Preface

The preface to the first edition of *Neuroscience in Medicine* began with a simple statement: "Neuroscience is a fascinating discipline." The interest that provoked the preparation of a second edition means that statement still rings true. The challenge remained to define the core material. I have attempted to restrict certain peripheral topics—the generalities of biosynthesis and gene expression, for example—in order to allow the remaining topics to include new material and, in some cases, to showcase developing areas—neuroimmunology, for example—in the hope that this will pique the interests of the reader and keep the volume fresh.

As in the first edition of *Neuroscience in Medicine*, the authors are selected from leaders in research on their chosen topics who also hold credentials as excellent teachers. Such individuals are rare and, not surprisingly, are very careful with their time. Happily, the authors involved here recognize the significance of their project and have generously made the necessary time commitments to it. Once the manuscripts were in hand, it was the editor's job to make the writing uniform, remove duplicative materials except where essential for ease of understanding, and incorporate additional critical material.

Neuroscience in Medicine is designed to reveal the basic science underlying disease and treatments for neural disorders. Though the chapters are intended to interdigitate, each chapter can be read as a stand alone—that is, each contains a complete discussion of the topic.

I am pleased that the "Clinical Correlations," a popular feature of the first edition, are again included. We have also been aided in our task by the art and editorial staff at Humana, whose help I gratefully acknowledge.

Two participants from the first edition of *Neuroscience in Medicine*, Dr. David K. Sundberg and Dr. Robert F. Spencer, passed away during the ten years since it was published. Their intellectual contribution, collegiality, and helpfulness was missed.

P. Michael Conn

2 Anatomy of the Spinal Cord and Brain

Bruce E. Maley

CONTENTS

1. INTRODUCTION

The central nervous system (CNS) is divided into a rostral *brain* and a caudal *spinal cord*. The brain is contained in the cranial cavity, and the spinal cord is located in the vertebral canal that is formed by the 31 vertebral foramina from the individual vertebra. The two are continuous with one another at the foramen magnum of the occipital bone. The twelve pairs of cranial nerves—which arise from the brain and the thirty-one pairs of spinal nerves originating from the spinal cord with their associated ganglia—are, by convention, part of the peripheral nervous system. Both the brain and spinal cord are organized into *gray matter* in which the neuronal cell bodies are located and *white matter*, which contains the long myelinated tracts of the CNS.

2. SPINAL CORD

The spinal cord, continuous with the brain's medulla oblongata, is a long cylinder beginning at the foramen magnum and extending to the second lumbar vertebra. It is divided into thirty-one segments composed of eight cervical, twelve thoracic, five lumbar, five sacral, and one coccygeal segment. Each spinal cord segment has an associated pair of spinal nerves that arise as a series of fine rootlets. Each spinal nerve is formed from *dorsal root fibers*, which are sensory fibers whose cell bodies are in spinal ganglia located outside the CNS and *ventral root fibers*, which are motor fibers originating from ventral horn cells in the spinal cord gray matter (Figs. 1,2). At cervical levels C1–C4, fibers from the accessory nerve (cranial nerve XI) originate from the lateral side of the spinal cord intermediate between the dorsal root fibers and ventral root fibers. In contrast, the vertebra column, which surrounds and protects the spinal cord, has seven cervical vertebra, twelve thoracic vertebra, five lumbar vertebra, five sacral vertebra typically fused into a single sacrum, and three to four coccygeal vertebra also fused into a common coccyx. Although the number of spinal cord segments is roughly equivalent to the thirty-three vertebra, each of its segments is relatively shorter than the corresponding vertebra. As a result, the spinal cord ends at the level of the second lumbar vertebra in adults. In infants, the spinal cord ends more caudally at the third lumbar vertebra. The remainder of the vertebral canal below the level of the second lumbar vertebra is composed of the obliquely oriented dorsal roots and ventral roots traveling to their proper point of exit from the vertebral canal at the appropriate intervertebral foramina.

The spinal has two noticeable swellings along its length—a *cervical enlargement* at lower cervical to upper thoracic levels to accommodate the increase of neurons for innervation of the upper limb and a *lumbar enlargement* at lumbar to upper sacral levels for innervation of the lower limb. At its termina-

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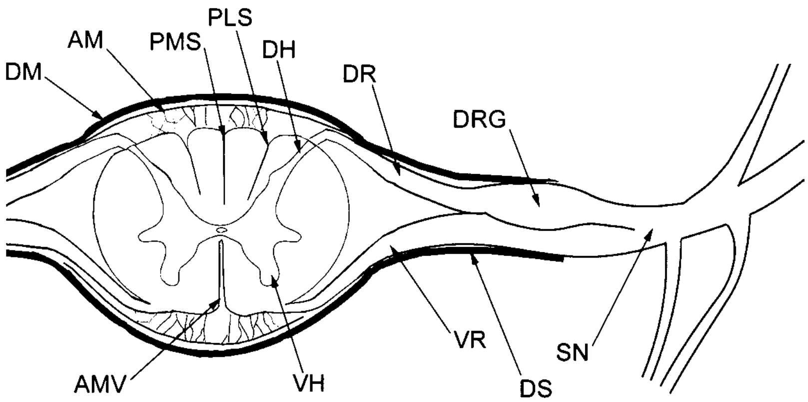

Fig. 1. Schematic diagram of a cross-section of the spinal cord. The gray matter occupies the central region of the spinal cord, and is composed of the ventral horn (VH) and dorsal horn (DH). The anterior median fissure (AMF) extends through the white matter to the gray matter. The posterior median sulcus (PMS) and posterolateral sulcus (PLS) are located on the posterior side of the white matter. The dorsal root (DR) originates from cell bodies in the dorsal-root ganglion (DRG) to enter the dorsal horn, and the ventral root (VR) begins as axons of the ventral horn. Dorsal-root fibers and ventral-root fibers unite distal to the dorsal-root ganglion to form the spinal nerve (SN). The dura mater (DM) covers the spinal cord and extends to the intervertebral foramen as a dura sleeve (DS). The arachnoid membrane (AM) lies deep to the dura mater and has fibrous strands that extend to the pia mater on the surface of the spinal cord.

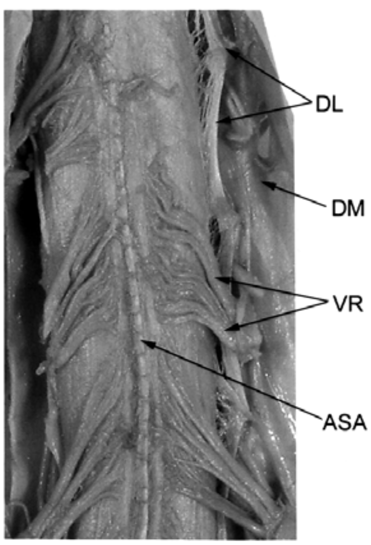

Fig. 2. Anterior surface of the spinal cord. The dura mater (DM) has been cut to reveal the ventral rootlets (VR) that comprise one ventral root of the spinal cord. The anterior spinal artery (ASA) lies in the anterior median fissure. Posterior to the ventral roots, the denticulate ligament (DL) is visible as a tooth-like extension from the surface of the spinal cord to the dura mater. Anterior surface of the brainstem. Midbrain, pons, and medulla are visible, as are the origin of cranial nerve III through XII.

tion, the spinal cord narrows into the *conus medullaris*, representing a reduction in neuronal cell bodies and myelinated tracts.

The spinal cord's anterior (ventral) surface has a deep *anterior median fissure* along its entire length, which typically contains the anterior spinal artery. The anterior median fissure extends deeply to the central gray matter, dividing the anterior half of the spinal cord into two separate cylinders. On its posterior (dorsal) side, several longitudinal depressions are visible—a midline *posterior median sulcus* and two *posterolateral sulci*, where the dorsal roots of the individual spinal nerves originate, on either side of the posterior median sulcus. A *posterior intermediate sulcus*, intermediate between the dorsal median sulcus and the posterolateral sulcus, is present beginning at upper thoracic levels. Its formation results from the location of two separate ascending sensory tracts, the fasciculus gracilis and fasciculus cuneatus, from the lower limb and upper limb, respectively (Figs. 1,3).

The spinal cord is divided into an outer layer of white matter and an inner core of gray matter. The *white matter* is composed of longitudinally oriented myelinated fiber tracts that ascend and descend the length of the spinal cord. The *gray matter* takes the shape of an "H" and is composed of paired dorsal horns and ventral horns. Between the first thoracic level and the second lumbar spinal cord level, the gray matter contains an additional horn (cell column), known as the intermediolateral cell column, intermediate between the ventral horn and dorsal

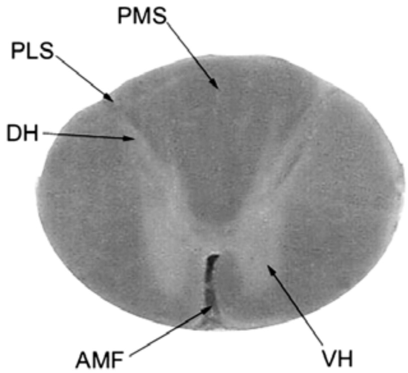

Fig. 3. Cross-section of the cervical spinal cord. The gray matter occupies the central region in the form of an "H." The ventral horn (VH) forms the legs of the "H," and the dorsal horn (DH) forms the arms of the "H." The white matter surrounds the gray matter. It has an anterior median fissure (VMH) and a posterior median fissure (PMF) that divide the white matter into left and right sides. The dorsolateral sulcus (DLS) is located at the entrance of dorsal-root fibers into the dorsal horn.

horn. Contained within the horizontal, interconnecting gray matter is the *central canal*, a part of the ventricular system of the CNS. The central canal is usually not patent its entire length.

2.1. Blood Supply of the Spinal Cord

The spinal cord receives its blood supply from three longitudinal arteries, which are supplemented from segmental vessels along the length of the spinal cord. Extensive anastomoses occur between the longitudinal arteries and the segmental arteries. The *anterior spinal artery* (Fig. 2) is the principal artery of the anterior two-thirds of the spinal cord, and the paired *posterior spinal arteries* are responsible for the posterior third of the spinal cord. The anterior spinal artery originates as a common trunk from the union of the paired vertebral arteries as they pass through the foramen magnum into the cranial cavity. The posterior spinal arteries arise either from the vertebral arteries or the posterior inferior cerebellar arteries, which are typically branches of the vertebral arteries. The anterior spinal artery runs the entire length of the anterior median fissure, although it reaches its largest diameter in the cervical and upper thoracic level and then begins to diminish in size as it descends further down the spinal cord. The posterior spinal arteries run the entire length of the spinal cord and are located in the posterolateral sulci. The vascular supply to the spinal cord is most attenuated between T3 and T9 levels, and this level of the spinal cord is most vulnerable to ischemia. The anterior spinal artery throughout its length receives anastomotic branches from segmental vessels that enter intervertebral foramina with the ventral and dorsal-root fibers. In cervical levels segmental arteries arise from vertebral arteries, the ascending cervical branch of the inferior thyroid artery and the deep cervical branch of the costocervical trunk. At thoracic levels, posterior intercostal arteries arising from the descending aorta supply segmental arteries to the spinal cord. At lumbar levels, lumbar arteries originating from the abdominal aorta supply blood, and sacral arteries from internal iliac arteries supply the lowest levels of the spinal cord. Each segmental artery at every level enters an intervertebral foramen to give origin to dorsal radicular and anterior radicular arteries that follow and supply the dorsal roots and ventral roots. Periodically, these give rise to *anterior medullary artery* and *posterior medullary arteries*, which anastomose with the anterior spinal artery and the posterior spinal artery. Typically, there are three medullary arteries supplying cervical spinal cord levels, two supplying thoracic levels and two for the lumbar spinal cord. The *great anterior medullary artery (of Adamkiewicz)*, located around the 8th to 11th thoracic level, is noticeable because of its large size and is responsible for supplementing the blood supply to the lumbar enlargement. Posterior medullary arteries are smaller and more numerous than the anterior medullary arteries, with an average of 3–5 for each spinal cord region. The anterior spinal artery and the two posterior spinal arteries supply the majority of the gray matter and white matter of the spinal cord, although occasional medullary branches arise from radicular arteries located on the surface of the spinal cord.

2.2. Venous Drainage of the Spinal Cord

The veins that drain the spinal cord begin as capillaries within it—as *intramedullary veins*, which drain into the more superficial *intradural (pial) veins* located external to the spinal cord in the pia mater. The *anterior median vein*, located in the anterior median fissure, is the most consistent of the intradural veins. Several less consistent veins may also be present, including the posterior median vein located in the posterior median sulcus, anterolateral veins located in the region of exit of the ventral roots, and posterior lateral veins located in or near the entrance of the dorsal roots. Each of these veins freely communicates with its neighbors, forming large anastomotic channels along the surface of the spinal cord. At the base of the skull the intradural veins unite to form several trunks that also drain into the posterior inferior cerebellar veins and vertebral veins of the cranial cavity. The intradural veins communicate with the *internal vertebral venous plexus* located in the epidural space of the vertebral canal along its entire length. The internal vertebral plexus can be divided into an *anterior internal vertebra venous plexus* located between the vertebral body and the spinal cord and a *posterior internal vertebral venous plexus* between the vertebral arch and the spinal cord. The internal vertebral venous plexus in turn drains more superficially into the *external vertebral venous plexus* surrounding the vertebral column. The external vertebral plexus consists of an *anterior external vertebral plexus* around the vertebral bodies and the *posterior external vertebral plexus* lying on the surface of the vertebral arch. Both the anterior and posterior external vertebral plexi anastomose with one another and drain into the systemic segmental veins, including the deep cervical veins, intercostal veins, lumbar veins, and lateral sacral veins.

2.3. Meninges of the Spinal Cord

The spinal cord is covered by three connective tissue layers known as the *meninges*. The most superficial layer is the *dura mater* (Fig. 2). The spinal dura mater begins at the foramen magnum and extends caudally as a sac to the second sacral vertebra. At each intervertebral foramen, the dura mater extends as a *dural sleeve* to cover the dorsal roots, ventral roots, and spinal ganglia. It ends at the external edge of the intervertebral foramen, where it becomes continuous with the epineurum of the spinal nerve. At the caudal end of the vertebral canal, the dura mater ends as the *dural sac,* a blind end sac. The *arachnoid membrane* (spider-like), the second meningeal layer, is deep to the dura mater and consists of a fine network of connective tissue fibers that extend to the surface of the spinal cord. It follows the contours of the dura mater and is present in the dural sleeves and the dural sac. The *pia mater* (delicate mother) is the deepest and thinnest meningeal layer, and is typically adherent to the surface of the spinal cord, following its fissures and sulci. It is a vascular layer containing arteries supplying the spinal cord and veins that drain the spinal cord. The *denticulate ligaments* are irregularly found, sawtooth-like lateral extensions of the pia mater that extend laterally from the side of the spinal cord between the dorsal roots and ventral roots to the overlying dura mater/arachnoid membrane. The pia mater extends beyond the spinal cord caudally as a fine filament, the *filum terminale* from the conus medullaris. It passes through the dural sac in the midst of the *cauda equina* to anchor to the coccyx. In the dural sac it is known as the filum terminale interna, and once it passes through the dura sac it is the filum terminale externa.

Several spaces are associated with the meninges of the spinal cord. The *epidural space* is superficial to the dura mater and contains significant amounts of fat that protect the spinal cord and the internal vertebral plexus of veins, which drain blood from the spinal cord to the more superficial external vertebral venous plexus. The *subdural space*, which is a potential space only under normal conditions, lies deep to the dura mater but superficial to the arachnoid membrane. The *subarachnoid space* separates the arachnoid membrane from the deeper pia mater. Cerebrospinal fluid (CSF), produced by the choroid plexus of the brain's ventricular system, is contained within the subarachnoid space, and allows the spinal cord to float within this space.

3. BRAIN

The brain is divided into a forebrain (prosencephalon), consisting of the cerebral cortex and thalamus, midbrain (mesencephalon), and hindbrain (rhombencephalon), composed of the pons, cerebellum, and medulla oblongata. The medulla oblongata, pons, and midbrain are collectively described as the brainstem. The brain is located in the cranial cavity. Its floor is divided into three horizontal shelves or fossae, from rostral to caudal, which are successively lower (Fig. 4). The anterior cranial fossa is composed of the crista galli and cribriform plate of the ethmoid, the greater wing of the sphenoid and frontal bones. The orbital surface, so named because it forms the roof of the orbit, supports the orbital surface of the frontal cortex. The ethmoid bone on either side of the midline crista galli is perforated (cribriform plate) to allow the olfactory nerves to pass from the nasal cavity into the paired olfactory bulbs, which are connected to the cortex by the posteriorly running olfactory tracts. Posterior to the greater wing of the sphenoid

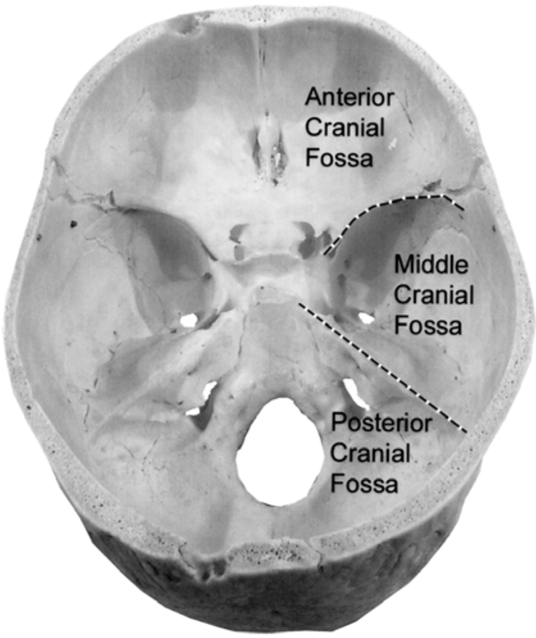

Fig. 4. Floor of the cranial cavity demonstrating the anterior cranial fossa, middle cranial fossa, and posterior cranial fossa.

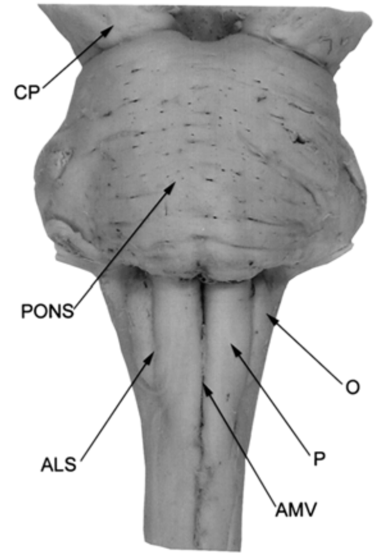

Fig. 5. Anterior surface of the brainstem. The cerebral peduncles (CP) of the midbrain are rostral to the pons. The medulla contains the pyramids (P), separated from the olive (O) by the anterior lateral sulcus (VLS). The pyramids are located on either side of the anterior median fissure (AMF).

is the middle cranial fossa. It extends to the petrous ridge of the temporal bone. The temporal cortex's inferior surface rests on the tegmen tympani of the temporal bones, and in the midline the depression of the sella turcica of the sphenoid bone houses the pituitary and infundibulum of the hypothalamus. The posterior cranial fossa is located posterior to the petrous ridge of the temporal bone and is bounded by the mastoid process of the temporal bone laterally and the clivus of the occipital bone medially. Its floor posteriorly contains the foramen magnum that allows continuation of the brainstem to the spinal cord. The brainstem and the cerebellum are contained in the posterior cranial fossa. Its roof is formed by the tentorium cerebelli of the dura mater.

3.1. Medulla Oblongata

The medulla oblongata, located in the posterior cranial fossa, is the most caudal portion of the brainstem and is continuous with the spinal cord at the foramen magnum (Fig. 5). Its anterior surface contains two prominent ridges along its length. The most medial pair of ridges is the *pyramids* formed by the corticospinal tracts, and the more lateral ridges are the *olives*, formed by the inferior olivary nuclei. Each pyramid is separated from the other by an *anterior median fissure* and from the more lateral olive by the *anterior lateral sulcus*. The anterior lateral sulcus contains the hypoglossal nerve (CN XII) fibers. The olive is bounded laterally by the *posterior lateral sulcus,* which contains the fibers of the glossopharyngeal nerve (CN IX), the vagus nerve (CN X) and the bulbar portion of the accessory nerve (CN XI). The posterior surface of the medulla contains the tubercle of the nucleus gracilis medially and the tubercle of the nucleus cuneatus laterally (Fig. 6). It opens into a diamond-shaped region known as the *rhomboid fossa*, which forms the floor of the fourth ventricle. The medulla oblongata is continuous rostrally with the pons. At the junction of the pons with the medulla, the abducens nerve (CN VI) arises medially, and both the facial nerve (CN VII) and vestibulocochlear nerve (CN VIII) originate in the lateral groove formed at the pons-medulla junction.

3.2. Pons

The pons, located in the posterior cranial fossa, lies against the basilar portion of the occipital bone (Fig. 5). It is continuous with the medulla oblongata caudally and the midbrain rostrally. Its anterior region contains pontine nuclei scattered among major descending tracts, and the posterior region

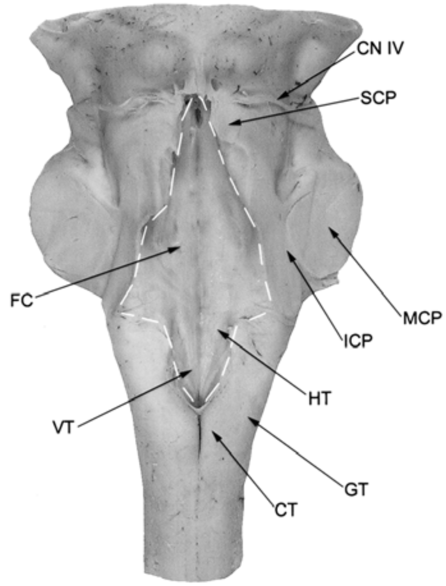

Fig. 6. Posterior surface of the brainstem, demonstrating the rhomboid. The rhomboid fossa (*outlined by dashed lines*) is visible after removal of the cerebellum. The facial colliculus (FC), hypoglossal trigone (HT), and vagal trigone (HT) are located on the floor of the rhomboid fossa. The cuneate tubercle (CT) and gracile tubercle (GC) are located caudal to the rhomboid fossa. Rostral to the rhomboid fossa cranial nerve IV is seen originating from the posterior surface of the brainstem. The inferior cerebellar peduncle (ICP), middle cerebellar peduncle (MCP), and superior cerebellar peduncle (SCP) are visible.

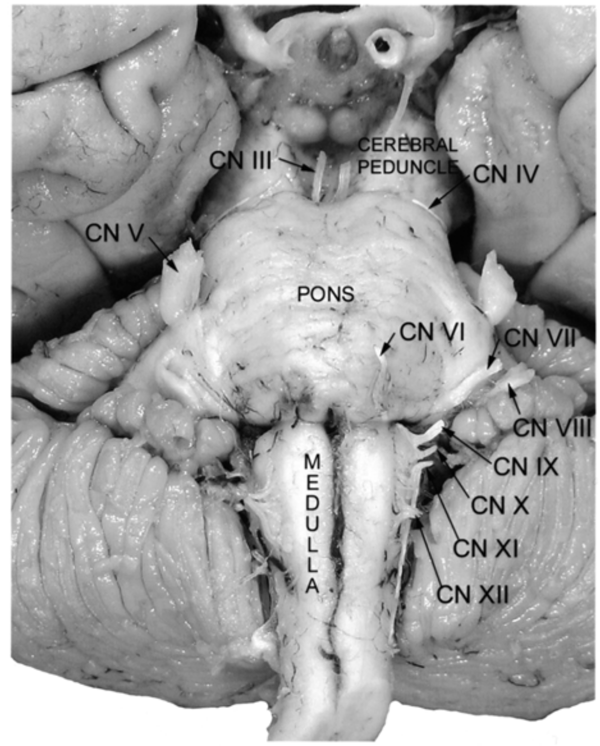

Fig. 7. Anterior surface of the brainstem. The medulla, pons, and cerebral peduncles (anterior representation of the midbrain) are labeled. The individual cranial nerves arising from each region of the brainstem are labeled. The midline oculomotor nerve (CN III) arises in the interpeduncular fossa (between the cerebral peduncles) rostral to the pons. The trochlear nerve (CN IV) wraps around the cerebral peduncle from the posterior surface of the midbrain. The trigeminal nerve (CN V) is a large nerve arising from the middle cerebellar peduncle of the pons. The abducens nerve (CN VI) arises from the midline of the pontomedullary junction, and the facial nerve (CN VII) and vestibulocochlear nerve (CN VIII) originate from the lateral region of the pontomedullary junction. The glossopharyngeal nerve (CN IX), vagus nerve (CN X), and accessory nerve (CN XI) arise lateral to the pyramid. The hypoglossal nerve (CN XII) arises in the ventrolateral sulcus between the pyramid and olive.

contains nuclei for CN VI, CN VII, and CN VIII (Fig. 7). The pons is expanded along its lateral sides for passage of fibers to the cerebellum in the *middle cerebellar peduncles*. The trigeminal nerve (CN V) arises from the anterior surface of the middle cerebellar peduncle. The pons' posterior surface contributes to the rostral half of the rhomboid fossa of the fourth ventricle (Fig. 6).

3.3. Midbrain

The midbrain, contained in the posterior cerebral fossa, is located between the pons caudally and the thalamus and hypothalamus superiorly. The cerebral aqueduct of the ventricular system passes through it. The anterior region is characterized by the prominent *cerebral peduncles* that define a depression described as the *interpeduncular fossa* (Figs. 5,7). The oculomotor nerves (CN III) arise from the midbrain medial to the cerebral peduncles in the interpeduncular fossa (Fig. 7). The posterior region of the midbrain, also known as the tectum, is composed of the *corpora quadrigemina*, four prominent tubercles consisting of the rostral *superior colliculi* (colliculus, singular), and the more caudal *inferior colliculi* (Fig. 8). The trochlear nerve (CN IV) is the only cranial nerve to arise posteriorly from the brainstem.

3.4. Cerebellum

The cerebellum is located in the posterior cranial fossa, immediately anterior to the tentorium cerebelli and posterior to the pons and medulla, where

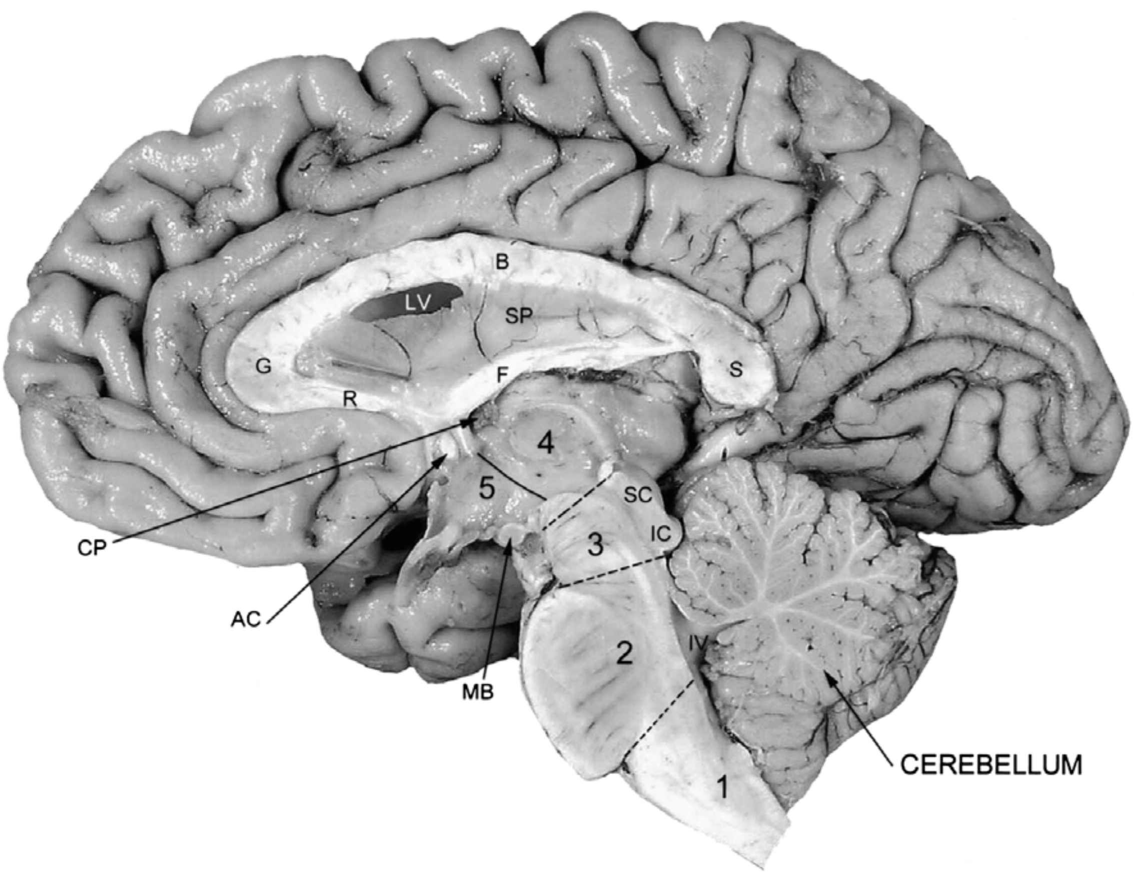

Fig. 8. Midsagittal section of the brain. The brainstem composed of the medulla oblongata **(1)**, pons **(2)** and midbrain **(3)** is visible. The cerebellum lies posterior to the caudal brainstem and forms the roof of the fourth ventricle (IV). The corpora quadragemina, made up of the superior colliculus (SC) and inferior colliculus (IC), is located posterior to the cerebra aqueduct. The diencephalons, containing the thalamus **(4)** and hypothalamus **(5)**, is rostral to the midbrain. The mammilary bodies (MB) are anterior prominences of the hypothalamus. The anterior commissure (AC) is rostral to the hypothalamus, and the fornix (F) arches over the thalamus. The corpus callosum is composed of the rostrum (R), genu (G), body (B), and splenium (S). The septum pellucidum (SP) separates the lateral ventricle (LV) of each cerebral hemisphere.

it completes the roof of the fourth ventricle along with its extensions, the superior medullary velum and inferior medullary velum (Figs. 8,9). The best way to visualize the physical arrangement of the cerebellum is to view it as a planar structure folded upon itself as a piece of paper is folded upon itself, so that its inferior edge is brought up in contact with its superior edge. The cerebellum is notable for its extensive, transversely oriented *folia* (Figs. 8,9). It is composed of two lateral *cerebellar hemispheres* that are continuous with the midline *vermis* (Figs. 9A,B). The separation of vermis from cerebellar hemispheres is less obvious on the superior surface than on the inferior surface of the cerebellum. Many fissures separate the cerebellum into its major lobes. The two most important fissures—the primary fissure and the posterolateral fissures—divide the cerebellum into three major lobes, anterior, posterior, and flocculonodular (Figs. 8,9). The *primary fissure* separates the anterior lobe from the posterior lobe and, the *posterolateral fissure* separates the posterior lobe from the flocculonodular lobe. The remaining fissures, such as the horizontal fissure and prepyramidal fissure, help to separate the cerebellum into additional lobules. The cerebellar hemisphere's lobules from its rostral to caudal edges are the anterior quadrangular, posterior quadrangular, superior semilunar, inferior semilunar, gracile, biventar, tonsil, and flocculus. The vermis lobules from its rostral to caudal edges are the lingula, central, culmen, declive, folium, tuber, pyramis, uvula, and nodulus.

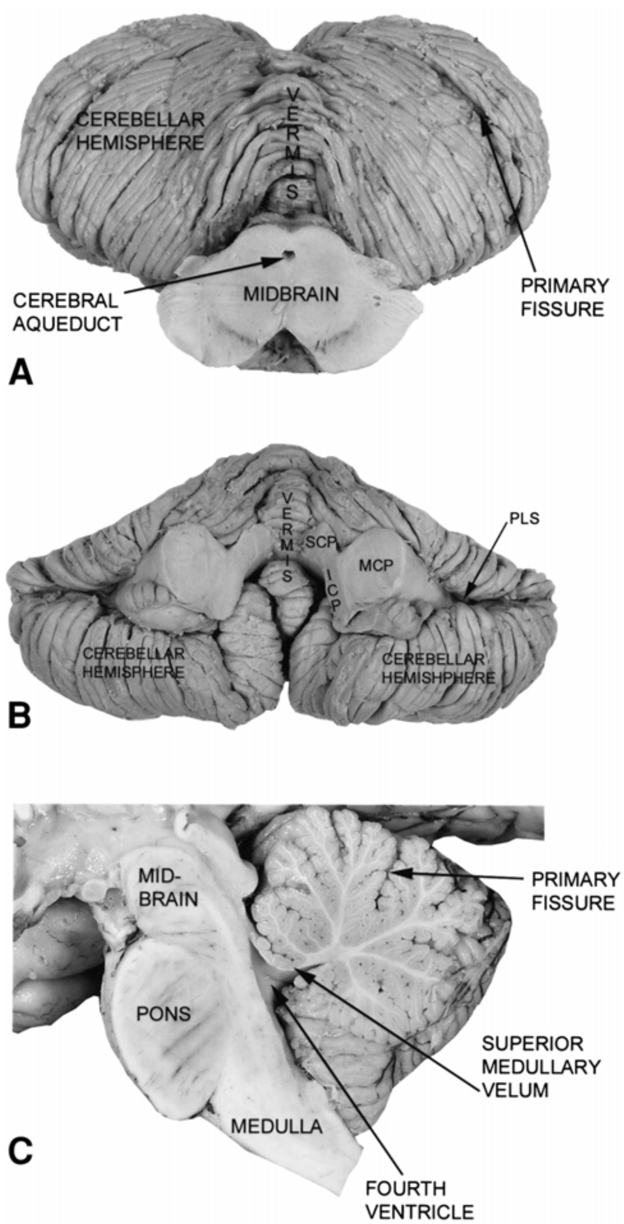

Fig. 9. (A) Anterior view of the cerebellum. The cerebellum, with its cerebellar hemispheres and vermis, lies posterior to the midbrain. The primary fissure separates the anterior lobe from the posterior lobe. The cerebral aqueduct is located in the midbrain. **(B)** Inferior view of the cerebellum. The two cerebellar hemispheres are present laterally, and the vermis is located in the midline. The posterolateral sulcus separates the posterior lobe from the flocculonodular lobe. The inferior cerebellar peduncle (ICP), middle cerebellar peduncle (MCP), and superior cerebellar peduncle (SCP) are visible. **(C)** Sagittal view of the cerebellum. The cerebellum lies posterior to the pons and medulla, and helps to define the roof of the fourth ventricle by its superior medullary velum and inferior medullary velum. The primary fissure separates the anterior lobe from the posterior lobe. The midbrain lies rostral to the pons.

3.5. Forebrain

The diencephalon and telencephalon comprise the forebrain (prosencephalon). The diencephalon is composed of the thalamus and hypothalamus, and is located between the midbrain caudally and the cerebral cortex rostrally (Fig. 8). The thalamus is located posterior to the hypothalamus. Posterior to the thalamus, the midline pineal body is connected to it by the habenular commissure. The third ventricle separates the two sides of the thalamus, and it extends ventrally down into the hypothalamus. Its separation from the thalamus is best visible from the midline, where the hypothalamic sulcus separates the two regions (Fig. 8). The hypothalamus, located on the anterior surface, connects to the pituitary through its tuberal (infundibular) region, which is located immediately posterior to the optic chiasm. Posterior to the tuberal region a pair of small swellings, known as mammillary bodies are formed by the mammillary nuclei of the hypothalamus (Fig. 8).

The two cerebral cortices comprise the majority of the brain, and each cortex is characterized by prominent folds, gyri (gyrus, singular) separated from each other by sulci (sulcus, singular), which invaginate into the depth of the cortex (Figs. 10,11). The cerebral cortex on each side is composed of an outer layer of gray matter, where the majority of neuronal cell bodies are located and a deeper layer of white matter formed by myelinated and unmyelinated axons from the neuronal cell bodies. The two cerebral cortices, are separated from one another on its superior side by the longitudinal fissure containing the falx cerebri of the dura mater, yet are connected deep in the longitudinal fissure by the corpus callosum. The corpus callosum is composed of myelinated axons that connect the two cortices and more caudal regions.

The cerebral cortex is divided by sulci or fissures into five lobes—the frontal, parietal, temporal, occipital, and insular cortices (Figs. 10–12). Several major sulci separate the major lobes from one another. The frontal cortex is separated from the parietal lobe by the central sulcus, a vertically running sulcus that begins at the longitudinal fissure in the midline and ends just short of the lateral sulcus on the lateral surface of the brain (Fig. 10). The lateral sulcus separates the temporal lobe from the frontal cortex and parietal cortex (Fig. 10). The parietal cortex on the lateral surface of the cerebral cortex is bounded by the central sulcus rostrally and

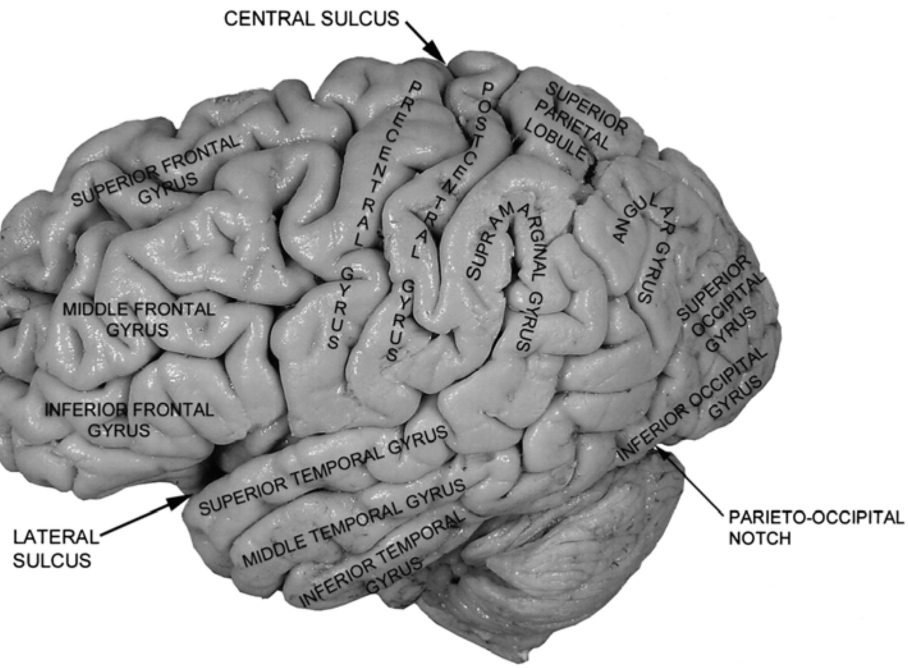

Fig. 10. Lateral surface of the cerebral hemispheres demonstrating the major gyri. The central sulcus separates the frontal cortex from the parietal cortex. The lateral sulcus separates the temporal cortex from the frontal and parietal cortices. An imaginary vertical line drawn from the parieto-occipital notch separates the parietal cortex from the occipital cortex.

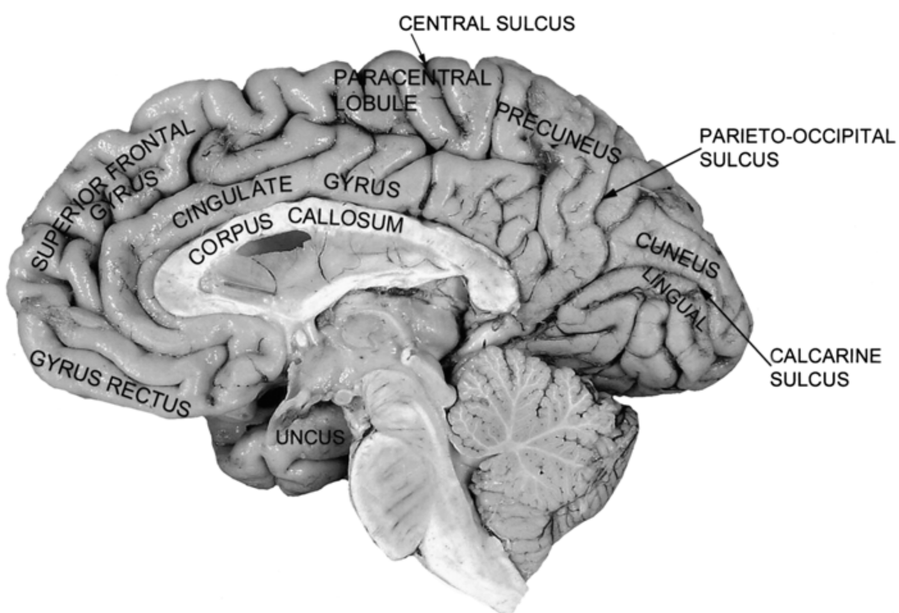

Fig. 11. Midsagittal section of the brain with cortical gyri labeled. The central sulcus extends medially into the longitudinal fissure. The parieto-occipital sulcus separates the parietal cortex from the occipital cortex. The calcarine sulcus separates the cuneus from the lingual gyrus.

is poorly delineated from the occipital lobe by a shallow indentation, parieto-occipital notch, just superior to the cerebellum (Fig. 10). On the medial surface, the separation between the parietal lobe and occipital lobe is more clearly defined by the vertically oriented parieto-occipital sulcus (Fig. 11). The

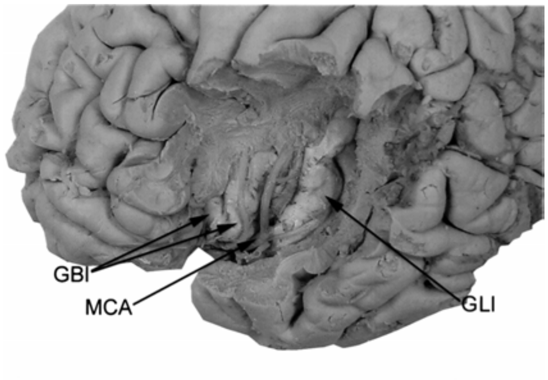

Fig. 12. Lateral surface of the cerebral cortex. The frontal operculum, parietal operculum, and temporal operculum have been removed to reveal the deeply located insula in the lateral sulcus. The middle cerebral artery (MCA) is located on the surface of the insula. Both gyrus longus insulae (GLI) and gyri brevi insulae (GBI) are present in the insula.

insular cortex lies deep inside the lateral sulcus and is most easily seen when the temporal cortex is pulled away from the frontal and parietal cortices (Fig. 12).

The frontal cortex is the most rostral portion of the cerebral cortices, and extends posteriorly to the central sulcus. It contains four prominent gyri on its lateral surface separated by corresponding sulci (Fig. 10). Three of its gyri (superior frontal gyrus, middle frontal gyrus, and inferior frontal gyrus) are horizontally oriented at the rostral end of the frontal cortex, and the fourth gyrus (precentral gyrus) is vertically oriented caudal to the first three gyri. The superior frontal gyrus begins anterior to the precentral gyrus and ends at the rostral pole of the brain. It is separated from the wide middle frontal gyrus by the superior frontal sulcus. The middle frontal cortex that is immediately inferior to the superior frontal gyrus is the broadest of the frontal gyri and also begins at the anterior border of the precentral gyrus. The inferior frontal sulcus is its inferior border, separating it from the inferior frontal gyrus. The inferior frontal gyrus is continuous inferiorly with the lateral orbital gyrus on the floor of the anterior cranial fossa. The frontal cortex on its inferior (orbital) surface is many times composed of four gyri that form an "H." These four gyri are the lateral orbital gyrus, anterior orbital gyrus, posterior orbital gyrus, and the medial orbital gyrus. The gyrus rectus is most medial, lying immediately lateral to the longitudinal fissure. Upon it lie the olfactory bulb and its centrally located olfactory tract.

The temporal cortex on its lateral surface lies inferior to the lateral sulcus, separating it from the frontal and parietal cortices (Fig. 10). Posteriorly, it is continuous with the parietal cortex. The temporal cortex contains three horizontally oriented gyri: superior temporal gyrus, middle temporal gyrus, and inferior temporal gyrus. The posterior surface of the superior temporal gyrus in the lateral sulcus is the transverse gyrus, which is associated with the auditory system. The superior temporal sulcus separates the superior temporal gyrus from the middle temporal gyrus, and the inferior temporal sulcus separates the middle temporal gyrus from the inferior temporal gyrus. The temporal cortex continues inferiorly and medially as a lateral occipitotemporal gyrus, a medial occipitotemporal gyrus, and the most medial parahippocampal gyrus, which has the uncus at its most anteromedial extent (Fig. 11).

The parietal cortex is located between the frontal cortex anteriorly and the occipital cortex posteriorly (Figs, 10,11). It is separated from the frontal cortex by the central sulcus and from the occipital cortex by the parieto-occipital sulcus. The most prominent gyrus is the vertically oriented postcentral gyrus immediately posterior to the central sulcus. The remainder of the parietal cortex lies posterior to the postcentral gyrus and is divided into a superior parietal lobule and an inferior parietal lobule. They are separated from each other by the intraparietal sulcus. On the lateral surface, the inferior parietal lobule can be divided into the supramarginal gyrus that arches over the posterior end of the lateral fissure, and the angular gyrus that arches over the superior temporal sulcus (Fig. 11).

On the superolateral surface, the occipital cortex appears as a continuation of the parietal cortex (Fig. 10). Only on the anterior edge of the cortex can a separation be discerned, where a slight indentation, parieto-occipital notch or pre-occipital notch, is present (Fig. 10). The remainder of the lateral surface of the occipital cortex has poorly defined gyri, although a superior occipital gyrus and an inferior occipital gyrus are often described. On its medial surface the vertically oriented parieto-occipital sulcus clearly separates it from the more anterior parietal cortex (Fig. 11). The horizontal calcarine sulcus separates several small gyri superior to it, collectively known as the cuneus, from the more inferior lingual gyrus.

The insula is located deep within the lateral sulcus. It is composed of two or more gyri brevi insulae and two or more gyri longus insulae (Fig. 12). The middle cerebral artery passes into the lateral sulcus on the surface of the insula. The portions of the frontal cortex, temporal cortex, and parietal cortex that form the border of the lateral sulcus and therefore cover the insula are described as the operculum. Thus, the frontal operculum is the part of the frontal cortex that helps to form the superior border of the lateral sulcus, and also participates in covering more rostral regions of the insula.

3.6. Arterial Supply of the Brain

The brain receives its blood supply from two paired arterial sources, the vertebra arteries and the internal carotid arteries (Fig. 13). The *vertebral arteries*, arising from the subclavian arteries at the base of the neck, ascend through the transverse foramina of the upper six cervical vertebral to enter the foramen magnum at the base of the skull. Once inside the cranial cavity, the two vertebral arteries unite on the anterior surface of the brainstem to form a single *basilar artery*. Prior to their union they each give rise to an arterial branch that joins with its opposite member to form the anterior spinal artery, which descends back through the foramen magnum to run along the anterior surface of the spinal cord. Each vertebral artery gives rise to the posterior inferior cerebellar artery that supplies the posterior surface of the cerebellum.

The *basilar artery* begins at the pontomedullary junction and courses along the anterior surface of the pons and midbrain until it terminates as the posterior cerebral arteries just rostral to the oculomotor nerve (Fig. 13). Before its termination it gives off several branches. Its first branch is typically the *anterior inferior cerebellar artery* which supplies the medial and lateral surface of the cerebellum. Multiple *pontine branches* arise from the basilar artery, supplying the pons as well as the midbrain. The *labyrinthine artery* arises in the midst of the pontine branches. It follows the facial nerve and vestibulocochlear nerve into the internal auditory meatus to supply the internal ear. The *superior cerebellar artery* arises from the basilar artery prior to the oculomotor nerve's origin, and is responsible for suppling the more superior surface of the cerebellum. The *posterior cerebral arteries*, which course around the cerebral peduncles to reach the posterior surface of the brainstem and caudal surface of the cerebrum, are the final pair of branches from the basilar artery. The posterior cerebral arteries communicate via posterior communicating arteries with the internal carotid artery.

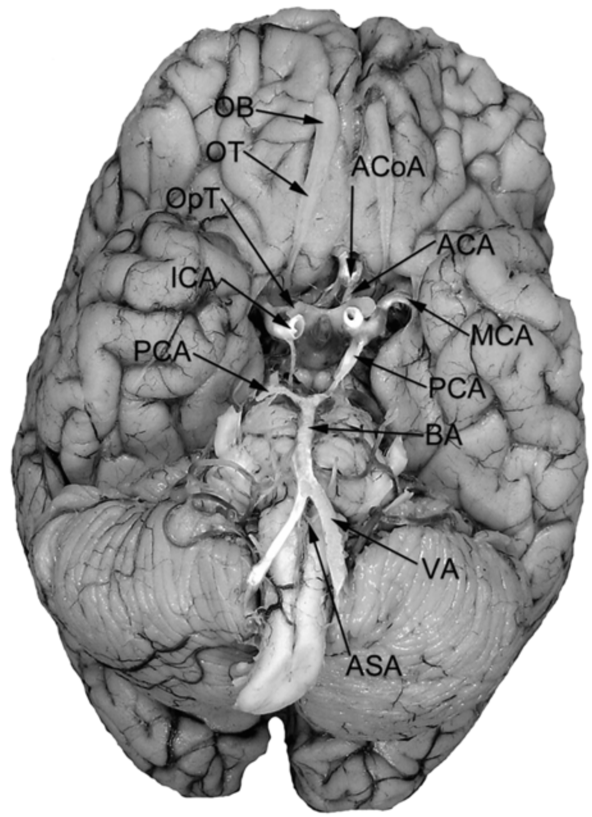

Fig. 13. Anterior surface of the brain, demonstrating circle of Willis and its associated arterial supply. The two vertebral arteries (VA) unite to form the basilar artery (BA). The anterior spinal artery (ASA) arises from the individual vertebral arteries prior to their union. The basilar artery terminates as the posterior cerebral arteries (PCA) It communicates with the internal carotid artery (ICA) via the posterior communicating artery (PCoA). The middle cerebral artery (MCA) originates from the internal carotid artery and enters the lateral sulcus, and the anterior cerebral artery (ACA) also arises from the internal carotid artery to enter the longitudinal fissure. A short vessel, the anterior communicating artery (AcoA), connects the two anterior cerebral arteries in the longitudinal fissure. In addition to the vascular supply on the anterior surface of the brain, the olfactory bulb (OB), olfactory tract (OT), and optic nerves (ON) are identified.

The *internal carotid artery*, one of two terminal branches of the common carotid artery, begins at the C4 level of the neck. It ascends through the neck without forming any branches and enters the skull through the serpentine-shaped carotid canal of the temporal bone to enter the cranial cavity. In the cranial cavity it is first located in the cavernous sinus of the sella turcica. Its first branch is the ophthalmic artery, which supplies the orbit. The internal carotid artery passes through the diaphragma sellae and immediately terminates as three branches to supply the cerebrum and diencephalon. The *posterior communicating artery* courses posteriorly to anastomose with the posterior cerebral arteries (Fig. 13). The *middle cerebral artery* arises from the lateral side of the internal carotid artery and courses laterally and posteriorly to enter the lateral fissure. It major branches can be divided into striate branches and cortical branches. The striate arteries are numerous, and are responsible for blood supply to the striatum. Cortical branches supply lateral surfaces of the cerebral cortex, including the orbital surface, precentral gyrus, middle frontal gyrus, inferior frontal gyrus, superior parietal gyrus, inferior, parietal gyrus, supramarginal gyrus, angular gyrus, superior temporal gyrus, middle temporal gyrus and inferior temporal gyrus. The *anterior cerebral artery* follows the corpus callosum—first anteriorly and superiorly and then posteriorly in the longitudinal fissure to supply medial surfaces of the cerebral cortex. In the first part of longitudinal fissure along the anterior surface, the two anterior cerebral arteries are connected by a very short *anterior communicating artery*. Central branches of the anterior cerebral artery supply the septum pellucidum, corpus callosum, and rostral portions of the basal ganglia. Cortical branches supply olfactory-bulb medial surfaces of the frontal and parietal cortex (gyrus rectus, medial orbital gyrus, superior frontal gyrus, middle frontal gyrus, cingulate gyrus, and the precuneate gyrus).

An anastomotic channel known as the circle of Willis is formed from branches of the internal carotid artery and the vertebral artery system. The arteries that contribute to the circle of Willis are the internal carotid artery anterior cerebral artery, anterior communicating artery, posterior communicating artery, and the posterior cerebral artery.

3.7. Venous Drainage of the Brain

Veins that drain the brain are tributaries of dural sinuses that ultimately empty into the internal jugular vein. They begin deep within the parenchyma of the brain and drain superficially, and can be divided into cerebral veins, cerebellar veins, and veins of the brainstem. The cerebral veins are composed of internal cerebral veins that drain the deep regions of the cerebrum and external cerebral veins located in the sulci and gyri. The superficial cerebral veins, located within the pia mater, are further divided into superior cerebral veins, middle cerebral veins, and inferior cerebral veins. The superior cerebral veins are located on the superolateral and medial surfaces of the cerebral cortex within their sulci, and drain directly into the superior sagittal sinus. The middle cerebral vein drains the lateral surface of the cerebral cortex, where they empty into the superior sagittal sinus via the superior anastomotic vein (Trolard's vein), or into the transverse sinus by way of the inferior anastomotic vein (Labbe's vein). The inferior cerebral veins are located on the anterior surface of the cerebral cortex. The more anterior branches drain into the superior cerebral veins, and the more posterior branches empty into the middle cerebral vein. The internal venous drainage of the cerebral cortex is conducted by the great cerebral vein (Galen's vein), and begins by its tributaries—the internal cerebral veins that drain the deep regions of the cerebral cortex. These in turn are formed by the thalamostriate and choroid veins. The great cerebral vein joins with the inferior sagittal sinus to empty into the straight sinus of the dural sinuses. The cerebellum is drained by the superior cerebellar veins and the inferior cerebellar veins on its surface. The superior cerebellar veins pass anteriorly and medially to enter the straight sinus, and the inferior cerebellar vein drains into the superior petrosal sinuses or transverse sinuses. The brainstem is drained by a venous plexus composed of anterior vessels that drain into the vertebral venous plexus, lateral venous plexus that drains into the inferior petrosal sinus, and a posterior plexus that drains into the great cerebral vein or straight sinus.

3.8. Ventricular System

The ventricular system of the brain is a series of cavities and passages connected to one another throughout the different brain regions. It contains cerebrospinal fluid (CSF), which is produced by the choroid plexus that is also located in the ventricles (Fig. 14). The ventricular system opens into the subarachnoid space, allowing CSF to surround the brain and spinal cord for support and protection. A *lateral ventricle* is contained within each cerebral hemisphere, and is separated by the septum pellucidum. Each lateral ventricle is in the form of a "C" and is subdivided into four interconnected regions. Its *frontal horn*, located in the frontal cortex, is continuous with the *body* located in both the frontal cortex and parietal cortex. Posteriorly, the body curves anterolaterally into the temporal cortex as

Fig. 14. Cast of the ventricular system of the human brain. The ventricular system of the brain was filled with latex, and the brain tissue was then removed to reveal the arrangement of the ventricular system. The two lateral ventricles are each composed of the frontal pole (F), body (B), posterior pole (P), and inferior pole (I). The lateral ventricles communicate with the midline third ventricle (III) via the interventricular foramen (InVF). The cerebral aqueduct (CA) allows communication between the third ventricle and the fourth ventricle (IV).

the *inferior horn*. The *posterior horn* extends from the body into the occipital cortex as it begins to curve into the inferior horn. The lateral ventricles communicate with the remainder of the ventricular system by the *interventricular foramen (of Monro)*, which is located at the midrostral end of the lateral ventricles anterior to the fornix. It connects each lateral ventricle to the midline thin, *third ventricle* between the two sides of the diencephalon. The *cerebral aqueduct*, located in the tectum of the midbrain, connects the third ventricle posteriorly with the fourth ventricle. The *fourth ventricle* is located between the cerebellum dorsally and the pons and medulla oblongata anteriorly. It is continuous with the central canal of the spinal cord. More importantly, the fourth ventricle opens into the subarachnoid space by the median foramen (of Majendie) and the lateral foramina (of Lushka), which are located in its roof. These foramina allow the CSF to move from the ventricular system into the subarachnoid space.

The subarachnoid space is enlarged in places, allowing accumulations of CSF between the arachnoid membrane and pia mater that help to cushion and protect the brain from the surrounding skull. The posterior *cerebellomedullary cistern*, the site of drainage of the lateral and median foramina openings from the fourth ventricle, is the largest of the subarachnoid spaces. It is located between the medulla and cerebellum posteriorly and is continuous with the subarachnoid space surrounding the dorsal side of the spinal cord. The *quadrigeminal cistern* (cistern of the great cerebral vein) is located posteriorly, but is located in the interval between the splenium of the corpus callosum and the superior surface of the cerebellum. It is continuous with the cerebellomedullary cistern caudally. The *pontine cistern* is located on the anterior surface of the pons between it and the more caudal medulla oblongata. It is continuous caudally with the subarachnoid space surrounding the ventral side of the spinal cord and the interpeduncular cistern more rostrally. The *interpeduncular cistern*, located between the cerebral peduncles, contains the origin of the oculomotor nerve (CNIII). This region is also described as the interpeduncular fossa on specimens that have had their meninges removed. The *chiasmatic cistern* is the rostral continuation of the interpeduncular cistern. It is located anterior and inferior to the optic chiasm on the anterior surface of the brain. This cistern is in turn continuous laterally with the subarachnoid space in the cranial fossa.

The CSF located in the ventricular system is produced by the *choroid plexus* found in the roof of the lateral ventricles, third ventricles, and fourth ventricles. The choroid plexus is a complex vascular system composed of pia mater covered by ependymal cells. Production of CSF by the choroid plexus results in circulation beginning in the lateral ventricle, through the third ventricle into the fourth ventricle, and out from the median and lateral foramina into the subarachnoid space. Once in the subarachnoid space, the CSF circulates throughout the subarachnoid space surrounding the brain and spinal cord, and is then reabsorbed into the venous system from the subarachnoid space at the superior sagittal sinus by tuft-like protrusions, the *arachnoid granulations* of the arachnoid membrane.

3.9. Meninges of the Brain

The dura mater of the cranial cavity is composed of a superficial *periosteal layer* and a deeper *meningeal layer*. The meningeal layer is continuous with the meningeal layer of the spinal cord in the vertebral canal at the foramen magnum, and the periosteal layer ends at the foramen magnum. Both layers in the cranial cavity are adherent to one another except in regions where the venous dural sinuses force them apart. The arachnoid membrane lies deep to the dura mater and is continuous with the arachnoid membrane of the vertebral canal. Like the arachnoid membrane in the vertebral canal, it has fibrous extensions down to the pia mater. The pia mater in the cranial cavity follows the surface of the brain and is found in sulci of the cerebral cortex, cerebellum, and the fissures of the brain. Along the posterior surface of the third ventricle and the rostral end of the fourth ventricle the pia mater invaginates into the ventricular spaces to contribute to the formation of the choroid plexus of these regions. Epidural and subdural spaces that are associated with the spinal cord are not present in the cranial cavity. The subarachnoid space is filled with CSF and surrounds the brain and allows it to float in the cranial cavity. It is continuous with the subarachnoid space of the vertebral canal surrounding the spinal cord. A number of enlarged regions of the subarachnoid space are present on the anterior and posterior sides of the brain, and have already been described.

Extensions of the meningeal layer of the dura mater are located in specific regions of the brain, and contain some dural sinuses used to drain blood away from the brain. The first is the vertically oriented *falx cerebri*, which extends into the longitudinal fissure between the two halves of the cerebral cortex. The second is the horizontally oriented *tentorium cerebelli*, attached from the occipital bone posteriorly to the petrosal ridge of the temporal bone anterolaterally. It is located between the anterior surface of the occipital cortex and the superior surface of the cerebellum. In the midline the tentorium cerebelli does not attach to any bony structure, forming the tentorial incisure which allows the brainstem to continue from the posterior cranial fossa into the middle cranial fossa. The third is the vertically oriented *falx cerebelli* located between the two cerebelli cortices. The fourth is the horizontal *diaphragma sellae* that covers the sella turcica. The falx cerebelli has the occipital sinus along is posterior free edge. The diaphragma sellae contains the cavernous sinus. Dural sinuses are modified venous structures contained within the dura mater of the cranial cavity. The *superior sagittal sinus* is present along the superior edge of the falx cerebri, where it is bounded by both the periosteal dura mater and the meningeal dural mater. It begins rostrally at the crista galli of the ethmoid bone and continues posteriorly to empty into the confluens of the sinuses. The superior sagittal sinus receives the CSF drainage by way of arachnoid villi that extend into its lumen. It also communicates with superficial veins of the scalp and emissary veins that drain the overlying bone of the skull. Along the inferior free edge of the falx cerebri the *inferior sagittal sinus* is contained entirely within the meningeal layer of the dural mater. It also begins at the crista galli and empties into the straight sinus at the anterior border of the junction of the falx cerebri and tentorium cerebelli. The *straight sinus* begins at the anterior border of the tentorium cerebelli, where it receives blood from the great cerebral vein (of Galen) and the straight sinus and empties posteriorly into the confluens of the sinuses. The *confluens of the sinuses*, located on the internal occipital protuberance of the occipital bone communicates with the superior sagittal sinus, straight sinus, occipital sinus, and transverse sinuses. The *transverse sinuses*, formed between the periosteal and meningeal layers of dura mater, is located along the posterior edges of the tentorium cerebelli, where it is in contact with the occipital and parietal bones. These drain blood from the confluens of the sinuses and the superior sagittal sinus anteriorly. The *sigmoid sinuses* are continuations of the transverse sinuses as they leave the tentorium cerebelli, and take a medial and inferior serpentine course along the surface of the occipital bone to help form the internal jugular vein. The *cavernous sinuses* are located deep to the diaphragma sellae on either side of the sella turcica of the sphenoid bone. They communicate with one another by *intercavernous branches*. The cavernous sinuses are unique to other dural sinuses because they contain the internal carotid artery and abducens nerve (CN VI) within their lumen, and the ophthalmic and maxillary divisions of the trigeminal nerve (CN V) and the oculomotor nerve (CN III) in its wall. Anteriorly, the cavernous sinus communicates with superficial veins of the face, the ophthalmic veins, and the pterygoid plexus. Posteriorly, the cavernous sinus communicates with the inferior petrosal sinus, superior petrosal sinus and the basilar plexus of veins. The *superior petrosal sinus*, located within the anterolateral border of the tentorium cerebelli, is located along the superior border of the petrous ridge of the temporal bone. It begins at the cavernous sinus and joins with the transverse sinus to empty into the sagittal sinus. The *inferior petrosal sinus* begins at the cavernous sinus and follows the temporo-occipital suture to the jugular foramen, where it forms the internal jugular vein with the sigmoid sinus.

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