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The Vertebrate Central Nervous System

INTRODUCTION

The brain evolved in ancestral chordates in conjunction with the evolution of the head as a specialized body region. One of the principal evolutionary events that preceded the sequences of head and brain evolution was a novel embryological event: the development of the mouth as a distinct body opening separate from the gut opening, which eventually becomes the anus. Animals that possess these characteristics are known as **deuterostomes**, which means “second mouth.” Deuterostomes comprise a number of groups of which the three major ones are echinoderms (starfishes and sea urchins), hemichordates (pterobranchs and acorn worms), and chordates. The latter include tunicates (sea squirts), cephalochordates (*Branchiostoma*, previously called *Amphioxus*), and vertebrates. Because some of the key evolutionary events in deuterostome and chordate evolution have been ones that occur relatively early in embryological development, we will begin this chapter with some of the early aspects of the embryological development of the brain in vertebrates.

Following the fertilization of a deuterostome egg, development proceeds with repeated cleavages of the cells. The pattern of cleavage is variable among the different groups of deuterostomes but in all groups results in the formation of a **blastula** [Fig. 3-1(A)], a sphere of cells around a central cavity, the **blastocoel**. Some differences also exist among deuterostomes in particular features of the course of development following the blastula stage, but a general pattern of development is consistent among all deuterostomes.

In vertebrates, the process of gastrulation [Fig. 3-1(B and C)] follows the blastula stage, with continued cell proliferation and the specification and arrangement of specific groups of cells relative to the parts of the body that they will eventually form. The **gastrula** initially consists of two cell layers: an outer layer of cells, the **ectoderm**, from which the skin and nervous system will form, and an inner layer, which consists initially of **endoderm**. The endoderm surrounds the cavity, called the **archenteron**, that will become the lumen of the gut. The archenteron expands during gastrulation, obliterating the blastocoel. The opening of the gut cavity is the **blastopore**.

As gastrulation proceeds, the roof of the archenteron, formed by the dorsal part of the inner layer of cells, differentiates to form mesodermal tissue, which in turn gives rise to a midline structure called the **notochord**, as well as to lateral sheets of tissue that will form muscle. The rest of the inner layer remains endoderm, the tissue of the gut. During the later stages of gastrulation, the ectoderm overlying the archenteron roof thickens to form the **neural plate**. A pair of folds develops along this plate and grows dorsally to meet and then fuses to form a tube, called the **neural tube** [Fig. 3-1(D)]. The lumen (inner space) of this tube forms the ventricular system, while the brain and spinal cord develop within the walls of the tube. The notochord induces the differentiation of a specific group of cells in the midline of the neural plate, called the **floor plate**, and these cells in turn regulate the further differentiation of neurons and the growth of axons within the neural tube. A population of cells that initially lie between the neural tube and the surface ectoderm, the **neural crest**, also contributes

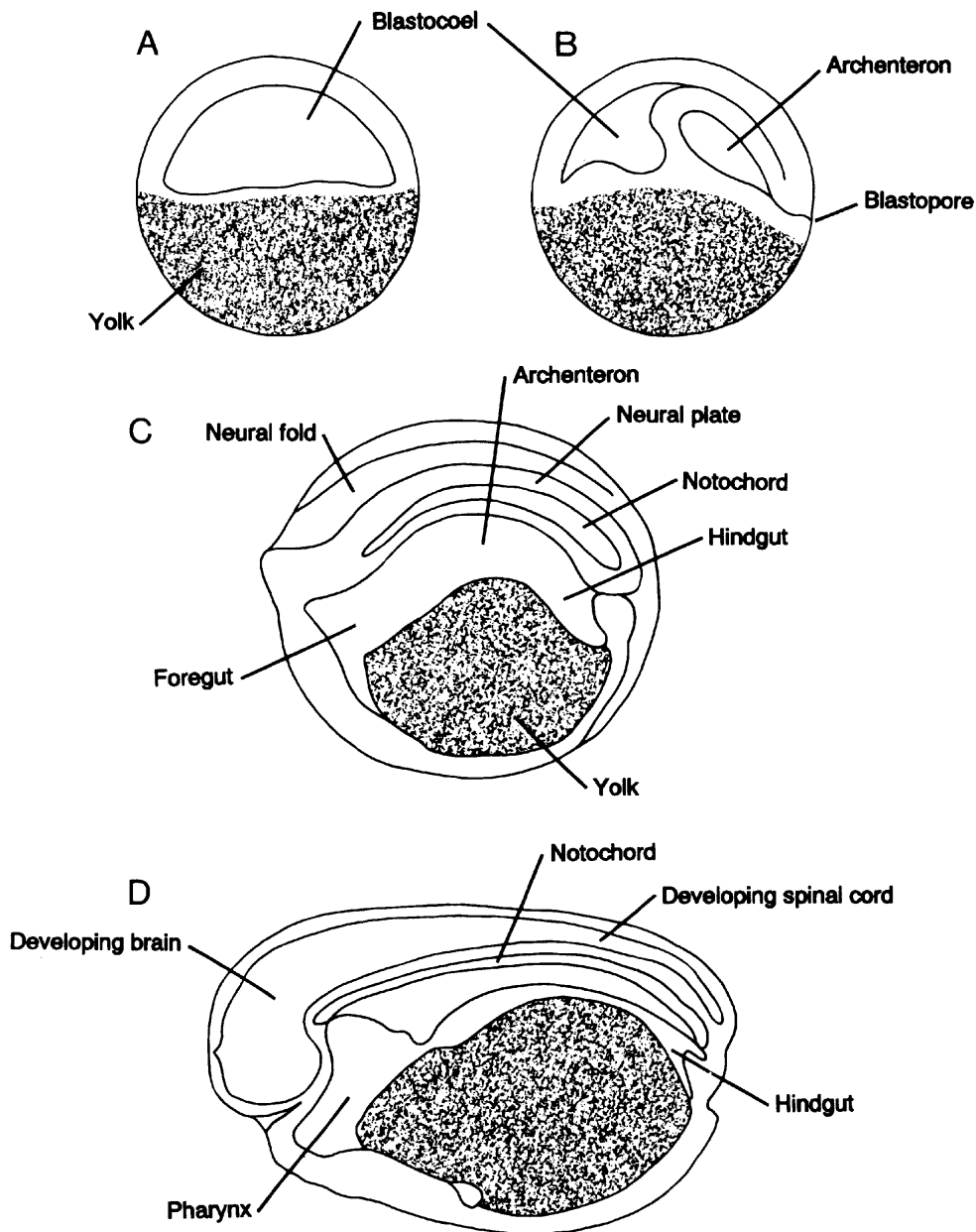


FIGURE 3-1. Drawings of sections through a gastrula (A) and stages of blastulation (B and C) to form a 3 mm embryo (D) in a frog.

to components of the developing nervous system, as do specific areas of neurogenic ectoderm in the head, called **placodes**.

THE BRAIN AND SPINAL CORD

In the head region of the earliest vertebrates, the neural crest and placodes were newly evolved tissues that resulted in the formation of paired sense organs and a new rostral (front) part of the head to house them. As the head developed special new functions, the central nervous system underwent a parallel development that provided the sensory innervation and motor control of the peripheral structures. A new rostral part of the brain, called the forebrain, was added in which sensory information could be analyzed, integrated, and remembered, allowing for sophisticated decision-making capabilities and for appropriate motor responses to a variety of stimuli.

The central nervous system consists of the brain and the spinal cord. Figure 3-2 illustrates the location of the brain and the rostral end of the spinal cord in the head of an adult vertebrate, a lizard in this example, and demonstrates some of the standard terms of orientation (also see the Appendix). The central nervous system traditionally has been divided into two great regions: the brain and the spinal cord. While this distinction is of some importance in medical education and neurology, it suggests a much greater dichotomy of function than actually exists. Indeed, this subdivision is often confusing to newcomers to the neurosciences because it emphasizes the relatively few differences and directs attention away from the many similarities between the two regions.

The boundary between the brain and spinal cord is not nearly as sharp as some textbooks suggest, nor does it correspond precisely to the junction of the skull and the vertebral column (spinal column or backbone), which surrounds and

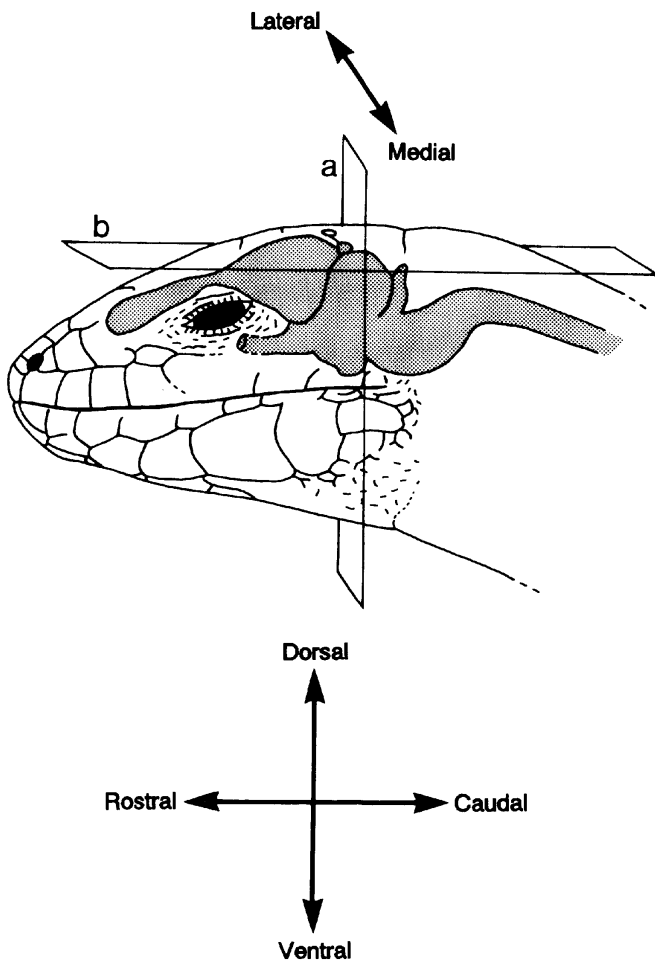


FIGURE 3-2. Lateral view of the head of a lizard (*Lacerta sicula*) with the position of the brain and the rostral part of the spinal cord (indicated by shading) shown *in situ*. Rectangle "a" represents the transverse plane, which runs from dorsal to ventral and medial to lateral. Rectangle "b" represents the horizontal plane, which is approximately parallel to the line of the mouth and runs from rostral to caudal and medial to lateral. The sagittal plane is parallel to the lateral view shown in the figure and runs from rostral to caudal and dorsal to ventral. Adapted from Senn (1979). Used with permission of Academic Press Ltd.

protects the spinal cord. Although a substantial portion of the brain consists of unique structures that have no counterpart in the spinal cord, much of the brain, especially its caudal region, is actually a continuation of the structures and general organization of the spinal cord.

The spinal cord is organized for the control of the body's limbs and trunk; similarly, the caudal brain is organized for the control of specialized structures in the head, such as the jaws, tongue, eye muscles and lids, and vocal organs. Moreover, the caudal brain and spinal cord share the task of control and regulation of the viscera, or internal organs, such as the heart, digestive system, and respiratory system.

CELLULAR ORGANIZATION OF THE CENTRAL NERVOUS SYSTEM

The cells in the brain and spinal cord are of two types: nonneural cells called glia, which fill in the spaces between

neurons and wrap around parts of neurons, and the neurons themselves. The neurons can be categorized into three broad categories. The first category is composed of Golgi Type I cells (see Chapter 2) that are the **afferent neurons**, which are cells that bring information about the internal and external environments into the central nervous system. The second category is composed of Golgi Type I cells that are **efferent neurons**, which are motor or effector cells that bring instructions from the central nervous system to the body's effector organs, that is, the muscles and glands. The third category consists of both Golgi Type I and II cells that are **interneurons**; these neurons account for the greatest proportion of the mass of the central nervous system (Fig. 3-3).

We should note that the terms "afferent" and "efferent" can be used in conjunction with the primary sensory and the motor or effector neurons, respectively, or in reference to the direction of information relay in the central nervous system. These terms refer to the direction of conduction and are also used in talking about interneurons. Afferent means "coming into," and efferent means "going out of." A long-axon interneuron coming into and terminating within a specified local-circuit population, which we will call A, is afferent to A. Another long-axon interneuron going from A to a different local-circuit population, which we will call B, is efferent from A and afferent to B.

The interneurons form the neural chain between the primary sensory afferent neurons and the efferent motor or effector neurons. Rarely does a primary sensory neuron make direct contact with a motor neuron. Rather, a few or many thousands of interneurons typically receive the flow of information from sensory neurons into the central nervous system, process that information, and send the resultant outflow of instructions to muscles or glands via the motor neurons. The interneurons determine whether the instructions will be for action or for inaction, whether a response will be rapid or leisurely, vigorous or delicate, towards an object or away from it.

As described in Chapter 2, interneurons form discrete neuronal populations, called **nuclei** (singular: **nucleus**). In addition to **nuclei**, there are also areas of layered sets of interneurons in the brain. Some of these layered areas are called **cortex**. Cortices are present in some of the more dorsal, or roof, areas of the brain. A number of cortical areas are present in the rostral part of the brain in some vertebrates, and cortex is also present in the roof of the middle part of the brain (midbrain) and of the hindbrain.

This general description of central nervous system organization applies to both the spinal cord and brain. The rostral-most parts of the brain have fewer primary sensory, afferent components and fewer effector, efferent components than are present in the brainstem. The rostral brain consists mostly of interneurons arranged in a variety of specialized local-circuit populations that are interconnected by long-axon, Golgi I interneurons. Ascending projections from nuclei in the brainstem bring sensory information and also feedback information up to the rostral brain, and descending projections from the rostral brain carry its output. The heavy concentration of interneurons in the rostral brain has served to focus attention on this region as the possible "executive" component of the central nervous system, with major responsibilities for decision making, mem-

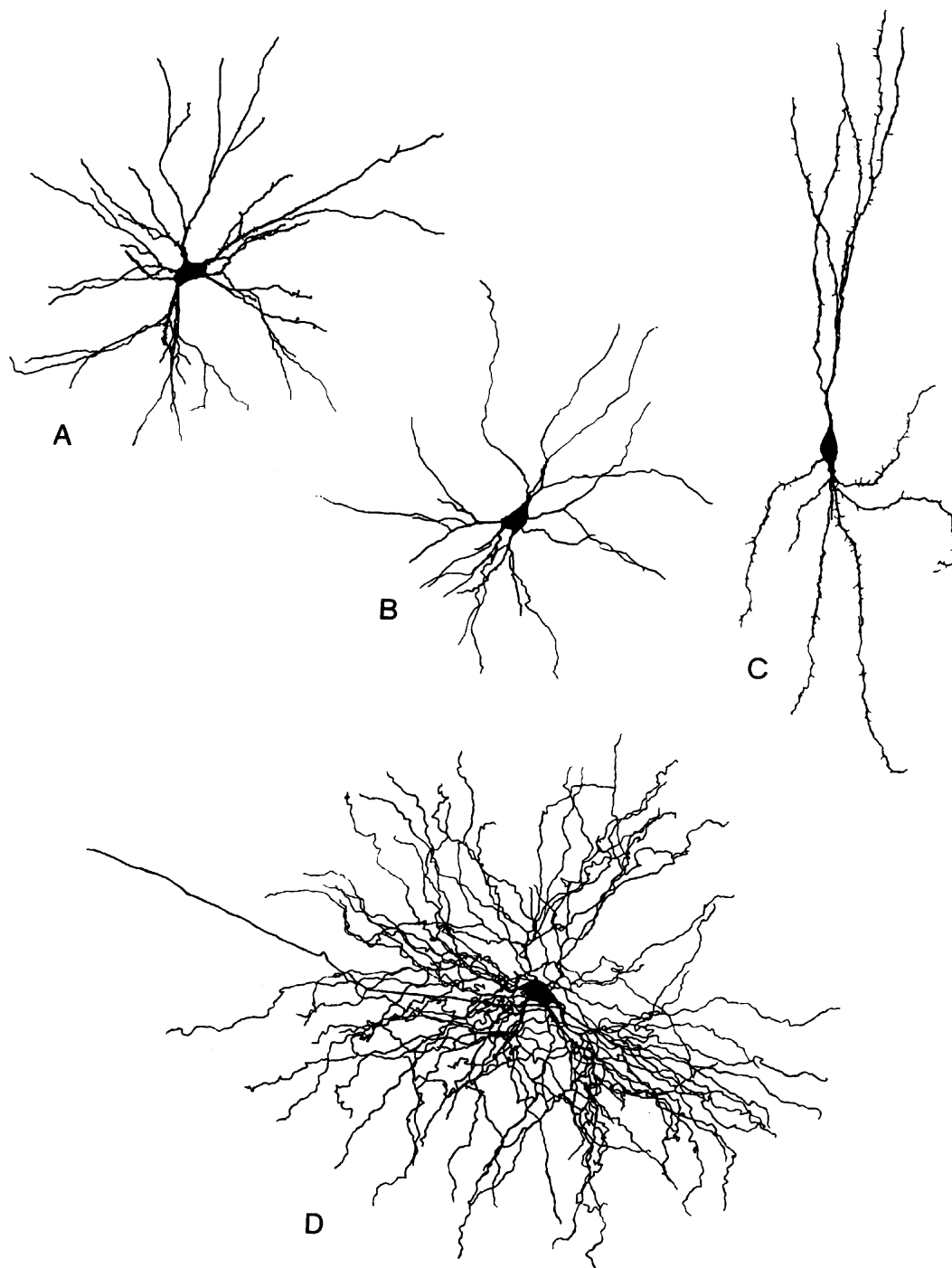


FIGURE 3-3. Examples of interneurons found in the forebrain in various mammals. (A and B) Both are from the dorsal thalamus of a cat, after Robson (1993); (C) is from the cerebral cortex of a monkey, after Lund and Lewis (1993); and (D) is from the dorsal thalamus of a monkey, after Havton and Ohara (1993).

ory, attention, communication, emotion, and other important, complex behavioral processes.

To summarize, the brain and spinal cord are organized to allow for the input of primary sensory information, the analysis and processing of the information, and the production and transmission of appropriate responses to the information. The axons of incoming, primary sensory, afferent neurons bring sensory information into the brain and spinal cord. Long-axon interneurons carry this information between multiple nuclei and cortices. Short-axon, local circuit interneurons within nuclei and cortices are involved with processing the information. Additional sets of long-axon interneurons carry the output for re-

sponses to the information to the outgoing, motor or effector neurons in the brain and spinal cord.

REGIONAL ORGANIZATION OF THE NERVOUS SYSTEM

The Spinal Cord

Both the brain and spinal cord can be subdivided into individual regions. The subdivisions of the spinal cord are named for regions of the spinal column through which the

spinal nerves exit on their way to the various parts of the body. Thus, the region of the cord from which nerves exit through the cervical (neck) bones is called the **cervical cord**. This is the most rostral division of the cord and is continuous with the most caudal region of the brain.

Proceeding caudally within the spinal cord, the remaining divisions are the **thoracic (chest) cord**, the **lumbar (abdominal) cord**, and the **sacral (pelvic) cord**. In addition to receiving primary somatic, afferent fibers from the skin, muscles and joints of the neck, body, limbs (if any) and tail (if any), the spinal cord also sends out motor, efferent fibers (axons) that control the muscles of these body parts. The latter are known as somatic efferent fibers.

From the thoracic and lumbar regions of the cord, a special group of efferent neurons sends its axons to innervate the smooth muscles of the digestive system and other internal organs and glands. These are known as **visceral efferent fibers**. The visceral efferents originating in the thoracic and lumbar spinal cord are known as the **sympathetic nervous system**. They function to provide a rapid activation of various internal organ systems such as the cardiovascular and respiratory systems when severe demands are placed on these systems or in times of emergency when quick action is required. This system serves "fight or flight" and related responses.

The sympathetic nervous system is complemented by another visceral efferent system, the **parasympathetic nervous system**, which is composed of visceral efferent neurons from the sacral division of the spinal cord and from the caudal regions of the brain. The parasympathetic system controls the same organs as does the sympathetic system, but it does so under normal conditions, when no special stresses are present. This system functions in promoting the digestion of food, allowing urination to occur, and other, related, normal functions of the organs. Thus, when a high-demand situation arises, the sympathetic system takes control; when the high-demand situation ceases, control returns to the parasympathetic system. The sympathetic and parasympathetic systems together are known as the **autonomic nervous system**.

The Brain

Figure 3-4 is a drawing of the brain and rostral spinal cord of a vertebrate, in this case a ray-finned fish, which will serve

as an example for the general organization of vertebrate brains. Each of the lobes and other swellings of the brain surface has a specific name, such as the optic lobe (tectum) or cerebellum. Groups of lobes or swellings are known by regional names, such as the mesencephalon (midbrain). Still more-encompassing regional names are forebrain and brainstem.

The nerves entering and leaving the brain are the **cranial nerves**. Like the spinal nerves, the cranial nerves carry primary sensory afferent neurons (in this case from the head rather than the body) into the central nervous system and motor or effector efferent neurons to control the muscles and glands of the head and neck. Although these nerves are given special names, such as trigeminal nerve and oculomotor nerve, the organization of at least some of them is essentially the same as that of the spinal nerves. Moreover, some of the interneuron networks of the more caudal cranial nerves are directly continuous with equivalent cell populations in the spinal cord.

Hindbrain. The caudal-most region of the brain is the **rhombencephalon** or **hindbrain**, which consists of the **medulla** and **pons**. The cranial nerves of this area include components that comprise most of the cranial division of the parasympathetic nervous system. However, a number of what have traditionally been called "special senses" are also represented by cranial nerves that enter the brain at this level. Such special senses are those that are unique to the head region, such as hearing and the sense of balance and acceleration. Other special senses, not present in all vertebrates, include the lateral line system for the detection of water displacement over the body surface and of electric fields in the aquatic environment and the infrared (IR) sense for the detection of body heat radiated by other animals. The cell bodies of the efferent neurons that control the muscles of the jaws and the superficial facial muscles, such as those of the lips and eyelids, are also located in this region of the brain.

In addition to the nuclei associated with some of the cranial nerves, the medulla and pons contain other nuclei and a number of fiber tracts. Many of the fiber tracts are long pathways between the spinal cord and the more rostral parts of the brain, while others are shorter and run between nuclei within this area. Some of the cell populations in the medulla and pons are more widely scattered and diffuse than most other nuclei in the brain. These scattered populations are collectively referred

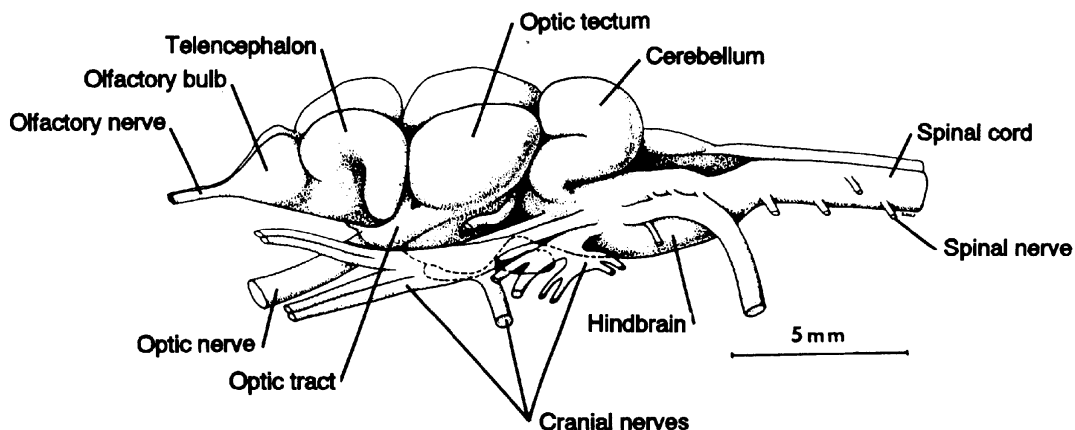


FIGURE 3-4. Drawing of a lateral view of the brain of a ray-finned fish, the longnose gar (*Lepisosteus osseus*). Adapted from Northcutt and Butler (1976).

to as the **reticular formation**. The nuclei of the reticular formation are involved in integrating inputs from a variety of sources, including the cranial nerve nuclei and more rostral parts of the brain. The reticular formation regulates and modulates activities elsewhere in the brain on the basis of the incoming information. A transverse section through the hindbrain in a fish (Fig. 3-5) illustrates the distribution of nerve cell bodies within the brain. Fiber tracts run in the areas in which there are few or no cell bodies. Closely related to the pons, both geographically and functionally, is the **cerebellum** (Fig. 3-4). The cerebellum is a cortical structure in the roof of the hindbrain. Among its other functions, the cerebellum is involved in balance, coordination, and the smooth execution of rapid movements.

Midbrain. The next major subdivision of the brain is the **mesencephalon** or **midbrain** (Figs. 3-4 and 3-5). The most prominent external feature of this area in most vertebrates is the **optic lobe**, or **optic tectum**, so named because of the large number of neurons of the optic nerve that terminate in it. The ventral portion of the mesencephalon, the region underneath the optic tectum, is known as the **tegmentum**. The

mesencephalic tegmentum contains a number of nuclei and fiber tracts, including the nuclei of two of the cranial nerves that control the movements of the eyes. The operation of the intraocular eye muscles, which control the pupil and the focus of the lens, are controlled from this region as well.

Forebrain. The **prosencephalon** or **forebrain** is the most rostral division of the brain. It contains two major parts: the **diencephalon** and the **telencephalon**. The diencephalon (= interbrain) lies rostral to the midbrain, caudal-ventral to the telencephalon, and medial to the axons that form the optic tract, the central nervous system continuation of the optic nerve. The diencephalon is a large division composed of six principal areas. The caudal part of the diencephalon contains a dorsal area called the **pretectum** and a more ventral area called the **posterior tuberculum**. More rostrally, four areas are present. In dorsal to ventral sequence, these areas are the **epithalamus**, the **dorsal thalamus**, the **ventral thalamus**, and the **hypothalamus**. Each of these areas are composed of a number of nuclei, and there are also major fiber tracts that pass through this region.

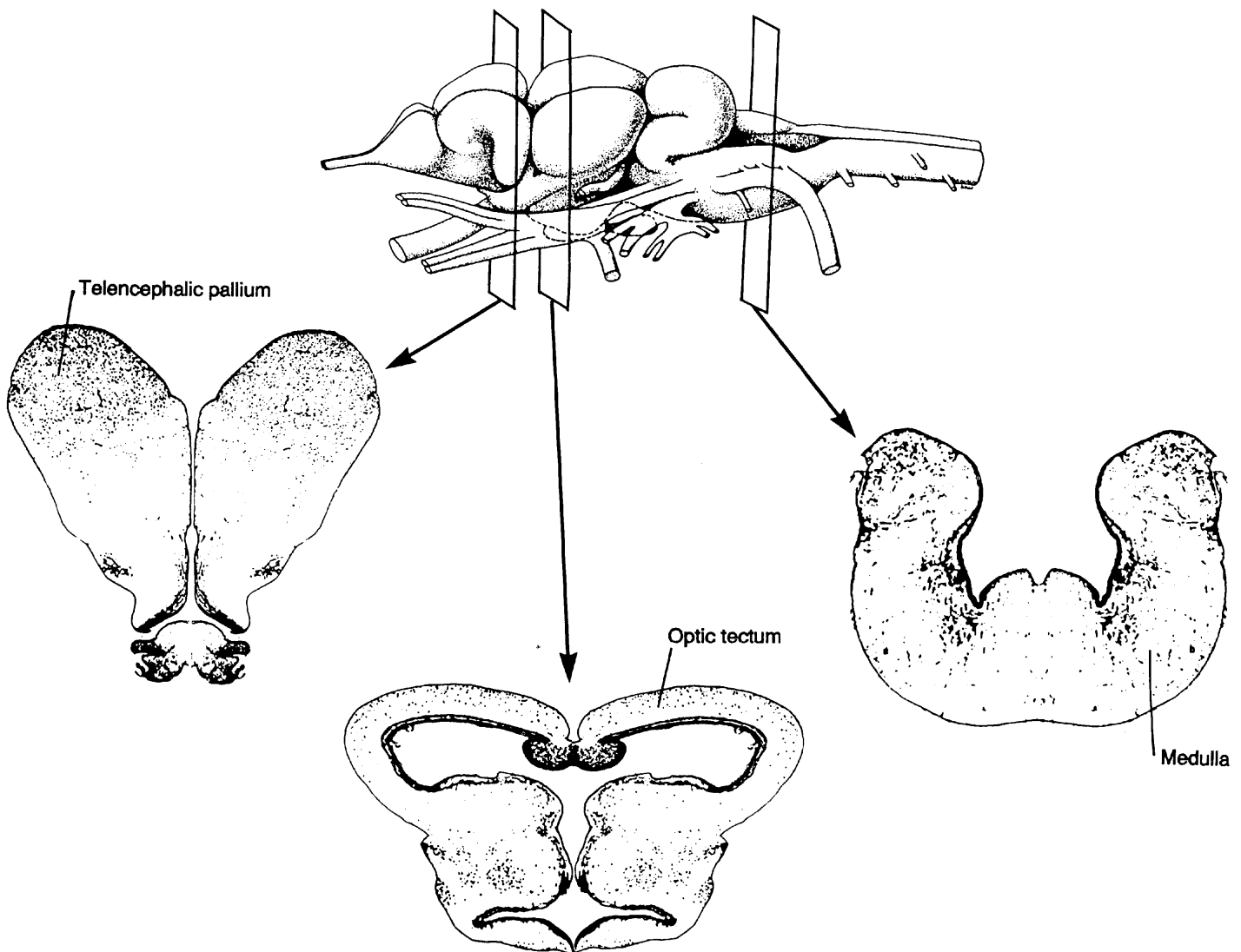


FIGURE 3-5. The brain of the longnose gar, as shown in Figure 3-4, with transverse sections through the telencephalon, midbrain, and hindbrain.

An additional neuroanatomical term frequently encountered is **brainstem**. This term sometimes refers to the more ventral parts of the brain except for any part of the telencephalon, that is, to the medulla and pons, the midbrain tegmentum, and the diencephalon. It is alternatively used to refer only to the medulla, pons, and midbrain tegmentum (and sometimes the midbrain tectum) without including the diencephalon. Context must be used to determine the specific sense in which this somewhat loose term is being used.

A number of the nuclei in the pretectum receive visual input from the retina and are involved in visuomotor behaviors. Pretectal nuclei and other visually related nuclei in the tegmentum influence eye movements in relation to prey and predator detection and to orientation of the body within space. The posterior tuberculum consists in part of a medially lying nucleus that contains neurons involved in regulating motor functions. In ray-finned fishes, more laterally lying nuclei of the posterior tuberculum are also present. These nuclei relay sensory inputs to the telencephalon. Similar nuclei may be present in cartilaginous fishes, but migrated posterior tubercular nuclei have not yet been identified in amphibians or land vertebrates.

The nuclei in the dorsal thalamus receive information via long-axon interneurons from the various sensory systems, which they transmit to various parts of the telencephalon. The nuclei in the dorsal thalamus constitute a gateway to the sensory areas of the telencephalon. A number of different parts within the telencephalon are involved in integrating the incoming sensory information for learning, memory, emotional responses, and motor responses.

Nuclei in the ventral thalamus are involved in modulating the activity of dorsal thalamic nuclei and also play a role, in concert with telencephalic structures, in motor control of the body and limbs. The epithalamus contains the **epiphysis** (pineal gland and related structures), which is located at the end of a stalk, the epiphyseal stalk. In some animals, such as reptiles, the pineal is a structure very similar to the eye. It contains light receptors and gives rise to primary sensory afferent neurons, which terminate in the epithalamus. In mammals and birds, the pineal is a glandular structure.

The hypothalamus is very much involved in the activities of the autonomic nervous system and the endocrine system. It controls the endocrine system's production of hormones by means of the **hypophysis** or **pituitary**, which is directly connected to the hypothalamus. The pituitary is located at the end of a stalk, the **infundibulum**, which is a direct outgrowth of the base of the hypothalamus. The hypothalamus thus is able to control and regulate behavior patterns that depend on the levels of hormones in the blood, such as sexual behavior, parental behavior, territoriality, migration, and hibernation, to name but a few. The hypothalamus also is concerned with feeding and drinking, aggression, temperature regulation, and a number of other important biological and behavioral functions.

The most rostral region of the brain, the **telencephalon** (Figs. 3-4 and 3-5), includes the **dorsal pallium**, or **cerebral hemisphere** (also called the **cerebrum**). At the rostral end of the cerebrum is the **olfactory bulb**, in which axons of olfactory receptor cells in the nasal mucosa terminate. In animals in which the sense of smell is highly developed, such as some sharks and bloodhounds, the olfactory bulb is rather impressive in size. In animals such as many birds and some mammals, in

which the sense of smell is not especially important for survival, the bulb is relatively small in comparison. The olfactory bulb projects to the **olfactory pallium** in the telencephalon via **olfactory tracts**, which can be short if the olfactory bulb lies adjacent to the telencephalon (as in the brain of the fish shown in Fig. 3-4) or elongated.

The cerebrum itself has a relatively smooth surface in most vertebrates. It is composed of nuclear areas in some vertebrate groups, such as cartilaginous and ray-finned fishes; in other vertebrate groups, particularly tetrapods, it is composed of both nuclei and cortex. In some animals, mostly among the mammals, although there are other instances as well, the surface of the cerebrum develops deep ridges and valleys known as convolutions. The ridges are called **gyri** (singular = **gyrus**) and the valleys are called **sulci** (singular = **sulcus**). The deepest of the sulci are known as **fiures**.

The telencephalon also includes several other major areas. The **limbic pallium** comprises a set of structures that include a cortical area known as the **hippocampus**, which is necessary for memory and is also involved in emotion. The hippocampus and some nuclei related to it, including the **septal nuclei** and **amygdala**, receive olfactory information from other telencephalic areas, which is integrated with other inputs. Several additional major areas lie in the more ventral part of the telencephalon and are involved with motor functions. These areas are collectively called the **striatum**, or **striatal nuclei**. They are interconnected with motor areas of the dorsal pallium and with nuclei in the more caudal parts of the brain.

The Meninges and the Ventricular System

The brain and spinal cord are covered by one or more layers of connective tissue, which are called the **meninges**, from the Greek word **meninx**, which means membrane. In fishes, only a single layer, the **primitive meninx**, is present. Amphibians and reptiles have two meningeal layers, an outer **dura mater** (meaning "hard mother") and an inner thin layer, the **secondary meninx**. In mammals and birds, three meningeal layers are present. The layer closest to the brain is a thin, vascular layer called the **pia mater** (meaning "tender mother"). The middle layer is a thin, avascular layer called the **arachnoid** due to its spider web-like appearance. The space between the pia mater and the arachnoid is the **subarachnoid space**. The outermost layer is the **dura mater** and is actually composed of two layers: an inner layer enclosing the central nervous system and an outer layer that lines the inside of the skull. The use of the word "mother" to describe these membranes comes from an ancient notion that they were the origin, or mother, of all membranes in the body.

Embryologically, the central nervous system develops from a hollow tube. The walls of the tube thicken to form the brain and spinal cord, and the hollow within the tube becomes the fluid-filled **ventricular system** of the adult. Instead of remaining a straight tube of uniform diameter, the ventricular system extends laterally into the variously expanded parts of the brain in different vertebrate groups, such as the olfactory bulbs, telencephalic hemispheres, the midbrain roof, and/or the cerebellum. This arrangement is shown in Figure 3-6.

In most groups of vertebrates, the ventricular system expands laterally within each of the telencephalic hemispheres,

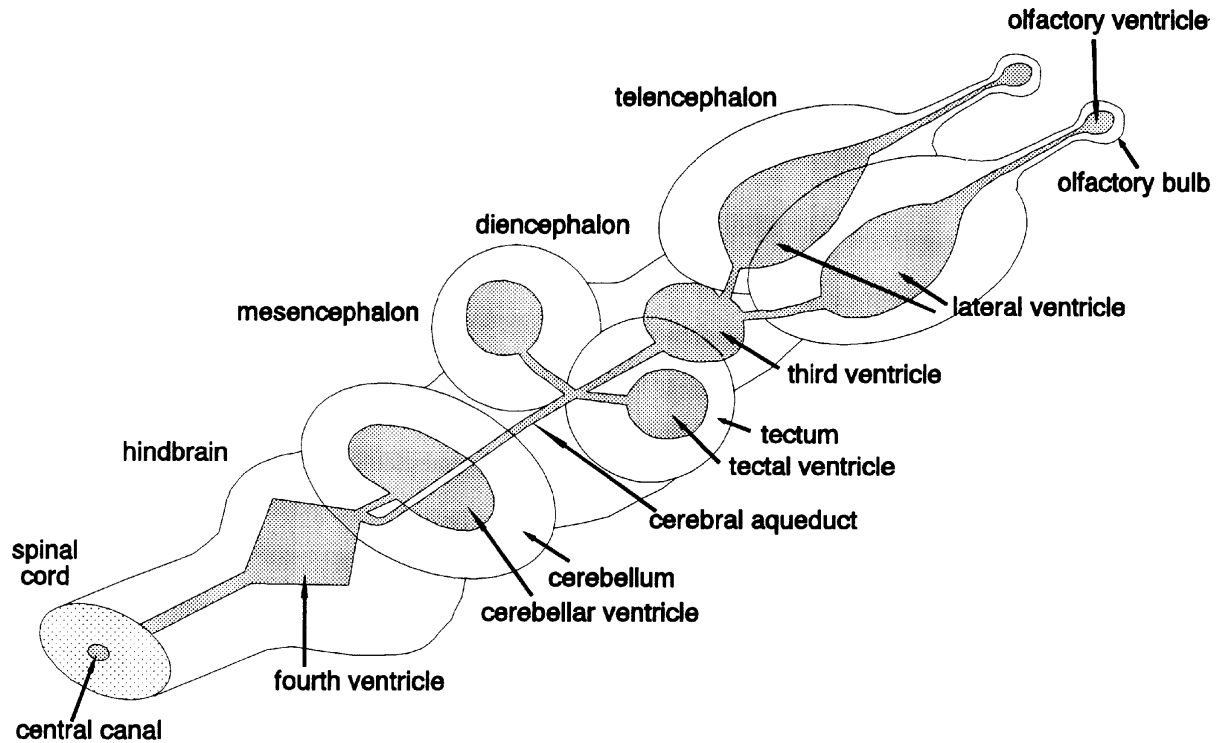


FIGURE 3-6. Dorsolateral schematic drawing of a vertebrate brain with the ventricular system, indicated by shading, projected onto it. Rostral is toward the upper right.

and this pair of laterally extending spaces are called the **lateral ventricles**. The lateral ventricles are in continuity, through paired openings called the **foramina of Monro**, with the unpaired, medial ventricular space of the diencephalon, called the **third ventricle**. The caudal continuation of the third ventricle is a narrow canal called the **cerebral aqueduct of Sylvius**, which in turn opens into the **fourth ventricle**, the unpaired, medial ventricular space of the hindbrain. The fourth ventricle is caudally continuous with the **central canal** of the spinal cord.

Parts of the ventricular walls consist of a thin ependymal epithelial layer and an inner, vascular meningeal layer, which together form the **tela choroidea**. A network formed by the blood vessels of the inner meningeal layer, called the **choroid plexus**, secretes **cerebrospinal fluid** into the ventricular spaces. The cerebrospinal fluid circulates in the ventricular system and also in the subarachnoid space; it reaches the latter by passing through three openings that connect the fourth ventricle with an enlarged part of the subarachnoid space, the **cisterna magna**. The three openings are a paired set, the **foramina of Luschka**, and an unpaired, medial foramen; the **foramen of Magendie**. After circulating, the cerebrospinal fluid passes out of the subarachnoid space into vascular sinuses through structures in the arachnoid called **arachnoid villi**, which act as one-way, pressure-sensitive valves. The cerebrospinal fluid provides support for the brain and cushions it from physical shocks by its buoyancy.

is relayed through various nuclei, being modified and sorted along the way. In later chapters, which cover various parts of the brain, a general idea of the basic organization of these systems will help you to make sense of the anatomy.

Sensory Systems

All of the receptors for touch, radiant-energy sense, pain, lateral line (for wave displacement and electrical field detection), hearing, vestibular sense, and gustatory sense have their initial points of termination within the central nervous system either in the spinal cord or in the medulla-pons region of the brain. The target cell populations of these primary pathways then project to more rostral levels of the brain. Most of the axons in the primary sensory pathways from the eyes terminate in part of the dorsal thalamus in the diencephalon and in the optic tectum. The olfactory pathways, in contrast to the more caudal sensory pathways, project directly into part of the telencephalon. Topographic organization is an important characteristic of all of these pathways; this feature provides for orderly maps of the sensory input within particular parts of the brain that correspond to the spatial map of the external world.

Each of the ascending sensory pathways to the telencephalon terminates in its own segregated region of the telencephalon. From here begins the complex and varied series of possible pathways that are the routes to other sensory, integrative, and motor systems. Functions including memory storage of sensory events and the consequences of reactions to them, decision making about subsequent reactions to such events, and the conscious awareness of these events reside within the telencephalon. In order to gain a general understanding of how ascending sensory systems are organized, we will briefly outline three of them here: the **auditory**, the **visual**, and the **somato-**

MAJOR SYSTEMS OF THE BRAIN

We now want to give you a very brief overview of some of the major systems of the brain. As we have discussed above, there are major sensory and motor systems in which information

sensory, which includes touch and position sense from the body.

The Auditory Pathway. In the auditory pathway, axons arise from neurons in the inner ear and pass into the brain in the **eighth (octaval) cranial nerve**. These axons synapse on the dendrites of neurons in an auditory nucleus in the hindbrain [Fig. 3-7(A)]. The neurons in this nucleus give rise to axons that pass rostrally in a tract (called the **lateral lemniscus**) and synapse on the dendrites of neurons within a part of the midbrain roof called the **torus semicircularis** in most vertebrates and the **inferior colliculus** in mammals. The torus semicircularis lies ventral and/or caudal to the optic tectum. Neurons within the torus semicircularis give rise to axons that terminate on the dendrites of neurons in an auditory nucleus in the dorsal thalamus. Neurons in the dorsal thalamic auditory nucleus give rise to axons that pass into the telencephalon (via tracts called the **forebrain bundles**) and terminate on the dendrites of neurons within one or more auditory regions of the dorsal pallium.

The Visual Pathways. Neurons in the retina give rise to axons that enter the brain via the **optic nerve** [Fig. 3-7(B)] and its continuation, the **optic tract**. The retinal axons terminate on the dendrites of neurons located either in the **optic tectum** of the midbrain (called the **superior colliculus** in mammals) or in a visual nucleus in the dorsal thalamus. Visual neurons in the optic tectum also give rise to axons that terminate on the dendrites of neurons in a second visual nucleus in the dorsal thalamus. Neurons in each of the two visual dorsal thalamic nuclei give rise to axons that pass into the telencephalon via the forebrain bundles and terminate on the dendrites of neurons in two or more visual areas within the dorsal pallium.

The Somatosensory Pathways. Axons that carry somatosensory information [Fig. 3-7(C)] enter the spinal cord and pass rostrally to terminate on the dendrites of neurons within two cell groups called the **dorsal column nuclei**. These nuclei lie in the junctional area between the spinal cord and the brainstem. Neurons in the dorsal column nuclei give rise to axons that pass rostrally in a tract called the **medial lemniscus**. Some of these axons terminate on the dendrites of neurons in a somatosensory part of the midbrain tectum. Other somatosensory axons from the dorsal column nuclei bypass the midbrain and terminate on the dendrites of neurons in a somatosensory nucleus in the dorsal thalamus. Neurons in the somatosensory part of the midbrain also give rise to axons that pass rostrally and terminate on the dendrites of neurons in a second somatosensory nucleus in the dorsal thalamus. Neurons in each of the two dorsal thalamic somatosensory nuclei give rise to axons that pass into the telencephalon via the forebrain bundles and terminate on the dendrites of neurons in two or more somatosensory areas within the dorsal pallium.

In the telencephalon, sensory information is relayed through multiple sets of long- and short-axon interneurons—to secondary, tertiary, and further sensory and association cortical areas, into the limbic system for memory, into multisensory association cortices for integration, and so on. When the information has been processed and assimilated, appropriate motor responses follow.

Motor Systems

Complex control mechanisms for motor responses derive from neurons in the motor pallial areas of the telencephalon, and/or from neurons in other dorsally lying structures, such as the roof of the midbrain and the cerebellum. Motor responses are also regulated by a number of structures including the **striatum**, also known as the **basal ganglia**, in the ventrolateral part of the telencephalon [Fig. 3-7(D)] and nuclear areas within the hindbrain. Mammals have motor neurons in the dorsal pallium of the telencephalon that give rise to axons that terminate on the dendrites of neurons within the striatum. In turn, neurons within the striatum give rise to axons that pass caudally and terminate within a number of nuclei in the brainstem, including a nucleus in the diencephalon. Neurons in the latter nucleus give rise to axons that terminate on the dendrites of neurons within the midbrain tectum.

Other neurons within the motor part of the dorsal pallium (long-axon interneurons) pass caudally via the same major bundles in which sensory axons ascend: the forebrain bundles. These axons collectively form a tract that is rather like a major interstate highway. They pass caudally to synapse on the dendrites of neurons within nuclei in the midbrain and the brainstem and, in some cases, directly on the dendrites of neurons in the spinal cord. The midbrain tectum also gives rise to axons that pass caudally in a tract called the **tectospinal tract** and terminate on the dendrites of neurons in brainstem motor nuclei and in the spinal cord. Motor nuclei of the cerebellum similarly contain neurons that give rise to axons that pass ventrally to terminate on the dendrites of neurons within brainstem nuclei. Neurons in the various brainstem motor nuclei give rise to axons that pass caudally and terminate on the dendrites of neurons in the spinal cord. The reticular formation of the brainstem is composed of a number of different nuclear areas that also are involved in these descending motor pathways.

DEVELOPMENT OF THE BRAIN

During the embryological development of the brain from the neural tube, the rostral part of the brain flexes ventrally [Fig. 3-8(A)]. A transverse, ventral fold develops on the ventral surface of the tube in the position where the pituitary gland will form. A pair of lateral bulges in the rostral part of the forebrain forms the cerebral hemispheres of the telencephalon. More caudally, the eyes grow out of the diencephalon, and the pineal gland develops in the dorsal part of the diencephalon [Fig. 3-8(B)].

The midbrain lies caudal to the ventral fold in the neural tube. Paired bulges in the roof of the midbrain expand to form the optic tecta (plural of tectum), or roof of the midbrain, while the more ventral part of the midbrain becomes the tegmentum (the main body of the midbrain). The dorsal portions of both the caudal midbrain and the rostral hindbrain enlarge to form the cerebellum [Fig. 3-8(B)].

Within the neural tube, a layer of **neurogenic cells** gives rise to the neurons. The neurogenic cells encircle the ventricular lumen. As neuron cell bodies are produced, they migrate away from the region of the lumen. The degree of migration differs markedly among different vertebrates and in different regions

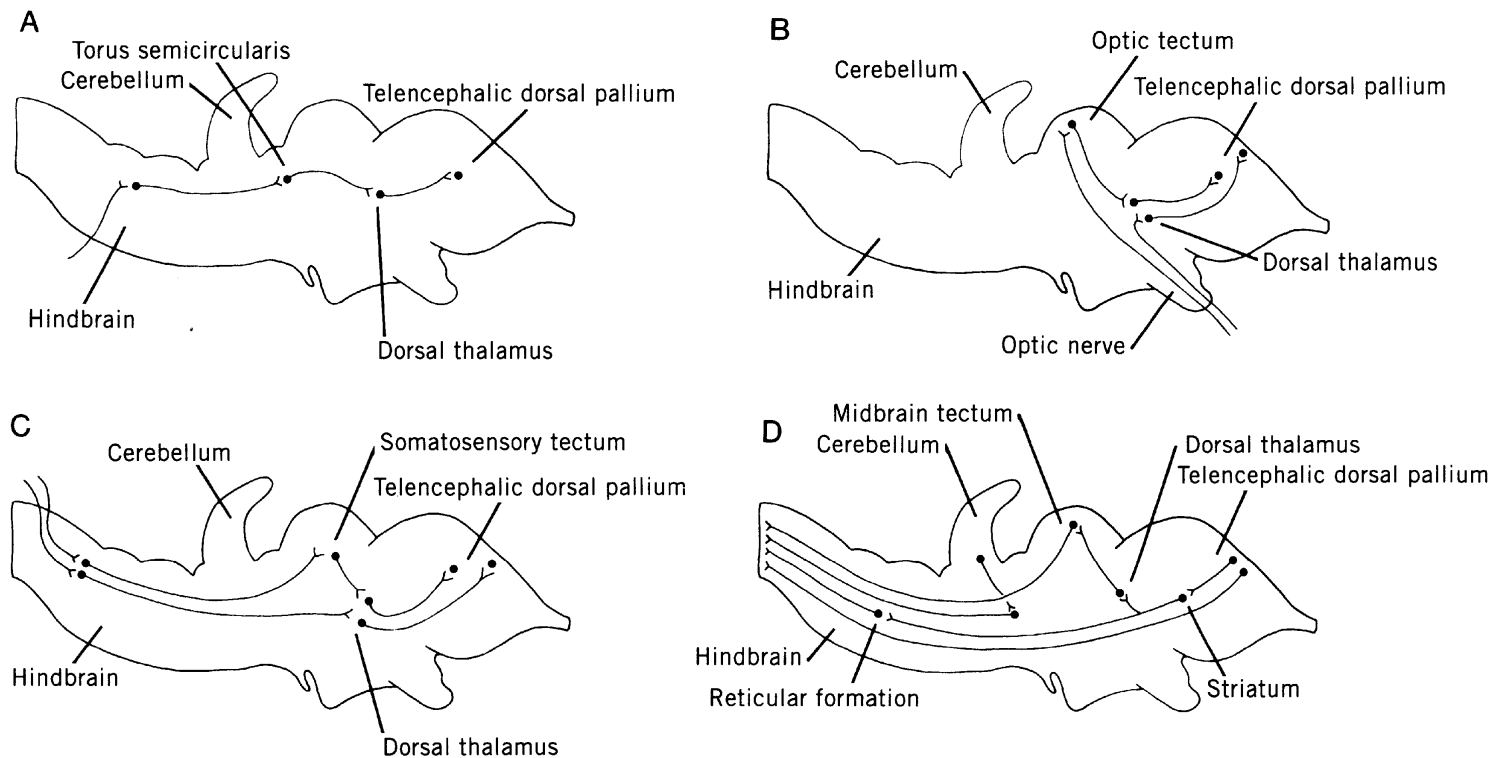


FIGURE 3-7. Schematic representation of the major sensory and motor pathways. Rostral is toward the right. Dots represent neuronal cell bodies, and lines represent the axons of the cell bodies with their terminal endings. Dendrites of cell bodies, on which the axons actually synapse, are not represented. (A) Ascending auditory pathways; (B) the two major ascending visual pathways; (C) the two major ascending somatosensory pathways; and (D) some of the descending motor pathways.

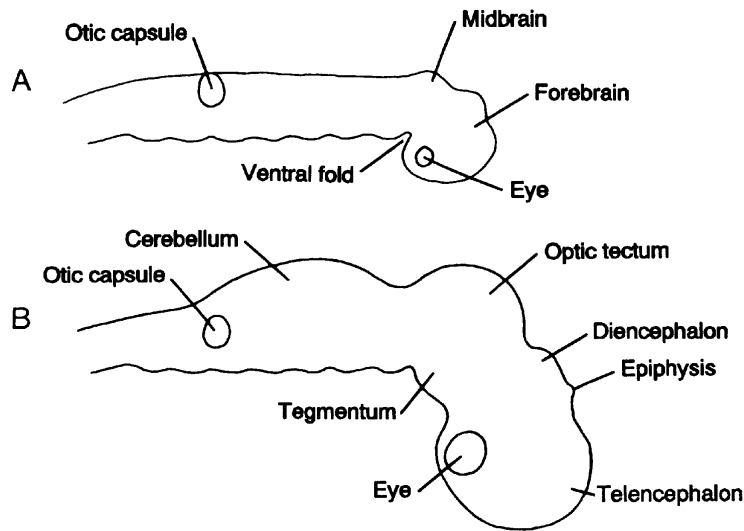


FIGURE 3-8. Diagram of the flexure of the neural tube during formation of the brain.

of the brain. The pattern of migration also varies, with nuclei and cortices being formed in different ways. In this section, we will examine some of the various ways in which the neurons are assembled into structures within different regions of the brain and among different groups of vertebrates.

The developmental processes involved in producing the individual neurons and their connections are complex and also subject to disruption by both local factors and more external influences. The timing of sequences in multiple groups of neurons must be properly phased for normal development to occur. The production and migration of populations of neurons to form nuclei and cortices also occurs in specifically timed sequences, since targets must be established for the growing, incoming axons to locate and reach.

Cortices and Nuclei

As we discussed above, two basic structural patterns for populations of neurons are **cortices**, which are laminated structures that tend to be located in the more dorsal parts of the brain, and **nuclei**, which are prevalent in the rest of the brain. Nuclei may consist of diffusely scattered, either loosely or more tightly packed cells or of cells aligned in a laminar pattern, reminiscent in some cases of cortex.

Cortical areas such as the cerebral cortex in mammals and the optic tectum in many vertebrates are formed by serial migrations of generated neurons. In the mammalian cerebral cortex, neurons that eventually lie in the outermost (layer I) and innermost (**subplate**) layer are produced first, but for the layers that form the bulk of the cortex, the sequence of production is altered. For most of the cortical layers, the neurons that lie nearer to the periventricular germinal zone (matrix) in the adult are produced earlier than those that lie nearer to the outermost layer of the cortex. The subsequently produced sets of neurons migrate through the layers of neurons formed earlier. This pattern of migration is called "**inside-out**." Following this series of migrations, which result in particular sets of neurons lying in particular layers, growth of axons and dendrites occurs, and connections, both distant and local, are established.

A component of the guidance system for afferent cortical axons has been found within the cortex. The distal end of each in-growing afferent axon is a specialized structure called a **growth cone**, which is the site of elongation of the axon. The deepest layer of cortical neurons, produced first and called the subplate, normally disappears by cell death after the axons from cells in the dorsal thalamus reach their appropriate cortical areas. The axons arrive before their main target cell layer (layer IV) has been generated, but they wait for these target cells to be formed and do not grow beyond that area. However, if the subplate cells are selectively destroyed, the arriving dorsal thalamic axons do not halt in the proper position but continue growing beyond their normal area of termination and on into adjacent, unrelated areas of cortex. The subplate cells thus seem to provide a necessary sign post for the growth cones of the afferent dorsal thalamic axons.

There is a high degree of specificity in the connections of cortical structures, made possible by their geometric configuration. Different afferent neurons terminate on different, specified parts—superficial to deep—of the dendritic trees of the cortical neurons. The entire area of a given cortical region is also frequently in receipt of specifically ordered projections, so that the point-to-point mapping of sensory or motor space from the external world of the animal is mapped in order onto the cortex. In-growing axons may sometimes form connections in the wrong location with reference to the map, but these axons later retract and then form connections in the place that is congruent with the map of external space. These adjustments occur as sensory information comes over the afferent axons and into the cortex.

The nuclei in the brain, as well as some of the cortices, are formed by cellular migrations that proceed in an "**outside-in**" pattern, the opposite of that in the mammalian cerebral cortex. In this case, the more superficial, lateral groups of neurons are generated first. There are additional spatiotemporal gradients that have been identified in the dorsal thalamus. Caudal nuclei develop earlier than more rostral ones, and ventral nuclei earlier than more dorsal ones. Thus, different areas of the periventricular matrix give rise to different sets of nuclei at different times.

While nuclei form by different migration patterns than in some cortices, a number of nuclei have point-to-point maps that correspond to those found in cortex. The nuclei that have such maps are generally those that project to or have reciprocal connections with cortical, mapped areas. In mammals, the **dorsal lateral geniculate nucleus**, the dorsal thalamic nucleus that projects to primary visual cortex, has a point-to-point map of visual space in each of its multiple, separate layers of cells. A similar map is present in a midbrain nucleus of many vertebrates, **nucleus isthmi**, which has reciprocal, point-to-point projections with the optic tectum. Maps are also established and maintained in other ascending sensory systems, including the auditory and lateral line systems and the somatosensory system.

As nuclei are formed by migrations of cells, given regions of the periventricular matrix may give rise to one or more specific nuclei. Such a region is called a “**field**.” The number of distinct nuclei that arise from a given field may be different in different groups of vertebrates. Also, all the cells or cell groups produced by a field during development may not be retained in the adult if the proper connections are not made at the proper time. Such occurrences would affect the phenotype and may well play a role in evolutionary change. A subtle alteration in timing or in the presence or absence of local molecular cues, produced by a mutation established in the genome, could result in the lack of a particular cell group in the adult and/or the appearance of a “new” cell group with new connections.

Differing Patterns of Development

Within each of the major groups of vertebrates, one marked difference in brain development is present that will be discussed in detail in Chapter 4—that of wide variation in the degree of migration of neurons, both cortical and nuclear, away from the periventricular matrix. Those vertebrates in which relatively limited migration occurs, that we have designated as Group I, include some species from each of the four major vertebrate radiations: agnathans (jawless vertebrates), cartilaginous fishes, ray-finned fishes, and sarcopterygians (fleshy lobed-finned fishes and their tetrapod descendants). Other species in each of the same four radiations (Group II) have much more extensive migration of neurons and the formation of multiple, distinct layers in cortical structures as well as a greater number of discretely recognizable and larger nuclei. Two other major differences in the development of the brain among different verte-

brates will be considered in this chapter. These developmental differences result in marked differences in the organization of the telencephalon.

In the initial phase of development from the closed neural tube, the telencephalon develops by a process called **evagination** in most vertebrates, that is, agnathans, cartilaginous fishes, and amphibians and amniotes. The central lumen of the neural tube enlarges to form the telencephalic ventricles as the pallial (dorsal) part of the telencephalon bulges outward and expands, that is, evaginates. This process is shown in Figure 3-9. Following evagination, the part of the pallium that was originally in the most dorsal position (A) around the central lumen comes to lie in the most medial part of the telencephalon. This pallial area forms the hippocampal formation and limbic pallium (the functions of which include memory and emotion) in the adult. The originally intermediate pallial area (B) becomes the dorsal pallium, which forms the major sensory, integrative and motor pallial areas in the adult. The originally most ventral pallial area (C) comes to lie most laterally and gives rise to the olfactory pallium.

In contrast, a different process takes place in the development of the telencephalon in ray-finned fishes. This process is called **eversion**. The part of the roof of the neural tube over the central lumen thins and elongates, and the hemispheres bend outward (Fig. 3-10). Following eversion, the originally most dorsal part of the pallium (A) comes to lie in the most lateral position in the telencephalon. The originally intermediate part of the pallium (B) lies most dorsally, as in other vertebrates. The originally most ventral pallial area (C) comes to lie in the most medial position in the telencephalon of the adult. Thus, in comparison with other vertebrates, the mediolateral positions of the hippocampal (A) and olfactory (C) pallial areas are reversed in the ray-finned fishes. The areas in the basal part of the telencephalon are similarly aligned in all vertebrates, as this region does not undergo either evagination or eversion (Figs. 3-9 and 3-10).

A second major difference in telencephalic development occurs between the mammals on one hand and the nonmammalian amniotes on the other. The dorsal part of the evaginated pallium (B in Fig. 3-9) forms the regions of six-layered cortex called **neocortex**, or **isocortex**, in mammals (Fig. 3-11), which occupies the bulk of the cerebral hemispheres. In diapsid reptiles, birds, and turtles, part of the dorsal pallium also forms a superficial cortical area, but a larger part expands in a medial

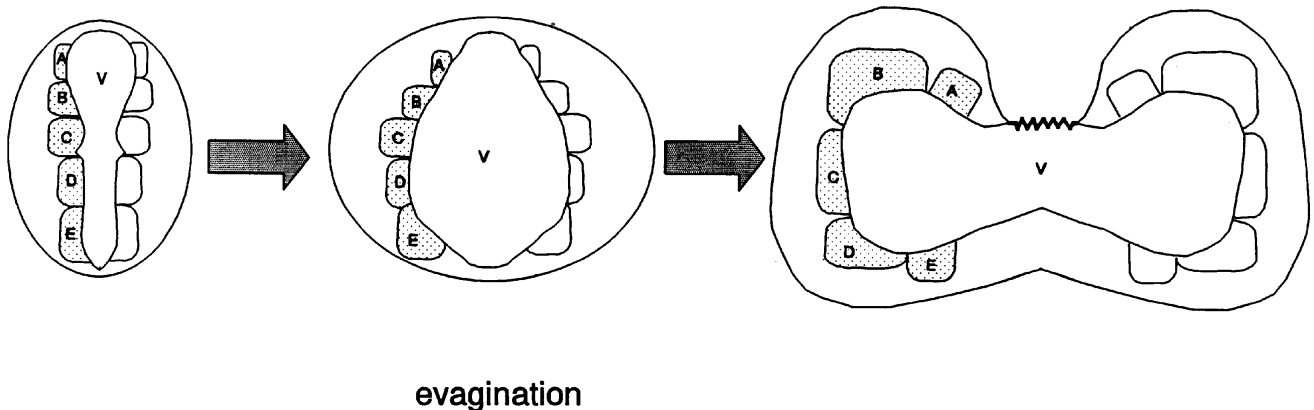


FIGURE 3-9. Diagram of the process of evagination in forebrain development, as occurs in most groups of vertebrates.

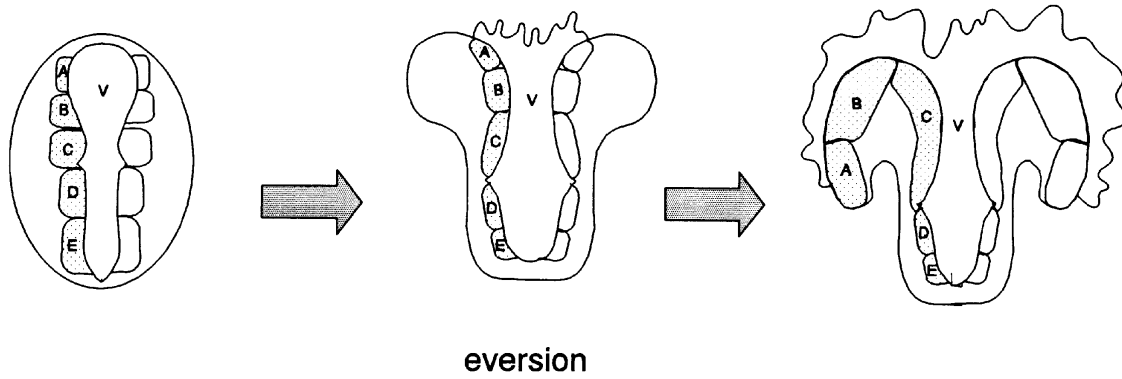


FIGURE 3-10. Diagram of the process of eversion in forebrain development, as occurs in ray-finned fishes.

direction to form a large, nuclear area called the **dorsal ventricular ridge** (Fig. 3-11). The dorsal ventricular ridge was long thought to represent a huge, basal telencephalic area for use in stereotyped motor behaviors, but many connectional and histochemical studies support the hypothesis that a large part of it is homologous as a collection of several embryologically derived fields to respective areas of part of mammalian isocortex.

The differences in the organization of both evaginated versus everted telencephalons and isocortex versus the dorsal ventricular ridge are differences of the topography of various groups of neurons. As discussed above, growth cones of axons require various local guidance cues in order to grow along the right path and reach their target. Developing dendrites require

the arrival of afferent axons within the proper time frame to continue developing and be maintained. Developmental differences can produce grossly different topographical relationships of areas in the telencephalon, but the other, multiple developmental factors necessary for the establishment of connections are obviously unaffected and sufficient despite the alterations of topography in these cases.

Ontogeny and Recapitulation

In closing this chapter, there is one final aspect of brain development to consider briefly. One of the most pervasive of "old wives' tales" is the notion that ontogeny recapitulates phylogeny: in other words, that the developmental sequence

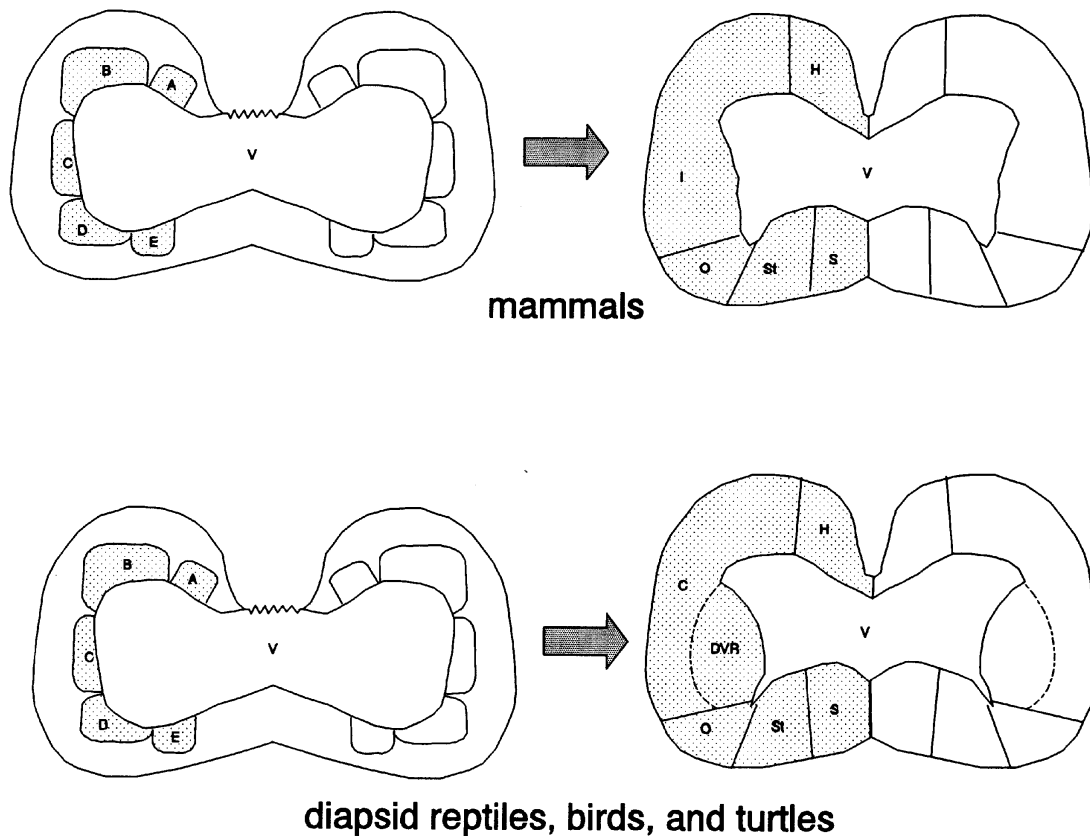


FIGURE 3-11. Diagram of the differential development of the dorsal pallium (indicated by the letter B) in mammals versus diapsid reptiles, birds, and turtles. Abbreviations: C, cortex; DVR, dorsal ventricular ridge; H, hippocampal formation; I, isocortex; O, olfactory cortex; S, septum; St, striatum; V, ventricle.

is a kind of rerun of the species' evolutionary history. In the late 1800s, Haeckel promoted the idea that evolutionary change results from the addition of new ontogenetic stages to the terminal phase of the ancestor's development. Such **terminal additions** to existing sequences of development would be the basis of ontogeny recapitulating phylogeny. Terminal additions do, in fact, occur in phylogeny, but the sequence of development in vertebrate brains does not recreate adult ancestral stages of the species' evolutionary history.

From our analysis of differences in the development of the telencephalon, we can see that for ontogeny to recapitulate phylogeny, particularly in terms of the now discredited *scala naturae*, a highly improbable series of events would have to occur to produce the brain of an adult mammal. The telencephalic pallium would first have to evaginate, as in agnathans and cartilaginous fishes, then undo the evagination and evert as in ray-finned fishes, then undo the eversion and evaginate as in amphibians, and finally have all of the dorsal pallium develop into isocortex. Nevertheless, attempts persist to perceive a recapitulation of phylogeny in ontogenetic sequences, as with long projection neurons developing before locally projecting ones and motor neurons before sensory ones. Many of these attempts are based on erroneous *scala naturae* thinking and also fail to take into account the multitude of features that were gained quite suddenly with the evolution of neural crest and placodes (see Chapter 9) in ancestral chordates.

As in many incorrect ideas, there nonetheless is a grain of truth in the ontogeny-phylogeny idea. In the early 1800s, Karl von Baer realized that developmental sequences do not recreate stages from "lower" to "higher" groups of animals. He did note, however, that resemblances occur among embryos within a group, and that the resemblances decrease as development proceeds. von Baer concluded that those features that are common to a group appear earlier in development than the more specialized features of individual taxa within the group. Thus, in the development of the brain of a seagull, for example, we would expect features common to chordates to develop first, followed by features common to vertebrates, and so on in sequence through features common to jawed vertebrates, sarcopterygians, tetrapods, amniotes, birds, and finally seagulls. von Baer thus believed that over evolution, there is conservation of a number of developmental stages. This concept is referred to as "**von Baerian recapitulation**," and a growing body of data supports it.

The von Baerian view makes sense when we note that adult phenotypes are produced by a series of ontogenetic sequences. Changes over evolution in the phenotype are the direct result of changes in the ontogenetic sequences, which in turn are produced by mutations established in the genome. Features that are common to all vertebrates, such as the neural tube, arise before more specialized features present only in one radiation, such as the dorsal ventricular ridge in nonmammalian amniotes. Given the complexity and interactions of developmental events, modifications in early sequences would have much more profound, and in most cases disruptive, effects than modifications in later sequences. The reduction of particular systems and the maintenance of neotenic (embryonic) characteristics in the adults of some groups may in fact result from relatively early modifications in the rates of cell proliferation and differentiation.

Although later modifications constitute terminal or near terminal additions, the radiations of extant vertebrates have been separated long enough that such terminal additions reflect their independent histories rather than allowing for the construction of a single line of evolutionary history. Differences in the development of the telencephalon between the major vertebrate radiations, as well as marked differences in the degree of migration of cells from the periventricular matrix within all four major radiations, clearly demonstrate the separateness and independence of the radiations over a long period of time. On the other hand, those features that are common to most or all groups, in developmental structures and sequences and in the adults, can be used to reconstruct the condition of the brain in the common ancestral vertebrate stock.

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