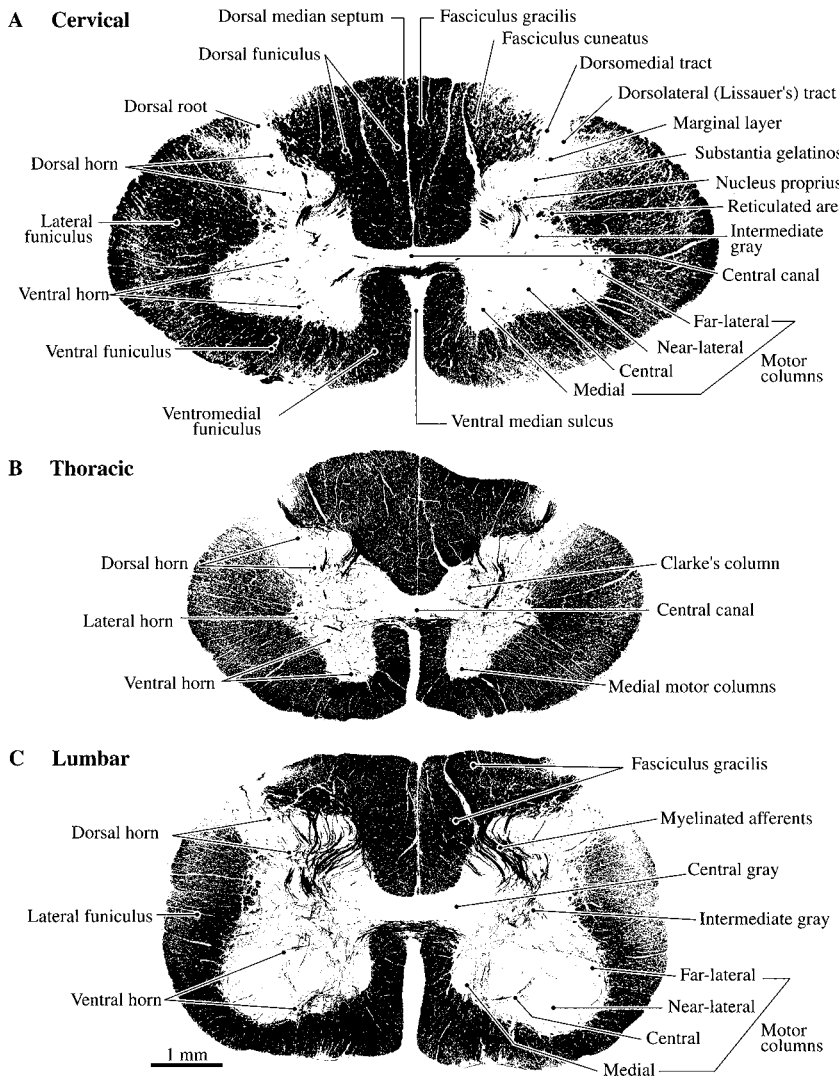


Photo 16-1 Histological axial sections through cervical, thoracic, and lumbosacral spinal cord
With permission from Altman, J., and S. A. Bayer. *Development of the Human Spinal Cord: An Interpretation Based on Experimental Studies in Animals*. Oxford and New York: Oxford University Press, 2001.

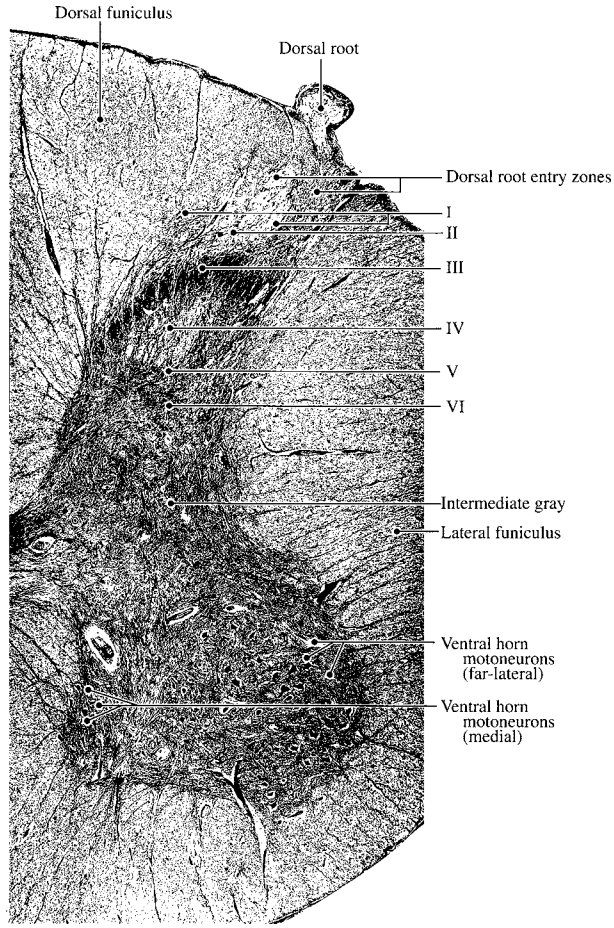


Photo 16-2 Gray matter horns
With permission from the estate of Dr. William DeMyer.

Draw a cross-section through the spinal cord; it is ovoid and has a thin fissure on its anterior side. The internal gray matter resembles a butterfly (or a bikini-top). Label the top of the diagram as "posterior" and the bottom as "anterior." The ratio of gray matter to white matter varies throughout the rostro–caudal length of the spinal cord.

In the lumbosacral spinal cord, the gray matter outsizes the white matter, whereas in the thoracic spinal cord, the white matter outsizes the gray matter. Why is this? At the bottom of the spinal cord, the ascending white matter tracts are narrow (they are just beginning to coalesce) and the descending white matter motor fibers have, for the most part, already terminated within the spinal cord gray matter, so they are also narrow. Conversely, in the thoracic cord, a high density of white matter lumbosacral afferent sensory fibers have accumulated and the white matter motor efferent bundles destined for the lumbosacral cord are still dense with fibers. Additionally, there are gray matter enlargements in both the lumbosacral and cervical spinal cord regions because of the high density of sensory and motor neurons required to innervate the distal extremities, which helps enlarge the relative size of the gray matter at those levels. But in the thoracic spinal cord, the gray matter size is small. Thoracic-innervated abdominal musculature requires less eloquent wiring than the lumbosacral-innervated footwork requisite for dancing or the cervical-innervated finger coordination required to play the piano. Thus, in the lumbosacral cord, the gray matter clearly outsizes the white matter and in the thoracic spinal cord, the white matter outsizes the gray matter. In the cervical spinal cord, both the gray and white matter are plump for reasons you can infer from the prior discussion.

Now, draw the *central canal* (the ventricular system extension into the spinal cord) in the center of the gray matter. By the second decade of life, this canal is mostly obliterated. Introduce the *posterior median septum*, which divides the posterior white matter into two halves. Label the parallel *anterior median fissure* in the anterior spinal cord.

The white matter of the spinal cord is segmented into posterior, lateral, and anterior funiculi (aka columns). Label the posterior white matter as the *posterior funiculus*, the middle white matter as the *lateral funiculus*, and the anterior white matter as the *anterior funiculus*. Certain disease processes preferentially involve certain columns.

The gray matter of the spinal cord divides into three different horns. On one side, label the dorsal gray matter as the *posterior horn*, the midsection as the *intermediate horn*, and the ventral gray matter as the *anterior horn*. The horns divide into Rexed laminae, numbered from I to IX; they will seem tedious at this point of the chapter, but we will introduce them here, anyway, because they fit well into this diagram. Skip ahead to more salient clinical anatomy and then return to this section at the end, if prefer.

The sensory laminae are laminae I–VI, they line the posterior horns of the spinal cord; the autonomic lamina is lamina VII: it lies in the intermediate horn of the gray matter; and the motor laminae are laminae VIII and IX, and they lie in the anterior horn of the gray matter. Label the posterior horn laminae from posterior to anterior in stepwise fashion from *lamina I* to *VI*; they begin just in front of the postero-lateral fasciculus (discussed later) and terminate just behind the intermediate gray matter zone of the spinal cord. The anterolateral system (ALS) fibers, which carry small fiber axons, synapse on laminae I, II, III, and V. Lamina I is called the *posterior marginal nucleus* and lamina II is called the *substantia gelatinosa*—it appears gelatinous on myelin staining because it lacks myelinated fibers. Interspinal white and gray matter regions (projections between levels in the rostro–caudal plane of the spinal cord) involve both ascending and descending pathways; laminae III and IV, which together form the *nucleus proprius*, primarily project along those interspinal pathways. Indicate that the main interspinal white matter tract is the *proprius fasciculus*, which surrounds the spinal cord gray matter.

Label *lamina VII* in the intermediate zone; it involves pathways of the spinocerebellar tracts and the visceromotor and viscerosensory nuclei of the spinal cord. Then label *laminae VIII* and *IX* in the anterior horn of the spinal cord gray matter just ventral to lamina VII; they are pure motor laminae.

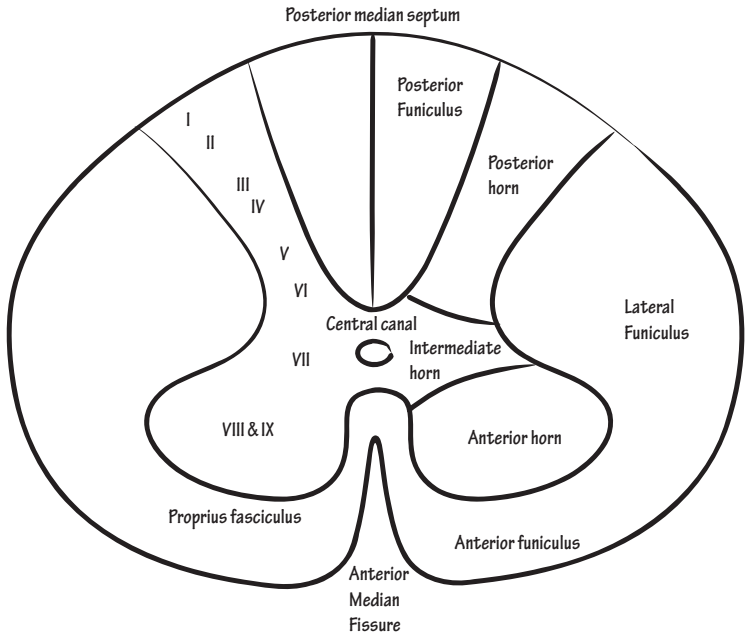


Figure 16-1 Overview of spinal cord axial cross-section

Now, we will draw the ascending pathways of the spinal cord. Introduce the *posterior intermediate septum*, which divides the posterior funiculus into medial and lateral segments. Label the medial segment the *gracile fasciculus* and the lateral segment the *cuneate fasciculus*. Write *thoracic level 6* over the posterior intermediate septum to indicate the gracile fasciculus carries large fiber sensory information from thoracic level 6 and below (i.e., the lower abdomen, pelvis, and lower extremities) and the cuneate fasciulus carries sensory information between thoracic level 7 and the face (i.e., the upper abdomen, trunk, upper extremities, and neck). A mnemonic for the *gracile* fasciculus is that ballerinas must have good sensory input from their toes to twirl *grace*fully. Sensory information from the face travels via the trigeminal nerve and synapses in the principal trigeminal sensory nucleus in the pons and spinal trigeminal nucleus, which spans from the pons to the upper cervical cord (C2–C3).

The gracile and cuneate fasiculi are jointly referred to as *posterior column* pathways because of their location in the posterior column of the spinal cord. They comprise large-diameter (10 μm), heavily myelinated, white matter axon bundles. Information ascends quickly (at a rate of 100 m/sec) along heavily myelinated large-diameter axons because of saltatory conduction. "Saltatory" means "to leap," and conjures a helpful image of how the action potentials move from one myelinated node of Ranvier to the next. In contrast, action potentials slowly propagate up the axons of unmyelinated sensory fibers, which do not allow this leap-frog ability.

The integrity of the posterior column pathway is routinely tested at the bedside in three different ways. First, let's demonstrate how to test joint-position perception. Close your eyes and ask a partner to move your fingertip up or down. The distance required for your fingertip to move before you sense its direction determines your joint-position perception ability; the less distance required, the better your joint-position sensation. Next, let's demonstrate two-point discrimination. Ask your partner to tap on your arm with two blunt tips side by side, so that you sense them as a single point. Then, in stepwise fashion, have your partner increase the distance between the points. How far apart the points have to be before you recognize them as two separate points, determines your two-point discrimination ability; the closer they are, the better your two-point discrimination. Why blunt points? So you don't recruit pain fibers, which are part of the anterolateral sensory system we will soon discuss. Now, let's show how to test vibratory sensation, which requires the use of a vibrating tuning fork. To use the tuning fork, strike its prongs so they vibrate strongly. The vibration is channeled to the blunt end of the instrument, which you place on the joint of an extremity, such as the distal interphalangeal joint of the thumb. As the tuning fork vibrates, its vibratory oscillations diminish; the smaller the amplitude of vibratory oscillations you are able to perceive, the better your vibratory sensory perception.

Patients with impairment of their posterior columns exhibit symptoms of difficulty ambulating in dim light because they lose the visual cues they rely upon in the absence of appropriate sensory perception, and they have signs of impaired joint-position sensation, impaired two-point discrimination, and diminished vibration sensation on examination. Lesions to the posterior columns of the spinal cord cause deficits on the same side of the body as the cord lesion because the posterior column fibers do not cross midline until they reach the medulla.

Certain diseases preferentially affect the posterior columns of the spinal cord. In tabes dorsalis (one of the many manifestations of neurosyphilis), the posterior columns are the only affected spinal cord region. Whereas in vitamin B_{12} deficiency, the posterior columns are affected along with the lateral columns, which contain descending corticospinal tracts (we will draw them with the descending pathways). The combination of posterior and lateral column pathology in vitamin B_{12} deficiency gives it the name "subacute *combined* degeneration."

In multiple sclerosis, vibration sensation is often markedly impaired out of proportion to joint-position sensation. The underlying pathology for this differential functional loss has been a topic of interest for many years because these modalities travel together in the spinal cord, and if anatomy were the only determining factor, then both should be affected equally.

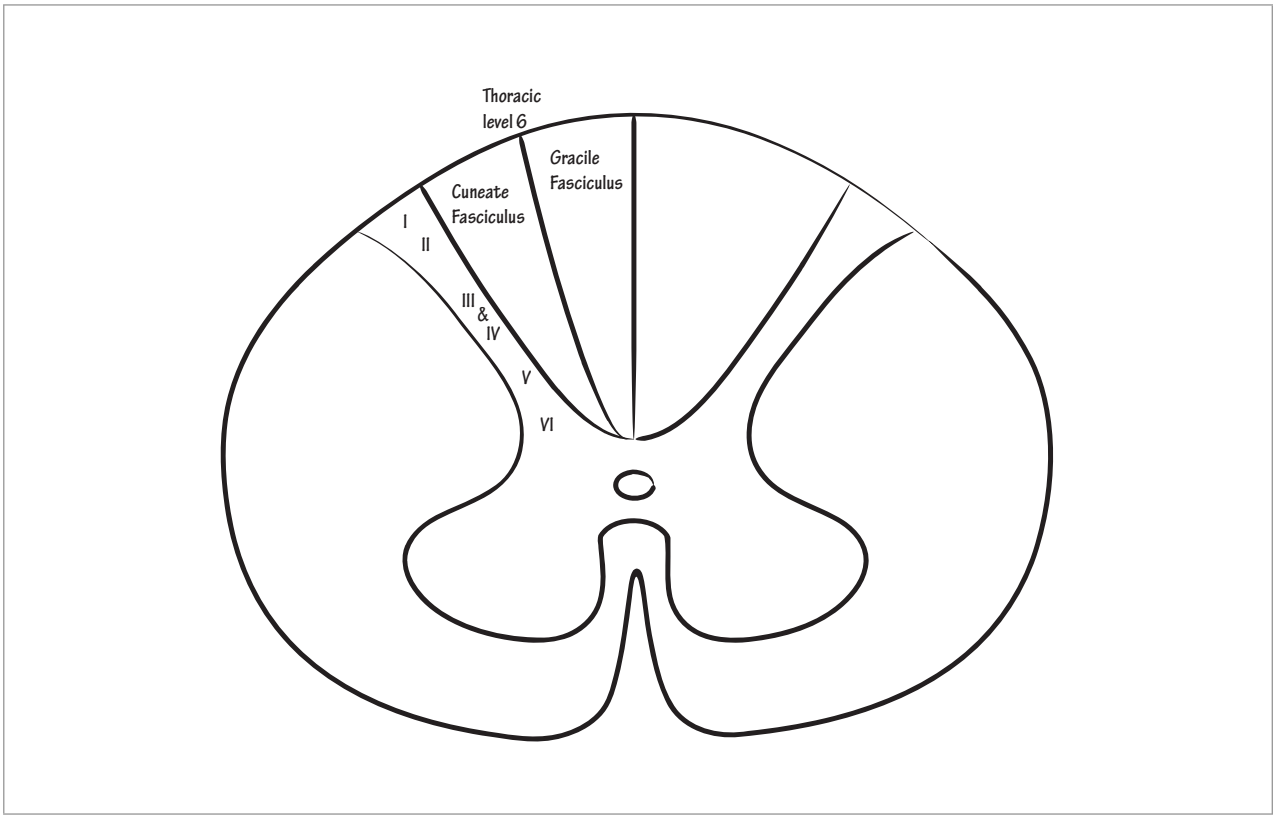


Figure 16-2 Incomplete axial section of ascending tracts

Now, label the long, narrow *anterolateral system* (*ALS*) in the anterior funiculus. The anterolateral system comprises small-diameter (0.5–5 μm) sensory pathways, which carry non-discriminative touch, pain, and thermal sensory information. These fibers have either very thin amounts of myelin or no myelin at all. Their variable size translates into variable speeds of transmission (1–30 m/sec); however, overall, action potentials ascend these axons much slower than the large fiber axons of the posterior columns. These small fiber nerves originate within both encapsulated and free nerve endings in the periphery and their cell body resides, as it does for nearly all sensory nerves, in the dorsal root ganglion. Whereas proprioceptive nerve fibers enter the spinal cord in the posterior columns, the anterolateral system pathways enter it through the *postero-lateral fasciculus* (aka *Lissauer tract*); it lies on the posterior surface of the spinal cord just behind the posterior horn.

The anterolateral system pathways are grouped into direct and indirect pathways based on whether they synapse directly in thalamus or indirectly in the thalamus, after relaying caudally in the brainstem. The direct spinothalamic pathway fibers of the anterolateral system enter the postero-lateral fasciculus and ascend or descend 3–5 levels before they synapse in lamina I. Then, they cross to the other side of the spinal cord in the ventral commissure; label the *ventral commissure* in the anterior funiculus just anterior to the intermediate zone of the gray matter. The direct spinothalamic fibers then join the long, narrow anterolateral system tract in the anterior funiculus opposite their side of origin. These fibers ascend the spinal cord and lateral brainstem and synapse directly in the thalamus.

The indirect anterolateral system fibers, on the contrary, enter the postero-lateral fasciculus and descend 1–2 levels before they synapse in lamina II or lamina III. Fibers from these laminae then project to laminae V and VIII, cross to the contralateral anterolateral system via the ventral white matter commissure, ascend the spinal cord, and synapse in different sites in the brainstem before they project to the thalamus. Thus, the anterolateral system comprises more than just the spinothalamic tract; it also comprises the spinoreticular, spinomesencephalic, spinobulbar, and spinohypothalamic tracts.

Let's note the two most salient points from the above information: (1) The anterolateral system tracts ascend or descend a variable number of levels within the postero-lateral fasciculus before they enter the spinal cord and (2) they cross midline within the spinal cord near their level of entry. The first point—that anterolateral system fibers either ascend or descend in the postero-lateral fasciculus—complicates the dermatomal levels affected with an anterolateral system lesion. If, for the sake of exercise, all anterolateral system fibers ascend 2 levels within the postero-lateral fasciculus, then what is the most superior anterolateral system dermatomal level that will be affected with a cervical level 4 lesion? The highest anterolateral system dermatomal level to be affected with a lesion at cervical level 4 will be the cervical level 6 fibers; they enter the spinal cord at cervical level 6 and ascend to cervical level 4. In contrast, the cervical level 4 fibers enter at level 4 and ascend to level 2; thus, they escape the lesion. Of course, in reality, anterolateral system fibers ascend and descend a variable number of levels, and therefore the inferior border of the deficit is indistinct.

The second point—that anterolateral system fibers cross midline at the spinal cord level at which they synapse—means a spinal cord lesion to the anterolateral system fibers on the *left* side of the spinal cord will cause clinical deficits on the *right* side of the body.

Now, we will indicate the somatotopic organization of the anterolateral system, which is similar to that of the corticospinal tract: the arms are medial and the legs are lateral. Use the clinical scenario of a cervical central cord lesion, such as a syringomelia (a fluid-filled cavity within the spinal cord), to help you remember this organization. In a cervical central cord lesion, the upper extremity anterolateral system and lateral corticospinal tracts, which we will soon draw, are affected before those of the lower extremity. This differentiation occurs for two reasons. (1) Because of the somatotopic organization of these fibers, a lesion expanding from central to peripheral within the spinal cord will affect the medial-lying arm fibers of both the anterolateral system and lateral corticospinal tract before affecting the lateral-lying leg fibers. (2) In a cervical central cord lesion, the disrupted anterolateral system fibers crossing the ventral commissure are arm fibers.

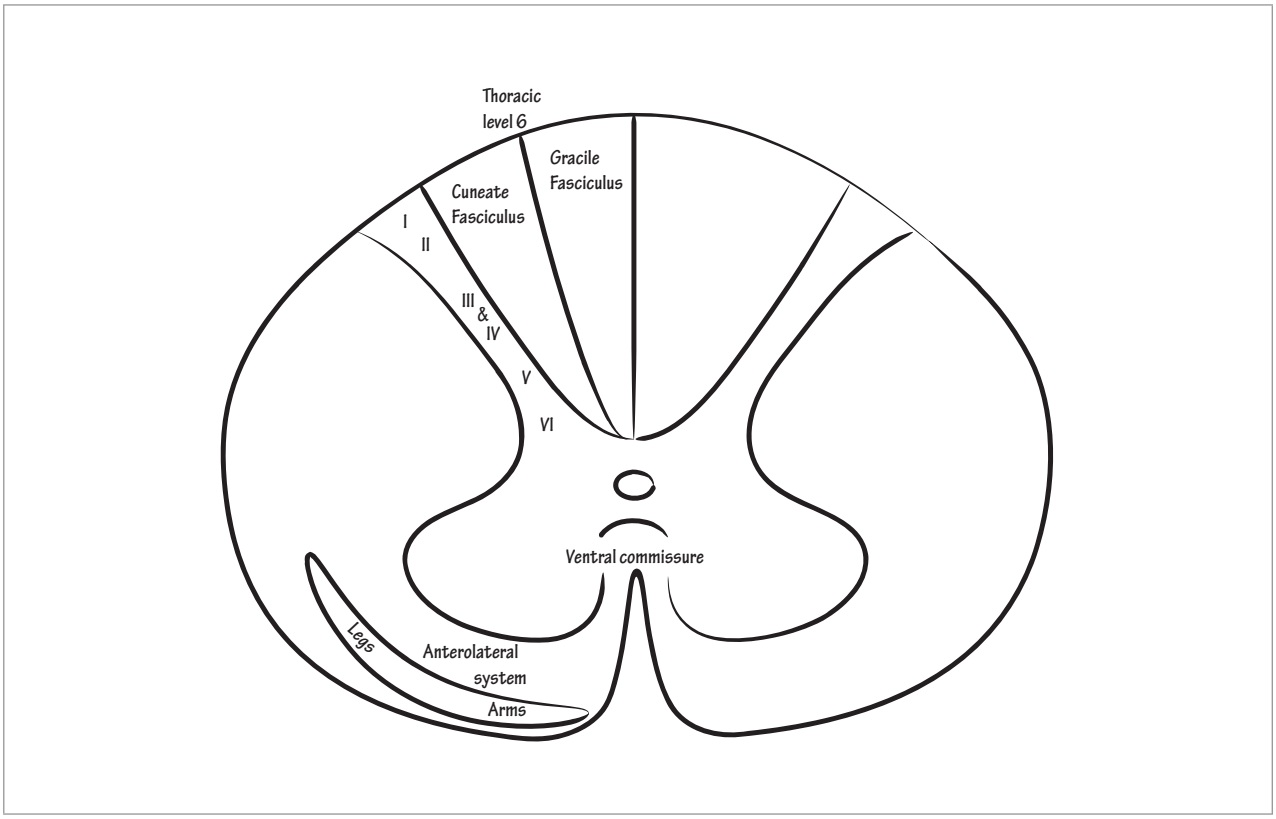


Figure 16-3 Incomplete axial section of ascending tracts

The spinocerebellar system carries sensory information from the body to the cerebellum. It sends proprioceptive information from peripheral mechanoreceptors to the ipsilateral cerebellum via large-diameter, heavily myelinated fibers. To help distinguish the role of the spinocerebellar fibers from that of the posterior column fibers, we divide large fiber sensory information into *static* and *dynamic* modalities.

Static sensory proprioception refers to non-motion related sensory tasks (joint-position sensation, two-point discrimination, vibratory sensation, and pain and temperature sensation), whereas dynamic sensory proprioception refers to motion-related sensory tasks. To demonstrate motion-related sensory input, ask a partner to touch a target and then his/her nose, first with eyes open and then with eyes closed. The movement is unaffected when the visual cue is removed because of dynamic sensory inputs, such as the spinocerebellar tracts.

We separate the spinocerebellar inputs into anterior and posterior spinocerebellar systems and subdivide these systems into tracts from the lower extremities and lower trunk and tracts from the upper extremities and upper trunk. Here, we begin with the lower extremity and lower trunk subdivision of the posterior spinocerebellar system. Along the postero-lateral wall of the spinal cord, label the *posterior spinocerebellar tract*, which carries lower limb and lower trunk sensory information from the dorsal nucleus of Clarke in lamina VII in the intermediate gray matter horn of the spinal cord to the cerebellum via the inferior cerebellar peduncle. The posterior spinocerebellar tract inputs are in peripheral receptors in the lower limbs and lower trunk. The information initially ascends along with the other large proprioceptive sensory fibers in the gracile fasciculus of the posterior column. At L2, posterior spinocerebellar fibers separate from the other large proprioceptive fibers and synapse in the dorsal nucleus of Clarke, which spans from L2 to T1 in lamina VII. The postsynaptic fibers then join the ipsilateral posterior spinocerebellar tract on the lateral edge of the spinal cord and ascend the spinal cord in the lateral funiculus. They pass through the inferior cerebellar peduncle and terminate in the ipsilateral cerebellum. A similar pattern holds true for the posterior spinocerebellar tract of the upper trunk and upper extremities, which is called the cuneocerebellar tract.

The posterior spinocerebellar fibers of the cuneocerebellar tract originate from T4 to C2 and join the posterior columns of the spinal cord along with other sensory proprioceptive fibers. They form their primary synapse in the lateral cuneate nucleus of the medulla rather than in the spinal cord. Like the lower limb and lower trunk fibers of the posterior spinocerebellar pathway, they enter the cerebellum through the ipsilateral inferior cerebellar peduncle.

Now, label the *anterior spinocerebellar tract*, which lies opposite to the posterior spinocerebellar tract on the antero-lateral wall of the spinal cord. Like the inputs to the posterior spinocerebellar tract, muscle spindle sensory afferents destined for the anterior spinocerebellar tract ascend the spinal cord in the posterior columns before they synapse in the intermediate zone of the spinal cord. However, these fibers synapse at L3–L5, just caudal to the dorsal nucleus of Clarke, which as mentioned earlier, spans from T1 to L2. These fibers cross within the ventral commissure of the spinal cord, along with fibers of the anterolateral system, and they move to the opposite side of the spinal cord to join the anterior spinocerebellar pathway. Even still, the anterior spinocerebellar fibers ultimately traverse back within the cerebellum to their side of origin, so the cerebellum maintains an ipsilateral relationship with the periphery.

Generally, the inferior and middle cerebellar peduncles are the inflow pathways to the cerebellum, and the superior cerebellar peduncle is the outflow pathway for fibers from the cerebellum. However, the anterior spinocerebellar pathway is an exception. The anterior spinocerebellar pathway ascends the spinal cord and lateral brainstem, and enters the cerebellum through the superior rather than the inferior cerebellar peduncle. Then, these fibers cross back to their original side, within the cerebellum, and terminate laterally in the cerebellar hemisphere; the posterior spinocerebellar and cuneocerebellar tracts terminate in the midline cerebellum. The hemispheres are devoted to limb function and the midline cerebellum is devoted to truncal coordination.

Now, just as the cuneocerebellar tract is the upper limb equivalent of the posterior spinocerebellar tract, the rostral spinocerebellar tract is the upper limb equivalent of the anterior spinocerebellar tract. These fibers synapse at C4–C8 in lamina VII. They never cross midline but ascend in the ipsilateral anterior spinocerebellar tract and terminate in the ipsilateral cerebellum through the inferior cerebellar peduncle.

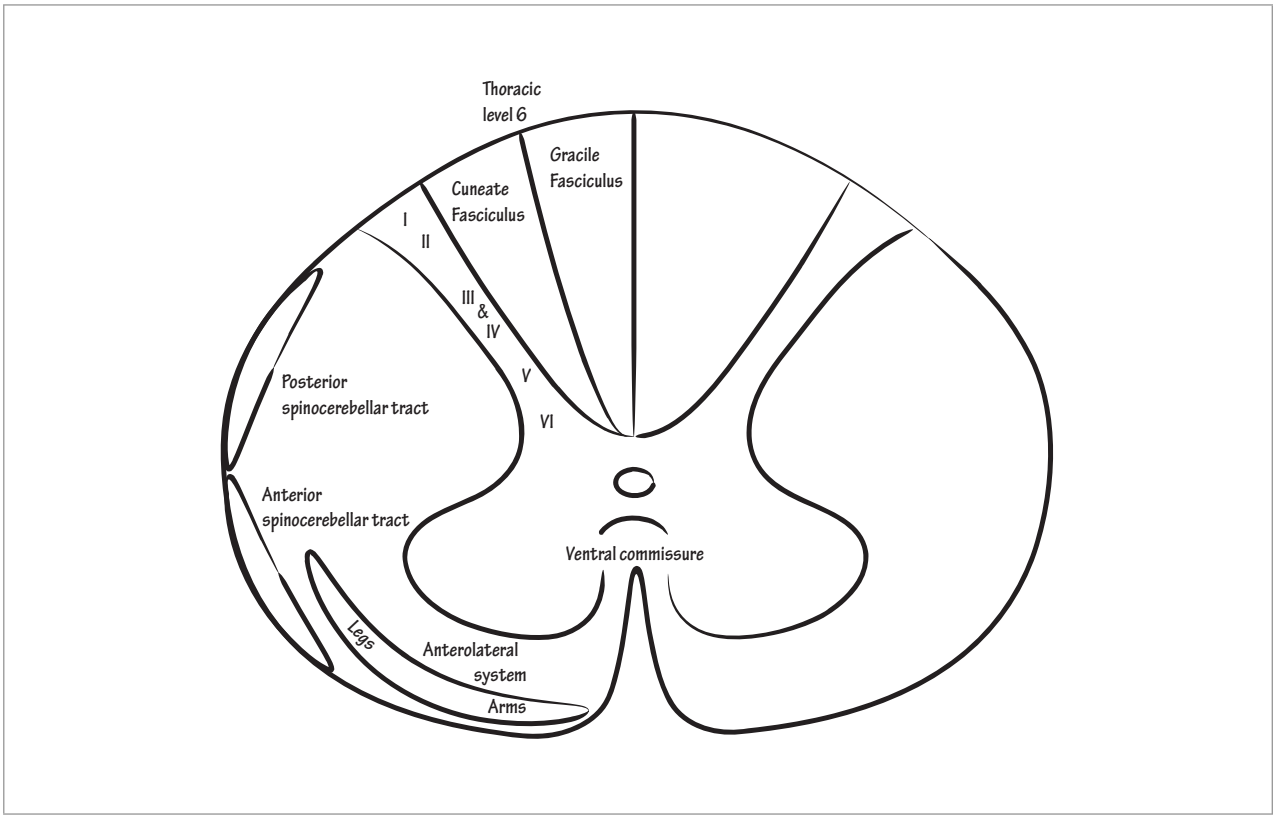


Figure 16-4 Complete axial section of ascending tracts

Next, turn your attention to the descending pathways of the spinal cord. Draw the *lateral corticospinal tract* in the lateral funiculus and the *anterior corticospinal tract* along the anterior median fissure in the anterior funiculus. As their names indicate, the corticospinal tract fibers originate in the cerebral cortex, specifically in the primary motor cortex (the precentral gyrus of the frontal lobe). They then pass through the ventral aspect of the brainstem. Roughly 90% of the fibers decussate at the medullary pyramids before they enter the cervical spinal cord as lateral corticospinal tract fibers. The remaining 10% of fibers remain uncrossed and descend in the spinal cord ipsilateral to their side of origin as anterior corticospinal tract fibers. In primates, the lateral corticospinal tracts are necessary for fine motor movements and the anterior corticopsinal tracts, alone, are sufficient for gross motor movements.

Most of the anterior corticospinal tract fibers ultimately cross in the spinal cord, which clouds the clinical implications of having both crossed and uncrossed corticospinal tract pathways. However, consider the following clinical phenomenon. When children with intractable epilepsy have their offending cerebral hemisphere removed or disconnected, they generally retain good gross motor function with the opposite side of their body and their primary motor deficit is with fine motor tasks of the opposite hand. Why should this be? The lateral corticospinal tract on the side opposite to the disconnected hemisphere is impaired, which manifests with poor fine motor skills; however, the intact anterior corticospinal tract on that side generates reliable gross motor movements. The other side of the body is normal because its lateral corticospinal tract is intact, which provides both gross and fine motor movements. Actually, motor function in these patients often improves after surgery because the seizure activity was more disruptive than the surgery.

Now, label the medial aspect of the lateral corticospinal tract as carrying *arm* fibers and the lateral aspect as carrying *leg* fibers. Which clinical syndrome will help you remember the somatotopic organization of this and the anterolateral pathways? Cervical central cord syndrome.

The corticospinal tract fibers synapse on anterior horn cells, exit the spinal cord via ventral nerve roots, pass through peripheral nerve bundles, and cross the neuromuscular junction to innervate muscle fibers. Lesions of corticospinal tract fibers in the spinal cord cause motor deficits on the same side of the body. Amyotrophic lateral sclerosis is an important disease that causes degeneration of both the corticospinal tracts and motor neurons.

Next, label the *hypothalamospinal tract* alongside the lateral corticospinal tract in the lateral funiculus. As its name indicates, this tract originates in the hypothalamus. During its descent through the lower half of the brainstem, it moves laterally so that when it reaches the spinal cord it is adjacent to the lateral corticospinal tract. It carries hypothalamic input for visceral motor activities, such as sympathetic-mediated eye changes as well as bowel, bladder, and sexual functions. Injury to the hypothalamospinal tract often results in Horner's syndrome, discussed in the "Peripheral Autonomic Nervous System" chapter.

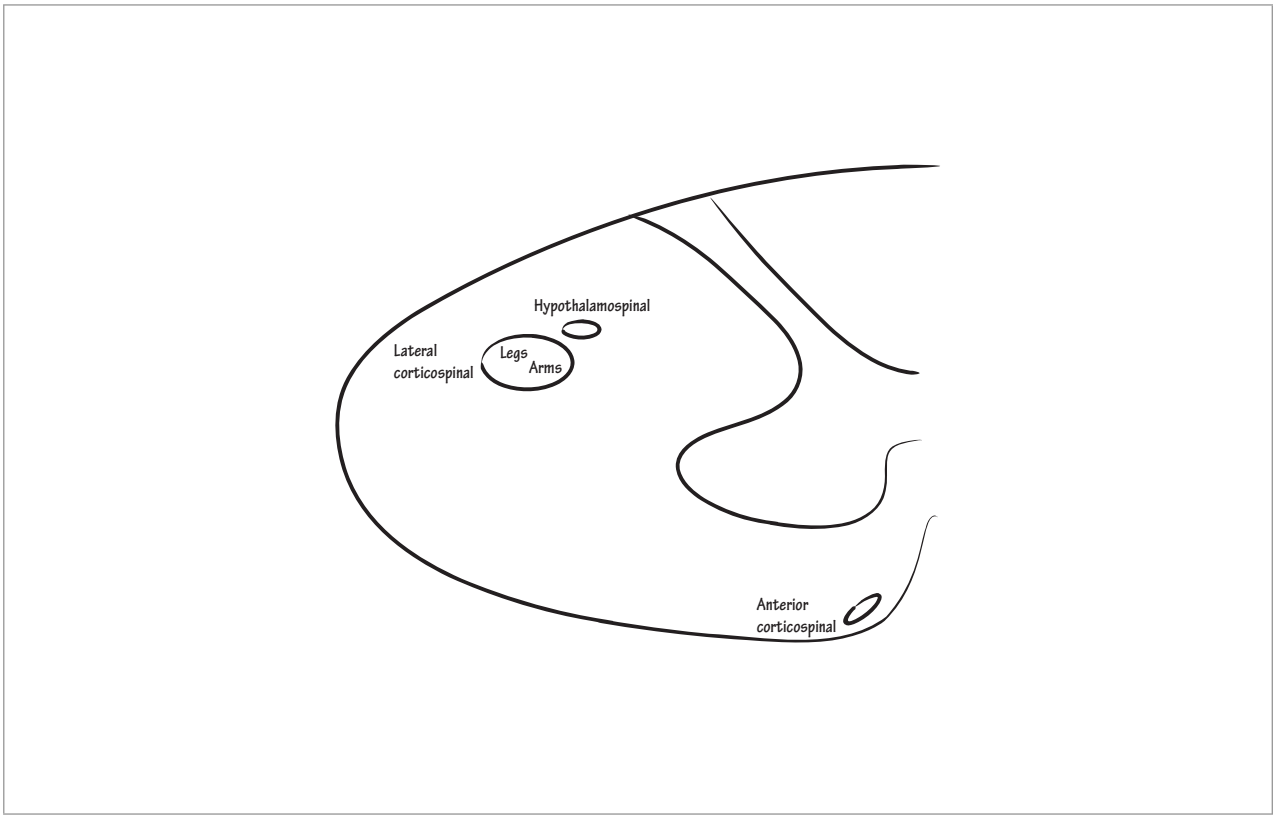


Figure 16-5 Incomplete axial section of descending tracts

Now, label the *rubrospinal tract*; it lies in front of the lateral corticospinal tract. Then, label the *medial* and *lateral reticulospinal tracts* that lie medially and laterally, respectively, in front of the anterior gray matter. Lastly, label the *medial* and *lateral vestibulospinal tracts*, which lie along the medial and anterior borders of the spinal cord. The action of these tracts will help you remember their location in the white matter as well as the organization of motor nuclei in the anterior horn gray matter.

Flex your arms at the elbows to demonstrate the action of the rubrospinal tracts. Then, extend your neck and upper and lower limbs to demonstrate the action of the reticulo- and vestibulospinal tracts. A lesion above the origination of the rubrospinal tract (i.e., above the red nuclei in the midbrain) will release cortical inhibition of the rubro-, reticulo-, and vestibulospinal tracts. In this circumstance, the action of rubrospinal tract supercedes that of the reticulo- and vestibulospinal tracts, which results in arm flexion at the elbows and lower extremity extension, so-called *decorticate posturing*. A lesion below the origination of the rubropsinal tract (i.e., in the pons and below) releases inhibition of the reticulo- and vestibulospinal tracts, which results in extension of the neck and all four limbs, so-called *decerebrate posturing*.

Now, let's address the posterior–anterior and medial–lateral somatotopy of the motor nuclei in the anterior horn gray matter. Label the posterior nuclei as the *flexor* muscles, the anterior nuclei as the *extensor* muscles, the medial nuclei as the *proximal* muscles, and the lateral nuclei as the *distal* muscles. For instance, in the anterior horn of the cervical spinal cord, the motor nuclei to the biceps (flexor muscles) are posterior, the nuclei to the triceps (extensors) are anterior, the nuclei to the cervical paraspinal muscles (proximal) are medial, and the nuclei to the hand muscles (distal) are lateral.

How are we able to use the cortico-, rubro-, reticulo-, and vestibulospinal tract locations in the white matter to help us remember this gray matter somatotopic organization? The white matter positions of these tracts relate to the gray matter positions of their related nuclei. Where are the anterior corticospinal tracts? Medial. What do they innervate? Proximal musculature. And proximal motoneurons lie medially in the anterior horn. The *lateral* corticospinal tract is necessary for fine motor tasks, which require distal musculature. Where do the motor nuclei of the distal muscles lie in the anterior horn? Laterally.

Now, look at the rubro-, reticulo- and vestibulospinal tracts; what functions do they provide? Most notably, the rubrospinal tract triggers flexion of the arms at the elbows and it is situated in the posterior aspect of the white matter; the flexor motoneurons are situated in the posterior part of the anterior horn gray matter. The reticulo- and vestibulospinal tracts provide neck and limb extension and are situated in the ventral spinal cord white matter; the extensor motoneurons are situated in the ventral portion of the anterior horn gray matter. As one last helpful corollary, the *medial* vestibulospinal tract provides stimulation to the proximal, axial muscle extensors, primarily the neck extensors, and it is located on the *medial* aspect of the spinal cord; again, motoneurons to proximal musculature lie medially.

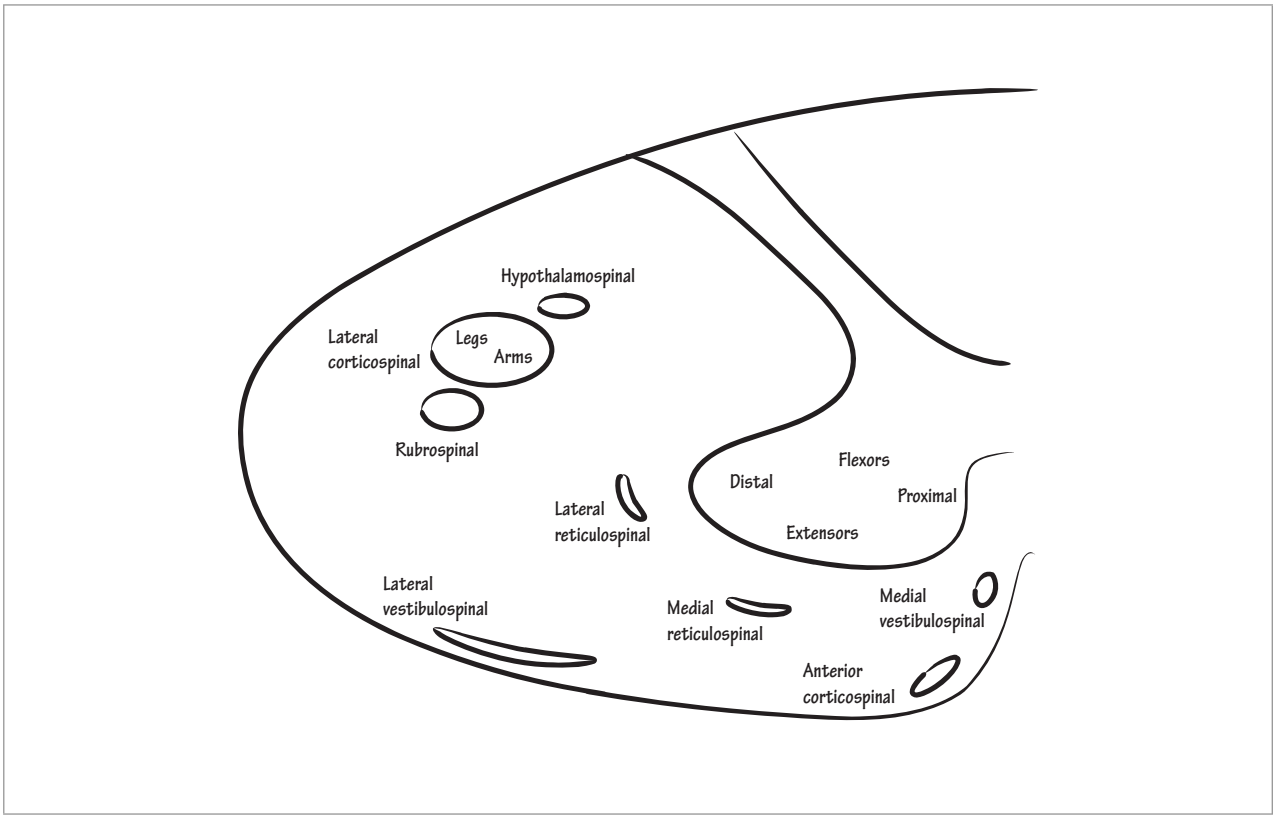


Figure 16-6 Complete axial section of descending tracts

Reflex Loops and Muscle Tone

A MUSCLE STRETCH reflex (aka myotatic reflex or deep tendon reflex) is a simple circuit that requires the following: muscle spindle cells, large sensory afferent fibers, spinal cord interneurons, motor neurons, motor efferent fibers, and a paired agonist–antagonist muscle group. In this chapter, we will use the patellar reflex (aka knee extensor reflex) as a prototypical muscle stretch reflex to learn about spinal reflexes. The common muscle stretch reflexes we test are at the biceps (C5, C6), triceps (C7, C8), patella (L3, L4), and achilles (S1). Also, in this chapter, we will discuss the related anatomy of muscle tone.

Draw a lower extremity flexed at the knee. Label the quadriceps (knee extensor) at the top and the hamstrings (knee flexor) at the bottom. In the center of the quadriceps, draw two thin, elliptical *muscle spindles*. These muscle spindles each contain a centrally located multi-nucleated cell body flanked on each side by several small muscle striations called *intra*fusal muscle fibers, which we will soon draw. Outside of these muscle spindles, draw large striated skeletal muscle fibers called *extra*fusal fibers that constitute the bulk of the muscle groups. In small muscle groups, such as the extraocular muscles, a motor neuron commands as few as 10 extrafusal muscle fibers; whereas in large muscle groups, such as the quadriceps, a single motor neuron commands as many as 1000 extrafusal muscle fibers.

Now, draw a cross-section of the spinal cord off to the side; it is not necessary to include the white matter tracts but only an outline of the gray matter horns. Next, return to the muscle spindles. In the contractile regions at the edges of each muscle spindle, draw several *intrafusal* muscle striations; they will be especially important when we discuss tone.

In the center of one of the muscle spindle fibers, draw a multi-nucleated cell body with nuclei clustered together, like marbles in a bag. Label this entire muscle spindle fiber as a *nuclear bag fiber*. In the center of the other muscle spindle fiber, draw a multi-nucleated cell body with its nuclei arranged in a line, like pearls a chain, and label it as a *nuclear chain fiber*. Both spindle fibers types are involved in sensing rate of change of muscle length and tension.

Annulospiral endings encircle the center of the nuclear bag fiber cell bodies and wavy *flower-spray endings* attach off-center within the nuclear chain fibers. Draw a *type I alpha* sensory fiber from the annulospiral endings. *Type II* sensory fibers project from the flower-spray endings; we leave them out for simplicity. Both fibers project to cell bodies in a *dorsal root ganglion* just outside the spinal cord.

Next, draw the central projection of the type I alpha sensory afferent from the dorsal root ganglion into the spinal cord through the postero-lateral sulcus. Show it synapse on an *alpha motor neuron* in the anterior aspect of the anterior horn of the spinal cord gray matter. Remember that motor neurons to extensor muscles, such as the quadriceps, are in the anterior aspect of the anterior horn. This direct synapse of sensory afferent fiber to motor efferent nucleus is unique and is called *mono*synaptic; most, if not all, nervous system circuitry elsewhere is *poly*synaptic.

Next, draw an *alpha motor fiber* projection from the motor neuron to the thigh. Show it cross the

neuromuscle junction and terminate in an *extra*fusal, striated muscle fiber of the quadriceps. Extrafusal muscle fibers provide muscle contraction, or muscle shortening, and produce limb movement: in this case, leg extension at the knee.

Now, review the preliminary steps of the myotatic reflex. The patellar tendon is stretched with the tap of a reflex hammer, which activates muscle spindle fibers that stimulate their annulospiral receptor endings to send a volley of afferent activity centrally via type I alpha sensory afferents. These afferents travel into the spinal cord through its postero-lateral sulcus and they synapse directly onto quadriceps motor neurons. The motor neurons send action potentials down alpha motor efferent axons across the neuromuscle junctions of extrafusal, striated quadriceps muscle fibers, which cause them to contract and the leg to extend at the knee.

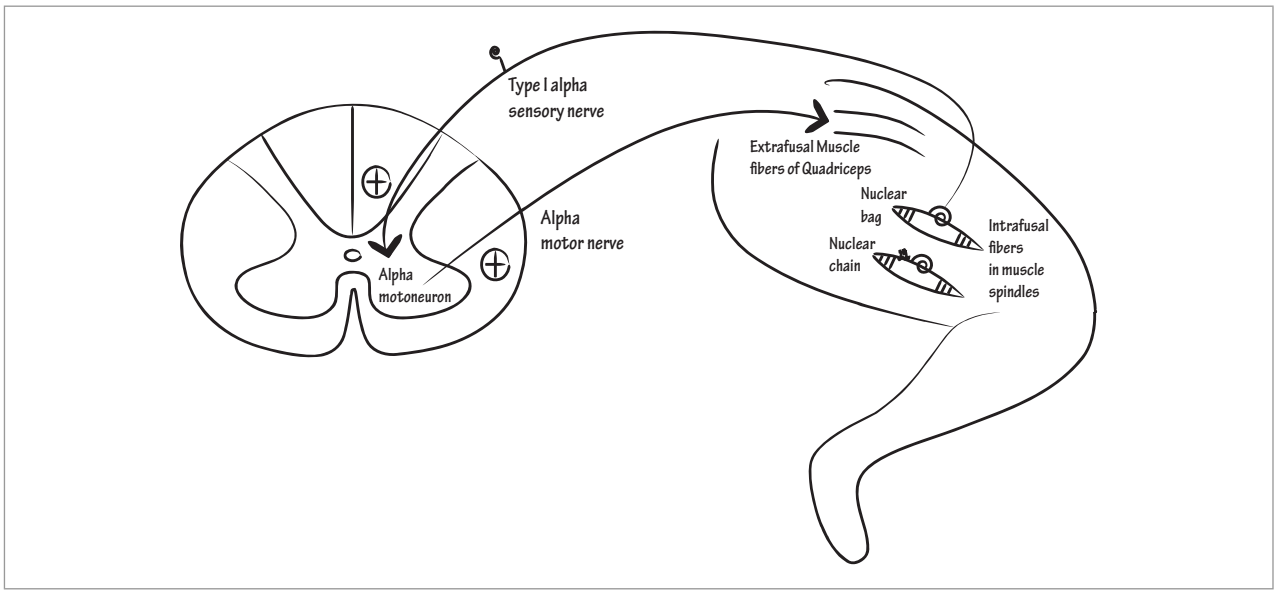


Figure 17-1 Muscle stretch reflex: excitatory loop

What if the hamstrings muscle, the flexor muscle of the thigh, also received this excitatory impulse at the same time? The leg would only stiffen and not move because both muscles of this agonist–antagonist pair would shorten simultaneously. So the hamstrings must be inhibited. Draw a projection from the type I alpha sensory fiber to a *Renshaw cell* (aka interneuron) in the anterior horn of the gray matter of the spinal cord. From the Renshaw cell, draw a short inhibitory projection to a hamstrings motor neuron in the posterior region of the anterior gray matter horn—remember that flexor motor neurons lie posterior within the anterior horn. Glycine is the inhibitory neurotransmitter in this pathway. Next, draw a large alpha motor fiber from the motor neuron to a striated muscle fiber in the hamstrings. When the muscle stretch reflex for the quadriceps is generated, the hamstrings is inhibited; it relaxes, and the knee is free to extend.

Inhibitory interneurons are important components to more than just the muscle stretch reflex. These interneurons, along with excitatory interneurons, are the lynchpins to more complicated spinal reflexes, such as the triple flexor reflex and the crossed extensor reflex. In the triple flexor reflex, for instance, a painful stimulus to the plantar surface of the foot causes automatic upward flexion of the foot (aka foot dorsiflexion) and flexion of the lower extremity at the knee and hip. Normally, the cortex modulates this reflex, but the reflex is uninhibited in cases where there is cortical injury. Clinicians scratch the bottom of comatose patients' feet to evaluate for this stereotyped response.

The crossed extensor reflex provides the opposite effect of the triple flexor reflex to the other leg; it generates downward flexion of the foot (aka plantar flexion) and extension of the lower extremity at the knee and hip. So that when the injured foot and leg draw up from the triple flexor reflex, the opposite foot and leg are able to support the person's weight. This spinal reflex occurs naturally in everyday life and is functionally protective. In contrast, the patellar muscle stretch reflex is only activated during the bedside examination and is not a protective response.

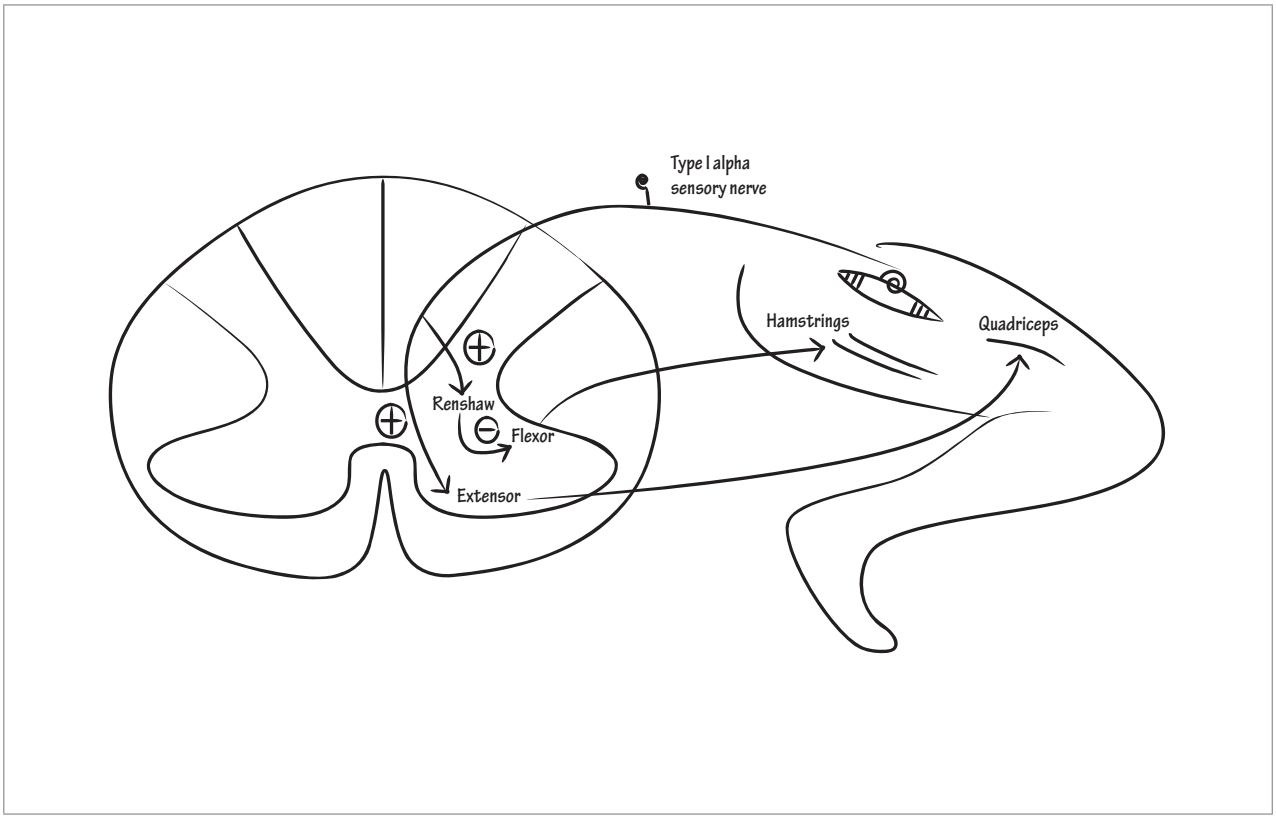
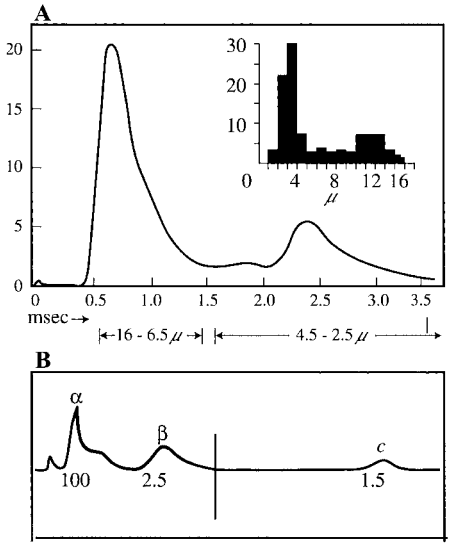


Figure 17-2 Muscle stretch reflex: inhibitory loop

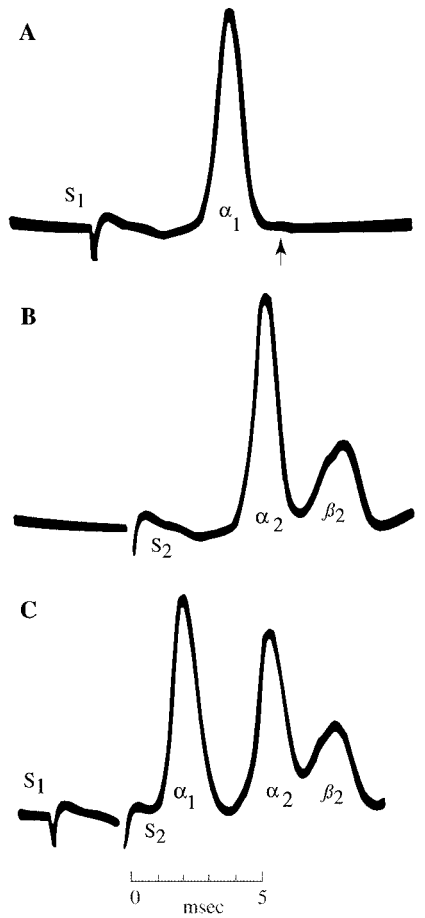
If you have ever performed a muscle stretch reflex, you will know that a key component to its arc is its termination. A delay in the relaxation phase of the muscle stretch reflex (aka Woltman's sign) is seen in patients with various disorders, such as symptomatic hypothyroidism. Here, we will draw an important neuroanatomical circuit involved in the relaxation phase of the muscle stretch reflex; however, bear in mind that there are a number of neurobiological influences on the relaxation of muscle contraction, which include myosin ATPase and calcium re-accumulation into the endoplasmic reticulum, which we will not draw here.

Draw a *Golgi tendon organ* in the tendonous insertion of the quadriceps to the patella. Then, draw a *type I beta* fiber projection from the Golgi tendon organ to a Renshaw interneuron in the anterior horn of the gray matter. For completeness, include a cell body in the dorsal root ganglion for the type I beta fiber. Next, draw an inhibitory synapse from the interneuron to the quadriceps motoneuron. The Golgi tendon organ signal runs through a type I beta fiber to a Renshaw cell, which then inhibits the motor neuron of the quadriceps.

How is the quadriceps able to receive excitatory stimuli from the muscle spindle fibers and inhibitory stimuli from the Golgi tendon organs, and still fire? The impulses must reach the motor neurons of the quadriceps at different times. One way of achieving this would be if afferent impulses ascended the type I alpha and beta fibers at different speeds; however, both type I alpha and type I beta fibers are between 12 and 20 micrometers in diameter and transmit signals at 80 to 120 meters/second. Instead, it is classically believed that muscle spindle fibers have a much lower threshold to fire than Golgi tendon organs. When the patella stretches with a tap from a reflex hammer, the muscle spindles fire. Only when the quadriceps contracts and shortens, does tension on the patella reach threshold for the Golgi tendon organs to fire, which is why they do not activate at the same time.



A. Compound action potential of a frog nerve composed of fibers of different diameters and conduction velocities. Insert shows the distribution of fibers of different diameter (μ) in the nerve. From Gasser (1943). **B.** Compound action potential of a human cutaneous nerve. The three peaks (α, β, c) indicate that the nerve is composed of three major groups (conduction velocities indicated below the tracing in meters/second). After Heinbecker et al. (1933); from Ottoson (1983).



Latencies and amplitudes of components of a compound action potential of the frog sciatic nerve to a weak electric shock (S_1 in **A**), a stronger shock (S_2 in **B**), and to two successive shocks (S_1 and S_2 in **C**). From Erlanger and Gasser (1937); after Brinley (1974).

Photo 17-1 The relationship of nerve diameters to their speeds of transmission.
With permission from Altman, J., and S. A. Bayer. *Development of the Human Spinal Cord: An Interpretation Based on Experimental Studies in Animals*. Oxford and New York: Oxford University Press, 2001.

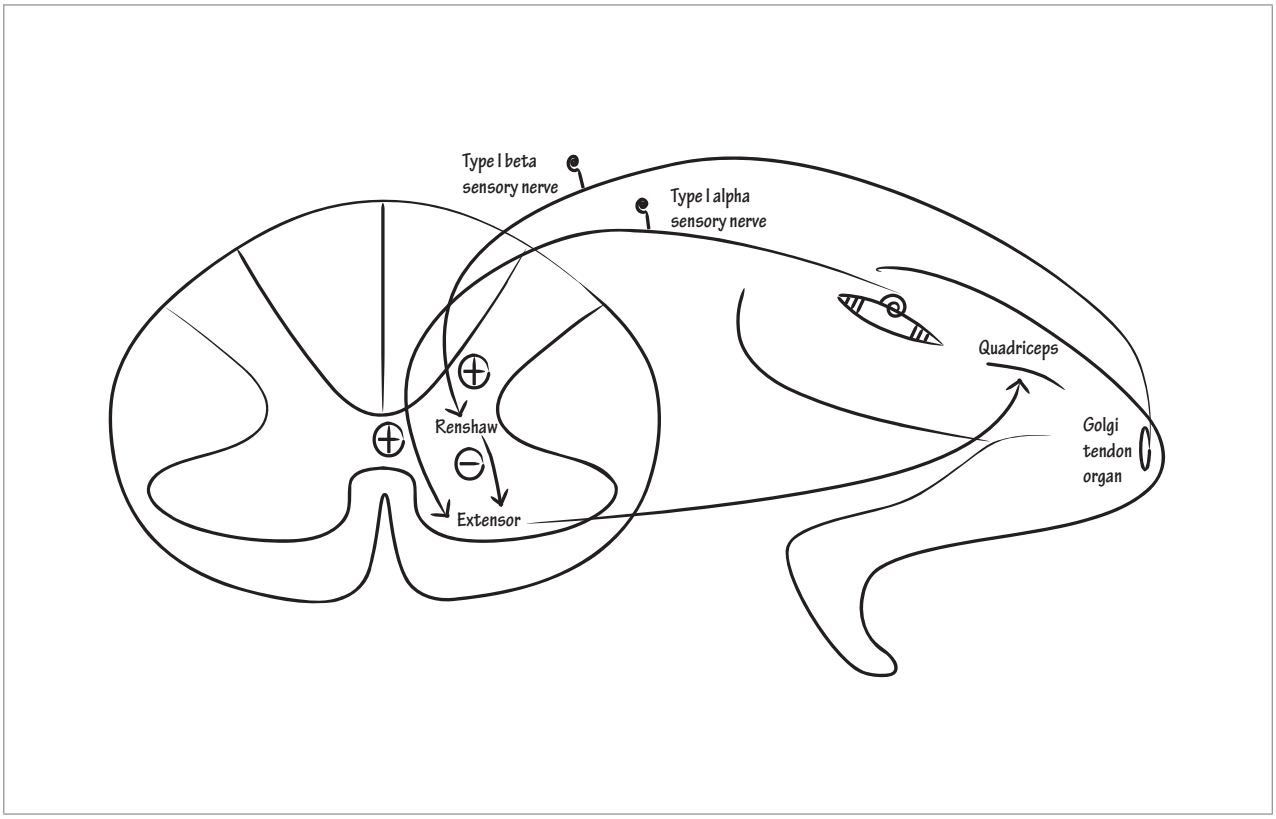


Figure 17-3 Cessation of muscle stretch reflex

Now, let's address muscle tone with the fusimotor system (aka gamma loop). Show a *gamma motor nerve* project from the anterior gray matter to the contractile intrafusal muscle fibers of the muscle spindle. Next, draw a *supraspinal* fiber projection onto the gamma motor neuron. In the gamma loop, an excitatory impulse descends from supraspinal centers (i.e., the brainstem and cerebral cortex as well as superior spinal levels) via the descending supraspinal pathways onto gamma motor neurons, which excite intrafusal muscle fibers via gamma motor nerves.

This system is classically used to help explain the maintenance of muscle tone as well as the effects of the Jendrassik maneuver on spinal reflexes. The Jendrassik maneuver is the use of mental computation or remote muscle contraction, such as wrist flexion or jaw clenching, to augment a distant muscle stretch reflex. It is commonly employed for difficult to elicit reflexes, such as the gastrocnemius reflex (aka ankle tendon jerk or Achilles reflex). Let's use the fusimotor system to simplistically explain the maintenance of muscle tone, if only for teaching purposes.

When gamma motor neurons incite intrafusal motor fibers to contract, or shorten, their muscle spindle cell bodies are naturally stretched. This stimulates annulospiral and flower-spray endings to send impulses via type I alpha and type II sensory fibers to their respective alpha motor neurons, which in turn send action potentials down their alpha motor axons to extrafusal muscle fibers causing them to contract, resulting in increased muscle tone. Indeed, when the supraspinal input to gamma motor neurons is severed (i.e., in an upper motor neuron lesion) muscle tone is lost and patients become flaccid or develop so-called spinal shock. It is not until days or weeks later that, through poorly understood mechanisms, tone increases. Ultimately spasticity occurs, which is a velocity-dependent increase in resistance.

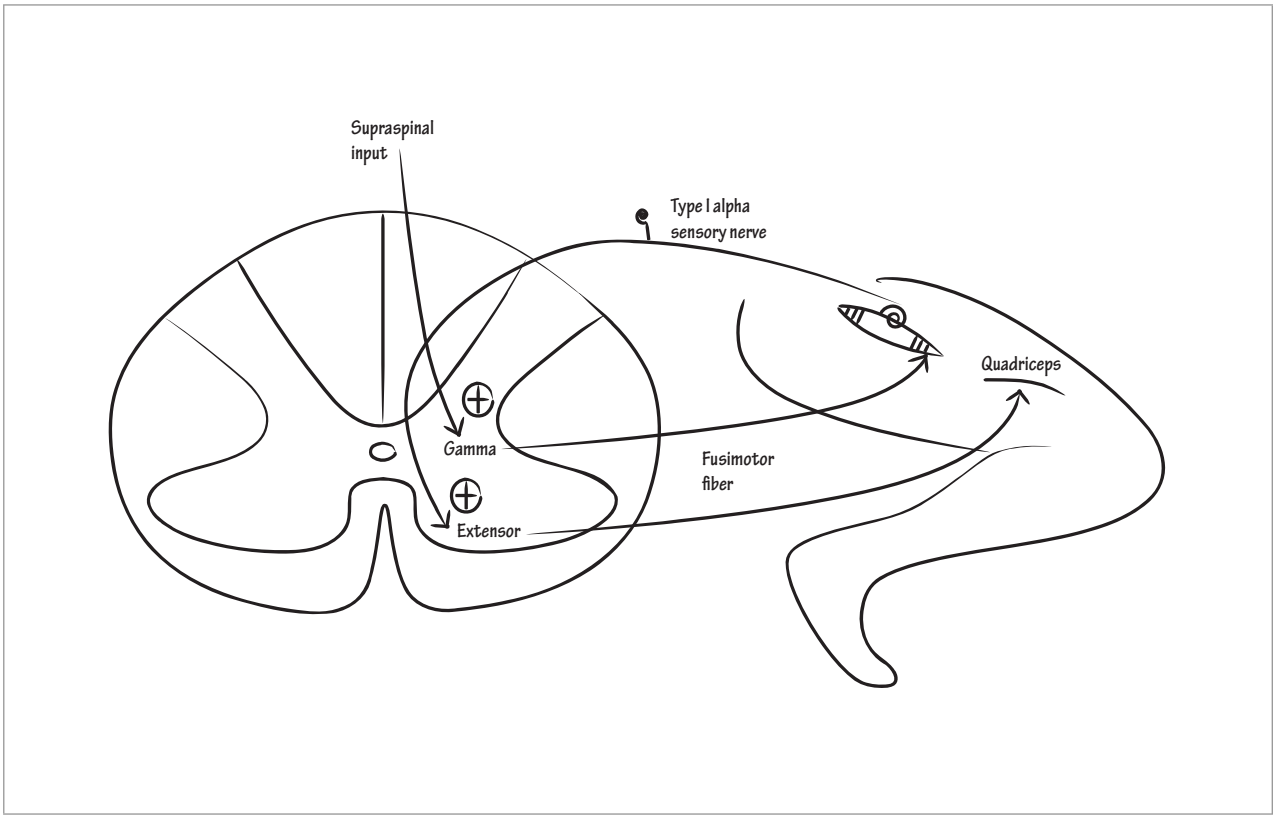


Figure 17-4 Muscle tone: fusimotor loop

Brainstem

THE BRAINSTEM IS arguably the most important anatomical region of the nervous system; all fibers that pass to and from the cerebrum go through it and it contains numerous neuronal pools requisite for survival. Despite its importance, it is suprisingly small—only 6 × 3 × 3 cm in size (54 cm^3 in volume), which means its neurons and axons are densely packed, and so we are able to localize brainstem lesions with remarkable precision. In this chapter, we will start with a basic approach to the overall brainstem and then cover each brainstem level in detail.

The superior border of the brainstem lies along the horizontal plane of the mammillary bodies and posterior commissure. The inferior border is the upper cervical spinal cord at the level of the pyramidal decussation.

We begin with an axial composite of the brainstem. The midbrain, pons, and medulla have many similarities, which we show with a compressed slice. While the intersegmental variability between the different rostro–caudal brainstem levels is important, before we delve into it, we will use our composite section to create a general construct of the brainstem. In this way, we will reduce the amount of gross memorization we need to do for each brainstem level. Listed next are the 12 different neuroanatomical groups of the brainstem fiber bundles and nuclei. They are as follows: the *corticofugal fiber pathway*, which comprises the corticospinal and corticobulbar tracts; the *supplementary motor nuclei*, which consists of the substantia nigra, red nucleus, pontine nuclei, and olivary nuclei; the *posterior column–medial lemniscus pathway* (the large fiber sensory pathway); the *antero-lateral system pathway*, which comprises the spinothalamic, spinoreticular, spinomesencephalic, and spinotectal tracts; the *trigeminothalamic tracts* (aka trigeminal lemniscus); the *cranial nuclei* of cranial nerves 3–10 and cranial nerve 12; the *neurobehavioral cells*, which comprise the periaqueductal gray, raphe nuclei, locus ceruleus nuclei, ventral tegmental nuclei, and the pedunculopontine and lateral dorsal tegemental nuclei; the *reticular nuclei*; the *supplementary motor* and *sensory tracts*, which are divided into tracts that are primarily ascending tracts—the medial longitudinal fasciculus and central tegmental tracts, and into pathways that are primarily descending tracts—the tectobulbo-, rubro-, reticulo-, and vestibulospinal tracts; the brainstem components of the *auditory system*—the trapezoid body, superior olivary nucleus, lateral lemniscus, and inferior colliculus; and the *cerebellar fibers* that relate to the brainstem—the spinocerebellar tracts, cerebellar peduncles, and the decussation of superior cerebellar fibers. The details of the spinocerebellar fibers are intricate; therefore, it is best to review them cohesively at the end rather than parse and discuss them as we go.

While at first glance this list is dizzying, it will become manageable as we work through the axial brainstem composite and then the individual brainstem sections at each level. Before we begin our drawing, however, let's clarify what we mean by neurobehavioral cells and the reticular formation (although this discussion may make better sense after you complete the chapter).

The neurobehavioral cells are devoted to behavioral function. They have diffuse projection patterns and their neurotransmitters are of particular pharmacologic interest.

The reticular formation historically belongs as a neurobehavioral cell group as it was long thought to function solely as a diffuse arousal, wakefulness center. However, current thinking is that the reticular formation consists of cells with highly specific targets. It is believed to function in a wide range of actions, including interneuronal motor activity for eye movements. This is why we categorize the reticular formation separately from the neurobehavioral cells.

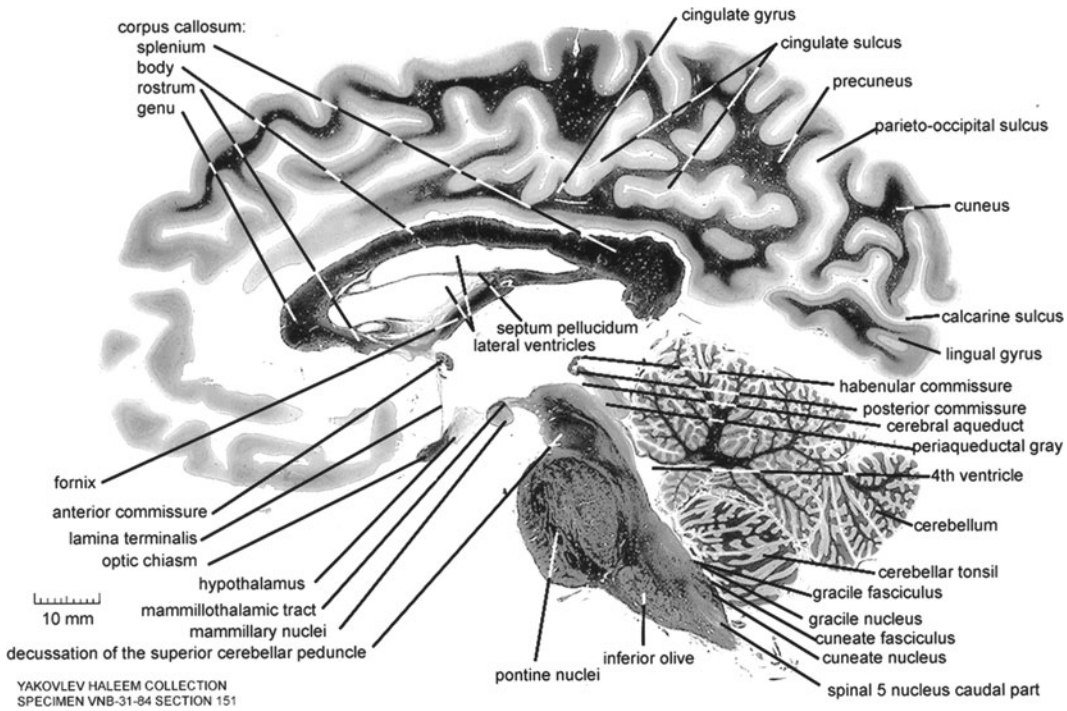


Photo 18-1 Midsagittal section of the brain
With permission from the Michigan State University: Brain Biodiversity Bank. https://www.msu.edu/~brains/

If you have time before we move on to our diagrams, let's discuss a few challenges in brainstem and related anatomical nomenclature. First, let's consider the derivation of some of the motor cell and motor fiber terminology. The corticospinal fibers pass through the medullary pyramids so their cortical cells of origin (the primary motor neurons in the brain) are referred to as pyramidal cells. These neurons are also referred to as Betz cells because it was classically believed that large-sized Betz cells were the predominant histological corticospinal cell type but this is no longer considered to be true.

The terminology for the cortical innervation of the cranial nerves is confusing. Historically, they were called corticobulbar fibers because they pass through the medullary bulb. However, some cortico-cranial nerve nuclei projections never reach as far inferior as the medullary bulb so the term corticobulbar was considered misleading, and in 1998, the official nomenclature was elaborated: the fibers became subcategorized based on their termination sites. The fibers that project to cranial nerve nuclei of the medulla are now called bulbar corticonuclear fibers, those to cranial nerve nuclei of the pons are called pontine corticonuclear fibers, and those to cranial nerve nuclei of the midbrain are called midbrain corticonuclear fibers. Authors often refer to these three groups collectively as corticonuclear fibers. However, this term is unsatisfactory and in this chapter we will stick with the original term corticobulbar, because it is succinct, historically well-established, and still widely used.

The term corticofugal is used to denote all of the relevant cortical motor projection fiber pathways that pass through the brainstem: corticobulbar, corticospinal, corticorubral, corticopontine, and corticoreticular.

The nomenclature of the central gray substance and the periaqueductal gray is often another source of confusion. The central gray area surrounds the midline cerebrospinal fluid channel throughout the brainstem and spinal cord; it is a continuation of the periventricular gray matter of the cerebral cortex. Within the midbrain, the central gray area is subcategorized as the periaqueductal gray area. "Central gray area" and "periaqueductal gray area" are occasionally used interchangeably, however, which muddles their meaning.

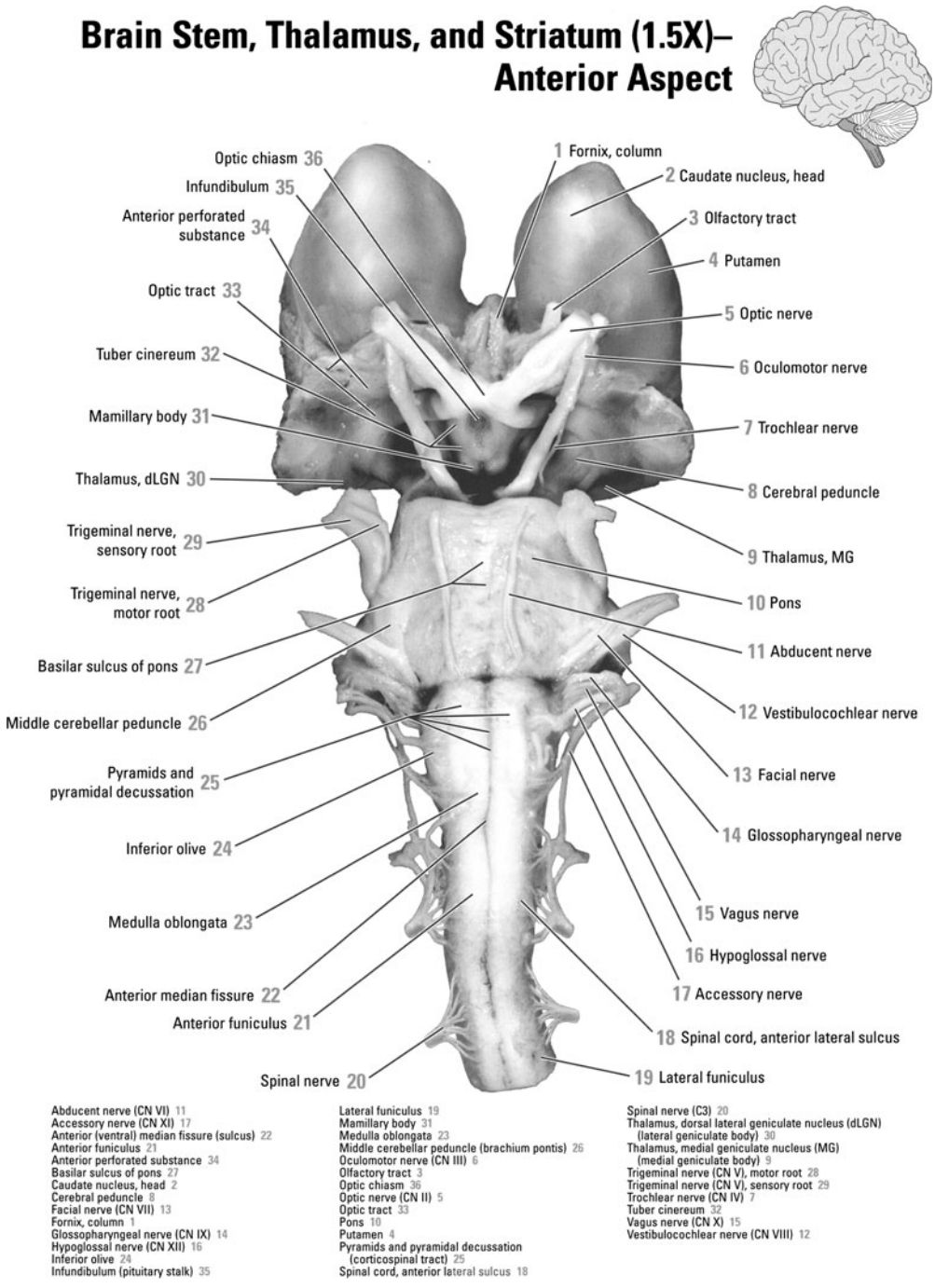


Photo 18-2 Anterior aspect of brainstem, thalamus, and striatum

From Woolsey, T. A., J. Hanaway, and M. H. Gado. *The Brain Atlas: A Visual Guide to the Human Central Nervous System*. 3rd ed. Hoboken, NJ: Wiley, 2008. Reproduced with permission of John Wiley & Sons Inc.

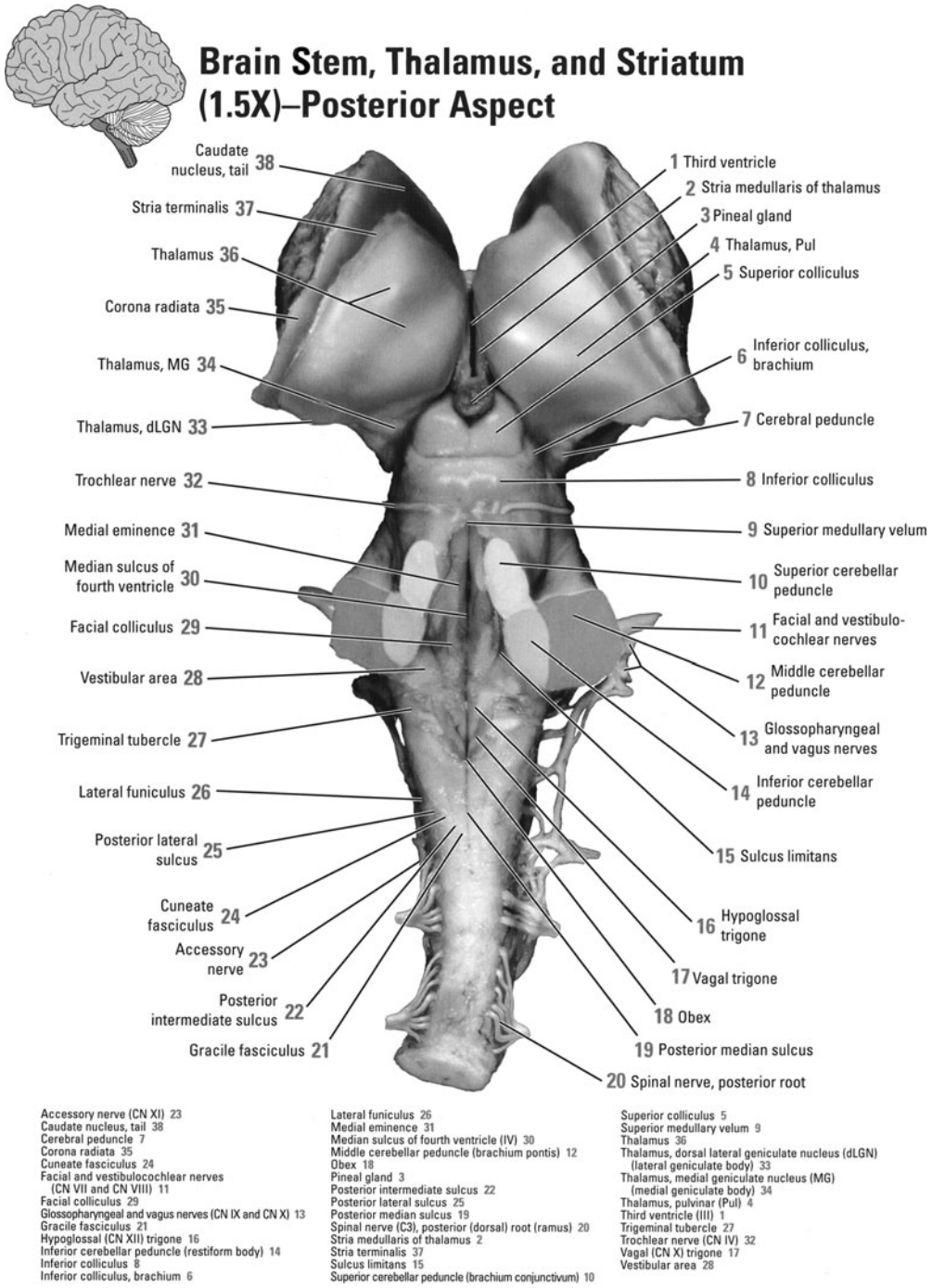


Photo 18-3 Posterior aspect of brainstem, thalamus, and striatum

From Woolsey, T. A., J. Hanaway, and M. H. Gado. *The Brain Atlas: A Visual Guide to the Human Central Nervous System*. 3rd ed. Hoboken, NJ: Wiley, 2008. Reproduced with permission of John Wiley & Sons Inc.

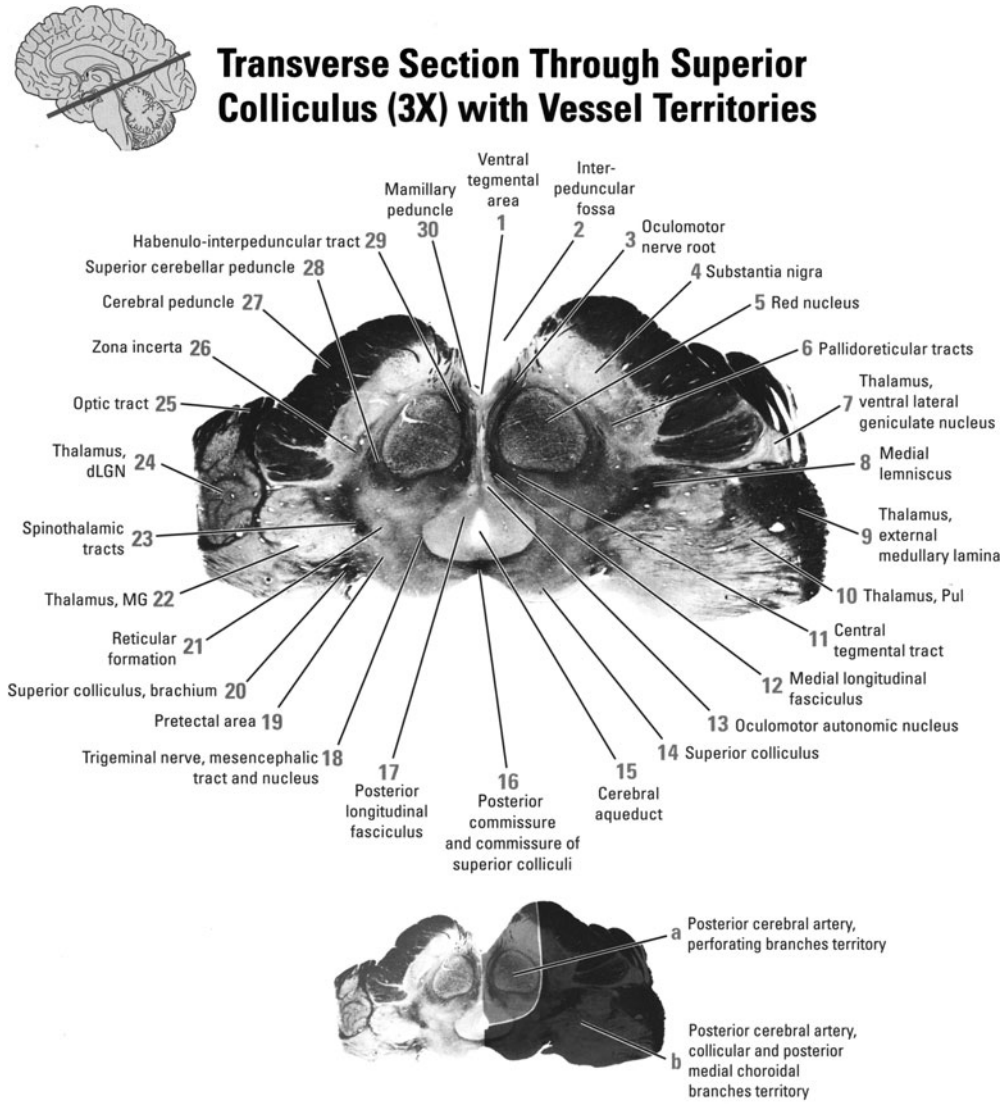


Photo 18-4 Axial section through the midbrain: the sections are in radiographic orientation

From Woolsey, T. A., J. Hanaway, and M. H. Gado. *The Brain Atlas: A Visual Guide to the Human Central Nervous System*. 3rd ed. Hoboken, NJ: Wiley, 2008. Reproduced with permission of John Wiley & Sons Inc.

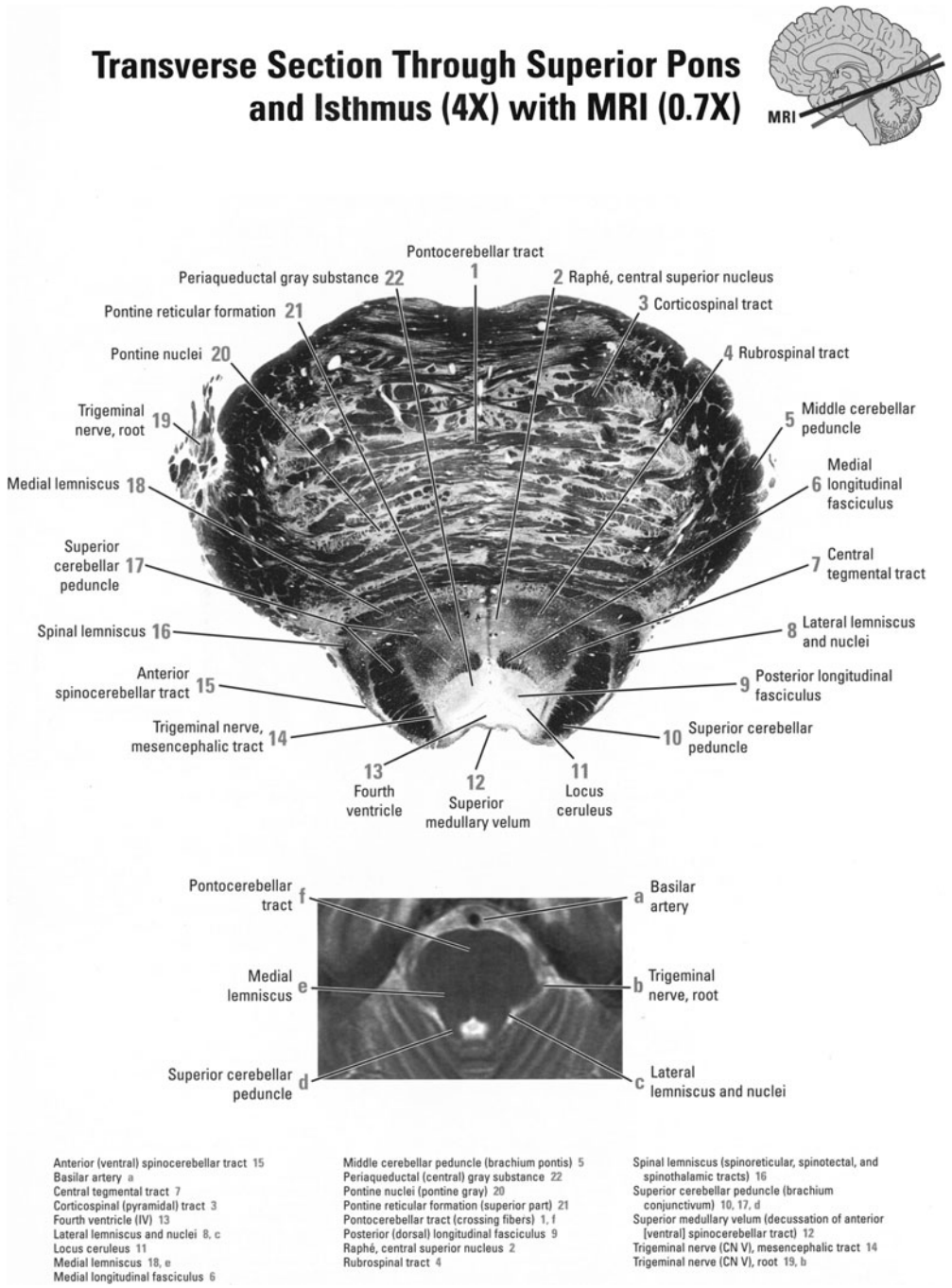
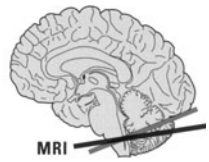
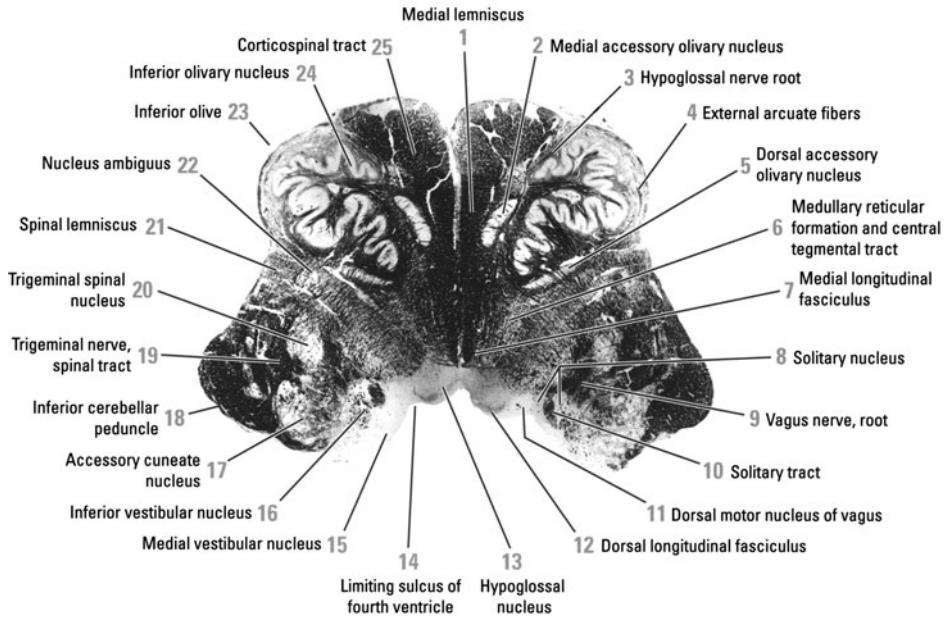


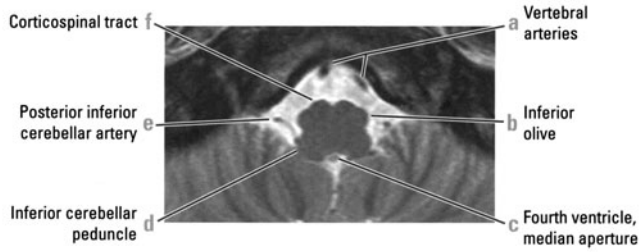
Photo 18-5 Axial section through the pons: the sections are in radiographic orientation

From Woolsey, T. A., J. Hanaway, and M. H. Gado. *The Brain Atlas: A Visual Guide to the Human Central Nervous System*. 3rd ed. Hoboken, NJ: Wiley, 2008. Reproduced with permission of John Wiley & Sons Inc.

Transverse Section Through Hypoglossal Nucleus (5X) with MRI (0.7X)







Accessory (lateral) cuneate nucleus 17
Anterior spinal artery territory d
Corticospinal (pyramidal) tract 25, f
Dorsal accessory olivary nucleus 5
Dorsal longitudinal fasciculus 12
Dorsal (posterior) motor nucleus of vagus (CN X) 11
External arcuate fibers 4
Fourth ventricle (IV), median aperture (foramen of *Magendie*) c
Hypoglossal nerve root (CN XII) 3
Hypoglossal nucleus (CN XII) 13
Inferior cerebellar peduncle, (restiform body) 18, d
Inferior olivary nucleus 24
Inferior olive 23, b
Inferior vestibular nucleus (CN VIII) 16
Limiting sulcus of fourth ventricle (IV) (sulcus limitans) 14
Medial accessory olivary nucleus 2
Medial lemniscus 1
Medial longitudinal fasciculus 7
Medial vestibular nucleus (CN VIII) 15
Medullary reticular formation (gigantocellular nucleus) and central tegmental tract 6
Nucleus ambiguus (ventral motor nucleus of vagus) (CN X) 22
Posterior inferior cerebellar artery e
Solitary nucleus 8
Solitary tract 10
Spinal lemniscus (spinoreticular, spinotectal, and spinothalamic tracts) 21
Trigeminal nerve (CN V), spinal tract 19
Trigeminal (CN V) spinal nucleus 20
Vagus nerve (CN X), root 9
Vertebral arteries a

Photo 18-6 Axial section through the medulla: the sections are in radiographic orientation

From Woolsey, T. A., J. Hanaway, and M. H. Gado. *The Brain Atlas: A Visual Guide to the Human Central Nervous System*. 3rd ed. Hoboken, NJ: Wiley, 2008. Reproduced with permission of John Wiley & Sons Inc.

The previous pages exhibit the different brainstem levels in radiographic orientation. When we draw the individual brainstem levels, we will draw them in anatomic orientation and then ultimately in radiographic orientation, as well, since this is how we commonly view them, clinically.

Now, let's draw the ovoid outline of the *axial brainstem composite* so we can position the 12 groups of brainstem nuclei and fibers. Divide the brainstem from anterior to posterior into its *basis*, *tegmentum*, and *tectum*. Throughout the rostro–caudal axis of the brainstem, the tectum is the thinnest layer. Use the left side of this diagram and the diagrams that follow to draw nuclei and the right side to draw tracts.

Within the basis, show the ventral-lying *corticofugal tracts* and dorsal-lying *supplementary nuclei*. Then, move to the tegmentum and show the *posterior column-medial lemniscus fibers* in the ventromedial tegmentum and move postero-laterally to show the *anterolateral system fibers*. Between them, draw the *trigeminothalamic fibers*. Then, populate the rest of the tegmentum with the *supplementary motor* and *sensory tracts*. Show the *cerebrospinal fluid space* in midline at the border of the tegmentum and tectum. Indicate the *neurobehavioral cells* and *recticular formation nuclei* surround it anteriorly. Then, draw *cranial nuclei* in the dorsal tegmentum. Next, indicate the *auditory system* in the lateral tegmentum. Finally, show the *cerebellar fibers* on the dorsolateral exterior of the brainstem. At every level of the brainstem, we will account for these 12 groups of fibers and nuclei. Certain groups are consistent throughout the brainstem, while others vary in their presence and position throughout its rostro–caudal axis.

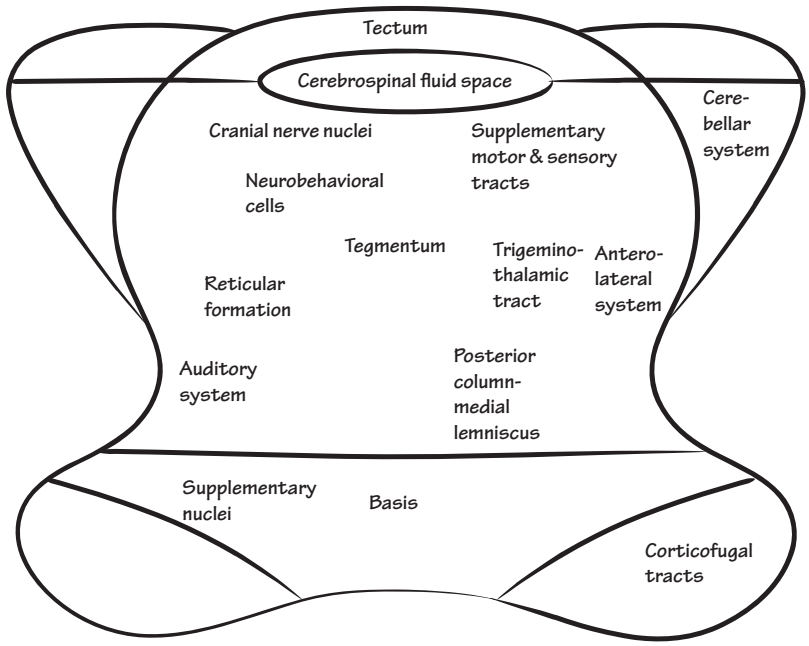


Figure 18-1 Axial brainstem composite

One clinically important feature of the brainstem is the rotation of the posterior column–medial lemniscus pathway. These fibers originate in the inferior medulla, cross midline, and rotate as they ascend the brainstem. To show this process, first draw axial brainstem sections at every level—*medulla*, *pons*, and *midbrain*. Also include a coronal *thalamus* and *cerebral hemisphere* so we can show the relay and termination of the posterior column-medial lemniscus fibers. Show the fiber origins of the *legs* in the *gracile nucleus* in the postero-medial medulla and the *arms* in the *cuneate nucleus* in the postero-lateral medulla. Then indicate the sensory fibers cross midline (decussate) as *internal arcuate fibers*. In the process, show they rotate their somatotopic orientation from medial–lateral to anterior–posterior: the leg fibers go from medial to anterior and the arm fibers go from lateral to posterior. Indicate that after the decussation, the internal arcuate fibers become the *medial lemniscus*. Then, show that as the medial lemniscus ascends the brainstem, it flips back to medial–lateral orientation: arm fibers medial, leg fibers lateral. And show it maintain this organization throughout its projection to the thalamus.

Indicate the *body* fibers (arms and legs) project to the *ventral postero-lateral nucleus* of the thalamus and show the *ventral postero-medial nucleus* of the thalamus receives *facial* fibers via the trigeminothalamic tract. We draw the pathway of the trigeminothalamic tracts separately in the "Pharyngeal Arch Cranial Nerves" chapter.

Next, draw the twisting *thalamocortical sensory projections* of the body fibers from the postero-lateral thalamic nucleus to the cerebral cortex. In their ascent, the sensory fibers again reverse their orientation: the leg fibers project medially and the arm fibers project laterally. Show the *leg* fibers project to the paracentral parietal lobe and the *arm* fibers project to the upper lateral convexity of the cerebral cortex. Then, show the *facial* fibers project from the postero-medial thalamic nucleus to the superior lip of the insular cortex.

Now, demonstrate this multi-step rotational ascent with your hand for easy reference. Place your right hand in front of you, palm down, with your fingers spread apart. Your thumb represents the leg fibers, your little finger the arm fibers. At the outset, we are in the posterior right side of the inferior medulla. To demonstrate the decussation of the internal arcuate fibers, move your hand across midline and bring it in towards you. In the process, rotate your hand into anterior–posterior orientation with your little finger behind your thumb: arm fibers posterior to leg fibers. Next, rotate your hand back into medial–lateral orientation and raise it to demonstrate the orientation reversal that occurs during the medial lemniscus ascent to the thalamus. Then, twist your hand over (palm up) and spread out your fingertips to demonstrate the thalamocortical projection fiber twist and termination in the sensory cortex.

Practice this multi-step rotational hand movement; it will be well worth knowing.

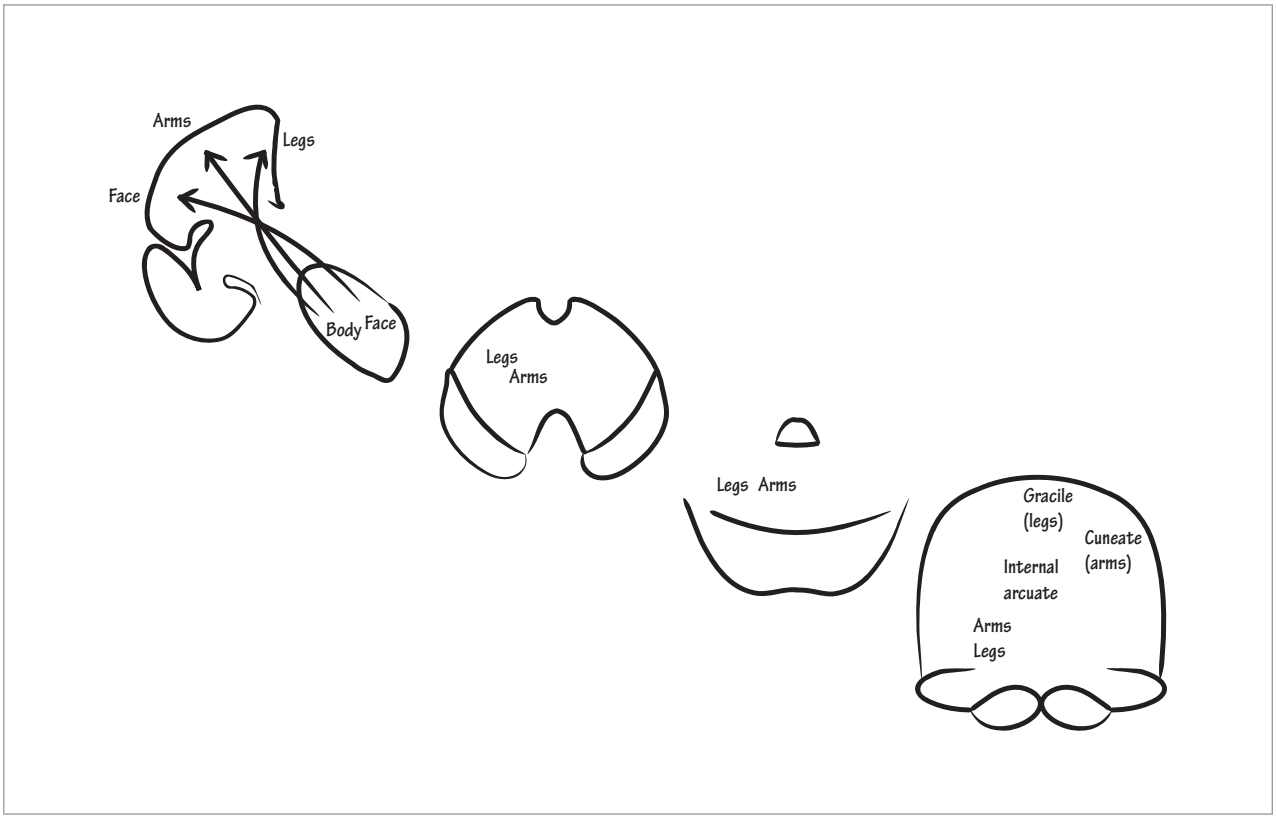


Figure 18-2 Posterior column–medial lemniscus sensory rotation

Next, let's draw the motor fiber descent through the brainstem; the motor fibers originate in parallel to the sensory fibers just in front of the central sulcus in the cerebral cortex. For this diagram, we need a coronal section through the brain: include the *cerebral cortex* and *internal capsule*; representative axial sections through each level of the brainstem—*midbrain*, *pons*, and *medulla*; and a section through the *medullo-cervical junction*. Show the origins of the different motor fibers: the *facial* fibers in the lateral cortex, *arm* fibers in the upper lateral convexity, and *leg* fibers in the paracentral frontal lobe. Draw the twisting descent of each fiber group through the subcortical white matter. The facial fibers descend medially, the leg fibers laterally, and the arm fibers between the two. Show them bundle in the internal capsule and pass into the ipsilateral cerebral peduncle in the midbrain. In the midbrain, the *facial* fibers lie medial to the *arm* fibers, and the arm fibers are situated medial to the *leg* fibers. The facial fibers are called corticobulbar fibers and synapse on different cranial nerve nuclei throughout their descent through the brainstem. In the pons, the descending motor fibers weave through large, fixed pontine nuclei. In the lower medulla, by definition, the corticobulbar fibers have completed their descent, so only the arm and leg corticospinal fibers remain; they descend through the base of the medulla in the ipsilateral medullary pyramid: arms medial, legs lateral.

As the corticospinal tract descends through the medullo-cervical junction, show it decussate and also shift postero-laterally. It positions itself in the lateral funiculus of the upper cervical spinal cord. During the decussation, the arm and leg fibers twist for a second time, so although they cross midline, the arms remain medial to the legs.

With our drawing complete, let's demonstrate the rotational descent of the motor fibers with our hand. During the sensory fiber demonstration, our thumb was the leg fibers and our little finger was the arm fibers; let's use the same representation here. We begin where we ended our sensory fiber rotation in the cerebral cortex with our hand turned palm up and our arm across our body. To demonstrate the twist and bundling of the motor fibers as they descend through the subcortical white matter and into the internal capsule, lower your hand and turn it over (palm down) as you bring your fingers together. Your pinky should be medial to your thumb. To demonstrate the motor fiber descent through the brainstem, simply continue to drop your hand.

Now, we need to demonstrate the pyramidal decussation in the caudal medulla and the second twist of the corticospinal fibers. This rotation is important because it keeps the leg fibers lateral to the arm fibers when the corticospinal tracts cross midline in the upper cervical cord. For this step, bring your hand across midline and turn your palm back up so that your thumb is lateral and your little finger is medial when they cross midline.

Practice this rotation a few times so you will know it when you need it.

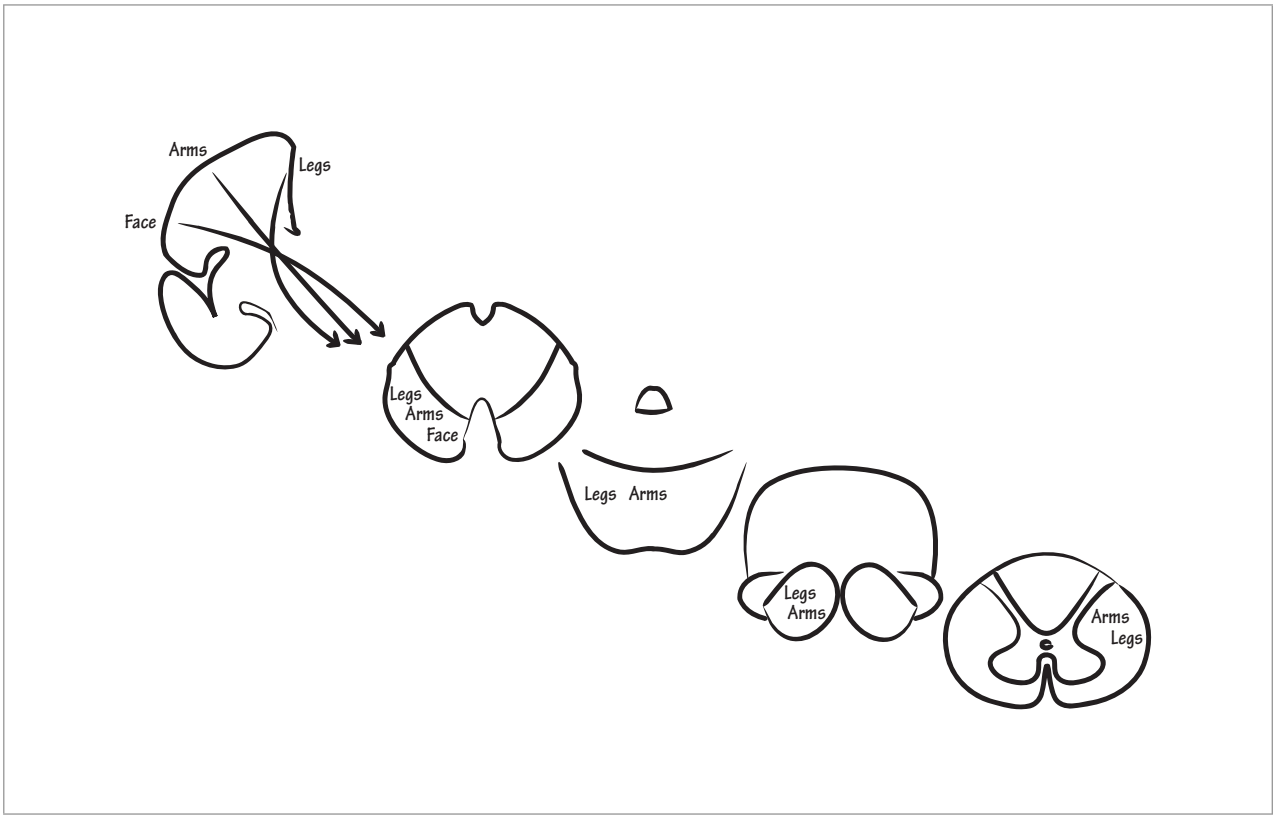


Figure 18-3 Corticofugal motor rotation

We have now completed an introduction to the brainstem that, in conjunction with the following cranial nerve chapters, will answer the majority of clinical brainstem anatomy questions. And yet, we still need a closer look at the specifics of each individual brainstem level, so now, let's draw axial sections of the midbrain, pons, and medulla.

Draw an outline of the midbrain and demarcate the basis, tegmentum, and tectum. Denote the *crura* in the ventral basis. We will begin with the corticofugal tracts that run through them. Divide the center of the crura into the *corticobulbar tracts*, medially, and the *corticospinal tracts*, laterally. Then, in the most medial portion of the crura, draw the *frontopontine tracts* and in the most lateral portion, draw the *parietopontine tracts*. The frontopontine and parietopontine fibers originate in the frontal and parietal cerebral cortices, respectively, descend through the midbrain cerebral peduncles, synapse in ipsilateral pontine nuclei, and project to the contralateral cerebellum. These fibers function in transferring information between the cerebrum and cerebellum.

Dorsal to the corticofugal fibers, draw the *substantia nigra*; it comprises supplementary nuclei that lie in the midbrain basis. We will soon draw the red nuclei, which are supplementary nuclei that lie within the tegmentum. The substantia nigra is so named because of its black appearance, which is due to the melanotic byproduct formed during the production of dopamine. Loss of dopaminergic cells in the substantia compacta of the substantia nigra results in Parkinson's disease.

Now, move to the ventral midbrain tegmentum and draw the additional tegmental supplementary nuclei: the circular *red nuclei*, just off midline. The red nuclei receive fibers from both the motor cortex and cerebellum and project fibers down the spinal cord via the rubrospinal tract. Cortical innervation of the red nucleus is ipsilateral, whereas cerebellar projections to the red nucleus are contralateral.

In the "Spinal Cord" chapter, we discussed that the rubrospinal tract causes arm flexion and the reticulo- and vestibulospinal tracts, which originate at lower brainstem levels, provide arm and leg extension. Thus, a lesion that occurs at or below the level of the red nucleus eliminates rubrospinal upper extremity flexor influence. Consequently, the limbs extend, which is called decerebration. If the lesion is above the red nucleus, the arms flex and the legs extend, which is called decortication.

Cerebellar innervation of the red nucleus is involved in motor performance. Clinical lesions of the red nucleus result in rubral tremor, which is a slow, coarse tremor that occurs at rest and is worsened with posture and action. Despite the tremor's name, red nucleus lesions comprise only a minority of the cases of rubral tremor; lesions in the superior cerebellar peduncle, posterior thalamus, and midbrain tegmentum cause most of them.

Notably, rubral circuitry involves the triangle of Guillain–Mollaret, which we will draw at the end. It comprises descending fibers from the red nucleus that pass through the central tegmental tract to the inferior olivary complex in the medulla; the inferior olivary complex then projects climbing fibers to the contralateral cerebellum; and the cerebellum then sends fibers contralaterally to the red nucleus where they originated, completing the triangle. Disruption in the triangle of Guillain–Mollaret results in a specific form of tremor called palatal tremor (aka palatal myoclonus).

If you want to learn about clinical aspects of palatal tremor, read on; otherwise, skip ahead. If there is no obvious lesion for palatal tremor, this dysrhythmic disorder is called essential palatal tremor and an ear-clicking noise will often be audible that is attributed to abnormal movements of tensor veli palatini. When a clear-cut lesion exists, this is known as secondary palatal tremor (aka acquired palatal tremor), and abnormal movement of levator veli palatini is believed to cause the tremor. In acquired palatal tremor, you will often find hypertrophy of the inferior olivary complex on brain imaging, which is compensatory to the disruption within the triangle of Guillain–Mollaret.

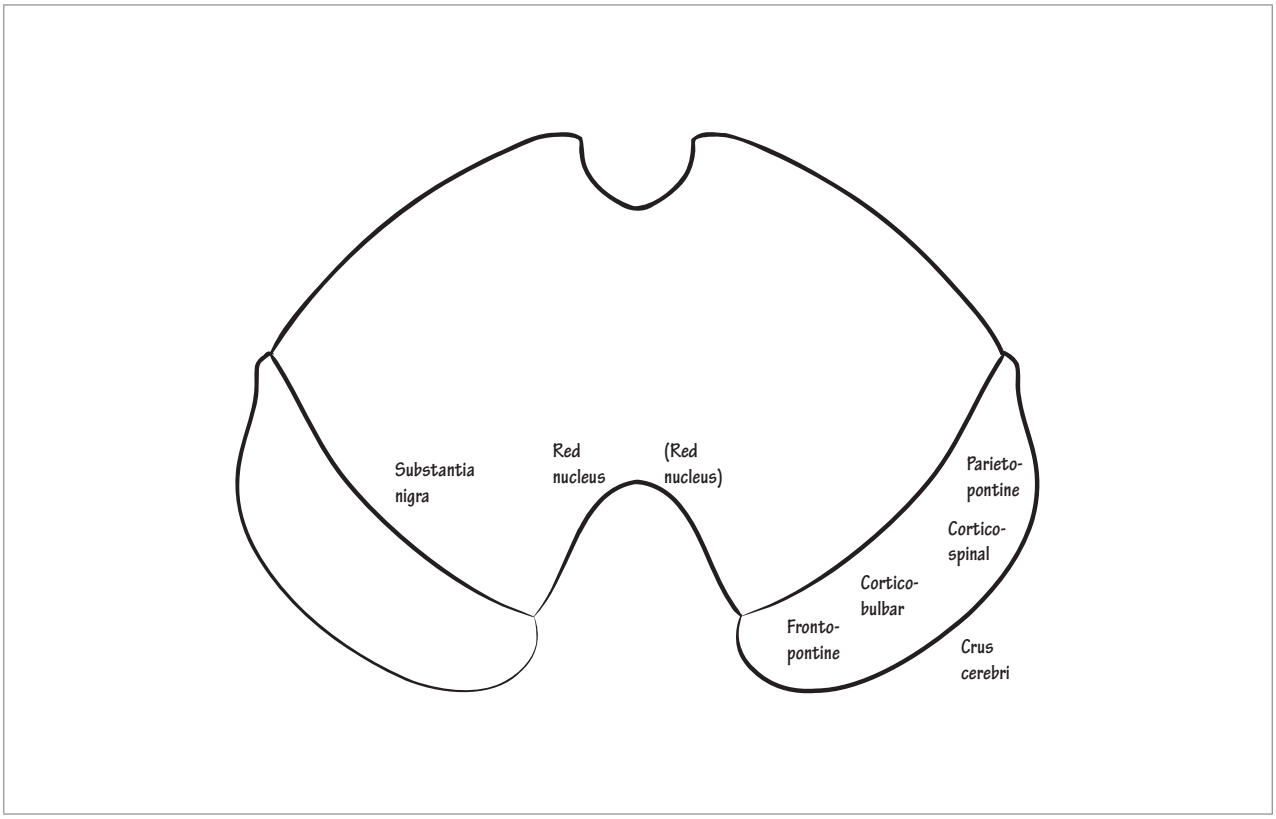


Figure 18-4 Incomplete axial midbrain

Now, return to our midbrain diagram. Lateral to the red nuclei, draw the *medial lemniscus* and postero-lateral to it, draw the spinothalamic tract fibers of the *anterolateral system*. In the pons and medulla, we will draw these sensory bundles (the spinothalamic tracts and medial lemniscus fibers) farther medially; but in the midbrain, the midline-positioned red nuclei push them out laterally. The only fiber bundle still left within the anterolateral system when it reaches the midbrain is the spinothalamic tract. The others either synapse at lower levels or disperse within the midbrain to various targets. The tracts that disperse within the midbrain are the spinomesencephalic tract ("mesencephalic" is Latin for "midbrain"), the spinoreticular fibers (which form synapses throughout the brainstem reticular formation along the rostro-caudal axis of the brainstem), and the spinotectal fibers, which target the midbrain tectum. Next, move farther inside the brainstem and draw both the *posterior* and *anterior trigeminothalamic tracts*.

Now, label the *cerebral aqueduct* as the cerebrospinal fluid space of the midbrain; it lies in midline at the border of the tegmentum and tectum. Encircle it with its neurobehavioral media. First, label the surrounding *periaqueductal gray* and then indicate the *raphe nuclei*, which run medially along the rostro-caudal length of the brainstem.

The periaqueductal gray is a key link in the suppression and modulation of pain and is involved in many other neurobehavioral functions, as well. While it is best known for its stores of opioid neuropeptides, it is also packed with monoamines, acetylcholine, and amino acids. Afferent tracts to the periaqueductal gray of note are the spinomesencephalic fibers from the anterolateral system, which provide localization information, and the dorsal longitudinal fasciculus (aka posterior longitudinal fasciculus), which provides input from the hypothalamus. The diverse chemoarchitecture of the periaqueductal gray coupled with its wide efferent connectivity to the prefrontal cortex, limbic regions, hypothalamus, spinal cord, and other brainstem areas involves it in numerous functions. Periaqueductal gray functions include far-reaching modulation of sympathetic responses (i.e., pupillary dilation and cardiovascular responses); parasympathetic-induced micturition; modulation of reproductive behavior; and even locomotion and vocalization. However, its best-known function is in pain modulation, and since the 1970s, neurosurgeons have been stimulating the periaqueductal gray area in chronic pain patients to achieve analgesia, albeit with mixed results.

The string of raphe nuclei are actually considered a subcategory of the reticular formation, which we discuss next; they are its medial division. Six subnuclei constitute the raphe system but we think about the raphe system as just two groups: the nuclei above the mid-pons and the nuclei below it. The rostral raphe group (aka oral raphe group) comprises the upper pontine and midbrain raphe nuclei. For reference, they are the caudal linear, dorsal raphe, and median raphe nuclei. The caudal raphe group comprises the lower pontine and medullary raphe nuclei. Again, for reference, they are the raphe magnus, raphe obscuris, and raphe pallidus nuclei. Efferent projections from the rostral raphe group ascend into the forebrain, whereas projections from the caudal raphe group descend to the lower brainstem and spinal cord. While the periaqueductal gray has a diverse chemoarchitecture, the raphe system was originally defined by its nearly universal serotinergic make-up. Despite the uniformity of its chemoarchitecture, it has diverse functions that include modulation of sleep-wake cycles, pain management, and motor activity, but it is best known for its regulation of mood and its role in hallucinogenic drug effects and the effects of serotonin-modulating psychotropic medications.

In short, the periaqueductal gray and raphe nuclei are the main neurobehavioral cell groups of the midbrain. For the periaqueductal gray, think opioids and pain suppression, and for the raphe nuclei, think serotonin and psychopharmacology.

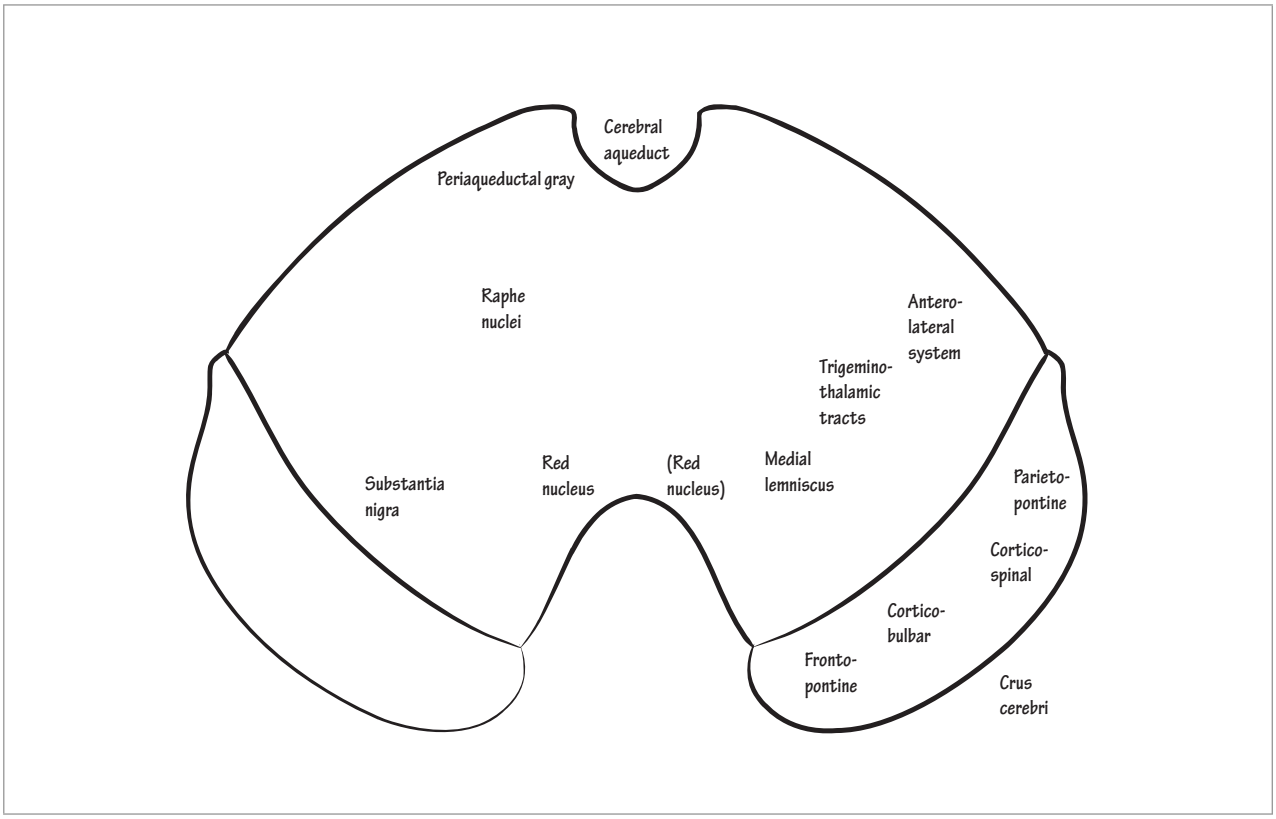


Figure 18-5 Incomplete axial midbrain

Lateral to the raphe nuclei, indicate the *reticular formation*, which encompasses a network of specifically arranged nuclei that span the rostro-caudal length of the brainstem. Initially, researchers believed the reticular formation was simply a "diffuse arousal network." This estimation was based on its apparent indistinct histology, and only recently have researchers begun to realize its histologic and functional specialization. While wakefulness is no longer believed to be the only purpose of the reticular formation, the recticular formation does project fibers via the central tegmental tract to the rostral intralaminar nuclei of the thalamus for arousal; this is the current, targeted version of the ascending reticular activating system. Like the raphe nuclear system, which is divided into rostral and caudal groups, the reticular formation is divided into medial and lateral fields. The medial field is involved in eye and head movements and postural control, whereas the lateral field is involved in autonomic functions, such as respiration, micturition, and blood pressure control. Interneurons of the pharyngeal arch cranial nerve derivatives and hypoglossal nuclei populate the lateral field.

Now, label the cranial nerves with nuclei in the dorsal midbrain tegmentum as *cranial nerves 3* and *4*. We dedicate the following few chapters to cranial nerve organization, so we will not provide any further explanation, here. Next, label the supplementary motor and sensory fiber tracts in midline, just in front of the periaqueductal gray; they are the *medial longitudinal fasciculus* and, lateral to it, the *central tegmental tract*. The medial longitudinal fasciculus carries ascending fibers from the contralateral interneurons of the abducens nucleus to the ipsilateral oculomotor nucleus and the central tegmental tract carries both ascending and descending fiber bundles. The ascending fibers of the central tegmental tract are the projection fibers from the reticular formation to the rostral intralaminar nuclei of the thalamus, which form the targeted ascending reticular activating system. We mentioned the role of the descending fibers of the central tegmental tract, which connects the red nucleus to the inferior olivary complex. What triangle does it help create? The triangle of Guillain–Mollaret. At lower levels, we will show the central tegmental tract shift progressively laterally along with the rubrospinal tract.

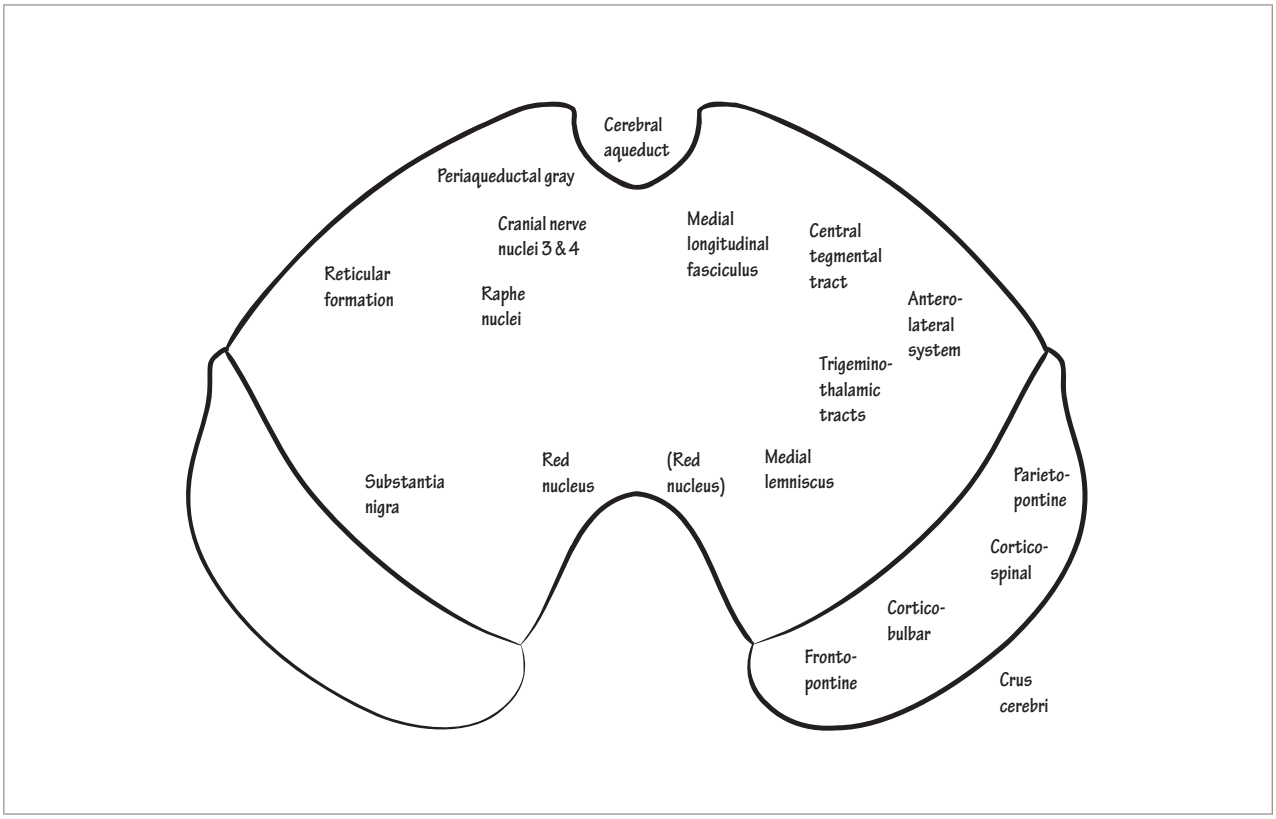


Figure 18-6 Incomplete axial midbrain

Now, include the nuclei of the tectum: the *superior* and *inferior colliculi* and the *posterior commissure*. The colliculi form four humps along the dorsal surface of the midbrain that are collectively grouped as the quadrigeminal plate (aka corpora quadrigemina), which is surrounded by the quadrigeminal cistern. The superior colliculus and posterior commissure are involved in eye movements. The inferior colliculus is the auditory component of the midbrain.

Within the center of the tectum is the posterior commissure. Decussating fibers from the pretectal nuclei pass through it to the contralateral Edinger–Westphal nucleus. The nucleus of the posterior commissure, itself, is responsible for sending upgaze fibers to the cranial nerve 3 and 4 nuclei. Large pineal tumors can compress the quadrigeminal plate and cause impairment of upgaze.

Draw the *tectobulbospinal tract*, which originates in the superior colliculus and decussates in front of the medial longitudinal fasciculus. It is a supplementary motor fiber pathway but we draw it here because it originates within the midbrain tectum. The tectobulbospinal tract serves in eye movement control as does the medial longitudinal fasciculus and both descend through the dorsal midline of the brainstem. Regional stimulation of the superior colliculus stimulates efferent impulses through the tectobulbospinal tract to the brainstem and upper cervical nuclei for eye and head movements.

Finally, show the *superior cerebellar peduncle fibers* decussate in the central midbrain tegmentum. The major outflow tracts from the cerebellar peduncles are through the superior cerebellar peduncles. These outflow fibers exit through the peduncles, cross within the midbrain tegmentum, and ascend to the thalamus. This midbrain decussation of the cerebellar outflow fibers explains the lateralized ataxia that often occurs in midbrain lesions.

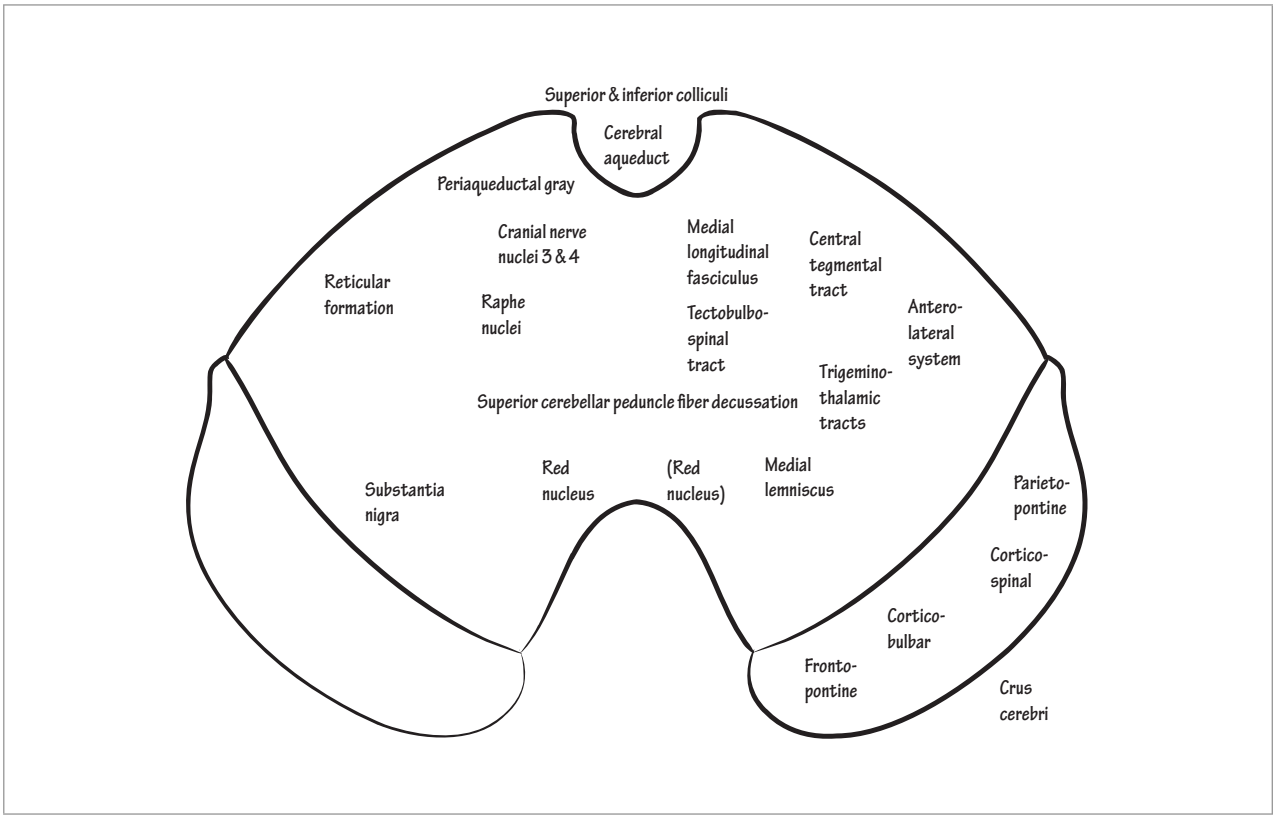


Figure 18-7 Complete axial midbrain

Before we move on to the pons, draw the midbrain upside down to review its anatomy. Why upside down? Because radiographic images are upside down relative to anatomic images. In the cerebral cortex, the difference produces right–left confusion, which is easy to work through; whereas in the brainstem, it causes anterior–posterior disorientation, which is often baffling. It is difficult to know which level of the brainstem you are viewing, if you are unaware of this difference in orientation. In radiographic images, identify the midbrain by its crura, which look like a pair of *Mickey Mouse ears*.

Draw the midbrain, now, in radiographic orientation and review its anatomy.

Photo 18-7 Anatomical orientation of midbrain
With permission from DeArmond, S. J., M. M. Fusco, and M. M. Dewey. *Structure of the Human Brain: A Photographic Atlas*. 3rd ed. New York: Oxford University Press, 1989.

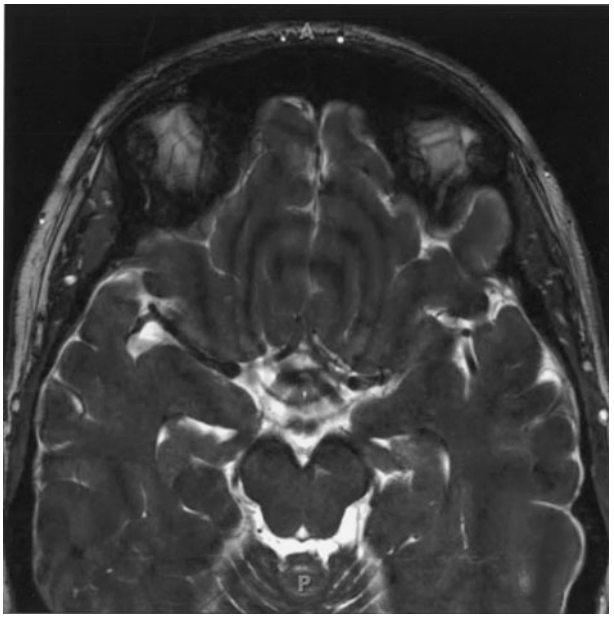


Photo 18-8 Radiographic orientation of midbrain

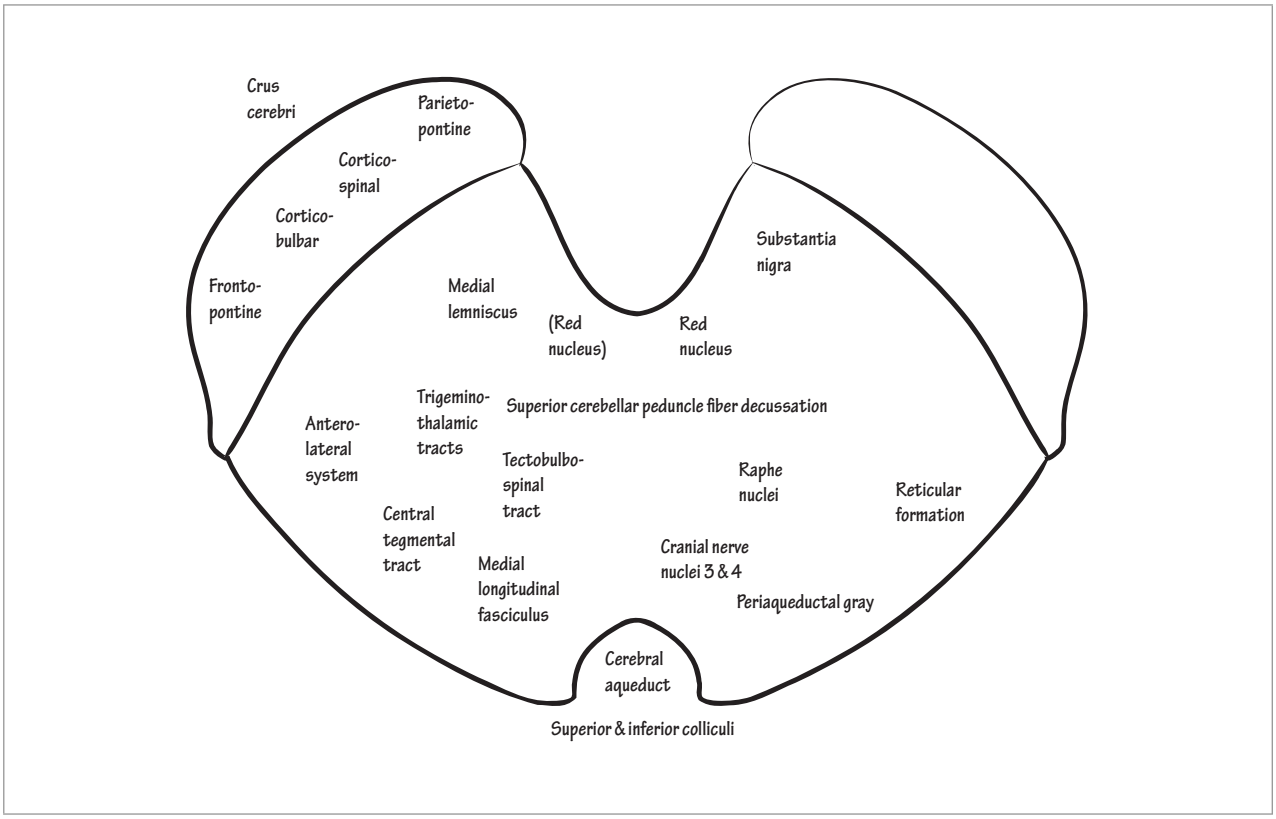


Figure 18-8 Radiographic axial midbrain

Next, let's draw the *pons* in anatomic orientation. First, draw its tear-drop shaped outline. Show its bulbous *basis*, which resembles a bag of marbles. This bulge comes from the numerous supplementary motor nuclei (the pontine nuclei), which we will draw next, and from the projection fibers to the cerebellum.

In the basis, draw the corticofugal tracts, which are the *corticospinal* and *corticobulbar tracts*; they are interspersed between large, scattered supplementary motor nuclei called *pontine nuclei*. Corticopontine fibers synapse on the pontine nuclei and project to the contralateral cerebellum to help in motor planning.

Now, move to the pontine tegmentum. Show the *medial lemniscus* in the ventral tegmentum, oriented in the medial–lateral plane. The red nuclei terminate above the pons, therefore, at the rostro-caudal level of the pons, the medial lemniscus lies medial, as its name indicates—unlike in the midbrain where, as discussed, it is pushed lateral. Next, show the *anterolateral system fibers* lateral to the medial lemniscus fibers. Farther interior, draw the *anterior trigeminothalamic tract*. In the next paragraph we explain why only the anterior bundle of the trigeminothalamic tract is present here, whereas both the anterior and posterior tracts were found in the midbrain. If you are uninterested in this explanation, skip ahead.

The anterior trigeminothalamic tract bundle is formed from fibers of the spinal trigeminal nucleus, which spans the upper cervical spinal cord through the pons; therefore, we find anterior trigeminothalamic projections here as well as in the medulla. On the contrary, fibers from the posterior trigeminothalamic tracts originate in the principal sensory nuclei in the pons but only first *bundle* in the midbrain; therefore, the posterior trigeminothalamic tract bundles are not found in the pons or the medulla. Note, the principal sensory nuclei also send fibers to the anterior trigeminothalamic tracts.

Now, let's show the medial-lying supplementary motor and sensory tracts of the pontine tegmentum. Indicate the *medial longitudinal fasciculus* and the *tectobulbospinal tract* descend through the dorsal midline tegmentum, whereas the *rubrospinal* and *central tegmental tracts* shift progressively laterally as they descend through the pons and medulla. Next, label the cerebrospinal fluid space of the pons as the *fourth ventricle* and show that the neurobehavioral *central gray area* surrounds it here and throughout the rest of the neuraxis (in the midbrain, the central gray is called the periaqueductal gray). Also, show the *raphe nuclei* in midline, in the medial aspect of the *reticular formation*, where they are throughout the rostro-caudal axis of the brainstem.

Now, indicate the presence of a different neurobehavioral cell type, the *locus ceruleus*; it lies in the lateral floor of the fourth ventricle and releases noradrenaline. Skip ahead, if that satisfies your knowledge of the locus ceruleus. Technically, the locus ceruleus spans from the caudal end of the periaqueductal gray in the lower midbrain to the facial nucleus in the midpons; however, it is convenient to associate the locus ceruleus with the pons. In distinction to the raphe nuclei, which are *predominantly* serotonergic, the locus ceruleus cells are *entirely* noradrenergic. The precursor of dopamine and noradrenaline is neuromelanin; therefore, the largest sites of neuromelanin in the brainstem are the substantia nigra, which produces dopamine, and the locus ceruleus, which produces noradrenaline.

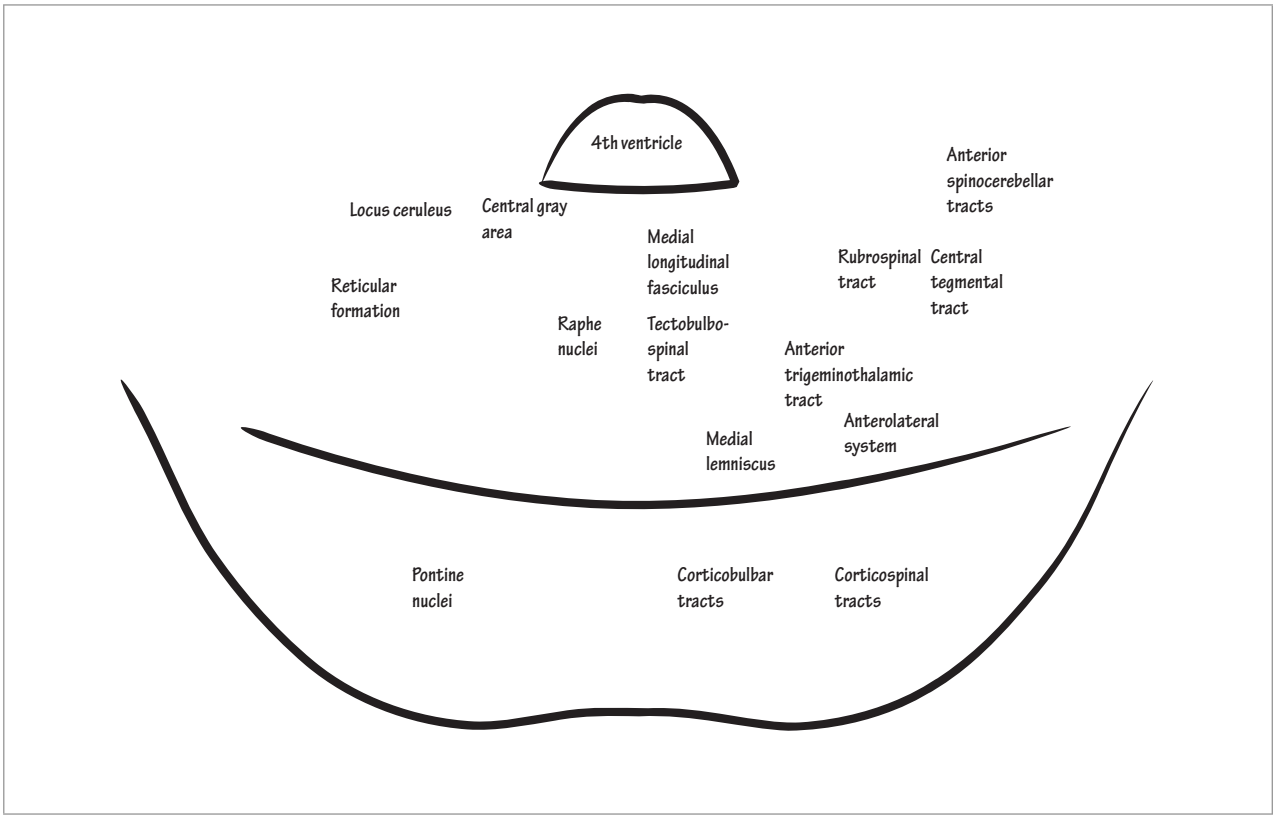


Figure 18-9 Incomplete axial pons

Stop, now, and remind yourself that (1) the most commonly discussed neurotransmitter class of the periaqueductal gray is the opioids, (2) the most abundant raphe nuclei neurotransmitter is serotonin, and (3) all locus ceruleus cells generate what type of neurotransmitter? Noradrenaline.

Now, indicate the presence of the nuclei of *cranial nerves 5*, *6*, and *7* in the dorsal pontine tegmentum. To represent the auditory system component of the pons, draw the *lateral lemniscus* in the lateral tegmentum and the *trapezoid body* and *superior olivary nucleus* in the antero-lateral tegmentum.

Next, draw the extensive cerebellar structures that attach to the pontine tectum. First, show the brachium conjunctivum of the *superior cerebellar peduncle* and then the *inferior cerebellar peduncle*, which comprises the restiform and juxtarestiform bodies. The superior cerebellar peduncle is functionally associated with the midbrain and the inferior cerebellar peduncle with the medulla; however, they technically lie at rostral and caudal levels of the pons, respectively. Next, show the *middle cerebellar peduncles* along the lateral aspects of the pontine basis; cerebellar afferent fibers pass through the basis and are an additional reason for its swollen topography. At the end of the chapter, we will discuss the presence of the anterior spinocerebellar fibers in the postero-lateral pons.

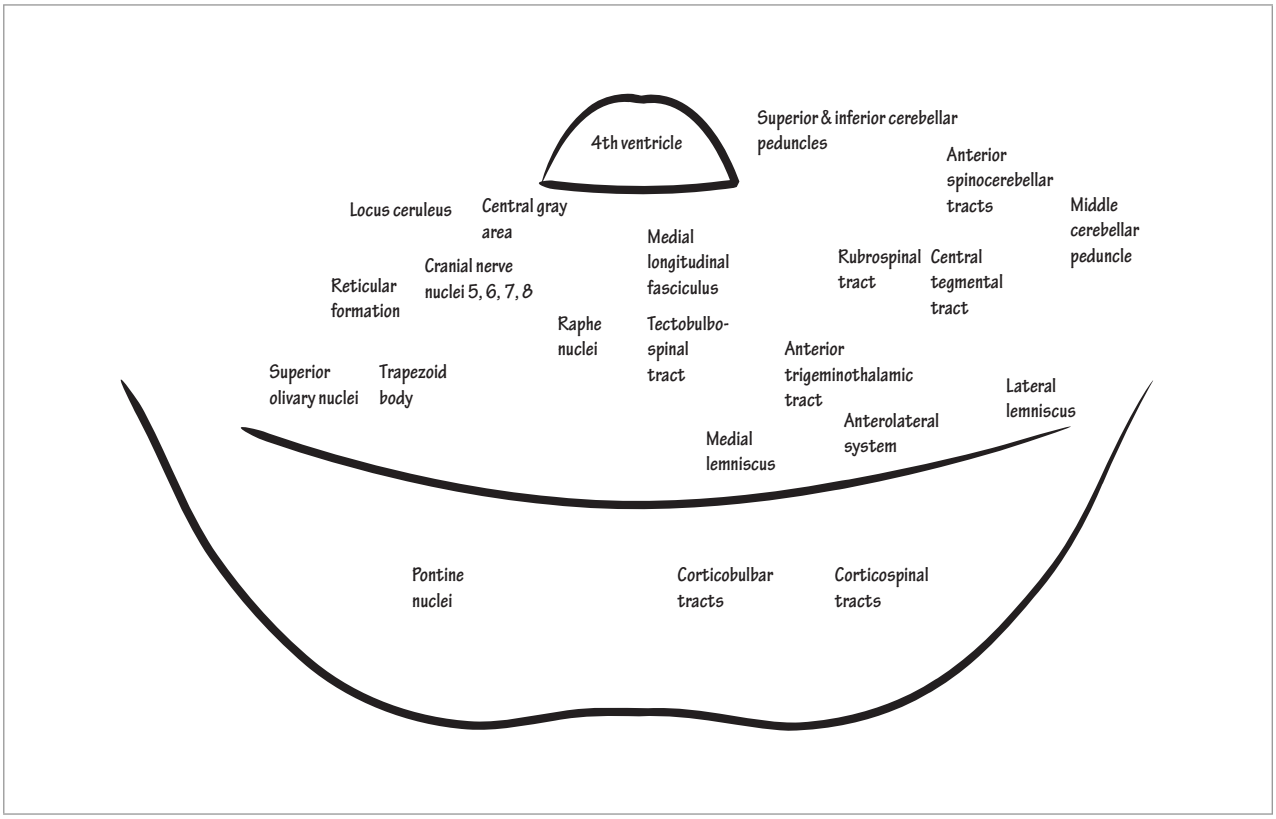


Figure 18-10 Complete axial pons

Just as we did with the midbrain, draw the pons in radiographic orientation and review its anatomy.

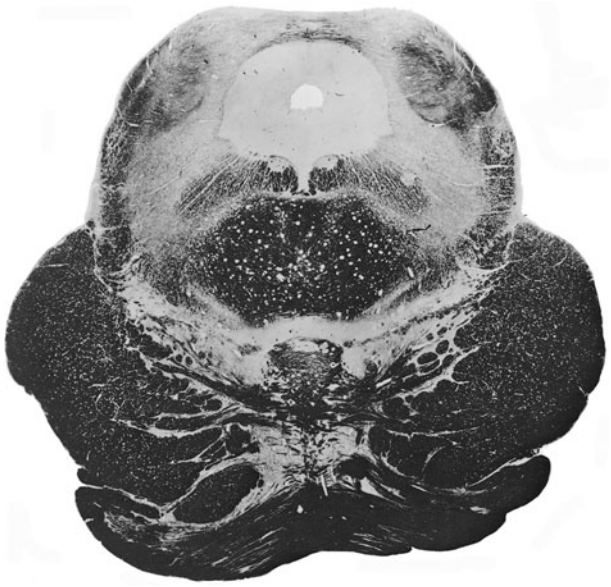


Photo 18-9 Anatomical orientation of pons
With permission from DeArmond, S. J., M. M. Fusco, and M. M. Dewey. *Structure of the Human Brain: A Photographic Atlas*. 3rd ed. New York: Oxford University Press, 1989.

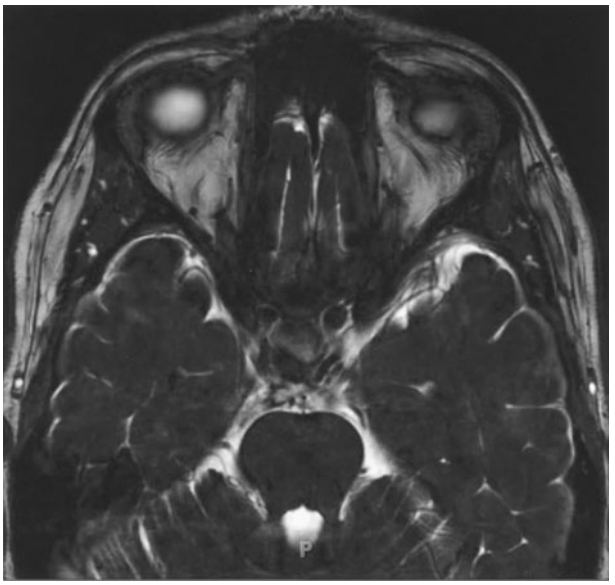


Photo 18-10 Radiographic orientation of pons

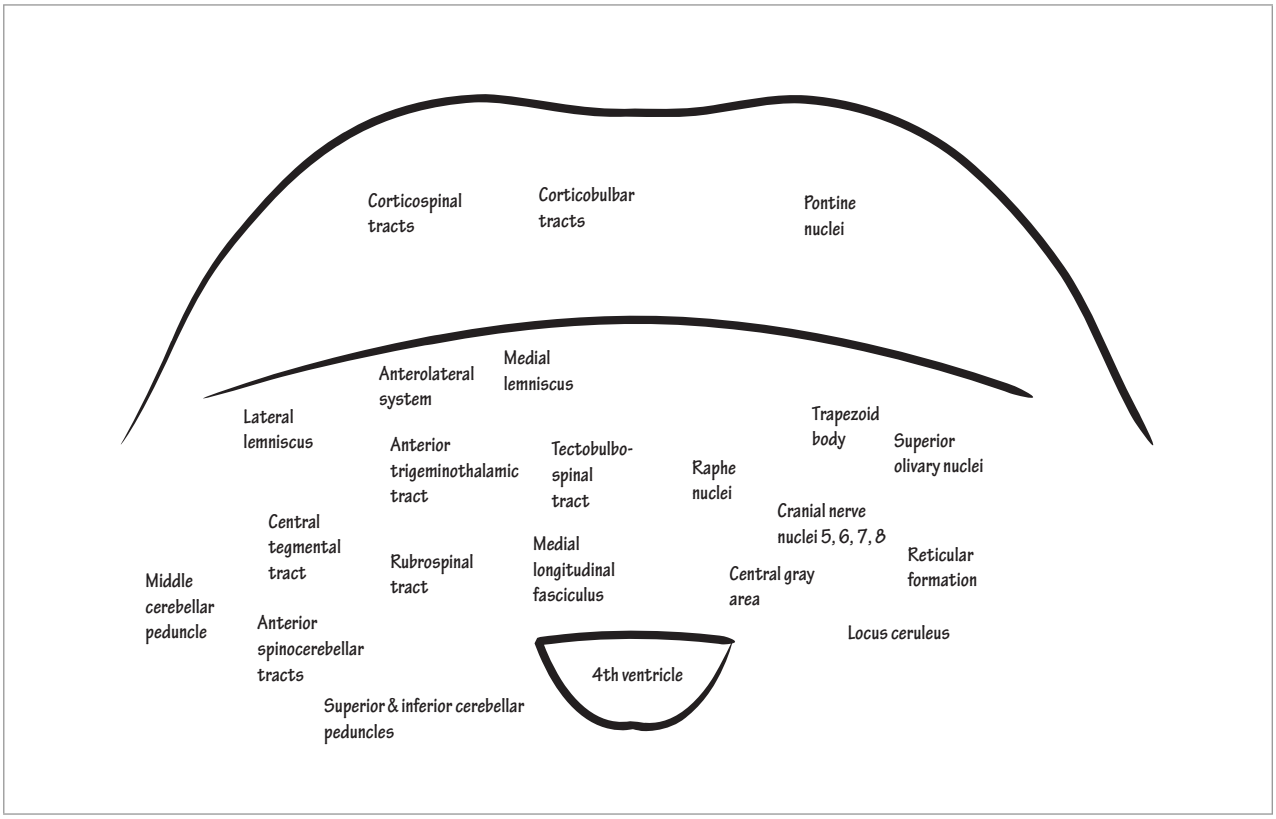


Figure 18-11 Radiographic axial pons

Now, let's draw a cross-section through the medulla. The medulla lacks a true basis or tegmentum, but we apply one, anyway. Before we detail the basis, first draw the *posterior column/internal arcuate/medial lemniscus sensory decussation*. In the dorsal medulla, show the posterior column nuclei: the *gracile nucleus*, medially, and the *cuneate nucleus*, laterally. Then, show the *internal arcuate fibers* project from these nuclei in posterior–anterior orientation to the contralateral medulla (where they become the *medial lemniscus*). Note that when these fibers ascend into the upper medulla, pons, and midbrain, they return to medial–lateral orientation.

Now, let's go through the rest of the medulla in an organized fashion. Along the anterior surface of the basis, draw the corticofugal pathway within the ovoid *medullary pyramids*. Indicate that only the *corticospinal tracts* destined for the spinal cord pass through it; the corticopontine fibers, as their name indicates, synapse in the pons and the corticobulbar fibers synapse throughout the brainstem.

The pyramidal shape of the pyramids is only perceivable when you look at the medulla along a rostro–caudal axis, out of the plane of this diagram. Ninety percent of the corticospinal fibers of the medullary pyramids decussate to form the contralateral lateral corticospinal tract, which descends through the postero-lateral spinal cord in the lateral funiculus. The remaining 10% descend ipsilaterally through the antero-medial spinal cord as the anterior corticospinal tract.

Next, draw the *inferior olivary complex* dorsolateral to the medullary pyramid. The olivary complex primarily receives afferent fibers from the spinal cord, but it also receives descending fibers through what tract? The central tegmental tract. Together with the red nucleus in the midbrain and the dentate nucleus in the contralateral cerebellum, the olivary complex forms the triangle of Guillain–Mollaret.

It is important to remember that projection fibers from the olivary nuclei to the contralateral cerebellum are called climbing fibers. While little is known about the function of the olivary nuclei, the histology of these efferent fibers is well described. Which cerebellar peduncle do these climbing fibers enter to reach the contralateral cerebellum? The inferior cerebellar peduncle.

Now, let's draw the medullary tegmentum. We already inserted the medial lemniscus. In the lateral tegmentum, draw the *anterolateral system*; it lies in a similar position to where it is situated in the spinal cord. Note that unlike in the midbrain, where there were only the spinothalamic fibers left within the anterolateral system, here, in the medulla, many ascending fiber groups are present: spinothalamic, spinoreticular, spinomesencephalic, and spinotectal. The spino-olivary and spino-vestibular fibers disperse within the medulla so we do not include them in this bundle. Certain spinocerebellar fibers join the anterolateral system, which we discuss at the end. Internal to these anterolateral system fibers, draw the *anterior trigeminothalamic tract* as we did in the pons. Next, in the midline tegmentum, from posterior to anterior, draw the *medial longitudinal fasciculus* and the *tectobulbospinal tract*. Then draw the *rubrospinal tract* in the lateral tegmentum.

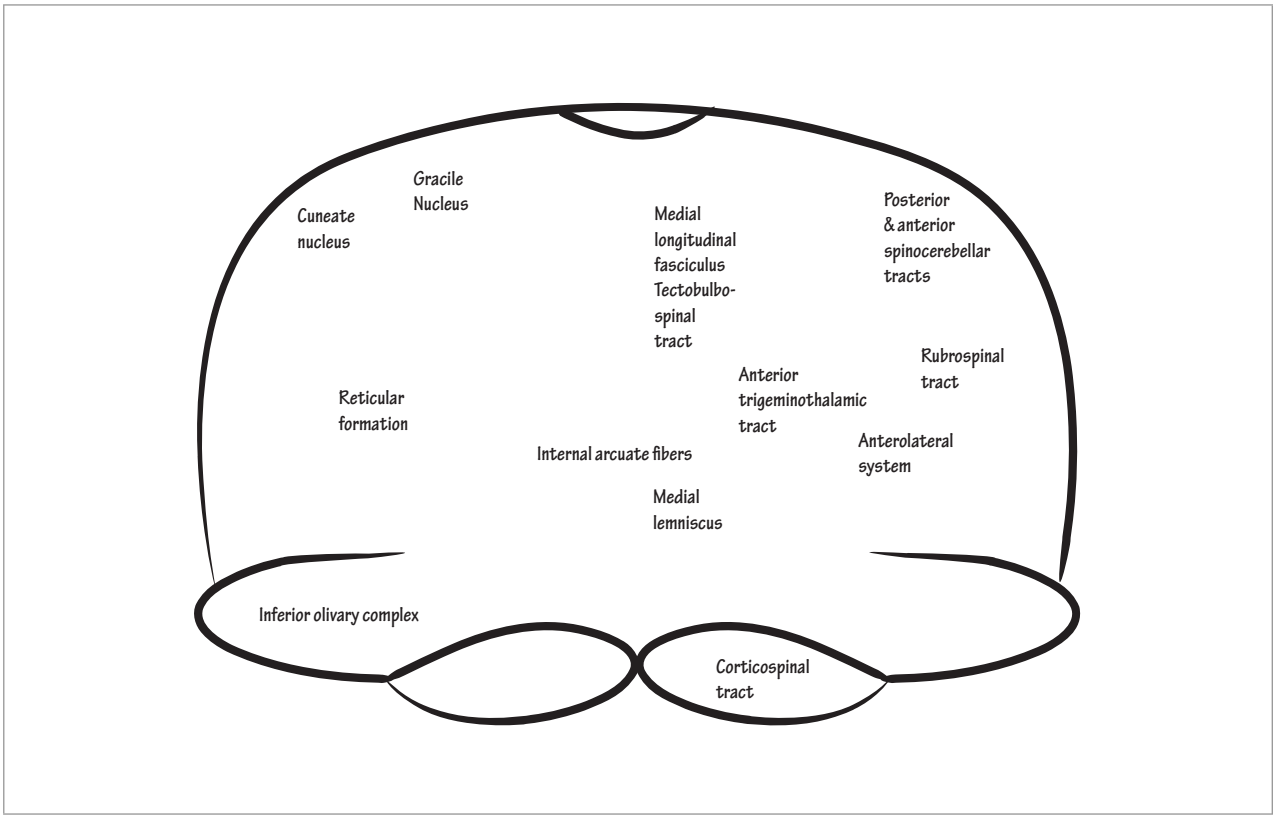


Figure 18-12 Incomplete axial medulla

Now, label the cerebrospinal fluid space of the medulla as the *fourth ventricle*, rostrally, and the *central canal*, caudally. Show the *obex* demarcates these two fluid spaces. Along the anterior border of the obex (in the floor of the fourth ventricle) label the *area postrema*. The area postrema is an important chemoreceptor trigger zone for emesis (aka vomiting). Medications and radiation are the primary activators of it. The area postrema is susceptible to medications because, being one of the rare circumventricular organs, it lacks a blood–brain barrier to diffusion of large molecules. Formerly, the area postrema was considered the "vomit center," but this concept is now out of vogue, as we understand that activation of many different areas potentially lead to emesis; for example, neurovestibular centers that produce motion sickness ultimately cause vomiting.

Next, label the region around the cerebrospinal fluid space as the *central gray area* as you did in the pons. Indicate the neurobehavioral cells that surround it are the *raphe nuclei*. Then, show the nuclei of *cranial nerves 8, 9, 10*, and *12* in the dorsal tegmentum. The auditory system component in the medulla is the cochlear nuclei of cranial nerve 8.

Lastly, as the cerebellar attachment to the posterolateral medulla, draw the *restiform body*; it joins the juxtarestiform body in the caudal pons to form the inferior cerebellar peduncle. Many ascending fiber tracts terminate in the restiform body, including the spinocerebellar fibers, which we will soon add to our drawing.

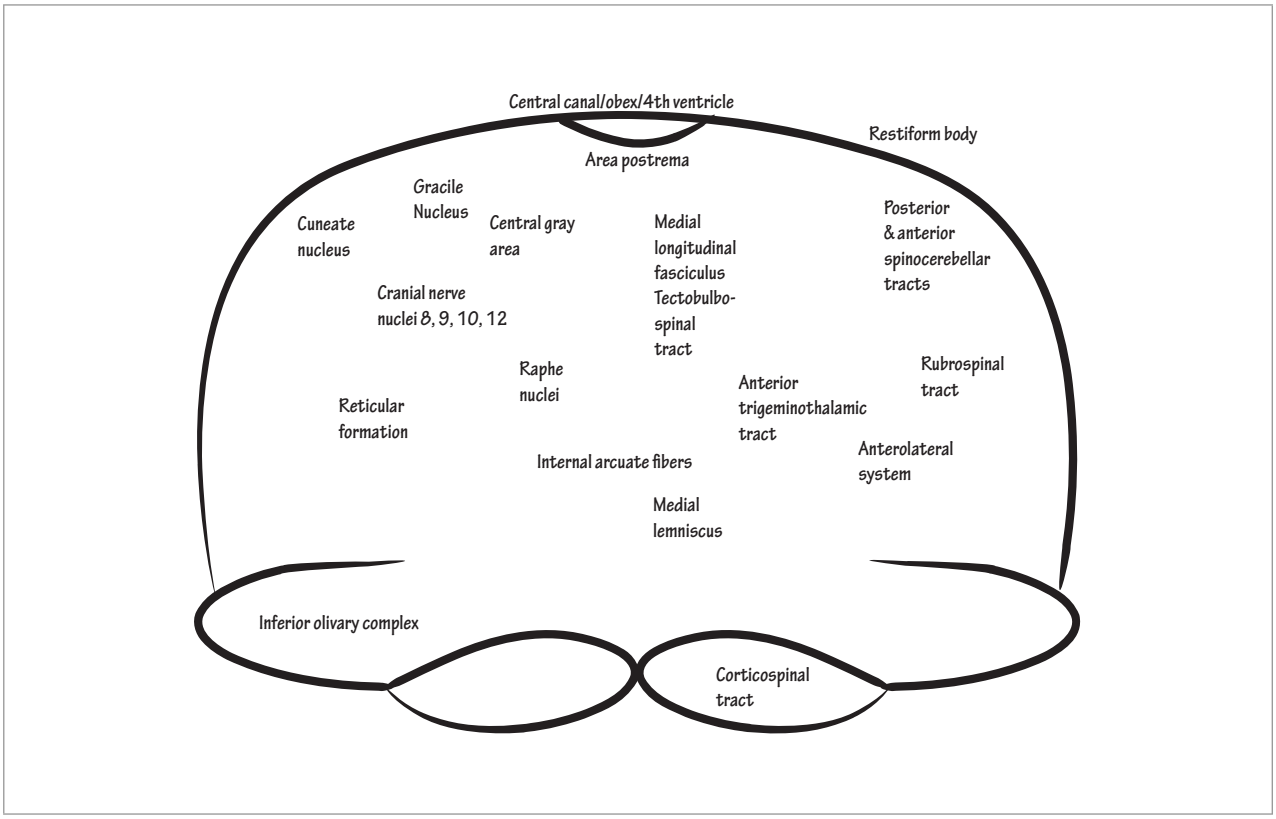


Figure 18-13 Complete axial medulla

Now, draw the medulla in radiographic orientation as you did for the midbrain and pons.

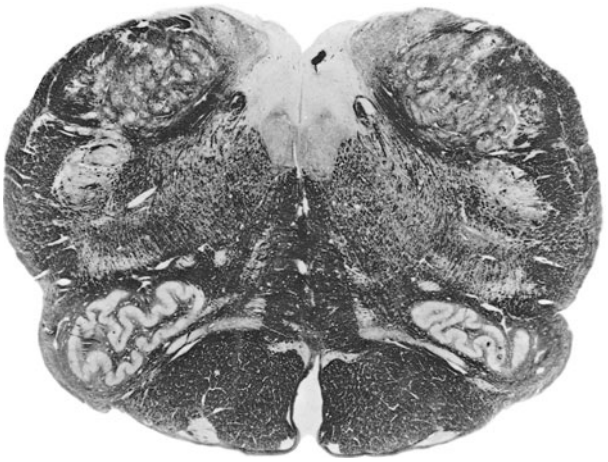


Photo 18-11 Anatomic orientation of medulla
With permission from DeArmond, S. J., M. M. Fusco, and M. M. Dewey. *Structure of the Human Brain: A Photographic Atlas*. 3rd ed. New York: Oxford University Press, 1989.

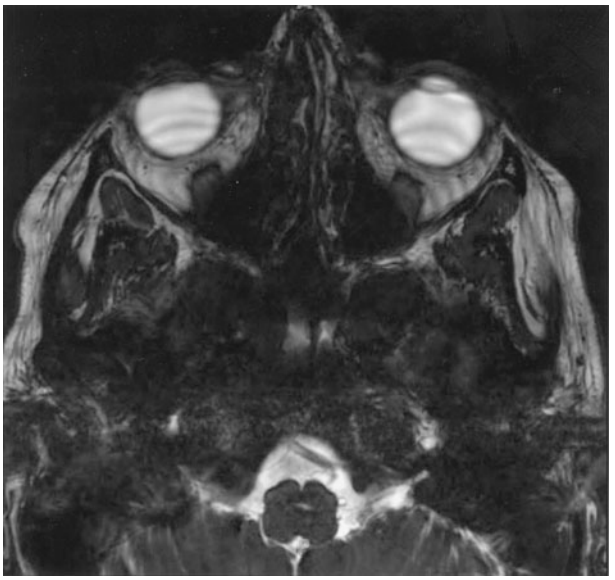


Photo 18-12 Medulla in radiographic orientation

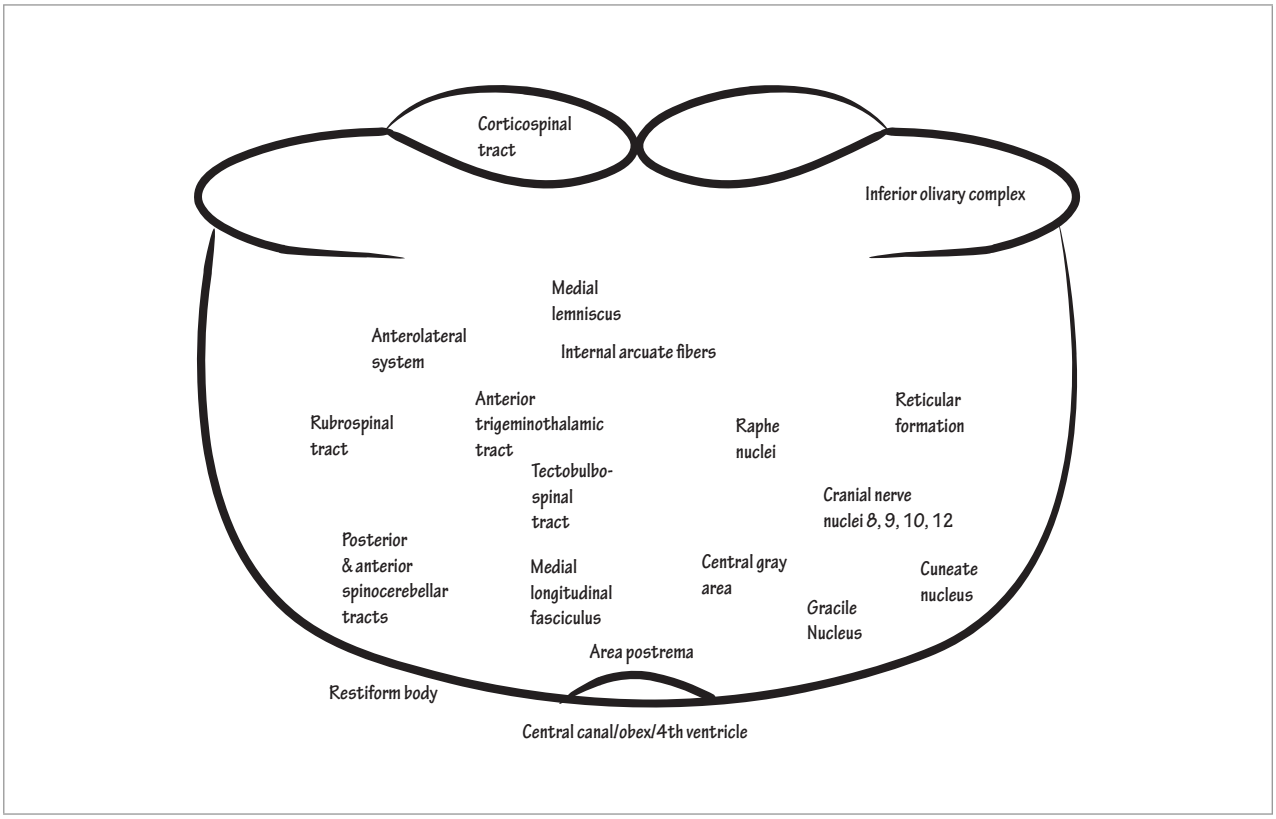


Figure 18-14 Radiographic axial medulla

Now, let's draw the spinocerebellar systems. This section is mostly a review of the spinocerebellar systems discussed in the "Spinal Cord" chapter. If you just want to know enough to label the spinocerebellar systems in the brainstem, skip to the end.

There are two spinocerebellar systems: posterior and anterior. In terms of their spinal cord course, but not their function, it is helpful to think of these systems as the cerebellar equivalent of the posterior column and anterolateral sensory systems. The posterior spinocerebellar tract is the lower limb tract of the posterior system. Its fibers enter the spinal cord through the posterior column and synapse in the dorsal nucleus of Clarke in the medial intermediate zone of the spinal cord gray matter from C8 to L2. As a side note, the preganglionic sympathetic fibers originate from T1 to L2 in the lateral intermediate zone, in the intermediolateral cell column; the posterior spinocerebellar fibers and preganglionic sympathetic fibers are unrelated, however. Fibers from the dorsal nucleus of Clarke project along the postero-lateral wall of the spinal cord to the dorsolateral medulla, and ascend into the cerebellum through the inferior cerebellar peduncle.

The cuneocerebellar tract is the upper limb division of the posterior spinocerebellar system. Fibers from T4 to C2 ascend in the posterior column and synapse in the lateral cuneate nucleus in the medulla (aka the accessory cuneate nucleus). They then project along with the posterior spinocerebellar tract fibers into the cerebellum through the inferior cerebellar peduncle.

The anterior system is divided into the anterior spinocerebellar and rostral spinocerebellar tracts. Fibers from the lower limb project into the intermediate zone (and ventral posterior zone) of the spinal cord, cross to the contralateral antero-lateral wall of the white matter, and ascend to the medulla. They continue to ascend through the pons and enter the cerebellum through the superior cerebellar peduncle. Then, they cross to the contralateral cerebellar hemisphere and end on their side of origin.

The rostral spinocerebellar tract is the upper limb division of the anterior spinocerebellar system. These fibers arise from the intermediate zone and remain uncrossed as they ascend through the lateral funiculus of the spinal cord and lateral medulla; they enter the cerebellum through the ipsilateral inferior cerebellar peduncle, except for the minority of fibers, which join the anterior spinocerebellar tract, instead, and enter through the superior cerebellar peduncle.

Now, label the *posterior* and *anterior spinocerebellar systems* in the lateral wall of the medulla, and label the *anterior spinocerebellar tract* of the *anterior spinocerebellar system* in the lateral wall of the pons. If it is unclear why we label the different brainstem levels this way, review the preceding paragraphs.

In Figure 18-15, we draw the *triangle of Guillain–Mollaret*. Begin with a coronal section through the brainstem and cerebellum. Connect the *red nucleus* to the *inferior olivary complex* through the *central tegmental tract*. Then, connect the inferior olivary complex to the *dentate nucleus* of the contralateral cerebellum. And finally, through the *dentatorubral tract*, show fibers exit from the dentate nucleus, deep in the cerebellum, and pass through the *superior cerebellar peduncle* to the opposite *red nucleus*. What geometric shape did we create? A triangle. The red nucleus, inferior olivary complex, and dentate nucleus of the contralateral cerebellum connect to form the triangle of Guillain–Mollaret.

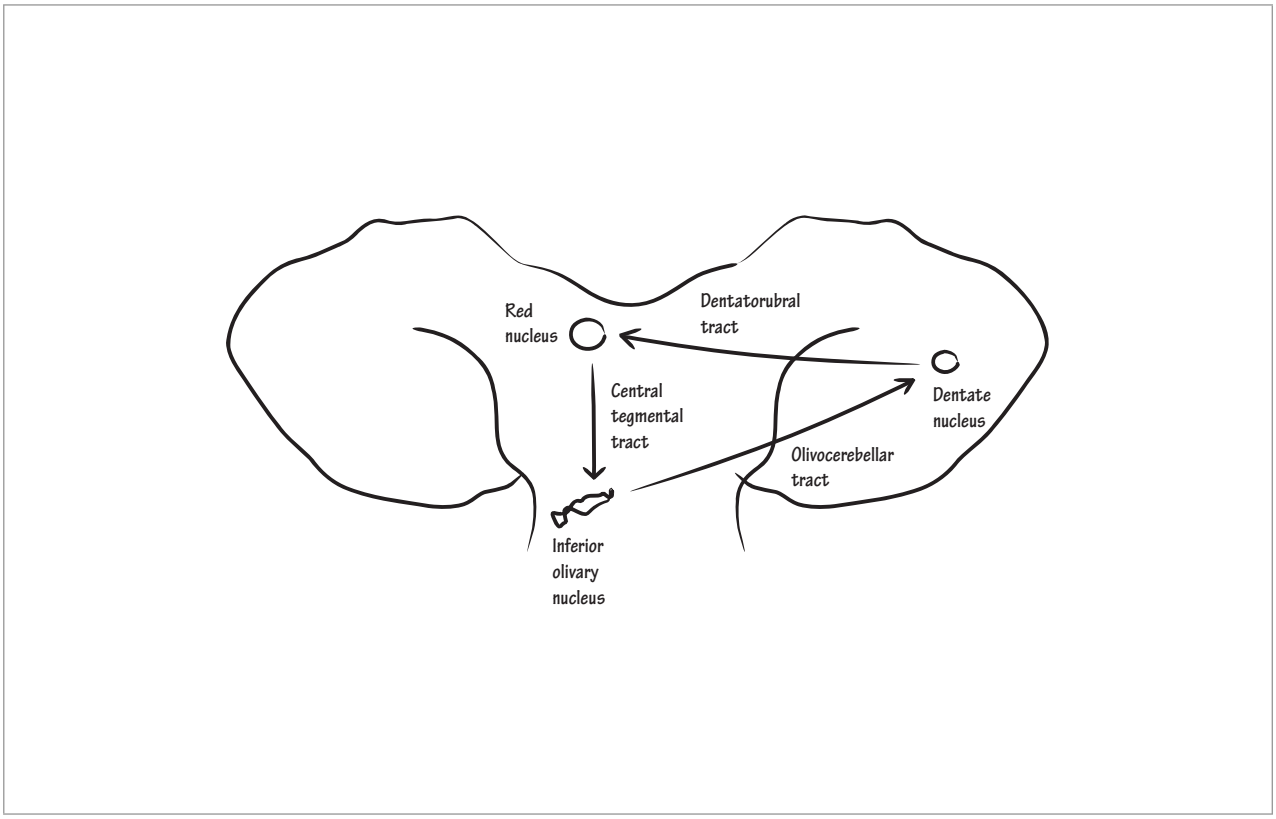


Figure 18-15 Triangle of Guillain–Mollaret

Cranial and Spinal Nerve Overview

IN THIS CHAPTER, we will learn the organization of the cranial and spinal nerves. In order to do so, we will first review the embryogenesis of cranial and spinal nerve development, which will require us to establish the anatomical landscape of the developing embryo. This approach requires extra work at the outset and, therefore, is often met with resistance. However, bear with this teaching method. Knowing the embryogenesis of these nerve groups will allow us to infer their anatomical positions and functions, long after we forget them. Moreover, the information we learn here about the neural plate and folding of the neural tube is of great clinical importance, and is a common board topic in its own right. At the end of the chapter, the highlights of this material are simplified and consolidated for use at the bedside. We must know the global topography of the cranial nuclei to practice neurology; the rest of the details are secondary.

Let's look at a human embryo three weeks into embryogenesis when it has a three-ring (aka trilaminar) structure: ectoderm on the outside, mesoderm in the middle, and endoderm on the inside. Each cell layer ultimately derives many different tissue types. The nervous system, itself, is derived from a small stretch of cells within the dorsal ectoderm called the neural plate. Formation of the neural plate is induced on day 16 by an underlying column of mesodermal cells called the notochord. After its formation, the neural plate quickly begins an infolding process called neurulation, which occurs in the rostral and caudal regions at separate times. Folding of the rostral plate is called primary neurulation and that of the caudal plate is called secondary neurulation. The end products of primary neurulation are the brain and majority of the spinal cord, whereas those of secondary neurulation are the sacrum and coccyx.

During primary neurulation, which occurs around day 18, the lateral margins of the neural groove thicken and form neural folds. By day 21, the neural folds appose at somite segment 4 in the middle of the embryo. Somites are segmented mesodermal tissue masses that run alongside the anterior–posterior axis of the neural tube. After apposition of the neural tube occurs at somite segment 4, the open anterior and posterior segments of the neural tube are called the anterior and posterior neuropores. Bidirectional tube closure occurs in zipper-like fashion, anteriorly and posteriorly, rather than in a single direction. The anterior neuropore closes on day 24 and the posterior neuropore closes on day 26. Failure of neural tube closure can affect the entire neural tube or be limited to one of the neuropores.

If the anterior neuropore does not close, anencephaly results, which means that cranial structures, such as the brain, do not form—an obviously neurologically devastating result. Failure of posterior neuropore closure results in spinal canal defects collectively called myeloschisis, which are subcategorized into different forms of spina bifida.

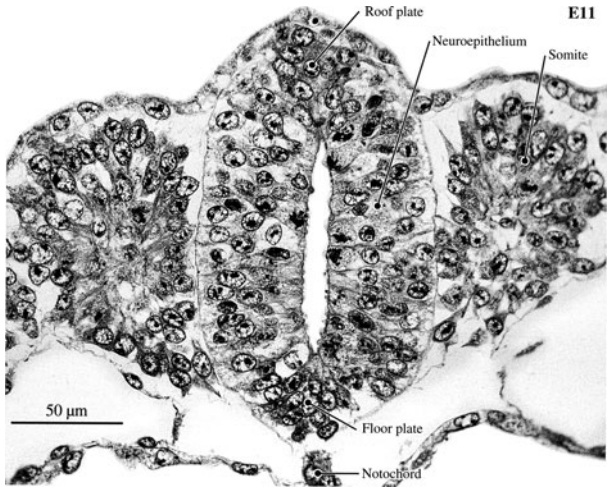
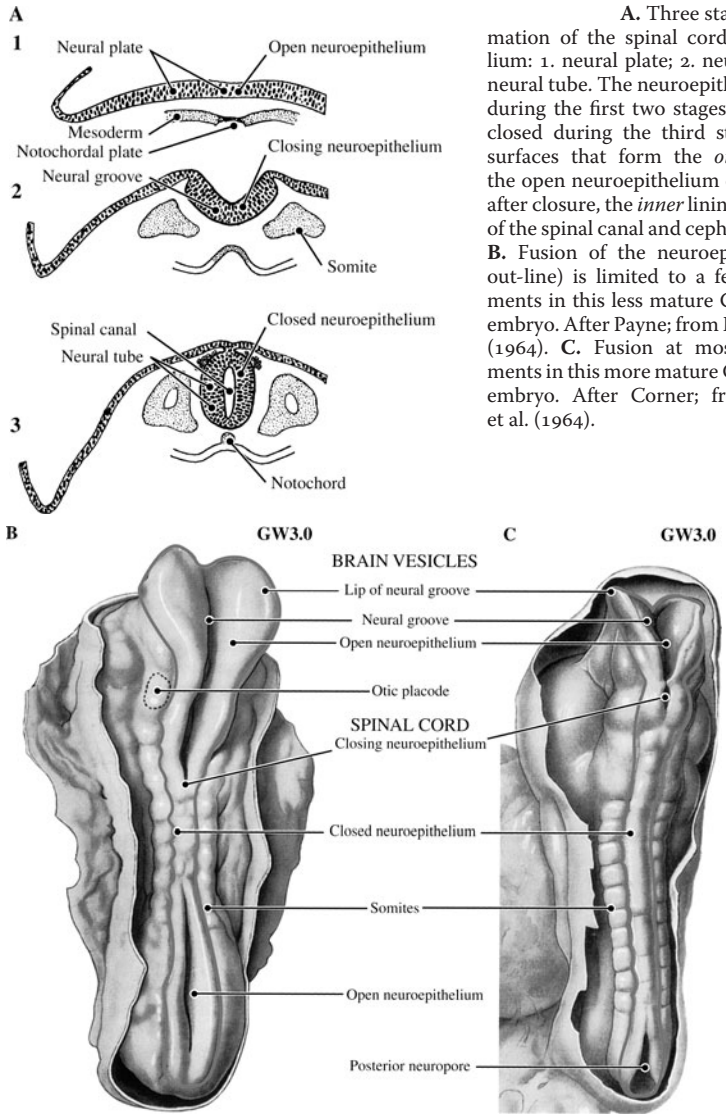


Photo 19-1 Neural tube coronal section

With permission from Altman, J., and S. A. Bayer. *Development of the Human Spinal Cord: An Interpretation Based on Experimental Studies in Animals*. Oxford and New York: Oxford University Press, 2001.



A. Three stages in the formation of the spinal cord neuroepithelium: 1. neural plate; 2. neural groove; 3. neural tube. The neuroepithelium is open during the first two stages and becomes closed during the third stage. The cell surfaces that form the *outer* lining of the open neuroepithelium come to form, after closure, the *inner* lining of the lumen of the spinal canal and cephalic ventricles. **B.** Fusion of the neuroepithelium (red out-line) is limited to a few spinal segments in this less mature GW3.0 human embryo. After Payne; from Hamilton et al. (1964). **C.** Fusion at most spinal segments in this more mature GW3.0 human embryo. After Corner; from Hamilton et al. (1964).

Photo 19-2 Neural tube model and coronal section

With permission from Altman, J., and S. A. Bayer. *Development of the Human Spinal Cord: An Interpretation Based on Experimental Studies in Animals*. Oxford and New York: Oxford University Press, 2001.

Now, let's draw the embryonic region of interest in the dorsum of the developing embryo. First, draw the *notochord*. We mentioned that it is formed from dorsal mesoderm and we already discussed its role in the induction of neural plate formation. It also serves as the structure around which the embryo forms and is the foundation upon which the vertebral column is built. When these events are complete, the notochord degenerates into the jelly-like substance of the intervertebral discs called nucleus pulposus. If notochord persists, it becomes chordoma (notochord tumor). Next, draw a coronal section through the dorsal half of the postneurulation *embryo*. Draw the *ectoderm* as the outer layer; it derives the epidermis and neuroectodermal tissue. Then draw *endoderm* at the bottom of the diagram; it comprises most of the ventral half of the embryo and it forms the gut and respiratory contents of the developing embryo.

In the dorsal midline of the embryo, draw the folded *neural tube*; draw it as oval-shaped and with a long, narrow *cerebrospinal fluid space* in its center. Dorsolateral to the neural tube, draw the *neural crests*, which are neural plate cell derivatives that give rise to the peripheral nervous system (including the chromaffin cells of the adrenal gland), meninges, certain pigmented cells, head mesenchyme, and branchial arch cartilages (discussed later). Draw *somite tissue masses* lateral to the notochord. The neural crest cells and somite tissue masses develop early in embryogenesis and the somite masses derive the sclerotome, myotome, and dermatome cells. We will include the somites along with their derivatives in this diagram, albeit an anachronism, for simplicity.

Choose a somite mass and draw three arrows from it: direct one to the notochord and label it *sclerotome*; draw another dorsally to the surface of the embryo and label it *dermatome*; and direct the last laterally to a tissue mass called *myotome*. First, indicate the sclerotome differentiates into *bone*. What specific type of bone does the sclerotome of the notochord become? Vertebral bone. Next, indicate the dermatome differentiates into *dermis*. It underlies the epidermis formed separately from the outer ectoderm. Finally, show the myotome becomes *muscle*.

An artery and nerve pair corresponds to each somite segment and wherever the products of that somite travel, the nerve and artery follow. This is the anatomical basis of how we systematically assess spinal cord as well as peripheral nervous segments when we test dermatomal and myotomal levels during the neurologic exam. From the peripheral distribution of the deficit, we localize the rostro–caudal level of the lesion within or peripheral to the central neuraxis.

With that embryogenesis as a background, let's take a closer look at the origin of the cranial and spinal nerves. Inside the neural tube, surrounding the lateral walls of the fluid space, draw two tissue masses. Divide each into a ventral *basal plate* and a dorsal *alar plate*. Along the horizontal meridian, draw a *sulcus limitans*, a small sulcus, into the lateral walls of the fluid space. The bilateral sulci separate the bilateral basal and alar plates. Somite nerve pairs emanate from these neural plates as nerve roots.

According to the law of Bell and Magendie, proposed by Charles Bell and François Magendie in the beginning of the 19th century, ventral roots are motor and dorsal roots are sensory. This functional division is extended centrally to the neural tube, as well. The basal plates, which produce the ventral roots, house motor cell columns; and the alar plates, which receive sensory roots, house sensory cell columns. Although the spinal roots originate separately, they combine within a short distance in the intervertebral foramina to form mixed spinal nerves. The ventral-motor/dorsal-sensory division that exists in early in embryogenesis in the neural tube persists throughout development, and is substantially preserved in the adult spinal cord and brainstem; it provides the basis for the organization of the spinal and cranial nerves, spinal cord, and brainstem.

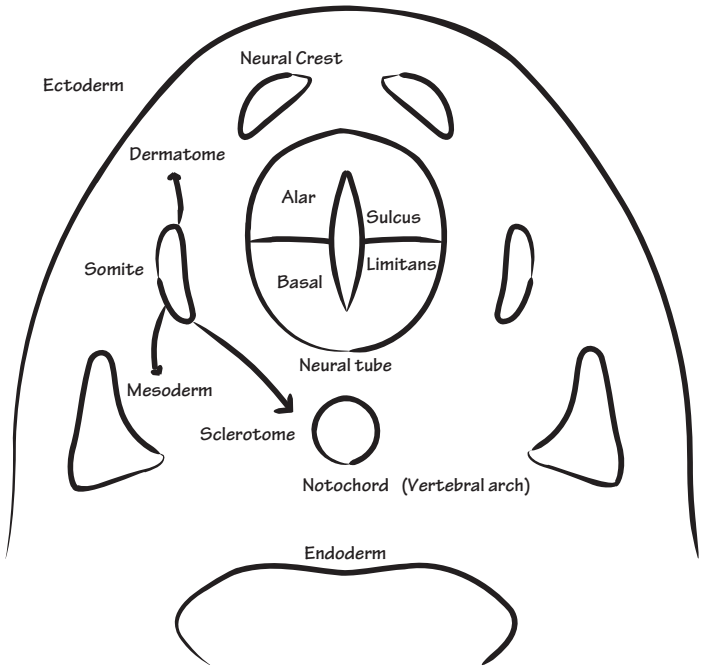


Figure 19-1 Embryo

Now, let's move from the early embryologic neural tube to the developed spinal cord and draw the spinal nerves. Afterward, we will draw the cranial nerves that emanate from the brainstem. We choose to draw the spinal nerves first because they will teach us about a homologous group of cranial nerves, and so it is easiest to learn the cranial nerves after we first learn the anatomy of the spinal nerves.

Draw a cross-section through the spinal cord. The gray matter is central and the white matter surrounds it, peripherally. In the center of the gray matter, draw the small *central canal*. Along the horizontal plane of the central canal, divide the spinal cord gray matter into *alar* and *basal plates*. Then, divide the gray matter into its three anatomical horns. From posterior to anterior, they are the *posterior*, *intermediate*, and *anterior horns*. The alar plate, which is sensory, corresponds to the posterior and posterior intermediate horns; the basal plate, which is motor, corresponds to the anterior and anterior intermediate horns.

In the following section, we will introduce functional cell columns, which will appear challenging at first glance, but as we work with these cell columns and incorporate them into our construct of the brainstem organization, they will come naturally.

The posterior and anterior horns are constituted with general somatic afferent (sensory) and general somatic efferent (motor) cell columns, respectively. These columns derive the paired somite nerves we discussed earlier. The intermediate horns house the general visceral cell columns, which communicate with body organs, such as smooth or cardiac muscle or glandular tissue.

Now, label the cell columns: *general somatic afferent* in the posterior horn, *general somatic efferent* in the anterior horn, *general visceral afferent* in the posterior intermediate horn, and *general visceral efferent* in the anterior intermediate horn. Note that here the somatic and visceral cell columns are given the qualification of "general" cell columns. Homologous cell columns also exist in the brainstem that derive "general" cell column cranial nerves, but in addition, "special" cell columns exist, which we will introduce later.

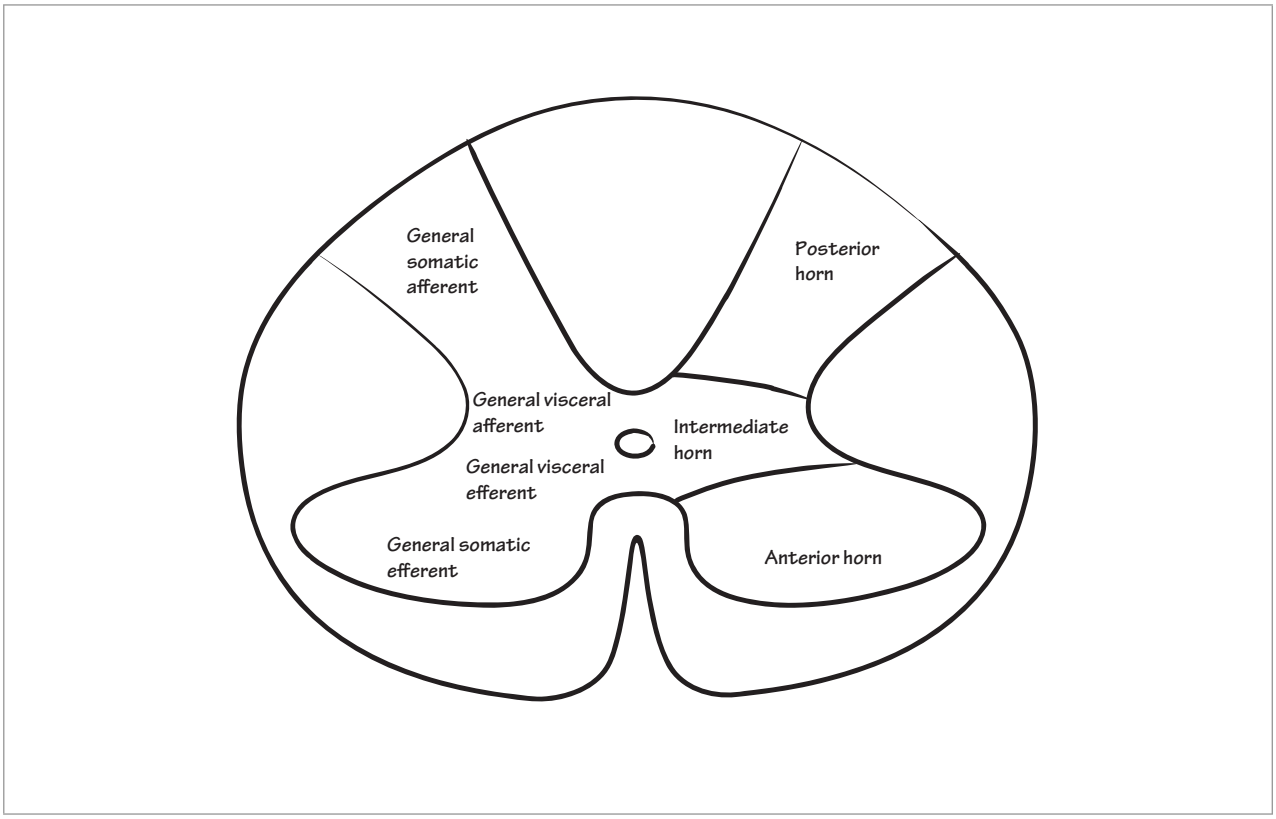


Figure 19-2 Axial spinal cord

Now, let's transition to the cranial nerve nuclei organization in the brainstem; there are two key anatomical differences between the spinal nerve and cranial nerve set-ups. First, how is the brainstem topographically different from the spinal cord and the layout of the neural tube? In the brainstem, the large fourth ventricle shifts the dorsal-lying alar plate laterally. To understand this shift, imagine holding a peeled orange. The alar plate lies dorsally and the basal plate lies ventrally. What happens when you open the orange along the dorsal midline? The dorsal-lying alar plates swing outward and end up dorsolateral to the basal plates. This occurs in the brainstem where the fourth ventricle is large (i.e., in the upper medulla, pons, and lower midbrain). A second difference between the brainstem cell columns and the neural tube and spinal cord is that the brainstem involves two additional cell column categories. One is the special visceral category, which has both efferent and afferent cell column subcategories, and the other is the special somatic afferent cell column.

The special visceral cell columns are part of the pharyngeal arch (aka branchial arch) cranial nerve derivatives, which appear during week 4 of embryogenesis as five bar-like ridges along the head and neck. Their related ectoderm, endoderm, and mesoderm form the skin and musculoskeletal structures of the face and neck. Each pharyngeal arch supplies the face and neck with cartilage, aortic arch vasculature, and a cranial nerve. Cranial nerve motor innervation of pharyngeal arch mesoderm occurs through special visceral efferent fibers. The taste buds lining the tongue are the sole sensory cells that derive the special visceral afferent cell column. These columns are most likely qualified as "special" because they originate from pharyngeal arch derivatives, rather than the segmented somites that span the neural tube and produce "general" somatic efferent fibers. Finally, as mentioned, an additional special sensory cell column exists in the brainstem called the special somatic afferent cell column; it carries fibers for hearing and balance.

For a thorough review of the origins of this classification scheme, read C. Judson Herrick's early 20th century work on the cranial nerve doctrine. However, for our purposes, just remember that the brainstem is different from the spinal cord and neural tube because (1) the fourth ventricle shifts the alar plate from a dorsal to a dorsolateral position and (2) special visceral cell columns and the special somatic afferent cell column exist within the brainstem.

Now, let's draw the cranial nuclear cell columns of the brainstem. In the brainstem section, we create an axial brainstem composite of the medulla, pons, and midbrain. Draw one side of that *axial brainstem composite*, now. Divide it from posterior to anterior into: tectum, tegmentum, and basis. The cranial nuclear cell columns lie within the dorsal tegmentum, just in front of the cerebropsinal fluid space. Although we draw their relative positions in great detail, all of the brainstem cranial nuclei lie in close proximity within the dorsal tegmentum.

Next, we will label the cranial nuclear cell columns, but before we do so, what structure demarcates the division between the afferent and efferent cell columns? The sulcus limitans. Draw the *sulcus limitans* into the wall of the fourth ventricle.

Now, we will label the cranial homologues of the spinal motor nerves from medial to lateral; they are the general somatic and general visceral efferent cell columns. Adjacent to midline, in the basal plate, draw the *general somatic efferent* cell column and lateral to it, label the *general visceral efferent* cell column.

Next, we will label the cranial homologues of the spinal sensory nerves. Move to the alar side of the sulcus limitans. In the most medial postion of the alar plate, draw the *general visceral afferent* cell column; and in the most lateral position, draw the *general somatic afferent* cell column. Leave some space between them.

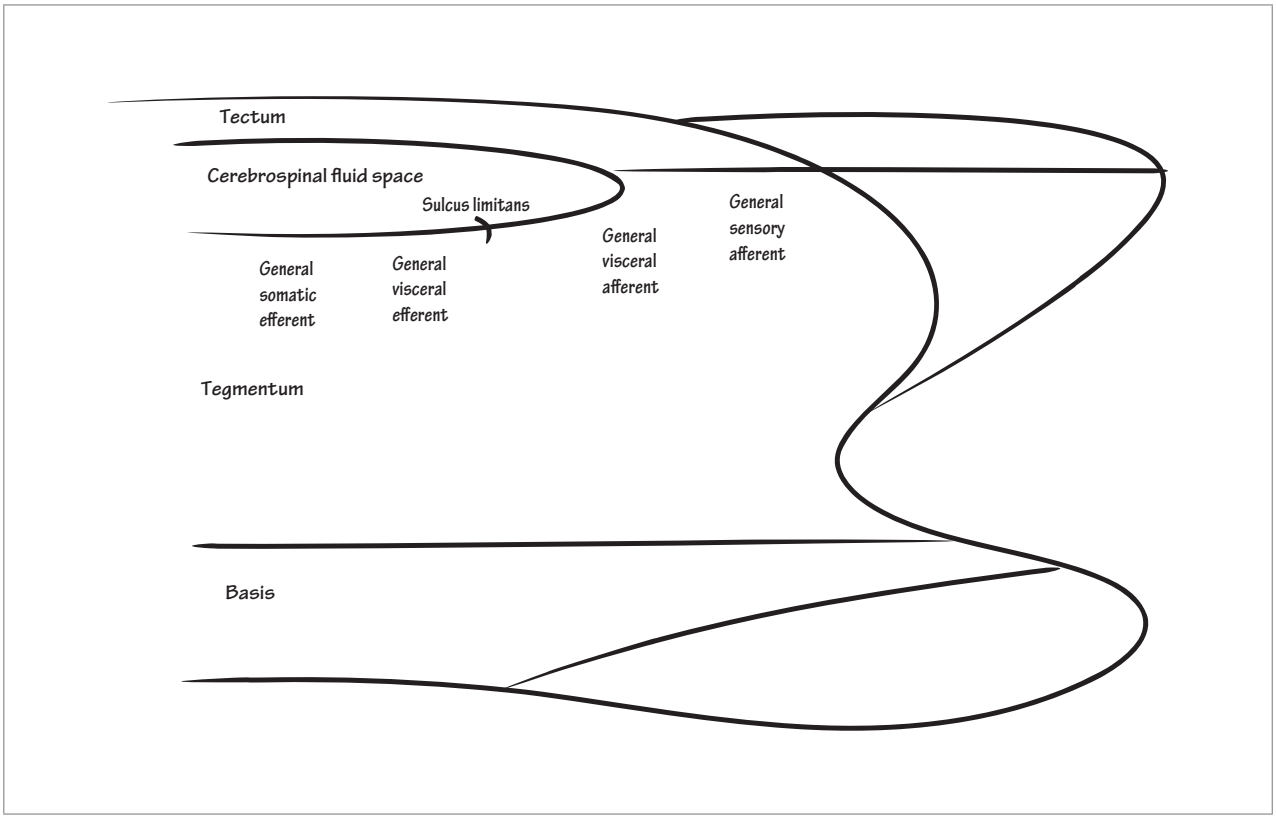


Figure 19-3 Incomplete axial brainstem composite of cranial nerve cell columns

Now, we need to address the pharyngeal arch special visceral cell columns and then the special somatic afferent cell column. The special visceral cell columns both hug the sulcus limitans. Draw the *special visceral efferent* cell column in the space between the general visceral efferent cell column and the sulcus limitans. Then join the *special visceral afferent* cell column with the general visceral afferent column in the medial alar plate. Both the special and general visceral afferent cell columns lie within the solitary nucleus, as we will later show. Finally, position the *special somatic afferent* cell column in between the general somatic afferent cell column and the visceral afferent columns.

We have completed the axial brainstem composite of the cranial nuclei and have learned the medial–lateral and dorsal–ventral axes of their arrangement. These orientational planes were sufficient to complete an overview of the spinal nuclei because the spinal nuclei are uniform along the rostro-caudal axis of the spinal cord. However, the cranial nerves vary along the rostro-caudal axis, so we need to introduce a coronal brainstem diagram to complete our overview.

Before we begin this diagram, let's discuss the general principle behind the rostro–caudal organization of the cranial nuclei. The cranial nuclei are numbered by their rostro–caudal positions as they exit the base of the brain. Cranial nerve 1 lies rostral to 2, 2 to 3, 3 to 4, and so on. As an overview, cranial nerve 1 comprises the olfactory filaments that lie within the nasal cavity and cranial nerve 2 is the set of optic nerves that run underneath the base of the brain. The cranial nuclei of 3 and 4 lie in midbrain; the cranial nuclei of 6–8 and the motor nucleus of 5 lie within the pons; and the cranial nuclei of 9, 10, and 12 lie within the medulla. The cranial nucleus of 11 lies in the cervical spinal cord, and the sensory cranial nuclei of 5 extend from the pons into the upper cervical spinal cord.

One way to recall this rostro–caudal organization is to imagine that you are a primordial fish swimming through the great sea. First, you smell food (cranial nerve 1, the olfactory nerve), then, it appears in your visual field as you swim toward it (cranial nerve 2, the optic nerve), next, you fix your eyes on it for which you use the cranial nerves for eye movements: cranial nerve 3 (the oculomotor nerve); cranial nerve 4 (the trochlear nerve); and cranial nerve 6 (the abducens nerve); you bite into it and chew using cranial nerve 5—motor (the trigeminal nerve); and as you taste it you smile using cranial nerve 7 (the facial nerve). Then, you steady yourself to devour the meal with cranial nerve 8 (the vestibulocochlear nerve); swallow it with cranial nerve 9 (the glossopharyngeal nerve) and cranial nerve 10 (the vagus nerve); you shrug your shoulders and turn your head from side to side with cranial nerve 11 (the accessory nerve); and satisfactorily lick your lips using cranial nerve 12 (the hypoglossal nerve). The exercise is fanciful but provides a vivid mneomic for the exit positions of the cranial nerves along the rostro-caudal axis of the brainstem.

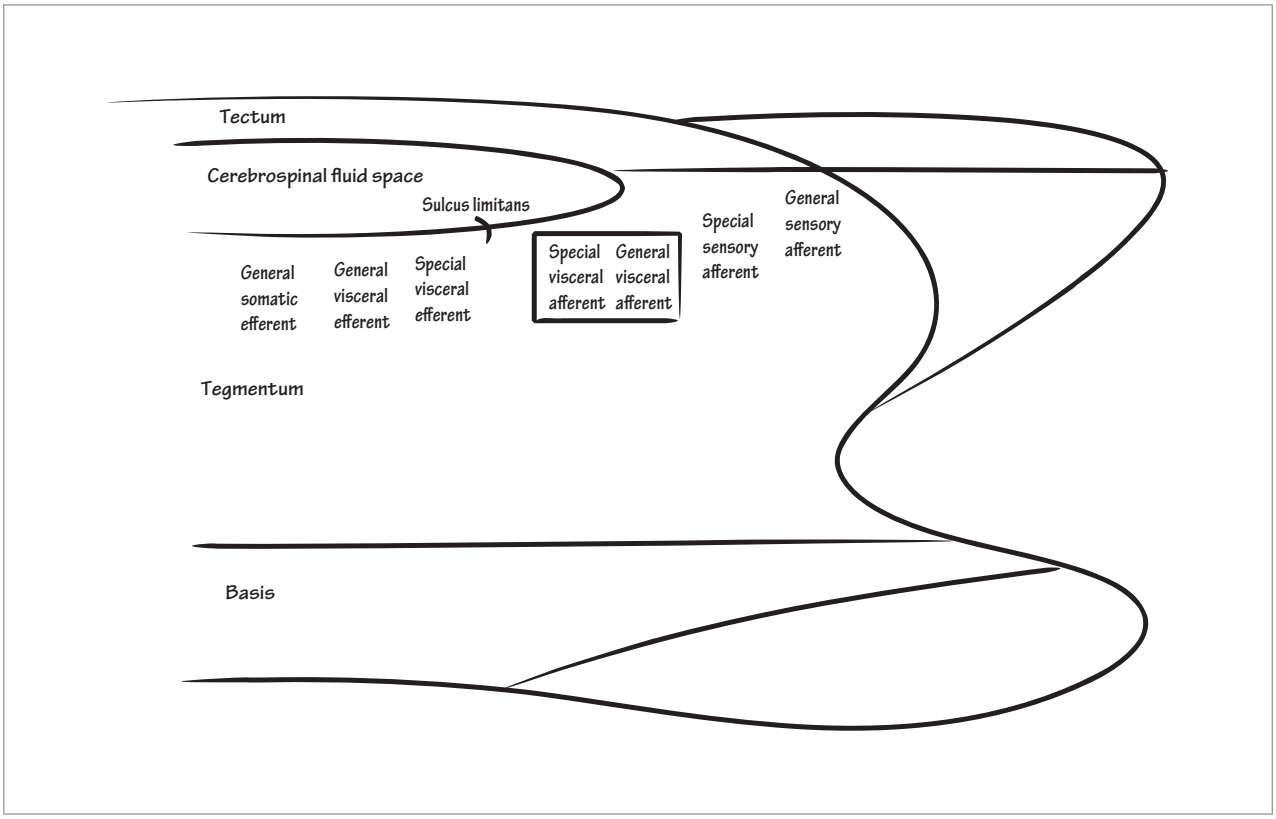


Figure 19-4 Complete axial brainstem composite of cranial nerve cell columns

Draw a coronal section through the brainstem and demarcate the general boundaries of the midbrain, pons, and medulla. Along the top of the brainstem, list the positions of the cell columns. Begin with the sulcus limitans, which as a reminder, divides each half of the brainstem into basal and alar plates. At the medial end of the basal plate (i.e., at the midline of the brainstem), label the *general somatic efferent* column. Lateral to it, label the *general visceral efferent* column. Within the medial alar plate, label the *general visceral afferent* column; and at the lateral end of the alar plate, label the *general somatic afferent* column; leave some room between them. Now go back and show the special visceral cell columns hug the sulcus limitans: label the *special visceral efferent* column on the basal side of the sulcus limitans and join the *special visceral afferent* column with the general visceral column on the alar side. Finally, label the *special somatic afferent* column in between the general somatic afferent column and the visceral afferent columns.

Though it is tempting to simply label these cell columns from medial to lateral, always use this same stepwise progression: it will be easier to remember their positions and will reinforce their functional classification scheme.

We think about the cranial nerves in three sets: the somatomotor (aka somitic), solely special sensory, and pharyngeal arch derivatives (aka branchial arch derivatives). Each of the different cranial nerve sets involves different groups of cell columns and overlap exists. For instance, general visceral efferent cells belong to both the somatomotor and pharyngeal arch sets and special somatic afferent fibers belong to the pharyngeal arch and solely special sensory sets.

Aside from these examples, the cell columns tend to group within certain nerve sets. The somatomotor set is almost entirely constituted by general somatic efferent cells; the solely special sensory set is entirely constituted by special somatic afferent cells; and the pharyngeal arch derivatives contain cells from all of the cell columns except for the general somatic efferent column.

The somatomotor set comprises cranial nerves 3, 4, 6, 12, and 11 and is considered the brainstem extension of the spinal nerves. Yet, this somatomotor cranial nerve set almost exclusively comprises somatic efferent cells, whereas spinal nerves comprise four different cell columns: somatic motor, somatic sensory, visceral motor, and visceral sensory. So what makes them spinal nerve homologues? They innervate somite tissue derivatives just as spinal nerves do. The only cell column other than the general somatic efferent column within this cranial nerve set is a single general visceral efferent nucleus—the Edinger–Westphal nucleus, which we discuss in detail in the "Eye Movements" chapter.

To demonstrate the actions of the somatomotor cranial nerve set, do the following: move your eyes in all directions using cranial nerves 3, 4, and 6; wiggle your tongue using cranial nerve 12; and shrug your shoulders and turn your head from side to side using cranial nerve 11. Notice that these movements involve midline muscles. This will help you remember that the location of the general somatic efferent cell column is in midline.

The solely special sensory set encompasses cranial nerves 1, 2, and 8. They are named *solely* special sensory because they have no motor component. Demonstrate the actions of the solely special sensory cranial nerves: smell the air around you using cranial nerve 1, olfaction; appreciate the visual scene before you with cranial nerve 2, vision; and focus on the page in front of you while you turn your head from side to side and then listen to the sounds around you with cranial nerve 8, vestibular and auditory function. Only cranial nerve 8 resides within the brainstem. Cranial nerve 1 comprises fibers that descend from the base of the brain through the cribiform plate into the nasal cavity and cranial nerve 2 is the set of optic nerves that run underneath the base of the brain.

Now, which of the cranial nerves constitute the pharyngeal arch set? Which are left? The somatomotor set comprises cranial nerves 3, 4, 6, 12, and 11, and the solely special sensory set comprises cranial nerves 1, 2, and 8. That leaves cranial nerves 5, 7, 9, and 10 to constitute the pharyngeal arch derivatives. The pharyngeal arch derivatives are the most complicated of the cranial nerves and are best understood in comparison to their gill arch homologues.

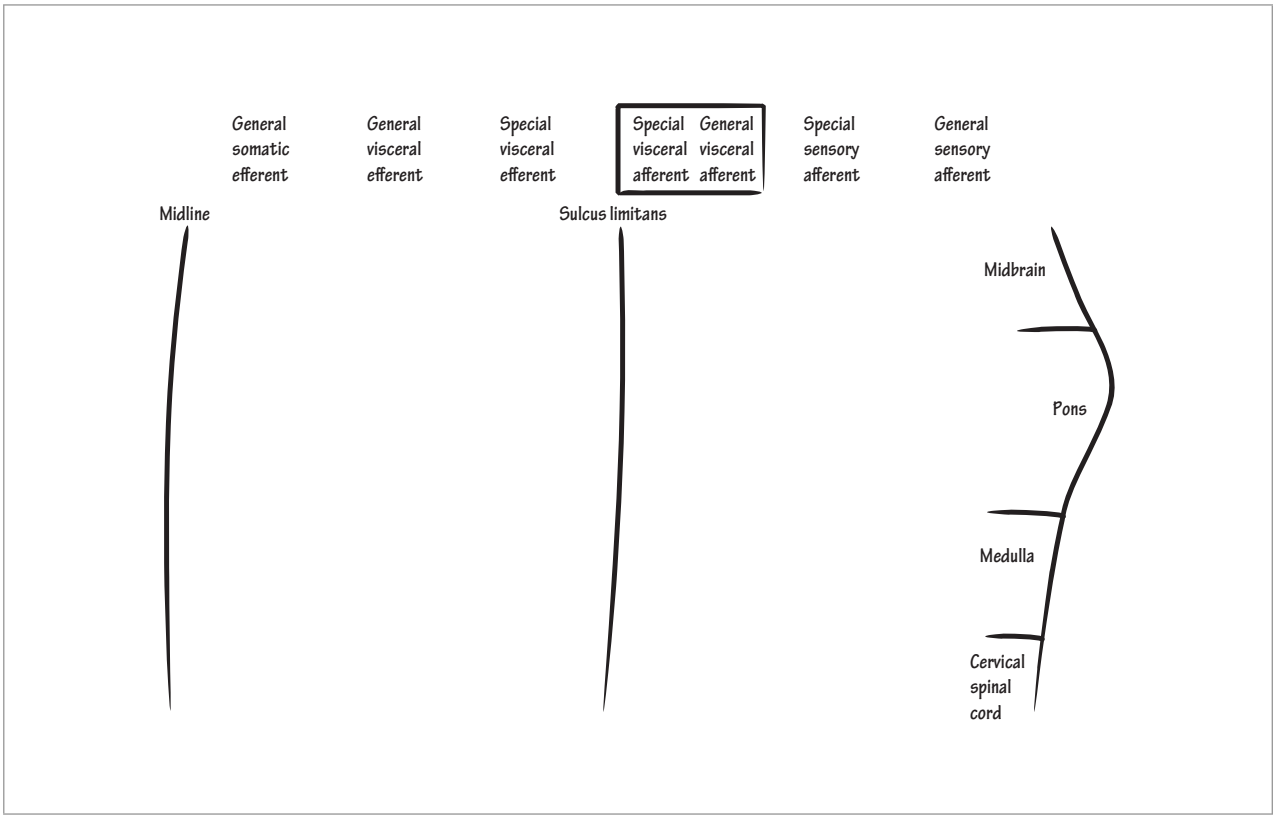


Figure 19-5 Complete coronal brainstem of cranial nerve cell columns

Fish use their gills to transfer oxygen from the surrounding water to their blood stream. In order to pump water across their gills, they perform coordinated jaw and gill cover movements. Cranial nerves 5, 7, 9, and 10 supply the adductor and abductor innervation of these muscles. In humans, oxygen to blood transfer occurs in the lungs so these cranial nerves are available to perform different motor functions carried by special visceral efferent fibers. The pharngyeal arch derivatives supply structures of the face (cheeks, jaws, and ears) and neck (pharynx, larynx, and upper esophagus) and stimulate muscles of mastication, swallowing, facial expression, and sound vocalization through special visceral motor fibers. To demonstrate the special visceral efferent functions, do the following: chew using cranial nerve 5 and swallow using cranial nerves 9 and 10; then, smile and raise your eyebrows using cranial nerve 7; and finally articulate a sound using cranial nerve 10.

The marine gill arch homology also informs us about the special visceral afferent function of taste. It is carried primarily by special visceral afferent fibers of cranial nerve 7 (from the anterior two-thirds of the tongue) and to a lesser degree by cranial nerves 9 and 10 (from the posterior one-third of the tongue). Taste buds are also found in the mouth and gills of fish, and they are also primarily innervated by cranial nerve 7.

Pharyngeal arch derivatives also provide general visceral functions through parasympathetic innervation of body organs, just like marine gill arch derivatives do. Through parasympathetic preganglionic cells, the general visceral cell columns of the cranial nerves send and receive information to and from the body viscera, such as the heart, lungs, and gut for homeostatic control. The only general visceral efferent cell that is not a part of the pharyngeal arch derivatives is the Edinger–Westphal nucleus of the somatomotor set.

The sole general visceral afferent nucleus is the solitary nucleus, which also houses special visceral afferent cells. The rostral solitary nuclear division is dedicated to the special visceral afferent function of taste and the caudal division is dedicated to general visceral afferent functions.

The last cell column of the pharyngeal arch derivatives, which also exists within the marine gill arches, is the general somatic afferent cell column. Cranial nerve 5 is the largest contributor to this cell column category in humans and the sole contributor in marine life: it carries somatosensory information from the face. However in humans, cranial nerves 7, 9, and 10 provide sensory coverage from the outer ear and external auditory canal and cranial nerve 10 covers a portion of the posterior dura (meninges). All of these sensory afferents synapse within the trigeminal nucleus. Thus, the spinal trigeminal nucleus receives fibers from more than just cranial nerve 5, the trigeminal nerve.

Now, we are able to complete our coronal brainstem diagram; you will need a separate sheet of paper to draw it because of its size. First, label the nerves of the somatomotor set, then the pharyngeal arch derivatives, and finally the solely sensory set. In the general somatic efferent column, in descending order, draw the nuclei of the *somatomotor set*. Indicate the position of the *oculomotor nucleus* of *cranial nerve 3* (the *oculomotor nerve*) in the rostral midbrain; the *trochlear nucleus* of *cranial nerve 4* (the *trochlear nerve*) in the caudal midbrain; the *abducens nucleus* of *cranial nerve 6* (the *abducens nerve*) in the central pons; the *hypoglossal nucleus* of *cranial nerve 12* (the *hypoglossal nerve*) in the medulla; and the *accessory nucleus* of *cranial nerve 11* (the *accessory nerve*) in the upper cervical spinal cord. The accessory nerve is classically considered to have both cranial and spinal divisions; however, current thinking is that the medullary cranial division does not truly exist and only the upper cervical spinal division is actually present.

Next, include the general visceral efferent nucleus the *Edinger–Westphal nucleus* of *cranial nerve 3* (the *oculomotor nerve*) in the rostral midbrain near the oculomotor nucleus.

Now, draw the nuclei of the *pharyngeal arch set*; start from where we left off with the nuclei of the general visceral efferent cell column. Indicate the position of the *superior salivatory nucleus* of *cranial nerve 7* (the *facial nerve*) in the central pons and the *inferior salivatory nucleus* of *cranial nerve 9* (the *glossopharyngeal nerve*) in the pontomedullary junction. The salivatory nuclei are so named because they provide secretomotor function to mucosal and glandular tissues in the face, which produce saliva. Next, indicate the *dorsal motor vagus nucleus* of *cranial nerve 10* (the *vagus nerve*) in the medulla.

Now, let's complete the cranial motor fibers; the last column is the special visceral efferent cell column. In the special visceral efferent cell column, in descending order, draw the *trigeminal motor nucleus* of *cranial nerve 5* (the *trigeminal nerve*) in the central pons; the *facial nucleus* of *cranial nerve 7* (the *facial nerve*) in the lower pons; and the *nucleus ambiguus* of *cranial nerve 10* (the *vagus nerve*) in the medulla.

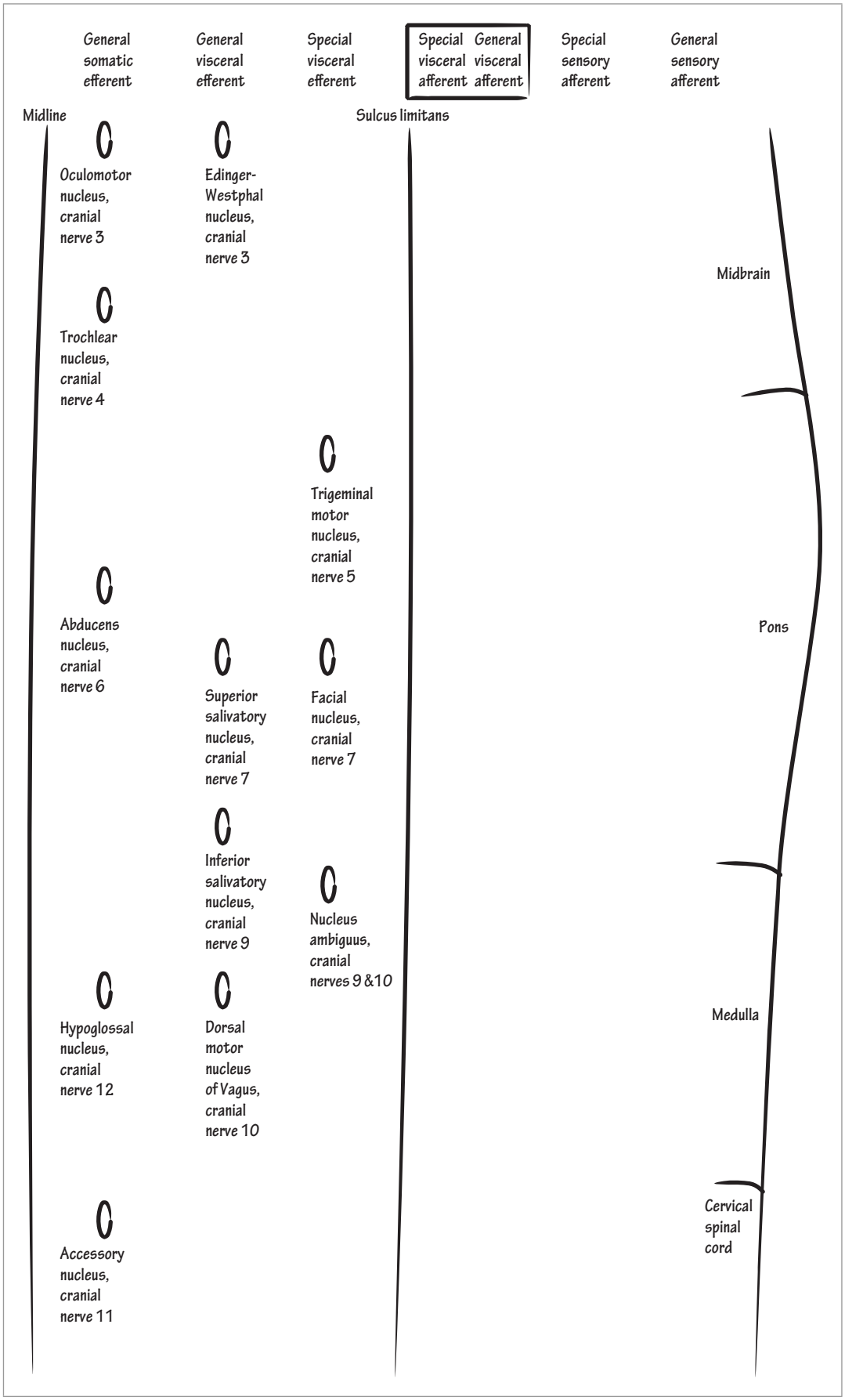


Figure 19-6 Incomplete coronal brainstem of cranial nerves

Next, turn to the sensory cells in the alar plate. Begin with the combined special and general visceral afferent cell columns. First, draw the rostral portion of the *solitary nucleus* of *cranial nerves 7, 9*, and *10* (the *facial, glossopharyngeal*, and *vagus nerves*); it is the special component of the visceral afferent cell column and primarily receives innervation from cranial nerve 7. Then draw the caudal portion of this nucleus; it receives the same fibers as the rostral portion but is primarily supplied by cranial nerve 10, instead.

Then, move to the general somatic afferent cell column at the lateral end of the alar plate. Indicate that the *trigeminal nucleus*, primarily of *cranial nerve 5* (the *trigeminal nerve*), is divided into three different subnuclei: the *mesencephalic nucleus* in the midbrain, *the principal sensory nucleus* in the pons, and *the spinal trigeminal nucleus* from the pons into the upper cervical spinal cord. *Cranial nerves 7, 9*, and *10* (the *facial, glossopharyngeal*, and *vagus nerves*) also supply the spinal trigeminal nucleus. As you might imagine from its length, the spinal trigeminal nucleus is further divided into three subnuclei: pars oralis, rostrally; pars interpolaris, in the middle; and pars caudalis, caudally.

Next, we will complete the diagram with the nuclei of the solely sensory set. While it comprises cranial nerves 1, 2, and 8, only the cranial nuclei of cranial nerve 8 are positioned within the brainstem. To remember that cranial nuclei 1 and 2 are in this cranial nerve set, however, still list the *olfactory cells* of *cranial nerve 1* (the *olfactory nerve*), which descend through the cribiform plate in the base of the skull, and the *neural retina* of *cranial nerve 2* (the *optic nerve*), which lies within the retinal layer of the eye. The optic nerves, themselves, pass underneath the base of the brain. Now, show that the *vestibulocochlear nucleus* of *cranial nerve 8* (the *vestibulocochlear nerve*) spans the pontomedullary junction.

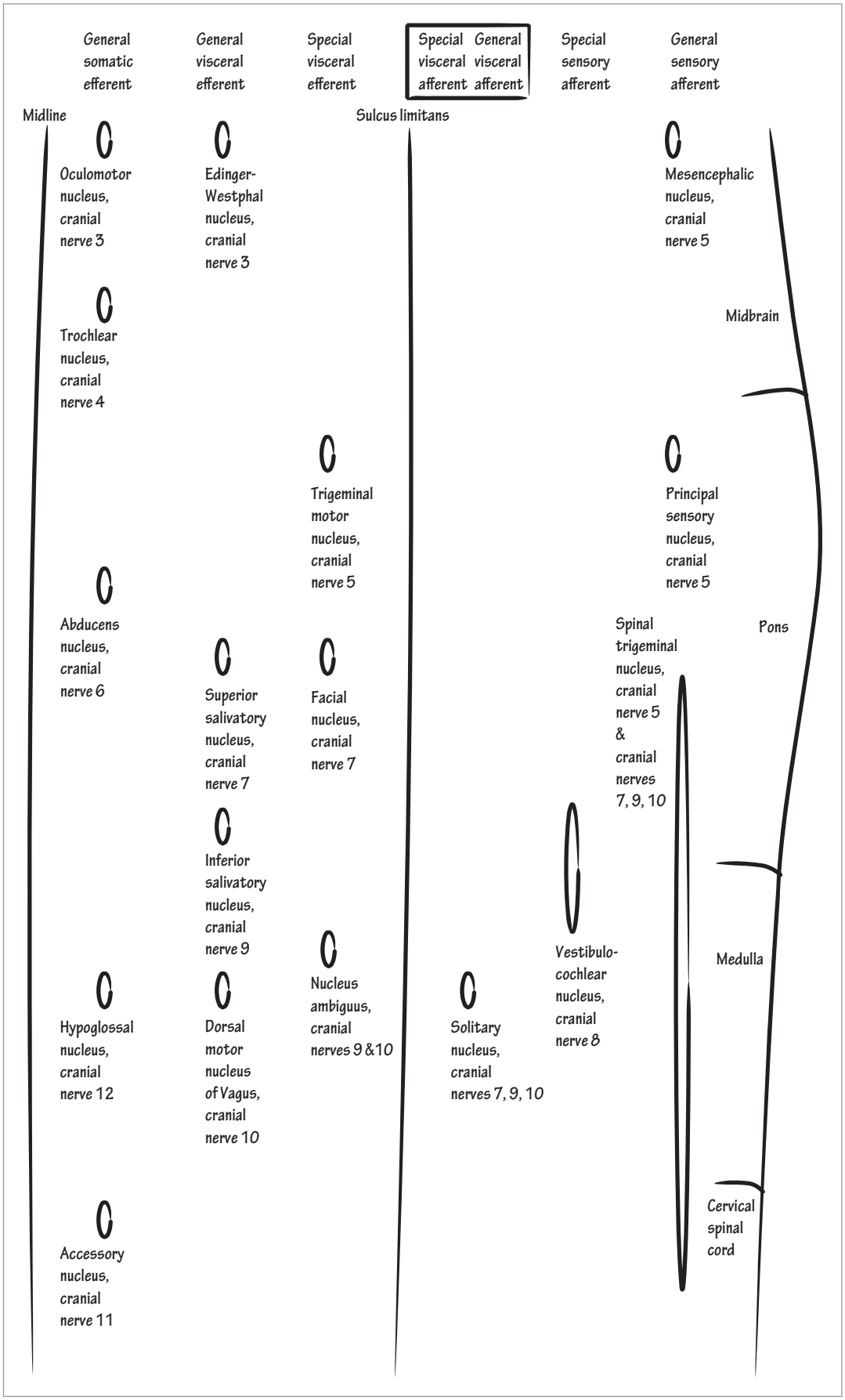


Figure 19-7 Complete coronal brainstem of cranial nerves

This completes our coronal brainstem cranial nuclei diagram; however, as promised, let's create a simplified version of this material. Draw another coronal brainstem. Across the top, use the *sulcus limitans* to divide the brainstem into a medial, *motor* division and a lateral, *sensory* division. Then divide the rostro–caudal axis of the brainstem into *midbrain, pons,* and *medulla*. Along the medial half of the motor division, draw the *cranial nucleus* of cranial nerve *3* in the rostral midbrain, *4* in the caudal midbrain, *6* in the pons, *12* in the medulla, and *11* in the cervical spinal cord. In the lateral motor region, draw the *cranial nucleus* of cranial nerve *5* in the rostral pons, *7* in the caudal pons, *9* in the rostral medulla, and *10* in the central medulla. In the medial sensory region, draw the *visceral cranial nuclei* of cranial nerves *7, 9*, and *10* in the medulla. At the lateral edge of the sensory side of the brainstem, show that the *cranial nucleus* of cranial nerve *5* spans the midbrain, pons, and medulla and indicate that it includes minor branches from *cranial nuclei* of cranial nerves *7, 9*, and *10*. In the midsensory region, draw the *cranial nuclei* of cranial nerve *8*, which spans the pontomedullary junction. This simplified depiction of cranial nerve organization will be an invaluable localizing tool to have in your memory bank for use at the bedside.

In the "Somatomotor Cranial Nerve" and "Pharyngeal Arch Cranial Nerve" chapters, we will specify the course and functions of these two groups of cranial nerves. We will learn the solely special sensory nerves in several different topical chapters: "The Olfactory System," "The Visual Pathways," "The Central Auditory Pathways," and "The Vestibular System."

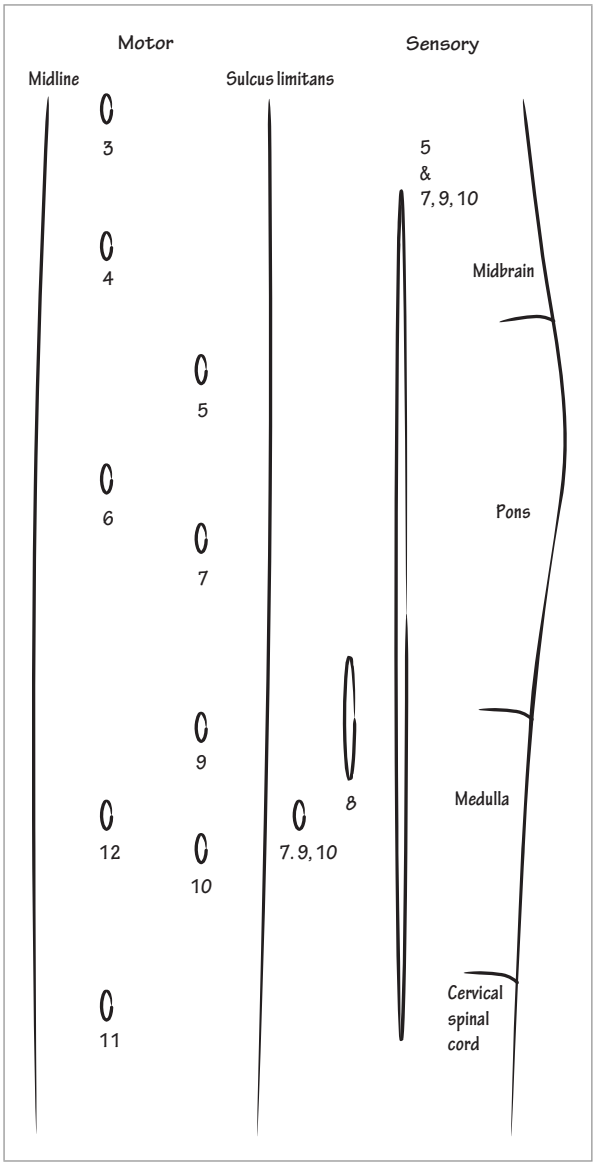


Figure 19-8 Simplified coronal brainstem of cranial nerves

Somatomotor Cranial Nerves

THE SOMATOMOTOR CRANIAL nerves comprise cranial nerves 3, 4, 6, 12, and 11. It is called "somatomotor" because these nerves innervate somite muscle derivatives. All of the somatomotor cranial nerves originate in midline and innervate midline musculature, and they are all general somatomotor nerves, except for cranial nerve 3, which has an additional general visceral motor cell column component. We discuss the visceral component of cranial nerve 3, the Edinger–Westphal nucleus, in the "Eye Movements" chapter in association with the pupillary light reflex.

Cranial nerve 11 is drawn and discussed in the "Cervical Plexus" chapter because it passes through the cervical triangle and not because it is a part of the cervical plexus. Over time, its role as a cranial nerve has been de-emphasized. Classically, it was believed that cranial nerve 11 had both spinal and cranial origins but current thinking is that only its spinal portion truly exits. It originates from C1–C4 nerve roots, which ascend through the foramen magnum. Then, it exits the cranium through the jugular foramen. Thus, cranial nerve 11 is actually a spinal nerve that also happens to meet the definition of a cranial nerve—it exits a major foramen in the base of the skull.

Now, let's introduce cranial nerves 3, 4, 6, and 12. All of their nuclei originate close to midline within the general somatic efferent cell column, and with the exception of cranial nerve 4, all of them proceed directly across the posterior fossa. Instead of exiting the ventral midbrain like cranial nerves 3, 6, and 12, cranial nerve 4 exits the dorsal brainstem contralateral to its side of origin. It then wraps around the brainstem and runs in midline to its end-target organ: the superior oblique extraocular muscle (on the side opposite to its origin). With the exception of the superior rectus subnucleus, which we will address later, cranial nerve 4 is the only somatomotor cranial nerve to innervate an end-target opposite to its side of origin.

Next, we will learn the six cardinal (aka primary) eye movements of the extraocular muscle targets of cranial nerves 3, 4, and 6. Each extraocular muscle is primarily responsible for one of the cardinal eye movements. Four of them have secondary and tertiary actions, as well, but we will first establish the primary movements.

We will draw the primary eye muscle–rotation relationships in coronal section. The muscles move both eyes in identical fashion, so we will just show the movements of one eye—the left eye. Show, now, that across the entire horizontal plane, the *medial rectus* directs the eye medially and the *lateral rectus* directs the eye laterally. Then show that when the eye is rotated laterally (aka abducted), *superior rectus* directs the eye superiorly and *inferior rectus* directs the eye inferiorly. When the eye is rotated medially (aka adducted), show that *superior oblique* directs the eye inferiorly and *inferior oblique* directs the eye superiorly. Note, we do not show the up and down movements of the eye when it is looking straight ahead because these movements are produced by the combined actions of multiple muscles.

Four of the six extraocular muscles—the obliques and the vertical recti muscles (superior and inferior)—also have secondary and tertiary actions.

If you only want to know the secondary and tertiary actions of these muscles well enough to answer test questions, memorize the following: (1) the superior muscles cause intorsion and the inferior muscles cause extorsion—"*superior* people do not *extort*" and (2) the vertical recti adduct the eye and the obliques abduct it—the assonance in the expression "*oblique* muscles rotate the eye *out*" will help you remember the second point. If you want to understand the neuroanatomy of the eye movements and not simply memorize their actions, proceed with the following several paragraphs.

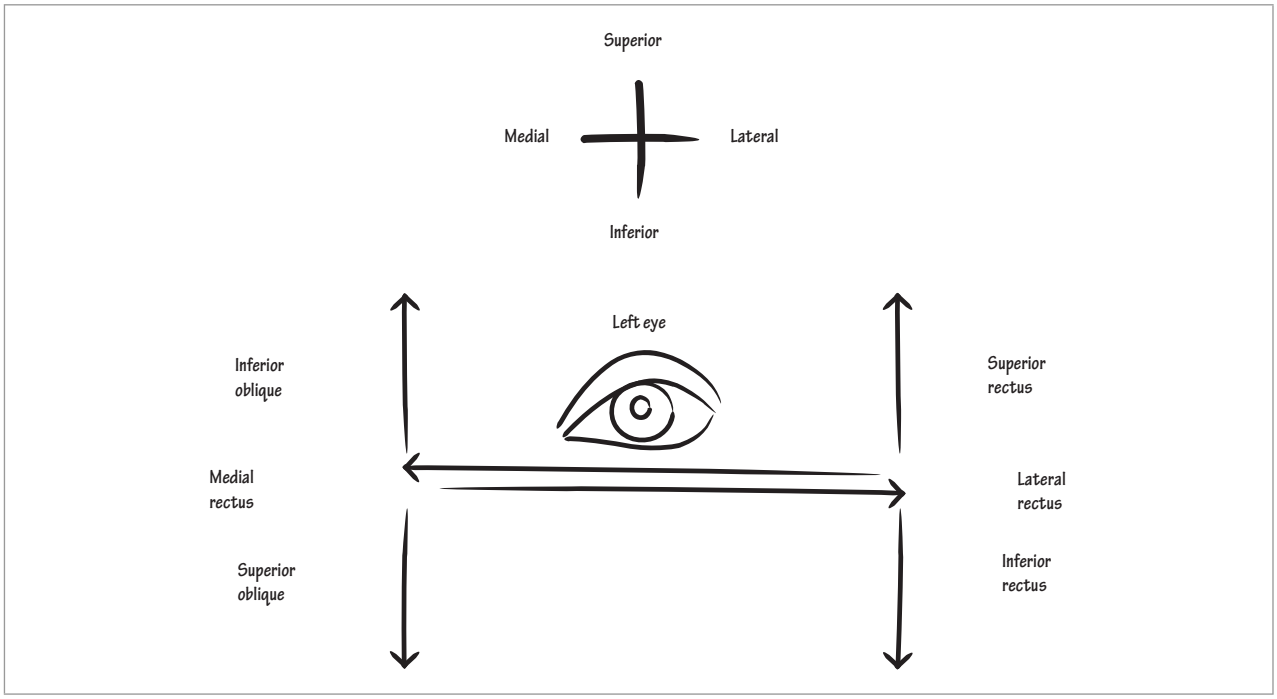


Figure 20-1 Cardinal eye movements

First, draw an axial section of an eye within the orbit. Draw the *orbit* as V-shaped. Its medial border lies along the anterior–posterior plane of the cranium, and its lateral border lies at an angle to it. At rest, your eyes look straight ahead in the anterior–posterior plane and not along the angle of the orbit; this will be important later in our discussion.

Next, attach the *medial* and *lateral recti* muscles to the medial and lateral aspects of the eyeball, respectively. Explore their forces on the eye. Imagine how the eye rotates when you separately pull the muscles. The medial rectus rotates the eye medially and the lateral rectus rotates it laterally. Next, draw an axial section with the eye rotated medially (adducted) and then laterally (abducted). How does the eye rotate in these positions when you pull the medial and lateral recti muscles? The same way: there is no difference in their action. In any eye position, the medial rectus rotates the eye medially and the lateral rectus rotates the eye laterally. Finally, in full adduction, the medial rectus is unable to rotate the eye any farther and in full abduction, the lateral rectus is unable to continue to rotate the eye. The medial and lateral recti muscles (the horizontal recti) are the only two extraocular muscles that have exclusively primary actions. As we work through the muscles, let's keep tabs on their innervation and rotational patterns in a separate table.

It is difficult to learn the muscle–eye actions by drawing them. If you refer to William DeMyer's *Technique of the Neurologic Examination* book, there is a detailed section on creating a model eyeball, which is an excellent way to understand the eye movements. Here, we will demonstrate how to use our hands to feel their rotational pull, instead. We start with the medial and lateral recti muscles because they are the easiest. Then we draw the actions and demonstrate the different forms of rotational pull of the vertical recti and oblique muscles.

Make a fist with your right hand to represent your right eyeball. Your thumb is your right medial rectus. Grip your thumb with your left hand and pull on it, keeping the eye within the globe (i.e., don't pull the eye out of its socket!). Notice that whether your fist is directed straight ahead, adducted, or abducted, the force from your left hand always rotates your wrist medially along the horizontal plane: the sole action of the medial rectus is medial rotation of the eye. To demonstrate the lateral rectus, use your right pinky finger as your right lateral rectus and grip it with your left hand. Pull your pinky and feel it rotate your fist laterally throughout the horizontal plane. Again, whether your fist is directed straight ahead, adducted, or abducted, the sole action of the lateral rectus is lateral rotation of the eye.

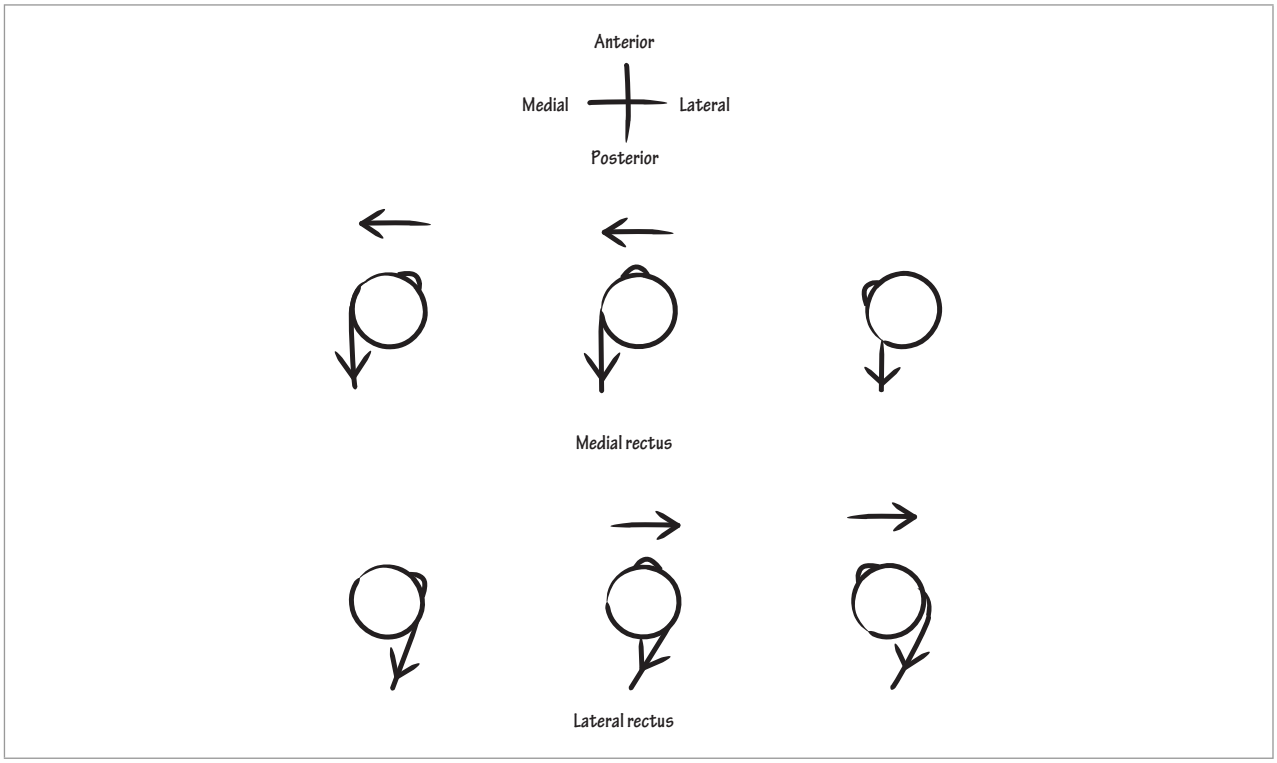


Figure 20-2 Horizontal recti: medial and lateral recti

Let's, now, use a similar approach for the superior and inferior recti muscles. First, draw an axial cut through the eye with it looking straight ahead. For all of the extraocular muscles, begin the diagram with the eye in the muscle's primary action position. We established their primary action positions in the cardinal eye movements diagram. For the superior rectus, draw the diagram with the eye in full abduction. Attach the *superior rectus* to its center. How will the resultant force from the superior rectus rotate the eye? Show that in abduction, the superior rectus causes eye elevation. Next, with the eye looking straight ahead, show that the superior rectus produces eye adduction. If you are confused by this action, move to the demonstration provided in the next paragraph to feel the eye action and then return to this diagram. Finally, draw the eye in full adduction. How does the superior rectus rotate the eye? Show that it rotates the eye internally around the anterior–posterior axis—it intorts it. In intorsion, the medial aspect of the eye depresses and the lateral aspect elevates.

You can feel the movements of the superior rectus on your wrist with a similar hand arrangement as we used for the medial and lateral recti. Use your closed right fist as your right eye and hook your left index finger over the top of it at an angle. Your left index finger is the right superior rectus. First, fully abduct your fist—it is now in the superior rectus' primary position of action, in line with the left index finger. Pull with your left index finger (the superior rectus). Your right fist (the eye) will rotate superiorly (i.e., elevate); the primary action of superior rectus is elevation. Then position your fist straight ahead and again pull across the top of it with your left index finger. You should feel your fist adduct (i.e., rotate medially around the vertical plane); the tertiary action of the lateral rectus is adduction. Secondary and tertiary actions are distinguished by their axes of rotation. Secondary actions rotate around the anterior–posterior axis and result in intorsion and extorsion movements, whereas tertiary actions rotate the eye around the vertical axis and result in medial and lateral movements (adduction and abduction). Finally, position the eye in full adduction and continue to pull. The fist is unable to rotate medially any farther, and instead it rotates internally around the anterior–posterior axis. If you have trouble generating this movement, it is because your wrist is too stiff. Loosen your wrist to mimic the fluidity of the eye within the orbit. The eye muscle always overpower the eye (i.e., your left finger should overpower your right fist).

Before we draw the inferior rectus, try to imagine its resultant forces. Let's see if you're right. First, show the eye in full abduction. Indicate that force from the inferior rectus depresses the eye: the primary action of the inferior rectus. Next, draw the eye positioned straight ahead. Attach the inferior rectus and show that it produces eye adduction, which is the same tertiary movement as that of the superior rectus. Then with the eye in adduction, what is the resultant force of the inferior rectus? Is it the same or opposite that of the superior rectus? How do the insertion points of the superior and inferior recti differ? The inferior rectus pulls from the bottom of the eye, whereas the superior rectus pulls from the top. In full adduction, the inferior rectus rotates the eye around the anterior–posterior axis in the opposite direction of the superior rectus: it extorts the eye.

Next, let's use our hands to feel the actions of the inferior rectus. Flip your right hand over (knuckles down) and hook your left index finger underneath your fist at an angle. Your right-hand knuckles still represent anterior and your wrist represents posterior. Fully abduct your fist so that it comes in line with the left index finger. Now, pull with the left finger; the downward/backward force of the inferior rectus depresses the eye. Then with your right fist directed straight ahead, pull backward/downward with your left hand and the right fist adducts. Finally, in full adduction, continue to pull down and back. The medial side rises and the lateral side depresses—the eye extorts.

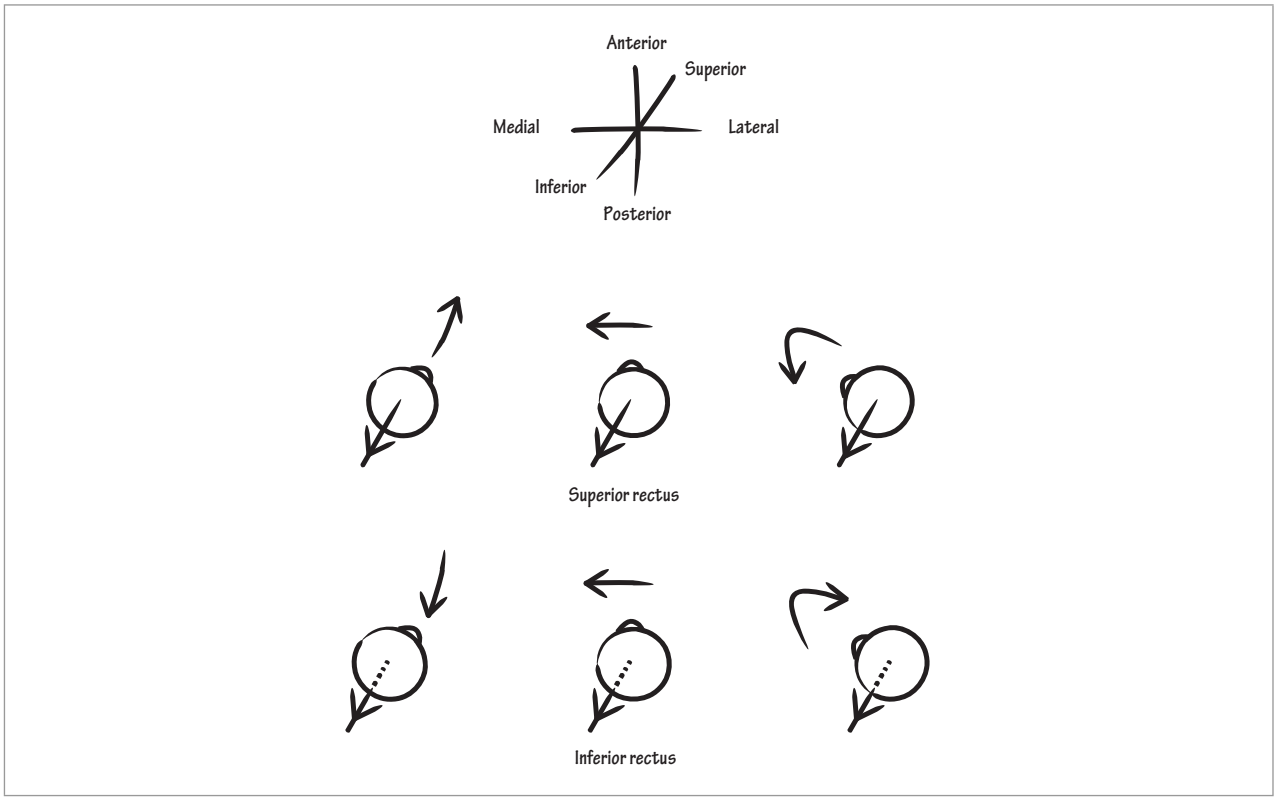


Figure 20-3 Vertical recti: superior and inferior recti

Now, let's draw the superior oblique in the axial plane. Show that the superior oblique runs across the superior surface of the eyeball, hooks around a pulley (aka trochlea), and runs along the medial wall of the orbit. Show that when the eye is in full adduction, the superior oblique depresses the eye: its primary action. Then with the eye looking straight ahead, show the superior oblique causes the eye to rotate around its vertical axis in abduction: its tertiary action. Finally, indicate that when the eye is fully abducted, further superior oblique force causes the medial side to depress and the lateral side to elevate. What type of movement is this? Intorsion: its secondary action.

It is challenging to conceptualize how to use your hands to recreate the forces of the superior oblique, but bear with this demonstration, if you want to learn their rotational pull. Your right fist is again the eyeball. Hook your left thumb around your right index finger. The left thumb is the trochlea (aka pulley) and the right index finger is the superior oblique. For this exercise, pay attention to the amount of spread in the web between your right index and middle fingers. When the right fist is fully adducted, there is no separation between these fingers and they are unable to spread apart. Force along the trochlea (left thumb) is fully distributed toward depressing the fist, its primary action. When the eye is looking straight ahead, the index and middle fingers are separated. With additional force along the trochlea, they further separate, which represents eyeball abduction, its tertiary action. When the eyeball can no longer abduct (i.e., when separation between the middle and index fingers is maximal), additional force causes intorsion of the eyeball, its secondary action—the medial side depresses and the lateral side elevates. Remember, the eye muscle overpowers the eye!

For the inferior oblique, let's abandon the axial view of the eyeball and draw it in a coronal plane. The full extent of the inferior oblique is best seen from this perspective. Show that when the eye is fully adducted, force from the inferior oblique causes elevation of the eye, its primary action. Then show that when the eye looks straight ahead, the inferior oblique causes abduction of the eye, its tertiary action. Finally, show that in full abduction, further inferior oblique force causes the lateral side to depress and the medial side to elevate, which is extortion, its tertiary action.

While we do not have to account for a trochlea to demonstrate the actions of the inferior oblique, we do have to reverse our anterior–posterior plane. In this demonstration, the knuckles are posterior and the wrist is anterior. What does this do to the medial-lateral perspective? When the wrist is facing toward the body, the eye is in adduction and when it is facing away from the body, the eye is in abduction. Grip your right index finger with your left hand to create the inferior oblique. With your wrist fully adducted, pull down with the left hand. Which direction does the wrist move? It elevates. In full adduction, force from the inferior oblique causes eye elevation: its primary action. When the eyeball is straight ahead, force from the inferior oblique causes the eye to abduct, its tertiary action. Gripping your right index finger with your left hand, pull in toward your body to demonstrate this—first the wrist will abduct. In full abduction, further force from the inferior oblique causes the eye to extort—its secondary action. The lateral side depresses and the medial side elevates.

Now, let's prepare our completed eye muscle table. If you have difficulty, remind yourself of the mnemonics for the secondary and tertiary extraocular actions. "Superior people do not extort" and "*oblique* muscles rotate the eye *out*."

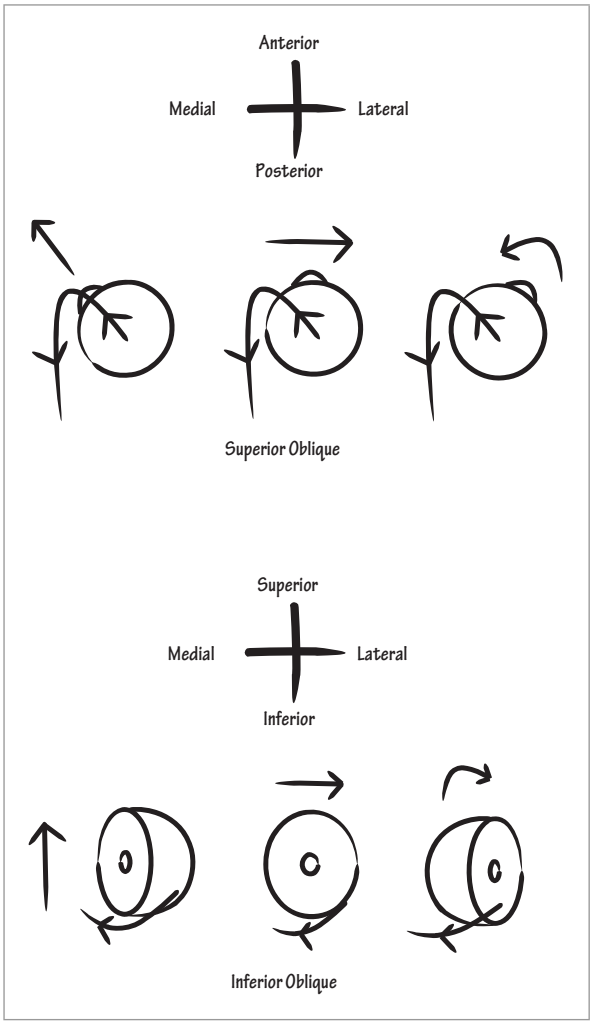


Figure 20-4 Oblique muscles: superior and inferior obliques

Cranial nerve	Muscle	Primary action	Tertiary action	Secondary action
3	Medial rectus	Adducts	X	X
6	Lateral rectus	Abducts	X	X
3	Inferior rectus	Depresses	Adducts	Extorts
3	Superior rectus	Elevates	Adducts	Intorts
3	Inferior oblique	Elevates	Abducts	Extorts
4	Superior oblique	Depresses	Abducts	Intorts

Figure 20-5 Eye movements table

Now that we understand the actions of the extraocular end-targets of cranial nerves 3, 4, and 6, we will draw their different origins and pathways through the cranium. We begin our diagram with a midsagittal section through the brainstem, and we will draw the cranial nerves in their rostro–caudal order. Start with the *oculomotor complex* of *cranial nerve 3* (the *oculomotor nerve*), which spans the rostral midbrain, within the ventral periaqueductal gray area just in front of the cerebral aqueduct. The oculomotor complex is a paired structure that straddles the midline and comprises several subnuclei. Show that its superior landmark is the *superior colliculus* and its inferior landmark is the *inferior colliculus*. The detailed anatomy of the oculomotor complex is interesting and frequently discussed in anatomy texts; however, it is of limited clinical yield because partial cranial nerve 3 palsies occur more frequently from selective cranial nerve fiber involvement than subnuclear lesions, yet we do include the detailed anatomy of the oculomotor nucleus at the end of this section for completeness. Draw the *oculomotor fascicles* fanning out as they pass ventrally through the midbrain and then show them re-converge before they enter the interpeduncular fossa.

Indicate the oculmotor nerve rootlets enter the interpeduncular fossa between the *posterior cerebral* and *superior cerebellar arteries*; and then continue the nerve's course lateral to the *posterior communicating artery*. Arterial aneurysms that injure cranial nerve 3 most commonly arise from the posterior communicating artery, but the superior cerebellar and posterior cerebral arteries are also potential culprits. Next, show cranial nerve 3 pass underneath the uncus of the temporal lobe. A third nerve palsy is often the first sign of uncal herniation (aka temporal lobe herniation)—a potential red flag of increased intracranial pressure. Herniation of the temporal lobe into the basilar cisterns causes compression of the brainstem and exiting fibers.

Then, show the oculomotor nerve pass through the rectangular-shaped *cavernous sinus*, then the oval-shaped *superior orbital fissure*, and finally, into the orbit through the *annulus of Zinn*—the entry site for all cranial nerves into the eye.

Within the orbit, the oculomotor nucleus divides into superior and inferior divisions (aka rami). The inferior division innervates the inferior rectus, inferior oblique, and medial rectus muscles; and the superior division innervates the superior rectus muscle. The inferior division also innervates the ciliary ganglion, which is the end-target of the visceral division of cranial nerve 3, and the superior division additionally innervates the levator palpebrae muscle, which causes eyelid opening.

While cranial nerve 3 innervates levator palpebrae, which opens the eyelids, cranial nerve 7 innervates orbicularis oculi, which closes them. Large basis pontine lesions result in the aptly named locked-in syndrome. In this syndrome, most muscles, including those of the eyes, are paralyzed; however, eyelid opening and closure are frequently spared. Eyelid opening and closure are often the only means of communication for patients with this unfortunate syndrome. These eye movements persist from the action–relaxation pattern of the levator palpebrae. The eyes open when levator palpebrae activates and closes when it passively relaxes. Orbicularis oculi, the muscle for active eyelid closure, is typically paralyzed from injurious involvement of the cranial nerve 7 nucleus or its exiting fibers, and does not participate in this action.

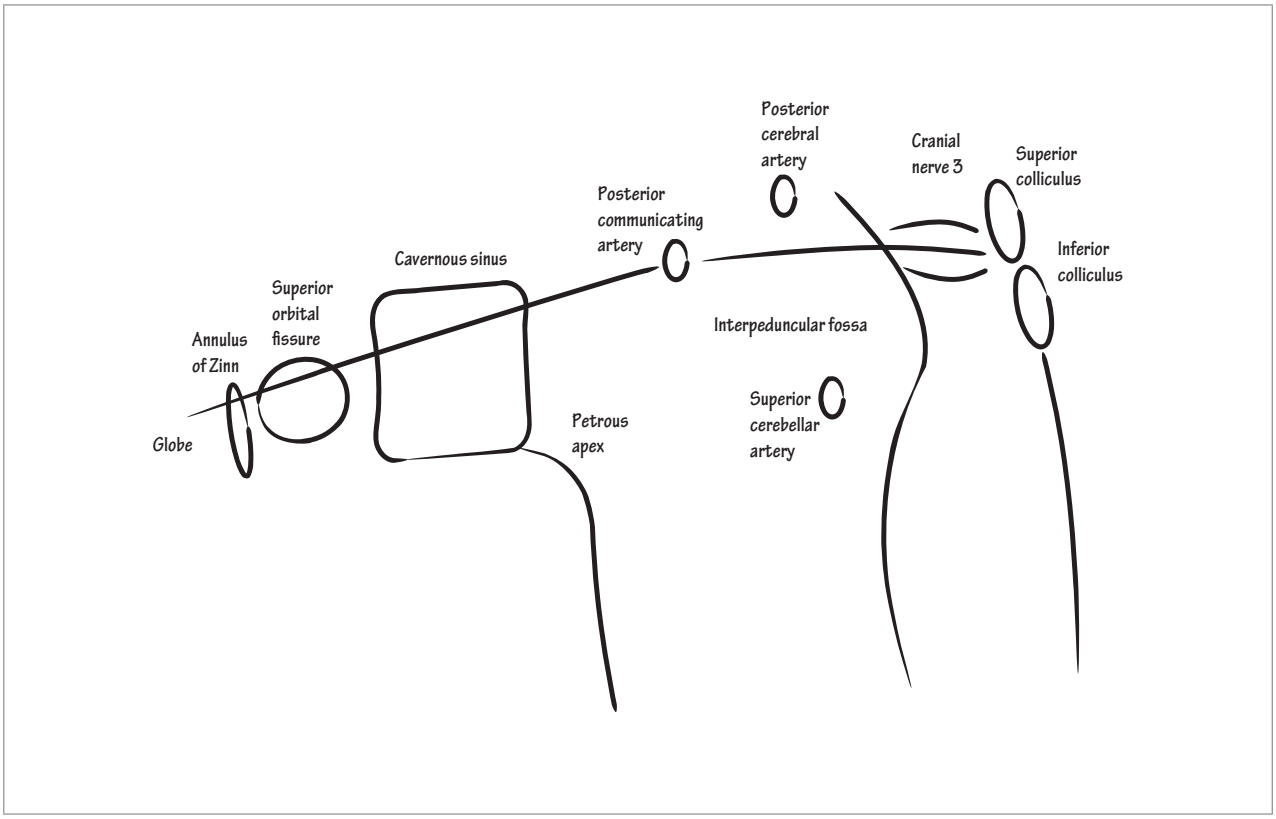


Figure 20-6 Midsagittal view of cranial nerve 3 course

The parasympathetic pupillary constrictor fibers, which we discuss in the "Eye Movements" chapter, cover the oculomotor nerve throughout its course. As a result, compressive cranial nerve 3 lesions cause pupillary dilation from external interruption of pupillary constrictor fibers, whereas non-compressive lesions spare the pupillary fibers. For this reason, third nerve palsies that occur in combination with pupillary involvement suggest the presence of an intracranial mass lesion and are considered medical emergencies until proven otherwise.

In a complete oculomotor nerve lesion, eye position, eyelid position, and pupillary response are affected. How do you think the eye appears? The intact lateral rectus, which is innervated by cranial nerve 6, and, secondarily, the superior oblique, which is innervated by cranial nerve 4, both abduct the eye, so it is "out." Both elevators, the superior rectus and inferior oblique, which are innervated by cranial nerve 3, are paralyzed, so the eye is "down." Thus, the eye appears "down and out." What about the eyelid? The levator palpebrae is disrupted so the eyelids slacken (i.e., the eyelid droops), which is called ptosis. Specifically, the distance between the upper and lower eyelids is narrowed, which is called a narrow palpebral fissure. What about the pupil? The pupillary constrictor fibers are disrupted so the pupil is unable to constrict from either direct light (ipsilateral pupillary illumination), indirect light (contralateral pupillary illumination), or near-convergence response, which we also discuss in the "Eye Movements" chapter.

Now, for those interested, we will go through the details of the oculomotor complex and learn how oculomotor subnuclear lesions cause partial oculomotor palsies. If you are uninterested in this topic, read just this paragraph and then skip ahead to cranial nerve 4. In the 1950s, R. Warwick created a classic model for the oculomotor complex. The model shows that the superior rectus subnuclei project contralaterally, the single levator palpebrae subnucleus projects bilaterally, and the remaining subnuclei project ipsilaterally. All you have to remember about the levator palpebrae and superior recti innervation is that for both of them, a single lesion to either subnucleus results in bilateral palsies. It is obvious why a lesion of the single levator palpebrae subnucleus causes bilateral levator palpebrae weakness: it innervates both muscles. But why does a lesion of either superior rectus subnuclei result in bilateral superior recti palsies when their innervation is contralateral? This is because when superior rectus fibers exit their subnucleus, they immediately pass through the contralateral subnucleus. Injury to one subnucleus affects its own fibers and the exiting fibers from the opposite subnucleus, as well, resulting in paralysis of both superior recti end-target muscles.

Now that we have learned the key points of Warwick's model, let's draw it. First, draw a sagittal view of the oculomotor complex. Label the top as *rostral*, bottom as *caudal*, left as *dorsal*, and right as *ventral*. Most of the subnuclei lie at a 45° angle to both the vertical and horizontal planes (i.e., they lie along a diagonal midway between the two planes), which makes its orientation conceptually challenging. Now, draw the long, narrow *ventral subnucleus* close to the ventral border; it innervates the *medial rectus*. Above it, draw the *intermediate subnucleus*, which innervates the *inferior oblique*, and above it, draw the *dorsal subnucleus*, which innervates the *inferior rectus*. Medial to these subnuclei, draw the hidden *superior rectus subnucleus*; it is the only subnucleus named for its end-target muscle rather than its anatomical position. Then, on the dorsocaudal surface, draw the small *central caudal subnucleus*, which innervates both *levator palpebrae*. On the rostral surface, draw the *visceral nucleus*, which is the *Edinger–Westphal nucleus*. This completes the oculomotor complex.

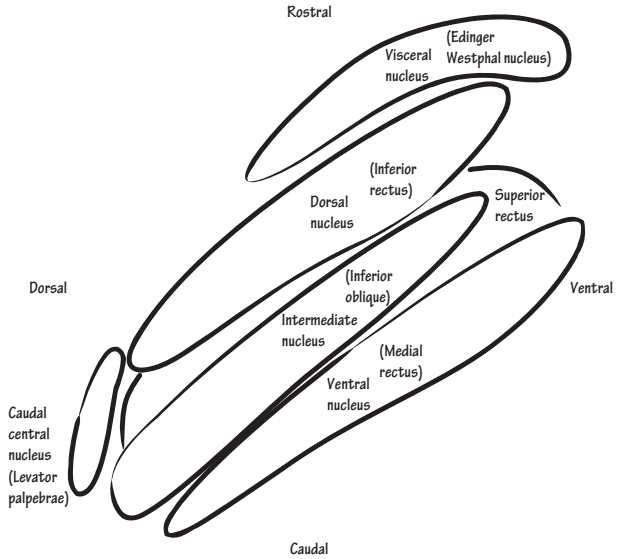


Figure 20-7 Oculomotor complex

Draw the trochlear nucleus of cranial nerve 4 (the trochlear nerve) in front of the *inferior colliculus*, which lies along the dorsal midbrain, beneath the superior colliculus. Note how the colliculi serve as landmarks of both the oculomotor and trochlear nuclei—the oculomotor nucleus spans vertically from the superior to the inferior colliculus, and the trochlear nucleus lies at the level of the inferior colliculus. Now, show cranial nerve 4 emerge from the trochlear nucleus, course posteriorly through the midbrain and exit the midbrain on its dorsal surface on the side opposite to its origin. Show it then pass outside the midbrain; all of the other cranial nerves of the somatomotor set, instead, pass directly ventrally through the brainstem. Show cranial nerve 4 enter the *prepontine cistern*, which lies beneath the interpeduncular cistern, and like the oculomotor nerve, show it pass between the *posterior cerebral* and *superior cerebellar arteries*, and run along the free edge of the tentorium. Then, show it pass through the *cavernous sinus* just below the oculomotor nerve: it passes along the lateral wall, which is out of the plane of this diagram. Finally, show it pass through the *superior orbital fissure* into the *orbit* through the *annulus of Zinn* to innervate the superior oblique muscle (on the side opposite its side of origin).

The trochlear nerve is frequently disrupted because it is the longest and thinnest of the cranial nerves. The presentation of a fourth nerve palsy is classic but subtle; it involves impairment of the primary action of the superior oblique, depression of the eye in adduction, and requires close observation to detect. When eye depression is impaired, the affected eye is higher (aka hypertropic) than the unaffected eye. As a result, the retinal images are disconjugate and manifest with subjective diplopia (aka double vision). To feel how nauseating this is, push on one of your eyes and generate double vision. To counteract this effect, patients tilt their head to bring their eyes into the same plane. Do they tilt their head toward or away from the side of the lesion? Let's find out. We'll use our fingers to analyze the diplopia from a cranial nerve 4 palsy. Hold your fists in front of you with your index fingers pointing straight ahead. Then, raise your right hand to simulate a lesion affecting the right cranial nerve 4—the right eye becomes hypertropic. Looking straight ahead, your index fingers lie along a diagonal. Which way do you have to tilt your head to bring your fingers into the same horizontal plane? To the left, to the side opposite the side of the lesion: in a fourth nerve palsy, patients tilt their head away from the hypertropic eye to compensate for its elevation.

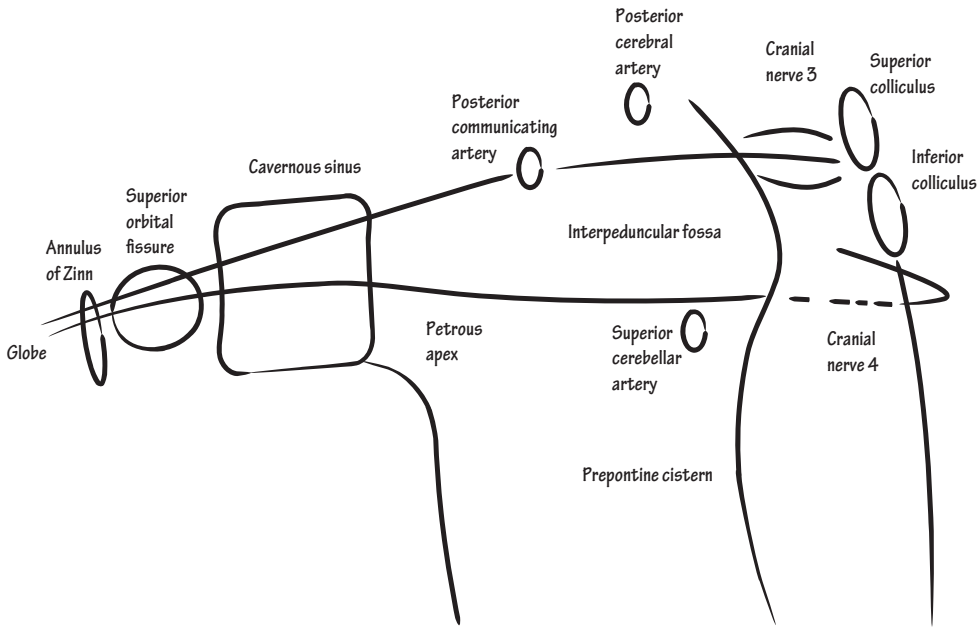


Figure 20-8 Midsagittal view of cranial nerve 3 and 4 course

Let's move on to cranial nerve 6. Show the *abducens nucleus* of *cranial nerve 6* (the *abducens nerve*) in the lower pons; it lies in the floor of the fourth ventricle. Show it pass ventrally through the pons and exit near the *anterior inferior cerebellar artery*. In the "Eye Movements" chapter, we draw the important interneuronal connections between the abducens and oculomotor nuclei through the medial longitudinal fasciculus, and in the "Pharyngeal Arch Cranial Nerves" chapter, we show cranial nerve 7 wrap around the abducens nucleus.

Next, show cranial nerve 6 cross the prepontine cistern and climb the *clivus*. From there it passes through three important landmarks. It penetrates the temporal bone dura and enters a channel in the basilar venous plexus called Dorello's canal. Show it penetrate the dura at the *petrous apex* and travel under the *petrosphenoidal ligament* (aka *petroclinoid ligament*) within Dorello's canal. In this stretch, the abducens nerve is in close proximity to the first division of cranial nerve 5 and the inferior petrosal venous sinus lies underneath them. This sinus is particularly susceptible to infection or extension of neoplastic disease. Therefore, injury to cranial nerve 6 often occurs at this site along with injury to the first division of cranial nerve 5 in a disease process that bears the eponym Gradenigo's syndrome. More frequently, however, disruption of cranial nerve 6 is a warning sign of increased intracranial pressure. Where the abducens nerve pierces the dura, the nerve is fixed, so with increased intracranial pressure, downward herniation of the brainstem applies traction on the abducens nerve. In this way, a cranial nerve 6 lesion is a harbinger of increased intracranial pressure and is a medical emergency until proven otherwise.

Next, show cranial nerve 6 pass through the cavernous sinus. It takes the most medial path through the cavernous sinus of all of the cranial nerves—it travels inferomedial to cranial nerve 3 and lateral to the cavernous portion of the internal carotid artery. Within the cavernous sinus, the pupillosympathetic fibers leave the internal carotid to join the first division of the fifth cranial nerve. As they do, over a very short distance, they run along cranial nerve 6: thus, a lesion in this location will result in a cranial nerve 6 palsy with an associated Horner's syndrome. Finally, show the abducens nerve pass from the cavernous sinus through the *superior orbital fissure* and through the *annulus of Zinn* into the orbit to innervate the *lateral rectus muscle*.

A cranial nerve 6 lesion causes an unmistakable presentation of lateral gaze palsy. Is the resultant diplopia a common complaint with near or far vision? Cranial nerve 3 produces eye convergence for near vision, whereas cranial nerve 6 produces divergence of the eyes for distance vision. So cranial nerve 6 lesions cause diplopia with attempted far vision.

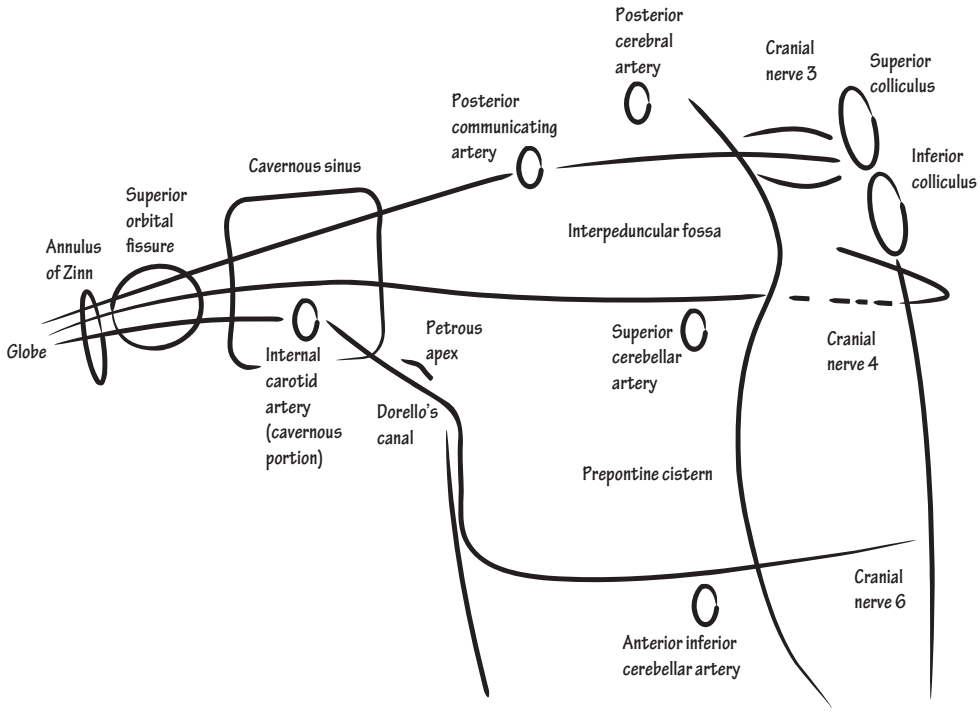


Figure 20-9 Midsagittal view of cranial nerve 3, 4, and 6 course

Now, let's leave the extraocular cranial nerves and address cranial nerve 12. In the terminal course of cranial nerve 12, it runs underneath the tongue (aka the glossus), which is why it is named the hypoglossal nerve. The hypoglossal nerve ends in the unnamed intrinsic muscle fibers and named extrinsic muscles (styloglossus, hypoglossus, and genioglossus) of the tongue. Palatoglossus is the only extrinsic tongue muscle not innervated by cranial nerve 12; it is innervated by the vagus nerve, instead. Of the three extrinsic muscles innervated by the hypoglossal nerve, genioglossus is the most clinically important. Whereas the other tongue muscles receive bilateral innervation, genioglossus receives solely contralateral innervation and, therefore, it is most helpful with localization. Protrude your tongue, now, to demonstrate the action of genioglossus.

To understand the action of all of these muscles, we will draw a sagittal view of them along with the mandible. Draw *styloglossus* swooping down from its supero-posterior origin, attaching underneath the tongue. Indicate it pulls the tongue up and back. Then draw *hypoglossus* angling toward the tongue from postero-inferior and indicate that it depresses the tongue. Finally, draw *genioglossus* targeting the underside of the tongue from antero-inferior.

Genioglossus provides tongue protrusion. In axial section, show that both sides of the *genioglossi* are directed at opposite angles toward the mandible. Their opposing lateral–medial angles cancel and the tongue is directed forward. As you can imagine, when one side of the genioglossus is impaired, the tongue moves forward and toward the side of the lesion, away from the intact side. Demonstrate this with your index fingers. Hold your fists in front of you and point your index fingers toward midline (they create a *V-shape*). Now drop one of your fists to demonstrate that when one side of the genioglossus muscle is impaired, the tongue pushes out and toward the side of the lesion, away from the intact side.

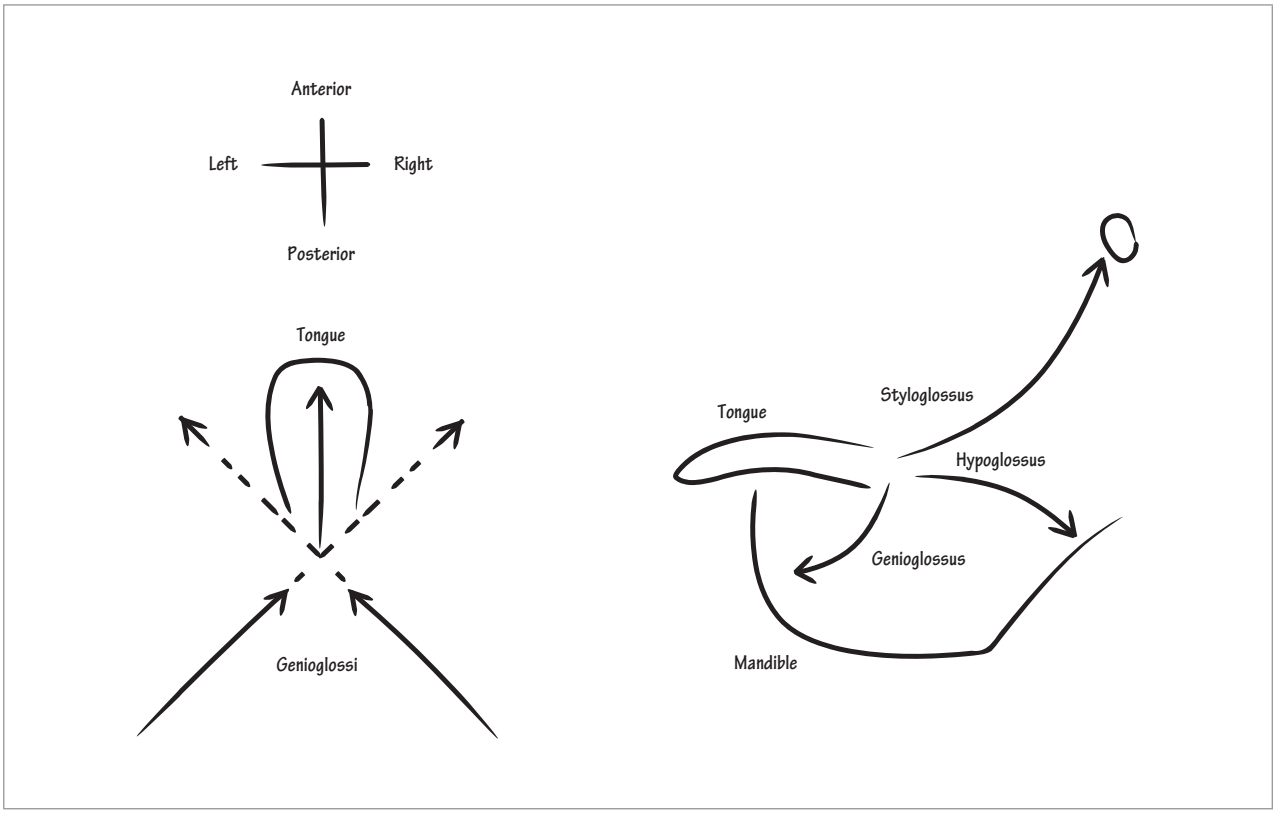


Figure 20-10 Muscle actions on tongue directions

The previous description involves a lower motor neuron or nerve lesion (i.e., a lesion within the hypoglossal nucleus or nerve). What happens when the lesion is proximal to the hypoglossal nucleus? In other words, is cortical hypoglossal innervation ipsilateral, contralateral, or bilateral? On the whole, it is believed to be bilateral but with the predominance of fibers originating from the contralateral side. Therefore, with most hemispheric lesions, tongue protrusion is normal, but if you see weakness from an upper motor neuron lesion, for instance a right-side hemispheric lesion, how will the tongue deviate? The left genioglossus will be weak so the tongue will deviate to the left (away from the side of the cortical lesion).

Now, let's draw the midsagittal central course of cranial nerve 12. Draw the *hypoglossal nucleus* of *cranial nerve 12* (the *hypoglossal nerve*) at the level of the *inferior olive* in the medulla. Show cranial nerve 12 pass ventrally through the medulla and exit between the inferior olive, laterally, and the medullary pyramid, medially. Then, show it cross the *premedullary cistern* and traverse the skull base through the *hypoglossal canal*. It runs near the internal carotid artery and carotid bulb as it descends in the medial nasopharyngeal carotid space. Which other cranial nerves are present in this space? (Hint: they communicate with autonomic receptors in the aortic arch and carotid bulb.) Cranial nerves 9 and 10. Finally, complete the course of the hyopglossal nerve as it terminates in the intrinsic and extrinsic tongue muscles.

The proximity of cranial nerve 12 to the internal carotid artery makes it susceptible to injury from carotid dissection. How does an injury within the carotid artery cause damage to a nerve that runs alongside it? When an artery dissects, clot often forms in its wall (between the tunica intima and tunica media layers) and this clot will potentially expand the wall enough to compress the adjacent nerves. Thus, in cranial nerve 12 lesions, especially when they occur in combination with lesions of cranial nerves 9 and 10, consider carotid dissection as a potential cause.

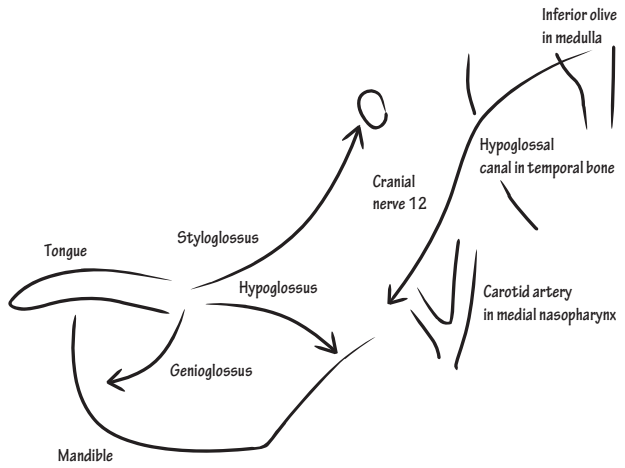


Figure 20-11 Midsagittal view of cranial nerve 12 course

Pharyngeal Arch Cranial Nerves

Cranial nerves 5, 7, 9, and 10 all share the same pharyngeal arch embryonic origin, which is described in the "Cranial and Spinal Nerve Overview" chapter. In that chapter, we drew and discussed the nerves as a group; here, we examine their individual anatomy. Multiple cell columns constitute the different pharyngeal arch nerves: special visceral efferent (skeletal motor), general visceral efferent (autonomic motor), special visceral afferent (taste), general visceral afferent (viscerosensory), and general somatic afferent (somatosensory).

We will draw the nerves in their rostro-caudal sequence along the brainstem, beginning with the trigeminal nerve. The trigeminal nerve comprises only special visceral efferent and general somatic afferent fibers, making it one of the most uniform of the pharyngeal arch derivatives, yet it is the most robust of all the cranial nerves because of its large sensory fiber volume.

In this chapter, we will first address the peripheral division of the trigeminal sensory system. It is the most important clinical aspect of the trigeminal nerve (and the most important aspect of the pharyngeal arch derivatives as a whole). The peripheral divisions of the trigeminal nerve are division 1 (ophthalmic), division 2 (maxillary), and division 3 (mandibular). From their names, you already get an idea of their distributions. Ophthalmic covers the eyes, maxillary covers the cheeks, and mandibular covers the jaw. Before we draw the sensory coverage of these branches, let's palpate their coverage on our face. First, tap just behind the top of your head—the trigeminal nerve covers the area in front of this point and the C2 dermatome, through the greater occipital nerve, covers behind it. Next, tap the corner of your eye and then the tip of your nose. Division 1 covers everything within these three points. Now, once again, tap the same superior-posterior point on your head. Then, tap your cheekbone (your maxilla) and then the corner of your mouth. Division 2 covers everything in between these points and division 1. For division 3, again start with the same superior-posterior point, first. Next, tap the tragus (it is the hard, anterior cartilaginous portion of the outer ear) and then underneath the chin (aka the mentum). Division 3 covers everything between these points and division 2.

Now, in the same manner in which we palpated its distribution, let's draw the trigeminal distribution. First, mark a dot on the superior-posterior curvature of the head, then at the corner of the eye, and then the tip of the nose. Now, connect these dots and label the region supero-anterior to it as *division 1* (aka the *ophthalmic division*). Next, mark a dot at the same superior-posterior point, then at the maxilla, and then the corner of the mouth. Join these dots and label the region between this line and division 1 as *division 2* (aka the *maxillary division*). Finally, mark a dot at the same superior-posterior point, then at the tragus, and then the mentum. Connect these dots and label the region between this line and division 2 as *division 3* (aka the *mandibular division*).

Two key details of facial sensory coverage are that cranial nerves 7, 9, and 10 cover the outer ear (aka the auricle) and that C2 or C3, depending on your reference, covers the angle of the mandible. In other

words, division 3 of the trigeminal nerve covers neither the outer ear nor the angle of the mandible.

Clinicians often use the sensory coverage of the angle of the mandible to differentiate between real and functional (i.e., non-neurologic) symptoms because the angle of the mandible should be unaffected in division 3 trigeminal nerve disease and most patients are unaware of this. Clinicians also test whether sensory loss crosses the superior pole of the head for the same reason. Tap along the top of your head from anterior to posterior to mimic this evaluation. The coverage of the trigeminal nerve extends posteriorly, beyond the superior pole, and thus "true" peripherally-mediated sensory loss should not stop abruptly at top of the head. It is clearly important to use these types of examination tools judiciously and within the context of the individual patient.

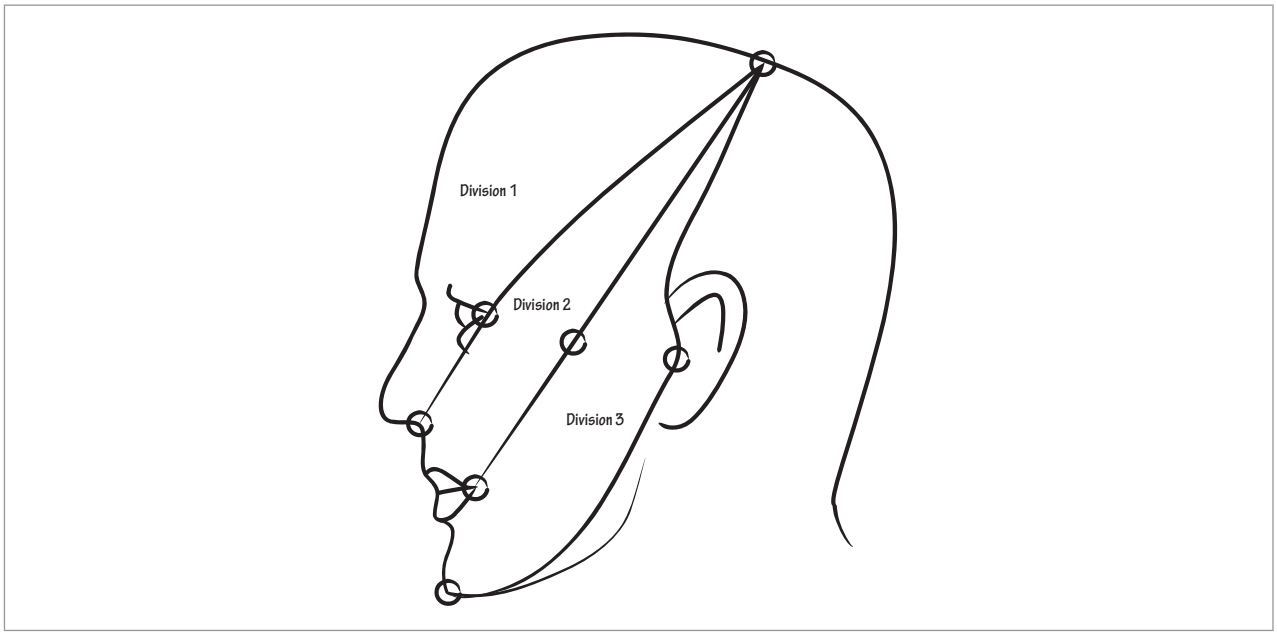


Figure 21-1 Trigeminal sensory map of face

In the following paragraphs, we will address the motor component of the trigeminal nerve along with its central sensory afferents. The main function of the trigeminal motor system is chewing. Chewing requires the medial and lateral pterygoids, masseter, and temporal (aka temporales) muscles. The lateral pterygoids open the jaw and the rest—the medial pterygoid, temporal, and masseter muscles—close it. The trigeminal motor fibers also innervate several clinically less relevant muscles that we will leave out of our discussion—tensor tympani, tensor veli palatini, mylohyoid, and the anterior bellies of the digastric.

Feel just above and in front of the angle of your mandible and clench and relax your jaw. The contracting muscles under your fingertips are the masseters. Next, look at your temples and cheeks; the temporal muscles fill out your facial contour. Atrophy of these muscles is an important potential clue to trigeminal neuronal degeneration.

The lateral pterygoids are arranged like the genioglossi. They aim at an angle to one another. Open your jaw and extend your mandible forward to activate your lateral pterygoids. As you did for the genioglossus, draw the *lateral pterygoids* at an angle to one another; show them pushing the mandible forward. In a lower motor neuron lesion (when a trigeminal motor nucleus or nerve or when a lateral pterygoid is damaged), the jaw deviates toward the injured side. Remember this the way we did for genioglossi. Point your index fingers toward one another to represent the lateral pterygoids. When one drops out, the remaining finger points toward the weak side.

Cortical innervation of the trigeminal motor nuclei is bilateral with contralateral predominance as it is for the hypoglossal nuclei. As a review, when upper motor neuron fibers are disrupted, what is the effect on tongue protrusion? Most often there is none. If tongue deviation occurs, it is toward the weak side of the body (away from the side of the cortical lesion). The same is true for jaw protrusion. With an upper motor neuron lesion, most often jaw deviation will be unaffected. If it is, the jaw deviates away from the side of cortical disruption toward the weak side of the body. For instance, in a right hemispheric lesion, the left trigeminal nucleus is unable to activate the left lateral pterygoid and so the jaw deviates to the left, away from the injured right cerebral hemisphere.

In addition to chewing, the motor component of cranial nerve 5 provides a muscle stretch reflex called the jaw jerk. Sensory afferents from their stretch receptors course centrally via the mandibular component (division 3) of cranial nerve 5 and, when the muscles of mastication are stretched, they activate the bilateral motor neurons of cranial nerve 5. To demonstrate this, relax your jaw and tap your chin. When you suddenly stretch your jaw muscles, afferent impulses to the trigeminal motor neurons signal the jaw muscles to snap shut. A brisk jaw jerk in certain clinical settings suggests pathologic disinhibition of suppressive corticonuclear fibers to cranial nerve 5.

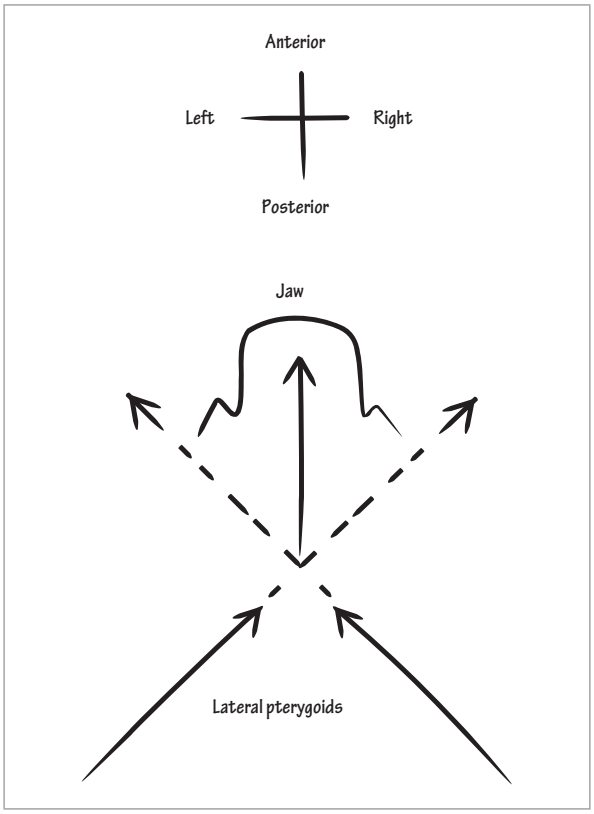


Figure 21-2 Lateral pterygoids

Now, let's draw the anatomy of the motor division of cranial nerve 5 in mid-sagittal cross section. Draw a mid-sagittal section through the brainstem and show the *trigeminal motor nucleus* in the mid-pons. Show the motor trigeminal nerve course ventrolaterally to exit the brainstem—all of the pharyngeal arch derivatives leave the brainstem along a ventrolateral path. Then, show the trigeminal nerve cross the *cerebellopontine angle cistern*. The somatomotor nerves pass through anterior cisternal spaces (the interpeduncular fossa [in front of the midbrain], prepontine cistern, and premedullary cistern) but the pharyngeal arch nerves and cranial nerve 8 pass through laterally positioned cisternal spaces named from combined cerellar-brainstem segments; as mentioned, the cisternal space for cranial nerve 5 is the cerebellopontine angle cistern.

Next, show cranial nerve 5 course over the apex of the petrous temporal bone and enter the middle cranial fossa. Then, draw the *trifurcated sensory ganglion of the trigeminal nerve* in *Meckel's cave*, a dural cavern in the posterolateral aspect of the cavernous sinus. The lateral position of Meckel's cave in the cavernous sinus again underscores the lateral course of cranial nerve 5. Sensory afferents from the periphery travel along branches of the trigeminal nerve and synapse in the trigeminal ganglion. From rostral to caudal, the trigeminal ganglion, which means the "three twins," contains ophthalmic, maxillary, and mandibular divisions.

Now, show that the motor fibers of the trigeminal nerve circumvent the trigeminal ganglion, itself, but join the mandibular division as it exits the middle cranial fossa through foramen ovale. In the periphery, the motor fibers separate into five different nerves that innervate the muscles of mastication. The nerve–muscle pairs are listed here for reference, only. The medial pterygoid nerve innervates the medial pterygoid, tensor veli palatini, and tensor tympani muscles; the lateral pterygoid nerve innervates the lateral pterygoid muscle; the masseteric nerve innervates the masseter muscle; the deep temporal nerve branches innervate the temporal muscle; and the mylohyoid nerve innervates the anterior belly of the digastric and mylohyoid muscles. It is not as hard as you might imagine to learn these nerve branch–muscle relationships when you consider that the nerves share the name of the most important muscle they innervate. Look back over them, now, with this in mind.

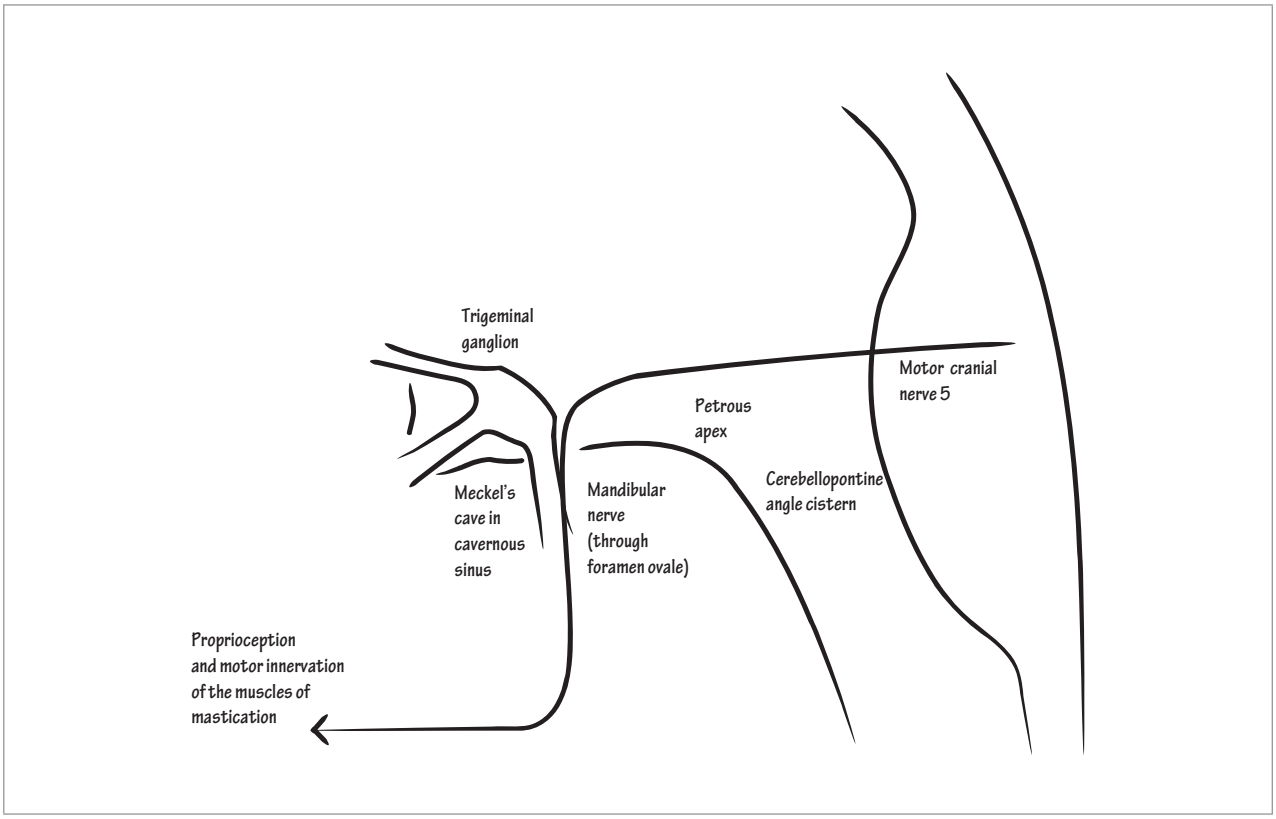


Figure 21-3 Motor trigeminal nerve

Next, add the trigeminal sensory nuclei to the brainstem. They are the midbrain *mesencephalic nucleus*, the pontine *principal sensory nucleus*, and the *spinal trigeminal nucleus*, which spans from the pons into the upper cervical spinal cord. The mesencephalic nucleus receives proprioceptive afferents from the muscles of mastication, which ascend through the mandibular division of the trigeminal nerve. The primary synapse of these nerve fibers is in the mesencephalic nucleus and not in the trigeminal ganglion, as you might imagine; it is the only instance where primary sensory afferents synapse in the central nervous system and not in a ganglion outside of it. Although these afferent fibers travel through the lowest division of the trigeminal nerve, they synapse in the uppermost portion of the central trigeminal nuclear complex. These are just some of the peculiarities of the central sensory component of the trigeminal nerve. The mesencephalic nucleus not only signals the motor nucleus to activate jaw closure through the jaw jerk reflex but also projects to the principal sensory and spinal trigeminal sensory nuclei.

The pontine principal sensory nucleus is often considered the trigeminal functional equivalent of the posterior column nuclei (i.e., the recipient of the large fiber, proprioceptive afferents from the trigeminal nerve) and the expansive spinal trigeminal nucleus, which runs from the pons into the upper cervical spinal cord, is often considered the trigeminal functional equivalent of the anterolateral system (i.e., the recipient of small fiber pain and temperature afferents from the trigeminal nerve). But, as mentioned above, the mesencephalic nucleus projects proprioceptive fibers to both of these nuclei—so, the spinal trigeminal nucleus also receives proprioceptive fibers. Thus, although we *are* able to distinguish the principal sensory nucleus as a large fiber reception area and the spinal trigeminal nucleus as a small fiber area, these nuclei are far too interconnected for us to put any clinical emphasis on this distinction.

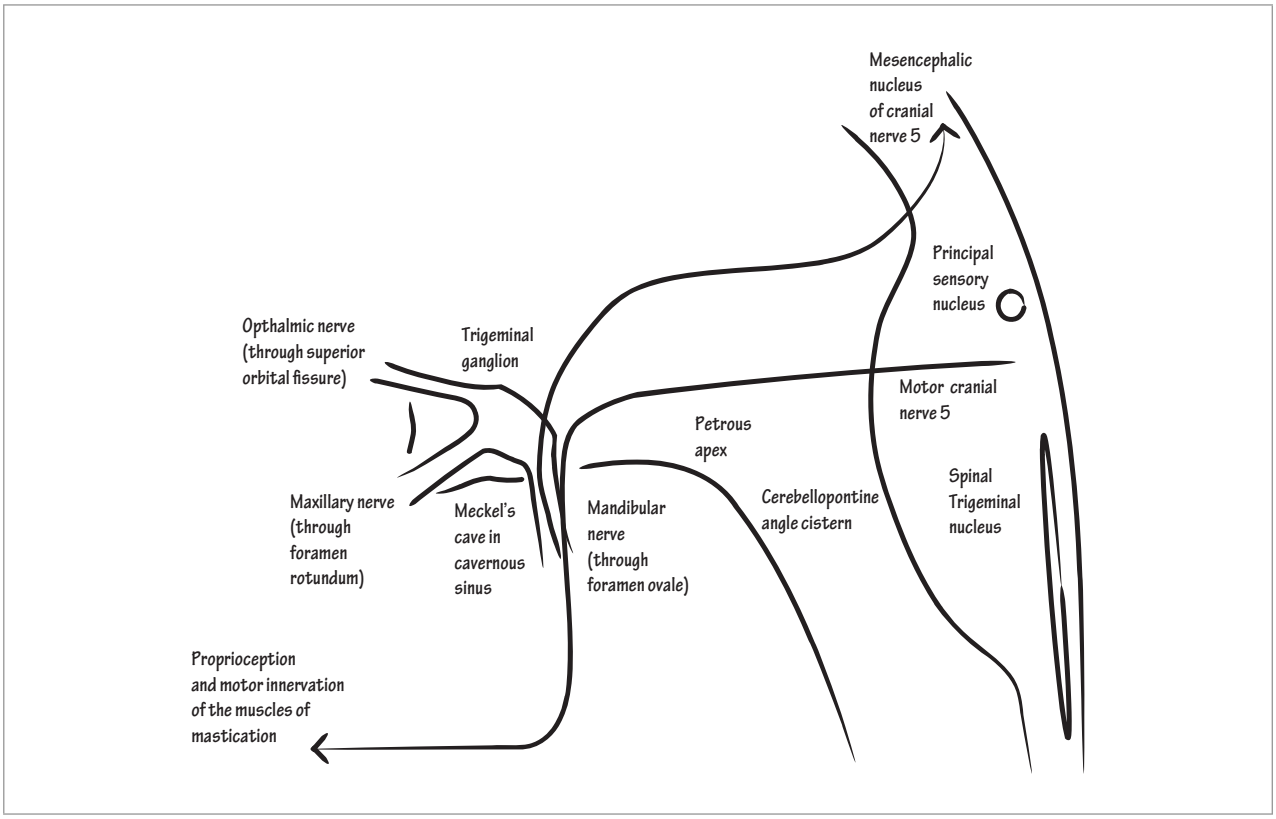


Figure 21-4 Complete trigeminal nerve

The central sensory afferents of the trigeminal nerve relay to the thalamus through the trigeminothalamic pathways. There are two trigeminothalamic tracts; they are the anterior trigeminothalamic tract (aka *ventral trigeminothalamic tract*) and posterior trigeminothalamic tract (aka *dorsal trigeminothalamic tract*). The anterior trigeminothalamic tract comprises principal sensory and spinal trigeminal fibers that project to the contralateral thalamus whereas the posterior trigeminothalamic tract comprises principal sensory fibers that project to the ipsilateral thalamus.

The organization of the trigeminothalamic pathways and of the principal sensory nucleus is interesting but of limited clinical value. The bullet points are that the oral cavity has bilateral central sensory projections and the other areas of the face have solely contralateral central projections. We include a diagram of the trigeminothalamic pathways and a description of the somatotopy of the principal sensory nucleus for those who are interested. If you are not, skip ahead to the section on the onionskin somatotopy of the trigeminal system; knowledge of it is of significant clinical value.

The *trigeminothalamic pathways* are best shown in coronal brainstem section. Show the *small* and *large fibers* enter the brainstem through the trigeminal nerve. Indicate the small fibers descend and synapse in the *spinal trigeminal nucleus*. Then, indicate they project contralaterally via the *anterior trigeminothalamic tract* to the *ventral posteromedial nucleus* of the *thalamus*. Remember, fibers from the rest of the body synapse in the ventral posterolateral nucleus of the thalamus.

Next, show the large fibers enter the brainstem and synapse in the *principal sensory nucleus*. One group synapses in the *ventrolateral* portion of the principal sensory nucleus while the other synapses in the *dorsomedial* portion. Indicate the ventrolateral principal sensory nucleus sends fibers contralaterally via the anterior trigeminothalamic tract along with those from the spinal trigeminal nucleus to synapse in the ventral posteromedial nucleus of the thalamus. Then, show the dorsomedial principal nucleus project fibers to the *ipsilateral ventral posteromedial nucleus* of the *thalamus* via the *posterior trigeminothalamic tract*.

The principal sensory nucleus lies in a small area in the dorsolateral pons. Within the principal nucleus, the dorsomedial portion receives fibers solely from the ipsilateral oral cavity whereas the ventrolateral portion receives fibers from all three divisions of the ipsilateral face. The somatotopic organization of the peripheral trigeminal map is turned on its side in the principal sensory nucleus. In the periphery, the sensory coverage of the face is divided into three horizontal divisions arranged from superior to inferior: division 1 for the upper face, division 2 for the middle face, and division 3 for the lower face. In the principal sensory nucleus, the divisions are arranged from anterior to posterior as follows: division 1 is the most anterior, division 2 lies in the middle, and division 3 is the most posterior. Since the principal sensory nucleus is relatively small, it is hard to imagine a lesion that would affect only one of its subdivisions (ventrolateral or dorsomedial). However, the principal sensory nucleus lies in the border-zone of the anterior and posterior vascular supply of the pons. The superior cerebellar artery supplies the dorsal portion of the nucleus and the long circumferential branch of the basilar artery supplies the ventral portion. So, a long circumferential branch stroke (aka *infarct*) will injure the ventrolateral portion of the principal sensory nucleus and result in loss of sensation on the side of the lesion. Meanwhile, the superior cerebellar artery will still supply the dorsomedial nucleus and maintain sensory supply to the oral cavity. On the contrary, a superior cerebellar infarct will damage the dorsomedial region and leave the ventrolateral region intact with variable clinical loss of oral cavity sensation since there is some redundancy of sensory coverage of this area by the ventrolateral region.

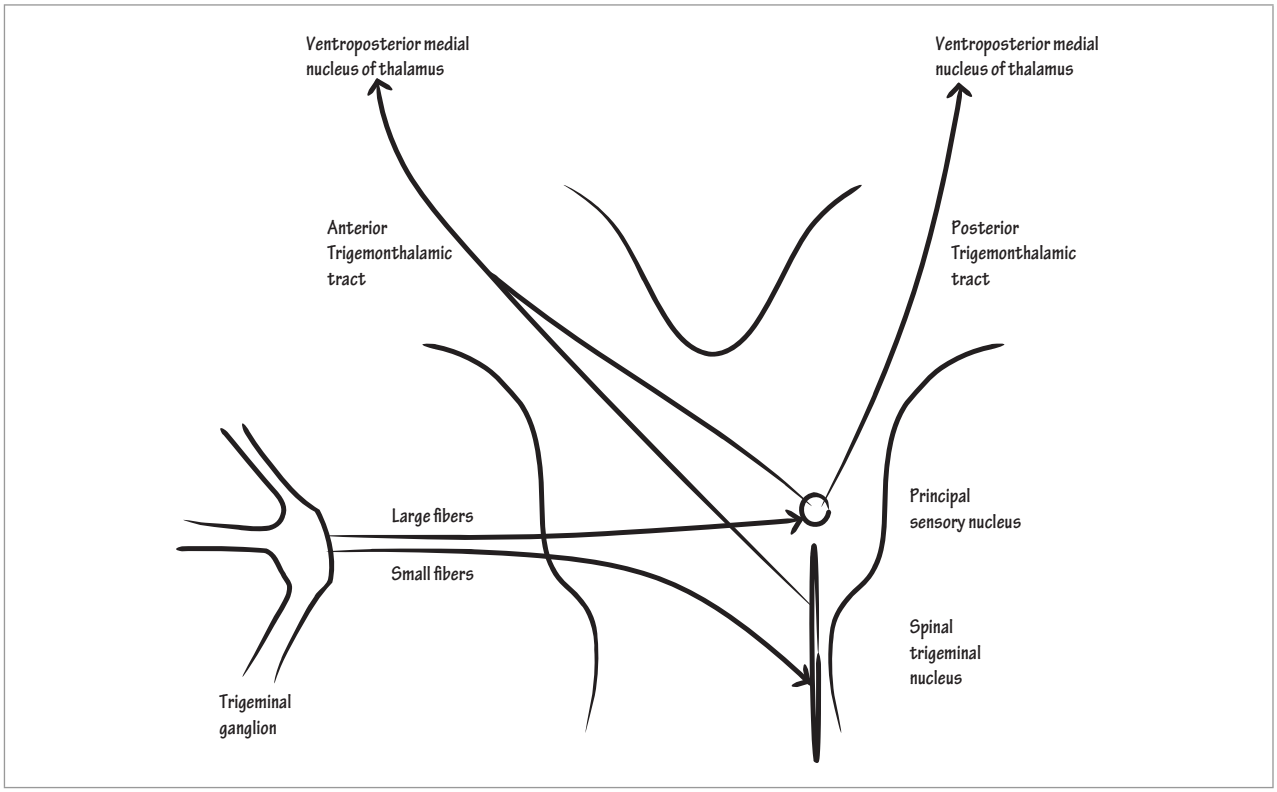


Figure 21-5 Trigeminothalamic tracts

While the principal sensory nucleus is small, the spinal trigeminal nucleus is quite long; it spans from the pons into the upper cervical cord, so partial spinal trigeminal nuclear lesions are common, which makes its somatotopy highly clinically relevant. The spinal trigeminal nucleus has three different cytoarchitectual regions: pars oralis, superiorly; pars interpolaris in the middle; and pars caudalis, inferiorly. When clinicians discuss the spinal trigeminal nucleus, they are most commonly referring to pars caudalis, which itself spans from the medulla into the upper cervical spinal cord. As already mentioned, it predominantly receives small fibers and has an onionskin somatotopy that is both interesting and important.

To understand the somatotopy of the spinal trigeminal nucleus, imagine a slightly distorted face as layers of an onion. The lips and perioral area constitute the outer-most layer; then as we peel inward, the next layer comprises the nose, eyes, and outer oral areas; then the cheeks and forehead; then the vertical band just in front of the ears; and finally the ears themselves, which cranial nerves 7, 9, and 10 cover.

This somatotopic arrangement is called onionskin or onion-peel organization and is preserved within the ventromedial nucleus of the thalamus. In the thalamic somatotopic map, the thumb reaches medially to the lips. Small thalamic ventral posteromedial nucleus infarcts often result in sensory loss restricted to the perioral region and thumb, the so-called cheiro-oral distribution.

The somatotopic features of the face in the spinal trigeminal somatotopic map are disproportionate to human features. They are stretched to fit into the proportions of the long, columnar spinal trigeminal nucleus. Imagine pulling a rubber mask off of your face: the distorted features of the mask resemble those in the somatotopic map of the spinal trigeminal nucleus. In terms of the rostro-caudal organization of the spinal trigeminal nucleus, the most superior portion receives the lips and perioral area and the most inferior component receives the outer ears. In terms of the anterior-posterior organization, the superior features of the face (e.g. the eyes) lie anterior and the inferior features (e.g. the jaw) lie posterior.

Now, we will draw the somatotopic organization of the spinal trigeminal nucleus. First, draw a side-on view of a normal-appearing face. To emphasize the concept of the onionskin somatotopy, first, slice a layer through the lips and perioral region; then a layer that includes the eyes, side of the nose, and outer oral region; then one that includes the forehead and cheeks; then the area in front of the ears; and then the ears, themselves. In the next schematic, draw a face that is stretched along the horizontal meridian to show how its somatotopy is distorted within the columnar spinal trigeminal nucleus. Alongside the face, draw a sagittal view of the brainstem; include the long spinal trigeminal nerve to show that the orientation of the face is such that the eyes are anterior and the jaw is posterior. At some point, you will read that the somatotopy of the spinal trigeminal nucleus is "inverted." It would be nice if we could sum up the anatomy of the spinal trigeminal nucleus in one word but we cannot, and while "inverted" may be the best single-word descriptor we have, it is misleading: avoid it if possible.

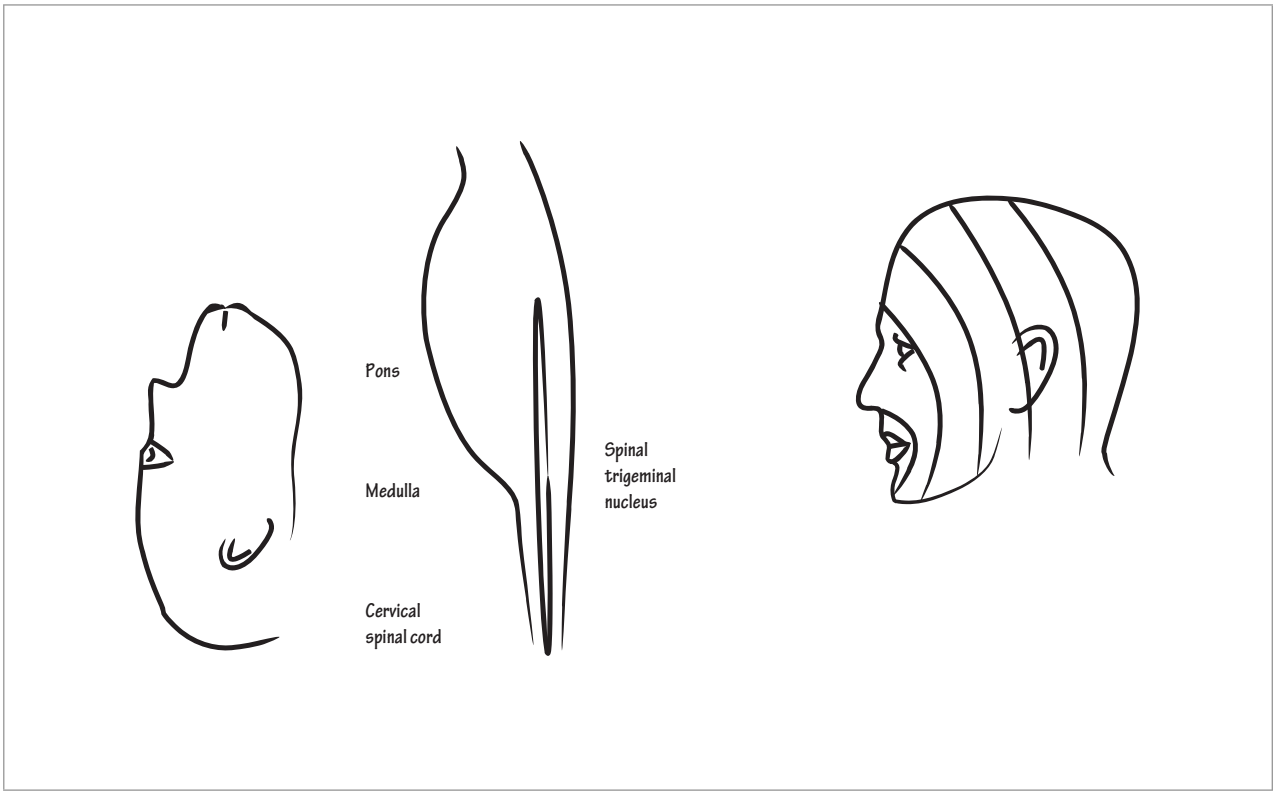


Figure 21-6 Trigeminal somatotopy. Adapted from Haines D., *Fundamental Neuroscience for Basic and Clinical Applications*, page 293, figure 18-15

Now, let's address cranial nerve 7, the facial nerve. This nerve comprises special visceral efferent fibers to the muscles of facial expression; general visceral efferent fibers for parasympathetic, glandular secretomotor action; special sensory afferent fibers that carry taste sensation from the anterior two-thirds of the tongue; and general somatic afferent fibers that provide sensory coverage to the external ear and external auditory canal. The innervational pattern of the motor division of cranial nerve 7 is the most commonly assessed aspect of its anatomy. When you learn it, you will easily be able to distinguish between upper and lower motor neuron cranial nerve 7 injuries, which are quite common. Stroke is the most common cause of upper motor neuron cranial nerve 7 lesions (i.e., lesions central to the cranial nerve 7 nucleus), whereas Bell's palsy is the eponym for lower motor neuron cranial nerve 7 lesions (i.e., lesions peripheral to and including the cranial nerve 7 nucleus).

Let's draw this important innervation pattern in a simple schematic so we can visualize the effects of central versus peripheral lesions. Draw a front-on view of the face. Above the face, draw the *cerebral hemispheres*. Raise your eyebrows and feel your forehead wrinkle. The *frontalis* muscle is responsible for this action, so label it as the upper facial muscle in our diagram. Next, force a smile. *Zygomatic major* is responsible for this action, so label it as the lower facial muscle in our diagram. A volitional smile (aka *forced smile*) is innervated through the corticobulbar tract whereas the origins of an involuntary smile (aka *emotional* or *mimetic smile*) lie within the basal ganglia and limbic system. To differentiate these, first, mimic a smile from a laugh-out-loud funny joke; this is an emotional smile. Then, mimic the smile that the Joker from the *Batman* series paints on his victims (a forced smile). At the bedside, we want to test the forced smile, so be careful not to make your patients laugh.

Now, draw *corticonuclear projection fibers* from one of the cerebral hemispheres to the contralateral *upper* and *lower divisions of the cranial nerve 7 nucleus*. Next, draw a *corticonuclear fiber* from the opposite cerebral hemisphere to the *upper division of the cranial nerve 7 nucleus*, only. The upper division receives bilateral projections whereas the lower division receives contralateral projections, only. Indicate the *cranial nerve 7 nucleus* projects to the *ipsilateral side of the face*: draw fibers from the upper portion of the cranial nerve 7 nucleus to the *frontalis muscle* and fibers from the lower portion of the cranial nerve 7 nucleus to *zygomatic major*.

What is the clinical presentation of a central (aka *upper motor neuron*) lesion? Is the contralateral upper face weak or strong? It is strong. Cortical projections from the injured hemisphere are disrupted but projections from the opposite hemisphere still supply the upper division of cranial nerve 7. And the lower face? The contralateral lower face is weak. It relies solely on cortical projections from the injured cerebral hemisphere. What about a peripheral (aka *lower motor neuron lesion*)? When cranial nerve 7, itself, is injured, there is disruption to innervation of the upper and lower face on the side of the injury.

At the bedside, keep in mind the following point: in a central lesion, the lower eyelid on the paretic side will commonly droop, secondary to lower facial weakness. This will cause the distance between the upper and lower eyelid (aka the palpebral fissure) to widen. The palpebral fissure on the normal side will thus appear narrow relative to the paralyzed side.

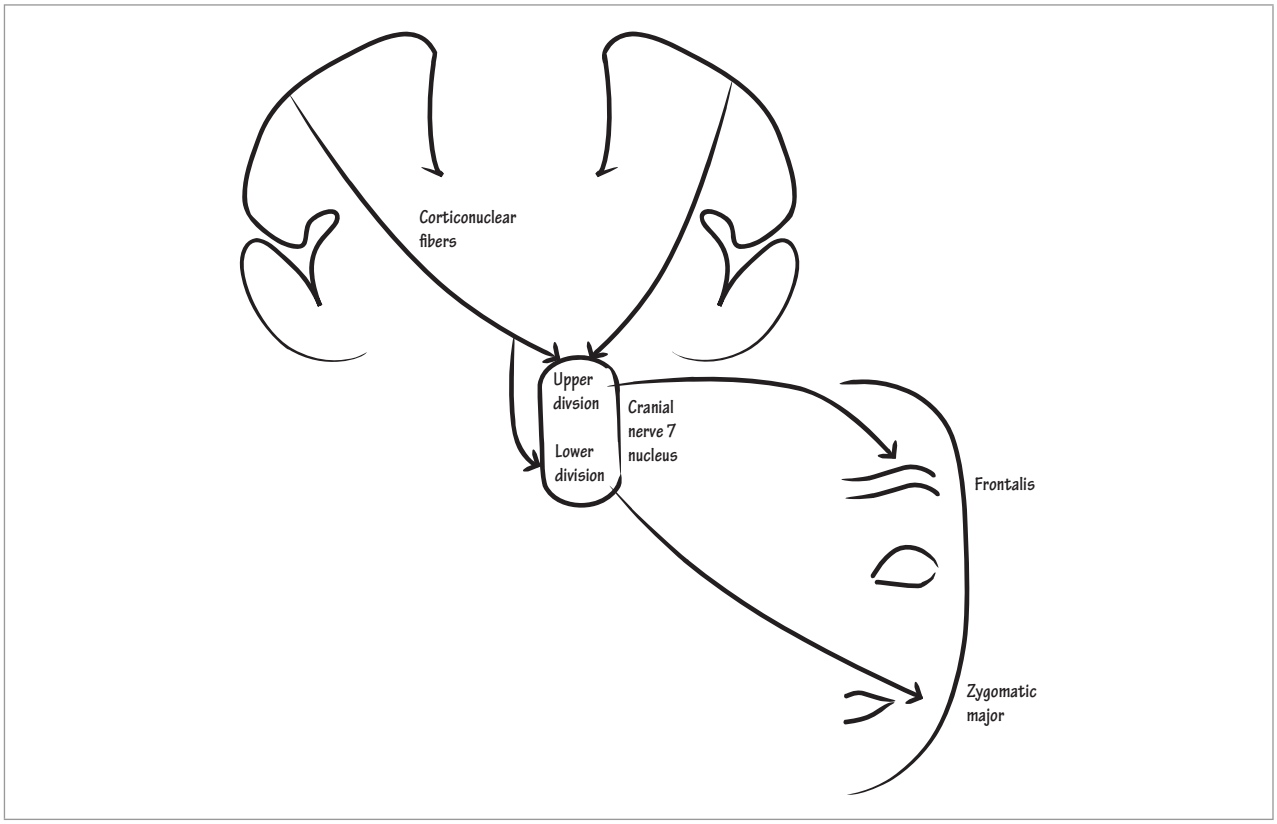


Figure 21-7 Cranial nerve 7 motor innervation to the face

Now, let's illustrate the course of cranial nerve 7 with a sagittal diagram. As a reminder, the facial nerve comprises fibers from the following cell columns: special visceral efferent (motor, muscles of facial expression), general visceral efferent (motor parasympathetic, glandular production), special visceral afferent (taste, from the anterior two-thirds of tongue), and general somatic afferent (sensory, from the external ear and external auditory canal). In sagittal section, draw the *facial nucleus* of the *motor* component of *cranial nerve 7* (the *facial nerve*) in the dorsal pons. In what is called an internal genu, show the special motor fibers course posteromedially around the abducens nucleus, which lies just off midline. As the special motor fibers reach the posterior surface of the pons, show them form an indentation called the *facial colliculus* in the floor of the fourth ventricle. Next, show the fibers double-back ventrally to complete the genu and then course ventrolaterally through the pons. Show them emerge from its ventrolateral surface. Next, draw the course of the other cranial nerve 7 fibers. They do not perform an internal genu around the abducens nucleus but instead originate lateral to the special motor nucleus and pass ventrolaterally through the pons along with the post-genu special motor roots. Indicate the emergence of these fibers from the pons at the *root exit zone* in the *pontomedullary junction*. Label the exiting special motor fibers as the *facial root proper* and the other exiting fibers as the *intermediate nerve*. But show that all of the cranial nerve 7 fibers bundle together as the *facial nerve*.

Now, add *cranial nerve 8* (the *vestibulocochlear nerve*) alongside the facial nerve and show both cranial nerves pass through the *cerebellopontine angle cistern*. As mentioned with cranial nerve 5, the pharyngeal arch derivatives pass laterally through the basal cisterns. Next, show both cranial nerves 7 and 8 pass through the *internal auditory canal* together. The internal auditory canal is a cavern within the temporal bone of the middle cranial fossa. It serves as passageway for cranial nerve 8, which courses from its peripheral origins in the inner ear through the temporal bone, into the cerebellopontine angle cistern, and centrally to the vestibulocochlear nucleus in the pontomedullary junction. The internal auditory canal also serves as a thoroughfare for cranial nerve 7, as drawn here.

Now, let's draw the peripheral course of cranial nerve 7. Pay particular attention to where along its course different fiber types split off from the main bundle. Note that while in our diagram we discuss the sensory and motor nerves as traveling in the same direction, this is not the actual progression: sensory nerves pass from peripheral to central and motor nerves travel in the opposite way. Still, it is easiest to understand the peripheral anatomy of cranial nerve 7, if we think of them all traveling together from central to peripheral.

The most proximal site where fibers leave the nerve is at the geniculate ganglion. Draw the *geniculate ganglion* near the vestibular labyrinth at the lateral portion of the internal auditory canal. Indicate that this ganglion houses the primary cell bodies of the *general somatic afferent fibers* (which carry sensory information from the outer ear and external acoustic meatus) and the *special visceral afferent fibers* (which carry taste from the anterior two-thirds of the tongue). The geniculate ganglion is analogous to the trigeminal ganglion of cranial nerve 5. What type of sensory cells does the geniculate ganglion house that the trigeminal ganglion does not? Special visceral afferent fibers. The trigeminal ganglion only receives general somatic afferent fibers.

At the geniculate ganglion, show the general visceral efferent fibers (parasympathetic motor fibers) divide into *upper* and *lower branches*. Indicate the *upper branch* follows the *greater petrosal nerve* (aka *major superficial petrosal nerve*) anteromedially toward the trigeminal ganglion in Meckel's cave. Then, show it drop down through foramen lacerum and exit the temporal bone at the pterygopalatine fossa, where it synapses on the *pterygopalatine ganglion*. Knowing that the greater petrosal nerve carries *parasympathetic fibers*, do you think its end target is close to or far from the ganglion? Close to. Remember from the "Peripheral Autonomic Nervous System" chapter that parasympathetic ganglia lie near to or within the wall of their target organ. The post-ganglionic fibers of the greater petrosal nerve innervate the lacrimal, nasal, and palatine glands.

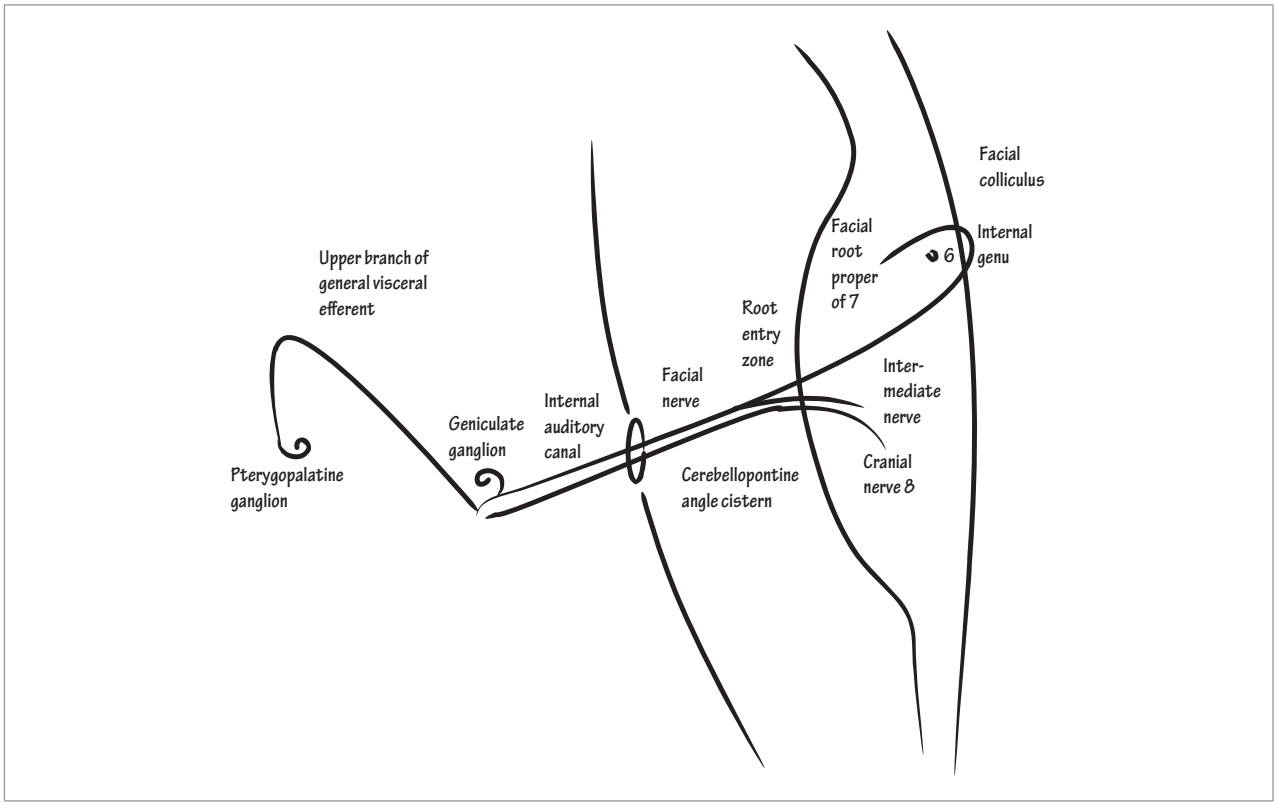


Figure 21-8 Incomplete cranial nerve 7

Now, indicate that the rest of the nerve fibers, including the lower branch of the general visceral efferent fibers, turn posterolaterally at the geniculate ganglion; label this the *tympanic segment*. Show the tympanic segment descend through the mastoid bone. During its descent, indicate the *stapedius nerve* (the special visceral efferent branch) peels away to innervate the *stapedius muscle*. It is easy to appreciate why the stapedius branch comes off within the *tympanic* segment near the vestibulocochlear labyrinth: this is its site of action. The stapedius contracts the neck of the stapes (a middle ear bone), and while it is classically and commonly thought that the stapedius prevents transmission of high-energy sounds through the middle ear ossicles, some believe it acts more eloquently to extract meaningful sound from loud background noise. Regardless, patients with stapedius paralysis complain that sound is too loud, so-called hyperacusis.

Show the facial nerve continue its descent a short distance and then indicate the special visceral afferent fibers (which carry taste from anterior two-thirds of tongue) and lower branch of the general visceral efferent fiber column (which are parasympathetic motor) split off together in the *chorda tympani*. The chorda tympani crosses through the middle ear and then exits the temporal bone through the petrotympanic fissure. Show it merge with *division 3* of *cranial nerve 5* as the *lingual nerve*. From there, show the special visceral afferent fibers spread out over the anterior two-thirds of the tongue and show the general visceral efferent fibers synapse in the *submandibular ganglion*. Indicate the post-synaptic fibers from the submandibular ganglion innervate the submandibular and sublingual glands in the floor of the mouth.

Next, show the *general somatic afferent* and *special visceral efferent fibers* finish their descent through the mastoid bone and exit through the *stylomastoid foramen*. Then, draw them split up and indicate the general somatic afferent fibers carry sensory information from the *pinna*, *external auditory canal*, and *tympanic membrane*—collectively called the *Ramsay-Hunt area*. Classic Ramsay-Hunt syndrome is caused by herpes zoster (which causes shingles) and involves blistering in the distribution of the general somatic afferent fibers of cranial nerve 7 (i.e., the pinna, external auditory canal, and tympanic membrane). There is considerable variation to the distribution of Ramsay Hunt syndrome, however, as there is differential involvement of the cranial nerve 7 and 8 fibers. Depending on the site of the herpes zoster infection along the course of cranial nerve 7, one of many clinical manifestations potentially occurs. If the nerve is affected where it runs with cranial nerve 8 in the internal auditory canal, cranial nerve 8 is affected and, accordingly, patients complain of tinnitus and vertigo.

Finally, show the special visceral efferent fibers innervate the *muscles of facial expression*, which we will learn next.

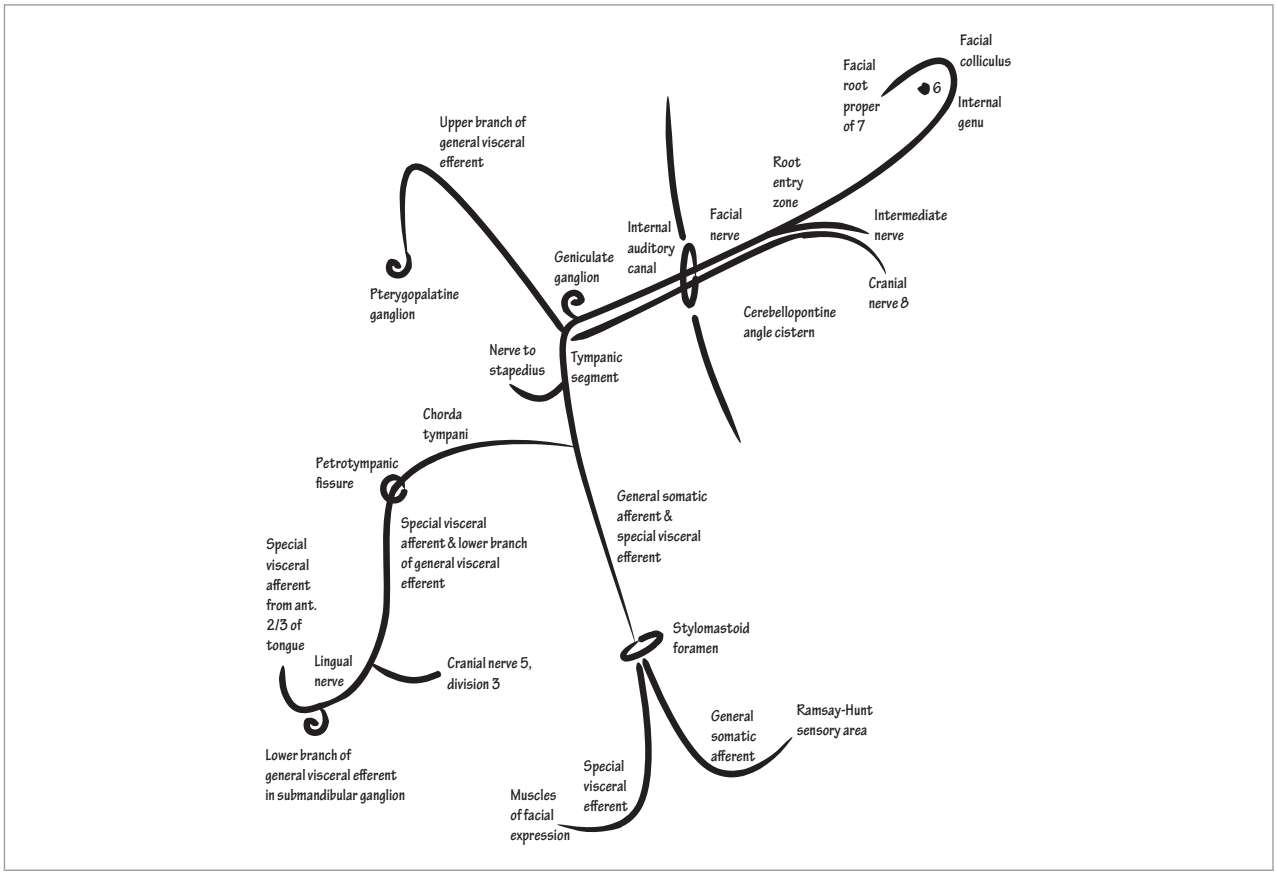


Figure 21-9 Complete cranial nerve 7

What were the important facial muscles we learned earlier? Frontalis and zygomatic major. Frontalis raises the eyebrows and zygomatic major generates a volitional smile. Now, close your eyes with *orbicularis oculi*; this eye sphincter muscle moistens and protects the eyes. When the facial nerve is damaged, the affected eye is dry from orbicularis oculi paralysis. Purse your lips together and use your mouth sphincter muscle to thrust them outward. If the sphincter muscle of the eye is orbicularis oculi, what do you think the sphincter of the mouth is called? *Orbicularis oris*.

We learned that frontalis raises our eyebrows but what wrinkles them? The corrugator. Activate the *corrugator* to furrow your eyebrows. Next, activate *risorius* to stretch your mouth horizontally. Your face will look like it is being pulled back in the wind. Finally, activate the *platysma* to stretch your neck and give yourself the appearance of a webbed neck.

For the sake of completeness, we now list all of the muscles of facial expression. It is not recommended you memorize them but instead think about their pattern of distribution. After the special visceral efferent fibers exit the stylomastoid foramen, they split from the general somatic afferent fibers and trifurcate. The posterior auricular nerve branch courses posteriorly; it innervates the auricular muscles directly behind the ear and the occipital muscle on the back of the skull. Another facial nerve branch passes inferiorly and innervates the posterior digastric and stylohyoid muscles. And the last, most prominent facial branch, travels anteriorly and divides into five smaller branches that run across the face and are listed next, from superior to inferior. The temporal nerve innervates frontalis, orbicularis oculi, corrugator, and procerus; the zygomatic nerve provides additional innervation to orbicularis oculi and innervates zygomatic major (also innervated by the buccal nerve listed next); the buccal nerve innervates buccinator, orbicularis oris, nasalis, levator labii superioris and alaeque nasi, zygomatic major and minor, and levator anguli oris; the mandibular nerve innervates orbicularis oris, mentalis, depressor anguli oris, depessor labii inferioris, and risorius; and the cervical nerve innervates platysma. If you notice, in our discussion of the muscles of facial expression at the start of this section, we learned at least one muscle from each of the anterior nerve branches.

Let's now review the facial nerve and provide a mnemonic for the organization of its peripheral nerve course. Cranial nerve 7 originates in the pons, crosses the posterior fossa through the cerebellopontine angle, and enters the temporal bone through the internal auditory canal. The sensory fibers form their primary synapse in the geniculate ganglion. The most proximal branch to peel away from the facial nerve bundle is the upper branch of the general visceral efferent fibers via the greater petrosal nerve through the pterygopalatine fossa. To feel for your pterygopalatine fossa, palpate laterally along the underside of your cheekbone (aka *zygomatic bone*) at the posterior end of your upper jaw. Also, with your tongue, feel behind your back upper tooth. Here, you will find the pterygopalatine fossa.

Next, the stapedius nerve branch peels away. Snap your fingers to activate this muscle (it contracts the stapes muscle during loud sounds). The next fiber groups that separate are the special visceral afferent fibers to the anterior two-thirds of the tongue and the lower branch of the general visceral efferent group to the submandibular and sublingual glands, in the floor of the mouth. With the tip of your tongue, now press against the floor of your mouth (this action denotes both the special visceral afferent fibers to the tongue and the general visceral efferent fibers to the glandular tissue in the floor of the mouth). The facial nerve exits through the stylomastoid foramen and splits into general somatic afferent and special visceral efferent fibers. Feel just behind your earlobe along the mandible for the stylomastoid foramen and then rub your ear to activate the general somatic afferent fibers. Finally, make a war face to activate your muscles of facial expression to denote the special visceral efferent fibers.

To summarize this sequence: (1) palpate your pterygopalatine fossa behind your upper jaw to denote the proximal branching of the upper general visceral efferent fibers in the greater petrosal nerve; (2) snap your fingers near your ear to activate your stapedius muscle, which peels away in the tympanic segment; (3) push the tip of your tongue into the floor of your mouth to signify the branching in the chorda tympani of the special visceral afferent fibers and the lower general visceral efferent fibers; (4) feel your stylomastoid foramen to denote the exit site of the general somatic afferent and special visceral efferent fibers: touch your outer ear to stimulate the general somatic afferent fibers of the Ramsay-Hunt area and make a war face by activating the special visceral efferent fibers.

When you know the peripheral course for cranial nerve 7, you can localize the site of cranial nerve 7 palsies based on the affected fiber groups. For instance, a facial palsy along the cranial nerve 7 bundle that involves the upper branch of the general visceral efferent fibers should involve the rest of the cranial nerve 7 fibers as well, because the upper branch of the general visceral efferent fibers (the greater petrosal nerve) is the most proximal fiber group to branch from the cranial nerve 7 bundle. On the contrary, a facial palsy that only involves the general somatic afferent fibers and the special visceral motor fibers is only possible with a distal injury (for instance, in the stylomastoid foramen).

Now, we will address cranial nerve 9 (the glossopharyngeal nerve), which comprises several cell fiber types. We learn about the glosssopharyngeal nerve in other chapters of this book, as well, so this section primarily serves as an opportunity to consolidate and complete our understanding of it. Start by drawing the four different central nuclei of cranial nerve 9 in sagittal section. They all group near one another within the medulla. First, draw the sensory nuclei: the *solitary nucleus* and the caudal-most portion of the *spinal trigeminal tract*. Then, draw the motor nuclei: the *inferior salivatory nucleus* and *nucleus ambiguus*. What cell column type constitutes each nucleus? The solitary nucleus

receives special visceral afferent fibers, which encode taste from the posterior one-third of the tongue (aka the base of the tongue) and general visceral afferent fibers, which are parasympathetic afferent fibers from chemoreceptors in the carotid body and baroreceptors in the carotid sinus. The spinal trigeminal tract receives glossopharyngeal general somatic afferent fibers, which cover sensation from the tonsils and pharynx and the Ramsay-Hunt area (the pinna, external auditory canal, and tympanic membrane), but most importantly from the soft palate as the afferent component of the gag reflex. The inferior salivatory nucleus provides general visceral efferent parasympathetic innervation to the parotid gland. The last nucleus of the glossopharyngeal nerve is the nucleus ambiguus. While its role is no longer considered *ambiguous*, it is mixed. Nucleus ambiguus primarily encodes special visceral efferent fibers to the stylopharyngeus muscle, but it also provides a minority of the general visceral efferent parasympathetic fibers for the chemo- and baroreceptor reflexes. The dorsal motor nucleus of the vagus of cranial nerve 10, however, produces the majority of these fibers.

How do we remember the roles of the inferior salivatory nucleus and nucleus ambiguus? The name of the inferior salivatory nucleus is its own reminder that the inferior salivatory nucleus provides salivation to the lower face. It is helpful, too, to remember that the superior salivatory nucleus of cranial nerve 7 also provides secretomotor parasympathetic action to the upper and lower face. What about nucleus ambiguus? If the inferior salivatory nucleus provides parasympathetic motor action, then nucleus ambiguus must be responsible for somatic motor function, and it primarily innervates the stylopharyngeus muscle. But the glossopharyngeal nerve is part of the efferent carotid chemo- and baroreceptor loops, as well, and nucleus ambiguus produces a minority of these general visceral efferent fibers.

Now, draw the origin of *cranial nerve 9* (the *glossopharyngeal nerve*) in the brainstem. It exits the brainstem through the ventrolateral medulla between the inferior cerebellar peduncle and olivary nucleus. Show the glossopharyngeal nerve course laterally in the posterior fossa through the *cerebellomedullary cistern* where it is joined by cranial nerves 10 and 11. All of them cross through the temporal bone of the middle cranial fossa through the *jugular foramen*.

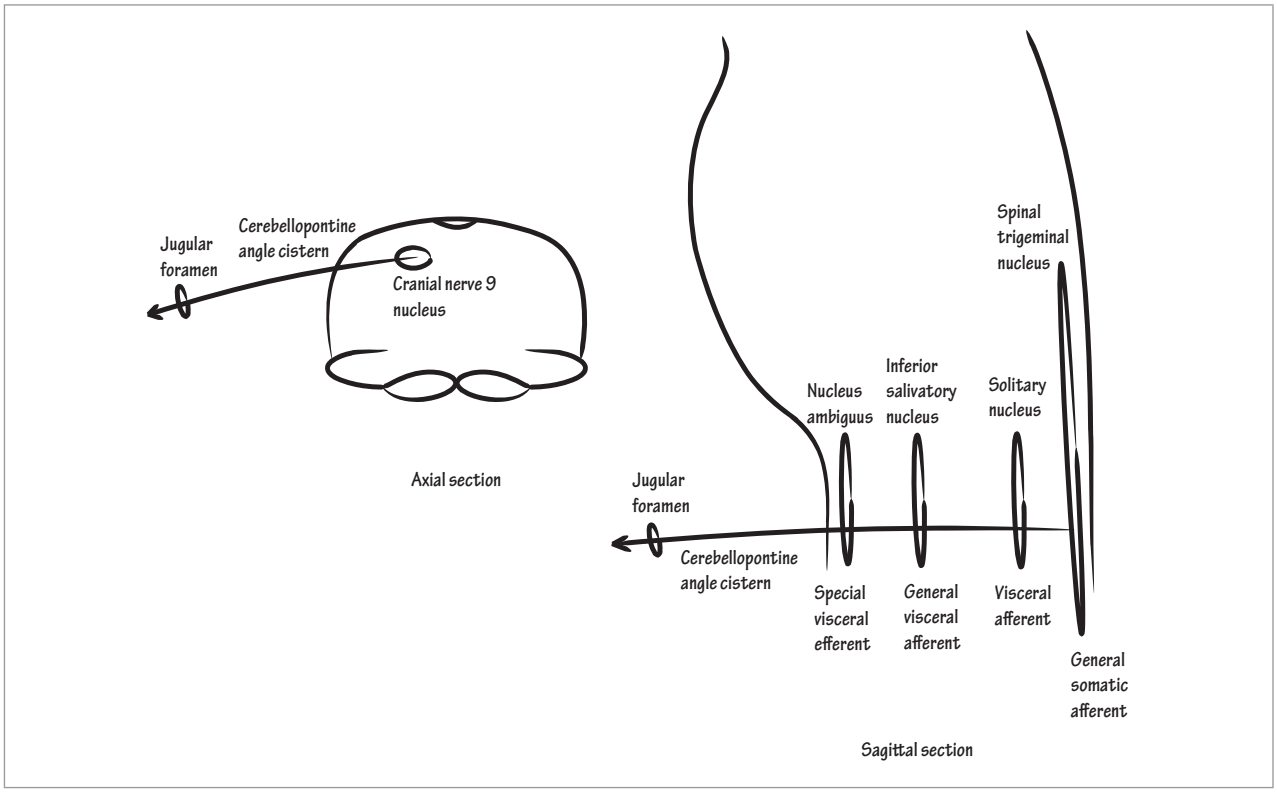


Figure 21-10 Incomplete cranial nerve 9

Next, draw the *superior* and *inferior ganglia of the glossopharyngeal nerve* within the jugular foramen. Indicate the superior ganglion contains the *general somatic afferent* cell bodies whereas the inferior ganglion contains the *general visceral afferent* cell bodies, which is anatomically fitting because the somatic afferent fibers come from the face and the general visceral afferent fibers come from below, from chemo- and baroreceptors in the thoracic cavity. As an aside, ganglia often form in areas of bony protection. Dorsal root ganglia form in or near intervertebral foramina, the trigeminal ganglion forms in Meckel's cave near the dural cavernous sinus, and the geniculate ganglion lies near the internal auditory canal.

Show that all of the glossopharyngeal fibers pass through the jugular foramen into the periphery except for the *general visceral efferent fibers*, which branch from the glossopharyngeal nerve within the jugular foramen. The visceral efferent fibers then cross through the tympanic cavity and exit along with the mandibular nerve through foramen ovale. Show their parasympathetic synapse at the otic ganglion. Then, indicate their post-synaptic fibers join the auriculotemporal branch of the mandibular nerve to innervate the secretomotor *parasympathetic tissue of the parotid gland*.

Although at the outset of this chapter, we established that cranial nerve 5 comprises only special visceral efferent and general somatic afferent fibers, clearly parasympathetic efferent and sensory cell fibers from cranial nerves 7 and 9 join distal branches of the trigeminal nerve to serve additional functions. And don't forget, the spinal trigeminal nucleus receives general somatic afferent fibers from cranial nerves 7, 9, and 10 to expand the sensory coverage of the trigeminal nuclear complex, as well.

Let's indicate the end-targets of each fiber type to complete our diagram of cranial nerve 9. Show the special visceral afferent fibers encode *taste fibers from the posterior one-third of the tongue* and the general somatic afferent fibers are somatosensory fibers from the *tonsils, pharynx*, and *Ramsay-Hunt area* (*pinna*, *external auditory canal*, *tympanic membrane*) but, most importantly, from the *soft palate*. Innervation from the soft palate is especially important because it is the afferent signal for the gag reflex, which is often tested at the bedside; we address the gag reflex in the cranial nerve 10 section, next, because cranial nerve 10 supplies its efferent component. Indicate the general visceral afferent fiber bundle receives parasympathetic sensory afferent fibers from the *carotid body* and the *carotid sinus*. Then, show nucleus ambiguus sends, primarily, special visceral efferent fibers to *stylopharyngeus*, which assists cranial nerve 10 innervated musculature in elevation of the pharynx for speech and swallowing. Also, show nucleus ambiguus sends general visceral efferent parasympathetic fibers to the *carotid body* and *carotid sinus*.

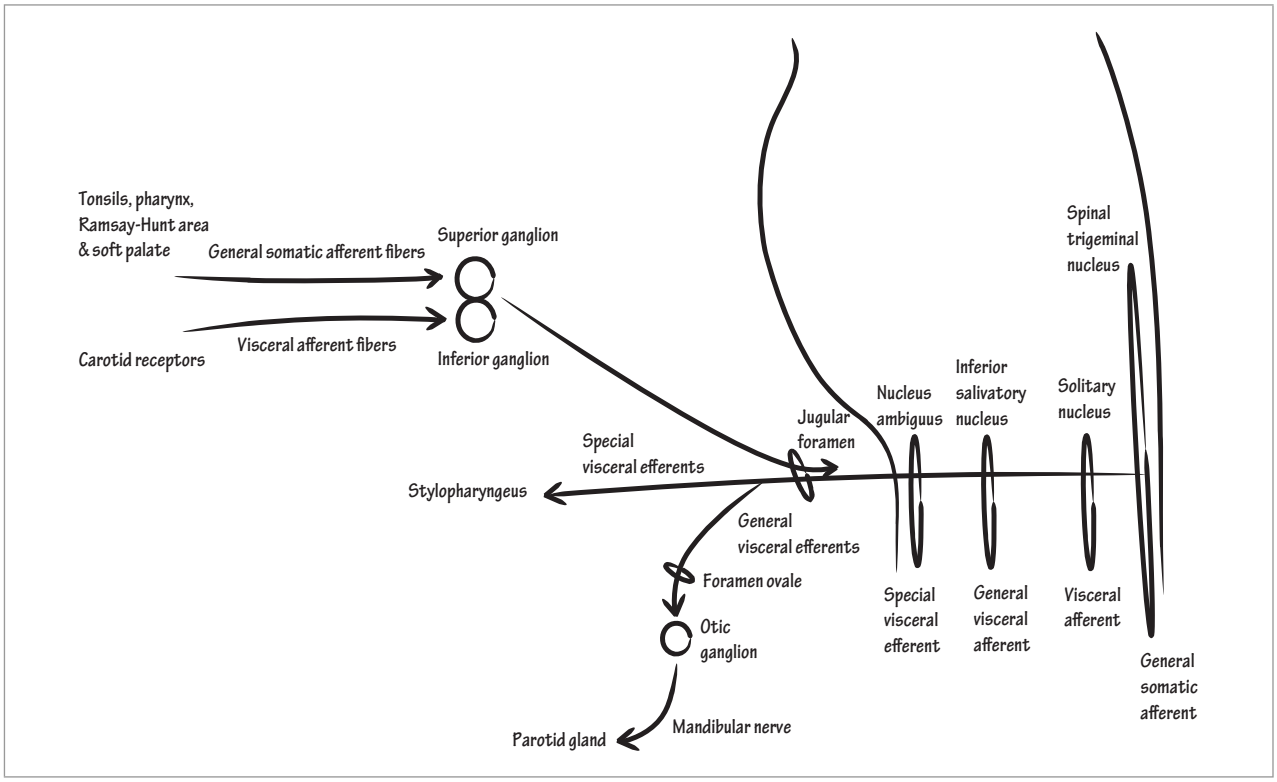


Figure 21-11 Complete cranial nerve 9

Now, let's address cranial nerve 10 (the vagus nerve). Cranial nerve 10 and cranial nerve 9 share similarities in their cell column arrangement, anatomical positions, nerve courses, and actions. They share the same general somatic sensory nucleus (the spinal trigeminal nucleus), visceral afferent nucleus (the solitary nucleus), and special visceral efferent nucleus (the nucleus ambiguus). Both pass through the cerebellomedullary cistern and through the temporal bone via the jugular foramen. Each has superior and inferior sensory ganglia with similar organizational patterns. Both cranial nerves are often tested together through autonomic heart rate and blood pressure challenges and the gag reflex. Lastly, they overlap in their special visceral afferent coverage of taste from the posterior one-third of the tongue and in their general somatic afferent sensory coverage.

Unlike cranial nerve 9, though, cranial nerve 10 wanders far into the abdomen where it is involved in motor and sensory gastric functions; this is the rationale for its name, the vagus nerve, which in Latin means the "wandering nerve." Additionally, unlike cranial nerve 9, cranial nerve 10 receives sensory fibers from the posterior fossa dura. Lastly, cranial nerve 10 widely innervates the pharyngeal musculature whereas cranial nerve 9's pharyngeal muscular innervation is limited to stylopharyngeus. Still, cranial nerves 9 and 10 share many important similarities and they are best understood, and remembered, when learned together.

Now, similar to how we drew cranial nerve 9, let's draw *cranial nerve 10* (the *vagus nerve*). First, draw the cranial nerve 10 sensory arrangement; show the special visceral and general visceral afferent fibers to the *solitary nucleus* and general somatic afferent fibers to the *spinal trigeminal nucleus*. Then, add special visceral efferent fibers from the motor cell column of *nucleus ambiguus*. For the most part, nucleus ambiguus originates *special* visceral efferent fibers, but as mentioned in the previous section, it also sends out *general* visceral efferent fibers via the glossopharyngeal nerve for autonomic cardiac responses. The general visceral efferent fibers of cranial nerve 10 come from the *dorsal motor nucleus of the vagus*, unlike those from cranial nerve 9, which come from the inferior salivatory nucleus. The vagal nerve fibers bundle together and exit ventrolaterally from the medulla.

Like we did with cranial nerve 9, show cranial nerve 10 cross the posterior fossa through the cerebellomedullary cistern and enter the middle cranial fossa through the jugular foramen. The jugular vein runs within the jugular foramen near to cranial nerve 10. A glomus body sits in the wall of the jugular bulb that is similar to the carotid body chemoreceptor of the carotid artery. Glomus jugulare tumors can compress cranial nerve 10 and cause dysarthria and dysphagia.

Next, indicate the *general visceral efferent fibers* act on the *chemoreceptors* of the *carotid body* and *baroreceptors* of the *carotid sinus*. We elaborated on carotid body and carotid sinus reflex loops and discussed the extensive parasympathetic innervation pattern of the vagus nerve in the "Peripheral Autonomic Nervous System" chapter.

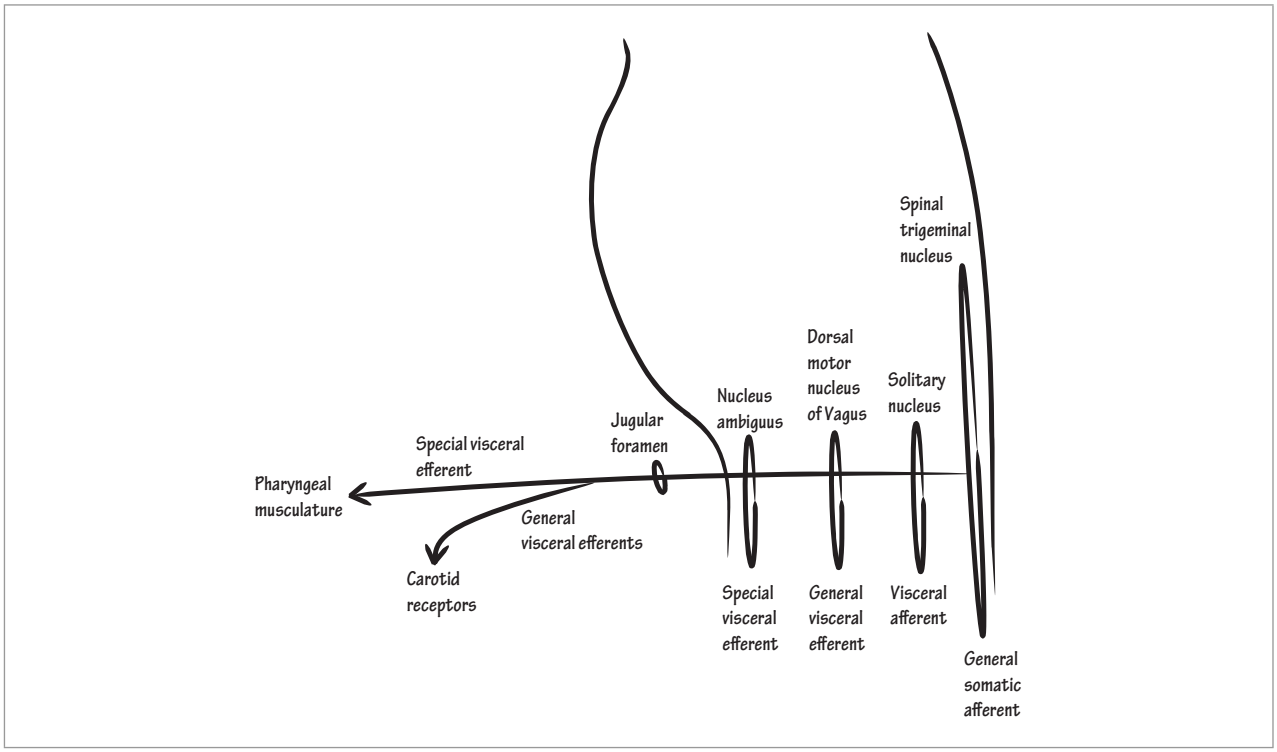


Figure 21-12 Incomplete cranial nerve 10

Now, show the vagal *special visceral efferent fibers* innervate *pharyngeal musculature*. Paralysis of the muscles of the soft palate results in failure of closure of the nasopharyngeal aperture; as a consequence, air escapes through the nose during speech and liquids are regurgitated into the nasal cavity during swallowing. In amyotrophic lateral sclerosis (ALS), there is loss of corticobulbar innervation to the nucleus ambiguus with resultant characteristic nasal pattern speech.

The gag reflex is a valuable clinical tool for testing the integrity of the cranial nerve 9 general sensory afferent fibers and the cranial nerve 10 special visceral efferent fibers. The innervation pattern of the palatine musculature is much like that of genioglossus from the hypoglossal nerve. Corticobulbar fibers from each hemisphere project to each nucleus ambiguus but the predominance of fibers come from the contralateral hemisphere. Thus, unilateral corticobulbar fiber disruption results in a mild degree of contralateral weakness (or none at all), but injury to the nucleus ambiguus itself, or the exiting fibers, causes severe unilateral weakness. When you evaluate for palatal weakness, look for the side of the palate that hangs lower and that is the side that is weak. As a warning, turn a blind eye to the uvula. Authors often remark that a weak palate directs the uvula to the opposite side and they suggest evaluating the direction in which it points to ascertain the side of weakness. This only adds another layer of unnecessary complexity to your evaluation: look at the palate and ignore the uvula.

To perform the gag reflex, brush the soft palate to stimulate the general somatic afferent sensory fibers of cranial nerve 9; this will stimulate cranial nerve 10 special visceral efferents from nucleus ambiguus and cause pharyngeal constriction resulting in a gag. This reflex is often performed in comatose patients to test the integrity of the brainstem.

Do you recall the sensory reception pattern of the glossopharyngeal nerve ganglia? It is the same for the vagus nerve. Show *general sensory afferent* fibers synapse in the *superior ganglion* and *visceral afferent* fibers synapse in the *inferior ganglion*. We remember the sensory reception pattern of the ganglia by the superior–inferior organization of their origins in the periphery. Indicate the general sensory afferent fibers emerge from the *Ramsay-Hunt area* (*pinna*, *external auditory canal*, *tympanic membrane*), *larnyx*, *pharynx*, and, importantly, *posterior fossa meninges*. Then, show the general visceral afferent fibers come from the *thoracoabdominal* and *esophageal-pharyngeal regions*: from the stomach and intestines, esophagus, heart, lungs, aortic arch, and pharynx. Finally, indicate the special visceral afferents come from the *posterior one-third of the tongue*.

The peripheral vagal fiber arrangement is of great interest to cardiothoracic surgeons. The bilateral vagus nerves each involve a superior laryngeal nerve, a recurrent laryngeal nerve, and thoracoabdominal nerve branches. For simplicity, we will only describe the peripheral to central course of the bilateral vagal nerves but, in actuality, they pass bidirectionally. The bilateral superior laryngeal nerves originate from the upper pharynx and tracheo-esophagus and pass directly into the cranium (they are the easiest to imagine). The bilateral recurrent laryngeal nerves originate from the lower tracheo-esophagus and loop under different great vessels before their cranial ascent. The left recurrent nerve swoops under the aortic arch and the right goes under the right subclavian artery. Both ascend from beneath these vessels into the cranium in between the carotid artery and jugular vein on their respective sides. During their ascent, they receive thoracoabdominal vagal branches.

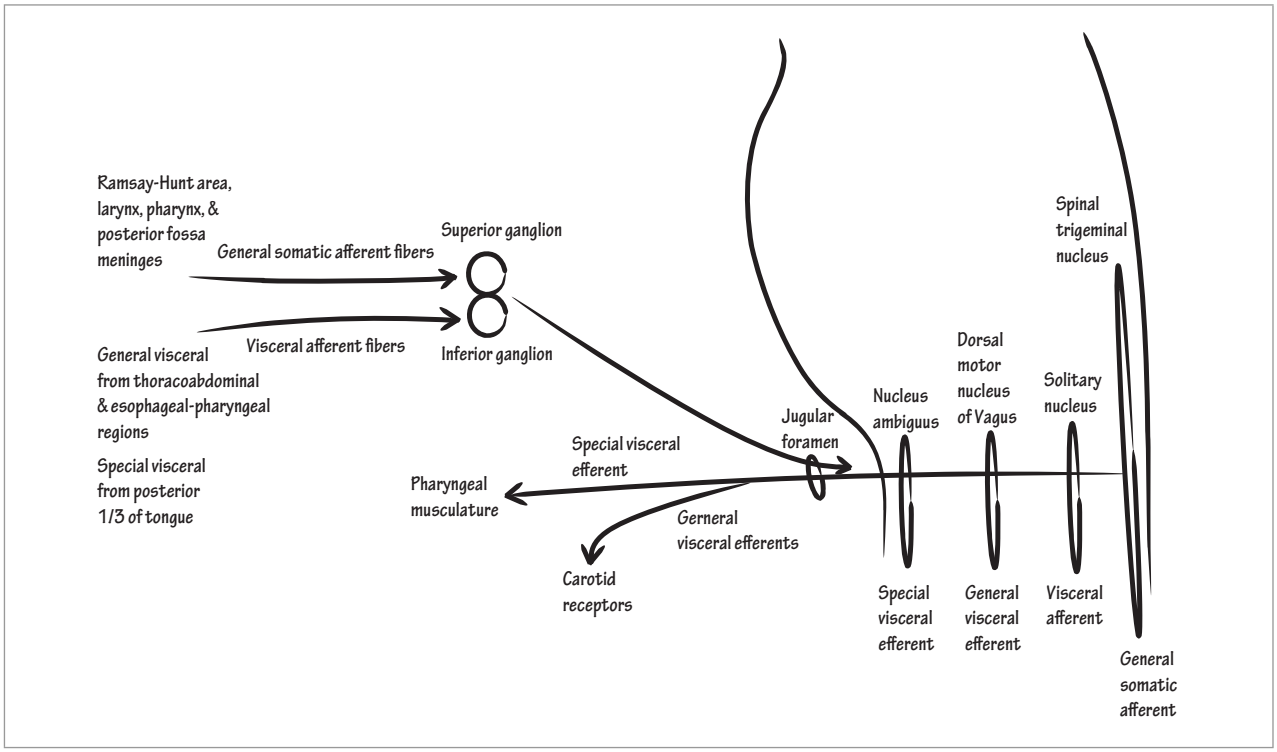


Figure 21-13 Complete cranial nerve 10

Vestibular System

IN THIS CHAPTER, we will draw the peripheral vestibulocochlear system and central vestibular system. The peripheral vestibulocochlear region comprises the outer ear; the external ear canal, which extends through the mastoid process; the middle ear, which encompasses the ossicles in the mastoid process; and the inner ear, which is the bony labyrinth in the temporal bone. The auditory component functions in sound perception and the vestibular component keeps us balanced despite constant motion and also helps us fixate our vision. Move your head about while reading this text. If your vestibular system is intact, you won't become nauseated or have much drop in visual accuity—just a one line drop on a Snellen visual chart (e.g., from 20/20 to 20/25). When the vestibular system is damaged, on the other hand, even slight movements are dizzying.

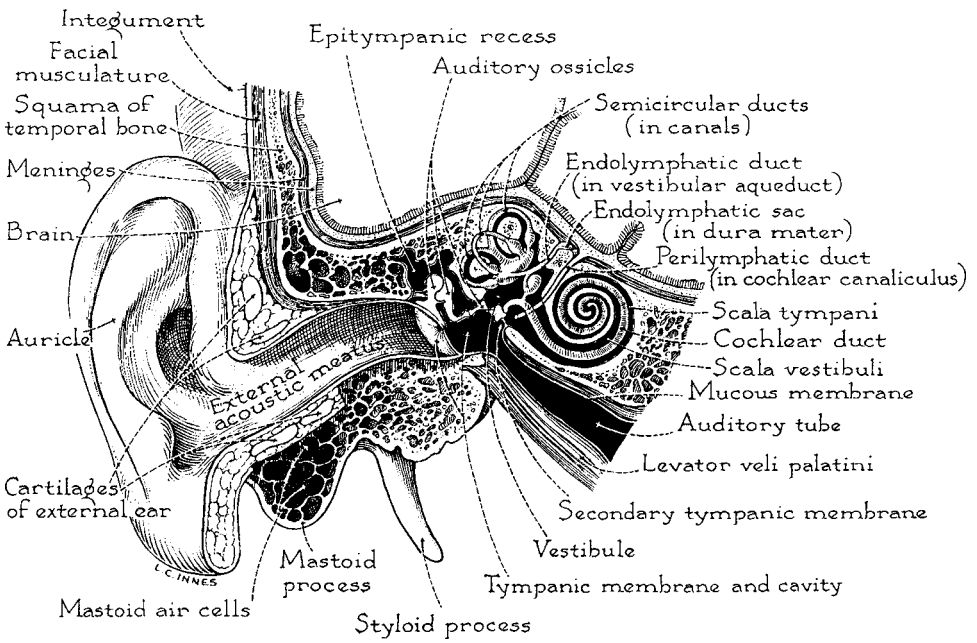


Photo 22-1 Outer, middle, and inner ear

With permission from Baloh, R. W., and V. Honrubia. *Clinical Neurophysiology of the Vestibular System*. 3rd ed., Contemporary Neurology Series 63. Oxford and New York: Oxford University Press, 2001.

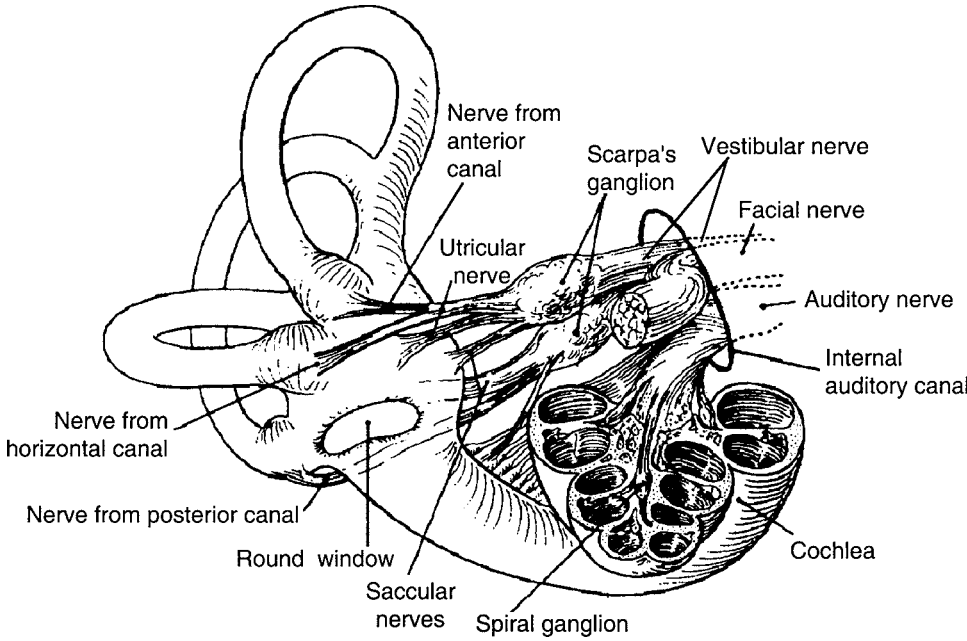


Photo 22-2 Inner ear

With permission from Baloh, R. W., and V. Honrubia. *Clinical Neurophysiology of the Vestibular System*. 3rd ed., Contemporary Neurology Series 63. Oxford and New York: Oxford University Press, 2001.

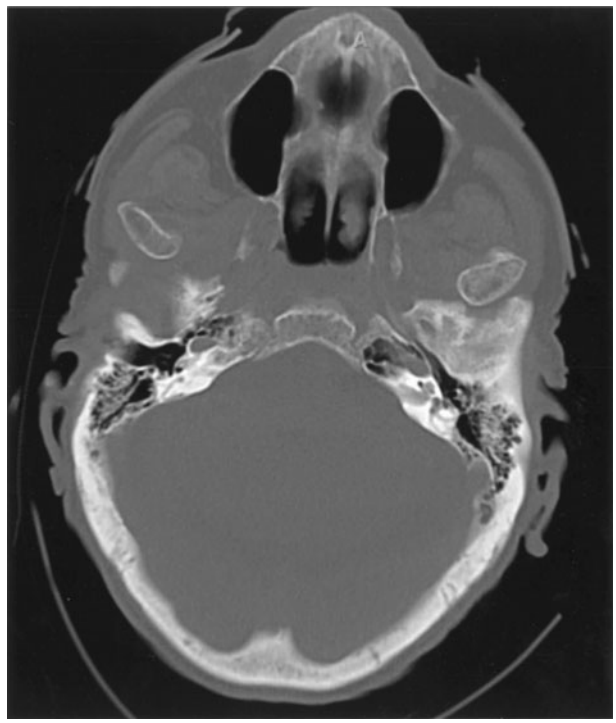


Photo 22-3 Computed tomography of the ear canals

In our first diagram, we will draw the four portions of the ear as they lie within the head: the outer ear, external ear canal, middle ear, and inner ear. Draw a coronal slice through the head of a subject who is facing toward you. The orientation of the diagram will become important when we draw the intricacies of the inner ear, specifically the orientation of the semicircular canals. First, draw the *outer ear* (aka *auricle* or *pinna*). Then, draw the *external ear* (aka *external acoustic meatus* or *auditory canal*) as it extends within the *mastoid process* and ends at the oval-shaped *tympanic membrane* (aka *ear drum*).

Next, draw the *middle ear*, which also lies within the *mastoid process*; it comprises three *ossicles*. From lateral to medial, the ossicles are the *malleus, incus*, and *stapes*, which are most easily remembered by the acronym "MIS." The ossicles are named for the Latin origins of their shapes. Malleus means "hammer," incus means "anvil," and stapes means "stirrup" and each, more or less, resembles these objects. Within the middle ear, draw the *eustachian tube* (aka *auditory tube*) descend from the middle ear into the nasopharynx. Swallow, now, and you will hear your ears "pop." You just contracted your tensor palati and levator palati muscles and opened your eustachian tubes to your nasopharynx, which allowed the pressure in your middle ears to equilibrate with the atmospheric pressure in your nasopharynx.

Next, we will draw the inner ear. It contains an outer, bony labyrinth, which is filled with perilymphatic fluid and an inner, membranous cavity, filled with endolymphatic fluid. Perilymphatic fluid has an electrolyte composition similar to *extra*cellular fluid (serum); it contains high sodium (140 milliequivalents/liter) and low potassium (10 milliequivalents/liter) concentrations. Endolymphatic fluid, on the other hand, has an electrolyte composition similar to *intra*cellular fluid; it contains low sodium (5 milliequivalents/liter) and high potassium (145 milliequivalents/liter) concentrations. Menière syndrome is an inner ear syndrome thought to be due to pathologically elevated endolymphatic sodium concentration. It presents with bouts of vertigo, low-frequency hearing loss, and ear fullness (aka *tinnitus*) that sounds like ocean rumbling. The next time you are at the beach, blow into a shell to mimic the sound. Patients with Menière syndrome are treated with salt-wasting diuretic medications and in severe, refractory cases sometimes vestibular ablation is performed. Are you aware of a drug that selectively causes vestibular ablation without affecting the cochlea and hearing? Aminogylcosides, specifically gentamicin, are toxic to vestibular hair cells but do not affect the cochlea, and are occasionally used to treat Menière syndrome in extreme circumstances.

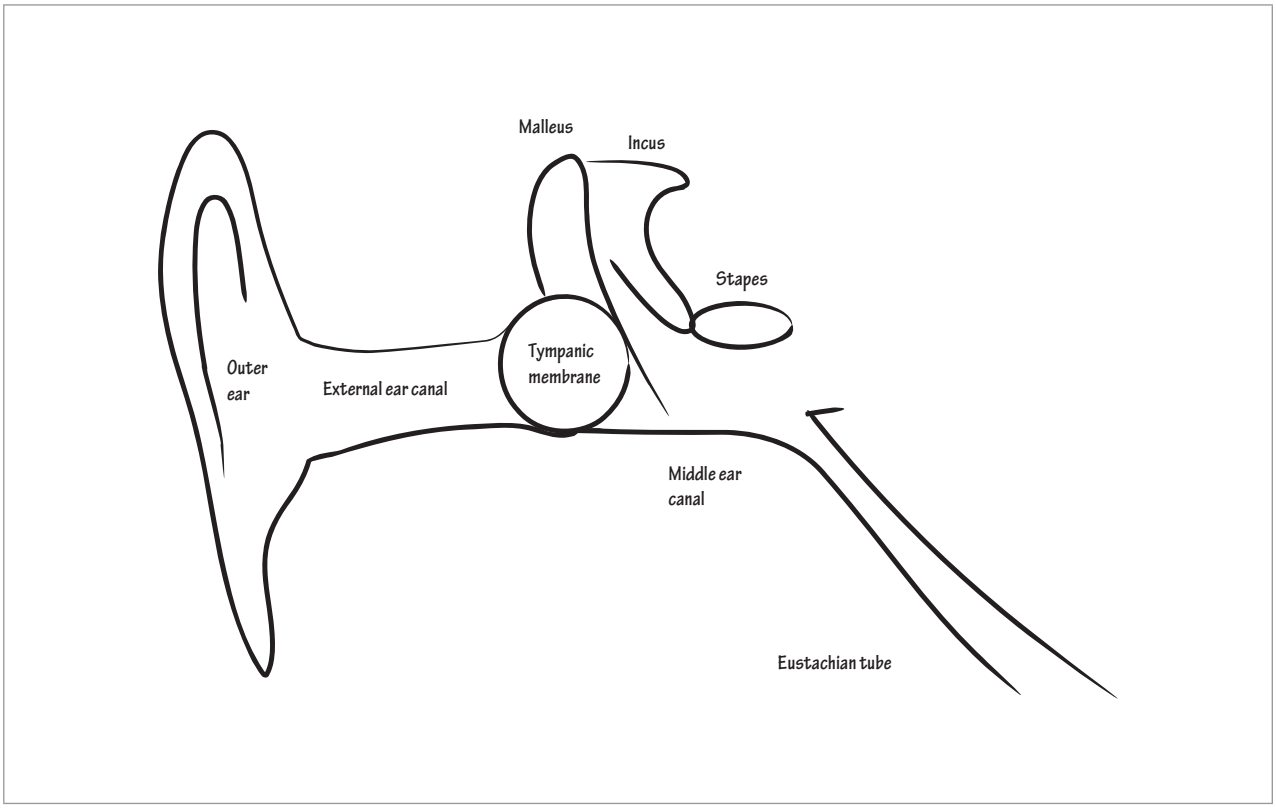


Figure 22-1 Incomplete ear

Now, we will draw the bony labyrinth of the inner ear. It lies within the petrous portion of the temporal bone. We divide the inner ear into three different parts: the semicircular canals, which lie supero-laterally and serve vestibular function; the cochlea, which lies antero-inferiorly and serves auditory function; and the vestibule, which lies between them and assists with both functions. We will begin with the *cochlea*, which bears resemblance to a snail's shell. Three ducts form within the cochlea: vestibular, cochlear, and tympanic. The vestibular and tympanic ducts are interconnected; *peri*lymphatic fluid runs between them. The cochlear duct is a membranous partition that separates the vestibular and tympanic ducts. It contains *endo*lymphatic fluid, and also the auditory sensory organ, the organ of Corti, along its basilar membrane. Fluid waves are transmitted down the vestibular duct to the tympanic duct, and in the process, they vibrate the cochlear duct and excite the organ of Corti. Show the inner loop is the *vestibular duct* (aka *scala vestibuli*), the middle duct is the *cochlear duct* (aka *scala media*), and the outer duct is the *tympanic duct* (aka *scala tympani*). Attach the *vestibule* onto the vestibular duct of the cochlea.

Then, on the lateral face of the vestibule, draw the *oval window*; it is the small window at the footplate of the stapes. The oval window is the connection between the middle and inner ears. Sound transduction is transmitted from the stapes of the middle ear across the oval window to the inner ear and fluid is displaced through the vestibular duct. Next, attach the *round window* to the tympanic duct. The tympanic duct shares its name with the flexible diaphragmatic covering of the round window, called the *secondary tympanic membrane* (aka *Scarpa's membrane*): remember that the *primary* tympanic membrane separates the outer ear canal from the middle ear. Show the oval window displace fluid through the vestibular duct, which empties into the tympanic duct at the apex of the cochlea (aka *helicotrema*). The round window bends out of the cochlea when a pressure wave is transmitted through the tympanic duct. Without the round window, the oval window would be unable to displace fluid because the perilymphatic fluid, itself, is incompressible.

Now, let's address the cochlear duct. High-frequency sounds activate hair cells at the base of the cochlea whereas low-frequency sounds activate hair cells at its apex. Sound reception within the cochlea is not a reflection of sounds created but rather of sounds received. So, if you try to relate the tonotopical arrangement of the cochlea to the sounds of different musical instruments, you will understand it backwards. Base instruments produce low, heavy booming sounds and narrow-diameter instruments create high-pitched sounds but the tonotopical arrangement of the cochlea is just the opposite. Tonotopy of the cochlea is determined by the basilar membrane width of the cochlea, which is thinnest and stiffest at the base of the cochlea and thickest and floppiest at its apex, so the broad base of the cochlea receives high-frequency sounds and the apex receives low-frequency sounds.

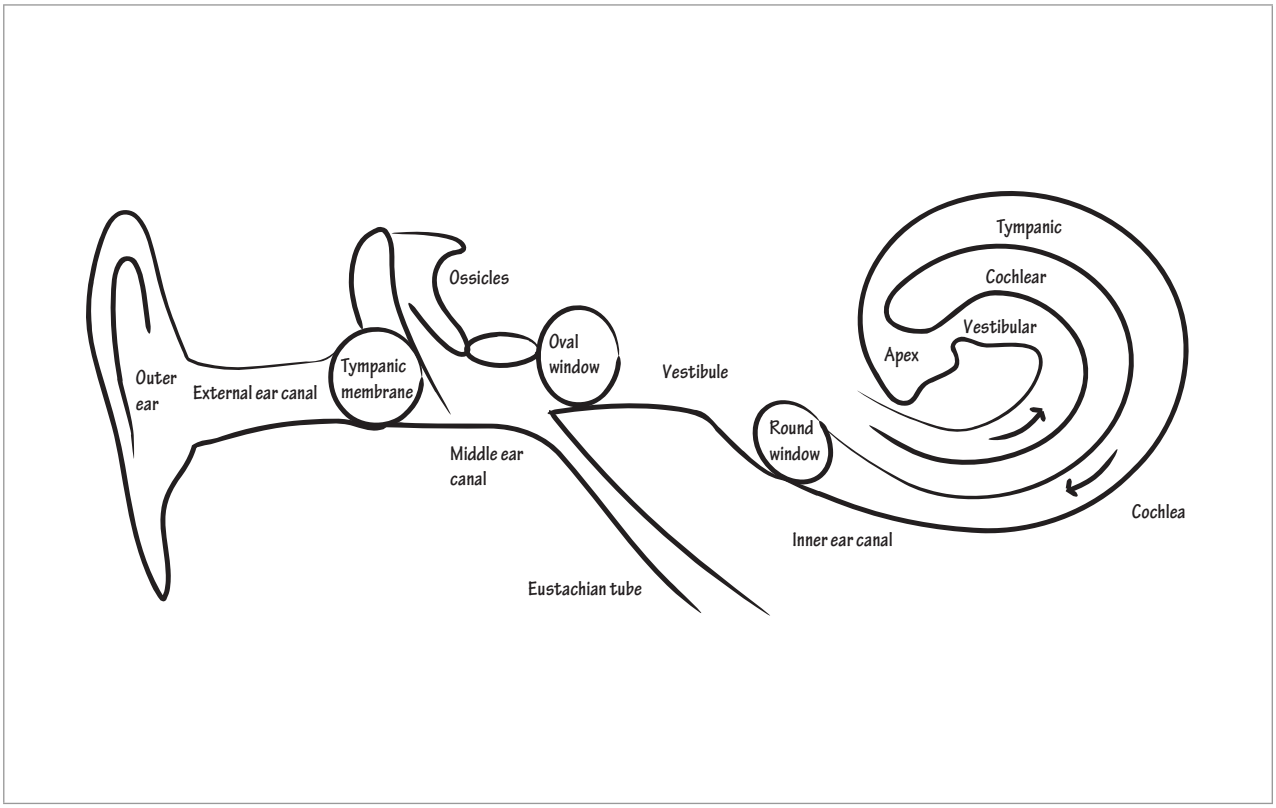


Figure 22-2 Incomplete ear

Draw the *cochlear* segment of the *vestibulocochlear nerve* as it exits the cochlear duct and traverses the *cerebellopontine angle* via the *internal acoustic meatus* (aka the internal auditory canal) to the *vestibulocochlear nucleus* in the *pontomedullary junction* of the brainstem. Prior to entering the internal acoustic meatus, the *cochlear* segment of the *vestibulocochlear nerve* joins the *cochlear ganglion* and the *vestibular* component of the *vestibulocochlear nerve* joins the vestibular ganglion known as Scarpa's ganglion. We will draw the components of the vestibulocochlear nucleus and its central projections when we draw the rest of the central portions of the vestibular and auditory systems at the end of this chapter and in the "Central Auditory Pathways" chapter.

Now, return to the vestibule. Show the two *otolith organs*: the *saccule* and the *utricle*. The otolith organs perceive linear acceleration (i.e., movement of the head through the environment). Move your head toward this book. Your otolith organs perceive the forward movement and the saccule detects downward gravitation pull. The semicircular canals, which we will draw next, detect rotation: spin your head about and you will maintain your balance.

Along the supero-lateral surface of the vestibule, attach the three semicircular canals in the following steps. First, draw the vertically oriented *anterior semicircular canal* facing antero-laterally. Then, draw the lateral-facing *horizontal semicircular canal* in the horizontal plane. Finally, draw the *posterior semicircular canal* in the vertical plane facing postero-laterally. All three semicircular canals lie in perpendicular to one another and together are able to perceive any of the three-dimensional directions of rotational acceleration (aka *angular acceleration*), which is the rotation of the head in the *x*, *y*, or *z* axis. The orientation of these semicircular canals is admittedly difficult to appreciate from this diagram. We will show how the canals act on eye movements in the next section of this chapter to elucidate their orientation, so continue on even if you are having trouble understanding their directionality.

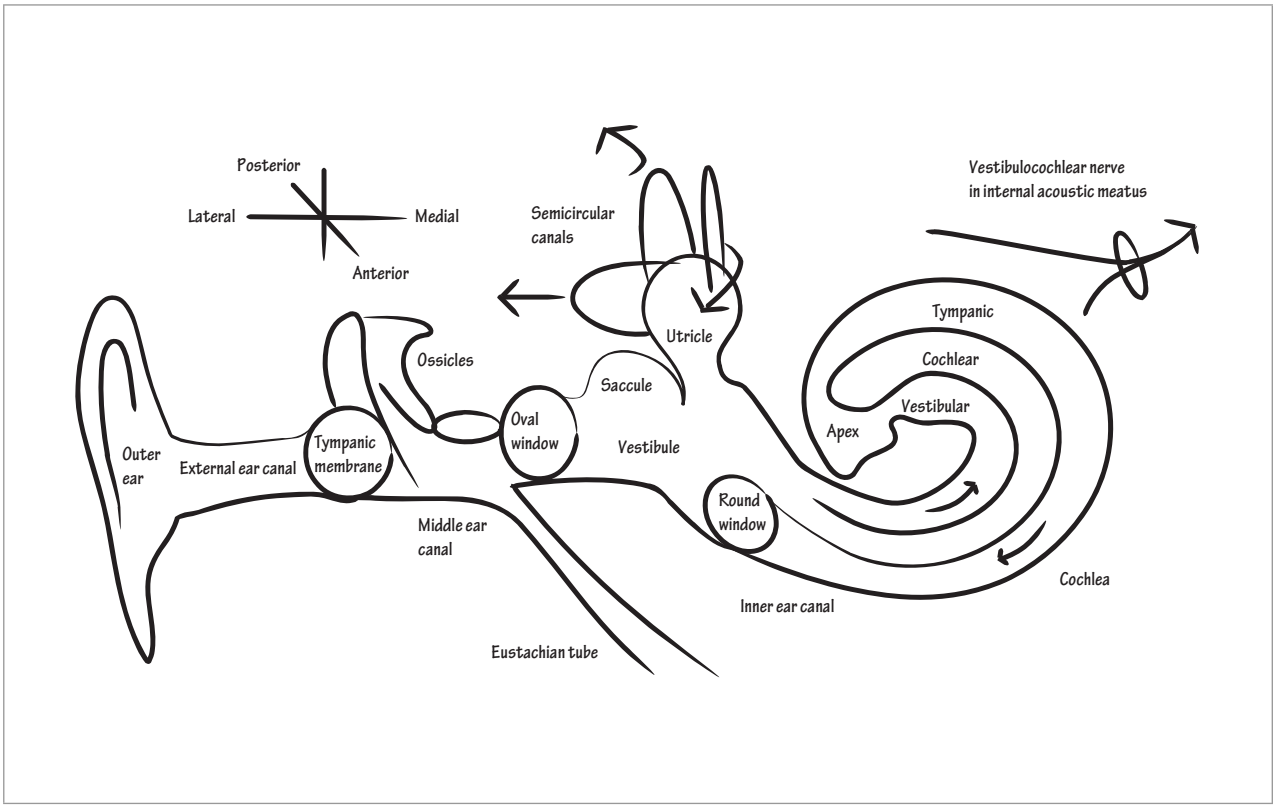


Figure 22-3 Complete ear

Now, we will generate an axial diagram looking down from above to clarify the planes of the semicircular canals. Draw an oval-shaped cranium. Label the anterior portion of the cranium at the top of the page and the posterior portion at the bottom. Include the nose to illustrate this orientation. Then, draw the left *anterior semicircular canal* facing antero-laterally and the left *posterior semicircular canal* in perpendicular to it, facing postero-laterally. Next, include the laterally facing left *horizontal canal*. Use arrows to illustrate the planes of orientation. Now, draw the right side semicircular canals, which are the mirror image of the left.

When the canals are activated, they produce eye movements in their plane of orientation. Together, show the left anterior canal and right posterior canal drive the eyes along a diagonal from left anterior to right posterior; the right anterior and left posterior canals drive the eyes along a diagonal from right anterior to left posterior; and the horizontal canals drive the eyes laterally. While the horizontal canals drive the eyes in the horizontal plane, the anterior and posterior canals drive the eyes in the vertical and torsional planes to achieve their designated movements.

Anterior canals produce upward movements and posterior canals produce downward movements. From the observer's perspective, the right side canals produce torsional movements in a clockwise direction whereas the left side canals produce torsional movements in a counterclockwise direction. Thus, from the observer's perspective, stimulation of the right anterior canal causes the eyes to move up and rotate clockwise.

In benign paroxysmal positional vertigo, debris within the canals stimulates eye movements through a negative pressure pathophysiology. It most often triggers the posterior canal. If the right posterior canal is activated, then, from the observer's perspective, the eyes are driven down and rotate clockwise; use your hands to feel the movement, if you are confused. Unfortunately, the movement is named by the direction of its nystagmus, which is the *fast phase* of the movement and occurs in the *opposite direction* of the slow-phase movement. From the observer's perspective, then, the nystagmus for right side anterior canal activation is downward and counterclockwise; for the left side anterior canal it is downward and clockwise; for the right posterior canal it is upward and counterclockwise; and for the left posterior canal it is upward and clockwise. The best way to remember this is to think about the clinical scenario in which you will test it. When testing for benign paroxysmal positional vertigo, you perform the Dix-Hallpike maneuver. To mimic this maneuver, turn your head toward the suspected problem ear (let's use the left side) and then lie flat on your back, with the culprit ear directed toward the floor. If the posterior canal is the problem, as it most commonly is, the upper pole of the nystagmus will be directed toward the down ear (i.e., the undermost ear), in this case, the left.

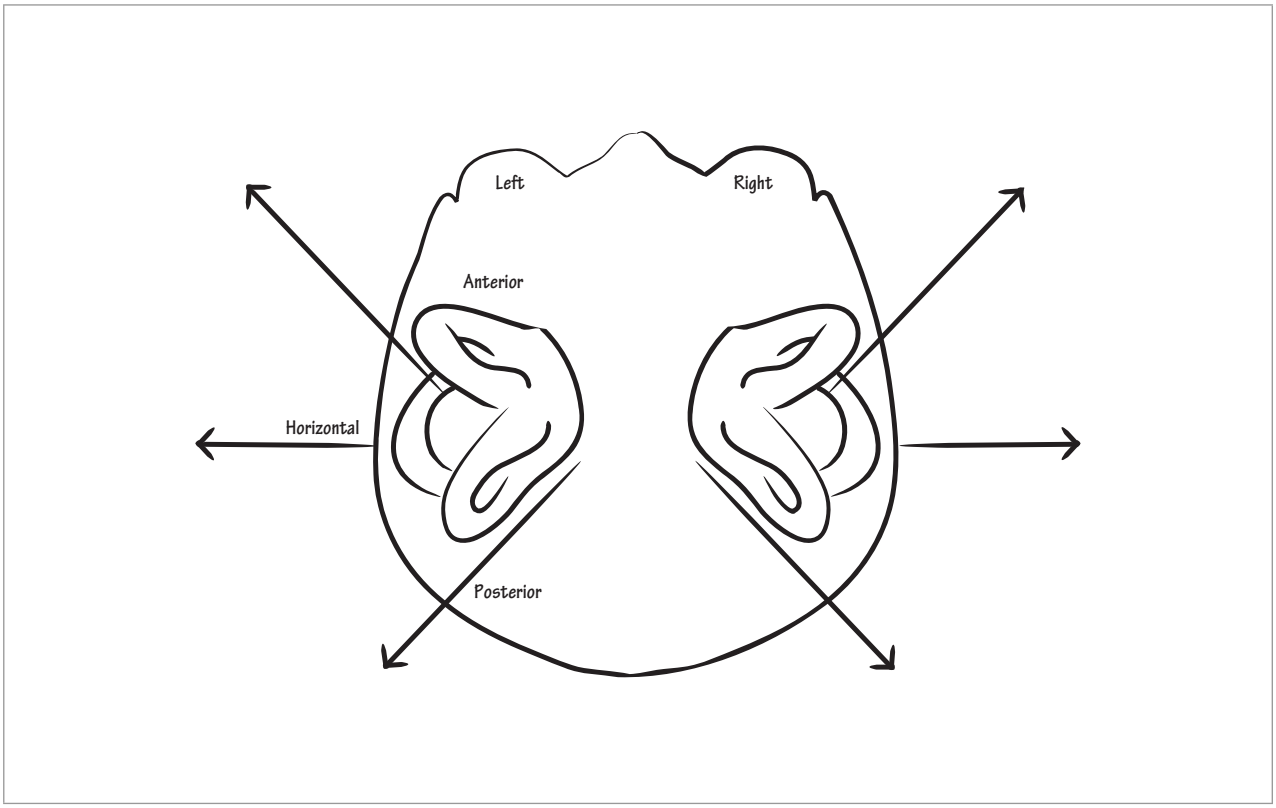


Figure 22-4 Semicircular canal directions

Now, we will draw the central vestibular pathways, which originate from the four vestibular nuclei that form the vestibular nuclear complex. The vestibular labyrinth provides the primary afferent fibers to the vestibular complex and also communicates with the midline cerebellum. The vestibular complex targets the ocular nuclei as part of the vestibulo-ocular pathway; spinal motor nuclei as part of the spinal vestibular pathway; and the midline cerebellum in its communication with the flocculonodular lobe. Drawing the central vestibular pathways is tedious. It involves differential involvement of the four vestibular subnuclei and varying degrees of ipsilateral and contralateral projections. The most important features of the central vestibular pathways are the following: (1) the vestibular complex helps control eye movements through the vestibulo-ocular pathway and helps maintain trunk and forelimb posture through the vestibulospinal and reticulospinal tracts, (2) both the vestibular labyrinth, itself, and the vestibular nuclei communicate with the flocculonodular lobe, (3) there is differential involvement of the vestibular nuclei in these different tasks—the medial vestibular nucleus is involved in all of the afferent and efferent pathways, the superior vestibular nucleus is involved in the vestibulo-ocular mechanism, and the lateral and inferior vestibular nuclei are involved in the vestibulospinal functions. If you know these points and learn the vestibulo-ocular pathway in the "Eye Movements" chapter and are not interested in drawing these pathways, skip to the next chapter.

To draw the vestibular complex and the central vestibular pathways, first draw a coronal section through the brainstem. Then, draw a small vestibular labyrinth off to its side. Show the vestibulocochlear nerve pass from the vestibular labyrinth through the internal acoustic meatus to the *vestibular nuclear complex* in the pontomedullary junction of the brainstem. Divide the vestibular complex into four separate nuclei: *superior, medial, lateral*, and *inferior*. For simplicity, we will only draw the most clinically relevant pathway, the vestibulo-ocular pathway, and then discuss the others.

Both the *superior* and *medial vestibular nuclei* are responsible for the *vestibulo-ocular reflex*. Show that they send fibers up the brainstem along the *medial longitudinal fasciculus* to the *opposite abducens nucleus*, which, as we will show in the "Eye Movements" chapter, then sends fibers back across midline to the oculomotor and trochlear nuclei in the midbrain.

Next, we will discuss how the medial, lateral, and inferior vestibular nuclei are responsible for the vestibulospinal reflex through two separate pathways. The medial and lateral nuclei send fibers directly to spinal motor neurons through the vestibulospinal tracts while the inferior nucleus sends its fibers first to the reticular formation and then on to the spinal cord via the reticulospinal tract.

Efferent *medial vestibular nucleus* fibers descend the medial longitudinal fasciculi and become the *medial vestibulospinal tracts*, which innervate cervical and upper thoracic motor nuclei. Note that the medial vestibulospinal pathway is responsible for *head* and *neck posture* maintenance. The *lateral vestibular nucleus* sends fibers down the ipsilateral *lateral vestibulospinal tract*, which are responsible for *forelimb antigravity posture*. Efferent *inferior vestibular nucleus* fibers synapse in the reticular formation and descend in the *reticulospinal tract* to provide additional *forelimb antigravity posture*.

These pathways complete the primary vestibular afferent pathways and the efferent vestibulo-ocular and vestibulospinal pathways. Next, let's discuss the afferent and efferent vestibulocerebellar pathways. The vestibular labyrinth and the vestibular nuclei, both, communicate with the midline cerebellum. Fibers from the *inferior* and *medial vestibular nuclear complex* ascend the ipsilateral brainstem and enter the *inferior cerebellar peduncle* in route to the *uvula* and *flocculonodular lobe* in the midline cerebellum, and primary vestibulocerebellar afferents from the *vestibular labyrinth*, itself, course into the brainstem at the pontomedullary junction and terminate in the *vermis* in the midline cerebellum. Finally, efferent cerebellovestibular fibers pass from the *midline cerebellum* to the bilateral *vestibular nuclear complexes*.

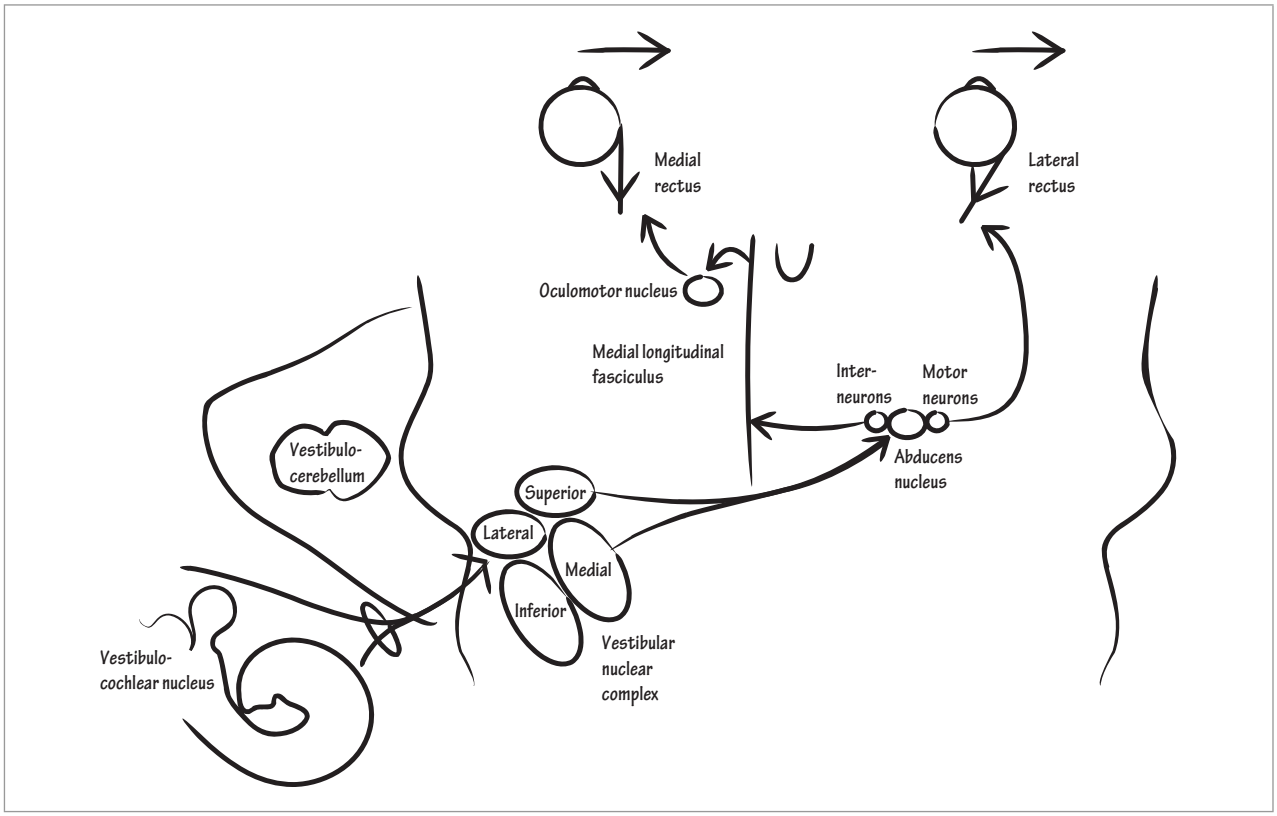


Figure 22-5 Central vestibular system: vestibulocochlear inputs, vestibular nuclear complex, vestibulocerebellum, and vestibulo-ocular pathway

Skull Base

SKULL ANATOMY (aka cranial bone anatomy) is outside of the strict domain of neuroanatomy but is still important to learn. Neuroanatomy books often provide a cursory review of skull anatomy and related anatomical subjects, such as facial musculature, the oral and nasal cavities, blood vessels of the head and neck, and the ear and vestibular structures. However, if you want a complete review of these topics, look for an anatomy book on the head and neck. In this chapter, we will draw and discuss the aspects of skull anatomy relevant to neurology. We will draw the skull base and label the cranial bones, then draw the cranial fossae, and afterwards the foramina at the base of the skull.

The cranial bones in the base of the skull, from anterior to posterior, are the frontal bone, which houses the cribiform plate; the sphenoid bones, which contain the anterior clinoid processes; the temporal bones; and the occipital bone. The parietal bones lie along the sides and superior surface of the skull. It's challenging to learn the jig-saw layout of these bones and if you are not interested in their details, skip ahead; otherwise, let's proceed.

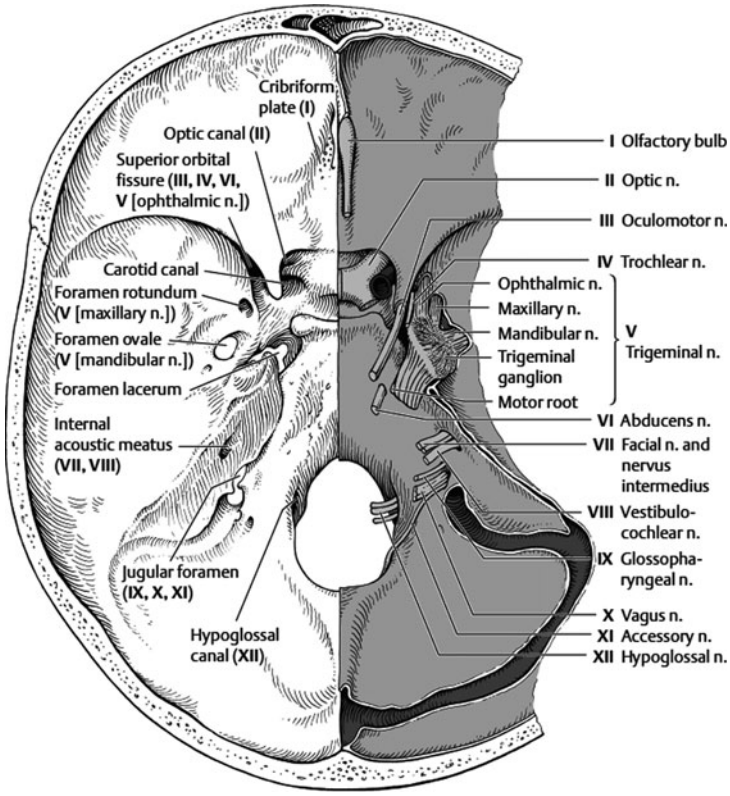


Photo 23-1 Sites of exit of the cranial nerves and neurovascular structures from the skull

From Baehr, M., Frotscher, M., and Duus, P. *Duus' Topical Diagnosis in Neurology: Anatomy, Physiology, Signs, Symptoms*. 4th completely rev. ed. Stuttgart and New York: Thieme, 2005 (Reprinted with permission).

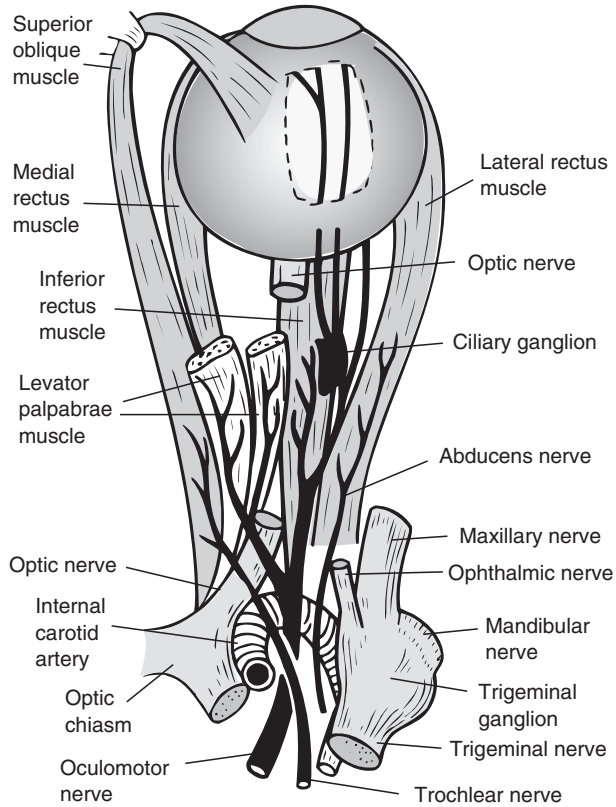


Photo 23-2 Axial view of cavernous sinus and orbit

With permission From Brodal, P. *The Central Nervous System: Structure and Function*. 3rd ed. New York: Oxford University Press, 2004.

Begin our drawing of the bones of the base of the skull with an outline of the skull in axial plane. We will only use half of the skull base in our diagram because both sides are the same. First, label the anterior one-third of the skull base as the *frontal bone*. In its midline, indicate the steeply peaked crista galli and the surrounding *cribiform plate* of the *ethmoid bone*. Next, show the sphenoid bone lies behind the frontal bone; it is divided into two sets of wings that look like opposing batwings. The anterior set is the lesser wing of the sphenoid bone and the posterior set is the greater wing of the sphenoid bone. First, draw the *lesser wing of the sphenoid bone*; draw its batwings oriented towards the occiput. Then, draw the *greater wing of the sphenoid bone* with its batwings oriented toward the frontal bone. The topography of the sphenoid wings is as follows. The lesser sphenoid wing angles up over the greater wing, and the greater wing slopes downward. Label the protuberance along the ridge of the lesser wing as the *anterior clinoid process*. The bilateral anterior clinoid processes are important orientational points for the different fossae and foramina of the base of the skull.

Now, draw one of the heart-shaped *temporal bones* posterior to the greater wing of the sphenoid bone. Divide it into medial and lateral halves. Label the lateral half as the *squamous portion* and the medial half as the *petrous portion*. The medial petrous portions of the temporal bones are sloped upward. Next, draw the *occipital bone* in the posterior-center of the skull base between the temporal bone and the greater wing of the sphenoid bone; it extends back to the occiput. In the anterior one-third of the occipital bone, draw the *foramen magnum*. This is the entry/exit site for the brainstem. In a separate diagram, we will draw the other major foramina in the base of the skull; they are the additional entry/exit sites for the cranial nerves and the key intracranial neurovascular structures. Along the lateral edges of the skull base, label the paired *parietal bones*. They, along with the frontal bone, comprise the superior surface of the skull and are not involved in the topography of the cranial fossae.

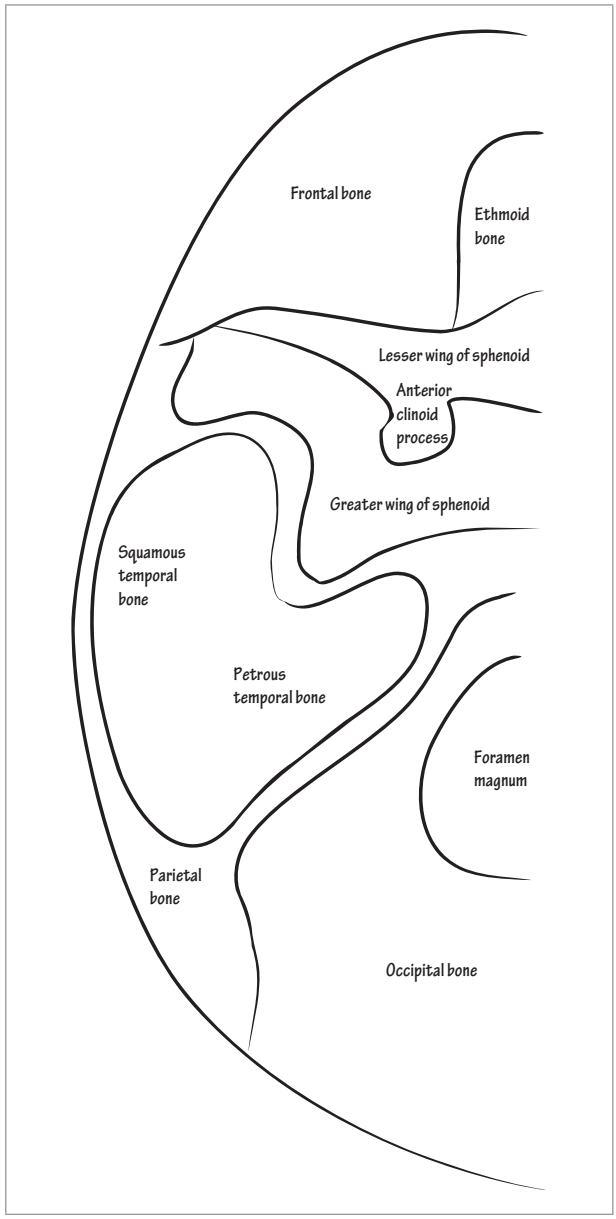


Figure 23-1 Bones of skull base

Now, we are able to demarcate the different cranial fossae. Simply put, the anterior cranial fossa lies in front of the anterior clinoid processes; the middle cranial fossa lies between the anterior clinoid processes and the petrous ridge of the temporal bones; and the posterior cranial fossa lies behind the petrous ridge of the temporal bone. The cranial fossae are depressions in the skull base that compartmentalize different regions of the base of the brain; they do not house all of the lobes of the brain as certain lobes lie superior to the plane of the skull base.

To draw these fossae, first draw a dotted line that runs along the lesser wing of the sphenoid bone. Anterior to the dotted line, show the skull forms a *ridge* and posterior to it, show the skull forms a *valley*. Label the *anterior cranial fossa* as the region from the ridge of the lesser wing of the sphenoid bone forward. What bones constitute the anterior cranial fossa? The frontal bone, ethmoid bone, and lesser wing of the sphenoid bone. What lobe of the brain sits inside this fossa? The frontal lobe. Next, dot a diagonal line through the petrous temporal bone from posterolateral to anteromedial. In front of the line, indicate the skull peeks into a *ridge* and behind it, show it slopes into a *valley*. Show the *middle cranial fossa* is the skull depression that spans from the lesser wing of the sphenoid bone to the petrous ridge of the temporal bone. What bones form the middle cranial fossa? The greater wing of the sphenoid bone, the squamous temporal bone, and the ridged portion of the petrous temporal bone. What lobe of the brain lies within it? The temporal lobe. Lastly, indicate the *posterior cranial fossa* comprises the petrous temporal valley and occipital bone. And what structures sit inside of it? The brainstem and cerebellum.

Now, draw a mid-sagittal section of the skull to highlight the different depths of the cranial fossae. In particular, we want to illustrate the vastly different depths of the anterior and posterior cranial fossae. In this mid-sagittal section, indicate the *anterior cranial fossa* lies in front of the *anterior clinoid process*, the *middle cranial fossa* lies between it and the *ridge of the petrous temporal bone*, and the *posterior cranial fossa* lies behind it. Show a significant step-down between the middle and posterior cranial fossae.

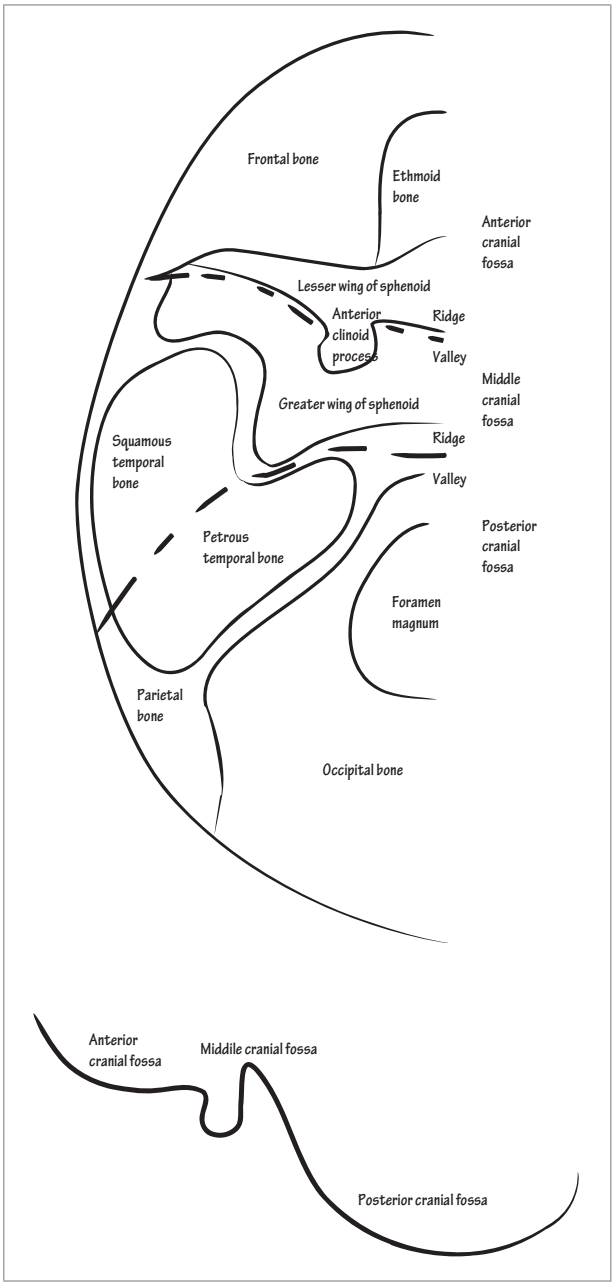


Figure 23-2 Cranial fossae

Now, we're ready to draw the foramina at the base of the skull. The cranial nerves and neurovascular structures are often damaged at these exit sites, so they are important to learn. Certain combinations of nerve and neurovascular injuries clue us to basal skull disease.

Let's start anteriorly with the most easily neglected foramina of the group. Draw a few small circles in the cribiform plate to show the *foramina of the cribiform plate*, which contain the *olfactory nerve bundles*. Underneath the cribiform plate lies the nasal cavity. When the cribiform plate is damaged, cerebrospinal fluid leaks into the nasal cavity and drips out of the nostrils (called rhinorrhea). Next, draw the *anterior clinoid process*; it is a landmark of the optic canal and superior orbital fissure. Medial to it, label the *optic canal* and lateral to it label the *superior orbital fissure*. Show the *optic nerve* traverses the optic canal and the *oculomotor*, *trochlear*, and *abducent nerves*, and the *first division of the trigeminal nerve* (aka *V1*, *the ophthalmic nerve*) pass through the superior orbital fissure. The first division of the trigeminal nerve contains three branches: nasociliary, frontal, and lacrimal, which are sometimes listed individually.

Let's stop and address the neurovascular structures that run through the aforementioned foramina. While they are less often discussed than the cranial nerves, they are easy to learn and are clinically relevant. The vessels that pass through the foramina share similar nomenclature. Show the *ophthalmic artery* traverse the optic canal and the *superior ophthalmic vein* passes through the superior orbital fissure. The ophthalmic artery is a direct branch of the internal carotid artery, which traverses the carotid canal. Indicate the *carotid canal* lies just behind the sella turcica along the same anterior–posterior plane as the optic canal. The foramen lacerum also lies at the position of the carotid canal. Classically, the carotid artery was believed to run through both the carotid canal and the foramen lacerum, but current thinking is that the foramen lacerum is so plugged with cartilage only the greater and deep petrosal nerves are actually able to pass through it.

Next, behind the superior orbital fissure, from anterior to posterior, label the *foramen rotundum* and *foramen ovale*. While the first division of the trigeminal nerve runs through the superior orbital fissure, the second and third divisions run through these foramina. Indicate the *second division of the trigeminal nerve* (aka the *maxillary nerve*) passes through foramen rotundum. Think about the *round* head of the *Star Wars* character R2D2 to associate the second division of the trigeminal nerve with foramen *rotund*um. Show the *third division of the trigeminal nerve* (aka the *mandibular nerve*) pass through foramen ovale. Another foramen to mention, but which we won't draw, is foramen mentum; it is distal to foramen ovale and strictly serves the distal mandibular nerve branch that provides sensory coverage to the mentum (aka chin).

Indicate *foramen spinosum* lies along the postero-lateral side of foramen ovale. You can think of foramen spinosum as the "meningeal foramen." It contains the *middle meningeal artery* as well as the *meningeal branch of the third division of the trigeminal nerve*. What type of hematoma is caused by damage to the middle meningeal artery? Epidural hematoma. The meningeal branch of the third division of the trigeminal nerve is one of several branches of the trigeminal nerve responsible for innervation of the meninges, specifically supratentorial innervation (i.e., innervation above the tentorium cerebelli). Infratentorial innervation (i.e., innervation below the tentorium cerebelli) is derived from the upper cervical spinal and vagus nerves. While the pathogenesis of migraine is incompletely understood, the trigeminal-innervated meninges is clearly involved in this form of headache. The brain parenchyma, itself, on the contrary, is insensate.

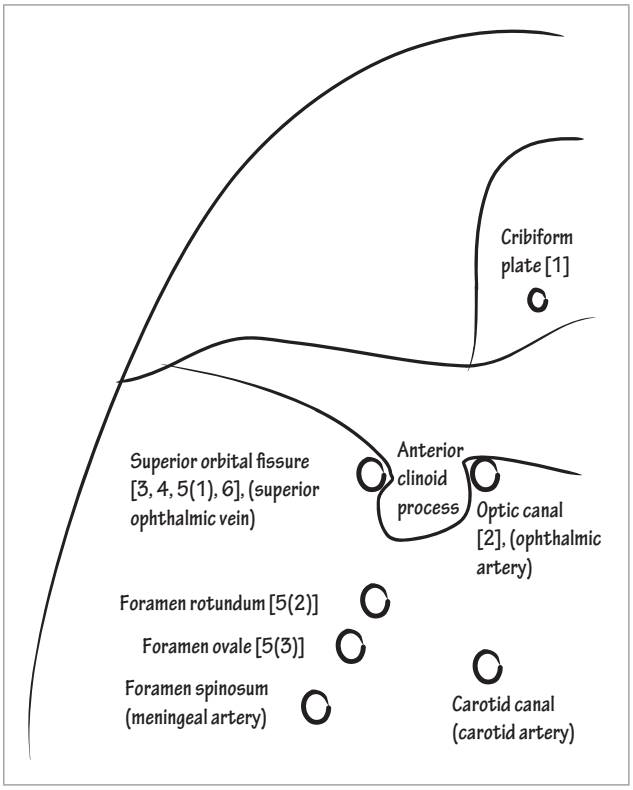


Figure 23-3 Incomplete skull base foramina

Next, draw the *internal acoustic meatus* along the ridge of the petrous temporal bone. Indicate both the *facial* and *vestibulocochlear nerves* run within it along with the *internal auditory artery*. Next, posterior to the internal acoustic meatus, draw the *jugular foramen*. Show the *glossopharyngeal*, *vagus*, and *accessory nerves* pass through it. What vein, do you imagine, joins them in the jugular foramen? The *internal jugular vein*.

Now, within the foramen magnum, label the *hypoglossal canal*. Show both the *hypoglossal nerve* and *venous plexus of the hypoglossal canal* pass through it. Then, indicate the *spinal accessory nerve* ascends through the foramen magnum. The spinal accessory nerve originates in the cervical spinal cord, passes up through the foramen magnum, and then out of the cranium through the jugular foramen. Finally, indicate the *vertebral arteries* and *spinal vessels* (the anterior and posterior spinal arteries and spinal vein) also pass through the foramen magnum.

The most effective way to remember the rostro-caudal organization of the foramina at the base of the skull is to consider the cranial nerves that run through them, which are numbered by their rostro-caudal sequence along the base of the brain. Cranial nerve 1 lies alone in the cribiform plate of the ethmoid bone; cranial nerve 2 lies medial to the anterior clinoid process in the optic canal; cranial nerves 3, 4, 6, and cranial nerve 5 (division 1) all lie within the superior orbital fissure; cranial nerve 5 (division 2) lies alone in foramen rotundum; cranial nerve 5 (division 3) passes through foramen ovale; cranial nerves 7 and 8 travel together in the internal acoustic meatus; cranial nerves 9, 10, and 11 pass through the jugular foramen; cranial nerve 12 runs alone through the hypoglossal canal; and cranial nerve 11 ascends through the foramen magnum.

As already mentioned, most of the foramina share the name of the neurovasculature that traverses them. The ethmoid vessels pass through the ethmoid bone; the ophthalmic artery runs through the optic canal; the internal carotid artery passes through the carotid canal; the superior ophthalmic vein passes through the superior orbital fissure; the labyrinthine vessels run through the internal acoustic meatus; the jugular vein passes through the jugular foramen; and the venous plexus of the hypoglossal canal runs through the hypoglossal canal. Several vessels pass through the foramen magnum: the vertebral arteries, anterior and posterior spinal arteries, and spinal vein.

It is impractical to organize the foramina by their fossae because many of them lie along fossa borders; we'll do so anyway, here, for those interested, but skip ahead, if you like. In the anterior cranial fossa, there is only one group of foramina, the foramina of the cribiform plate. In the middle cranial fossa are the optic canal and superior orbital fissure, which lie along its anterior border, and the carotid canal, foramen rotundum, foramen ovale, and foramen spinosum. Within the posterior cranial fossa, just posterior to the ridge of the petrous temporal bone, lie the internal acoustic meatus and jugular foramen. Other foramina in the posterior cranial fossa are the hypoglossal canal and foramen magnum.

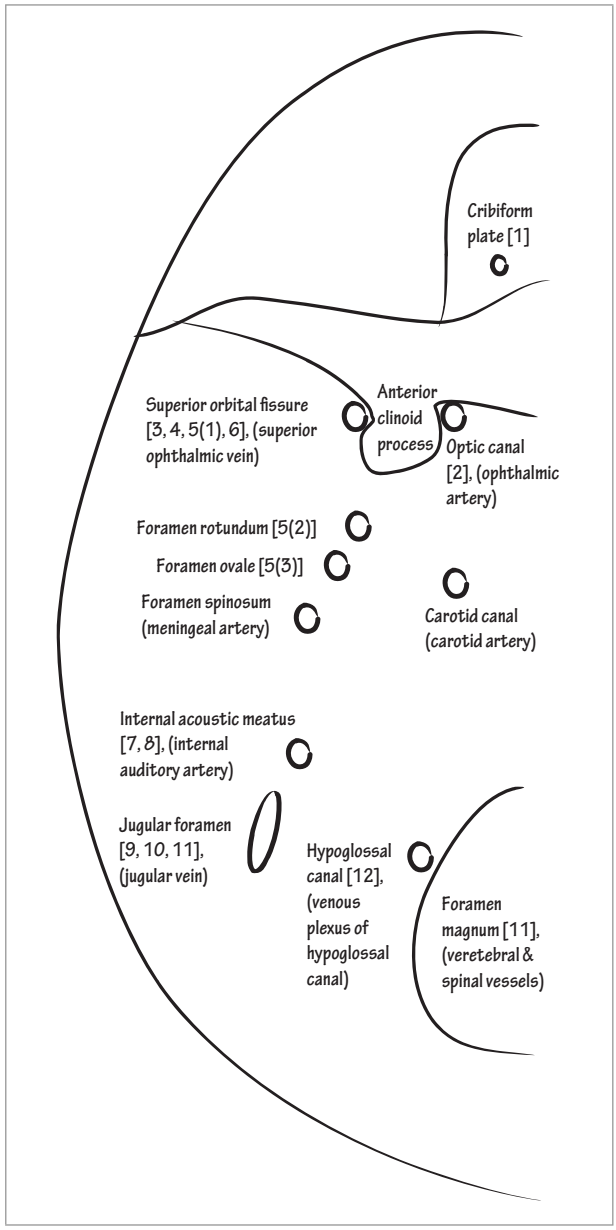


Figure 23-4 Skull base foramina

We will now draw the anatomy of the cavernous sinus, which is a venous sinus. However, air-filled sinuses also exist within the skull and it is important not to confuse them with the venous sinuses; the air-filled sinuses include the sphenoid sinuses, maxillary sinuses, frontal sinus, and mastoid air cells. The cavernous sinus diagram will teach us about the anatomical relationships between it, the superior orbital fissure, foramen rotundum, and the carotid canal. As well, in the cavernous sinus diagram, we will also include the air-filled sphenoid sinuses to distinguish the different forms of skull sinuses.

In a coronal diagram, draw the *sphenoid bone* along the base of the diagram. In the center of the sphenoid bone, draw a trapezoid. Label its concave roof as the *sella turcica* and fill the roof with the *pituitary body*. Next, draw two sphenoid sinuses within the figure but note that occasionally only one sphenoid sinus exists. Label one of the *sphenoid sinuses* by its name and the other by its contents, as *air-filled*.

Next, draw the bilateral venous *cavernous sinuses* outside the walls of the trapezoidal portion of the sphenoid bone. On one side, show the bilateral cavernous sinuses are filled with *venous trabeculations* (unlike the air-filled sphenoid sinus). Above the cavernous sinuses, draw the *optic nerves* and the overlying *base of the brain*, and off to the sides of the cavernous sinuses, draw the *temporal lobes*.

Now, let's draw the contents of one of the bilateral cavernous sinuses. The arrangement of the cranial nerves is as follows: along the lateral wall of the cavernous sinus, from superior to inferior, show the *oculomotor nerve* (*cranial nerve 3*), *trochlear nerve* (*cranial nerve 4*), *first division of the trigeminal nerve* (*cranial nerve 5(1)*), and *second division of the trigeminal nerve* (*cranial nerve 5(2)*). In the center of the cavernous sinus, draw the *abducens nerve* (*cranial nerve 6*) and a portion of the *internal carotid artery* directly over it. Then, draw another portion of the *internal carotid artery* in coronal cross section between the roof of the cavernous sinus and the optic nerve. The carotid artery doubles-back across the top of the cavernous sinus, as we will show in our sagittal section through the base of the brain, next.

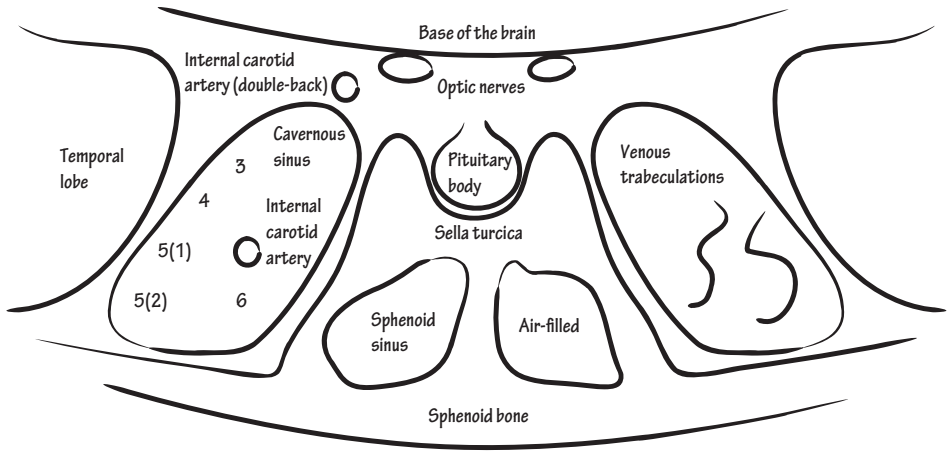


Figure 23-5 Coronal cavernous sinus

In this next diagram, we will draw a sagittal view of the cavernous sinus; Meckel's cave; internal carotid artery; major regional foramina; and relevant cranial nerves. The perspective is slightly oblique: the posterior portion is shifted laterally and the anterior aspect is shifted medially.

Let's begin with the bony portions of this region. Along the top of the diagram, draw the *anterior clinoid process*. Then, show the *sphenoid bone* along the inferior border of the diagram; it forms a valley. Along the posterior border, draw the *petrous temporal bone* and the *sella turcica* on the posteromedial side. The sella turcica is the sphenoid depression along the roof of the sphenoid bone in which the pituitary body sits. Label the *optic canal* medial to the anterior clinoid process. Then, within the cavernous sinus, draw the *superior orbital fissure* and *foramen rotundum*. Draw a dashed line to separate the *cavernous sinus*, anteriorly, from *Meckel's cave* behind it. In the floor of Meckel's cave, draw *foramen ovale*.

Now, show the *optic nerve* run medial to the anterior clinoid process and through the optic canal. Within Meckel's cave, draw the *trigeminal ganglion*. Indicate the *third division of the trigeminal ganglion* (*cranial nerve 5(3)*) drops immediately through *foramen ovale* and never enters the cavernous sinus. On the contrary, show both the *first and second divisions of the trigeminal nerve* (*cranial nerves 5(1)* and *5(2)*) pass anteriorly through the cavernous sinus. Indicate the first division originates superior to the second division, crosses the sinus, and exits through the *superior orbital fissure* and the second division crosses the sinus and exits through *foramen rotundum*.

Cranial nerves 3, 4, and 6 originate in the midline of the upper midbrain, lower midbrain, and mid-pons, respectively. Show the *oculomotor nerve* (*cranial nerve 3*), *trochlear nerve* (*cranial nerve 4*), and *abducens nerve* (*cranial nerve 6*) pass through the cavernous sinus above the first division of the trigeminal nerve, and exit through the superior orbital fissure.

Think of the internal carotid artery in four separate parts: cervical, petrous, cavernous, and cerebral. In the cervical part, the internal carotid ascends through the anterior neck; in the petrous part, it crosses through the temporal bone; in the cavernous part, it passes through the cavernous sinus; and in the cerebral part, it ascends into the brain. That is probably all you need to know about the internal carotid artery, but complete the following if you want to understand its course in more detail.

First, show the *cervical part* ascend through the anterior neck. Next, show the *petrous part* cross horizontally through the petrous temporal bone. The *cavernous part* should be drawn in three separate steps. Show the artery ascend into the cavernous sinus in the first vertical portion. Some authors label this segment separately as the *lacerum segment* because it runs above (not through) the foramen lacerum. Next, show the carotid artery jut forward within the cavernous sinus in the horizontal portion. Lastly, indicate it exits the cavernous sinus in the second vertical portion. Now, draw the *cerebral part* of the internal carotid artery. It begins as the carotid exits the cavernous sinus. Show that in the proximal portion of the cerebral part, the carotid gives off the *ophthalmic branch*, which joins the optic nerve in the optic canal. Then, indicate the cerebral part doubles-back across the top of the cavernous sinus and subsequently ascends into the brain. Some authors further subdivide the cerebral segment into three different segments. They label the short, inferior stretch where it runs near the anterior clinoid process as the *clinoid segment*, the segment where it gives off the ophthalmic artery and doubles-back over the roof of the cavernous sinus as the *ophthalmic segment*, and the segment where it gives off the posterior communicating artery and ascends into the cerebrum as the *supraclinoid segment* (aka *communicating segment*).

Although we divide the carotid into four simple parts (cervical, petrous, cavernous, and cerebral), the standard numbering system for the internal carotid artery accounts for its subdivisions. It is numbered as follows: cervical segment (C_1), petrous segment (C_2), lacerum segment (C_3), cavernous segment (C_4), clinoid segment (C_5), ophthalmic segment (C_6), and supraclinoid segment (C_7).

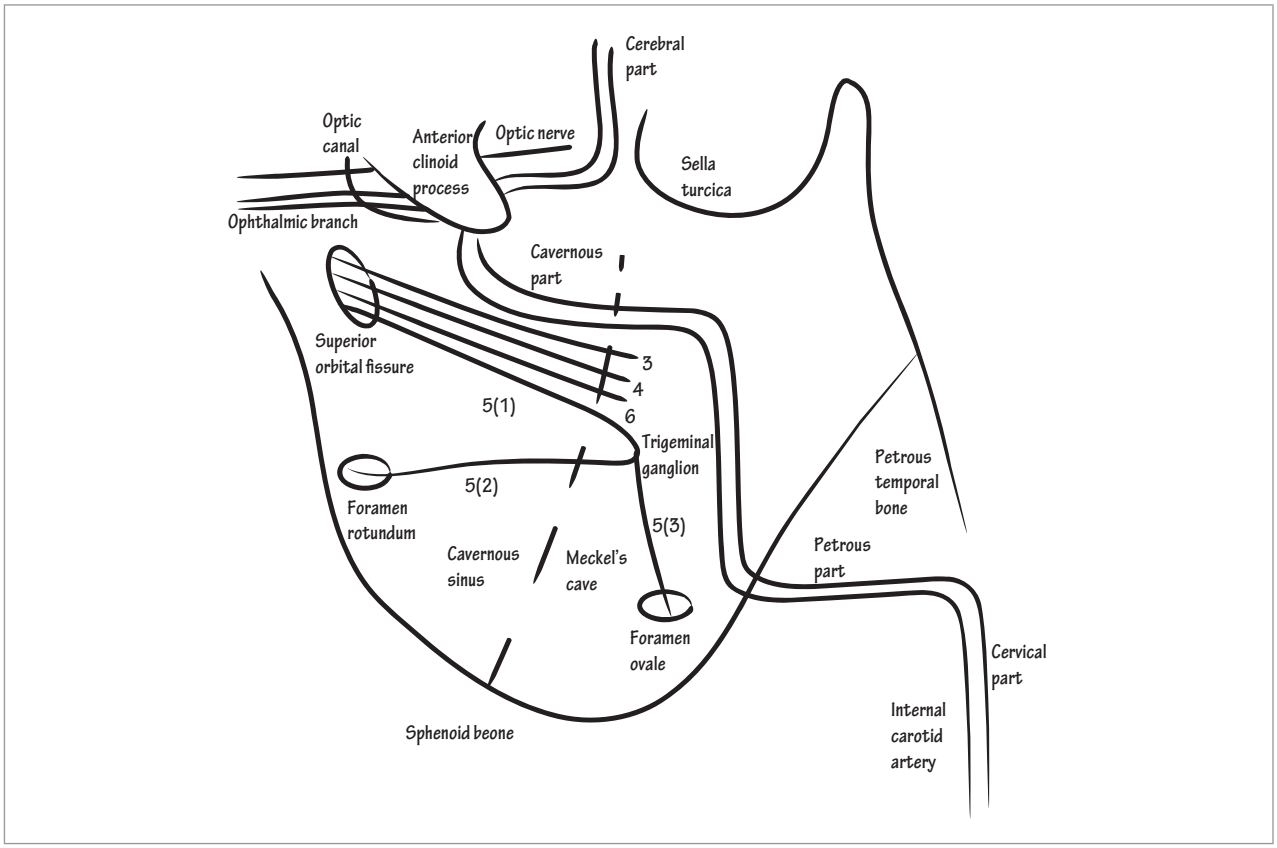


Figure 23-6 Oblique view of cavernous sinus

Cerebellum

IN THIS CHAPTER, we will learn the gross structure and functional pathways of the cerebellum. Amazingly, the cerebellum is packed with more neurons than the cerebrum and yet it is able to fit into the compact posterior fossa because of its unique crystalline structure. To learn the anatomy of the cerebellum, we will begin with a mid-sagittal section; then we will create a coronal view of the anterior cerebellum in its folded state; then of the posterior cerebellum in its unfolded state; and afterward, we will learn the cerebellar somatotopic map.

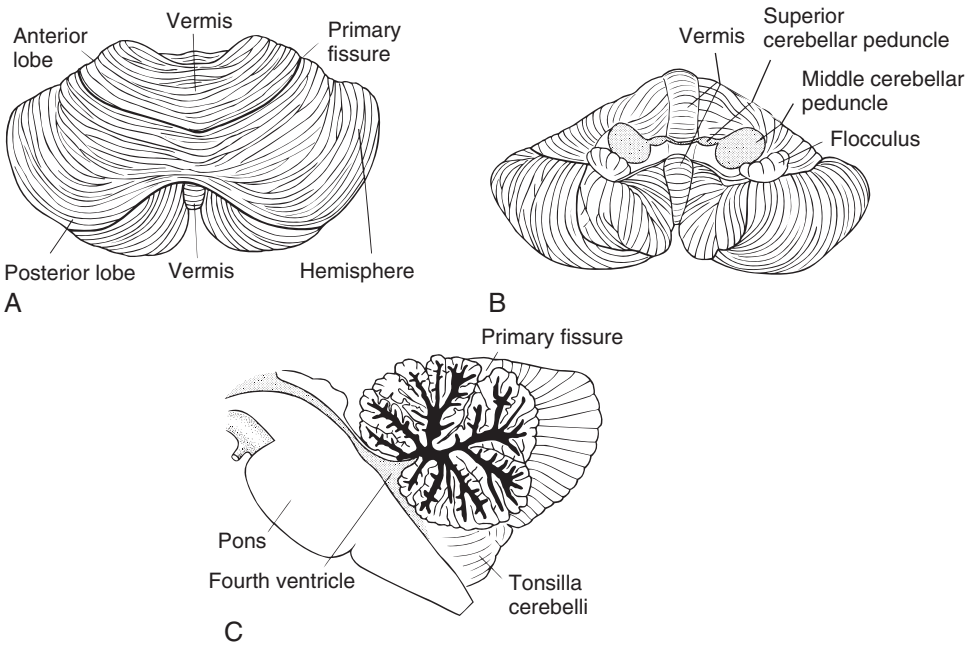


Photo 24-1 External surfaces of the cerebellum
With permission from Brodal, P. *The Central Nervous System: Structure and Function*. 3rd ed. New York: Oxford University Press, 2004.

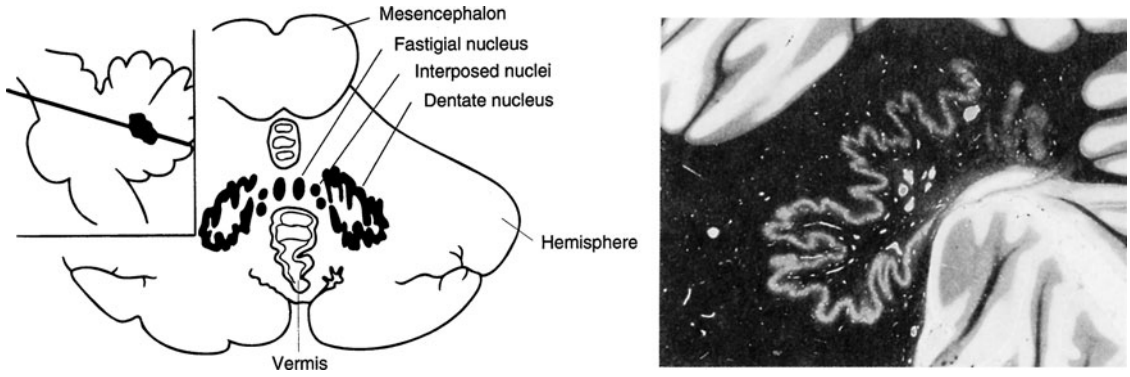


Photo 24-2 Deep cerebellar nuclei
With permission from Brodal, P. *The Central Nervous System: Structure and Function*. 3rd ed. New York: Oxford University Press, 2004.

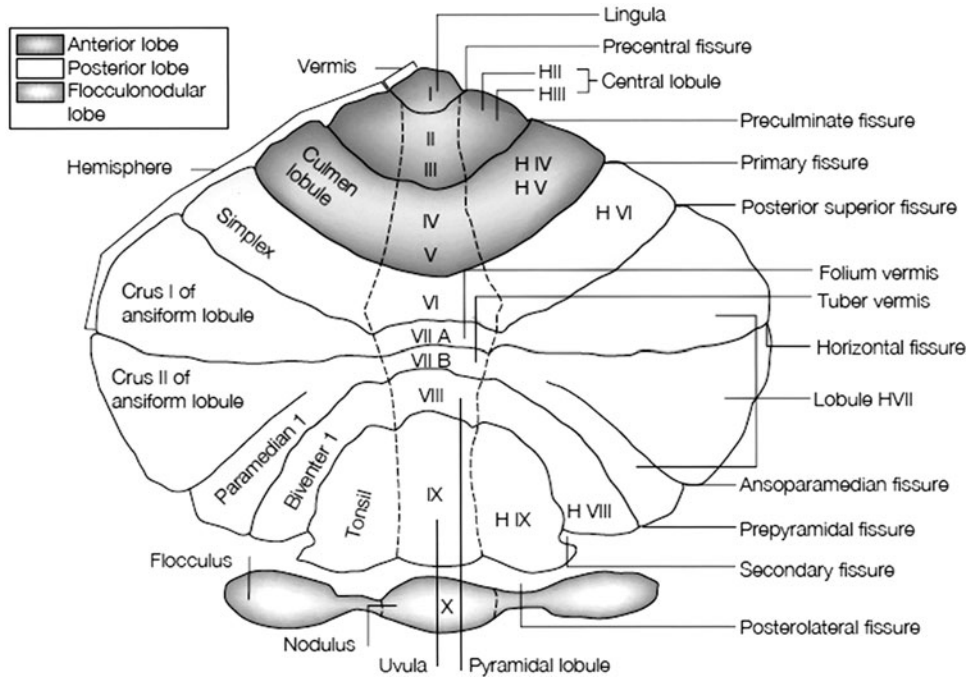


Photo 24-3 Unfolded cerebellum
Reprinted by permission from Macmillan Publishers Ltd.: *Nature Reviews Neuroscience*: Manni, E., L. Petrosini. A Century of Cerebellar Somatotopy: A Debated Representation. *Nat Rev Neurosci* 5, no. 3 (2004): 241–249.

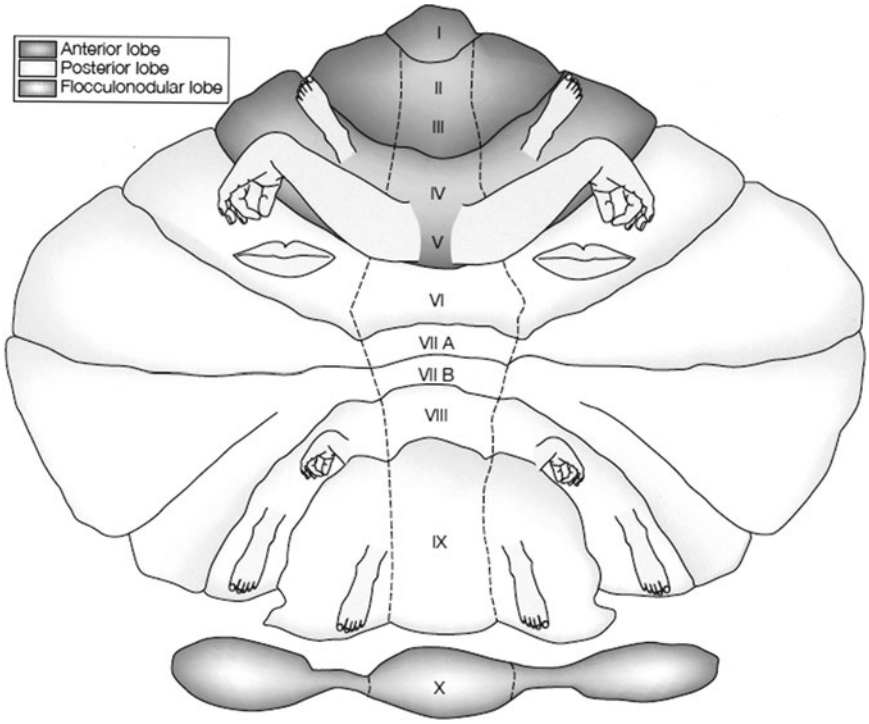


Photo 24-4 Cerebellar somatotopy

Reprinted by permission from Macmillan Publishers Ltd.: *Nature Reviews Neuroscience*: Manni, E., Petrosini, L. A Century of Cerebellar Somatotopy: A Debated Representation." *Nat Rev Neurosci* 5, no. 3 (2004): 241–249.

Let's now draw the mid-sagittal section of the cerebellum. First, draw the triangular-shaped fourth ventricle, and around it, draw the oval-shaped cerebellum. Next, create a small fissure along the rostral-posterior surface of the cerebellum; label it as the *primary fissure*. The primary fissure divides the majority of the cerebellum into anterior and posterior lobes. Label the anterior-superior cerebellum as the *anterior lobe* and the posterior-inferior cerebellum as the *posterior lobe*. Next, just beneath the inferior lip of the fourth ventricle, label the *nodulus*; show the *posterolateral fissure* separates it from the posterior lobe. Laterally, out of the plane of this diagram, the posterolateral fissure separates the posterior lobe from the flocculus, which is the lateral corollary of the midline vermian nodulus. The flocculus and nodulus are often paired as the flocculonodular lobe because of their shared phylogeny. Label the cerebellar tonsils in front of the inferior posterior cerebellar lobe; they are particularly important to pay attention to on radiographic imaging for reasons we will discuss later.

The primary and posterolateral fissures comprise the two main cerebellar fissures. Additional fissures divide the midline cerebellum into 10 different lobules. It is unnecessary for us to label all 10 of them but we will introduce their numbering scheme to familiarize ourselves with their organization. Lobule 1 sits in the anterior-superior position and lobule 10 is in the anterior-inferior position; the other lobules are labeled in stepwise progression as you trace clockwise (in this orientation) around the cerebellum. Indicate, now, the cerebellar region above the superior lip of the fourth ventricle as *lobule 1* (aka the *lingula*). Next, show a small fissure separates it from *lobule 2* and another fissure separates lobule 2 from *lobule 3*. Together, lobules 2 and 3 form the *central lobule*. For simplicity, we skip lobule 4 and will skip lobules 7 and 8, but we are able to imagine their positions.

Indicate the primary fissure separates *lobules 5* and *6* and, as already shown, the anterior and posterior cerebellar lobes. Next, at the anterior-inferior edge of the posterior lobe, draw *lobule 9*. In front of it is the

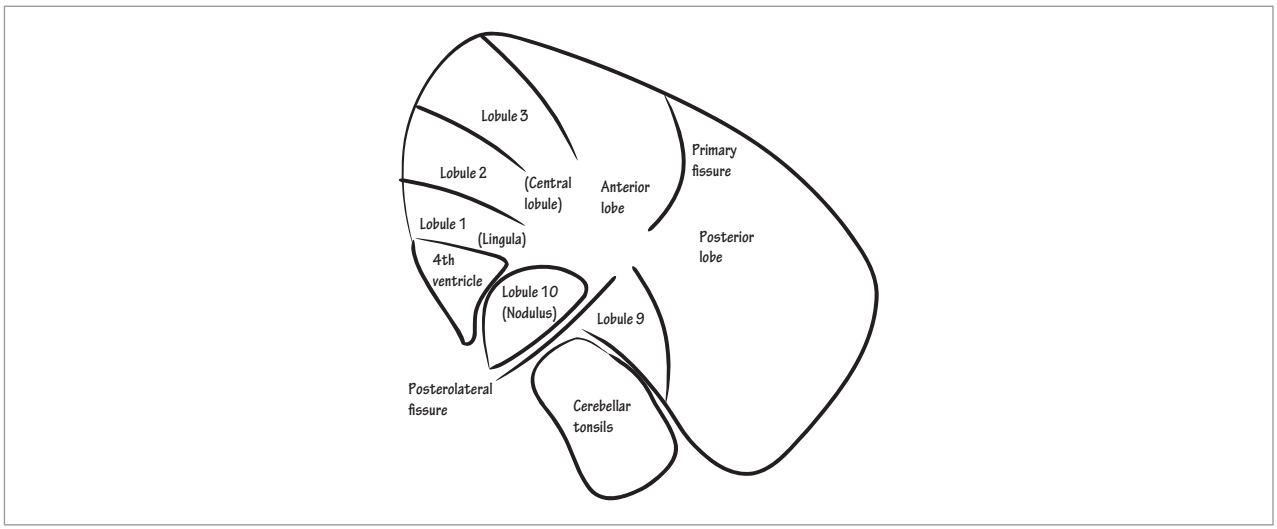


Figure 24-1 Sagittal view of cerebellum

previously drawn posterolateral fissure and also the nodulus, which is *lobule 10*; it lies below the inferior lip of the fourth ventricle. The 10 numerically labeled lobules comprise nine named lobules. Lobules 2 and 3 form the central lobule, as shown; lobules 4 and 5, together, form the culmen; and lobule 7 comprises both the folium and tuber.

Now, we will draw a coronal slice through the anterior cerebellum. On one half, we will label the deep cerebellar nuclei and on the other half, we will label the major external structures of the anterior surface of the cerebellum. Let's begin with an outline of the anterior cerebellum, which has a saddlebag appearance.

On the structural side of the diagram, above and below the fourth ventricle we will show the midline portions of the vermis. Superiorly, label the vermian *lingula* (lobule I) and *central lobule* (lobules II and III), and inferiorly, label the *nodulus* (lobule X). Next, label the *superior*, *middle*, and *inferior cerebellar peduncles* around the lateral border of the fourth ventricle. Remember, the inferior and middle cerebellar peduncles receive afferent (inflow) fibers to the cerebellum and the superior cerebellar peduncle is the passageway for efferent (outflow) fibers from the cerebellum. The anterior spinocerebellar tract is the exception; it enters the cerebellum through the superior cerebellar peduncle.

Beneath the lateral portion of the inferior cerebellar hemisphere, label the *flocculus*. Lastly, label the *cerebellar tonsils* just off midline, near the nodulus; they occasionally extend into the spinal canal and cause headaches or radiating pain. Sometimes, however, they are found on radiographic imaging extending into the spinal canal but are entirely asymptomatic. Arnold-Chiari malformations involve cerebellar tonsillar hernation along with various other midline malformations.

Now, let's label the deep cerebellar nuclei, which span the medial one-third of the hemisphere. From medial to lateral, they are the *fastigial, globose, emboliform*, and *dentate nuclei*. Their names form the acronym "F'GED," reminiscent of the expression "F'ged about it," popularized in the film *Donnie Brasco*. The dentate nucleus is of particular interest because it is involved in the important cerebrocortical-ponto-cerebellocortical-dentato-rubro-thalamo-cerebrocortical pathway. Notice that in this pathway, fibers synapse first in the cerebellar cortex and then in its deep dentate nucleus; we will draw the complete pathway when we describe the pontocerebellar functional module later in this chapter.

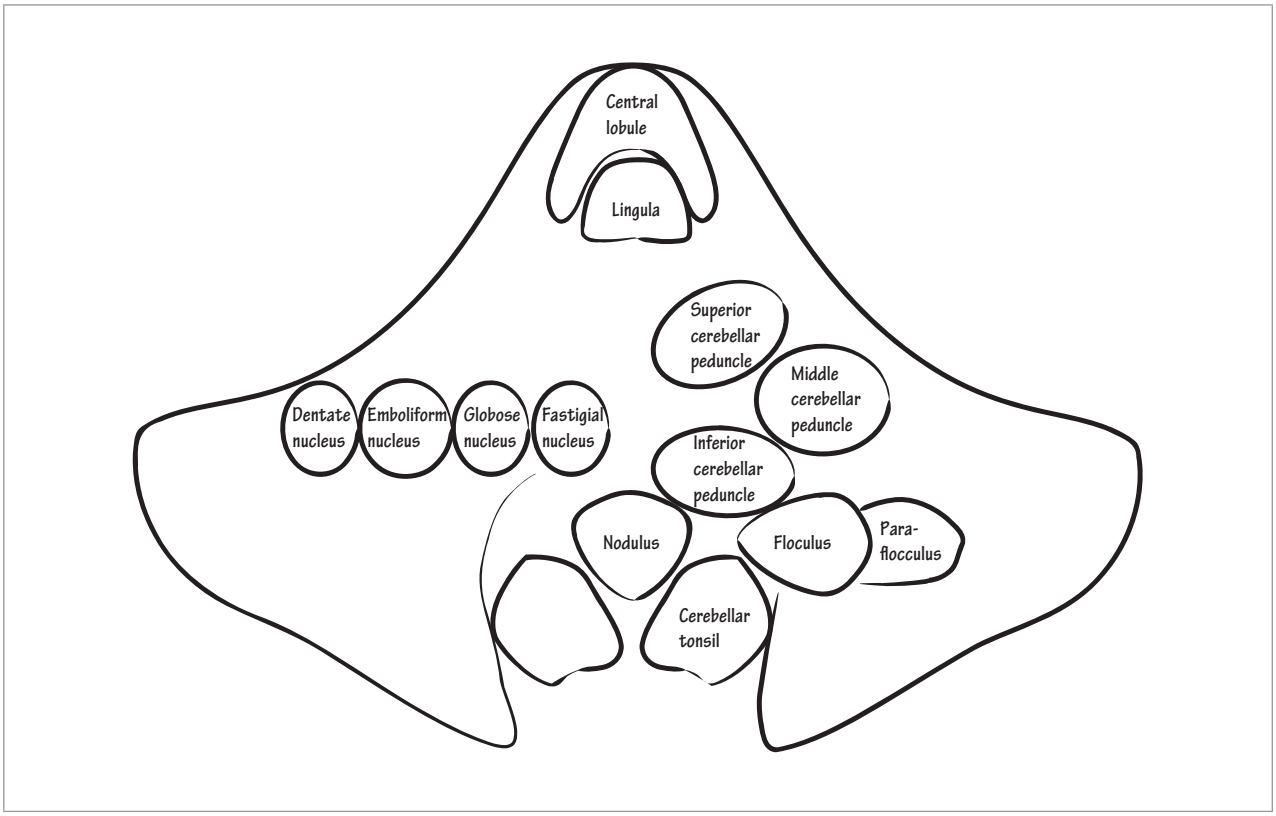


Figure 24-2 Anterior coronal view of cerebellum

In our next diagram, we will draw the posterior surface of the cerebellum in its unfolded state. In the unfolded state, we are able to include the flocculus and nodulus; they lie in the center of the anterior surface of the cerebellum so we must unfold it to see them. Imagine a sagittal view of the cerebellum: peel back its anterior upper and lower lips to unfold it.

Now, draw an outline of the oblong, unfolded cerebellum. First, divide the cerebellum into an inner, midline region and an outer region; the inner segment is thin compared to the large outer segment. Show that the *vermis* comprises the majority of the midline cerebellum; we will show the flocculonodular lobe below it, soon. There are 10 numbered lobules in the vermis that correlate to the lobules of the cerebellar hemispheres, but they are beyond our interest, here. Next, divide the outer cerebellum with the horizontal *primary fissure* into a top one-third and a bottom two-thirds. Label the top one-third as the *anterior lobe* (aka *paleocerebellum*) and the bottom two-thirds as the *posterior lobe* (aka *neocerebellum*).

Next, near the bottom of the cerebellum, draw a horizontal line for the *posterolateral fissure*. Label the bottom portion of the vermis as the *nodulus*. Attach a foot to the nodulus and label it the *flocculus*. Together, indicate the flocculus and nodulus form the *flocculonocular lobe* (aka *archicerebellum*). They are phylogenically the oldest part of the cerebellum.

Finally, let's include the cerebellar arterial territories, which we also learn in the "Arterial Supply to the Central Nervous System" chapter. The paired vertebral arteries each directly supply the posterior-inferior cerebellar arteries (the PICAs). Then, the vertebrals join to form the basilar artery. The anterior-inferior cerebellar arteries (the AICAs) emerge from the lower basilar artery and the superior cerebellar arteries (the SCAs) emerge from the upper basilar artery. Show the *posterior-inferior cerebellar arteries* perfuse the flocculonodular lobe and medial portion of the posterior-inferior cerebellum; the *anterior cerebellar arteries* perfuse the lateral posterior lobes; and the *superior cerebellar arteries* perfuse the anterior lobes and the superior portion of the posterior lobes.

So far in this chapter, we have focused on cerebellar structure but we are also able to parse the cerebellum into three different functional modules that each contain a section of cerebellar cortex, specific white matter afferent and efferent pathways, and certain deep cerebellar nuclei. We will discuss the functional modules, next.

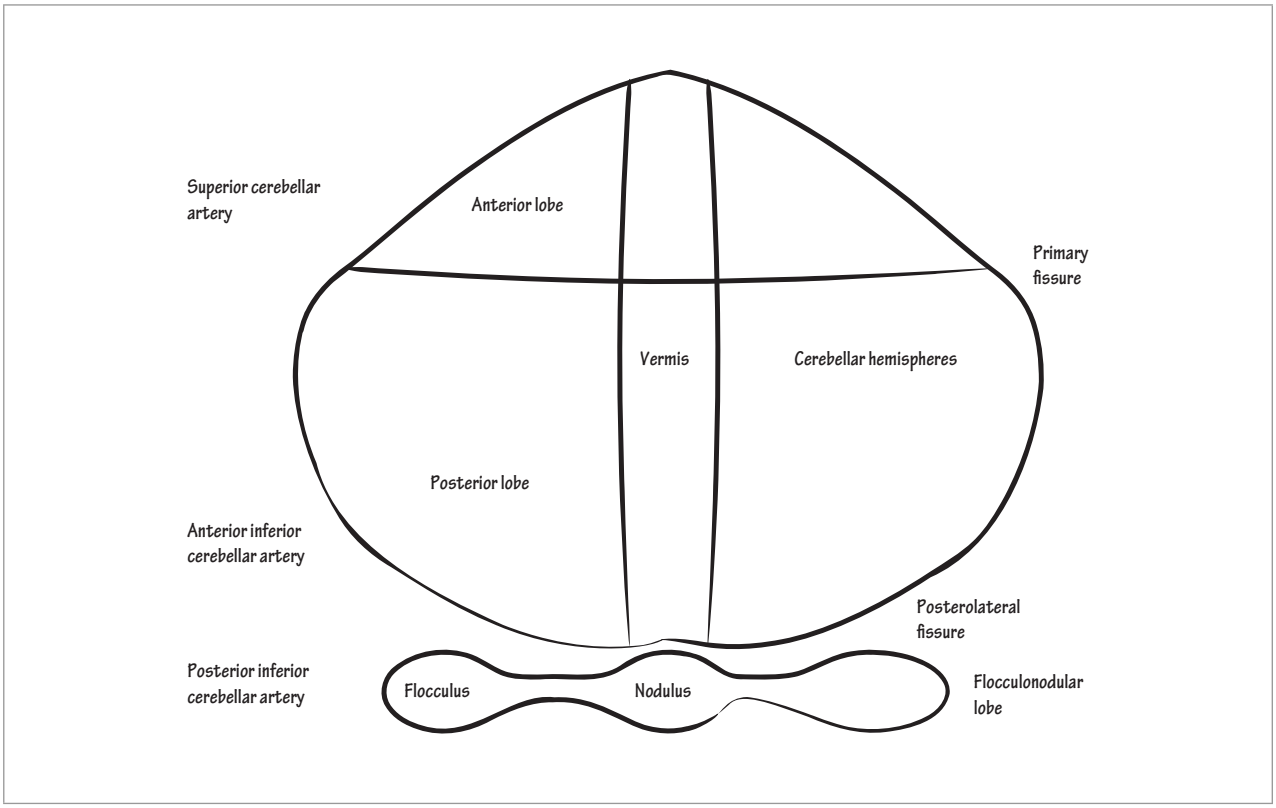


Figure 24-3 Posterior coronal view of unfolded cerebellum

The *vestibulocerebellar module* (aka *archicerebellum*) encodes balance and eye movements. Its cerebellar cortex comprises the *flocculonodular lobe* and the *paraflocculus* of the posterior vermis; its afferent and efferent pathway system comprises the *vestibulocerebellar fibers* and *olivocerebellar fibers*; and its deep cerebellar nucleus is the *fastigial nucleus*. In the "Vestibular System" chapter, we discussed that vestibulocerebellar fibers from the vestibular labyrinth and vestibular nuclear complex travel up the inferior cerebellar peduncle and terminate in the flocculonodular lobe and uvula, and we also discussed that the cerebellum sends fibers back to the bilateral vestibular nuclear complexes. Here we learn that the fastigial nucleus originates those efferent fibers; it is the deep cerebellar nucleus of the vestibulocerebellar module.

The olivocerebellar fiber pathway of the vestibulocerebellar module is important because of its histology. The cerebellum is composed of three different histological fiber types and the inferior olivary nucleus is its only source of climbing fibers. The other histological fiber types are the mossy fibers, which originate in sensorimotor areas of the spinal cord, brainstem, and deep cerebellar nuclei, and the multilayered fibers, which originate in behavioral centers such as the locus ceruleus, raphe nuclei, and hypothalamus.

The *spinocerebellar module* (aka *paleocerebellum*) provides postural stability. Its cerebellar cortex comprises the *vermis* and the *intermediate zone* just lateral to it. It has a wide variety of afferent and efferent pathways and involves numerous deep cerebellar nuclei. It is unnecessary to remember all of the pathways and nuclei of this module. Instead, pay close attention to the overall difference between this module and the vestibulocerebellar module. The vestibulocerebellar module provides orientation, as through the vestibulo-ocular system—it keeps the world straight; whereas the spinocerebellar module provides postural balance and stability—it keeps us upright.

It should come as no surprise that the major afferent pathways of the spinocerebellar module are the *spinocerebellar tracts*, which we drew in the "Spinal Cord" and "Brainstem" chapters. Additional afferent pathways of the spinocerebellar module come from the vestibular nuclei, pontine nuclei, reticular fibers, and inferior olivary nuclei. Efferent fibers from the spinocerebellar module exit through the superior cerebellar peduncle and synapse either directly in the spinal cord or secondarily in the spinal cord via the reticular and rubral nuclei, or they synapse in the thalamus or olive. Aside from the olivary climbing fibers, all of these afferent and efferent fibers are mossy fibers. The cerebellar nuclei of the spinocerebellar module are the medial three nuclei: the *fastigial nucleus* (the main cerebellar nucleus of the vestibulocerebellar module) and the *globose* and *embolliform nuclei*.

The *pontocerebellar module* (aka *neocerebellum*) involves the *cerebellar hemispheres* and functions in goal-directed movements. Its primary pathway is the *cerebrocortical-ponto-cerebellocortical-dentato-rubro-thalamo-cerebrocortical pathway*. Although the name of this pathway is a mouthful, its logical progression makes it relatively easy to remember. The pathway is important because it explains how the motor cortex enacts smoothness of limb movement. The *dentate nucleus*, as stated in the pathway's name, is the main deep cerebellar nucleus of the pontocerebellar module.

Now, let's draw the pontocerebellar module pathway. Draw a coronal section through the brain and brainstem and include the cerebellum. Indicate the pathway originates in the *primary motor cortex* and show the motor cortex sends descending fibers to the *pons*, where they synapse and project to the contralateral cerebellum through the middle cerebellar peduncle. Show these fibers synapse in the *cerebellar hemispheric cortex*, which then projects fibers to the ipsi-cerebellar *dentate nucleus*. Next, indicate the dentate nucleus sends exiting fibers out through the superior cerebellar peduncle. Show these fibers decussate (cross midline) at the level of the midbrain and send connections to the *red nucleus* in the midbrain before they synapse in the *ventral lateral nucleus* of the *thalamus*. Finally, indicate the thalamus projects back to the motor cortex. From there, the cortex sends out post-cerebellar modified impulses through the corticospinal tracts.

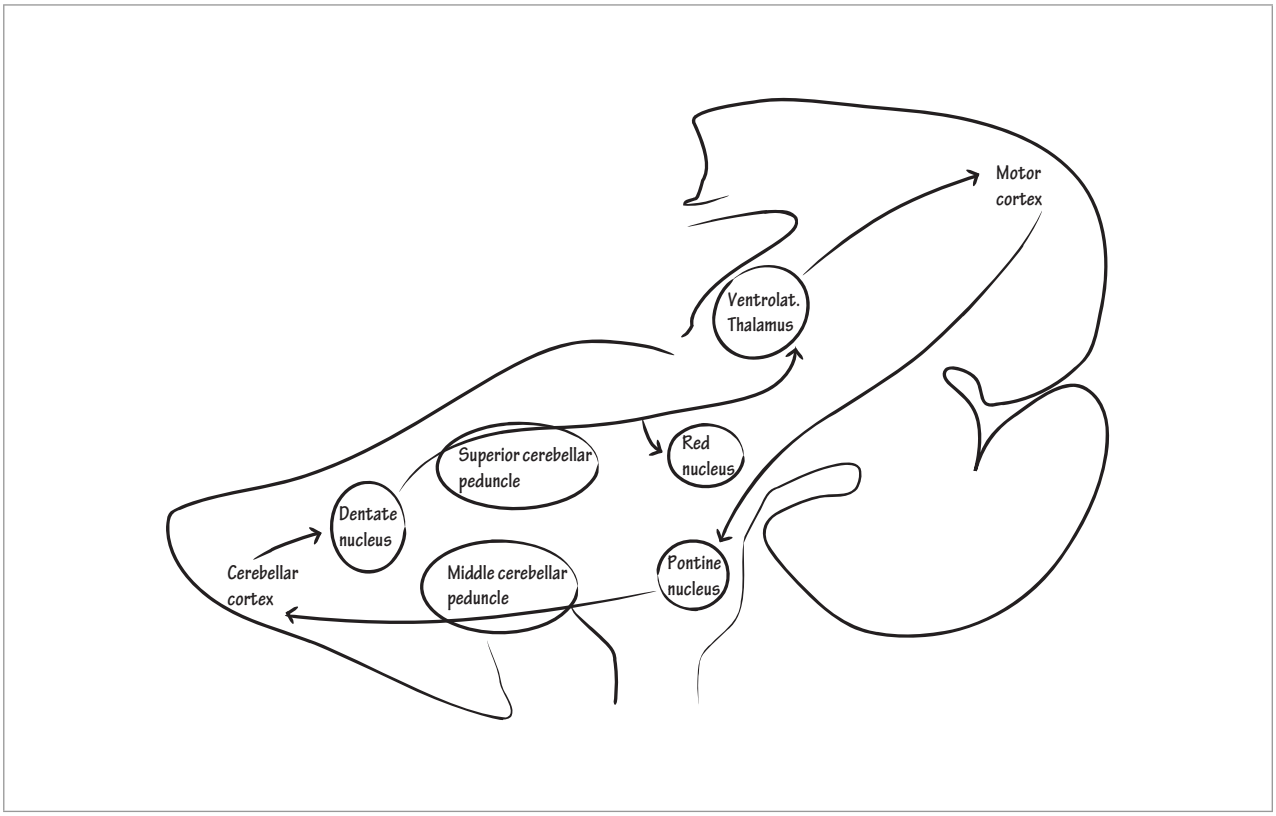


Figure 24-4 Pontocerebellar module

Now, let's address the somatotopic organization of the cerebellum. Somatotopic maps of the cerebellum were introduced in 1904 and anatomists have used various electrophysiological and imaging modalities to refine them since. Two important points regarding cerebellar somatotopy hold true: (1) unilateral cerebellar lesions affect the ipsilateral side of the body and (2) the midline (vermian) cerebellum provides input to the face and trunk while the cerebellar hemispheres provide input to the limbs. To sit still in a chair, you need midline cerebellar input, and to reach smoothly into the environment, you need cerebellar hemispheric input. Patients with midline cerebellar lesions exhibit neck, trunk, and pelvic imbalance (aka *axial imbalance*) and patients with cerebellar hemispheric injury have limb incoordination (aka *appendicular incoordination*), which causes dysmetria (they over or undershoot a target) and dysynergy (they exhibit irregular stops and accelerations); tremor often accompanies the limb incoordination.

Truncal and appendicular control are tested separately. With one heel, rub your foot up and down your opposite shin: this is called heel–knee–shin testing. Of the two divisions, it primarily tests truncal control. To detect truncal incoordination, patients must sit upright; if they lie flat in bed, their posture is stabilized. Next, with your finger, tap a distant target and then tap your nose. This is called finger–nose testing and it evaluates the integrity of the appendicular division of cerebellar control. Often clinicians only test finger-to-nose and neglect to test heel-knee-shin, but appendicular testing is normal in midline cerebellar disorders, such as alcoholic degeneration of the cerebellum. Thus, neither test is a substitute for the other.

In this last section, we will draw a cerebellar somatotopic map from the functional imaging work of W. Grodd and colleagues. First, overall, cerebellar innervation is ipsilateral: the right cerebellar hemisphere encodes the right-side limbs and the left hemisphere encodes the left. Separate somatotopic maps exist within both the anterior and posterior cerebellar lobes and while the maps in each lobe are similar, they are not the same. In both lobes, the trunk and face lie in midline and the limbs extend from just off-center out laterally. In the unfolded somatotopic cerebellar map, the legs lie at the top of the anterior lobe and the arms lie at the bottom. In the posterior lobe, the arms lie at the top and the legs lie at the bottom. So, in the anterior lobe, the body is oriented head-down and in the posterior lobe it is oriented head-up: the heads meet in the middle.

If you want to know the specifics of Grodd's map, read on, otherwise go to the next chapter. In high-resolution somatotopic cerebellar maps, the large contiguous body parts appear fractured. The limbs are splintered into small, noncontiguous patches with contralateral, bilateral, and ipsilateral representation intermixed. Despite this, remarkably, at a gross level the somatotopic map we described in the previous paragraph remains accurate and we are able to use it clinically.

First, reproduce the unfolded, ovoid cerebellum. Again, divide it into an inner vermian region and outer hemispheric regions. One-third of the way from the top of the outer segment, draw the *primary fissure*, which separates the cerebellar hemispheres into *anterior* and *posterior lobes*. The trunk and face are strewn throughout the vermis, so just write *trunk* and *face* along midline.

Next, focus on the anterior and posterior lobes of the cerebellar hemispheres. In the anterior lobe, imagine someone lying in a bathtub with his/her arms and legs coming out of the water, extending laterally. The arms lie at the bottom of the anterior lobe and the legs lie at the top. Underneath the dangling hands, on each side, draw the somatotopic representation of the entire mouth; both sides of the mouth are encoded in the bilateral hemispheres. Next, let's draw the somatotopic organization of the posterior lobe; it is organized head-up. The arms lie at the top of the posterior lobe and the legs lie at the bottom; think of someone poised to kick a soccer ball. The mouth is absent in the posterior lobe hemispheres unlike in the anterior lobes (where it is represented bilaterally).

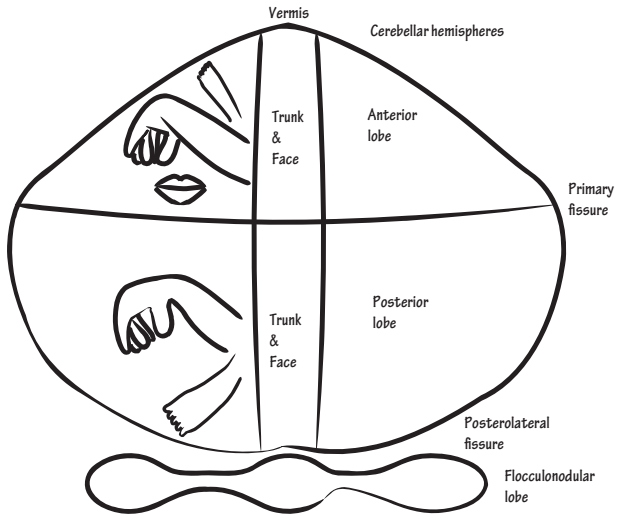
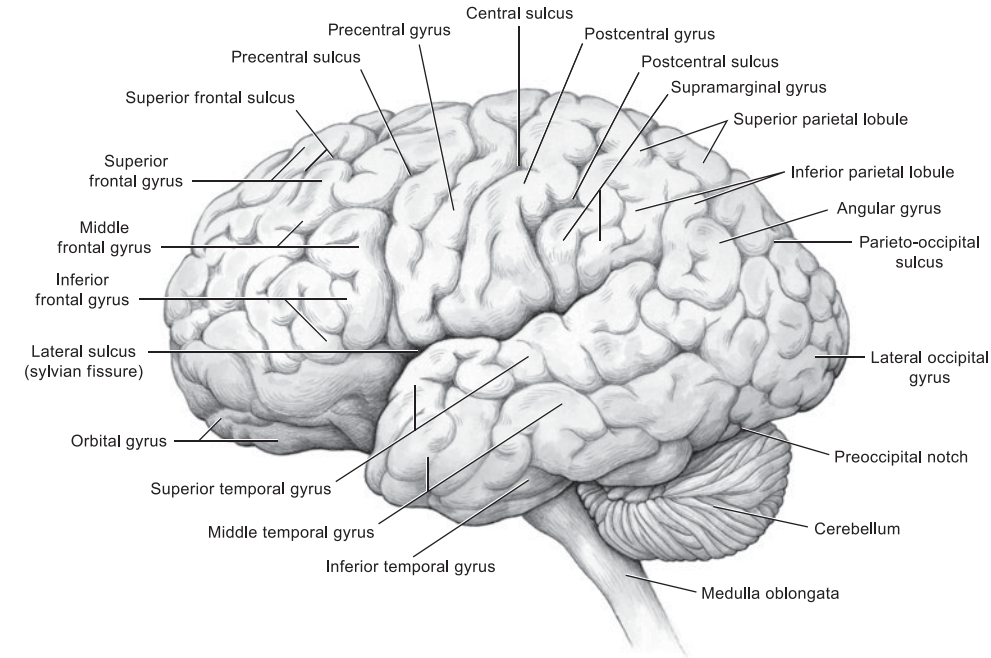


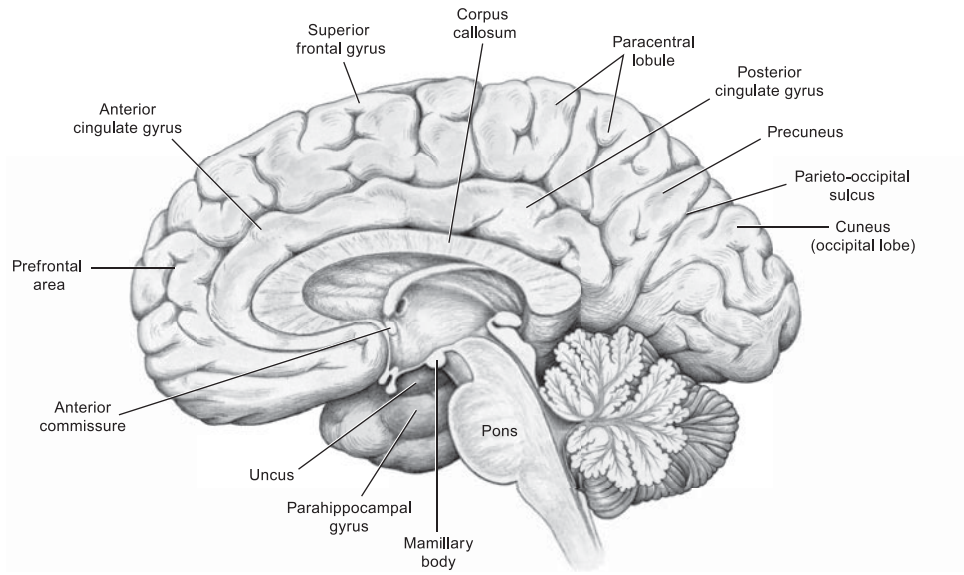
Figure 24-5 Cerebellar somatotopy

Surfaces of the Brain

In this chapter, we will draw the lateral, medial, and under surfaces of the brain, as well as the Sylvian fissure, and insular cortex. In addition, we will draw highlights of the Brodmann functional maps and Penfield's somatotopic homunculus. On each cerebral surface, we will divide the brain into its lobes and then divide the lobes into their gyri and sulci.

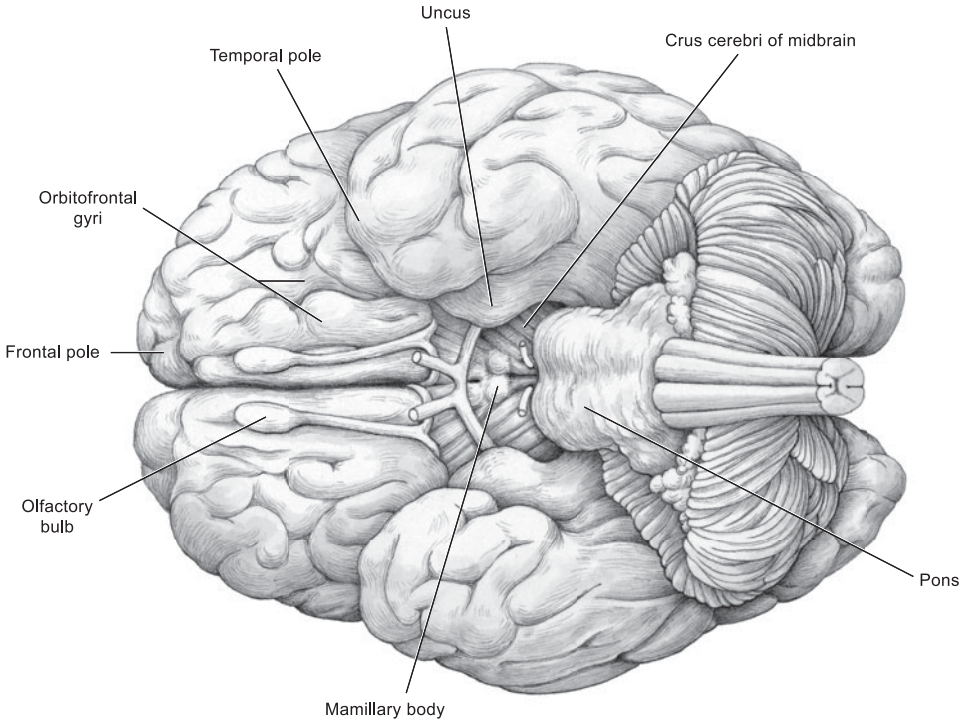


A



B

Photo 25-1 Medial and lateral cerebral surfaces
With permission from Devinsky, O., and M. D'Esposito. *Neurology of Cognitive and Behavioral Disorders*, Contemporary Neurology Series. Oxford and New York: Oxford University Press, 2004.



C

Photo 25-2 Undersurface of cerebrum

With permission from Devinsky, O., and M. D'Esposito. *Neurology of Cognitive and Behavioral Disorders*, Contemporary Neurology Series. Oxford and New York: Oxford University Press, 2004.

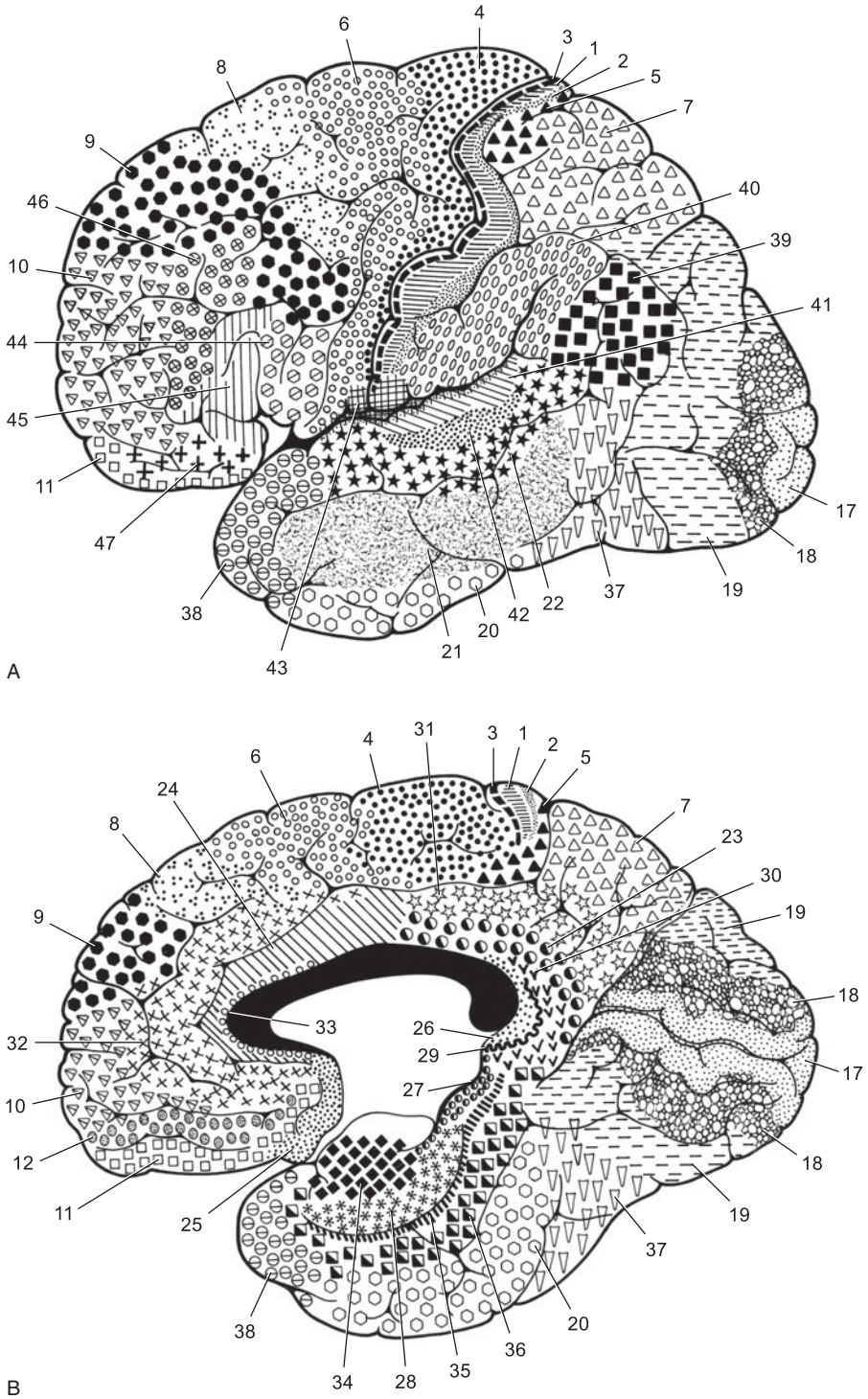


Photo 25-3 Brodmann's map

With permission from Devinsky, O., and M. D'Esposito. *Neurology of Cognitive and Behavioral Disorders*, Contemporary Neurology Series. Oxford and New York: Oxford University Press, 2004.

Close your fist, now, to represent the topography of the brain. The fingers represent the gyri and the grooves between them are the sulci. What advantage is there to this contour? It increases the brain surface's area: approximately two-thirds of the brain's surface lies within these sulcal valleys. The cerebellum, which was drawn in the preceding chapter, is a good example of how important tissue folding can be; it is condensed into a space much smaller than the remainder of the brain but its convolutions give it a larger surface area.

In addition to the cortical sulci, there are also much deeper invaginations into the brain, called cortical fissures. The distinction between a sulcus and a fissure is that sulci merely indent the outer surface of the brain whereas fissures extend through the entire cerebral wall and alter the contour of the deep-lying ventricular system. A good example of this is the Sylvian fissure; it extends so far into the ventricular system that it forms temporal horns into the lateral ventriclular system. Although a semantic distinction between sulci and fissures does exist, these terms are often inter-exchanged, regardless. The Sylvian fissure, itself, is commonly referred to as the lateral sulcus and the calcarine sulcus, which does not affect the ventricular system, is often called the calcarine fissure.

Now, let's begin our diagram of the lateral surface of the brain. Draw an outline of the lateral aspect of a cerebral hemisphere and show the *Sylvian fissure* (aka *lateral sulcus*) runs diagonally from anterior-inferior to posterior-superior along the inferior one-third of the brain. Then, draw the *central sulcus* from the top of the brain to the Sylvian fissure. Label the area anterior to the central sulcus as the *frontal lobe*.

Next, label the *inferior preoccipital notch* along the posterior undersurface of the brain. Then, show the *superior preoccipital notch* on the posterior-superior aspect of the brain in the vertical plane of the inferior preoccipital notch. In our drawing of the medial aspect of the cerebral hemisphere, we will show that the parieto-occipital sulcus is the medial corollary to the superior preoccipital notch.

Draw a dotted (i.e., imaginary) line between the inferior preoccipital notch and the superior preoccipital notch. Posterior to this dotted line, label the *occipital lobe*. Next, draw a dotted horizontal line from the Sylvian fissure to the anterior border of the occipital lobe. Label the area above this horizontal line as the *parietal lobe* and the horn-shaped region below it as the *temporal lobe*. We have now drawn the four cerebral lobes visible on the lateral surface of the brain. The fifth lobe, the *limbic lobe*, is only present on its medial surface and is not represented in this diagram. We will draw it after we draw the lateral hemispheric gyri and sulci.

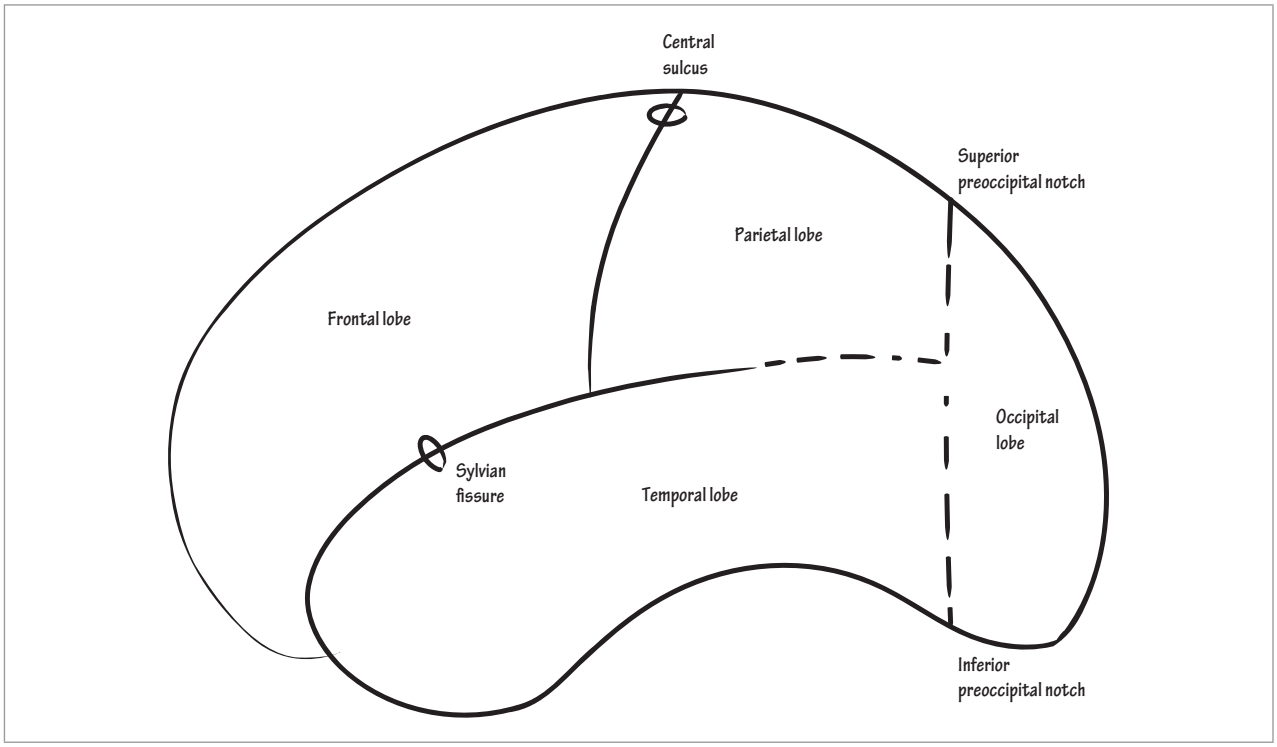


Figure 25-1 Cerebral lobes on lateral surface

Now, let's draw the gyri and sulci of the lateral surface of the brain. Redraw the *central sulcus* and label the *Sylvian fissure*. Divide the anterior frontal lobe into three horizontally distributed gyri using two parallel sulci that follow the contour of the outer surface of the brain. Label the sulci as the *superior frontal* and *inferior frontal sulci*. Then, indicate the *superior frontal gyrus* lies above the superior frontal sulcus, the *middle frontal gyrus* lies in between it and the inferior frontal sulcus, and the *inferior frontal gyrus* lies between the inferior frontal sulcus and the inferior border of the frontal lobe. The inferior frontal gyrus contains a pars orbitalis, pars triangularis, and pars opercularis. Later in this chapter, we will draw these three, specific areas as they relate anatomically to the Sylvian fissure.

While the superior, middle, and inferior frontal gyri make up the vast majority of the anterior frontal lobe, the precentral gyrus in the posterior frontal lobe is particularly important. It contains the primary motor neurons, which are arranged in the somatotopic motor homunculus, which we will draw at the end. The anterior boundary of the precentral gyrus is the vertically-oriented *precentral sulcus*; draw it in front of and in parallel to the central sulcus. Then, label the *precentral gyrus* in between these sulci. With that complete, label the undersurface of the frontal lobe as the *orbitofrontal cortex*. Its details are drawn along with rest of the undersurface of the brain later in this chapter.

Now, turn your attention to the parietal lobe. As a corollary to the frontal lobe precentral motor gyrus, the parietal lobe has a postcentral sensory gyrus. As you might imagine, it is bound by the central and postcentral sulci. Draw the vertically-oriented *postcentral sulcus* posterior to the central sulcus, and label the *postcentral gyrus* that lies between them. Just as the precentral gyrus contains the primary motor homunculus, the postcentral gyrus contains the primary sensory homunculus. The somatotopic maps of the motor and sensory homunculi correspond to one another.

Next, divide the remainder of the parietal lobe into the *superior parietal lobule* and the *inferior parietal lobule* with the horizontally-oriented *intraparietal sulcus*. The inferior parietal lobule further divides into the supramarginal and angular gyri. Both gyri straddle a sulcus or fissure in saddle-bag formation; put another way, they each wrap around the posterior termination of a sulcus or fissure in an upside-down "U" shape. First, show the *supramarginal gyrus* envelops the posterior end of the Sylvian fissure. Then, before we draw the angular gyrus, indicate the *superior temporal sulcus* runs horizontally through the upper third of the temporal lobe into the parietal lobe. After you finish drawing it, draw the *angular gyrus* around its posterior termination.

Now, let's complete the temporal lobe. We already established the position of the superior temporal sulcus. So, next, indicate the *inferior temporal sulcus* runs through the lower one-third of the temporal lobe. Three horizontally-oriented gyri constitute the temporal lobe as they do the frontal lobe. Label the *superior temporal gyrus* above the superior temporal sulcus, the *middle temporal gyrus* between the superior and middle temporal sulci, and the *inferior temporal gyrus* underneath the inferior temporal sulcus.

For the occipital lobe, simply label its lateral surface as the *occipital gyri* (aka *lateral occipital gyri*); the occipial pole serves as the primary visual cortex.

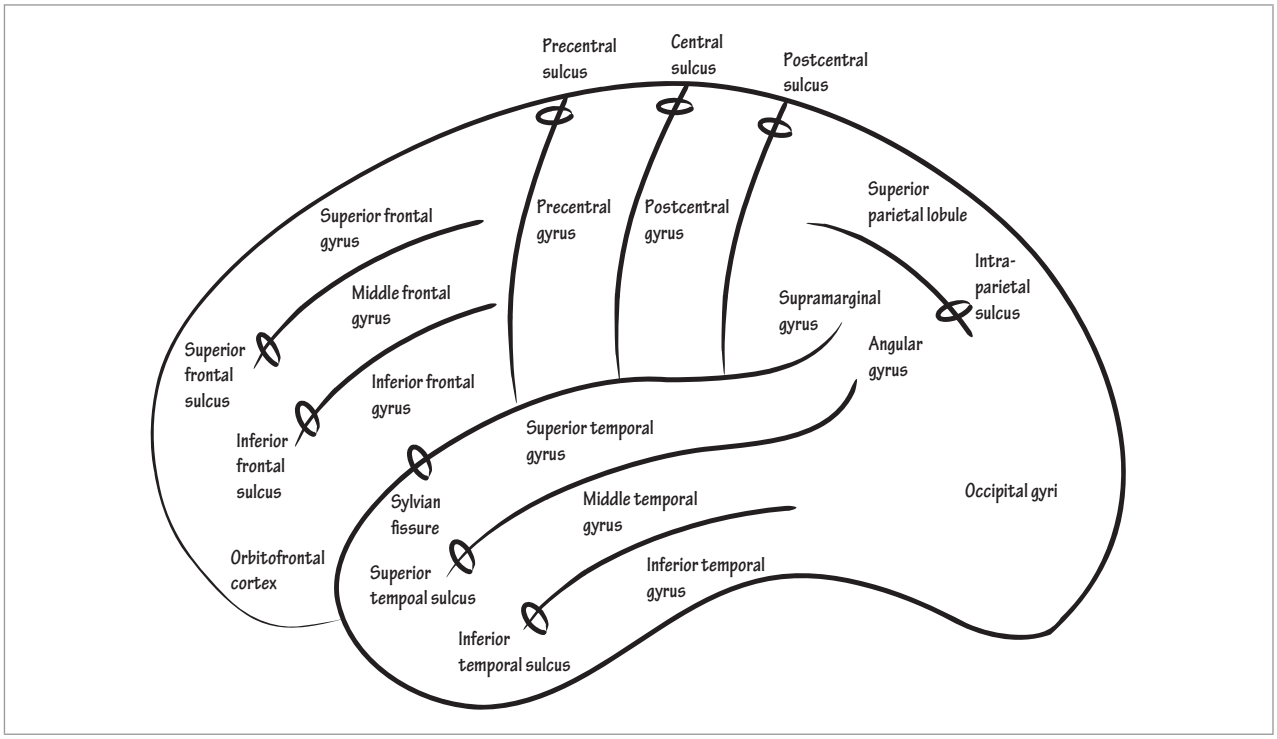


Figure 25-2 Gyri and sulci on lateral surface

Now, we will draw the medial surface of the brain; first, we will divide it into five lobes: frontal, parietal, limbic, temporal, and occipital. Then, we will subdivide these lobes into their gyri and sulci. The anatomy of the medial surface of the brain is potentially tedious. For practical purposes, simply think of the central sulcus as the division between the frontal and parietal lobes; the parieto-occipital sulcus as separating the parietal lobe from the occipital lobe; the inferior preoccipital notch as the division between the occipital and temporal lobes; and the limbic lobe as lying centrally, in a "C-shape," around the corpus callosum. In regards to the bullet points of the medial gyri and sulci, the primary gyrus of the frontal lobe is the superior frontal gyrus; the primary gyrus of the parietal lobe is the precuneus; the cuneus and lingual gyri are the primary gyri of the occipital lobe; the parahippocampal and occipitotemporal gyri constitute most of the temporal lobe; and the cingulate and parahippocampal gyri constitute the majority of the limbic lobe. Note, we group the parahippocampal gyrus with both the temporal and limbic lobes because not everyone considers the limbic lobe a separate anatomic lobe. With that background, now let's begin our drawings.

Draw an outline of the medial face of the right cerebral hemisphere. Include in this drawing the corpus callosum and the underlying diencephalon, which comprises the thalamic structures (we define the diencephalon, and discuss the embryology of the cerebral hemispheres, in the "Thalamus" chapter). First, we will demarcate the boundaries of the *limbic lobe*, which lies in the center of the brain. Draw the *cingulate sulcus* above and in parallel to the corpus callosum and the *collateral sulcus* in the temporal horn of the brain in parallel to its inferior border. These sulci delineate the limbic lobe.

Next, draw the anatomy of the *central sulcus* on the medial surface of the brain. Label the region anterior to the central sulcus as the *frontal lobe*. The frontal lobe spans from the frontal pole to the central sulcus. Next, draw the *parieto-occipital sulcus*, which originates along the posterior convexity of the brain and extends along the same anterior-inferior/posterior-superior diagonal as the collateral sulcus. What lobes of the brain does the parieto-occipital sulcus partition? Label the region above and in front of the parieto-occipital sulcus as the *parietal lobe* and the area below and behind it as the *occipital lobe*. Now, we are ready to demarcate the boundary between the parietal and limbic lobes. Draw a line joining the cingulate and collateral sulci; the limbic lobe lies in front of the line and the parietal lobe lies behind it.

No true topographic boundary separates the temporal lobe from the occipital lobe so we will create an imaginary one to satisfy our purposes. Identify the *inferior preoccipital notch* on the posterior undersurface of the brain as you did in our lateral surface diagram. Draw a dotted vertical line from the inferior preoccipital notch to the parieto-occipital sulcus. The occipital lobe ends at this dotted line. Indicate the *temporal lobe* lies in front of it.

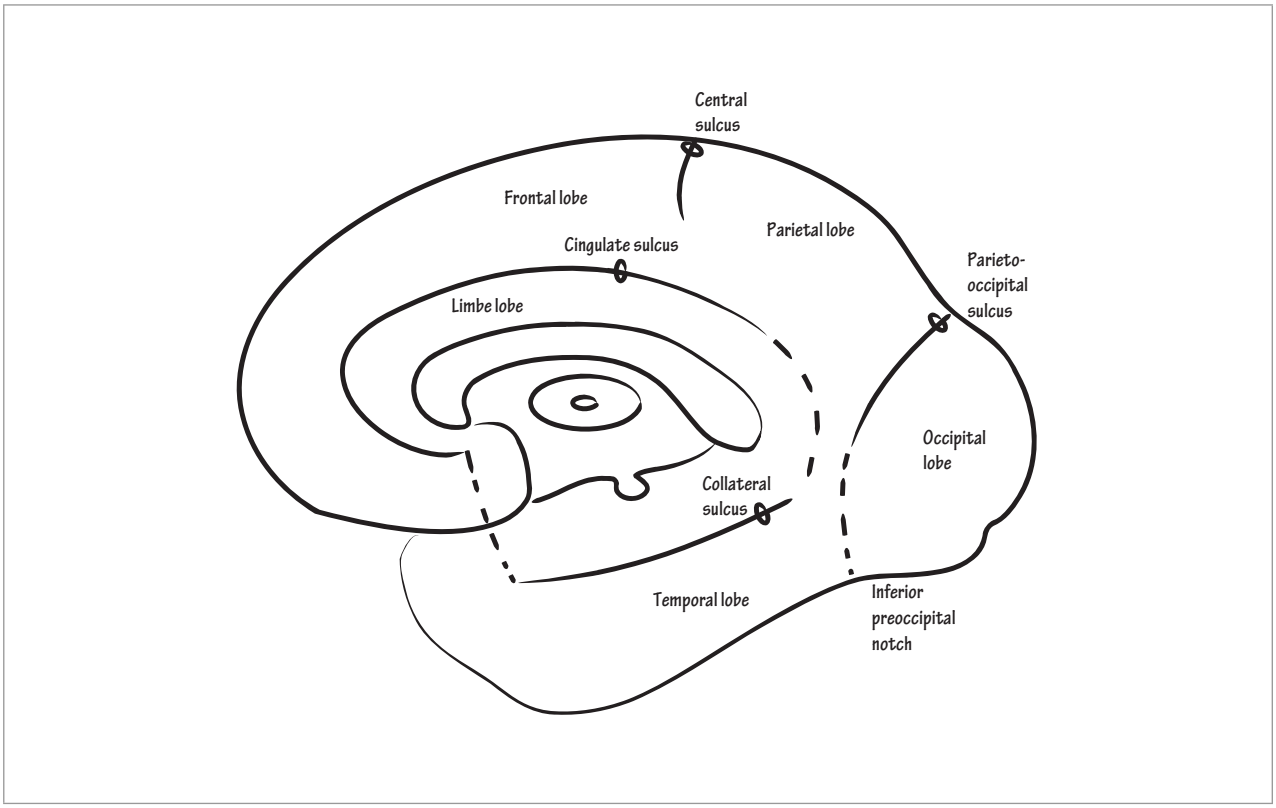


Figure 25-3 Cerebral lobes on medial surface

We are now ready to create a diagram of the gyri and sulci of the medial surface of the brain. First, redraw the cingulate, collateral, central, and parieto-occipital sulci. At the inferior tip of the parieto-occipital sulcus, draw the *calcarine sulcus*. It extends bidirectionally, that is, anteriorly and posteriorly. Posteriorly, it divides the occipital lobe into two gyri; label the superior one as the *cuneus* and the inferior one as the *lingual gyrus*.

Next, let's complete the temporal lobe. On the inferior aspect of the medial face of the temporal lobe, draw the *occipitotemporal sulcus* beneath and in parallel to the collateral sulcus. In between the occipitotemporal sulcus and the collateral sulcus, label the broad *occipitotemporal gyrus* (aka *fusiform gyrus*). In addition to being a part of the temporal lobe, is also a part of the occipital lobe, as its name reveals. Some authors divide the occipitotemporal gyrus into medial and lateral divisions; they label its posterior portion as the medial occipitotemporal gyrus and its anterior portion as the lateral occipitotemporal gyrus.

Now, we will complete the frontal lobe. The superior frontal gyrus (aka medial frontal gyrus) constitutes the majority of the medial surface of the frontal lobe. The remainder is constituted by the anterior paracentral gyrus. First, in the posterior frontal lobe, just anterior to the central sulcus, label the *paracentral sulcus*. Label the vast area from the paracentral sulcus to the anterior pole of the frontal lobe as the *superior frontal gyrus* (aka *medial frontal gyrus*). Then, in between the central sulcus and the paracentral sulcus, label the *anterior paracentral gyrus*. What, do you imagine, is the lateral hemispheric corollary to the anterior paracentral gyrus? The precentral gyrus. This point is important in regards to the motor homunculus; the majority of the motor homunculus lies along the lateral, precentral gyrus, but the leg hangs over the convexity of the brain and dangles along the anterior paracentral gyrus.

The major gyrus of the medial parietal lobe is the precuneus but the posterior paracentral gyrus is present, as well, and to draw it, we need to show that the *marginal branch of the cingulate sulcus* extends from the posterior cingulate sulcus to the top of the brain posterior and in parallel to the central sulcus. Now, just as we drew the anterior paracentral gyrus between the central and paracentral sulci, here draw the *posterior paracentral gyrus* (aka *posterior paracentral lobule*) between the marginal branch of the calcarine sulcus and the central sulcus. The posterior paracentral gyrus is the medial extension of the postcentral gyrus and, as such, it contains the leg component of the sensory homunculus. Label the area between the marginal branch of the cingulate sulcus and the parieto-occipital sulcus as the *precuneus*. What did we name the superior occipital area that lies inferior to the precuneus? The cuneus.

Finally, let's label the major gyri and sulci of the limbic lobe; it primarily comprises the cingulate gyrus, superiorly, and the parahippocampal gyrus, inferiorly. First, indicate the *callosal sulcus* runs along the dorsal surface of the corpus callosum. Next, in between the callosal and cingulate sulci, in the superior region of the limbic lobe, label the *cingulate gyrus*. Then, in the inferior region of the limbic lobe, label the *parahippocampal gyrus* above the collateral sulcus. We will draw the limbic lobe in further detail in the "Limbic System" chapter.

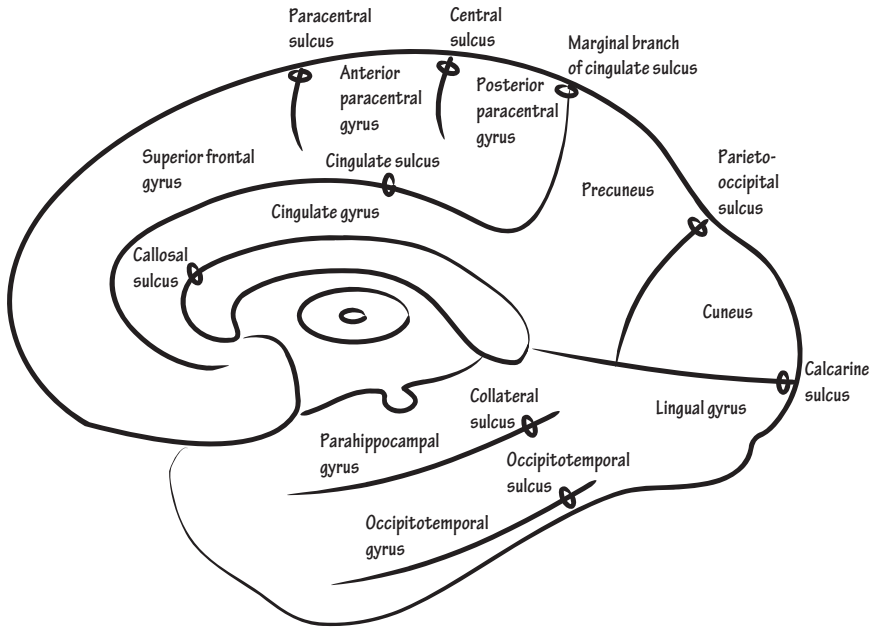


Figure 25-4 Gyri and sulci on medial surface

Next, we will draw the undersurface of the brain. Begin with an outline of the undersurface of both cerebral hemispheres. Also, include in this diagram the optic chiasm and an axial section through the midbrain for orientational purposes.

We will use one side of the drawing to label the lobes of the brain as well as their gyri and sulci. First, draw the temporal horn of the temporal lobe in the anterior two-thirds of the cerebral hemisphere. Distinguish the *temporal lobe* from the *frontal lobe* above and in front of it. Just inside the medial border of the frontal lobe, in anterior–posterior orientation, draw the *olfactory sulcus*. Show the *olfactory bulb* and *tract* run within it, which gives it its name. Medial to the olfactory sulcus, label the *gyrus rectus* and lateral to the olfactory sulcus, label the *orbital gyri*. The orbits of the eyes, fittingly, lie underneath the orbital gyri. Now, where the cerebral hemispheres touch posteriorly, draw an imaginary horizontal dotted line to separate the temporal lobes, anteriorly, from the *occipital lobes*, posteriorly.

Within the temporal lobe, draw the following three anterior–posterior oriented sulci: the *collateral sulcus*, medially; the *occipitotemporal sulcus*, centrally; and the *inferior temporal sulcus*, laterally. Label the anterior portion of the collateral sulcus as the *rhinal sulcus*. Notice, the undersurface of the temporal lobe is also its medial surface because the temporal lobe is sloped. Label the *parahippocampal gyrus* medial to the collateral sulcus and the *occipitotemporal gyrus* lateral to it. Then, label the *uncus* in the anteromedial temporal lobe. As mentioned when we drew the occipitotemporal gyrus in the medial face of the temporal lobe, the occipitotemporal gyrus is a particularly broad gyrus that extends into the occipital lobe.

Now, turn your attention to the opposite side of our diagram where we will draw the medial–lateral anatomy of the Sylvian fissure. The region surrounding the optic chiasm is the anterior perforated substance, which is perforated by short branches of the proximal middle cerebral artery. Show the *internal carotid artery* just lateral to the optic chiasm. Next, with a caret sign, denote the origin of the *Sylvian fissure*, which is called the *vallecula*. Then, draw the *stem* of the Sylvian fissure from the apex of the vallecula to the lateral edge of the temporal lobe. The proximal middle cerebral artery (aka the M1 branch) travels in the stem of the Sylvian fissure. To complete the Sylvian fissure, we need to draw another lateral face of the cerebral hemisphere.

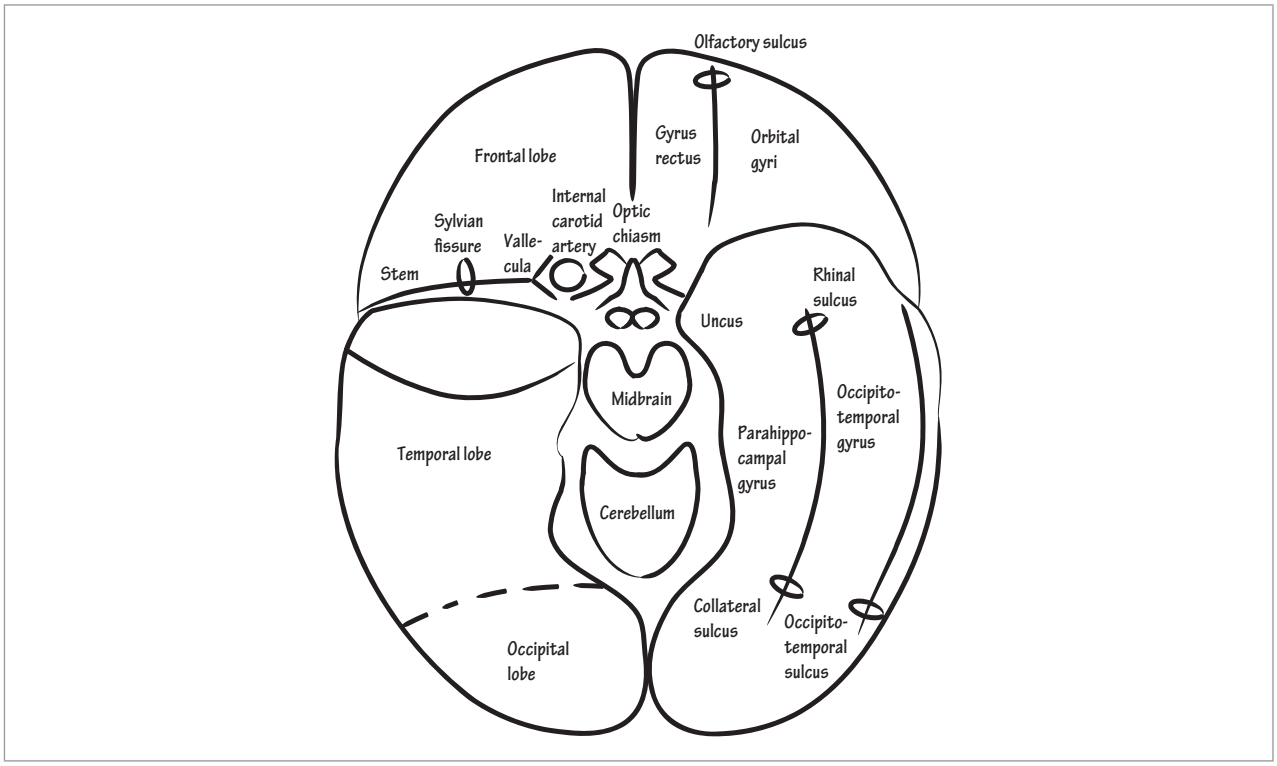


Figure 25-5 Gyri and sulci on undersurface

Draw an outline of the lateral cerebral hemisphere and include the central sulcus for orientational purposes; don't draw the complete Sylvian fissure yet, though—we will draw it in stages. Imagine the Sylvian fissure comprises anterior-inferior and posterior-superior divisions. When we drew the lateral surface of the frontal lobe, we established that the inferior frontal gyrus subdivides into pars orbitalis, pars triangularis, and pars opercularis. We will use the anterior-inferior Sylvian fissure to demarcate these divisions and we will again show how its posterior-superior division separates the parietal and temporal lobes and indents the supramarginal gyrus.

First, draw the anterior-inferior portion of the Sylvian fissure; show it follow the curvature of the superior cerebral hemisphere. At the mid-point of the anterior-inferior segment of the Sylvian fissure, draw a "V" onto it; the legs of the "V" form rami extensions from the Sylvian fissure. Label the lower leg of the "V" as the *anterior horizontal ramus* and the upper leg as the *anterior ascending ramus*: the anterior horizontal ramus runs horizontally and the anterior ascending ramus runs superiorly. As mentioned, these rami subdivide the inferior frontal gyrus. Beneath the anterior horizontal ramus, label the *pars orbitalis*; it is closest to the orbit. Then, label the triangular-shaped *pars triangularis* in between the two rami. Finally, label the *pars opercularis* above the ascending horizontal ramus. Operculi are cortical coverings over the insula, which we will draw next. The frontal, parietal, and temporal lobes each contribute opercular divisions and the pars opercularis is the frontal lobe's opercular contribution.

Next, let's draw the posterior-superior division of the Sylvian fissure. Begin with the horizontally directed *posterior horizontal ramus*; it separates the temporal and anterior parietal lobes. Now, complete the Sylvian fissure with its short *posterior ascending ramus*. The supramarginal gyrus forms around this posterior termination of the Sylvian fissure.

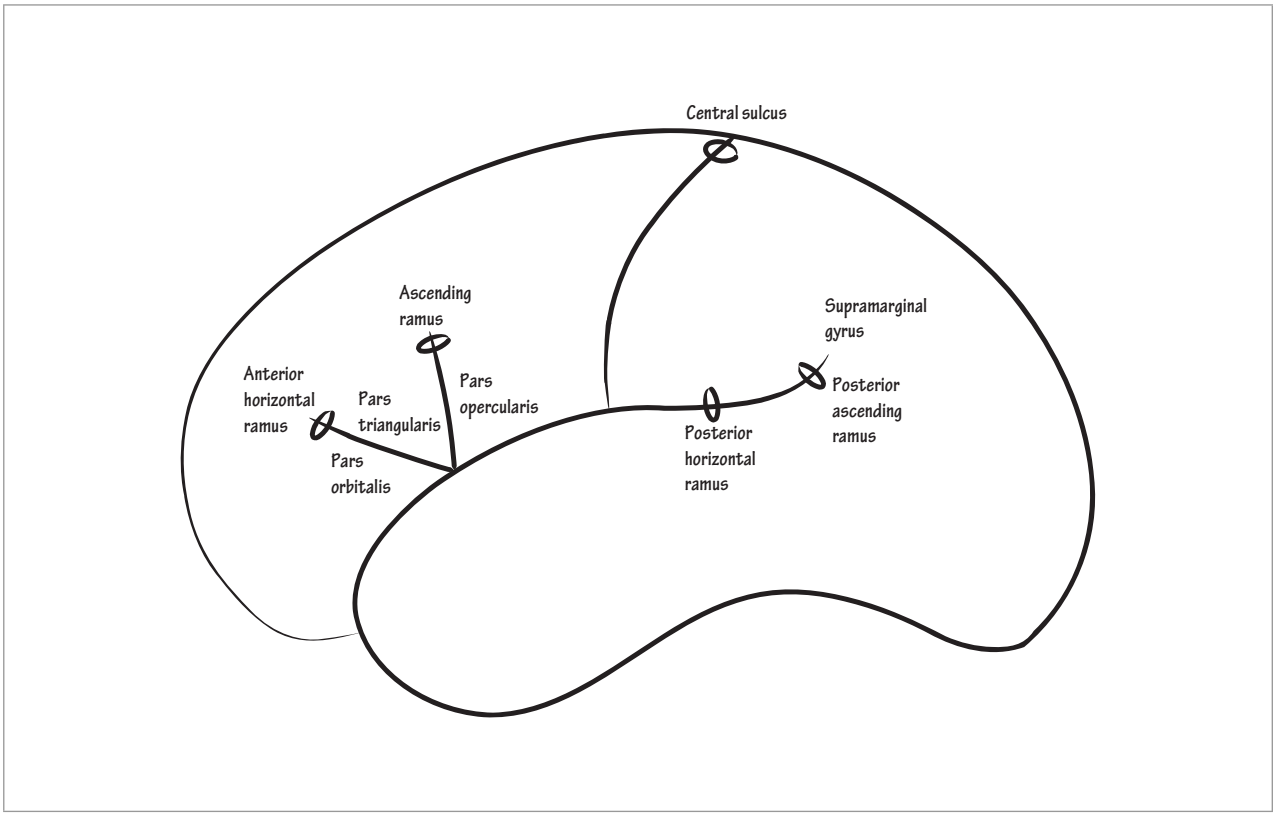
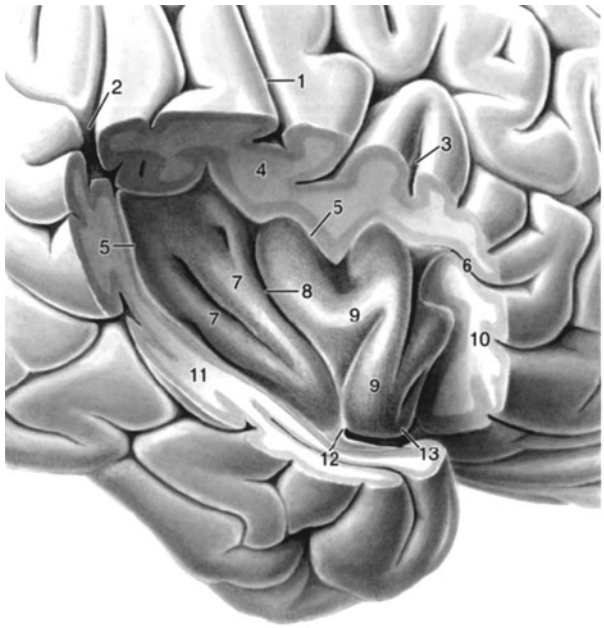


Figure 25-6 Sylvian fissure

Now, we will draw the insular cortex, which underlies the operculum. The opercula and the transverse temporal gyri are clinically important aspects of insular anatomy. Begin with an outline of the lateral cerebral hemisphere but this time show the covering of the insula as peeled back. Within the insula, show the C-shaped *circular sulcus*, which surrounds the deep insular cortex. Surrounding the circular sulcus, label the *frontal*, *parietal*, and *temporal opercula*.

Next, draw the *central sulcus of the insula*, which runs in parallel to the Sylvian fissure that overlies it. Show the central sulcus of the insula divides the insula into *short gyri*, anteriorly, and *long gyri*, posteriorly. Label the *transverse temporal gyri* (aka *transverse gyri of Heschl*) in the posterior insula. Show they extend out across the superior temporal gyrus. The transverse temporal gyri comprise the primary auditory cortex.



1 Central sulcus
2 Lateral sulcus, posterior branch
3 Lateral sulcus, ascending branch
4 Frontoparietal operculum
5 Circular sulcus of the insula
6 Lateral sulcus, anterior branch
7 Long gyrus of the insula
8 Central sulcus of the insula
9 Short gyri of the insula
10 Frontal operculum
11 Temporal operculum
12 Limen insulae
13 Anterior pole of the insula

Photo 25-4 Insular cortex
With permission from Nieuwenhuys, R., C. Huijzen, J. Voogd, and SpringerLink (Online service). *The Human Central Nervous System*. Berlin, Heidelberg: Springer, 2008.

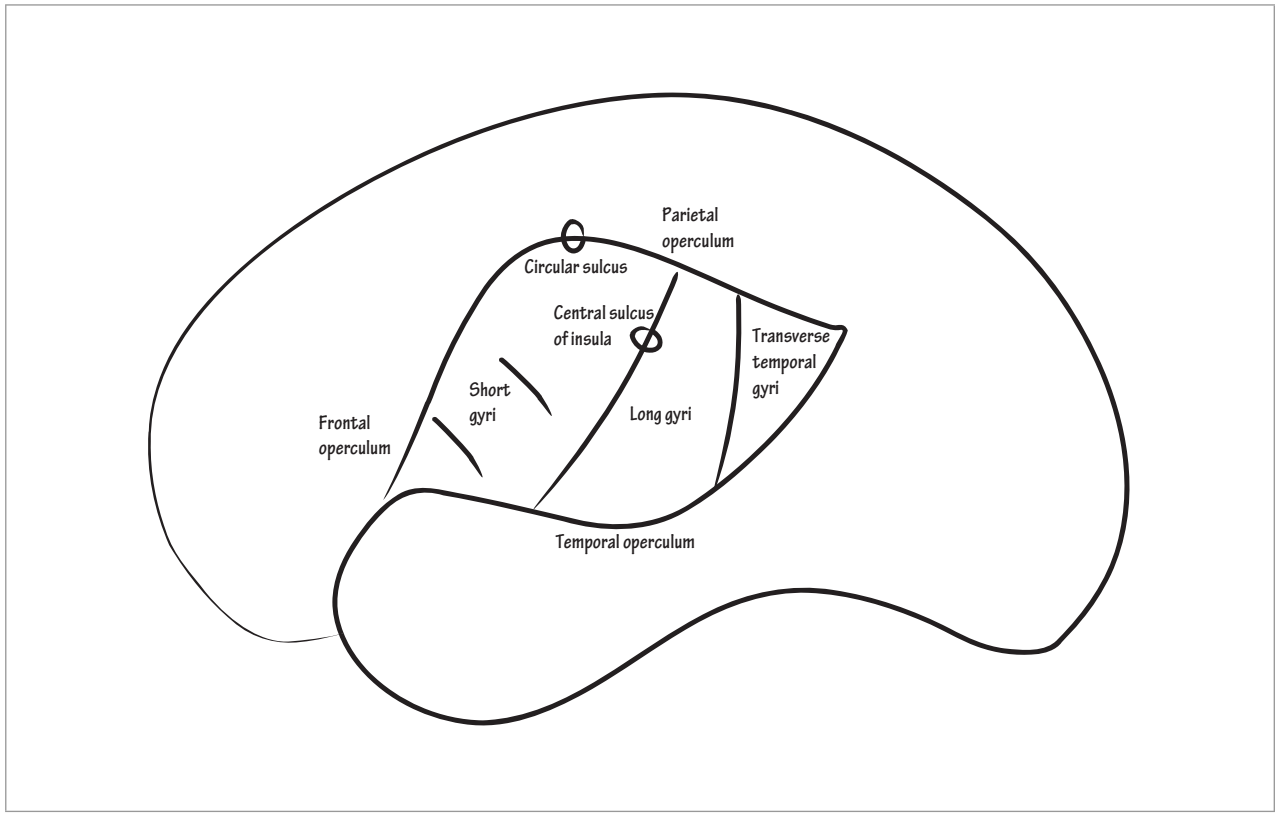


Figure 25-7 Insular cortex

At the turn of the twentieth century, Korbinian Brodmann developed cytoarchitectural maps of the human brain that distinguish 47 different cytoarchitectural areas. His maps are still used today in neuroanatomical vernacular. It would be impractical and of limited help to learn all of the 47 different areas, but we need to learn the commonly referenced ones. The complete maps are also included in this chapter for reference.

Draw a lateral surface of the cerebral hemisphere and include the central sulcus. In front of it, label *area 4*, which is the primary motor cortex. Behind it, within the postcentral gyrus, from anterior to posterior, label *areas 3, 2, 1*; they constitute the primary sensory cortex. We draw the somatotopic maps of the primary motor and sensory cortices in the next diagram. Now, in front of area 4, label *area 6*, which lies within the broad premotor and supplemental motor area. In front of it, label *area 8*. As we will discuss in the "Eye Movements" chapter, the frontal eye fields of monkeys lie in area 8, but recent functional imaging studies show they lie in humans in areas 4 and 6.

Now, in front of area 8, label *area 9*, which along with *area 46*, below it, comprise the dorsolateral prefrontal cortex; it is important for executive planning (i.e., sequential task completion). Next, show that *area 44* is pars opercularis and *area 45* is pars triangularis; together, they comprise Broca's area. Then, show the primary auditory cortex is in *areas 41* and *42* and Wernicke's area is in the posterior portion of *area 22*. Both Broca's and Wernicke's areas are important language centers. Finally, label the primary occipital cortex as *area 17* and the secondary and tertiary occipital cortices as *areas 18* and *19*, respectively; they are important visual reception areas.

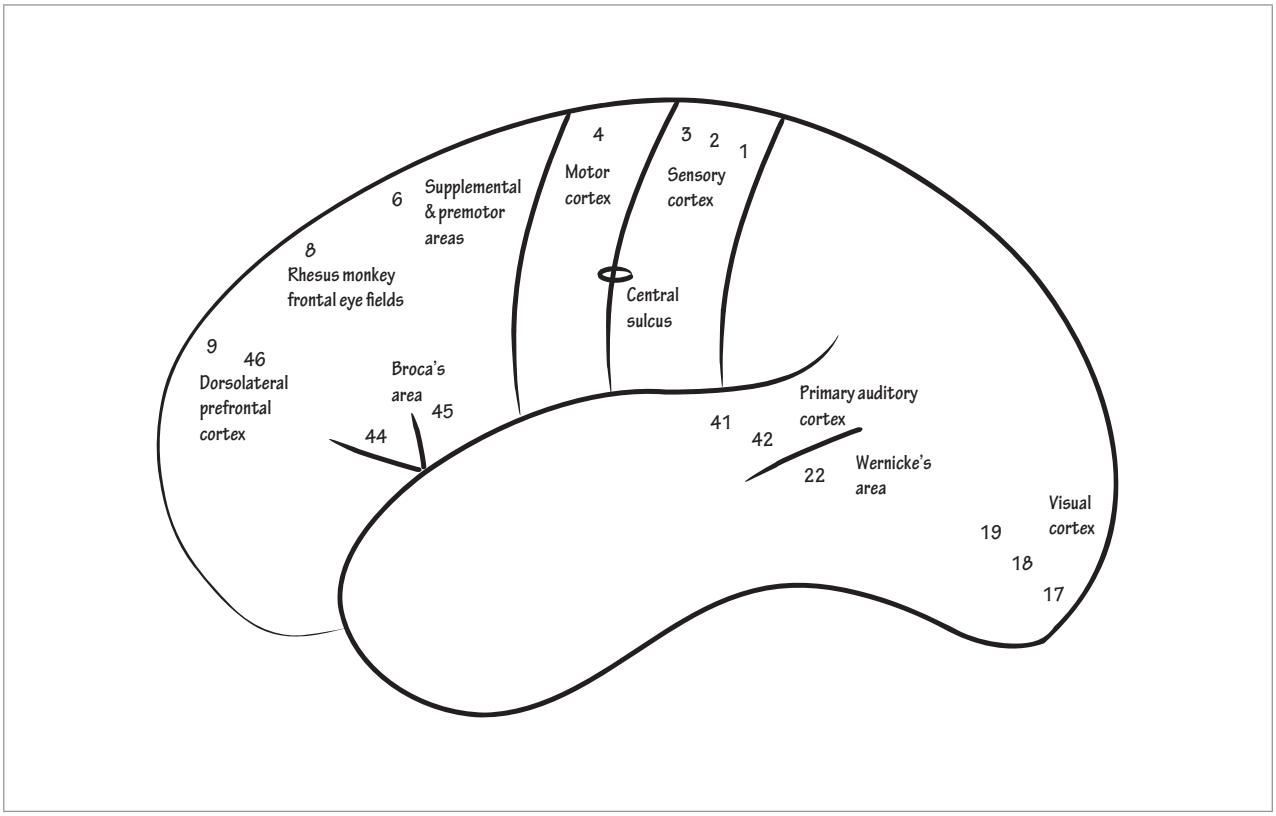


Figure 25-8 Brodmann map highlights

The cortical map of the sensory and motor fibers within the cerebral cortex is called the homunculus; it is the representation of sensory coverage and motor control of different body parts. Each body region's cortical size is determined by the amount of nervous system tissue dedicated to it rather than the actual body size. The mouth and hand, for instance, are disproportionately large because so much nervous system tissue is devoted to fine motor and sensory innervation.

In our diagram, we will use a coronal section to show the homunculus as it was drawn in Wilder Penfield's *The Cerebral Cortex of Man*. Start with the *throat* and *tongue*; label them overlying the frontal operculum. Then, label the *face* higher up along the precentral gyrus. March even higher along the precentral gyrus and label the *thumb* and *rest of the hand*. Above the hand, on the upper convexity of brain, indicate the *arm* and *torso*. Label the *hip* hanging over the convexity and the *leg* and *foot* dangling down along the medial surface of the brain into the paracentral lobule. For orientational purposes, consider the crossing corpus callosum fibers and the cingulate cortex that lie above it. Note that while the foot stretches down the medial surface of the brain, it stops short of the cingulate gyrus.

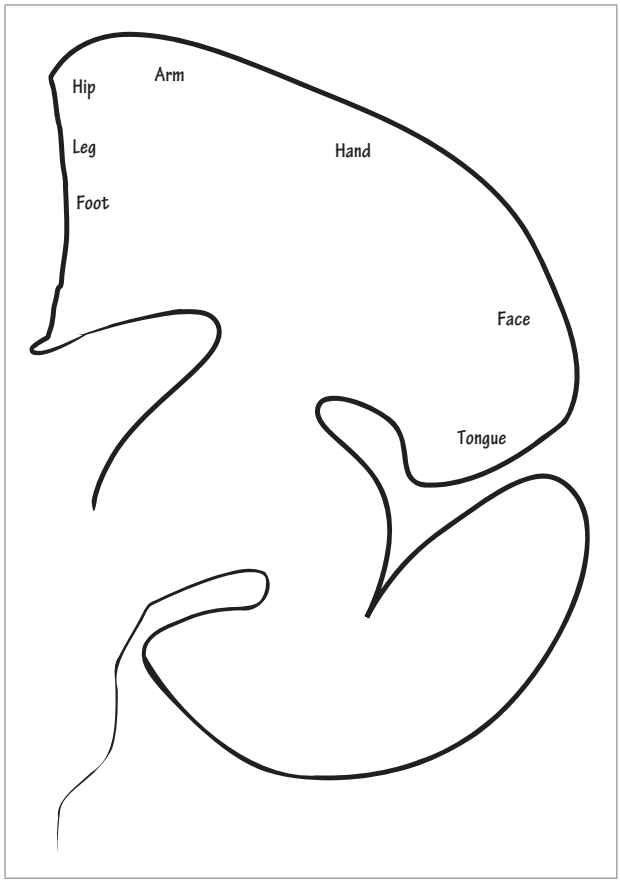


Figure 25-9 Homunculus

White Matter Pathways

WHITE MATTER PATHWAYS are the train-tracks of the nervous system. If they are interrupted, impulses stagnate. Historically, the number of publications on white matter has paled in comparison to that on gray matter. However, now, with diffusion tensor imaging and other radiographic techniques dedicated to imaging the white matter pathways, much is being learned about their anatomy. Recent attempts to clarify white matter anatomy using audiographic and diffusion spectrum imaging techniques were compiled in a remarkable book entitled *Fiber Pathways of the Brain*, by Jeremy Schmahmann and Deepak Pandya. Images from that book are included at the start of this chapter.

White matter bundles are organized as association, striatal, or cord fibers. Association fibers connect cerebral cortical areas within the same hemisphere, striatal fibers communicate between the cortex and basal ganglia, and cord fibers connect areas on opposite sides of the brain. In this chapter, we will draw prototypical examples of these white matter pathways as well as specific white matter tracts.

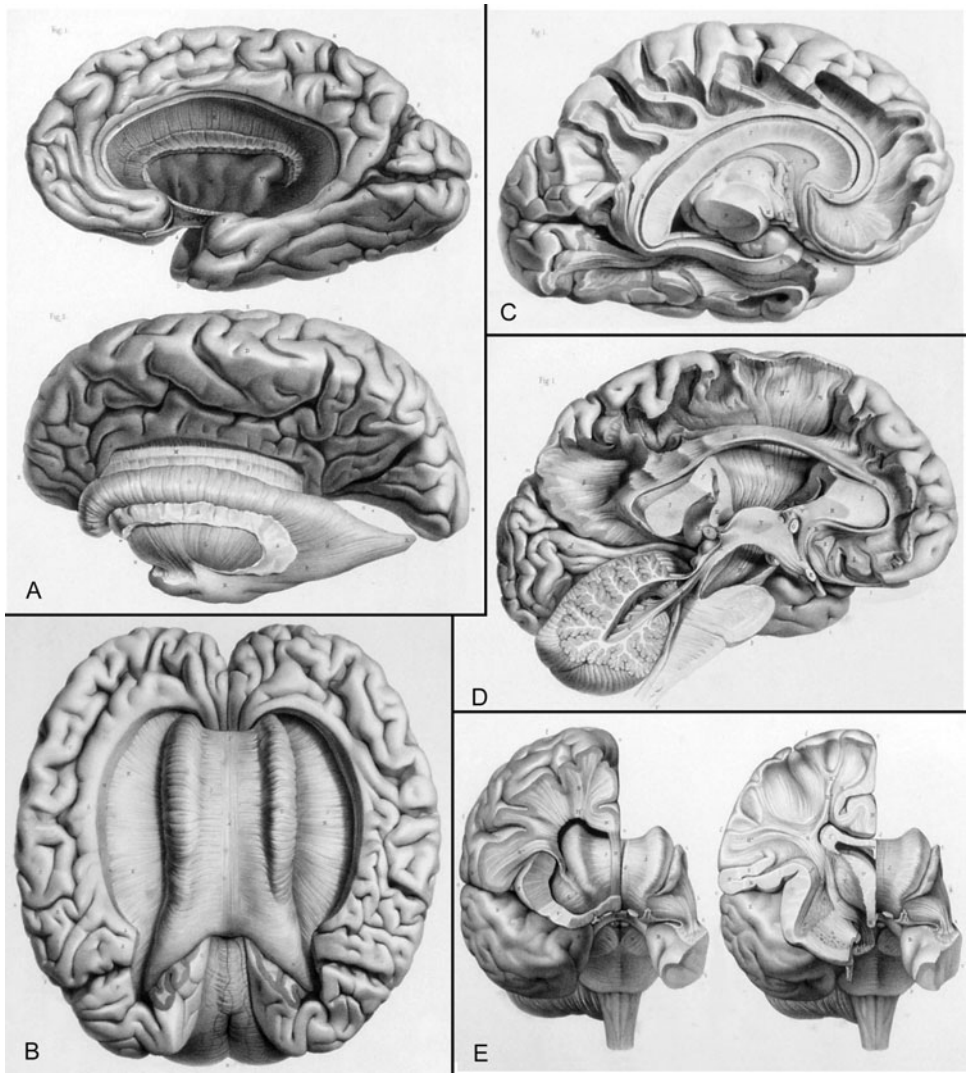


Photo 26-1 Achille-Louis Foville's illustrations of white matter, 1844
With permission from Schmahmann, J. D., and D. N. Pandya. *Fiber Pathways of the Brain*. New York: Oxford University Press, 2006.

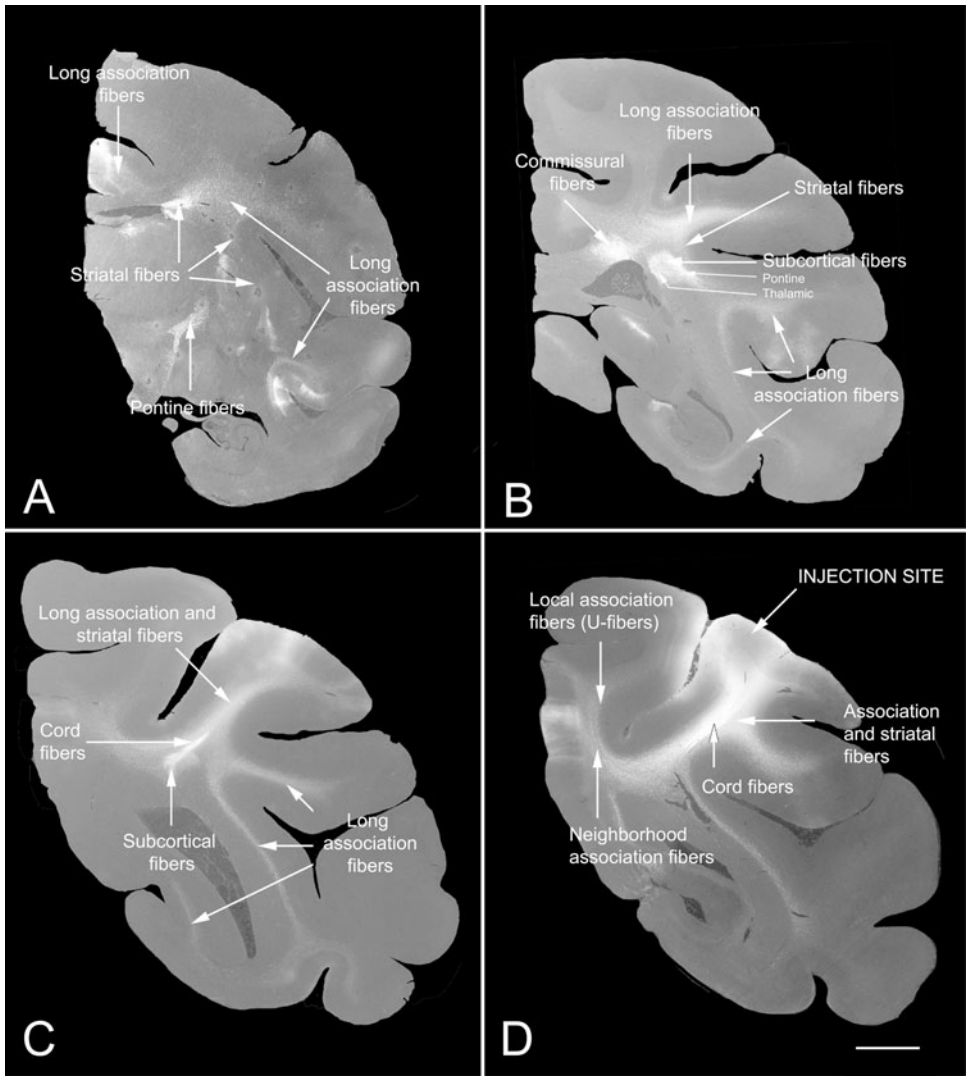


Photo 26-2 Dark-field photomicrographs of rostral to caudal coronal sections to illuminate white matter pathways
With permission from Schmahmann, J. D., and D. N. Pandya. *Fiber Pathways of the Brain*. New York: Oxford University Press, 2006.

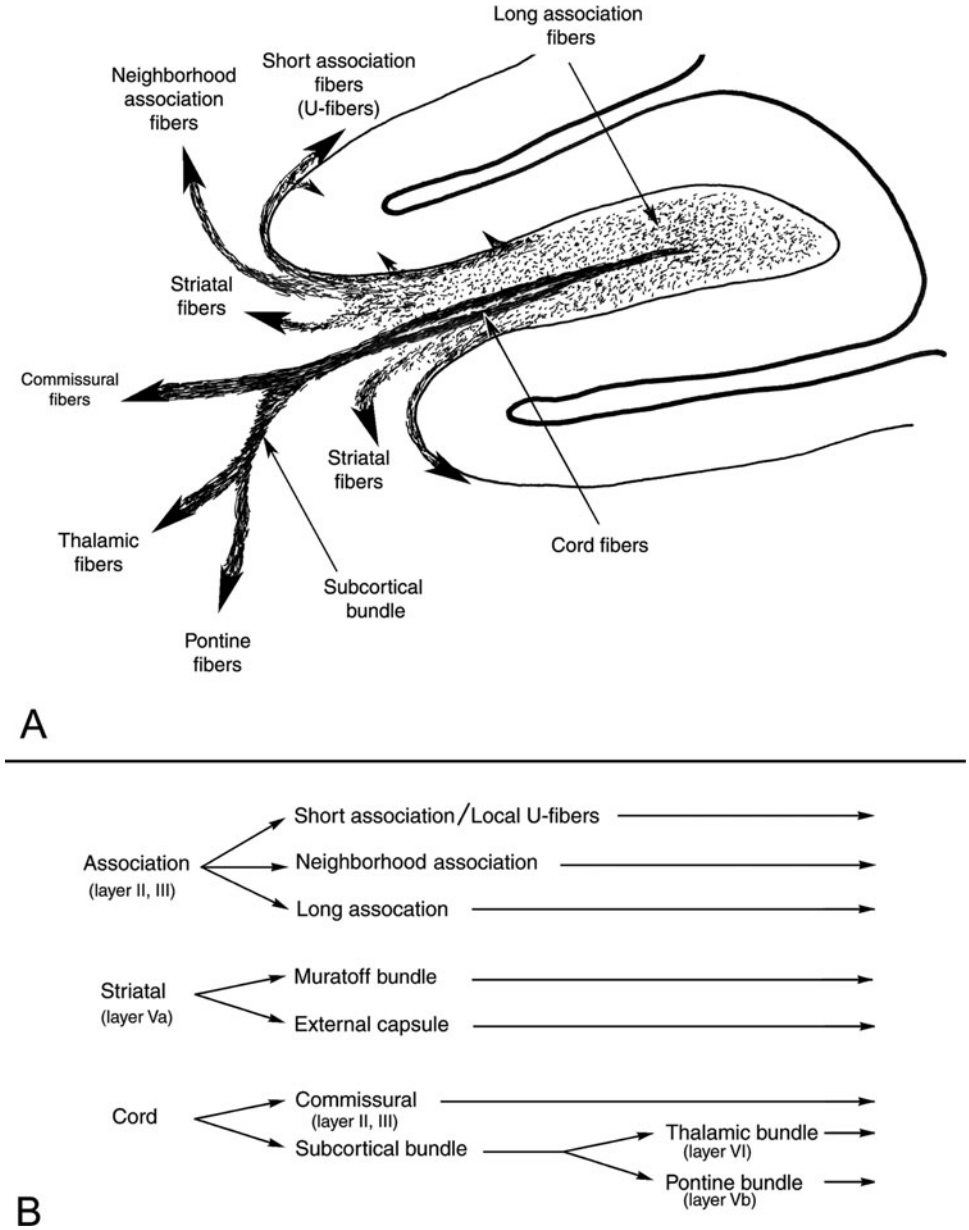


Photo 26-3 Organization of white matter

With permission from Schmahmann, J. D., and D. N. Pandya. *Fiber Pathways of the Brain*. New York: Oxford University Press, 2006.

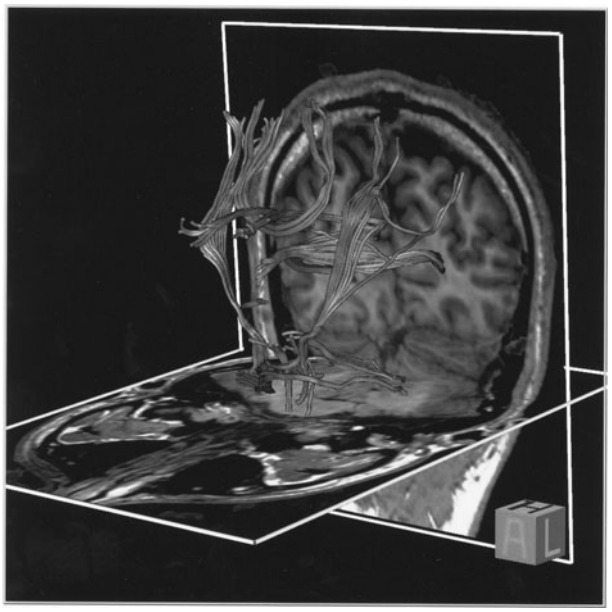


Photo 26-4 Diffusion tensor imaging reconstruction of multiple pathways

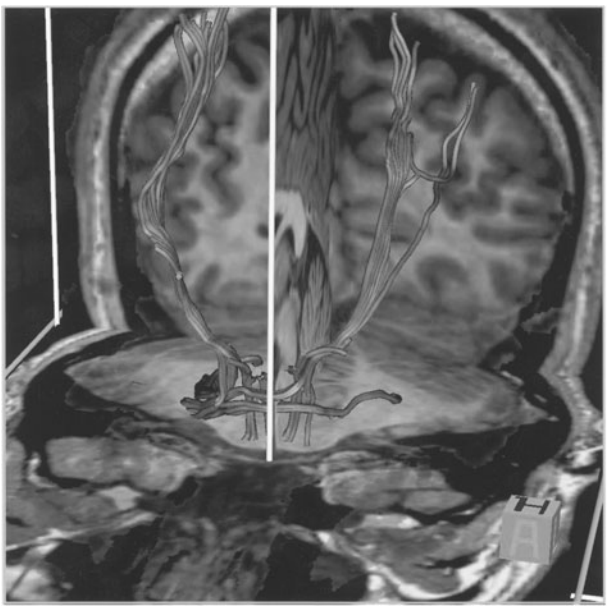


Photo 26-5 Diffusion tensor imaging reconstruction of cortico-ponto-cerebellar pathways

Let's begin our drawing of the three types of white matter pathways with the association fibers. Draw a coronal section through the neuraxis; include a single sulcus along the surface of the cerebral cortex for reference. There are three subtypes of association fibers that differ based on the distance they travel, but all three connect cortical areas within the same side of the brain. First, draw a short-stretching association fiber called a *cortical U-fiber* (aka *arcuate bundle*). Cortical U-fibers travel between gyri, superficially, just underneath sulci. Then, draw a middle-distance stretching association fiber called a *neighborhood fiber*. Neighborhood fibers extend into the "deep white matter" to connect areas farther away from one another than the cortical U-fibers do. Finally, draw a *long association fiber*. Long association fibers extend deep into the brain and connect ipsi-hemispheric regions the farthest distance away. Later, we will use a sagittal view of the brain to draw the different named long association fibers.

Next, draw a prototypical *striatal fiber* projection from the cortex to the basal ganglia (aka *striatum*). Projections from throughout the cortex synapse in the basal ganglia and are evidence of the widespread role of the basal ganglia in behavior as well as motor function.

Now, we will draw the cord fibers, which connect opposite sides of the nervous system. They form the dense aggregate of deep white matter underneath the cortical gray matter. The cord fibers are subdivided into transverse-oriented commissural and vertically oriented subcortical projection bundles. Draw a *commissural fiber* connection from one side of the cortex to the other through the corpus callosum. Then, draw a *subcortical projection fiber* from the cortex to the opposite side of the brainstem. Ascending projection fibers from the spinal cord often cross in the brainstem, synapse in thalamus, and ascend to the cortex.

Next, we will draw named association fibers in sagittal section. However, our first two association fiber types—the short-length U-fibers and middle-distance neighborhood fibers—are unnamed. We still want to include them in this diagram, though, so we will simply represent them, again, as representative, prototypical fibers. The long association fibers, on the other hand, are individually named.

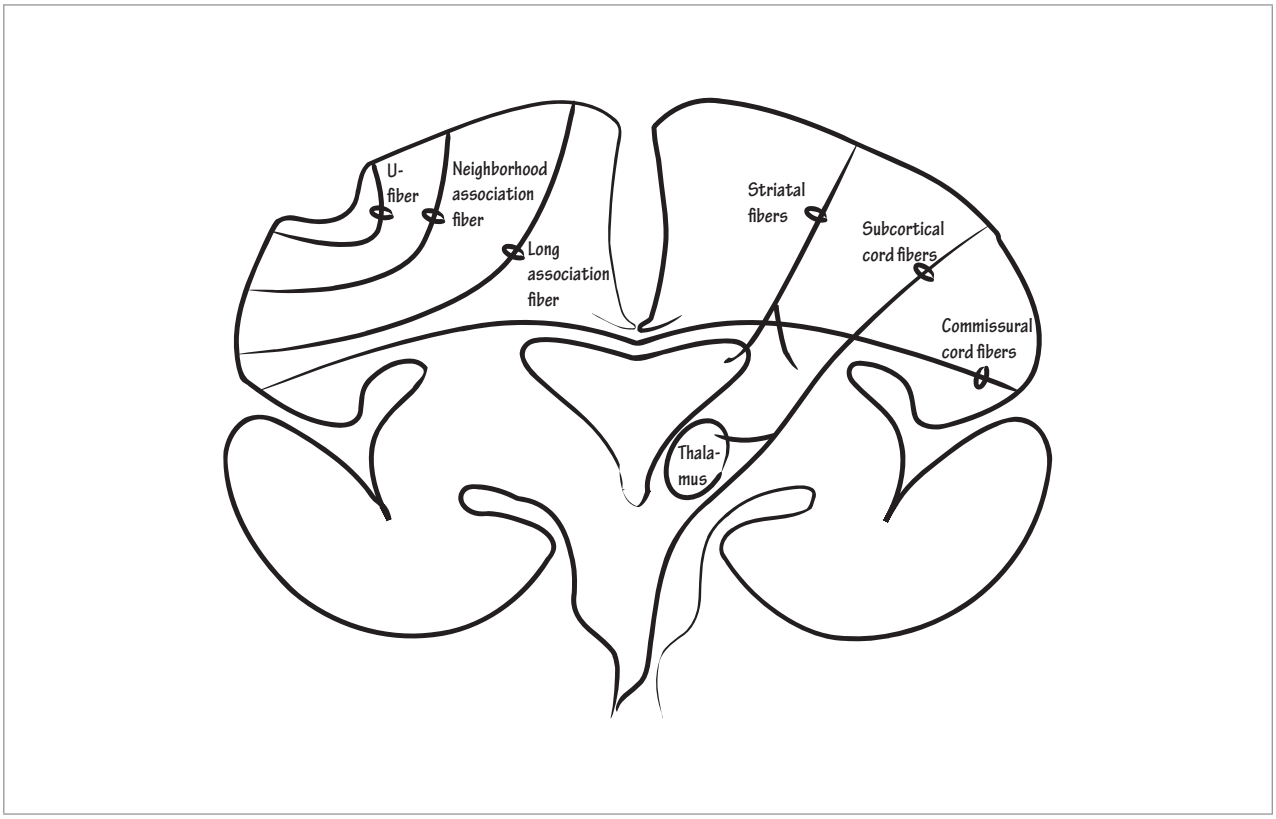


Figure 26-1 Coronal overview of white matter tracts

In sagittal view, now, draw a prototypical *U-fiber*. Often, certain white matter diseases, such as subtypes of multiple sclerosis, spare the U-fibers, which is a distinguishing feature of them on radiographic imaging. Next, draw a prototypical *neighborhood association bundle*; it dips deeper into the brain and connects areas farther away from one another than the U-fibers do.

The long association fibers are named based on their anatomical location. Draw the *superior longitudinal fasciculus* from the frontal to the occipital cortex passing through the parietal cortex (i.e., through the superior cerebral white matter). The width of the superior longitudinal fasciculus spans from the medial to the lateral cerebrum, and so it is subcategorized into three different fasciculi based on their medial to lateral positions, but we leave out the subcategorization here for simplicity. Historically, the superior longitudinal fasciculus was synonymous with the arcuate fasciculus and these fiber bundle names were used interchangeably. With modern imaging techniques, the pathways are distinguishable, however.

Show the *arcuate fasciculus* originate in the superior temporal region and arc laterally around the corpus callosum to the frontal lobe. The ability to repeat language, which is called language conduction, has long been assigned to the arcuate fasciculus. Ask someone to repeat the sentence, "No ifs, ands, or buts . . . " The sentence has to be heard and processed, which takes place in the superior temporal area, and then transferred to the frontal motor speech area to be repeated. Language conduction will sometimes persist despite deficits in language understanding or expression.

Details regarding language processing and language disorders (aka aphasias) are described in the "Language" chapter but we include a summary here of the names of many important aphasias as they relate to preservation or impairment in the ability to repeat. If language conduction is unimpaired but a motor aphasia exists, it is called a transcortical motor aphasia and if language conduction is unimpaired but a sensory (i.e., understanding) aphasia exists, it is a transcortical sensory aphasia. If conduction is disrupted along with speech production, it is a motor (aka *Broca's*) aphasia, and if conduction is disrupted along with language understanding, it is a sensory (aka *Wernicke's*) aphasia. If conduction is impaired with both motor and sensory deficits, it is a global aphasia. Finally, if conduction is impaired but there is preservation of both motor and sensory language, it is a conduction aphasia.

While conduction is classically assigned to the arcuate fasciculus, present evidence suggests the arcuate fasciculus is more generally involved in spatial orientation of sound and that it does not have any specific role in language conduction. Language conduction, it is currently argued, is actually dependent on the superior longitudinal fasciculus and the striatal fiber extreme capsule, drawn next. However, until this line of thinking becomes more widely accepted, you should probably still consider the arcuate fasciculus as responsible for language conduction.

Now, draw the *uncinate fasciculus*, which spans from the orbital prefrontal cortex to the anterior temporal lobe. This white matter bundle has a wide range of roles in behavior. It is believed to combine sensory perception modalities with emotional response regulation and help to provide the capacity for decision-making skills.

The cingulum is a main white matter bundle of the limbic system and it travels through the limbic gyrus. Draw the *cingulum* passing through the cingulate gyrus, isthmus and parahippocampal gyrus, now. Interestingly, cingulotomy (i.e., cingulum fiber transection) was unsuccessfully used to treat psychosis in the mid-twentieth century and was abandoned, but is now used, in certain instances, for the treatment of obsessive-compulsive disorder and intractable pain.

Next, draw the *inferior longitudinal fasciculus* from the parieto-occipital cortex to the temporal cortex. It plays a role in the ventral occipitotemporal visual pathway. The visual system has both primary receptive and secondary processing areas. In 1982, Ungerleider and Mishkin proposed that there are ventral and dorsal pathways for visual processing, which we will discuss in detail in the "Visual Pathways" chapter, but as an introduction, the primary visual receptive area lies in the occipital cortex and ventral and dorsal white matter pathways carry visual information through the secondary processing areas. The ventral occipitotemporal visual pathway is believed to recognize and identify objects, and so it is called the "what" pathway. The "where" pathway corollary to the ventral occipitotemporal "what" pathway is the fronto-occipital pathway; it processes visual spatial information. Draw the *fronto-occipital pathway*, now, in the superior cortex from the parieto-occipital to the prefrontal area. As a visual spatial pathway, the fronto-occipital pathway carries spatial information from the parietal lobe to the frontal lobe and guides the activation of movement; it "shows it the way."

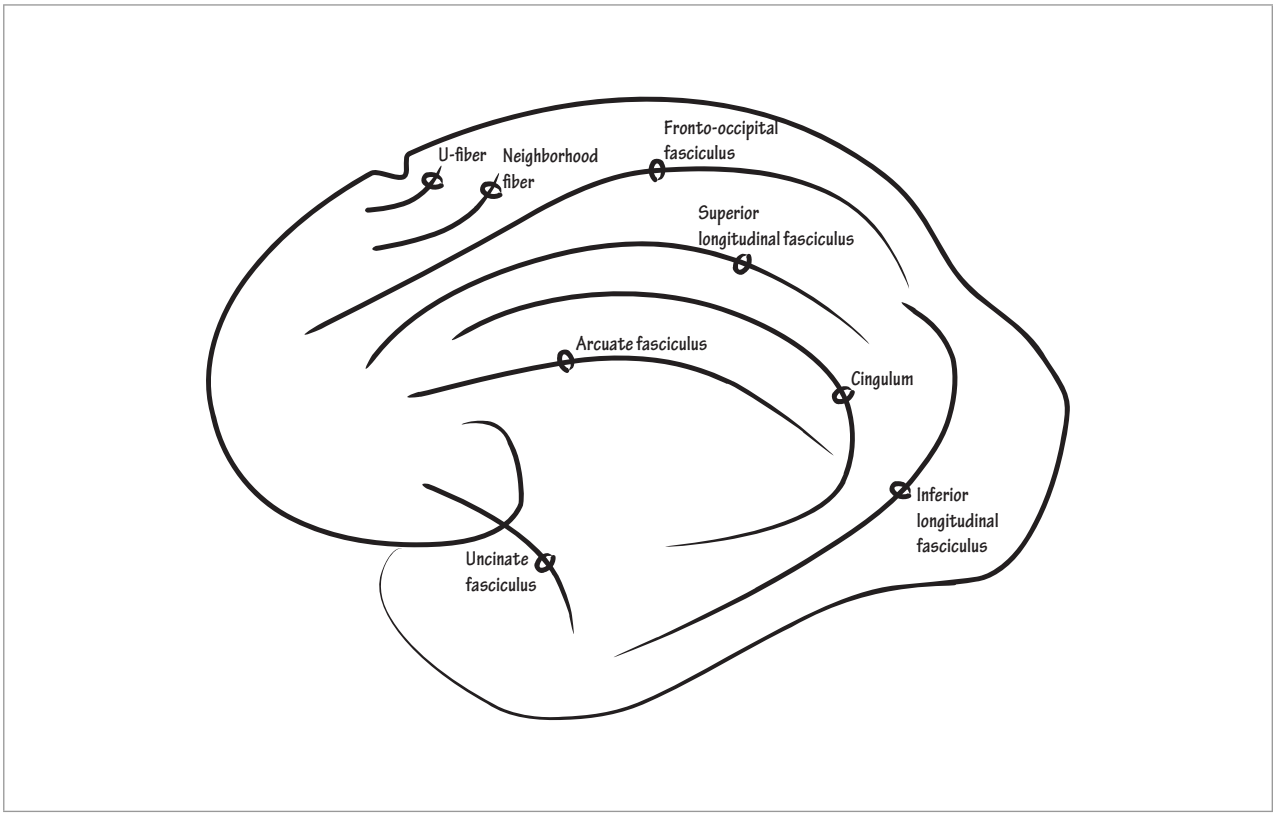


Figure 26-2 Sagittal view of white matter tracts

Within the basal ganglia, the *external* capsule descends from the cortex in between the putamen and claustrum and the *extreme* capsule makes its descent in between the claustrum and insula. The extreme capsule connects the middle temporal and prefrontal cortices; it is important in nonarticulatory language components such as syntax and grammar.

Now, let's address the commissural fibers, which interconnect corresponding areas of cerebral cortex; the two main ones are the anterior commissure and the corpus callosum. The corpus callosum lies superior to the anterior commissure and connects dorsal cortical areas while the anterior commissure connects ventral areas. To show both in the same drawing, we will use an axial plane through the ventral surface of the brain. Hash the *anterior commissure* bundle, which connects the bilateral posterior frontal and also the bilateral anterior temporal lobes. Then, draw the *corpus callosum* fibers. They connect the bilateral hemispheres from the frontal pole (the rostral tip of the frontal lobes) to the occipital pole (the caudal tip of the occipital lobes). Indicate the frontal fibers are called the *anterior forceps* (aka *forceps minor*) and the occipital fibers are called the *posterior forceps* (aka *forceps major*). The four regions of the corpus callosum are only all able to be seen in sagittal view, so let's draw a separate sagittal section to show them, now.

Label the anterior-inferior tip as the *rostrum*, the anterior-superior section as the *genu*, the length of the corpus callosum as the *body*, and the caudal portion as the *splenium*. The genu fibers correspond to the anterior forceps, the splenial fibers to the posterior forceps, and the body fibers to the mid-portion of the callosum. The rostral fibers run beneath the genu and are inferior to the plane of the axial section.

Other smaller commissural fiber pathways include the hippocampal commissure, which lies inferior to the splenium of the corpus callosum and connects the bilateral hippocampal formations and the diencephalic commissures—the posterior and habenular commissures.

The function of the commissural fibers, specifically the corpus callosum, has aroused great interest throughout the past several centuries. While it has long been understood to involve interhemispheric communication, the full extent of its function remains to be determined. Sophisticated functional analysis of the corpus callosum suggests a role for it in both sensory integration and high-level cognitive processing. Historically, much of our knowledge of the corpus callosum came from callosal resection surgeries, called callosotomies, which are still done to prevent transmission of epileptic activity between the cerebral hemispheres (i.e., to stem the propagation of seizures), and also from commissural fiber disruption injuries, which result in disconnection syndromes.

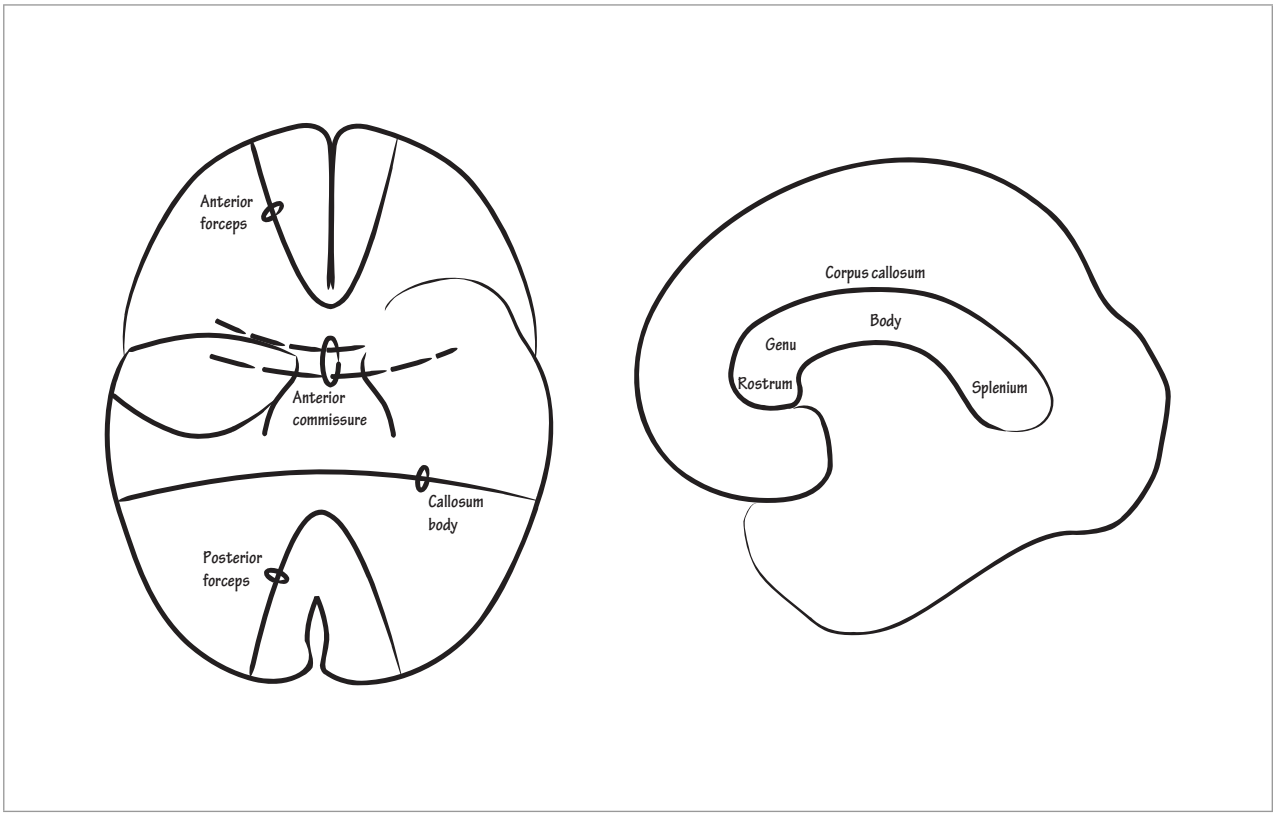


Figure 26-3 Commissural fibers

In 1892, Dejerine described the first disconnection syndrome, called alexia without agraphia. Patients with this disorder are unable to read but are still able to write. Try to imagine a single lesion that could cause this form of impairment. In order for it to occur, there must be loss of visual input to the language center without destruction of the language center, itself; otherwise, the patient would not be able to write. Also, patients with this disorder have partial preservation of vision, so there can only be injury to one visual cortex. The commissural pathway through the splenium of the corpus callosum connects the right occipital cortex to the left superior temporal gyrus, where the language center exists. So, the classic lesion in alexia without agraphia lies in the left occipital lobe (preventing it from communicating visual material to the language center) and extends into the splenium of the corpus callosum, which prevents inflow from the intact right occipital lobe to the left-lateralized language center (i.e., disconnecting it from the language center).

As a practical point, the lesion is often shown in anatomical drawings, which are oriented differently than radiographic images. In axial anatomical drawings, left is on the left and right is on the right but in radiographic images left is on the right and right is on the left. It is easy to confuse what you have learned about this syndrome, if you do not pay attention to this orientational difference.

Another disconnection syndrome that receives attention from both neurologists and Hollywood, alike, is called alien hand syndrome (aka *alien limb sign*). It was cinematized most memorably in Stanley Kubrick's *Dr. Strangelove*. There are three forms of alien hand syndrome, each with a discrete anatomical localization; however, most often patients present with symptoms from overlapping forms of the disorder. Perhaps the most fascinating of the three manifestations is the intermanual conflict or so-called self-oppositional behavior displayed with the "diagonistic dyspraxic" form. In this disorder subtype, one hand is in direct conflict with the other, most commonly the left with the right. To show yourself what is meant by self-oppositional behavior, open a desk drawer with your right hand and then immediately slam it shut with your left. This syndrome is reportedly caused by a lesion in the ventral-posterior portion of the body of the corpus callosum.

A second form of alien hand syndrome, the frontal variant, manifests with involuntary grasping. With one hand, involuntarily grasp at any object within arm's reach. Also, curse or scold your hand for its disobedience, as patients with this form of the disorder often report "rebuking their hand." This category of alien hand syndrome is termed the frontal variant because it is found with a lesion to the medial frontal lobe on the side opposite the alien hand.

Finally, there is a sensory variant to the alien hand syndrome that occurs with limb anesthesia or hypesthesia. In this form of the disorder, the hand is ataxic. Let your hand dangle out away from your body and try to forget its existence. Patients with the sensory variant are generally unaware of their limb or even frankly deny it's theirs. Lesions in the parieto-occipital cortex cause this iteration of alien hand syndrome, and corticobasal degeneration, a neurodegenerative cause of dementia, is a common etiology for it.

Other important clinical aspects regarding the corpus callosum are the frequency with which it fails to develop and the wide range of diseases that target it. Congenital failure of the corpus callosum to fully develop is known as callosal agenesis and occurs either in isolation or as part of a syndrome. One such syndrome is Arnold-Chiari malformation, in which there is also cerebellar tonsillar herniation and other midline abnormalities. Another is Dandy-Walker syndrome, in which there is associated enlargement of the fourth ventricle and also agenesis of midline cerebellar structures. Aicardi syndrome involves callosal agenesis along with retinal lesions; patients with this disorder present at three to four months of age with seizures and mental retardation. Callosal agenesis also occurs in birth defects such as schizencephaly, in which the cerebral hemisphere contour has multiple clefts, as well as holoprosencephaly, in which there is failure of division of the cerebrum resulting in a single-lobed brain.

Acquired forms of corpus callosum abnormalities occur from a wide range of causes, including demyelinating disorders, such as multiple sclerosis. Also, certain tumors characteristically invade the corpus callosum; they include: glial tumors, such as glioblastoma multiforme; lymphomas; and lipomas. Head trauma has also been shown to affect the callosum. Marchiafava-Bignami is the name of a rare cause of necrotic layering of the corpus callosum. It was originally described from the autopsies of three Italian men known to have been heavy red wine drinkers but has subsequently been found in both alcoholics and non-alcoholics, alike. Vitamin B

complex deficiency is now considered the cause of this disorder.

The subcortical cord projection fibers are divided into ascending and descending pathways. The thalamocortical fibers constitute the primary ascending pathway (aka *corticopetal pathway*) and the corticofugal pathway descends from the cortex through the brainstem as the primary descending pathway. The corticofugal fibers are subdivided into corticospinal fibers, which synapse in the medullary pyramids, and corticobulbar fibers (aka corticonuclear fibers), which synapse throughout the brainstem. For a detailed description of the nomenclature of the corticobulbar fibers, refer to the "Brainstem" chapter.

In the next diagram, we will draw the corticofugal fibers but let's stop and discuss the term "deep white matter," first.

The cord fibers form the "deep white matter" region between the cortex and the diencephalon. It is anatomically divided into the centrum semiovale and corona radiata. The name corona radiata stands for "radiating crown"; however, its radiating appearance is only appreciable in detailed anatomical dissection. On radiographic imaging, we are able to use the lateral ventricles to differentiate whether we are viewing the centrum semiovale or the corona radiata. The centrum semiovale lies above the level of the lateral ventricles and the corona radiata lies at their level.

Within the diencephalon, the corticofugal fibers bundle together as the internal capsule, which we will draw now. For this diagram, draw an axial section through the diencephalon at the level of the basal ganglia. Label the head of the caudate, thalamus, and combined globus pallidus and putamen (aka *lentiform nucleus*); the internal capsule fills the V-shaped wedge in between these nuclei.

The internal capsule divides into an *anterior limb*, a *genu* (where the anterior and posterior limbs meet), and a *posterior limb*. The posterior limb is subdivided into three different parts whose names have undergone revision but whose organization remains the same. The portions of the posterior limb were named based on their relationship with the lentiform nucleus: the area between the thalamus and lentiform nucleus was the thalamolenticular part; the sublenticular part was posterior to the thalamolenticular part and below the lentiform nucleus; and the retrolenticular part was posterior to the sublenticular part and behind the lentiform nucleus. With the updated nomenclature, the thalamolenticular part became the posterior limb and the sublenticular and retrolenticular parts are now considered their own separate limbs rather than subcategories of the posterior limb.

Now, let's draw the internal capsule using the revised nomenclature. Draw all five limbs: the *anterior limb* between the caudate and lentiform nucleus; the *genu*, which is the bend in the internal capsule where the anterior and posterior limbs meet; the *posterior limb* between the thalamus and the lentiform nucleus; the *sublenticular limb* behind the posterior limb (its fibers run underneath the lentiform nucleus); and the *retrolenticular limb* behind the sublenticular limb (it runs posterior to the lentiform nucleus).

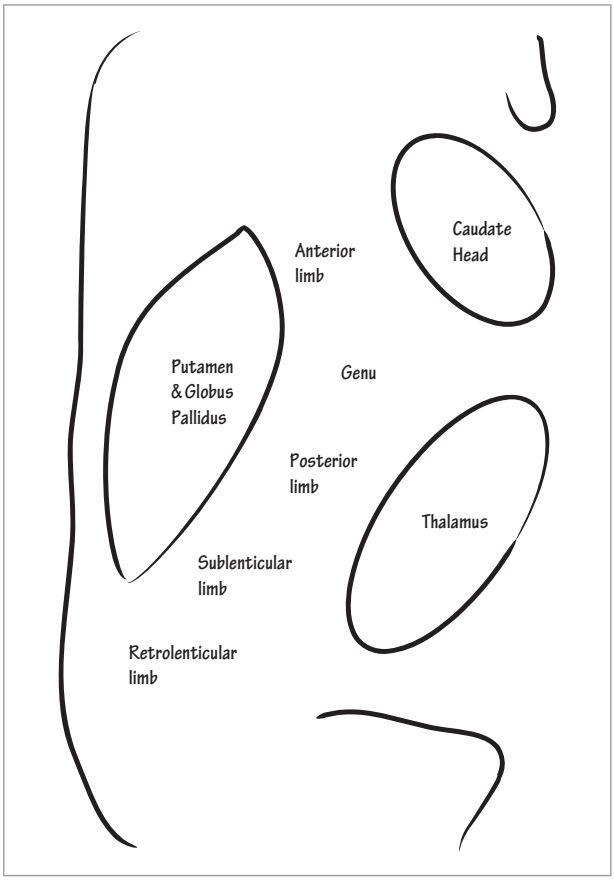


Figure 26-4 Axial internal capsule

In the next diagram, we will draw the fibers that pass through the internal capsule. Most important to clinical neurology is the position of the motor fibers during their descent through the genu and posterior limb. They are arranged somatotopically so that fibers for the face pass through the genu and fibers for the lower extremity descend through the posterior portion of the posterior limb. A common clinical entity is the pure motor stroke that occurs with an isolated infarction of the genu and posterior limb of the internal capsule. Now, let's create the functional diagram for the fiber pathways of the internal capsule. In sagittal view, draw the internal capsule as a broad-based triangle sitting on its apex; the internal capsule gradually dips down through the anterior limb, reaches its lowermost point in the genu and then rises again throughout the posterior limb: in this view, it looks like a pair of Speedo swim-trunks. Label the left half of the figure as the *anterior limb*, the central portion as the *genu*, and divide the right half into the *posterior*, *sublenticular*, and *retrolenticular limbs*.

The fiber pathways of the internal capsule descend at differing angles rather than directly vertically, which complicates our diagram. Those of the anterior limb pass through in an anterior-superior to posterior-inferior direction and those of the posterior portion travel through in a posterior-superior to anterior-inferior direction.

Indicate the anterior limb consists of fibers from the *prefrontal* and *anterior cingulate cortices*. Then, show the genu and posterior limbs comprise the *motor fibers*; specify the genu receives the *facial fibers* and that the *arm* and *leg fibers* are arranged from anterior to posterior along the posterior limb. Then, indicate the sublenticular limb comprises *parietal fibers* and that the *temporal* and *occipital fibers* pass through the retrolenticular limb.

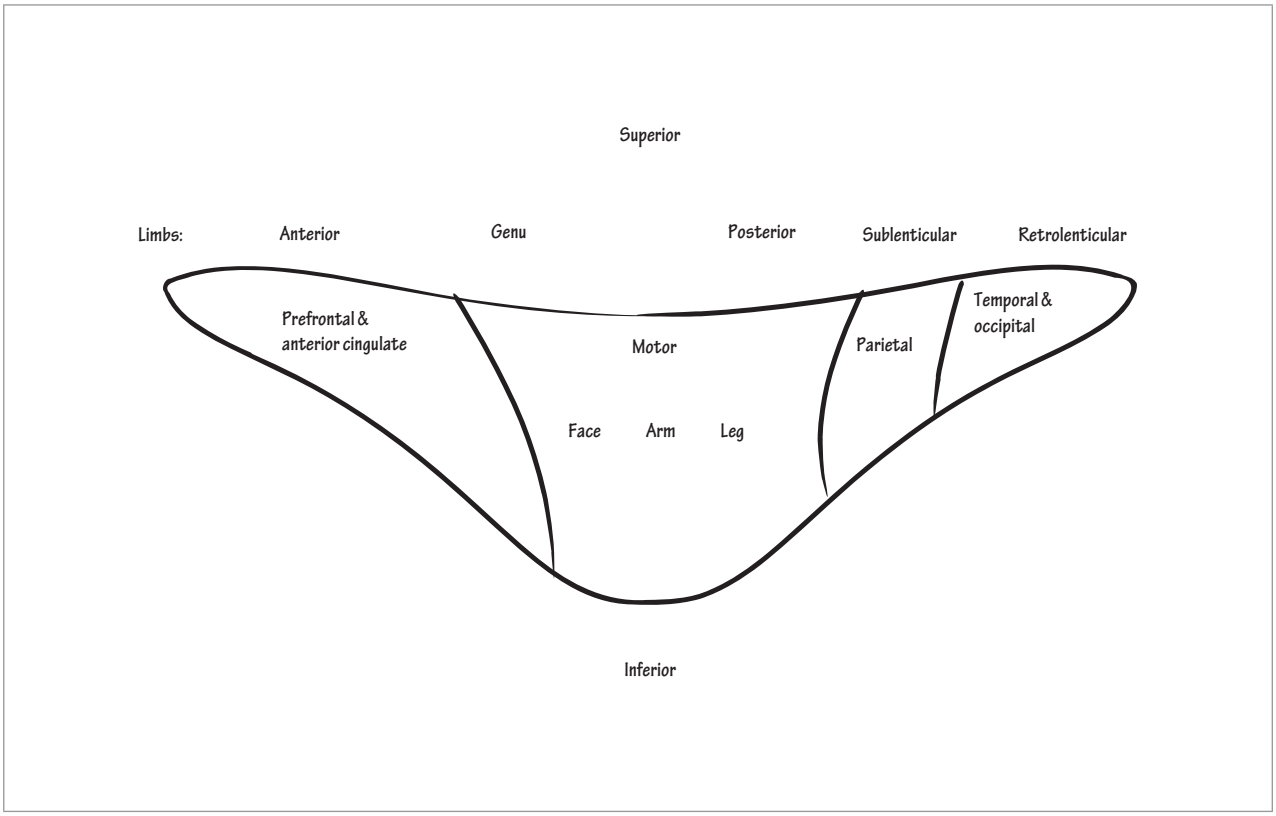


Figure 26-5 Coronal functional internal capsule map

Basal Ganglia

THE BASAL GANGLIA lie deep within the brain and surround the diencephalon, which comprises the thalamic structures. They were classically considered a solely motor area, but are now understood to play an intrinsic role in neurobehavioral activities, as well. Basal ganglia motor disorders are commonly divided into hypokinetic (slow, rigid movement) versus hyperkinetic (fast, chaotic movement) disorders. Parkinson's disease is the classic hypokinetic disorder and Huntington's disease is the classic hyperkinetic disorder. Perhaps the most disabling features of these two disease states, however, are their neurobehavioral dysfunctions—cognitive slowing/dementia and psychosis, and it is important to think about them in the management of movement disorders patients.

In this chapter, we will draw the structural anatomy of the basal ganglia and their classic motor circuitry. No such commonly replicated circuitry diagram exists for the neurobehavioral functions of the basal ganglia, so we will learn them through a discussion at the end.

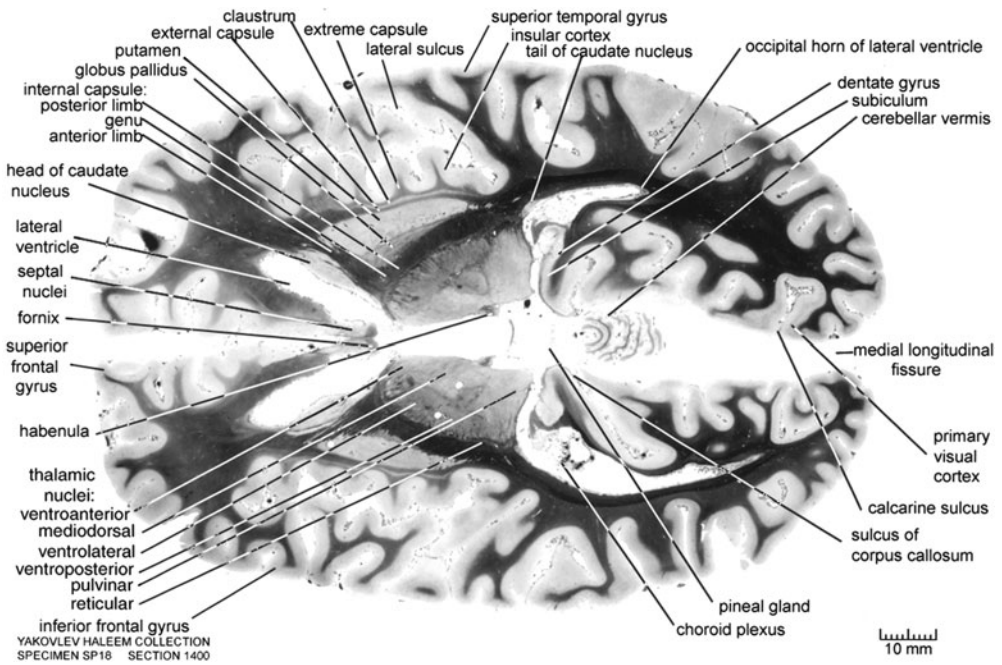


Photo 27-1 Axial anatomic section of basal ganglia
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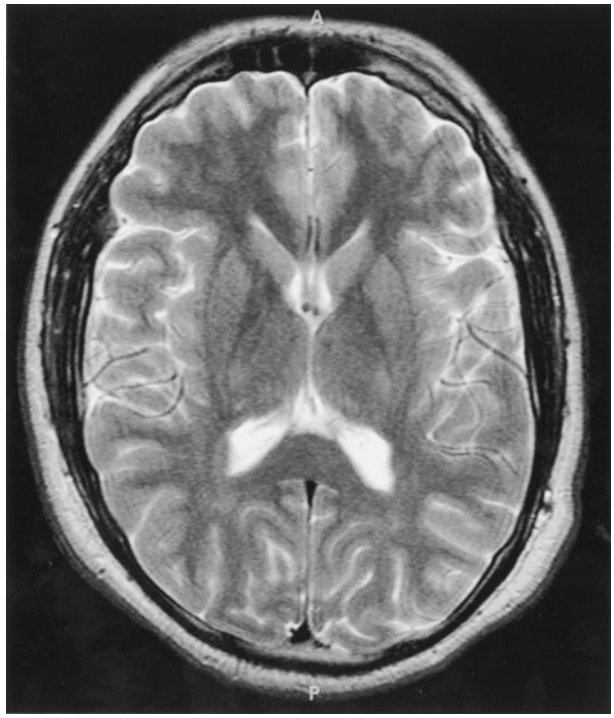

Photo 27-2 Axial radiographic section through basal ganglia

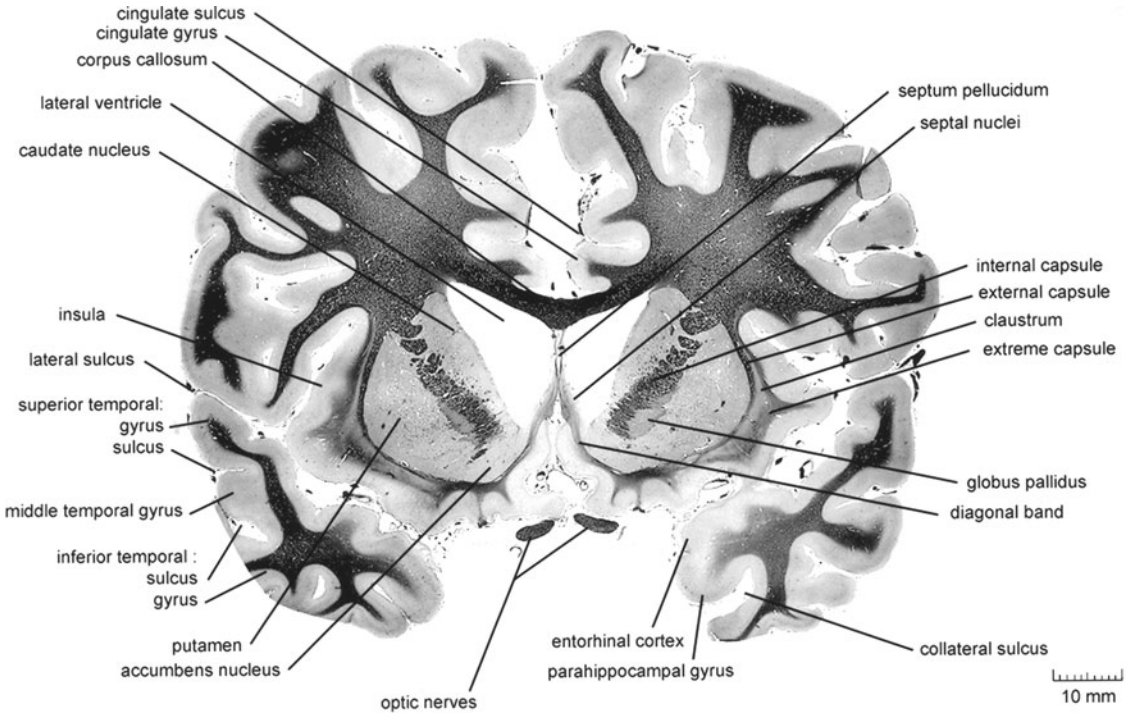

Photo 27-3 Coronal anatomic section through the anterior basal ganglia
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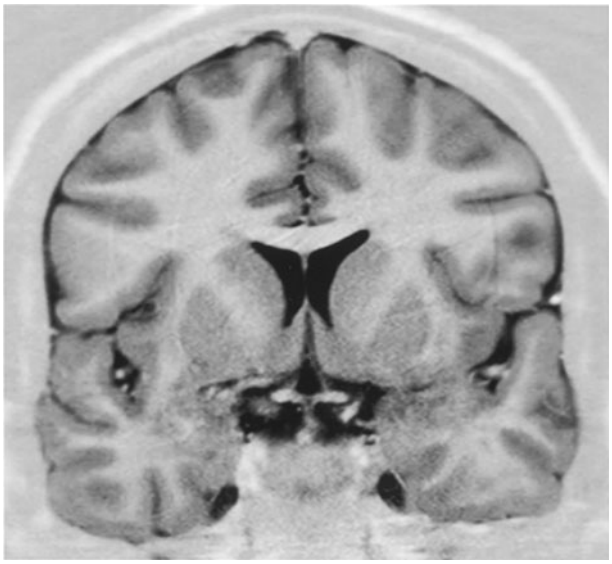

Photo 27-4 Coronal radiographic section through anterior basal ganglia

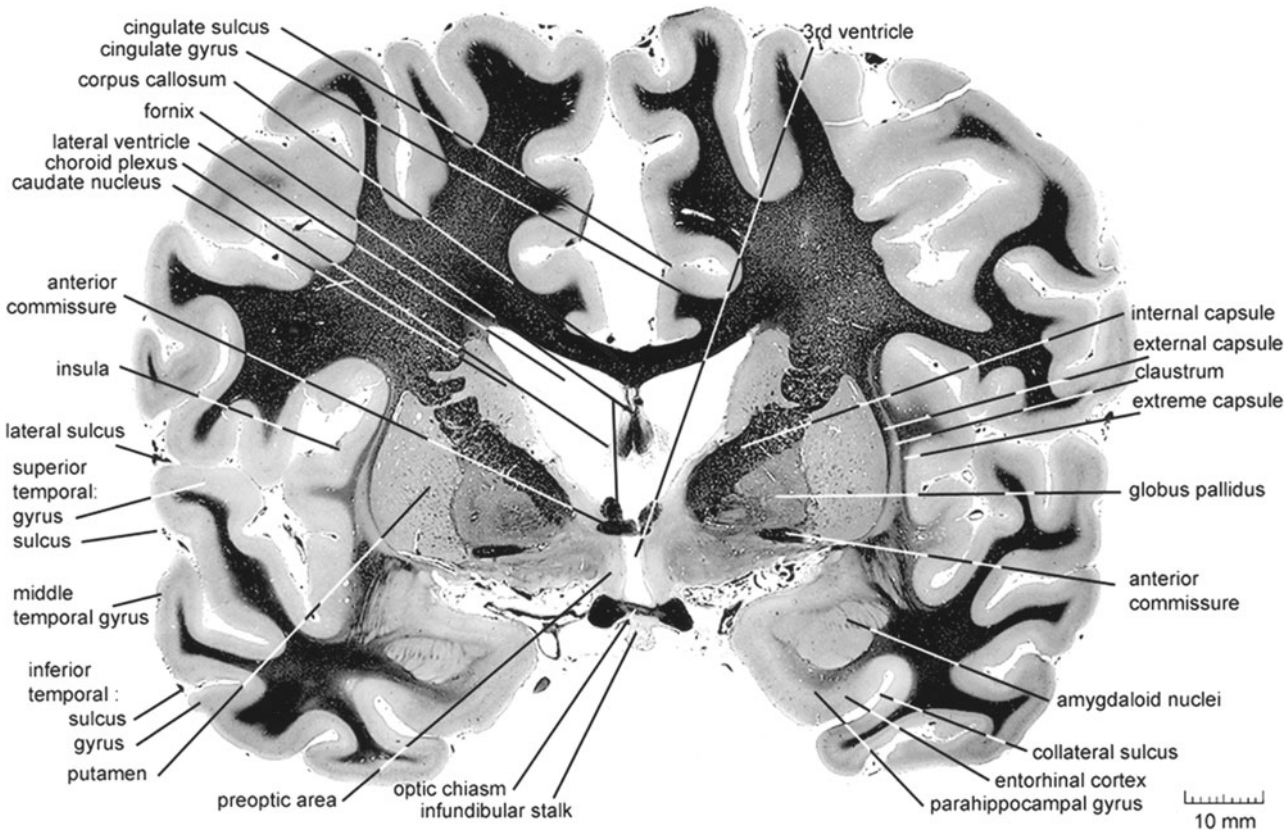

Photo 27-5 Coronal anatomic section through the basal ganglia posterior to nucleus accumbens
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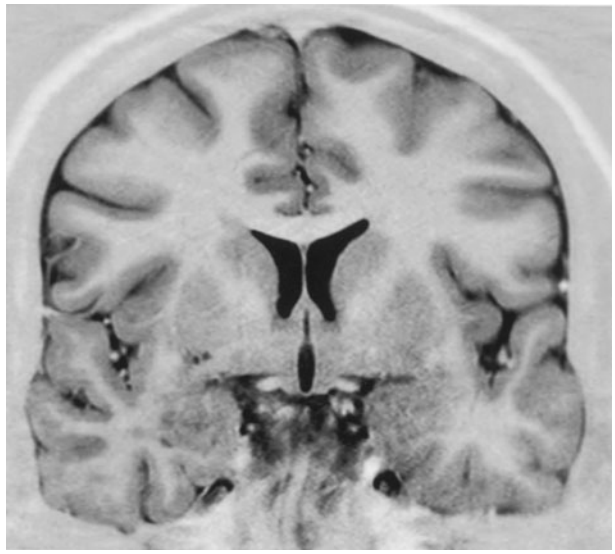

Photo 27-6 Coronal radiographic section through basal ganglia posterior to nucleus accumbens

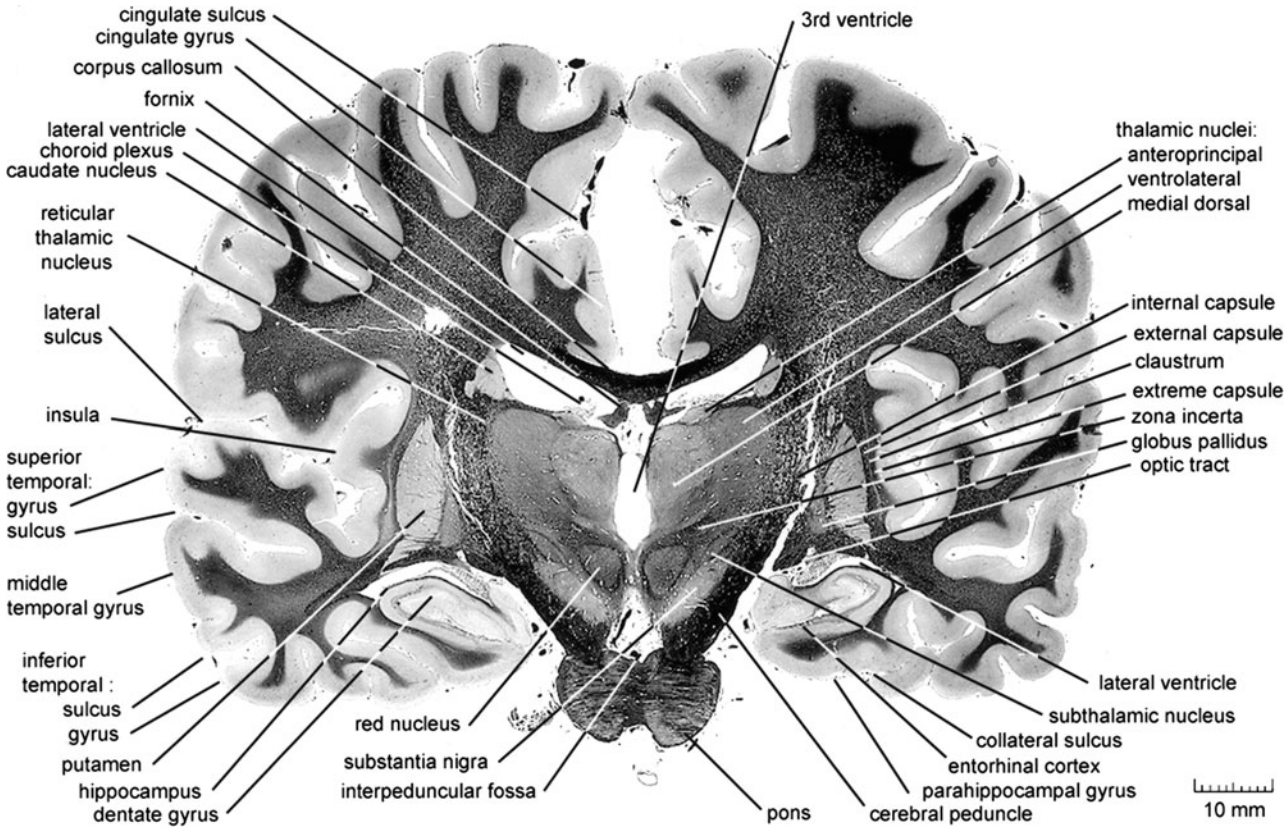

Photo 27-7 Coronal anatomic section through the Forel fields
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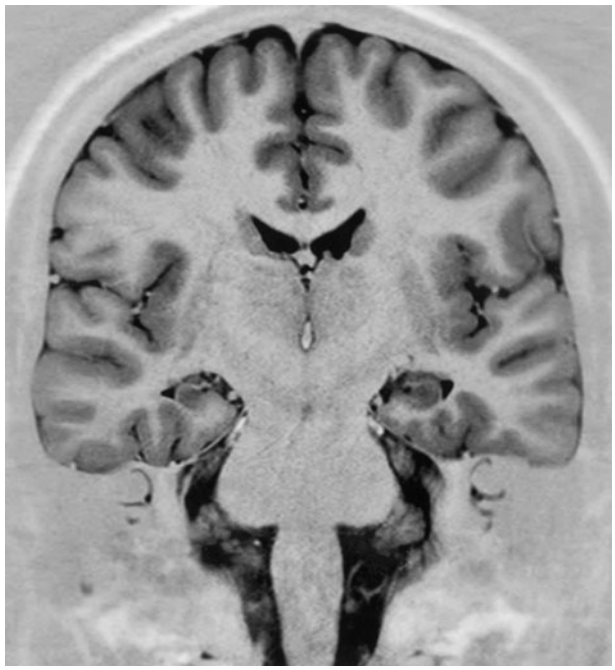

Photo 27-8 Coronal radiographic section through Forel fields

The biggest challenge to the basal ganglia is their nomenclature. If your time is short, skip this section and go on to the structural anatomy diagram, but if you have the time, we will wade through this tedious but revelatory subject matter together, now. Let's begin with the term "basal ganglia." While a "ganglion" is by definition a neuronal aggregation in the *peripheral* nervous system, the basal ganglia refer to nuclei in the *central* nervous system. It is likely for this reason that in the most recent edition of the *Terminologia Anatomica*, the term basal ganglia was revised to the "basal nuclei;" we will use both of these terms interchangeably throughout the book. Some authors use the term the "basal motor nuclei" but this neglects their involvement in neurobehavioral function so we avoid it here.

In this diagram, we will build the nomenclature of the basal nuclei from the term *corpus striatum*. Show the corpus striatum comprises the *caudate*, *putamen*, and *globus pallidus*. We owe the term "corpus striatum" to Thomas Willis' seventeenth-century description of the basal nuclear region. Willis described medullary "rays or beams" (aka striations) connecting the caudate and the putamen, and so the caudate and putamen collectively became known as the *striatum*.

The globus pallidus and putamen appear connected but are structurally separated by the lateral medullary lamina. However, because of their proximity, they were collectively named the *lentiform nucleus*, given their lens-shaped appearance. In the early eighteenth century, scientist Karl Burdach first divided the lentiform nucleus into its core, the globus pallidus, and shell, the putamen, but it was only in the twentieth century that scientists realized these subdivisions have different embryologic origins.

Early in development, the globus pallidus, which is a diencephalic structure, migrates into the medial wall of the putamen, which is a telencephalic structure—imagine throwing a marble into a mound of mud (for a discussion of the embryology of the diencephalon and telecenphalon, refer to the "Thalamus" chapter). This migration formed the globus pallidus core and surrounding putaminal shell. Bundles of myelinated fibers traversing the globus pallidus give it its characteristic pale appearance, and its pallor is the root of its original name, pallidum, so now, write *pallidum* beside globus pallidus. Since the globus pallidus is derived from the phylogenetically older portion of the brain, the diencephalon, it is also known as the *paleostriatum*, whereas the caudate and putamen are from the phylogenetically newer part of the brain, the telencephalon, and so they are called the *neostriatum*; label the diagram with these synonyms.

In addition to the caudate, putamen, and globus pallidus, the definition of the corpus striatum also encompasses several fibers pathways which traverse the *prerubral fields* (aka *Fields of Forel*), named after

their proximity to the red nucleus; although these fields are variably listed as part of the diencephalon. The prerubral fibers include the *ansa lenticularis*, *lenticular fasciculus*, *subthalamic fasciculus*, and *thalamic fasciculus*. We will include these pathways in our caudal coronal sections through the basal nuclei.

Aside from the corpus striatum and prerubral pathways, several other structures are commonly lumped with the basal ganglia. The nucleus accumbens is clinically important in drug addiction and is the antero-inferior anatomical connection between the caudate and putamen. The caudate and putamen originate as one structure but during embryologic development, the internal capsule fibers descend through them and almost completely separate them except at the nucleus accumbens, where they remain connected. Both the external capsule and the claustrum are grouped with the basal ganglia: the external capsule surrounds the lateral wall of the putamen, and the claustrum lies between it and the insula. Originally, the amygdala was included with the basal nuclei but it is now joined with the limbic system. However, we can still appreciate how the amygdalo-stria terminale pathway, hippocampal-fornix pathway, and lateral ventricles share the C-shaped appearance of the caudate, and how all of them run close to one another. We demonstrate this C-shape embryologic development in the "Meninges and Ventricular System" chapter.

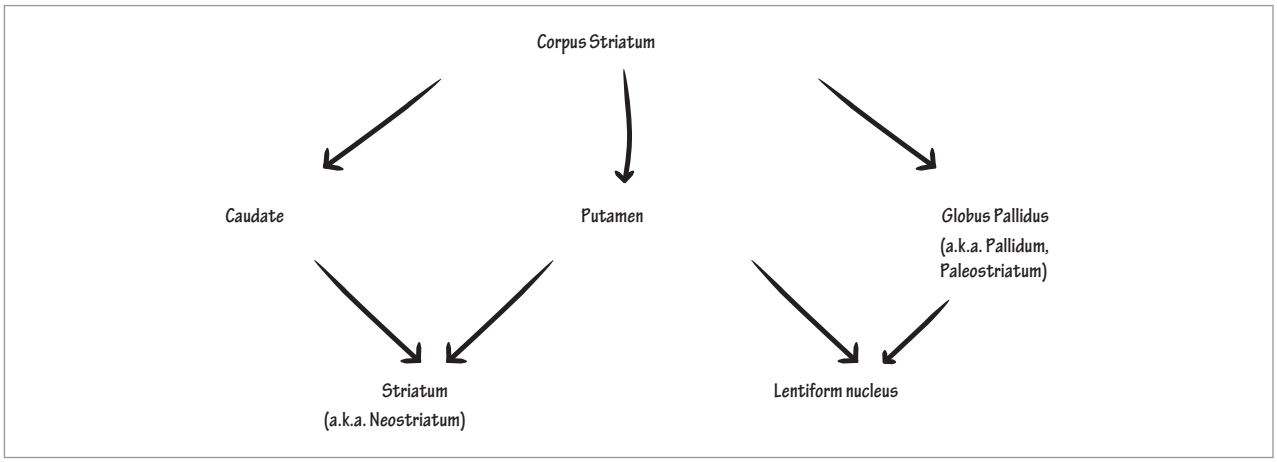

Figure 27-1 Basal ganglia nomenclature

Now, let's draw the basal nuclei in axial section. Begin with an axial outline of the anterior two-thirds of the brain. While we are unable to include all of the related basal nuclei structures in one axial slice (because the basal ganglia lie across several different rostro-caudal levels), we will draw the clinically relevant structures we do see at this level. Draw the *caudate nucleus head* along the lateral wall of the anterior horn of the lateral ventricle. Then, in the anterolateral wall of the posterior horn of the lateral ventricle, draw the *caudate nucleus tail*.

Next, outside of the lateral ventricles, draw the lens-shaped lentiform nucleus. Divide it into the *putamen* and *globus pallidus* with the *lateral medullary lamina*. The medial medullary lamina further subdivides the globus pallidus into the globus pallidus internal segment (aka globus pallidus medial segment) and globus pallidus external segment (aka globus pallidus lateral segment). The internal segment joins the substantia nigra pars reticularis as the major outflow component of the basal nuclei, as we will show in the motor circuitry section of this chapter. In contrast, the midbrain substantia nigra pars compacta is the major producer of dopaminergic cells, and loss of these cells is central to the pathology of Parkinson's disease.

The thalamus and internal capsule are not a part of the basal nuclei but we draw them here because they are important landmarks. Draw the thalamus between the anterior and posterior horns of the lateral ventricle. Then show the *anterior limb of the internal capsule* between the head of the caudate and the lentiform nucleus and the *posterior limb of the internal capsule* between the thalamus and the lentiform nucleus. Next, draw the *extreme capsule* outside the lateral edge of the putamen; it is an important corticostriatal fiber bundle. Draw the *claustrum* lateral to it. While the claustrum's function remains poorly understood, we look at the claustrum radiographically quite frequently. In strokes, early changes on head computed tomography (head CT) are subtle, and loss of gray–white matter differentiation is often the only clue one has occurred. The best place to look for this gray–white matter differentiation loss is in the region of the extreme capsule and claustrum.

Finally, show the presence of the *insular cortex* at the level of the basal nuclei; it is the infolding of the lateral cerebral cortex. The insular cortex is especially important in sound perception as well as many other functions, including autonomic nervous system operations.

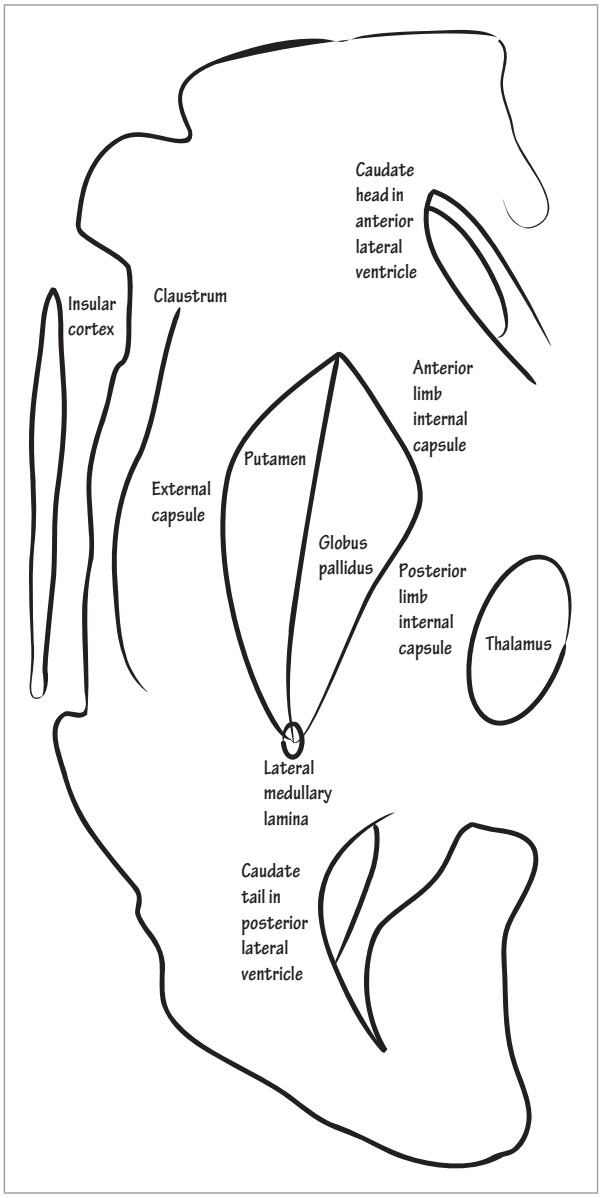

Figure 27-2 Axial section through basal ganglia

Now, draw two coronal sections through the anterior portion of the basal nuclei. Use only one side of the brain in each section. Draw the first coronal section in the plane of the optic chiasm. For orientational purposes, include the optic chiasm, the medial temporal and frontal lobes, the frontal horn of the lateral ventricle, and the insular cortex. Next, draw the striatum, which is a combination of the *caudate nucleus head* in the frontal lateral ventricle; the *putamen*; and the *nucleus accumbens*, which is the medio-inferior connection between the caudate and putamen. As mentioned in the nomenclature section, it is an embryological remnant from when the caudate and putamen were a single structure.

Next, draw the *diagonal band of Broca* (aka the *medial septal band*) medial to the nucleus accumbens—it is not part of the basal nuclei but its anatomy is best understood in this view. The diagonal band of Broca comprises cholinergic fibers that communicate with the hippocampus much as the basal nucleus of Meynert does; we will draw it in the next coronal section. Between the head of the caudate and the putamen, draw the *anterior limb of the internal capsule*: it is *anterior* because we are in the plane of the optic chiasm.

Where in this coronal slice is the globus pallidus? Behind us (posterior to the plane of this diagram). The putamen forms a shell around the globus pallidus, so its anterior-posterior extent is more limited than that of the putamen. Finally, add the white matter *external capsule* lateral to the putamen and the gray matter *claustrum* between it and the insular cortex.

Now, draw a coronal section in the plane of the anterior commissure; we are continuing to move posteriorly. The external boundaries of this more caudal diagram are the same as the first except that under the cerebrum, draw *optic tracts* rather than the optic chiasm: the optic tracts lie posterior to the optic chiasm. Again draw the *caudate nucleus head* in the lateral wall of the frontal lateral ventricle. Below and lateral to it, draw both the *globus pallidus* and the surrounding *putamen*. Next, show anterior limb internal capsule fibers between the lentiform nucleus and the head of the caudate. Indicate those fibers end in the horizontal crossing fibers of the *anterior commissure*. Next, again draw the white matter *external capsule* outside of the putamen and the gray matter *claustrum* that runs between the external capsule and the insula.

Now, let's draw a few structures unrelated to the basal nuclei that are best visualized in this section. In midline, show the *anterior commissure* separates the frontal lateral ventricles, above, from the *third ventricle*, below. Indicate the hypothalamus lies along the wall of the third ventricle and then draw the surrounding *substantia innominata* (aka *innominate substance*). The substantia innominata is the basal forebrain region beneath the anterior commissure and is best known for housing the nucleus basalis of Meynert. Structurally, the nucleus basalis of Meynert lies close to the basal nuclei but functionally it plays a role in cholinergic transmission to the hippocampus and cortex for memory formation (like the diagonal band of Broca/medial septal band). It is similar to the neurobehavioral cells of the dorsal brainstem in that its widespread cholinergic neurons are reminiscent of the serotinergic connections of the brainstem raphe nuclei and the noradrenergic connections of the pontine locus ceruleus nuclei.

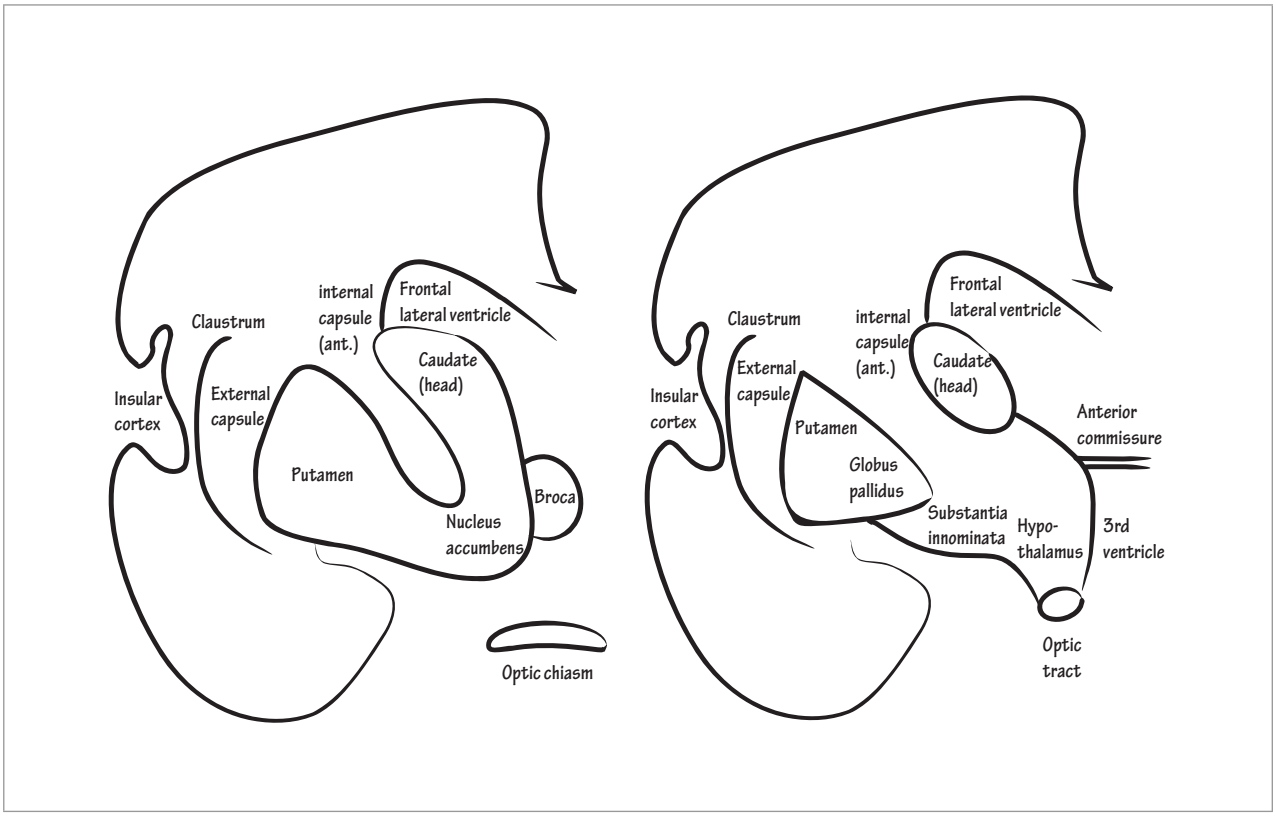

Figure 27-3 Coronal sections through basal ganglia

In the next coronal section, we will draw the fiber pathways of the corpus striatum, which traverse the prerubral fields (aka the fields of Forel). Draw a coronal section through the basal nuclei in the plane of the cerebral peduncles. Show the lateral ventricle and the midline third ventricle. Draw the *caudate nucleus body* in the lateral wall of the frontal lateral ventricle. Show the *thalamus* and *lentiform nucleus*, and draw the posterior limb internal capsule fibers that run between them. Now, within the cerebral peduncle, draw the *substantia nigra*, and above it, draw the *red nucleus*. We show the substantia nigra and red nucleus in this same coronal section for simplicity, but technically, the substantia nigra lies anterior to the red nucleus. If you see them together, the brain was sectioned at an angle.

Lateral to the red nucleus and beneath the thalamus, draw the *subthalamic nucleus*. Between the thalamus and subthalamic nucleus, draw the *zona incerta*; it is an important target of descending cortical projection fibers and an important landmark in the prerubral fields. In more posterior planes, the zona incerta wraps around the lateral edge of the thalamus.

With this anatomy in place, we are able to draw the *prerubral fields* (aka *fields of Forel*, or *Forel's field H*). There are three field subcategories: field H, field H1, and field H2. Indicate that *field H* lies medial to the zona incerta and divides the prerubral fields into superior and inferior regions. Show that *field H1* is the upper region: it lies superior to the zona incerta and underneath the thalamus, and indicate that *field H2* is the lower region: it lies inferior to the zona incerta but above red nucleus. Fiber pathways from the basal nuclei, the red nucleus, and thalamus all pass through the prerubral fields.

In our definition of the corpus striatum, we listed four fiber bundles: the ansa lenticularis, lenticular fasciculus, subthalamic fasciculus, and thalamic fasciculus. These bundles traverse the prerubral fields and we will draw them, now. Let's start with the *lenticular* and *thalamic fasciculi*. They are two stages in a single bundle that passes through all three divisions of the prerubral fields. Show the *lenticular fasciculus* originates in the globus pallidus interna, crosses the internal capsule, passes through field H2 and then turns upward within field H. Indicate it becomes the *thalamic fasciculus* when it traverses field H1 and enters the thalamus, specifically through the ventral anterior, ventral-lateral, or centromedian nuclei. The thalamic fasciculus comprises many different fiber projections that target the thalamus.

Now, show fibers from the globus pallidus that loop around the internal capsule and reach the thalamus through the *ansa lenticularis*. Specifically indicate they originate in the globus pallidus interna, loop under the internal capsule and subthalamic nucleus, and pass through field H into field H1 to join the thalamic fasciculus.

Next, draw the *subthalamic fasciculus*, which comprises fibers that project from the *external* segment of the globus pallidus to the subthalamic nucleus and then back to the *internal* segment of the globus pallidus. They constitute the fiber bundles of the indirect pathway, which we will diagram in the next section along with the other motor circuitry.

What other important motor pathway runs through the Forel fields? Hint—the pre*rubral* fields. The dentatorubrothalamic pathway. Let's talk through this pathway; it is drawn in the "Cerebellum" chapter: the cerebral motor cortex projects to pontine nuclei, which project to the contralateral cerebellar cortex, which projects to the dentate nucleus of the deep cerebellum, which projects through the superior cerebellar peduncle to the contralateral red nucleus, which projects to the thalamus, which projects back to the motor cortex on the side of origin. In the rubral-thalamic extent of the pathway, it runs through the thalamic fasciculus in field H1.

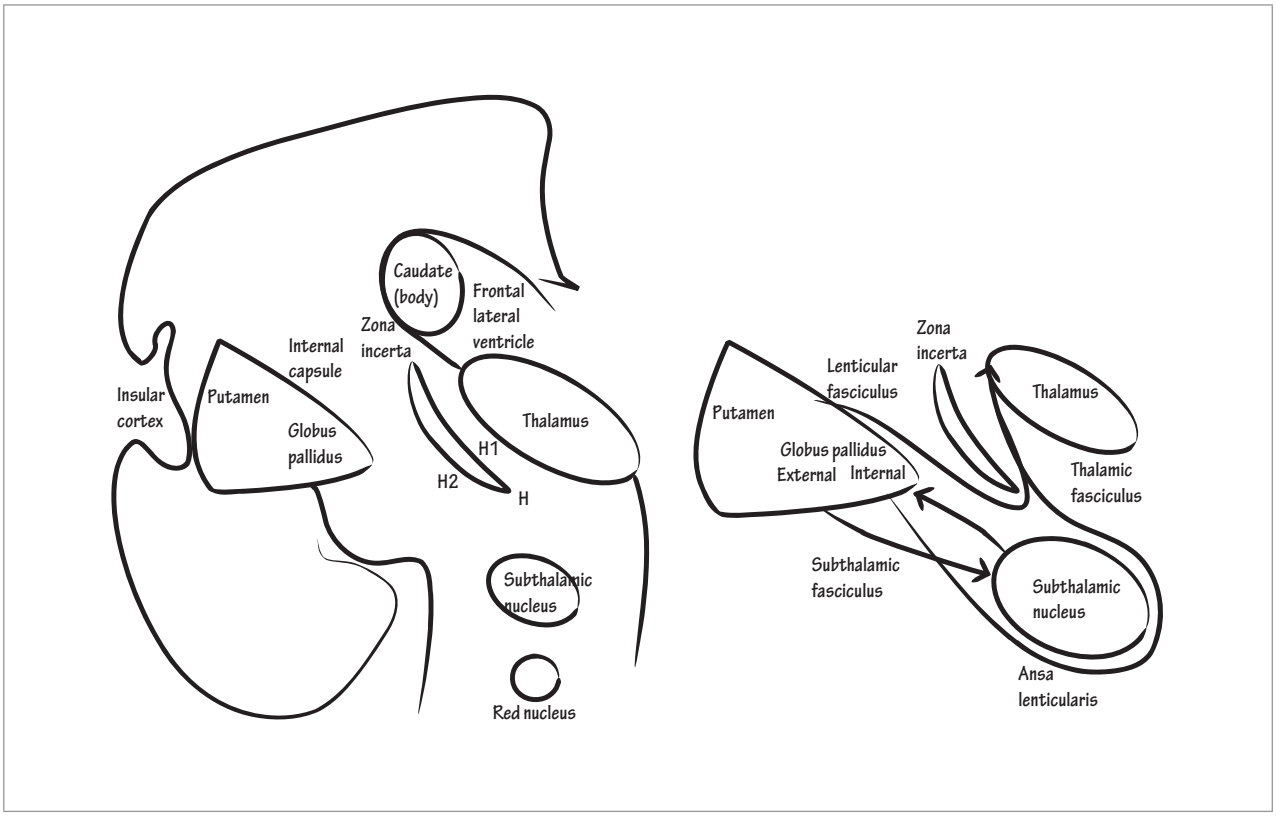

Figure 27-4 Forel fields

Now, we will draw the motor circuitry. The determination of the basal nuclei motor circuitry was monumental in movement disorders and seemingly no chapter about the basal nuclei is complete without a description of the direct and indirect motor pathways, and for good reason: the motor circuitry elucidates the clinical consequences of discrete basal ganglia lesions and provides a blueprint for basal ganglia manipulation. Unfortunately, you'll never remember the motor circuitry, if you don't periodically think about it (and, unfortunately, you probably won't), but no matter, you'll get the joy of relearning it every time you have to.

Here, we will draw a flow diagram of the motor circuitry, beginning with the direct pathway. First, indicate the *motor cortices* project corticostriatal fibers to the *putamen*; the putamen, as we will show, sends impulses through the indirect and direct pathways. Next, show the putamen projects to both the globus pallidus interna and substantia nigra reticulata through the direct pathway. The substantia nigra reticulata and globus pallidus interna are anatomically distinct but functionally equivalent so we label them as the combined *globus pallidus interna/substantia nigra reticulata*. This combination tonically inhibits the thalamus, so draw projection fibers from the globus pallidus interna/substantia nigra reticulata to the *thalamus*. Then show further projection fibers from the thalamus back to the *motor cortex*; the cortex then sends fibers through the corticobulbar and corticospinal pathways to the periphery.

Now, qualify each projection as excitatory or inhibitory. First, show that the pathways from the putamen to the globus pallidus interna/substania nigra reticulata and from the globus pallidus interna/substantia nigra reticuluata to the thalamus are both *inhibitory*. These two inhibitory fiber pathways, in essence, cancel one another out. Next, show that the rest of the fiber projections within the direct pathway are excitatory. Overall, then, the direct pathway is an excitatory pathway.

In summary, in the direct pathway, the motor cortex excites the putamen; the putamen, then, inhibits the globus pallidus interna/substantia nigra reticulata from inhibiting the thalamus; which frees the thalamus to further excite the motor cortex.

The specific cortical regions and thalamic nuclei of interest in the basal motor circuitry are as follows: the sensorimotor cortex originates the corticostriatal efferents that project to the putamen, and the globus pallidus interna/substantia nigra reticulata project to the ventral-anterior and ventral-lateral nuclei of the thalamus.

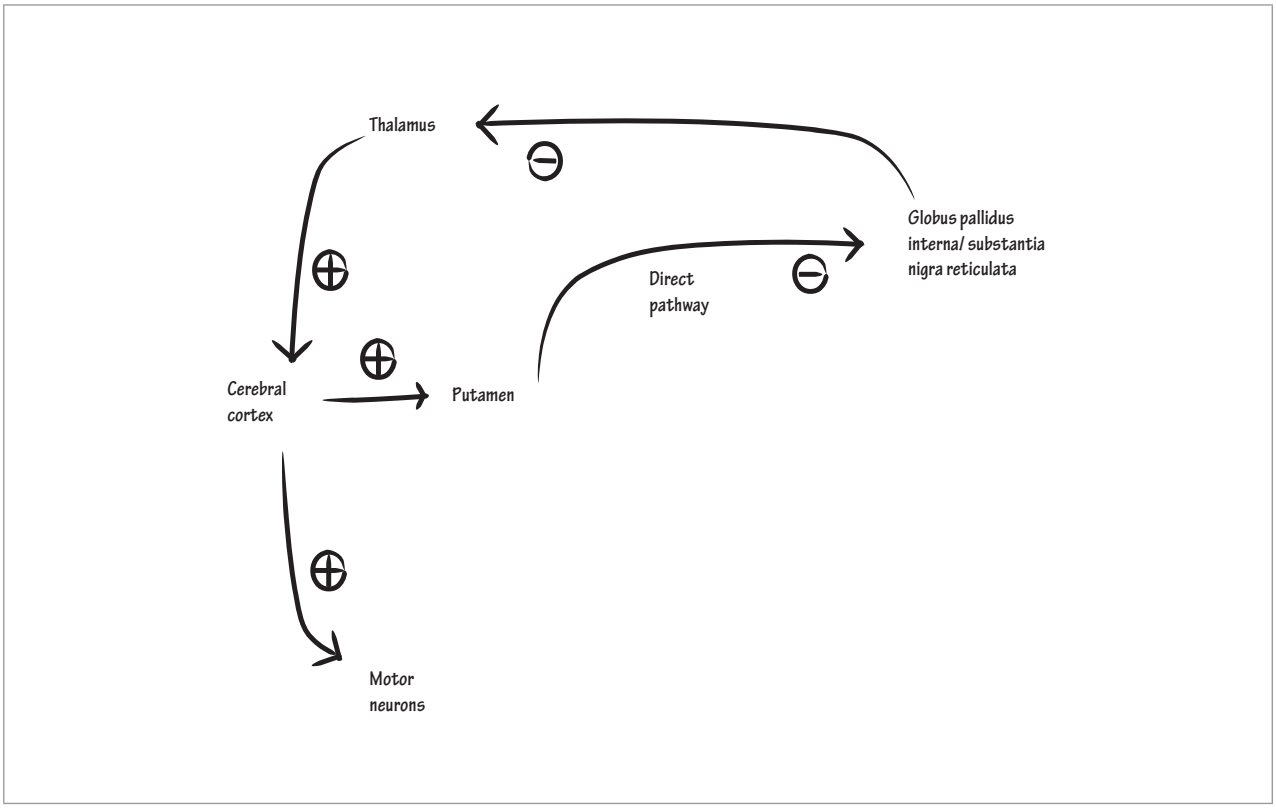

Figure 27-5 Incomplete motor circuitry

Next, we will add the indirect pathway to our diagram. The indirect pathway incorporates several of the same steps as the direct pathway; yet, they ultimately have opposite effects. Let's look at their similarities, first. Both synapse in the globus pallidus interna/substantia nigra reticulata, which inhibits the thalamus. And both begin the same way, with corticostriatal excitation of the putamen. But in the indirect pathway, the putamen projects *indirectly* to the globus pallidus interna/substantia nigra reticulata through the globus pallidus externa. After receiving projection fibers from the putamen, the globus pallidus externa then sends fibers either to the globus pallidus interna/substantia nigra reticulata, immediately, or through the subthalamic nucleus, first. But both tracts have the same end result; we will soon show why.

For the moment forget about the passage of fibers to the subthalamic nucleus. Think about the indirect pathway as being just like the direct pathway but that fibers first go through the globus pallidus externa, which adds an additional inhibitory step, so that ultimately the indirect and direct pathways have opposing effects. In the indirect pathway, putaminal inhibition of the globus pallidus externa releases the globus pallidus externa's hold on the globus pallidus interna/substantia nigra reticulata. The globus pallidus interna/substantia nigra reticulata is then free to inhibit thalamic excitation of the motor cortex. In other words, there are three inhibitory steps in a row, which overall, makes the pathway inhibitory.

Now, let's add the details of the indirect pathway. First, show the putamen send inhibitory fibers to the *globus pallidus externa*. Then, show the globus pallidus externa send inhibitory fibers directly to the globus pallidus interna/substantia nigra reticulata. Next, show the globus pallidus externa send inhibitory fibers to the *subthalamic nucleus*, which sends excitatory fibers to the globus pallidus interna/substantia nigra reticulata. As you can see, though, the end result is the same in both circumstances. Whether the indirect pathway acts through the subthalamic nucleus or not, it always frees the globus pallidus interna/substantia nigra reticulata to inhibit the thalamus from excitation of the cortex.

Ballismus is a hyperkinetic movement disorder, which consists of wild *ballistic* movements of the limbs; it is classically considered to be secondary to a contralateral subthalamic nucleus lesion.

Parkinson's disease results from a loss of dopaminergic cells in the substantia nigra compacta, so to understand its pathophysiology we need to include the *substantia nigra compacta*, here. Label it in the flow diagram near the putamen. It serves to energize movement, which means it must have opposite effects on each pathway. It must excite the direct pathway and inhibit the indirect pathway or the effects of both would cancel one another out. But how does it release a single neurotransmitter, dopamine, and perform opposing actions? The difference lies in the dopamine receptors in the putamen. The direct pathway putaminal cells express dopamine 1 and 5 receptors, which are excitatory; whereas the indirect putamen cells express dopamine 2, 3, and 4 receptors, which are inhibitory. Thus, dopamine acts on both pathways to generate the same ultimate effect: it excites movement.

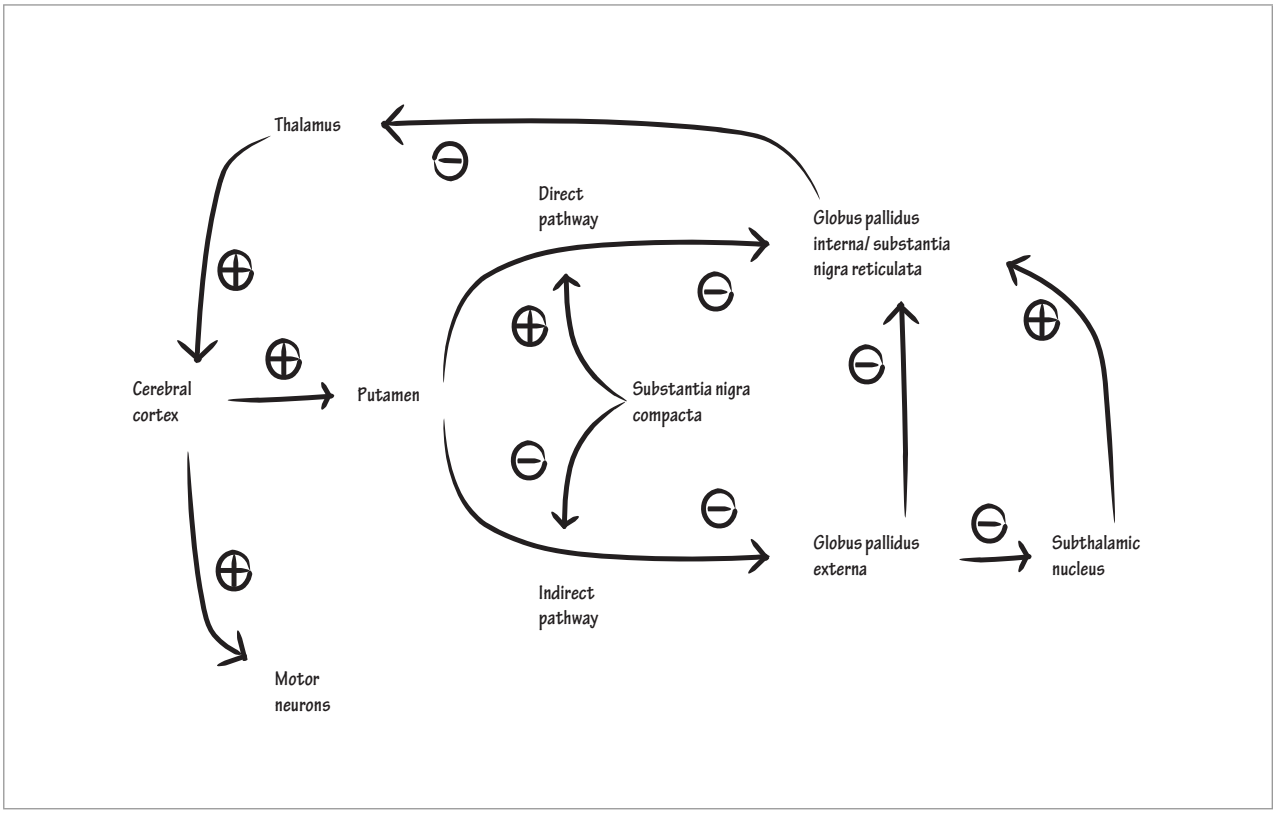

Figure 27-6 Complete motor circuitry

The timing of activation in motor circuitry is important for movement. In the scaling model of motor performance, we imagine that the direct pathway initiates movement—it acts as the gas pedal, and the indirect pathway terminates it—it acts as the brake. However, according to this model, thalamic lesions should also result in bradykinesia and Parkinsonism (i.e., a slowing of movement), but they do not.

A complementary theory suggests that pathologic oscillatory firing patterns of basal nuclei (in addition to synchronous firing patterns in previously asynchronous neuronal populations) result in the clinical manifestations of movement disorders. According to this model, the pathophysiology found in hypokinetic movement disorders, such as Parkinsonism, is similar to that found in hyperkinetic movement disorders, such as Huntington's diease, dystonia, and chorea; they all involve pathologic firing patterns.

Indeed, pallidotomy and deep brain stimulation of basal nuclei are used for both hypokinetic and hyperkinetic movement disorders. Researchers propose that the separation of thalamocortical fibers from the disruptive signals of the pathologic basal nuclei produces the beneficial effect. This model of aberrant signaling rather than structural damage as the cause of clinical disorder has been extended to language dysfunction (aka aphasia) and transcranial magnetic inhibition of the cerebral cortex is being tested to improve it.

Now, let's address one last brainstem nucleus important in movement disorders and related nervous system functions, which is the pedunculopontine nucleus. Nearby is the para*median* pontine reticular formation (PPRF), which is best known for its control of saccadic eye movements and, indeed, many movement disorders involve impaired initiation or termination of saccades, most notably progressive supranuclear ophthalmoplegia (commonly referred to as PSP), but the pedunculopontine nucleus lies *lateral*, near the superior cerebellar peduncle. The pedunculopontine nucleus acts on lower spinal motor neurons for gait production. Pedunculopontine nucleus injuries result in difficulty with gait initiation and maintenance, such as in the festinating/freezing gait of Parkinson's disease. Also, as is further discussed in the "Sleep Neurocirctuitry" chapter, the pedunculopontine nucleus is active in rapid-eye movement sleep (aka REM sleep or dream sleep), which involves rapid saccadic eye movements and muscle atonia. During REM sleep, current thinking is that the magnocellular medullary reticular formation and the human equivalent of the rat sublaterodorsal nucleus produce muscle atonia to prevents us from acting out our dreams. If muscle tone is uninhibited during dream sleep, as in REM sleep behavior disorder, people are capable of performing wild, unconscious, sometimes dangerous behaviors during their dream sleep.

In the beginning of this chapter, we mentioned the importance of neurobehavioral aspects of the basal ganglia. While, they are addressed in relevant sections throughout the rest of this book, let's consolidate a few key points about them, now. First, it is helpful to divide the striatum into upper (aka dorsal) and lower (aka ventral) divisions. The dorsal striatum functions in motor activities and the ventral striatum, as mentioned in regards to the nucleus accumbens, operates in reward and behavior.

Indeed, the frontal motor cortex projects to the upper/outer caudate and putamen (aka the dorsolateral striatum) and the medial and orbital prefrontal cortices, which are involved in behavior and emotion, project to the ventral striatum. While dorsolateral striatal lesions primarily produce movement disorders, they also cause coexistent apathy and amotivation, as well. Ventral striatal lesions, instead, result in irritability and addiction, and are linked to obsessive compulsive disorder.

The caudate nucleus head, specifically, is involved in neurobehavioral function. Right parietal lobe spatial attention communicates with the right caudate head and left frontal lobe language production projects to the left caudate head. Both caudate heads are involved in memory consolidation.

Arterial Supply to the Central Nervous System

IN THIS CHAPTER, we will diagram both the arterial vessel pattern and the vascular territories of the central nervous system. Our goal is to learn the course of each vessel and the major region it supplies. Fluoroscopic cerebral arteriography and non-invasive imaging modalities, such as magnetic resonance imaging (MRI), give us excellent views of arterial circulation and bolster our knowledge of vascular territories. From these technologies, and a long history of pathologic studies, we know that the central nervous system vascular territories are highly variable. Therefore, when we review an MRI of a stroke (aka infarct), we should look at the central area of injury to determine the infarcted vessel and avoid temptation to determine the vessel territory by reviewing its borders. In this chapter, we will specifically focus on the central region each vessel supplies and try to neglect the vessel borders.

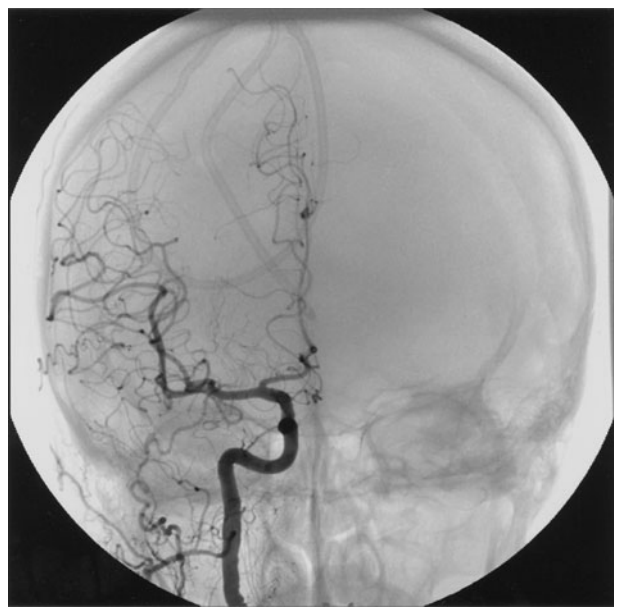

Photo 28-1 Cerebral angiography of internal carotid system

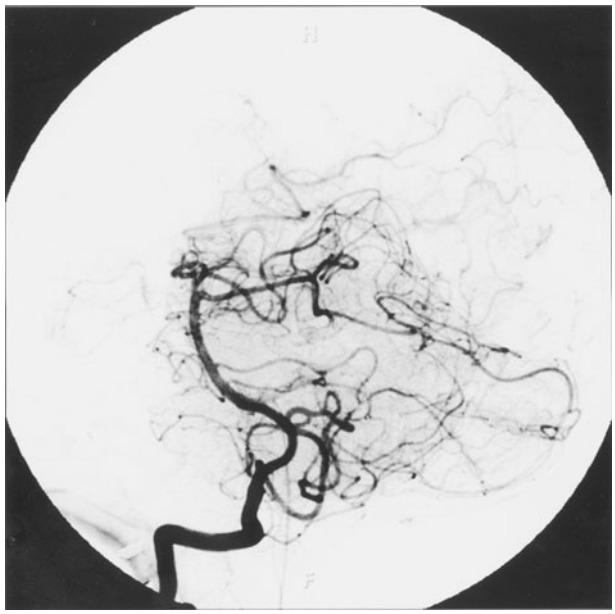

Photo 28-2 Cerebral angiography of vertebrobasilar system

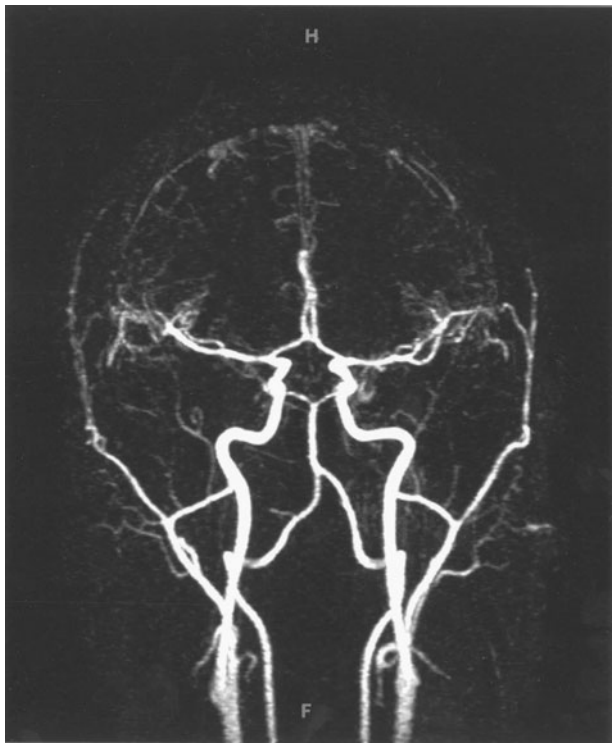

Photo 28-3 Magnetic resonance angiography of cerebral vasculature

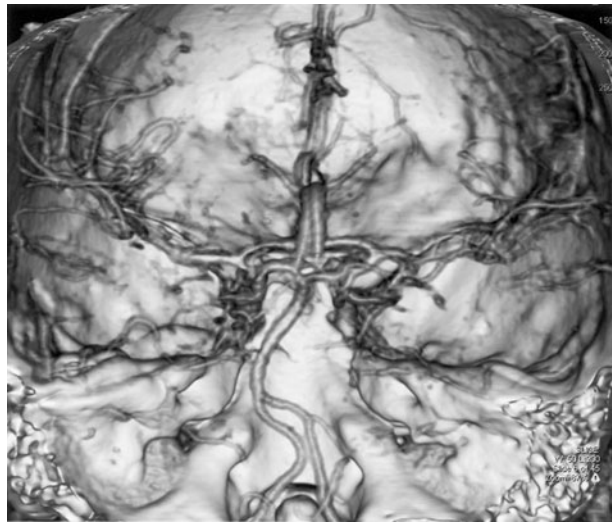

Photo 28-4 Reconstructed computed tomography of Circle of Willis

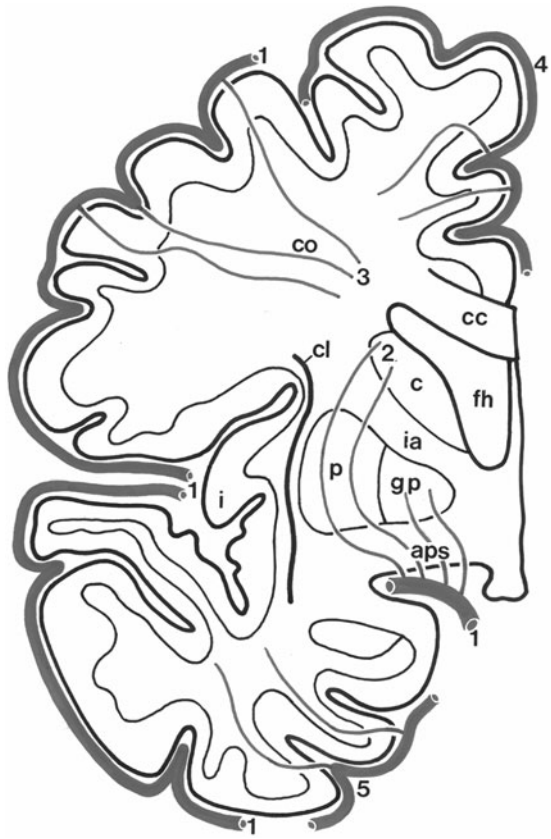

Photo 28-5 Coronal section of leptomeningeal arteries and lenticulostriate perforators 1 – middle cerebral artery, 2 – perforating arteries, 3 – medullary arteries, 4 – anterior cerebral artery, 5 – posterior cerebral artery
From Bogousslavsky, J., and L. R. Caplan. *Stroke Syndromes*. 2nd ed. Cambridge and New York: Cambridge University Press, 2001. Reprinted with the permission of Cambridge University Press.

The major cerebral arterial vessels are the anterior, middle, and posterior cerebral arteries. The internal carotid artery feeds the anterior and middle cerebral arteries, and the vertebral–basilar system feeds the posterior cerebral arteries. Feel the pulsating internal carotid arteries in your anterior neck, near the trachea. Then palpate your vertebrae; the vertebral arteries ascend alongside the upper cervical vertebral column. The internal carotids pass through the cavernous sinus before they split into anterior and middle cerebral arteries; see the "Skull Base" chapter for details about the course of the internal carotid arteries. The vertebral arteries combine in the posterior fossa to form the basilar artery, which ascends the brainstem and bifurcates at the top of the midbrain into the posterior cerebral arteries.

The major cerebral vessels have both perforating and leptomeningeal branches. The perforating branches supply the deep structures (e.g. the diencephalon and basal ganglia) and the leptomeningeal branches supply the superficial structures (e.g. the cortical and subcortical regions). In this first diagram, we will draw the *Circle of Willis*, which Thomas Willis first described in 1664; it lies along the base of the brain. The Circle of Willis will help us learn the vascular supply of the brain and interpret cerebral arteriography. In our diagram, we will draw the leptomeningeal branches of the Circle of Willis on one side and the perforating branches on the other.

Let's stage our diagram so that we learn the most commonly discussed arteries first and then add the more advanced vasculature. Never lose sight of the simple idea that two main arterial systems exist—an anterior internal carotid artery system and a posterior vertebral-basilar system. When evaluating a stroke, if you are able to determine which system is involved, or if both are, you'll never be far from localizing the infarcted vessel.

Start our diagram with the anterior-lying *internal cerebral arteries*; show axial sections through them. Next, show the *middle cerebral arteries* originate from the internal carotids and extend laterally. Then, indicate the *anterior cerebral arteries* branch anteriorly from the internal carotids. Next, at the bottom of the diagram, show the two *vertebral arteries* join to form the *basilar artery*, and indicate its rostral ascent up the brainstem. Show it bifurcate into the postero-laterally directed *posterior cerebral arteries*.

Connect the middle and posterior cerebral arteries with the *posterior communicating arteries*. Then, show the *anterior communicating artery* connects the two anterior cerebral arteries. Proximal to the anterior communicating artery is the A1 segment of the anterior cerebral artery and distal to it is the A2 segment. The posterior cerebral artery is divided in similar fashion, that is, proximal to the posterior communicating artery is the P1 segment and distal to it is the P2 segment. P3 and P4 are successively distal segments.

The M1 branch of the middle cerebral artery is the proximal segment that arises from the internal cerebral artery (it passes laterally along the Sylvian fissure toward the insula). When the artery travels up across the insula, it is the M2 branch, and then when it passes back down along the underside of the operculum it is the M3 branch. Finally, it becomes the M4 branch when it travels out across the surface of the brain. There are two main divisions to the M4 branch: an anterior–superior division and a posterior–inferior division. Often, strokes will occur in one M4 division and not the other. It is clinically important to recognize if only one division is affected, because the other division is still at risk for additional infarct.

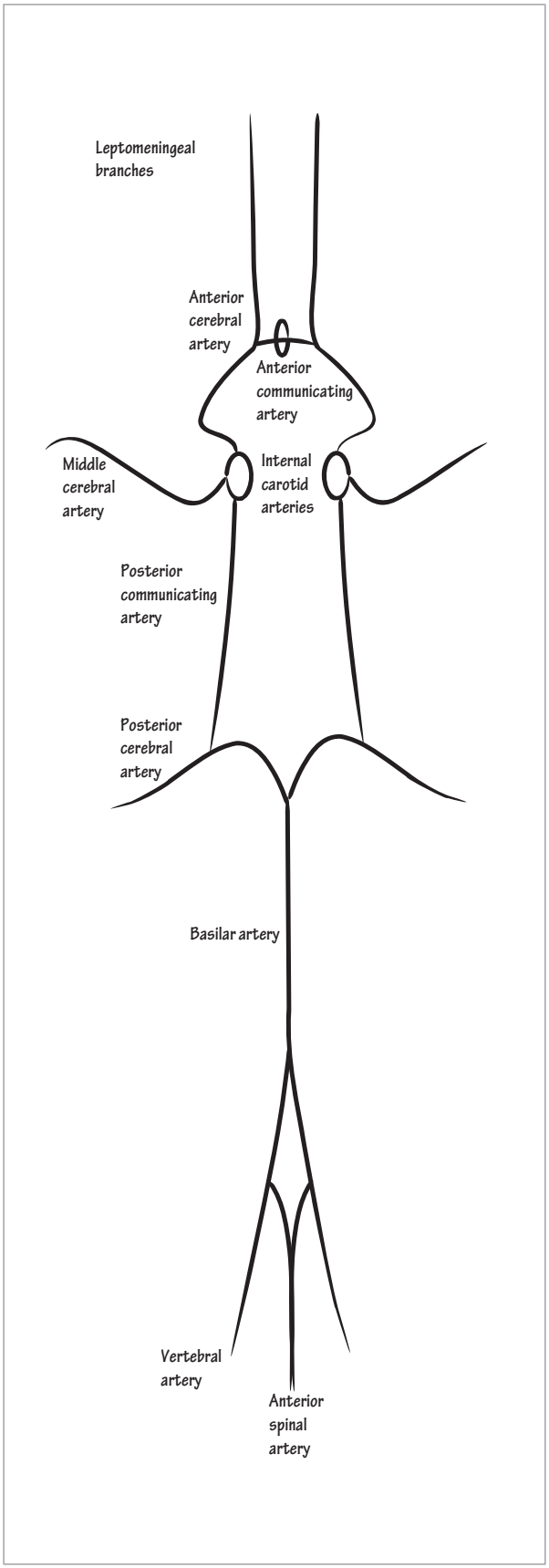

Figure 28-1 Incomplete Circle of Willis

Now, show branches of the vertebral arteries join together in midline to form the *anterior spinal artery*. Let's take a moment to discuss spinal cord vasculature. Spinal cord arterial vasculature comprises the anterior and posterior spinal arteries; they run rostro-caudally down the length of the spinal cord. Both originate from the vertebral arteries in the posterior fossa of the cranial vault. The anterior spinal artery is a singular artery that runs down the front of the cord and the posterior spinal arteries run down the bilateral posterolateral aspects of it. Paired horizontally-mediated segmental arteries (aka radicular arteries or spinal medullary arteries) originate from the aorta and help supply these two longitudinal arteries throughout their descent. The radicular arteries originate from the somite derivatives, as discussed in the "Cranial and Spinal Nerve Overview" chapter. As we age, there is involution of many of the segmental arteries so that in adulthood only a few persist.

In the lower thoracic, upper lumbar region (most commonly between T8 and L1), and usually on the left-hand side, a large segmental artery exists called the artery of Adamkiewicz. Surgeons need to pay particular attention to this vessel as injury to it will likely lead to paraplegia given its lower thoracic/upper lumbar location. The other segmental arteries are important but none supply the spinal arteries as impressively as the artery of Adamkiewicz.

The anterior spinal artery covers the anterior two-thirds of the spinal cord, and the posterior spinal arteries cover the posterior one-third of it. As an exercise, look back over the diagrams we have drawn in the "Spinal Cord" chapter and see how anterior and posterior spinal infarcts will differentially affect the cord. Interestingly, it is possible that an anterior spinal infarct will affect the arm fibers of the lateral corticospinal tracts without affecting the leg fibers and vice versa (a posterior spinal artery infarct can affect the leg and not the arm fibers), because the border of the anterior and posterior spinal arterial territories lies within the corticospinal tract systems in the lateral funiculi.

The spinal venous system is much less distinct; it involves extensive communication with surrounding venous plexuses. Most notably, its low-pressure state and valveless chambers expose the spinal canal to the spread of intrathoracic or intrabdominal abscesses and neoplastic metastases.

Next, we will draw one side of the bilateral cerebellar vessels. Draw the *posterior inferior cerebellar artery* off the vertebral artery, the *anterior inferior cerebellar artery* off the posterior basilar artery, and the *superior cerebellar artery* off the anterior basilar artery.

On the opposite side of the diagram, we will draw the deep perforators. First, draw the *anterior choroidal* branch of the internal carotid artery and then show the *lenticulostriate branches* of the middle cerebral artery. Next, show the thalamic perforators, from medial to lateral they are: the *paramedian thalamic artery*, *posterior choroidal artery*, and the *inferolateral thalamic artery*. Finally, show the basilar perforators, which are the *paramedian basilar branches*, *short circumferential branches*, and *long circumferential branches*.

The Circle of Willis is worth knowing well so draw and redraw it.

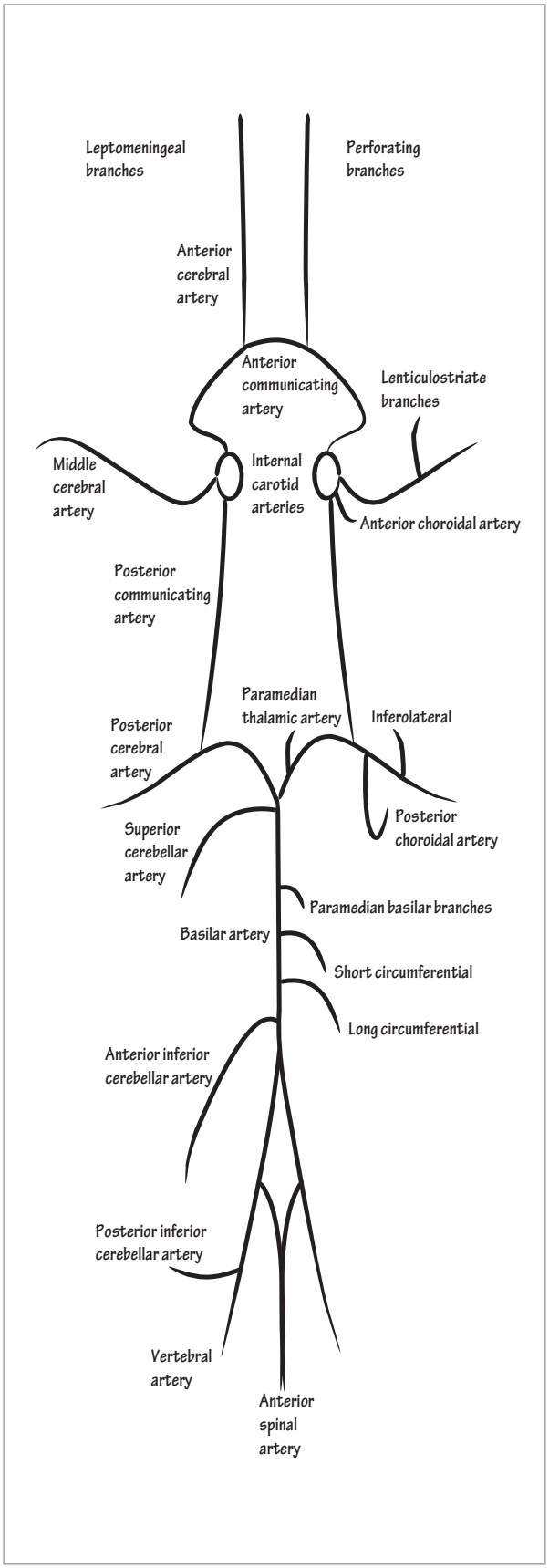

Figure 28-2 Complete Circle of Willis

In this diagram, we will draw the vascular territories of the leptomeningeal branches of the anterior, middle, and posterior cerebral arteries. We will use two axial sections: one that is superior within the brain and the other that is inferior. In this diagram, indicate the *anterior cerebral artery* supplies the *entire medial superior cerebrum* and the *anterior portion of the medial inferior cerebrum*; the middle cerebral artery supplies the *entire lateral superior cerebrum* and the *anterior two-thirds of the lateral inferior cerebrum*; and the *posterior cerebral artery* supplies most of the *inferior posterior cerebrum* (specifically, the *posterior one-third of the lateral inferior cerebrum* and the *posterior half of the medial inferior cerebrum*). This completes the leptomeningeal branch territories; however, the inferior axial section of our current diagram provides the best opportunity to view the deep perforator vascular territory of the anterior choroidal artery, so show the *anterior choroidal artery perforators* feed the deep medial inferior temporal region, now.

As mentioned in the introduction, the cerebral vascular territories are variable and our goal is to learn the central region each cerebral artery supplies, but infarction also occurs in the border-zones, themselves, and causes "watershed strokes." These strokes occur from low blood flow states. Cerebral autoregulation is a physiologic mechanism that maintains relatively constant cerebral pressure despite fluctuations in systemic pressure, but when systemic pressure is outside of the autoregulation curve, there is the possibility for brain injury. During precipitous drops in blood pressure, the areas between the major vascular territories, the border-zones (aka watershed territories), are starved of blood.

The somatotopic sensorimotor area between the middle and anterior cerebral arteries encodes the proximal arms and legs. So patients with watershed strokes often manifest with "man in a barrel syndrome," meaning they have trouble lifting their arms and legs but their hands and feet are fine. To demonstrate this clinical effect, sit with your arms at your side and wiggle your fingers and toes but be unable to raise your arms or your legs.

Now that we know the leptomeningeal vascular territories, we are able to answer most of the clinical cerebral vascular questions that arise; however, we do need to learn the perforating vessels, as well. Unfortunately, this is a challenge and requires patience—bear with this next section.

Let's summarize the deep perforators before we draw them. First, the anterior, middle, and posterior arteries all have perforating branches and so does the internal carotid artery; the rest of the perforating branches are the anterior and posterior choroidal arteries, the anterior and posterior communicating arteries, and the paramedian and inferolateral thalamic arteries. Fortunately, the names of these vessels will help us remember their territories. In the following section, as we did with the leptomeningeal vessels, focus on the general region each artery supplies. We include a detailed list of the structures each vessel supplies to help us understand the territory, not for memorization.

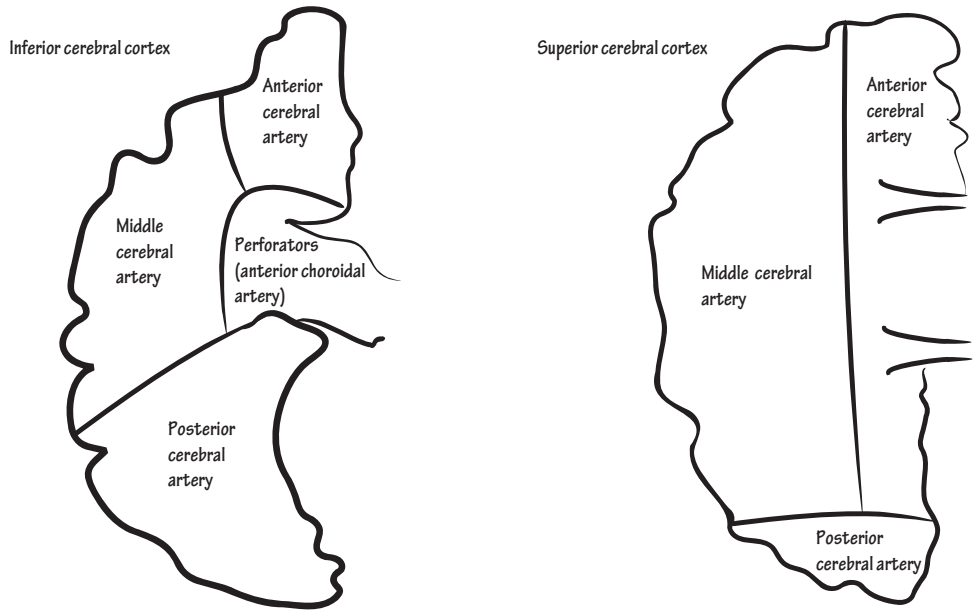

Figure 28-3 Leptomeningeal vascular territories

While the perforating branches supply many rostro-caudal levels of the brain, we will show their vascular territories, here, with a single axial section through a level just above the brainstem, through the basal ganglia/diencephalon. Draw the following anatomical landmarks: the lentiform nucleus (i.e., the globus pallidus–putamen combination), head of the caudate, thalamus, and write in the hypothalamus (since drawing it would be nondistinct). In the leptomeningeal diagram, we added the *anterior choroidal artery* perforators and showed that they supply the *medial temporal lobe* (uncus, hippocampus, amygdaloid body). In this section, show their supply extends superiorly to the *medial–posterior–inferior basal ganglia region* (lower posterior internal capsule, lateral geniculate nucleus, medial globus pallidus, and tail of the caudate). Next, show the perforating branches of the *internal carotid artery* supply the *genu of the internal capsule* and the area immediately surrounding it. Show the *anterior communicating artery* supplies the *anterior hypothalamus* and that the *posterior communicating artery* (aka the premammillary artery or anterior thalamoperforating artery or tuberothalamic artery) supplies the *posterior hypothalamus* and *anterior thalamus*. Indicate the *anterior cerebral artery perforating branches* (including the *recurrent artery of Heubner*) supply the *anterior basal ganglia region* (anterior–inferior head of the caudate, anterior–inferior portion of the anterior limb of the internal capsule and surrounding lentiform nucleus, and medial anterior commissure).

Then, show the *perforating branches of the middle cerebral artery* (aka lenticulostriate arteries) supply the *superior and lateral basal ganglia region* (superior portions of the caudate and internal capsule and the lateral portions of the globus pallidus and anterior commissure). Indicate the *paramedian thalamic artery* (aka thalamoperforating artery) supplies the *intralaminar and medial thalamus* and that the *inferolateral thalamic artery* (thalamogeniculate branch) supplies the *lateral thalamus*. Finally, show the posterior choroidal artery is highly variable in its vascular supply of the *medial–lateral axis of the thalamus*.

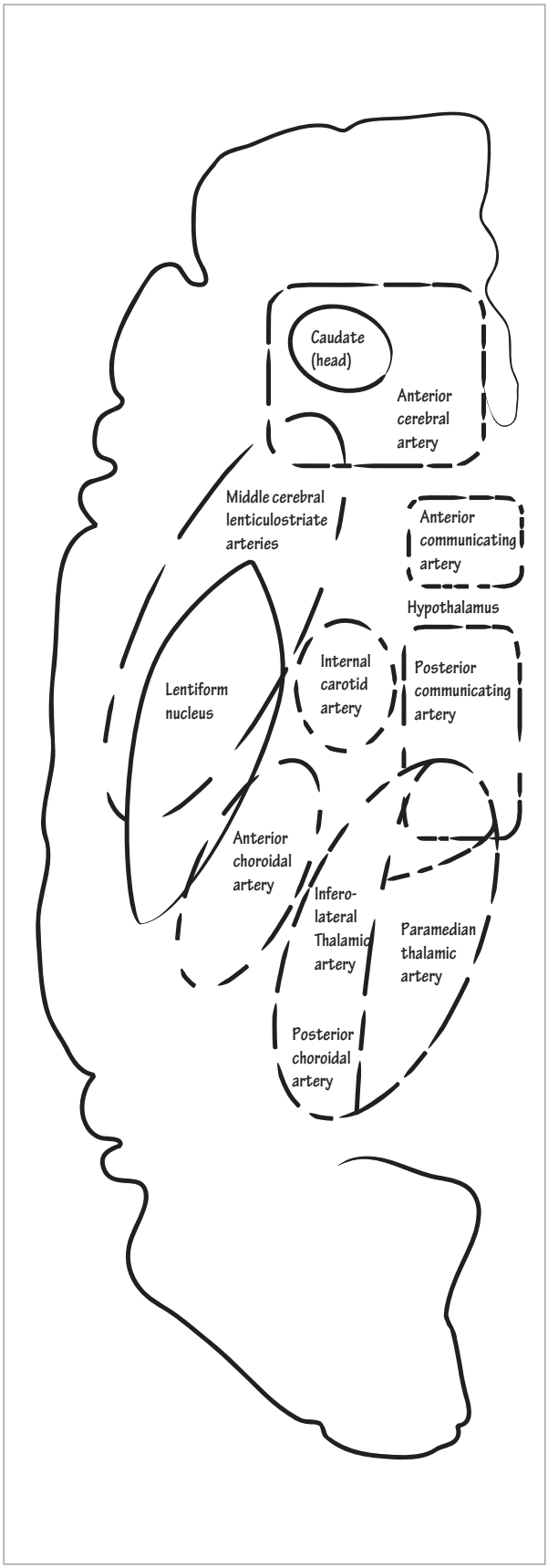

Figure 28-4 Deep perforator vascular territories

Now, we will draw and label the arterial vascular supply of the brainstem using axial cuts through the medulla, pons, and midbrain. Fortunately, the vascular pattern of each brainstem level can be divided into four general vascular groups: anteromedial, anterolateral, lateral, and posterior. The anteromedial group is oriented along the anterior–posterior plane, and the anterolateral, lateral, and posterior groups are oriented along the medial–lateral plane. Paramedian arteries supply the anteromedial group; short circumferential arteries, which originate in midline and wrap a short distance around the outside of the brainstem, supply the anterolateral group; long circumferential arteries, which also originate in midline but wrap a long way around the outside of the brainstem, supply the lateral group; and large lateral-lying vessels supply the posterior group.

Let's begin with an outline of an axial composite of the medulla, pons, and midbrain. Divide it into right and left sides. On the left side indicate the *anteromedial group* territory lies in anterior–posterior orientation along the medial one-third of the anterior brainstem. Then divide the remaining lateral and posterior two-thirds into three groups that lie along the medial to lateral plane. They are, from anterior to posterior, the *anterolateral*, *lateral*, and *posterior* groups.

Next, on the other side, indicate the arterial groups that supply each of these four territories. As listed previously, the *paramedian arteries supply* the anteromedial group, the *short circumferential arteries* feed the anterolateral group, *the long circumferential arteries* supply the lateral group, and the *large vessels* feed the posterior group.

At certain levels, the arterial groups vary in size. In the medulla, the anterolateral group is small; in the pons, the posterior group is small; and in the midbrain, the anterolateral group is quite large, but otherwise this organizational pattern is consistent.

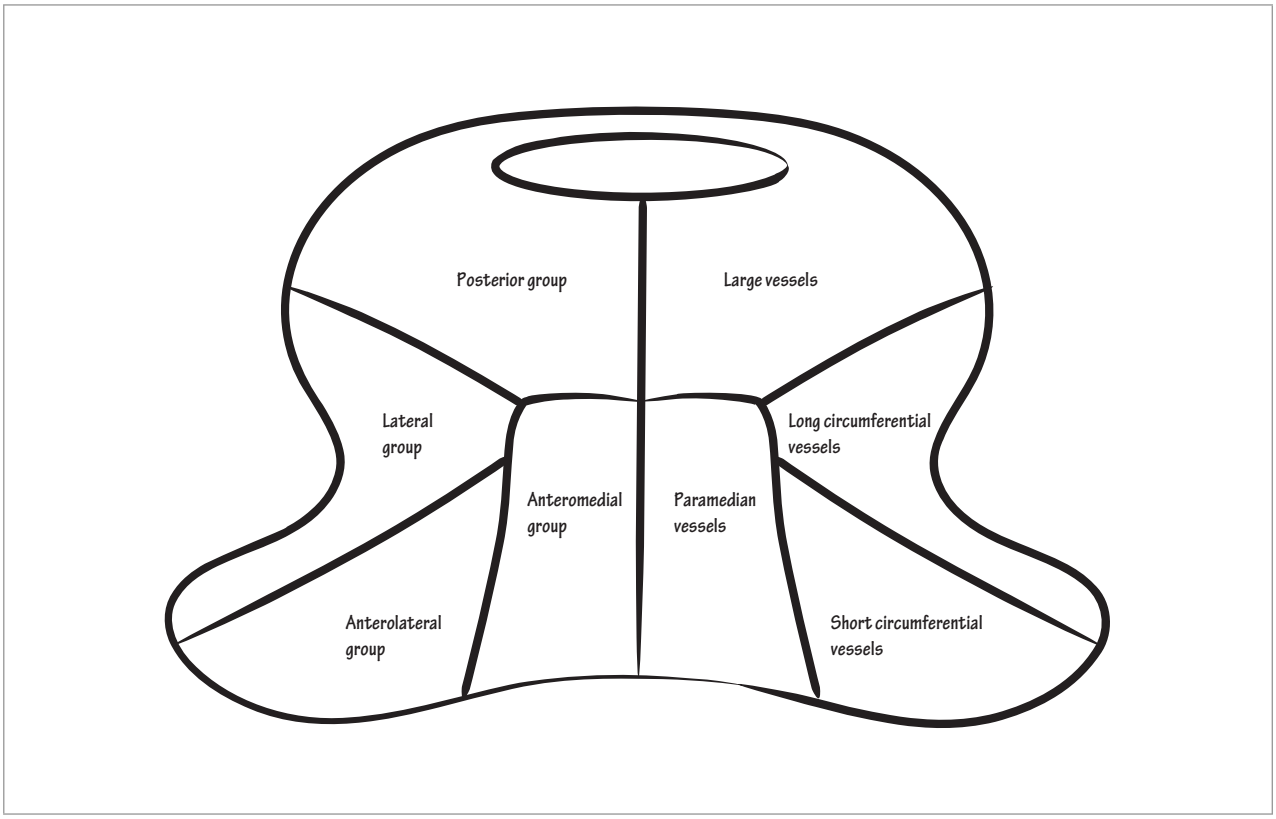

Figure 28-5 Brainstem vascular supply

We will now make a table of the specific vessels that supply the brainstem. If you are uninterested in this, just pay attention to the next few highlights and then skip ahead to the vascular supply of the cerebellum. First, the posterior inferior cerebellar artery (PICA) is of particular clinical importance; it supplies the anterolateral, lateral, and posterior medulla (i.e., all but the anteromedial portion) and an occlusion of this vessel results in a lateral medullary syndrome (aka Wallenburg's syndrome). Next, note that the anterior and posterior spinal arteries help supply the medulla, which people are often surprised to learn. Pay attention to the short and long branches of the basilar artery, which supply the anterolateral and lateral pontine groups. Disease of these vessels may result in pontine basis strokes, which occasionally lead to locked-in syndrome, discussed in the "Somatomotor Cranial Nerves" chapter. Finally, the posterior cerebral arteries supply the anterior midbrain, and in basilar arterial stroke, clot will often pass up to the top of the basilar artery and block blood-flow to the bilateral posterior cerebral arteries.

Let's begin our table with the paramedian arteries, which supply the anteromedial group. Indicate that in the medulla, the paramedian arteries are the *anterior spinal artery* and *vertebral artery*; in the pons, they are the *paramedian branches of the basilar artery*; and in the mibrain, the paramedian artery is the *posterior cerebral artery* (*PCA*).

Next, let's learn the arteries that comprise the short circumferential arteries, which supply the anterolateral group. In the medulla, they are *anterior spinal artery* and *posterior inferior cerebellar artery*; in the pons, they are the *short circumferential branches of the basilar*, and in the midbrain, they are the *collicular artery* and *posteromedial choroidal artery*.

Now, let's indicate the arteries that constitute the long circumferential arteries, which supply the lateral group. For the medulla and midbrain, they are the same as the anterolateral group; that is, in the medulla, they are the *anterior spinal artery* and *posterior inferior cerebellar artery*, and in the midbrain, they are the *collicular artery* and *posteromedial choroidal artery*. In the pons, show the *long circumferential branches of the basilar* supply the lateral group (note, the short circumferential branches supply the anterolateral pontine group).

Lastly, indicate the arteries that comprise the large vessels, which supply the posterior group. In the medulla, indicate they are the *posterior spinal artery* and *posterior inferior cerebellar artery*; in the pons, they are the *superior cerebellar artery* (*SCA*) and *anterior inferior cerebellar artery* (*AICA*); and in the midbrain, they are the *superior cerebellar artery*, *collicular artery*, and *posteromedial choroidal artery*.

While the process of writing out this table was ugly, in tabular form, certain consistencies in the vascular territories at each brainstem level become apparent; it's worth looking for them now.

	Medulla	Pons	Midbrain
Paramedian vessels (anteromedial group)	Anterior spinal artery Vertebral artery	Paramedian branches of the basilar	Posterior cerebral artery
Short circumferential vessels (anterolateral group)	Anterior spinal artery Posterior inferior cerebellar artery	Short circumferential branches of the basilar	Collicular artery Posteromedial choroidal artery
Long circumferential vessels (lateral group)	Anterior spinal artery Posterior inferior cerebellar artery	Long circumferential branches of the basilar	Collicular artery Posteromedial choroidal artery
Large vessels (posterior group)	Posterior spinal artery Posterior inferior cerebellar artery	Superior cerebellar artery Anterior inferior cerebellar artery	Superior cerebellar artery Collicular artery Posteromedial choroidal artery

Figure 28-6 Brainstem vessels table

The cerebellum is supplied by three arteries: the posterior inferior cerebellar artery (PICA), anterior inferior cerebellar artery (AICA), and superior cerebellar artery (SCA). We will show their vascular territories by drawing three sections through the cerebellum from inferior to superior. Also, in each section, we will include the related brainstem level (medulla, pons, or midbrain) for visual reference. First, indicate the *posterior inferior cerebellar artery*, which has both *medial* and *lateral* divisions, feeds the inferior cerebellum. Next, the middle rostro-caudal cerebellar level is supplied by all three cerebellar vessels: show the *anterior inferior cerebellar artery* supplies its anterior segment, the *superior cerebellar artery* supplies its lateral segment, and the *posterior inferior cerebellar artery* supplies its medial segment. Finally, show the *superior cerebellar artery*, which has both *medial* and *lateral branches* (like the posterior inferior cerebellar artery), supplies the superior cerebellum. The lateral superior cerebellar branch extends inferiorly and the medial branch extends superiorly.

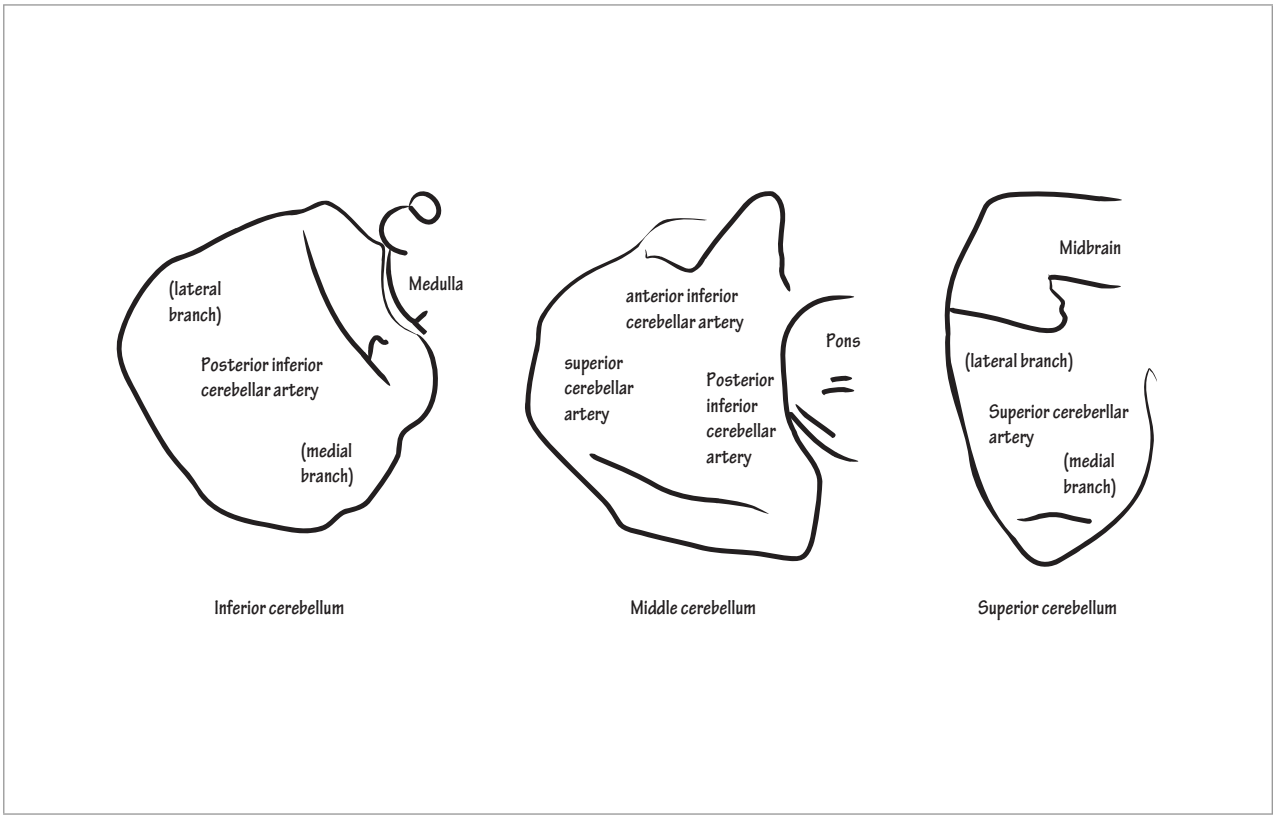

Figure 28-7 Cerebellar arterial supply

Thalamus

In this chapter, we will draw the nuclei of the thalamus. Informational pathways flow into the thalamus from all areas of the central nervous system. Thalamic nuclei process, integrate, and relay sensory, motor, and behavioral information and project it throughout the cerebral cortex. These cortical areas then return modulated information to the thalamus, which forms a reciprocal topographic connection between the thalamus and the cerebral cortex. In some instances, the cerebral cortex, itself, provides the initial projection to the thalamus, such as the cortical projections that exist to the dorsomedial nucleus of the thalamus.

The thalamus is one of the main structures of the diencephalon. We refer to the diencephalon throughout this book, so let's take a moment to explain what it is. Remember from the "Cranial and Spinal Nerve Overview" chapter that in the first few weeks of development, the neural tube forms anterior and posterior neuropores. At the time the anterior neuropore closes—during the fourth week of gestation—three brain vesicles form, called primary brain vesicles. They are the prosencephalon (aka the forebrain); the mesencephalon (aka the midbrain); and the rhombencephalon (aka the hindbrain). During the next week of embryogenesis, the fifth week, the primary brain vesicles develop into secondary vesicles. The mesencephalon remains undivided but the vesicles below and above it split. The rhombencephalon divides into the metencephalon, which comprises the pons and cerebellum, and the myelencephalon, which contains the medulla. And the prosencephalon divides into the telencephalon and the diencephalon. The diencephalon becomes everything between the midbrain and the basal ganglia and the telencephalon develops into the cerebral hemispheres and everything above the diencephalon. More specifically, the telencephalon becomes the lobes of the brain, white matter, and basal ganglia, and the diencephalon forms the thalamic structures.

Let's list the diencephalic components in detail. They are the thalamus, epithalamus (habenula and pineal body), subthalamus and Forel fields, metathalamus (medial geniculate body and lateral geniculate body), hypothalamus, and also the surrounding non-thalamic structures (optic chiasm, optic tract, third ventricle, anterior and posterior commissures, and other related areas). We learn about these structures throughout the book; here, we will focus on the thalamus only.

The thalamus comprises relay, association, and diffusely projecting nuclei, which are categorized on the basis of their cerebral cortical targets, that is, relay nuclei project to primary cortical areas, association nuclei project to association cortices, and diffusely projecting nuclei project to widespread targets throughout the cerebral cortex. As we learn the nuclei, we will point out the association nuclei because they are not obvious; on the contrary, the relay and diffusely projecting nuclei will be readily apparent. Despite this established organization scheme, it is best to learn the specific functions of the different thalamic

nuclei and their inputs and outputs rather than rely on generalizations about the classes of thalamic nuclei. The functions of these nuclei are too specific and important for that level of generalization to be effective. Because the thalamic nuclei are involved in so many important nervous system pathways, thalamic anatomy, in essence, is a primer for nervous system anatomy, in general.

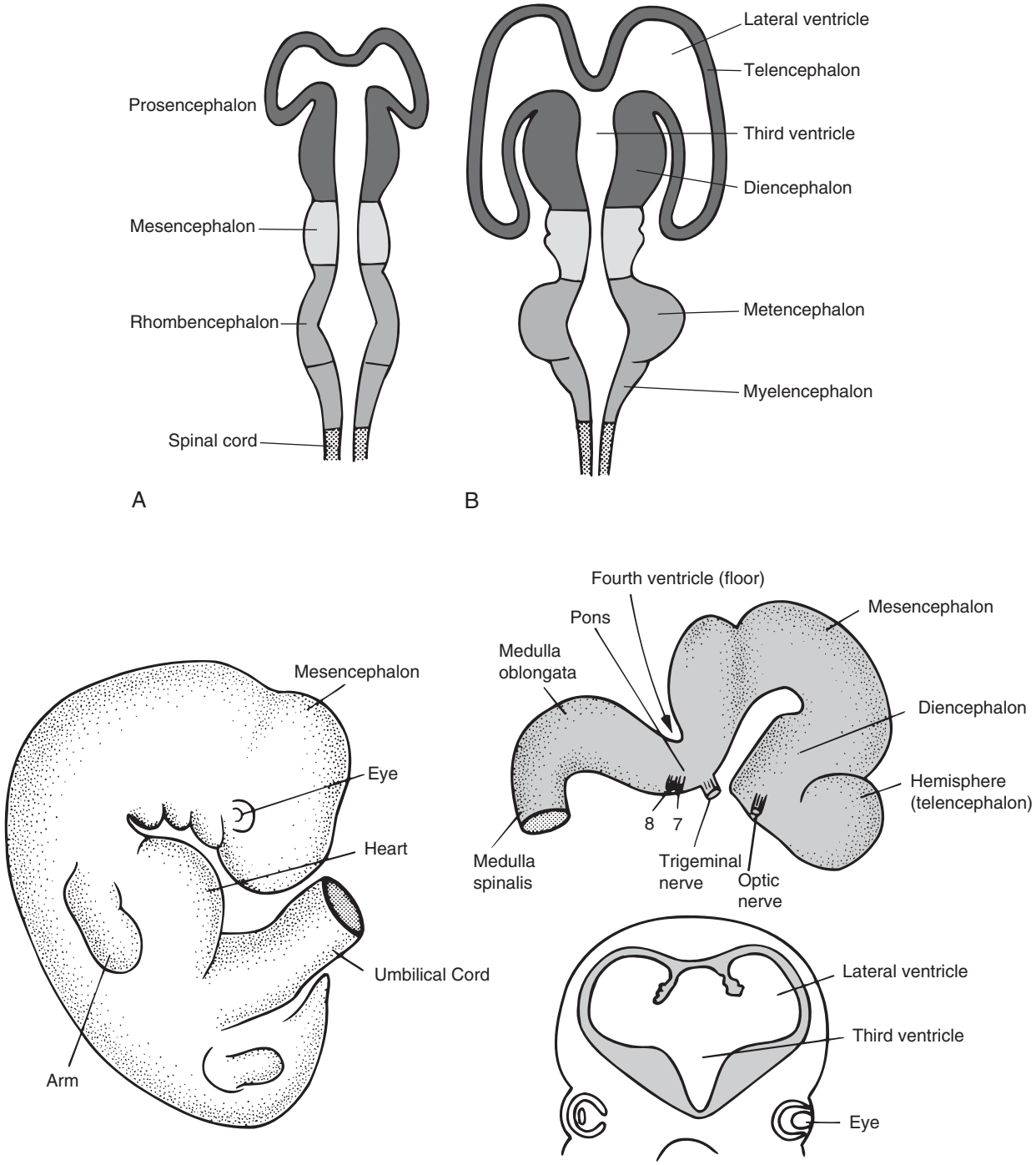

Photo 29-1 Vesicle development during embryogenesis: A – primary brain vesicles, B – secondary brain vesicles
With permission from Brodal, P. *The Central Nervous System: Structure and Function*. 3rd ed. New York: Oxford University Press, 2004.

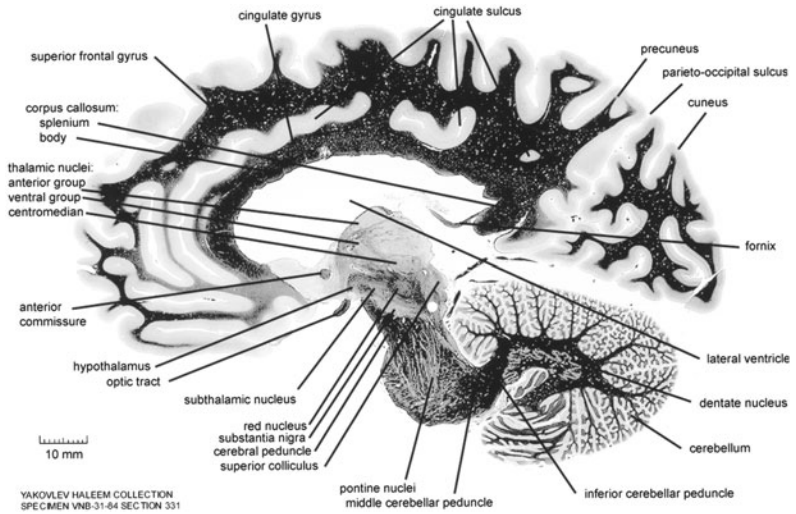

Photo 29-2 Mid-sagittal anatomical section to highlight the diencephalic thalamic structures
With permission from the Michigan State University: Brain Biodiversity Bank. https://www.msu.edu/~brains/

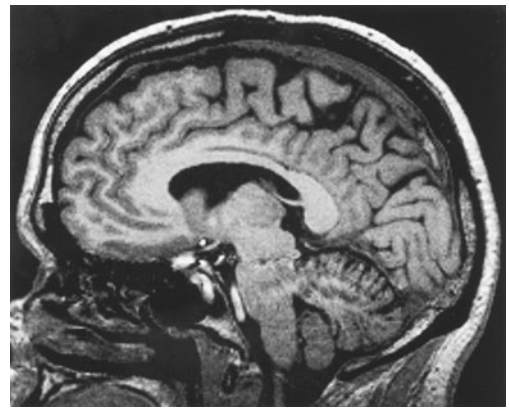

Photo 29-3 Mid-sagittal radiographic section to highlight the diencephalic thalamic structures

First, draw the egg-shaped appearing thalamus. Open its middle so we are able to show the ventral posteromedial nuclei and midline thalamic nuclei. Next, section the thalamus by drawing the Y-shaped *internal medullary lamina* diagonally along its anterior–posterior axis. Label the triangular wedge in the anterior thalamus as the *anterior nuclear group*, which is important in the classic memory circuit the Papez circuit, discussed in detail in the "Limbic System" chapter. The Papez circuit originates in the hippocampus, passes via the fornix to the mammillary nuclei, and then to the anterior nucleus of the thalamus via the mammillothalamic tract. The anterior thalamic nucleus projects to the *cingulate gyrus* and prefrontal cortex, and the memory circuit ultimately terminates back in the hippocampus.

Next, label the *ventral nuclear group* in the ventro-lateral thalamus; it is a widely important relay group. Label the constituents of this group from anterior to posterior along the ventro-lateral thalamus as the *ventral anterior*, *ventral lateral*, and *ventral posterior nuclei*, and the *medial* and *lateral geniculate bodies*, which attach to their respective sides of the ventro-posterior thalamus.

Indicate the ventral anterior nucleus is involved in *motor skills*, the ventral lateral nucleus in *coordination*, and the ventral posterior nucleus in *sensation*. With that in mind, which nervous system regions connect with each of the nuclei? Indicate the ventral anterior nucleus receives projections from the *basal ganglia* (specifically, the *globus pallidus interna* and *substantia nigra*) and the cortical *supplementary motor area*. Then, show the ventral lateral nucleus receives afferent information from the contralateral

cerebellum. Which pathway involves the cerebellar fibers that project to the contralateral ventral lateral nucleus? The cerebrocortico–ponto–cerebellocortico–dentato-rubro–thalamo–cerebrocortical pathway discussed and drawn in the "Cerebellum" chapter. Through it, fibers project from the cerebral cortex to the pons across midline to the contralateral cerebellar cortex to the deep cerebellar dentate nucleus, then back across midline, again, to the contralateral red nucleus, and then to the ventral lateral thalamus, which projects to the cerebral cortex.

The ventral posterior nucleus is the main sensory relay station of the thalamus and receives sensory afferents from the lower brainstem sensory nuclei, including the gracile and cuneate nuclei and the trigeminal sensory nuclei. Indicate the ventral posterior nucleus subdivides into *lateral* and *medial* nuclei. The ventral posterolateral nucleus receives somatosensory information from the *body* and the ventral posteromedial nucleus receives it from the *face*. The sensory information in the thalamus has a very specific "onion-peel" somatosensory map in which the fist is adjacent to the mouth. Patients with a ventral posteromedial stroke present with cheiro-oral syndrome. On the side opposite the damaged thalamus, they have impaired sensation around the mouth and in the fist. The efferent target of the ventral posterolateral and ventral posteromedial nuclei is the primary somatosensory cortex, which is in the post-central gyrus. Note, a secondary somatosensory cortex also exists, which we will discuss when we address its major afferent supplier—the posterior nucleus of the posterior thalamic nuclear group.

Show, now, the medial geniculate body receives auditory information from the *inferior colliculus* and projects to the *transverse gyri of Heschl* in the *insular cortex* and the lateral geniculate body receives visual information from the *optic tract* and projects to the primary visual cortex in the *posterior occipital lobe*. Reciprocal projections exist from the cortex to the thalamus that modulate thalamic outflow.

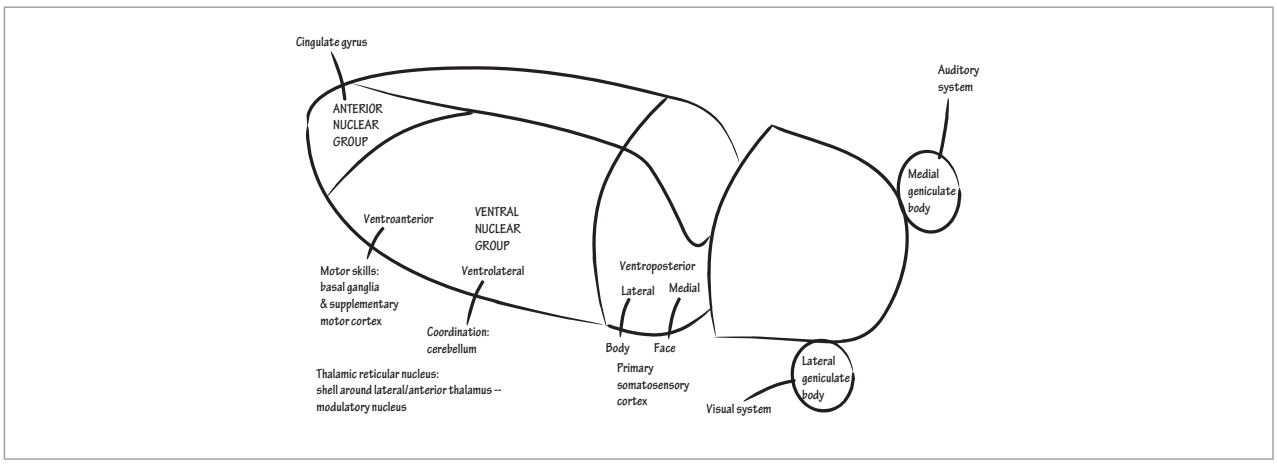

Figure 29-1 Incomplete thalamus

Ventral and posterior to the thalamus, itself, indicate the *posterior thalamic nuclear group*, which is a widespread conglomeration of nuclei. Note that the posterior thalamic nuclei lie posterior to the thalamus and not within the posterior thalamus—that portion is dedicated to the pulvinar of the lateral nuclear group, instead, which we will draw soon. Here, we will only draw one tiny nucleus—the *posterior nucleus*, which attaches to the posterior tip of the thalamus. Show it project to the *secondary somatosensory cortex* in the inferior parietal cortex, which is involved in cortical processing of pain and temperature sensation.

The *lateral nuclear group* runs the anterior-posterior length of the thalamus. Show it comprises the thin territory in between the ventral group and intramedullary lamina, and indicate that the posterior third of the thalamus is a subcategory of the lateral nuclear group called the *pulvinar*. It seems more appropriate to categorize the pulvinar with the posterior nuclear group because it makes up the *posterior thalamus*, but it is organized with the lateral nuclear group, instead: the posterior thalamic nuclear group refers to the nuclei behind the thalamic body that are affiliated with it and not the actual posterior thalamus.

Anteriorly, indicate the lateral nuclear group connects with the *limbic system*. Then, posteriorly, show it connects with the *visual attention system* in the pretectal nucleus and the *cortical visual system* in temporoparietal association areas. Its connections with the visual association areas make it an association group.

On the medial aspect of the thalamus, label the *medial nuclear group*, which largely consists of the dorsomedial nucleus. The medial nuclear group connects the limbic centers with the frontal lobe. It has afferent connections from the amygdala, hippocampus, and basal forebrain and efferent connections to the prefrontal, premotor, and frontal eye field regions of the frontal lobe. The frontal association cortex is its main target, which makes the medial nuclear group an association group.

Now, show the internal medullary lamina contains the *intralaminar group*. Indicate it has widespread inputs and outputs involved in the *maintenance of arousal*. As discussed the in the "Brainstem" chapter, it receives specialized fibers from the reticular formation that assist in the maintenance of arousal. At one point, arousal was thought to be due to a general, non-specific activation network, but now the specialized nature of the neurobiology of wakefulness is better understood.

Show the *midline nuclear group* encases the ventromedial portion of the thalamus; it lies in the midline of the central nervous system, along the third ventricle. Given this location, what behavioral role do you expect it to serve? What other important diencephalic structure surrounds the third ventricle? The hypothalamus, which is the command center of the autonomic central nervous system. Indicate the midline nuclear group of the thalamus is involved in *visceral function*.

Lastly, the thalamic reticular nucleus forms a shell around the lateral, superior, and anterior-inferior thalamus; it is a diffuse modulatory nucleus that communicates widely with the thalamus and cerebral cortex. The thalamic reticular nucleus is morphologically related to the zona incerta, which channels input into the thalamus (we draw the zona incerta in the "Basal Ganglia" chapter). If we draw the thalamic reticular nucleus, we will obstruct the view of the rest of the thalamus so simply label it in our diagram and indicate its function.

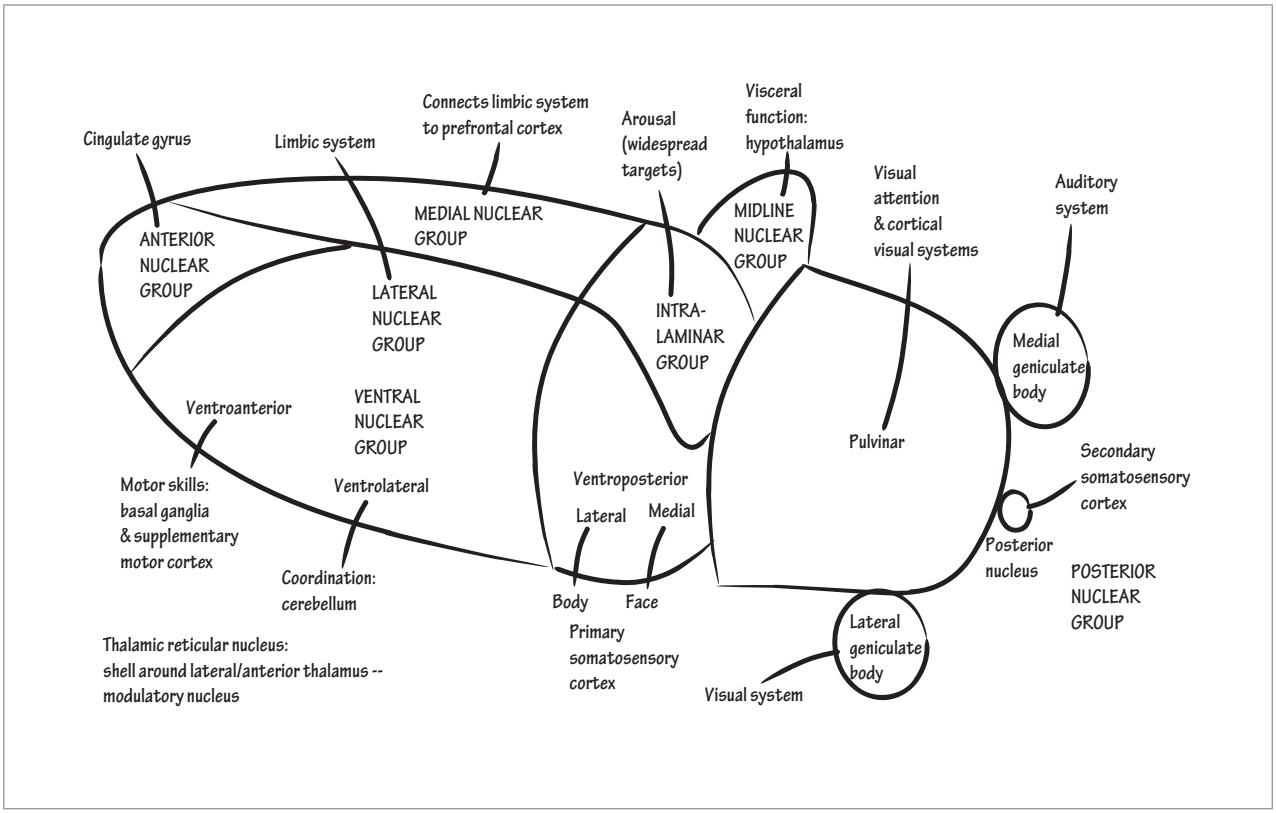

Figure 29-2 Complete thalamus

Hypothalamus

IN THIS CHAPTER, we will draw several figures of the hypothalamus: first, one of its borders, then its nuclei, followed by a drawing of its relationship to the pituitary gland, and finally, its afferent and efferent fibers. Unlike the thalamus, which is not well-suited to generalizations, the hypothalamus is best learned through categorizations and simplifications, because the nuclei of the hypothalamus are cumbersome to remember, often non-distinct, and their functions are, in many instances, poorly understood. Regardless, if we stay above its anatomical muck, the hypothalamus will be an interesting part of the brain for us to learn because it plays such an important role in behavior.

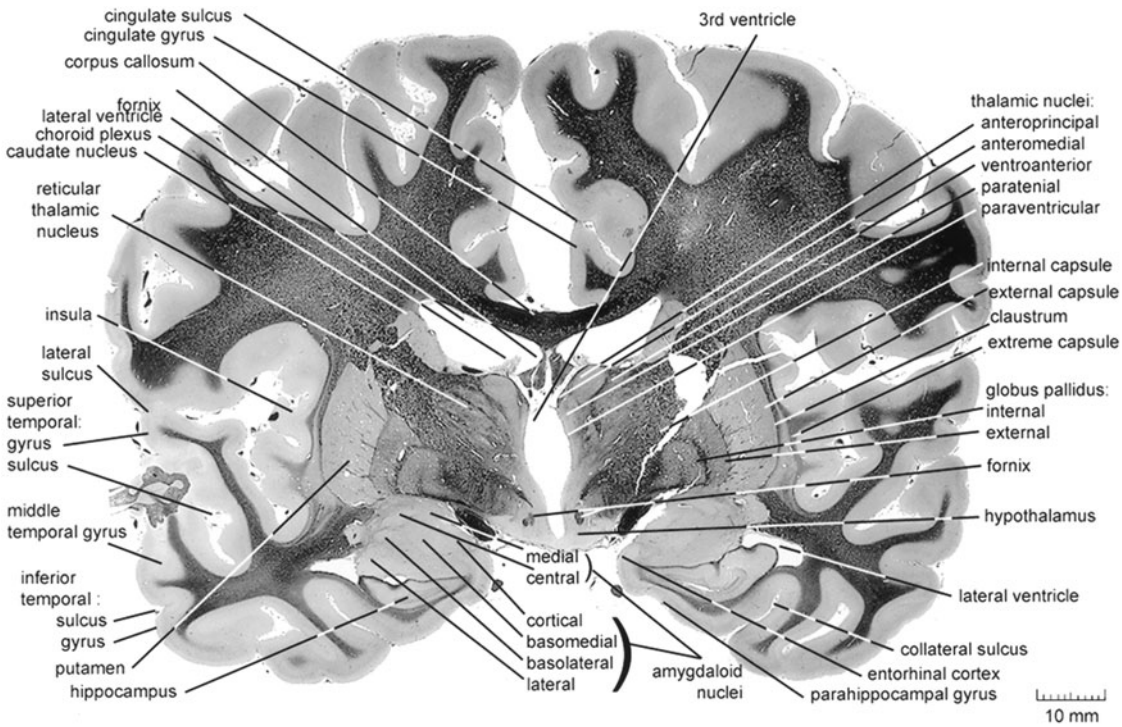

Photo 30-1 Coronal section through the brain to show the hypothalamus
With permission from the Michigan State University: Brain Biodiversity Bank. http://www.msu.edu/~brains/

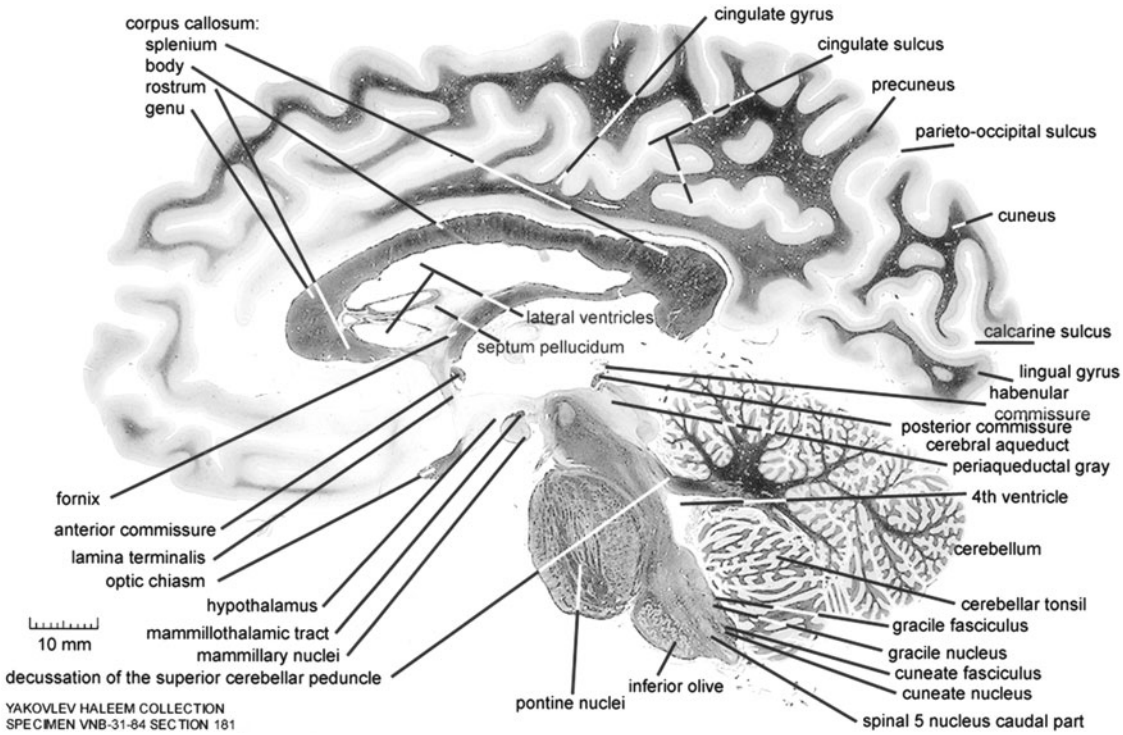

Photo 30-2 Sagittal section through the brain to show the hypothalamus
With permission from the Michigan State University: Brain Biodiversity Bank. http://www.msu.edu/~brains/

To draw the boundaries and surrounding structures of the hypothalamus, first draw the *lamina terminalis*; it is the anterior hypothalamic border and it extends from the *anterior commissure*, superiorly, to the *optic chiasm*, inferiorly. Indicate the *frontal lobe* lies just anterior to the lamina terminalis; the lamina terminalis is the most anterior division between the diencephalon and telencephalon. Posterior to the anterior commissure, draw the *hypothalamic sulcus*, which is the superior border of the hypothalamus. Draw the *thalamus* above it. The fornix wraps around the top of the thalamus and begins its descent near the anterior commissure; we will show it pass through the hypothalamus and synapse in the mammillary bodies in the clinically important Papez circuit.

Now, along the undersurface of the hypothalamus, let's draw the *infundibulum*, *posterior pituitary gland*, and a section through the *mammillary bodies*. The infundibulum (aka pituitary stalk) is the funnel-shaped connection between the posterior pituitary gland and the hypothalamus. Neuronal fibers descend from the hypothalamus through the infundibulum directly into the posterior pituitary gland. Next, draw the *anterior pituitary gland*; it is derived from Rathke's pouch. While neuroectoderm derives the posterior pituitary gland, hypothalamus, and rest of the central nervous system, the anterior pituitary gland is an outcropping of the embryologic alimentary tract, which has functional and anatomical implications. While the hypothalamus directly communicates with the posterior pituitary gland, it indirectly communicates with the anterior pituitary gland through a vascular plexus. The hypothalamus sends hormones through the bloodstream to reach the anterior pituitary gland rather than communicating through neuronal channels as it does with the posterior pituitary gland.

The posterior border of the hypothalamus is relatively indistinct so we will create a border for it from some important landmarks. Draw the anterior surface of the *midbrain* just behind the mammillary bodies. Show the *quadrigeminal plate* and the *pineal body* that hangs above it. The hypothalamus terminates in front of these two parenchymal structures and behind the mammillary bodies.

Now, draw a coronal composite of the hypothalamus to show its medial and lateral borders. In the center, draw the narrow *third ventricle*, which is the medial border of the hypothalamus. Whenever you want to find the hypothalamus on radiographic imaging, look for the third ventricle and the hypothalamus surrounds it. Next, laterally, draw an outline of the *internal capsule* (it lies along the postero-lateral border of the hypothalamus) and on the inferior border, draw one of the *mammillary bodies* (they lie along the postero-inferior border of the hypothalamus). Then, as compared to the *posterior*-lying structures we just drew, dot the following *anterior* structures. Dot an outline of the *anterior commissure* across the top of the third ventricle and dot outlines of the *pituitary stalk*, *pituitary gland*, and the *optic chiasm and tract* along its bottom.

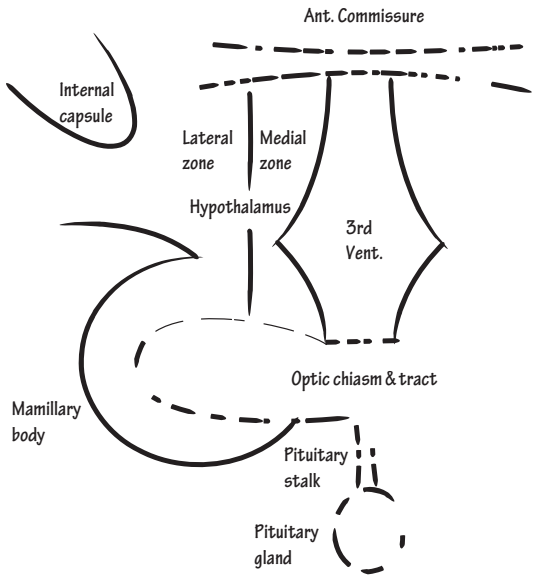

Figure 30-1 Coronal view of the hypothalamus

For the most part, the nuclei and fiber tracts of the hypothalamus naturally organize themselves into medial and lateral zones. The medial zone contains the hypothalamic nuclei and, with small exception, the lateral zone contains the hypothalamic fiber tracts. The medial zone can be further categorized into anterior, middle, and posterior groups of hypothalamic nuclei. However, before we begin indicating the various groups of nuclei and their functions, it is important to realize that the hypothalamus does not have the exactness of functional localization that other areas of the nervous system do. Although we would like to make certain regions "control centers," this often comes at the cost of introducing error into our thinking; still, as mentioned in the introduction, we need a simple model of the hypothalamus to remember anything about it at all.

One schema that generally holds true is that the anterior or rostromedial hypothalamus is involved in parasympathetic functions and the posterior or caudolateral hypothalamus is involved in sympathetic functions. The rostromedial hypothalamus is active in states of satiety, restfulness, and decreased temperature, whereas the caudolateral hypothalamus is active in states of hunger, anxiousness, and increased temperature. Keep the above in mind as we mire ourselves in the details of hypothalamic anatomy.

Now, we will draw the hypothalamic nuclei; we divide them into anterior, middle, and posterior groups. Here, we will use a sagittal diagram as we did for the hypothalamic borders. First, indicate the *anterior group* of nuclei. Just above the optic chiasm, draw the *suprachiasmatic nucleus*; behind it, just above the optic tract, indicate the *supraoptic nucleus*; then, above the supraoptic nucleus, draw the *anterior nucleus*; and above it, show the *paraventricular nucleus*. Neurons of the suprachiasmatic nucleus are the "master clock." They receive light–dark information from the retinae, and are important in circadian rhythms. The suprachiasmatic nucleus projects to the paraventricular nucleus, which stimulates the pineal gland to generate melatonin, which helps us transition to a sleep state. The position of these nuclei near the optic chiasm helps us remember their function in circadian rhythms, which are entrained to light-dark cycles. Neurons of the supraoptic and paraventricular nuclei produce oxytocin and antidiuretic hormone (ADH) (aka vasopressin), which is released into circulation after it is transported down the supraopticohypophysial tract to the posterior pituitary gland, drawn later. Neurons of the anterior nucleus, itself, are ill defined anatomically and their functional role remains unclear.

Now, label the *preoptic nucleus* above the suprachiasmatic nucleus and in front of the anterior nucleus. The preoptic nucleus develops with the telencephalon, whereas the hypothalamus is part of the diencephalon, so oftentimes, authors categorize the preoptic nucleus as its own entity, separate from the anterior group of hypothalamic nuclei. The preoptic nucleus contains neurons that produce gonadotropin-releasing hormone (Gnrh), which is transported to capillaries of the anterior pituitary gland through the tuberoinfundibular tract, drawn later. It is also heavily involved in sleep promotion through its effects on other hypothalamic nuclei and brainstem nuclei.

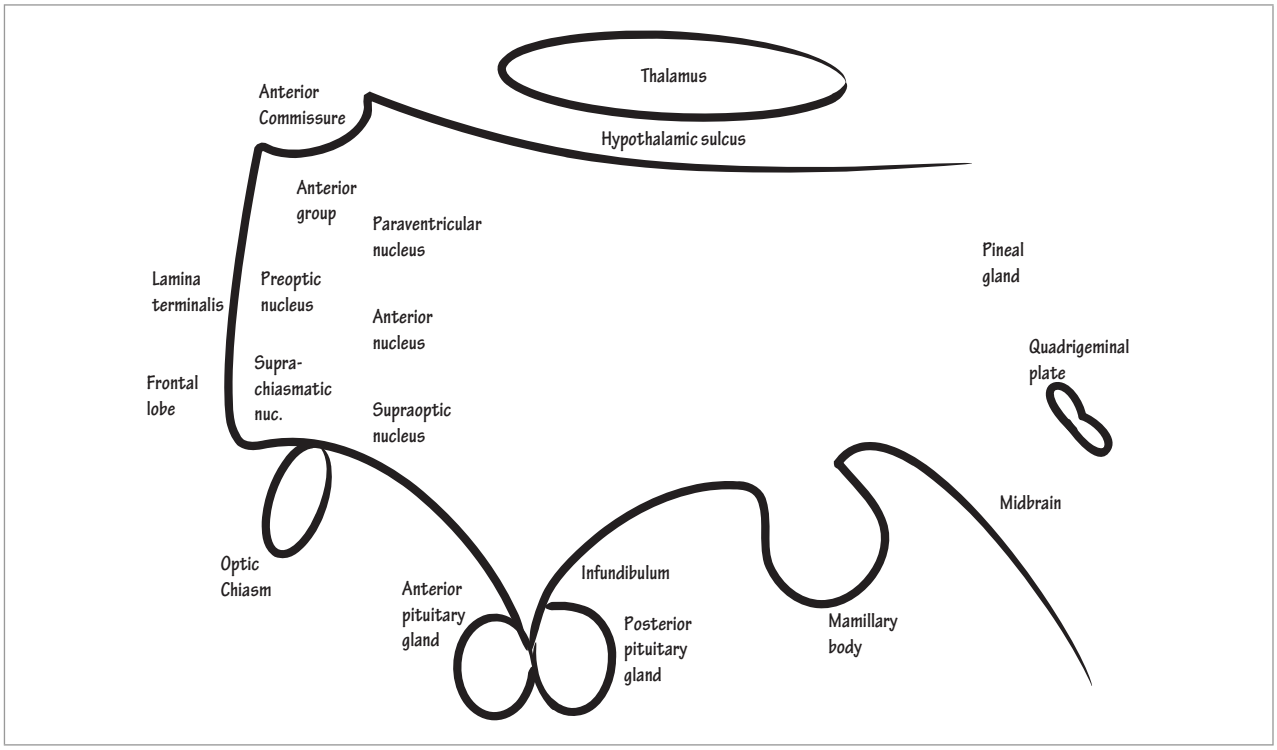

Figure 30-2 Incomplete hypothalamic nuclei

Next, we will draw the middle nuclear group (aka the tuberal region), which comprises both medial and lateral groups of its own. The medial group consists of the dorsomedial nucleus, ventromedial nucleus, and arcuate nucleus (aka infundibular nucleus). The lateral group comprises the tuberal nuclei and the lateral nucleus (aka tuberomammillary nucleus). All of the middle nuclear group nuclei are involved in energy homeostasis and contain varying degrees of leptin and other energy hormone receptors. Recently, leptin has been shown to be an important anorexigenic signal and there is much hope for its pharmacologic role in promoting weight loss.

Classically, there is a two-hypothalamic center model for food intake; the medial nuclei form the "satiety" center and the lateral hypothalamus makes up the "feeding" center. Unfortunately, however, the drive to eat is more complicated than this model predicts. But it does fit with our simple construct that rostromedial nuclei are involved in states of rest and caudolateral nuclei are involved in states of activity.

Now, indicate the *medial group* of *middle hypothalamic nuclei*. From superior to inferior, just behind the anterior nuclear group, label the *dorsomedial nucleus*, *ventromedial nucleus*, and *arcuate nucleus* (aka *infundibular nucleus*). The dorsomedial nucleus and the surrounding dorsal hypothalamus function in the physiologic response to psychological stress. The arcuate nucleus plays a role in hormonal output and has recently been described as the central integrator of metabolic stimuli in what is called the melanocortin pathway. The original name of the arcuate nucleus was the infundibular nucleus, which comes from its position in the infundibular region. Later, we will draw its connections to the anterior pituitary gland.

Next, draw the *lateral group* of *middle hypothalamic nuclei*. As mentioned earlier, the lateral zone of the hypothalamus predominantly comprises afferent and efferent fiber pathways, but it also contains two sets of hypothalamic nuclei: the tuberal nuclei and the lateral nucleus (aka tuberomammillary nucleus). We draw them here but they are actually lateral to the plane of this section. The tuber cinereum lies posterior to the infundibulum; it is the anatomical landmark from which the "tuberal nuclei" receive their name. The *lateral nucleus* is interspersed amongst the tuberal nuclei. Its original name, the tuberomammillary nucleus, refers to its position within the tuber cinereum, near the mammillary body. The lateral nucleus is involved in reward behavior and is clinically important in feeding and addiction. Notably, it is the only source of histamine production in the brain; histamine is a key wake-promoter, as discussed in the "Sleep Neurocircuitry" chapter.

Now, we will turn our attention to the *posterior group of nuclei* (aka the *mammillary region*). Label the *mammillary nuclei* within the mammillary bodies and the *posterior nucleus* above them. The mammillary nuclei are involved in memory consolidation in the Papez circuit. The posterior nuclei extend to the periaqueductal gray area, which surrounds the central aqueduct in the midbrain; and they form important connections with this diverse neurobehavioral center. There are other nuclei in this group, including the intermediate nucleus (aka intercalate nucleus) and the lateral mammillary nucleus, which lie lateral to the mammillary and posterior nuclei, but they are relatively minor, so we will leave them out of our drawing.

To review, aside from the lateral and tuberal nuclei, the hypothalamic nuclei lie medially within the hypothalamus. Broadly organized, the rostromedial nuclei act parasympathetically and the posterolateral nuclei act sympathetically. More specifically, the anterior group is involved in circadian rhythm maintenance, including stimulation of melatonin production and release from the pineal gland, and the release of oxytocin, anti-diuretic hormone, and gonadotropin-releasing hormone; the middle group is involved in energy homeostasis, including feeding and reward behavior, response to psychological stress, and wakefulness; and the posterior group is involved in short-term memory storage and behavioral functions in connection with the periaqueductal gray area.

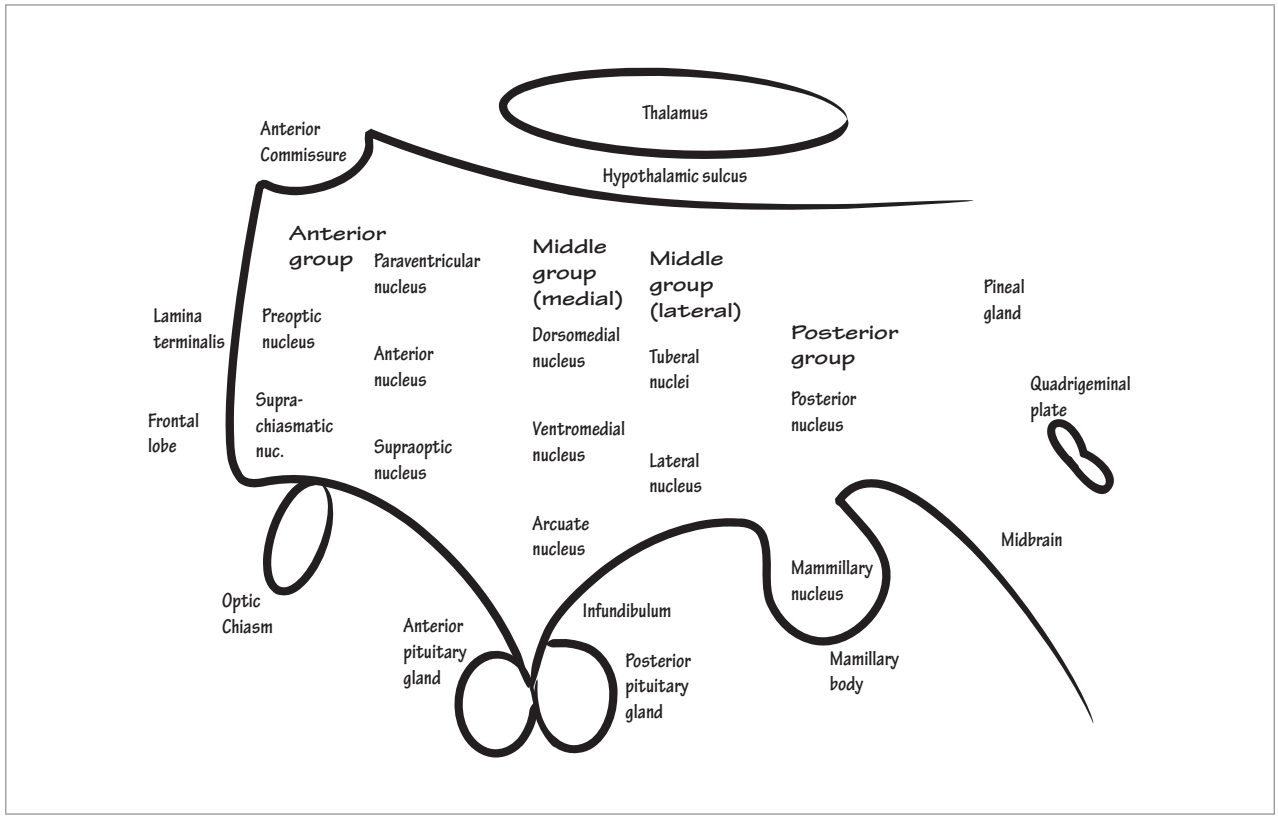

Figure 30-3 Complete hypothalamic nuclei

The connections between the hypothalamus and pituitary gland (aka hypophysis) are clinically important, so we pay particular attention to them. First, indicate the anterior hypothalamic nuclear group, specifically the *supraoptic* and *paraventricular nuclei*, communicates directly with the *posterior pituitary gland* through the *supraopticohypophysial tract*. These nuclei control the production of oxytocin and anti-diuretic hormone. The posterior pituitary gland releases these hormones into a *capillary plexus* and they enter the systemic circulation through hypophysial veins. The name of this tract is difficult to remember, but it is telling. The pathway originates in the supraoptic area of the hypothalamus above the optic tract and terminates in the posterior pituitary gland (aka neurohypophysis).

Next, illustrate the *tuberoinfundibular tract*, which originates in the middle hypothalamic nuclear group (aka the tuberal group) and in the anterior hypothalamic nuclear group in the zone immediately surrounding the third ventricle (aka the periventricular zone), and terminates in the infundibulum. Hormones from the infundibulum are sent to the anterior pituitary gland. Again, the tuberoinfundibular tract's name is challenging but revealing. It originates in the tuberal areas and does not pass directly into the anterior pituitary gland (aka adenohypophysis) but stops in the infundibulum. While the supraoptic and paraventricular nuclei send hormones directly to the posterior pituitary gland through the supraopticohypophysial tract, hypothalamic hormones that travel through the tuberoinfundibular tract reach the anterior pituitary gland secondarily via portal veins.

Show the tuberoinfundibular tract empties into a *primary capillary plexus* in the infundibulum that connects to a *secondary capillary plexus* in the anterior pituitary gland via *portal veins*. Hormones from the tuberal region are *releasing hormones* that regulate the ultimate release of the hormones of the anterior pituitary gland, which are corollaries of the hypothalamic-releasing hormones. The anterior pituitary gland hormones are thyrotropin hormone, growth hormone, the gonadotropins (follicle stimulating hormone [FSH] and leutinizing hormone [LH]), prolactin, and adrenocorticotropin. The acronym "FLAT PiG" will help you remember them; it stands for FSH, LH, Adrenocorticotropin, Thyrotropin, Prolactin, and Growth hormone.

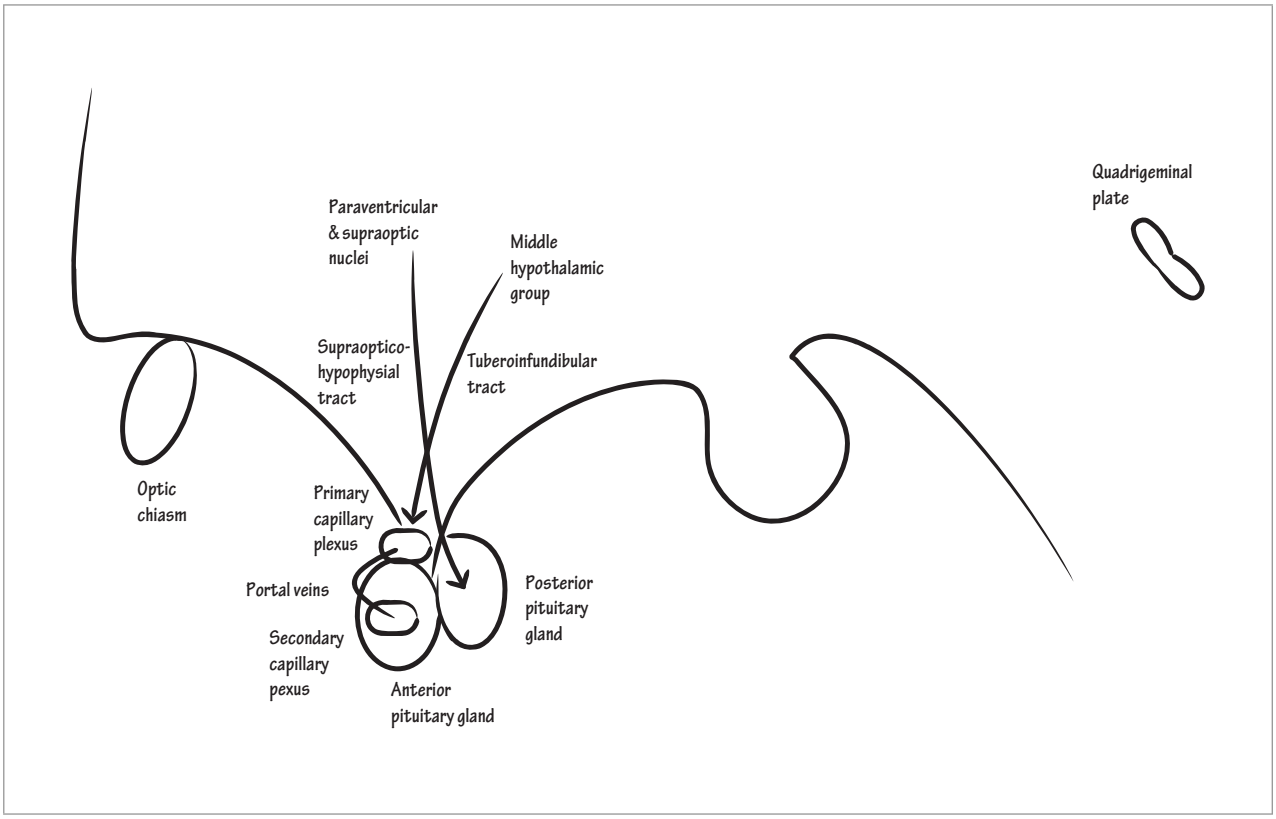

Figure 30-4 Relationship of the hypothalamus to the pituitary gland

Now, we will include the afferent and efferent fiber tracts of the lateral hypothalamus. Label the anatomical areas that communicate with hypothalamus. In front of the hypothalamus, label the *retina*, *basal olfactory system*, and *septal nuclei*; below and lateral to it, label the *amygdala* and the *hippocampal complex*; behind it, label the *reticular formation* and *periaqueductal gray area* of the brainstem; and above it, label the *midline thalamic nuclei* and the *anterior nucleus of the thalamus*. The structures that surround the hypothalamus gives us an appreciation of its function, that is, it receives sensory encoding of light and smell, is involved in memory and emotion, and plays a role in other neurobehavioral functions, as well. On the contrary, the hypothalamus is uninvolved in motor, somatosensory, or cerebellar activities, which are the predominate roles of the surrounding basal and thalamic nuclei.

Draw fibers from the *optic chiasm* to the *suprachiasmatic nucleus*: the terminal portion of the *retinohypothalamic pathway*. The optic nerves pass visual information from both retinae to the optic chiasm. Remember, the suprachiasmatic nucleus is part of the anterior group of hypothalamic nuclei and is involved in the maintenance of circadian rhythms.

Next, draw the *medial forebrain bundle*, which originates in the *basal olfactory system* and *septal nuclei*. Indicate it passes through the hypothalamus and synapses in the *reticular formation* of the brainstem. The medial forebrain bundle diffusely communicates autonomic visceral information to the hypothalamus. In contradistinction, the lateral forebrain bundle, which passes lateral to the hypothalamus (and does not interact with it), communicates planned motor movements to the internal capsule and basal nuclei. The medial forebrain bundle contains unmyelinated fibers and the lateral forebrain bundle contains myelinated fibers, which is a structural distinction that helps reinforce their functional difference; the medial forebrain bundle is involved in slowly changing behaviors and the lateral forebrain bundle is involved in fast-changing activities.

Draw the *fornix*, which originates in the *hippocampal complex*, and show it pass across the pineal body, over the top of the thalamus, and split at the anterior commissure into both *pre-* and *postcommissural bundles*. Indicate the precommissural fibers pass in front of the *septal nuclei* and show the postcommissural fibers descend through hypothalamus to the *mammillary nuclei*. Remember, the mammillary nuclei are part of the posterior group of hypothalamic nuclei and are involved in memory processing. The pathway of the fornix together with the postcommissural bundle forms the first step in the Papez ciruit. The second step in the Papez circuit involves the *mammillothalamic tract* (aka *mammillothalamic tract of Vicq d'Azyr*), which you should draw, now, as an efferent pathway from the *mammillary nuclei* to the *anterior nucleus of the thalamus*.

To complete the efferent hypothalamic projection fibers from the mammillary body, indicate the *mammillary nuclei* also project to the *brainstem tegmentum* through the *mammillotegmental tract*.

Now, draw the *stria terminalis*, which predominantly travels back and forth between the amygdala and the nucleus of the stria terminalis, but also passes through the hypothalamus. Afferent fibers to the hypothalamus originate in the *amygdala* and follow a similar course as the fornix; they travel up along the dorsal surface of the thalamus and send fibers to the *anterior hypothalamic nuclear group*, specifically the paraventricular nucleus (which stimulates melatonin production and excretion from the pineal body and produces anti-diuretic hormone) and the *middle hypothalamic nuclear group* (which is involved in energy homeostasis, reward behavior, wakefulness, and the physiological response to psyschological stress). We will draw and discuss the amygdala, which is an important behavioral center, in the "Limbic System" chapter.

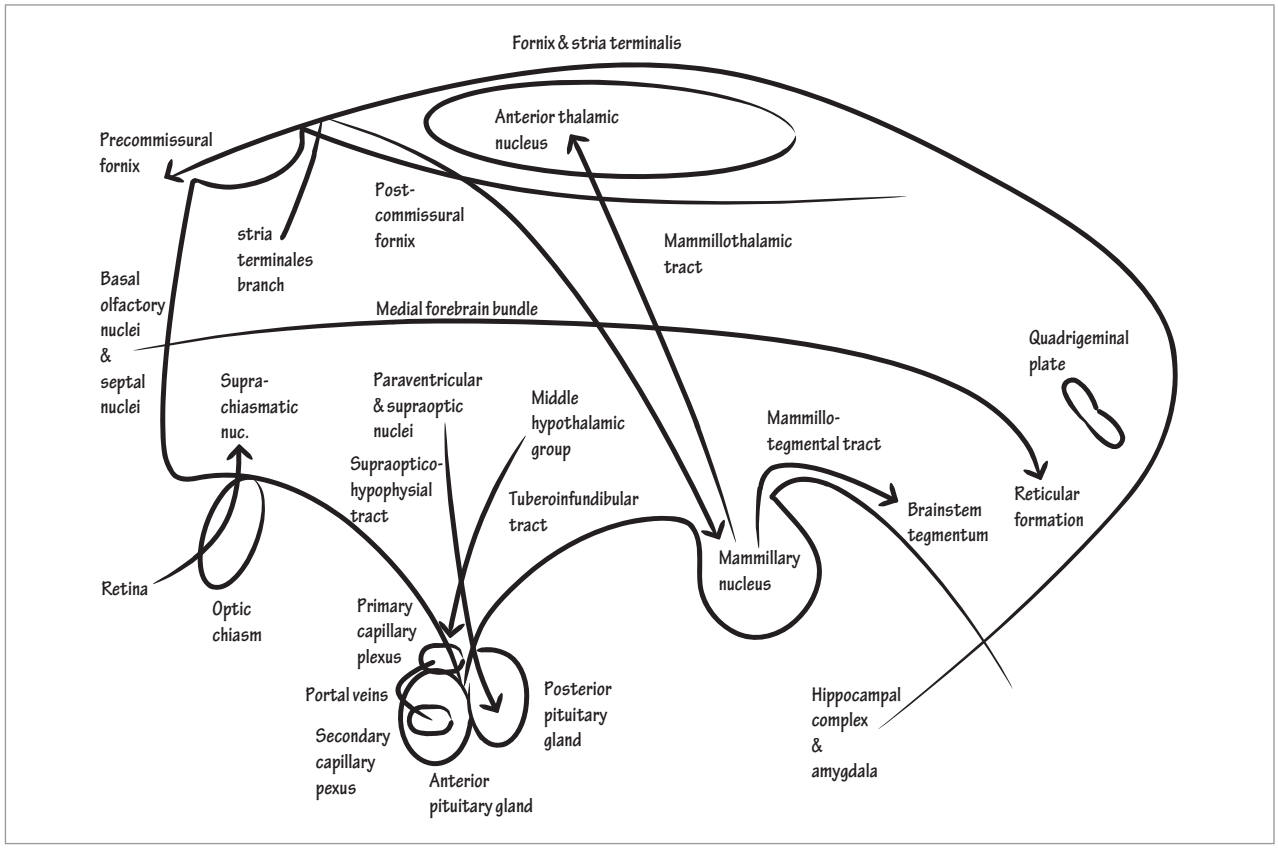

Figure 30-5 Complete hypothalamic fibers

The hypothalamospinal, hypothalamomedullary, and posterior longitudinal fasciculus (aka dorsal longitudinal fasciculus or dorsal longitudinal fasciculus of Schütz) are important descending pathways. The hypothalamospinal tract carries sympathetic fibers ipsilaterally from the hypothalamus to the intermediolateral cell column of the spinal cord to provide sympathetic stimulation to the face. When these fibers are interrupted, loss of sympathetic innervation occurs, resulting in Horner's syndrome, which consists of miosis, ptosis, facial flushing, anhidrosis, and enophthalmosis; we discussed it in the "Peripheral Autonomic Nervous System" chapter.

The hypothalamomedullary tract passes from the hypothalamus to the medulla and terminates in several cranial nerve nuclei. The solitary nucleus and the dorsal nucleus of the vagus nucleus are important autonomic nervous system sensory and motor cranial nerve nuclei, and through the hypothalamomedullary tract, the hypothalamus influences both of them.

The posterior longitudinal fasciculus passes from the nuclei of the hypothalamus to the periaqueductal gray area where it influences pain response and modulates other neurobehaviors.

We will now list several other pathways to and from the hypothalamus—skip to the next chapter, if you are uninterested in them. They are listed here for reference, only. The ventral amygdalofugal and hypothalamoamygdaloid pathways send fibers between the amygdala and the lateral hypothalamus, septal nuclei, and preoptic area; these fibers pass beneath the lentiform nucleus (i.e., the globus pallidus and putamen combination). The thalamohypothalamic and hypothalamothalamic pathways send fibers between the dorsomedial thalamus and the lateral hypothalamic and lateral preoptic nuclei. The corticohypothalamic pathway projects from the prefrontal cortex to the lateral hypothalamus.

Limbic System

THE LIMBIC SYSTEM is fascinating but, unfortunately, inconsistencies in its nomenclature make it a frustrating subject to learn. Even the term the "limbic system" has many different accepted definitions. Paul MacLean coined it in the mid-twentieth century to group the limbic lobe with functionally-related areas of the brain but many different iterations of the term have since evolved. In this chapter, we will address the constituents of the limbic lobe and then use the Papez circuit to introduce the functionally-related areas of the limbic system.

The limbic lobe, as defined by Paul Broca in 1878, comprises the medial, central-lying area of the brain that surrounds the diencephalon (the thalamic area). The limbic lobe comprises the subcallosal gyrus, cingulate gyrus, parahippocampal gyrus, and the hippocampal formation. It was originally called the "rhinencephalon" because of its connection to the olfactory system; the role of the olfactory system in human behavior was overemphasized at the time and was appropriately deemphasized by James Papez in 1937 at the same time he introduced the Papez circuit.

In its original description, the Papez circuit was proposed to transfer emotive sensory information from the hippocampus to the cingulate gyrus and from there to other areas of the neocortex; at that time, the hippocampus was believed to be crucial to the origination of emotion. We now, however, assign that role to its rostral-lying neighbor, the amygdala, and we ascribe the role of declarative memory to the hippocampus. Although originally Papez was mistaken about the function of his circuit, the pathway still became fundamental to our understanding of memory, and it brought attention to such structures as the mammillary bodies and the anterior thalamus.

MacLean included the Papez circuit structures in his 1952 definition of the limbic system and since that time the number of recognized limbic system structures has steadily grown. Many authors now include the following as parts of the limbic system: basal forebrain areas such as the septal and preoptic areas; diencephalic areas such as the hypothalamus, habenula, and midline thalamus; and brainstem areas such as the paramedian mesencephalon (aka midbrain). In this chapter, we will divide the limbic system into primary limbic areas and secondary areas of involvement; we will draw the primary areas and simply discuss the secondary areas as they are all explored in other chapters of the book.

The primary limbic areas can be divided into gray and white matter regions. Historically, Broca defined the primary limbic gray matter areas as the cingulate, parahippocampal, and subcallosal gyri, and the hippocampal formation. It comprises two main gyral loops that encircle the diencephalon: the limbic and intralimbic gyri. Essentially, the limbic gyrus is the outer loop, which encompasses the cingulate and parahippocampal gyri and connecting areas and the intralimbic gyrus is the inner loop, which comprises the hippocampus and related areas.

More specifically, the limbic gyrus contains the cingulate gyrus and its isthmus, the parahippocampal gyrus, and the subcallosal gyrus. And the intralimbic gyrus comprises the paraterminal gyrus,

hippocampus, and indusium griseum. Other primary limbic gray matter areas are the anterior perforated substance and gyrus fasciolaris. The primary white matter tracts in the limbic system are the cingulum, amygdalofugal tract, stria terminales, stria medullaris, longitudinal stria, and fornix.

Toward the end of the chapter, we will draw the detailed anatomy of the hippocampus and we will address the amygdala, which lies in front of it. To find the amygdala on a radiographic image, look for the anterior hippocampus in the antero-medial portion of the temporal horn of the lateral ventricle. When you find it, look rostrally (at images more anterior) to see the amygdala (MRI images are included, here, to show these structures).

Bilateral amygdala destruction results in the clinically important Klüver Bucy syndrome. This devastating syndrome involves psychic blindness, loss of avoidance—manifesting with hypermetamorphosis (the incessant exploration of objects within the environment), and hypersexuality. The Klüver Bucy syndrome was first described from the results of bilateral removal of the amydgaloid bodies in monkeys, but a variety of diseases naturally cause this syndrome in humans: herpes simplex encephalitis, the neurodegenerative fronto-temporal dementia named Pick's disease, and anoxic-ischemic lesions in the anterior medial temporal lobes. Also, in the past, surgeons performed bilateral temporal lobectomies to treat intractable seizures emanating from the temporal lobes; unfortunately, the results of these surgeries were sometimes dreadful. Currently, these surgeries are limited to unilateral, sometimes restricted, temporal lobe resections to avoid causing Klüver Bucy syndrome and other neurologic problems. As well, before surgery, the patients' behavioral functions are mapped using a variety of methods to limit untoward effects.

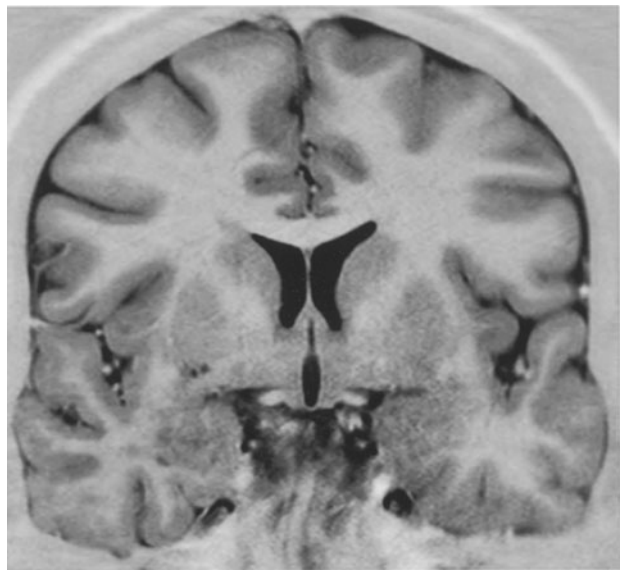

Photo 31-1 Coronal radiographic section through the amygdala

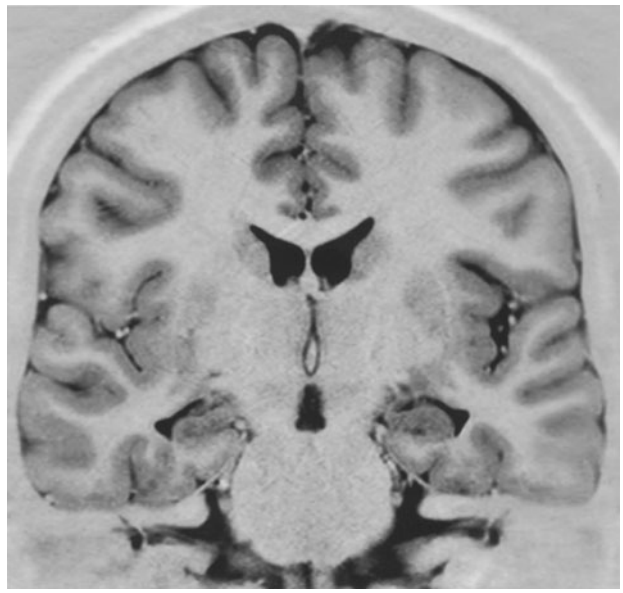

Photo 31-2 Coronal radiographic section through the hippocampus

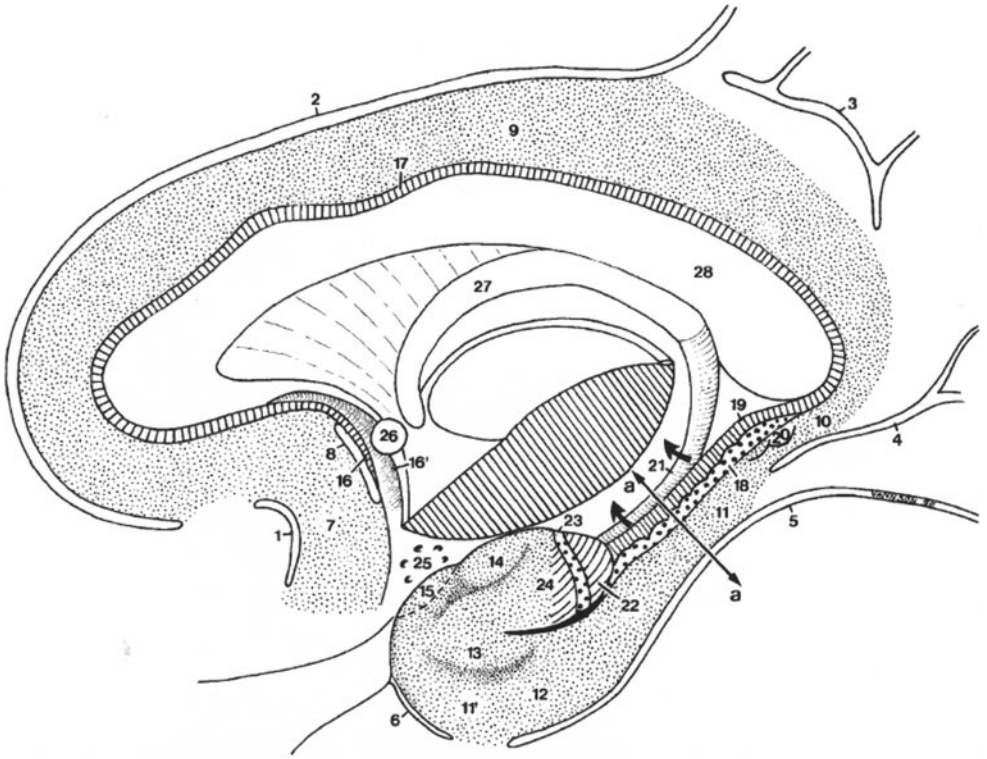

Photo 31-3 Illustration of the limbic system. 1 – anterior paraolfactory sulcus, 2 – cingulate sulcus, 3 – subparietal sulcus, 4 – anterior calcarine sulcus, 5 – collateral sulcus, 6 – rhinal sulcus. Limbic gyrus: 7, subcallosal gyrus, 8 – posterior paraolfactory sulcus, 9 – cingulate gyrus, 10 – isthmus, 11 – parahippocampal gyrus. 12 – entorhinal area, 13 – ambient gyrus, 14 – semilunar gyrus, 15 – prepiriform cortex. Intralimbic gyrus: 16 – prehippocampal rudiment and paraterminal gyrus, 17- indusium griseum. Hippocampus: 18 – gyrus dentatus, 19 – cornu Ammonis, 20 – gyri of Andreas Retzius, 21 – fimbria, 22 – uncal apex, 23 – band of Giacomini, 24 – uncinate gyrus, 25 – anterior perforated substance, 26 – anterior commissure, 27 – fornix, 28 – corpus callosum

With permission from Duvernoy, H. M. *The Human Hippocampus: Functional Anatomy, Vascularization and Serial Sections with Mri.* 3rd ed. Berlin and New York: Springer, 2005.

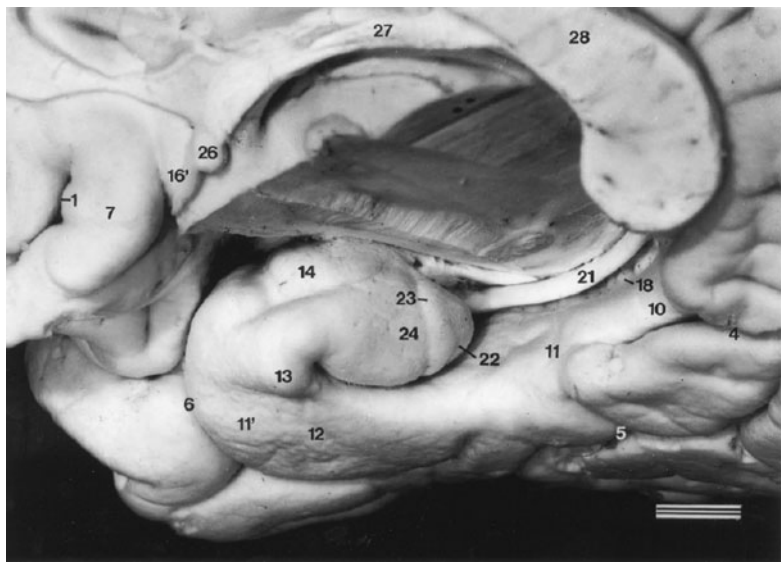

Photo 31-4 Anatomical correlate of Photo 31-3

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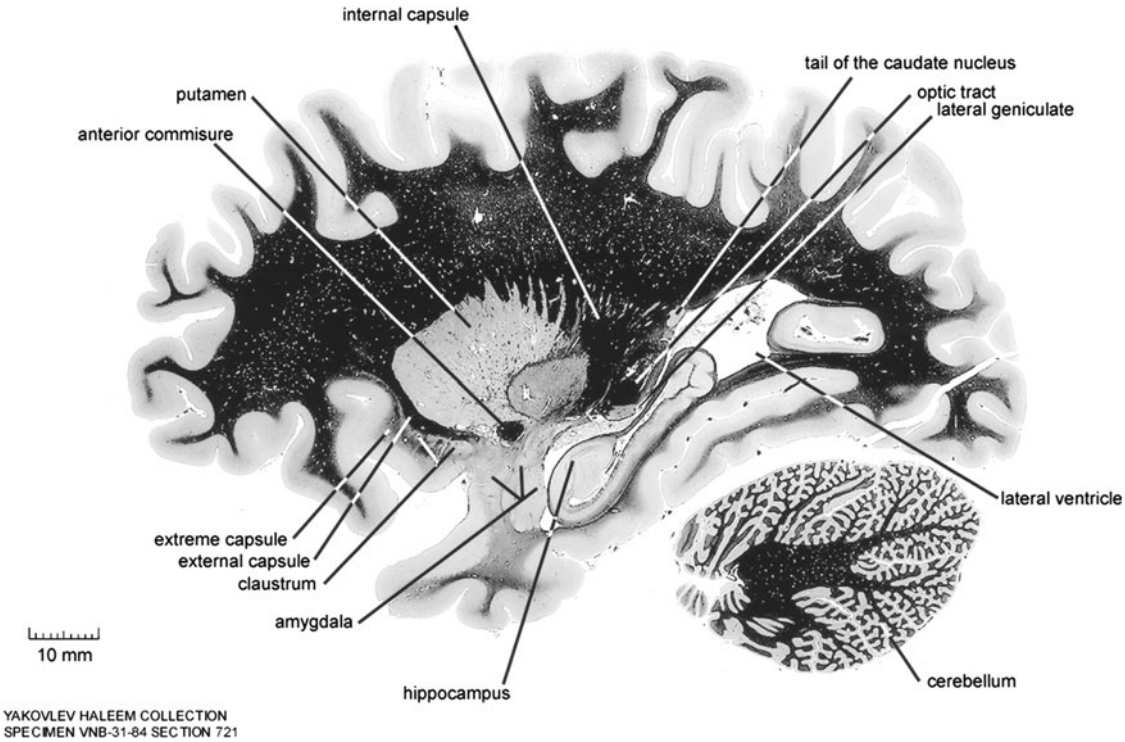

Photo 31-5 Oblique anatomical section through the brain to highlight the length of the hippocampus
With permission from the Michigan State University: Brain Biodiversity Bank. https://www.msu.edu/~brains/

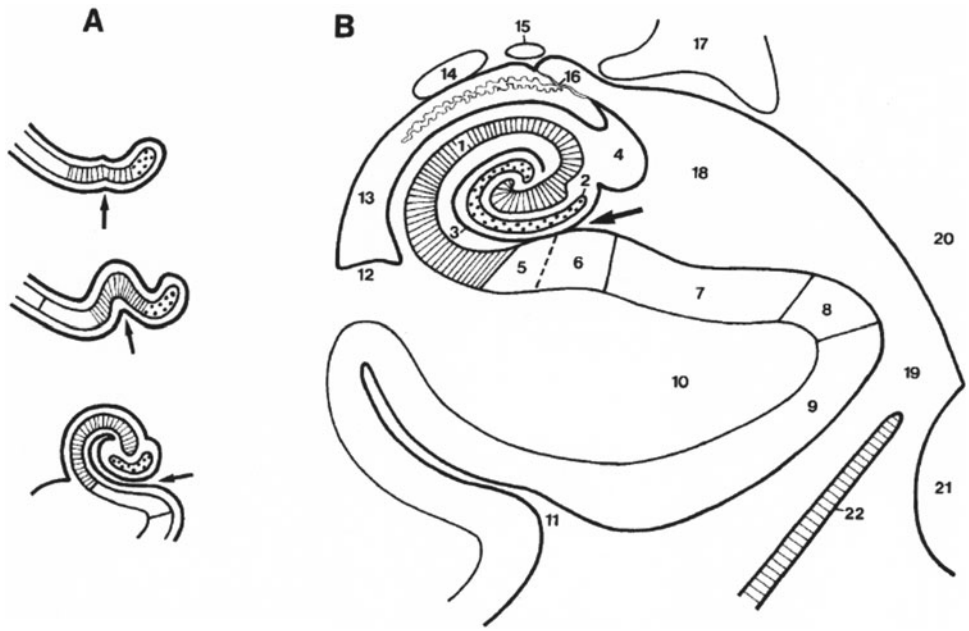

Photo 31-6 Coronal illustration of hippocampus. 1 – cornu Ammonis, 2 – gyrus dentatus, 3 – hippocampal sulcus, 4 – fimbria, 5 to 8 – subiculum, 9 – entorhinal area, 10 – parahippocampal gyrus, 11 – collateral sulcus, 12 – collateral eminence, 13 – temporal horn lateral ventricle, 14 – tail of caudate, 15 – stria terminalis, 16 – choroid fissure and choroid plexus, 17 – lateral geniculate body, 18 and 19 – ambient cistern, 20 midbrain, 21 – pons, 22 – tentorium cerebelli
With permission from Duvernoy, H. M. *The Human Hippocampus: Functional Anatomy, Vascularization and Serial Sections with Mri.* 3rd ed. Berlin and New York: Springer, 2005.

Now, let's draw the primary limbic areas. We begin with a drawing of the limbic gyrus. Draw the central portion of a medial face of a cerebral hemisphere. Include the corpus callosum and key portions of the diencephalon. Remember, the limbic gyrus comprises the cingulate gyrus and its isthmus and the parahippocampal and subcallosal gyri. First, draw the *cingulate gyrus* above and in parallel to the superior–anterior corpus callosum. The cingulate gyrus comprises the bulk of the fronto-parietal portion of the limbic gyrus. Indicate it is bounded dorsally by the *cingulate sulcus* and ventrally by the *callosal sulcus*. The cingulate gyrus is functionally divided into anterior and posterior regions. Label the anterior region as being involved in *emotion/behavior* and the posterior region in *learning/memory*.

Interestingly, this functional–anatomical relationship is analogous to that of the amygdala and hippocampus. The amygdala sits anterior to the hippocampus and is involved in emotional behavior, whereas the hippocampus sits just behind it and is involved in declarative memory. As well, recall the arrangement of the hypothalamus, which is a secondary limbic area (through its connections to the cingulate gyrus, amygdala, and hippocampus)—the anterior hypothalamic nuclei are involved in behavior whereas the posterior nuclei, specifically the mammillary nuclei, are involved in memory.

Clinically, midline frontal lesions in the region of the anterior cingulate gyrus cause abulia (a lack of motivation). Patients with a lesion to the anterior cingulate gyrus present with a paucity of speech, called akinetic mutism. It is often mistaken for a primary language disturbance but these patients' language, itself, is intact; they simply lack the drive to speak.

Next, let's address the major temporal lobe component of the limbic gyrus. Draw the *parahippocampal gyrus*, which lies in parallel to the inferior border of the temporal lobe. The parahippocampal gyrus lies superficial to the amygdala and hippocampus, which gives it its name—"para-hippocampal" gyrus. On the superior–anterior aspect of the parahippocampal gyrus, draw the thumb-like gyral tissue fold—the *uncus*. It is a medial temporal gyral bulge that folds back along the superior edge of the parahippocampal gyrus. The uncus is often the first part of the brain to herniate over the tentorium cerebelli when brain swelling occurs. This form of herniation is called "uncal herniation" and we will describe it further later in the chapter.

To complete the gray matter of the limbic gyrus, first label the posterior region between the parahippocampal and cingulate gyri as the *isthmus of the cingulate gyrus*. Then, label the *subcallosal gyrus* underneath the rostrum of the corpus callosum in a region called the septal area. We will draw the detailed anatomy of the septal area at the end of the chapter.

Next, we will add the intralimbic gyrus, which as its name suggests, runs internal to the limbic gyrus. Draw the *hippocampus* internal to the parahippocampal gyrus. It stretches from the posterior tip of the uncus to the inferior tail of the corpus callosum. During embryogenesis, the hippocampus originates at the rostrum of the corpus callosum; during development, it follows the lateral ventricles in a backward, downward, forward involution to reach its target destination—the same migration the ventricular system makes.

Next, label the *indusium griseum* along the corpus callosum. The indusium griseum is a prehippocampal rudiment, flanked by white matter longitudinal striae. These gray and white matter structures mark the trail of the involution of the hippocampus. Finally, label the poorly formed *paraterminal gyrus* within the septal area.

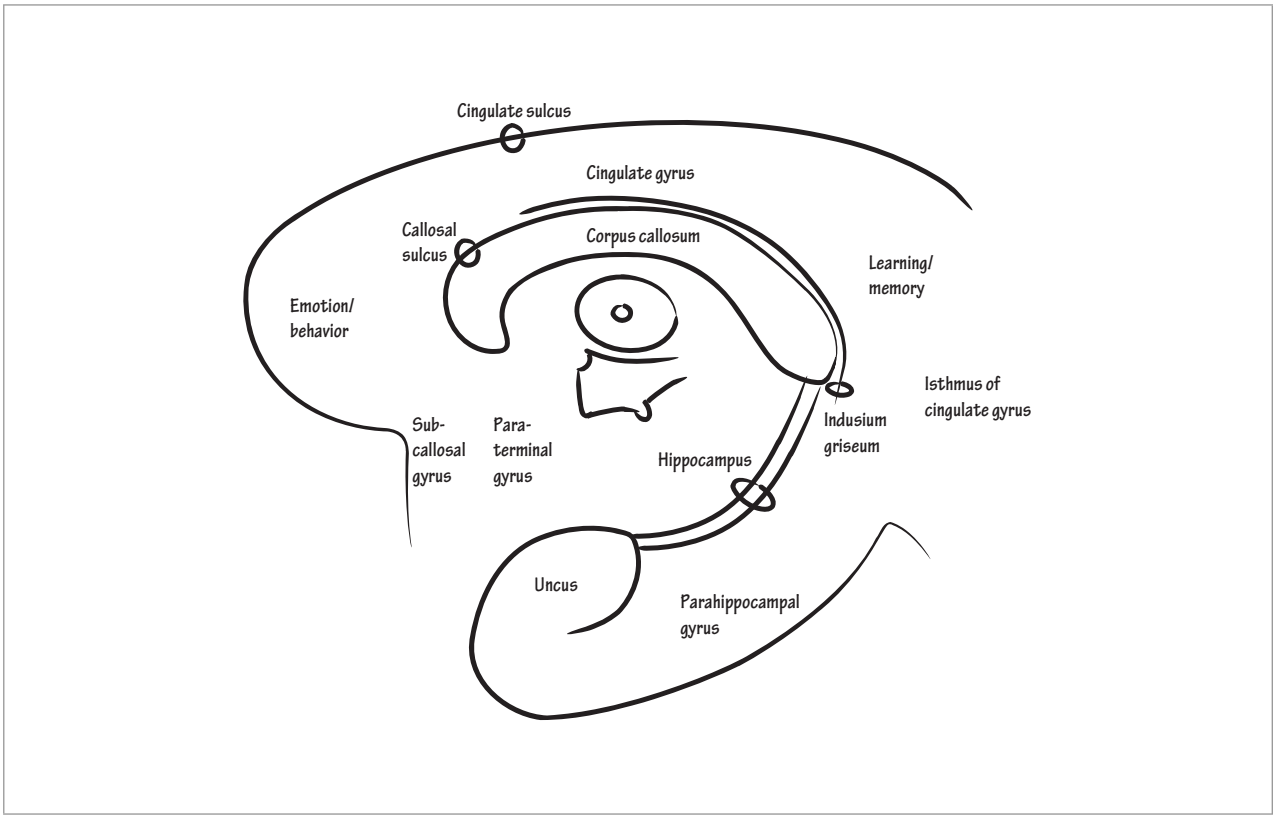

Figure 31-1 Limbic and intralimbic gyri

We draw the olfactory system in detail in its own chapter but let's show the limbic-related portion of the olfactory system, here, since historically, at least, the olfactory area was an important part of the limbic lobe. Pay special attention to the amygdala portion of this section.

On the ventral surface of the frontal lobe, draw the round *olfactory bulb* and its tail, the *olfactory tract*. Olfactory sensory information travels underneath the posterior frontal lobe along the olfactory tract. Although it is tempting to think of the olfactory bulb, tract, and striae as parts of the olfactory nerve, only the short filaments that line the nasal cavity constitute the olfactory nerve. These filaments communicate with olfactory bulb through the cribiform plate.

Now, label the gap between the posterior-inferior frontal lobe and anterior-superior temporal lobe as the *anterior perforated substance*, although it is not a direct part of the olfactory system. Internal to the anterior perforated substance (i.e., just above it [out of the plane of this diagram]) lies the substantia innominata, which houses the basal nucleus of Meynert. This nucleus has cholinergic connections with the hippocampus and the cortex and is important in memory. The lenticulostriate vessels that arise off of the proximal branch of the middle cerebral artery (aka the M1 branch) perforate the anterior perforated substance.

Now, indicate the olfactory tract splits into *medial* and *lateral olfactory striae* at the anterior edge of the anterior perforated substance. Draw the medial olfactory stria passing through the septal area. In the "Olfactory System" chapter, we will show that medial stria fibers also cross to the contralateral side and communicate with the contralateral olfactory bulb. Next, indicate the *lateral olfactory stria* travel from the olfactory tract to the primary olfactory areas in the anterior temporal lobe: the amygdala, periamygdaloid complex, and the piriform cortex. Other primary olfactory areas are the anterior olfactory nucleus and olfactory tubercle. Of all of these structures, the amygdala has the most prominent role in the limbic system.

Label the almond-shaped *amygdala* (aka *amygdaloid body*) in the postero-lateral portion of the uncus—the supero-medial thumb-shaped fold of the parahippocampal gyrus. The amygdala is divided into three groups: corticomedial, central, and basolateral. The corticomedial group is connected to the olfactory system through the lateral olfactory stria. The central group connects with the hypothalamus and, as you might imagine, is involved in autonomic function, and the basolateral group connects with the hippocampus and provides an emotional attachment to memory.

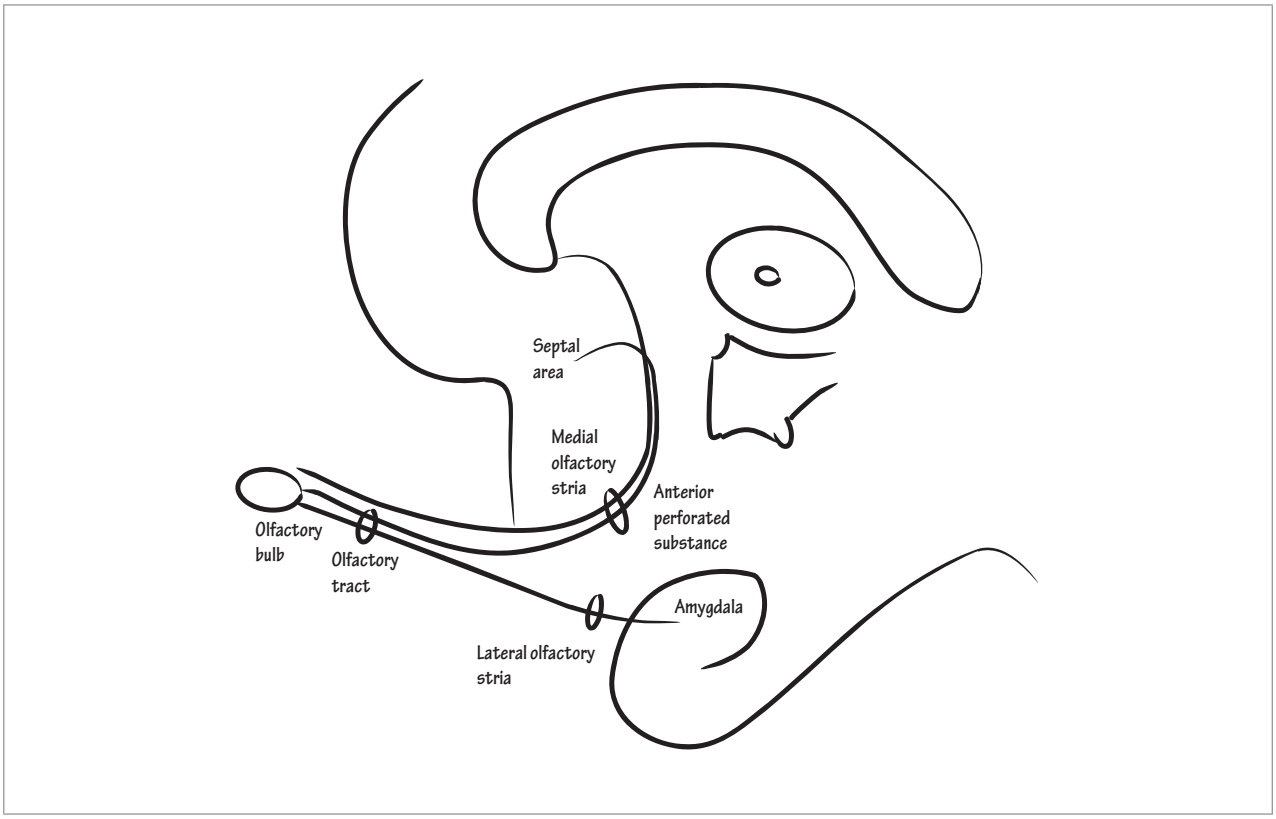

Figure 31-2 Limbic-related olfactory structures

Now, we will draw the main white matter pathways of the limbic system: the cingulum, fornix, stria terminalis, amygdalofugal pathway, and the stria medullaris thalami. We will begin with the C-shaped fornix and stria terminalis, which are the large white matter pathways of the hippocampus and amygdala, respectively. The fornix originates in the hippocampus and the stria terminalis originates in the amygdala. Both follow the parahippocampal gyrus postero-superiorly, bend anteriorly underneath the corpus callosum, and descend to their target areas.

The fornix divides at the anterior commissure into pre- and postcommissural fibers. The precommissural fibers, along with the majority of stria terminalis fibers, communicate with the septal area. Within the septal area, the stria terminalis fibers synapse in the bed nucleus of the stria terminalis. The postcommissural fibers of the fornix descend through the hypothalamus and communicate with the mammillary nuclei as part of the Papez ciruit. With this discussion as a background, let's now draw the major fiber tracts of the limbic system.

First, draw the highly important white matter tract the *cingulum*; it passes through the limbic gyrus and connects the cingulate and parahippocampal gyri.

Now, indicate the *fornix* originates from *alvei* along the bilateral *hippocampi*. On each side of the brain, alveus fibers combine to form flat *fimbria*, which then form the bilateral crus of the fornix. The bilateral crus join as the singular body of the fornix. To recap, alvei lead to fimbrae, fimbrae to the bilateral crus fornices, which become the singular fornix.

Next, show the fornix bends underneath the corpus callosum in a tight radius. The termination of the fornix is tricky to imagine: the pre-commissural fornix pathway terminates bilaterally, lateral to the bed nucleus of the stria terminalis (lateral to the plane of this diagram), and the post-commissural pathway descends through the hypothalamus to the mammillary bodies.

Next, draw the *stria terminalis*; it originates in the amygdala, follows the fornix under the corpus callosum, and communicates with the *bed nucleus of the stria terminalis* in the superior septal area. Other stria terminalis fibers communicate with the hypothalamus, specifically the paraventricular nucleus of the anterior group of nuclei, which produces anti-diuretic hormone (aka vasporessin), and the middle group of hypothalamic nuclei, which produce hormones involved in the physiologic response to psychologic stress.

The ventral-lying *amygdalofugal pathway* is the ventral corollary to the stria terminalis. Show that it connects the amygdala to the septal area, specifically the substantia innominata (aka innominate substance). This connection involves the medial septal pathway—the diagonal band of Broca, which is a cholinergic pathway important in memory.

The last important limbic system pathway to draw is the stria medullaris (aka stria medullaris thalami or stria thalami). The stria medullaris is a midline limbic system pathway that connects the basofrontal septal area to the diencephalic eptihalamus. The epithalamus consists of the habenula and the pineal gland. Draw the *habenula* on the posterosuperior portion of the thalamus and show the *stria medullaris* runs from the septal area to it. Of note, the habenula projects to the mesencephalic reticular formation through the habenulointerpeduncular tract; it is for this reason that certain authors consider the midbrain as a secondary limbic area.

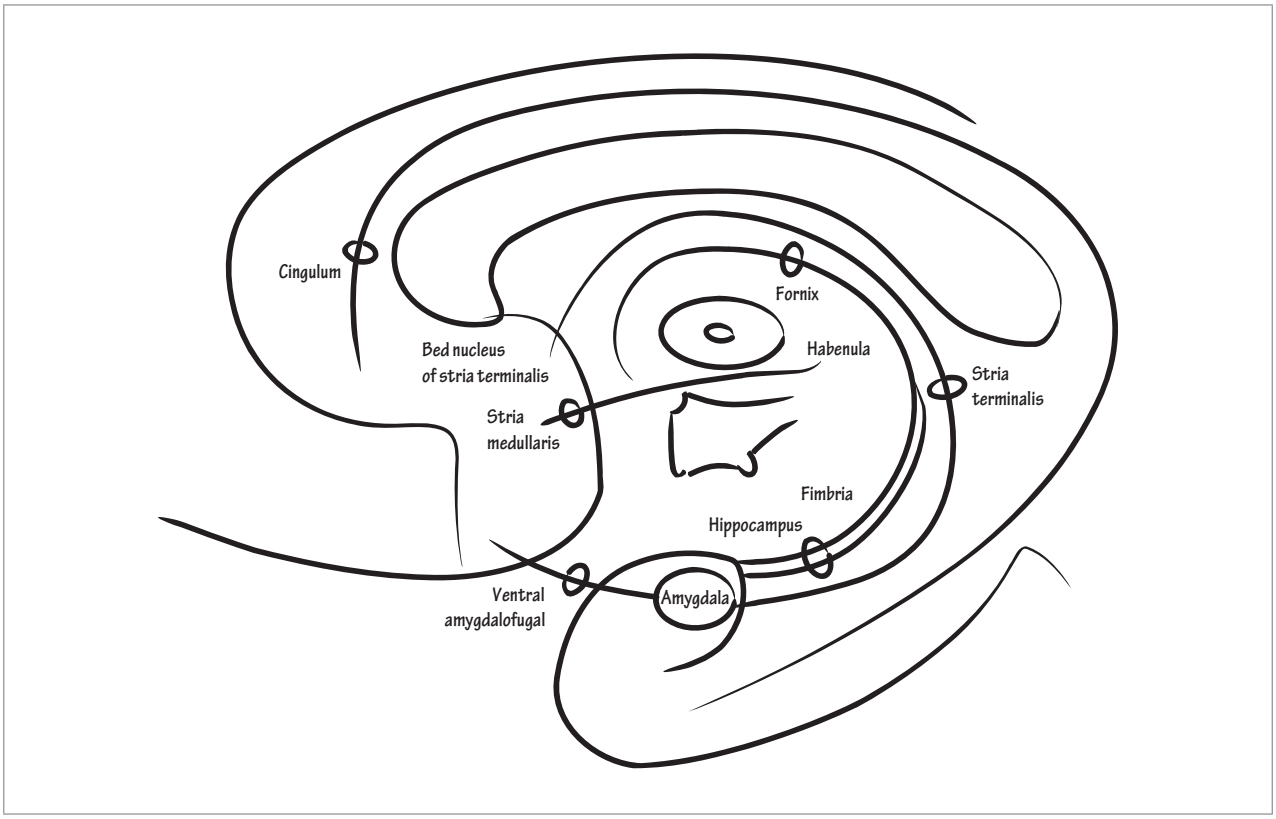

Figure 31-3 Limbic system pathways

We have now drawn the primary gray and white matter areas of the limbic system and have discussed certain secondary areas, as well. We have three drawings left to complete our understanding of the limbic system. In the first, we will draw a coronal section through the hippocampal formation and parahippocampal area, then we will draw the complete connections of the Papez circuit, and lastly we will draw the detailed anatomy of the basofrontal area.

Before we draw the hippocampus, it is important to know that most often when people refer to the hippocampus, they mean the hippocampal formation, which includes the hippocampus proper, subiculum, and dentate gyrus (which is different from the dentate nucleus of the cerebellum). The anterior hippocampus lies in the inferomedial portion of the temporal horn of the lateral ventricle. What lies in front of it? The amygdala. Hippocampal anatomy is confusing but important so let's draw it in a few small steps and let's include a few related landmarks for orientational purposes. To orient ourselves to the coronal plane of the hippocampus, in the corner of the page, draw a coronal section through the brain in the plane of the anterior temporal horn of the lateral ventricle.

In coronal perspective, draw the lateral border of the brainstem along with the temporal horn of the lateral ventricle. Indicate the thin line of *choroid plexus* that separates the ventricle from the medially adjacent cerebrospinal fluid cistern—the *ambient cistern*, which flanks the midbrain. At the end of this chapter, we discuss why during uncal hernation, the medial temporal lobe first herniates into the ambient cistern.

Now, let's draw the hippocampal formation, entorhinal cortex, and the parahippocampal gyrus in multiple steps. First, draw a double-sided "S"-shape formation underneath the lateral ventricle within the temporal lobe. Next, divide the "S"-shape into its superior turn, horizontal stretch, and inferior turn. Note that the inner fold of the superior turn is contiguous with the outer fold of the inferior turn and vice-versa. Label the superior turn as the *cornu ammonis*; it resembles a ram's horn and was dubbed "cornu ammonis" after the Egyptian god Amon who bore a ram's head. The cornu ammonis is sectioned into four regions: CA4 to CA1 (cornu ammonis section 4 to section 1), each with varying histologies. Also, the *dentate gyrus* is present in this region; draw it as a double-sided "C"-shape that cups the terminal portion of the superior turn of the hippocampus. Then, label this terminal portion as *CA4*. Its position inside the concavity of the dentate gyrus is its distinguishing anatomical feature. Next, label *CA3* along the rise of the superior turn and *CA2* along its descent. CA4 to CA2 encompass large, ovoid neurons; the relative density of their somata increases as you go from CA4 to CA2. The last region is *CA1* (aka the Sommer sector). Label it along the inferior portion of the superior turn. Unlike the other regions, it is composed of triangular-shaped neurons and is particularly susceptible to anoxia. Hypoxic-ischemic disease often causes isolated neuronal dropout in CA1, and selective injury to CA1 serves as an important pathological marker of anoxic injury.

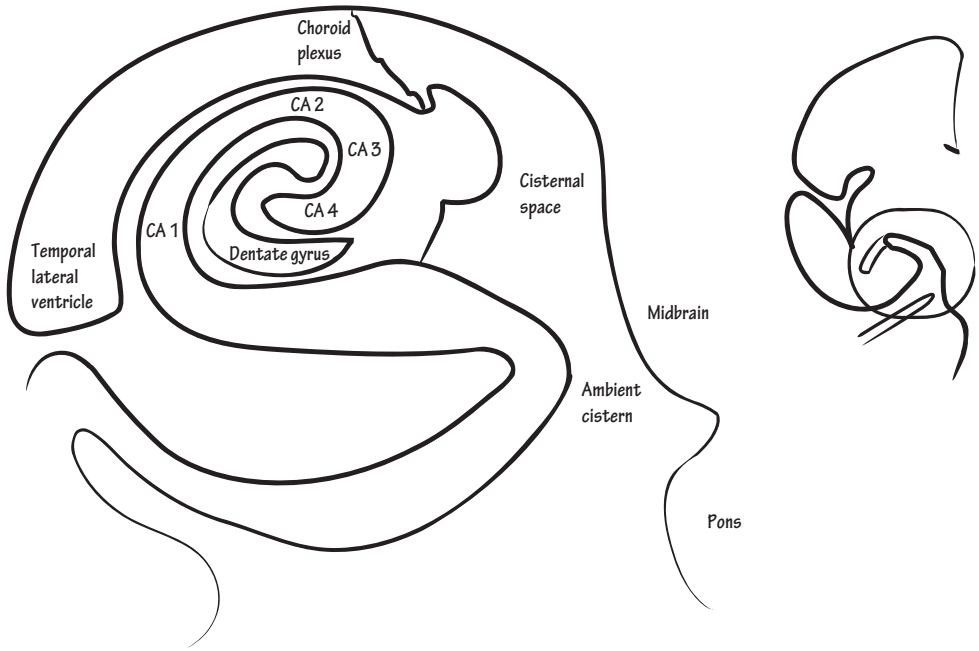

Figure 31-4 Incomplete hippocampus. Adapted from Duvernoy, H.M. *The Human Hippocampus: Functional Anatomy, Vascularization, and Serial Sections with Mri.* 3rd ed. Berlin and New York: Springer, 2005

Now, label the horizontal stretch of the S-shape as the *subiculum* and the entire inferior turn as the *entorhinal cortex*. Inside the inferior turn, label the *parahippocampal gyrus* of the temporal lobe. Then, draw the *occipitotemporal gyrus* and label the sulcus between the parahippocampal and occipitotemporal gyri as the *collateral sulcus*.

Finally, draw a hump-shaped connection between the medial tip of the lateral ventricle and the subiculum. The hump represents the *fimbria* of the fornix.

Now that we've had a close look at the medial temporal region, let's take this opportunity to discuss uncal herniation. Draw the *tentorium cerebelli* underneath the temporal lobe. The most medial-lying portion of the temporal lobe is the uncus of the parahippocampal gyrus. As a point of orientation, the uncus lies anterior to the plane of the hippocampus so it is out of the plane of this diagram. We know this is so because earlier we drew the almond-shaped amygdala deep within the *posterior* portion of the uncus. Since the amygdala lies anterior to the hippocampus, the uncus must also be anterior to the plane of the diagram.

The most medial portion of the uncus is called the ambient gyrus and it effaces the ambient cistern, which it first enters during uncal herniation. What are two helpful clinical signs of uncal cerebral herniation? First, on the side of the brain that herniates, the pupil dilates because the uncus compresses the third nerve as it exits the midbrain. Second, there is a "false localizing sign" that occurs when the uncus herniates against the midbrain cerebral peduncle. This pressure forces the contralateral cerebral peduncle against the opposite tentorium and forms a groove in the peduncle known as Kernohan's notch, named after Kernohan and Woltman who published their findings on this phenomenon in 1929. Because the cerebral peduncle compression occurs on the contralateral side, limb weakness results on the same side as the herniating brain. Thus, this is considered a *false* localizing sign.

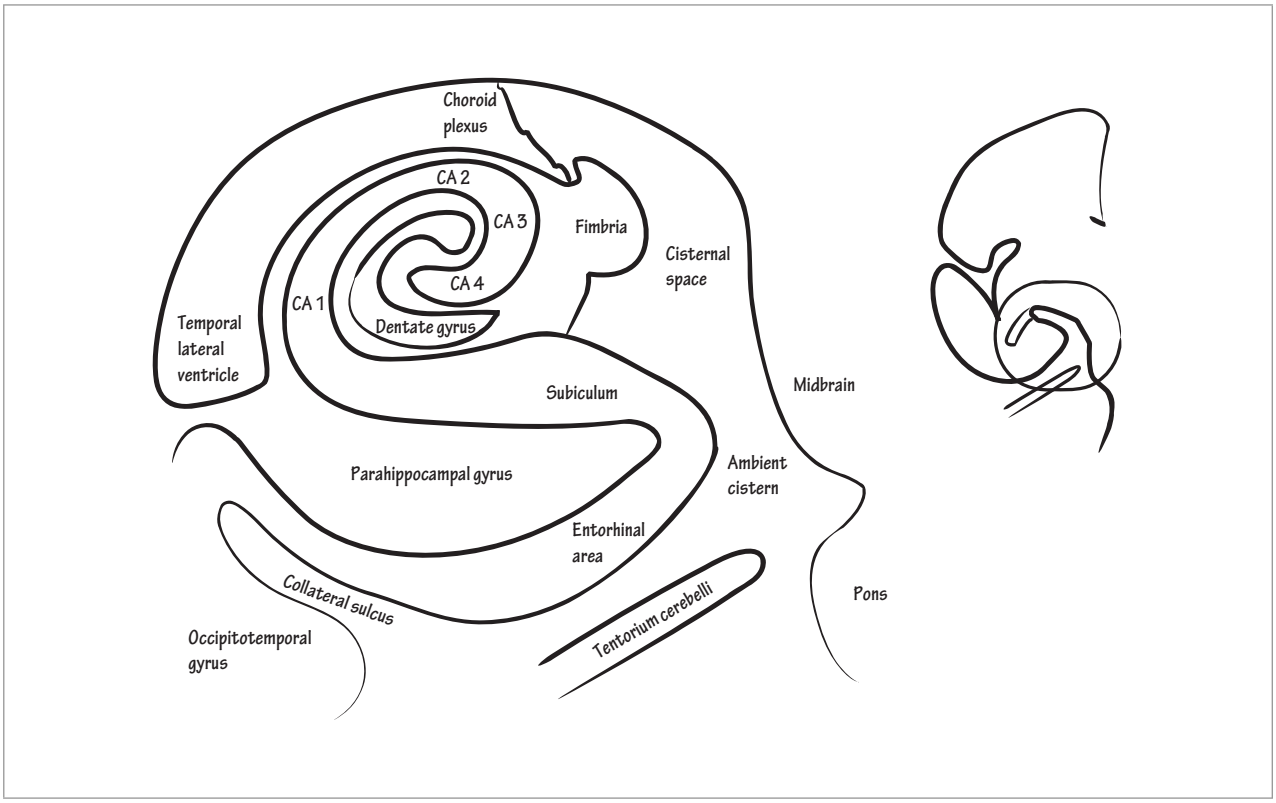

Figure 31-5 Complete hippocampus. Adapted from Duvernoy, H.M. *The Human Hippocampus: Functional Anatomy, Vascularization, and Serial Sections with Mri*. 3rd ed. Berlin and New York: Springer, 2005

Now, let's discuss the functional circuitry of the hippocampal formation in declarative memory. Many areas, including the parietal association cortex and the occipital and temporal cortices, provide input to the hippocampal formation and the hippocampus projects to the temporal and prefrontal areas and the cingulate gyrus through the Papez circuit. But memory formation also involves complicated intrahippocampal circuitry; connections exist throughout the hippocampal formation (dentate gyrus, cornu ammonis, and subiculum).

The intrahippocampal pathways are divided into a polysynaptic pathway and a direct pathway. In both pathways, fibers originate in the entorhinal cortex and project to CA1. The major difference is that in the direct pathway, fibers travel directly from the entorhinal cortex to CA1, whereas in the polysynaptic pathway, they do so through multiple steps. In the polysynaptic pathway, fibers from the entorhinal cortex first synapse in the dentate gyrus; this initial step is referred to as the perforant pathway because the fibers perforate through the subiculum without synapsing in it. From the dentate gyrus, fibers of the polysynaptic pathway project to CA3, and finally to CA1.

From CA1, fibers from both the direct and polysynaptic pathways project to the subiculum and then to the fimbria of the fornix. Note that although the subiculum lies adjacent to the entorhinal cortex, it is not involved in the intra-hippocampal circuitry until the end of the pathway when it sends fibers to the fornix. If you remember nothing about the steps of the intrahippocampal pathways, know that the entorhinal cortex is the main input area from the cortex to the hippocampus and the subiculum is the main output area back to the cortex, which is a revision of the longstanding opinion that CA1 was the main output area to the cortex.

The output to the cingulate gyrus through the Papez circuit is discussed in several chapters of this book because it involves so many different areas of the central nervous system. It involves primary limbic system areas—the hippocampus of the limbic lobe and cingulate gyrus; the mammillary bodies of the hypothalamus; and the anterior nucleus of the thalamus. Now, draw the central portion of the medial cerebral hemisphere. Indicate the origins of the Papez circuit in the *hippocampus*. Next, show *fornix* fibers project from it in a tight radius underneath the corpus callosum. Show that at the anterior commissure, the fornix splits into *precommissural* and *postcommissural fibers*. The precommissural fibers are not a part of the Papez circuit but instead synapse in the septal area and the nucleus accumbens of the ventral striatum, which is involved in drug addiction. Show the postcommissural fibers descend through the hypothalamus and synapse in the *mammillary nuclei*. Indicate the mammillary nuclei project fibers via the *mammillothalamic tract* to the anterior thalamus, which sends fibers to the cingulate gyrus. Then, show the cingulate gyrus sends fibers via its main white matter pathway, the *cingulum*, back to the hippocampus through the *entorhinal cortex*. Also, indicate the cingulate gyrus projects fibers throughout the *neocortex*. This completes the Papez circuit.

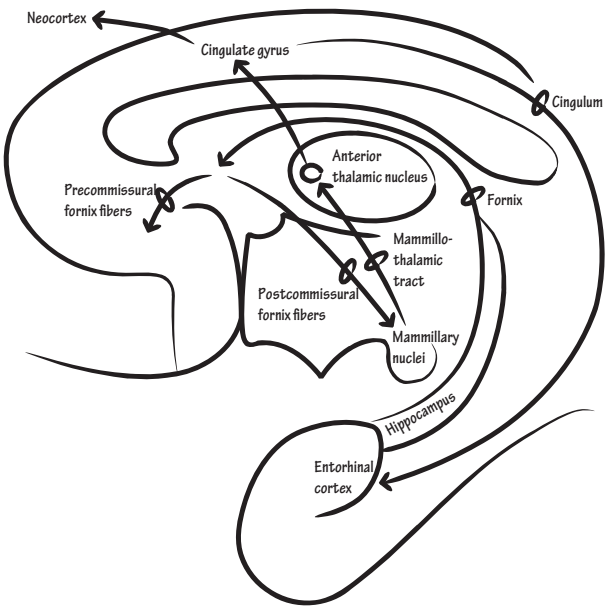

Figure 31-6 The Papez circuit

Now, turn your attention to the basal forebrain. Underneath the rostrum of the corpus callosum, there are several structures that are all defined under the umbrella term the *septal area*. Other names for this region are the *subcallosal area* and *paraolfactory area*—these terms are loosely synonymous with the septal area. This figure involves detailed neuroanatomy and is fine to skip, but do read the explanation regarding the septal nuclei; they are commonly referenced.

To draw the septal area, first draw the anterior brain, that is, include the rostral corpus callosum, thalamus, hypothalamus, and frontal lobe. In this diagram, we will first label the septal nuclei and then the following structures, from anterior to posterior: the anterior paraolfactory sulcus (aka subcallosal sulcus), subcallosal gyrus, posterior paraolfactory sulcus, and the paraterminal gyrus.

Label the *septal nuclei* just in front of the anterior commissure at the base of the septum pellucidum. Although the septal nuclei are anatomically related to the septum pellucidum, the two are histologically and functionally dissimilar. The septal nuclei are cellular and play a role in both pleasure-seeking behaviors and aggression restraint whereas the septum pellucidum is an acellular fibrous tissue fold that separates the frontal horns of the lateral ventricles. In septo-optic dysplasia, the septum pellucidum is missing, the optic nerves and tracts are hypoplastic, and the hypothalamic-pituitary axis is dysfunctional.

Underneath the rostral segment of the corpus callosum, draw the vertically oriented *anterior paraolfactory sulcus* (aka *subcallosal sulcus*). Posterior to this sulcus, label the *subcallosal gyrus*. Behind the subcallosal gyrus, draw the *posterior paraolfactory sulcus*. Then, show the *paraterminal gyrus* lies between it and the lamina terminalis. Which of these gyri is part of the limbic gyrus and which is part of the intralimbic gyrus? The subcallosal gyrus is the anterior–inferior extent of the limbic gyrus and the paraterminal gyrus is the anterior–inferior extent of the intralimbic gyrus.

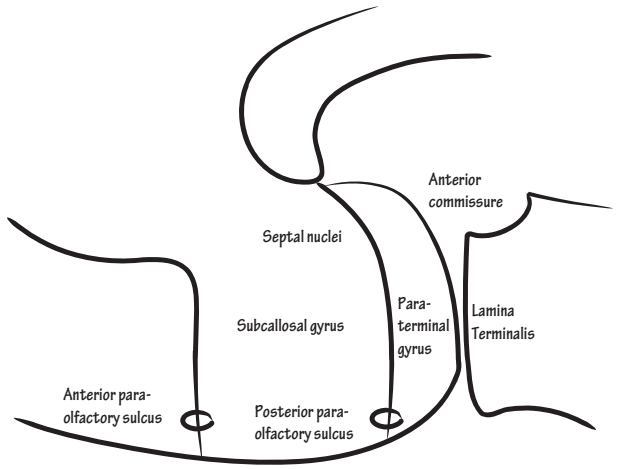

Figure 31-7 The basofrontal area

Olfactory System

THE OLFACTORY SYSTEM is a less important sensory system in humans than in many other animal classes but its anatomy has been well studied and, as discussed in the preceding chapter, it has important secondary connections to memory and behavioral brain regions. In Parkinson's disease and Alzheimer's dementia, loss of olfactory function is an early symptom of disease, and research is ongoing to use olfactory testing to help diagnose these clinical disorders in their early stages.

The olfactory system encompasses small bilateral cortical outgrowths, called the olfactory bulbs and tracts, which communicate with the primary olfactory cortices in the anterior temporal lobes. The olfactory bulbs and tracts have cerebral cytoarchitecture and are involved in bidirectional communication with the brain and olfactory nerves. A common misconception is that the olfactory bulbs and tracts are, themselves, the peripheral olfactory nerves, because they have a gross appearance similar to peripheral nerves. The actual olfactory nerves, however, are tiny filaments in the nasal walls that are often overlooked.

A unique feature of the olfactory system is that it bypasses the thalamus when it synapses in the primary olfactory cortex. It is most likely able to do this because it has a different form of cerebral cytoarchitecture than other somatosensory cortical areas. We will take time in this chapter to learn the different forms of cerebral cytoarchitecture as it is relevant to our discussion of the anatomy of the olfactory system.

In this chapter, we will use three separate drawings to illustrate the olfactory nerves, bulbs, and tracts and the primary olfactory cortex and we will rely on our drawing of the limbic system to show certain secondary olfactory structures, which are not depicted here. The first drawing will be a sagittal view through the midline nasal cavity, which will highlight the arrangement of the olfactory nerves and bulb and will show the microanatomy of the olfactory bulb. The second drawing will be a ventral perspective of the anterior one-third of the brain and will help display the olfactory system from the bulb to the primary olfactory cortex. The third diagram will be a schematic for nerve impulse through the olfactory system.

Let's begin our first diagram with a sketch of the midline human nasal cavity. Include the frontal and nasal bones, the palate and sella turcica (aka pituitary fossa), the nasal turbinates, and tongue. Next, draw the anterior portion of the medial face of a cerebral hemisphere and specify that the *cribiform plate* lies underneath it; the cribiform plate is a part of the ethmoid bone and it separates the cranial vault from the nasal cavity below it. Show small perforations in the cribiform plate through which the olfactory nerve axons extend. This midline drawing illustrates how a dural tear to the basal frontal cavity can cause *rhinorrhea*, a cerebrospinal fluid leak through the cribiform plate into the nasal cavity, when the cribiform plate and dura are compromised.

Now, draw the *neuronal* portions of the nerves within the nasal cavity and show their *axons* ascend through the porous cribiform plate into the cranial vault. These tiny filaments are cranial nerve 1, the olfactory nerve. As mentioned in the introduction, they are the extent of the nerve; the remainder of what we will draw is an extension of the cerebrum.

Next, draw an enlarged *olfactory bulb* on the inferior surface of the frontal lobe. The layout of the olfactory bulb is much like that of the retinal layer of the eye; there are several different cell layers designed for the relay and modification of nerve transmission. Label the most inferior layer of the bulb as the *glomerular layer*, which houses the olfactory glomeruli. The glomeruli make direct contact with the axonal processes of the olfactory nerves that cross through the cribiform plate. Next, draw a single *bipolar neuron* to represent the other three cell layers. From inferior to superior, they are the external plexiform layer, which houses tufted cells; the mitral cell layer, which houses mitral cells; and the granular cell layer, which houses granule cells. Show the ascending axons of the olfactory bulb form the *lateral olfactory tract*. It is easy to imagine that information flows from the olfactory nerve to the bulb and down the tract, but communication also occurs in the opposite direction, as well: the primary olfactory cortex, which we will draw next, also sends impulses to the olfactory bulb.

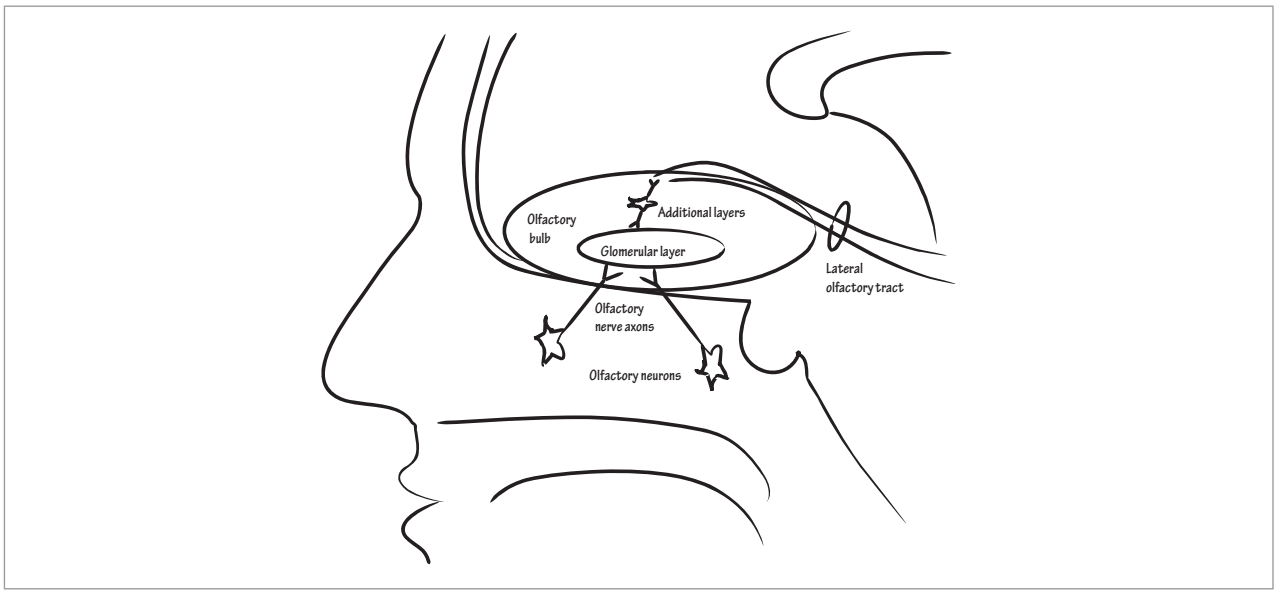

Figure 32-1 Sagittal view of enlarged olfactory afferents in the nasal cavity and basal frontal lobe

Now, let's draw the primary olfactory cortex. Begin with the underbelly of the frontal and anterior-temporal portions of the brain. Next, in the frontal lobe, draw the *olfactory bulb* and *tract* and show they lie within the *olfactory sulcus*. Also, let's take the opportunity to include a few structures that are unrelated to the primary olfactory cortex but that we are able to visualize from this perspective. Draw the midline-lying *optic chiasm*, *pituitary stalk*, *mammillary bodies*, and the *anterior perforated* substance. Use both sides of the brain so we have enough room to label all of the structures we will discuss.

As a side note, the olfactory bulb is often listed as the *main* olfactory bulb. This is because the majority of vertebrates have an accessory olfactory system in addition to their main olfactory system. But this accessory olfactory system is not found in mammals with the following exception: the vomeronasal organ, which is the primary sensory organ within the accessory olfactory system, is found in the nasal septum of human fetuses.

Before the olfactory tract reaches the anterior perforated substance, indicate it becomes the *olfactory trigone*, a small triangular area with its apex in the olfactory sulcus. At the olfactory trigone, show the olfactory tract split into two separate *striae*: the *lateral stria* and *medial stria*. Later, we will show that the *lateral stria* synapses in the lateral portion of the primary olfactory cortex and the *medial stria* synapses in the medial frontal lobe in the paraolfactory area and sends fibers to the contralateral olfactory bulb.

Now, let's draw the olfactory cortex, which has primary and secondary components. The olfactory bulb and tract directly communicate with the primary areas and indirectly with the secondary areas. The primary olfactory cortex comprises the anterior olfactory nucleus, olfactory tubercle, piriform cortex, amygdala, and perimaygdaloid cortex. Indicate the most anterior of these structures is the *anterior olfactory nucleus*, which lies in the anterior tip of the olfactory tract. In some texts, its position is shown at the posterior end, near the olfactory trigone. Situate the nucleus medially as a cue to its functional role in the flow of olfactory information, which we will draw later. The anterior olfactory nucleus has multi-layered cytoarchitecture and is more aptly referred to as *anterior olfactory cortex* than as a nucleus. It serves to organize and store olfactory information.

Next, label the *olfactory tubercle*, which lies just behind the medial olfactory stria in the anterior perforated substance. This structure is often discussed but its existence in humans is controversial.

Then, within a cross-section of the anterior temporal lobe, label the following primary olfactory cortical structures: superolaterally, label the *amygdala*; superomedially, label the *periamygdaloid complex*; and inferomedially, label the *piriform cortex*. Our understanding of the neurobiology of olfaction, in large part, comes from studies of the piriform cortex, which in rats is clearly the largest primary olfactory cortical area. But the relative significance of the human piriform cortex remains to be determined.

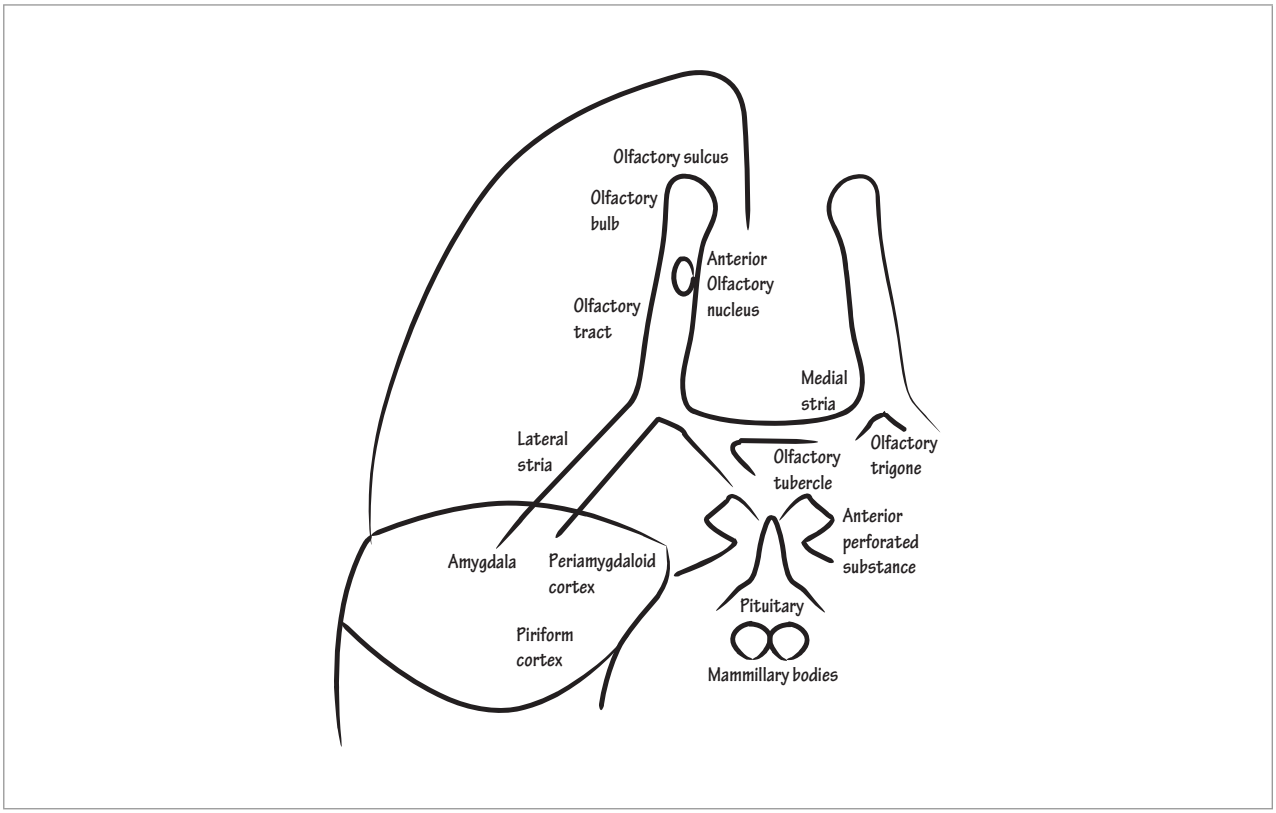

Figure 32-2 Primary olfactory cortex and anatomically related structures

The secondary olfactory structures mostly lie within the limbic system; we will simply discuss them as they are diverse and drawn elsewhere in the book. The secondary areas are the orbitofrontal cortex, lateral hypothalamus, insula, anterior hippocampus, and indusium griseum. The contralateral olfactory bulb is also a secondary area for reasons that will become clear when we draw the flow of olfactory information. The lateral entorhinal cortex is listed as a primary or secondary olfactory area. Functionally, it is logical why the aforementioned secondary areas connect with the olfactory system. The hypothalamus and insula are central autonomic centers, the anterior hippocampus and indusium griseum are memory areas, and the orbitofrontal cortex is a behavioral center: the sense of smell influences all of them.

The lateral entorhinal cortex and the dorsomedial thalamus assist in communication between the primary olfactory cortex and the secondary olfactory structures. However, the thalamus is not involved in the flow of information between the olfactory tract and the primary olfactory cortex. Do any other sensory systems bypass the thalamus before making their primary cortical synapse? No. How does primary olfactory information bypass the thalamus? As mentioned at the beginning of the chapter, the answer is likely related to the difference in the cytoarchitecture between the primary olfactory cortex and other primary somatosensory areas.

So, now, let's learn the cytoarchitecture of the brain. Primary somatosensory areas contain six-layered cortex, called *neocortex*; the primary olfactory cortex contains an evolutionarily older cytoarchitecture that is three to five layers and is called *paleocortex*; the hippocampus, the phylogenically oldest cortical region, contains three-layered *archicortex*. Alternative nomenclature for this cytoarchitecture classification also exists. Six-layered neocortex is called *isocortex*, three to five layered paleocortex is called *periallocortex*, and three-layered archicortex is called *allocortex*. Thus, isocortex is synonymous with neocortex and has six layers; periallocortex is synonymous with paleocortex and has three to five layers; and allocortex is synonmyous with archicortex and has three layers.

Now, let's detail the flow of information from the olfactory bulb to the primary olfactory cortex. Only the lateral olfactory tract directly joins the olfactory bulb. The medial division of the olfactory tract begins at the anterior olfactory nucleus located farther posterior. Yet for simplicity, in this diagram, we will unify the olfactory tracts. As well, we will simplify the flow of information: olfactory information is bidirectional but here we will only show it pass from the olfactory bulb to the cortex to keep our diagram clear.

First, show the olfactory cortical impulse originate in the *olfactory bulb* and pass down the *olfactory tract*. Laterally, it travels along the *lateral olfactory stria*, which synapses in the *temporal olfactory area*. From there, information is sent and received from secondary olfactory regions. Next, draw the *anterior olfactory nucleus* at the anterior extent of the medial olfactory tract. Show a nerve impulse travel down the ipsilateral medial olfactory tract to the ipsilateral *medial stria*, cross the *anterior commissure* to the contralateral medial stria, and travel up the contralateral medial olfactory tract to the *secondary olfactory bulb*. Because of this arrangement, the olfactory bulbs are considered both primary and secondary olfactory areas.

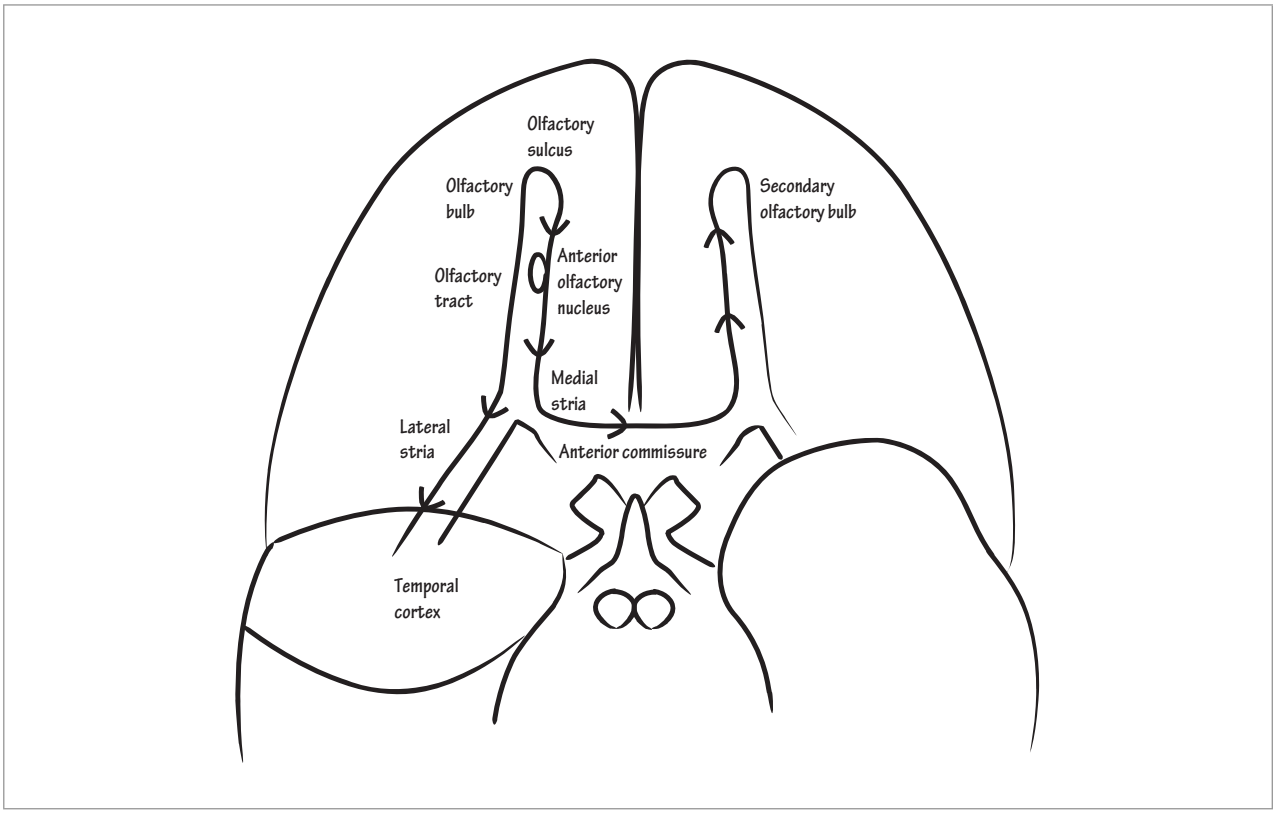

Figure 32-3 Afferent flow of olfactory information

Visual Pathways

IN THIS CHAPTER, we will draw the most overtly relied upon sensory system—the visual sensory system, and in the next chapter, we will learn the eye movements. Let's begin with an axial section through the eyeball and include the posterior optic nerve attachment. In the anterior eye, draw the *lens*; indicate it separates the *anterior chamber* in front of it from the *vitreous space* behind it. The anterior chamber and vitreous space contain aqueous and vitreuous humor, respectively.

Next, adjacent to the anterior plane of the lens, draw an *iris*; immediately behind the irises are the *posterior chambers*. They play a role in the flow of aqueous humor. Draw the *ciliary bodies*, which line the inner surface of the eyeball and produce aqueous humor. Aqueous humor first enters the posterior chamber and then flows into the anterior chamber. At the angle between the iris and the cornea, the iridocorneal angle, indicate there is a small canal called the *canal of Schlemm*, which is responsible for the reabsorption of aqueous humor. Blockage of the canal of Schlemm causes failure of reabsorption, which increases intraocular pressure and results in narrow-angle glaucoma.

Now, draw wire-like *zonules* connecting the lens to the ciliary bodies. When the ciliary bodies are relaxed (flattened), the zonules are stretched and the lens is flattened. During the near response (i.e., when the eyes respond to near objects), lens thickening (aka accommodation) occurs in order to change the depth of the visual field to place the nearby object in focus. To produce lens thickening, the ciliary bodies contract (i.e., shorten) and the zonules relax (i.e., slacken).

To demonstrate this principle for yourself, do the following. Extend a finger to represent a relaxed ciliary body. Then make a "V" with your opposite hand's thumb and index finger and touch their tips to the ends of the relaxed ciliary body. The "V" represents the taut zonules that stretch the lens (flatten it). Contract the ciliary body (i.e., shorten your stretched finger) and the zonules fold in on themselves, that is, they lose their tensile strength. The zonules no longer stretch the lens and it thickens.

Now, indicate the outermost layer of the eye is the *sclera*—the "white of the eye." Anteriorly, it is called the *cornea*. The cornea is transparent to allow light to enter the eye. Label the layer internal to the sclera as the *uvea* (aka *vascular layer*). It is the extension of the meningeal arachnoid and pia mater layers and is where the vasculature to the eye lies. The densely pigmented part of the uvea is referred to as choroid. The choroid catches all of the light that passes through the photoreceptor layer, which we will draw next.

Internal to the uvea, draw the *retinal layer*. The photoreceptor layer is the outermost sublayer of the retina; it lies just inside the choroid of the uvea. Light is detected by the photoreceptor layer and whatever aberrant light passes through it, the choroid layer catches.

The retina has 10 anatomic layers but for simplicity, we will group them into three functional layers. Label the outermost functional layer as the *photoreceptor layer*; inside it, label the *bipolar layer*; and label the innermost retinal layer as the *ganglion cell layer*. The photoreceptor layer serves for photon absorption; it comprises the five outermost retinal layers: the retinal pigment epithelium, rods and cones,

the outer nuclear and plexiform layers, and the outer limiting membrane. The bipolar layer serves as an intermediary transduction layer and comprises the inner nuclear layer, only. The ganglion layer lies inside it and receives transduction from the bipolar layer and propagates the visual potential down the optic nerve. The ganglion layer comprises the inner plexiform layer, ganglion cell and nerve fiber layers, and the inner limiting membrane. In short, light is absorbed in the photoreceptor layer of the retina, transitioned through the bipolar layer, and propagated to the optic nerve fibers via the ganglion layer.

Now, show the *subarachnoid space* surrounds the optic nerve fibers. Together, they are bundled within an optic nerve sheath. Increased pressure in the subarachnoid space results in increased optic nerve tissue pressure, which, in turn, causes impairment of axoplasmic transport and axonal swelling.

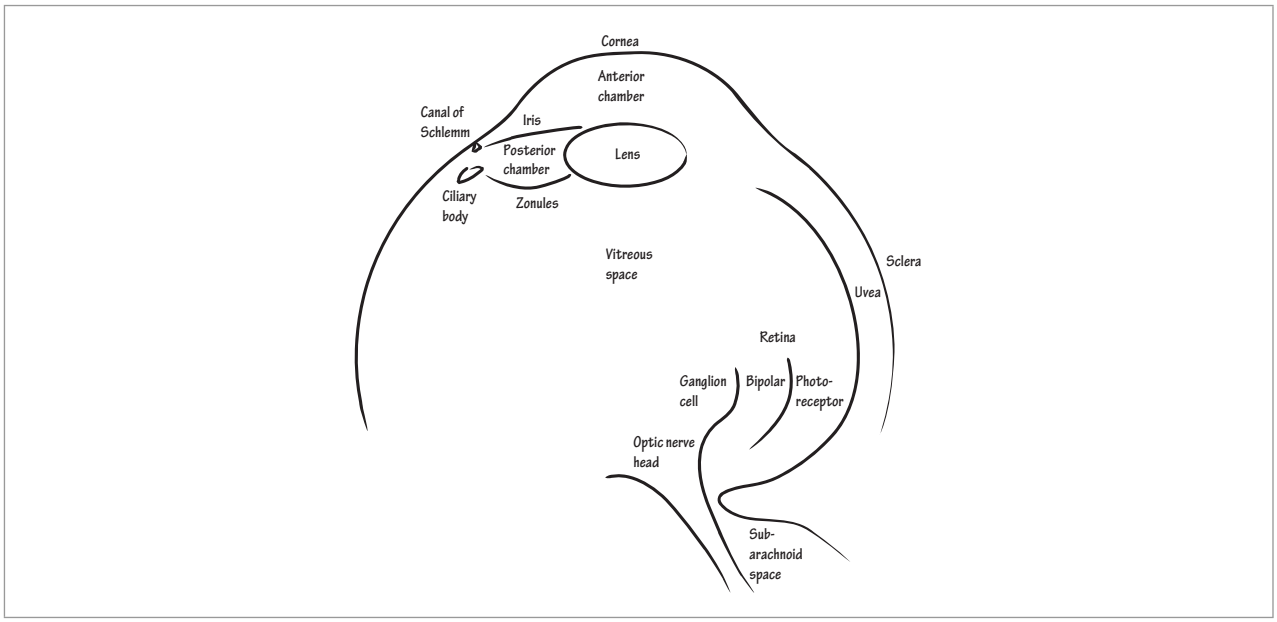

Figure 33-1 Axial section of the eye and optic nerve

Here, let's define the anatomy of the retina with a coronal section through the back of the eye. Label the central point of the retina as the *macula*, which means "spot," and the center of the macula as the *fovea*, which means "pit." The macula lies in the middle of the retina and splits the retina into *nasal* and *temporal hemiretinae*; the optic nerve lies in the nasal hemiretina. The visual world divides into right and left fields, both of which further subdivide into temporal and nasal hemifields; the nasal hemiretinae receive light from the temporal visual hemifields and the temporal hemiretinae receive light from the nasal visual hemifields.

Next, draw the optic nerve medial to the macula (in the nasal hemiretina). Show that it comprises a central *optic cup* that is encircled by an *optic disk*. The optic nerve head becomes engorged when the intracranial pressure is elevated because the nerve is covered by an extension of the intracranial leptomeninges (the arachnoid mater and pia mater combination) so increased pressure is transmitted along the nerve. The visual blind spot corresponds to the optic nerve head in the retina. The retina does not detect the corresponding region of the visual field because no photoreceptors are present in the optic nerve head, and thus, increased intracranial pressure enlarges the blind spot. To demonstrate the blind spot for yourself, hold your thumb out in front of you. Close your opposite eye. Now rotate your arm out laterally while you stare straight ahead. Within about 10° of rotation, your thumbnail disappears and then within another few degrees, it reappears. The visual stretch where the thumbnail disappears corresponds to the retinal optic nerve head. Clinically, testing a patient's blind spot is especially important in the syndrome of intracranial hypertension as enlargement of the blind spot may be the first visual field deficit you will be able to elicit on examination.

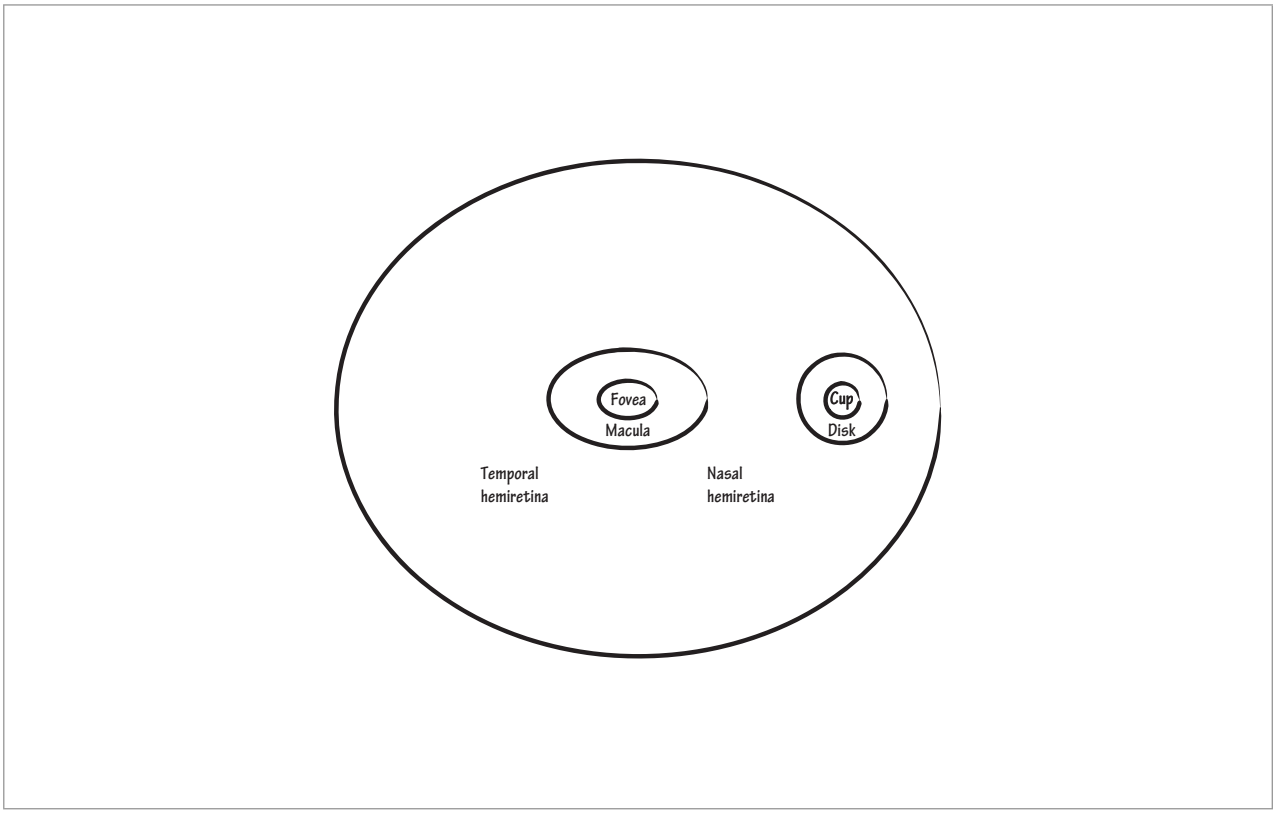

Figure 33-2 Retina

Now, let's draw the visual pathways from the retinae to the occipital cortex. Begin with an axial section through the brain, including the eyeballs. Indicate the right nasal visual hemifield projects to the left temporal retinal hemifield and the right temporal visual hemifield projects to the right nasal retinal hemifield. Indicate the *temporal nerve fibers* from each retina project to the ipsilateral *lateral geniculate body* and the *nasal nerve fibers* cross in the *optic chiasm* and project to the contralateral *lateral geniculate* body.

Also, show that after the nasal retinal fibers cross in the optic chiasm, the *inferior nasal hemiretinal fibers* loop into the proximal contralateral optic nerve before projecting down the optic tract. This redundant loop is called the *anterior Wilbrand's knee*. The inferior nasal hemiretinal field corresponds to which visual field quadrant? The superior temporal visual field. A posterior Wilbrand's knee also exists wherein the ipsilateral superior nasal fibers form a redundant loop in the ipsilateral optic tract before crossing in the chiasm. This loop is disrupted far less often than the anterior Wilbrand's knee, however.

When the optic nerve is interrupted just anterior (i.e., proximal) to the optic chiasm, the clinical condition of anterior junction syndrome occurs. What are the deficits in anterior junction syndrome? The optic nerve is affected, so there is loss of visual input from the ipsilateral eye. Also, the contralateral inferior nasal retinal fibers are affected because of the anterior Wilbrand's knee. Anterior junction syndrome should prompt investigation of the region just proximal to the optic chiasm.

The chiasm, itself, is highly susceptible to injury because of the propensity for mass lesions to grow within the pituitary body and from out of the sella turcica, which is the depression in the sphenoid bone where the pituitary gland sits. Indeed, the most common tumor to damage the optic chiasm is a pituitary adenoma. Meningiomas and craniopharyngiomas are also common sellar tumors. A Rathke's cleft cyst is a benign mucous containing sellar cyst that arises from Rathke's pouch, which is the portion of the alimentary canal that derives the anterior pituitary gland.

What are the visual deficits from a sellar mass that grows up into the optic chiasm? The nasal retinal hemifields are affected because they cross in the optic chiasm, so there are bitemporal visual hemifield deficits. The inferior fibers are affected first if the mass grows upward, so the superior visual fields are first affected.

Between the optic chiasm and the lateral genticulate bodies, optic fibers pass through the optic tracts. They contain ipsilateral temporal retinal fibers and contralateral nasal retinal fibers. Lesions within the optic tracts, themselves, are rare. They result in the same class of deficit as all lesions posterior to the optic chiasm, called post-chiasmatic lesions. Post-chiasmatic lesions cause contralateral homonymous visual field deficits.

What does this mean? Let's use a left post-chiasmatic lesion as an example. In post-chiasmatic lesions, the ipsilateral temporal retinal fibers and the contralateral nasal retinal fibers are affected. So, (1) the contralateral nasal visual field is affected from injury to the ipsilateral temporal hemiretina fibers and (2) the contralateral temporal visual field is affected from injury to the contralateral nasal hemiretina fibers. These visual hemifields sum to the full visual field contralateral to the side of the post-chiasmatic lesion.

Within the lateral geniculate nuclei, there are six retintopic layers that divide into parvocellular and magnocellular subtypes. The parvocellular subtypes are projections from small ganglion cells sensitive to color and shape and the magnocellular subtypes are projections from larger ganglion cells sensitive to motion.

The macula projects to the posterior lateral geniculate nucleus and the peripheral retinal images project to the anterior lateral geniculate nucleus. From there, the posterior lateral geniculate nucleus projects to the posterior portion of the occipital cortex (aka the occipital pole). The anterior lateral geniculate nucleus projections are more complicated; we address them in the last section, but the topographic organization of the lateral geniculate body is preserved in its projections to the occipital cortex. For now, simply indicate the *optic radiations* project from the lateral geniculate nuclei to the *primary occipital cortex*.

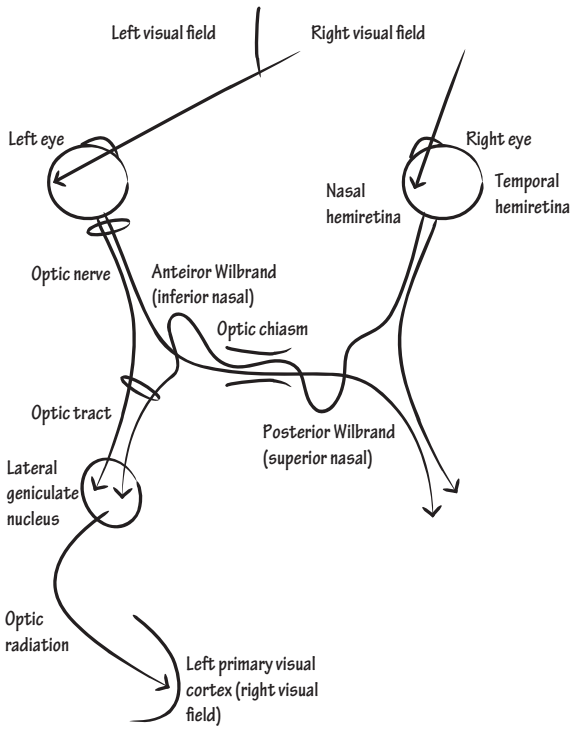

Figure 33-3 Optic pathways (axial view)

Here, let's draw the optic pathways. Draw a cerebral hemisphere; the optic radiations travel deep within the cerebrum. Let's start by drawing the Sylvian fissure for orientational purposes. Now, indicate the *superior visual world* projects to the *inferior retina* and the *inferior visual world* projects to the *superior retina*. Then, show the retinal fibers bundle as the *optic nerve*, which becomes the *optic tract* posterior to the *optic chiasm*. Next, indicate the optic tract synapses in the *lateral geniculate nucleus*. Show that *macular* images organize posteriorly and peripheral images organize anteriorly in the lateral geniculate nucleus.

Now, draw the *optic radiations*. Show the *superior bundle* projects along the occipital horn of the lateral ventricle in the superior temporal and inferior parietal lobes. Indicate it terminates in the superior *primary visual cortex* in the posterior occipital lobe. Next, show the *inferior bundle* (aka *Meyer's loop*) fans out over the anterior pole of the temporal horn of the lateral ventricles and projects back through the inferior temporal lobe to the inferior *primary occipital cortex* in the posterior occipital lobe, as well. Injury to the inferior bundle is more common than to the superior bundle, so superior visual field defects are more common than inferior field defects. If a lesion only occurs in one optic radiation, it results in quadrantanopia, which means only the respective superior or inferior quadrant of the visual field is affected.

The cortical representation of the macula lies at the occipital pole. Next, we will show where the peripheral retinal images lie.

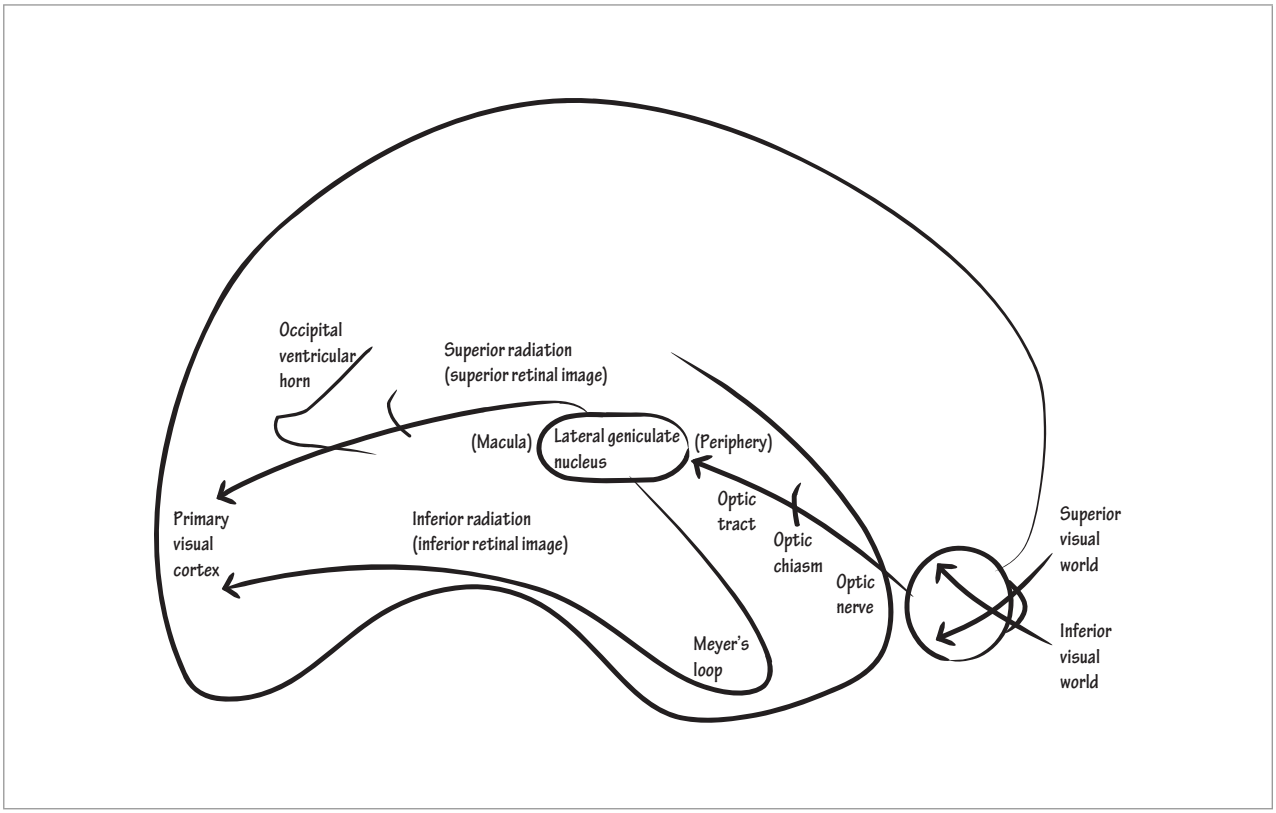

Figure 33-4 Optic radiations (lateral view)

Now, let's draw the visual cortex, itself; you will find our diagram at the end of the chapter. Draw a lateral cerebral hemisphere. Label the *occipital visual area* in the occipital lobe, the *ventral stream* in the temporal lobe, the *dorsal stream* in the parietal lobe, and the *frontal visual area* in the frontal lobe. The occipital visual area is the primary visual cortex—it encodes basic visual features; the ventral stream is the "what" pathway; the dorsal stream is the "where" pathway; and the frontal area contains the frontal eye fields, which enact eye movements.

Next, draw both the medial and lateral faces of a cerebral hemisphere. On the lateral face, label the occipital pole as area *V1* (aka *striate cortex*). This is the primary cortical processing area for macular retinal images. Areas *V2* and *V3* (aka *extrastriate cortex*) are the primary cortical processing areas for peripheral retinal images. Draw V2 in front of V1 and V3 in front of V2; here, the topographic orientation is the same as in the lateral geniculate body. On the medial face, show V1 lies along the calcarine fissure; V2 lies immediately above and below V1; and V3 lies immediately above and below V2. "VP" is routinely used to designate the ventral division of V3 (the area below V2), but here, we simply label both the dorsal and ventral divisions as V3. Thus, in the medial hemisphere, the primary visual cortices are arranged in horizontal rows and in the lateral hemisphere, they are arranged in vertical columns.

Close your eyes for a moment and create a visual world with the sounds and smells you sense. Patients with bilateral lesions in V1 have bilateral blindness but are unaware of their deficit; this is called Anton syndrome. When asked directed questions about their environment, patients with Anton syndrome answer confidently but inaccurately, which is called confabulation. It is helpful, even if it turns out not to be entirely true, to imagine that their confabulation is based on a visual world created from their other, intact senses.

Now, let's address color processing. What color is your shirt? Take a closer look at it; you will see it is not a single color or even a pattern of colors but that it actually comprises innumerable colors from the widely different wavelengths of light that reflect off of it. So what gave you such a uniform impression of your shirt color when it is actually so heterogenous? Cortical processing of color information requires high-level cognitive processing, which primarily takes place in the inferior occipito-temporal lobe. In both the medial and lateral hemispheres, label this inferior occipito-temporal region as area *V4/V8*, which corresponds to the lingual and fusiform gyri. Currently, there is debate about what constitutes the anterior border of V4, which is why we denote this area as V4/V8. The grayscale images throughout this book give you an idea of the visual appearance of the world for someone with a deficit in color perception (aka achromatopsia): it appears drained of color.

Other disorders of color processing also exist. Imagine mixing red and white paint. What color results? Pink. If you are unable to answer this question, you have color agnosia, a color recognition disorder. If you are able to recognize the color name but are unable to say it or understand it when it is spoken, and your language is otherwise intact, you have color anomia.

Color recognition and color naming disorders also lie in the occipitotempoal region but are separate from each other and separate from the location for color perception disorder (achromatopsia). Some authors include the V4 color perception area as part of the "what" ventral stream area.

In the lateral hemisphere, in the temporo-parietal-occipital junction, label area *V5*—the motion detection area. It is also called human MT+ (hMT+) because it is the homologue of the middle temporal and middle superior temporal areas in the macaque monkey, which is an important animal research model for the visual systems. We discuss the role of this area in smooth pursuit eye movements in the next chapter. As mentioned in that chapter, lesions in area V5 cause disorders of motion perception (aka cerebral akinetopsia). A well-studied patient with cerebral akinetopsia, known as L.M. described that when pouring coffee, it appeared frozen, like a glacier. Correspondingly, when crossing the street, cars would at first seem distant but then, suddenly, very near. Just as some authors include V4 with the "what" pathway, some authors include V5 motion perception as part of the "where" dorsal stream area.

The *parvocellular* cells of the retina detect the "what" properties of the visual world and, accordingly, the ventral stream is referred to as the "P" pathway. Controversy exists regarding the hierarchical and anatomical organization of the ventral stream recognition system. Let's consider two opposing ways the ventral stream could be arranged. It could be that faces, places, and all other objects are encoded in hierarchical fashion; wherein, it would require minimal visual cognitive ability to recognize simple objects but high-level cognitive ability to recognize

complicated objects. In this system, people who lost their ability to recognize rudimentary objects would certainly be unable to recognize complex ones, such as faces. An alternative organizational system would be one that is location-specific. Visual cortical areas would encode specific object classes and no hierarchy of complexity would exist. In this system, encoding of faces, places, and other objects would have individual locations. Face recognition could be disturbed in the setting of preserved rudimentary object recognition and vice versa. It is unclear, yet, which methodology is the dominant organizational system in the human visual cortex. Therefore, here we will simply present the main types of cognitive visual disorders that exist and label their common localizations, and we will skip trying to validate or disprove either organizational hypothesis.

The visual object recognition area lies midway along the medial–lateral plane of the inferior occipito-temporal surface. Loss of object recognition is called *visual object agnosia*. Classically, there are two categories of visual object agnosia: *apperceptive* and *associative*. Patients who are unable to perceive objects have apperceptive agnosia and those with intact visual object perception but impaired recognition (i.e., they are unable to tell you what an object is) have visual object associative agnosia. Think of an example to distinguish these two types of disorders. For instance, try to draw your desk. Patients with apperceptive visual agnosia will be unable to draw it or tell you what it is; whereas, patients with visual associative agnosia will be able to draw it, but will be unable to tell you what it is. Why is visual apperceptive agnosia an agnosia at all and not just a visual impairment? Because visual perception is otherwise intact; for instance, visual acuity and color detection are normal. When object agnosia occurs from a lesion in the dominant hemisphere, there is often a profound associated language disturbance, including loss of word meaning. This occurs in the left temporal variant of frontal temporal dementia (aka semantic dementia).

Recognition for *familiar faces* lies laterally in the inferior temporo-occipital cortex in the *fusiform gyrus*. A deficit for recognition of familiar faces, such as those of family, friends, and colleagues is called *prosopagnosia*. There are two points of interest regarding prosopagnosia: (1) the right fusiform gyrus is more often involved in familiar face recognition than the left (isolated lesions of the right fusiform gyrus have the potential to cause prosopagnosia but isolated lesions of the left do not) and (2) it remains to be determined if the fusiform gyrus is specific for the recognition of human faces or if it responds to any over-trained visual stimulus (i.e., cars in people who are car experts, birds in bird-watchers, and so on).

Place recognition lies medially in the inferior temporo-occipital cortex in the *parahippocampal gyrus*. It encodes visual memory of environmental scenes and buildings. Let's not confuse this with the dorsal visual area, which we will discuss next; it is responsible for encoding orientation of the body in space. While patients with dorsal stream lesions are unaware of parts of their bodies, patients with parahippocampal gyral lesions have difficulty recognizing familiar environments.

The magnocellular retinal cells detect the "where" properties of the visual world, and so the dorsal "where" stream (aka "how stream") is referred to as the "M" pathway. The caudal portion of the intraparietal sulcus is the site of *stereoscopic processing*. Binocular disparity, discrimination of object size, and surface orientation information are pooled in this area to make stereoscopic sense of the world. Thus, stereoscopic processing is more than simple physics, more than a reconciliation of binocular vision; it involves higher level cognitive processing. The remainder of the intraparietal sulcus serves as the *reach area*. This area is involved in visually-guided pointing, grasping, and object manipulation. Think of it as the "show me the way" area. It tells the motor cortex where to move to produce a desired effect. Lesions in the intraparietal sulcus present with *optic ataxia* and *oculomotor apraxia*. Optic ataxia is an impairment of reaching for objects in the environment and oculomotor apraxia is impairment of volitional eye movements to command; we will explain these further, soon.

The superior parietal lobule and inferior parietal lobule are the primary areas of *body* or *spatial awareness* (different from parahippocampal place recognition). Superior and inferior parietal lobule lesions result in *hemineglect*. Patients with this disorder have remarkable deficits in attending to a particular side of the body (most commonly the left side of the body from right hemispheric lesions).

Let's show how to examine optic apraxia, optic ataxia, and hemineglect at the bedside. Oculomotor apraxia is an impairment of directing the eyes toward a target to command. To mimic oculomotor apraxia,

pretend as though you've been asked to look at your hand but are unable to. Patients with optic ataxia, on the contrary, are able to look at objects but are unable to reach for them because of an inability to process visual cues appropriately. To demonstrate this, reach for an object in front of you but miss it.

Patients with *simultagnosia* also have a visual attention problem, but it is not specific to either half of the world or to any object type. They are simply only able to visualize one object at a time. To mimic this disorder, only allow yourself to attend to one object in the world in front of you at a time: block everything else out. Simultagnosia is a diffusely localizing visual disturbance. Ventral, occipito-temporal lesions cause a mild form of the disorder whereas dorsal, occipito-parietal lesions, cause a more severe form of it.

Oftentimes, patients present with simultagnosia along with optic apraxia and optic ataxia. Together, these symptoms constitute *Bálint syndrome*, named after the Hungarian neurologist Rezsö Balint. The complete syndrome suggests wide-spread bilateral occipito-parietal lesions.

Hemineglect, as discussed, is commonly found in right parietal lesions, which cause left-side neglect. At the bedside, one of the simplest ways to test for it is to hold a patient's left hand in front of his/her eyes and ask whose hand it is. Patients with severe neglect will say it is your hand (i.e., the examiner's hand).

In addition to hemineglect, patients with right parietal lesions also commonly demonstrate anosognosia, the "unawareness of impairment." Anton syndrome is a specific, visual form of anosognosia. Anosognosia is rarely found from left hemispheric injuries and is argued to be a right frontoparietal disorder because certain motor-sensory findings commonly accompany anosognosia, such as left visual and tactile neglect and left motor problems. But evidence shows that the right insular cortex, thalamus, and pons are also involved with the right frontoparietal region, and together, they form an awareness circuit.

Throughout the past 60 years, neuropsychologists have developed models to explain anosognosia. One of the first neuropsychologists to do so was Stanley Geschwind. He argued that right-side lesions disconnect the left hemisphere from any knowledge of the injury, and that disconnection is the cause of anosognosia. Certain, more recent models have been described, which emphasize the role of emotional dysregulation in anosognosia and propose that without a functioning right hemisphere, which is the "emotionally-astute hemisphere," the mind is unable to adjust to the massive effects of the injury and denies their existence.

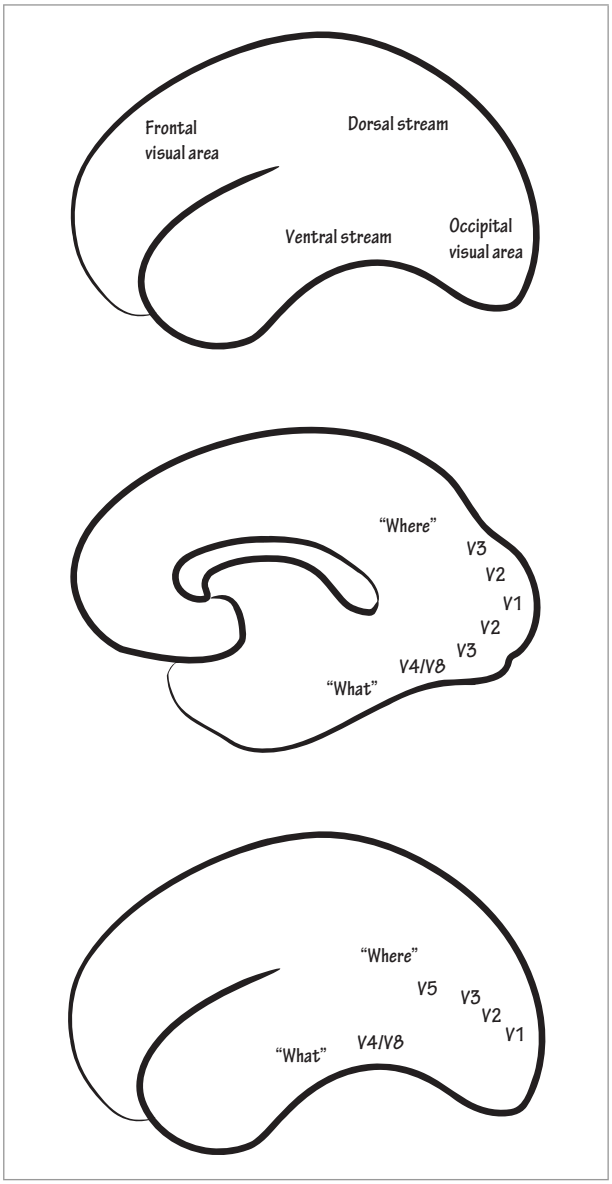

Figure 33-5 Visual cortex

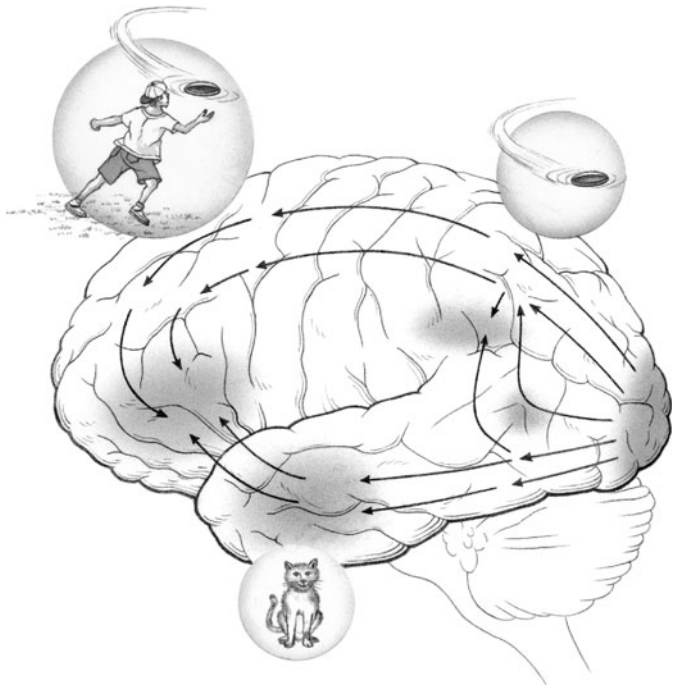

Photo 33-1 Dorsal and ventral streams. Visual information regarding movement of the frisbee is transmitted to the parietal lobe, which processes and passes that spatial information forward to the motor cortex so the frisbee can be caught. The stationary cat is recognized in the posterior temporal lobe and semantically labeled in the anterior temporal lobe (semantics are discussed in chapter 36)

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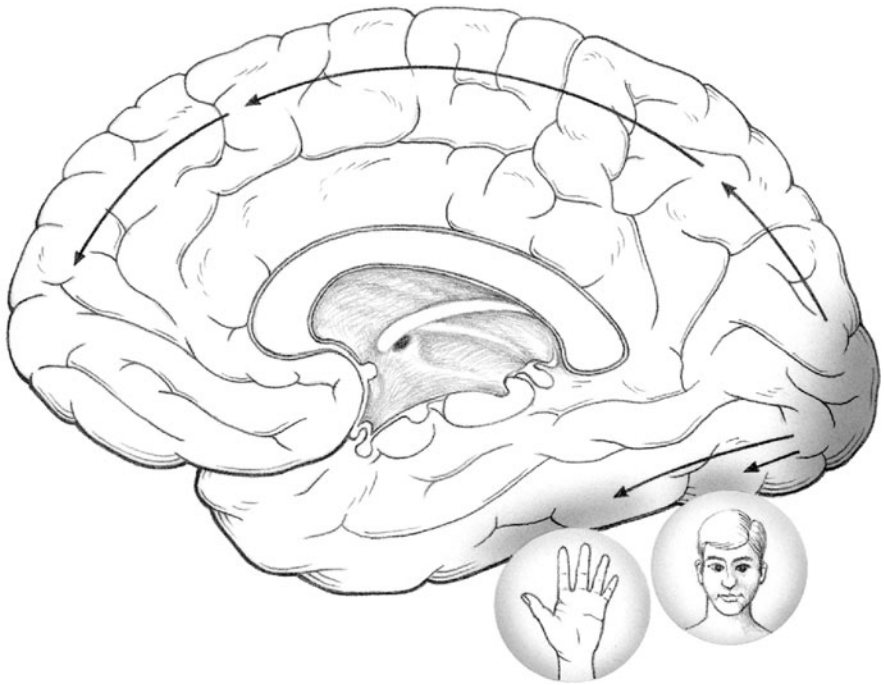

Photo 33-2 Dorsal and ventral streams. Other objects (the face and hand) are recognized in other regions of the temporal lobe (an example of non-hierarchical recognition)

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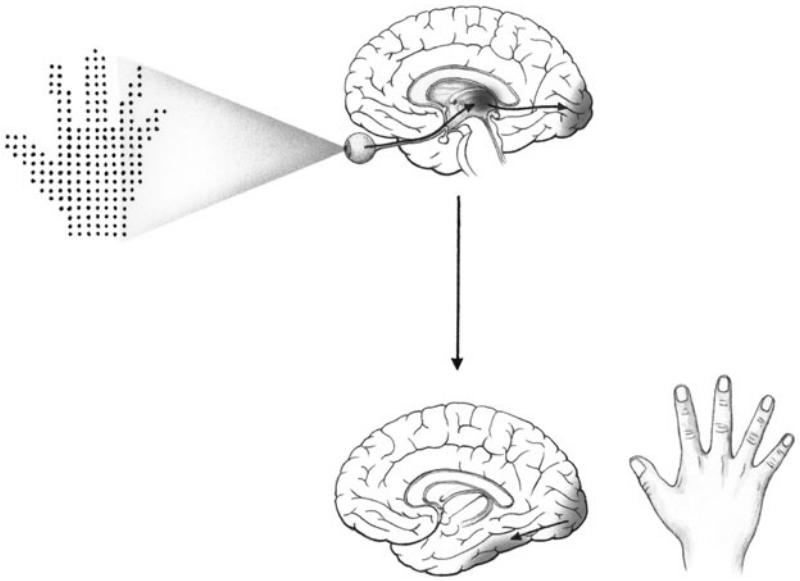

Photo 33-3 Bottom-up processing: individual components are perceived in the retina, processed in the lateral geniculate nucleus, and transmitted to the visual cortex

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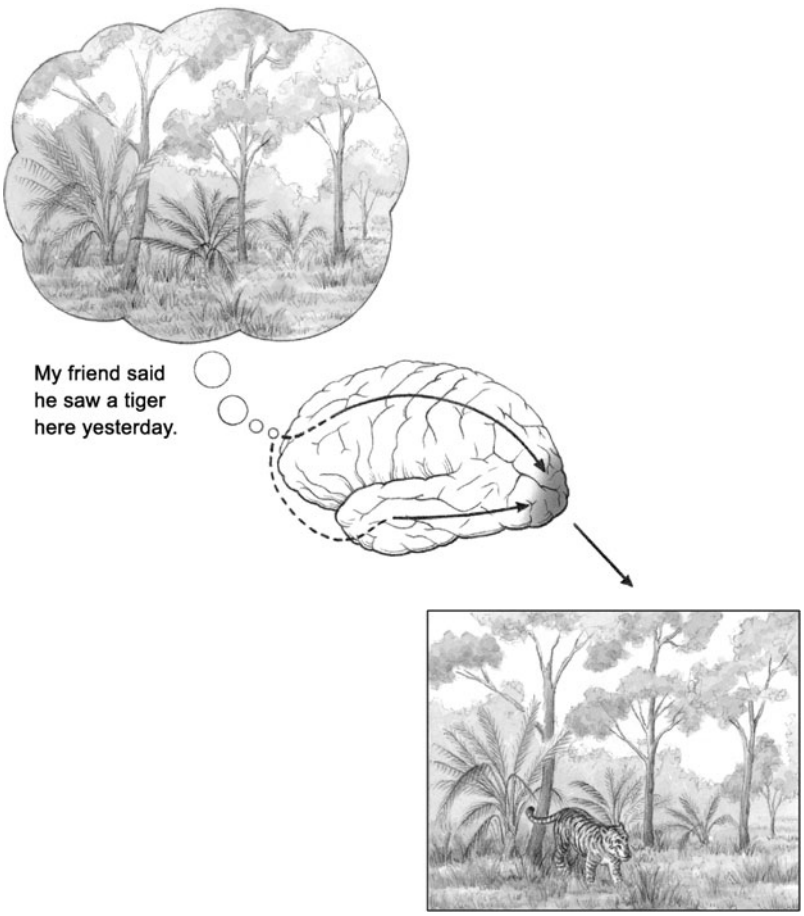

Photo 33-4 Top down processing: higher cortical function affects visual perception. "Here, a person who is forewarned of a recent tiger sighting misinterprets ambiguous environmental cues and 'sees' a tiger that is not present."

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Eye Movements

THERE ARE MANY different classes of eye movements dedicated to keeping the visual world in focus; two main categories are those that keep the world steady on the retina and those that keep the object of focus in the center of vision, in the fovea. Different areas of the nervous system initiate different eye movements but they all share the same final brainstem pathways. One brainstem pathway is for conjugate eye movements, which drive the eyes in the same direction (horizontally or vertically), and the other is for vergence eye movements, which drive the eyes in opposite directions (inward or outward). Let's start with a discussion of the different types of eye movements and then learn their anatomy.

We begin with the eye movements that keep the world stabilized on the retina. First, pick a word on the page and focus on it. *Visual fixation* mechanisms keep the image on your retina despite constant, unappreciable head movements. During appreciable head movements, *vestibulo-ocular* mechanisms keep the image on your retina. Rotate your head back and forth while reading the words on this page to demonstrate how vestibulo-ocular movements allow you to keep them in focus. During formal visual acuity testing, you will not lose more than one line on the Snellen eye chart with brief head rotations. If you lose these vestibulo-ocular mechanisms, you will experience oscillopsia. To demonstrate what oscillopsia feels like, bob your head up and down without focusing on anything in particular; people with vestibular loss have to deal with this constant bouncy sensation all of the time.

Ear, nose, and throat specialists (ENTs) have elaborate methods for evaluating vestibulo-ocular mechanisms, whereas clinical neurologists evaluate vestibulo-ocular reflexes at the bedside in a more limited fashion. One setting is during the brainstem reflex examination of comatose patients through water irrigation of the ear canal (aka calorics); comatose patients are unable to visually fixate, which is important because visual fixation can interfere with the test. Let's use caloric testing to learn about vestibulo-ocular mechanisms.

Before you perform this test, make sure your patient's tympanic membranes are intact or you will inject water into their middle ears. First, you inject cold water into one ear canal at a time. The eyes will to slowly deviate toward the side of the cold water irrigation and then slowly drift back to midline. Warm water has the opposite effect; the eyes deviate away from the stimulus and then slowly drift back. The caloric vestibular response is from thermal convection on the semicircular canal in the vertical plane; it displaces the cupula, which stimulates eye movement. The position of the head determines which semicircular canal is in the vertical plane and thus the deviation of the eyes. When sitting straight up, the patient's horizontal semicircular canal is in a plane at a 30° angle to the Earth's horizontal. Tilt the patient's head back 60° and you move it into the vertical plane. It just so happens that most comatose patients are already lying in bed with their heads tilted back at this angle, anyway, so they are in the appropriate position for vestibulo-ocular testing.

Only do this test on comatose patients; alert patients will become sick, if you do it on them. However, if you did inject cold water into an alert patient (and the patient was able to suppress visual fixation) the eyes would rotate toward the side of the cold water injection and then flick back toward midline. The rotation is the slow phase and the quick saccadic movement back is the nystagmus. There is an acronym for the direction of the response to cold water irrigation, which is "COWS." It stands for "Cold Opposite, Warm Same." What is the problem with this acronym? It refers to the nystagmus and not the original eye deviation. Why is this a problem? This test is used on comatose patients and they do not exhibit a nystagmus response, only a slow-phase response.

We are able to use our fists to demonstrate the directionality of this pathway. Make your fists represent the peripheral labyrinths and your index fingers the direction of gaze. Point your fingers in a "V" shape toward one another. Cold water effectively turns off the vestibular labyrinth (i.e., it mimics a labyrinthine injury). Drop your right fist to show a right side peripheral vestibular lesion. Only the left vestibular labyrinth remains; it drives the eyes toward the right, toward the side of the lesion. On the contrary, warm water mimics a stimulatory effect and drives the eyes away from the side of irrigation. But vestibular stimulation is uncommon compared to vestibular injury so think about the cold water and not the warm water effect. We will diagram the vestibulo-ocular pathway later in the chapter.

During sustained rotation, *optokinetic* mechanisms keep the image stabilized on the retina and provide clarity of vision despite sustained rotation. Spin yourself in a swivel chair. What do you see? Periods of image clarity followed by a periods of image re-setting. We are able to test optokinetic mechanisms at the bedside with the subject sitting still with an optokinetic drum or strip of cloth, however. Have a subject count the stripes on the drum while it is rotated or on the cloth while it is moved across his/her field of vision. The subject will experience a feeling of self-rotation and will exhibit the characteristic eye movements of optokinetic tracking.

Optokinetic movements combine two important conjugate eye movements: smooth pursuit and saccadic nystagmoid eye movements. The smooth pursuit eye movements stabilize the moving image on the fovea and the saccadic eye twitches reset the eyes to the center of the orbit. To demonstrate smooth pursuit movements for yourself, hold your thumb in front of you and lock your vision on your thumbnail using visual fixation. Next, as you move your thumb in either direction, track it with your eyes. Your *smooth pursuit eye movements* allow you to keep it centered on the fovea.

As discussed, during sustained rotation, *involuntary corrective saccadic nystagmus* resets the eyes to their primary position, but *volitional saccadic eye movements* also exist. To demonstrate volitional saccadic eye movements, pick a target in your periphery and then with a quick dart of your eyes bring it into the center of your vision.

In all of the eye movement classes we have discussed so far, our eyes are driven in the same direction, but in vergence eye movements, they move in opposite directions (inward or outward) to bring a near or far target into focus. Demonstrate convergence eye movements, which are when the eyes rotate inward (the right eye toward the left and the left eye toward the right). First, fixate on your thumbnail. Then, bring your thumb in towards you and your eyes will exhibit *convergence eye movements*. If you move your thumb away from you, your eyes will rotate outward, known as *divergence eye movements*.

The two general classes of eye movements: conjugate and vergence, project through different brainstem pathways, which we will draw, now. Later we will draw their diverse initiation centers.

Begin our drawing of the final common pathway of *conjugate horizontal eye movements* with a coronal section through the brainstem. At the top of the diagram, draw an axial section through a pair of eyes. Attach a *medial rectus muscle* to the right eye and a *lateral rectus muscle* to the left eye. Next, in the left side of the mid-pons, draw the *left abducens nucleus of cranial nerve 6*, just off the midline. Divide the abducens nucleus into the lateral-lying *abducens motoneurons* and the medial-lying *abducens internuclear neurons*. Show the motoneurons innervate the ipsilateral lateral rectus muscle.

Next, draw the *medial rectus subdivision* of the *right oculomotor nucleus of cranial nerve 3* lying just off midline in the right side of the midbrain. Show the left abducens internuclear neurons project fibers that cross midline, ascend the brainstem along the *right medial longitudinal fasciculus*, and terminate in the right oculomotor nucleus. Finally, show fibers from the oculomotor nucleus exit the brainstem and innervate the ipsilateral medial rectus muscle. This completes the final pathway for horizontal conjugate eye movements.

In short, the abducens nucleus is responsible for lateral rotation (aka abduction) of its ipsilateral eye and also projects to the opposite third nerve nucleus, which provides medial rotation (aka adduction) of the opposite eye. The medial longitudinal fasciculus is the white matter tract the abducens internuclear fibers ascend to reach the oculomotor nucleus. This system allows the eyes to remain yoked during horizontal conjugate eye movements.

One important clinical syndrome where horizontal conjugate eye movements become unyoked is called *internuclear ophthalmoplegia* (aka *INO* or *MLF syndrome*). As its name implies, internuclear ophthalmoplegia involves paralysis of eye movements from disruption of the projection fibers between the sixth and third nerve nuclei. It results from disruption of one of the medial longitudinal fasciculus tracts and often occurs from a demyelinating lesion, stroke, or tumor.

On evaluation, there is total paralysis of the adducting eye and horizontal nystagmus of the abducting eye. The patient may experience symptoms of double vision as the abducting eye attempts to rotate laterally and the patient may also feel an illusion of oscillatory, or bouncy, movement of the environment (we demonstrated oscillopsia earlier). Both the sign of the abducting eye nystagmus as well as the symptoms of diplopia and oscillopsia will often resolve within a week of the injury.

What would occur if both medial longitudinal fasciculus tracts were injured? Would either eye be able to adduct? No. Could both eyes still abduct? They could, but they both would have nystagmus. Bilateral internuclear opthalmoplegia lesions are not uncommon because the medial longitudinal fasciculus tracts run close together in the midline of the brainstem. Typically, demyelinating plaques, hemorrhages, or tumors are the cause since they can extend across the midline; on the contrary, strokes are generally restricted to unilateral vascular territories.

Another clinical syndrome that involves the final common pathway for conjugate eye movements is the *one-and-a-half syndrome*, which often results from an injury to the abducens nucleus and the medial longitudinal fasciculus on the same side. What are the resultant eye movements in a right one-and-a-half syndrome, for instance, a right abducens and right medial longitudinal fasciculus lesion? Right eye abduction is paralyzed due to injury to the right abducens motoneurons. Left eye adduction is paralyzed due to injury to the right abducens internuclear neurons. Left eye abduction is intact, but with nystagmus from the right medial longitudinal fasciculus lesion. Right eye adduction is paralyzed from injury to the right medial longitudinal fasciculus. So of the two complete potential horizontal eye movements, the only intact movement is left eye abduction (i.e., left eye lateral gaze), and it has nystagmus. Thus, one-and-a-half of the two complete eye movements are impaired, which is why it is called one-and-a-half syndrome.

An additional cause of one-and-a-half syndrome is a lesion in the para-pontine reticular formation, which we will discuss along with the control centers for conjugate eye movements. At that time, you will see how a lesion to it along with an ipsilateral medial longitudinal fasciculus lesion will also result in one-and-a-half syndrome.

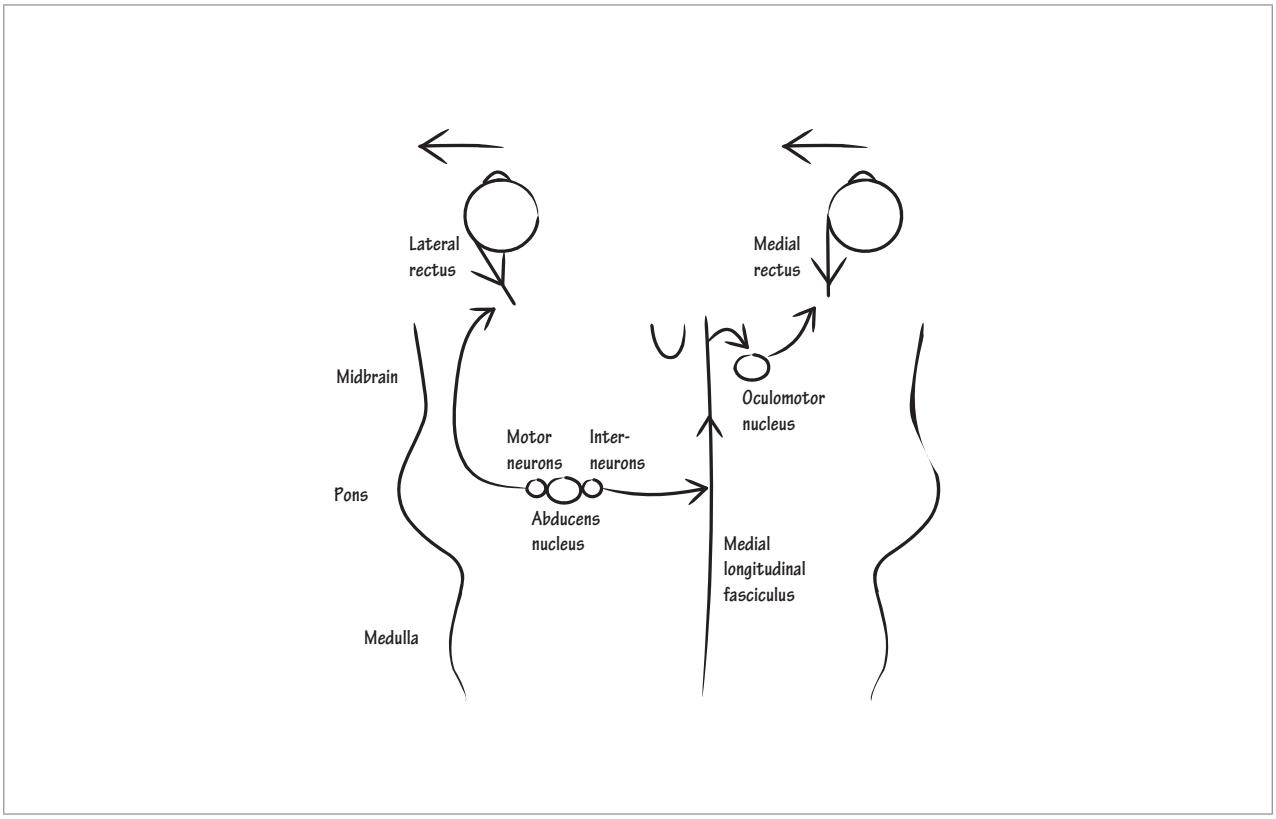

Figure 34-1 Horizontal eye movements in coronal section

Now, let's create a diagram for vertical eye movements. Here, we will limit our diagram and discussion to the location of the nuclei involved in vertical eye movements and to how anatomical lesions differentially affect up and down gaze; with certain exception, the vertical pathways, themselves, are cumbersome and poorly understood.

Other than the nucleus of the posterior commissure, which lies along the dorsal surface of the superior midbrain, the nuclei for vertical conjugate eye movements are all ventral to the cerebral aqueduct. Draw a sagittal section through the midbrain. On the superior–dorsal surface of the midbrain, label the *nucleus of the posterior commissure*. Anterior to it, in front of the cerebral aqueduct, draw the *rostral interstitial nucleus of the medial longitudinal fasciculus* (riMLF). Then, along the rostral–caudal plane of the riMLF, in descending order, draw the *interstitial nucleus of Cajal*, *oculomotor nucleus*, and *trochlear nucleus*. These nuclei complete the nuclei of the vertical eye movements; notice that they are confined to the midbrain.

Indicate, now, that interruption of the fibers that run through the posterior commissure and, more specifically, the nucleus of the posterior commissure, itself, result in *loss of upgaze with preservation of downgaze*. Many nuclei are involved in upgaze, but the nucleus of the posterior commissure is the one site where upgaze can be paralyzed without any downgaze paralysis.

Upgaze paralysis occurs as part of the dorsal midbrain syndrome. As its name implies, the dorsal midbrain syndrome involves disruption of the fibers and nuclei on the dorsal surface of the midbrain. It is easy to imagine how increased cerebrospinal fluid pressure in the quadrigeminal plate cistern, which overlies the dorsal midbrain, will cause downward pressure on the dorsal midbrain or how a pineal-based tumor or cyst could grow and compress the dorsal midbrain. Indeed, these are two of the more common causes of dorsal midbrain syndrome. You can remember this syndrome by the expression the "setting sun sign," which describes the tonic downward deviation of the eyes that occurs acutely in dorsal midbrain syndrome.

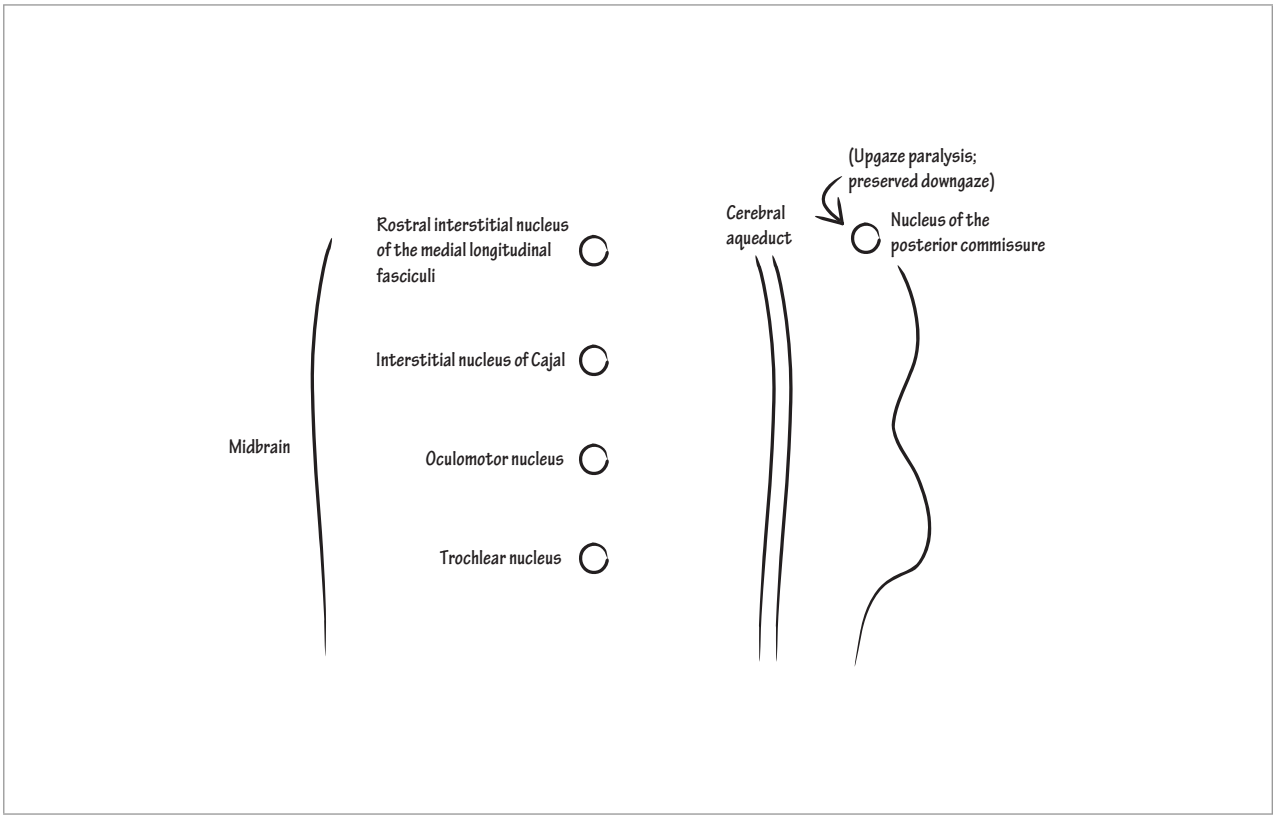

Figure 34-2 Vertical eye movement in sagittal section: upgaze paralysis

In progressive supranuclear palsy, an atypical Parkinsonian disorder, downgaze is affected before upgaze. Here, we will show how upgaze vertical eye movement is preserved in the presence of downgaze paralysis (for this diagram, we will need to show a few simple fiber pathways). In this section, we will introduce the vertical burst and gaze holding centers, but we will discuss their role in eye movements in greater detail later in the chapter. Feel free to skip to those discussions while you work through this drawing.

Draw a coronal brainstem section through the midbrain just ventral to the cerebral aqueduct. Note that the nucleus of the posterior commissure lies dorsal to the plane of this coronal section so it is not shown here. At the superior surface of the diagram, draw the *bilateral rostral interstitial nuclei of the medial longitudinal fasciculi* and, in descending order, draw the paired *interstitial nuclei of Cajal*, the paired *oculomotor nuclei*, and then the paired *trochlear nuclei*.

Divide the oculomotor and trochlear nuclei into *upgaze* and *downgaze subnuclei*. The oculomotor subnuclei actually combine into one giant nuclear complex, which we drew in the "Somatomotor Cranial Nerves" chapter, but we separate them here for practical purposes. Label one of the rostral interstitial nuclei of the medial longitudinal fasciculi as the major *burst command center* for vertical conjugate eye movements; draw fibers from the command center to the *bilateral upgaze subnuclei* and to *unilateral downgaze subnuclei* in both the oculomotor and trochlear nuclei (don't worry about whether the fibers project ipsilaterally or contralaterally; that is beyond our purposes, here). Indicate that injury to one of the rostral interstitial nuclei of the medial longitudinal fasciculi results in *downgaze paralysis with preservation of upgaze eye movements*. This is because there is redundant innervation to the upgaze nuclei; each rostral interstitial nucleus innervates both of the oculomotor subnuclei for upgaze, but they each only unilaterally innervate the oculomotor and trochlear subnuclei for downgaze. In reality, pure downgaze paralysis with upgaze preservation from a rostral interstitial medial longitudinal fasciculus lesion is rare. More commonly, it results in contralesional torsional nystagmus.

Lastly, label the interstitial nuclei of Cajal as the *gaze-holding center* for vertical eye movements. Many different manifestations occur with a lesion in the interstitial nucleus of Cajal but perhaps the most relevant is gaze-evoked nystagmus.

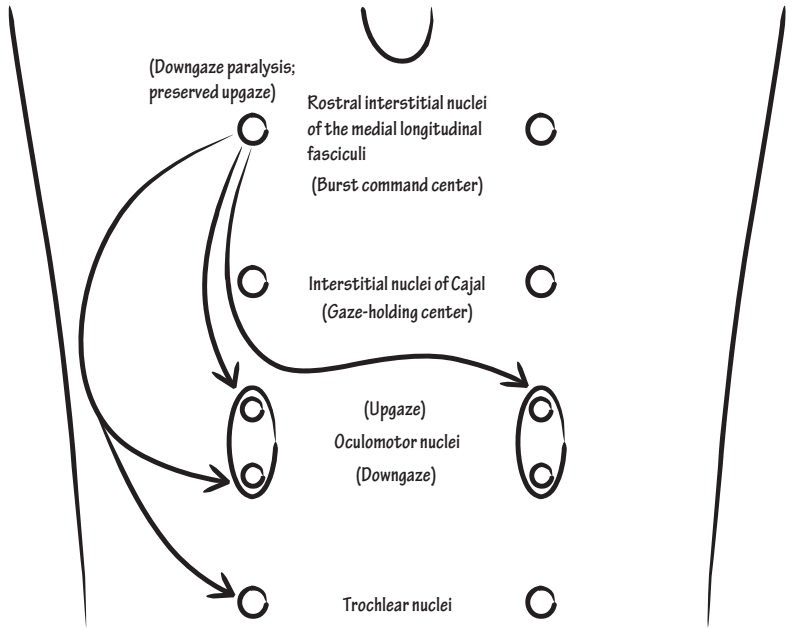

Figure 34-3 Vertical nuclei in coronal section: downgaze paralysis

Now, let's remind ourselves of what vergence eye movements are. Follow your thumbnail toward your nose. As you do, both of your eyes turn inward to keep the image on similar regions of each retina. To demonstrate what happens when they fail to converge, do the following. Hold both fingertips out in front of you. Visually fixate on one of them. The peripheral fingertip will be mildly doubled. Continue to fixate on the stationary fingertip as you bring the peripheral one toward you; the degree of its doubling will increase. Binocular disparity (aka diplopia), such as what you've experienced, results when the eyes fail to *converge* with near vision.

Convergence eye movements play a role in what is called the near triad or near response. The other features of the triad are the pupillary near response (different from the pupillary light reflex) and the lens thickening response (aka the accommodation reflex); together they both improve image resolution. While lens thickening is imperceptible to the examiner, evaluation of pupillary constriction to near objects is one of the key aspects of the neurologic examination.

To demonstrate the *near triad* (aka *near response*), ask a partner to visually fixate on an object as you bring it toward his/her nose. In addition to eye convergence, you will notice the pupils constrict. Pupillary constriction optimizes light ray diffraction for image resolution. Lens thickening (aka the accommodation reflex) imperceptibly occurs from intraocular ciliary muscle contraction and reduces image blur. Now, let's reexamine the appearance of the peripheral image. Again, hold your finger out in front of you. While you read this text, pay attention to the image of your fingertip in the periphery. In addition to being doubled, it is also hazy. Your pupils and your lens are adjusted for the words on the page and not for the peripheral image. Images farther or closer to the text are naturally blurred.

An important distinction between the anatomical pathways for conjugate and convergence eye movements is that the conjugate pathway loops into the pons and lower half of the brainstem, whereas the convergence pathway remains in the upper brainstem. Inward eye movements rely on the medial recti muscles, which are innervated by the third nerve nuclei, which lie within the midbrain. Thus, there is no reason for the convergence eye movement pathway to descend through the brainstem in order to activate the eyes to turn inward. Divergence eye movements have a separate pathway, however. Pontine tegemental nuclei (e.g., the nucleus reticularis tegmenti pontis) activate the abducens nucleus for divergence, but we leave them out of our diagram for practical purposes. The convergence movements are of more interest to us, since clinically we routinely test inward movements with the near triad when we ask patients to follow an object toward their nose. We use convergence movements to distinguish middle longitudinal fasciculus lesions from oculomotor or medial rectus lesions as we will discuss at the end of this section.

To draw the near triad, let's begin with an exaggerated axial section through the midbrain; this is the brainstem control center for convergence eye movements. We will use this same set-up when we draw the pupillary light reflex in the next section. In the midline of the midbrain, draw the circular *cerebral aqueduct*. Lateral to it, show the *supraoculomotor area*—the main command center for convergence movements. It projects to *oculomotor motoneurons* adjacent to it.

The near triad involves pupillary constriction as well as convergence, so next, draw the bilateral *Edinger–Westphal nuclei* of the oculomotor nucleus; they stimulate pupillary constriction. Then, draw axial sections through both eyes. Along the medial aspect of one eye draw a *medial rectus* muscle, which produces inward eye movement, and behind the other, draw the *ciliary ganglion*—it innervates the *pupillary constrictor muscles* (aka *sphincter pupillae*), which produce pupillary constriction.

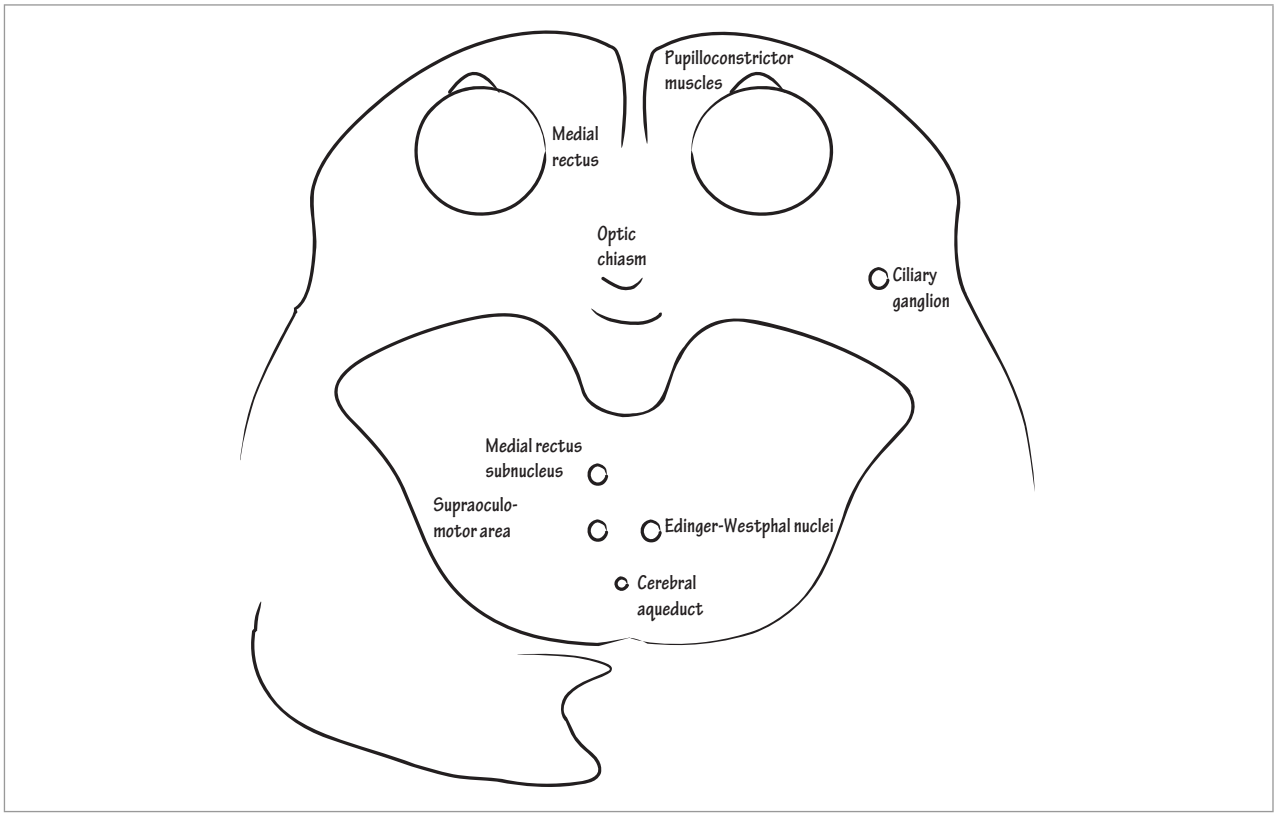

Figure 34-4 Incomplete near triad in axial section

Next, draw a *lateral geniculate nucleus* along the posterolateral aspect of the midbrain. Then, draw the *primary occipital cortex* (aka *striate cortex*) in the postero-medial occipital lobe. It projects to the visual association areas, which comprise the secondary occipital cortex, parietal, cerebellar, and frontal cortices. These cortices project to the supraoculomotor area in the midbrain.

Now, let's complete the pathways for the near triad. Draw afferent fiber pathways from the back of each retina to the *lateral geniculate nucleus*. Be sure to show that the afferent nasal fibers cross within the *optic chiasm*. Next, show projection fibers from the lateral geniculate nucleus to the primary occipital cortex. Fibres project from the primary occipital cortex to the visual association areas, which we leave out for simplicity; then, from the visual association areas to the supraoculomotor area; then, from the supraoculomotor area to the oculomotor nucleus, which projects to the medial rectus muscle and produces inward eye movement (the same occurs on the opposite side, so both eyes turn inward).

Now, go back to the supraoculomotor area and show projections to the bilateral Edinger–Westphal nuclei. Indicate projections to the ciliary ganglion and then to the pupillary constrictor muscle, which produces pupillary constriction. Note, the projections from the supraoculomotor nucleus to the bilateral Edinger–Westphal nuclei are a simplified version of the actual projections, which are beyond the scope of this book.

The pupillary light reflex involves many of the same nuclei and fibers as the near triad; it produces parasympathetic-induced pupillary constriction. Like the near response, its anatomical pathway remains in the upper brainstem. We described the sympathetic pathway for pupillary *dilation* in the "Peripheral Autonomic Nervous System" chapter, but we will draw the parasympathetic pupillary light reflex, here, because it relates anatomically to the near triad.

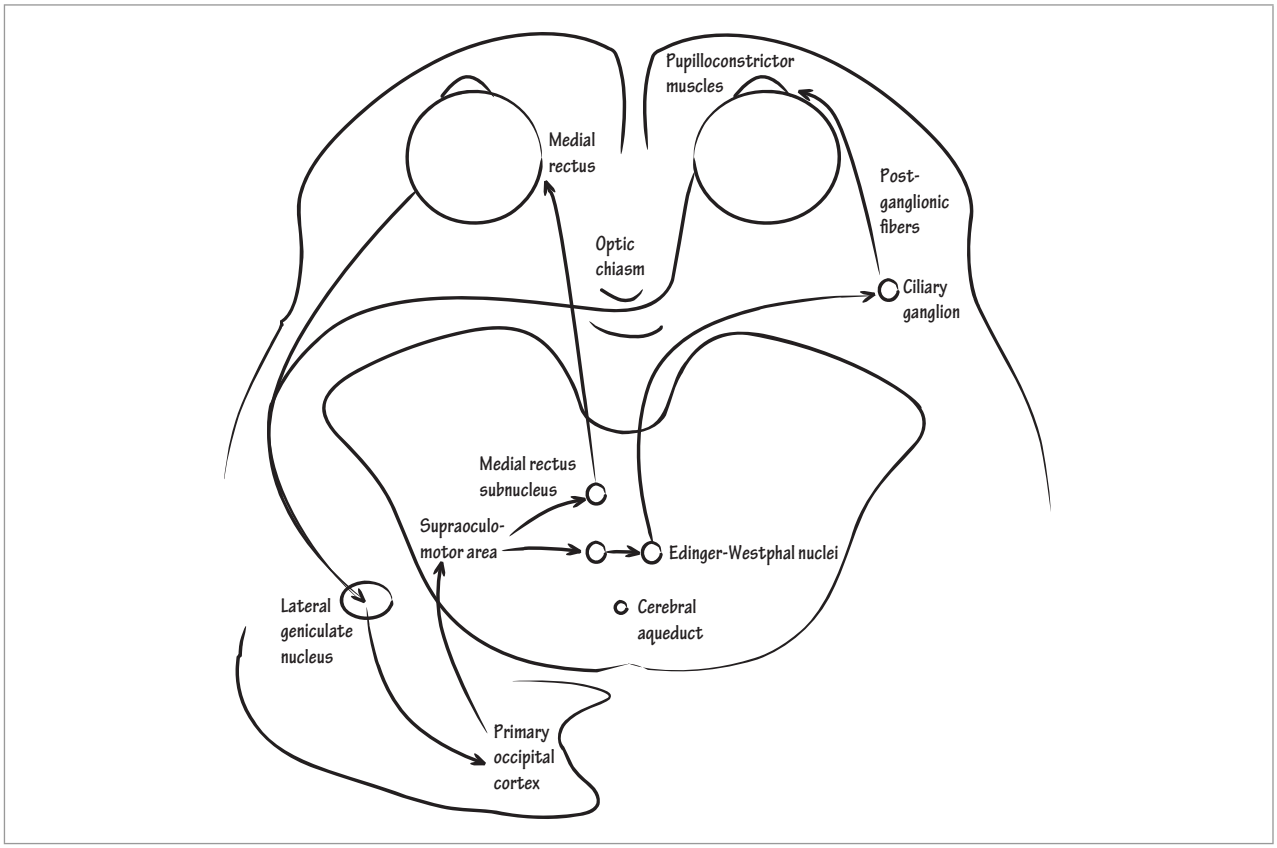

Figure 34-5 Complete near triad in axial section

Begin our set-up for the *pupillary light reflex* as you did for the near triad; first, draw an exaggerated midbrain. Include the cerebral aqueduct and the bilateral Edinger–Westphal nuclei. Here, we do not need the supraoculomotor area or the medial rectus oculomotor subnuclei. Instead, draw the *pretectal olivary nucleus* (aka *olivary nucleus of the superior colliculus*) in the posterolateral midbrain. The posterolateral region of the midbrain is the pretectal area. The term "tectum" refers to the posterior brainstem. From anterior to posterior, the brainstem is arranged as the basis, tegmentum, and tectum. Label the posterior midbrain as the *posterior commissure*. It carries projections from the pretectal olivary nucleus to the opposite Edinger–Westphal nucleus creating redundancy within the pupillary light reflex pathway.

Set up the rest of the diagram the same as the near triad but exclude the lateral geniculate nucleus, primary occipital area and visual association areas. The optic tracts synapse directly on the pretectal olivary nuclei, anterior to the lateral geniculate nucleus.

Now, draw the afferent optic nerve and tract fibres destinated for the left cerebral hemisphere. Show their projections through the pretectal area to the olivary pretectal nucleus. From the olivary pretectal nucleus, show bilateral projections to the Edinger–Westphal nuclei. Then, show one of the Edinger–Westphal nuclei projects to its ipsilateral ciliary ganglion and from there to the pupillary constrictor muscles for pupillary constriction.

To demonstrate the pupillary light reflex, shine a bright light on one of your partner's eyes. What happens? Both pupils constrict. Why? For two reasons; first, when light strikes the retina, the temporal retina projects ipsilaterally and the nasal retina projects contralaterally. Thus, there is bilateral perception of the light in the proximal portion of the pathway. Second, each pretectal olivary nucleus projects bilaterally to the Edinger–Westphal nuclei, so redundancy exists in that step of the pathway, as well.

Now, review our discussion of dorsal midbrain syndrome, which causes the "setting sun" sign of upgaze paralysis with forced downgaze. Considering what we learned about the anatomy of the pupillary light reflex, might it also be affected in dorsal midbrain syndrome? Indeed, in dorsal midbrain syndrome, the pupils react sluggishly to light but normally to near response. Similarly, patients with syphilis can develop Argyll–Robertson pupils, which react to near accommodation but not illumination. This is presumably because of injury to the pre-tectal and posterior commissural areas with preservation of the supraoculomotor area.

As a final point about dorsal midbrain syndrome, patients also develop convergence–retraction nystagmus, that is, when they try to initiate upward eye movements, they have reflex convergence eye movements. Considering the anatomy of the upgaze center and its proximity to the center for eye convergence, it is understandable that upgaze and convergence could become inappropriately yoked when there is damage to the dorsal midbrain.

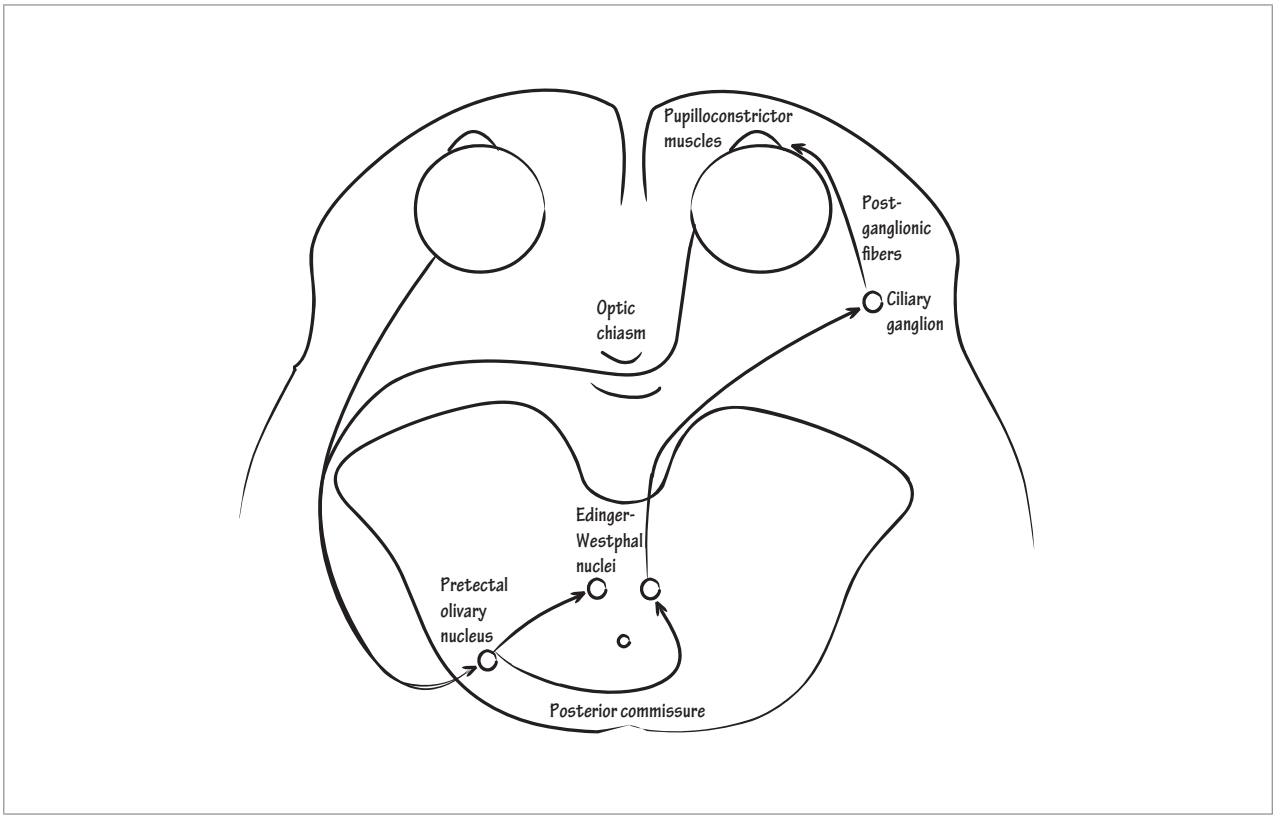

Figure 34-6 Pupillary light reflex in axial section

We have now completed the final common pathways for conjugate and convergence eye movements and have drawn the pathways for the near response and pupillary light reflex. In this next section, we will add cortical and infracortical input to the final common pathways to produce the saccadic, vestibulo-ocular, and smooth pursuit eye movements we introduced at the beginning of the chapter.

To diagram the *horizontal saccadic eye movements*, draw a coronal brainstem section and include the *abducens nucleus* in the left pons. Also, draw a lateral right cerebral hemisphere in the corner of the diagram. Label the *frontal eye field* area at the intersection of the superior frontal sulcus and the precentral sulcus. The frontal eye fields lie in Brodmann area 8 in macaque monkeys—the animal model most commonly used to study the visual pathways, but in humans, the frontal eye fields lie in Brodmann areas 4 and 6. This is why you will see inter-textual contradictions regarding their location.

Before we continue the diagram, let's demonstrate the actions of the frontal eye fields with our fists. Your fists represent the cerebral hemispheres. Hold them in front of you and point your index fingers inward in a "V" to show that the right cerebral hemisphere drives the eyes to the left and the left cerebral hemisphere drives the eyes to the right. When a destructive lesion, such as a stroke, occurs in the right frontal eye field, which direction do the eyes deviate? Set your right hand at your side; the only eye movement that remains is from your left hemisphere, which drives your eyes to the right. Thus, with a destructive right frontal lesion, the eyes look to the right.

What happens when an excitatory event, such as a seizure, occurs in your right frontal eye field? Shake your right fist to show that the right index finger is supercharged and overpowers the left; as a result, the eyes are forced to the left.

Now, let's explain why the eyes deviate this way. Fibers from the frontal eye fields project both directly and indirectly to the brainstem. A simple construct for the direct pathway is as follows: the right frontal eye field sends descending fibers to the left abducens nucleus. Then, the internuclear fibers of the left abducens project via the right medial longitudinal fasciculus to the right oculomotor nucleus, which innervates the right medial rectus. Meanwhile, the motor neurons of the left abducens nucleus project to the left lateral rectus. Thus, when stimulated, both eyes deviate to the left.

For important mechanistic reasons, both the direct and indirect pathways are more complicated than we have discussed here, but the overall nature of the horizontal saccadic eye movements is understood from this model. If you get lost in the details of the following section, refer back to it.

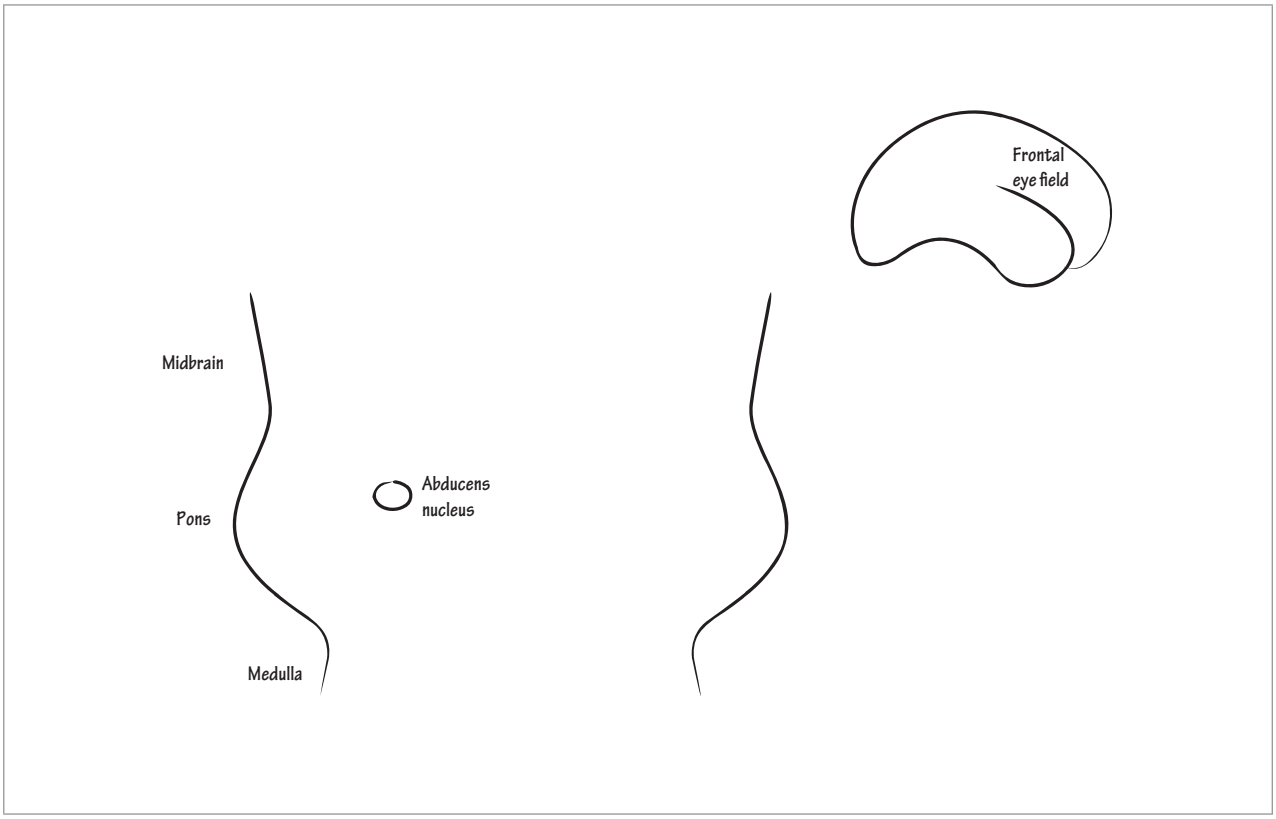

Figure 34-7 Incomplete conjugate horizontal eye movements in coronial section

In your diagram, show the direct pathway projection fibers from the *right frontal eye field*; they descend through the brainstem, decussate in the midbrain, and synapse in *burst neurons* within the *paramedian pontine reticular formation* rostral to the abducens nucleus. We alluded to this region in our discussion of one-and-a-half syndrome. It is a central pontomedullary region that contains rostrally located burst neurons and caudally located inhibitory neurons. The burst neurons of the paramedian pontine reticular formation are analogous to those of the rostral interstitial medial longitudinal fasciculi for vertical eye movements and we will soon explain what they do.

The indirect pathway sends fibers to the burst neurons through the superior colliculus. Show that projection fibers from the right frontal eye field synapse in the ipsilateral *superior colliculus* and then project to burst neurons in the contralateral paramedian pontine reticular formation. For a long time, the importance of the superior colliculus in saccadic eye movements went unrecognized because isolated lesions of the superior colliculus are rare, but experimental inactivation of the superior colliculus has shown that it is actually more significant in saccadic eye movements than the direct pathway. The superior colliculus, itself, is divided into a dorsal "visuosensory" division and a ventral "motor" division. The dorsal division receives an organized retinotopic map of the contralateral visual field and the ventral division sends efferent projections to the brainstem to stimulate eye movements.

Now, draw projection fibers from the burst neurons to their ipsilateral *abducens nucleus*; these are excitatory fibers. Then, draw *inhibitory cells* caudal to the abducens nucleus and *omnipause cells* at the level of the abducens nucleus, in midline. Show *burst neuron* projection fibers to the ipsilateral inhibitory cells, and then, projection fibers from the inhibitory fibers to the *contralateral abducens nucleus*. These inhibitory projections prevent the contralateral abducens nucleus from firing.

Thus, burst neurons directly excite their ipsilateral abducens nucleus and, through the inhibitory cells, indirectly inhibit their contralateral abducens nucleus. As a result, both abducens nuclei are prevented from firing at the same time.

Now, draw inhibitory projection fibers from the *omnipause cells* to the *burst neurons* and *inhibitory neurons*. Omnipause cells are tonically activated except immediately before and during saccadic eye movements (i.e., except when the burst neurons are needed to initiate an eye movement). When the omnipause cells are injured, there is opsoclonus, which are saccadic oscillations without intersaccadic pauses. Opsoclonus can occur from brainstem infection or paraneoplastic disease (a neurologic disorder secondary to systemic cancer). Jerk your eyes in multiple directions to demonstrate opsoclonus (don't get a headache doing it!). In horizontal gaze, opsoclonus is referred to as ocular flutter or saccadomania. Current thinking is that opsoclonus is more related to aberrant omnipause circuitry than actual destruction of the nucleus, itself.

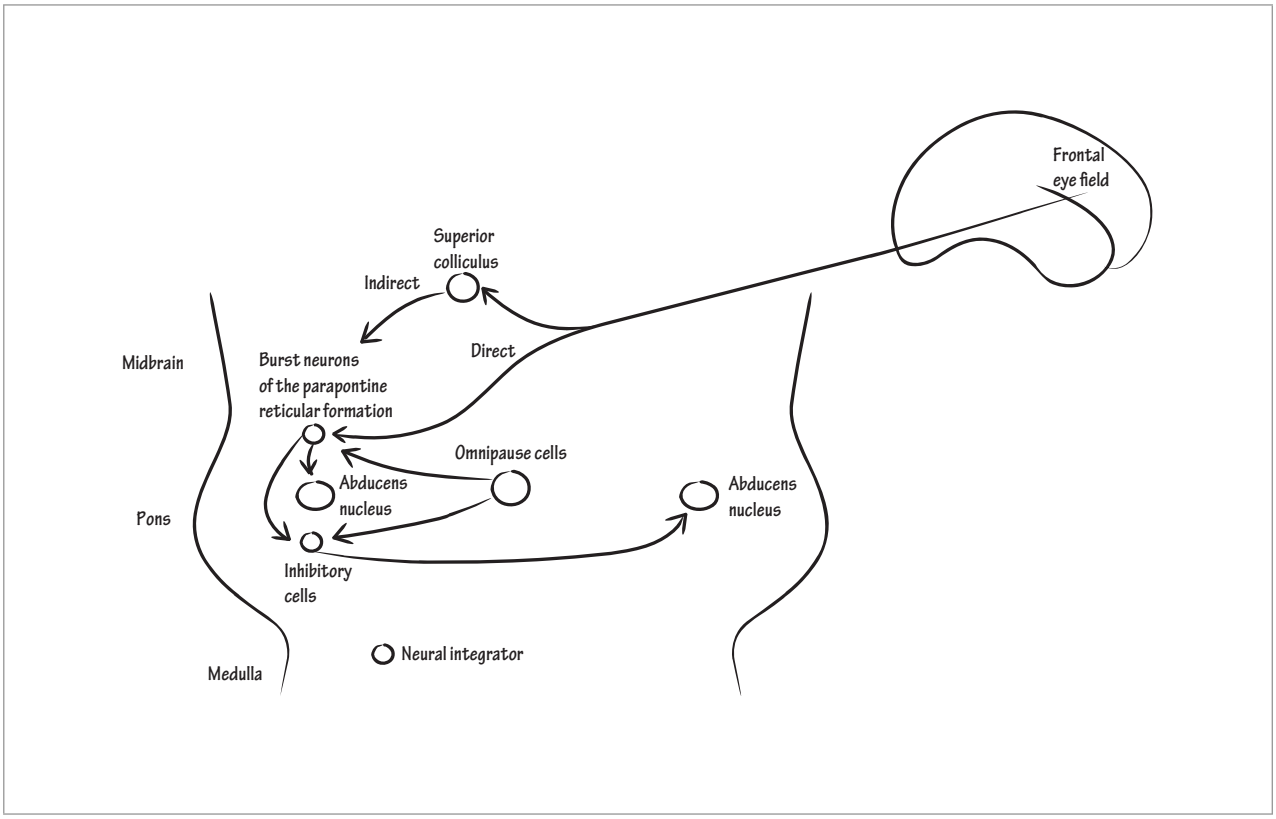

Figure 34-8 Complete conjugate horizontal eye movements in coronal section

Let's review the key anatomical structures we have discussed so far. The frontal eye fields send fibers via the direct and indirect pathways to the contralateral burst neurons in the paramedian pontine reticular formation, which are tonically inhibited by omnipause cells. When a saccadic movement is planned, the omnipause cells deactivate and the burst cells are uninhibited. They send excitatory impulses to the ipsilateral abducens nucleus and also to inhibitory neurons, which inhibit the contralateral abducens nucleus from firing. The activated ipsilateral abducens nucleus excites the ipsilateral lateral rectus muscle and, indirectly, the contralateral medial rectus muscle through the final common pathway for horizontal eye movements. The end result is that the eyes are deviated away from the activated frontal eye field.

The above discussion addresses two of the three important features of saccadic eye movements: the inter-eye movement *pause* and the *pulse* (i.e., the phasic muscle contraction that moves the eyes quickly). But what about the tonic contraction of the eye muscles that holds them steady within the orbit? It is called the *step*, and it requires the *neural integrator*, which lies in the rostral medulla, medial to the vestibular nucleus. Its position next to the vestibular nucleus is appropriate because, as we will draw, the vestibular nucleus is an important mediator of eye movements. The neural integrator for horizontal gaze holding is the prepositus hypoglossi nucleus, which lies in the perihypoglossal nuclear complex. For vertical gaze holding, the neural integrator is the interstitial nucleus of Cajal. A leaky neural integrator causes gaze-evoked nystagmus because visual fixation is disrupted.

Now, let's draw the *vestibulo-ocular eye movements*. First, show the vestibular nuclei lie at the pontomedullary junction. Then, draw projection fibers from the right *peripheral vestibular labyrinth* to the right *medial vestibular nucleus*. Next, show the medial vestibular nucleus projections to the contralateral *abducens nucleus*. From there, fibers are sent along the final common pathway for conjugate eye movements. The abducens nucleus innervates its lateral rectus muscle (contralateral to the vestibular labyrinth) and sends fibers via the medial longitudinal fasciculus to the contralateral oculomotor nucleus to innervate the medial rectus (ipsilateral to the vestibular labyrinth). Thus, stimulation of the right vestibular labyrinth causes the contralateral lateral rectus and ipsilateral medial rectus muscles to drive the eyes to the left (away from the right-side labyrinth).

To demonstrate the vestibulo-ocular response, fix your eyes on a target and turn your head to the right. Your eyes remain on the target but shift to the left within their orbits. Your peripheral vestibular labyrinths tell your eyes how much they need to move to compensate for your head turn to keep the image on the fovea. Imagine that by turning your head to the right, you are activating your right inner ear to drive your eyes to the left and inhibiting your left inner ear from driving your eyes to the right.

We are able to test the integrity of this system in comatose patients with the cold water calorics test we mentioned at the beginning of the chapter or simply by rotating the patient's head in the horizontal plane. With an intact vestibulo-ocular system, the eyes glide within their orbits to counteract the head turn. This is called the doll's eyes reflex (aka oculocephalic response). Unfortunately, it is an anachronism because doll's eyes today are fixed within their orbits and do not glide. Modern dolls actually give the appearance of a dysfunctional vestibulo-ocular system; if you turn their heads, their eyes remain in primary gaze (they stay fixed within the orbit rather than glide in the opposite direction of the head turn as they should).

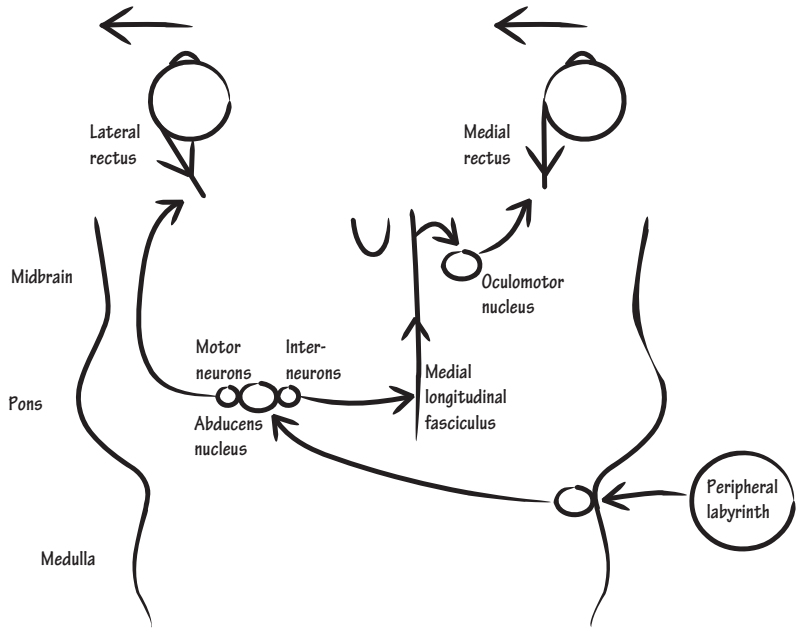

Figure 34-9 Vestibulo-ocular eye movement pathway in coronal section

Let's, now, turn our attention to smooth pursuit eye movements. Smooth pursuit circuitry stimulates the eyes to move in the direction of the activating hemisphere (i.e., the right hemisphere initiates eye movements to the right and the left to the left). These movements are stimulated by the V5 visual cortex, which projects both directly and indirectly to the ipsilateral dorsolateral pontine nucleus. Through a polysynaptic pathway, the dorsolateral pontine nucleus indirectly activates the ipsilateral abducens nucleus, which drives the eyes toward the original activating hemisphere.

To draw this pathway, let's first draw a lateral face of a cerebral hemisphere. Label the occiput as *V1* (aka the *striate cortex*). Visual information passes from the lateral geniculate body in the thalamus through the optic radiations to V1. Indicate V1 projects to *V5* (aka *middle temporal* and *middle superior temporal areas*), which lies at the temporal–parietal–occipital junction, just posterior to the superior temporal sulcus. From there, V5 projects both directly and indirectly to the ipsilateral dorsolateral pontine nucleus in the dorsolateral pons. First, show the direct projection from V5 to the *dorsolateral pontine nucleus*. Then indicate that through the indirect pathway, V5 projects to the *frontal eye field*, at the junction of the precentral sulcus and superior frontal sulcus, and subsequently, to the ipsilateral dorsolateral pontine nucleus. From the dorsolateral pontine nucleus, show fibers project across midline to the contralateral *vestibulocerebellum* (flocculonodular lobe) and then back across midline to the *abducens nucleus*. The abducens nucleus then activates the final common pathway for conjugate eye movements, and the eyes deviate toward the cortical side of activation.

The bilateral posterior cerebral arteries supply the occipital pole, which is where macular representation exists. If a target moves at a predictable rate, it will stay in the cortical macular area where there is this double arterial supply. Thus, even in large posterior circulation strokes, macular representation will often remain intact, because of its bilateral vascular supply. And, accordingly, so will smooth pursuit eye movements. On the contrary, a restricted lesion in V5 will impair ocular tracking without causing more widespread visual deficits.

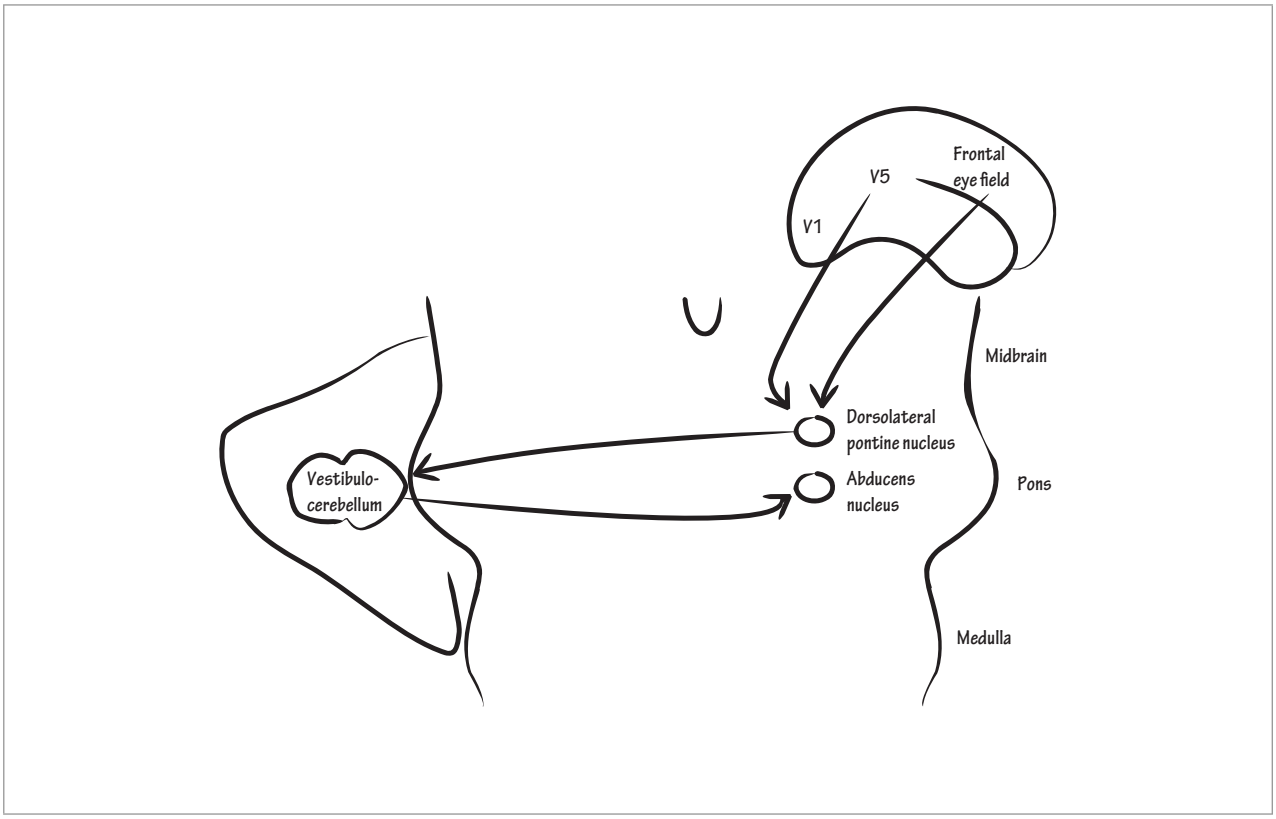

Figure 34-10 Smooth pursuit eye movements in coronal section

Central Auditory Pathways

THE CENTRAL AUDITORY pathway originates in the cochlear nuclei, forms multiple synapses as it ascends the brainstem, synapses in the diencephalon, and terminates in the auditory cortex. Interestingly, each cerebral hemisphere receives similar input from both cochlear nuclear complexes. So what does this mean, clinically, when there is a unilateral lesion to any of the steps in the central auditory pathway? It means that hearing is preserved from the duplication of auditory information in the contralateral cerebral hemisphere. Why does the auditory system have this central duplication of sensory information when other sensory systems, such as the visual system and somatosensory system, do not?

Consider the peripheral receptors of the visual and somatosensory systems. They are topographically designed to encode for stimulus localization. But this is not the case for the cochlea; it is arranged tonotopically rather than topographically. The base of the cochlea encodes high-frequency sounds and the apex encodes low-frequency sounds. This tonotopic cochlear arrangement informs the brain about sound frequency but not location; therefore, sound localization must occur through other means.

How can each cerebral hemisphere use information from both cochlea to determine the location of sound? Listen for a sound. Do you think it is the same at both of your ears? No, there are differences in its time of arrival and also its sound intensity at each ear. These are the two main interaural (between ear) differences: the interaural time difference (ITD) and the interaural level difference (ILD), where "level" refers to sound level or sound intensity. The auditory system relies on these features for binaural localization of sound, and that is probably why there is duplication of auditory information in the cerebral cortices.

The above argument suggests that sound localization must be binaural. But plug one of your ears, close your eyes, and snap your fingers at different places in space. Can you still localize the sound stimulus? Probably pretty well. Of course, there are sensory cues coming from the position of your arm in space that we are unable to remove, but there are also properties of the sound that allow it to be localized through the monaural sound localization system. In monaural sound localization, the outer ear shapes the sound as it transfers it to the ear canal in order to determine its directional plane. This process is called the head-related transfer function; it involves filtering of sounds by the outer ear in order to provide spectral cues for monaural sound localization, and its central anatomical pathway involves a unilateral projection from each cochlear nucleus.

In summary, each hemisphere receives similar but not identical auditory information from both cochlea. Clinically, it is difficult to appreciate a central auditory pathway lesion because of central duplication of most of the tracts, but not all of them are duplicated and we will want to account for their varying degrees of duplicity in our diagram. In order to avoid getting bogged down in the intricacies of the auditory pathways, however, we will draw the auditory system in two stages: first, we'll draw its nuclei, and second, its tracts.

Before we begin our first diagram, let's consider a common clinical application of the auditory system:

the brainstem auditory evoked response. In brainstem audiometry, a click stimulus generates a cochlear potential; it initiates a sequential response from each of the auditory nuclei, which is recorded in waveform format. Response amplitude is on the *Y*-axis and time latency is on the *X*-axis. The stimulus generates a downward deflection, and then a wave is formed for each step in the auditory pathway, that is, the auditory nerve, cochlear nucleus, superior olivary nucleus, inferior colliculus, medial geniculate nucleus, and finally, the transverse gyri of Heschl. There is also a response in the lateral lemniscus, which is the pathway for fibers from the superior olive to the inferior colliculus, which we will draw next.

Neurophysiologists use brainstem response recordings to determine the specific site of interruption of impulses through the central auditory pathway. Brainstem audiometry is an evoked potential test, and evoked potential tests for the visual and somatosensory sensory systems also exist. These tests are targeted to specific sensory systems but are often used to cast a broad net to capture any subclinical disease, such as asymptomatic abnormalities in multiple sclerosis.

Before we begin our first drawing, we should mention that an important component of the auditory system is the preservation of tonotopy (localization of tone) throughout the auditory system. The cochlear nuclei receive a range of low to high frequency sounds. Their anterior portion is dedicated to low frequency (apical) sounds, whereas their posterior portion is dedicated to high frequency (basal) sounds. Spherical bushy cells respond to low-frequency sounds and are sensitive to interaural time differences, whereas globular bushy cells respond to high-frequency sounds and are believed to mediate interaural level differences. In this way, there is a relationship between tonotopy and binaural localization of sound.

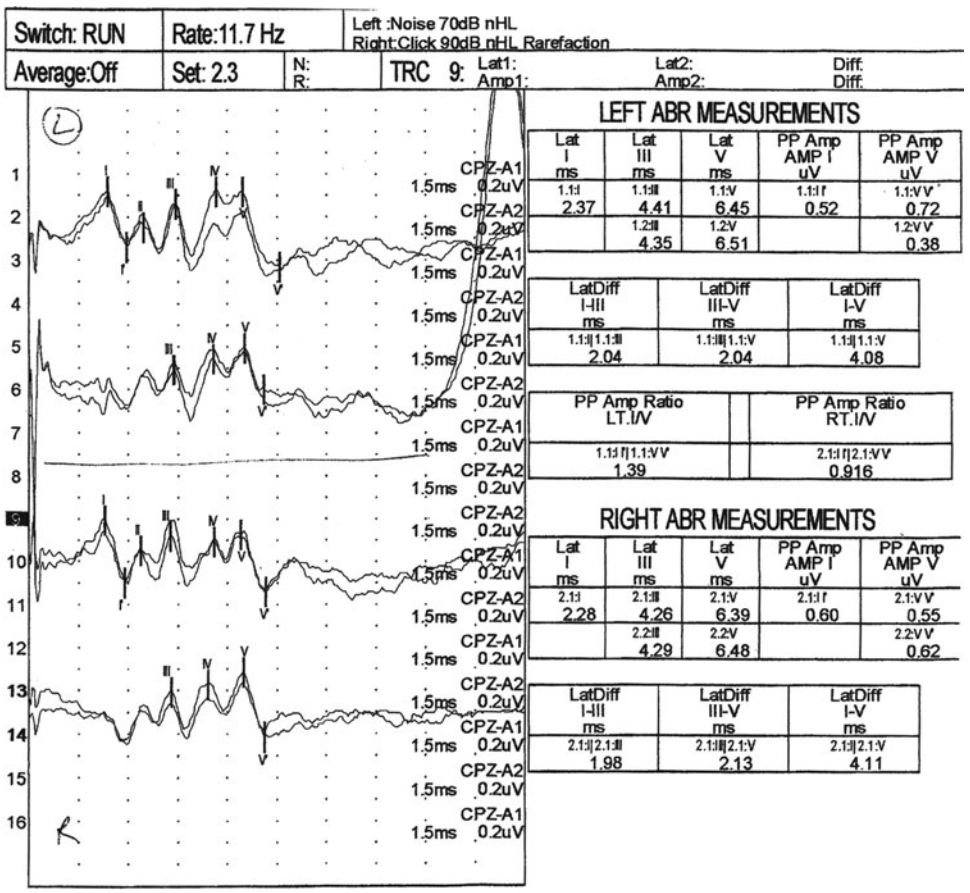

Photo 35-1 Brainstem auditory evoked potentials in the left (top) and right (bottom) ears. Wave I is from cranial nerve 8 fibers near the internal auditory canal, II is from fibers near the brainstem, III is from the cochlear nucleus, IV is from the superior olivary nucleus, V is from the inferior colliculus, VI and VII (not seen here) are from the medial geniculate nucleus. Debate exists about the exact structures responsible for many of the waveforms

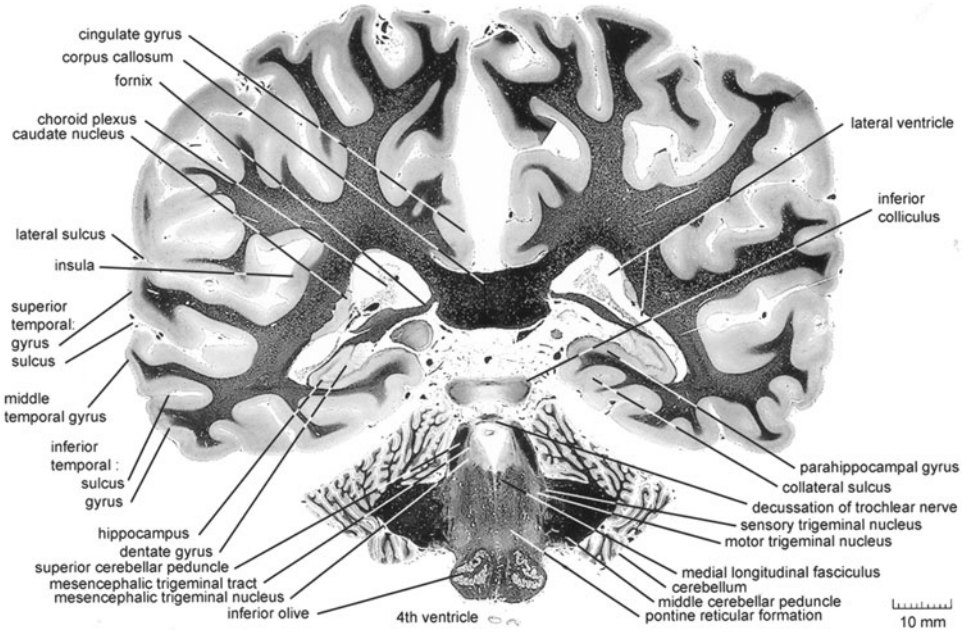

Photo 35-2 Coronal section through the brain to highlight several central auditory structures
With permission from the Michigan State University: Brain Biodiversity Bank. https://www.msu.edu/~brains/

To diagram the central auditory nuclei, we could use cross sections through the brainstem. However, the origins and synapses of the auditory pathway span junctions in brainstem levels, so this method becomes problematic. You will notice that different texts place the nuclei of the auditory system at different brainstem levels because they really span the junctions between levels. Some books show the inferior colliculi in the midbrain and some in the pons, whereas some texts show the medial geniculate bodies in the midbrain and others in the diencephalon. To avoid this confusion, we'll use a coronal view through the brain and brainstem. In coronal section, we lose the dorsal–ventral axis of the brainstem, but no matter; all of the brainstem auditory structures lie mid-dorsally, anyway.

Now, draw a coronal section through the cerebral hemispheres, diencephalon, and brainstem. Begin at the lateral pontomedullary junction with the *cochlear nuclei*. Next, in the medial medulla, draw the *superior olivary nucleus*; then, move rostrally to the medial pontine/midbrain junction and label the *inferior colliculus*; next, move up another level to the dorsolateral midbrain/diencephalon junction and label the *medial geniculate body*. Finally, move to the superior temporal cortex and deep within it label the *transverse gyri of Heschl*—the primary auditory cortex.

The cochlear nuclei are subdivided into posterior and anterior nuclei (aka the dorsal cochlear nucleus and ventral cochlear nucleus, respectively). They are oriented around the restiform nucleus of the inferior cerebellar peduncle. Draw a unilateral axial cross section through the rostral medulla to show their positions. Indicate the *restiform body* of the inferior cerebellar peduncle. The restiform and juxtarestiform bodies comprise the nuclei of the inferior cerebellar peduncle; it and the middle cerebellar peduncle receive most of the afferent fibers to the cerebellum. Now, in posterior–anterior orientation around the restiform body, draw the *posterior cochlear nucleus* and the *anterior cochlear nucleus*.

In this same axial section, draw the *medial superior olivary nucleus*. Then, show the *trapezoid body* fibers project from the anterior cochlear nucleus to the superior olivary nucleus. We will explain the purpose of these fibers in the next section.

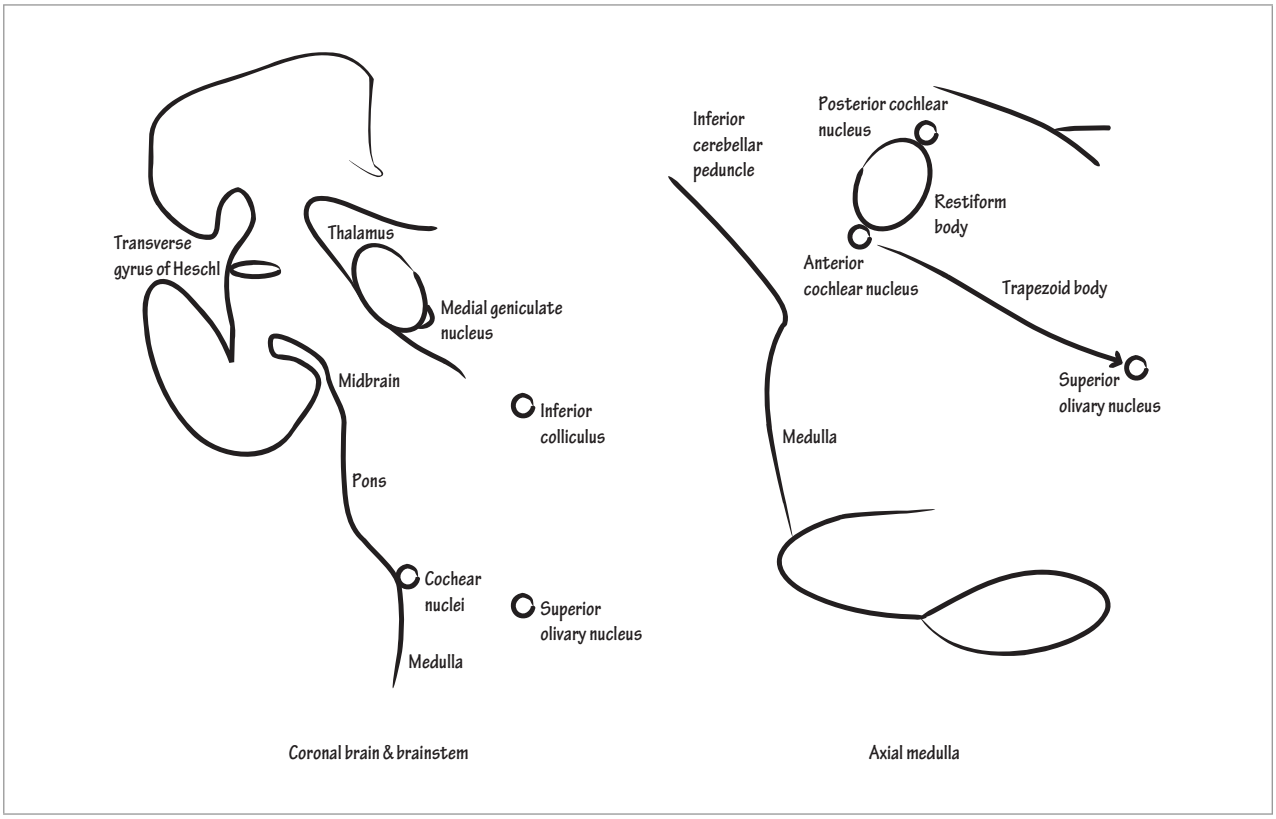

Figure 35-1 Central auditory nuclei

Now, let's draw a simplified diagram of the auditory pathways. Even imagining the actual pathways is dizzying. For instance, in the actual auditory system, there are nine distinguishable nuclei that each send projection fibers with varying degrees of unilaterality and bilaterality to their targets, and there are also varying degrees of internuclear communication between each of the paired targets of the auditory system. There are descending and ascending internuclear communication pathways, as well. It is impossible for us to show all of these fiber tracts but we will show a few ascending pathways of the auditory system to highlight the functional anatomy of the auditory system. If you want to skip these diagrams, just learn the following highlights.

As discussed, there are two pathways for sound localization—one is binaural and the other is monaural. Fibers project from the cochlear nuclei and the superior olive up the lateral lemniscus to the inferior colliculus, and then to the medial geniculate. To remember this core portion of the central auditory pathway, use the mnemonic "S-L-I-M." Note that we have learned the corollaries to these nuclei and pathways elsewhere: the inferior olivary nucleus, medial lemniscus, superior colliculus, and lateral geniculate nucleus. The central auditory pathway then projects from the medial geniculate nucleus to the primary auditory cortex, which comprises the transverse gyri of Heschl, deep to the superior temporal gyri in the Sylvian fissure. The primary auditory cortex then projects to the secondary auditory association cortices.

First, let's draw the pathway for binaural sound localization. Draw a bilateral version of the central auditory nuclear diagram. Show projection fibers from the *anterior cochlear nucleus* to the bilateral *superior olivary nuclei*. Label these projection fibers as the *anterior acoustic striae*. Indicate that these projection fibers form a trapezoidal shape and are aptly named the paired *trapezoid bodies*. Next, draw *lateral lemniscus* projection fibers from both of the superior olivary nuclei to their ipsilateral *inferior colliculi*. The corollary of the lateral lemniscus is the medial lemniscus sensory fibers that originate in the large fiber sensory nuclei in the medulla and ascend through the medial tegmental brainstem. Next, draw projections from each inferior colliculus to its ipsilateral *medial geniculate nucleus* via the *brachium of the inferior colliculus*. And finally, draw projections from each medial geniculate nucleus to its respective transverse gyri of Heschl, deep to the superior temporal gyrus in the Sylvian fissure. The auditory association cortex surrounds the primary auditory cortex.

Now, we will add the monaural sound localization pathway. The posterior acoustic stria is the monaural corollary to the binaural anterior acoustic striae. Show the *posterior cochlear nucleus* send fibers via the *posterior acoustic stria* directly to the contralateral *lateral lemniscus*. The distinguishing feature of the posterior acoustic stria is that it skips the projection to the superior olivary nucleus and goes directly to the contralateral inferior colliculus via the lateral lemniscus. Thus, unlike the anterior cochlear nucleus, which sends fibers to both superior olivary nuclei, the posterior cochlear nucleus sends fibers only to the opposite side of the brainstem. Posterior acoustic striae projections ascend the brainstem in the lateral lemnsicus just as the anterior acoustic striae do: they synapse at the inferior colliculus, project to the medial geniculate body through the brachium of the inferior colliculus, and terminate in the primary auditory cortex.

An intermediate acoustic stria also arises from the posteroanterior nucleus, which is intermediate to the anterior and posterior nuclei. It is believed to channel feedback from the superior olive to the outer hair cells of the cochlea.

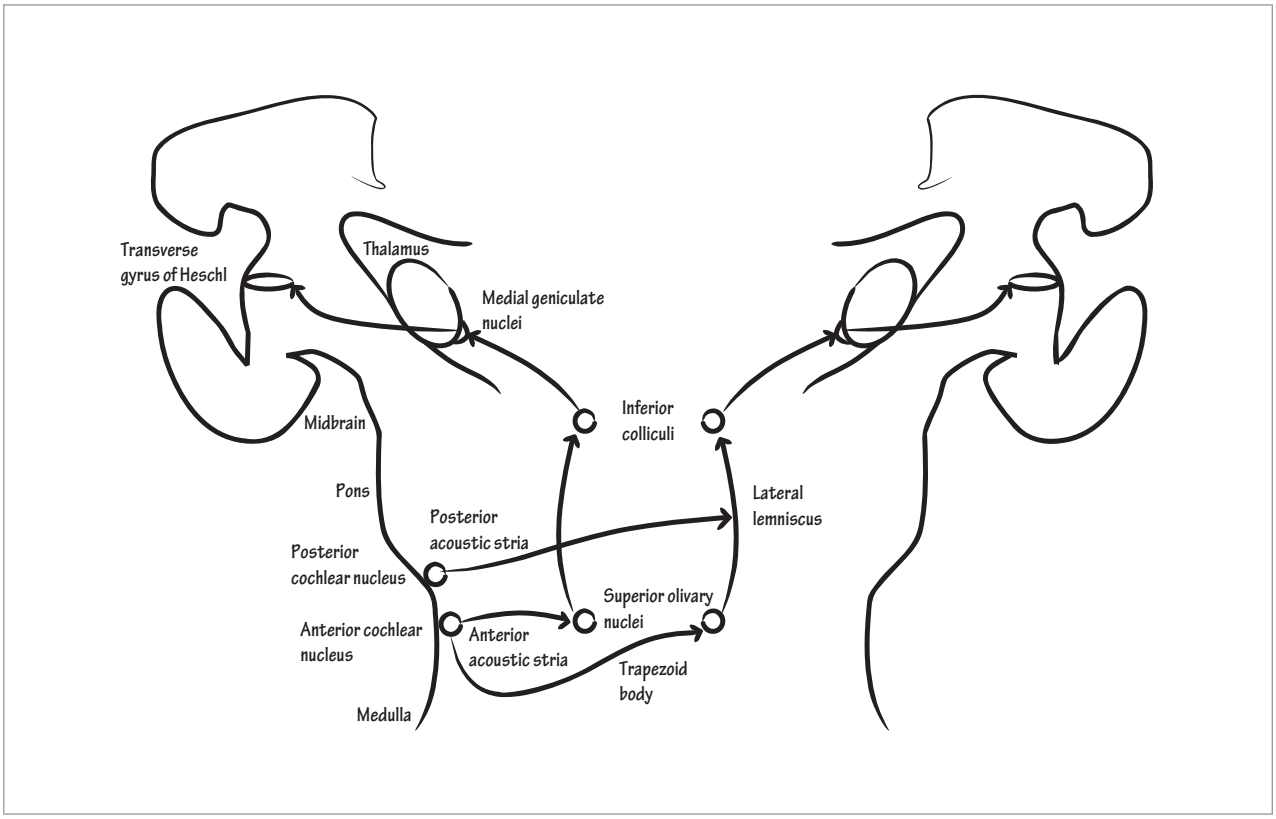

Figure 35-2 Central auditory pathways

Language

IN THIS CHAPTER, we will learn the neuroanatomy of language in two steps. First, we will learn the language disorders (aka aphasias), because clinically, we consider language anatomy in terms of its disorders. However, the anatomical basis of the aphasias is broad, imprecise, and redundant; so after that we will study the specific steps in the perception, processing, and production of language to fully understand its anatomy.

There are seven major clinical language disorders: Broca's aphasia (aka expressive aphasia, nonfluent aphasia, or motor aphasia), Wernicke's aphasia (aka fluent aphasia, receptive aphasia, or sensory aphasia), global aphasia, conductive aphasia, transcortical motor aphasia, transcortical sensory aphasia, and mixed transcortical aphasia. We begin with the classic Broca's and Wernicke's aphasias. The most distinguishing feature between the two is language fluency. In Broca's aphasia, patients are nonfluent, meaning they express fewer than three or four words in a sentence, and their speech is hesitant. Broca's aphasia is sometimes dysarthric, hypophonic, dystonic, spastic, or hyperkinetic, while the motor component in Wernicke's aphasia is unaffected and speech remains fluent.

Grammar is another distinguishing feature. Broca's aphasics are agrammatic—they omit or simplify grammar, whereas Wernicke's aphasics demonstrate paragrammatism, which means their grammar is present but imprecise due to semantic ambiguity.

Prosody refers to spoken intonation and inflection; it communicates a substantial portion of meaning and is severely affected in Broca's aphasia. In an excited tone, exclaim, "the horse is here!" then ask, "the horse is here?" Now, imagine being unable to differentiate the two. Broca's aphasics have difficulty with both understanding and generating prosody. Think of the droll, hackneyed high school teacher Ben Stein played in the film *Ferris Bueller's Day Off*—"Bueller? . . . Bueller?". Stein's delivery is more nasal than monotone, but you understand from the example how flat Broca-type speech can sound. When Broca's aphasics do generate prosody, it is often disrupted. Wernicke-type speech remains melodious and uninterrupted; it is just absent any meaning.

Empty speech typifies Wernicke's aphasia. It is filled with single unrelated words, circumlocutions, tangents, and, as mentioned, paragrammatism. Paraphasic speech involves inappropriate substitutions of phonemes (aka syllables) or whole words. Say "men" when you mean "pen" or "fork" when you mean "knife" to demonstrate paraphasic errors. Wernicke's aphasics even generate new words, called neologisms.

Wernicke's aphasia is often called comprehension aphasia because language comprehension is devastated. A lack of insight (aka anosognosia) often accompanies Wernicke's aphasia and patients with this disorder often have an inappropriately bright affect. Although at first glance this may seem like a silver-lining, their lack of awareness severely impedes rehabilitation of their disorder.

Unfortunately, because Broca's aphasia is often imagined to be the direct opposite of Wernicke's

aphasia, clinicians often misbelieve that Broca's aphasics must have normal language comprehension. As a rule, comprehension is abnormal in Broca's aphasics, but to a more mild degree, and unless we are vigilant about testing for it, it may go unnoticed.

Repetition is impaired in both Broca's and Wernicke's aphasias. Ask someone to repeat "ball," then "baseball," then "baseball player," and if they are able to repeat more than four syllables, ask them to repeat a full sentence; it is helpful to determine the degree of repetition impairment and reevaluate it over time to monitor for improvement or worsening of the language disorder.

A common cause of Broca's aphasia is left middle cerebral artery stroke, so Broca's aphasics often have accompanying right side hemiparesis and hemisensory loss of the arm more so than the leg; buccofacial apraxia; and right side visual field impairment in the inferior greater than the superior visual field. On the contrary, the main associated neurologic finding in Wernicke's aphasia is right side visual field deficit because it is generally a left-posterior neuroanatomical disorder.

Lastly, in Broca's aphasia, initiation difficulty, sound substitutions, omissions or transpositions of syllables, slow rate, equal stress, and inappropriate stops and starts are all characteristic. Demonstrate all of them by saying the following sentence in a flat, monotone voice. "(G)at . . . drink- . . . -ilk from the bowel."

Broca's area is limited to the frontal operculum within the left inferior frontal gyrus, specifically the pars opercularis (Brodmann area 44) and pars triangularis (Brodmann area 45). Broca's aphasia, however, is not necessarily confined to Broca's area but instead involves much more wide-reaching brain regions and is broadly considered a left frontal–insular–basal ganglia disorder.

Wernicke's area is confined to the superior temporal gyrus and its adjacent insular region. The insular region involves the planum temporale, which is a poorly defined region posterior to the transverse gyri of Heschl in the plane of the Sylvian fissure, bounded by the superior temporal gyrus laterally. But the neuroanatomical regions affected in Wernicke's aphasia, like those of Broca's aphasia, are much more wide-reaching: they span throughout the temporal and inferior parietal lobes.

In the second part of this chapter, we will study in more detail the different anatomical components of language fluency and sentence structure affected in Broca's aphasia, and we will learn about the properties of phoneme perception and semantic memory, which are affected in Wernicke's aphasia.

Next, consider what is meant by global aphasia. This is most easily thought of as a combination of Broca's and Wernicke's aphasias. There is dysfunction in speech output and language understanding with an inability to repeat. The distinguishing feature between global aphasia and Broca's aphasia is the severity of the comprehension impairment. In global aphasia, by definition, there is no more than single-word comprehension. Point to objects when their names are spoken. That is the upper limit of what globally aphasic patients are able to do. During their recovery, global aphasics regain language comprehension first and often progress to Broca's aphasia or transcortical motor aphasia (discussed momentarily).

Isolated impairment in repetition is called conduction aphasia; in it, language comprehension and speech production are normal but the transfer of lanaguage from the Wernicke's to the Broca's area is disrupted. Classically, we assign this transfer to the arcuate fasciculus but, as discussed in the "White Matter Pathways" chapter, current thinking is that the superior longitudinal fasciculus may actually be responsible for language conduction, instead. Although repetition impairment is the key examination feature of conduction aphasia, the most noticeable characteristics of conduction aphasia are paraphasic errors and hesitancy.

A retained ability to repeat distinguishes the transcortical aphasias from the Broca's and Wernicke's aphasias. Generally speaking, transcortical sensory aphasia is Wernicke's aphasia without repetition impairment and transcortical motor aphasia is Broca's aphasia without repetition impairment. Because the transcortical aphasias involve more restricted language abnormalities, they teach us much about semantic language processing. Language semantics involve the relationships between words and their meaning. Transcortical sensory aphasia is a restricted impairment in single-word language understanding. Patients with this disorder follow commands well, repeat just fine, and even argue without difficulty, but they are unable to point to a city on a map or name objects: they are unable to complete single-word tasks.

Language processing studies have identified that semantic comprehension localizes to the antero-ventral and posterior temporal lobes with specialization of knowledge stores of living things (e.g., animals and insects) in the antero-ventral temporal lobes and of man-made objects (e.g., tools) in the posterior temporal lobes. Collectively, these regions are the temporal network.

Transcortical motor aphasia is also a disorder of semantics but of an inability to retrieve information from the semantic word stores. It is a nonfluent aphasia with intact repetition and ostensibly normal language comprehension. Patients with transcortical motor aphasia produce terse, delayed responses with intact grammar and uncontrolled repetition (aka echolalia). To demonstrate echolalia, listen to a commercial jingle sometime and find yourself repeating what you hear.

The localization of transcortical motor aphasia is classically ascribed to the dorsolateral frontal cortex, which is consistent with the role of this region in executive planning and, specifically, in the planning of speech output. The caudate head interacts with this cortical region, and indeed, white matter lesions to it along the frontal horn of the lateral ventricle often cause transcortical motor aphasia.

Patients with abulia, an amotivational syndrome, demonstrate a lack of initiation of speech with normal language comprehension and normal language fluency once they begin speaking, which is similar to transcortical motor aphasia. But the localization pattern is different: lesions to the medial frontal cortex cause abulia, whereas we noted, the dorsolateral frontal cortex is injured in transcortical motor aphasia.

Mixed transcortical aphasia, much like global aphasia, is a combination of transcortical motor and sensory aphasia, with speech nonfluency and impaired language comprehension but intact repetition. While you might imagine the syndrome necessitates both frontal and posterior lesions, in reality large frontal lesions, alone, will impair comprehension. Possibly because impairments in the inferior and middle frontal regions disrupt working memory and syntax processing. Complex syntax comprehension, specifically, localizes to the inferior frontal gyrus pars triangularis.

Anomic aphasia is the mildest form of aphasia and involves word retrieval or word-finding problems. In essence, it is extremely mild transcortical motor or sensory aphasia. The only deficit is in naming, and the underlying cause is either due to impairment of semantic comprehension from ventral temporal or posterior temporal lesions or impairment in word-retrieval from dorsolateral injury. This is the "tip of the tongue" phenomenon in which you "know you know" a certain name but just can't "bring it to mind."

Now, let's create a diagram that will provide a shorthand way to evaluate language disorders. First, draw a lateral view of the brain. Indicate the presence of *Broca's area* in the frontal operculum of the inferior frontal gyrus; *Wernicke's area* in the posterior superior temporal gyrus and the underlying planum temporale; and also the *arcuate fasciculus* that has been classically considered to connect them. Then, indicate the *dorsolateral frontal network* for the planning of language and the *temporal network* for language comprehension. Write repetition/conduction aphasia over the arcuate fasciculus; transcortical motor aphasia over the dorsolateral frontal network; and transcortical sensory aphasia over the temporal network. This shorthand sketch will come in handy at the bedside.

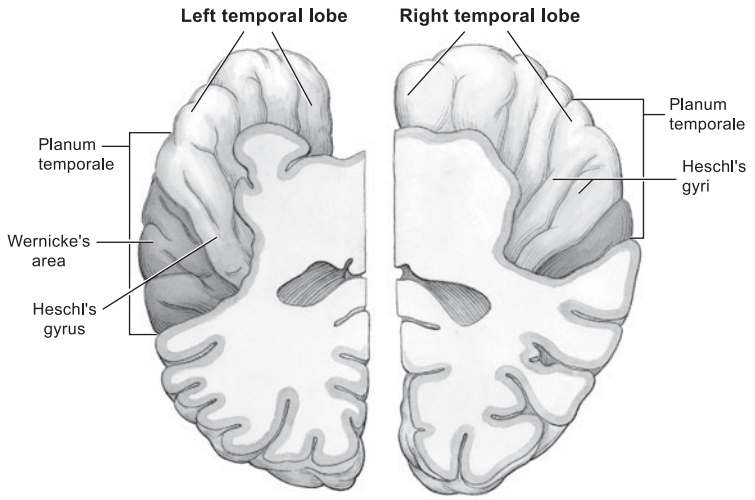

Photo 36-1 Axial sections to show the related anatomy of Wernicke's area, the transvere gyri of Heschl, and the planum temporale

With permission from Devinsky, O., and M. D'Esposito. *Neurology of Cognitive and Behavioral Disorders*, Contemporary Neurology Series. Oxford and New York: Oxford University Press, 2004.

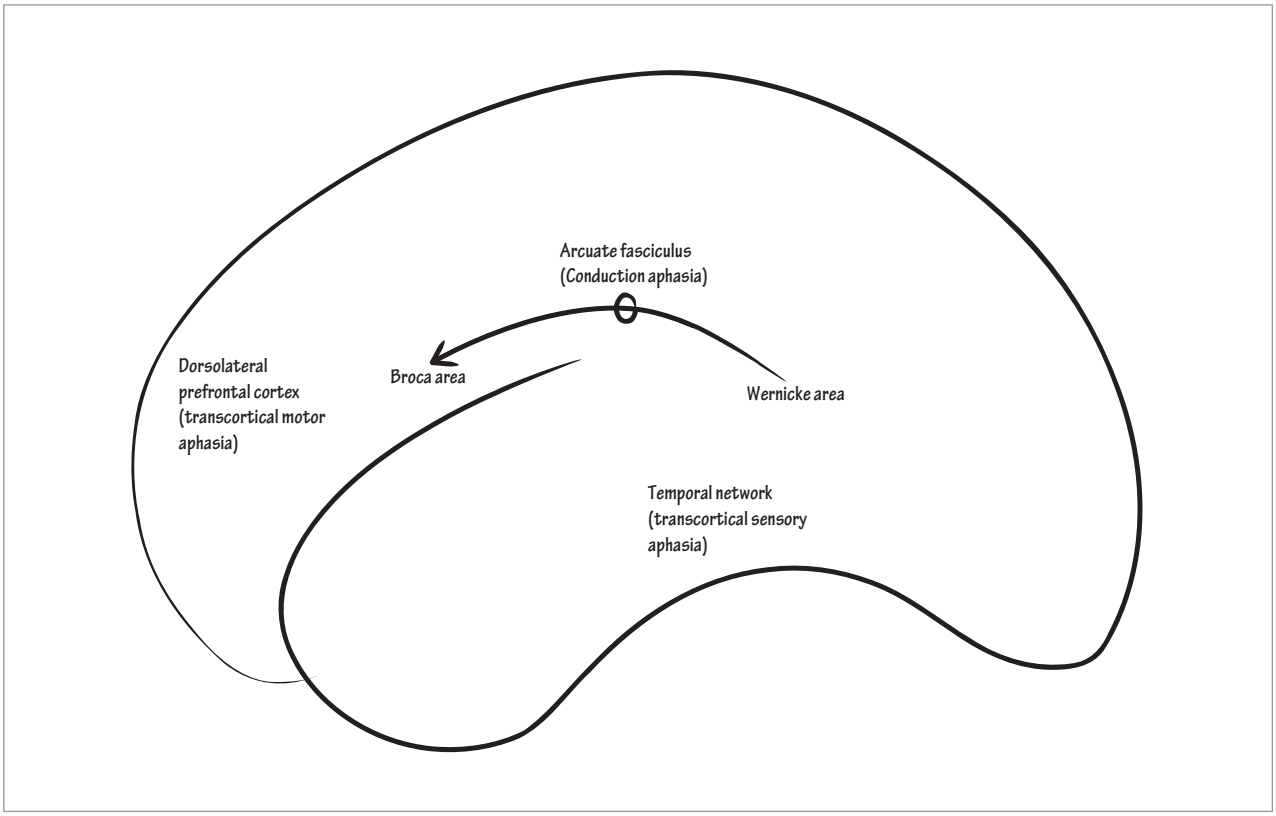

Figure 36-1 Shorthand diagram of classic language model

Now let's work through the neuroanatomy of language from a language processing and production standpoint. First, let's look at the components of speech production, which are collectively impaired in Broca's aphasia. We divided speech production into motor output (i.e., articulation) and speech syntax (i.e., grammar and sentence construction). Broca's area, itself, divides into a posterior, motor region: the pars opercularis, and an anterior, syntax region: the pars triangularis; opercularis is hard to pronounce, which will help you remember its role in articulation. In addition to the pars opercularis, the motor network involves the insula, motor and premotor cortices of the mouth and head, supplemental motor area, and basal ganglia. And, in addition to the pars triangularis, the syntax network involves the rest of the inferior frontal gyrus and also the posterior temporal region; this is a particularly vast region, and so it is best to subdivide the syntax network into complex sentence comprehension and general language comprehension. Complex sentence production and understanding involves the frontal area, whereas general language comprehension involves the posterior temporal region.

Language processing begins with language perception. Although we discuss the auditory and visual processing of language, here, we should also remember that language perception is tactile in Braile. Auditory perception of language is referred to as phoneme perception. Imagine hearing a tone or more complicated nonspeech sound. These are perceived in the auditory cortex separate from phonemes (aka speech sounds). Now, say the word "man" and then the non-word "lan," which are both phonemes. Phoneme perception takes place in the superior temporal gyrus and the superior temporal sulcus, below it. Bilateral superior temporal gyri and sulci lesions produce pure word deafness, which is isolated phoneme perception impairment. Patients with this disorder are able to read and write because the visual word form area is preserved; we will discuss it in the next section. Is their nonspeech auditory perception normal? Yes, by definition, the remainder of the auditory cortex is intact. Pure word deafness is seen during the recovery from Wernicke's aphasia, as well as in the neurodegenerative process of fronto-temporal lobar dementia, and in Landau–Kleffner syndrome.

In contrast to pure word deafness, which is a language disorder, auditory agnosia is a disorder of selective nonspeech hearing loss. Imagine the sounds of car engines, animal-calls, and music. Auditory agnosia is a selective loss of recognition of these sounds. The syndrome is rare and may involve several different regions, but most often it is caused by right superior temporal lobe lesions.

In the first part of the chapter, we discussed conduction aphasia and how patients with conduction aphasia exhibit paraphasic errors secondary to poor phonologic access. Access to phonological representations (i.e., word sounds) occurs within the posterior superior temporal gyrus and sulcus and the supramarginal gyrus. Deficits in this region result in conduction aphasia, which manifests with impairment in repetition but most prominently with paraphasic errors of speech and paragraphic errors of writing.

The primary site of written code is classically ascribed to the left angular gyrus. In the classic model, written codes are perceived by the visual cortex during reading and used by the motor system for writing. A lesion of the left angular gyrus, itself, then, results in an inability to read (aka alexia) and also write (aka agraphia). In the "White Matter Pathways" chapter, we discussed how disruption of visual input to this area results in the disconnection syndrome of alexia without agraphia. Alexia without agraphia (i.e., impaired reading but intact writing) occurs when visual input to the left angular gyrus is disrupted but the angular gyrus, itself, is spared. It occurs from a lesion of the left primary visual cortex that extends into the splenium of the corpus callosum to interrupt crossing fibers from the right visual cortex, so they are disconnected from the left angular gyrus. These patients have a right visual field defect from the left visual cortex lesion but their visual fields are otherwise intact.

Similar to how we separated phonological perception from general auditory perception, we can also define a specific higher level visual language perception area, called the visual word form area, in the left fusiform gyrus (aka occipitotemporal gyrus). On the right side of the brain, the fusiform gyrus is dedicated to the perception of familiar faces, but on the left side, it is dedicated to recognizing visual word and non-word combinations. It is believed that enhancement of reading speed occurs on a cellular level where neuronal plasticity of letter combination recognition relates to the frequency of their visualization. Destruction of the visual word form area, then, amounts to an inability to recognize the combination of letters, and patients with a lesion in the visual word form area read one letter at a time, so-called letter-by-letter dyslexia.

We discussed semantic language processing in the first part of this chapter and described the transcortical aphasias that result from select disruption of regions within this network. There, we introduced the role of the antero-ventral temporal lobe in the knowledge of living things, the posterior temporal lobe in the knowledge of man-made objects, and the dorsolateral prefrontal cortex in semantic memory retrieval. Certain more memory-specific regions are also involved in semantic language processing, as well, such as the posterior cingulate gyrus and parahippocampal gyrus. In the "Limbic System" chapter, we divided the cingulate gyrus into anterior, behavioral and posterior, memory centers. Here, again this division is reinforced: the posterior cingulate gyrus, and not the anterior portion, is involved in semantic memory.

Let's consider a couple of clinical correlates for semantic memory disorders and disorders that affect the anterior temporal lobes. Semantic dementia is a disorder that presents with vocabulary incomprehension and language production problems. It involves primary degeneration in the ventral and anterior temporal lobes on the left side more so than the right. Herpes encephalitis also has a tendency to affect the anterior temporal lobes and it causes semantic memory deficits, as well.

Memory

THE STUDY OF MEMORY overlaps neuropsychology with other areas of cognitive neuroscience. To learn the neuroanatomy of memory, we need to define the forms of memory content and steps in memory processing as well as the different memory time spans.

Memory content is classically divided into semantic and episodic forms. Family members' birthdays, anniversaries—things you have to force yourself to remember—are semantic memories; whereas the memories of experiences you've enjoyed together are episodic memories. Facts constitute your semantic memory; experiences make up your episodic memory. When it comes to friends and family, the episodes are better remembered than the facts. But, now, consider a lion's color: where or when did you learn this? Unless the first time you saw a lion was up-close, in person, a memorable event, indeed, you've probably forgotten where and when you first learned its color—it was discarded from your episodic memory long ago but the knowledge of the lion's color is encoded within your semantic memory.

Now, let's divide memory storage another way: into declarative (aka implicit) and nondeclarative (aka explicit) memories. The episodic and semantic memories we discussed are divisions of declarative memory. Nondeclarative memory subdivides into priming, which is the memory process wherein a familiar subject matter is easiest to remember, and procedural memory. Procedural memories are the memories we call upon for mechanistic actions: riding a bike, swimming, skipping—things we do "without thinking."

What about memory time and processing? Memories are categorized broadly into two time spans: short and long, but short-term memory is further subdivided into sensory memory, which is momentary, and working memory, which is brief but significantly longer than sensory memory. Sensory memory is the transitory retention of a primary sensory stimulus. Visual sensory memory is retained for an exceedingly short period of time (a third of a second). Auditory sensory memory retention is longer, which is why we are able to make sense of conversation. Working memory keeps "something in mind" for a period of seconds or a few minutes and then the memory is either processed into a long-term memory or discarded.

Lions populate sub-Saharan Africa and India and are one of four big cats in the genus Panthera. The other three are the leopard, tiger, and jaguar. What of that information can you recall? Review it. You are using your working memory, which at any one time will hold 7 ± 2 items or bits of information.

Now try to remember the following words: leopard, cow, lion, bus, tiger, hat, jaguar, and shirt. Repeat them without looking. Although there are eight items in that list, you did well with them, presumably, for two separate reasons. First, you were able to combine the lions, tigers, jaguars, and leopards into a single chunk—big cats, and you could combine the shirt and hat into street clothes; in total, you decreased the memory load to 4 bits (big cats, street clothes, cow, bus), which is called memory chunking. Here, you did this consciously, but memory chunking occurs subconsciously all the time. Although the

average working memory storage is only 7 bits, information is always being "chunked" to ease the working memory load. This relates to remote memory recall, as well, because items are stored long-term in chunks. You've probably forgotten your last phone number, but if you were told the first few digits of it, you might recite the whole thing. For the second exercise, note that we were already primed to remember the big cats from our discussion of them: it is easier to recall new information about a subject matter you are already familiar with or that is "on your mind."

The processing of memory involves encoding and consolidation, storage, and retrieval. Encoding and consolidation is the transfer of information from short to long-term memory; for instance, the transfer of the definition of big cats from working to long-term memory. Storage, as you might imagine, is the stockpiling of information in accessible brain regions, and retrieval is the accessing of that information.

Next, we will address the classic model for the neuroanatomical underpinnings of memory and then updates to it. Sensory perception is the first step in forming a memory and it occurs in all primary sensory areas. Sensory memories are transferred from sensory areas through the parahippocampal gyrus to the hippocampus for encoding and consolidation. Encoding and consolidation occurs within the limbic lobe, primarily through the Papez circuit and amygdaloid circuit. After being encoded and consolidated within the limbic system pathways, these memories are stored throughout the neocortex, and the frontal lobes retrieve them as they are needed.

While this model for memory held sway throughout the mid-twentieth century in this form, during the latter part of the century, Lynn Nadel and colleagues discovered another layer of interconnectivity between the hippocampus and the neocortex in the formation of memory, which they called memory trace. According to the multiple memory trace theory, in addition to encoding and consolidating memories, the hippocampus also binds with the neocortex for memory storage and together they build a context or "spatial scaffold" for memories. Each time a memory is retrieved, the hippocampal–neocortical ensemble is strengthened by the formation of an additional memory trace.

Two clinical conditions inform our understanding of memory. The first is Korsakoff syndrome, which is secondary to thiamine deficiency; it involves damage to multiple regions including the mammillary bodies and anterior thalamic nuclei, which are important structures of the Papez circuit. The second is the patient H.M. who underwent bilateral medial temporal lobe resections for intractable epilepsy. To understand the memory dysfunction of H.M. and patients with Korsakoff syndrome, we need to introduce the terms anterograde and retrograde amnesia.

Patients with anterograde amnesia are unable to form new memories whereas those with retrograde amnesia are unable to retrieve old memories. The sole apparent disruption in H.M. and in patients with Korsakoff syndrome involves the transfer of information from short to long-term memory. For example, people who came daily to visit H.M. were strangers anew every day, and yet other aspects of his memory—sensory memory, working memory, remote storage of older memories, and memory retrieval—appeared unaffected. Korsakoff patients display a similar inability to remember new events, but they confabulate (they unconsciously fabricate answers), if they don't know the truth. Both in H.M.'s situation and in Korsakoff syndrome, only anterograde amnesia appears impaired; retrograde retrieval seems unscathed. But proponents of the multiple memory trace theory argue that in H.M. and in other patients with bilateral hippocampal damage, long-term memories are, in fact, altered because the contextual component of long-term memory is stored in the hippocampal formation and it is lost.

Let's compress our understanding of memory into the clinically useful, albeit simplistic, analogy of the file clerk, the inbox, and the file cabinet. In this analogy, the frontal lobes are the file clerk, the limbic system is the inbox, and the neocortical–hippocampal ensemble is the file cabinet. Memories enter the inbox and the file clerk moves them to the file cabinet in an organized manner and systematically retrieves them when they are needed.

When the inbox is jammed, no new memories can come in; when the file cabinets are a mess, memories are unable to be stored; and when the file clerk is problematic, memories can't be filed or retrieved. In transient global amnesia, the inbox is jammed temporarily, whereas in the case of H.M. it was removed permanently. In frontotemporal lobar dementia, the file clerk is ineffective and chaotic.

Apraxia

APRAXIAS ARE notoriously difficult to conceptualize and, unfortunately, inconsistently defined throughout the literature. In some ways trying to imagine them is like looking at a three-dimensional painting: let your mind go and the image will become clear, but if you focus on any particular element within it, the image will fragment into numerous, insubstantial pieces. In this chapter, we will first establish the common definitions of frequently discussed apraxias, so we will be able to look for them at the bedside and answer board questions about them. Then, we will disassemble these definitions in order to understand their limitations. If you just want a simple mental construct for the apraxias, it is better to accept the imaginary, three-dimensional painting than to analyze its fragments; however, to do so, you need to accept that what you are viewing is unreal.

Ideational apraxia is impairment in the mental formulation of a multi-step action—difficulty in *ideating* it. The term conceptual apraxia was introduced to define impairments in the formulation of single-step tasks. What differentiates ideational and conceptual apraxias is the number of mental steps it takes to complete a task, but both are impairments in conceptualization. Examples of ideational and conceptual apraxias are categorically bizarre. For instance, the next time you're hungry, eat with a toothbrush and brush your teeth with a spoon to demonstrate their effects.

Mechanistically impaired actions, on the contrary, characterize ideomotor apraxias; they involve problems such as spatial disorganization, impaired sequencing, and timing errors. To demonstrate ideomotor apraxia, use the correct utensil to eat but do so with difficulty. For instance, over-grip your spoon and overshoot your mouth. Limb-kinetic apraxia is, in some sense, a subtler form of ideomotor apraxia. Again, the conceptualization of the action is intact, but the performance of finely graded finger movements is impaired. After dinner, pick up a violin and clumsily mash at the neck of the instrument rather than finely pressing its strings to demonstrate limb-kinetic apraxia.

Ideational, ideomotor, and limb-kinetic apraxia form the backdrop of the apraxias. These definitions provide a clear, three-dimensional picture of apraxia. So, with our well formed image in mind, let's learn the general anatomy of the apraxias.

First, praxis predominantly originates in the left hemisphere; on the contrary, awareness (gnosia) originates in the right. However, the left hemisphere sends transcallosal fibers to the right hemisphere for programming and, thus, both hemispheres participate in praxis. Left hemispheric lesions result in bilateral impairments. When right hemispheric lesions cause apraxia, as they infrequently do, they cause only contralateral (i.e., left side) deficits.

In the early twentieth century, H. Liepmann established the concept of the motor engram, a space–time plan for actions, which localizes to various brain regions to produce praxis. The bulk of evidence suggests the frontal and parietal lobes are the primary generators of praxis, but the temporal and occipital lobes, frontoparietal subcortical white matter, and basal nuclei are all involved in praxis, as well. If we want to restrict our localization of praxis, we say it

involves the left inferior parietal and left dorsolateral frontal lobes.

Knowing what we do about the organization of motor and spatial cortical localization, it would make sense if posterior lesions caused spatial apraxia and anterior lesions caused motor apraxia, but this is not the case: both types of apraxia come from both regions. Still, lack of awareness of mistakes appears to be a uniquely posterior phenomenon.

Apraxia is common to certain clinical conditions. Corticobasal degeneration is a distinct entity that involves apraxia along with akinetic-rigid muscle tone, asymmetric lateralizing sensory loss, and alien hand syndrome; corticobasal degeneration has its own unique pathology. On the contrary, the combination of Parkinsonism plus apraxia is called corticobasal *syndrome*, which is a more heterogenous diagnosis. It involves different pathologic hallmarks, including those of the dementias (Alzheimer's disease and frontotemporal dementia) and those of the movement disorders (dementia with Lewy bodies and progressive supranuclear palsy).

Now, let's add numerous distinctions and specifications to our construct of the apraxias, and in the process, destroy our clear vision of them. Dissociations are often used to distinguish types of apraxias. They include whether patients are able to make a motion with a tool (called a transitive action) or whether they are able to make an imaginary motion (called an intransitive action) and differences in meaningful versus meaningless gestures; distal versus proximal movements; novel versus imagined movements; the effects of verbal commands versus imitation; and pantomime versus tactile difficulties. Naturally, from these dissociations, terms for many different distinguishable apraxias evolve.

Conduction apraxia is commonly referenced and involves being better at following verbal commands than pantomiming to command. To demonstrate this apraxia, imagine that when you are asked to perform a task, you can do it, but when you are shown how to do it, you fall apart. An extreme form of conduction apraxia is called visuo-imitative apraxia. Tactile apraxia is apraxia to transitive actions: patients are unable to use a hammer but are able to perform intransitive gestures normally—for instance, they salute on command. Construction apraxia is impairment in perceiving details and understanding their interrelationships. To demonstrate this, be unable to copy a drawing or build a tower with blocks. If an apraxia involves select body parts, it is named by the part. Buccofacial apraxia involves the mouth and face, facial apraxia involves the face without the mouth, and oral apraxia involves only the mouth.

The cumbersome nature of the dissociations burdens our view of apraxia but we still understand it—until we consider the practical evaluation of apraxia. From the outset, to distinguish apraxia from motor-sensory impairment requires close examination. How do you know the deficit is not just from a primary motor or sensory problem? Presume you establish the presence of a true apraxia. You will be able to categorize it as ideational/conceptual, ideomotor, or limb-kinetic, but when you entertain the numerous dissociations, a cohesive interpretation will seem impossible.

Unfortunately, as our recognition of these dissociations grows, it becomes increasingly paralyzing to perform and interpret a simple apraxia examination. Knowing what you do now, what would you ask a patient to do at the bedside? Salute? Copy a drawing? Mail a letter? Can you convince yourself of the type of apraxia before you account for all of the different dissociations or is your interpretation incomplete without them?

If you scrutinize the components of the three-dimensional image of apraxia, it will fragment into a myriad of scattered bits. So, now, go back to the beginning with a blank stare and regain clarity on the subject matter.

Sleep Neurocircuitry

In 1914, renowned French neurologists Joseph Dejerine and Jacques Lhermitte emphatically denied the possibility of a brain sleep center. Their view was shared by most scientists that sleep was simply the absence of sensory input to the brain and not an active brain process. In 1916–1917, however, Baron Constantin von Economo documented pathologic–anatomic correlations of patients who had died from encephalitis lethargica (aka von Economo's encephalitis), which demonstrated clear sleep and wake central nervous system centers.

Encephalitis lethargica causes a myriad of clinical manifestations, the most relevant of which are severe hypersomnia (excessive sleepiness) or extreme insomnia (inability to fall or stay asleep). Some patients with this disorder also manifest with eye movement abnormalities and Parkinsonian rigidity, which relate to the location of its pathology in the midbrain and diencephalon. Von Economo incorporated anatomical findings of hypothalamic and upper brainstem lesions into a construct of sleep–wake anatomy that resembles our current model of it. In his 1931 paper entitled *Sleep as a Problem of Localization*, von Economo writes "the inflammation in cases associated with insomnia is localized anteriorly in the lateral wall of the third ventricle, near the corpus striatum, while it is localized in cases showing disturbances of ocular muscles with sopor (stupor) in the posterior wall of the third ventricle near the nuclei of the oculomotorius in the cap of the interbrain." In this statement, he proposes that the center for sleep lies in the anterior hypothalamus and the center for wakefulness lies in the posterior hypothalamus and upper brainstem. Von Economo's work held little sway in his time, however.

It wasn't until the 1940s and 1950s that neurophysiologists Giuseppe Moruzzi and H. W. Magoun performed a series of electroencephalographic studies that proved the existence of an active arousal generator in the brainstem reticular formation, which was coined the ascending reticular activating system. The reticular activating system was proven to receive widespread sensory information from the periphery and indirectly activate the cerebral cortex by way of diffuse projection fibers to the thalamus. Their model is still clinically useful, today. Lesions in the upper brainstem do cause coma and stimulation of the reticular formation does promote wakefulness; however, animals with chronic reticular formation lesions often regain wakefulness over time, which is incongruent with their model.

In the 1960s and 1970s, this inconsistency prompted further investigation into the construct of sleep and wakefulness, and new observations confirmed the importance of the posterior hypothalamus and the basal forebrain in the model of wakefulness, as von Economo had earlier suggested. More recently, the marked specificity of the reticular formation has become clear. It is now viewed as a highly specialized system, active in numerous, varied functions beyond just wakefulness, including motor activities such as saccadic eye movements.

Over the last 60 years, the main neurotransmitters involved in the promotion of sleep and wakefulness have been identified. They are the cholinergic neurons of the pedunculopontine and lateral dorsal

tegmental nuclei in the upper brainstem; the histaminergic neurons of the tuberomammillary nuclei in the middle nuclear group of the hypothalamus; and the catecholamine-producing neurons, which include the dopaminergic neurons of the substantia nigra and ventral tegmental area in the midbrain; norepinephrine neurons in the pontine tegmentum; noradrenergic neurons in the locus ceruleus of the pons; and the upper brainstem group of serotinergic raphe nuclei. The role of the neuropeptide orexin (aka hypocretin) has most recently gained attention. It is excreted from the posterior hypothalamus and serves as a stabilizer of the "flip-flop switch," which is a bistate circuit that coordinates abrupt transitions in sleep–wake states.

The role of these neurotransmitters in combination with our understanding of sleep–wake anatomy has led to an interrelated model for sleep–wake circuitry that is an elaboration of what von Economo proposed in the early 1900s. It involves multi-system pathways in the basal forebrain, diencephalon, and upper brainstem.

In our current model, three states of consciousness exist: wakefulness, non-rapid eye movement sleep (NREM sleep), and rapid eye movement sleep (REM sleep). In NREM sleep, electroencephalography (EEG) demonstrates slow brain wave activity, whereas in REM sleep, it shows rapid eye movements and fast brain wave activity similar to that of wakefulness. Loss of muscle tone occurs during REM sleep, exclusively, presumably to prevent us from acting out our dreams.

In this chapter, we will draw the important tristate generators, modulators, and afferent and efferent pathways of wake, NREM sleep, and REM sleep states. We will begin with a diagram of the arousal cells, but we need to organize them based on a discussion of the direct and indirect pathways for wakefulness, which originate in select areas of the upper brainstem, forebrain, and diencephalon. One pathway synapses in the thalamus and the other synapses directly in the lateral hypothalamus, basal forebrain, and cerebral cortex. The projection to the thalamus is important for arousal but also for the inactivation of sensory gating.

Sensory gating is the inhibition of sensory information to the cerebral cortex during sleep. During sleep, T-type calcium channels, more specifically $Ca_v3.1$ T-type calcium channels in the rostral midline of the thalamus inhibit firing of sensory information from the thalamus to the cortex. Thus, as early twentieth century neurologists

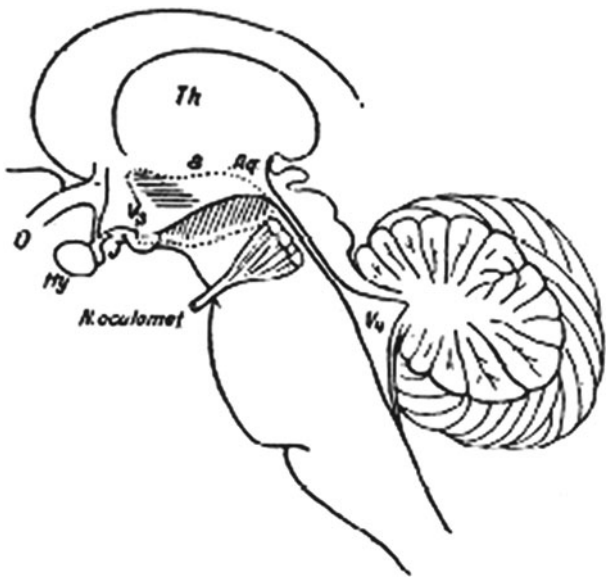

Photo 39-1 von Economo's anatomical drawing of the sleep centers. The anterior hypothalamus is indicated with horizontal lines and is the sleep center and the posterior hypothalamus is indicated with diagonal lines and is the wakefulness center

From von Economo, C. "Sleep as a Problem of Localization." *The Journal of Nervous and Mental Disease* 71, no. 3 (1930): 249–259.

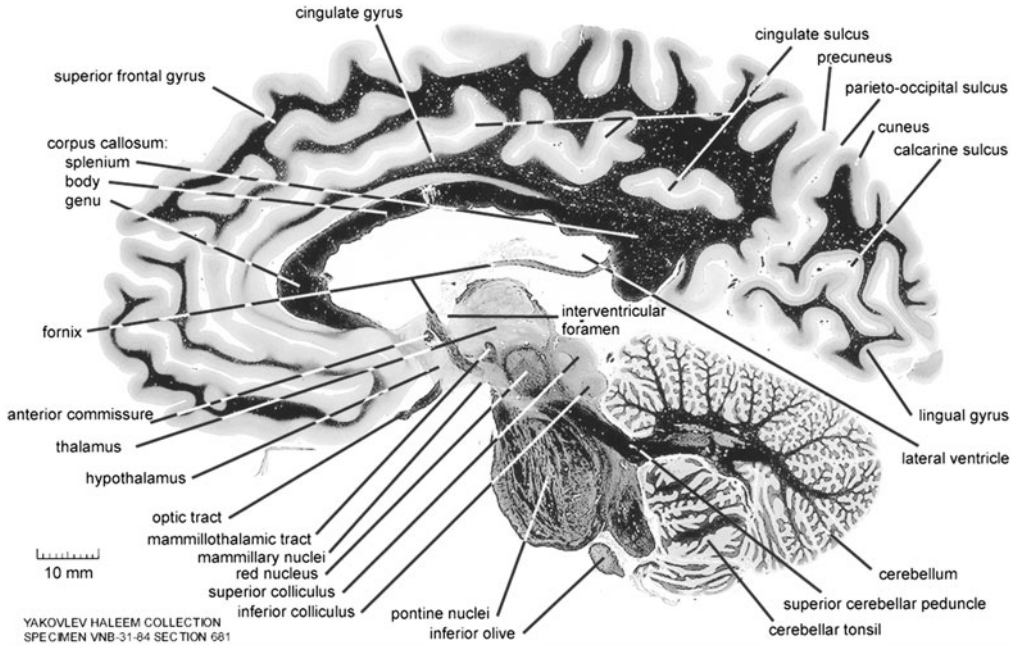

Photo 39-2 Mid-sagittal section through the brain to show the structural anatomy of the sleep and wakefulness centers
With permission from the Michigan State University: Brain Biodiversity Bank. https://www.msu.edu/~brains/

suggested, in this manner, sleep does involve a period of decreased sensory flow to the cerebral cortex. Tonic firing of wake-promoting cells results in inactivation of the T-type calcium channels (i.e., they inhibit sensory gating) and, on the contrary, rhythmic burst firing of sleep-promoting cells de-inactivates the T-type calcium channels and promotes sensory gating.

Let's draw the wakefulness cells beginning with those that indirectly stimulate the cortex through the thalamus. Draw a mid-sagittal section through the brain and brainstem. Show the paired brainstem cholinergic neurons: the *lateral dorsal tegmental nucleus* in the midbrain and the *pedunculopontine nucleus* in the pons. They are neurobehavioral cells and so they lie within the dorsal tegmentum. These cells are active during REM sleep, which differentiates them from the other brainstem arousal cells (the monoaminergic neurons).

Next, we will draw the wakefulness cells that send fibers directly to the cerebral cortex. We will start with the upper brainstem monoaminergic nuclei. In the pons, draw the noradrenergic *locus ceruleus*; in the midbrain, the dopaminergic *substantia nigra* and, just behind it, the dopamine-producing *ventral tegmental area*; and in the upper pons and midbrain, draw the upper brainstem group of serotinergic *raphe nuclei*. Amphetamines inhibit the reuptake of monoaminergic neurotransmitters from the synaptic cleft to promote wakefulness. Next, let's move to the hypothalamus. Draw the middle group *lateral nucleus* (aka *tuberomammillary nucleus*) in the center of the hypothalamus. It is the sole source of histamine in the brain, which is important in the initiation phase of wakefulness. As a pharmacological corollary, anti-histamines, such as diphenhydramine (aka *Benadryl*), make us drowsy. Lastly, include the cholinergic *basal forebrain nuclei* in the ventral surface of the frontal lobe. Remember, the cholinergic basal nucleus of Meynert in the substantia innominata of the basal forebrain is important in the neurobiology of memory, and cholinergic medications are used to augment the production of acetylcholine from these nuclei in patients with dementia.

In addition to their role in wakefulness, the cholinergic pedunculopontine and lateral dorsal tegmental neurons are active during REM sleep and are called "REM-on" neurons, whereas the monoaminergic neurons are not active during REM sleep and are called "REM-off" neurons. Monoaminergic reuptake inhibitors (i.e., antidepressants such as serotonin-reuptake inhibitors) promote monoaminergic activity and inhibit the generation of REM sleep.

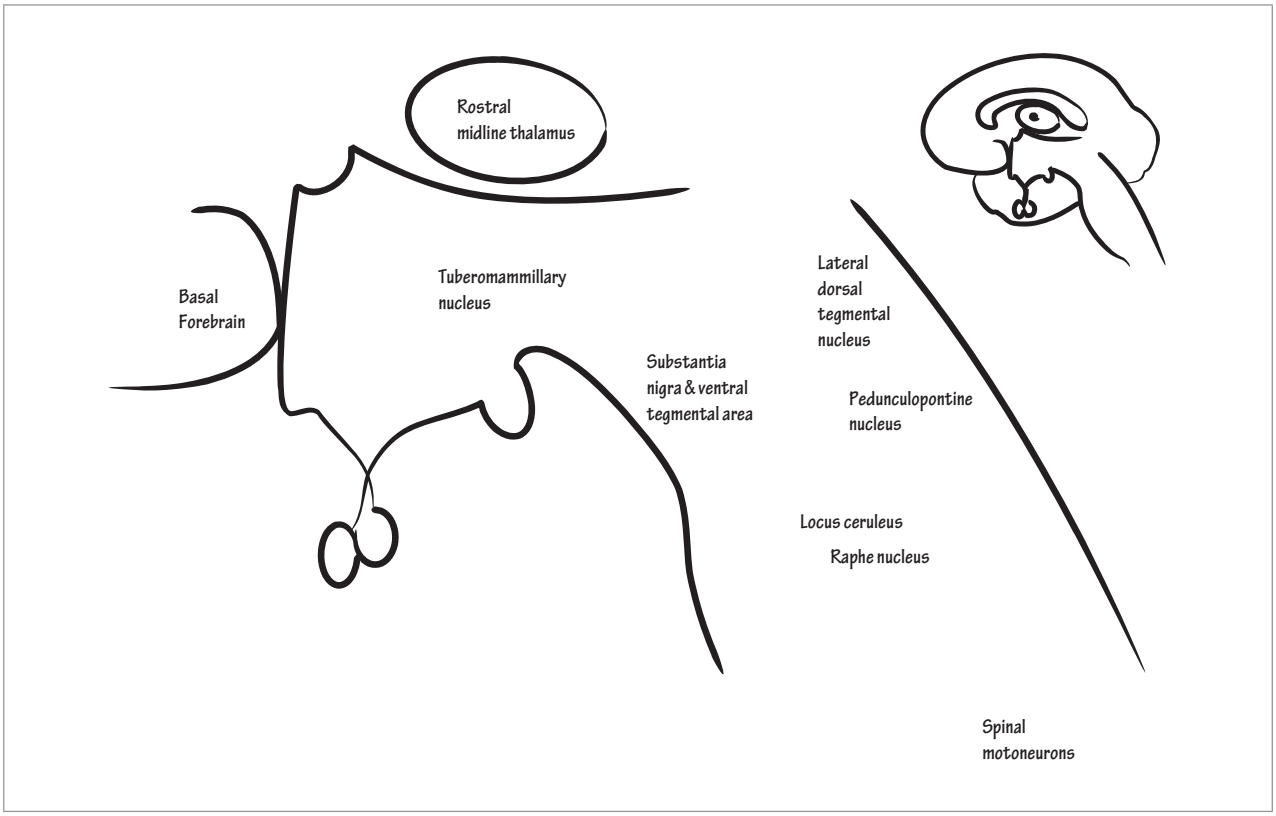

Figure 39-1 Cells for wakefulness

Now that we have drawn the cells related to wakefulness, let's draw the ones that promote sleep. In the anterior nuclear group of the hypothalamus, the ventrolateral and median preoptic nuclei play important roles in sleep promotion. Evidence suggests that the ventrolateral preoptic nucleus is important for sleep consolidation and the median preoptic nucleus helps in homeostatic sleep drive and sleep initiation. For simplicity, only include the *ventrolateral preoptic nucleus* in this diagram—it is the better recognized of the two. The ventrolateral preoptic nucleus is subdivided into cluster and extended groups that promote different types of sleep states (NREM and REM phases).

The ventrolateral preoptic nuclear cluster primarily stimulates the histaminergic tuberomammillary hypothalamic nuclei of the middle group, which produce NREM sleep. The extended ventrolateral preoptic nucleus inhibits the monoaminergic locus ceruleus and raphe nuclei in the promotion of REM sleep.

Mutual inhibition between the sleep–wake centers allows for coordinated transitions in sleep–wake states through a flip–flop switch. A flip–flop circuit is an electrical engineering term for a switch that avoids transitional states; the circuit is in either one of two states but not in a blend of both. If you are tired when you lie down, you quickly fall asleep, and when you're ready to rise, you suddenly wake up. The arousal center inhibits the sleep center and vice-versa to promote this switch effect. But what prevents unwanted flip–flopping between states? A neuropeptide called orexin that is released from the posterior hypothalamus.

In the posterior hypothalamus, draw the *perifornical lateral hypothalamic area* (in reference to the hippocampal-fornices that pass through the lateral hypothalamus). This area produces the neuropeptide orexin (aka hypocretin)—orexin and hypocretin are structurally similar neuropeptides that are functionally equivalent, that is, they both stabilize the flip–flop switch and their names are used synonymously. Loss of orexin production through gliosis or other injury to the perifornical hypothalamic area in the posterior–lateral hypothalamus results in narcolepsy with cataplexy, which consists of intrusion of sleep during wakefulness and inappropriate wakefulness during sleep. Interestingly, the overall sleep time in patients with narcolepsy is equivalent to that of the rest of the population but the fragmentation of sleep leads to sleepiness.

Now we know what keeps us awake and asleep, but what drives the flip–flop switch to the sleep state? Of particular interest is the build-up of adenosine with normal brain metabolism. Broadly, adenosine appears to promote sleep, and NREM sleep, in turn, reduces adenosine levels. There is some evidence that caffeine, which is second only to oil in global financial importance, is believed to act on adenosine receptors to promote wakefulness.

Many proteins have significant diurnal changes and have been associated with causing sleepiness. The circadian rhythm influences on sleep are discussed in the "Hypothalamus" chapter. Briefly, the suprachiasmatic region of the hypothalamus is an important promoter of sleep–wake cycles; it stimulates the neighboring hypothalamic paraventricular nucleus to activate the pineal body to produce and release melatonin, which promotes sleep.

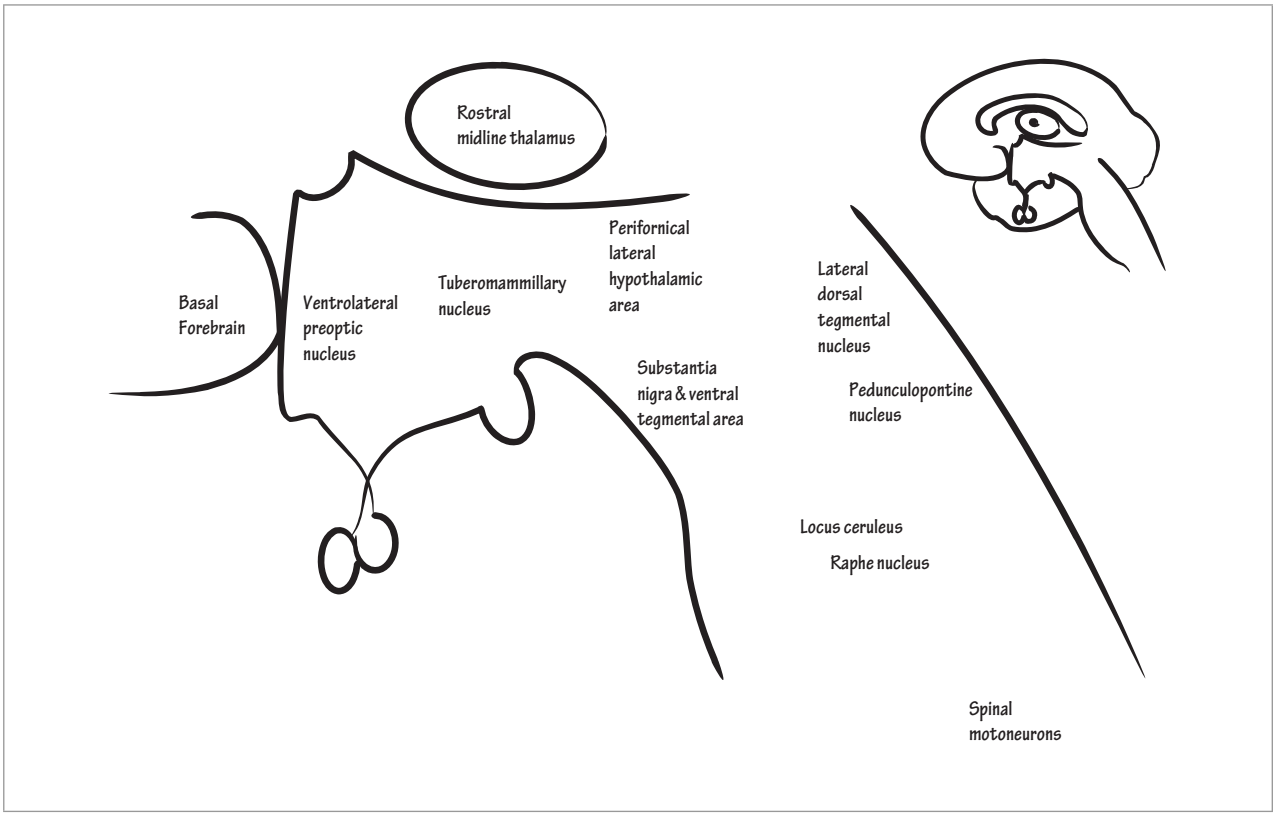

Figure 39-2 Cells for sleep and wakefulness

Now let's draw a flow diagram to show the projections from the sleep–wake centers involved in the flip–flop circuit. First, write out the different wake-promoting cells and their neurotransmitters: the *monoaminergic upper brainstem nuclei*, the *histaminergic middle group hypothalamic nucleus*, and the *cholinergic lateral dorsal tegmental* and *pedunculopontine nuclei* and *basal forebrain cholinergic nuclei*. Then, write out the end target—the *cerebral cortex*. Next, draw efferent fibers from the cholinergic lateral dorsal tegmental and pedunculopontine nuclei to the *rostral, midline thalamus*. From the thalamus, draw *thalamocortical* projection fibers to the cerebral cortex. This is the indirect wake-promoting pathway. Next, show direct activating efferent fibers to the cerebral cortex from the monoaminergic upper brainstem nuclei, the middle group hypothalamic nucleus, and the basal forebrain cholinergic nuclei.

Label the *ventrolateral preoptic hypothalamic* nucleus as the sleep promoter. Show that it sends inhibitory fibers to the wake-promoting cells. Then show that the wake-promoting cells send inhibitory fibers back to the sleep center. This establishes the bistate model.

Next, label the stabilizer of the flip–flop circuit, the orexin cell group in the *perifornical lateral hypothalamic area*. Show that it sends stabilizing fibers to the arousal cells. Finally, draw inhibitory fibers from the ventrolateral preoptic hypothalamic nucleus to the perifornical lateral hypothalamic area. This completes the flip–flop circuit portion of our diagram.

Now, in this last section, let's add a simplified version of the pathway for muscle atonia during REM sleep. In NREM sleep, dreams are simplistic, if present; they involve passive activities, such as listening to a song, so muscle atonia is unnecessary. But in REM sleep, dreams are complex and vivid. In REM sleep behavior disorder, muscle atonia is lost and patients act out their dreams. The pathologic region in REM sleep behavior disorder in humans is still unproven but lesions in the rat medullary magnocellular reticular formation and sublaterodorsal nucleus cause loss of muscle atonia during REM sleep. Add the *sublaterodorsal nucleus* and the *magnocellular reticular formation* to the ponto-medullary junction and draw an inhibitory line from them to *spinal motoneurons* in the spinal cord.

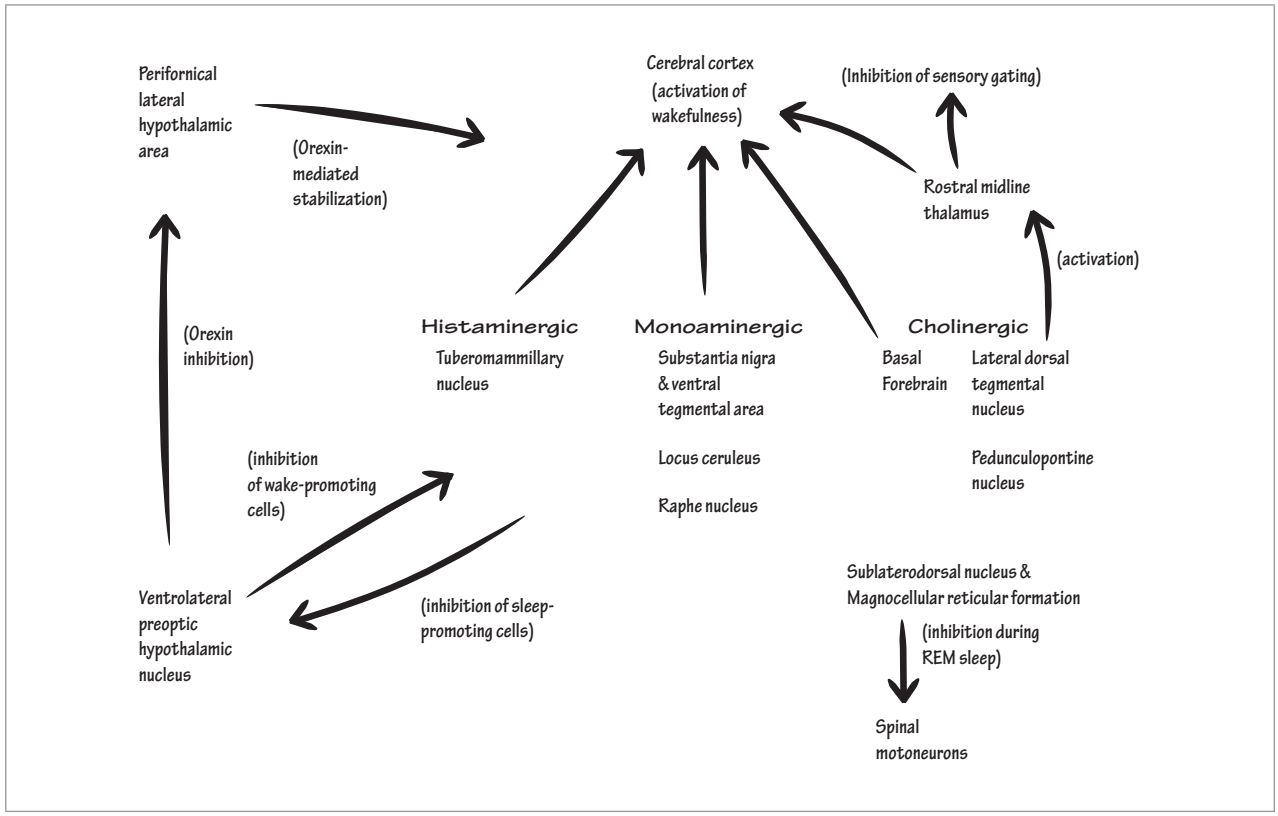

Figure 39-3 Bistate model of sleep and wakefulness with inhibition of spinal motor neurons during REM sleep

Frequently Used References

Aids to the Examination of the Peripheral Nervous System. 4th ed. Edinburgh: Churchill Livingstone, 2000.

Baloh, R. W., and V. Honrubia. *Clinical Neurophysiology of the Vestibular System*. 3rd ed., Contemporary Neurology Series 63. Oxford and New York: Oxford University Press, 2001.

Bogousslavsky, J., and L. R. Caplan. *Stroke Syndromes*. 2nd ed. Cambridge and New York: Cambridge University Press, 2001.

Brodal, P. *The Central Nervous System: Structure and Function*. 3rd ed. Oxford and New York: Oxford University Press, 2004.

Davis, L. E., M. K. King, and J. L. Schultz. *Fundamentals of Neurologic Disease: An Introductory Text*. New York, NY: Demos Medical Pub., 2005.

DeMyer, W. *Technique of the Neurologic Examination: A Programmed Text*. 3d ed. New York: McGraw-Hill, 1980.

——. *Neuroanatomy*. 2nd ed., The National Medical Series for Independent Study. Baltimore: Williams and Wilkins, 1998.

Devinsky, O., and M. D'Esposito. *Neurology of Cognitive and Behavioral Disorders*, Contemporary Neurology Series. Oxford and New York: Oxford University Press, 2004.

Duvernoy, H. M. *The Human Hippocampus: Functional Anatomy, Vascularization and Serial Sections with Mri*. 3rd ed. Berlin and New York: Springer, 2005.

Federative Committee on Anatomical Terminology. *Terminologia Anatomica: International Anatomical Terminology*. Stuttgart and New York: Thieme, 1998.

Fehrenbach, M. J., and S. W. Herring. *Illustrated Anatomy of the Head and Neck*. Philadelphia: W. B. Saunders, 1996.

Feinberg, T. E., and M. J. Farah. *Behavioral Neurology and Neuropsychology*. 2nd ed. New York: McGraw-Hill Medical Publishing Division, 2003.

Haines, D. E. *Fundamental Neuroscience*. 3rd ed. Philadelphia: Churchill Livingstone, 2006.

Harnsberger, H. R., and A. J. Macdonald. *Diagnostic and Surgical Imaging Anatomy. Brain, Head & Neck, Spine*. 1st ed. Salt Lake City: Amirsys, 2006.

Kiernan, J. A., and M. L. Barr. *Barr's the Human Nervous System: An Anatomical Viewpoint*. 8th ed. Philadelphia: Lippincott Williams & Wilkins, 2005.

Leblanc, A. *Encephalo-Peripheral Nervous System: Vascularisation, Anatomy, Imaging*. Berlin and New York: Springer, 2001.

Leigh, R. J., and D. S. Zee. *The Neurology of Eye Movements*. Oxford University Press.

Manto, M.-U., and M. Pandolfo. *The Cerebellum and Its Disorders*. Cambridge and New York: Cambridge University Press, 2002.

Masland, R. H. *The Senses: A Comprehensive Reference*. 1st ed. 6 vols. Amsterdam and Boston: Elsevier, 2008.

Netter, F. H. *Atlas of Human Anatomy*. 4th ed. Philadelphia, PA: Saunders/Elsevier, 2006.

Netter, F. H., Ciba Pharmaceutical Products inc., and CIBA-GEIGY Corporation. *The Ciba Collection of Medical Illustrations: A Compilation of Pathological and Anatomical Paintings*. Summit, NJ: Ciba Pharmaceutical Products, 1959.

Noback, C. R. *The Human Nervous System: Structure and Function*. 6th ed. Totowa, NJ: Humana Press, 2005.

Nolte, J., and J. B. Angevine. *The Human Brain in Photographs and Diagrams*. 3rd ed. Philadelphia: Mosby/Elsevier, 2007.
Parent, A., and M. B. Carpenter. *Carpenter's Human Neuroanatomy*. 9th ed. Baltimore: Williams & Wilkins, 1996.
Purves, D. *Neuroscience*. 3rd ed. Sunderland, MA: Sinauer Associates, Publishers, 2004.
Samuels, M. A. *Office Practice of Neurology*. New York: Churchill Livingstone, 1996.
Schiefer, U., H. Wilhelm, and W. M. Hart. *Clinical Neuro-Ophthalmology: A Practical Guide*. Springer.
Schmahmann, J. D., and D. N. Pandya. *Fiber Pathways of the Brain*. New York: Oxford University Press, 2006.
Schünke, M., L. M. Ross, E. D. Lamperti, E. Schulte, and U. Schumacher. *Head and Neuroanatomy*. Stuttgart and New York: Thieme, 2007.
Schwartzman, R. J. *Neurologic Examination*. 1st ed. Malden, MA: Blackwell Pub., 2006.
Woolsey, T. A., J. Hanaway, and M. H. Gado. *The Brain Atlas: A Visual Guide to the Human Central Nervous System*. 3rd ed. Hoboken, NJ: Wiley, 2008.

Additional References

Al-Shekhlee, A., B. E. Shapiro, and D. C. Preston. "Iatrogenic Complications and Risks of Nerve Conduction Studies and Needle Electromyography." *Muscle Nerve* 27, no. 5 (2003): 517–26.
Altman, J., and S. A. Bayer. *Development of the Human Spinal Cord: An Interpretation Based on Experimental Studies in Animals*. Oxford and New York: Oxford University Press, 2001.
Andersen, P. *The Hippocampus Book*. Oxford and New York: Oxford University Press, 2007.
Anderson, M. P., T. Mochizuki, J. Xie, W. Fischler, J. P. Manger, E. M. Talley, T. E. Scammell, and S. Tonegawa. "Thalamic Cav3.1 T-Type Ca2+ Channel Plays a Crucial Role in Stabilizing Sleep." *Proc Natl Acad Sci U S A* 102, no. 5 (2005): 1743–8.
Arbelaez, A., A. Pajon, and M. Castillo. "Acute Marchiafava-Bignami Disease: Mr Findings in Two Patients." *AJNR Am J Neuroradiol* 24, no. 10 (2003): 1955–7.
Baehr, M., M. Frotscher, and P. Duus. *Duus' Topical Diagnosis in Neurology: Anatomy, Physiology, Signs, Symptoms*. 4th, completely rev. ed. Stuttgart and New York: Thieme, 2005.
Benarroch, E. E. "Enteric Nervous System: Functional Organization and Neurologic Implications." *Neurology* 69, no. 20 (2007): 1953–7.
Benarroch, E. E. "Suprachiasmatic Nucleus and Melatonin: Reciprocal Interactions and Clinical Correlations." *Neurology* 71, no. 8 (2008): 594–8.
Berkovic, S. F., and P. F. Bladin. "Rubral Tremor: Clinical Features and Treatment of Three Cases." *Clin Exp Neurol* 20, (1984): 119–28.
Bhattacharyya, N. *Brainstem Auditory Evoked Response*. Emedicine from WebMD, 2009. http://emedicine.medscape.com/article/836277-overview.
Bielefeldt, K., J. A. Christianson, and B. M. Davis. "Basic and Clinical Aspects of Visceral Sensation: Transmission in the Cns." *Neurogastroenterol Motil* 17, no. 4 (2005): 488–99.
Binder, J. The Functional Neuroanatomy of Language and Aphasia. Paper presented at the annual American Academy of Neurology, April 12–19, 2008.
Binder, J. R., J. A. Frost, T. A. Hammeke, P. S. Bellgowan, J. A. Springer, J. N. Kaufman, and E. T. Possing. "Human Temporal Lobe Activation by Speech and Nonspeech Sounds." *Cereb Cortex* 10, no. 5 (2000): 512–28.
Binder, J. R., J. A. Frost, T. A. Hammeke, S. M. Rao, and R. W. Cox. "Function of the Left Planum Temporale in Auditory and Linguistic Processing." *Brain* 119 Pt 4, (1996): 1239–47.
Bingham, N. C., K. K. Anderson, A. L. Reuter, N. R. Stallings, and K. L. Parker. "Selective Loss of Leptin Receptors in the Ventromedial Hypothalamic Nucleus Results in Increased Adiposity and a Metabolic Syndrome." *Endocrinology* 149, no. 5 (2008): 2138–48.
Biran, I., and A. Chatterjee. "Alien Hand Syndrome." *Arch Neurol* 61, no. 2 (2004): 292–4.
Boeve, B. F., D. W. Dickson, E. J. Olson, J. W. Shepard, M. H. Silber, T. J. Ferman, J. E. Ahlskog, and E. E. Benarroch. "Insights into Rem Sleep Behavior Disorder Pathophysiology in Brainstem-Predominant Lewy Body Disease." *Sleep Med* 8, no. 1 (2007): 60–4.
Boeve, B. F. et. al. "Pathophysiology of Rem Sleep Behaviour Disorder and Relevance to Neurodegenerative Disease." *Brain* 130: 18.
Bogousslavsky, J., F. Regli, and A. Uske. "Thalamic Infarcts: Clinical Syndromes, Etiology, and Prognosis." *Neurology* 38, no. 6 (1988): 837–48.
Budson, A. E., and B. H. Price. "Memory Dysfunction." *N Engl J Med* 352, no. 7 (2005): 692–9.
Burger, K. M., S. Tuhrim, and T. P. Naidich. "Brainstem Vascular Stroke Anatomy." *Neuroimaging Clin N Am* 15, no. 2 (2005): 297–324.
Buttner-Ennever, J. A., and A. K. Horn. "Anatomical Substrates of Oculomotor Control." *Curr Opin Neurobiol* 7, no. 6 (1997): 872–9.
Carrera, E., and J. Bogousslavsky. "The Thalamus and Behavior: Effects of Anatomically Distinct Strokes." *Neurology* 66, no. 12 (2006): 1817–23.
Cervero, F. "Sensory Innervation of the Viscera: Peripheral Basis of Visceral Pain." *Physiol Rev* 74, no. 1 (1994): 95–138.

Chai, T. C., and W. D. Steers. "Neurophysiology of Micturition and Continence." *Urol Clin N Am* 23, no. 2 (1996): 221–36.

Conn, P. M., and G. F. Gebhart. *Essentials of Pharmacology*, Essentials of Medical Education Series. Philadelphia: Davis, 1989.

Crocker, A., R. A. Espana, M. Papadopoulou, C. B. Saper, J. Faraco, T. Sakurai, M. Honda, E. Mignot, and T. E. Scammell. "Concomitant Loss of Dynorphin, Narp, and Orexin in Narcolepsy." *Neurology* 65, no. 8 (2005): 1184–8.

Damasio, H., T. J. Grabowski, D. Tranel, R. D. Hichwa, and A. R. Damasio. "A Neural Basis for Lexical Retrieval." *Nature* 380, no. 6574 (1996): 499–505.

DeArmond, S. J., M. M. Fusco, and M. M. Dewey. *Structure of the Human Brain: A Photographic Atlas*. 3rd ed. New York: Oxford University Press, 1989.

DeLong, M. R., and T. Wichmann. "Circuits and Circuit Disorders of the Basal Ganglia." *Arch Neurol* 64, no. 1 (2007): 20–4.

Dement, W. C., M. H. Kryger, and T. Roth. *Principles and Practice of Sleep Medicine*. Philadelphia: Saunders, 1989.

Dieterich, M. "Central Vestibular Disorders." *J Neurol* 254, no. 5 (2007): 559–68.

Donkelaar, H. J., A. Hori, M. Lammens, and SpringerLink (Online service). *Clinical Neuroembryology Development and Developmental Disorders of the Human Central Nervous System*. Berlin, Heidelberg: Springer-Verlag Berlin Heidelberg, 2006.

Doyle, B Howling like dogs: Metaphorical language in Psalm 59. Paper presented at the annual international meeting for the Society of Biblical Literature, June 19–22, in Berlin, Germany, 2002.

Dupont, S., V. Bouilleret, D. Hasboun, F. Semah, and M. Baulac. "Functional Anatomy of the Insula: New Insights from Imaging." *Surg Radiol Anat* 25, no. 2 (2003): 113–9.

Ferber, R., and M. H. Kryger. *Principles and Practice of Sleep Medicine in the Child*. Philadelphia: Saunders, 1995.

Finger, S. *Origins of Neuroscience: A History of Explorations into Brain Function*. New York: Oxford University Press, 1994.

Gallucci, M., S. Capoccia, A. Catalucci, and SpringerLink (Online service). *Radiographic Atlas of Skull and Brain Anatomy*. Berlin, Heidelberg: Springer-Verlag Berlin Heidelberg, 2007.

Gorno-Tempini, M. L. Left Frontal Speech and Language System. Paper presented at the annual American Academy of Neurology, April 12–19, 2008.

Gorno-Tempini, M. L., and C. J. Price. "Identification of Famous Faces and Buildings: A Functional Neuroimaging Study of Semantically Unique Items." *Brain* 124, no. Pt 10 (2001): 2087–97.

Gorno-Tempini, M. L., C. J. Price, O. Josephs, R. Vandenberghe, S. F. Cappa, N. Kapur, and R. S. Frackowiak. "The Neural Systems Sustaining Face and Proper-Name Processing." *Brain* 121 Pt 11, (1998): 2103–18.

Hamilton, R. Magnetic Stimulation in the Treatment of Stroke and Aphasia. Paper presented at the annual American Academy of Neurology, April 12–19, 2008.

Harnsberger, H. R., and A. J. Macdonald. *Diagnostic and Surgical Imaging Anatomy. Brain, Head & Neck, Spine*. 1st ed. Salt Lake City: Amirsys, 2006.

Haymaker, W., and B. Woodhall. *Peripheral Nerve Injuries, Principles, of Diagnosis*. 2d ed. Philadelphia, PA: Saunders, 1953.

Herman, J. P., M. M. Ostrander, N. K. Mueller, and H. Figueiredo. "Limbic System Mechanisms of Stress Regulation: Hypothalamo-Pituitary-Adrenocortical Axis." *Prog Neuropsychopharmacol Biol Psychiatry* 29, no. 8 (2005): 1201–13.

Herrero, M. T., C. Barcia, and J. M. Navarro. "Functional Anatomy of Thalamus and Basal Ganglia." *Childs Nerv Syst* 18, no. 8 (2002): 386–404.

Hillis, A. E. The Functional Neuroanatomy of Language: Evidence from Acute Stroke. Paper presented at the annual American Academy of Neurology, April 12–19, 2008.

Hotson, J. R., and R. W. Baloh. "Acute Vestibular Syndrome." *N Engl J Med* 339, no. 10 (1998): 680–5.

Jensen, T. S., G. F. Gebhart, and D. L. Hammond. *Proceedings of the 7th World Congress on Pain*, Progress in Pain Research and Management. Seattle: IASP Press, 1994.

Johnson, R. D. "Descending Pathways Modulating the Spinal Circuitry for Ejaculation: Effects of Chronic Spinal Cord Injury." *Prog Brain Res* 152, (2006): 415–26.

Kopell, B. H., and B. D. Greenberg. "Anatomy and Physiology of the Basal Ganglia: Implications for Dbs in Psychiatry." *Neurosci Biobehav Rev* 32, no. 3 (2008): 408–22.

Kryger, M. H., T. Roth, and W. C. Dement. *Principles and Practice of Sleep Medicine*. 4th ed. Philadelphia, PA: Elsevier/Saunders, 2005.

Leranth, C., and T. Hajszan. "Extrinsic Afferent Systems to the Dentate Gyrus." *Prog Brain Res* 163, (2007): 63–84.

Lucchelli, F., and H. Spinnler. "A Reappraisal of Person Recognition and Identification." *Cortex* 44, no. 3 (2008): 230–7.

Lustig, L. R., and J. K. Niparko. *Clinical Neurotology: Diagnosing and Managing Disorders of Hearing, Balance and the Facial Nerve*. London and New York: Martin Dunitz, 2003.

Maleki, J., A. A. LeBel, G. J. Bennett, and R. J. Schwartzman. "Patterns of Spread in Complex Regional Pain Syndrome, Type I (Reflex Sympathetic Dystrophy)." *Pain* 88, no. 3 (2000): 259–66.

Manni, E., and L. Petrosini. "A Century of Cerebellar Somatotopy: A Debated Representation." *Nat Rev Neurosci* 5, no. 3 (2004): 241–9.

May, B. J. "Role of the Dorsal Cochlear Nucleus in the Sound Localization Behavior of Cats." *Hear Res* 148, no. 1–2 (2000): 74–87.

McDowall, L. M., J. Horiuchi, and R. A. Dampney. "Effects of Disinhibition of Neurons in the Dorsomedial Hypothalamus on Central Respiratory Drive.' *Am J Physiol Regul Integr Comp Physiol* 293, no. 4 (2007): R1728–35.

Mendell, J. R., J. T. Kissel, and D. R. Cornblath. *Diagnosis and Management of Peripheral Nerve Disorders*, Contemporary Neurology Series. Oxford: Oxford University Press, 2001.

Miller, A. D., and R. A. Leslie. "The Area Postrema and Vomiting." *Front Neuroendocrinol* 15, no. 4 (1994): 301–20.

Miller, B. Brain Circuits in Cognition: An Overview. Paper presented at the annual American Academy of Neurology, April 12–19, 2008.

Monti, J. M., and D. Monti. "The Involvement of Dopamine in the Modulation of Sleep and Waking." *Sleep Med Rev* 11, no. 2 (2007): 113–33.

Morris, J. G., J. Lee, and C. L. Lim. "Facial Sweating in Horner's Syndrome." *Brain* 107 Pt 3 (1984): 751–8.

Moscovitch, M., R. S. Rosenbaum, A. Gilboa, D. R. Addis, R. Westmacott, C. Grady, M. P. McAndrews, B. Levine, S. Black, G. Winocur, and L. Nadel. "Functional Neuroanatomy of Remote Episodic, Semantic and Spatial Memory: A Unified Account Based on Multiple Trace Theory." *J Anat* 207, no. 1 (2005): 35–66.

Nadel, L., A. Samsonovich, L. Ryan, and M. Moscovitch. "Multiple Trace Theory of Human Memory: Computational, Neuroimaging, and Neuropsychological Results." *Hippocampus* 10, no. 4 (2000): 352–68.

Nakamura, M., I. Miyazawa, K. Fujihara, I. Nakashima, T. Misu, S. Watanabe, T. Takahashi, and Y. Itoyama. "Preferential Spinal Central Gray Matter Involvement in Neuromyelitis Optica. An Mri Study." *J Neurol* 255, no. 2 (2008): 163–70.

Nieuwenhuys, R., C. Huijzen, J. Voogd, and SpringerLink (Online service). "The Human Central Nervous System." Berlin, Heidelberg: Springer Berlin Heidelberg, 2008.

Nolte, J., and J. B. Angevine. *The Human Brain: In Photographs and Diagrams*. St. Louis and London: Mosby, 1995.

Orfei, M. D., R. G. Robinson, G. P. Prigatano, S. Starkstein, N. Rusch, P. Bria, C. Caltagirone, and G. Spalletta. "Anosognosia for Hemiplegia after Stroke Is a Multifaceted Phenomenon: A Systematic Review of the Literature." *Brain* 130, no. Pt 12 (2007): 3075–90.

Patten, J. *Neurological Differential Diagnosis*. 2nd ed. London and New York: Springer, 1996.

Penfield, W., and T. Rasmussen. *The Cerebral Cortex of Man; a Clinical Study of Localization of Function*. New York: Macmillan, 1950.

Petreska, B., M. Adriani, O. Blanke, and A. G. Billard. "Apraxia: A Review." *Prog Brain Res* 164, (2007): 61–83.

Preston, D. C., and B. E. Shapiro. *Electromyography and Neuromuscular Disorders: Clinical-Electrophysiologic Correlations*. 2nd ed. Philadelphia: Butterworth-Heinemann, 2005.

Raphaeli, G., A. Liberman, J. M. Gomori, and I. Steiner. "Acute Bilateral Paramedian Thalamic Infarcts after Occlusion of the Artery of Percheron." *Neurology* 66, no. 1 (2006): E7.

Rolland, A. S., M. T. Herrero, V. Garcia-Martinez, M. Ruberg, E. C. Hirsch, and C. Francois. "Metabolic Activity of Cerebellar and Basal Ganglia-Thalamic Neurons Is Reduced in Parkinsonism." *Brain* 130, no. Pt 1 (2007): 265–75.

Rosen, H. J., S. C. Allison, G. F. Schauer, M. L. Gorno-Tempini, M. W. Weiner, and B. L. Miller. "Neuroanatomical Correlates of Behavioural Disorders in Dementia." *Brain* 128, no. Pt 11 (2005): 2612–25.

Rossi-Durand, C. "Proprioception and Myoclonus." *Neurophysiol Clin* 36, no. 5–6 (2006): 299–308.

Rucker, J. C. "An Update on Acquired Nystagmus." *Semin Ophthalmol* 23, no. 2 (2008): 91–7.

Russell, S. M. *Examination of Peripheral Nerve Injuries*. New York: Thieme, 2006.

Saleem, S. N., A. H. Said, and D. H. Lee. "Lesions of the Hypothalamus: Mr Imaging Diagnostic Features." *Radiographics* 27, no. 4 (2007): 1087–108.

Samuels, M. A. *Office Practice of Neurology*. New York: Churchill Livingstone, 1996.

Saper, C. B., T. E. Scammell, and J. Lu. "Hypothalamic Regulation of Sleep and Circadian Rhythms." *Nature* 437, no. 7063 (2005): 1257–63.

Schmahmann, J. D., and D. N. Pandya. "Disconnection Syndromes of Basal Ganglia, Thalamus, and Cerebrocerebellar Systems." *Cortex* 44, no. 8 (2008): 1037–66.

Schmahmann, J. D., D. N. Pandya, R. Wang, G. Dai, H. E. D'Arceuil, A. J. de Crespigny, and V. J. Wedeen. "Association Fibre Pathways of the Brain: Parallel Observations from Diffusion Spectrum Imaging and Autoradiography." *Brain* 130, no. Pt 3 (2007): 630–53.

Schwartzman, R. J. "Explaining Reflex Sympathetic Dystrophy." *Arch Neurol* 56, no. 5 (1999): 521–2.

Schwartzman, R. J., and A. Popescu. "Reflex Sympathetic Dystrophy." *Curr Rheumatol Rep* 4, no. 2 (2002): 165–9.

Seeley, W. W. Frontal Lobe Anatomy, Networks, and Function. Paper presented at the annual American Academy of Neurology, April 12–19, 2008.

Spinazzola, L., L. Pia, A. Folegatti, C. Marchetti, and A. Berti. "Modular Structure of Awareness for Sensorimotor Disorders: Evidence from Anosognosia for Hemiplegia and Anosognosia for Hemianaesthesia." *Neuropsychologia* 46, no. 3 (2008): 915–26.

Stefani, A., A. M. Lozano, A. Peppe, P. Stanzione, S. Galati, D. Tropepi, M. Pierantozzi, L. Brusa, E. Scarnati, and P. Mazzone. "Bilateral Deep Brain Stimulation of the Pedunculopontine and Subthalamic Nuclei in Severe Parkinson's Disease." *Brain* 130, no. Pt 6 (2007): 1596–607.

Stein, D. J. "Depression, Anhedonia, and Psychomotor Symptoms: The Role of Dopaminergic Neurocircuitry." *CNS Spectr* 13, no. 7 (2008): 561–5.

Storer, K. P., J. Toh, M. A. Stoodley, and N. R. Jones. "The Central Canal of the Human Spinal Cord: A Computerised 3-D Study." *J Anat* 192, Pt 4 (1998): 565–72.

Sundin, L., and S. Nilsson. "Branchial Innervation." *J Exp Zool* 293, no. 3 (2002): 232–48.

Swanson, L. W. *Brain Architecture: Understanding the Basic Plan*. Oxford and New York: Oxford University Press, 2003.

Szymusiak, R., and D. McGinty. "Hypothalamic Regulation of Sleep and Arousal." *Ann NY Acad Sci* 1129 (2008): 275–86.

Tanaka, Y. "[Responsible Lesion for Diagnostic Dyspraxia]." *Rinsho Shinkeigaku* 34, no. 3 (1994): 274–5.

Tatu, L., T. Moulin, J. Bogousslavsky, and H. Duvernoy. "Arterial Territories of Human Brain: Brainstem and Cerebellum." *Neurology* 47, no. 5 (1996): 1125–35.

——. "Arterial Territories of the Human Brain: Cerebral Hemispheres." *Neurology* 50, no. 6 (1998): 1699–708.

Tazoe, T., T. Kida, T. Wasaka, M. Sakamoto, T. Nakajima, Y. Nishihira, and T. Komiyama. "Attenuation of the Effect of Remote Muscle Contraction on the Soleus H-Reflex During Plantar Flexion." *Clin Neurophysiol* 116, no. 6 (2005): 1362–9.

Thakkar, M. M., S. C. Engemann, K. M. Walsh, and P. K. Sahota. "Adenosine and the Homeostatic Control of Sleep: Effects of A1 Receptor Blockade in the Perifornical Lateral Hypothalamus on Sleep-Wakefulness." *Neuroscience* 153, no. 4 (2008): 875–80.

Uchino, A., Y. Takase, K. Nomiyama, R. Egashira, and S. Kudo. "Acquired Lesions of the Corpus Callosum: Mr Imaging." *Eur Radiol* 16, no. 4 (2006): 905–14.

van de Beek, W. J., R. J. Schwartzman, S. I. van Nes, E. M. Delhaas, and J. J. van Hilten. "Diagnostic Criteria Used in Studies of Reflex Sympathetic Dystrophy." *Neurology* 58, no. 4 (2002): 522–6.

van den Top, M., and D. Spanswick. "Integration of Metabolic Stimuli in the Hypothalamic Arcuate Nucleus." *Prog Brain Res* 153, (2006): 141–54.

Viskontas, I. V. Human Memory: from Cells to Systems. Paper presented at the annual American Academy of Neurology, April 12–19, 2008.

Vodusek, D. B. "Anatomy and Neurocontrol of the Pelvic Floor." *Digestion* 69, no. 2 (2004): 87–92.

von Economo, C. "Sleep as a Problem of Localization." *J Nerv Ment Dise* 71, no. 3 (1930).

Voogd, J., and M. Glickstein. "The Anatomy of the Cerebellum." *Trends Neurosci* 21, no. 9 (1998): 370–5.

Wan, I. Y., G. D. Angelini, A. J. Bryan, I. Ryder, and M. J. Underwood. "Prevention of Spinal Cord Ischaemia During Descending Thoracic and Thoracoabdominal Aortic Surgery." *Eur J Cardiothorac Surg* 19, no. 2 (2001): 203–13.

Warwick, R. "A Study of Retrograde Degeneration in the Oculomotor Nucleus of the Rhesus Monkey, with a Note on a Method of Recording Its Distribution." *Brain* 73, no. 4 (1950): 532–43.

Webster, G. F., R. V. Iozzo, R. J. Schwartzman, A. J. Tahmoush, R. L. Knobler, and R. A. Jacoby. "Reflex Sympathetic Dystrophy: Occurrence of Chronic Edema and Nonimmune Bullous Skin Lesions." *J Am Acad Dermatol* 28, no. 1 (1993): 29–32.

Willoughby, E. W., and N. E. Anderson. "Lower Cranial Nerve Motor Function in Unilateral Vascular Lesions of the Cerebral Hemisphere." *Br Med J (Clin Res Ed)* 289, no. 6448 (1984): 791–4.

Wilson-Pauwels, L., E. J. Akesson, and P. A. Stewart. *Cranial Nerves*. 2nd ed. Hamilton, ON and London: B C Decker, 2002.

Zadikoff, C., and A. E. Lang. "Apraxia in Movement Disorders." *Brain* 128, no. Pt 7 (2005): 1480–97.

Zee, P. C., and P. Manthena. "The Brain's Master Circadian Clock: Implications and Opportunities for Therapy of Sleep Disorders." *Sleep Med Rev* 11, no. 1 (2007): 59–70.

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