15

Overview of the Midbrain

INTRODUCTION

In all vertebrates, a group of structures collectively known as the midbrain, or mesencephalon, links the sensory, motor, and integrative components of the hindbrain with those of the forebrain. The midbrain contains three major regions: the **tectum,** the **tegmentum,** and the **isthmus** (Fig. 15-1). One important feature of the midbrain is the presence of areas within the tectum, or roof, that receive topographically organized projections from the auditory, visual, and somatosensory systems, which form maps of the animal's sensory space. A second feature of the midbrain is the presence of nuclei intrinsic to the region and of ascending and descending fiber tracts that pass through it. Finally, like the hindbrain, the midbrain also contains several nuclei that control the distribution of certain critical neurotransmitters to other brain regions.

The tectum contains laminated structures—particularly the **optic tectum** and the **torus semicircularis.** The optic tectum receives its major input from the optic tract, which is the central continuation of the optic nerve. The optic tectum is involved in integrating the spatial aspects of visual and other sensory inputs and with spatially oriented motor responses. The torus semicircularis receives its major input from ascending auditory projections and, where present, from the lateral line system. The sensory maps in the midbrain roof are in register with each other; thus, visual and somatosensory stimuli, for example, that arise from the same part of the space around the animal result in neuronal activity in the same part of the optic tectum. Auditory stimuli are mapped onto parts of the torus semicircularis that are interconnected in a point-to-point manner with parts of the optic tectum that likewise correspond in spatial register. Both the optic tectum and the torus semicircularis project rostrally to nuclei in the dorsal thalamus.

The main part of the midbrain tegmentum lies ventral to the tectum and is separated from the hindbrain by a transitional area called the isthmus, or isthmal tegmentum. Parts of the tegmentum consist of the rostral continuations of areas present in the hindbrain: the reticular formation, the somatic motor and other columns of cranial nerve nuclei, and ascending and descending fiber systems. Additional nuclei, related to visuospatial functions, motor activities, ascending feedback for the integration and adjustment of motor activities, and relay to the forebrain of ascending sensory information, are also present. The midbrain tegmentum is thus a gateway (or clearinghouse) for incoming sensory information and outgoing motor responses to and from the forebrain. It assists the more rostral parts of the brain with analysis and modulation of the information.

In some species, especially in those with more laminar brains (Group I: see Chapter 4), not many experimental studies of connections have been done on tegmental nuclei. In these cases, we frequently do not yet know which populations of the cells that lie along the ventricular surface may project to a specific target and thus may correspond to particular nuclei in animals with more elaborated brains. Pinpointing these groups of cells must await future studies, but we need to note that a greater number of nuclei are present in these brains than can be identified for now. Specializations of nuclei and areas in the brainstem occur in correlation with the presence of specialized capabilities such as electroreception, motor adaptation for specialized forms of swimming, and motor adaptations for locomotion on land. In this chapter, we will present a generalized overview of the structures and systems of the isthmus, the tegmentum proper, and the tectum.

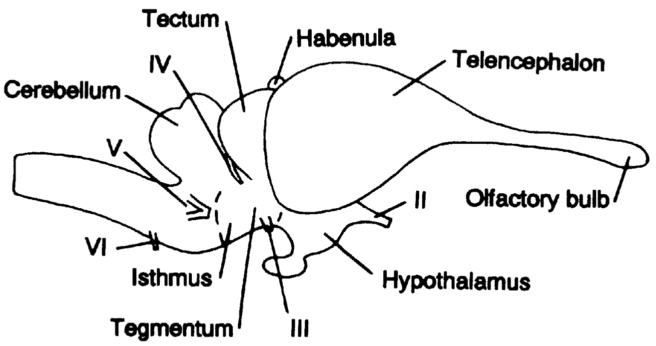

FIGURE 15–1. Lateral view of the brain of a crocodile, with the approximate boundaries of the isthmus, tegmentum, and tectum indicated by broken lines. Cranial nerves are indicated by Roman numerals. Data from ten Donkelaar and Nieuwenhuys (1979). Used with permission of Academic Press, Ltd.

THE ISTHMUS

The isthmus lies at the rostral end of the hindbrain. Within the isthmus are rostrally projecting cell groups, such as the locus coeruleus and raphe, cranial nerve nuclei including the trochlear, oculomotor, and mesencephalic nucleus of the trigeminal nerve, and the rostral parts of some of the structures of the hindbrain, such as the reticular formation. A major ascending tract from the cerebellum, the brachium conjunctivum, is present as are numerous other ascending and descending fiber tracts. Some of these structures are shown in a sagittal view of a rat brain for orientation in Figure 15-2 and in a generalized, schematic diagram in Figure 15-3(A), which is an amalgamation of structures present in this region in various vertebrates. The relative positions of some isthmal structures are shown in a lamprey and a crocodile in Figures 15-4 and 15-5. A partial list of structures in the isthmus is given in Table 15-1.

The rostral part of the **reticular formation** extends into the isthmus and lies in its central part. The reticular formation (as discussed in Chapter 13) has widespread connections with a number of structures. It gives rise to the **reticulospinal tract,** which courses through the ventral part of the tegmentum and is important in motor control.

The **nuclei of the raphe** lie near the midline. Cells in the raphe contain the neurotransmitter **serotonin** (5-hydroxytryptamine). These cells, along with serotonin-containing cells located more rostrally in the hypothalamus of the diencephalon, project to other brainstem nuclei, to motor cells in the spinal cord, to the optic tectum and other sensory processing structures, and to wide areas of the telencephalon. Serotonin has a variety of functions, including effecting the excitability of neurons in the forebrain. It plays a role in regulating mood and in perceptual integration.

The **locus coeruleus** is a nucleus that contains darkly pigmented cells bordering the central gray around the fourth ventricle. The cells are filled heavily enough with pigment to be visible to the unaided eye in fresh, unfixed tissue. Cells in the locus coeruleus contain the neurotransmitter **norepinephrine,** a catecholamine. Norepinephrine is present in some of the neuronal pathways that regulate movements and in others that participate in cognitive functions and affect. The locus coeruleus projects to the cerebral cortex in the telencephalon and to the cerebellar cortex.

The **trochlear nucleus,** which gives rise to cranial nerve IV, lies in the dorsal part of the tegmentum. It is interconnected with the oculomotor and abducens nuclei and with vestibular nuclei by the **medial longitudinal fasciculus.**

Nucleus isthmi is present in the isthmus in some vertebrates. It is called the **parabigeminal nucleus** in mammals. Nucleus isthmi is reciprocally connected with the optic tectum in a point-to-point manner, and the map of visual space in the tectum is also topographically represented in this nucleus.

An **isthmo-optic nucleus** is present in the dorsomedial part of the isthmal region [rostral to the level shown in Fig. 15-3(A)] in some vertebrates. Unlike nucleus isthmi, this nucleus does not have tectal connections. Neurons of the isthmo-optic nucleus project centrifugally to the retina.

The **interpeduncular nucleus** lies in the ventral part of the isthmus. It receives descending projections from the habenula in the diencephalon, which receives input from olfactory and limbic related areas of the telencephalon. The tract between the habenula and the interpeduncular nucleus is the **fasciculus retroflexus.** The interpeduncular nucleus sends efferent projections to other areas within the dorsal part of the tegmentum.

The **brachium conjunctivum** is a tract that carries fibers from the contralateral cerebellum to the **red nucleus** in the tegmentum proper. The red nucleus projects to the spinal cord via the **rubrospinal tract,** which courses through the ventral part of the isthmus.

Ascending tracts carrying sensory information also course through the isthmus and tegmentum. The **spinal lemniscus,** a continuation of the lateral funiculus of the spinal cord, carries pain and temperature information. The **medial lemniscus** carries somatosensory information: touch, proprioception, and vibration senses. The **lateral lemniscus** carries ascending auditory projections in all animals and, in many, ascending electrosensory and/or mechanosensory lateral line projections.

We have included the **corticospinal** and **corticopontine tracts** here, as they are large and prominent in mammals. These tracts arise in the cerebral cortex and form large structures called the **cerebral peduncles** on the lateral edge of the tegmentum. The term "interpeduncular nucleus" is derived from the position of this nucleus in the **interpeduncular fossa** between the cerebral peduncles in mammals.

THE TEGMENTUM PROPER

The tegmentum lies ventral to the tectum in the midbrain. The tegmentum contains some nuclei involved in motor control, such as the cuneiform nucleus, substantia nigra, and ventral tegmental area, as well as the red nucleus, which receives ascending cerebellar projections. Many ascending and descending tracts pass through or originate in the tegmentum. Some tegmental structures are shown in the sagittal view of a rat brain in Figure 15-2 and in the generalized, schematic diagram of a transverse section in Figure 15-3(B). Figures 15-4 and 15-5 show the relative positions of some tegmental structures in a lamprey and a crocodile. A list of

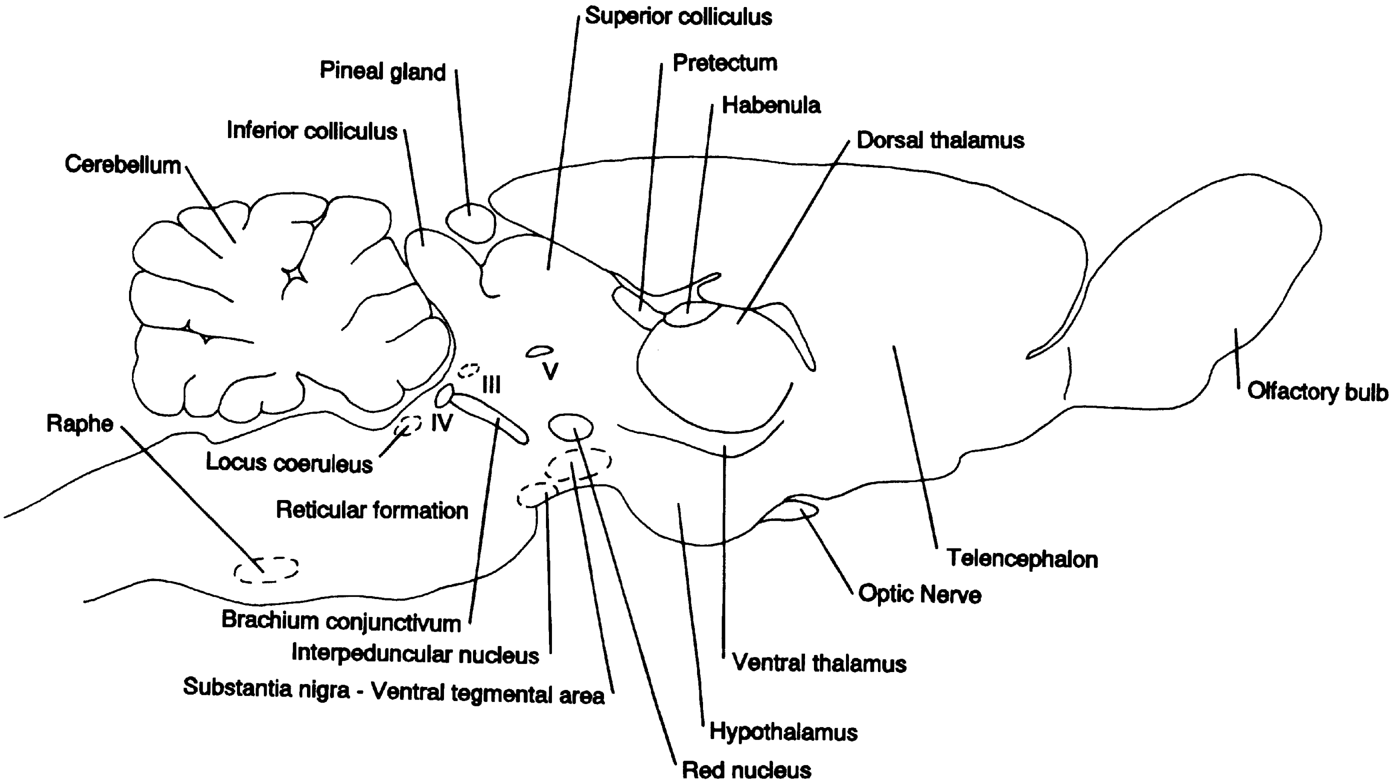

FIGURE 15–2. Drawing of a parasagittal section through the brain of a rat, showing the locations of some of the structures in the midbrain. Some nuclei, shown in broken lines, that are out of the plane of section have been projected onto this section to show their rostrocaudal and dorsoventral position relative to other structures. Cranial nerve nuclei are indicated by Roman numerals, with V indicating the mesencephalic nucleus of the trigeminal nerve. Data from Pelligrino et al. (1979). Used with permission of Plenum Publishing Corp. and the author.

a number of the structures in the tegmentum is provided in Table 15-2.

The **cuneiform nucleus** lies in the central part of the tegmentum. This nucleus projects to the reticular formation in the medulla, which in turn projects to the spinal cord. Stimulation of parts of the cuneiform nucleus and other nuclei in this area results in movements of the limbs. The area is called the **midbrain locomotor region** (MLR).

Large neurons of the mesencephalic nucleus of the trigeminal nerve (see Chapter 11) lie within the deep layers of the optic tectum. These neurons receive proprioceptive information from jaw muscles and are part of a monosynaptic reflex arc for regulation of the movements of the muscles.

The **oculomotor nucleus** lies in the dorsal part of the tegmentum in a medial position. It gives rise to the oculomotor nerve, which courses ventrally through the tegmentum to exit the brain. The **red nucleus** lies immediately lateral to the fibers of the oculomotor nerve. The nucleus is so named because of its pinkish color, due to the presence of abundant blood vessels, in fresh specimens of some animals. It receives cerebellar input as well as descending projections from the telencephalon. Thus, the red nucleus can integrate and coordinate motor signals from both sources. The red nucleus projects to the spinal cord via the rubrospinal tract.

The **substantia nigra** and **ventral tegmental area** lie near the red nucleus. The cells of these nuclei contain the catecholamine dopamine. They project to a number of sites in the diencephalon and telencephalon and are involved in the initiation and control of movements. In humans, loss of cells in the substantia nigra results in the tremors, rigidity, and other symptoms of Parkinson's disease.

The **medial longitudinal fasciculus** lies next to the oculomotor nucleus and, as discussed above, interconnects the oculomotor, trochlear, and abducens nuclei with vestibular nuclei. The **fasciculus retroflexus** is also present at this level, carrying fibers from the habenula to the interpeduncular nucleus in the isthmus.

The **brachium conjunctivum** projects to the red nucleus, carrying fibers from the cerebellum. The tract lies ventromedial to the nucleus, as its fibers enter the nucleus to terminate there. Other ascending tracts pass through the tegmentum on the way to the tectum and to nuclei in the diencephalon. These include the spinal lemniscus and medial lemniscus, which carry pain and somatosensory information as discussed above.

Tracts that descend through the tegmentum include the corticospinal and corticopontine tracts, present in mammals, which form the cerebral peduncle on the lateral surface of the tegmentum. Other descending tracts include corticoreticular and corticobulbar projections. Fibers from a variety of sources cross to the contralateral side in the tegmentum via the **posterior commissure.** There is also a **tectal commissure** interconnecting the optic tecta.

The **torus lateralis** is a bulge on the lateral side of the tegmentum that is present in ray-finned fishes but has not been

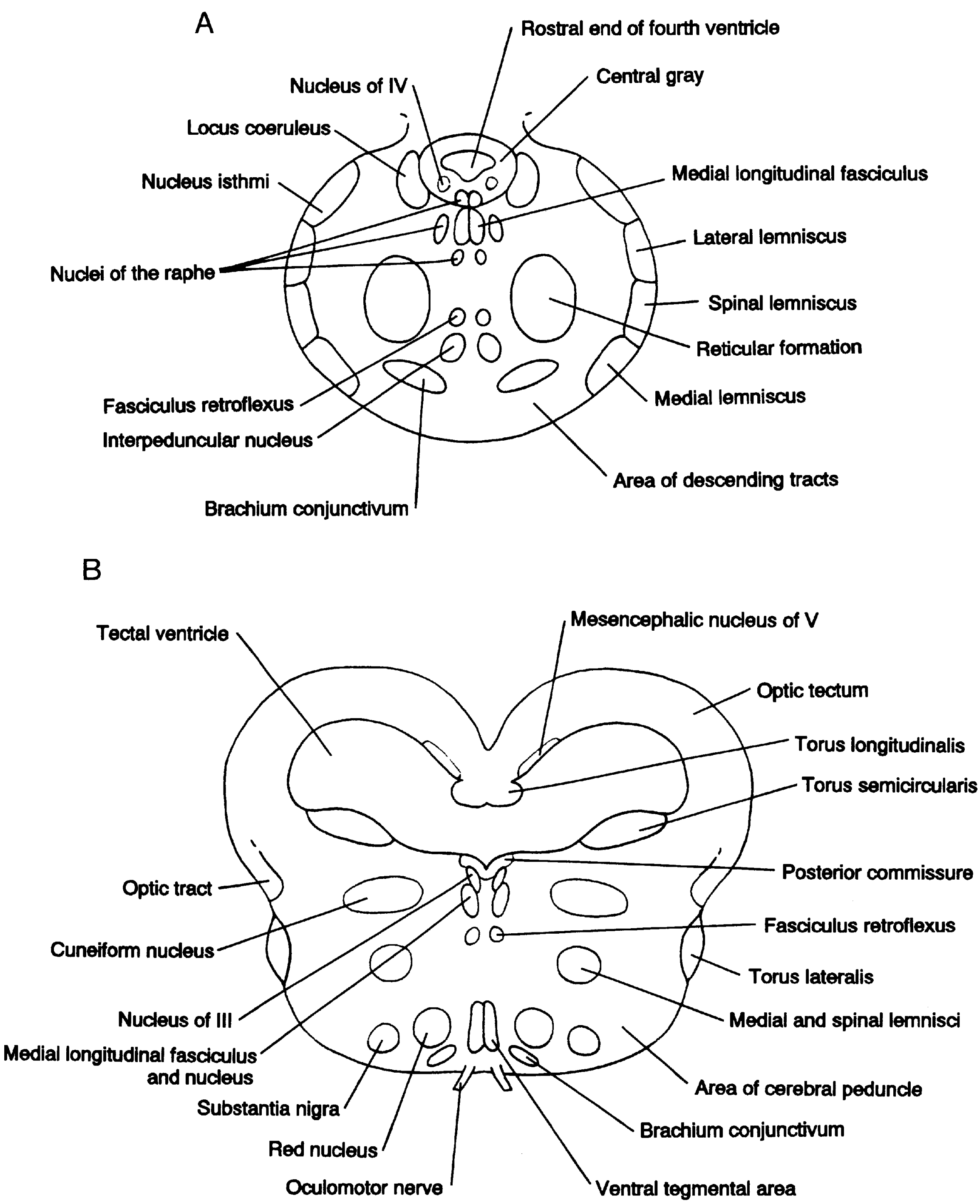

FIGURE 15–3. Schematic transverse sections through the isthmus (A) and the tegmentum and tectum (B) in a generalized vertebrate. The structures shown are not all present in any single species.

identified in other vertebrates. It has been found to project to the telencephalon, but its other connections and functions are unknown.

THE TECTUM

The two prominent structures within the tectum are the **optic tectum** and **torus semicircularis.** These two structures occur in all vertebrates and form rounded bulges over the tegmentum. In mammals, they are called the **superior colliculus** and **inferior colliculus,** respectively. Colliculus is Latin for "little hill," which each bulge resembles. A third structure—the **torus longitudinalis**—is present at the medial end of the optic tectum in ray-finned fishes. The optic tectum, torus semicircularis, and torus longitudinalis are shown in Figure 15-3(B).

The optic tectum is formed by a lobe on each side of the brain (Figs. 15-1 and 15-2). It is most properly called by its full name, to distinguish it from the entire midbrain roof, but is also referred to simply as the tectum in some contexts. In many nonmammalian vertebrates, the optic tectal lobes are relatively

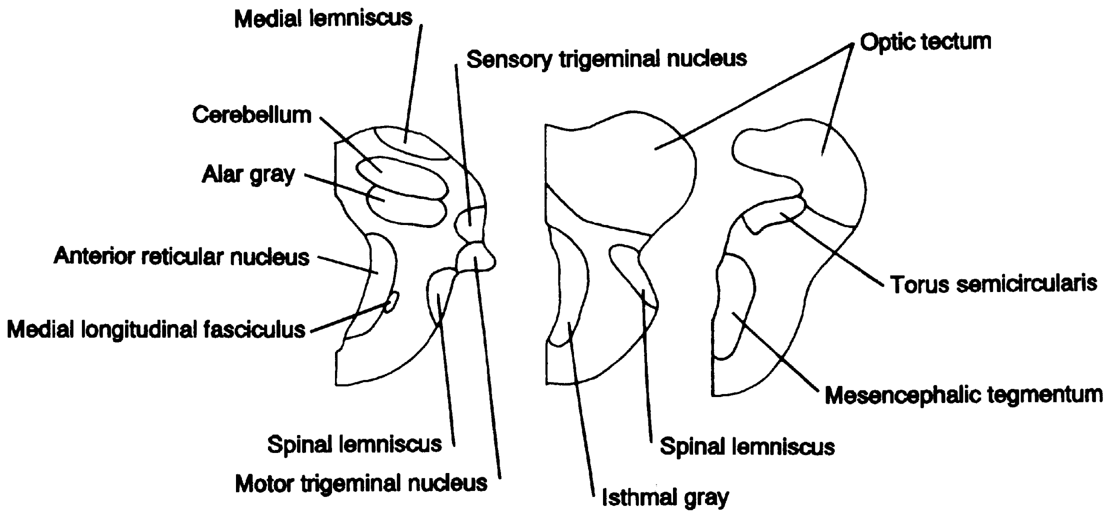

FIGURE 15–4. Drawings of transverse hemisections through the right midbrain of a lamprey, with the most caudal section on the left. Data for the most caudal section is from Northcutt (1979) and for the more rostral sections from Kennedy and Rubinson (1977). Note that in this figure and in figures in this and succeeding chapters on the midbrain, the ventricle is generally not labeled. Material from Northcutt (1979) used with permission of Elsevier.

expanded, and the third ventricle extends laterally into each tectal lobe, forming the tectal ventricle. The optic tectum consists of various layers of cells and fibers, with the dendrites of many cells oriented in a radial fashion and with afferent fibers coursing through it parallel to the surface. The cell and fiber layers can be divided into superficial, central, and periventricular zones. The optic tectum has multiple sources of input, among which are the visual and somatosensory systems. The optic tract terminates in the superficial and central zones, while somesthetic information terminates in the deeper part of the central zone. The inputs of both these modalities are mapped topographically and are in register with each other in regard to their spatial location of origin.

As a result of the expansion of the tectal lobes, the torus semicircularis lies ventral to the tectal ventricle in most cases. In mammals, the inferior colliculus lies caudal to the superior colliculus, rather than in a more ventral position, because the superior collicular lobes are not expanded laterally and the ventricle does not extend into them.

The torus semicircularis is the site of termination of auditory and lateral line fibers from the lateral lemniscus. The topography of these fibers is maintained so that there is a map of lateral line and/or auditory space in the torus semicircularis. The torus semicircularis is also reciprocally connected with the optic tectum, and the maps of visual and somatosensory space in the optic tectum and of auditory/lateral line space in the

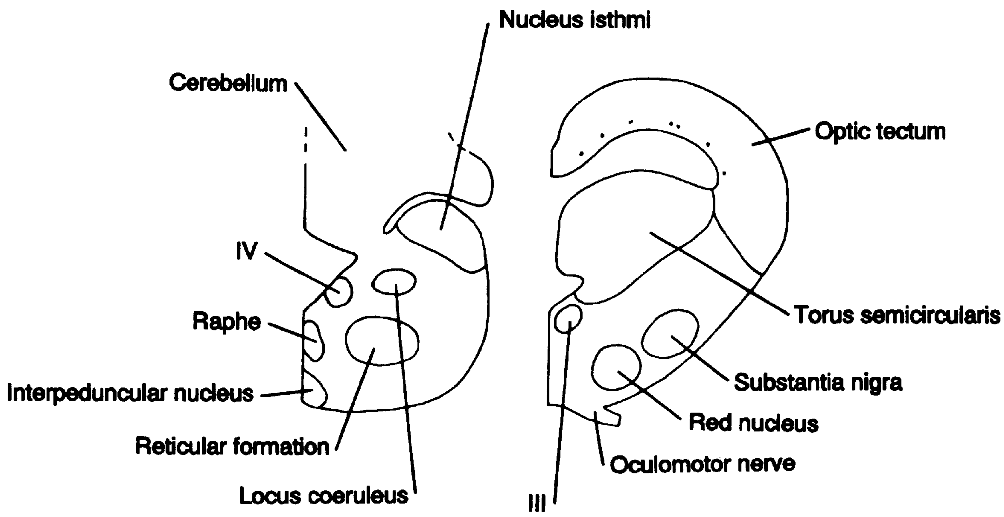

FIGURE 15–5. Drawings of transverse hemisections through the right midbrain of a crocodile, with the more caudal section on the right. Roman numerals indicate cranial nerve nuclei. The dots in the optic tectum represent cell bodies of the mesencephalic nucleus of the trigeminal nerve. Data from ten Donkelaar and Nieuwenhuys (1979). Used with permission of Academic Press Ltd.

TABLE 15-1. Some of the Nuclei and Tracts in the Isthmus

Reticular formation	Motor, autonomic, and activating system
Nuclei of the raphe	Serotonin-containing cells that have widespread connections
Locus coeruleus	Catecholamine-containing cells that project to cerebral and cerebellar cortices
Trochlear nucleus	Nucleus of cranial nerve IV
Nucleus isthmi	Connected with optic tectum
Isthmo-optic nucleus	Projects to the retina
Interpeduncular nucleus	Receives projections from the habenula in the diencephalon
Fasciculus retroflexus	Tract between habenula and interpeduncular nucleus
Brachium conjunctivum	Tract from cerebellum to red nucleus
Spinal lemniscus	Carries ascending pain and temperature information
Medial lemniscus	Carries ascending somatosensory information
Lateral lemniscus	Carries ascending auditory and lateral line information
Rubrospinal and reticulospinal tracts	Carry descending projections from red nucleus and reticular formation to spinal cord
Corticospinal, corticopontine, and other descending tracts	Carry descending projections from telencephalon to spinal cord and nuclei in the brainstem

TABLE 15-2. Some of the Nuclei and Tracts in the Tegmentum Proper

Cuneiform nucleus	Projects to reticular formation
Mesencephalic nucleus of the trigeminal nerve	Proprioception for jaw muscles; the cells lie in the deep part of the tectum
Oculomotor nucleus	Nucleus of cranial nerve III
Red nucleus	Receives cerebellar and descending projections and projects to spinal cord
Substantia nigra	Catecholamine-containing cells project to basal ganglia in the telencephalon
Ventral tegmental area	Catecholamine-containing cells similar to those in substantia nigra
Medial longitudinal fasciculus	Interconnects oculomotor and vestibular nuclei
Fasciculus retroflexus	Tract from habenula to the interpeduncular nucleus
Brachium conjunctivum	Tract from cerebellum to the red nucleus
Spinal lemniscus	Carries ascending pain and temperature information
Medial lemniscus	Carries ascending somatosensory information
Corticospinal and corticopontine tracts	Carry descending information from the telencephalon
Posterior and tectal commissures	Carry a variety of decussating fibers
Torus lateralis	Connections mostly unknown

torus semicircularis are maintained in register in both structures. Descending projections involved in motor movements to orient the head and/or body to novel stimuli in the environment arise from both the optic tectum and the torus semicircularis, and the mapping of space allows for rapid and precise orienting movements. This is equally important to the frog needing to catch a fly for lunch as to the human orienting to whatever goes bump in the night, or to motion in one's peripheral visual field. In addition to descending projections, the optic tectum and the torus semicircularis both project rostrally to nuclei in the diencephalon, which in turn project to the telencephalon.

The torus longitudinalis is a small structure that is unique to ray-finned fishes. It is involved in relaying motor inputs to the optic tectum, and thence to the reticular formation.

FOR FURTHER READING

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16

Isthmus

INTRODUCTION

We have previously discussed a number of isthmic nuclei and tracts, such as the reticular formation, the trochlear and oculomotor nuclei, and the medial longitudinal fasciculus. Other tracts that pass through the tegmentum proper and the isthmus, including the medial and spinal lemnisci and a number of the descending tracts, are also covered elsewhere in conjuction with the specific systems to which they belong. This chapter focuses on the comparative anatomy of five isthmal structures: the **nuclei of the raphe,** the **locus coeruleus, nucleus isthmi,** the **isthmo-optic nucleus,** and the **interpeduncular nucleus.** Drawings of sections through the isthmus show a number of the nuclei and fiber tracts for a variety of animals with laminar brains (Group I)—a lamprey (Fig. 16-1), a nonteleost ray-finned fish (Fig. 16-2), a lungfish (Fig. 16-3), and an amphibian (Fig. 16-4)—and for some animals with elaborated brains (Group II)—a hagfish (Fig. 16-5), a teleost (Fig. 16-6) and, among amniotes, a mammal (Fig. 16-7) and a bird (Fig. 16-8).

NUCLEI OF THE RAPHE

Group I

The word raphe, derived from the Greek word for seam, refers to the midline of the brainstem. In most vertebrates, the nuclei of the raphe extend into the isthmus. In lampreys, the raphe has cells which contain serotonin but is confined to the hindbrain proper, even though this system is quite extensive within the hindbrain. It gives rise to widely distributed projections to the telencephalon, diencephalon, tectum, interpeduncular nucleus, and reticular formation. In squalomorph sharks and ratfishes, the raphe lies dorsal and caudal to the interpeduncular nucleus. The raphe nuclei in ratfishes are known to have serotonin-containing cells. These cells are also distributed through more lateral areas within the brainstem.

Among nonteleost ray-finned fishes, the serotonin system in the raphe is known to be extensive in gars. It extends caudally to upper spinal cord levels. In the isthmus (Fig. 16-2), the area of the serotonin-containing cells extends lateral to the raphe itself.

Differences occur in the degree of lateralization of this system in amphibians. In frogs, the serotonin-containing cells of the raphe extend from medullary to isthmic tegmental levels in the area of the midline and also extend into more lateral areas in the tegmentum. In urodele amphibians, however, the serotonin-containing cells are confined to the raphe nuclei in the area of the midline.

Group II

In hagfishes, the nucleus of the superior raphe extends rostrally to the level of the caudal isthmus (Fig. 16-5). Serotonin-containing cells are mostly confined to the area of the midline. In galeomorph sharks, skates, and rays, the rostral part of the raphe also extends into the isthmus, a part of it lying dorsal to the caudal part of the interpeduncular nucleus. Serotonin-containing cells are numerous within the raphe and also are distributed through a number of more laterally lying sites in the hindbrain.

The column of the raphe nuclei extends into the caudal part of the isthmus in teleosts (Fig. 16-6). The medially lying raphe nuclei have serotonin-containing cells, but this system is relatively limited in teleosts. The column of serotonin-containing cells in the raphe does not extend caudally through the medulla and into the spinal cord in most teleosts as it does in

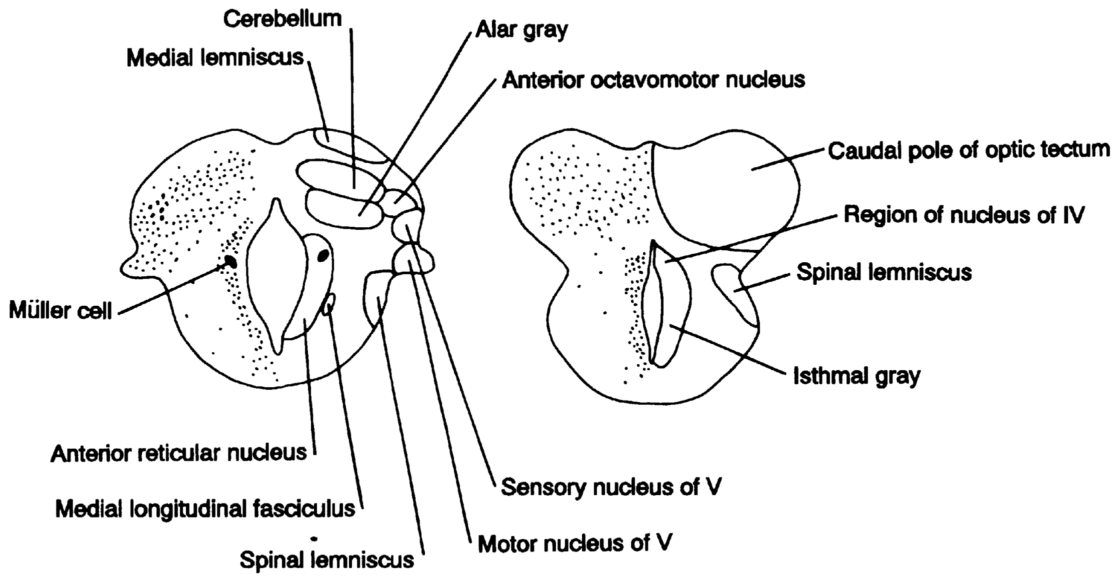

FIGURE 16-1. Drawings of transverse hemisections in lampreys (*Petromyzon marinus* and *Ichyomyzon unicuspis*), with mirror-image drawings, through isthmal levels, with the more caudal section on the left. Adapted from Kennedy and Rubinson (1977) and Northcutt (1979). The latter material used with permission of Elsevier. Please note that in this and most succeeding similar illustrations in the book, scales are not shown. The approximate scale can be determined in most cases by reference to Chapter 4, in which scales are shown on drawings of whole brains.

lampreys, cartilaginous fishes, and nonteleost ray-finned fishes such as gars. One exception to the limited extent of the system in teleosts is in mormyrid fishes where serotonin-containing cells extend throughout the brainstem. In most teleosts, the serotonin-containing cells are also limited in their lateral extent, being confined to the area of the midline. This lack of lateral migration of the cells contrasts with the more laterally migrated reticular formation and a number of other nuclei in teleosts.

In amniotes (Fig. 16-7), the serotonin-containing cells lie both within the nuclei of the raphe and more laterally in the tegmentum. This lateralization of the serotonin system is pronounced in mammals and most extensive in birds. In both mammals and birds, some serotonin-containing cell somata extend as far laterally as nuclei such as the locus coeruleus (discussed below), where they intermingle with the catecholamine-containing cells of that region. The number of such intermingling serotonin-containing cells is relatively few in mammals but quite high in birds. The functional consequences of having the cell somata intermingled have not yet been determined.

In mammals, widespread ascending serotoninergic projections of the raphe have been found to the cerebral cortex in the telencephalon, nuclei within the diencephalon, the superior colliculus in the roof of the midbrain, and the cerebellum. These projections have also been found to be topographically organized.

Evolutionary Perspective

The serotonin system is well developed and extends laterally from midline areas in most vertebrates. Hagfishes, teleosts, and urodele amphibians are the exceptions, having relatively reduced systems in which the cells are confined to the area of the midline. While we cannot determine whether or not lateralization of the serotonin system was present in the common ancestor of hagfishes and all other vertebrates, this condition does appear to have arisen very early in vertebrate evolution. Lateralization of the system has been maintained in most groups and, in some cases, augmented. The system has been secondarily reduced in teleosts and in urodele amphibians.

LOCUS COERULEUS

Group I

The presence of a locus coeruleus, which means "sky-blue place" in reference to the color of its catecholamine-containing cells, has not yet been investigated in lampreys, but this nucleus has been found in ratfishes along the border of the fourth ventricle. In nonteleost ray-finned fishes such as gars, the locus coeruleus is a small group of catecholamine-containing cells (indicated by the large dots in Fig. 16-2) in the isthmus, and within the telencephalon, there are only a few catecholamine-containing axons. The locus coeruleus is thus quite small, especially in contrast to the extensive serotonin system of the raphe. In amphibians, the catecholamine-containing cells of the locus coeruleus lie on the ventromedial wall of the fourth ventricle.

Group II

The presence of a locus coeruleus has not yet been investigated in hagfishes. Among cartilaginous fishes with elaborated brains, a circumscribed group of cells forms the locus coeruleus in galeomorph sharks, lying in the caudal part of the isthmus along the border of the fourth ventricle. This nucleus has not yet been identified in skates, but a locus coeruleus with scattered, catecholamine-containing cells has been found in a closely related animal, the guitarfish, caudal to the isthmus at the level of the trigeminal motor nucleus. The locus coeruleus projects to the spinal cord, cerebellum, and telencephalon. In teleosts,

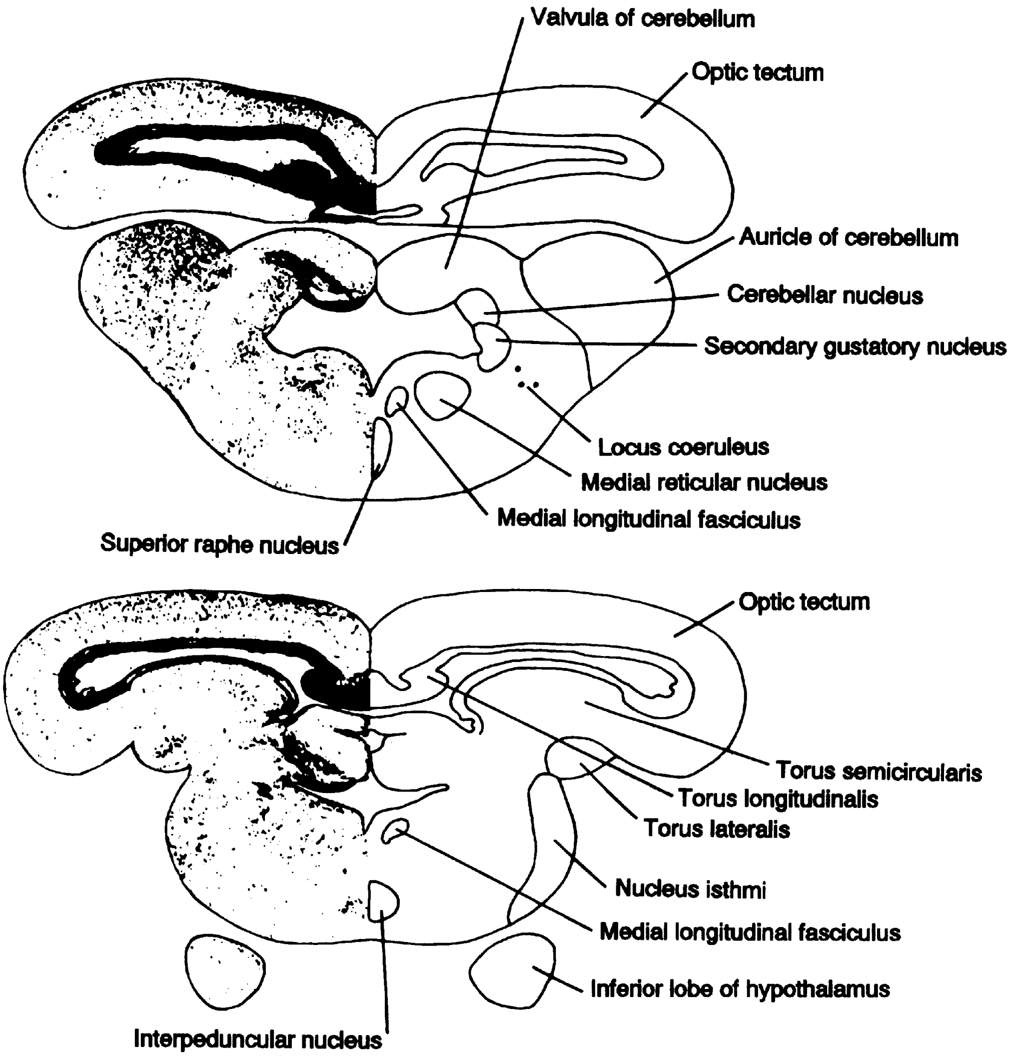

FIGURE 16-2. Transverse hemisections in a longnose gar (*Lepisosteus osseus*), with mirror-image drawings, through isthmal levels, with the more caudal section at the top. Adapted from Northcutt and Butler (1980). Used with permission of Elsevier.

the locus coeruleus (Fig. 16-6), with numerous, large catecholamine-containing cells, lies dorsal to the reticular formation. In contrast with the serotonin system, the locus coeruleus is larger in teleosts than in nonteleost ray-finned fishes, and there is dense innervation of a number of areas within the midbrain

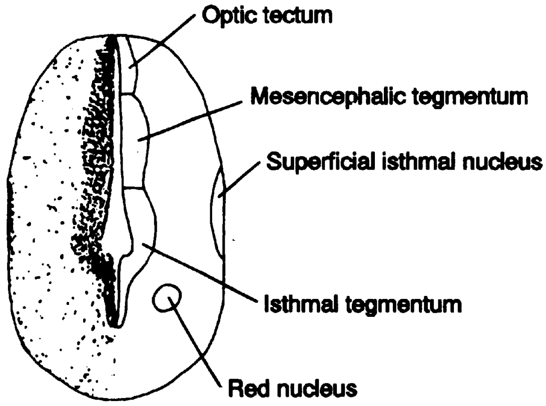

FIGURE 16-3. Transverse hemisection in a lungfish (*Protopterus annectens*), with a mirror-image drawing through the isthmus. Adapted from Northcutt (1977) with additional data from Northcutt and Ronan (1985).

and forebrain, including part of the telencephalon, by catecholamine-containing fibers.

In amniotes, the locus coeruleus lies along the lateral edge of the rostral end of the fourth ventricle (Figs. 16-7 and 16-8). It is a relatively larger nucleus in birds than in mammals, diapsid reptiles, or turtles. In amniotes, the catecholamine-containing cells of the locus coeruleus project topographically to various parts of the forebrain, midbrain, hindbrain, and spinal cord. Like the serotonin-containing neurons of the raphe, the locus coeruleus plays a role in affecting the activity of sensory neurons and the general level of activity of the pallium in the telencephalon.

Evolutionary Perspective

A locus coeruleus is a common feature of the brains of jawed vertebrates. Whether or not it is also present in lampreys and hagfishes, we can conclude that this group of catecholamine-containing cells with widespread projections evolved early in vertebrate history.

In some cases, this set of cells seems to be developed in inverse proportion to the serotonin system of the raphe. In

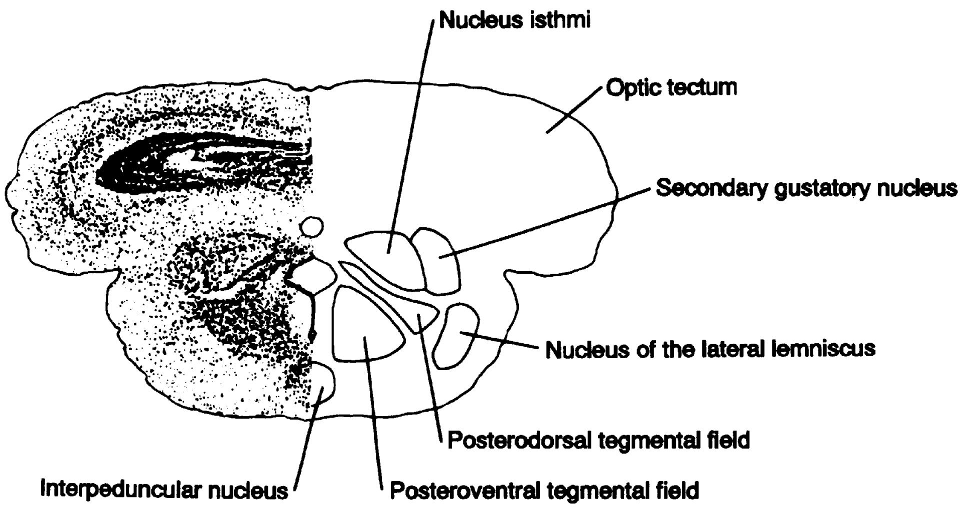

FIGURE 16-4. Transverse hemisection in a leopard frog (*Rana pipiens*), with a mirror-image drawing, through the isthmus. Adapted from Wilczynski and Northcutt (1977).

nonteleost ray-finned fishes, the locus coeruleus is relatively small while the serotonin-containing raphe cells are extensive. In teleost fishes, the reverse is true. However, in amniotes, serotonin-containing cells are numerous in the raphe and also extensively invade more lateral areas of the tegmentum, and the locus coeruleus is also well developed and has numerous and widespread projections.

NUCLEUS ISTHMI

Group I

A nucleus isthmi has not been identified in lampreys or in squalomorph sharks or ratfishes. In nonteleost ray-finned fishes, nucleus isthmi is present on the lateral edge of the isthmus (Fig. 16-2). In frogs, nucleus isthmi is a large and prominent nucleus that lies ventral to the caudal part of the optic tectum (Fig. 16-4). Nucleus isthmi is reciprocally and topographically connected with the optic tectum in both nonteleost ray-finned fishes and anuran amphibians. In the tegmentum of the coelacanth and lungfishes, a nucleus called the **superficial isthmal nucleus** has been identified (Fig. 16-3). However, this nucleus, unlike the nucleus isthmi of ray-finned fishes and amphibians, receives retinal projections and may thus be a different, unrelated cell group. Its other connections are unknown.

Group II

A nucleus isthmi has not been found in hagfishes. A nucleus has been labeled nucleus isthmi in galeomorph sharks and skates. It corresponds in position to the nucleus named isthmi in squalomorph sharks but appears to lack reciprocal connections with the optic tectum. Nucleus isthmi is present and large in teleosts (Fig. 16-6), with a distinctive lamina of cells surrounding a relatively cell-free, central neuropil. It is reciprocally and topographically connected with the optic tectum.

Nucleus isthmi is called the **parabigeminal nucleus** in mammals and lies rostrally, at the level of the tegmentum proper. Parabigeminal roughly translates to "next to the two sets of twins," the two sets of twins being the two paired sets of the inferior and superior colliculi (= the torus semicircularis

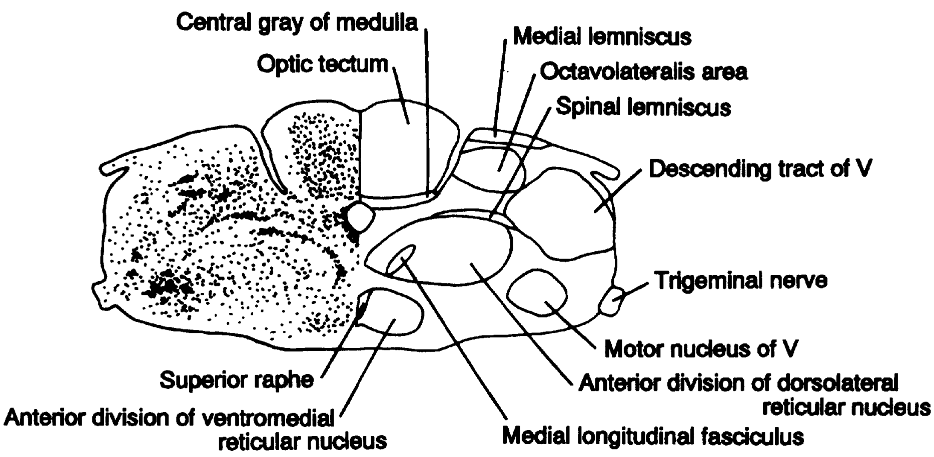

FIGURE 16-5. Drawing of a transverse hemisection in a hagfish (*Eptatretus stouti*), with a mirror-image drawing, through the isthmus. Adapted from Ronan and Northcutt (1990). Used with permission of S. Karger AG.

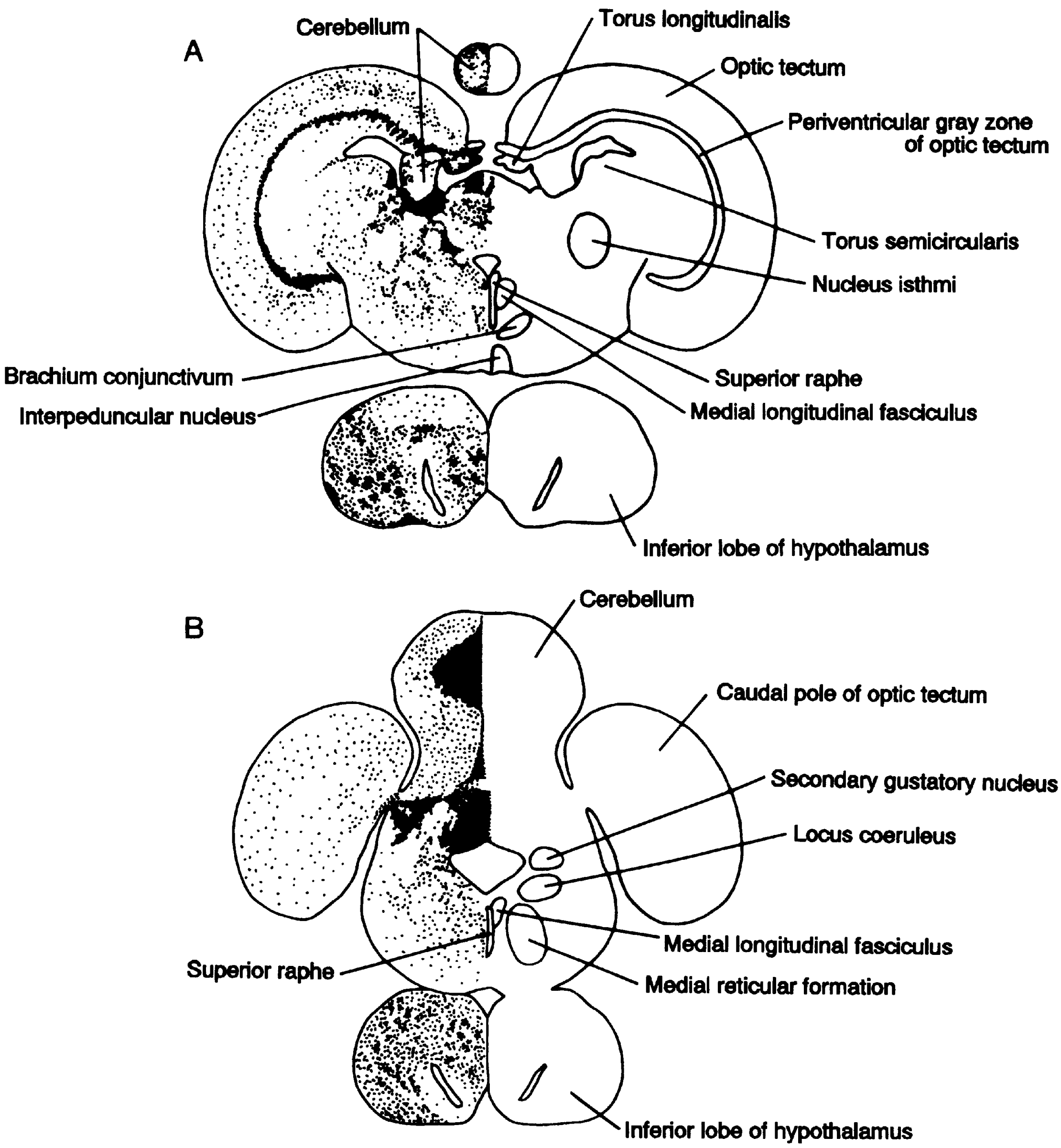

FIGURE 16-6. Drawing of transverse hemisections in a teleost (*Lepomis gibbosus*), with a mirror-image drawing, through isthmal levels, with the more caudal section at the bottom. Adapted from Parent et al. (1978).

and optic tectum, respectively). The nucleus is reciprocally and topographically connected with the optic tectum in amniotes, as it is in fishes and amphibians. In mammals, the parabigeminal nucleus has also been found to project to a major visual nucleus in the dorsal thalamus, the dorsal lateral geniculate nucleus. In the latter nucleus, parabigeminal projections overlap another set of afferent projections to it from the superior colliculus.

Electrophysiological studies in mammals have found that the responses of parabigeminal cells to light stimuli are very like the responses of tectal cells. The tectal and parabigeminal cells are most responsive to a point of light moving in a specific direction, that is, they are "direction selective." They do not selectively respond to the size or the speed of the light stimulus. The parabigeminal nucleus has been characterized as a "satellite" system for the optic tectum, used to monitor and modulate the responses of the tectal cells. Given the properties of the isthmal/parabigeminal cells, one can surmise that this nucleus helps the optic tectum help a frog to catch a fly by adjusting for the directional component of the fly's movement. It would in like manner assist the optic tectum of fishes and amniotes in capturing moving prey.

In diapsid reptiles and turtles, nucleus isthmi lies in a dorsolateral position in the isthmal region. It has reciprocal connections with the optic tectum. Three nuclei present in the isthmal region in birds (Fig. 16-8), nucleus isthmi pars parvocellularis, nucleus isthmi pars magnocellularis, and nucleus semilunaris, receive tectal projections and project back to the optic tectum. These three nuclei may be homologous as a field to the nucleus isthmi of other vertebrates.

Evolutionary Perspective

A nucleus isthmi that is reciprocally and topographically connected with the optic tectum and that does not receive a direct retinal input is present in ray-finned fishes, amphibians, and amniote vertebrates. Such a nucleus has not been found

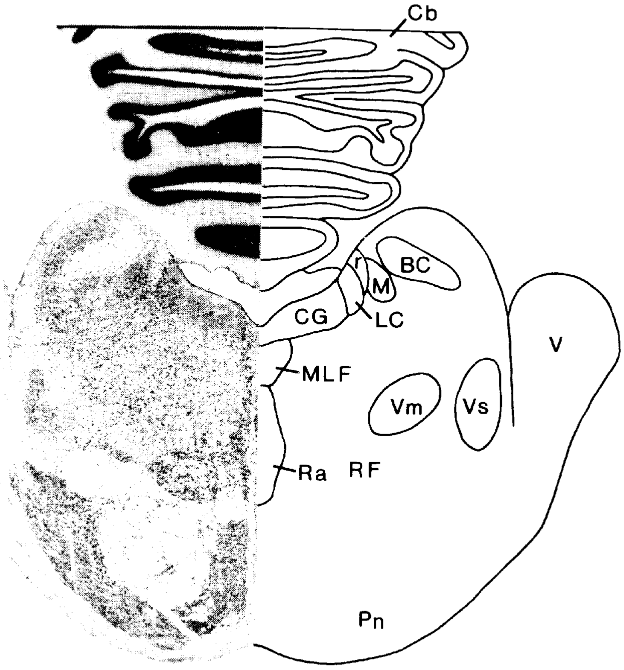

FIGURE 16-7. Transverse hemisection with mirror-image drawing through the isthmal region in a racoon (*Procyon lotor*). Abbreviations: BC, brachium conjunctivum; Cb, cerebellum; CG, central gray; LC, locus coeruleus; M, mesencephalic trigeminal nucleus; MLF, medial longitudinal fasciculus; Pn, pontine nuclei; r, mesencephalic root; Ra, raphe; RF, reticular formation; V, trigeminal nerve; Vm, motor trigeminal nucleus; Vs, principal sensory trigeminal nucleus. Photograph courtesy of Wally Welker.

in lampreys or hagfishes or in any cartilaginous fishes. Nucleus isthmi thus does not appear to have been present in the common ancestral stock of all vertebrates but to have evolved in the ancestral stock that gave rise to both ray-finned fishes and sarcopterygians.

If this nucleus is indeed absent in the coelacanth and in lungfishes, it was presumably secondarily lost as a result of the general process of reduction of the brain within these taxa. The lack of migration of most cell groups throughout the brain in the coelacanth, lungfishes, and urodele amphibians appears to be the result of a trend to secondary simplification related to neoteny (the retention of embryonic characteristics in the adult). These groups of vertebrates are in fact excellent examples of the principal that brain evolution is multidirectional; there is not a single trend from simple to complex, as complex can also give rise to simple. Phylogenetic analysis of such simplified and reduced structures is particularly difficult, however, as many features of the morphology of the ancestral adult phenotype have been lost.

ISTHMO-OPTIC NUCLEUS

Group I

An isthmo-optic nucleus, that is, a group of neurons located in the caudal mesencephalon that project to the retina, has been found in a fragmented distribution both among and within various vertebrate groups. Tegmental retinopetal projections have been found in lampreys and in two nonteleost ray-finned fishes, bichirs and gars, but are absent in another nonteleost ray-finned fish, sturgeons. Similar projections also appear to be absent in Group I sharks as well as in amphibians.

Group II

Isthmo-optic neurons that project to the retina have been found in hagfishes in the medial, rostral part of the mesencephalic tegmentum. The nucleus in hagfishes that contains the majority of the retinopetal cells is called the **nucleus of the posterior commissure** (rostral to the level shown in Fig. 16-5; see Fig. 20-5); additional retinopetal cells lie scattered in an area lateral to this nucleus. An isthmo-optic nucleus has not been found in any Group II cartilaginous fish. Isthmo-optic neurons have been found in one teleost, a pike, but are absent in other teleosts studied.

Among amniotes, isthmo-optic neurons have been found in crocodiles and turtles. Only a few such neurons are present in lizards, and no retinopetally projecting neurons are present in the tegmentum of snakes. In birds, an isthmo-optic nucleus is present in the dorsal, medial part of the tegmentum; this nucleus is cytoarchitectonically well defined in some species, such as in the pigeon, as shown in Figure 16-8. A smaller number of retinopetal neurons also lie scattered in an area ventral to the isthmo-optic nucleus. The avian isthmo-optic nucleus is particularly well developed in birds that feed by pecking, such as pigeons, as opposed to those that feed on-the-wing, such as swifts and swallows. This nucleus in birds and its centripetal innervation of the retina may thus be involved in searching for and/or pecking at food on the ground.

Evolutionary Perspective

Retinopetally projecting isthmo-optic neurons are present in lampreys, hagfishes, some but not all nonteleost ray-finned fishes, at least one teleost, and, among amniotes, in some diapsid reptiles, and in birds and turtles. Such neurons appear to be absent in all cartilaginous fishes, at least one nonteleost ray-finned fish (sturgeons), most teleosts, amphibians, snakes, and mammals. From this distribution, the evolutionary history of isthmo-optic neurons cannot be clearly discerned, particularly among jawed vertebrates.

Due to their presence in both hagfishes and lampreys, isthmo-optic neurons were probably present in the earliest vertebrates and thus plesiomorphic for vertebrates. This population of neurons may have been lost in the common ancestral stock of jawed vertebrates, however, and subsequently regained independently within two groups of vertebrates—in some of the ray-finned fishes and in nonmammalian amniotes. Among the latter, since isthmo-optic neurons are present in lizards, crocodiles, and birds, their absence in snakes appears to be an apomorphy. Another possibility, that isthmo-optic neurons were retained in ancestral jawed vertebrates and subsequently lost multiple times cannot be entirely ruled out, however. Thus, whether the isthmo-optic neurons present in nonmammalian amniotes are homologous or homoplaseous to those in some ray-finned fishes cannot be determined from the present data.

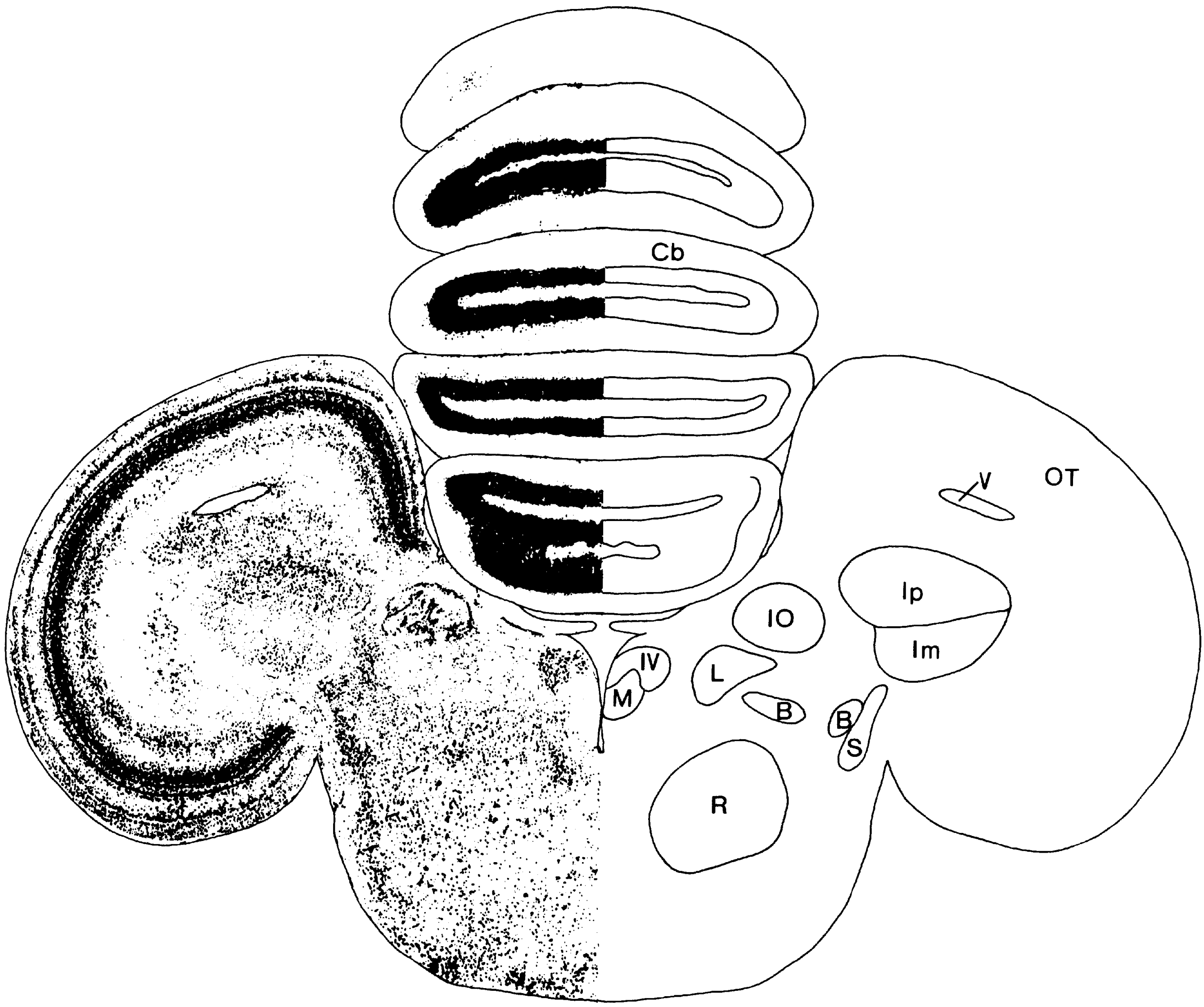

FIGURE 16-8. Transverse hemisection through the isthmal region in a pigeon (*Columba livia*) on the left with a mirror-image drawing on the right. Adapted from Karten and Hodos (1967). Abbreviations: B, brachium conjunctivum; Cb, cerebellum; Im, nucleus isthmi, pars magnocellularis; IO, isthmo-optic nucleus; Ip, nucleus isthmi, pars parvocellularis; L, locus coeruleus; M, medial longitudinal fasciculus; OT, optic tectum; R, nucleus reticularis pontis oralis; S, nucleus semilunaris; IV, nucleus of the trochlear nerve. Used with permission of the Johns Hopkins University Press.

INTERPEDUNCULAR NUCLEUS

Group I

An interpeduncular nucleus has recently been identified in the ventral part of the mesencephalon in lampreys, based on a major afferent input from the habenula via the fasciculus retroflexus. The interpeduncular nucleus in squalomorph sharks lies medial to the rostral part of the reticular formation and immediately rostral to the raphe and caudal to the ventral tegmental area. The fasciculus retroflexus traverses the medial tegmental region to project to the interpeduncular nucleus. In nonteleost ray-finned fishes, the interpeduncular nucleus (Fig. 16-2) and fasciculus retroflexus lie in similar positions. The interpeduncular nucleus is rather small and cell sparse in these fishes. In frogs, the interpeduncular nucleus is well developed and lies in the isthmus (Fig. 16-4).

Group II

In hagfishes, a large interpeduncular nucleus (and a large habenula) are present, but the interpeduncular nucleus lies farther rostrally than in most animals. In these fishes, it lies in a ventromedial position at levels through the diencephalon rather than in the isthmus or caudal tegmentum. The position of the fasciculus retroflexus has not been established.

The interpeduncular nucleus is larger and more distinct in cartilaginous fishes with elaborated brains than in squalomorph sharks. It lies in a medial position in the ventral tegmentum and receives projections via the fasciculus retroflexus. In teleosts (Fig. 16-6) and amniotes, the interpeduncular nucleus lies in the ventromedial part of the tegmentum, and the fasciculus retroflexus projects to it from the habenula. In mammals, the cerebral peduncle lies lateral to the nucleus.

Evolutionary Perspective

The fasciculus retroflexus, the habenula in the diencephalon from which it arises, and the interpeduncular nucleus to which it projects are common features of vertebrates and are assumed to have been present in the ancestral stock of all vertebrates. This system is the route by which input from olfactory and limbic related areas of the telencephalon reaches the tegmentum and can be integrated there with other incoming sensory information for coordination with the appropriate motor responses.

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