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# Understanding Vertebrate Brain Evolution[1]

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**SYNOPSIS. Four major questions can be asked about vertebrate brain evolution: 1) What major changes have occurred in neural organization and function? 2) When did these changes occur? 3) By what mechanisms did these changes occur? 4) Why did these changes occur? Comparative neurobiologists have been very successful in recognizing major changes in brain structure. They have also made progress in understanding the functional significance of these changes, although this understanding is primarily limited to sensory centers, rather than integrative or motor centers, because of the relative ease of manipulating the relevant stimuli. Although neuropaleontology continues to provide important insights into *when* changes occurred, this approach is generally limited to recognizing variation in overall brain size, and sometimes brain regions, as interpreted from the surface of an endocranial cast. In recent years, most new information regarding *when* neural changes occurred has been based on cladistical analysis of neural features in extant taxa. Historically, neurobiologists have made little progress in understanding *how* and *why* brains evolve. The emerging field of evolutionary developmental biology appears to be the most promising approach for revealing *how* changes in development and its processes produce neural changes, including the emergence of novel features. *Why* neural changes have occurred is the most difficult question and one that has been the most ignored, in large part because its investigation requires a broad interdisciplinary approach involving both behavior and ecology.**

## INTRODUCTION

In thinking about brain evolution in vertebrates, or the evolution of any structure in any group, it is useful to consider what questions can be asked about the topic. In the case of brain evolution, there are four major questions (Northcutt, 2001): 1) *What* changes in brain organization and function have occurred over time? 2) *When* did these changes occur? 3) *How* did these changes occur (*i.e.,* what were the underlying mechanisms responsible for them)? and 4) *Why* did these changes occur? Each of these questions is best answered by an approach very different from that appropriate for any of the others. Neuroanatomists generally focus on the question of *what* has happened, using descriptive and experimental techniques, within the context of a comparative approach. This approach minimally involves describing brain centers, determining their pathways, and recognizing possible homologues of these centers and pathways across major vertebrate radiations (Butler and Hodos, 1996; Nieuwenhuys *et al*., 1998). As I hope to demonstrate in this paper, this is the most limited use of the comparative approach, which can also be a valuable tool to infer *how* and *why* brains evolve.

Comparative neurophysiologists and, more recently, neuroethologists, have used a wide range of experimental techniques to unravel the functions of specific centers and circuits (Camhi, 1984; Gazzaniga, 2000). Much of this work has been directed towards understanding the function of one sensory center or another because of the relative ease of manipulating biologically relevant sensory stimuli; correspondingly, there has been less progress in understanding integrative and motor functions. One notable exception is the organization of spinal and medullary locomotor centers (see Grillner *et al*., 1995 for a recent review).

In a short article such as this, it is impossible even to begin to do justice to the myriad morphological and functional details that are presently known about the organization and evolution of vertebrate brains. It is possible, however, to recognize a number of anatomical trends in their evolution and to speculate on the possible significance of those trends.

Paleontologists continue to provide critical information on the time frame within which certain neural changes occurred (Jerison, 1973, 1990; Forey and Janvier, 1994). Unfortunately, fossil endocasts can provide information only on overall brain size and those features that can be recognized and interpreted from the surface of an endocast. Most new information on *when* neural changes occurred is based on cladistical analysis of the feature in question. Cladistics is usually thought of as a method for revealing taxonomic relationships, but given the existence of a well corroborated hypothesis of such relationships, it is also the most powerful tool we have for determining the polarity of brain characters (*i.e.,* which characters are primitive features and which are derived) and, thus, where and when these changes occurred. This type of analysis, however, can provide only a relative date for any given neural change. Paleontological data regarding the suspected time of origin of a taxonomic group are still critical for refining estimates of *when* changes in neural characters occurred. Several examples will demonstrate some of the problems encountered when trying to determine *when* a particular neural event occurred in evolution.

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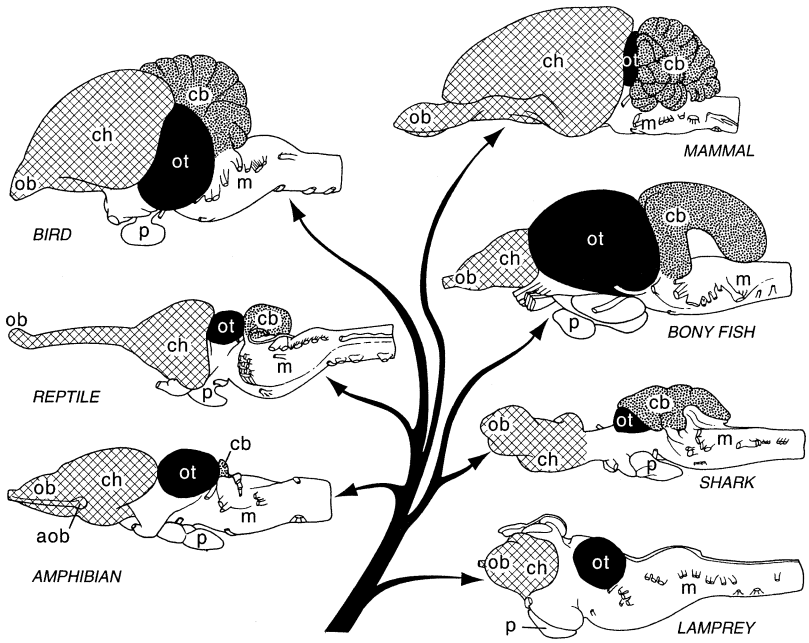


FIG. 1. Lateral views of the brains of a number of extant vertebrate species (the brains are not drawn to the same scale). While there is tremendous variation in both overall brain size (see Fig. 2) and the size of most brain divisions, most vertebrates possess brains that can be divided into the same number of divisions. **aob,** accessory olfactory bulb (cross-hatched); **cb,** cerebellum (stippled); **ch,** cerebral hemispheres (cross-hatched); **m,** medulla oblongata; **ob,** olfactory bulb (cross-hatched); **ot,** optic tectum (black); and **p,** pituitary gland. Modified from Braun and Northcutt (1999).

Although comparative neurobiologists have been relatively successful in establishing *what* changes characterize brain evolution in vertebrates, and even *when* these changes occurred, there has been little progress in understanding *how* and *why* such changes occurred. This is in part due to an erroneous approach to assessing these changes. The most frequently used paradigm, which can be termed an adult transformation paradigm, assumes that evolution of whole organisms or specific organs occurs as a series of transformations from one adult form to another adult form. Evolution does not occur by the transformation of adult structures, however; rather, it occurs by ontogenetic changes over time (Garstang, 1922). In addition, for applicants of the erroneous adult transformation paradigm, it is common to attribute evolutionary changes automatically to mutation-and-selection, with no further specification. One neuroanatomical wit has rightfully referred to such superficial explanations as "evobabble." There is no question that mutation, recombination, selection, and drift are mechanisms that drive all evolutionary changes, but these concepts in and of themselves are not very informative explanations. If we accept that evolution occurs by ontogenetic changes over time, evolutionary developmental biology may provide a substitute for the adult transformation paradigm and may prove more efficacious for studying *how* evolutionary changes occur. Although this paradigm has emerged only recently as a novel way of viewing the evolution of neural characters, two examples can be discussed.

*Why* neural changes occur is the most difficult question that can be asked and one that has been largely ignored. This is because it requires an interdisciplinary approach that involves recognizing the set of neural and other features that allow a group of organisms to interact with the world in a unique way. In order to do this, it is necessary to characterize the anatomy, physiology and behavior of a group within the context of its life history strategy (Stearns, 1992). One example of a major change in the neural organization of ray-finned fishes will be explored from this perspective.

## WHAT CHANGES HAVE OCCURRED IN BRAINS?

After 200 yr of anatomical descriptions and more than 50 yr of experimental anatomical and physiological studies, there are considerable data regarding *what* changes have occurred in vertebrate brains. In the last 20 yr, cladistics has also emerged as a powerful tool for analyzing variation in brain characters (Northcutt, 1984, 1995; Wullimann and Northcutt, 1990; Striedter, 1991, 1992; Butler, 1994*a*, *b*; Nieuwenhuys, 1998*a*).

Given this extensive body of information on brain variation, it is possible to reach at least three major conclusions regarding brain evolution in vertebrates: 1) All vertebrates, with the exception of the agnathans, which appear to lack a cerebellum, have the same number of brain divisions (Fig. 1); 2) Brain size has increased independently in some members of each vertebrate radiation (Fig. 2); and 3) Increases in brain size have frequently resulted in increases in the number of neural centers, increases in the number of neuronal cell

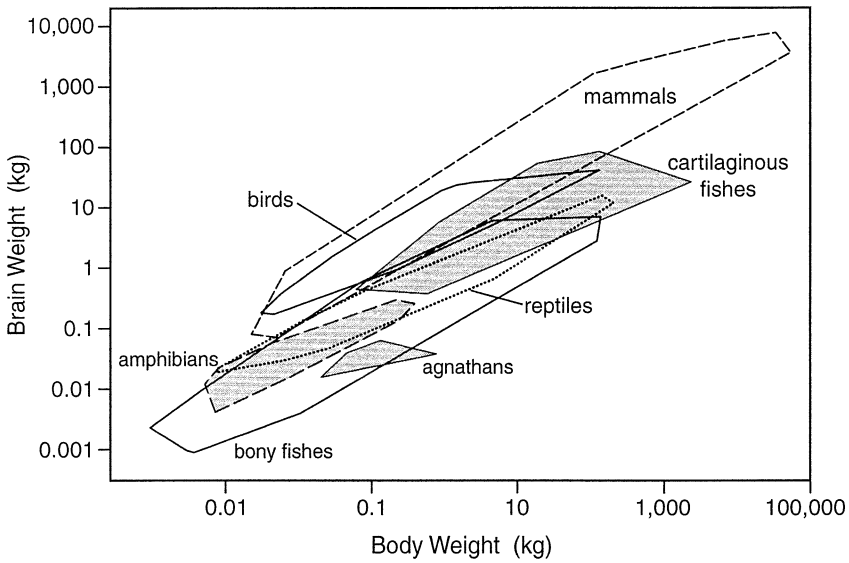


FIG. 2. Brain weights plotted against body weights and expressed as minimal convex polygons in a double logarithmic graph for each of the major vertebrate groups. Each polygon encloses the available data for a given group. For most of these groups, there is a ten-fold range in brain size for any given body size. Furthermore, within each group, the largest brains are also generally the most complex brains. Redrawn from van Dongen (1998).

classes within a center, and probably, increases in behavioral complexity.

*Brain divisions*

Even a superficial examination of the external anatomy of the brains of each vertebrate radiation (Fig. 1) reveals that most vertebrates possess the same number of brain divisions. The absence of a cerebellum in hagfishes and lampreys appears to be the only exception. Both hagfishes and lampreys do possess a thin band of cells located medial to the lateral line centers of the medulla (Ronan and Northcutt, 1998), which has been interpreted as a primitive cerebellum (Larsell, 1967), but more recent experimental studies (Kishida *et al*., 1987; Weigle and Northcutt, 1998) fail to support Larsell's claim.

The conservative nature of major brain divisions across living vertebrates suggests that much of the organization of these brains must have arisen with the origin of vertebrates or shortly thereafter. Unfortunately, as is frequently the case, the fossil record tells us far too little about the brains of transitional forms. The recent discovery of two Lower Cambrian chordates, *Yunnanozoon* (Chen *et al*., 1995) and *Haikouella* (Chen *et al*., 1999; Holland and Chen, 2001), from the Chengjiang Lagerstätte do provide some information. Although *Yunnanozoon* is known from only a few specimens, *Haikouella* is represented by several hundred, which has facilitated reconstruction of its body, including its central nervous system. *Haikouella* was a small, lancelet-like animal, some two to four centimeters in length, which appears to have been a filter feeder, like lancelets, based on its buccal tentacles, endostyle, and well developed pharynx with paired slits. Unlike lancelets, however, *Haikouella* possessed a small number of pharyngeal bars that may have been composed of mucocartilage, as in modern lampreys (Holland and Chen, 2001). These pharyngeal bars also appear to have supported gills similar to those of living craniates. If so, pharyngeal movements in *Haikouella* must have been powered by branchiomeric muscles, as in living craniates, rather than by water moving through the pharynx via ciliary currents, as in lancelets. In turn, the pharyngeal bars of *Haikouella* were probably derived from neural crest, as were the sensory components of the cranial nerves that innervated its pharyngeal muscles. If this suit of pharyngeal characters was present in *Haikouella*, then this animal should have possessed a hindbrain very comparable to that in living craniates. Indeed, it may have, as it appears that *Haikouella*'s brain was fairly large and was divided into two or three distinct rostrocaudal lobes. There is also evidence that *Haikouella* may have possessed laterally paired eyes, which, if present, indicate that a diencephalon/midbrain was probably also present at this point. There is no evidence that other special sensory organs (olfactory and octavolateralis organs) existed, however. In spite of this, Chen *et al*. (1999) claim that the rostral part of the brain was bilobed. Thus it is possible that *Haikouella* may also have had cerebral hemispheres, although this would be particularly surprising based on the absence of olfactory organs, as most comparative neurobiologists have argued that the cerebral hemispheres arose primarily as olfactory centers.

Shu and colleagues (1999) also discovered two fossil chordates, *Haikouichthys* and *Myllokunmingia*, from the Lower Cambrian Chengjiang deposits, and these appear to have been true craniates. The head is better preserved in *Haikouichthys* and shows indications of nasal and otic capsules, as well as sclerotic cartilages. If these initial observations are corroborat-

ed, there is every reason to believe that the brain of *Haikouichthys* possessed the same major brain divisions as exist in living vertebrates.

*Brain size*

Viewed across all vertebrate radiations, brain size varies approximately 30-fold for a given body size (Fig. 2), an astounding evolutionary statistic. The relationship between brain size and body size is highly ordered. In most vertebrate radiations, brain size varies approximately 10-fold, and brain size increases with body size, although this increase is not proportional. Rather, it is allometric, with slopes ranging from 0.21 (agnathans) to 0.74 (mammals). Brain size also varies in an orderly manner between and within vertebrate radiations. Agnathans generally have the smallest brains for their body size, with hagfishes having brains that are two to three times larger than lampreys of the same body size (Northcutt, 1985). Although a small number of bony fishes have brains of the same relative size as those in agnathans, most bony fishes have considerably larger brains for the same body size (Fig. 2). Within bony fishes, non-neopterygians (bichirs, paddlefish, and sturgeons) have relatively smaller brains than those in the vast majority of teleosts (van Dongen, 1998). This is also true of the living lobe-finned fishes (lungfishes and coelacanths), which have relatively smaller brains than most amphibians and reptiles. Among amphibians, frogs generally have relatively larger brains than salamanders, and the brains of reptiles are generally two to three times larger than the brains of most amphibians of the same body size.

Both birds and mammals have brains that are 6–10 times larger than the brains of reptiles of the same body size. Among birds, the largest brains for body size are seen in perching birds, woodpeckers, and parrots, while the relatively smallest brains are found in pigeons and chicken-like birds (van Dongen, 1998). Similarly, mammals have brain sizes that are 10 times larger than those in reptiles of the same body size. Primates and cetaceans have the largest brains for their body size, while non-placental mammals, marsupials, insectivores, and rodents have the relatively smallest brains. Much of this variation in relative brain size among mammals may be due to developmental constraints, in that selection for an increase in the size of a single brain center is likely to lead to an overall increase in brain size (Finlay and Darlington, 1995). Surprisingly, many cartilaginous fishes have brains as large for their body size as those of birds and mammals (Bauchot *et al*., 1976; Northcutt, 1977; Demski and Northcutt, 1996). Among cartilaginous fishes, carcharinid sharks and myliobatid rays have the relatively largest brains, while squalomorph sharks and skates have the smallest brains for a given body size.

If lancelets and the fossil ostracoderms (Forey and Janvier, 1994) are considered out-groups to living craniates, then the brains of the earliest craniates must have been very small for their body size. An out-group analysis of brain variation among living craniates suggests that brain size has increased independently in some members of each vertebrate radiation, as previously proposed (Northcutt, 1985). It is clear, however, in the extensive overlap in relative brain size among living bony fishes, amphibians, and reptiles, that many members of each radiation have not increased relative brain size, and some even decreased it. Although it is not possible to identify the precise selective pressure(s) responsible for specific increases (or decreases) in relative brain size, one or more selective pressures must certainly have been operative in each vertebrate radiation. In some cases selection may have acted for a change in body size, and the increased/decreased brain size may only reflect this general change. In other cases, a change in brain size may have been selected for directly, with little or no change in body size. In any case, when relative brain size has increased, what are the organizational consequences of that increase?

*Consequences of relative brain enlargement*

Relative brain size appears to have increased independently in some members of each vertebrate radiation, such that six separate morphoclines (the arrangement of homologous character states in different taxa into a linear sequence from primitive to derived states [Hennig, 1966; Eldredge and Cracraft, 1980]) can be recognized: 1) lampreys—hagfishes; 2) squalomorph sharks—galeomorph sharks; 3) polypteriforms—teleosts; 4) amphibians—reptiles; 5) reptiles—birds; and 6) reptiles—mammals (Northcutt, 1985). Most of these clines can be characterized by increases in the number of neural centers in one or more brain regions, increases in the number of neuronal classes within neural centers, and, probably, increases in behavioral complexity.

*Increase in neural centers*. Surprisingly, there are few quantitative data correlating the change in the number of neural centers in a given brain area with increasing brain size relative to body size. Clearly, some divisions of the brain, such as the medulla, appear to change very little in vertebrate phylogeny. For example, it is possible that the brainstem reticular formation is divided into the same number of nuclei in all jawed vertebrates (Cruce *et al*., 1999). On the other hand, the total number of brainstem nuclei appears to vary from approximately 20 to 50 across anamniotes and reptiles (Nieuwenhuys, 1977). Other divisions of the brain, such as the cerebellum, have also changed very little. A cerebellum comprised of a central body (corpus cerebelli) and paired auricles (flocculo-nodular lobes) apparently arose with, or slightly prior too, the origin of jawed fishes themselves. Increases in the relative size of the cerebellum have occurred independently in galeomorph sharks, myliobatiform rays, teleosts, reptiles, birds, and mammals. In all these groups, except reptiles, the corpus has become convoluted into multiple folia, and, in the case of birds and mammals, has divided into medial (cerebellar vermis) and lateral (cerebellar hemispheres) anatomical and/or functional divisions. Similar increases in the number of deep cer-

ebellar nuclei also characterize the expansion of the cerebellum in birds and mammals.

The optic tectum (Table 1) exhibits even more variation than the medulla or cerebellum. In all craniates, it is divided into a varying number of alternating cellular and fibrous layers or laminae. Each cellular layer comprises different neuronal classes, receives different kinds of sensory inputs, and projects to different neural centers. Tectal cell layers, therefore, can be viewed as unique functional divisions. The available data on tectal lamination clearly show an increase in the number of tectal laminae along a morphocline from hagfishes to amniotes, but there are interesting exceptions. The tectum in lampreys has as many, or more, layers than the tectum in hagfishes, and may actually be larger in relative or absolute size, even though the whole brain is larger in hagfishes of the same body weight. This is likely related to the fact that vision is less well developed in hagfishes. Unfortunately, there are few quantitative data on the relative sizes of major brain divisions in most craniates.

Tectal lamination may increase from squalomorph sharks, such as *Squalus*, to galeomorph sharks, such as *Scyliorhinus* (Table 1), but this is difficult to evaluate because of the small data base and the fact that there is limited agreement on the number of tectal laminae among sharks and other chondrichthyans. On the other hand, it is clear that tectal lamination in ray-finned fishes increases along a morphocline from polypteriformes, such as bichirs, to teleosts, such as goldfish, and it will almost certainly be even higher in those marine teleosts that have well developed vision. A similar increase in tectal lamination also occurs in lobe-finned fishes, along a morphocline from coelacanths and lungfishes to amphibians (Table 1). Although the tectum in reptiles is more laminated than in lobe-finned fishes and salamanders, it does not appear to be more laminated than in anuran amphibians. It is not clear whether the large number of tectal laminae in frogs has been selected for independently or actually represents the primitive condition for amphibians. On the other hand, tectal lamination is almost identical in reptiles and birds and is more restricted in mammals (Table 1). The fact that tectal laminae are fewer in mammals may be related to their suspected nocturnal origin, which may have been marked by the decreased importance of visual stimuli and an increased reliance on audition and olfaction. In this context, further information on tectal lamination in highly visual rodents and primates would be of great interest.

The increase in number of neural centers with increase in relative brain size is best illustrated in the forebrain (Wicht and Northcutt, 1992), particularly the cerebral hemispheres (Table 2). Except for chondrichthyan fishes, each of the craniate morphoclines listed at the beginning of this section exhibits striking increases in the number of neural centers. In each case, most of the increase has occurred in the roof of the telencephalon, *i.e.,* in the pallial centers. For example, hagfishes have independently evolved a highly laminated cerebral cortex, comparable in many ways to the cerebral cortex of mammals. Most of the increase in number of centers in ray-finned fishes also occurs in the pallium, where three subdivisions can be recognized in bichirs and some 13 in teleosts (Northcutt and Braford, 1980). The most striking example of increase in neural centers with increase in relative brain size, however, occurs in mammals. In a morphocline from rodents to primates, there is a five-fold increase in the number of cortical subdivisions. In this context, the apparent absence of an increase in neural centers in the morphocline from squalomorph sharks to galeomorph sharks is particularly surprising, as there is an increase of approximately four-fold in the relative size of the telencephalon (unpublished observations). This apparent absence of an increase may, however, be due to the lack of data, as we do not have descriptions of the telencephalon in the most derived galeomorph sharks, such as the hammerhead sharks.

*Increase in cell classes*. There are far fewer data on how the number of cell *classes* varies with relative increase in size. Almost certainly, there are more cell classes in the cerebral cortex of a mammal than in the entire telencephalon of a lamprey, but there are only three brain centers for which there are sufficient data to measure the effect of relative increases in the size of a neural center on the number of cell classes in that center: the cerebellum, the olfactory bulb, and the optic tectum. In the first two, the number of cell classes (approximately five in each structure) is relatively constant. The optic tectum, however, shows considerable variation in the number of cell classes (Table 1). A morphocline from anamniotes to amniotes is characterized by an increase in the number of cell classes. Closer examination of the data, however, suggests that there is no increase in number of cell classes in the lamprey—hagfish morphocline or in the reptile—mammal morphocline. Given the information on tectal lamination in agnathans and mammals presented earlier, this should not be surprising. Unfortunately, there are, again, insufficient data to evaluate the squalomorph—galeomorph shark morphocline, and this is also true for the number of telencephalic cell classes in each of the morphoclines. Based on other measures, however, the telencephalon is the structure most likely to have the highest variation in cell classes.

*Increase in behavioral complexity*. The effect of increased relative brain size on behavior is one of the thorniest issues in comparative neurobiology. Late in the 19th century, relative brain size was believed to be linked to intelligence (Marsh, 1874; Romanes, 1883). It was generally assumed that mammalian evolution, in particular, was characterized by a progressive increase in brain size, especially in the cerebral hemispheres, which correlated with a progressive increase in intelligence. As late as 1966, Alfred S. Romer would write:

> "The brain of the creodonts was generally of relatively small size and their intelligence presumably

TABLE 1. *Variation in number of tectal layers and cell classes.*

| Species | Number of layers | Number of cell classes | Source |
|---|---|---|---|
| Hagfish | | | |
| *Eptatretus burgeri* | 4 | 5–6 | Iwahori *et al*., 1996 |
| River lamprey | | | |
| *Lampetra fluviatilis* | 5 | 5 | Heier, 1948 |
| Marine lamprey | | | |
| *Petromyzon marinus* | 7 | 5 | Kennedy and Rubinson, 1984 |
| Spiny dogfish | | | |
| *Squalus acanthias* | 7 | unknown | Northcutt, 1979 |
| Nurse shark | | | |
| *Ginglymostoma cirratum* | 5 | 7 | Ebbesson, 1984 |
| Chain dogfish | | | |
| *Scyliorhinus canicula* | 6–13 | 8 | Farner, 1978<br>Smeets, 1981<br>Repérant *et al*., 1986<br>Manso and Anadón, 1991 |
| Bichir | | | |
| *Polypterus palmas* | 10 | 12 | Northcutt, 1983 |
| Longnose gar | | | |
| *Lepisosteus osseus* | 11 | unknown | Northcutt, 1983 |
| Bowfin | | | |
| *Amia calva* | 13 | 14 | Northcutt, 1983 |
| Goldfish | | | |
| *Carassium auratus* | 15 | 8–14 | Ramon, 1899<br>Leghissa, 1955<br>Meek and Schellart, 1978<br>Northcutt, 1983 |
| Coelacanth | | | |
| *Latimeria chalumnae* | 4 | unknown | Northcutt and Neary, 1975 |
| African lungfish | | | |
| *Protopterus dolloi* | 3 | 2 | Clairambault *et al*., 1974<br>Clairambault and Flood, 1975 |
| Tiger salamander | | | |
| *Ambystoma tigrinum* | 8 | 3 | Herrick, 1942<br>Roth et al., 1990 |
| Green frog | | | |
| *Rana esculenta* | 9–14 | 8–9 | Ramón, 1894<br>Székely and Lazar, 1976 |
| Red-eared turtle | | | |
| *Pseudemys scripta* | 14 | 22 | Huber and Crosby, 1933 |
| Wall lizard | | | |
| *Podarcis* (*Lacerta*) *muralis* | 14 | 15 | Ramón, 1896 |
| Tegu lizard | | | |
| *Tupinambis nigropunctatus* | 14 | 18 | Butler and Ebbesson, 1975 |
| Teiid lizard | | | |
| *Pantodactylus schrieberi* | 14 | 25 | Quiroga, 1978 |
| House sparrow | | | |
| *Passer domesticus* | 15 | 27 | Cajal, 1911 |
| Domestic cat | | | |
| *Felis catus* | 5–7 | 17 | Cajal, 1911<br>Kaneseki and Sprague, 1974 |

TABLE 2. *Variation in number of telencephalic cell groups.*

| Species | Number of cell groups | Source |
|---|---|---|
| Hagfish | | |
| *Eptatretus stouti* | 13 | Wicht and Northcutt, 1992 |
| lamprey | | |
| *Lampetra fluviatilis* | 6 | Nieuwenhuys and Nicholson, 1998 |
| Ratfish | | |
| *Hydrolagus collei* | 15 | Smeets, 1998 |
| Spiny dogfish | | |
| *Squalus acanthias* | 18 | Smeets, 1998 |
| Skate | | |
| *Raja clavata* | 14 | Smeets, 1998 |
| Bichir | | |
| *Polypterus palmas* | 12 | Northcutt and Braford, 1980 |
| Shovelnose sturgeon | | |
| *Scaphirhynchus platorynchus* | 13 | Northcutt and Braford, 1980 |
| Green sunfish | | |
| *Lepomis cyanellus* | 26 | Northcutt and Braford, 1980 |
| Coelacanth | | |
| *Latimeria chalumnae* | 11 | Nieuwenhuys, 1998*b* |
| South American lungfish | | |
| *Lepidosiren paradoxa* | 10 | Nieuwenhuys, 1998*c* |
| Tiger salamander | | |
| *Ambystoma tigrinum* | 11 | ten Donkelaar, 1998*a* |
| Green frog | | |
| *Rana esculenta* | 15 | ten Donkelaar, 1998*b* |
| Greek tortoise | | |
| *Testudo hermanni* | 22 | ten Donkelaar, 1998*c* |
| Tegu lizard | | |
| *Tupinambis teguixin* | 28 | ten Donkelaar, 1998*c* |
| Domestic pigeon | | |
| *Columba livia* | 33 | Karten and Hodos, 1967 |
| Domestic rat | | |
| *Rattus norvegicus* | 66 | Paxinos and Watson, 1986 |

> low. This may have been a main cause of the early extinction of almost all members of the group; for with replacement of the slow-footed and stupid herbivores of early Tertiary time by the swifter modernized ungulates, intelligent group pursuit (as in the wolf pack) or clever stalking (as in the case of cats) became necessary for the capture of prey.''

In 1973, Jerison attempted to establish a quantitative measure of intelligence with his concept of the encephalization quotient (EQ), which was the ratio of actual brain size to expected ''average'' brain size. The latter was defined by the allometric function for brain: body relations initially proposed by Snell (1892) in the form of $E = kP^{\alpha}$, where E and P are brain and body weights, respectively, and k and $\alpha$ are constants. For example, a taxon with an EQ of 6, the actual value calculated by Jerison for humans, would have a brain six times larger than that in the ''average'' mammalian taxon. Jerison (1973) assumed that since the brain size of an ''average'' mammal was sufficient to maintain basic sensory and motor functions, the ''excess'' brain weight represented neurons that could be utilized for higher mental functions. The concepts of intelligence and the encephalization quotient have been repeatedly questioned, however. First of all, it has proven difficult if not impossible to establish a definition of intelligence, as a biological property of an organism, that is free of value judgment (Butler and Hodos, 1996). Secondly, the actual value of an expected brain size will depend on the choice of a reference group, and an expected brain size can therefore change substantially, depending on the taxonomic level selected (van Dongen, 1998).

In spite of these problems, most of us believe that our behavior is more complex than that of a rat, and that this is due to our relatively larger brain. Indeed, most biologists would not quibble with the intuitively based conclusion that brain complexity and behavioral

complexity are somehow linked. Brains exist to process information, which allows an animal to solve problems, which in turn contributes to that animal's fitness. As brains increase in size, the number of the neurons and their interconnections also increase, thus expanding the available equipment for processing information. This increased ability to process information allows an animal to construct a more complex perceptual world, which in turn should reveal increased opportunities for problem solving, prompting behavior to become more complex and adaptive. Of course, this scenario may apply only to populations that are under K-selection, *i.e.,* a population in a stable environment, where individuals develop slowly, live longer, grow larger, and invest heavily in a small number of offspring. It may not apply to populations under r-selection, where individuals develop rapidly, reproduce quickly and have large numbers of offspring with relatively small brains (Eisenberg, 1981).

If we accept that relative brain size is correlated with behavioral compexity, how can behavioral complexity be measured objectively? Unfortunately, this is not simply a matter of measuring observable motor behavior, as this tells us nothing about cognition, which includes another thorny concept, consciousness. For example, there is little question that Great Apes and African Parrots have a sense of self and personal experience over time (Heyes and Huber, 2000; Pepperberg, 2000), but how do we compare the behavior of these animals to one another or to ourselves? At present there is no satisfactory answer to this question. Our best hope for one may lie in the field of cognitive neuroscience, whose researchers are, perhaps, beginning to understand how our own brains really work.

## WHEN DO BRAINS CHANGE?

The question of *when* brains change can be answered in a mechanistic and/or historical context. Mechanistically, brains change either by chance or in response, directly or indirectly, to a change in selective pressures. Historically, changes in brain size or organization are correlated with phylogenetic changes, in particular the origin of a new radiation. Unfortunately, most comparative neurobiologists have not taken the next step and attempted to identify correlations between brain changes and the ecological changes that accompany the origin of a new vertebrate radiation. Although a correlational approach can be problematic, and does not necessarily imply causation, correlations between brain changes and a new ecology can be identified, and different scenarios can be proposed to account for them. Often these scenarios embody hypotheses that can be tested.

As an example of such a correlation, an increase in brain size and the origin or elaboration of a cerebellum are correlated with the origin of jawed fishes. Given the ecology of jawed fishes, it is highly probable that these neural changes are related to new ways of feeding and more active locomotion (Olson, 1966; Chatterjee, 1997; Hotton *et al*., 1986; Kemp, 1982). Although this hypothesis can not be tested directly, it is supported by the fact that similar increases in brain size and cerebellar/motor center elaboration occur with the origin of birds and the origin of mammals, both of which events were accompanied by ecological changes that also involved new ways of feeding and more active locomotion.

Answering the question of *when* brains change in an historical context can also be difficult. The sister groups most closely related to each of the living vertebrate radiations are usually extinct, which precludes examination of their brain anatomy. Even when fossil endocasts are available, they are of limited value if the braincase was far larger than the brain. For example, there are no endocasts available for the earliest reptiles, the cotylosaurs, and the endocasts for the earliest synapsid (mammal-like) reptiles tell us very little, as much of the brain case was not ossified, and the endocasts thus provide no useful information on even the size of the forebrain and midbrain (Hopson, 1979).

Even when useful endocasts exist, their interpretation may be contentious. An out-group analysis of living craniates suggests that the cerebellum arose with the origin of jawed vertebrates, as noted in the first section. However, a cerebellum has been included by Forey and Janvier (1994) in reconstructions of the brains of several groups of fossil agnathans: heterostracans, galeaspids, and osteostracans. Unfortunately, the roof of the fourth ventricle in lampreys is greatly expanded dorsally, so that an endocast might suggest the presence of an extensive cerebellum, but whether one existed is very much open to question. If Forey and Janvier's interpretations are accurate, then a cerebellum arose with the common ancestor of the fossil agnathans listed above and only expanded with the origin of jawed vertebrates. If the absence of a cerebellum in hagfishes and lampreys is a primitive condition for craniates, as discussed earlier in this paper, then a cerebellum arose only with the origin of jawed vertebrates. Given the difficulties inherent in endocast interpretation, it is possible that we will never know the precise time of origin of the vertebrate cerebellum.

In some cases, however, endocasts can provide critical and less dubious information. The telencephalon of living reptiles and birds is expanded laterally, so that it has a distinct heart-shape when viewed dorsally. This distinctive form appears to be primarily due to a large expansion of the lateral wall, termed the dorsal ventricular ridge (DVR), which protrudes into the lateral ventricle. Because of the phyletic continuity of the DVR in living reptiles and birds, and its numerous similarities in topography, histology, and connections in these two groups, there is little question that the DVR of reptiles and birds is homologous as a telencephalic neural center. In contrast, the telencephalon in living mammals does not appear to have a DVR. It has been suggested, however, that their predecessors did have such a ridge, and that its cells migrated to the surface of the telencephalon during development to form part of the cerebral cortices which characterize

all living mammals (Karten, 1969, 1991). This inference can not be supported or refuted by the endocasts of the mammal-like cynodont therapsid reptiles, but these endocasts do provide considerable details and limit our interpretations of what may have happened. Cynodonts very clearly had well developed olfactory bulbs and inner ears, and the cerebellum appears to have already assumed the appearance of a mammalian cerebellum, which is characterized by lateral hemispheres and a distinct flocculus. The cerebral hemispheres, however, are remarkably long and narrow, and they do not resemble the cerebral hemispheres of living reptiles, birds, or mammals!

On the other hand, the endocasts of other reptiles, such as the archosaurs (crocodiles, pterosaurs, and dinosaurs), indicate that their cerebral hemispheres were probably characterized by a well developed DVR (Hopson, 1979). If a DVR existed in the telencephalon of cynodont reptiles, it was relatively poorly developed. In any case, the cynodont endocasts do not indicate an expansion of the cerebral cortices in synapsids. This must have occurred at a later time, because widened, mammal-like endocasts do not appear until the Late Jurassic (Rowe, 1996).

As noted earlier, modern birds have brains that are six to ten times larger than those in living reptiles of the same body size (Fig. 2). Do endocasts give any indication of when avian brains began to enlarge? Fortunately, the endocast of *Archaeopteryx* has been reconstructed (Jerison, 1968), and its brain appears to have been intermediate between that of living reptiles and that of living birds, by any estimate of its body weight (250 g to 500 g). As additional data accumulate, however, the differences in relative brain size in fossil reptiles and fossil birds, will likely disappear. Estimates of brain size for some of the ostrich-like carnivorous dinosaurs (ornithomimosaurs) indicate that their relative brain size falls within the range of living birds (Russell, 1972). Thus, it appears that increased relative brain size was being selected for in *Archaeopteryx* and in theropod dinosaurs in general.

## HOW DO BRAINS CHANGE?

Phylogenetic changes in brains occur only by changes in an ancestral ontogeny. If this is the case, how can changes in an ancestral ontogeny be reconstructed, since the ancestors of most craniate radiations are extinct?

If a taxon is of interest because of particular traits, and there is a well corroborated hypothesis of phylogeny for that taxon, it is possible to do an out-group analysis of the development of those traits (Northcutt, 1990). Although the development of any trait is a continuous process, stages of that development must be designated in order to describe it. For example, development of the telencephalon can be divided into these stages: neurectoderm, neural plate, neural tube, forebrain vesicle, evaginated hemispheres, etc. For purposes of an out-group analysis, these stages can be treated in the same manner as one would treat adult

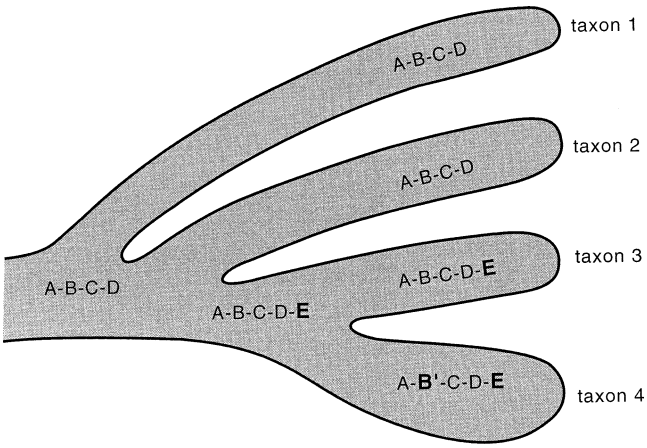


FIG. 3. An out-group analysis of the stages (A–E) in the development of a theoretical structure in four taxa. If there is a highly corroborated hypothesis of the phylogeny of these taxa (indicated in gray), it is possible to determine which stages are primitive (normal print) and which are derived (bold print). In this example, a pair-by-pair analysis of sister groups indicates that: 1) The primitive sequence of developmental stages for this structure is A-B-C-D in the common ancestor; 2) Stage E in Taxa 3 and 4 must have arisen by the addition of a terminal stage in the common ancestor shared by Taxa 3 and 4; 3) Stage B in Taxon 4 is a uniquely derived, nonterminal change.

traits (Fig. 3). The proviso in dealing with developmental stages, however, is that each stage must be causally linked to the preceding stage (*i.e.*, development of any given stage is dependent on development of the stage immediately before it). A matter of practical concern is: how do we know how many stages to recognize in the development of a given character, and is it possible to compare traits in different taxa where the traits do not have the same number of developmental stages? In practice, it is not difficult to determine how many stages to recognize in the development of a given trait, since developmental stages are traditionally recognized on the basis of a distinct morphology. For example, in telencephalic development, as outlined above, no further stages *can* be recognized. One could divide each of these stages into early, middle, and late, but this would make sense only if a new morphological event characterized each of these substages. In addition, it is not difficult to compare traits with a different number of developmental stages in different taxa. In the case illustrated in Figure 3, the number of stages in the development of a hypothetical trait differs in the four separate taxa, but stages A, B, C, and D are homologous across all these taxa. This is true even for stage B′ in taxon 4, since this change has occurred in only one taxon and can be viewed as a derived stage, homologous to the primitively retained stage in the other taxa. Similarly, stage E is homologous in taxa 3 and 4 but is a uniquely derived stage of the clade formed by taxa 3 and 4 and has no homologue in taxa 1 and 2.

Because the evolution of structures has traditionally been viewed as trait transformation in adults, there are few examples of how an out-group analysis of devel-

opmental stages allows the reconstruction of an ancestral ontogeny and the determination of where and when changes have occurred. Two examples can be described, however: the evolution of the lateral line system in anamniotic vertebrates (Northcutt, 1997) and the evolution of the telencephalon in amniotes (Striedter, 1997).

The lateral line system of fishes and many amphibians comprises lines of mechanoreceptive neuromasts distributed over the head and trunk. These lines vary in number among anamniotes, and they occur on the surface of the skin in lampreys and amphibians but in ectodermal grooves or canals in most fishes. In addition to neuromasts, many anamniotes also have a second class of receptors, *i.e.*, ampullary electroreceptors. The presence of these ampullary organs varies greatly among anamniotes, but an out-group analysis of their distribution in adult anamniotes suggests that they were present in primitive vertebrates and retained in living lampreys, cartilaginous fishes, lobe-finned fishes and basal ray-finned fishes (bichirs, sturgeons and paddlefishes). Ampullary organs do not occur in gars and bowfins, two of the three groups of neopterygian fishes, nor are they found in most teleost fishes, but they do appear to have re-evolved at least twice (and more likely three or more times) in five groups of teleosts (Northcutt, 1997). How did this variation in lateral line receptors evolve?

An out-group analysis of the development of the lateral line system in living vertebrates (Northcutt, 1997) reveals that cephalic ectodermal thickenings, termed placodes, are the basic ontogenetic unit responsible for their development and that six (at least) pairs of these placodes must have occurred in the earliest jawed fishes. The development of a primitive lateral line placode can be divided into eight stages: 1) initial formation of the placode; 2) generation of the neuroblasts that will form the sensory neurons that innervate the receptors generated by a placode; 3) elongation of the placode to form a sensory ridge; 4) differentiation of neuromast primordia along the central length of the sensory ridge; 5) differentiation of electroreceptor primordia within the sensory ridge in two lateral zones that flank the developing neuromasts; 6) eruption of neuromasts to the surface, forming lines on the skin; 7) opening of ampullary electroreceptors to the surface and flanking of each neuromast by ectodermal ridges; and 8) fusing of ectodermal ridges to form a canal that encloses the neuromasts (Northcutt *et al.*, 1994). Terminal truncation (a heterochronic change) in the primitive sequence of placodal development has occurred in one or more placodes in each radiation of anamniotes, with the most extensive truncations occurring in lepidosirenid lungfishes and extant amphibians (Northcutt, 1997). The most extensive nonterminal change in the primitive sequence of placodal development is the failure of electroreceptors to form within the lateral zones of the elongating sensory ridges (Northcutt, 1997). This change appears to have occurred independently in ancestral neopterygian bony fishes and many amphibians. The redevelopment of electroreceptors in osteoglossomorph and ostariophysine fishes represents an additional nonterminal change in placodal patterning (Northcutt, 1997).

As noted in the section "When Do Brains Change", there is no agreement on the mammalian homologue of the DVR in reptiles and birds. Amazingly, this has remained an intractable problem to comparative vertebrate neuroanatomists (see the symposium proceedings edited by Braford, 1995), despite accumulated histochemical and connectional data on the telencephalon of adult tetrapods. Striedter (1997) offered a novel solution to the problem with an out-group analysis of the development of the telencephalon in tetrapods. Although his analysis was based on descriptive developmental data published by different authors over a period of 75 yr, he was able to divide telencephalic development into a number of stages. In the first stage, the telencephalic hemispheres of all tetrapods can be divided into a roof area, or pallium, and a floor area, or subpallium, separated by relatively cell-free zones. In the second stage, the pallium can be divided into lateral (lateral pallium) and medial longitudinal zones. In the third stage, the medial longitudinal zone can be further divided into dorsal (dorsal pallium) and dorsomedial (medial pallium) longitudinal zones. Stage three appears to be the terminal stage of telencephalic development in amphibians, but additional stages can be recognized in reptiles, birds, and mammals. In these stages, various pallial subdivisions differentiate along divergent lines, varying in their number and in their relative growth. In spite of this variation, Striedter (1997) suggests that a stage can be recognized in all amniotes in which the lateral pallium can be divided into a superficial sheet of cells, termed the piriform cortex, and more deeply located anterior and posterior cell masses. He believes that the anterior deep cell mass in reptiles and birds greatly increases its size to become the DVR, whereas the homologous cell mass in mammals does not increase greatly and becomes the endopiriform nucleus, which is often considered a ventral part of the claustrum.

Only time will tell if Striedter's novel conclusion will become widely accepted, but there is no question that his hypothesis can be tested by continued developmental studies. In this context, it is important to note that an out-group analysis of multiple ontogenies is only the first step in determining how neural or other structures change over time. An out-group analysis can strongly suggest where and when an ontogenetic trajectory has been altered by one or more changes, but additional studies are needed to determine the cellular interactions and genetic bases of these changes.

## WHY DO BRAINS CHANGE?

The cerebral hemispheres of ray-finned fishes develop in a radically different way than do the cerebral hemispheres of all other vertebrates (Fig. 4). In all vertebrates, the forebrain vesicle initially forms a simple hollow tube (Fig. 4A), with a germinal layer that can

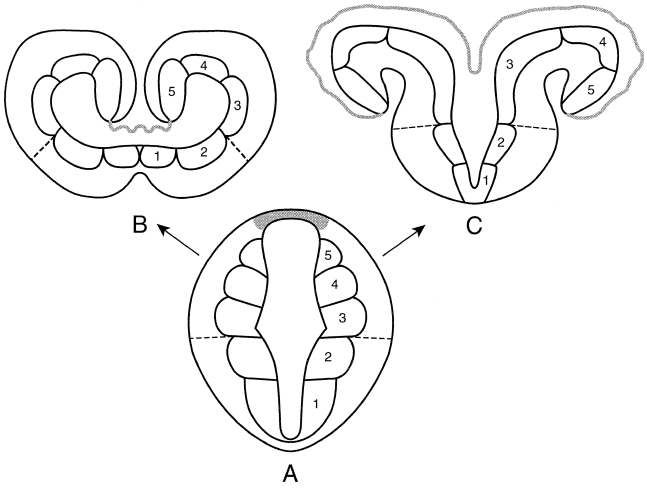


FIG. 4. Schematic representation of transverse sections through the initial forebrain vesicle (A), the evaginated cerebral hemisphere of an amphibian (B), and the everted cerebral hemispheres of a ray-finned fish (C). The topography of the germinal zones (1–5) and their derivatives are profoundly altered by the process of evagination versus eversion, as is the extent of the choroid plexus (gray). Both types of cerebral hemispheres can be divided (dashed line) into a ventral subpallium (1, 2) and a dorsal pallium (3–5). While the topographical relationships of the cell groups of the subpallium are hardly changed, the topography of the pallial cell groups of ray-finned fishes is reversed lateromedially when compared to the pallial cell groups of an amphibian. Modified from Northcutt (1995).

be divided into a ventrodorsal series of zones (1–6, Fig. 4A) lying adjacent to the central lumen or prosencoel. In all vertebrates except ray-finned fishes, the lateral walls of the rostral half of the forebrain vesicle expand more rapidly than do the floor or roof and bulge out to form cerebral hemispheres (Fig. 4B). This evagination of the lateral walls also results in the inversion of the initial, most dorsal segment (zone 5) of the dorsal half (pallium) of the forebrain vesicle. In ray-finned fishes, however, the pallium (zones 3–5) thickens and everts (Fig. 4C), so that the initial most dorsal pallial segment (zone 5) comes to lie lateral to the remaining pallium. The cerebral hemispheres of all ray-finned fishes that have been examined are everted (Nieuwenhuys *et al*., 1998), and an out-group analysis (Northcutt, 1995) indicates that this is a derived pattern for vertebrates. Although everted cerebral hemispheres have been known to exist in ray-finned fishes for at least 80 yr (Holmgren, 1922), no satisfactory explanation has been offered for the selective advantage of eversion.

The answer may lie in a comparison of the life histories, particularly the markedly different body size and reproductive strategies, of ray-finned fishes and other fishes. In general, body size in ray-finned fishes is several orders of magnitude smaller than in other fishes, particularly cartilaginous fishes, and ray-finned fishes generally produce large numbers of young with short gestation periods (a few days). In contrast, the much larger cartilaginous fishes produce small numbers of young that require long gestation periods (several months).

An examination of the fossil record (Carroll, 1988; Maisey, 1996) suggests that these size differences are very ancient. For example, most Devonian sharks are estimated to have had body lengths between 1 and 2 m, whereas most Devonian ray-finned fishes are estimated to have had body lengths less than 15 cm (Maisey, 1996). If large body lengths are primitive for jawed fishes, which is also true for many placoderms, then a marked reduction in body size may have occurred with the origin of ray-finned fishes. Although we may never understand why ray-finned fishes have reduced body size, it is clear that their larvae are generally so small that they can feed only on extremely tiny (50–100 micron) prey (Gerking, 1994).

The larvae of ray-finned fishes are able to feed on such small prey because they have enlarged their eyes, which increases visual acuity, and accelerated their optic development (Easter and Nicola, 1996; Shand, 1997; Shand *et al*., 1999). The consequences of the acceleration in optic development may be that, initially, there is insufficient intracranial space for the development of evaginated cerebral hemispheres, and, further, telencephalic eversion along the dorsomedial margin of the greatly enlarged eyes may also be delayed until the heads of the larvae are sufficiently enlarged to accommodate development of the cerebral hemispheres. These ideas are presently being tested in collaboration with Dr. Georg Striedter of the University of California, Irvine by examining the relative timing and development of the cerebral hemispheres, the eyes, and other cephalic sensory organs in ray-finned fishes and other anamniotic vertebrates. If these ideas are correct, telencephalic eversion in ray-finned fishes was never selected for directly but is a consequence of reduction in body size and acceleration in optic development in the larvae.

## FUTURE DIRECTIONS

In spite of 50 plus years of experimental anatomical and physiological studies of vertebrate brains, there are still vast gaps in our understanding of how they are organized. We know nothing about the physiology of the cerebral cortices in hagfishes, very little about the forebrain organization of cartilaginous fishes, almost nothing about the biological significance of variation in the cerebellum across vertebrates, and virtually nothing about the organization of higher motor centers in any group of vertebrates except mammals. Any comparative neuroanatomist would be hard pressed to list the neural specializations for feeding in ray-finned fishes or flight in birds. We are so intent on constructing a model of how ''the brain'' is organized that we forget that each vertebrate radiation has evolved unique suits of neural characters that are responsible, in part, for their being able to interact with the world in unique ways.

If Garstang's hypothesis is correct, it will be possible to understand vertebrate brain evolution only within the context of brain development. If this is true, the vast body of data on the organization of adult verte-

brate brains represents only the tip of the ontogenetic iceberg. We know almost nothing about the development of most brain centers and pathways across vertebrates. There is every reason—in fact it is necessary—to assume that there is at least as much variation, if not more, in developing brains as in adult brains. A number of developmental ''models'' (*e.g.*, zebrafish, clawed frogs, chicks and mice) are proving useful in providing insights into many aspects of neural development, but they do not allow us to address most questions concerning the developmental modifications required for the origin of novel features (*e.g.*, the origin and evolution of electroreception).

Finally we need to focus our attention on how ecological factors alter development and thus phylogeny. Many, perhaps most, unique neural characters will be understood only within the broader framework of life history strategies. In spite of Robert Frost's fantasy that some day our arms and legs might atrophy so that only our beached brains remain with the single wish that the tide will rise to ''keep our abstract verse from being dry,'' brains do not exist in isolation but as parts of complex organisms changing over time.

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## REFERENCES

Bauchot, R., R. Platel, and J. M. Ridet. 1976. Brain-body weight relationships in Selachii. Copeia 1976:305–310.

Braford, M. R., Jr. (ed.) 1995. Evolution of the forebrain. Brain Brehav. Evol. 46:181–338.

Braun, C. B. and R. G. Northcutt. 1999. Morphology: Brain and cranial nerves. *In* R. Singer (ed.), *Encyclopedia of paleontology,* pp. 185–192. Fitzroy Dearborn Publishers, Chicago.

Butler, A. B. 1994*a*. The evolution of the dorsal thalamus of jawed vertebrates, including mammals: Cladistic analysis and a new hypothesis. Brain Res. Rev. 19:29–65.

Butler, A. B. 1994*b*. The evolution of the dorsal pallium in the telencephalon of amniotes: Cladistic analysis and a new hypothesis. Brain Res. Rev. 19:66–101.

Butler, A. B. and S. O. E. Ebbesson. 1975. A Golgi study of the optic tectum of the tegu lizard, *Tupinambis nigropunctatus*. J. Morphol. 146:215–228.

Butler, A. B. and W. Hodos. 1996. *Comparative vertebrate neuroanatomy*. Wiley-Liss, Inc., New York.

Cajal, S. Ramón y. 1911. Histologie du système nerveux de l'homme et des vertébrès, Vol. II. Maloine, Paris. Trans. from the Spanish by L. Azoulay; trans. from the French by N. Swanson and L.W. Swanson. Oxford University Press, New York, 1995.

Camhi, J. M. 1984. *Neuroethology*. Sinauer Associates Inc. Publishers, Sunderland, Massachusetts.

Carroll, R. L. 1988. *Vertebrate paleontology and evolution*. W.H. Freeman and Company, New York.

Chatterjee, S. 1997. *The rise of birds*. Johns Hopkins University Press, Baltimore, Maryland.

Chen, J.-Y., D.-Y. Huang, and C.-W. Li. 1999. An early cambrian craniate-like chordate. Nature 402:518–522.

Chen, J.-Y., J. Dzik, G. D. Edgecombe, L. Ramskld, and G.-Q. Zhou. 1995. A possible Early Cambrian chordate. Nature 377:720–722.

Clairambault, P. and C. Flood. 1975. Les centres visuels primaires de *Protopterus dolloi* Boulenger. J. Hirnforsch. 16:497–509.

Clairambault, P., E. Capanna, M. Chanconie, and G. Pinganaud. 1974. Architectural pattern of the diencephalon and mesencephalon of the African lungfish *Protopterus dolloi*. Boll. Zool. 41:107–122.

Cruce, W. L. R., S. L. Stuesse, and R. G. Northcutt. 1999. Brainstem neurons with descending projections to the spinal cord of two elasmobranch fishes, thornback guitarfish, *Platyrhinoidis triserita*, and horn shark, *Heterodontus francisci*. J. Comp. Neurol. 403:534–560.

Demski, L. S. and R. G. Northcutt. 1996. The brain and cranial nerves of the white shark: An evolutionary perspective. *In* A. P. Klimley and D. G. Ainley (eds.), *Great white sharks. The biology of* Carcharodon carcharias, pp. 121–130. Academic Press, New York.

Easter, S. S., Jr. and G. N. Nicola. 1996. The development of vision in the zebrafish (*Danio rerio*). Dev. Biol. 180:646–663.

Ebbesson, S. O. E. 1984. Structure and connections of the optic tectum in elasmobranchs. *In* H. Vanegas (ed.), *Comparative neurology of the optic tectum,* pp. 33–46. Plenum Press, New York.

Eisenberg, J. F. 1981. *The mammalian radiation: An analysis of trends in evolution, adaptation and behavior*. University of Chicago Press, Chicago.

Eldredge, N. and J. Cracraft. 1980. *Phylogenetic patterns and the evolutionary process*. Columbia University Press, New York.

Farner, H.-P. 1978. Untersuchungen zur Embryonalentwicklung des Gehirns von *Scyliorhinus canicula* (L). II. Das Tectum opticum und dessen Stratification. J. Hirnforsch. 19:333–344.

Finlay, B. L. and R. B. Darlington. 1995. Linked regularities in the development and evolution of mammalian brains. Science 268: 1578–1584.

Forey, P. and P. Janvier. 1994. Evolution of the early vertebrates. Am. Sci. 82:554–565.

Garstang, W. 1922. The theory of recapitulation: A critical re-statement of the biogenetic law. Zool. J. Linnean Soc. London 35: 81–101.

Gazzaniga, M. S. (ed.) 2000. *The new cognitive neurosciences,* 2nd ed. MIT Press, Cambridge.

Gerking, S. D. 1994. *Feeding ecology of fish*. Academic Press, New York.

Grillner, S., T. Deliagina, Ö. Ekeberg, A. El Manira, R. H. Hill, A. Lansner, G. N. Orlovsky, and P. Wallén. 1995. Neural networks that co-ordinate locomotion and body orientation in lamprey. Trends Neurosci. 18:270–279.

Heier, P. 1948. Fundamental principles in the structure of the brain. A study of the brain of *Petromyzon fluviatilis*. Acta Anat. 5:7–213.

Hennig, W. 1966. *Phylogenetic systematics* (translated by D. D. Davis and R. Zangerl). University of Illinois Press, Urbana.

Heyes, C. and L. Huber. (eds.) 2000. *The evolution of cognition*. MIT Press, Cambridge, Massachusetts.

Herrick, C. J. 1942. Optic and postoptic systems in the brain of *Amblystoma tigrinum*. J. Comp. Neurol. 77:191–354.

Holland, N. D. and J. Chen. 2001. Origin and early evolution of the vertebrates: New insights from advances in molecular biology, anatomy, and palaeontology. BioEssays 23:142–151.

Holmgren, N. 1922. Points of view concerning forebrain morphology in lower vertebrates. J. Comp. Neurol. 34:391–459.

Hopson, J. A. 1979. Paleoneurology. *In* C. Gans, R. G. Northcutt, and P. Ulinski (eds.), *Biology of the Reptilia,* Vol. 9, pp. 39–146. Academic Press, London.

Hotton, N., III, P. D. MacLean, J. J. Roth, and E. C. Roth. 1986.

*The ecology and biology of mammal-like reptiles*. Smithsonian Institution Press, Washington, DC.
Huber, G. C. and E. C. Crosby. 1933. The reptilian optic tectum. J. Comp. Neurol. 57:57–164.
Iwahori, N., K. Nakamura, and A. Tsuda. 1996. Neuronal organization of the optic tectum in the hagfish, *Eptatretus burgeri*: A Golgi study. Anat. Embryol. 193:271–279.
Jerison, H. J. 1968. Brain evolution and *Archaeopteryx*. Nature 219: 1381–1382.
Jerison, H. J. 1973. *Evolution of the brain and intelligence*. Academic Press, New York.
Jerison, H. J. 1990. Fossil evidence on the evolution of the neocortex. *In* E. Jones and A. Peters (eds.), *Cerebral cortex*, Vol. 8A, *Comparative structure and evolution of cerebral cortex,* Part 1, pp. 285–309. Plenum Press, New York.
Kanaseki, T. and J. M. Sprague. 1974. Anatomical organization of pretectal nuclei and tectal laminae in the cat. J. Comp. Neurol. 158:319–338.
Karten, H. J. 1969. The organization of the avian telencephalon and some speculations on the phylogeny of the amniote telencephalon. Annals N.Y. Acad. Sci. 167:164–179.
Karten, H. J. 1991. Homology and evolutionary origins of the ''neocortex.'' Brain Behav. Evol. 38:264–272.
Karten, H. J. and W. Hodos. 1967. *A stereotaxic atlas of the brain of the pigeon* (Columba livia). The Johns Hopkins Press, Baltimore.
Kemp, T. S. 1982. *Mammal-like reptiles and the origin of mammals*. Academic Press, New York.
Kennedy, M. C. and K. Rubinson. 1984. Development and structure of the lamprey optic tectum. *In* H. Vanegas (ed.), *Comparative neurology of the optic tectum,* pp. 1–13. Plenum Press, New York.
Kishida, R., R. C. Goris, H. Nishizawa, H. Koyama, T. Kadota, and F. Amemiya. 1987. Primary neurons of the lateral line nerves and their central projections in hagfishes. J. Comp. Neurol. 264: 303–310.
Larsell, O. 1967. *The comparative anatomy and histology of the cerebellum from myxinoids through birds*. The University of Minnesota Press, Minneapolis.
Leghissa, S. 1955. La struttura microscopica e la citoarchitettonica del tetto ottico dei pesci teleostei. Z. Anat. Entw. Gesh. 118: 427–463.
Maisey, J. G. 1996. *Discovering fossil fishes*. Henry Holt and Company, New York.
Manso, M. J. and R. Anadón. 1991. The optic tectum of the dogfish *Scyliorhinus canicula* L: A Golgi study. J. Comp. Neurol. 307: 335–349.
Marsh, O. C. 1874. Small size of the brain in tertiary mammals. Amer. J. Sci. 7:81–86.
Meek, J. and N. A. M. Schellart. 1978. A Golgi study of goldfish optic tectum. J. Comp. Neurol. 182:89–122.
Nieuwenhuys, R. 1977. The brain of the lamprey in a comparative perspective. Ann. N.Y. Acad. Sci's. 299:97–145.
Nieuwenhuys, R. 1998*a*. Comparative neuroanatomy: Place, principles and programme. *In* R. Nieuwenhuys, H. J. ten Donkelaar, and C. Nicholson (eds.), *The central nervous system of vertebrates,* Vol. 1, pp. 273–326. Springer-Verlag, Berlin.
Nieuwenhuys, R. 1998*b*. The coelacanth *Latimeria chalumnae*. *In* R. Nieuwenhuys, H. J. ten Donkelaar, and C. Nicholson (eds.), *The central nervous system of vertebrates,* Vol. 2, pp. 1007–1043. Springer-Verlag, Berlin.
Nieuwenhuys, R. 1998*c*. Lungfishes. *In* R. Nieuwenhuys, H.J. ten Donkelaar, and C. Nicholson (eds.), *The central nervous system of vertebrates,* Vol. 2, pp. 939–1006. Springer-Verlag, Berlin.
Nieuwenhuys, R., H. J. ten Donkelaar, and C. Nicholson. 1998. *The central nervous system of vertebrates,* 3 vols. Springer-Verlag, Berlin.
Nieuwenhuys, R. and C. Nicholson. 1998. Lampreys, Petromyzontoidea. *In* R. Nieuwenhuys, H. J. ten Donkelaar, and C. Nicholson (eds.), *The central nervous system of vertebrates,* Vol. 1, pp. 397–495. Springer-Verlag, Berlin.
Northcutt, R. G. 1977. Elasmobranch central nervous system organization and its possible evolutionary significance. Amer. Zool. 17:411–429.
Northcutt, R. G. 1979. Retinofugal pathways in fetal and adult spiny dogfish, *Squalus acanthias*. Brain Res. 162:219–230.
Northcutt, R. G. 1983. Evolution of the optic tectum in ray-finned fishes. *In* R. E. Davis and R. G. Northcutt (eds.), *Fish neurobiology,* Vol. 2, pp. 1–42. University of Michigan Press, Ann Arbor.
Northcutt, R. G. 1984. Evolution of the vertebrate central nervous system: Patterns and processes. Amer. Zool. 24:701–716.
Northcutt, R. G. 1985. Brain phylogeny. speculations on pattern and cause. *In* M. J. Cohen and F. Strumwasser (eds.), *Comparative neurobiology: Modes of communication in the nervous system,* pp. 351–378. Wiley, New York.
Northcutt, R. G. 1990. Ontogeny and phylogeny: A re-evaluation of conceptual relationships and some applications. Brain Behav. Evol. 36:116–140.
Northcutt, R. G. 1995. The forebrain of gnathostomes: In search of a morphotype. Brain Behav. Evol. 46:275–318.
Northcutt, R. G. 1997. Evolution of gnathostome lateral line ontogenies. Brain Behav. Evol. 50:25–37.
Northcutt, R. G. 2001. Changing views of brain evolution. Brain Res. Bull. 55:663–674.
Northcutt, R. G. and M. R. Braford, Jr. 1980. New observations on the organization and evolution of the telencephalon of actinopterygian fishes. *In* S. O. E. Ebbesson (ed.), *Comparative neurology of the telencephalon,* pp. 41–98. Plenum Press, New York.
Northcutt, R. G., K. C. Catania, and B. B. Criley. 1994. Development of lateral line organs in the axolotl. J. Comp. Neurol. 340: 480–514.
Northcutt, R. G. and J. H. Kaas. 1995. The emergence and evolution of mammalian neocortex. Trends Neurosci. 18:373–379.
Northcutt, R. G. and T. J. Neary. 1975. Observations on the optic tectum of the coelacanth, *Latimeria chalumnae*. Amer. Zool. 15: 806.
Olson, E. C. 1966. Community evolution and the origin of mammals. Ecology 47:291–302.
Paxinos, G. and C. Watson. 1986. *The rat brain in stereotaxic coordinates,* 2nd ed. Academic Press, Sydney.
Pepperberg, I. M. 2000. *The Alex studies*. Harvard University Press, Cambridge, Massachusetts.
Quiroga, J. C. 1978. The tectum opticum of *Pantodactylus schreiberii*, Wiegmann (Teiidae, Lacertilia, Reptilia). J. Hirnforsch. 19:109–131.
Ramón, P. 1896. El structura de encéfalo del cameléon. Rev. Trimest. Micrograf. 1:46–82.
Ramón, P. 1899. El lóbulo de los peces (teleosteos). Rev. Trimest. Micrograf. 4:87–107.
Ramón, P. 1922. El cerebro de los batracios. *In* Libro en honor de D.S. Ramón y Cajal, Tomo I, pp. 13–59, Madrid.
Repérant, J., D. Miceli, J. P. Rio, J. Peyrichoux, J. Pierre, and E. Kirpitchnikova. 1986. The anatomical organization of retinal projections in the shark *Scyliorhinus canicula* with special reference to the evolution of the selachian primary visual system. Brain Res. Rev. 11:227–248.
Romanes, G. J. 1883. *Animal intelligence*. Kegan, Paul, Trench, London.
Romer, A. S. 1966. *Vertebrate paleontology,* 3rd ed. University of Chicago Press, Chicago.
Ronan, M. and R. G. Northcutt. 1998. The central nervous system of hagfishes. *In* J. M. Jørgensen, J. P. Lomholt, R. E. Weber, and H. Malte (eds.), *The biology of hagfishes,* pp. 452–479. Chapman and Hall, London.
Roth, G., C. Naujoks-Manteuffel, and W. Grunwald. 1990. Cytoarchitecture of the tectum mesencephali in salamanders: A Golgi and HRP study. J. Comp. Neurol. 291:27–42.
Rowe, T. 1996. Coevolution of the mammalian middle ear and neocortex. Science 273:651–654.
Russell, D. A. 1972. Ostrich dinosaurs from the Late Cretaceous of Western Canada. Can. J. Earth Sci. 9:387–402.
Shand, J. 1997. Ontogenetic changes in retinal structure and visual

acuity: A comparative study of coral-reef teleosts with differing post-settlement lifestyles. Environ. Biol. Fishes. 49:307–322.
Shand, J., K. D. Doving, and S. P. Collin. 1999. Optics of the developing fish eye: Comparisons of Matthiessen's ratio and the focal length of the lens in the black bream *Acanthopagrus butcheri* (Sparidae, Teleostei). Vis. Res. 39:1071–1078.
Shu, D.-G., H.-L. Luo, S. Conway Morris, X.-L. Zhang, S. X. Hu, L. Chen, J. Han, M. Zhu, Y. Li, and L.-Z. Chen. 1999. Lower Cambrian vertebrates from south China. Nature 402:42–46.
Smeets, W. J. A. J. 1981. Retinofugal pathways in two chondrichthyans, the skark *Scyliorhinus canicula* and the ray *Raja clavata*. J. Comp. Neurol. 195:1–11.
Smeets, W. J. A. J. 1998. Cartilaginous fishes. *In* R. Nieuwenhuys, H. J. ten Donkelaar, and C. Nicholson (eds.), *The central nervous system of vertebrates,* Vol. 1, pp. 551–654. Springer-Verlag, Berlin.
Snell, O. 1892. Die Abhängigkeit des Hirngewichtes von dem Körpergewicht und den geistigen Fähigkeiten. Arch. Psychiat. Nervenkrankh 23:436–446.
Stearns, S. C. 1992. *The evolution of life histories*. Oxford University Press, Oxford.
Striedter, G. F. 1991. Auditory, electrosensory and mechanosensory lateral line pathways through the forebrain in channel catfishes. J. Comp. Neurol. 312:311–331.
Striedter, G. F. 1992. Phylogenetic changes in the connections of the lateral preglomerular nucleus in ostariophysan teleosts: A pluralistic view of brain evolution. Brain Behav. Evol. 39:329–357.
Striedter, G. F. 1997. The telencephalon of tetrapods in evolution. Brain Behav. Evol. 49:179–213.
Székely, G. and G. Lázár. 1976. Cellular and synaptic architecture of the optic tectum. *In* R. Llinás and W. Precht (eds.), *Frog neurobiology,* pp. 407–434. Springer-Verlag, Berlin.
ten Donkelaar, H. J. 1998*a*. Urodeles. *In* R. Nieuwenhuys, H. J. ten Donkelaar, and C. Nicholson (eds.), *The central nervous system of vertebrates,* Vol. 2, pp. 1045–1150. Springer-Verlag, Berlin.
ten Donkelaar, H. J. 1998*b*. Anurans. *In* R. Nieuwenhuys, H. J. ten Donkelaar, and C. Nicholson (eds.), *The central nervous system of vertebrates,* Vol. 2, pp. 1151–1314. Springer-Verlag, Berlin.
ten Donkelaar, H. J. 1998*c*. Reptiles. *In* R. Nieuwenhuys, H. J. ten Donkelaar, and C. Nicholson (eds.), *The central nervous system of vertebrates,* Vol. 2, pp. 1315–1524. Springer-Verlag, Berlin.
van Dongen, P. A. M. 1998. Brain size in vertebrates. *In* R. Nieuwenhuys, H. J. ten Donkelaar, and C. Nicholson (eds.), *The central nervous system of vertebrates,* Vol. 3, pp. 2100–2134. Springer-Verlag, Berlin.
Weigle, C. and R. G. Northcutt. 1998. On the phylogenetic origin of the cerebellum: Tracing studies in the silver lamprey *Ichthyomyzon unicuspis*. Eur. J. Neurosci. 10, Abstract 68.01.
Wicht, H. and R. G. Northcutt. 1992. The forebrain of the Pacific hagfish: A cladistic reconstruction of the ancestral craniate forebrain. Brain Behav. Evol. 40:25–64.
Wullimann, M. F. and R. G. Northcutt. 1990. Visual and electrosensory circuits of the diencephalon in mormyrids: An evolutionary perspective. J. Comp. Neurol. 297:537–552.