Brains of Primitive Chordates

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Introduction

Craniates (which include the sister taxa vertebrata and hyperotreti, or hagfishes) represent the most complex organisms in the chordate phylum, particularly with respect to the organization and function of the central nervous system. How brain complexity has arisen during evolution is one of the most fascinating questions facing modern science, and it speaks directly to the more philosophical question of what makes us human. Considerable interest has therefore been directed toward understanding the genetic and developmental underpinnings of nervous system organization in our more 'primitive' chordate relatives, in the search for the origins of the vertebrate brain in a common chordate ancestor. We describe some of the principal features of the central nervous systems of hemichordates, cephalochordates, and urochordates – taxa of increasing genetic relatedness to craniates. The central nervous systems of these taxa show a variety of forms, from a hardly specialized basiepithelial nerve plexus (hemichordates) to a few small ganglia with a tail nerve cord (urochordates), a swimming spinal cord with a barely recognizable cerebral vesicle (cephalochordates), and a fully developed brain and spinal cord (craniates). It is important to emphasize that although the term primitive may be construed as implying a lower rank in evolutionary sequence, we use it strictly with respect to extant brain complexity. Each of these groups has in fact existed for substantial periods of evolutionary time and represents highly adapted lifeforms in their own right. We focus here on shared aspects of central nervous system structure and development that may relate to a common evolutionary origin but also indicate some of the specialized structural features that bear witness to the degree of divergence and range of derived characters that have arisen in the several hundred million years since these groups split from that origin.

Phylogenetic Relationships

Originally constructed solely through comparative analysis of morphological traits, phylogenetic trees are being increasingly tested and revised on the basis of gene sequence comparisons. Such analysis, although providing a more direct link to the evolutionary clock, is nevertheless hampered by differing rates of evolution, both among species and among genes, and a still largely deficient fossil record. Until recently, it was widely accepted, both on morphological and molecular grounds, that cephalochordates and craniates were sister taxons, with urochordates being more distant craniate relatives and with hemichordates being more closely related to echinoderms (Figure 1(a)). The molecular data only weakly supported a coherent chordate taxon, however, indicating that apparent morphological similarities among chordates are imposed on deep divisions among the extant deuterostome taxa. Recent analysis of a substantially larger number of genes has reversed the positions of cephalochordates and urochordates, promoting the latter to the most closely related craniate relatives (Figure 1(b)).

Comparative Appearance of Brains, Spinal Cords, and Nerves

Primitive Craniates (Cyclostomes)

The jawless cyclostomes, lampreys and hagfish, constitute a basic clade of craniates that shows the major features of brain organization also found in gnathostomes (jawed vertebrates). Externally, the brain of extant cyclostomes consists of a bilaterally symmetric rostral enlargement, the forebrain (telencephalon), each side of which is composed of an olfactory bulb and a cerebral hemisphere (Figure 2). Each hemisphere is connected to the single, bipartite diencephalon. The diencephalon gives rise to a number of neural appendages. Ventrolaterally are located the paired optic nerves leading to the lateral eyes. Dorsally lies a single enlargement, the habenula, that in lampreys, but not hagfish, has an attached pineal organ. Ventrally is located the pituitary gland. The central ventricle of the diencephalon is continuous with the ventricle in the midbrain, the hindbrain, and the central canal of the spinal cord, all of which are greatly reduced in hagfish. Lampreys have a dorsal central opening in the midbrain that is covered by a choroid plexus, a uniquely derived feature of lampreys not shared by other craniates. Lampreys, like gnathostomes, have an oculomotor nerve leaving the midbrain ventrally and a trochlear nerve exiting lateral to the cerebellum, neither of which do hagfish possess. Caudal to the small cerebellum in lampreys is the rhombencephalon (hindbrain) with a large choroid plexus covering the IVth ventricle. A small ventricle is also found in hagfish, but there is no trace of a
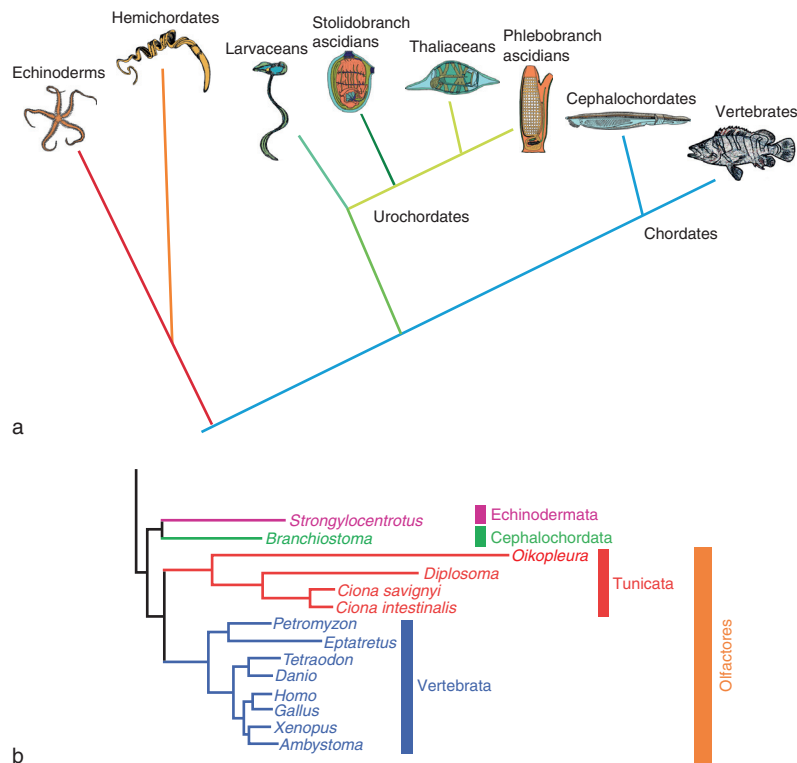
Figure 1 (a) Conventional scheme of phylogenetic relationships among chordates and related taxa. (b) A revised scheme based on more recent gene sequence analysis. Adapted from original image by Dr. Billie Swalla, University of Washington.

choroid plexus and the presence of a cerebellum has been questioned.

Lampreys have all the hindbrain nerves found in gnathostomes (trigeminal, abducens, facial, otic or stato-acoustic, glossopharyngeus, and vagus), with the possible exception of the hypoglossal nerve. The relative positions and fiber compositions of these nerves are very similar but not identical in cyclostomes and gnathostomes. For example, the abducens nerve root is almost integrated into the trigeminal nerve root in lampreys, whereas it is always a separate ventral nerve root at a more caudal level in gnathostomes. Moreover, gnathostomes have three distinct motor neuron populations in the brain stem, each innervating a different type of peripheral target: the somatic motor neurons that innervate somitomere-derived musculature, the branchial motor neurons that innervate branchial arch-derived musculature, and the visceral motor neurons that innervate neural crest-derived parasympathetic ganglia of the head and body. In contrast, cyclostomes as a group lack the somatic motor neurons of the hypoglossal nucleus and have no visceral motor neurons since no cranial parasympathetic ganglia are known to exist. However, the hindbrain of lampreys contains so-called branchiomotor neurons, the axons of which exit dorsally and innervate

branchial arch-derived muscle. To emphasize differences between gnathostomes and cyclostomes, the hagfish hindbrain, while recognizable as such, is unusually shaped, which relates to differences in its internal organization. The organization of cranial nerves in hagfish, other than the apparent absence of the entire extraocular muscle-related nerves, shows a number of deviations from gnathostome vertebrates. Hagfish have three completely segregated parts of the trigeminal nerve, two otic (stato-acoustic) nerves, no recognizable vagal ganglion, and a facial nerve that exits dorsal to the otic nerves.

The spinal cord in craniates is a continuous extension of the neural tissue of the hindbrain. Adult cyclostomes have unusually shaped spinal cords that are dorsolaterally flattened. Lampreys, like gnathostomes, have separate dorsal and ventral roots, but unlike in gnathostomes, these do not converge to form mixed spinal nerves and are asymmetrically distributed between the left and right side. A similar but more pronounced asymmetry of spinal nerves is exhibited by cephalochordates and has been suggested to be primitive for chordates because an asymmetric pattern is also found in hagfish and some gnathostomes. In hagfish, as in gnathostomes, the dorsal and ventral nerve roots converge, except in
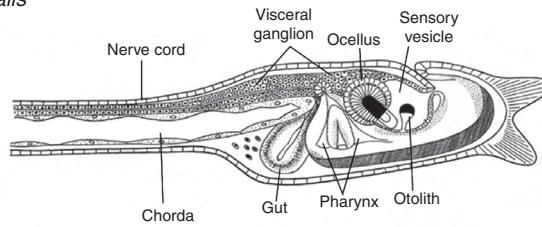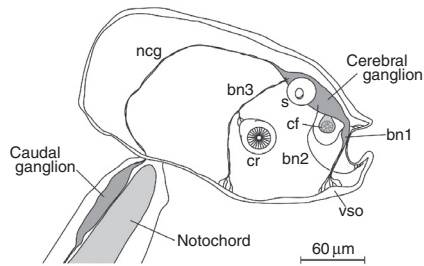
Saccoglossus cambrensis
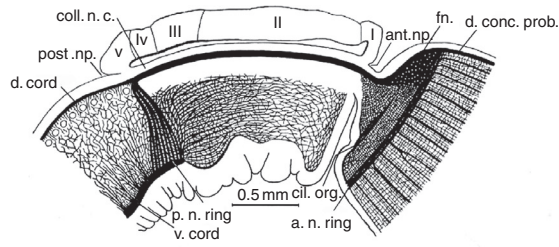
Branchiostoma floridae
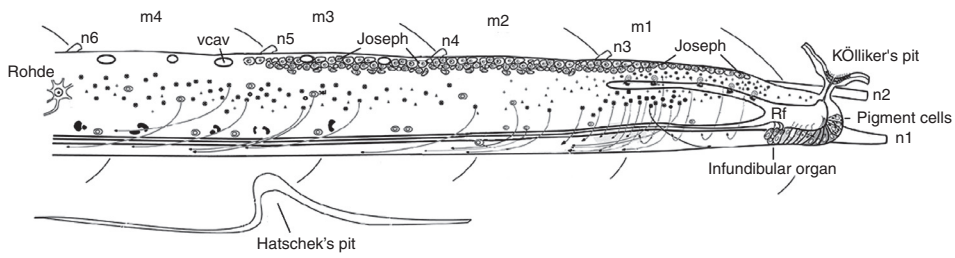
Ciona intestinalis
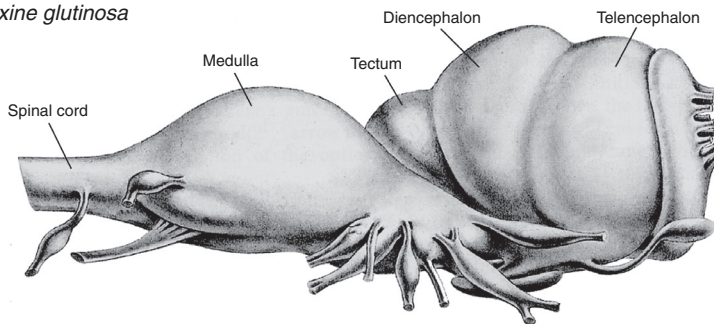
Oikopleura dioica

Myxine glutinosa

Figure 2 Continued

the tail region. It is believed that convergent dorsal and ventral roots is a derived feature of gnathostomes and that the superficial similarity of this feature in hagfish is independently derived. The fiber composition of spinal nerves is highly variable among cyclostomes and fits neither the cephalochordate nor the basal gnathostome composition. Consequently, their relationship to the nerves of cephalochordates and urochordates is problematic.

As in craniates, somatic motor neurons are distributed along the length of the spinal cord in cycolostomes and provide independent innervation of each segment of body musculature (Figure 3). Cyclostomes do not have autonomic ganglia and lack spinal visceral motor neurons that innervate such ganglia (Figure 4). It appears that autonomic ganglia arose with gnathostomes through the advent of migratory neural crest cells. This innovation has led to the formation in higher craniates of preganglionic parasympathetic motor neurons in the brain stem and the sacral part of the spinal cord and preganglionic sympathetic motor neurons in the thoracic and upper lumbar spinal cord (Figure 4).

Cyclostomes have dorsally located intramedullary sensory neurons (dorsal cells), which appear to be homologous to the Rohan–Beard cells of anamniote craniates, as well as sensory neurons in dorsal root ganglia. Dorsal root ganglia and proximal cranial ganglia are derived from migratory neural crest in craniates; in cyclostomes, spinal dorsal root ganglia are generated by neural crest, whereas cranial ganglia derive from placodes. In contrast to their craniate counterparts, the dorsal root ganglion cells in cyclostomes express modulatory neurotransmitters such as serotonin and neuropeptides and may therefore have more derived functions, although they do appear to transmit nociceptive signals in lampreys.

In many chordates, large neurons with descending axons have been identified in the rostral region of the neuraxis. Using cytological criteria, one can identify certain large reticulospinal neurons in the rhombencephalon of lampreys (the Müller and Mauthner cells) that have long descending axons that extend the length of the spinal cord. Similar neurons are found in hagfish, but Mauthner cells cannot be identified among them, and whether the other large cells are homologous to Müller cells is unclear.

Cephalochordates

The central nervous system of cephalochordates is a simple tube that does not show any obvious enlargement at the rostral pole comparable to the brain

Figure 2 A comparison of the basic anatomical structure of the hemichordate, cephalochordate, urochordate, and craniate central nervous systems. Enteropneust hemichordates (represented by *Saccoglossus cambrensis*) have an epidermal nerve network that shows condensations in certain areas. At the base of the proboscis is an anterior nerve ring (a.n. ring) that is next to the ciliary organ (cil.org.), which is adjacent to the oral opening (asterisk). The collar region has a collar nerve cord (coll.n.c.), an invaginated part of the epidermis with anterior and posterior neuropores (ant.np., post. np.) that lies dorsal to the buccal cavity. At the third body division, the metasome, the collar nerve cord becomes confluent with the dorsal nerve cord (d.cord) and, through the posterior nerve ring (p.n.ring), with the larger ventral cord. Neither true nerves nor major sensory organs are apparent in this simple epithelial nerve net. Cephalochordates (represented by an adult specimen of *Branchiostoma floridae*) have a hollow nerve cord that is fairly uniform in diameter throughout its length. There is a recognizable vesicular expansion at the anterior end, with a number of specialized appendages and neuron groups that provide indications of cephalic elaboration. Among these are Kölliker's pit (believed by some to be an olfactory organ), the pigmented cells of the single frontal eye, the infundibular organ (which gives rise to Reissner's fiber; Rf) and preinfundibular zone (possibly containing an organ of balance), and a dorsal column of putative photoreceptors called Joseph cells. The first nerve (n1) is ventral, and all other nerves are dorsal. Muscle segments (m) are located along the entire length of the nervous system. Urochordates have small nervous systems with a recognizable tripartite organization, consisting of a rostral ganglion (termed the cerebral ganglion in appendicularians and the sensory vesicle in ascidians), a caudal ganglion (termed the visceral ganglion in ascidians), and a caudal nerve cord. This organization is maintained throughout life in appendicularians (exemplified here by *Oikopleura dioica*), whereas ascidians (represented here by *Ciona intestinalis*) lose this organization at metamorphosis from larva to adult, in line with the transition from pelagic to sessile lifestyle. The rostral ganglion is intimately associated with a statocyst (s, containing an otolith) and in ascidian larvae also an ocellus. In appendicularians, there is also a ciliated funnel (cf), an outgrowth of the cerebral ganglion believed to be homologous to the pituitary gland. Several brain nerves (bn) connect the rostral ganglion to peripheral sensory and motor structures. The rostral ganglion is connected to the caudal ganglion by a nerve trunk (ncg) in appendicularians and by a cellular 'neck' region in ascidians. The nerve cord of ascidians is evidently nearly aneuronal, consisting predominantly of ependymal cells, whereas in appendicularians it contains neurons, including motor neurons. Craniates (shown is the hagfish, *Myxine*) have a brain that develops from invaginated ectoderm that becomes completely transformed into nervous tissue but remains confined within the former epithelial basement membrane. Major subdivisions that can be identified on the basis of external and internal features include (in anteroposterior order, right to left in the figure) the telencephalon (forebrain), diencephalon, mesencephalon (midbrain), and rhombencephalon (pons and medulla oblongata, or the hindbrain). Several distinct cranial nerves pass through the basement membrane to connect the brain with various sensory organs that provide chemical (olfaction and taste), mechanical (touch, proprioceptive, auditory, and vestibular), and visual (eyes) input. The brain integrates this input with information about internal states and uses this to generate motor output that is effected via motor neurons in the brain stem and spinal cord. The image of amphioxus is reproduced from Wicht H and Lacalli T (2005) The nervous system of amphioxus: Structure, development, and evolutionary significance. *Canadian Journal of Zoology* 83: 122–150. The image of *Saccoglossus Cambrensis* is reproduced from Bullock TH and Horridge GA (1965) *Structure and Function in the Nervous Systems of Invertebrates*. San Francisco, CA: W. H. Freeman. The image of *Myxine glutinosa* is reproduced from Nieuwenhuys R, Donlekaar HJT, and Nicholson C (1998) *The Central Nervous System of Invertebrates*. New York: Springer.
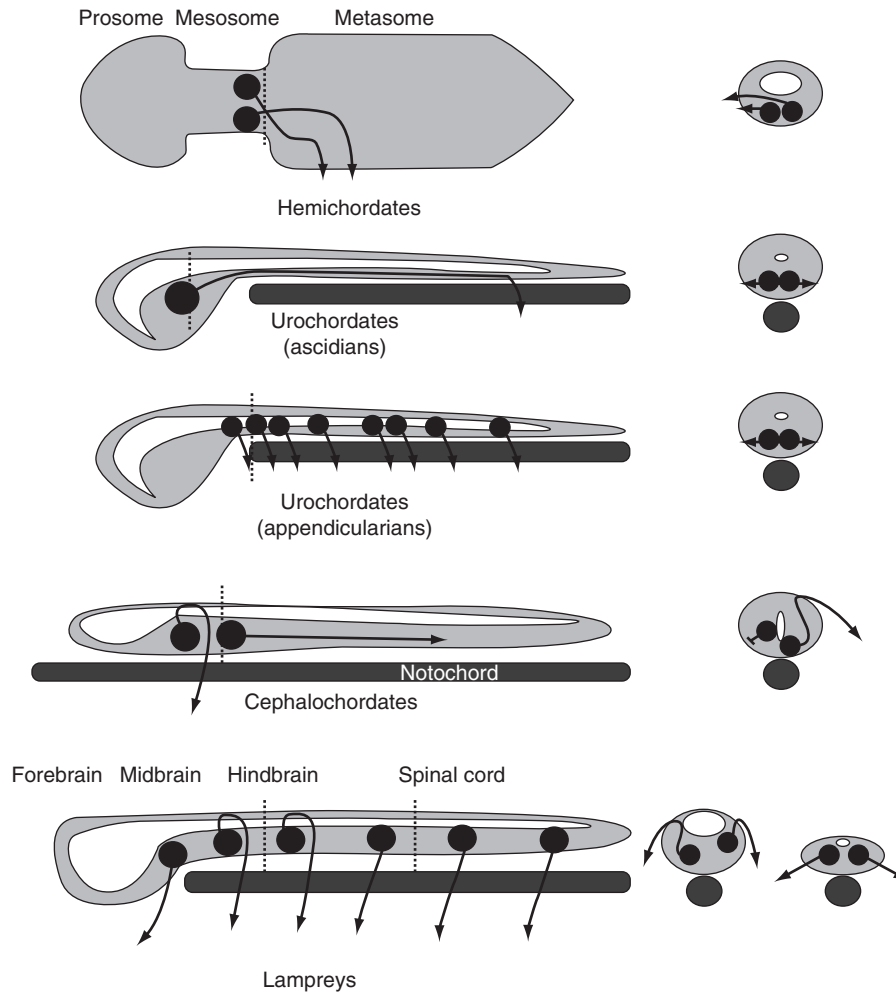
Figure 3 The distribution of motor neurons is shown from the dorsal aspect (hemichordates) or lateral aspect (others) as well as in transverse projections viewed in the caudal direction from the levels indicated by the dotted lines. Motor neurons in hemichordates are predominantly located in the caudal half of the collar cord, and their axons typically cross the basal membrane individually to reach muscle fibers. In ascidian urochordate larvae, all motor neurons are concentrated in the caudal ganglion and project caudally through the nerve cord to reach muscle fibers of the tail. In appendicularian urochordates, motor neurons are also present in the nerve cord and project directly to adjacent muscles. Cephalochordates have three types of motor neurons (only two are shown). One type is the somatic motor neuron that extends an axon along the spinal cord margin to innervate muscular processes that form synapses abutting the cord. The second type is the visceral motor neuron that projects through the dorsal root to innervate the pterygial muscle. The third type innervates muscle cells of the notochord at the ventral spinal cord margin. Lampreys have only somatic motor neurons in the spinal cord, whose axons project out through ventral roots, and in their hindbrain only dorsal exiting motor neurons, referred to as branchiomotor neurons because they innervate muscle derived from branchial arches. Lampreys also have three populations of ocular motor neurons in the midbrain/hindbrain region, some of which have the appearance of somatic motor neurons.

of craniates, hence the alternate name 'acrania' for this taxon. The hollow tube has a central canal that shows a vesicular enlargement at the anterior pole, into which the processes of frontal eye sensory cells extend. Like craniates, cephalochordates (as well as urochordates) have a unique structure that extends throughout the central canal, Reissner's fiber, which may provide a topological landmark for comparing different brain regions (Figure 5). Another structure of similar utility is the notochord, which shows a striking difference in its relationship to the brain in cephalochordates and craniates. In both taxa, the

notochord lies subjacent to the entire length of the spinal cord. In craniates, it extends rostrally to end at the transition from hindbrain to midbrain, whereas in cephalochordates it extends beyond the rostral aspect of the neural tube. The notochord is known to have a major inductive influence on the developing brain and spinal cord of craniates through the release of diffusible signaling proteins. This influence and the resultant regional patterning is therefore likely to be shifted rostrally along the neuraxis of cephalochordates relative to craniates, potentially contributing to the acraniate nature of the cephalochordates.
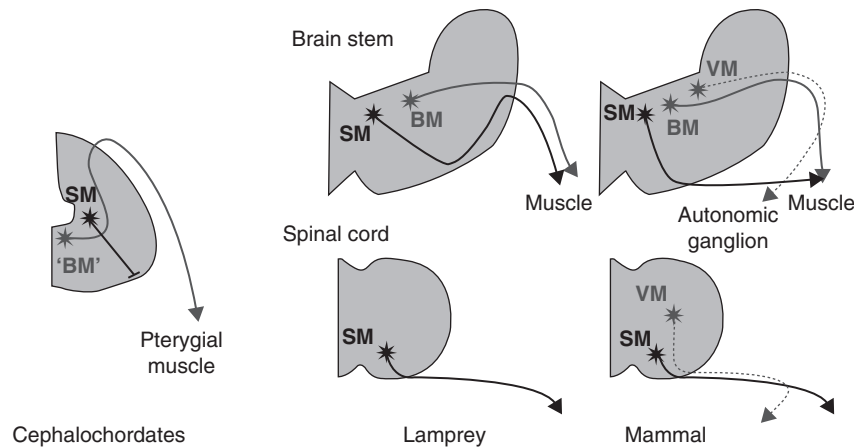
Figure 4 Motor neurons and their projections are compared in craniates and cephalochordates. Two motor neuron types have been characterized in cephalochordates – the branchiomotor neurons, which innervate the pterygial muscle and exit through dorsal roots, and the somatic motor neurons, which do not exit the neural tube but rather form synapses with muscle processes at the lateral margin of the spinal cord. The lamprey brain stem has mainly branchiomotor neurons (BM) that project through dorsal roots. Whether the abducens is a somatic motor nucleus in lampreys as indicated (SM) is unclear because its motor neurons also project through a dorsal root. The lamprey spinal cord has only somatic motor neurons that exit through the ventral root. Mammals have evolved visceral motor neurons (VM) in the spinal cord that migrate into a distinct position and project to autonomic ganglia. In mammals, there is also the addition of visceral motor neurons in several cranial nerves that project to the parasympathetic ganglia. These visceral motor neurons can be regarded as special branchiomotor neurons.
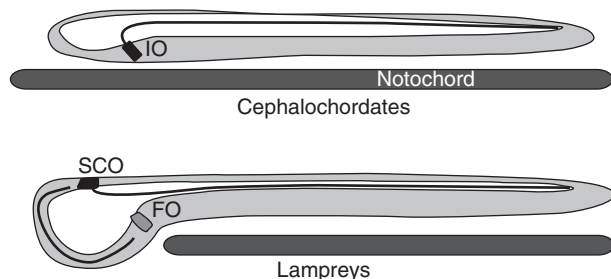

Figure 5 In one proposal for the evolutionary origin of the forebrain, the flexural organ (FO) and the subcommisural organ (SCO) represent a split of a single original cell population, represented by the infundibular organ (IO) in cephalochordates, thereby intercalating a novel population (black line). If this is accepted, then the entire area between the SCO and FO of craniates could be viewed as a craniate neomorph, in which case the entire telencephalon and large areas of the thalamus of craniates would have no equivalent in cephalochordates.

The cranial and spinal nerves of cephalochordates are difficult to compare with those of craniates. First, they are distributed too far rostrally, leaving virtually no space for what is typically considered the brain. There are no true ventral roots in the sense of motor neuron axons leaving the spinal cord. Rather, the somatic muscles extend processes that contact the ventrolateral margin of the spinal cord where they appose synapses from central processes of motor neurons (Figures 3 and 4). Moreover, the notochord is composed of muscle fibers that similarly contact the ventral spinal cord where they receive synapses from ventromedial motor axons. Motor neurons are found throughout the spinal cord and as far rostral as the

primary motor center between the second and third dorsal nerves. An additional set of motor neurons are the so-called visceral motor neurons. These are the most ventral neurons in the nervous system, situated virtually at the floor plate in the anterior portion of the nerve cord. The axons of these cells exit through the dorsal roots and supply the pterygeal muscle with cholinergic endings. There is in fact only one true ventral nerve, the first (most rostral) nerve. All other nerves are dorsal and become increasingly more caudal on the right than on the left side – an asymmetry that by far exceeds anything found in other chordates.

There are no dorsal root ganglia anywhere along the neuraxis of cephalochordates, in line with the apparent lack of a migratory neural crest population. Sensory projections arise from dorsally located intramedullary sensory neurons, similar to those found in cyclostomes. In addition, there is evidence for the presence of peripheral sensory neurons located in the epithelial lining of the buccal and atrial body cavities that project centripetal axons into the nerve cord. Paired sensory organs are conspicuously absent in cephalochordates. However, there is an unpaired frontal eye, putative balance and olfactory organs, and certain primordia of mechanosensors and chemosensors may be present among the numerous single or multicellular sensory organs. Among these are small encapsulated clusters of sensory cells located in branches of the first two brain nerves, the corpuscles of Quatrefages, believed to have a mechanosensory function.

Other features of the cephalochordate anterior neuraxis are the conspicuous lamellar body, believed to be

homologous to the vertebrate pineal gland but present only in larvae, the infundibular organ, whose name implies a proposed homology to the ventral diencephalic region, and the dorsally located Joseph cells, which are putative photoreceptors. Conspicuously pigmented individual ocelli are distributed along the length of the spinal cord. How these various features relate to the internal divisions of the craniate brain and spinal cord is unclear, leaving open the question of the existence of brain subdivisions, although gene expression studies have begun to shed some light on this issue.

In the rostral neuraxis of juvenile cephalochordates, two pairs of larger interneurons with descending axons have been identified and termed 'ventral giant cells of the primary motor center,' potentially homologous to the large reticulospinal neurons of cyclostomes. Another system of large neurons, the Rohde cells, are situated dorsally in the anterior region, starting at what is considered to be the transition from brain to spinal cord, and have descending axons in the spinal cord. A separate population of Rohde cells is located in the caudal spinal cord.

Urochordates

The urochordate subphylum includes the ascidians, the thaliaceans, and the appendicularians. Nearly all ascidians, some thaliaceans, and all appendicularians have a free-swimming larval stage with a notochord and a small central nervous system that appear homologous to the same structures in craniates. In contrast to the rather uniform appearance of the neuraxis of cephalochordates, the larval ascidian and larval and adult appendicularian central nervous systems are organized into an obvious tripartite structure (**Figure 2**). The three divisions are (1) a rostral ganglion (totaling approximately 215 cells in the ascidian *Ciona* and approximately 75 cells in the appendicularian *Oikopleura*), which contains sensory receptor structures, including an ocellus and/or an otolith, followed by (2) a caudal ganglion (containing approximately 45 cells in *Ciona* and approximately 25 neurons in *Oikopleura*), from which extends (3) a caudal nerve cord (containing approximately 65 cells, mostly ependymal, in *Ciona*, and approximately 30 neurons and 25 support cells in *Oikopleura*). In addition, the rostral and caudal ganglia are connected by a nerve trunk in appendicularians or a slender 'neck' region containing nerve cells in ascidians. Other urochordate taxa seem to exhibit primarily variations in size but not in structure. The ganglia of urochordates have the organization of an invertebrate ganglion, with cell bodies at the periphery and a neuropil in the center. Several nerves that vary considerably between species have been traced from adult ganglia, reaching up to 75 nerves in certain salps. These nerves appear to be mixed sensory and motor nerves and are asymmetric in several species, potentially related to the overall body asymmetry.

The organization of motor projections varies among urochordates. In ascidian larvae, all the motor neurons (three to five pairs in different species) are located in the caudal ganglion and project along the predominantly aneural nerve cord before exiting to innervate the peripheral muscle. In appendicularians, both the caudal ganglion and the nerve cord contain motor neurons, whose axons project laterally to the peripheral muscle either directly or after extending some distance in the cord.

Comparisons between urochordates and cephalochordates claim similarities in sensory organs within the central nervous system, in particular the infundibular sensory cells and otolith. The ciliated funnel, which extends to one side of the rostral ganglion, is believed to be homologous to the pituitary. However, the interpretation of homologies for most sensory cells and sensory organs outside the central nervous system is contended. Some adult urochordates have fairly complex eyes attached to the cerebral ganglion. There is a marked asymmetry in the organization of central and peripheral sensory structures.

No large neurons with descending axons that might be homologous to the large reticulospinal neurons of craniates have been described in urochordates, although there are some large cells within the rostral ganglion that could subserve a similar function.

Hemichordates

Hemichordates are not grouped within the chordates but share a number of chordate features, including a rudimentary notochord-like structure, the stomochord. Whether the simple nervous system of hemichordates should be referred to as a central nervous system is unclear. The overall organization is that of a basiepithelial plexus that shows regional concentrations in the three parts of the body, the protosome (the preoral proboscis), the mesosome (the postoral collar), and the metasome (or trunk, with rostral gill slits). The intraepithelial nerve plexus is well developed on the basement membrane but remains epithelial even in the invaginated collar region, which is hollow and opens through two neuropores (**Figure 2**). Concentrations of longitudinal strands of cells and fibers also exist on the trunk, where they form a dorsal and a larger ventral cord. The proboscis has a well-developed nerve plexus and numerous sensory cells. Except for the preoral ciliary organ with its abundance of sensory cells, there are no specialized sense organs. Concerning nerves, it appears that muscles are supplied by nerve fibers that cross the basement membrane singly and diffusely without forming obvious peripheral nerves.

Large neurons have been described in hemichordates, clustered in the caudal part of the collar cord and also scattered in more rostral and caudal areas. Some of these neurons have uncrossed or crossed axons that extend toward the ventrolateral longitudinal muscles and therefore may be motor neurons. Others have been compared to the Mauthner and Müller cells of craniates.

Molecular Patterning of the Neuraxis during Development

Despite their overall anatomical differences, the central nervous systems of the primitive chordates exhibit similarities to craniates with respect to the molecular mechanisms responsible for regional patterning during development, along both anteroposterior and dorsoventral axes. Shared by all chordates and the hemichordates is the expression of *otx* genes in the most rostral region of the central nervous system and the expression of *hox* genes starting more caudally; in all these taxa except cephalochordates, the *engrailed* gene (*en*) is expressed in the region between *otx* and *hox* genes, and in all save the hemichordates *pax* genes of the Pax-2/5/8 class are expressed in the very most rostral region (Figure 6). These elements alone provide support for proposed homologies between specific portions of the primitive chordate nervous
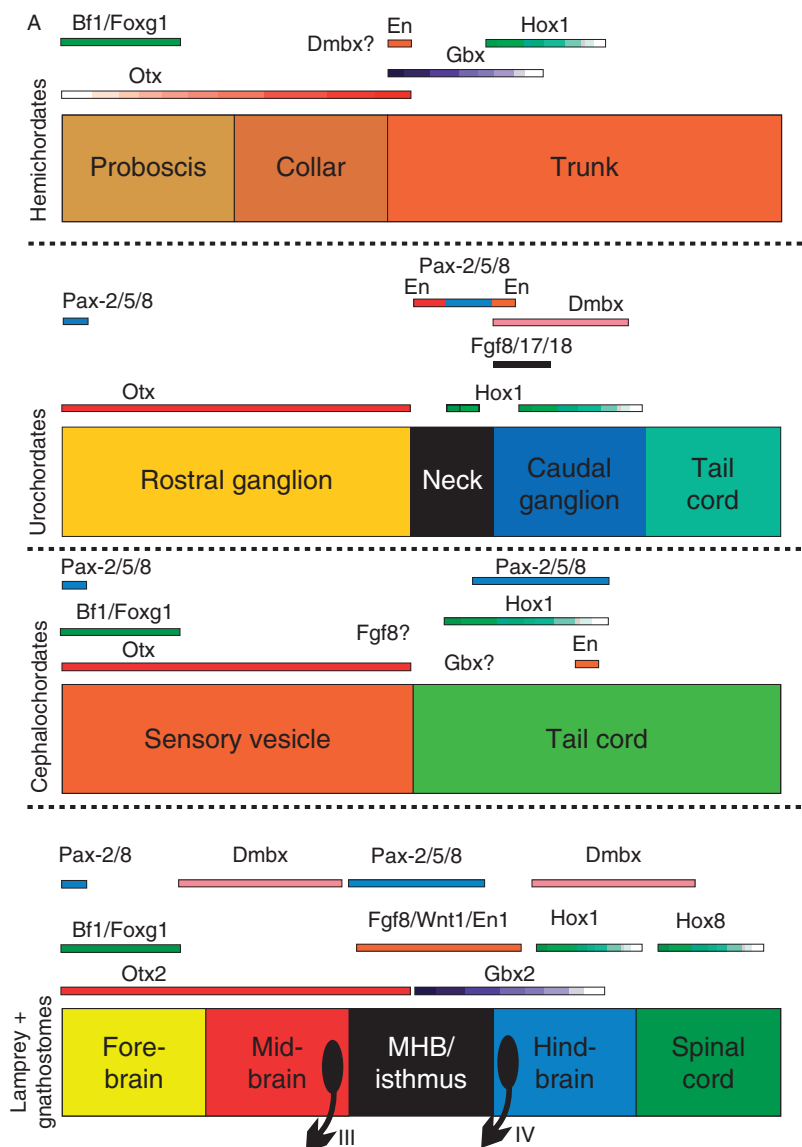

Figure 6 Gene expression patterns define regions along the anteroposterior axis. Several relationships are highly conserved, including the rostral expression of *pax2/5/8* and *otx* genes and a more caudal expression of *hox* and *en* (*engrailed*) genes. These gene expression patterns provide support for defining putative forebrain and hindbrain homologs in cephalochordates and urochordates. Intermediate gene expression patterns exhibit too many variants to support a clear homology with the midbrain and midbrain/hindbrain boundary (MHB), however.

systems and the brain subdivisions in craniates. On this basis, both urochordates and cephalochordates would appear to have homologs of the craniate forebrain, hindbrain, and spinal cord. Less compelling is the presence of a region homologous to the midbrain and the midbrain/hindbrain boundary (MHB), the latter of which is an important inductive organizer region in the craniate brain. Although certain genes that delineate the MHB in craniates, such as Pax2/5/8, are expressed in the general vicinity of the expected MHB location, the specific gene combination criteria that define the MHB in craniates are not met in any of the primitive chordates. This may mean that the definitive MHB and midbrain are later evolutionary elaborations of the neuraxis.

These genes, whose expression regionalizes the anteroposterior neuraxis (**Figure 6**), may be ancestrally related to the overall rostrocaudal patterning of the deuterostome body, and the degree of pattern conservation may reflect the fact that the neural tube evidently evolved only once in ancestral chordates. The presence of a similar anteroposterior pattern in the basiepithelial nerve plexus of hemichordates suggests that this anteroposterior regionalization predates the invagination of the neural tube from external ectoderm. A similar anteroposterior sequential pattern of some of the key genes in the insect nervous system lends support to this idea.

An alternative approach to deducing anteroposterior homologies between craniate and noncraniate nervous systems is to assess the location of specific neuron types known to bear a specific topographic relationship to given craniate brain subdivisions. Catecholaminergic neurons, which express the enzyme tyrosine hydroxylase (TH), provide a good example because these have very focal distributions within the craniate brain. In cephalochordates, TH- and catecholamine-positive neurons are found near the anterior end of the neural tube and near the first two dorsal nerves. This has been interpreted to indicate similarities with the di-, mes-, and rhombencephalic catecholaminergic neuron groups of craniates. TH-positive neurons are also present within the rostral ganglion of urochordates, providing support for a diencephalic or mesencephalic character there. Catecholamine-positive neuron populations have not been described in hemichordates.

Neural Crest, Placodes, and Their Derivatives

One of the fundamental evolutionary advances that characterizes craniates is the appearance of the neural crest and ectodermal placodes, from which are derived a large spectrum of peripheral structures and cell types, notably through the process of epithelial delamination that generates migratory mesenchyme. Restricting our focus to neural structures, the neural crest gives rise to all peripheral ganglia in the trunk, including sensory, autonomic, and enteric ganglia, and together with specific placodes, all of the cranial autonomic ganglia. It also gives rise to Schwann cells, which provide myelination of peripheral nerves. The placodes, which are local thickenings of the embryonic cranial ectoderm, invaginate to form sensory structures and associated neural epithelia and ganglia, in addition to contributing to some autonomic ganglia. The elaboration of sensory and motor function in the cranial region provided by the advent of neural crest and placodes clearly facilitated a more rapid acquisition of the predatory behavioral repertoire exhibited by craniates.

The substantial divergence in peripheral sensory and motor structures and limitations in the embryonic data have made the search for neural crest and placode precursors in noncraniates a difficult field. In hagfish, neural crest and placodes are clearly present at embryonic stages, but there is little direct evidence that they generate migratory cell populations, possibly limiting the scope and spatial range of the derivatives they can produce. Definitive migratory neural crest appears to be lacking in cephalochordates and urochordates. In particular, neural crest-specific genes do not appear to be expressed in the lateral margins of the neural tubes of these taxa as they are in craniates. Nevertheless, there are small populations of migratory neural cells in both taxa that have been proposed to have an evolutionary relationship to the neural crest. Possible placode-like structures have been identified both in amphioxus and in urochordates, and the expression of some placode-specific genes in these structures strengthens the argument that they may represent the early origins of certain craniate placodes. The first brain nerves of appendicularians, for example, express a gene profile and possess cell types consistent with a homology to the craniate olfactory placode, and similar evidence provides support for a homology between the appendicularian ciliary funnel and the adenohypophysis. In amphioxus, Hatschek's pit has also been proposed as an adenohypophyseal homolog, but here the gene expression data are weaker. A number of other small peripheral sensory structures in appendicularians express placode-specific genes, but their relationship to craniate placodes is less clear. It has been suggested that specific mechanoreceptors may represent precursors of the lateral line placode derivatives. Beyond these proposals, the evidence for placodal homologies is currently weak, and even the placodal nature of these best documented cases is still controversial.

See also: Allometric Analysis of Brain Size; Brain Development: The Generation of Large Brains; Brain Fossils: Endocasts.

Further Reading

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