Human Structure & Function | 2020

A Laboratory Guide for Learning Functional Human Neuroanatomy

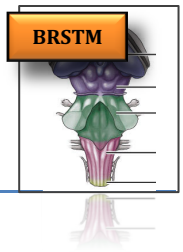
Internal Anatomy of the Brainstem and Spinal Cord

LABORATORY PROTOCOL

1. **Spinal cord**
   - Learning objective: ***recognize the internal distinctions among spinal cord levels.***
   - Specimens: one CNS specimen (with brain and spinal cord attached) available in lab
   - Activities:
     - Open to **Figure 1.5** and the associated chart, and open the histological atlas of the brainstem and spinal cord ("Brainstem Cross-Sectional Atlas") in ***Sylvius4 Online*** (see the *Sylvius Self-Study Exercise*—Medullary Surface)
     - Find each of the features listed in the chart and described in the text as you can on the sectional, histological views of the human spinal cord. (Do the spinal cord **Challenge.**)

2. **Do the brainstem Challenges**
   - Learning objective: ***describe the relation between major external features of the brainstem, including the cranial nerves, and internal gray matter and white matter structures in each embryological division.***
   - Resources: ***Sylvius4 Online***
   - Activities (to be done remotely):
     - Work through **Challenges 3.2–3.4** by referring to the charts and figures associated with descriptions of various sections through the medulla, pons and midbrain. Find each of the features listed in the charts and described in the text as you in the Brainstem Atlas found in ***Sylvius4 Online***.
     - Identify internal features of the brainstem that account for distinctive external features of each embryological subdivision; refer to the Brainstem Atlas in ***Sylvius4 Online*** for additional sections and annotations.

3. **Examine slabs through human brainstem specimens**
   - Learning objective: ***recognize the principal features of the brainstem that are visible with the unaided eye, including major gray matter and white matter structures in each embryological division.***
   - Specimens: thin gross slabs cut through the brainstem
   - Activities (to be done in the gross anatomy lab):
     - Repeat **Challenges 3.2–3.4** using gross sections through the human brainstem, referring to the charts and figures associated with the text and the Brainstem Atlas in ***Sylvius4 Online***.



Internal Anatomy of the Brainstem and Spinal Cord

- Find as many of the visible gray and white matter features listed in the chart and described in the text as you can on actual specimens of the human brainstem.
- Refer to **Figures 3.12–3.15** and identify the regions in wet slabs through the human brainstem containing cranial nerve nuclei (refer also to the Brainstem Atlas in ***Sylvius4 Online***).
- Refer to **Figures 3.19 & 3.22** and find the "black substance" in the midbrain and pons.

4. **Predict the impairments with brainstem stroke**
   - Learning objective: ***discuss functional impairments associated with vascular lesions that are typical in the brainstem.***
   - Resources: brain or brainstem models; ***Sylvius4 Online***
   - Activities (to be done remotely):
     - Work through **Challenge 3.5** by referring to **Figure 3.16** and the charts and figures associated with descriptions of various sections through the brainstem
     - Refer to the Brainstem Atlas in ***Sylvius4 Online*** for additional sections and annotations as needed.
     - Identify the vessels that supply major medial and lateral regions of the brainstem.

Introduction

Of chief importance in understanding the organization of the brainstem and spinal cord is knowledge of what is localized in each embryological subdivision and in any transverse section from any level. This is a significant challenge for every student of neuroanatomy. But be encouraged! You already took the first step toward mastery of this knowledge since you now are familiar with the external features of each brainstem subdivision and each major level of the spinal cord. In this lab, you will relate this knowledge of superficial anatomy to internal anatomy, and discover additional important features of the brainstem and spinal that are not discernible from gross inspection of their surface features.

But before beginning a detailed study of the internal anatomy of the brainstem and spinal cord, it will be helpful to familiarize yourself with some common conventions that are used to describe the deep structures of the central nervous system.

Terminology and general principles

As you studied in the histology labs, the simplest classification of central nervous tissue is **white matter** and **gray matter** (**Figure 3.1**). The gray matter (so-named because it looks grayish or brown in fresh specimens, as you have already seen) is made up of neuronal cell bodies, their dendrites, and the terminal arborizations of both local axons and those from distant sources; and of course, the glial cells and vascular

Internal Anatomy of the Brainstem and Spinal Cord

endothelium that is resident in gray matter. The dendrites and the axons that form synapses with them are sometimes referred to as "neuropil." The white matter is made up of the axons that connect separated areas of gray matter; and of course, the glial cells and vascular endothelium that is resident in white matter. The myelin that ensheathes many of these axons gives the white matter its glistening light tan (white) appearance. Note that an individual neuron can contribute to both gray and white matter. Axons projecting from one part of the brain to another usually group together in bundles. Likewise, neurons that serve similar functions often form clusters or columns.

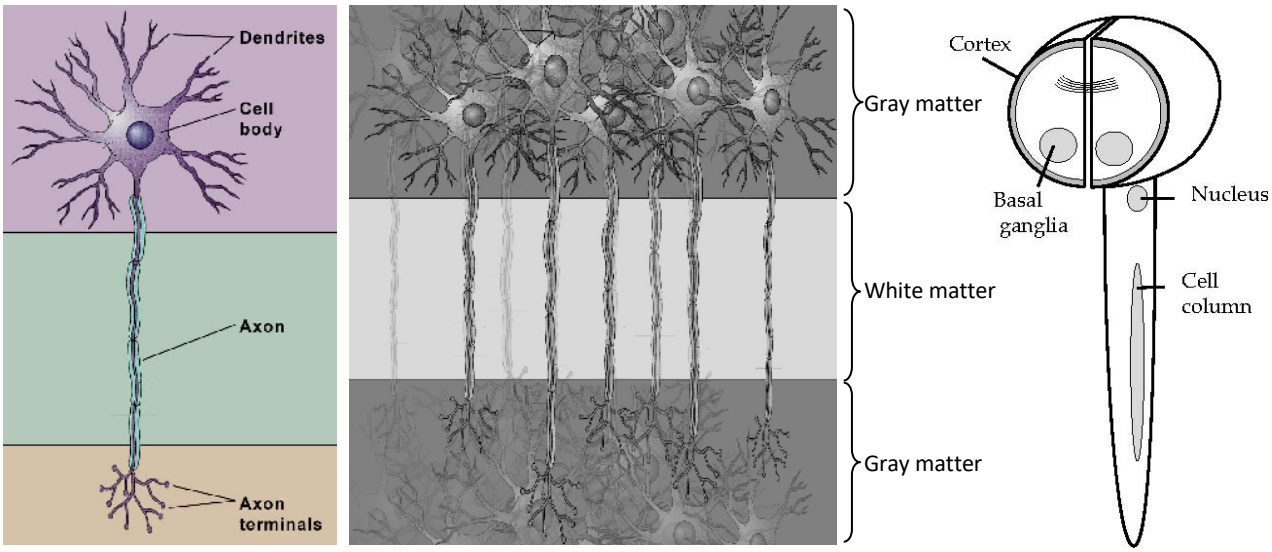


Figure 3.1. Gray and white matter in the central nervous system. *Left*, Drawings depicting the composition of both types of neural tissue (Illustration courtesy of Pyramis Studios, Durham NC). *Right*, Drawing of the organization of gray and white matter in the brain and spinal cord; cortex, basal ganglia, nucleus, and cell column are all examples of gray matter in the central nervous system. (Illustration by N.B. Cant)

Common terms used to refer to white matter bundles and gray matter clusters:

Terms used to refer to gray matter

Column
Cortex (plural: cortices; L., bark)
Ganglion (plural: ganglia; Gr., swelling)
Layer
Nucleus (plural: nuclei)

The large number of terms used to refer to similar structures may seem annoying, but it is not unlike the case in non-medical English usage. Consider, for example, the many terms that refer to roadways (street, avenue, boulevard, interstate, path, road, highway, etc.).

Terms used to refer to white matter

These five terms are used to refer to bundles of axons:

Column
Fasciculus (L., fascia, band or bundle)
Funiculus (L., funis, cord)
Lemniscus (L. from Gr., lemniskos, fillet, ribbon)
Tract

These terms also refer to bundles of axons; typically, those that can be seen from the surface of the brain:

Brachium (L., arm)
Peduncle (L., pes, foot, stalk)

These terms refer to the crossing of axons from one side of the CNS to the other. A **commissure** contains axons crossing from one location to its counterpart on the other side. A **decussation** contains axons that travel to a contralateral location in a non-corresponding region of the central nervous system.

Commissure (L., joining together)
Decussation (L., decussare, to cross in the form of an "X")

Many nuclei and tracts in the central nervous system are much longer than they are wide, calling to mind a column or a rod. (Note that the word 'column' is used to refer to both white matter and gray matter.) Although the terms that refer to white matter structures are not used interchangeably, they all refer to essentially the same constituent—axons (often heavily myelinated axons in a compact bundle) connecting one area of gray matter to another.

You will also encounter the following terms used to refer to general regions of the CNS:

tectum (L., roof)—used to refer to brainstem structures located dorsal to the ventricular system. In mammals, this term has become synonymous with the dorsal midbrain.

tegmentum—this term refers to structures that form the core of the brainstem. It can be thought of (very loosely) as the part of the brainstem that is most like the spinal cord in the sense that the cell groups in the tegmentum have functions similar to those of cell groups in the spinal cord. Thus, the brainstem tegmentum includes the cranial nerve nuclei, most long tracts, and loosely arranged groups of interneurons and projection neurons known collectively as the reticular formation. For the most part, the structures that lie outside the tegmentum have no counterparts in the spinal cord. Many division-specific features of the brainstem reside ventral to the tegmentum.

base—the ventral aspect of the brain. The term 'basal' is synonymous with 'ventral.' For example, the bulbous portion of the pons is in the base of the pons ("basilar pons" or "basis pontis"), which is ventral to the tegmentum.

floor, **wall**—usually used with respect to structures that bound the ventricles (e.g., the floor of the fourth ventricle corresponds to the part of the pons and medulla that forms the ventral boundary of the ventricle).

From the viewpoint of clinical practice, the most important general principle of organization in the central nervous system is that each ***CNS function*** (e.g., perception of sensory stimuli, control of motor behavior, memory, decision-making, etc.) ***involves groups of neurons—interconnected through synapses—that are spatially distributed throughout several CNS subdivisions***. Groups of neurons that together subserve a particular function are called a 'system'; for example, there are the visual, motor, and somatic sensory systems. The structures containing the neurons and axons of a particular system are collectively referred to as a 'pathway'. (The term 'system' has a functional connotation, whereas the term 'pathway' refers to

Internal Anatomy of the Brainstem and Spinal Cord

the structures involved.) Note that *somatic sensory receptors and muscles on one side of the body and the visual hemifields are represented in the opposite side of the forebrain*—a fact will be emphasized repeatedly over the remaining weeks of the course. Knowledge of the crossing of sensory and motor pathways as they ascend or descend provides critical information to the clinician who is localizing neurological injuries (lesions).

If damage to the CNS at every level gave rise to exactly the same signs and symptoms, it would not be worthwhile for you to learn the details of neuroanatomy. However, as neurologists and neuroscientists recognized long ago, the neurons involved in specific functions occupy specific locations in the CNS. Even those systems that are represented in multiple subdivisions bear different physical relationships to one another from one subdivision to the next. Because neurons that subserve specific functions occupy specific locations, the combinations of neurological signs and symptoms exhibited by particular patients often provide detailed information about the location of damage.

The internal anatomy of the spinal cord

The following discussion of the internal anatomy of the spinal cord will introduce some of the general principles of organization that also hold true for the brainstem. A cross-section through the spinal cord is illustrated schematically in **Figure 3.2**. The gray matter forms the interior of the spinal cord; it is surrounded on all sides by the white matter. The white matter is subdivided into **dorsal** (or posterior), **lateral**, and **ventral** (or anterior) **columns**. Each of these columns contains bundles of axons related to specific functions. For example, the lateral columns are made up partly of axons that travel from the cerebral cortex to form synapses with motor neurons in the ventral horn. The dorsal columns carry much of the ascending sensory information from mechanoreceptors (note ascending blue axon in **Figure 3.2**).

The gray matter of the spinal cord is divided into **dorsal** and **ventral** (or posterior and anterior) '**horns**.' The dorsal horn is the part of the gray matter that receives sensory information entering the spinal cord via the dorsal roots of the spinal nerves. The ventral horn contains the cell bodies of lower motor neurons that send their axons out via the ventral roots to terminate on striated muscles. Thus, one important general rule of organization is that neurons in the spinal cord that process sensory information are spatially separate from motor neurons. (See Table A1 of *Neuroscience, 6th Ed.*, for more detail on the internal organization of spinal gray matter.)

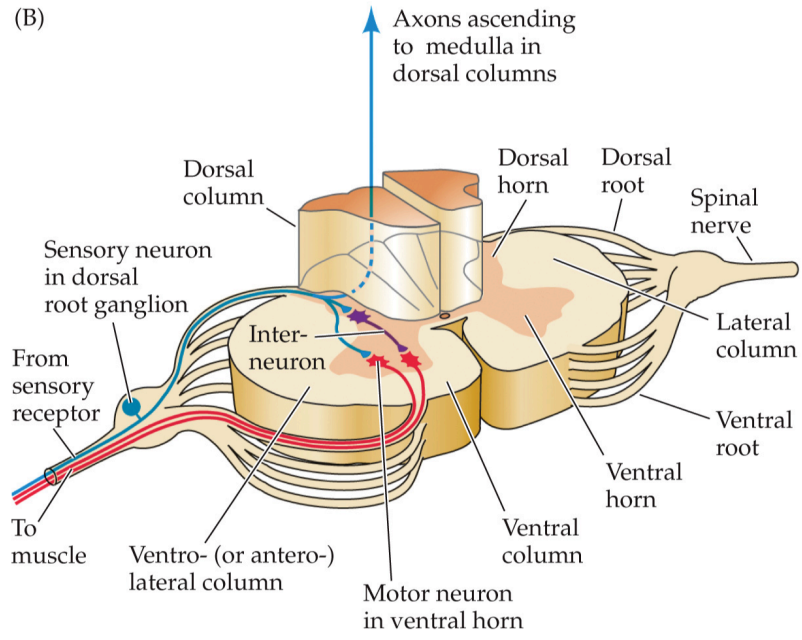


Figure 3.2. Diagram of the internal structure of the spinal cord. The general layout is the same at all levels, although specific details differ from one level to the next. (Figure A6B from *Neuroscience, 6th Ed.*)

Internal Anatomy of the Brainstem and Spinal Cord

As seen in the previous lab, the inputs and outputs of the spinal cord are arranged segmentally into the 31 pairs of spinal nerves. However, the gray matter of the spinal cord is not obviously segmented. It can be thought of as continuous columns (ventral horn) and layers (dorsal horn) of cells that run the length of the cord, with important differences in the size of the dorsal and ventral horns at different levels (**Figure 3.3**). The dorsal and ventral horns are largest where they supply the upper and lower limbs, because there are significantly greater numbers of outgoing and incoming nerve fibers at those levels and commensurately more neural circuitry (interneurons) involved in processing incoming and outgoing signals (**Figure 3.4**). There is also variation along the length of the cord in the number of fibers in the columns of white matter (and, therefore, in their relative size). The amount of white matter is greatest at cervical levels and least at sacral levels. This is because ascending and descending fibers from and to all levels must pass through the cervical cord.

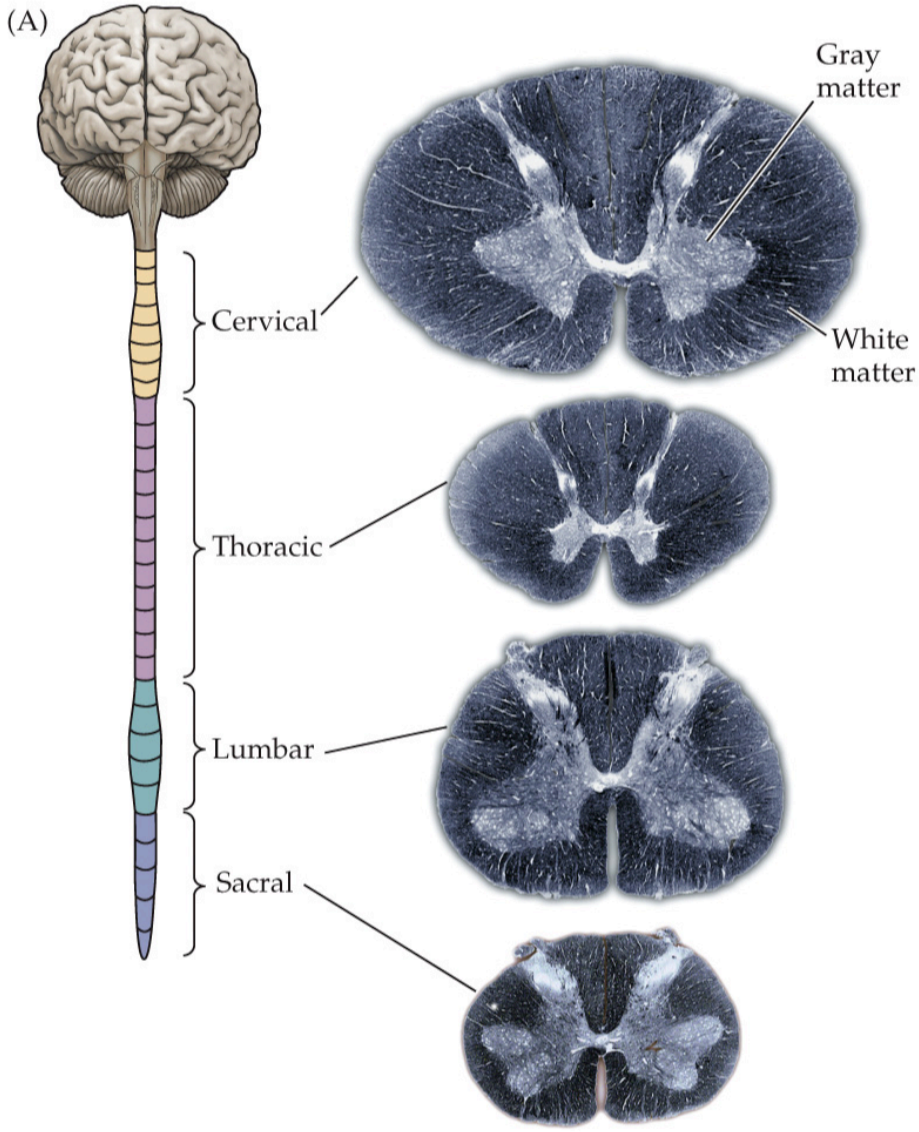
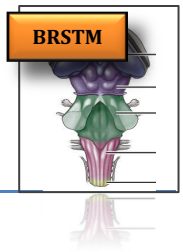


Figure 3.3. Cross-sections through the human spinal cord at four levels (shown at approximately the same magnification). Sections were prepared to emulate myelin staining (i.e., dark staining of myelin along axons). Thus, white matter appears dark and gray matter appears lighter. Note the swellings in cervical and lumbar cord segments, known as the cervical and lumbosacral enlargements of the spinal cord, respectively. As you might expect, these swellings accommodate the added neural circuitry related to the structure of the limbs that receive central innervation from the dorsal root ganglia and spinal cord. (Figure A6A from *Neuroscience, 6th Ed.*)



Internal Anatomy of the Brainstem and Spinal Cord

Challenge 3.1—internal anatomy of the spinal cord

With reference to **Figures 3.3** & **3.4** and the chart below, carefully inspect the internal features of the spinal cord that are present in each segment, as well as those that are different (or present in only in one segment). To complete this challenge, ***spend some time browsing the spinal cord sections in Sylvius4 Online, and find each of the internal features identified across the upper row in the chart in the Sylvius4 Online spinal cord***.

	Internal features								
Spinal cord segment	**Dorsal horn**	**Lateral horn**	**Ventral horn**	**White matter**	**Gracile tract**	**Cuneate tract**	**Lateral cortico-spinal tract**	**Ventral cortico-spinal tract**	**Antero-lateral system**
Cervical segments (8)	✓	--	✓	+++++	+++	+++	+++	+	++++
Thoracic segments (12)	✓	✓	✓	++++	+++	+ / --	++	+	+++
Lumbar segments (5)	✓	--	✓	+++	+++	--	++	+	++
Sacral segments (5)	✓	--	✓	++	++	--	+	+	+
Coccygeal segment (1)	✓	--	✓	+	+	--	--	+	+

Legend: ✓ indicates the structure's presence; **--** indicates the structure's absence; **+**'s indicate the tract's relative abundance across segments.

Internal Anatomy of the Brainstem and Spinal Cord

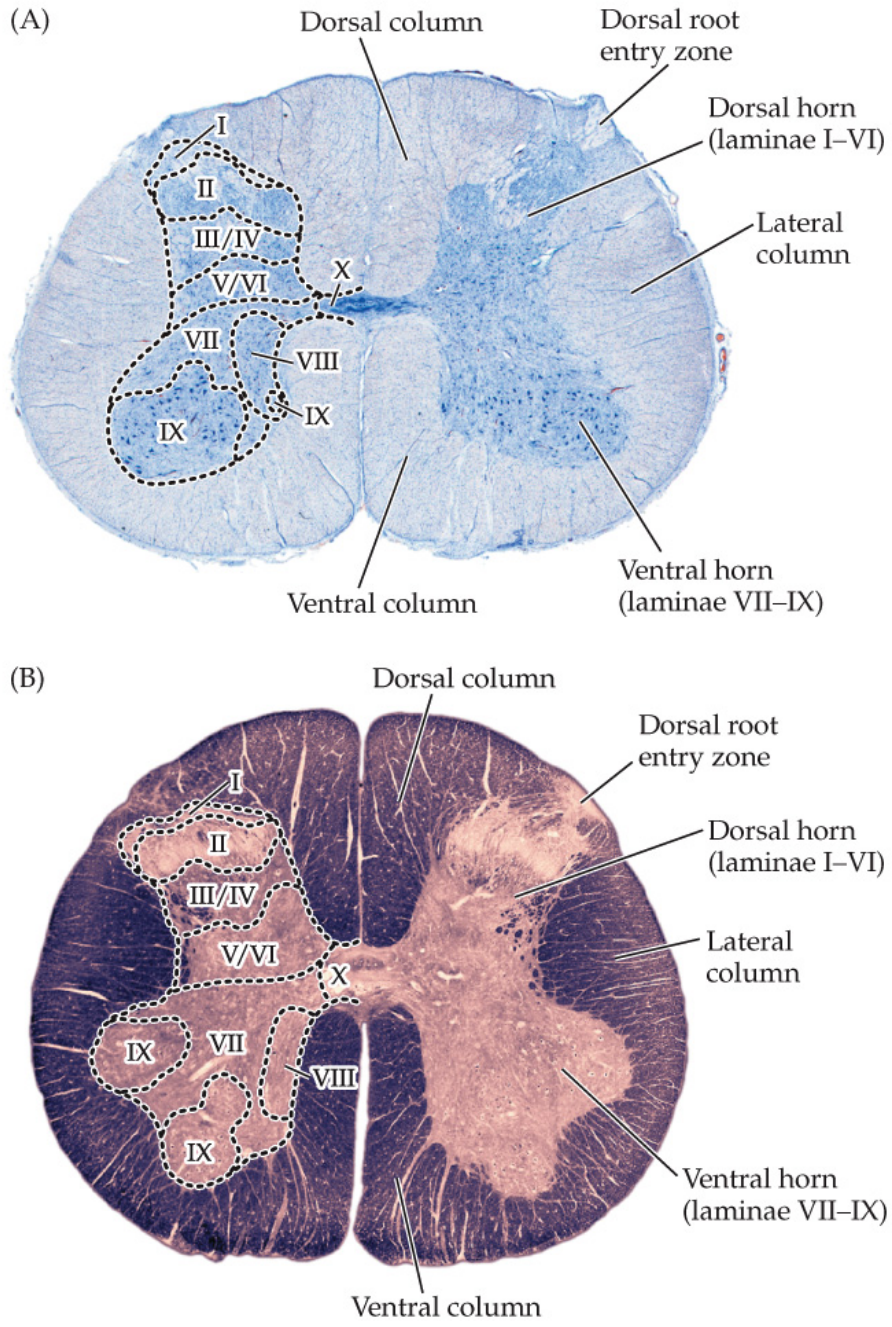
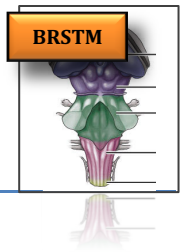


Figure 3.4. Cross-sections through a lumbar segment of the human spinal cord. (A) Nissl stain highlighting cell bodies. (B) Facsimile of a myelin stain highlighting (in dark tones) white matter. (Figure A7 in *Neuroscience, 6th Ed.*)



Internal Anatomy of the Brainstem and Spinal Cord

The internal anatomy of the brainstem

The internal organization of the brainstem is considerably more complicated than that of the spinal cord. However, two factors work in your favor as you study its features. First, important general principles of organization of the spinal cord also hold true for the brainstem. Second, much of the complexity of the brainstem is contributed by cell groups and axon tracts that will not be considered in this course. In the following discussion, the general plan of organization of the brainstem is presented first. Next, the prominent internal features that characterize each subdivision are identified. Then, we will focus on the cranial nerve nuclei and a set of neuromodulatory nuclei that will figure prominently in discussions during considerations of neuropsychiatry and psychopharmacology in your ***Body and Disease*** course. An understanding of the functions and locations of these nuclei is essential for diagnosing (and treating) neurological injury, dysfunction and disease, as well as mental illness and a spectrum of dysfunctions manifest in human behavior.

It would be convenient if each subdivision of the brainstem were sufficiently homogeneous along its length that one cross-section could serve as a 'typical' representative for the entire subdivision. However, the brainstem changes continuously along its length—the subdivision into three parts is somewhat arbitrary. As a compromise between examining three sections (one for each subdivision) and hundreds, four sections of the brainstem are shown first to serve as representatives, with additional sections shown later when we consider systematically the nuclei associated with the cranial nerves. Once you understand the organization of these four levels and the way various pathways traverse them, you should be able to identify the location of any section through the brainstem and the important pathways represented in it.

In the figures that follow, major landmarks in each of the subdivisions are identified in sections prepared to enhance the appearance of myelin (again, it is conventional to prepare sections of the brainstem and spinal cord with stains that make the white matter appear dark). As usual, be sure to focus on the structures identified in the figure legends in **bold font**. Our purpose here is to help you recognize the distinctive features of the embryological subdivisions of the spinal cord and brainstem, and to introduce you to some of the gray matter (nuclei) and white matter (tracts; peduncles) that you will study in more detail elsewhere in the course. We will return to these same sections frequently as the course progresses. These same sections and several intervening sections are fully annotated in ***Sylvius4 Online***.

Caudal medulla

A representative section through the caudal medulla is presented in **Figure 3.5**. Note that the general shape of this section ("13-medulla" in ***Sylvius4 Online***) is similar to that of the spinal cord (c.f. Figure 3.4). But, although the internal organization bears a resemblance to that of the spinal cord, there are some obvious differences. First, the **medullary pyramids** occupy the base of the caudal medulla and, at this level, they decussate forming the **pyramidal decussation**. In the spinal cord, the anterior columns do not contain so many fibers (and do not have the same pyramidal shape). On the other hand, the lateral columns are quite large in the cervical spinal cord, but there are relatively few myelinated axons in the lateral part of the caudal medulla. In the pyramidal decussation, the axons in the pyramids not only cross the midline, they also move laterally to enter the lateral columns of the spinal cord. This change in relative location of the axons explains why the anterior columns of the spinal cord are smaller in size and why the lateral columns are larger when the spinal cord is compared to the caudal medulla. A second difference

between the spinal cord and caudal medulla is that in the spinal cord, the dorsal columns are made up exclusively of white matter. In the caudal medulla, you can still see bundles of axons dorsally but now cell groups—the **dorsal column nuclei**, the **gracile nucleus** and the **cuneate nucleus**—have appeared in the same location. These nuclei are second-order sensory nuclei that will be discussed in a later session of this course. Finally, note that a cell group that resembles the dorsal horn is also present in the caudal medulla. This is a nucleus known as the **spinal trigeminal nucleus** (further subdivided here into magnocellular and gelatinosa layers), and it is continuous with the dorsal horn of the spinal cord. This important nucleus serves comparable functions in comparison to the dorsal horn, except for representation of a different region of the body, the face.

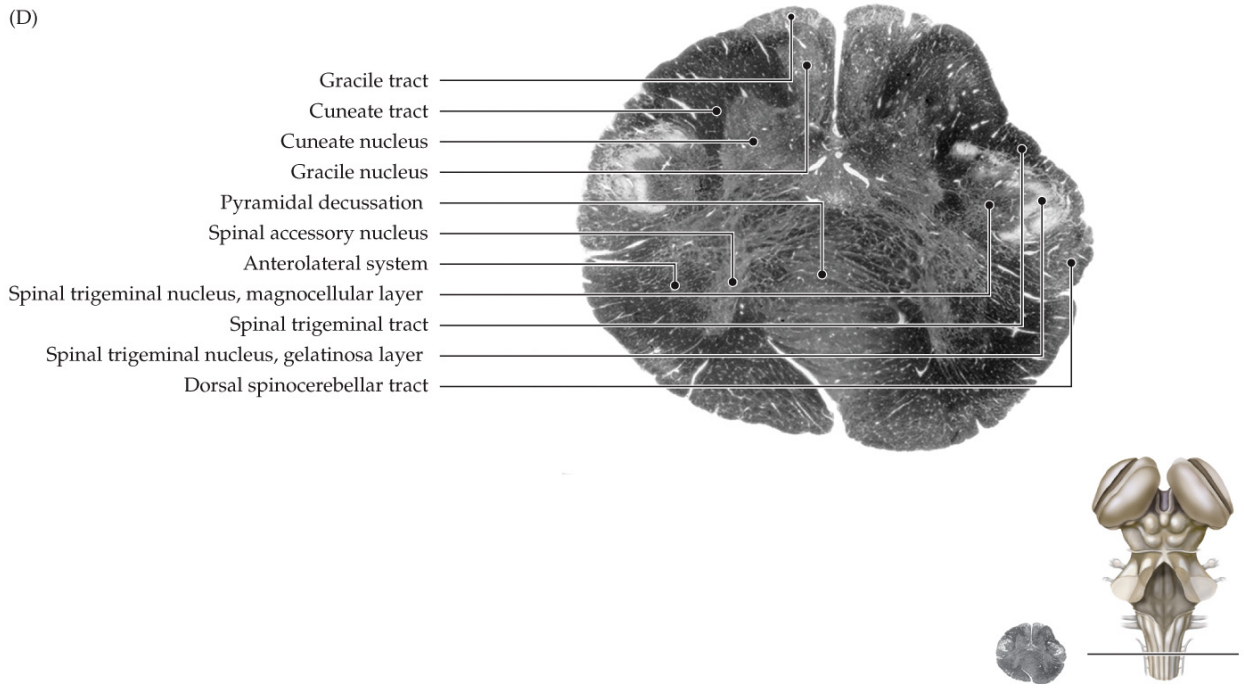
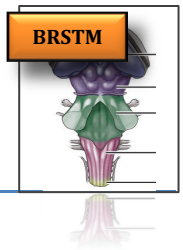


Figure 3.5. Transverse section of the caudal medulla oblongata acquired and prepared to simulate myelin staining; section in inset printed at actual size. (Atlas Plate 6D in *Neuroscience*, 6th *Ed.*)



Internal Anatomy of the Brainstem and Spinal Cord

Sylvius Self-Study Exercise
–*Internal brainstem features*

The **Brainstem Cross Sectional Atlas** in ***Sylvius4 Online*** contains 14 sections through the brainstem and four spinal cord sections featuring segmentation of well over 100 neuroanatomical structures. This atlas should be used to fill-in the gaps between the four sections illustrated in this chapter of your Laboratory Guide.

As you work through these chapter figures and the associated legends, find the same structures one at a time in the **Brainstem Cross Sectional Atlas** in ***Sylvius4 Online*.** The sections shown here are actually re-labeled versions of the same sections that are in ***Sylvius4 Online***. As suggested in a previous PDF, you may wish to look-up each labeled term (and each term that appears in **bold** in the figure legends) in ***Sylvius***'s **Visual Glossary** module; there, you can 'bookmark' each term for further study and review.

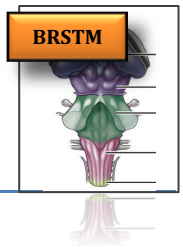
Since we are not yet studying the functional significance of many of these structures (we will do so in the first week of January), you should click on the structures identified in the figures, and when you do so, that structure becomes selected and a brief overview of that structure, including its function, becomes available in the text window.

> ***TIP***—click on the loudspeaker icon at the bottom of the text window to hear the proper pronunciation of any term that is unfamiliar to you.

> ***TIP***—to increase the magnification of the image, grab the lower-right corner of the image window and pull the window to its maximum extent.

Rostral medulla

A representative section through the rostral medulla is presented in **Figure 3.6**. The rostral medulla is easy to identify and is not likely to be confused with any other part of the brain (section shown is "9-medulla" in ***Sylvius4 Online***). It features the large nuclei known as the paired **inferior olivary nucleus** (this is what accounts for the outward bulging seen superficially as the inferior olive). This nucleus is part of an extensive group of brainstem nuclei that project to the cerebellum. Together with the medullary pyramids, which are now a prominent feature of the medulla, they form the ventral base of the rostral medulla. A prominent fiber bundle on the lateral surface of the medulla is the incipient **inferior cerebellar peduncle** (not yet attached to the cerebellum at this point). The thin roof of the fourth ventricle (IV) has been torn off of this specimen. You can see that the tegmentum of the medulla contains many different cell groups. Some will be discussed later. In addition to the **spinal trigeminal tract** and **spinal trigeminal nucleus**, note the presence of the **medial lemniscus** on either side of the midline. This white matter structure conveys somatosensory signals from the dorsal column nuclei to the thalamus. Similarly, in the lateral tegmentum, note the presence of a compact bundle of fibers called the **anterolateral system**, which also conveys somatosensory signals to the thalamus, as will be studied in a later session.



Internal Anatomy of the Brainstem and Spinal Cord

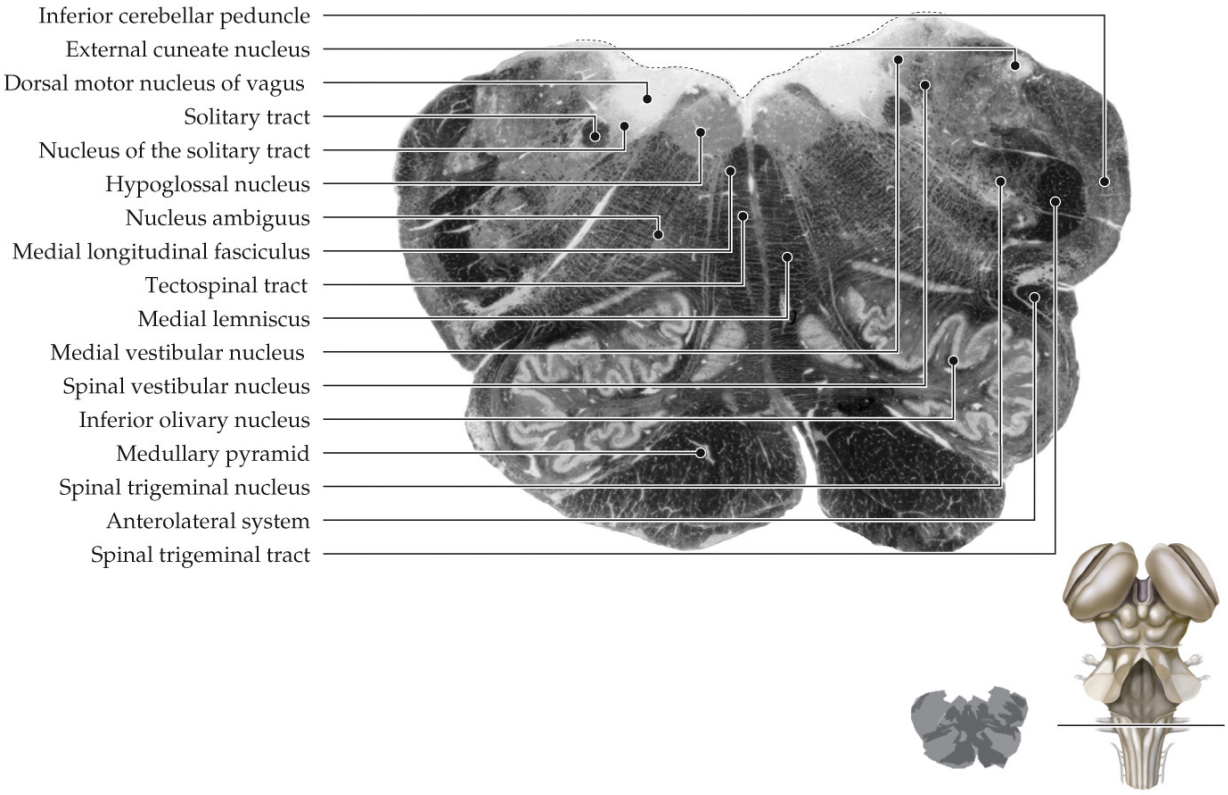
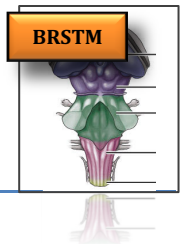


Figure 3.6. Transverse section of the rostral medulla oblongata acquired and prepared to simulate myelin staining; section in inset printed at actual size. (Atlas Plate 6C in *Neuroscience, 6th Ed.*)

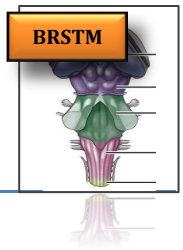
Challenge 3.2—internal anatomy of the medulla

With reference to **Figures 3.5** & **3.6** and the chart below, carefully inspect the internal features of the medulla from its caudal union with the spinal cord to the pons. ***Spend some time browsing the six medullary sections in Sylvius4 Online, and find each of the internal features described in the chart below.***



Internal Anatomy of the Brainstem and Spinal Cord

Subdivision	Surface feature	Internal structure
Caudal medulla (Figure 3.5)	**Gracile tract** (dorsal surface) • pair of extended longitudinal bulges or columns on either side of a midline furrow formed by the underlying gracile tract • continuation of the tract of the dorsal spinal cord	**Gracile tract & nucleus** • medial superficial bundle of myelinated axons from the dorsal column of the spinal cord • just deep to the gracile tract is the **gracile nucleus**, a compact gray matter structure whose neurons receive the synapses made by gracile tract axons
	Cuneate tract (dorsal surface) • pair of extended longitudinal bulges or columns just lateral to the gracile tracts formed by the underlying cuneate tract • continuation of the tract of the dorsal spinal cord	**Cuneate tract & nucleus** • lateral superficial bundle of myelinated axons from the dorsal column of the spinal cord • at the superior "head" of the cuneate tract is the **cuneate nucleus**, a compact gray matter structure whose neurons receive the synapses made by cuneate tract axons
	Pyramidal decussation (ventral surface) • see **Medullary pyramids** below • apparent "stitching" of fibers that cross the midline	**Pyramidal decussation** • see **Medullary pyramids** below • midline crossing of dense bundles of myelinated axons that run the longitudinal extent of the ventral brainstem • accounts for the formation of the **lateral** and **ventral** (**anterior**) **corticospinal tracts** of the spinal cord
Middle to rostral medulla (Figure 3.6)	**Medullary pyramids** (ventral surface) • pair of extended longitudinal bulges or columns on either side of a deep midline furrow	**Medullary pyramids** • dense bundle of myelinated axons that run the longitudinal extent of the ventral brainstem; these axons are also known as the **corticospinal tract** • these same axons are present in the **internal capsule**, **cerebral peduncles**, basilar pons, and about 95% are present in the **lateral columns** of the spinal cord
	Inferior olive (ventral-lateral surface) • pair of elongated bulges just lateral to the pyramids; a shallow furrow separates the pyramid and olive on each side	**Inferior olivary nucleus** • prominent nucleus of the ventral-lateral medulla just dorsal to the medullary pyramids • note the highly convoluted bands of gray matter that account for the superficial, ventral-lateral bulge
	Hypoglossal nerve (XII) (ventral-lateral surface) • exits through ventral-medial surface between the **medullary pyramid** and the **inferior olive**	**Hypoglossal nerve roots & nucleus** • nerve roots emerge between the **medullary pyramid** and the **inferior olive** • trace these nerve roots dorsally to their origin in the **hypoglossal nucleus**, located along the dorsal midline of the tegmentum



Internal Anatomy of the Brainstem and Spinal Cord

Middle pons

A representative section through the middle of the pons is presented in **Figure 3.7**. This section is attached to the cerebellum (a dead giveaway that we are in the pons) by the massive **middle cerebellar peduncles**. The base of the pons is made up of a mix of cells—the **pontine gray matter**—and transversely coursing **pontocerebellar fibers** that arise from the cells in the pontine gray matter and travel into the cerebellum via the middle cerebellar peduncle. Not all the fibers in the base of the pons are running transversely. Note that some appear to be traveling perpendicular to the plane of section. These are the **corticobulbar** and **corticospinal fibers**, and many will emerge on the base of the medulla as the medullary pyramids. The medial lemniscus continues to run through the brainstem; but by this level, it has twisted by a quarter-turn and is now oriented in the medial-lateral plane (c.f. **Figure 3.6** where it is oriented in the dorsal-ventral plane). The fibers of the anterolateral system remain in the lateral tegmentum. However, the tegmentum of the pons contains different nuclei at different levels. Here in the middle of the pons, additional nuclei associated with the trigeminal brainstem complex are evident (which we will identify below). Consult the section on the "peduncles" from the last laboratory session to understand why you see both the middle and the **superior cerebellar peduncle** in this same section.

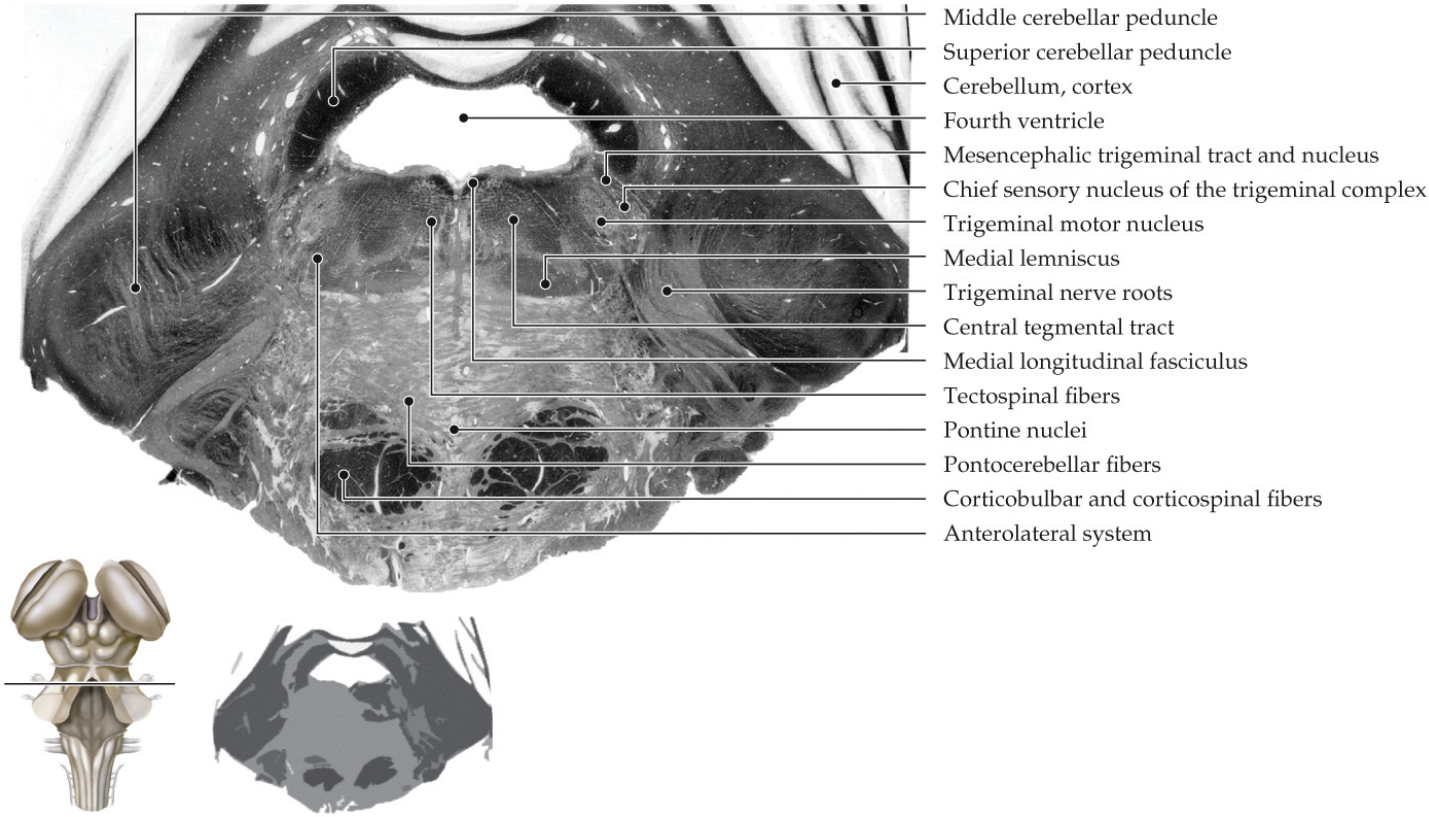
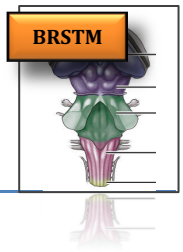


Figure 3.7. Transverse section of the middle pons ("6-pons" in ***Sylvius4 Online***) acquired and prepared to simulate myelin staining; section in inset printed at actual size. (Atlas Plate 6B in *Neuroscience, 6th Ed.*)



Internal Anatomy of the Brainstem and Spinal Cord

Challenge 3.3—internal anatomy of the pons

With reference to **Figure 3.7** and the chart below, carefully inspect the internal features of the pons. As you did for the medulla, ***spend some time browsing the sections in Sylvius4 Online, and find each of the internal features described in the accompanying chart.***

Subdivision	Surface feature	Internal structure
Middle of pons (**Figure 3.7**)	**Middle cerebellar peduncle** (ventral-lateral surface) • massive system of transverse fibers that "bridge" the longitudinal axis of the brainstem; these fibers originate in the basal region of the pons and continue around its ventral-lateral aspect to enter the cerebellum	**Pontocerebellar fibers & middle cerebellar peduncle** • the ventral half of the pons (also called the *basilar pons*) contains gray matter, longitudinal axons, and transverse fibers called the **pontocerebellar fibers** that decussate and form the *contralateral* middle cerebellar peduncle • these fibers arise from a scattering of gray matter in the basilar pons, called the **pontine nuclei**, and terminate in the *contralateral* cerebellum • also in the basilar pons are prominent fascicles of axons from the cerebral cortex that project to various nuclei of the brainstem and the spinal cord; collectively, these axons are the **corticobulbar/corticospinal fibers**
	Trigeminal nerve (V) (ventral-lateral surface) • enters/exits pons by penetrating the transverse, pontocerebellar fibers	**Trigeminal nerve roots & nucleus** • trace the nerve V roots to their origin in the trigeminal nuclear complex; at this level, note the location of the **trigeminal motor nucleus** and, just lateral to it, the **principal (chief sensory) nucleus** • now, keep your eye in this same general region and section caudally: in this same dorsal-lateral position in the caudal pons and throughout the medulla, the **spinal trigeminal nucleus** and the **spinal trigeminal tract** are present (the spinal nucleus can be further subdivided)
Caudal pons (not shown here—consult section "7-pons" in ***Sylvius4 Online***)	**Abducens nerve (VI)** (ventral-medial surface) • enters/exits near the midline at the pontomedullary junction (most medial of the three nerves that emerge from this junction)	**Abducens nerve roots & nucleus** • explore the medial tegmentum of the pons and locate nerve VI roots; note how they course through the basilar pons just lateral to the corticobulbar/corticospinal fibers • trace these nerve roots dorsally to their origin in the **abducens nucleus**, which is located along the dorsal tegmental midline
	Facial nerve (VII) (ventral-lateral surface) • enters/exits through ventral-lateral surface at pontomedullary junction (middle of the three nerves that	**Facial nerve roots & nucleus** • explore the lateral tegmentum of the pons and locate nerve VII roots; note how they trace a most unusual trajectory around the dorsal aspect of the abducens nucleus

	emerge from this junction, just medial to CN VIII)	• in this image, it may not be possible to trace these nerve roots all the way back to their origin in the **facial nucleus**, which is located just medial and ventral to the trigeminal nuclear complex • nerve VII roots exit the facial nucleus medially, then course dorsally around the abducens nucleus, and finally ventral-laterally (this is how CN VII ends up being lateral to CN VI)
	Vestibulocochlear nerve (VIII) (ventral-lateral surface) • enters through ventral-lateral surface at pontomedullary junction (most lateral of the three nerves that emerge from this junction, just lateral to CN VII)	**Vestibular nuclear complex** • explore the lateral tegmentum of the pons and locate nuclei of the vestibular nuclear complex (you may not find any CN VIII roots); you will find the vestibular nuclei dorsal to the trigeminal nuclear complex and spinal trigeminal tract • find the **superior, lateral** and **medial vestibular nuclei** • section down and locate the **spinal vestibular nucleus** • And what about the cochlear division? It terminates in a superficial nucleus of the dorsal-lateral upper medulla called the **cochlear nucleus**. Although not labeled in ***Sylvius4 Online***, it is visible in section "8-Medulla" as it wraps around the dorsal-lateral surface of the inferior cerebellar peduncle

Midbrain (mesencephalon)

A representative section through the midbrain is presented in **Figure 3.8**. Given the location of this section, it is not surprising that it cuts through the **superior colliculus**, (but avoids the inferior colliculus, which is in the caudal midbrain; see "3-midbrain" in ***Sylvius4 Online***). The space between the colliculi is the **cerebral aqueduct**. The **cerebral peduncles** form the base of the midbrain. Two very large nuclei lie dorsal to them. These are the **substantia nigra** (subdivided into 'pars compacta' and 'pars reticulata') and the **red nucleus**; they are discussed in a later session. Just lateral and dorsal to the red nucleus are the same two systems of somatosensory fibers that have been present in every section through the brainstem: the **medial lemniscus** and the **anterolateral system**. (A small part of the dorsal thalamus, including the medial and lateral geniculate nuclei, are also included in this section.)

Internal Anatomy of the Brainstem and Spinal Cord

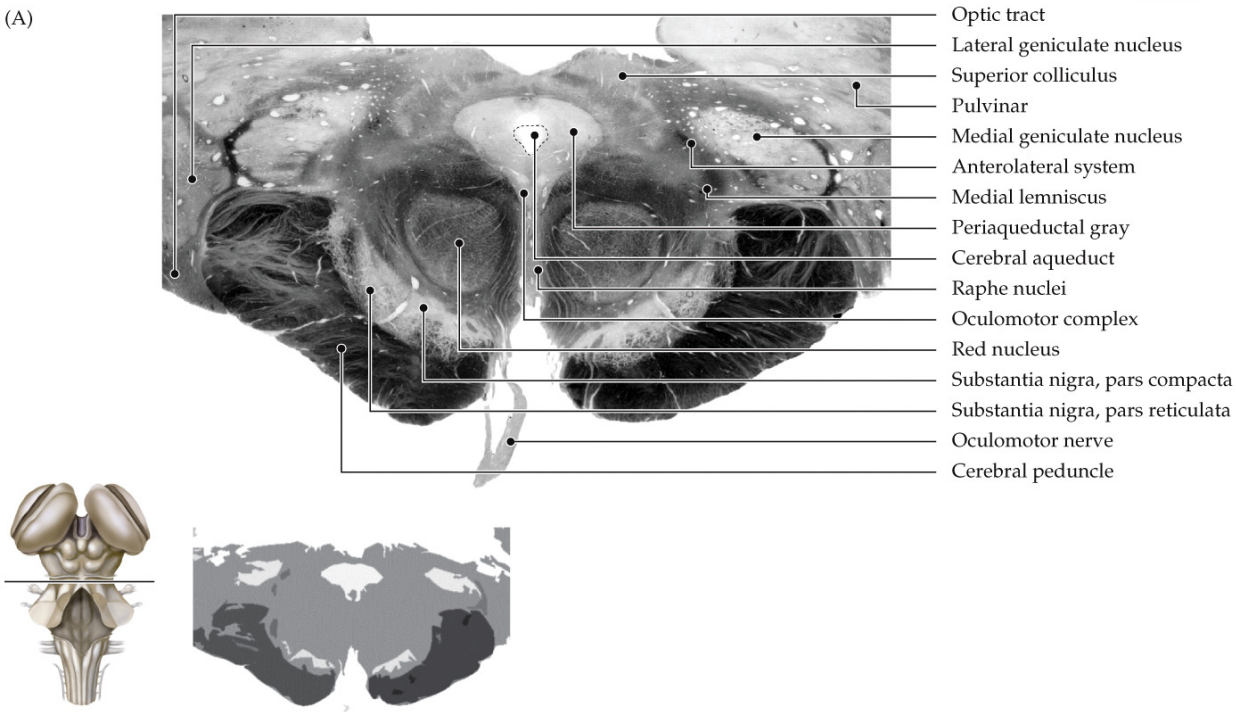
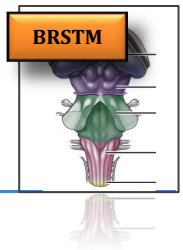


Figure 3.8. Transverse section of the rostral midbrain ("2-midbrain" in ***Sylvius4 Online***) acquired and prepared to simulate myelin staining; section in inset printed at actual size. (Atlas Plate 6A in *Neuroscience, 6th Ed.*)

Challenge 3.4—internal anatomy of the midbrain

With reference to **Figure 3.8** and the chart on the following page, carefully inspect the internal features of the midbrain. As you did for the medulla and pons, now ***spend some time browsing the sections in Sylvius4 Online, and find each of the internal features described in the chart.*** In addition, browse the most rostral section in the Brainstem atlas ("1-midbrain-diencephalon junction") and locate one additional structure that will become important in a later session: the **subthalamic nucleus**. Note how this nucleus occupies a position that—like the substantia nigra—lies just dorsal to the fibers of the cerebral peduncle. However, the subthalamic nucleus is rostral to the substantia nigra and represents the principle feature of the diencephalic division known as the "subthalamus". Please be sure that you can differentiate the substantia nigra from the subthalamic nucleus!



Internal Anatomy of the Brainstem and Spinal Cord

Subdivision	Surface feature	Internal structure
Midbrain (**Figure 3.8**)	**Cerebral peduncles** (ventral surface) • large, longitudinal "stalks" (peduncle means stalk) that occupy the ventral midbrain	**Cerebral peduncles** • "cerebral peduncle" refers to the entire ventral midbrain; however, it is common to use the term "cerebral peduncle" to refer specifically to these fiber systems (the proper term for the ventral peduncles is *pes* or *basis pedunculi*) • the cerebral peduncles comprise efferent fibers of the cerebral cortex that terminate in the brainstem and spinal cord; these fibers are referred to collectively as the **corticobulbar / corticospinal fibers**, indicating that some of these fibers terminate among brainstem nuclei ("bulbar" refers to the brainstem and cranial nerve nuclei) and other fibers terminate in the spinal cord • it is important to recognize the course of these fibers from their origin in the cerebral cortex through brainstem: cerebral cortex → subcortical white matter → **internal capsule** → **cerebral peduncle** → basilar pons → **medullary pyramids** → **lateral** and **anterior** (**ventral**) **corticospinal tract** • there are about 20 million axons in each cerebral peduncle; can you guess how many axons are present in each medullary pyramid by simply noting the difference in size of these two structures?[1] (the large majority of these axons in the cerebral peduncle never reach the spinal cord) • now consider the tegmentum of the midbrain; just dorsal to the cerebral peduncles (pes pedunculi) there is an important gray matter nucleus called the **substantia nigra**, which has two divisions (pars compacta and pars reticulata), and in a similar position but just a bit more rostral is the **subthalamic nucleus**; you will learn much more about these nuclei when we study the basal ganglia • and just dorsal to the substantia nigra, is a large, spherical gray matter structure called the **red nucleus**, which you will study when we consider cerebellar systems
	Oculomotor nerve (III) (ventral surface) • exits through ventral surface just medial to cerebral peduncles (in the interpeduncular fossa)	**Oculomotor nerve roots & nuclear complex** • trace these nerve roots dorsally to their origin in the nuclei of the oculomotor complex along the midline of the dorsal tegmentum; here you will find two divisions: the **oculomotor nucleus** and the **Edinger-Westphal nucleus** • this nuclear complex is embedded within a large region of gray matter that surrounds the **cerebral aqueduct**, termed the **periaqueductal** (or **central**) **gray**
	Inferior colliculi (dorsal surface) • inferior pair of the four bumps that are visible in brainstem model/illustration, but are normally covered by the cerebellum	**Inferior colliculi** • the inferior colliculi are gray matter structures that occupy a position just dorsal and lateral to the periaqueductal gray (see section "3 - Midbrain") • together with the superior colliculi, they form the "roof" of the midbrain (above the cerebral aqueduct); for this reason, these four bumps are also called the **tectum** (*tectum* means *roof*)

[1] There are roughly half a million axons in each medullary pyramid.

		• the **trochlear nerve** exits the dorsal surface of the brainstem just caudal to the inferior colliculus (see **Brainstem Model** in **Surface Anatomy** module of ***Sylvius4 Online***) • although that nerve is not visible in section 3 – Midbrain, you can see the small **trochlear nuclei** where you should expect to find somatic motor nuclei, along the midline of the dorsal tegmentum
	Superior colliculi (dorsal surface) • superior pair of the four bumps that are visible in brainstem model/illustration	**Superior colliculi** • in the rostral midbrain, the superior colliculi are laminated gray matter structures that occupy a position just dorsal and lateral to the periaqueductal gray matter (see section labeled "2 - Midbrain" in ***Sylvius4 Online***) • together with the inferior colliculi, they form the "roof" (tectum) of the midbrain (above the cerebral aqueduct)

Now that you have been introduced to many important internal gray matter and white matter structures of the brainstem, you are now ready to continue this process as we turn our attention to two categories of gray matter structures that are critical for understanding neurological function and human behavior: the **nuclei of the cranial nerves** and the **neuromodulatory nuclei** of the brainstem. After working through the remaining sections of this lab, you should be able to recognize components of important sensory, motor and modulatory systems in each of the embryological divisions of the brainstem.

The cranial nerve nuclei

The cranial nerve nuclei are made up of the neurons in the brainstem that receive primary sensory inputs or that give rise to motor outputs. Just as the spinal cord receives sensory information from the body surface and deeper tissues and sends motor axons to striated muscles and to the autonomic ganglia, similar inputs and outputs exist for the head and neck region. In addition, there are specialized sensory inputs in the head that do not have equivalents in the spinal cord. These include the inputs for hearing, balance and taste. The motor outputs are just a little more complicated as well. There are nuclei that innervate the extrinsic eye muscles and the tongue. Since the muscles that are innervated are derived from **somites**, these motor neurons are exactly equivalent to those in the ventral horn, which also innervate muscles derived from somites. In addition, there are nuclei in the brainstem that innervate the muscles derived from the **branchiomeres** of the pharyngeal arches (jaw muscles, muscles of facial expression, and muscles of the pharynx and larynx). There is only one such cell group in the spinal cord; it innervates the trapezius and sternocleidomastoid muscles, which are also derived from branchiomeres. It is included with the cranial nerve nuclei, since it gives rise to the spinal part of cranial nerve XI. Finally, there are cell groups in the brainstem that form part of the visceral motor (autonomic) system and send axons to autonomic ganglia in organs throughout the body. By working through the **Challenges** above, you have already encountered many of these nuclei. Let's now build a stronger appreciation for the organization of these nuclei in each division of the brainstem recalling some of what you learned already about the functions of the cranial nerves.

The organization of the sensory and motor neurons in the spinal cord and brainstem are similar, for reasons that are clear when one considers the development of these two regions of the neural tube—as

explained in **Figure 3.9**. Sensory neurons, which are derived from the alar plate and located dorsally in the spinal cord, are located laterally in the medulla and pons. Motor neurons, which are derived from the basal plate and located ventrally in the spinal cord, are located medially in the medulla, pons, and midbrain.

Nevertheless, the internal organization of the brainstem is considerably more complicated than that of the spinal cord. However, two factors work in your favor as you study its features. First, important general principles of organization of the spinal cord also hold true for the brainstem. Second, much of the complexity of the brainstem is contributed by cell groups and axon tracts that will not be considered in this course.

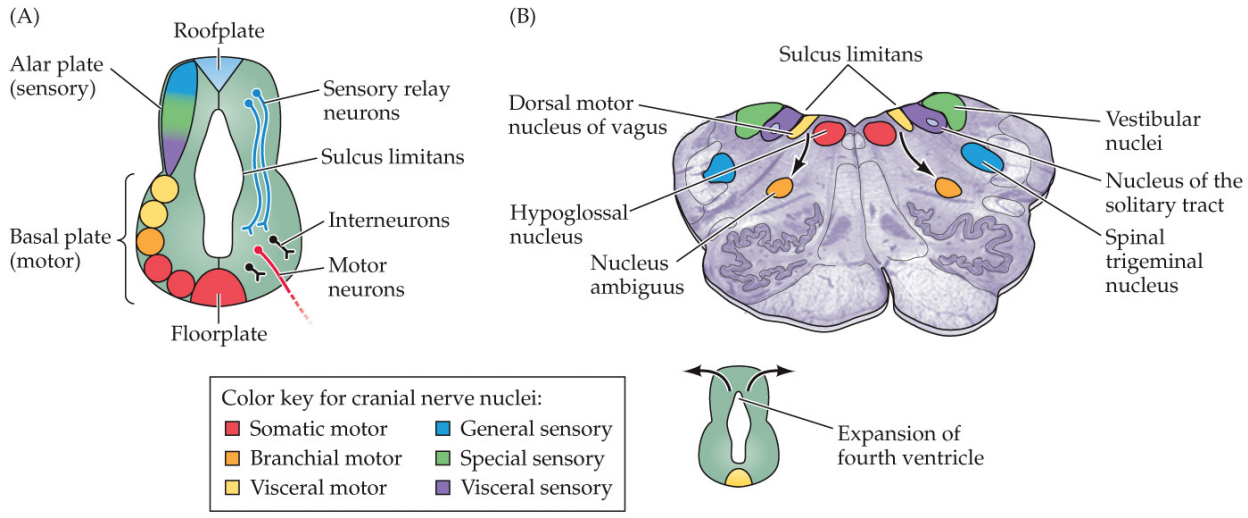


Figure 3.9. **Embryological derivation of internal structure in the brainstem.** (A) Illustration of a transverse section through the developing neural tube demonstrating the division of the alar plate from the basal plate by the sulcus limitans. The alar plate differentiates into the dorsal horn of the spinal cord and the sensory nuclei of the brainstem. The basal plate differentiates into the ventral horn of the spinal cord and the motor nuclei of the brainstem. (B) Representative transverse section from the brainstem (middle medulla) illustrating the location and identity of alar and basal plate derivatives. With expansion of the fourth ventricle, the alar plate derivatives develop lateral to the basal plate derivatives, like the opening of a book, with the floorplate in the position of the binding of the book (see inset). Note the secondary migration (curved ventrally pointing arrows) of branchial motor nuclei, such as the nucleus ambiguus, to an intermediate position in the brainstem tegmentum. (Figure A10 from *Neuroscience, 6th Ed.*)

One further point can be made from **Figure 3.9**. In the medulla, the basal plate that gives rise to somatic motor nuclei also gives rise to the motor neurons that will innervate the branchiomeric muscles. These motor neurons migrate from the midline into the ventral-lateral part of the tegmentum and send their axons out in nerves that exit the brain laterally (i.e., V, VII, IX, X, and XI). The somatic motor neurons, on the other hand, send their axons out ventrally (in a line with ventral roots of the spinal cord), except for the trochlear nucleus (as noted previously). Oddly, the parasympathetic preganglionic neurons (visceral motor neurons) in the medulla and pons also send their axons out laterally; in the spinal cord (and in the

Internal Anatomy of the Brainstem and Spinal Cord

midbrain), the autonomic preganglionic axons leave in the ventral roots. All of the sensory inputs enter the brain laterally.

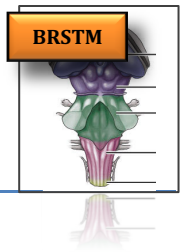
If you take the time to appreciate the organization of the cranial nerve nuclei in the brainstem, it will be much easier to learn how the **ten pairs of cranial nerves** supply sensory inputs to or derive motor output from the **16 pairs of cranial nerve nuclei**. How do these nuclei relate to the components of the cranial nerves that you studied in the last lab? **Table A2** lists the cranial nerve nuclei and sensory ganglia from which the sensory and motor components of each nerve arise.

TABLE A2 ■ The Cranial Nerves and Their Primary Functions

Cranial nerve	Name	Sensory and/or motor	Major function	Location of cells whose axons form the nerve
I	Olfactory nerve	Sensory	Sense of smell	Nasal epithelium
II	Optic nerve	Sensory	Vision	Retina
III	Oculomotor nerve	Motor	Eye movements; pupillary constriction and accommodation; muscle of upper eyelid	Oculomotor nucleus in midbrain; Edinger-Westphal nucleus in midbrain
IV	Trochlear nerve	Motor	Eye movements (intorsion, downward gaze)	Trochlear nucleus in midbrain
V	Trigeminal nerve	Sensory and motor	Somatic sensation from face, mouth, cornea; muscles of mastication	Trigeminal motor nucleus in pons; trigeminal sensory ganglion (the gasserian ganglion)
VI	Abducens nerve	Motor	Eye movements (abduction or lateral movements)	Abducens nucleus in pons
VII	Facial nerve	Sensory and motor	Controls the muscles of facial expression; taste from anterior tongue; lacrimal and salivary glands	Facial motor nucleus in pons; superior salivatory nuclei in pons; geniculate ganglion
VIII	Vestibulocochlear (auditory) nerve	Sensory	Hearing; sense of balance	Spiral ganglion; vestibular (Scarpa's) ganglion
IX	Glossopharyngeal nerve	Sensory and motor	Sensation from posterior tongue and pharynx; taste from posterior tongue; carotid baroreceptors and chemoreceptors; salivary gland	Nucleus ambiguus in medulla; inferior salivatory nucleus in pons; glossopharyngeal ganglia
X	Vagus nerve	Sensory and motor	Autonomic functions of gut; cardiac inhibition; sensation from larynx and pharynx; muscles of vocal cords; swallowing	Dorsal motor nucleus of vagus; nucleus ambiguus; vagal nerve ganglion
XI	Spinal accessory nerve	Motor	Shoulder and neck muscles	Spinal accessory nucleus in superior cervical cord
XII	Hypoglossal nerve	Motor	Movements of tongue	Hypoglossal nucleus in medulla

The sixteen cranial nerve nuclei can be most easily remembered if they are assembled into functional groups and anatomical location (**Table A3**—from Purves et al., *Neuroscience, 6th Ed.*; **Figure 3.10**). Three of the groups are motor nuclei: a somatic motor group, a branchial motor group, and a visceral motor (parasympathetic preganglionic) group. The other three groups are sensory nuclei: general sensory, special sensory, and visceral sensory.

Table A3 illustrates the point that most of the cranial nerves are connected to only one or two cranial nerve nuclei. Only three nerves carry components from more than two nuclei. These nerves—VII, IX, and X—each carry four components: a branchial motor component, a parasympathetic component, a somatic sensory component, and a visceral sensory component (taste and general visceral sensation). These three nerves lack a somatic motor component.



Internal Anatomy of the Brainstem and Spinal Cord

TABLE A3 ■ Classification and Location of the Cranial Nerve Nuclei[a]

LOCATION	SOMATIC MOTOR	BRANCHIAL MOTOR	VISCERAL MOTOR	GENERAL SENSORY	SPECIAL SENSORY	VISCERAL SENSORY
Midbrain	Oculomotor nucleus (III) Trochlear nucleus (IV)		Edinger–Westphal nucleus (III)	Trigeminal sensory: mesencephalic nucleus (V, VII)		
Pons	Abducens nucleus (VI)	Trigeminal motor nucleus (V) Facial nucleus (VII)	Superior salivatory nucleus (VII) Inferior salivatory nucleus (IX)	Trigeminal sensory: principal nucleus (V, VII, IX, X) Trigeminal sensory: spinal nucleus (V, VII, IX, X)	Vestibular nuclei (VIII) Cochlear nuclei (VIII)	Nucleus of the solitary tract (VII, IX, X)
Medulla	Hypoglossal nucleus (XII)	Nucleus ambiguus (IX, X) Spinal accessory nucleus (XI)	Nucleus ambiguus (X) Dorsal motor nucleus of vagus (X)			

[a]Associated cranial nerves are shown in parentheses.

Location of the cranial nerve nuclei in brainstem cross-sections

A schematic overview of how these nuclei are arranged in the mature brainstem is presented in **Figure 3.10** and **3.11**. Three points should be taken from these figures. (1) The cranial nerve nuclei lie in the tegmentum of the brainstem, as do many of the major ascending and descending tracts. (2) Just as in the spinal cord, the nuclei that receive sensory inputs via the cranial nerves are spatially separate from those that give rise to motor output, with the sensory nuclei located laterally and the motor nuclei located medially. (3) The cranial nerve nuclei that serve comparable functions are aligned in the longitudinal axis of the brainstem, even when comparable nuclei (e.g., somatic motor nuclei) are distributed across brainstem subdivisions (cf. **Figure 3.9**). The spatial segregation of sensory and motor functions provides an important clue for localization of focal damage in the brainstem. Thus, an understanding of the functions and locations of cranial nerve nuclei is essential for diagnosing (and treating) neurological injury, dysfunction and disease.

Internal Anatomy of the Brainstem and Spinal Cord

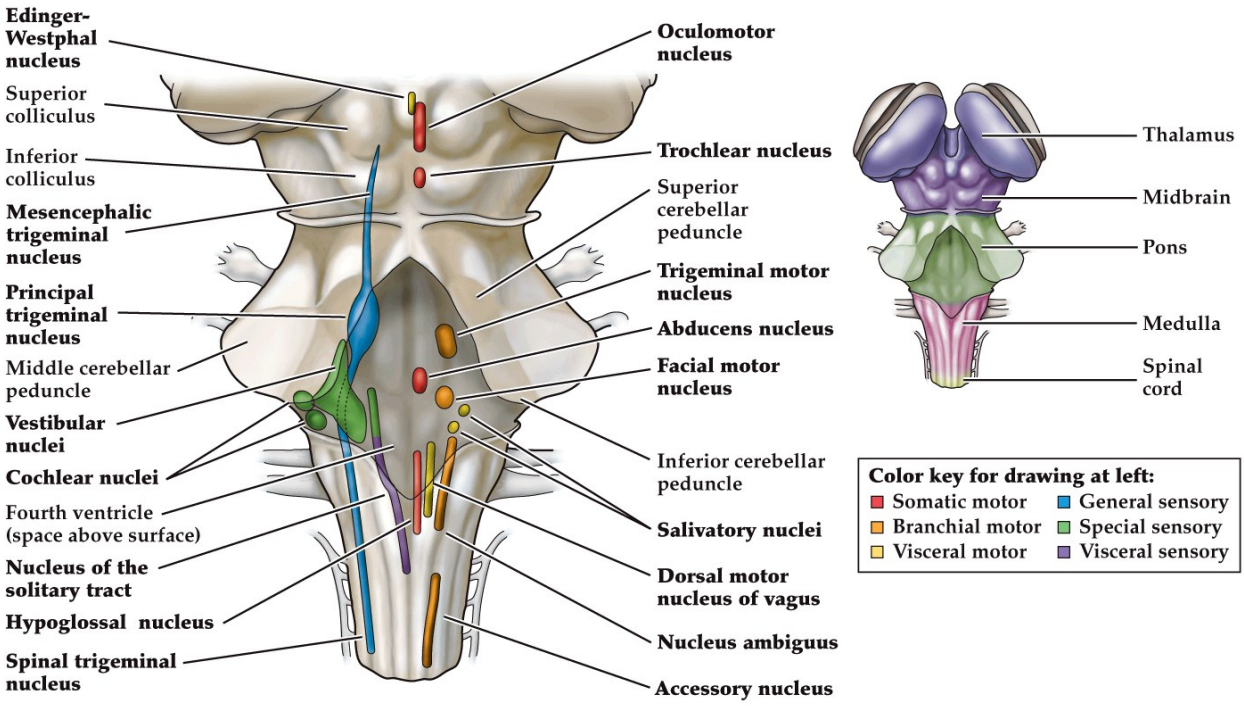
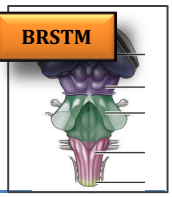
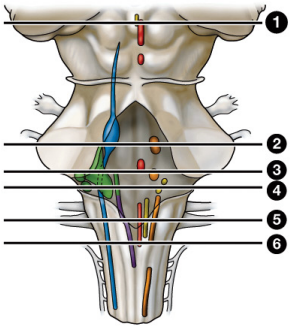


Figure 3.10. At left, a "phantom" view of the dorsal surface of the brainstem shows the locations of the brainstem cranial nerve nuclei that are either the target or the source of the cranial nerves. (See Table A2 for the relationship between each cranial nerve and cranial nerve nuclei and Table A3 for a functional scheme that localizes cranial nerve nuclei with respect to brainstem subdivision and sensory or motor function.) With the exception of the cranial nerve nuclei associated with the trigeminal nerve, there is fairly close correspondence between the location of the cranial nerve nuclei in the midbrain, pons, and medulla and the location of the associated cranial nerves. At right, the territories of the major brainstem subdivisions are indicated (viewed from the dorsal surface). (Figure A9 from *Neuroscience, 6th Ed.*)

Figure 3.11 (next page). Transverse sections through the brainstem along the rostral–caudal axis show the locations of the cranial nerve nuclei; ascending and descending tracts are indicated in each representative section. The identity of the nuclei (somatic sensory or motor; visceral sensory or motor; branchial motor; special sensory) is indicated using the color key. Each motor group forms an interrupted column of cells that lie in the same relative location (relative to the midline and ventricle) along the length of the brainstem (the nucleus ambiguus is also the source of cardio-inhibitory outflow and should also be co-listed under visceral motor.) Note: the sections are NOT drawn to scale; you should be sure to appreciate the relative proportions of the different subdivisions when you examine slabs of the human brainstem in the lab. (Figure A9 from *Neuroscience, 6th Ed.*)

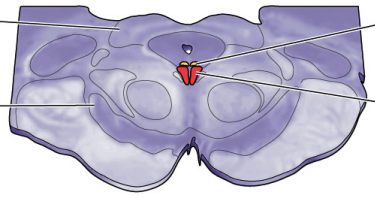


Internal Anatomy of the Brainstem and Spinal Cord

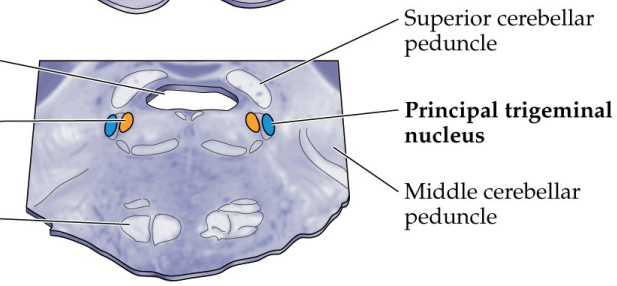


Color key for cranial nerve nuclei:
- Somatic motor
- Branchial motor
- Visceral motor
- General sensory
- Special sensory
- Visceral sensory

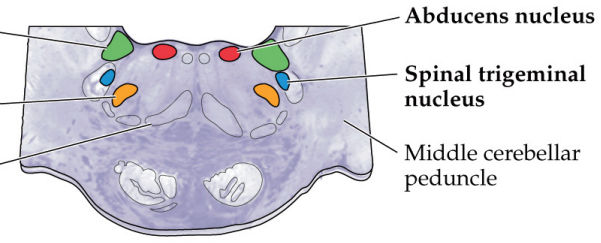
1 Midbrain



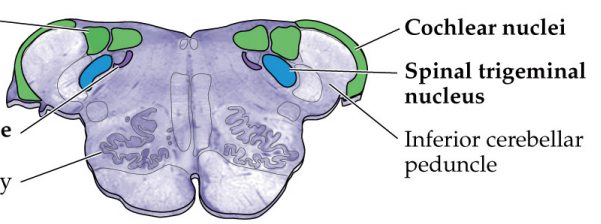
2 Middle pons



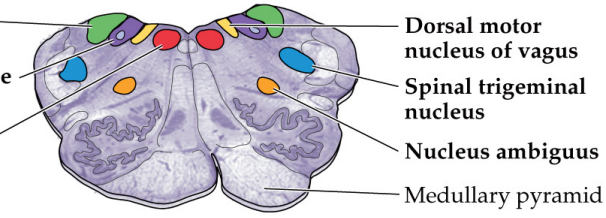
3 Lower pons



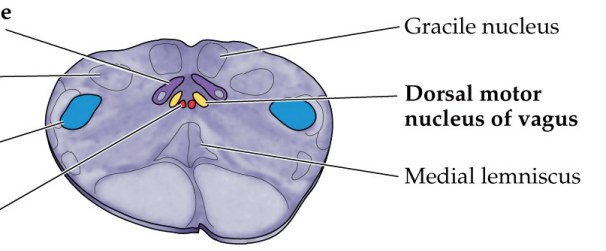
4 Upper medulla

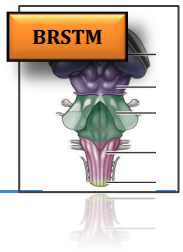


5 Middle medulla



6 Caudal medulla





Internal Anatomy of the Brainstem and Spinal Cord

Some of the cross-sections that were introduced earlier are reproduced and colorized in **Figures 3.12–3.15**. The locations of most of the cranial nerve nuclei listed in **Tables A2** & **A3** are indicated on these sections.

Rostral medulla

A representative section through the rostral medulla with important cranial nerve nuclei identified is presented in **Figure 3.12**. The rostral medulla is a good place to start because a representative of each motor column is present (labeled on right side of section), and most of the sensory nuclei are also present (labeled on left side of section). Of the motor nuclei, the **hypoglossal nucleus** is closest to the midline. Next to it is the **dorsal motor nucleus of the vagus nerve**. The **nucleus ambiguus**—true to its name—is difficult to delineate in the myelin-stained human brain. The **nucleus of the solitary tract** is easy to spot, because it is associated with an isolated myelinated tract (the **solitary tract**, of course) that terminates in the nucleus. (The fibers in the tract come from nerves VII, IX, and X.) The **vestibular nuclei** (a collection of discrete nuclei) are large and can be seen in sections through much of the rostral medulla and caudal pons. The trigeminal nucleus in the medulla is known as the **spinal trigeminal nucleus**. Axons travel into it via the **spinal trigeminal tract**, which is just lateral to the nucleus.

Internal Anatomy of the Brainstem and Spinal Cord

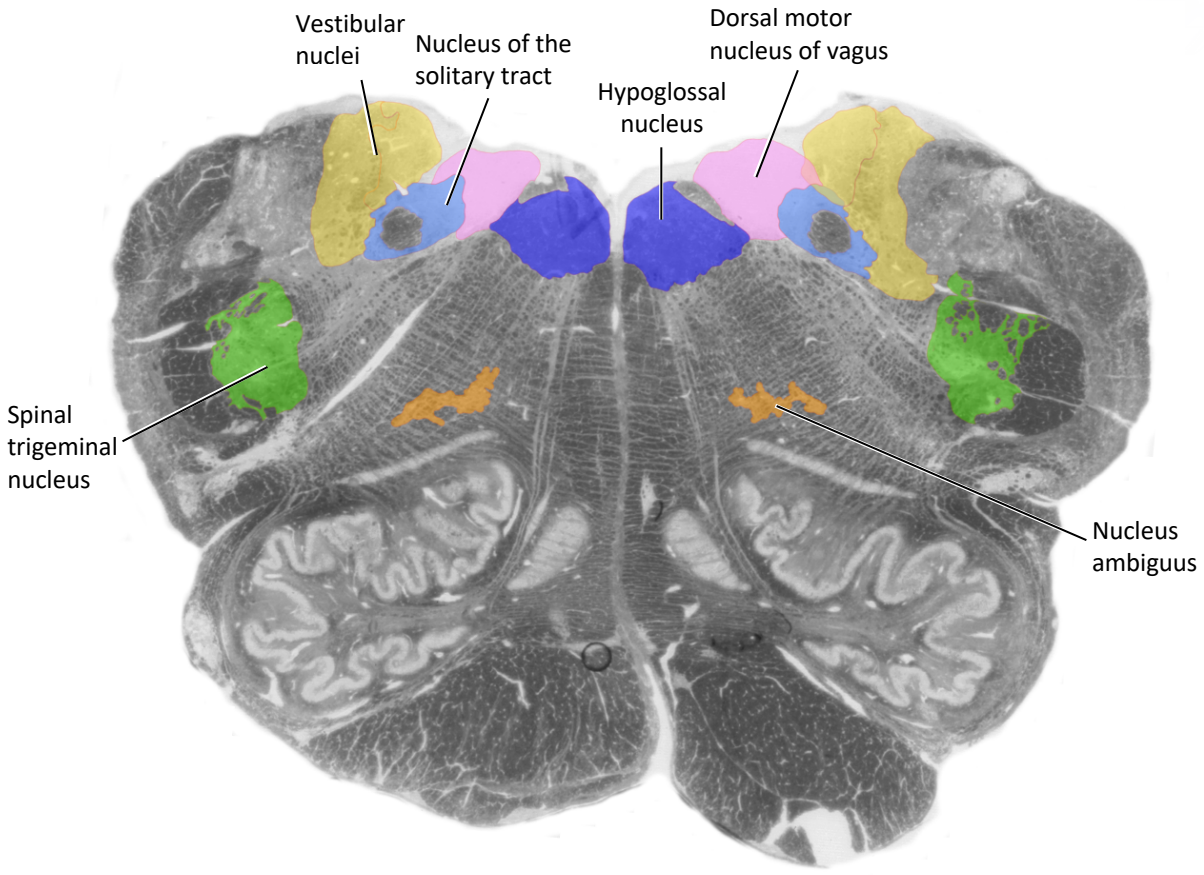
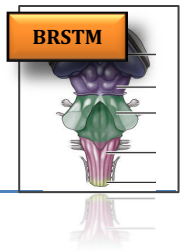


Figure 3.12. Representative section through the rostral medulla with important cranial nerve nuclei identified. (Section shown is "9-medulla" in ***Sylvius4 Online***)



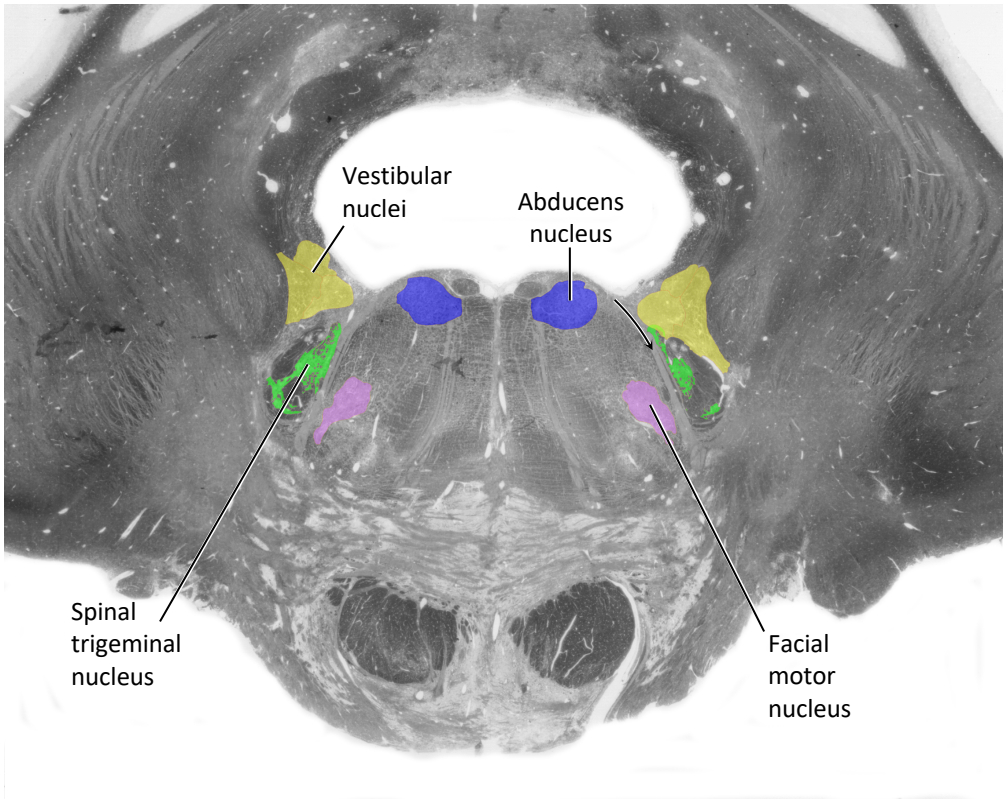
Internal Anatomy of the Brainstem and Spinal Cord

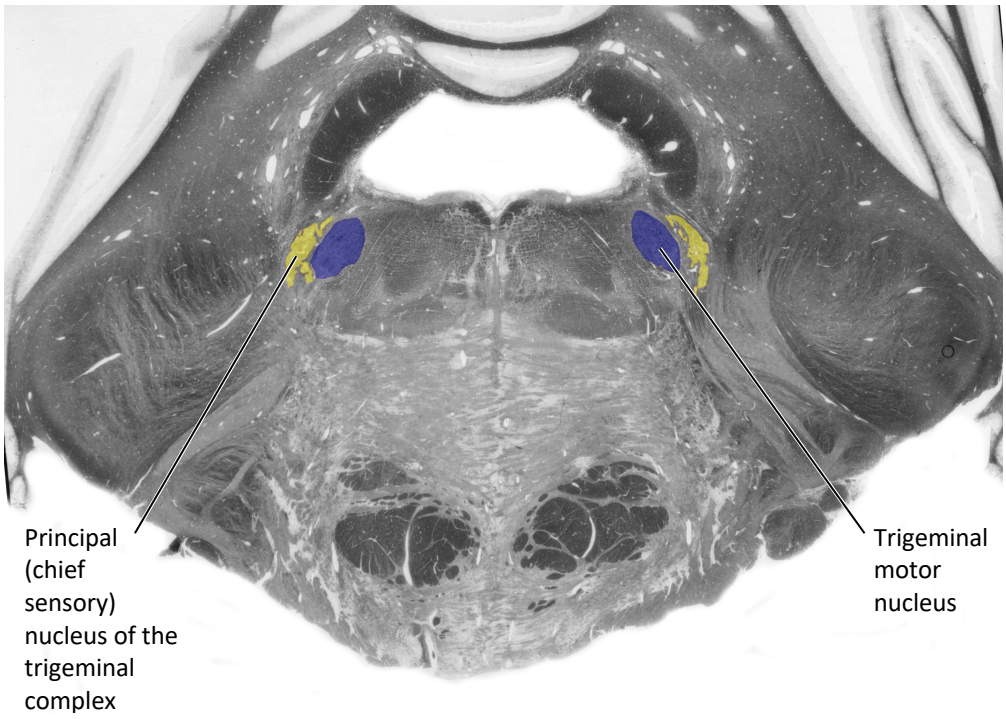
Pons

Two sections are necessary to demonstrate the cranial nerve nuclei of the pons: a section from the caudal pons (upper section in **Figure 3.13**) and a section through the level of the root of the trigeminal nerve (lower section in **Figure 3.13**). Three motor nuclei can be identified in the pons. In the caudal pons, the **abducens nucleus** occupies the location next to the midline, and the **facial motor nucleus** is located ventral-laterally in the tegmentum. The myelinated axons indicated by the arrow are the axons that are leaving the seventh motor nucleus to enter the seventh nerve. These axons loop over the abducens nucleus before they exit laterally, forming what is known as the 'genu' of the seventh nerve. Parts of two nuclei that could be seen in the medulla are also seen here in the caudal pons—the **spinal trigeminal nucleus** and the **vestibular nuclei**. The final motor nucleus in the pons is the motor nucleus of the fifth nerve, also known as the **trigeminal motor nucleus**, which is rostral to the seventh motor nucleus. It is separated from the chief sensory nucleus of the trigeminal nerve by a bundle of myelinated fibers that are either entering or leaving via the fifth nerve (which gets to these nuclei by plunging through the middle cerebellar peduncle).

Figure 3.13 (on next page). Caudal (upper section; "7-pons" in ***Sylvius4 Online***) and middle of pons (lower section; "6-pons" in ***Sylvius4 Online***).

Internal Anatomy of the Brainstem and Spinal Cord





Internal Anatomy of the Brainstem and Spinal Cord

Midbrain

There are three motor nuclei that can be identified in the midbrain. Like the pons, to localize these cranial nerve nuclei of the midbrain, it is necessary to show two representative sections. **Figure 3.14** is a section taken through the caudal midbrain (very near the ponto-mesencephalic junction). At this level, the **trochlear nucleus** is the most caudal of these three, and is very small. It is located along the dorsal midline, since it is a somatic motor nucleus.

The other two motor nuclei of the midbrain are present in the mid-to-rostral midbrain, which is represented in **Figure 3.15**. Here, the **oculomotor nucleus** occupies a dorsal-medial position; again, because it too is a somatic motor nucleus (see **Tables A3**). You can see some of the myelinated axons that are forming the third nerve medial to the substantia nigra and the cerebral peduncle. The other cranial nerve nucleus of the midbrain is the very small Edinger-Westphal nucleus, which lies immediately dorsal-lateral to the oculomotor nucleus. Its position is consistent with its embryological and functional derivation as a preganglionic parasympathetic (motor) nucleus.

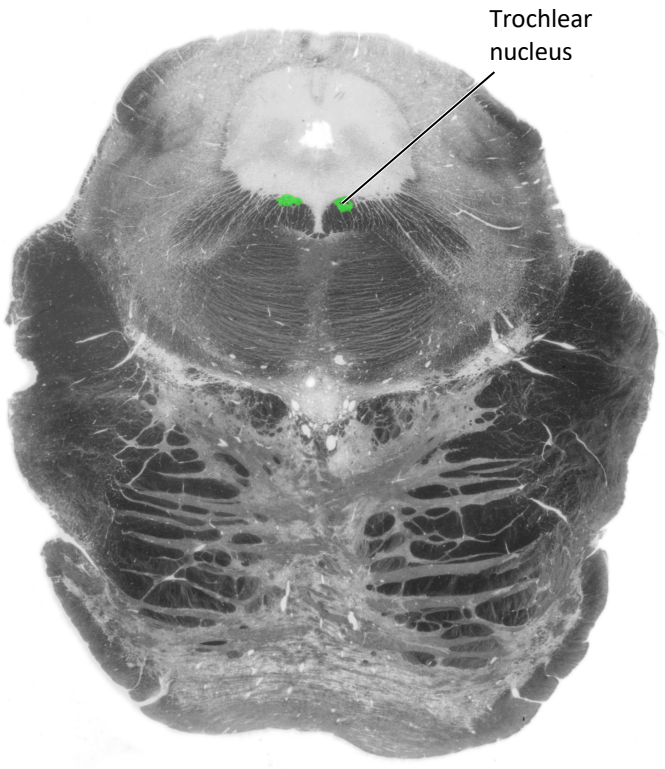


Figure 3.14. Section through the caudal midbrain. (Section shown is "3-midbrain" in ***Sylvius4 Online***)

Internal Anatomy of the Brainstem and Spinal Cord

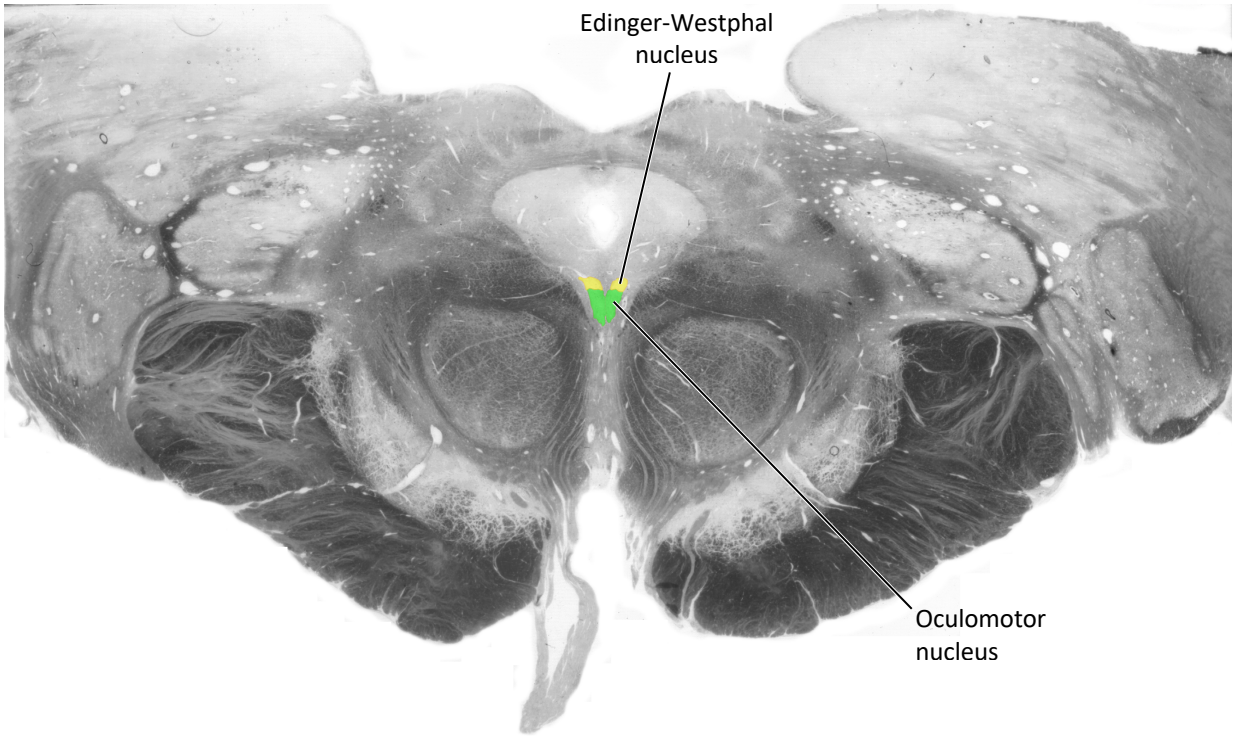


Figure 3.15. Section through the mid-to-rostral midbrain. (Section shown is "2-midbrain" in ***Sylvius4 Online***)

Only four of the cranial nerve nuclei are not identified in the preceding figures. The **spinal accessory nucleus** is found in the first few cervical segments of the spinal cord. Very few people in the world know just where the **superior** and **inferior salivatory nuclei** are located (somewhere in the dorsal tegmentum of the caudal pons and rostral medulla). The **cochlear nucleus** is located just at the junction of the medulla and pons, where this nucleus wraps around the lateral aspect of the inferior cerebellar peduncle (visible, but unlabeled in ***Sylvius4 Online***, section "8 – Medulla").

You should now be able to easily identify the brainstem subdivisions from which each section is taken. You should also be able to identify each of the cranial nerve nuclei (except for the four mentioned in the preceding paragraph). To consolidate your understanding of the surface anatomy of the brainstem and of sections through it, identify the point at which each cranial nerve enters or leaves the brainstem, and determine the approximate trajectory of the axons as they travel to or from this point to the cranial nerve nuclei with which they are connected. By the end of this laboratory experience, you should be able to view a cross section through the brainstem and identify the landmarks that characterize the subdivision, the level of the brainstem from which it was taken, and the locations of the cranial nerves and nuclei that are present. Make sure that you can identify all of the structures (in **bold**) discussed in this text and identified in the figures.

Internal Anatomy of the Brainstem and Spinal Cord

Signs and symptoms associated with specific lesions of the brainstem

Figure 3.16 contains examples of four different lesions that are commonly seen after vascular accidents involving the brainstem. Consider each of these sections in turn, and work through **Challenge 3.5**: predicting the functional impairments that result from stroke in the perforating and circumferential vessels that supply the brainstem.

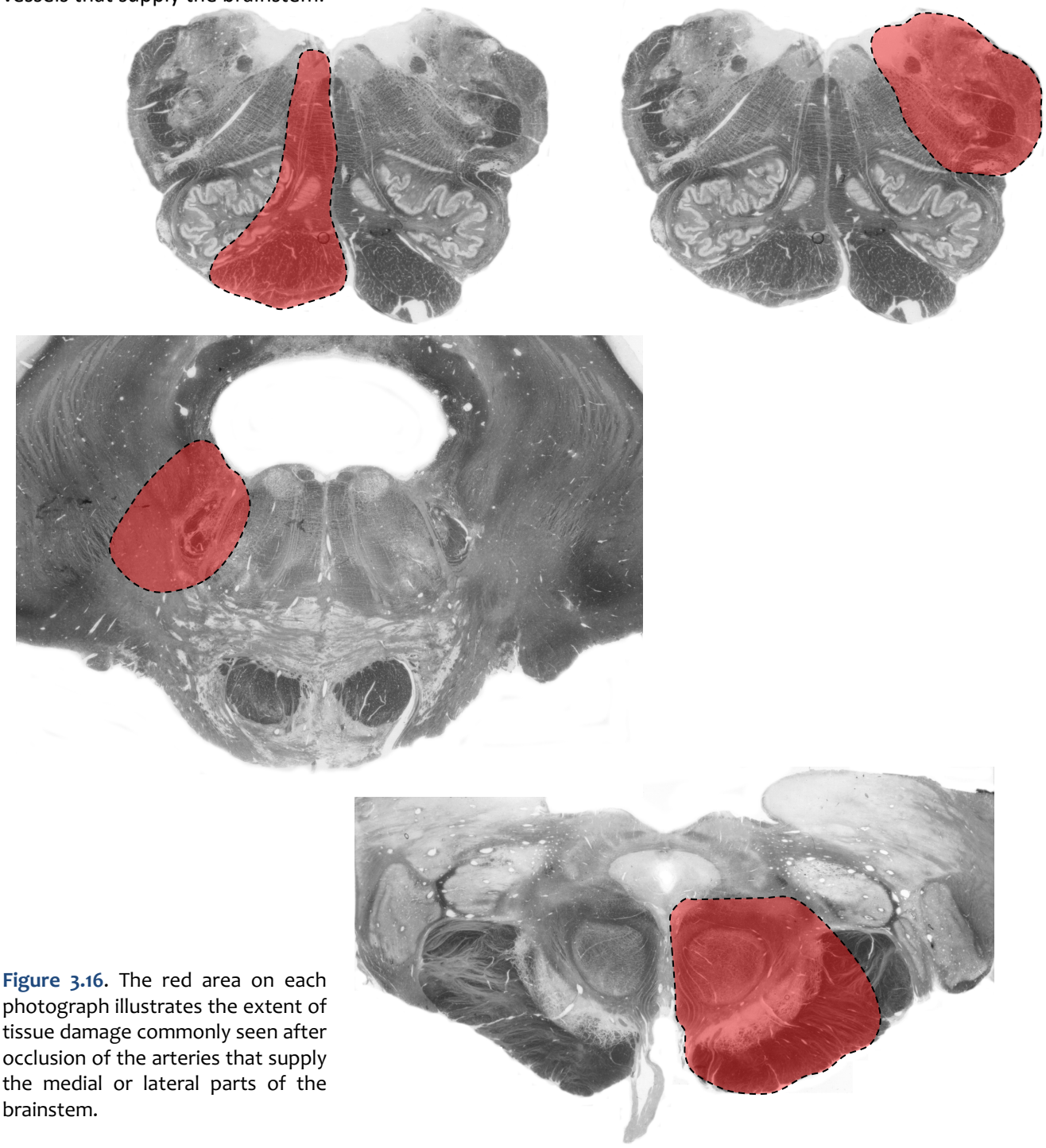


Figure 3.16. The red area on each photograph illustrates the extent of tissue damage commonly seen after occlusion of the arteries that supply the medial or lateral parts of the brainstem.

Internal Anatomy of the Brainstem and Spinal Cord

Challenge 3.5—predicting functional impairment post stroke

Selective occlusion or hemorrhage of specific arteries and arterioles that supply the brainstem can lead to damage that is preferentially localized to its medial or lateral parts. This is because, as detailed in a previous lab, the vascular supply to the medial brainstem is distinct from that to the lateral brainstem. Using this information, as well as the sections in ***Sylvius4 Online***, ***identify which cranial nerve structures are likely to be damaged in each of the lesions indicated in*** **Figure 3.16**. Once you identify the nerves involved, ***discuss among your teammates what functional impairments are likely associated with each of these brainstem strokes***.

Neuromodulatory nuclei of the brainstem

In contrast to the cranial nerve nuclei that mediate particular unimodal sensory or motor functions, other nuclei of the brainstem have widespread projections throughout the CNS and serve to "modulate" neural activities, rather than "drive" neuronal output. Neurons in these modulatory nuclei synthesize and secrete a variety of small molecule neurotransmitters, including biogenic amines and acetylcholine, as well as a diverse set of neuropeptide transmitters. The actions of these neurotransmitters are typically mediated by G-protein coupled (metabotropic) receptors and are more slowly developing and long-lasting than the ionotropic actions of conventional fast neurotransmitter systems (e.g., glutamate and GABA). This is the principal reason why these widespread projection systems are considered "neuromodulatory" in nature.

Neuromodulatory systems are implicated in a wide range of behaviors (ranging from central homeostatic functions to cognitive phenomena). It is therefore not surprising that dysregulation of the neuromodulatory systems—the biogenic amine neurotransmitters in particular—are implicated in most disorders of human behavior. It should also be of no surprise that many drugs of abuse act on these same biogenic amine pathways. The pharmacology of amine synapses is critically important in psychiatry, with drugs affecting the synthesis, receptor binding, uptake or catabolism of these neurotransmitters being among the most important agents in the armamentarium of modern neuropharmacology.

Here, we will focus on four systems that can have profound effects on conscious states, cognition, and emotion: the mesencephalic **dopamine systems**, the pontine **adrenergic** and **cholinergic** systems, and the **serotonergic systems** of the pons and medulla. In the laboratory phase of this session, you will clearly see with the unaided eye evidence of the dopaminergic and adrenergic nuclei. You will see the general area where cholinergic and serotonergic nuclei are localized, but they will not be as clearly distinguishable.

Dopamine

The cell bodies of the neurons that release dopamine as a neuromodulator are localized mainly to the ventral midbrain (mesencephalon), where they are organized into two principle divisions: a more loosely organized medial **ventral tegmental area** and a more tightly organized division of the substantia nigra known as the **substantia nigra, pars compacta**. The general distribution of projections from these divisions is illustrated in **Figure 3.17**. The locations of the cell bodies of origin of these projections is shown in **Figure 3.18**.

Internal Anatomy of the Brainstem and Spinal Cord

It is useful to differentiate three main systems of dopaminergic projections that emanate from these mesencephalic dopaminergic nuclei to the forebrain. Since they are all directed toward medial structures in the forebrain, they are often discussed with the prefix, “meso-” (a contraction of “mesial”, meaning directed toward the midline).

- **Mesostriatal** or **nigrostriatal**: projections from the *substantia nigra, pars compacta* to the *striatum*, which is a principal input division of the basal ganglia (to be discussed in the next neuroanatomy lab);
- **Mesolimbic**: projections from the *ventral tegmental area* to components of the *limbic forebrain*, including the ventral division the striatum, known as the *nucleus accumbens*;
- **Mesocortical**: projections mainly from the *ventral tegmental area* to the *prefrontal cortex*.

The functions of these three streams of dopaminergic projections to the forebrain will be discussed in later sessions in this course. For now, suffice it to summarize their functions as follows:

- **Mesostriatal** or **nigrostriatal**: facilitation of motor program selection and movement initiation. An important degenerative condition that we will study elsewhere is Parkinson’s disease, which results from the loss of mesencephalic dopaminergic neurons. The cardinal signs associated with Parkinson’s disease (e.g., bradykinesia) are attributable to loss of the nigrostriatal projection.
- **Mesolimbic**: facilitates the activation of effortful, motivated behavior and reward circuitry in the limbic forebrain and prefrontal cortex. Plasticity in this projection has been implicated in addiction and the expression of addictive behavior. In a different context, over activity of the mesolimbic pathway is thought to be important in the “positive” symptoms associated with psychosis and schizophrenia, such as forced ideations and hallucinations.
- **Mesocortical**: facilitates executive functions in prefrontal lobe circuitry, including working memory, behavior choice, and attentional aspects of motor initiation. Dysfunction or injury to the mesocortical dopaminergic pathway may contribute to the cognitive deficits seen in Parkinson’s disease, and in the “negative” symptoms associated with schizophrenia.

Internal Anatomy of the Brainstem and Spinal Cord

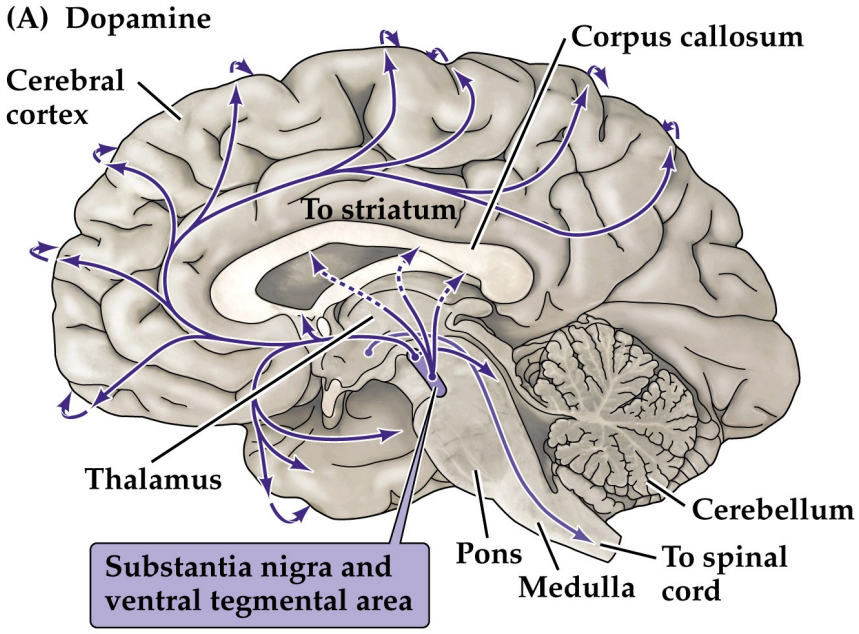


Figure 3.17. Distribution of dopaminergic systems in the central nervous system. Shown are neurons and their projections (arrows) that contain dopamine. Curved arrows along the perimeter of the cortex indicate the innervation of lateral cortical regions not shown in this midsagittal view. Mesocortical dopaminergic projections are mainly distributed to the prefrontal cortex. (Figure 6.15A from *Neuroscience*, 6th *Ed.*)

The mesencephalic dopaminergic nuclei are visible to the unaided eye in gross specimens by the presence of a dark pigment named *neuromelanin*, which accumulates across the lifespan in the cell bodies of catecholaminergic neurons (**Figure 3.18**). Neuromelanin is a polymer made from 5,6-dihydroxyindole monomers; evidently, its accumulation is benign with respect to the metabolic and biosynthetic activities of catecholaminergic neurons. It is this pigment that gives the appearance of "dark substance" in the pars compacta division of the substantia nigra and in the ventral tegmental area ("substantia nigra" means "dark substance"). At autopsy, the brain from an individual with idiopathic Parkinson's disease would be expected to exhibit far less "dark substance" due to the degeneration of the dopaminergic neurons.

Internal Anatomy of the Brainstem and Spinal Cord

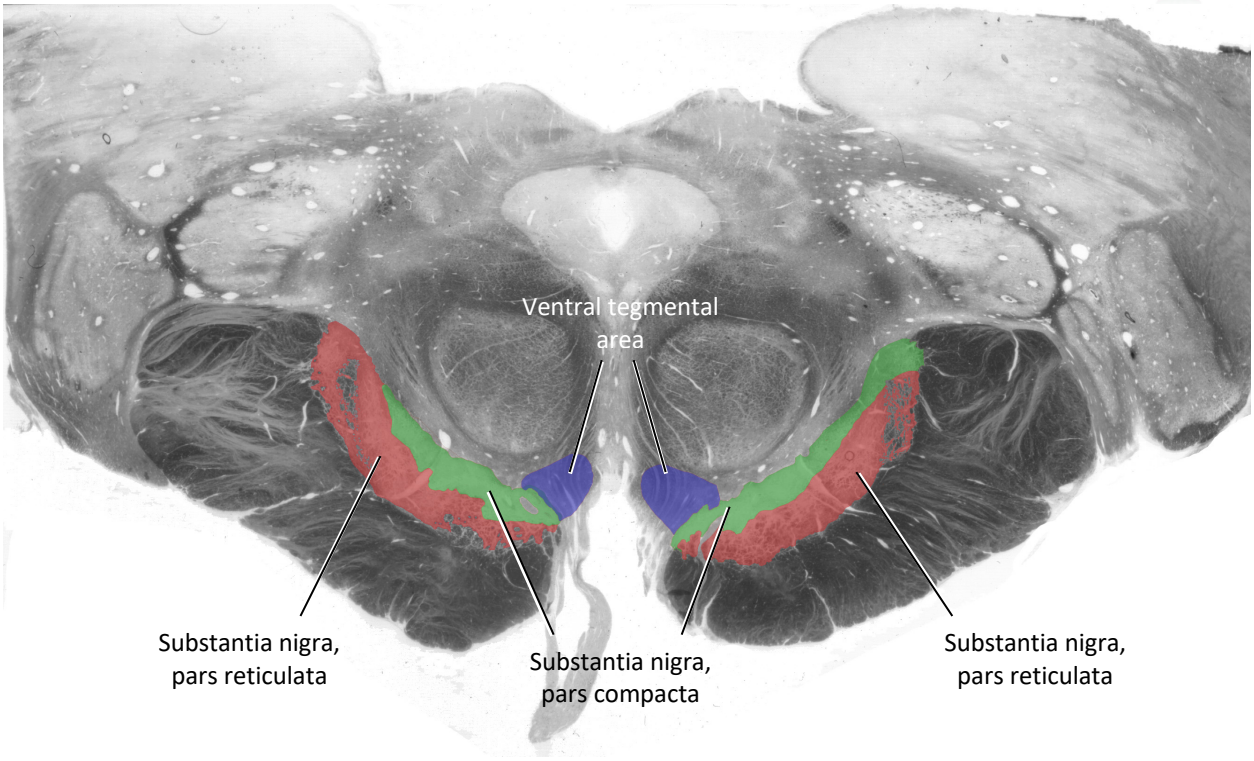
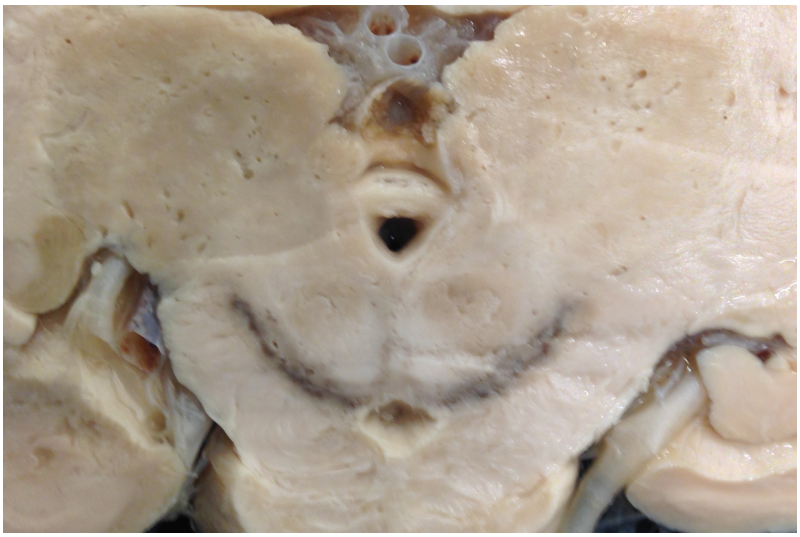


Figure 3.18. Histological section through the midbrain indicating the ventral tegmental area (blue) and the basic divisions of the substantia nigra: pars compacta (green) and pars reticulata (red). (Section shown is "2-midbrain" in ***Sylvius4 Online***)

Figure 3.19. Photograph of a gross specimen sectioned in the coronal plane through the midbrain. Note the presence of neuromelanin (the dark pigment) in the substantia nigra, pars compacta and the ventral tegmental area.



In addition to the mesencephalic dopaminergic neurons, dopaminergic neurons with more specialized functions are localized to the retina, the olfactory bulbs, the hypothalamus (where they function to inhibit prolactin release from the anterior pituitary), and the medulla.

Internal Anatomy of the Brainstem and Spinal Cord

Norepinephrine

The cell bodies of the neurons that release norepinephrine (noradrenaline) as a neuromodulator in the brain are localized mainly to a distinctive, needle-shaped nucleus of the rostral pons called the **locus coeruleus**. However, there are also noradrenergic neurons scattered in the lateral tegmentum of the pons and medulla. Ascending noradrenergic projections from the locus coeruleus (and lateral tegmentum) reach the entire forebrain (**Figure 3.20**). The location of the locus coeruleus is indicated in **Figure 3.21**.

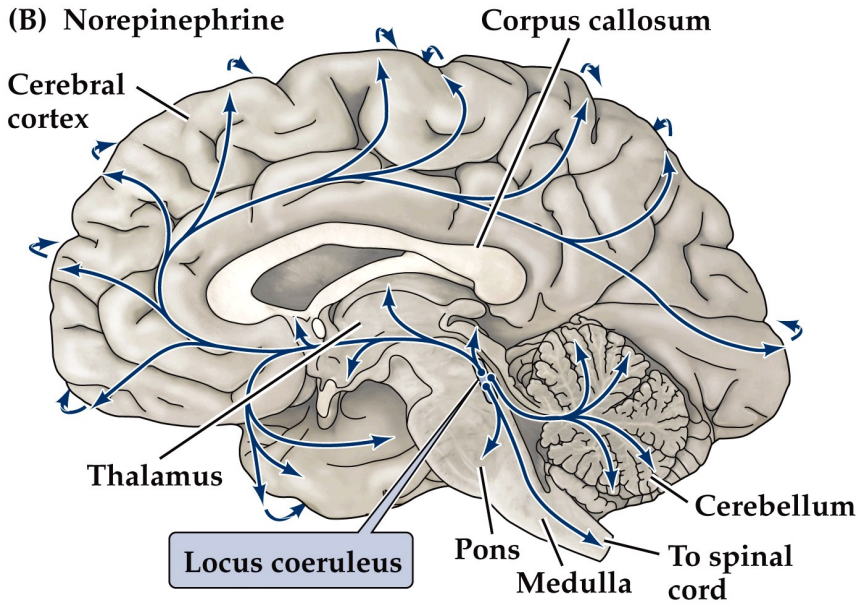


Figure 3.20. Distribution of noradrenergic systems in the central nervous system. Shown are neurons and their projections (arrows) that contain norepinephrine. Curved arrows along the perimeter of the cortex indicate the innervation of lateral cortical regions not shown in this midsagittal view. (Figure 6.15B from *Neuroscience*, 6th *Ed.*)

Internal Anatomy of the Brainstem and Spinal Cord

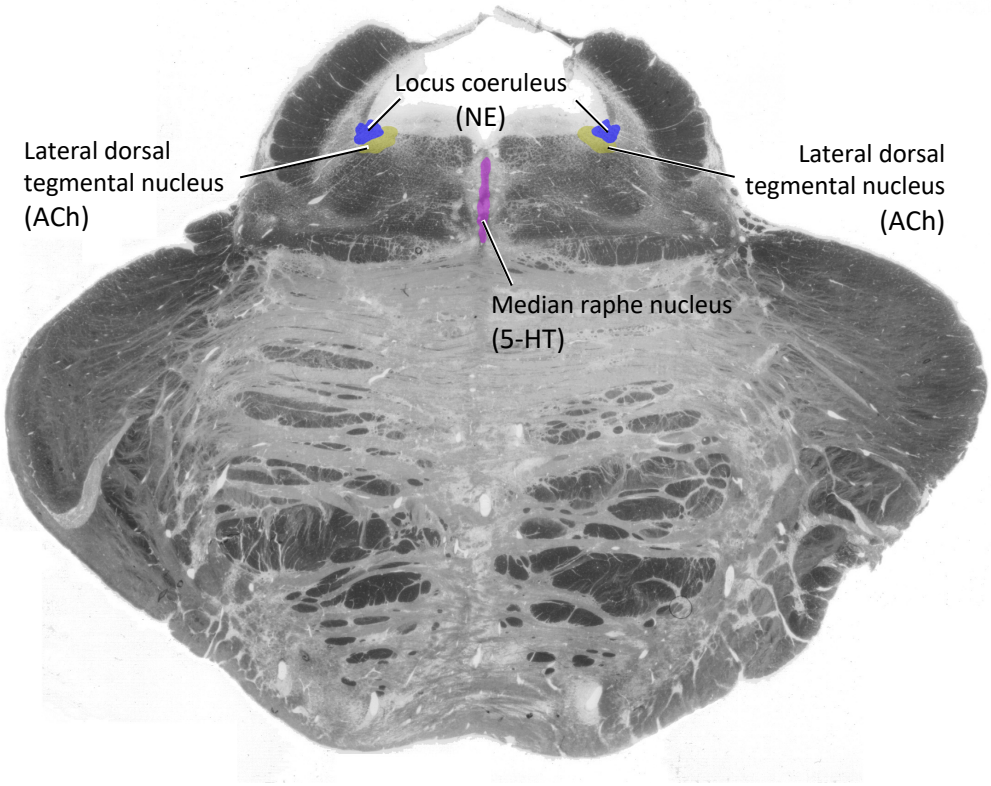


Figure 3.21. Histological section through the rostral pons indicating the bilateral, noradrenergic locus coeruleus (blue) and cholinergic lateral dorsal tegmental nuclei (green), and the serotonergic median raphe nucleus (pink). Respectively, these nuclei synthesize and release the neurotransmitters norepinephrine (NE), acetylcholine (ACh), and serotonin, also known as 5-hydroxytryptamine (5-HT). (Section shown is "5-pons" in ***Sylvius4 Online***)

The widespread projections of the locus coeruleus influences sleep and wakefulness, attention, and feeding behavior. They also contribute to transient stress-related responses helping to mediate a heightened state of vigilance and synergizing with sympathetic activation of visceral motor effectors. In the cerebral cortex, the effects of noradrenaline can be suppressive or facilitative (depending on the receptors expressed by postsynaptic structures), but in the thalamus, the effects generally are facilitative. Noradrenaline, together with serotonin, appears to have a role to play in the central modulation of pain in the brainstem and spinal cord. It also is implicated in mood disorders, such as depression and bipolar disorder, and in a variety of anxiety disorders.

Like dopaminergic neurons, the noradrenergic neurons of the locus coeruleus accumulate neuromelanin, which gives the locus coeruleus its characteristic "blue spot" appearance ("locus coeruleus" means "blue spot"). Although, in most brain specimens sectioned grossly through the pons, the pigment coloration of the locus coeruleus is indistinguishable to the unaided eye from the substantia nigra, pars compacta (**Figure 3.22**).

Internal Anatomy of the Brainstem and Spinal Cord

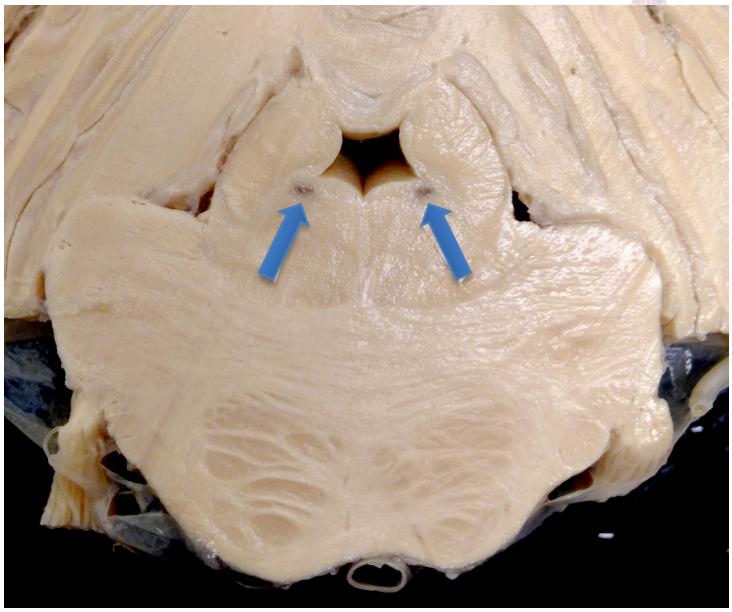


Figure 3.22. Photograph of a gross specimen sectioned in the coronal plane through the rostral pons. Note the presence of neuromelanin (the dark pigment) in the paired locus coeruleus ("blue spot"), indicated by the arrows.

Serotonin (5-hydroxytryptamine)

Serotonin is found primarily in groups of neurons in the median "seam" of the pons and rostral medulla; these neurons are organized into narrow midline nuclei called the **raphe nuclei** ("raphe" means "seam"). The raphe nuclei have widespread projections throughout the central nervous system (**Figure 3.23**). The location of the pontine raphe is indicated in **Figure 3.21**.

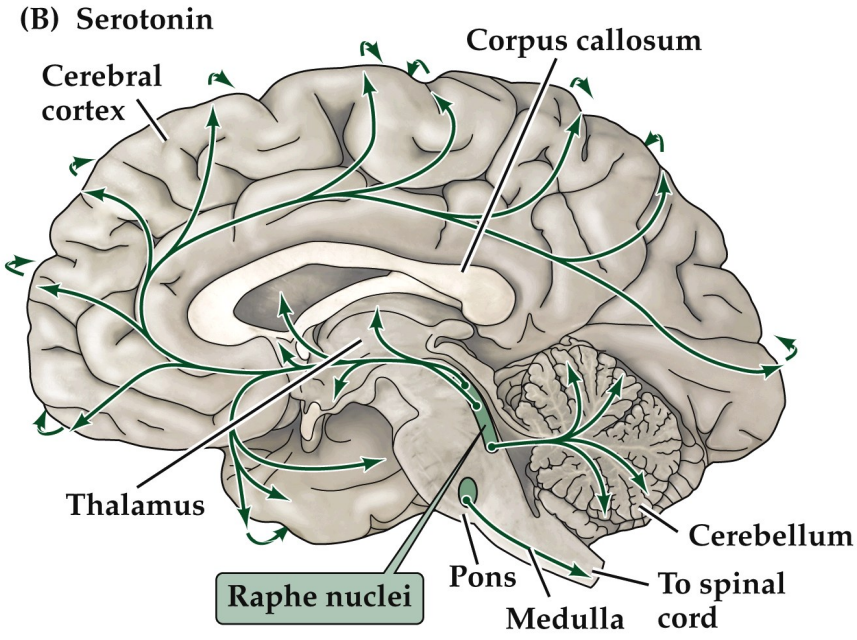
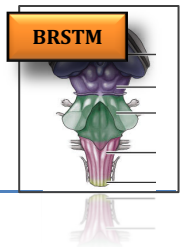


Figure 3.23. Distribution of serotonergic systems in the central nervous system. Shown are neurons and their projections (arrows) that contain serotonin. Curved arrows along the perimeter of the cortex indicate the innervation of lateral cortical regions not shown in this midsagittal plane of section. (Figure 6.17B from *Neuroscience, 6th Ed.*)



Serotonin occupies a place of prominence in neuropharmacology because a large number of antipsychotic drugs that are valuable in the treatment of depression and anxiety act on serotonergic pathways. Many antidepressant drugs are *selective serotonin reuptake inhibitors* (SSRIs) that inhibit the uptake of serotonin by specific presynaptic transporters. Serotonin has been shown to modulate a variety of behaviors, including emotion, circadian rhythms, motor behaviors, and states of arousal. Impairments in the function of serotonin receptors have been implicated in numerous psychiatric disorders, such as depression, anxiety disorders, and schizophrenia. Activation of serotonin receptors also mediates satiety and decreased food consumption, which is why serotonergic drugs may be useful in treating eating disorders.

Acetylcholine

Acetylcholine (ACh) was the first substance identified as a neurotransmitter. In addition to the function of ACh as the neurotransmitter at skeletal neuromuscular junctions, as well as at the neuromuscular synapse between the vagus nerve and cardiac muscle fibers, ACh serves as a transmitter at synapses in the ganglia of the visceral motor system and at a variety of sites within the central nervous system. Although its actions in the brain are not as well understood as they are in the periphery, ACh does seem to function as a neuromodulator at central cholinergic synapses generally serving to increase the depolarizing response of neurons to glutamatergic inputs.

Cholinergic neurons with widespread projections are found mainly in two locations in the brain: in the ponto-mesencephalic junction of the brainstem, and in the basal forebrain. Neurons of the brainstem cholinergic projection system are found mainly in the **lateral dorsal tegmental nuclei** (see **Figure 3.21**) and the nearby **pedunculopontine tegmental nucleus**. Neurons in these nuclei give rise to projections that diffusely innervate so-called non-specific nuclei of the thalamus, which in turn project to widespread regions of the cerebral cortex where they have a general effect promoting arousal. In addition to their role in arousal, these cholinergic tegmental nuclei also play a role in the function of motor systems, maintaining widespread connections to the basal ganglia, the superior colliculus, the deep nuclei of the cerebellum, and to premotor circuits distributed throughout the brainstem and spinal cord. For example, these descending cholinergic projections appear to play a role in the initiation of locomotion.

Direct cholinergic projections to the cerebral cortex arise from neurons in the nucleus basalis (of Meynert), which is a component of the **basal forebrain**. Other cholinergic projections in the forebrain come from the medial septal nuclei and the nucleus of the diagonal band (of Broca)—also components of the basal forebrain; these are mainly directed toward the amygdala and hippocampus in the medial temporal lobe.

In addition to cholinergic neurons with long-ranging projections, the central nervous system also contains cholinergic interneurons with more short-range local connections. Among the more important clinically are the large, cholinergic interneurons of the striatum, an important division of the basal ganglia that you will identify in the final lab session and study elsewhere in the course.