

9

Reticular Formation and Limbic System

CHAPTER OBJECTIVE

- To provide a brief overview of the structure and function of the reticular formation
- To present the parts of the limbic system and its functions

A 24-year-old medical student is rushed by ambulance to the emergency department after an accident on his motorcycle. On examination, he is found to be unconscious and shows evidence of severe injury to the right side of his head. He fails to respond when spoken to, and he does not make any response to deep painful pressure applied over his supraorbital nerve. The plantar reflex is extension, and the corneal, tendon, and pupillary reflexes are absent. The patient is clearly in a deep coma. Further neurologic examination reveals nothing that might add to the diagnosis. A computed tomography scan shows a large depressed fracture of the right parietal bone of the skull.

After a week in the intensive care unit, the patient's condition changes. He suddenly shows signs of being awake but not aware of his environment or inner needs. To the delight of his family, he follows them with his eyes and responds in a limited manner to primitive postural and reflex movements; he does not, however, speak and does not respond to commands. Although he has sleep-wake

cycles, he does not respond appropriately to pain. The patient's neurologic condition is unchanged 6 months later.

The neurologist determines that the patient is awake but not aware of his surroundings. He explains to the family that the part of the brain referred to as the *reticular formation* in the brainstem had survived the accident and is responsible for the patient apparently being awake and able to breathe without assistance. However, because his cerebral cortex is dead, the patient will remain in this vegetative state.

Not very long ago, the reticular system was believed to be a vague network of nerve cells and fibers occupying the central core of the brainstem with no particular function. Today, it is known to play a key role in many important activities of the nervous system.

Limbic system was a term loosely used to describe the part of the brain between the cerebral cortex and the hypothalamus, a little understood area of the brain. Today, it is known to play a vital role in emotion, behavior, drive, and memory.

RETICULAR FORMATION

The reticular formation, as its name suggests, resembles a net (reticular) that is made up of nerve cells and nerve fibers. The net extends up through the axis of the central nervous system (CNS) from the spinal cord to the cerebrum. It is strategically placed among the important nerve tracts and nuclei. It receives input from most of the sensory systems and has efferent fibers that descend and influence nerve cells at all CNS levels. The exceptionally long dendrites of the neurons of the reticular formation permit input from widely placed ascending and descending pathways. Through its many connections, it can influence skeletal muscle activity, somatic and visceral sensations, the autonomic and endocrine systems, and even the level of consciousness.

columns { median - intermediate n.
 medial - large n.
 lateral - small n.

General Arrangement

The reticular formation consists of a deeply placed continuous network of nerve cells and fibers that extend from the spinal cord through the medulla, the pons, the midbrain, the subthalamus, the hypothalamus, and the thalamus. The diffuse network may be divided into three longitudinal columns: the first occupying the median plane, called the **median column**, and consisting of intermediate-size neurons; the second, called the **medial column**, containing large neurons; and the third, or **lateral column**, containing mainly small neurons (Fig. 9-1).

With classic neuronal staining techniques, the groups of neurons are poorly defined; therefore, tracing an anatomical pathway through the network is difficult. However, with the new techniques of neurochemistry

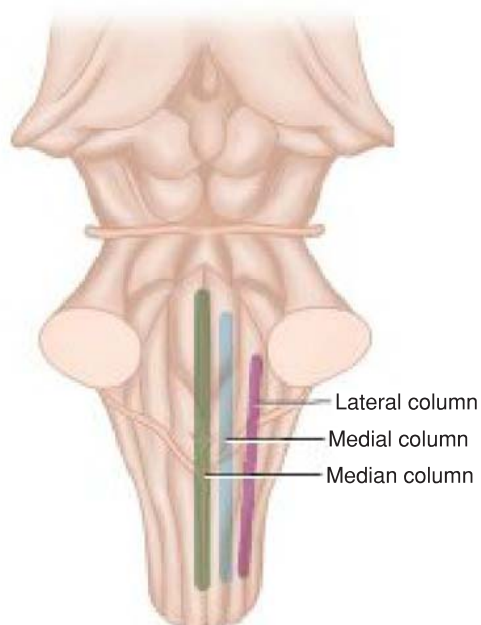


Figure 9-1 Diagram showing the approximate positions of the median, medial, and lateral columns of the reticular formation in the brainstem.

and cytochemical localization, the reticular formation is shown to contain highly organized groups of transmitter-specific cells that can influence functions in specific CNS areas. The monoaminergic groups of cells, for example, are located in well-defined areas throughout the reticular formation.

Polysynaptic pathways exist, and both crossed and uncrossed ascending and descending pathways are present, involving many neurons that serve both somatic and visceral functions.

Inferiorly, the reticular formation is continuous with the interneurons of the gray matter of the spinal cord, while superiorly, impulses are relayed to the cerebral cortex; a substantial projection of fibers also leaves the reticular formation to enter the cerebellum.

Afferent Projections

Many different afferent pathways project onto the reticular formation from most parts of the CNS (Fig. 9-2). Spinoreticular and spinothalamic tracts and the medial lemniscus project from the spinal cord. Ascending afferent tracts including the vestibular, acoustic, and visual pathways project from the cranial nerve nuclei. The cerebelloreticular pathway projects from the cerebellum,

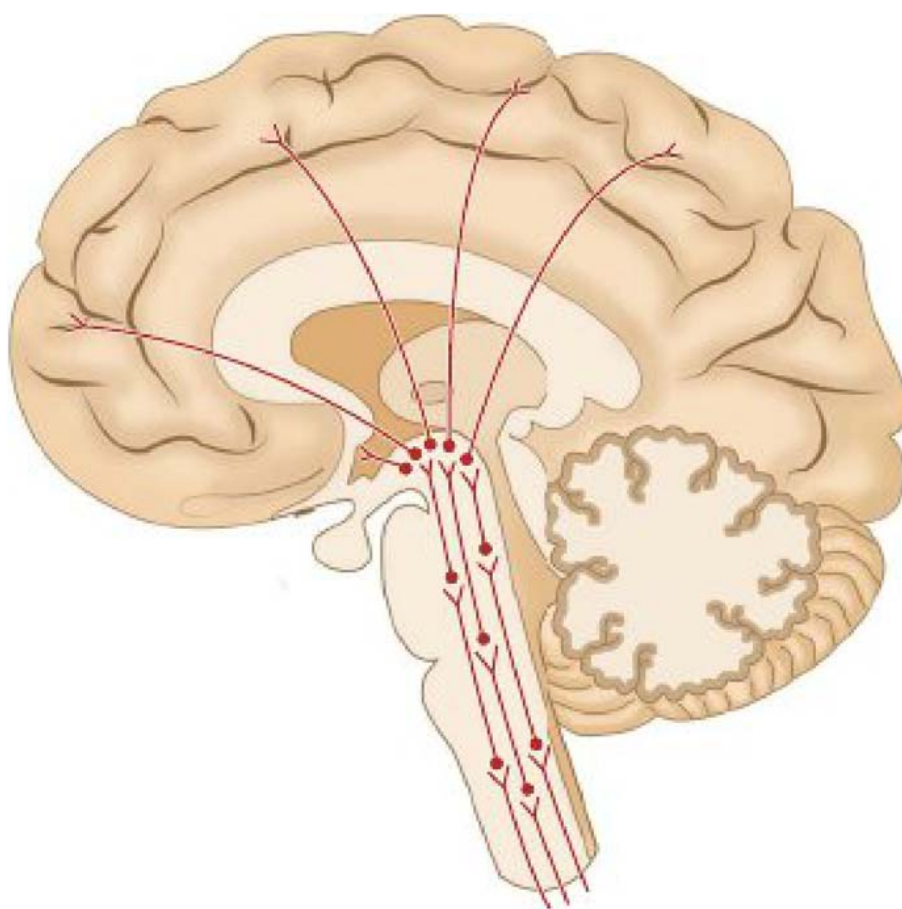


Figure 9-2 Diagram showing the afferent fibers of the reticular formation.

and further afferent tracts project from the subthalamic, hypothalamic, and thalamic nuclei and from the corpus striatum and limbic system. Other important afferent fibers arise in the primary motor cortex of the frontal lobe and from the somesthetic cortex of the parietal lobe.

Efferent Projections

Multiple efferent pathways extend down to the brainstem and spinal cord through the reticulobulbar and reticulospinal tracts to neurons in the motor nuclei of the cranial nerves and the anterior horn cells of the spinal cord. Other descending pathways extend to the sympathetic outflow and the craniosacral parasympathetic outflow of the autonomic nervous system (ANS). Additional pathways extend to the corpus striatum, the cerebellum, the red nucleus, the substantia nigra, the tectum, and the nuclei of the thalamus, subthalamus, and hypothalamus. Most regions of the cerebral cortex receive efferent fibers as well.

Functions

Given the vast number of connections of the reticular formation to all parts of the nervous system, not surprisingly, it serves many functions. A few of the more important functions are considered here.

1. **Control of skeletal muscle.** Through the reticulospinal and reticulobulbar tracts, the reticular formation can influence the activity of the α and γ motor neurons. Thus, the reticular formation can modulate muscle tone and reflex activity. It can also bring about reciprocal inhibition; for example, when the flexor muscles contract, the antagonistic extensors relax. The reticular formation, assisted by the vestibular apparatus of the inner ear and the vestibular spinal tract, plays an important role in maintaining the tone of the antigravity muscles when standing. The so-called respiratory centers of the brainstem, described by neurophysiologists as being in the control of the respiratory muscles, are now considered part of the reticular formation.
2. **Control of facial expression muscles.** The reticular formation is important in controlling the muscles of facial expression when associated with emotion. For example, when a person smiles or laughs in response to a joke, the motor control is provided by the reticular formation on both sides of the brain. The descending tracts are separate from the corticobulbar fibers. This means that a person who has suffered a stroke that involves the corticobulbar fibers and exhibits facial paralysis on the lower part of the face is still able to smile symmetrically (see Fig. 11-25).
3. **Control of somatic and visceral sensations.** By virtue of its central location in the cerebrospinal axis, the reticular formation can influence all ascending pathways that pass to supraspinal levels. The influence may be facilitative or inhibitory. In particular, the reticular formation may have a key role in the "gating mechanism" for the control of pain perception (see p. 146).
4. **Control of the ANS.** Higher control of the ANS, from the cerebral cortex, hypothalamus, and other

subcortical nuclei, can be exerted by the reticulobulbar and reticulospinal tracts, which descend to the sympathetic outflow and the parasympathetic craniosacral outflow.

5. **Control of the endocrine system.** Either directly or indirectly through the hypothalamic nuclei, the reticular formation can influence the synthesis or release of releasing or release-inhibiting factors and thereby control the activity of the hypophysis cerebri.
6. **Influence on biologic clocks.** By means of its multiple afferent and efferent pathways to the hypothalamus, the reticular formation probably influences the biologic rhythms.
7. **Reticular activating system.** Arousal and the level of consciousness are controlled by the reticular formation. Multiple ascending pathways carrying sensory information to higher centers are channeled through the reticular formation, which, in turn, projects this information to different parts of the cerebral cortex, causing a sleeping person to awaken. In fact, state of consciousness is now thought to be dependent on the continuous projection of sensory information to the cortex. Different degrees of wakefulness seem to depend on the degree of activity of the reticular formation. Incoming pain sensations strongly increase the activity of the reticular formation, which, in turn, greatly excites the cerebral cortex. **Acetylcholine** plays a key role as an excitatory neurotransmitter in this process.

Thus, the reticular formation, almost totally ignored in the past, is now being shown to influence practically all activities of the body.

Papez circuit, 1937 James Papez
 • mammillary bodies
 • ant. thalamic nucleus
 • subcallosal
 • cingulate
 • parahippocampal gyri
 • amygdaloid n.
 • hippocampal formation

LIMBIC SYSTEM

- emotional reactions

The word *limbic* means **border or margin**, and the term *limbic system* was loosely used to include a group of structures that lie in the border zone between the cerebral cortex and the hypothalamus. Research has now shown that the limbic system is involved with many other structures beyond the border zone in the control of emotion, behavior, and drive; it also appears to be important to memory.

Anatomically, the limbic structures include the subcallosal, the cingulate, and the parahippocampal gyri, the hippocampal formation, the amygdaloid nucleus, the mammillary bodies, and the anterior thalamic nucleus (Fig. 9-3). The alveus, the fimbria, the fornix, the mamillothalamic tract, and the stria terminalis constitute the connecting pathways of this system.

Hippocampal Formation

The hippocampal formation consists of the hippocampus, the dentate gyrus, and the parahippocampal gyrus.

The **hippocampus** is a curved elevation of gray matter that extends throughout the entire length of the floor of the inferior horn of the lateral ventricle (Fig. 9-4). Its anterior end is expanded to form the **pes hippocampus**. It is named *hippocampus* because it resembles a **seahorse** in coronal section. The convex ventricular

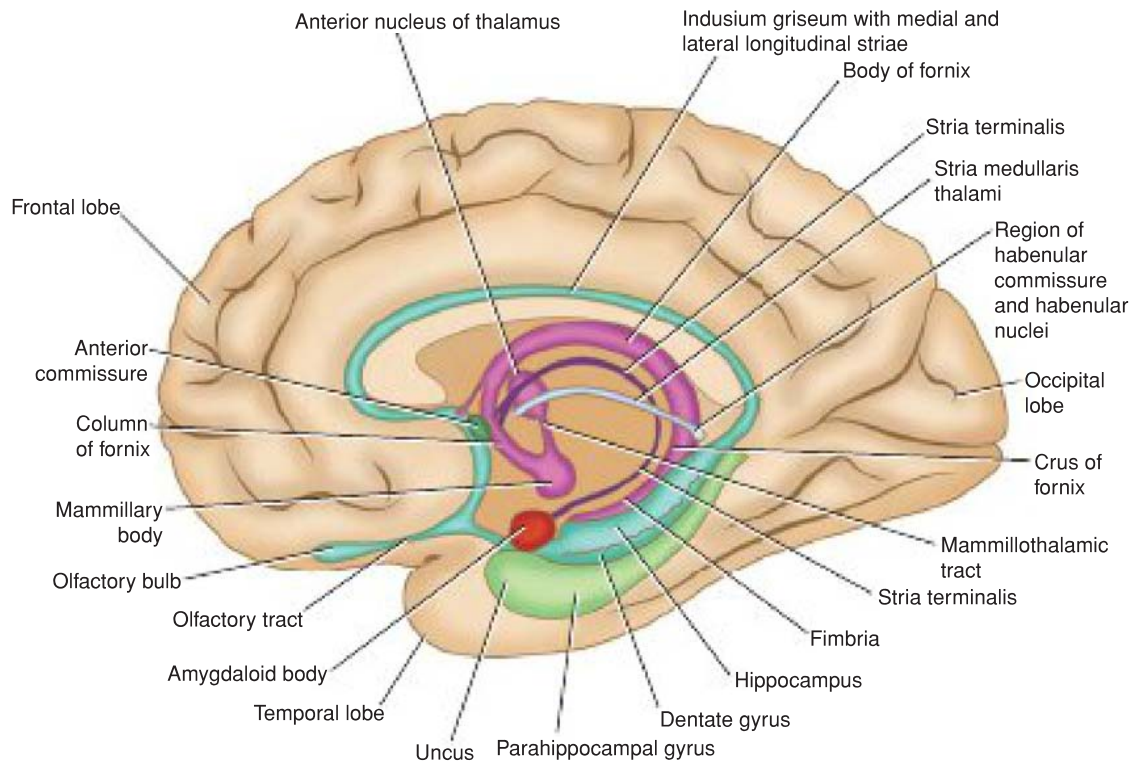


Figure 9-3 Medial aspect of the right cerebral hemisphere showing structures that form the limbic system.

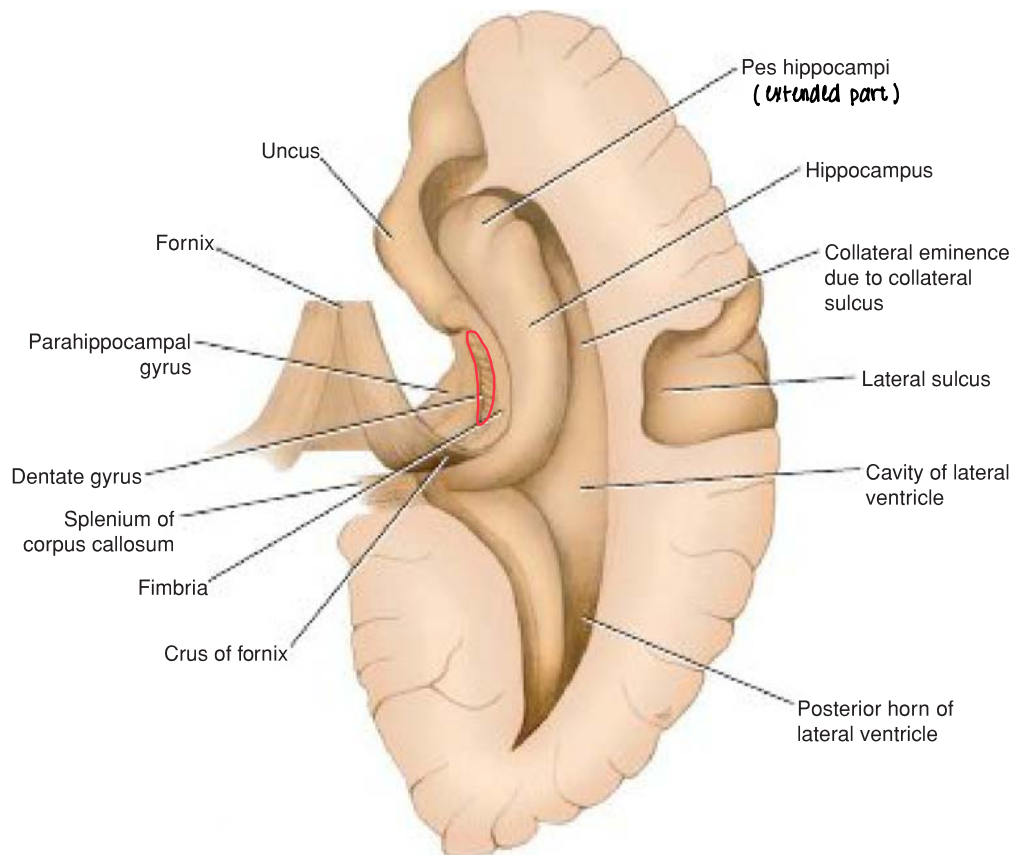


Figure 9-4 Dissection of the right cerebral hemisphere exposing the cavity of the lateral ventricle, showing the hippocampus, the dentate gyrus, and the fornix.

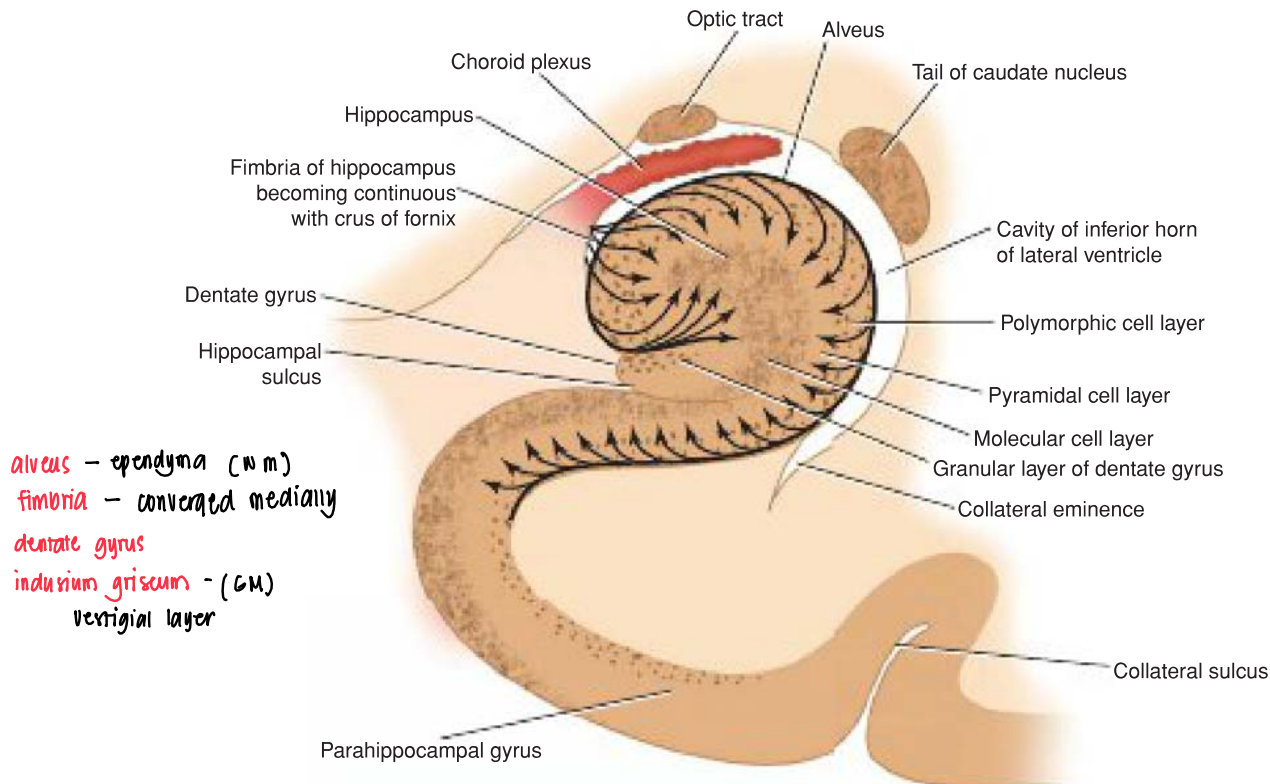


Figure 9-5 Coronal section of the hippocampus and related structures.

surface is covered with ependyma, beneath which lies a thin layer of white matter called the **alveus** (Fig. 9-5). The alveus consists of nerve fibers that have originated in the hippocampus, and these converge medially to form a bundle called the **fimbria**. The fimbria, in turn, becomes continuous with the crus of the fornix. The hippocampus terminates posteriorly beneath the splenium of the corpus callosum.

The **dentate gyrus** is a narrow, notched band of gray matter that lies between the fimbria of the hippocampus and the parahippocampal gyrus (see Fig. 9-4). Posteriorly, the gyrus accompanies the fimbria almost to the splenium of the corpus callosum and becomes continuous with the **indusium griseum**. The indusium griseum is a thin, vestigial layer of gray matter that covers the superior surface of the corpus callosum (Fig. 9-6). Embedded in the superior surface of the indusium griseum are two slender bundles of white fibers on each side called the **medial** and **lateral longitudinal striae**. The striae are the remains of the white matter of the vestigial indusium griseum. Anteriorly, the dentate gyrus is continued into the **uncus**.

The **parahippocampal gyrus** lies between the hippocampal fissure and the collateral sulcus and is continuous with the hippocampus along the medial edge of the temporal lobe (see Figs. 9-4 and 9-5).

Amygdaloid Nucleus

The **amygdaloid nucleus** is so named because it resembles an almond. It is situated partly anterior and partly

superior to the tip of the inferior horn of the lateral ventricle (see Fig. 7-14). It is fused with the tip of the tail of the caudate nucleus, which has passed anteriorly in the roof of the inferior horn of the lateral ventricle. The stria terminalis emerges from its posterior aspect. The amygdaloid nucleus consists of a complex of nuclei that can be grouped into a larger **basolateral group** and smaller **corticomedial group**.

The mammillary bodies and the anterior nucleus of the thalamus are considered elsewhere in this text.

Connecting Pathways of the Limbic System

The connecting pathways of the limbic system are the **alveus**, the **fimbria**, the **fornix**, the **mammillothalamic tract**, and the **stria terminalis**.

The **alveus** consists of a thin layer of white matter that lies on the superior or ventricular surface of the hippocampus (see Fig. 9-5). It is composed of nerve fibers that originate in the hippocampal cortex. The fibers converge on the medial border of the hippocampus to form a bundle called the **fimbria**.

The fimbria now leaves the posterior end of the hippocampus as the **crus of the fornix** (see Fig. 9-4). The crus from each side curves posteriorly and superiorly beneath the splenium of the corpus callosum and around the posterior surface of the thalamus. The two crura now converge to form the **body of the fornix**, which is applied closely to the undersurface of the corpus callosum (see Fig. 9-3). As the two crura come together, they are connected by transverse fibers called

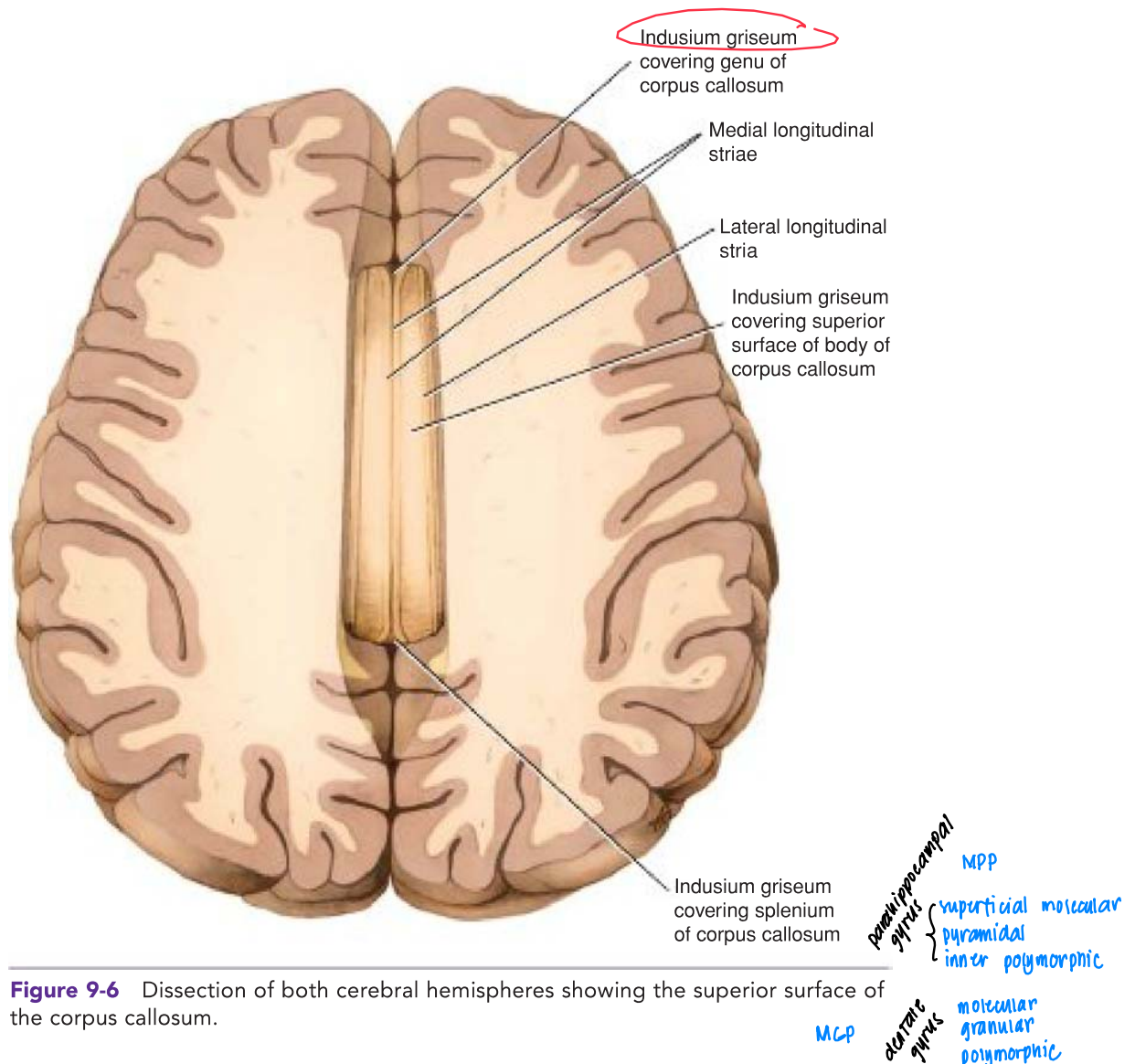


Figure 9-6 Dissection of both cerebral hemispheres showing the superior surface of the corpus callosum.

the **commissure of the fornix** (see Fig. 7-16). These fibers decussate and join the hippocampi of the two sides.

Anteriorly, the body of the fornix is **connected to the undersurface of the corpus callosum** by the **septum pellucidum**. Inferiorly, the body of the fornix is related to the tela choroidea and the ependymal roof of the third ventricle.

The body of the fornix splits anteriorly into two anterior **columns of the fornix**, each of which curves anteriorly and inferiorly over the interventricular foramen (foramen of Monro). Then, each column disappears into the lateral wall of the third ventricle to reach the **mammillary body** (see Fig. 9-3).

The **mammillothalamic tract** provides important **connections between the mammillary body and the anterior nuclear group of the thalamus**.

The **stria terminalis** emerges from the posterior aspect of the amygdaloid nucleus and runs as a bundle of nerve fibers posteriorly in the roof of the inferior horn of the lateral ventricle on the medial side of the tail of the caudate nucleus. It follows the curve of the caudate nucleus and comes to lie in the floor of the body of the lateral ventricle.

Hippocampal Structure and the Dentate Gyrus

The cortical structure of the parahippocampal gyrus is **six layered** (see Fig. 9-5). As the cortex is traced into the hippocampus, there is a **gradual transition from a six- to a three-layered arrangement**. These three layers are the ① **superficial molecular layer**, consisting of nerve fibers and scattered small neurons; ② **pyramidal layer**, consisting of many large pyramid-shaped neurons; and ③ **inner polymorphic layer**, which is similar in structure to the polymorphic layer of the cortex seen elsewhere.

The **dentate gyrus** also has three layers, but the pyramidal layer is replaced by the **granular layer**. The granular layer is composed of densely arranged rounded or oval neurons that give rise to axons that terminate on the dendrites of the pyramidal cells in the hippocampus. A few of the axons join the fimbria and enter the fornix.

Afferent Connections of the Hippocampus

Afferent **connections of the hippocampus** may be divided into **six groups** (Fig. 9-7):

1. Fibers arising in the **cingulate gyrus** pass to the hippocampus.

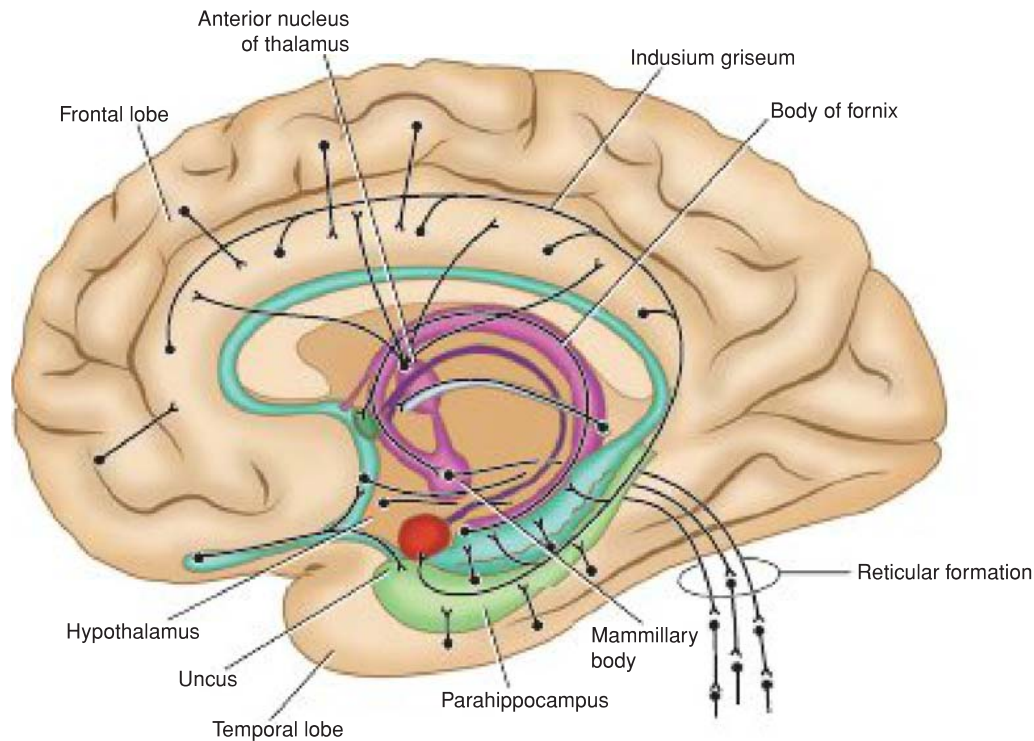


Figure 9-7 Diagram showing some important afferent and efferent connections of the limbic system.

- Fibers arising from the **septal nuclei** (nuclei lying within the midline close to the anterior commissure) pass posterior in the fornix to the hippocampus.
- Fibers arising from **one hippocampus** pass across the midline to the opposite hippocampus in the commissure of the fornix.
- Fibers from the **indusium griseum** pass posteriorly in the longitudinal striae to the hippocampus.
- Fibers from the **entorhinal area or olfactory-associated cortex** pass to the hippocampus.
- Fibers arising from the **dentate and parahippocampal gyri** travel to the hippocampus.
- Fibers join the **stria medullaris thalami** to reach the **habenular nuclei**.

Consideration of the above complex anatomical pathways indicates that the structures comprising the limbic system not only are interconnected but also **send projection fibers to many different parts of the nervous system**. Physiologists now recognize the importance of the **hypothalamus** as being the **major output pathway of the limbic system**.

Limbic System Functions

The limbic system, via the hypothalamus and its connections with outflow of the ANS and its control of the endocrine system, is able to **influence many aspects of emotional behavior**. These include particularly the reactions of **fear and anger** and the emotions associated with **sexual behavior**.

Evidence also suggests that the hippocampus is concerned with **converting recent memory to long-term memory**. A **lesion** of the hippocampus results in the individual being **unable to store long-term memory**. Memory of remote past events before the lesion developed is unaffected. This condition is called **anterograde amnesia**. Note that injury to the **amygdaloid nucleus and the hippocampus** produces greater memory loss than injury to either one of these structures alone.

Evidence does not show that the limbic system has an olfactory function. Its various afferent and efferent connections provide pathways for the integration and effective homeostatic responses to a wide variety of environmental stimuli.

Efferent Connections of the Hippocampus

Axons of the large pyramidal cells of the hippocampus emerge to form the alveus and the fimbria. The fimbria continues as the crus of the fornix. The two crura converge to form the body of the fornix. The body of the fornix splits into the two columns of the fornix, which curve downward and forward in front of the interventricular foramina. The fibers within the fornix are distributed to the following regions (see Fig. 9-7):

- Fibers pass posterior to the anterior commissure to enter the **mammillary body**, where they end in the **medial nucleus**.
- Fibers pass posterior to the anterior commissure to end in the **anterior nuclei of the thalamus**.
- Fibers pass posterior to the anterior commissure to enter the **tegmentum of the midbrain**.
- Fibers pass anterior to the anterior commissure to end in the **septal nuclei, the lateral preoptic area, and the anterior part of the hypothalamus**.



Clinical Notes

Reticular Formation

The reticular formation is a continuous network of nerve cells and fibers that extend through the neuroaxis from the spinal cord to the cerebral cortex. The reticular formation not only modulates the control of motor systems but also influences sensory systems. By means of its multiple ascending pathways, which project to different parts of the cerebral cortex, it is believed to influence the state of consciousness.

Loss of Consciousness

In experimental animals, damage to the reticular formation, which spares the ascending sensory pathways, causes persistent unconsciousness. Pathologic lesions of the reticular formation in humans can result in loss of consciousness and even coma. It has been suggested that the loss of consciousness that occurs in epilepsy may be due to inhibition of the activity of the reticular formation in the upper part of the diencephalon.

Limbic System

Because the anatomical connections of the limbic system are extremely complex and their significance is not fully understood, committing all of them to memory is unnecessary. The results of neurophysiologic experiments, which have included stimulation and ablation of different parts of the limbic system in animals, are not entirely clear. Nevertheless, certain important roles have been inferred: (1) The limbic structures are involved in the development of sensations of emotion and with the visceral responses accompanying those emotions, and (2) the hippocampus is concerned with recent memory.

Schizophrenia

The symptoms of schizophrenia include chronically disordered thinking, blunted affect, and emotional withdrawal. Paranoid delusions and auditory hallucinations may also be present. Clinical research has shown that if the limbic receptors to dopamine are blocked by a pharmacologic agent, the worst symptoms of schizophrenia are lessened. Phenothiazine

administration, for example, blocks the dopamine receptors in the limbic system. Unfortunately, this drug, as well as most other antipsychotic drugs, has major motor side effects on the dopaminergic receptors within the extrapyramidal system, producing abnormal involuntary movements. Research is now concentrating on finding a drug that will block the limbic dopamine receptors but without effect on the receptors of the extrapyramidal system (substantia nigra–corpus striatum).

Clearly, no direct evidence exists to suggest that excessive production of dopamine by certain neurons actually contributes to schizophrenia.

Amygdaloid Complex Destruction

Unilateral or bilateral destruction of the amygdaloid nucleus and the para-amygdaloid area in patients suffering from aggressive behavior in many cases results in a decrease in aggressiveness, emotional instability, and restlessness; increased interest in food; and hypersexuality but no memory disturbance. Monkeys that have been subjected to bilateral removal of the temporal lobes demonstrate what is known as Klüver–Bucy syndrome. They become docile and show no evidence of fear or anger and are unable to appreciate objects visually. They have increased appetite and sexual activity. Moreover, the animals indiscriminately seek partnerships with male and female animals.

Precise stereotactic lesions in the amygdaloid complex in humans reduce emotional excitability and bring about normalization of behavior in patients with severe disturbances. No loss of memory occurs.

Temporal Lobe Dysfunction

Temporal lobe epilepsy may be preceded by an aura of acoustic or olfactory experience. The olfactory aura is usually an unpleasant odor. The patient is often confused, anxious, and docile and may perform automatic and complicated movements, such as undressing in public or driving a car, and then, following the seizure, may have no memory of what occurred previously.

Key Concepts

Reticular Formation

- The reticular formation consists of a deeply placed, continuous network of nerve cells and fibers that extend throughout the medulla, pons, midbrain, subthalamus, hypothalamus, and thalamus.
- It is organized into three longitudinal columns: median, medial, and lateral.
- These columns can modulate 1) muscle tone and reflex activity, 2) somatic and visceral sensations, 3) autonomic nervous system, 4) endocrine functions, 5) biologic clocks, and

- 6) the reticular activating system (arousal and consciousness).

Limbic System

- This group of structures controls emotion, behavior, drive, and memory and includes the subcallosal, cingulate, and parahippocampal gyri, the hippocampal formation, the amygdaloid nucleus, the mammillary bodies, and the anterior thalamic nucleus.
- The hippocampal formation consists of the hippocampus, dentate gyrus, and parahippocampal gyrus.

Clinical Problem Solving

1. While discussing the neurologic basis of emotions during a ward round, a neurologist asks a third-year medical student what she knows about the Klüver–Bucy syndrome. What would be your answer to that question? Does Klüver–Bucy syndrome ever occur in humans?
2. A 23-year-old woman with a 4-year history of epileptic attacks visits her neurologist. A friend of hers vividly describes one of her attacks. For a few seconds before the convulsions begin, the patient complains of an unpleasant odor, similar to that encountered in a cow shed. This is followed by a shrill cry as she falls to the floor unconscious. Her whole body immediately becomes involved in generalized tonic and clonic movements. Clearly, this patient has a generalized form of epileptic seizure. Using your knowledge of neuroanatomy, suggest which lobe of the brain was initially involved in the epileptic discharge.
3. A 54-year-old man dies in the hospital with a cerebral tumor. He had always been intellectually very bright and could easily recall events in his childhood. For the past 6 months, his family had noticed that he had difficulty in recalling where he had placed things, such as his pipe. He also had difficulty in recalling recent news events, and, just before he died, he could not remember that his brother had visited him the day before. Using your knowledge of neuroanatomy, suggest which part of the brain was being affected by the expanding and highly invasive tumor.

Answers and Explanations to Clinical Problem Solving

1. The Klüver–Bucy syndrome consists of the signs and symptoms found in monkeys following bilateral removal of the temporal lobe. The monkeys become docile and unresponsive and display no signs of fear or anger. They have increased appetite and sexual activity, which is often disinhibited. They are able to see objects but are unable to recognize the objects. Humans in whom the amygdaloid area is destroyed do not usually demonstrate this syndrome. It has, however, been described in humans following the bilateral removal of large areas of the temporal lobes.
2. The olfactory aura that preceded the general convulsions of the epileptic attack would indicate that the temporal lobe of the cerebral cortex was initially involved.
3. An autopsy study revealed extensive invasion of the hippocampus, fornix, and mammillary bodies in both cerebral hemispheres. The hippocampus is apparently involved in the storage and categorizing of afferent information related to recent memory.

Review Questions

Directions: Each of the numbered items in this section is followed by answers. Select the ONE lettered answer that is CORRECT.

1. The following statements concern the reticular formation:
 - (a) Reticulobulbar and reticulospinal tracts form the afferent pathways from the reticular formation to the motor nuclei of the cranial nerves and the anterior horn cells of the spinal cord, respectively.
 - (b) The reticular formation extends through the neuroaxis from the spinal cord to the midbrain.
 - (c) The main pathways through the reticular formation may easily be traced from one part of the CNS to another using silver stains.
 - (d) Superiorly, the reticular formation is relayed to the cerebral cortex.
 - (e) Afferent pathways project into the reticular formation from only a few parts of the CNS.
2. The following statements concern the functions of the reticular formation:
 - (a) It influences the activity of the α and γ motor neurons.
 - (b) It opposes the actions of the vestibular spinal tract.
 - (c) It does not bring about reciprocal inhibition during contraction of the prime mover muscles.
 - (d) It plays no part in maintaining the tone of the antigravity muscles.
 - (e) It cannot modulate reflex activity.