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Sensory system evolution at the origin of craniates

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The multiple events at the transition from non-craniate invertebrate ancestors to craniates included the gain and/or elaboration of migratory neural crest and neurogenic placodes. These tissues give rise to the peripherally located, bipolar neurons of all non-visual sensory systems. The brain was also elaborated at or about this same time. Were the peripheral and central events simultaneous or sequential? A serial transformation hypothesis postulates that paired eyes and an enlarged brain evolved before the elaboration of migratory neural crest–placodal sensory systems. Circumstantial evidence for this scenario is derived from the independent occurrence of the combination of large, paired eyes plus a large, elaborated brain in at least three taxa (cephalochordates, arthropods and craniates) and partly from the exclusivity of the diencephalon for visual system-related distal sensory components versus the restricted distribution of migratory neural crest–placodal sensory systems to the remaining parts of the neuraxis. This scenario accounts for the similarity of all central sensory system pathways due to the primary establishment of descending visual pathways via the diencephalon and midbrain tectum to brainstem motor regions and the subsequent exploitation of the same central beachhead by the migratory neural crest–placodal systems as a template for their organization.

Keywords: cephalochordates; cerebral vesicle; visual system

1. INTRODUCTION

The transition from an invertebrate chordate ancestral condition to that of the first true craniates (hagfishes and vertebrates) was marked by multiple seminal changes (Northcutt 1996). These changes included the gain of a neurocranium and alterations in the embryological development of the paraxial mesoderm in the head region that resulted in the gain of a muscular pharynx in the branchiomeric region. They also encompassed numerous changes in the nervous system. The brain was markedly enlarged and elaborated in conjunction with the formation of paired eyes. Migratory neural crest and neurogenic placodes were gained (and/or elaborated); these tissues produce the bipolar sensory neurons of the peripheral nervous system.

Major new insights have been made recently into how this transition occurred as the result of the duplication of regulatory genes, and a credible scenario describing the elaboration of craniate characters from a cephalochordate-like ancestral condition has been postulated (Holland & Graham 1995). Questions remain, however, including: whether the elaboration of the craniate brain occurred simultaneously with the gain of migratory neural crest and craniate placodal systems; whether all aquatic craniate sensory systems evolved simultaneously or not; how all of the central pathways for these sensory systems evolved; why the central pathways for all the different modalities have such similar organization; and how the branchiomeric motor column evolved in concert with the branchiomeric muscles of the visceral arches. This paper addresses the evolution of craniate sensory system components in the central and peripheral nervous systems.

2. MIGRATORY NEURAL CREST AND PLACODES

Many of the changes at the non-craniate–craniate transition can be attributed to the gain (and/or elaboration) of migratory neural crest and neurogenic placodes (Northcutt 1996). In the early stages of nervous system morphogenesis in craniates, a population of ectodermal cells at the lateral aspect of the invaginating neural tube forms the neural crest. Some of the neural crest cells remain near the neural tube and give rise to or contribute to the sensory bipolar neurons of spinal and cranial nerve ganglia, while other neural crest cells migrate ventrolaterally to give rise to or contribute to a host of tissues, including the motor ganglia of the peripheral nervous system, calcitonin and chromaffin cells of the gut, the bars of the visceral arches, the neurocranium and sensory capsules of the paired sense organs, dermal skeleton, melanocytes and teeth (Northcutt 1996). Neurogenic placodes (subsequently referred to simply as placodes) consist of thickened patches of epithelium lateral to the region of the neural crest, which give rise to most or all of the bipolar sensory neurons of the olfactory and terminal nerves (and the vomeronasal nerve in tetrapods), the taste-receptive cranial nerve components, and the vestibulocochlear and lateral line nerves, as well as to the receptor cells for the last two systems (Northcutt 1996).

3. CRANIATE CENTRAL SENSORY PATHWAYS

The changes within the central nervous system at the non-craniate–craniate transition cannot be accounted for by effects and/or products of the more lateral region of the developing nervous system—the migratory neural crest and placodes. The forebrain, midbrain, and hindbrain were all markedly expanded, and a host of multisynaptic, central pathways for ascending sensory system projections to the telencephalon were established. Any plausible scenario of craniate brain evolution must account for the gain of these multisynaptic central pathways, which—as the general condition across craniates—all exhibit the same pattern of organization. All sensory system pathways have bipolar afferent neurons that either innervate receptor cells or transduce sensory information themselves at their distal processes (see Hodos & Butler 1997). For the retina, these bipolar neurons are neural tube derivatives. For all non-visual sensory systems, the bipolar neurons are part of the peripheral nervous system and are derived from migratory neural crest and/or placodes.

In all sensory systems, the bipolar neurons project to multipolar neurons that lie within the central nervous system. Since these bipolar-receptive neurons are the initial multipolar neurons in the sensory pathway, they are referred to here as first-order multipolar neurons. The pattern of projections for the latter sets of neurons is similar for all sensory systems, as shown in figure 1. From all sets of first-order multipolar neurons that are located caudal to the telencephalon, projections arise that are either to the midbrain roof and thence to the diencephalon and/or to the diencephalon directly. The retinal ganglion cells give rise to both midbrain-relay and direct pathways, while the other, neural crest–placodal, sensory systems each give rise to both pathways or to one or the other. From the diencephalic site for each sensory pathway, projections to the telencephalon arise. A variation on the theme is with the olfactory system (not included in figure 1); projections from olfactory bipolar neurons are to first-order multipolar neurons that are located within the olfactory bulb, and relay to the diencephalon occurs via the olfactory pallium rather than via the tectum.

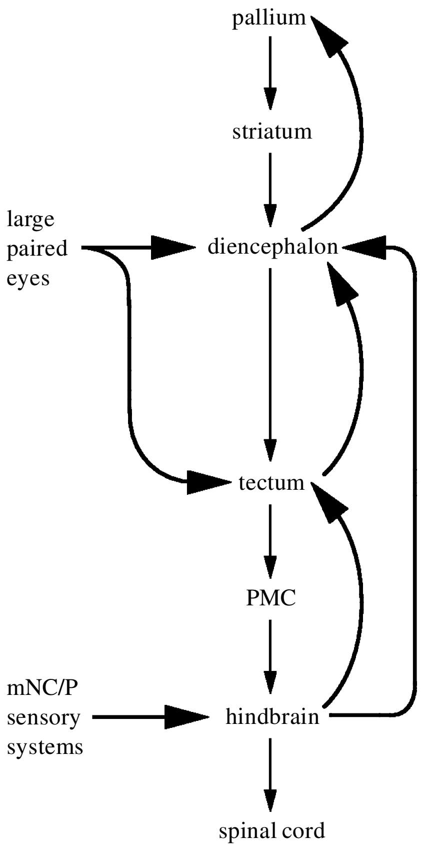

Figure 1. Diagram of the overall, generalized plan of ascending sensory systems (thick arrows) and descending motor pathways (thin arrows). The basic plan of sensory systems is a relay from bipolar neurons to first-order multipolar neurons, which then project, as shown with the thick arrows (from the retina and hindbrain in this figure) to the diencephalon directly or indirectly and from the diencephalon to the telencephalon. For the sake of illustrating the main point, a number of pathways are omitted from this figure, including ascending projections from the spinal cord (such as the spinothalamic pathway) and projections from the diencephalon to the striatum in the telencephalon. Also omitted are telencephalic sensory systems, which are a variation on the same theme; the olfactory system, for example, projects to the diencephalon via its own area of the pallium, and a subsequent relay then occurs from the diencephalon to a different pallial region. mNC/P, migratory neural crest/placodes; PMC, primary motor centre.

4. THE ANCESTRAL CHORDATE CONDITION

Recent anatomical work and new findings on homeobox genes and their expression patterns indicate that the extant cephalochordate *Branchiostoma*, the lancelet, may in fact be a reasonable approximation of the actual common ancestor of modern lancelets and their craniate cousins, at least in most respects. Lacalli (1996) and his co-workers have demonstrated rostral specializations in the neural tube of lancelets that appear to be homologous to some of the rostral neural tube structures in craniates. In the lancelet, a cerebral vesicle is present and has a frontal organ, or eye, consisting of pigmented and associated cells at its rostral end that may be homologous to the paired eyes of craniates. This vesicle also contains other structures that may be homologous to the epiphysis of vertebrates (which hagfishes lack) and the infundibular region of craniates. Caudal to these structures is a region that may encompass the midbrain and hindbrain regions of craniates. Gene expression studies support these interpretations (Holland & Graham 1995; Holland *et al.* 1996).

However, a credible precursor of the craniate brain is not the only relevant neural tissue that lancelets and their invertebrate chordate relatives have to offer. Holland *et al.* (1996) have identified gene expression patterns in the lancelet that indicate the presence of neural crest-precursor tissue in the epidermis dorsal to the developing neural tube. Likewise, Wada *et al.* (1998) have found similar evidence in ascidians, which are the chordate outgroup to lancelets and craniates, indicating the existence of placodal tissue that gives rise to a sensory organ homologous to the craniate ear. These findings are exciting but not entirely surprising, since the existence of a wide variety of peripheral sensory neurons with projections into the central nervous system in invertebrates is well documented and extensively studied, one example being the proprioceptive hair cell sensory system in squid (Preuss & Budelmann 1995). Thus, before the first true craniates appeared, cephalopods and arthropods had exploited the developmental path to large brains and paired eyes, and in the ancestral invertebrate chordate line, neural crest, placodal and brain precursors were in place. With the evolutionary stage thus fully set, can we now reconstruct the sequence of the play?

5. CONCURRENT GAIN AND SERIAL TRANSFORMATION HYPOTHESES

That the elaboration of migratory neural crest and craniate placodes with their resultant production of cell types, including the bipolar neurons of the peripheral nervous system, occurred at the same time as the elaboration of the brain (and the rest of the central nervous system) has been suggested (Holland & Graham 1995; Northcutt 1996) and is referred to here as the 'concurrent gain hypothesis'. Northcutt (1996) has proposed that these events occurred from changes in neurulation that involved the formation of transverse and longitudinal neural folds rostral and lateral to the developing neural plate. In the developing amphibian *Xenopus*, the rostral part of the neural plate has been found to give rise to major portions of the diencephalon, including the neural retinas, and of the midbrain and hindbrain, while the transverse and longitudinal neural folds give rise to the telencephalic hemispheres and also contribute to some of the alar parts of more caudal brain regions (Eagleson & Harris 1990). As Northcutt (1996) discussed, the more lateral parts of the neural folds and laterally adjoining ectodermal tissue give rise to neural crest and placodes. Thus, Northcutt (1996) has postulated that the gain of neural folds during the embryological development of the earliest craniates would account for the gain of major parts of the craniate brain in conjunction with the migratory neural crest and placodal derivatives.

Alternatively, that the elaboration of migratory neural crest and placodes in craniates did not occur simultaneously with the elaboration of the brain has also been suggested. Thomson (1988), for example, speculated that paired sensory organs and an enlarged forebrain evolved before the neural crest, due to changes in signalling from rostral mesodermal tissue. A plausible scenario that explains how elaboration of the brain in the craniate ancestral line occurred and that accounts for the gain of paired, lateral eyes and an expanded alar plate with multiple, ascending, sensory system pathways, has not, however, previously been offered.

A 'serial transformation hypothesis' that expands on Thomson's (1988) idea and postulates that at least part of the brain was elaborated in the ancestral craniate line before migratory neural crest and placodes is proposed here (and see Butler 2000) to provide such a scenario. Based on the work of Eagleson & Harris (1990) and Northcutt's (1996) findings and analysis, the rostral part of the neural plate of developing craniates would appear to give rise to the parts of the brain that are homologous to the cerebral vesicle of lancelets. As mentioned in §4, a region homologous to the craniate hindbrain has been identified caudal to the cerebral vesicle (Holland & Graham 1995). The rostral neural plate derivatives of paired eyes, diencephalon and mesencephalon, along with hindbrain regions, could thus have been elaborated before the gain of the neural folds with their derivatives, including the telencephalic hemispheres, migratory neural crest and placodes.

Several lines of circumstantial evidence support the plausibility of a serial transformation. First, one can note that across all bilaterally symmetrical animals, the presence of an enlarged, elaborated brain is often linked with the presence of large, paired, lateral eyes. Further, this combination has arisen multiple times independently in cephalopods, arthropods and craniates, and can arise with or without the elaboration of the migratory neural crest–placodal sensory systems that are present in craniates. In contrast, in the normal phenotypes of bilaterally symmetrical animals, the reverse combination of elaborated migratory neural crest–placodal sensory systems with an enlarged, elaborated brain but without large, paired, lateral eyes has never arisen. The implication of this pattern is that the genesis of the paired-eye visual system plus brain combination may result from different regulatory constraints than the migratory neural crest–placodal sensory systems.

Another noteworthy observation is that no neural crest and/or placodal-derived bipolar sensory neurons project to alar plate first-order multipolar neurons that are predominantly located within the craniate diencephalon. Such projections to first-order multipolar cell groups exist at most other levels of the neuraxis: telencephalon, hindbrain and spinal cord. A possible explanation for this situation is the prior establishment of visual first-order multipolar neurons in the diencephalon (i.e. the retinal ganglion cells) as a population that is thus different from all other sets of first-order multipolar neurons for the other, later-evolved sensory systems. Further, the central projections of the visual multipolar neurons could have established an alar plate beachhead in the diencephalon and mesencephalon, which could be subsequently exploited by the ascending projections from the neural crest–placodal sensory systems.

The idea of such an alar plate beachhead established by the visual system has some interesting implications for the evolution of similarly organized, multisynaptic sensory systems in craniate brains. The visual system pathways that would have been established at this juncture would involve retinal projections to the diencephalon and mesencephalon and relays from these sites to more caudal, motor-related and motor neuronal groups of the brainstem and spinal cord. As shown schematically in figure 2, such descending pathways could form the template for the subsequently evolved ascending pathways of the other systems. Just as the first-order multipolar neurons of the visual system project to the diencephalon and mesencephalon, ascending projections from the migratory neural crest and placodal systems could do likewise by using the same pathfinder system and thus participate in determining the descending output to motor systems. The fact that the central pathways of re-evolved and additionally evolved neural crest–placodal systems—such as the occurrence of the electrosensory system in some teleost fishes and the infrared system in snakes, respectively—use the same template lends credence

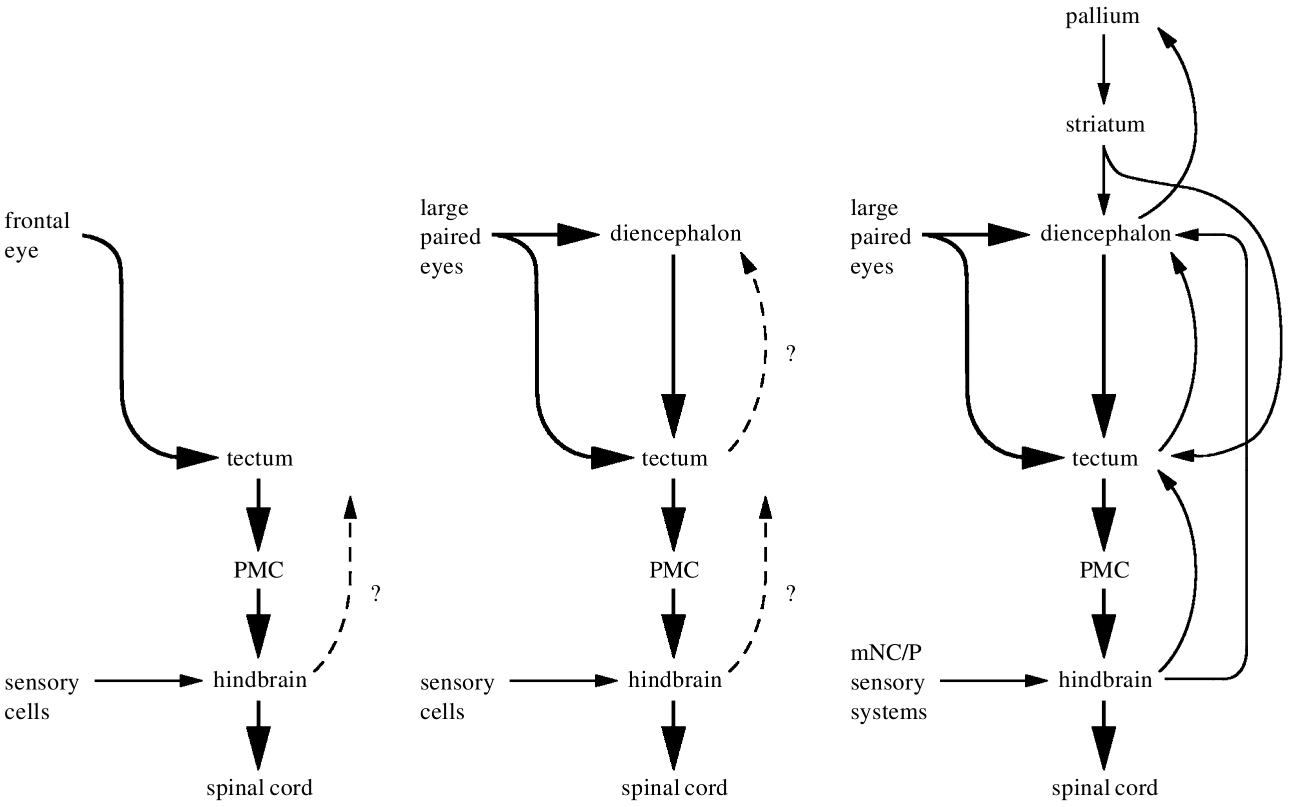

Figure 2. Summary of the evolution of similarly organized central sensory pathways according to the serial transformation hypothesis proposed here. The condition in extant lancelets (Lacalli 1996) is diagrammed on the left, showing projections of the frontal eye to the tectal region and thence to motor-related regions of the brainstem. The middle diagram shows the hypothesized intermediate condition of transitional craniate ancestors with elaboration of the hindbrain, mesencephalon and diencephalon with paired eyes. The alar plate beachhead in the diencephalon and mesencephalon allows the elaboration of the descending visual pathways consistent with the condition in lancelets. The diagram on the right shows the condition of the first true craniates with the subsequent gain of the telencephalic hemispheres and the elaboration of migratory neural crest–placodal sensory systems (Northcutt 1996). The similarity of organization of these systems to that of the visual pathways is due to their exploitation of the same alar plate beachhead. mNC/P, migratory neural crest/placodes; PMC, primary motor centre.

to this idea. The concurrent gain of the telencephalic hemispheres with the original neural crest–placodal set of systems would have supplied an additional rostral target for these sensory pathways that was added on to the existing diencephalic–mesencephalic–hindbrain template.

The signalling protein encoded by the gene sonic hedgehog, *Shh*—and/or its downstream effects—stands out as an excellent candidate for effecting the elaboration of the paired eyes and neural tube in the ancestral line that led to the first true craniates. *Shh* plays a role in the dorsoventral specification of the neural tube and in the formation of paired lateral eyes as opposed to the default cyclopean condition (Rubenstein & Beachy 1998). The upregulated expression of an ancestral homologue of *Shh* in a lancelet-like ancestral invertebrate could have caused the formation of lateral eyes and an elaborated diencephalon and mesencephalon. *Shh* expression effects include the activation of the proneural gene *achaete-scute*, which participates in signalling neurogenesis, as discussed by Kerszberg & Changeux (1998). In fact, a computer simulation of primary neurulation recently published by Kerszberg & Changeux (1998) corresponds closely to the morphogenetic events postulated for this first part of the serial transformation. This simulation had restricted epidermal cell movements in the horizontal plane, which resulted in the infolding of the neural plate to produce a neural tube but without the formation of neural folds. In the actual ancestral situation, embryological development with this condition could have resulted in an elaborated hindbrain, midbrain and diencephalon with paired eyes. The later gain of significant horizontal ectodermal movements would have then allowed the formation of the neural folds with their derivatives, defining the emergence of the first true craniate taxon.

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