

Segmental Organization of the Head, Brain, and Cranial Nerves

“TWELVE” CRANIAL NERVES

Traditionally, 12 cranial nerves have been recognized, and the list of them, numbered with Roman numerals, has been taught to many generations of students. The nerves have been named according to various attributes, such as their appearance (vagus = wanderer), the region of innervation (facial), or their function (oculomotor = moving the eye). These nerves have been classified according to their function (sensory or motor) and their direction of conduction with respect to the brain (afferent, meaning towards, or efferent, meaning away from). The nerves were also classified according to the types of tissue that they were believed to innervate, either somatic or visceral. The branchiomeric muscles, innervated by some of the cranial nerves, were erroneously believed to be visceral in nature, as were some of the sense organs, such as those of taste and smell. Other senses were classified as “special somatic” since they are not as directly related to the gut as taste and smell appeared to be. The “special somatic” senses included vision (optic nerve), balance and hearing (vestibular and cochlear nerves), and mechanoreception and electroreception (lateral line nerves). Unfortunately, the embryological development of the brain and the cranial nerves was not correctly understood when the nerves were so classified, and hence the traditional classification schemes are to a greater or lesser degree misleading.

A list of the traditionally recognized 12 cranial nerves is shown in Table 9-1. This list is useful for the study of human neuroanatomy, for which it was devised, but it is inadequate for the comparative neuroanatomy of all the vertebrate classes. There are, in fact, many more than 12 cranial nerves. The termi-

nology used in this text for all of the cranial nerves preserves the original Roman numeral designations of the “traditional” 12. These designations are so firmly established in the literature and so universally used that changing to a new set of numbers would be counterproductive.

SEGMENTAL DEVELOPMENT OF THE VERTEBRATE BRAIN

The central nervous system, in spite of the complexity of its structural components, is basically a hollow tube, the lumen of which is the central canal and the brain ventricles. During embryonic development, the neural tube is formed by the folding of the neural plate, as discussed in Chapter 3. In the rostral part of the neural tube, which will eventually become the brain, a rostrocaudal series of bulges, called **neuromeres**, then develops. The neuromeres, which are serial brain segments, were identified in the early 1900s, and formed the basis of a **neuromeric theory**. This theory postulated that the neuromeres are specified by genetic fate determinants and constitute longitudinal and transverse segmental divisions, or compartments, of the neural tube that have independent and individual developmental fates.

In the hindbrain (rhombencephalon), the neuromeres are called **rhombomeres** (Fig. 9-1); at least seven rhombomeres are present, and they are delineated by a series of transverse grooves on the external and internal surfaces of the neural tube. In the midbrain (mesencephalon) and forebrain (prosencephalon), a series of transverse grooves is not readily apparent, but neuromeres are present there as well (Fig. 9-2). The neuromeres

Symbol	Name	Innervation
I	Olfactory	Olfactory epithelium
II	Optic	Retina
III	Oculomotor	Internal and external eye muscles
IV	Trochlear	External eye muscles
V	Trigeminal	Jaw muscles; touch to face, snout and oral cavity
VI	Abducens	External eye muscles
VII	Facial	Taste buds; facial muscles; salivary and tear glands
VIII	Vestibulocochlear	Cochlea, vestibular organs
IX	Glossopharyngeal	Taste buds; pharynx; salivary glands
X	Vagus	Taste buds; viscera of thorax and abdomen; larynx; pharynx
XI	Spinal accessory	Neck and shoulder muscles
XII	Hypoglossal	Tongue

in the midbrain are called **mesomeres** and those in the forebrain **prosomeres**. To date, six prosomeres (p1–p6) and two mesomeres (m1 and m2) have been recognized.

The individual segmental specification of the rhombomeres has recently been correlated with the expression patterns of certain regulatory genes. These regulatory genes are involved in specifying anterior–posterior axial patterning in the developing embryo. Over the past decade, a new area of research on such regulatory genes has blossomed. One group of these genes are referred to as **homeobox-containing genes** (or **Hox** genes), because they contain a specific sequence of DNA nucleotide base pairs called the **homeobox**. Homeobox sequences are widely distributed in vertebrate genes, and are homologues of genes identified in the fruit fly *Drosophila* and various other invertebrates. Homeobox genes control segmental development by their role as DNA-binding transcriptional regulators, thus affecting the expression of a number of other genes involved in the developmental process. Similar regulatory genes with a variety of names, such as the “zinc-finger” gene (*Krox-20*) and **paired box (Pax)** genes, are also involved in the pattern specification of the brainstem.

A different and unique combination of homeobox-containing genes and other regulatory genes are expressed in each of the rhombomeres. In the upper part of Figure 9-1, the extent of each black bar indicates the part of the brainstem in which activity for the particular gene listed at the left has been detected. For example, the *Hox 2.8* gene is active in a long

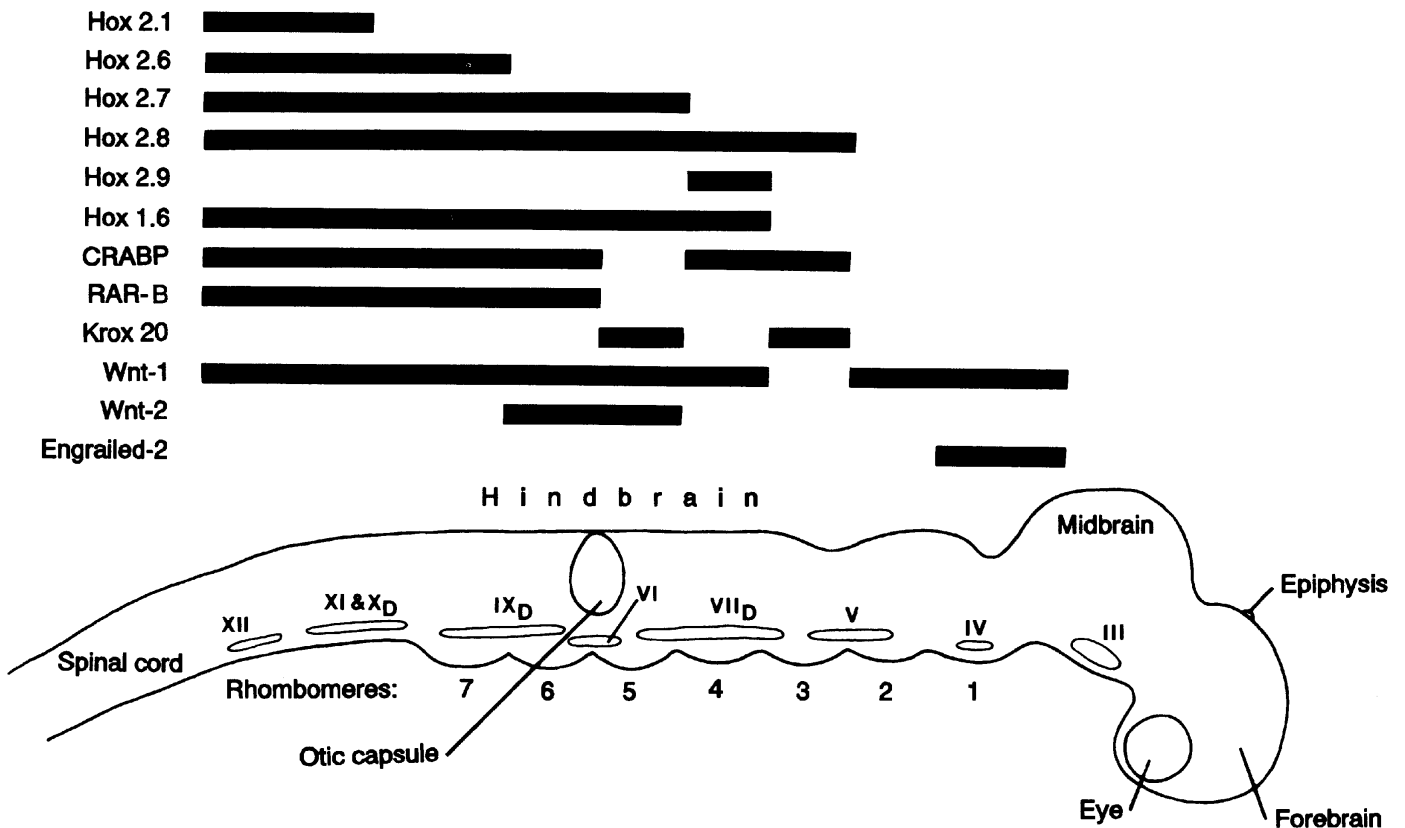


FIGURE 9-1. Schematic sagittal section through the developing chick brain, showing the expression patterns (indicated by the bars) of homeobox-containing and similar regulatory genes in the hindbrain and midbrain and the location of the populations of neurons for a number of the cranial nerve nuclei. The latter are indicated by Roman numerals, consistent with the terminology and classification of cranial nerves discussed in this chapter. Rhombomeres are indicated by Arabic numbers 1–7. Adapted from Noden (1991). Used with permission of S. Karger AG.

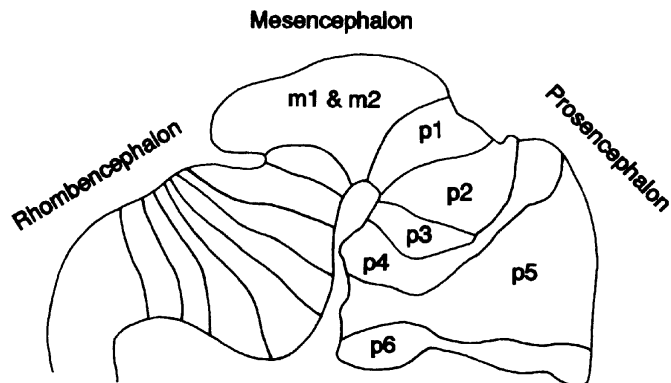


FIGURE 9-2. Drawing of a schematic lateral view of the developing brain of a chick embryo, with the segmental neuromeric divisions projected onto it. The prosomeres are identified as p1–p6 and the two mesomeres as m1 and m2. Adapted from Puelles and Rubenstein (1993). Used with permission of Elsevier.

area extending from the 2–3 rhombomere boundary caudally through the caudal-most part of the brainstem, whereas the *Krox-20* gene has two discrete areas of activity, one in rhombomere 3 and the other in rhombomere 5. The total pattern of gene activity thus forms a bar code or fingerprint-like profile that is unique for each individual rhombomere.

Whether the combined activity of these genes determines the specific identity of each rhombomere, the cranial nerve nuclei within the rhombomere, or both has not yet been established, however. During embryological development, the neuron cell bodies that form the motor nuclei of cranial nerves, which lie within the **basal plate** (the lower part of the tube) of adjacent pairs of neuromeres, migrate caudally within the neural tube to reach their final rhombomeric positions. Motor neurons of the seventh, ninth, and tenth cranial nerves and some of the neurons of the fifth and lateral line cranial nerves migrate over distances of one to three rhombomeres. How the activity of the regulatory genes specifies the various pools of motor nerve neurons in relation to the rhombomeric segments is thus unclear.

In the midbrain and forebrain, a number of similar, putative regulatory genes also have been identified recently that appear to specify the mesomeres and prosomeres. These include genes referred to as the *engrailed* homologue, *En-2*, as well as *Krox-20* in the midbrain (Fig. 9-2) and as *Wnt-1*, *Wnt-3*, *Wnt-3A*, *Wnt-4*, *Dix-1*, *Dix-2*, *Nkx-2.2*, and so on, in the forebrain. The same genes also have been discovered in a variety of invertebrates and vertebrates, and their names often reflect particular traits, such as the “zinc-finger” regulatory gene of the hindbrain mentioned above.

THE VERTEBRATE HEAD: SEGMENTAL ORGANIZATION

Understanding the organization of the cranial nerves depends on an appreciation of the segmental nature of the brain and head and of the embryonic derivation of the nerves, their ganglia, and the structures that they innervate. Questions that have been debated for a long time are whether or not the

brain and other tissues of the head are in fact developed in a segmental fashion and, if so, which structures are within each segment. Although neuromeres have yet to be identified in the developing spinal cord, the spinal cord in adult vertebrates clearly is a segmented structure. Each segment of the spinal cord has dorsal and ventral pairs of spinal nerves that innervate each successive segment of the body, but the segmental organization of the brain has not been as easily understood.

Recent advances from studies of the embryology of the head, using modern transplant and marking techniques, have led to a new understanding of the development of the head and brain in vertebrates through an understanding of the roles of two ectodermal (outer body layer) derivatives, called **neural crest** and **placodes**, and the role of mesoderm (middle body layer) in this process. In addition to the process of segmentation of neuromeres within the neural tube itself, at least some of these other tissues interact in a segmental fashion during the development of the brain and sensory organs. To approach this topic, first we need to review briefly some of the components of the skeleton of the head and then consider their relationship to the striated musculature, the neural crest, and placodes.

Gills and Arches

The skeleton of the head in vertebrates contains three components: the **chondrocranium**, which encloses the special sense organs and forms part of the braincase; the **splanchnocranium** (or **visceral arches**), which supports and moves the gills and, in jawed vertebrates, contributes to the jaws, and the **dermatocranium** (or **dermal bones**), which contributes to the braincase and the jaws. In vertebrates that have gills, the first step in the development of the gills is the formation of a paired series of pouches that arise as evaginations (out-growths) from the pharynx in the throat region. The visceral arches are a series of cartilaginous or bony arches that lie between the pharyngeal pouches. The cartilage of the visceral arches is mostly derived from neural crest tissue, as we will discuss below.

The first visceral arch, which is the **mandibular arch** in jawed vertebrates, lies rostral to the first pharyngeal pouch, and the second visceral arch, or **hyoid arch**, lies between the first and second pharyngeal pouches. Most jawed fishes have five additional visceral arches, which are called the first through the fifth **branchial arches**. The term branchial refers to the gills. In cartilaginous fishes, the mandibular arch consists of a dorsal palatoquadrate cartilage and a lower mandibular cartilage that form the upper and lower jaws, respectively. In bony fishes and tetrapods, the dermatocranium contributes substantially to the bony part of the jaws; remnants of the palatoquadrate and mandibular cartilages are retained in bony fishes, however, and the cartilaginous articulation of the jaws in non-mammalian tetrapods is derived from the mandibular arch. The dorsal part of the hyoid arch, called the hyomandibular cartilage, suspends the palatoquadrate cartilage in bony fishes, and its ventral part extends ventrally into the mouth and pharynx. In tetrapods, the hyomandibular forms one of the auditory ossicles, while most of the branchial arches are incorporated into the various cartilages of the throat (hyoid, thyroid, cricoid, etc.).

The Striated Musculature of the Head

One of the major breakthroughs in understanding the development of the head and central nervous system was the recent identification of the embryonic source of all of the striated muscles in the head. In the body, a part of the mesoderm called the **hypomere** (or **lateral plate mesoderm**) gives rise to the nonstriated, visceral muscles and connective tissues of the gut, while more dorsal mesoderm, called the **epimere** (or **paraxial mesoderm**) forms **somites** (segmental mesodermal divisions) that give rise to the striated muscles of the body (Fig. 9-3). The **branchiomeric muscles** (associated with the gills or throat cartilages) within the head were long thought to be derived from a rostral extension of the lateral plate mesoderm and therefore of visceral origin, and the cranial nerves supplying them were therefore classified as visceral motor nerves. Only the extrinsic muscles of the eye and the muscles of the tongue were thought to be somatic muscles, that is, derived from the embryonic paraxial mesoderm. The fact that the supposedly visceral, branchiomeric muscles are striated, like the eye muscles and the tongue, was an unresolved problem and ignored by most. These beliefs, which were the basis of the venerable classification of cranial nerves that is widely taught today, are, however, not supported by contemporary embryology.

Interspecies transplantation studies and cell lineage tracing studies have allowed a reexamination of the fate of the mesoderm within the head, revealing a rather different story. In the developing head, the paraxial mesoderm forms a longitudinal, segmented series of slightly elevated bulges called **somitomeres** (Fig. 9-4). The more ventrally lying, lateral plate mesoderm does not contribute to somitomere formation, so the somitomeres have no component that could be argued to be developmentally visceral. The somitomeres are delineated by a series of shallow depressions, rather than being completely divided into separate masses like the somites of the body. These somitomeres give rise to all of the striated muscles of the head (Fig. 9-4), just as the somites of the epimere in the body give rise to the striated muscles of the trunk and limbs. Thus, the voluntary, striated muscles in the head, which are innervated by cranial motor nerves, are all somatic muscles, and thus, their motor

nerves are all somatic motor nerves. The lateral mesoderm of the head only contains precursors of cells that make a minor contribution to some of the throat cartilages and neighboring bone.

Neural Crest and Placodes

Studies of the movement and fate of neural crest cells and other populations of ectoderally derived cells have also revealed new findings about the development of the brain and head. Neural crest cells arise within the neural fold tissue lateral to the neural tube. These cells are segmentally specified at their point of origin by the pattern of expression of *Hox* regulatory genes, and they carry their segmental identity as they migrate ventrally between the paraxial mesoderm and the surface ectoderm (Fig. 9-5). The neural crest gives rise to many structures throughout the body, including nerves and sensory ganglia in the trunk, chromaffin cells, which secrete adrenalin, in the medulla of the adrenal gland, all pigment cells, and the Schwann cells that supply the myelin sheathing around peripheral nerves. In the head, neural crest cells migrate between the pharyngeal pouches. These cells form the cartilage of the branchial arches and the smooth muscle of the aortic arches. Within the rest of the head, neural crest gives rise to the anterior part of the neurocranium and to the meninges, the connective tissue layers that cover the brain. It also gives rise to a number of the cranial nerves and their sensory ganglia.

Parts of the surface ectoderm also contribute to the formation of cranial nerves and sensory ganglia. Patches of neurogenic tissue form within the ectoderm. These patches are called placodes, and they give rise to additional components of the nervous system. Neural crest cells migrate beneath the placodes, and the placodes then begin to produce neuroblasts (nerve cell precursors). A dorsolateral series, a ventrolateral series, and additional unclassified sets of placodes form the sensory receptors and ganglia of some of the cranial nerves. While neural crest occurs throughout the head and body, placodes are present only in the head.

Segmentation of the Head

The head in vertebrates differs from the rest of the body in two significant ways: lateral plate mesoderm is present but makes only modest contributions to cartilage and bone rather than giving rise to muscle, and placodes are present. The contributions of placodes and neural crest result in the formation of the paired sense organs and the anterior part of the neurocranium, that is, the rostral part of the head, which is thus new in vertebrates. This formation of a new part of the head due to the presence of placodes and neural crest and its implications for the origin of vertebrates was recognized by Carl Gans and R. Glenn Northcutt in 1985.

Like the body, the head is segmented, that is, composed of repeating units. These units may or may not be serially homologous to the segments of the spinal cord, but they exhibit organizational similarities. The segmental units include the expression patterns of regulatory genes, morphological neuroepithelial units (neuromeres), populations of motor neurons for cranial nerves, morphological paraxial mesodermal elements (somitomeres), and streams of segmentally specified neural

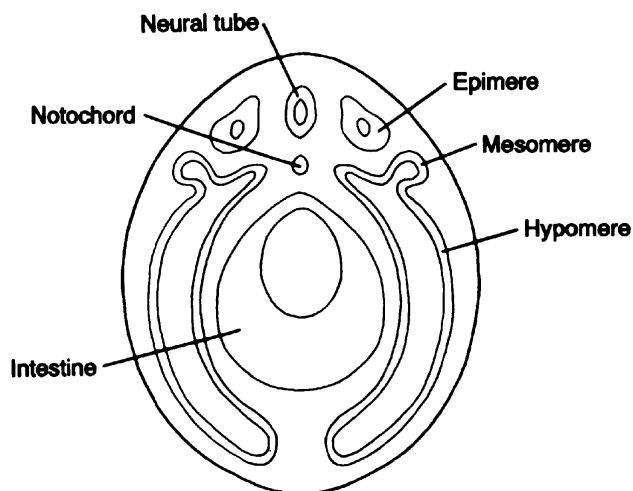


FIGURE 9-3. Schematic transverse section through a vertebrate embryo to show the organization of the epimeric and hypomeric parts of the mesoderm in the body.

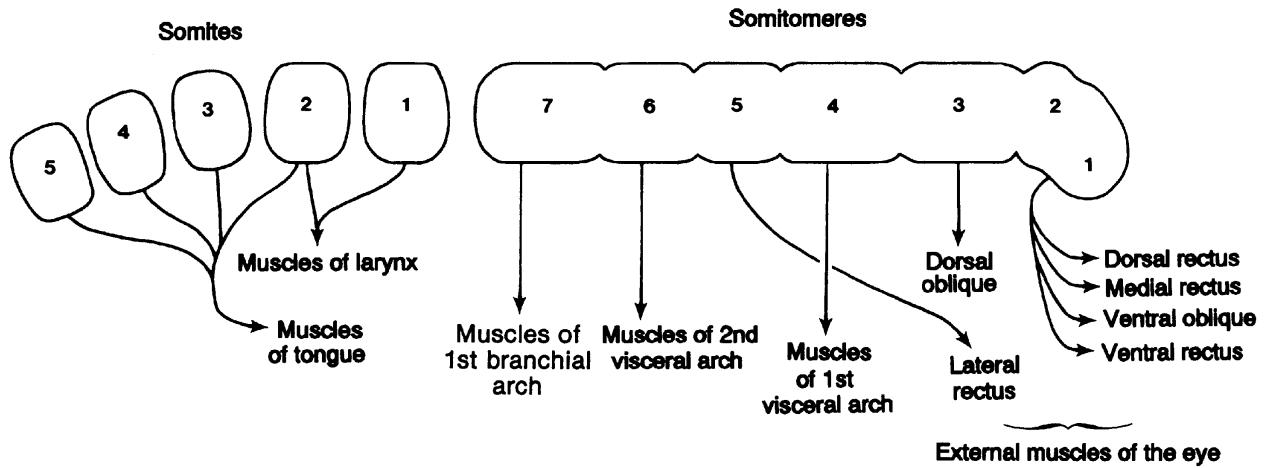


FIGURE 9-4. Schematic sagittal section through the epimeric mesoderm in the head and the muscles that each part of it gives rise to. Adapted from Noden (1991). Used with permission of S. Karger AG.

crest cells. Some of the cranial nerves are organized like segmented, spinal nerves. Other cranial nerves, including those derived from placodes, are unique to the head.

In creating a model of head segmentation, a simple, 1:1 correspondence among specific neuromeres, somitomeres, and visceral arches has not yet been defined across vertebrates. The series of rhombomeres that form the hindbrain is highly conserved among vertebrates, but variation occurs in the loca-

tion of some of the cranial nerve motor nuclei (Fig. 9-6). The series of somitomeres is also highly conserved, but a precise, topographic registration of somitomeres with neuromeres has yet to be confirmed.

Figure 9-7 shows a structural comparison among neurula stages of developing embryos of *Branchiostoma* (*Amphioxus*), a lamprey, a shark, and a chick. The neurula stage is reached with the first development of the nervous system following

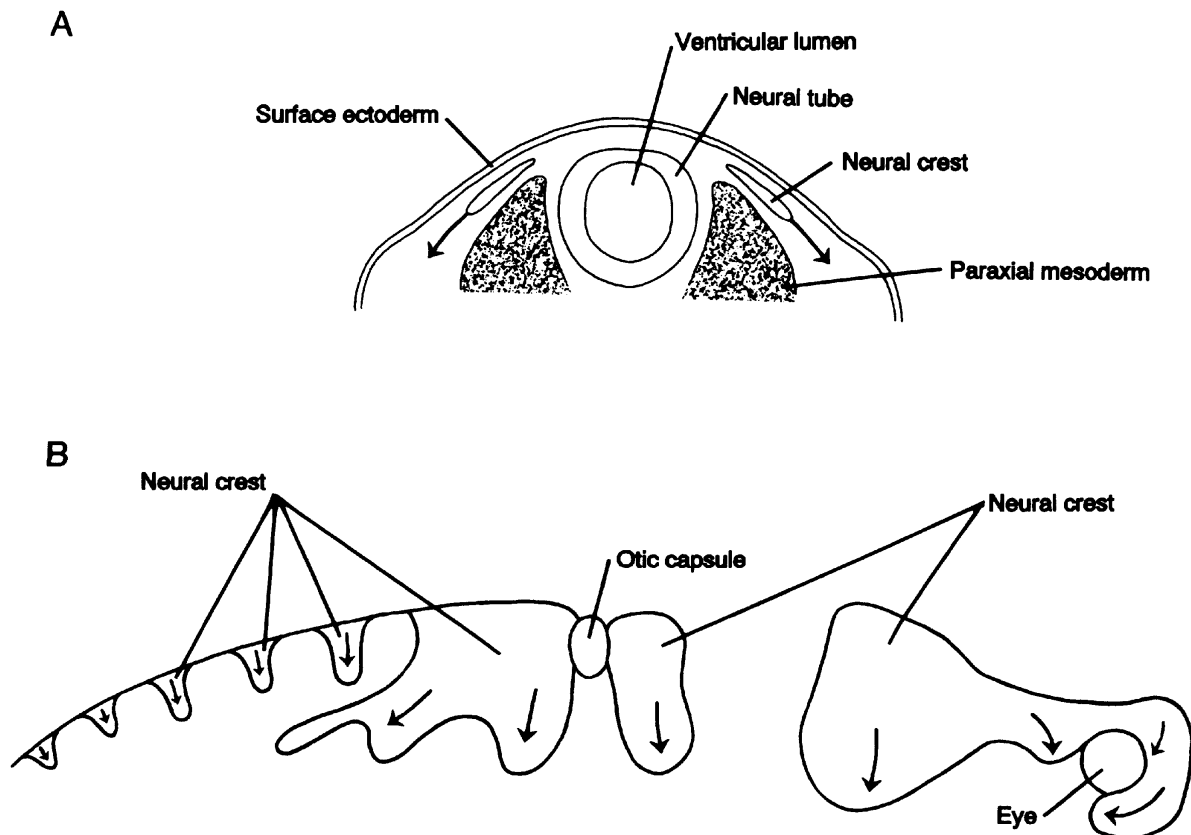


FIGURE 9-5. (A) Schematic drawing of a transverse section through the developing neural tube in the dorsal part of a vertebrate embryo, with arrows indicating the direction of migration of the neural crest. (B) A drawing to show the migration of the neural crest as seen in a parasagittal section. Adapted from Noden (1991) and used with permission of S. Karger AG.

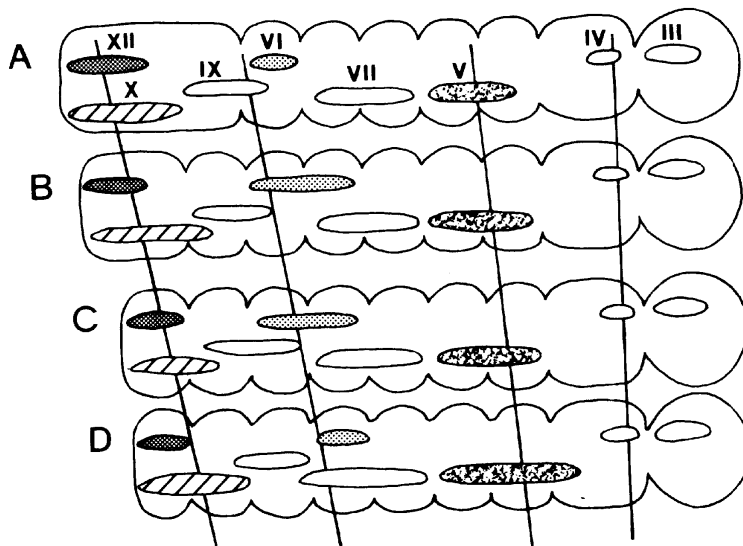


FIGURE 9-6. Schematic drawing to show the relationships between neuromeres and cranial nerve motor nuclei in a variety of vertebrate groups. Shadings and lines are used to facilitate comparisons of the relative positions and extent of the cranial nerve nuclei, which are indicated by their Roman numerals. (A) Elasmobranch, (B) teleost fish, (C) nonmammalian amniote, and (D) mammal. Adapted from Gilland and Baker (1992). Used with permission of S. Karger AG.

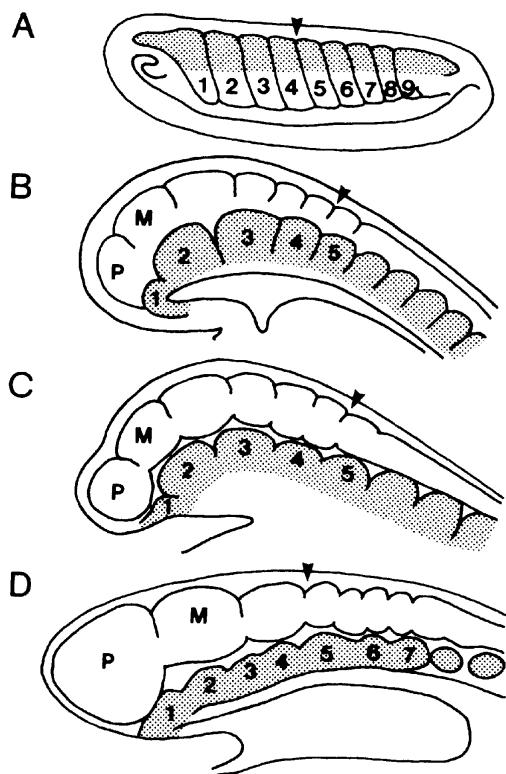


FIGURE 9-7. Drawings of parasagittal sections through early developmental stages of *Branchiostoma* (A) and three vertebrates—a lamprey (B), a shark (C), and a chick (D)—to show the comparative alignment of neuromeres, somitomeres (indicated by light shading), and the rostral limit of expression of the *Hox-3* (H3) regulatory gene (arrowheads). Comparable somitomeres are indicated by numbers, the prosencephalon by P and the midbrain by M. Rhombomeres are unnumbered. Adapted from Gilland and Baker (1992). Used with permission of S. Karger AG.

gastrulation. The dashed lines indicate homologous regions, showing that neuromeric units and somitomeric units do not have the same 1:1 relationship in all cases; nonetheless, a similar rostral to caudal sequence is maintained.

Two neurobiologists, E. Gilland and R. Baker, published a paper in 1992, which provides a new perspective for the evolution of the vertebrate head from this comparison. The rostral expression border of the *Hox-3* (H3) regulatory gene is indicated in each species shown in Figure 9-7. The position of H3 has been demonstrated experimentally in *Branchiostoma* and the chick but is theoretical for the lamprey and the shark. As Gilland and Baker discuss, the position of H3 in *Branchiostoma* implies that the first five somites of *Branchiostoma* are homologous as a field to the somitomeric region of jawed vertebrates. They argue that if this hypothesized homologous relationship is supported by further data, such as additional comparative information on homeobox gene expression patterns, then the cranial region of amniotes can be compared with the entire primary gastrula of *Branchiostoma*. In other words, the head of vertebrates may be the homologue of the primary gastrula of *Branchiostoma*.

THEORETICAL HEAD SEGMENTS

A head segment (or the concept of a head segment) encompasses elements of each of the segmentally organized tissues in the vertebrate head. Thus, a model head segment would contain a rostrocaudally defined portion of the neuromeres, at least some of the cranial nerve neurons, somitomeres, neural crest, visceral arches, and related tissues. Placodes may be influenced by segmentally specified neural crest but may not in themselves be segmentally organized. Since the rostrocaudal alignment of the various segmental tissues varies among differ-

ent groups of vertebrates, the definitive head segment cannot yet be identified. Nonetheless, we can examine the organization of the cranial nerves with a theoretical model of head segments.

The overall organizational pattern that emerges reveals the presence of up to four separately derived nerves—**dorsal**, **ventral**, **dorsolateral**, and **ventrolateral**—for each side of each head segment. All four nerves are not present in all head segments, but we have illustrated all four schematically in Figure 9-8 to make the segmental organizational pattern clear. Figure 9-8 models a pair of somitomeres for each head segment. The more rostral somitomere of each pair gives rise to one or more of the muscles of the eye or to the muscles of the tongue. The more caudal somitomere of each pair, except the first, gives rise to branchiomeric muscles.

A ventral nerve for a given model segment is derived from cells in the ventral part of the neural tube. This nerve is the somatic motor nerve for the muscle(s) derived from the more rostral of the two somitomeres. This arrangement appears to correspond to that seen in the spinal cord, with the ventral nerve carrying somatic motor fibers.

In addition, a dorsal nerve for the segment is derived from the neural tube and is the somatic motor nerve for the branchio-

meric muscles(s) that are derived from the more caudal of the two somitomeres. In contrast to the ventral nerve, the dorsal nerve also has axons from cells derived from neural crest, which are sensory axons. This sensory component may correspond to that seen in the dorsal axons of the spinal cord. However, the presence of the somatic motor fibers in this dorsal nerve is unlike the condition of the dorsal spinal nerves, which are purely sensory.

The sensory ganglion cells of two additional nerves in the segment may be derived from placodes. Additional research is needed to clarify the origin from placodes and/or neural crest of a number of cranial nerve sensory ganglia. Further work is needed to correlate the embryological derivation of specific populations of sensory neurons with the specific identity of the sensory receptors that they innervate. The dorsolateral nerve of a model segment is known to be derived from the dorsolateral series of placodes. In the third head segment, multiple dorsolateral nerves are in fact present, and the placodes give rise to the receptors and sensory ganglion cells of the auditory, vestibular, and lateral line systems. A ventrolateral nerve for the segment can be modeled, subject to further research findings, as deriving in the hindbrain from the ventrolateral (or epibran-

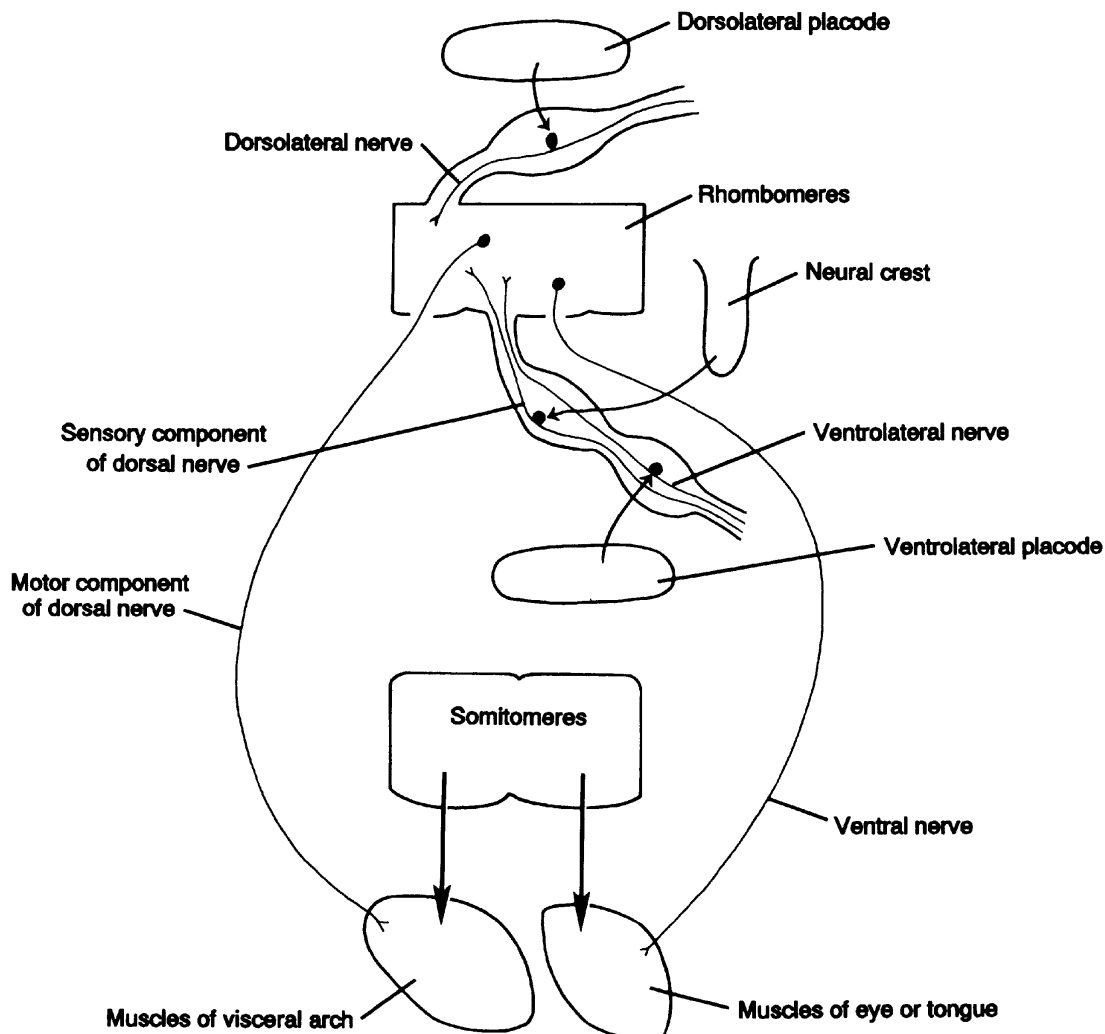


FIGURE 9-8. Schematic drawing of a model head segment to show the organizational plan of the cranial nerves. Rostral is toward the right. The embryological derivation of ganglion cells for a number of the cranial nerves has yet to be confirmed.

chial) series of placodes, which are thought to give rise to the sensory ganglion cells for the sense of taste, and in the telencephalon from more rostral placodes for other cranial nerves.

The most rostral cranial nerves are associated with the forebrain, which lies rostral to the first model head segment. Some forebrain cranial nerves are derived from placodes, which we have somewhat arbitrarily assigned to the ventrolateral category, but no dorsal, ventral, or dorsolateral nerves are present in the forebrain. Additionally, the forebrain has two unique nerves, derived from evaginations of the brain itself: the optic and the epiphyseal nerves.

From the above description, it should be apparent that there is a general scheme of organization of the cranial nerves. For a model head segment (Fig. 9-8), up to four separate cranial nerves are present: (1) a dorsal nerve, with a component derived from the neural tube that innervates branchiomic muscles and a component derived from neural crest cells that is sensory; (2) a ventral nerve derived from the neural tube that is motor; (3) a sensory nerve derived from dorsolateral placodes; and (4) a sensory nerve derived from ventrolateral placodes and/or neural crest. As discussed above, the modeled embryological derivation of some of these components may be modified as further data become available. Variation occurs in the presence of some of the nerves among different model head segments, but the differential patterns of organization of the cranial nerves in each segment can be understood in terms of the basic theme. The model segments of the head thus resemble the actual segments of the spinal cord in having dorsal and ventral nerves, but model head segments additionally have motor components of dorsal nerves and dorsolateral and ventrolateral nerves contributed by placodes and/or neural crest.

nerves actually comprise two separate nerves each. The facial, glossopharyngeal, and vagus nerves each contain the components of a dorsal, segmental, cranial nerve and a ventrolateral cranial nerve derived from the series of epibranchial placodes. In each of these cases, we refer to the former as a separate nerve from the latter. Thus, for example, we refer to the "dorsal facial (VII_D) nerve" and the "ventrolateral facial (VII_V) nerve" rather than to just the "facial (VII) nerve." In cases where only one of the segmental nerves (i.e., dorsal, ventral, ventrolateral, or dorsolateral) is contained in a designated nerve or where a placodal component of a nerve remains undesignated, we do not use an adjective to modify the original name of the nerve. For example, although the trigeminal nerve is a dorsal cranial nerve that also has a placodal component, it is not subdivided here into dorsal and either ventrolateral or dorsolateral components. We refer to it simply as the trigeminal (V) nerve.

The model presented in Figure 9-9 is a neuromere-somitomere model of the development of the head and the cranial nerves. It is based on several recent publications, including those of Northcutt (1990), Noden (1991), and Walker and Liem (1994). This model may be subject to revision as new data continue to be obtained. For example, data and analyses published by Gilland and Baker (1992, 1993) and by Northcutt (1993) suggest a revised numbering system for the somitomeres such that somitomeres 1-3 as shown here would be the prechordal plate (mesoderm that is located rostral to the rostral end of the notochord), and seven somitomeres would then be recognized in the region presently considered to be somitomeres 4-7. Still other designations of the somitomeres have also been proposed. The rostrocaudal order of neuromere-somitomere model units remains relatively constant, however, and that order is the key point to keep in mind in analyzing the organization of the cranial nerves.

SEGMENTAL ORGANIZATION OF THE INDIVIDUAL CRANIAL NERVES

We will now examine the organization of cranial nerves in the forebrain and in a rostrocaudal series of head segments. These segments only represent a hypothetical, generalized vertebrate scheme, since a simple, 1:1 correspondence of neuromeres, somitomeres, and other segmental tissues of the head has not been defined across all vertebrate groups. With the overall scheme of a model head segment that was presented in Figure 9-8 in mind, the organization of the various, individual cranial nerves can be understood. Figure 9-9 is a comprehensive diagram that illustrates the cranial nerves of the forebrain and the successive head segments (or **holobranchs**) along with the neuromeres, somitomeres, and currently hypothesized contributions from neural crest and placodes. Some of the contributions from neural crest and placodes may be subject to revision as further data indicate. The alignment of the head segments with the neuromeres and somitomeres in Figure 9-9 is based only on our generalized, theoretical model of vertebrate head segmentation, as discussed above. Table 9-2 summarizes the segmental organization of the head and the cranial nerves.

The original terminology used for the cranial nerves has been modified only slightly for the new scheme. As we will discuss below, three of the traditionally recognized, 12 cranial

The Forebrain

The first several cranial nerves are associated with the forebrain, which lies rostral to the first model head segment. The most rostral cranial nerve is the **terminal nerve**. At least some of the ganglion cells of the terminal nerve are derived from a rostral, **olfactory placode** [Fig. 9-9(B)]. Some of the terminal nerve ganglion cells may derive from other sources, including neural crest and/or the forebrain itself. The dendrites of terminal nerve neurons are distributed over the nasal septum, and the axons project to cilia in the forebrain; this nerve may play a role in reproductive behaviors.

Cranial nerve I, the **olfactory nerve**, also is derived from the olfactory placode. It carries olfactory information into the telencephalon. The **vomerinal nerve** is another cranial nerve that is present in some but not all vertebrates and is associated with the olfactory nerve and likewise derived from the olfactory placode. This nerve also plays a role in chemical detection. It projects, however, to a different area of the telencephalon than the olfactory nerve. An additional placode present in this region (but not illustrated in Fig. 9-9) is the **adenohypophyseal placode**. The olfactory organ and adenohypophysis arise from a single placode in lampreys, and a single rostral placode may thus be the plesiomorphic condition for vertebrates.

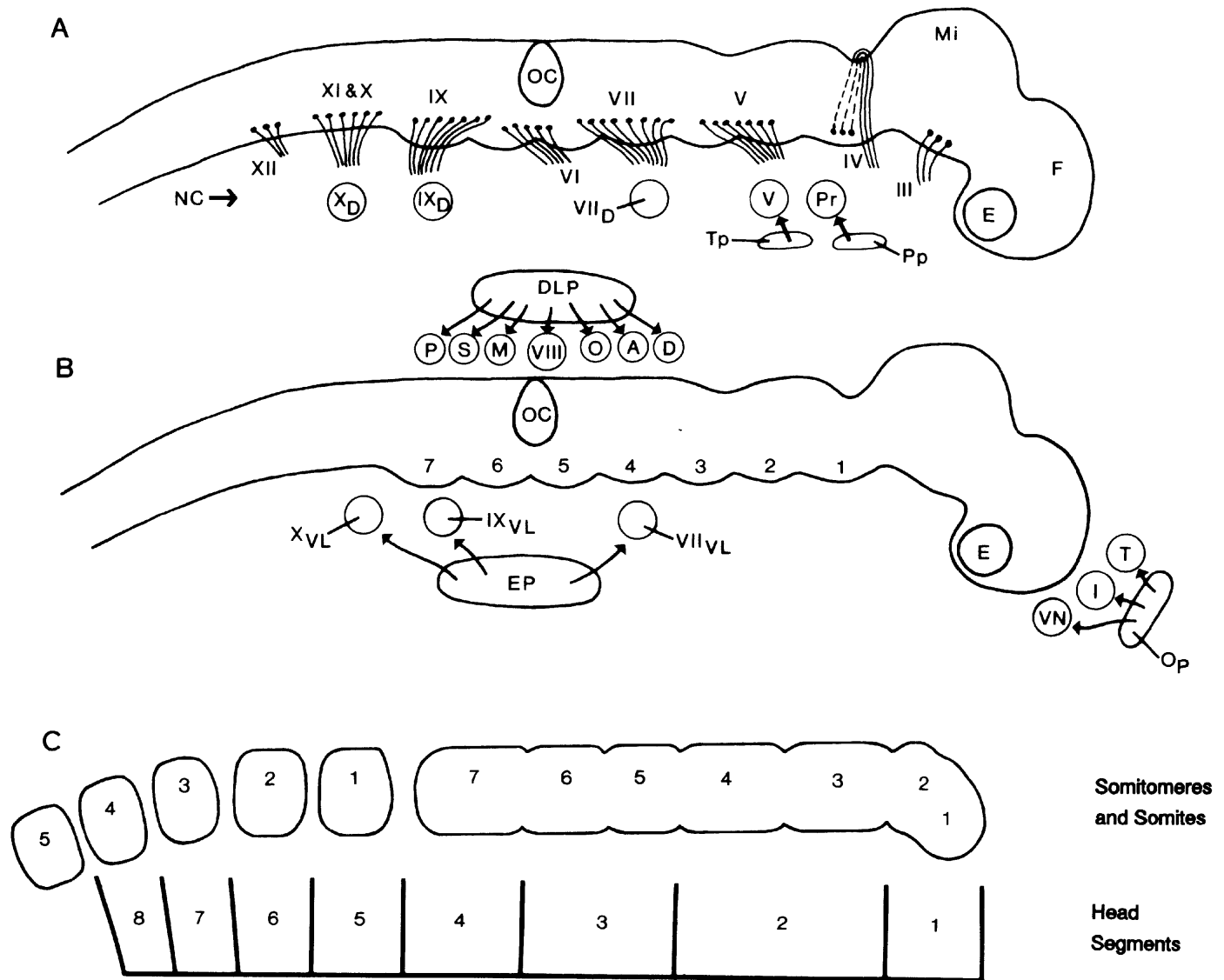


FIGURE 9-9. Schematic drawing of parasagittal sections through the neural tube (A and B) and the somitomeric mesoderm aligned with the model head segments (C). Rostral is toward the right and dorsal toward the top. The derivation of cranial nerve ganglia from neural crest (NC) and the trigeminal (T_p) and profundus (P_p) placodes and the location of their nuclei within the neural tube are shown in A. The derivation of cranial nerve ganglia and nerves from the dorsolateral (DLP) and ventrolateral, epibranchial (EP) series of placodes and the rostral olfactory (O_p) placode are shown in B. The rhombomeres are indicated by Arabic numerals 1–7 in B. The somitomeres (Arabic numerals 1–7) and rostral series of somites (Arabic numerals 1–5) along with model head segments (Arabic numerals 1–8) are shown in C in vertical alignment with the neural tube. Cranial nerve components are identified by their Roman numerals or by the abbreviations: A, anterodorsal lateral line; D, anterodorsal lateral line; M, middle lateral line; O, otic lateral line; P, posterior lateral line; Pr, profundus; S, supratemporal lateral line; T, terminal; and VN, vomeronasal. Other abbreviations: OC, otic capsule; E, eye; F, forebrain; Mi, midbrain. Adapted from Noden (1991). Used with permission of S. Karger AG.

The **optic nerve**, cranial nerve II, arises from neurons in the retina, and the **epiphyseal nerve** (which in a number of groups of vertebrates has two divisions, a pineal nerve and a more rostral epiphyseal nerve) arises from neurons in the epiphysis. These cranial nerves should probably be considered as parts of the brain rather than as cranial nerves because, whereas other sensory nerves are derived from either neural crest and/or from placodes, the receptors and sensory ganglion cells of the retina in the eye and of the epiphyseal photoreceptor system are derived from evaginations of the neural tube. Only the lens of the eye, and probably the lens of the parietal eye

where present, are derived from placodal tissue. We thus have classified these nerves as evaginated sensory afferents.

The telencephalon thus has three nerves, the terminal, olfactory, and vomeronasal nerves, which are derived from placodes. We rather arbitrarily classify these nerves as ventrolateral nerves derived from a rostral placode; they are, however, different and distinct from the ventrolateral nerves that are derived from the more caudally lying series of epibranchial placodes and that are discussed below. The optic and epiphyseal nerves of the diencephalon are photosensory and may be nerves that are uniquely derived from the neural tube or may

TABLE 9-2. Head Segmentation and Cranial Nerve Organization

Head Segment	Origin	Visceral Arch	Branchial Arch	Neural Tube-Derived or Dorsal Cranial Nerve	Ventral Cranial Nerve	Dorsolateral Cranial Nerve	Ventrolateral Cranial Nerve
				II, Epiphyseal			T, VN, I
1	Somitomeres 1, 2			Profundus	III	LL _{AD}	
2	3, 4	1		V	IV	LL _{AV}	
3	5, 6	2		VII _D	VI	Otic, VIII	VII _{VL}
4	7	3	1	IX _D		LL _M	IX _{VL}
5	Somites 1	4	2	X _D	XII	LL _{ST} , LL _P	X _{VL}
6	2	5	3	X _D	Occipital		X _{VL}
7	3	6	4	X _D	Occipital		X _{VL}
8	4	7	5	X _D	Occipital		X _{VL}

represent the sensory components of dorsal nerves. Dorsolateral and ventral nerves, as present in the more caudal parts of the brain, are clearly absent in the forebrain.

The First Head Segment

The first head segment in our model contains the first two somitomeres [Fig. 9-9(C)]. The more rostral somitomere, and possibly the more caudal one, give rise to the extrinsic eye muscles (listed in Fig. 9-4) that are innervated by cranial nerve III, the **oculomotor nerve**. Thus, the oculomotor nerve [Fig. 9-9(A)] is the somatic motor nerve of the ventral part of the first head segment. The more caudal somitomere of this segment does not give rise to any branchiomic muscle.

The **profundus placode** is currently not assigned to either the dorsolateral or ventrolateral series of placodes. It gives rise to most or all of the ganglion cells of the **profundus nerve** [Fig. 9-9(A)]; the possibility exists that the profundus ganglion also contains some cells derived from neural crest. The profundus is a sensory nerve, supplying a surface area on the snout of fishes. In the coelacanth *Latimeria*, the profundus nerve additionally supplies the mucosa of a series of rostral tubes that contain separately innervated electroreceptors. The profundus nerve has no motor component, as does the more caudal trigeminal nerve, but it can be considered to be the dorsal nerve of the first head segment. In mammals, in which the profundus nerve is called the **ophthalmic branch of the trigeminal nerve**, the ganglia of the profundus and trigeminal nerves merge. No ventrolateral nerve derived from an epibranchial placode is present in the first head segment. Dorsolateral nerves will be discussed in conjunction with the third head segment.

The Second Head Segment

Somitomeres 3 and 4 are the paraxial mesoderm of the second model head segment. Somitomere 3 gives rise to the dorsal oblique muscle of the eye. The dorsal oblique is innervated by cranial nerve IV, the **trochlear nerve**, which is the ventral nerve of the second (mandibular) model head segment [Fig. 9-9(A)]. Somitomere 4 gives rise to the branchiomic

muscles of the jaw. The dorsal nerve of this segment is the **trigeminal nerve**, cranial nerve V, which has a somatic motor component innervating the muscles of the jaw and a somatic sensory component. The ganglion cells of the sensory component of this dorsal nerve lie in the proximal part of the trigeminal ganglion and may arise from both neural crest and/or a **trigeminal placode** [Fig. 9-9(A)]. Further studies are needed to clarify the embryological origin of all of the cells in both the profundus and trigeminal placodes. The second head segment, like the first, lacks ventrolateral nerves derived from placodes. Dorsolateral nerves will be discussed in conjunction with the third head segment.

The Third Head Segment

The paraxial mesoderm of the third (hyoid) model head segment is derived from somitomeres 5 and 6. Somitomere 5 gives rise to the lateral rectus muscle of the eye. The lateral rectus is innervated by the ventral, somatic motor nerve of the third head segment, cranial nerve VI, the **abducens nerve** [Fig. 9-9(A)], which courses rostrally to reach the muscle. Somitomere 6 gives rise to the branchiomic muscles of the face. These muscles are innervated by the motor fibers in the dorsal nerve of the third head segment, the **dorsal facial nerve**, cranial nerve VII_D. Like the trigeminal nerve of the second head segment, the dorsal facial nerve also has a somatic sensory component. The ganglion cells for this sensory component are presumably derived from neural crest and lie in the proximal part of the ganglion of the nerve.

The third head segment is the central-most segment for nerves derived from **dorsolateral placodes** [Fig. 9-9(B)]. The dorsolateral series of placodes gives rise to the receptors and ganglion cells of a multiple set of nerves. Three **preotic placodes** (Table 9-3) give rise to the ganglion cells and receptors of three **lateral line nerves**—**anteroventral** (LL_{AV}), **anterodorsal** (LL_{AD}), and **otic** (O)—for electroreception and/or mechanoreception. An **octaval placode** gives rise to the receptors within the membranous labyrinth of the inner ear and to the ganglion cells of the vestibular and cochlear rami of the **octaval** (VIII) **nerve**. The **vestibular ramus** carries balance and posi-

TABLE 9-3. Lateral Line and Octaval Placodes and Nerves

Placodes	Nerves
Preotic	Anteroventral lateral line Anterodorsal lateral line Otic lateral line
Octaval	Cochlear ramus of eighth Vestibular ramus of eighth
Postotic	Middle lateral line Supratemporal lateral line Posterior lateral line

tion senses, and the **cochlear ramus** carries hearing. Three **postotic placodes** give rise to the ganglion cells and receptors of three additional lateral line nerves—**middle** (LL_M), **supratemporal** (LL_{ST}), and **posterior** (LL_P). We have illustrated the six lateral line placodes and the octaval (vestibulocochlear) placode as primarily associated with the third segment. Alternatively, as shown in Table 9-2, these dorsolateral placodes may be serially related to a number of head segments, such that the anterodorsal placode is the dorsolateral placode of the first head segment, the anteroventral placode is of the second, the otic and octaval placodes are of the third, the middle is of the fourth, and the supratemporal and posterior are of the fifth and more caudal segments. Further research is needed to clarify whether such registry of dorsolateral placodes and rhombomeres exists.

The third head segment also has a ventrolateral nerve, derived from a ventrolateral, **epibranchial placode**, which is thought to innervate taste buds. This nerve is the **ventrolateral facial nerve** [VII_{VL} , in Fig. 9-9(B)]. The neuron cell bodies of the axons of this nerve lie in the distal part of the ganglion of the facial nerve and are derived from placode.

The Fourth Head Segment

There is only one somitomere associated with the fourth model head segment. Within this segment, somitomere 7 gives rise to muscle associated with the first branchial arch (third visceral arch). These muscles are innervated by somatic motor fibers in the **dorsal glossopharyngeal nerve**, cranial nerve IX_D . The dorsal glossopharyngeal nerve also has a somatic sensory component, and neural crest cells give rise to the ganglion cells of these sensory fibers in the proximal ganglion of the nerve. The dorsal glossopharyngeal nerve is thus the dorsal nerve of the fourth head segment [Fig. 9-9(A)], and somitomere 7 resembles the more caudal of the two somitomeres present in the more rostral head segments. A more rostral somitomere apparently does not develop in the fourth head segment, and, correspondingly, no ventral, purely somatic motor nerve is present.

The dorsolateral nerve of the fourth head segment may be the middle lateral line nerve, as discussed above. The ventrolateral nerve of this segment, derived from an epibranchial placode, is the **ventrolateral glossopharyngeal nerve** (IX_{VL}). The ganglion cells for the sensory fibers that are thought to innervate

the taste buds are derived from placode and lie in the distal ganglion of the nerve [Fig. 9-9(B)].

The Fifth Head Segment

A series of somites are present caudal to somitomere 7, which gives rise to muscles of the larynx and tongue, as well as to hypobranchial muscles (those below the gill arches in the neck), in the fifth model head segment. The ventral, somatic motor nerve, which comprises three separate nerves in most fishes, is derived from the neural tube of this segment and is cranial nerve XII, the **hypoglossal nerve** [Fig. 9-9(A)]. The hypoglossal nerve innervates the muscles of the tongue in tetrapods. The **dorsal vagus nerve**, cranial nerve X_D , is the dorsal nerve of the fifth head segment. The ganglion cells of the sensory component of the dorsal vagus nerve are derived from neural crest and lie in the proximal ganglion of the nerve. The **accessory nerve**, cranial nerve XI (not included in Table 9-2), is also associated with the fifth head segment but is not as clearly understood. It is present in a wide range of vertebrates rather than being present only in amniotes as previously believed. In birds and mammals, the accessory nerve is a composite nerve, with a spinal motor nucleus that is plesiomorphic for at least jawed vertebrates and a bulbar portion of the nucleus derived from the vagus.

The supratemporal and posterior lateral line placodes supply the dorsolateral nerve component for the fifth (and more caudal) head segment, as discussed above. The ventrolateral, epibranchial series of placodes gives rise to a ventrolateral nerve of the fifth head segment, the **ventrolateral vagus nerve** (X_{VL}). The ganglion cells of this nerve are thought to innervate taste buds for this head segment. They are derived from placode and lie in the distal ganglion of the nerve [Fig. 9-9(B)].

We have not included some cranial nerve components in this analysis for the sake of the clarity of the overall pattern. As in the spinal cord segmental nerves, there are also autonomic and visceral (i.e., innervating viscera of the body) sensory components of cranial nerves. In addition, there are efferent components in a number of the sensory cranial nerves that terminate on the sensory receptor cells. These additional components, however, do not negate the overall scheme presented above.

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