Chapter 1

Introduction

Introduction

Human behavior is a direct reflection of the anatomy and physiology of the central nervous system. The goal of the behavioral neuroscientist is to uncover the neuroanatomical substrates of behavior. Complex mental processes are represented in the brain by their elementary components. Elaborate mental functions consist of subfunctions and are constructed from both serial and parallel interconnections of several brain regions. An introduction to the nervous system covers general terminology and the ventricular system.

Major Subdivisions

The nervous system is divided anatomically into the central nervous system (CNS) and the peripheral nervous system (PNS).

- The CNS is made up of the brain and spinal cord.
- The PNS consists of the cranial nerves and spinal nerves.

Physiologically, the nervous system can be divided into somatic and visceral (autonomic) divisions.

- The somatic nervous system deals with the contraction of striated muscle and the sensations of the skin (pain, touch, temperature), the innervation of muscles and joint capsules (proprioception), and the reception of sensations remote to the body by way of special senses. The somatic nervous system senses and controls our interaction with the environment external to the body.
- The autonomic nervous system controls the tone of the smooth muscles and the secretion of glands. It senses and controls the condition of the internal environment.

Common Terms

The neuraxis is the long axis of the brain and spinal cord (Figure 1.1). A cross-section (transverse section) is a section taken at right angles to the neuraxis. The neuraxis in the human runs as an imaginary straight line through the center of the spinal cord and brainstem (Figure 1.1). At the level of the junction of the midbrain and diencephalon, however, the neuraxis changes orientation and extends from the occipital pole to the frontal pole (Figure 1.1). The neuraxis located above the midbrain is the neuraxis of the cerebrum and is sometimes called the horizontal neuraxis. A cross-section taken perpendicular to the horizontal neuraxis is called a coronal (frontal) section.

With regard to the neuraxis of the spinal cord and brainstem:

- Dorsal (posterior) means toward the back.
- Ventral (anterior) means toward the abdomen.
- Rostral means toward the nose.
- Caudal means toward the tail.
- The sagittal (midsagittal) plane is the vertical plane that passes through the neuraxis. Figure 1.1 is cut on the sagittal plane.
- The parasagittal plane is parallel to the sagittal plane but to one side or the other of the midline.
- A horizontal section is a cut of tissue taken parallel to the neuraxis (Figure 9.1).
- A cross-section (transverse section) is a cut taken perpendicular to the neuraxis (Figures 10.1–10.3 and 10.5).

With regard to the neuraxis of the cerebrum (horizontal neuraxis):

- Dorsal (superior) means toward the top (crown) of the skull.
- Ventral (inferior) means toward the base of the skull.
- Rostral (anterior) means toward the nose.
- Caudal (posterior) means toward the occipital bone of the skull.
- The sagittal (midsagittal) plane is the vertical plane that passes through the neuraxis.
- The parasagittal plane is parallel to the sagittal plane but to one side or the other of the midline.

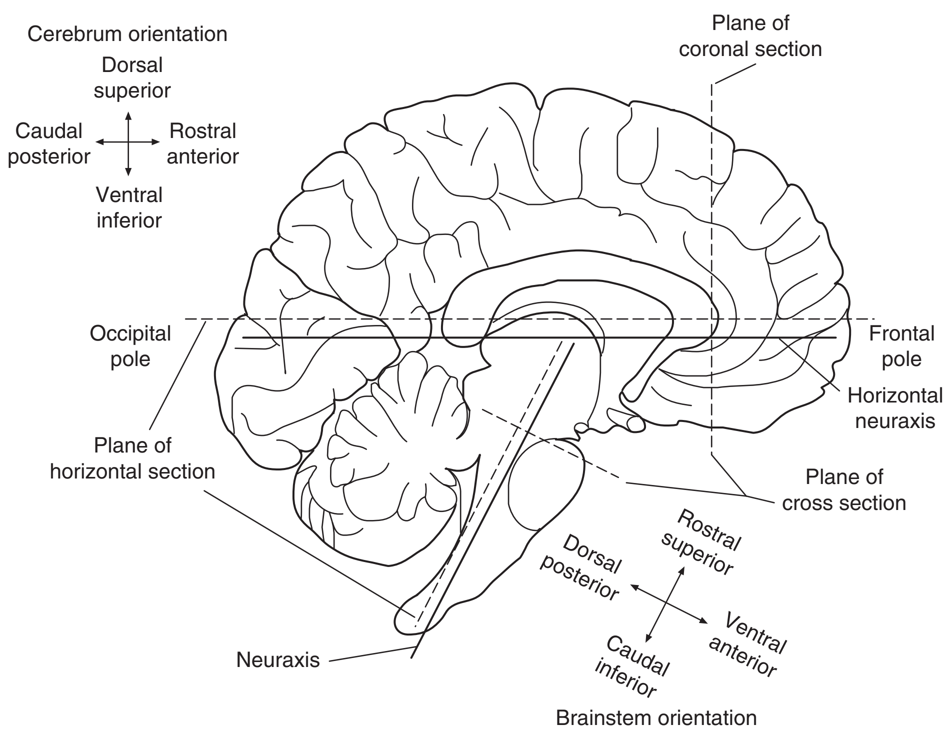

Figure 1.1 The neuraxis is the long axis of the spinal cord and brain. The neuraxis of the human brain changes at the junction of the midbrain and diencephalon. Caudal to this junction, orientation is as shown in the lower right (Brainstem orientation). Rostral to this junction, orientation is as shown in the upper left (Cerebrum orientation).

- A horizontal section is a cut of tissue taken parallel to the horizon.
- A coronal section (transverse section) is a cut taken perpendicular to the neuraxis.

Other terms that relate to the CNS:

- Afferent means to or toward and is sometimes used to mean sensory.
- Efferent means away from and is sometimes used to mean motor.
- Ipsilateral refers to the same side. Contralateral refers to the opposite side.

The CNS differentiates embryologically as a series of subdivisions called encephalons. Each encephalon can be identified in the adult brain. In many regions of the brain, the embryological terminology is applied to adult brain subdivisions:

- The prosencephalon is the most anterior of the embryonic subdivisions and consists of the telencephalon and diencephalon. The cerebrum of the adult corresponds with the prosencephalon.
  ‡ The telencephalon consists of the two cerebral hemispheres. These include the superficial gray matter of the cerebral cortex, the white matter beneath it, and the corpus striatum of the basal ganglia.
  ‡ The diencephalon is made up of the thalamus, the hypothalamus below it, and the epithalamus located above it.
- The brainstem lies caudal to the prosencephalon. It consists of the following:
  ‡ The mesencephalon (midbrain):
  ‡ The rhombencephalon, which is made up of the following:
    - The metencephalon, which contains the pons and cerebellum
    - The myelencephalon (medulla oblongata)

Ventricular System

The central canal of the embryo differentiates into the ventricular system of the adult brain. The ventricular cavities are filled with cerebrospinal fluid (CSF), which is produced by vascular tufts called choroid plexuses. The ventricular cavity of the telencephalon is represented by the lateral ventricles (Figure 1.2).

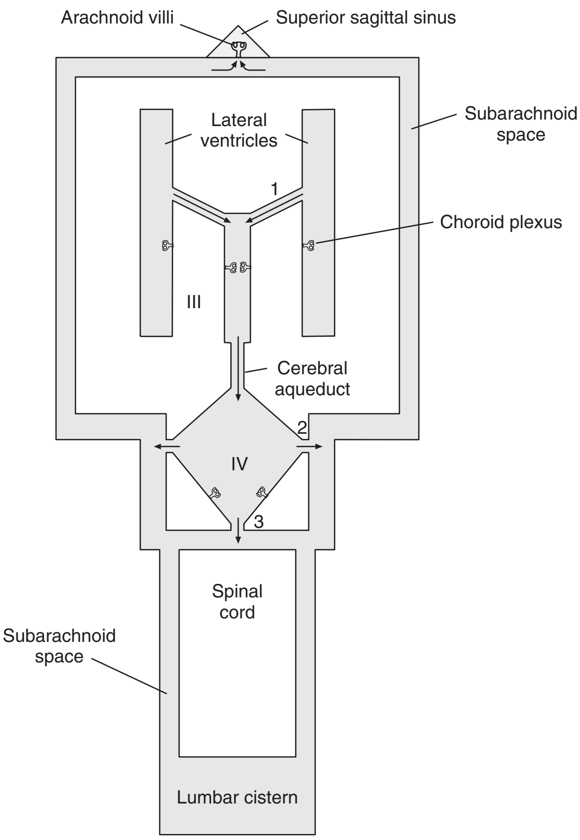

Figure 1.2 Cerebrospinal fluid (CSF) is produced by tufts of choroid plexus that are found in all four ventricles. CSF exits the lateral ventricles through the interventricular foramina (of Monro) (1). CSF exits the ventricular system through the lateral apertures (of Luschka) (2) and the median (aperture of Magendie) (3). CSF is reabsorbed into the blood by way of the arachnoid villi that project into the superior sagittal sinus.

The lateral ventricles are the first and second ventricles. They connect to the third ventricle of the diencephalon by the interventricular foramina (of Monro). Continuing caudally, the cerebral aqueduct of the midbrain opens into the fourth ventricle. The fourth ventricle occupies the space dorsal to the pons and medulla and ventral to the cerebellum. Cerebrospinal fluid (CSF) flows from the fourth ventricle to the subarachnoid space through the median aperture (of Magendie) and the lateral apertures (of Luschka). Most of the CSF is produced by the choroid plexus of the lateral ventricles, although tufts of choroid plexus are found in the third and fourth ventricles as well.

The lateral as well as the third ventricles has been noted to be enlarged in a number of psychiatric disorders, particularly schizophrenia (Daniel, Goldberg, Gibbons, and Weinberger, 1991; Elkis, Friedman, Wise, and Meltzer, 1995). Enlargement of the ventricles usually reflects atrophy of surrounding brain tissue. The term "hydrocephalus" is used to describe abnormal enlargement of the ventricles. In the condition known as normal pressure hydrocephalus, the ventricles enlarge in the absence of brain atrophy or obvious obstruction to the flow of the CSF. Normal pressure hydrocephalus is classically characterized by progressive dementia, ataxia, and incontinence (Friedland, 1989). However, symptoms may range from apathy and anhedonia to aggressive or obsessive-compulsive behavior or both (Abbruzzese, Scarone, and Colombo, 1994).

Clinical Vignette 1.1

A 61-year-old male reported that his work performance was slipping. He was forgetting names and dates more than usual. Because of recent losses in his family, he assumed he was depressed. He saw a psychiatrist (his wife had a history of depression), who prescribed an antidepressant. Soon after this he had an episode of urinary incontinence. A neurology consultation was obtained and revealed the presence of gait problems. A computed tomographic scan showed enlarged ventricles without enlarged sulci (which would have indicated generalized brain atrophy). The diagnosis of normal pressure hydrocephalus was made. Progressive improvement of the patient's clinical condition was seen following the installation of a ventricular shunt.

References

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Chapter 2

Anatomy of the Gross Brain

The brain is that portion of the central nervous system that lies within the skull. Three major subdivisions are recognized: the brainstem, the cerebellum, and the cerebrum. The cerebrum includes both the cerebral hemispheres and the diencephalon.

Brainstem

The brainstem is the rostral continuation of the spinal cord. The foramen magnum, the hole at the base of the skull, marks the junction of the spinal cord and the brainstem. The brainstem consists of three subdivisions: the medulla, the pons, and the midbrain (Figure 2.1).

Medulla

The caudal limit of the medulla lies at the foramen magnum. The central canal of the spinal cord expands in the region of the medulla to form the fourth ventricle (IV in Figure 1.2). Cranial nerves associated with the medulla are the hypoglossal (XII), spinal accessory (XI), vagus (X), and the glossopharyngeal (IX).

Pons

The pons lies above (rostral to) the medulla (Figure 2.1). The bulk of the medulla is continuous with the pontine tegmentum. The tegmentum consists of nuclei and tracts that lie between the basilar pons and the floor of the fourth ventricle (IV in Figures 1.2 and 10.2). The basilar pons consists of tracts along with nuclei that are associated with the cerebellum. The fourth ventricle narrows at the rostral end of the pons to connect with the cerebral aqueduct of the midbrain (Figures 1.2, 10.2, 10.3, 10.4). Cranial nerves associated with the pons are the statoacoustic (VIII), facial (VII), abducens (VI), and trigeminal (V).

Midbrain

The dorsal surface of the midbrain is marked by four hillocks, the corpora quadrigemina (tectum). The caudal pair is the inferior colliculi (Figure 10.3; auditory system), and the cranial pair is the superior colliculi (Figure 10.5; visual system). The ventricular cavity of the midbrain is the cerebral aqueduct. Most nuclei and tracts found in the midbrain lie ventral to the cerebral aqueduct and together make up the midbrain tegmentum (Figure 2.1). The basilar midbrain contains the crus cerebri ("motor pathway" in Figures 10.3 and 10.4) and the substantia nigra, one of the basal ganglia. Cranial nerves associated with the midbrain are the trochlear (IV) and oculomotor (III).

Ischemia (particularly transient ischemia) of the midbrain tectum can result in visual hallucinations (peduncular hallucinosis). Auditory hallucinations have also been reported with lesions of the tegmentum of the pons and lower midbrain (Cascino and Adams, 1986). The sounds have the character of noise: buzzing and clanging. To one patient, the sounds reportedly had a musical character like chiming bells.

Clinical Vignette 2.1

A 71-year-old retired man had no prior history of psychiatric or neurological problems. While at home with his two sons, daughter and wife, he suddenly experienced weakness in all four extremities and started seeing policemen entering the front door of his house. He became irritable and fearful that the police would take him away. He was brought to the emergency room (ER). A neurological examination was normal, and the hallucinations ceased. The patient was released, with follow-up at the psychiatry clinic. Three days later he was brought to the ER completely comatose due to a brainstem stroke. In retrospect, patient's attack was found to be a brainstem transient ischemic attack (TIA), which caused him to experience peduncular hallucinosis.

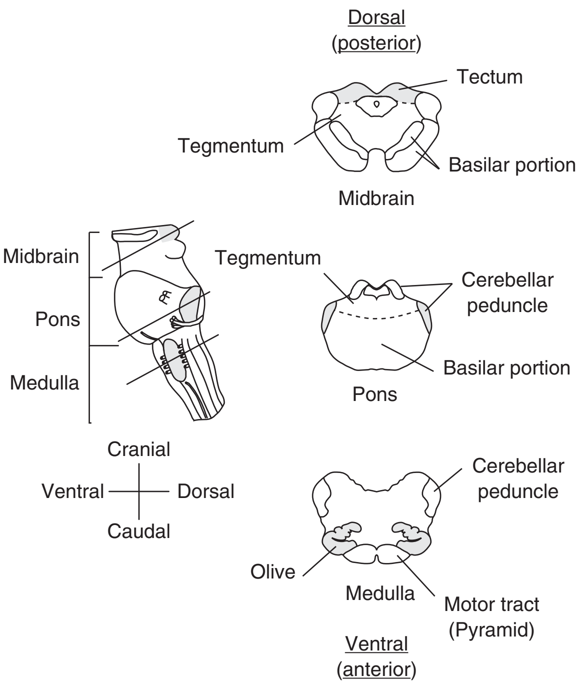

Figure 2.1 The brainstem consists of the medulla, pons, and midbrain. A lateral view of the brainstem (left) is marked to indicate the level from which each of the cross-sections (right) is taken. See Chapter 10 for significant structure found in each cross-section. Cranial refers to the top of the head and caudal refers to the spinal cord.

Cerebellum

The cerebellum overlies the pons and medulla of the brainstem and occupies the posterior cranial fossa (Figure 2.2). It is connected to the brainstem by three paired cerebellar peduncles (Figures 10.1 and 10.2). The cortex of the cerebellum is gray and a layer of white matter lies deep in it. Although it represents only about 10% of the brain, it contains more than four times the number of neurons in the cerebral cortex.

The gray matter of the cerebellum is folded into folia separated by sulci (Figure 2.4). A strip of cortex in the midline is the vermis; the lateral cerebellum is the hemisphere. The primary, horizontal, and posterior fissures separate the cerebellar cortex into an anterior, posterior, and flocculonodular lobe. Functionally, there are three regions: the vestibulocerebellum (archicerebellum), the spinocerebellum (paleocerebellum), and the cerebrocerebellum (neocerebellum). The vestibulocerebellum is represented by the flocculonodular lobe and functions in support of balance and eye movements. The spinocerebellum occupies the remainder of the vermis and a medial strip of the hemisphere: the paravermal area. The spinocerebellum supports paraxial musculature involved with trunk and leg motion. The cerebrocerebellum occupies the lateral hemisphere and functions in speech and skilled movements. The three lobes are divided into ten lobules (Figure 2.5). The lobules extend into the vermis, where they are grouped into as few as three or four subregions to facilitate imaging studies (DelBello, Strakowski, Zimmerman, Hawkins, and Sax, 1999). Input to the cerebellum is from the spinal cord (spinocerebellar tracts) and brainstem. Input to the cerebellum from the motor cortex of the cerebrum represents “copies” of signals sent to control striated muscles. Other input represents sensory feedback used by the cerebellum to determine if the motor actions dictated by the motor cortex were performed in a smooth and coordinated fashion. The cerebellum is positioned to modify the output of motor neurons to improve motor coordination. Output from the cerebellar cortex is through three cerebellar nuclei. The fastigial nucleus serves the vestibulocerebellum. The interposed nucleus serves the spinocerebellum, and the dentate nucleus serves the cerebrocerebellum.

The cerebellum also plays a role in affective and higher cognitive functions. The vermis has functional connections with limbic structures (amygdala and hippocampus) as well as direct connections with the red nucleus, a motor nucleus located in the midbrain (Figure 10.5). The cerebellar hemisphere may be more involved with cognitive functions such as strategic planning, learning, memory, and language (Schmahmann, 1991; Schmahmann and Sherman, 1998). Activation of cerebellar nuclei has been demonstrated during cognitive processing (Kim, Ugurbil, and Strick, 1994; Kim, et al., 2001). Transcranial magnetic stimulation of the cerebellum has been shown to affect language and verbal working memory (Grimaldi, et al., 2014).

Dysfunction of the cerebellum has been identified with truncal ataxia involving paraxial musculature (involvement of vermis and paravermal areas), limb ataxia and dysarthria (anterior and posterior portions of hemispheres), and oculomotor deficits including nystagmus (flocculonodular lobe). In 1998, Schmahmann and Sherman described the cerebellar cognitive affective syndrome sometimes referred to as Schmahmann syndrome. The syndrome includes disturbances in executive function (organizing and

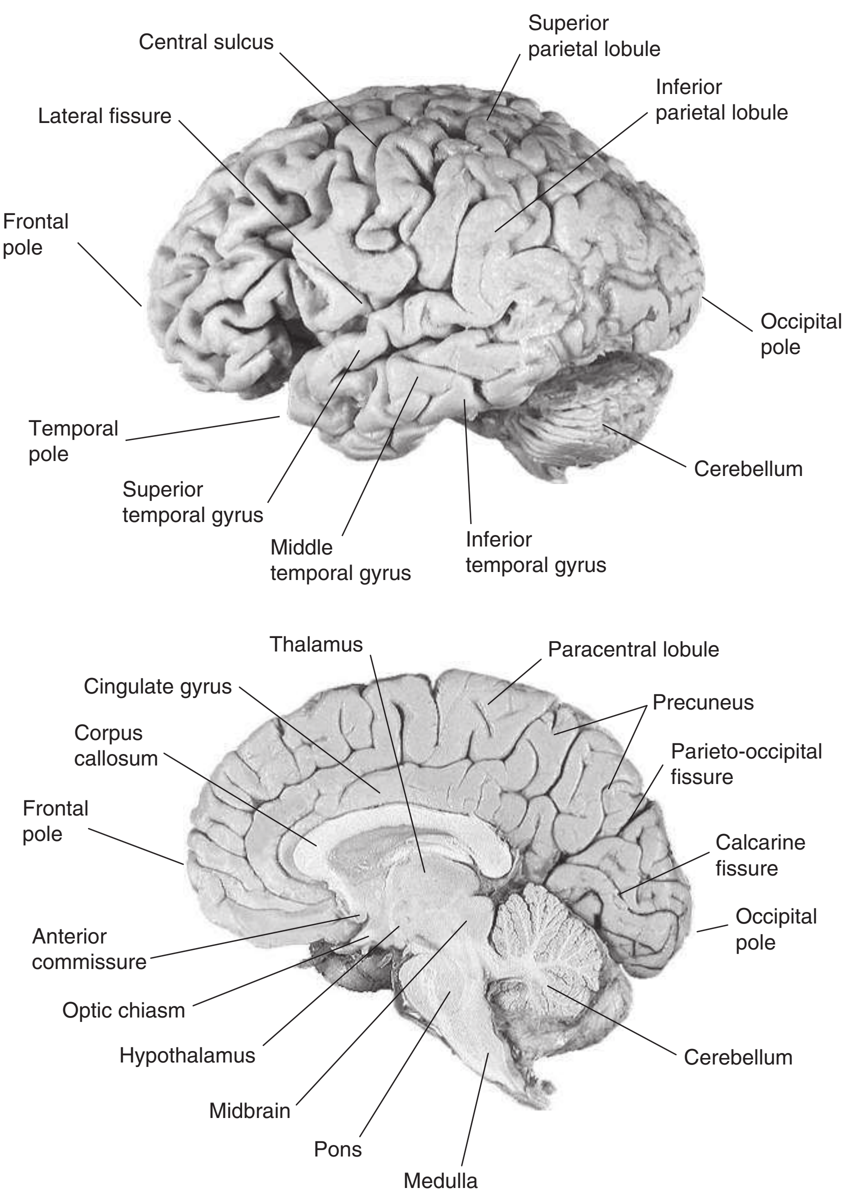

Figure 2.2 Lateral (above) and medial (below) views of the gross brain. Compare with Brodmann areas, Figure 2.3.

planning daily tasks), language (agrammatism and stuttering), and personality (social withdrawal, hyperactivity, and irritability). Visuospatial difficulties resemble simultanagnosia (Schmahmann, Weilburg, and Sherman, 2007). The syndrome is associated with damage to the "cognitive cerebellum," which includes lobules VI–IX extending from the vermis to the lateral extent of the hemisphere. Lobule VII sends signals to the prefrontal cortex. Impairments are more prominent with large, bilateral damage, especially in the posterior lobes. Damage in vermal regions is associated with disruption of affect (Manto and Mariën, 2015). Posterior fossa syndrome (cerebellum mutism syndrome) may be a subtype of Schmahmann syndrome (Mariën et al., 2013).

A smaller vermis was reported in several studies of patients with schizophrenia and alcohol dependence (Varnäs et al., 2007). Overall cerebellar volume is unchanged, but the vermis was smaller in patients with bipolar disorder or depression (Mills, Delbello, Adler, and Strakowski, 2005; Monkul et al., 2008).

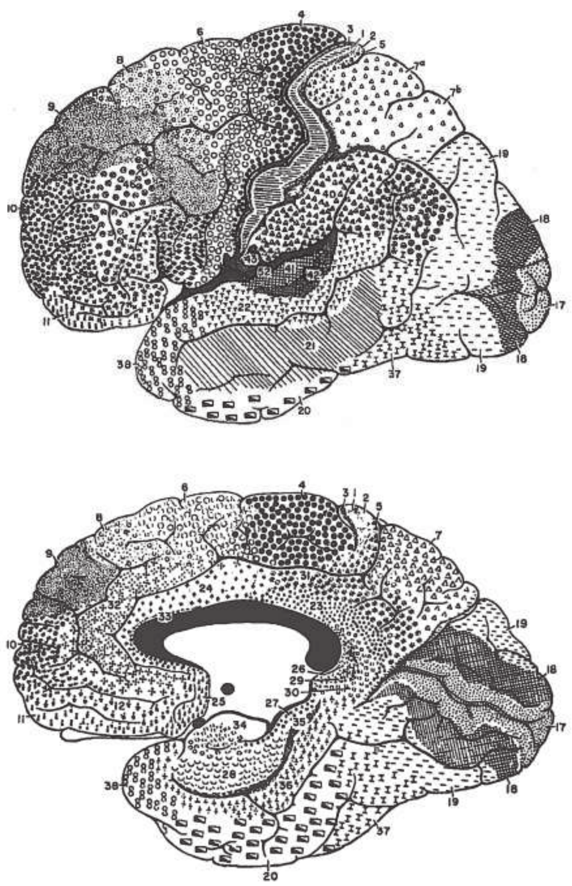

Figure 2.3 The cytoarchitectonic regions of the cortex, as described by Brodmann. Compare with the surface of the brain, Figure 2.2.

Total brain size in children with autism was found to be normal at birth using head circumference. However, 90% of 2–4-year-old autistic children had significantly larger (18%) brains compared with controls. Comparing both groups as 5–15 year olds showed no difference (Courchesne et al., 2001). The authors hypothesized that the overgrowth is restricted to childhood and is followed by a period of slowed growth (Sparks et al., 2002).

Decreased cerebellar hemisphere size was reported in autism (Murakami, Courchesne, Press, Yeung-Courchesne, and Hesselink, 1989), An analysis of MRI imaging of 50 subjects showed decreased vermal size in 86% but increased vermal size in 12% (Courchesne et al., 1994).

Decreased vermal size has been reported in autism (Kaufmann et al., 2003), but Hodge et al. (2010) report that the volume reduction is restricted to the anterior vermis of autistic and non-autistic children with specific language impairment. In contrast, children with Williams syndrome, who typically exhibit hypersociality and heightened affective expression, possess a significantly larger posterior vermis (Schmitt, Eliez, Warsofsky, and Reissa, 2001). Cerebellar abnormalities in autism have been linked to deficits in shifting attention, language impairment, stereotyped behavior, and reduced exploration (Akshoomoff and Courchesne, 1992; Pierce and Courchesne, 2001).

Higher blood flow to the cerebellum was reported in patients with posttraumatic stress disorder (Bonne et al., 2003), and reduced cerebellar size was described in attention-deficit/hyperactivity disorder (Castellanos et al., 2002; Valera, Faraone, Murray, and Seidman, 2007).

Decreased cerebellar hemisphere size was reported in patients with schizophrenia (Bottmer et al., 2005). A model has been proposed suggesting that abnormalities in connectivity within the cerebellum or between the cerebellum and other brain structures may be responsible for the "cognitive dysmetria" seen in schizophrenia (Andreasen, Paradiso, and O'Leary, 1998).

Cerebrum

The diencephalic portion of the cerebrum consists of the thalamus (Chapter 9), the hypothalamus, and the epithalamus (Chapter 8). The thalamus is an integrative center through which most sensory information must pass in order to reach the cerebral cortex and the level of consciousness. The hypothalamus serves as an integrative center for control of the body's internal environment by way of the endocrine and autonomic nervous systems (Figure 8.1). The pituitary gland (hypophysis) extends ventrally from the base of the hypothalamus. The epithalamus consists of the habenula and pineal gland. The ventricular cavity of the diencephalon is the third ventricle (III in Figure 1.2). The optic nerve (II) is associated with the diencephalon (Figure 8.3).

The cerebral hemisphere includes the cerebral cortex and underlying white matter, as well as a number of nuclei that lie deep to the white matter. Traditionally, these nuclei are referred to as the basal ganglia (Chapter 7). One of these forebrain nuclei, the amygdala (Figure 11.1), is now included as part of the limbic system (Chapter 11–12).

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More Information

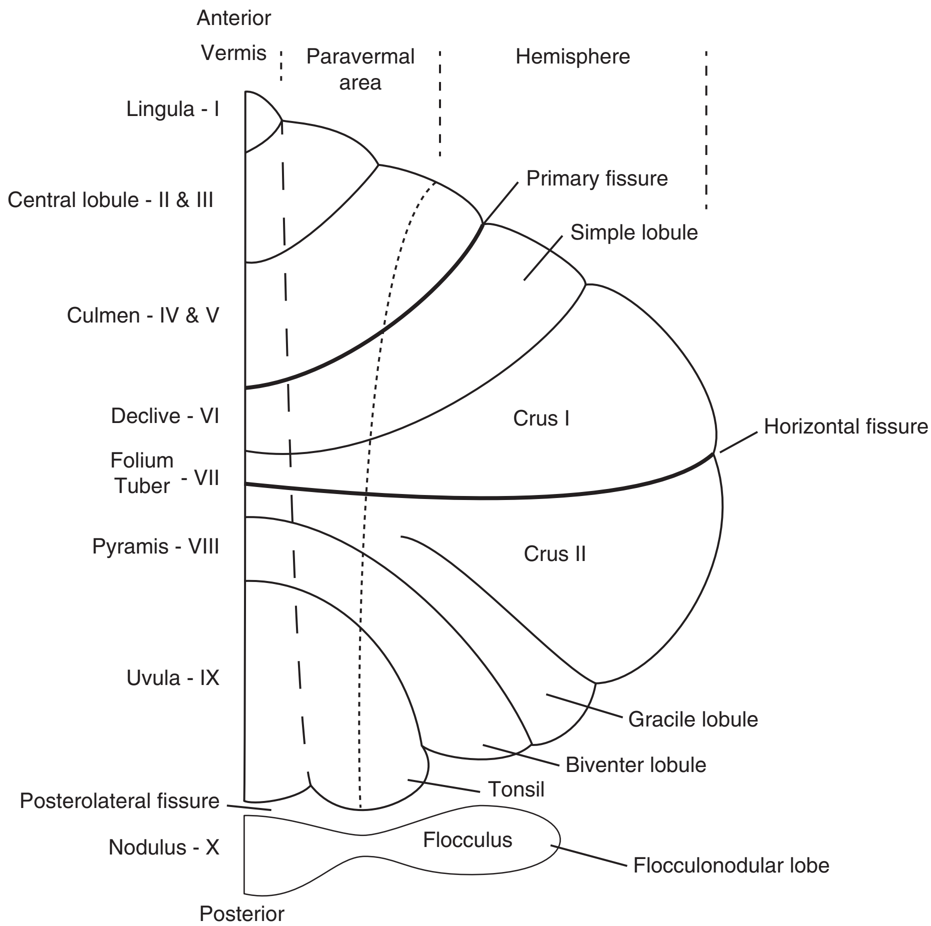

Figure 2.4 The posterior surface of the cerebellum showing the three anatomical lobes and three functional regions.
The anterior and posterior lobes are separated by the primary fissure. The vermis and paravermal cortex, excepting the nodulus, are involved with coordination of paraxial trunk musculature.
The cerebrocerebellum made up of the hemisphere functions in support of limb movements, speech, and procedural learning.
The flocculonodular lobe is involved with balance and eye movements.

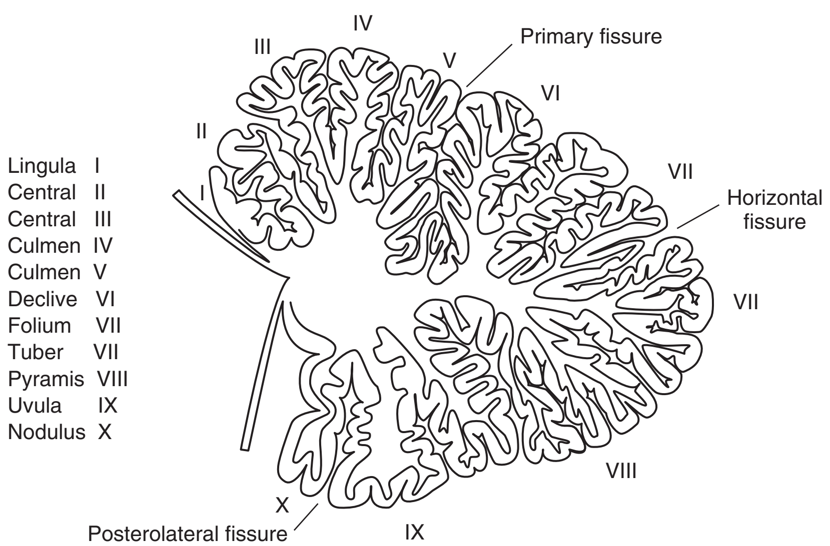

Figure 2.5 The cerebellar vermis consists of ten lobules. They are grouped into three or four for analysis in brain imaging.

The surface of the cortex is marked by ridges (gyri) and grooves (sulci). Several of the sulci are quite deep, are called fissures, and help demarcate lobes. The most prominent fissure is the longitudinal cerebral fissure (sagittal or interhemispheric fissure), which is located in the midline and separates the two hemispheres. Each of the hemispheres is divided into four separate lobes: frontal, parietal, occipital, and temporal.

The frontal lobe lies rostral to the central sulcus and dorsal to the lateral fissure (Figures 2.2 and 2.3). An imaginary line drawn from the parieto-occipital sulcus to the preoccipital notch separates the occipital lobe from the rest of the brain (Figure 5.1). A second imaginary line, perpendicular to the first and continuing rostrally with the lateral fissure, divides the parietal lobe above from the temporal lobe below. The smaller insular cortex is revealed by spreading apart the lips of cortex above and below the lateral fissure.

The limbic system (limbic lobe) is made up of contributions from several areas. The parahippocampal gyrus and uncus can be seen on the ventromedial aspect of the temporal lobe (Figure 5.4). The hippocampus and amygdaloid nucleus lie deep to the ventral surface of the medial temporal lobe (Figure 11.1), and the cingulate gyrus lies along the deep medial aspect of the cortex (Figure 12.1). These structures are joined together by fiber bundles and form a crescent or limbus of paralimbic cortex (see paralimbic system, Chapter 12).

The basal ganglia represent an important motor control center.

- The neostriatum is made up of the caudate nucleus and putamen (Figure 7.1).
- The paleostriatum consists of the globus pallidus.
- Two additional nuclei that are included as basal ganglia are the subthalamic nucleus (subthalamus) and the substantia nigra.

The internal capsule is made up of fibers that interconnect the cerebral cortex with other subdivisions of the brain and spinal cord. The anterior and posterior commissures as well as the massive corpus callosum interconnect the left side with the right side of the cerebrum (see corpus callosum, Chapter 13).

Vasculature

Two major systems supply blood to the brain (Figure 2.6). The vertebral arteries represent the posterior supply and course along the ventral surface of the spinal cord, pass through the foramen magnum, and then merge medially as the basilar artery on the ventral aspect of the medulla. The basilar artery splits at its rostral terminus to form the paired posterior cerebral arteries.

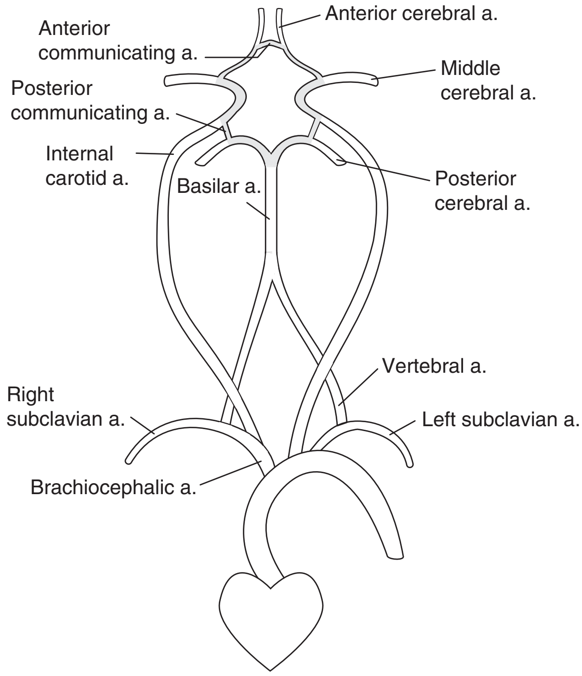

Figure 2.6 Principal arteries serving the brain. The shaded vessels make up the cerebral arterial circle (of Willis).

The internal carotid system represents the anterior supply and arises at the carotid bifurcation. Major branches of the internal carotid include the anterior cerebral and the middle cerebral arteries. The vertebral-basilar and internal carotid systems join at the base of the brain to form the cerebral arterial circle (of Willis).

The cerebral cortex is served by the three major cerebral arteries (Figures 2.7 and 2.8).

- The anterior cerebral artery supplies the medial aspect of the frontal and parietal cortices, with terminal branches extending a short distance out of the sagittal fissure onto the lateral surface of the brain.
- The posterior cerebral artery serves the medial and most of the lateral aspect of the occipital lobe, as well as portions of the ventral aspect of the temporal lobe.

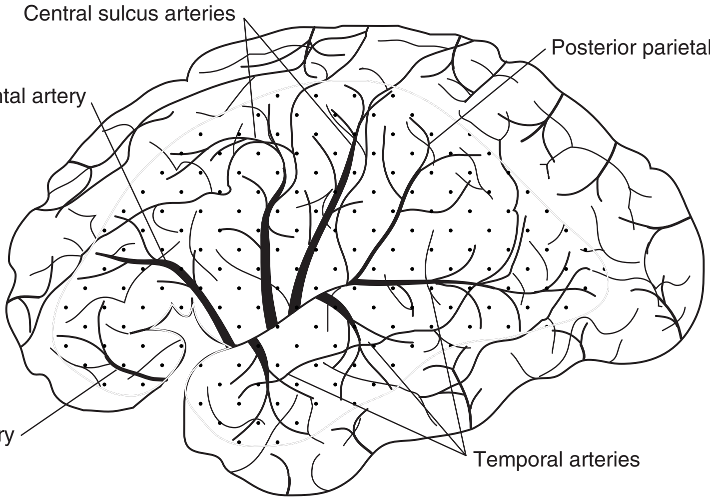

Figure 2.7 The stippled area represents the cortex served by the middle cerebral artery. The vessels emerging from the longitudinal cerebral fissure are the terminal branches of the anterior cerebral artery (after Waddington, 1974. Compare with Figure 2.6).

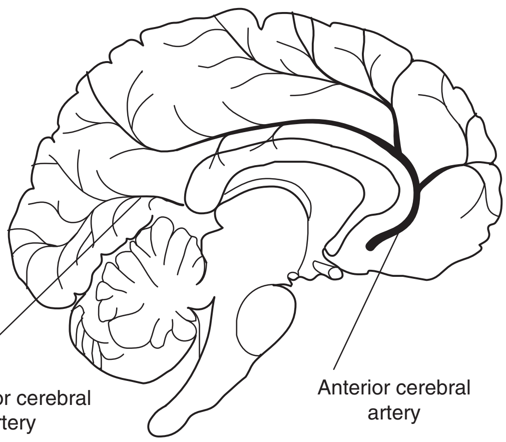

Figure 2.8 The distribution of the anterior cerebral artery (right) and the posterior cerebral artery (left) on the medial aspect of the brain.

- The large middle cerebral artery serves the remainder of the cortex, including the majority of the lateral aspect of the frontal, parietal, and temporal cortices.

The blood–brain barrier is a physiological concept based on the observation that many substances, including many drugs, which may be in high concentrations in the blood are not simultaneously found in the brain tissue. The location of the barrier coincides with the endothelial cells of the capillaries found in the brain. These endothelial cells, unlike those found in capillaries elsewhere in the body, are joined together by tight junctions. These tight junctions are recognized as the anatomical basis of the blood–brain barrier.

Blood flow to the brain was reported to be reduced in elderly patients diagnosed with major depressive disorder when compared with age-matched control subjects. Overall blood flow was reduced by 12%. The distribution of the effect was uneven, and there were brain regions in which the reduction was even greater (Sackeim et al., 1990).

Electroencephalogram

The electroencepalogram (EEG) uses large recording electrodes placed on the scalp (Figure 2.9). The activity seen on the EEG represents the summated activity of large ensembles of neurons. More specifically, it is a reflection of the extracellular current flow associated with the summed activity of many individual neurons. Most EEG activity reflects activity in the cortex, but some (e.g., sleep spindles) shows activity in various subcortical structures. The record generated reflects spontaneous voltage fluctuations. Abnormalities in the brain can produce pathological synchronization of neural elements that can be seen, for example, as spike discharges representing seizure activity. The detection of seizure activity is one of the most valuable assets of the EEG.

