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Paedomorphosis and Simplification in the Nervous System of Salamanders

Abstract

Comparative neuroanatomists since Herrick [1914] have been aware of the paradox that the brain of amphibians, especially salamanders, is less complex than one would expect based on their phylogenetic position among the Tetrapoda. Many features of the brain are less differentiated in salamanders than in tetrapod outgroups, including chondrichthyans and bony fishes, and for some brain characters, the salamander brain is even more simple than that of the agnathans. Here, we perform a cladistic analysis on 23 characters of four sensory systems (visual, auditory, lateral line and olfactory) and the brain. Our taxa include myxinooids, lampreys, chondrichthyans, actinopterygians, *Latimeria*, *Neoceratodus* and the lepidosirenid lungfishes, amniotes, frogs, caecilians, salamanders and bolitoglossine salamanders. Of the 23 characters we examined, 19 are most parsimoniously interpreted as secondarily simplified in salamanders from a more complex ancestral state, two characters are equally parsimonious under both hypotheses, one character (well developed ipsilateral retinotectal projections) is more complex in bolitoglossine salamanders than in vertebrates generally, and only one character (migration of neurons in the medial pallium) is most parsimoniously interpreted as retention of the plesiomorphically simple condition. Secondary simplification of the salamander brain appears to result from paedomorphosis, or retention of juvenile or embryonic morphology into adulthood. Paedomorphosis is correlated with an increase in genome size, which in turn is positively correlated with cell size, but negatively correlated with cell proliferation and differentiation rates. Available data suggest that, although increasing genome size and paedomorphosis tend to compromise the function of the salamander brain, compensating mechanisms have evolved that may restore or even enhance brain function.

Key Words

Brain
Evolution
Development
Paedomorphosis
Amphibians

Introduction

The brain is often viewed as having increased in functional and morphological complexity during the phylogenesis of vertebrates. This 'orthogenetic' view of brain evolution is exemplified by the following evolutionary trends,

which have emerged from a variety of comparative studies: (1) an increase in relative brain size; (2) an increase in the relative size of certain parts of the brain, such as the fore-brain or the cortex; (3) an increase in the number of nerve cells and the number of different cell types; (4) an increase in morphological differentiation of nerve cells; (5) an

increase in the number of anatomically distinct groups of nerve cells, such as nuclei, laminae or columns; and (6) an increase in the number and/or selectivity of pathways [Romer, 1970; Jerison, 1973; Sarnat and Netsky, 1974; Kuhlenbeck, 1977; Bauchot, 1978; Northcutt, 1978a, 1981; Ebbesson, 1980, 1984; Hofman, 1982; Starck, 1982; Bullock, 1984; Deacon, 1988; Hodos, 1988].

Such trends encourage the idea that 'encephalization' has increased during vertebrate phylogeny. This idea fits nicely into the unrealistic, but traditional, view of evolution as a linear sequence of changes in form and function from the most 'primitive' vertebrates (e.g., agnathans and cartilaginous fishes) to mammals, with humans as the ultimate achievement (a modernized version of the ancient 'scala naturae').

The idea of unidirectional evolutionary progress has been replaced by the view that the vertebrate classes have evolved independently, in a radiative, divergent pattern, with only one of many pathways leading to hominids [Northcutt, 1984a]. It is no longer appropriate to speak of 'primitive' and 'advanced' organisms, arranged along a ladder of increasing complexity. One refers instead to primitive ('plesiomorphic') and derived ('apomorphic') *traits* of a taxon. Organisms are mosaics of both primitive and derived characteristics.

Nevertheless, it is still widely accepted that, within vertebrate clades, taxa which diverged later (teleosts versus chondrosteans; birds versus amphibians) possess relatively more complex brains than taxa which are more basal. Increases in relative brain size and in forebrain complexity are now believed to have occurred independently within each class of vertebrates, most prominently in chondrichthyans, actinopterygians, birds and mammals [Northcutt, 1984a]. The idea that the complexity of the brain increases during phylogenesis within these independent lineages has been retained.

Recent neurobiological studies from our own and other laboratories [Northcutt, 1987] suggest that a broader view of brain evolution is necessary: some vertebrate brains, most prominently those of amphibians, have decreased in anatomical complexity during their evolution. Here, we present evidence that the evolution of the salamander nervous system is characterized by secondary simplification, which gives the impression that the brains of salamanders are more primitive than the phylogenetic position of salamanders, as tetrapods, implies.

The evolutionary status of amphibian brains has always created difficulties. The brains of frogs, and especially of caecilians [Kuhlenbeck, 1922] and salamanders [Herrick, 1948; Leghissa, 1962], appear to be simpler than those of

chondrichthyans and actinopterygians, and even of lampreys in some respects. Despite an awareness that salamanders are not phylogenetically basal among vertebrates, their brains were viewed by leading comparative neuroanatomists as exemplifying the ancestral state of the vertebrate brain [Herrick, 1948, pp. 13–14; Leghissa, 1962].

We will argue that secondary simplification in amphibians arises from paedomorphosis, a form of heterochronic evolution in which traits that characterize juveniles of ancestral taxa appear in the adult stage of descendant taxa. Paedomorphosis commonly involves different degrees of retardation, reduction or absence of traits in otherwise fully developed organisms, as compared with phylogenetic outgroups. Thus, a mosaic of fully adult traits, weakly expressed traits, and missing traits appears in terminal ontogenetic stages [Gould, 1977; Alberch et al., 1979].

Paedomorphosis has been important in the evolution of all three living orders of amphibians, in the ancestry of the Lissamphibia [Bolt, 1977, 1979; Milner, 1988], and in the evolution of early small tetrapods in general [Carroll, 1986]. Only recently has the concept of paedomorphosis received attention in comparative neurobiology [Northcutt, 1987].

We will argue that paedomorphosis results from increased genome size in the salamander lineage. Our hypothesis of paedomorphic simplification solves the old dilemma of the 'primitive' salamander brain, but creates a new dilemma. How has the functional integrity of the salamander brain been maintained during evolution in the face of simplification? We will suggest that ontogenetic repatterning provides an escape from developmental constraints and permits the evolution of compensatory mechanisms that maintain or may even improve brain function, as exemplified by the depth perception mechanisms of bolitoglossine salamanders.

Our study proceeds within the following phylogenetic framework (fig. 1). Recent morphological [de Queiroz and Cannatella, 1987; Trueb and Cloutier, 1987; Milner, 1988] and biochemical [Larson and Wilson, 1989; Larson, 1991] studies support the hypothesis that the Lissamphibia (present-day amphibians: orders Anura [frogs], Caudata [salamanders], and Gymnophiona [caecilians]) constitute a monophyletic taxon, which is the living sister taxon of the Amniota. The closest non-tetrapod relative of this group among living fishes is the Dipnoi [Meyer and Wilson, 1990]. *Latimeria* and the Dipnoi both serve as living outgroups for the Tetrapoda, but we follow Holmes [1985], Schultze [1987], and Edwards [1989] in considering some extinct osteolepid rhipidistians, rather than the Dipnoi [Rosen et al., 1981], to be the sister group of tetrapods.

Fig. 1. A cladogram of the vertebrate taxa included in this study. We follow Meyer and Wilson [1990] in considering the Dipnoi to be the sister group of the Amniota. ¹The sister group of bolitoglossine salamanders varies among the characters. For some characters, families of salamanders other than the Plethodontidae were used. For other characters, tribes of the Plethodontidae other than Bolitoglossini were used. For each character, the outgroup taxon is given in the text.

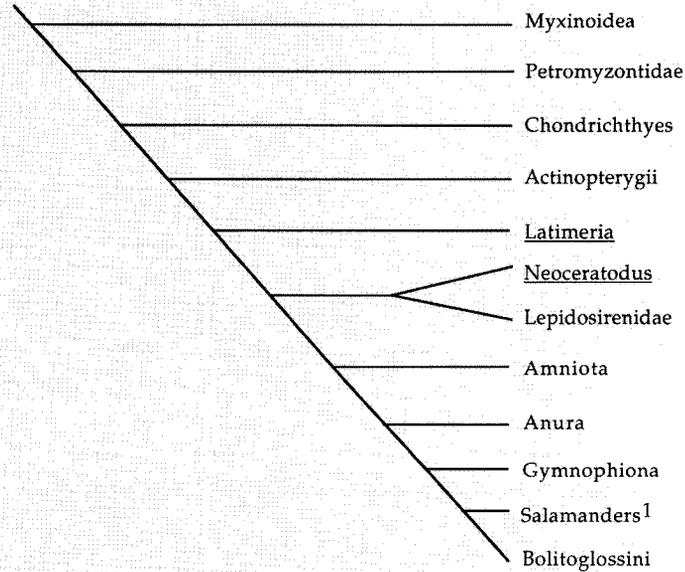
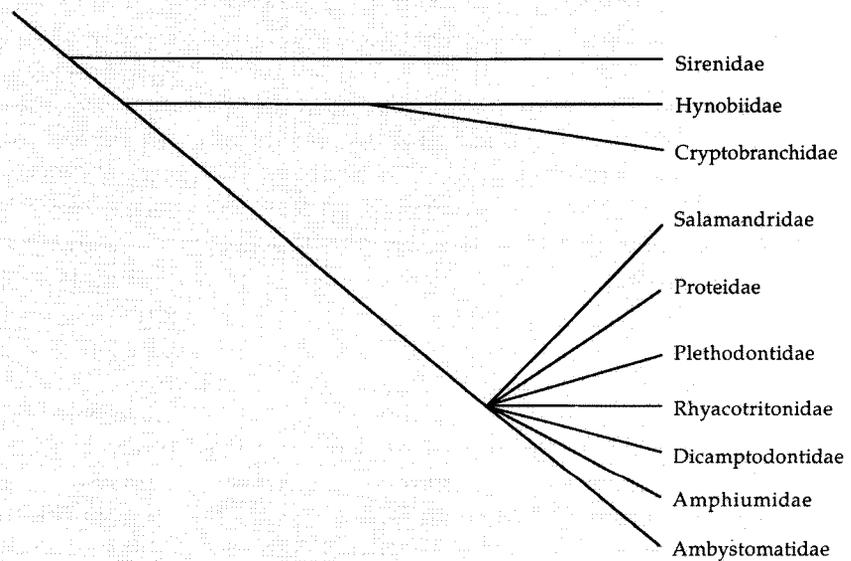


Fig. 2. Consensus tree of the salamander families from Sever [1991]. Note that the sister group of the family Plethodontidae is unresolved.



We consider the order Caudata to be a monophyletic taxon. There is no generally accepted cladistic hypothesis for the living salamander families [Hecht and Edwards, 1977; Duellman and Trueb, 1986; Larson and Wilson, 1989; Larson, 1991]. A consensus tree based on morphological characteristics [Sever, 1991] is shown in figure 2. The family Plethodontidae possesses a number of derived morphological characteristics, but its sister group is unre-

solved. Recent molecular evidence suggests that the Plethodontidae may be a relatively basal group, in a cladistic sense, within the order Caudata [Larson, 1991 in contrast to Hecht and Edwards, 1977; Duellman and Trueb, 1986]. Within the family Plethodontidae (fig.3), the tribe Bolitoglossini possesses the largest number of derived morphological traits [Wake, 1966; Hecht and Edwards, 1977; Duellman and Trueb, 1986; Lombard and Wake, 1986].

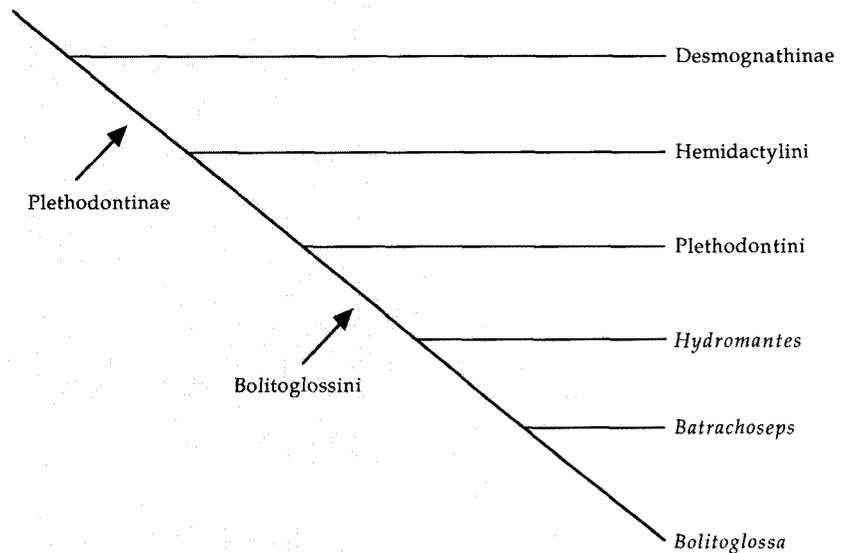


Fig. 3. A cladogram showing the relationships among the subfamilies and tribes of plethodontid salamanders [Lombard and Wake, 1986].

However, many of the derived traits may be autapomorphies (i.e., uniquely derived characteristics not shared with other taxa).

We review available data on the morphology and development of the sense organs and the central nervous system of salamanders and compare their degree of differentiation to that of outgroups. We concentrate on traits that previously have been cited as evidence for the primitiveness of the salamander brain.

Visual System

The salamander retina has been described as poorly developed [Leghissa, 1962]. Nevertheless, it has the same layered structure and the same cellular elements found in most other gnathostome vertebrates. There are three types of photoreceptors (rods, cones and double cones) and four types of interneurons (horizontal, bipolar, amacrine and interplexiform cells) [Dowling, 1987].

Morphological Types of Retinal Ganglion Cells

Salamanders have four types of retinal ganglion cells (RGCs), which differ in the size and shape of the soma and dendritic arbor, and in the pattern of dendritic arborization within the inner plexiform layer [Linke and Roth, 1989]. Despite some arbitrariness in the morphological classification of vertebrate RGCs, salamander RGCs are morphologically less complex than those of other vertebrate

groups. A striking difference between the salamander retina and all other vertebrate retinas is the absence of 'giant' cells (i.e., RGCs that are much larger than the others) [Linke and Roth, 1989]. These 'giant' cells, when present, are the last to form during retinal development [Rapaport and Stone, 1983], which suggests that their absence in salamanders may be pedomorphic.

The number of types of retinal ganglion cells is unknown in caecilians. Using the same criteria as applied to salamanders, the number of RGC types is greater in anurans than in salamanders. The number of types reported varies: 7 in *Rana pipiens* [Frank and Hollyfield, 1987], 5 in *Rana ridibunda* [Kalinina, 1976], and 3 (with 12 subtypes based on dendritic arborization) in *Xenopus laevis* [Straznický and Straznický, 1988].

Among amniotes, the number of RGC types may be as high as 21 in turtles [Woodbury and Ulinski, 1986; Kolb et al., 1988]. Nothing is known about the morphology of RGCs in dipnoans or *Latimeria*. In the teleost *Ictalurus*, there are 11 types of RGCs [Dunn-Meynell and Sharma, 1986], in the goldfish *Carassius auratus* there are 4, with 15 subtypes [Hitchcock and Easter, 1986], and in the percormorph teleosts *Navodon* and *Sebastiscus* there are 6 types of RGCs [Ito and Murakami, 1984]. The shovel-nosed ray possesses 3–4 types of retinal ganglion cells [Collin, 1988], and the lamprey *Ichthyomyzon unicuspis* possesses 4 types [Fritsch and Collin, 1990]. Nothing is known about the morphology of RGCs in hagfishes.

In summary, all vertebrates that have been studied, except lampreys and chondrichthyans, have a greater number of morphological types of RGCs than salamanders (fig. 4). The small number of types of RGCs in salamanders may represent retention of the primitive condition, or may represent secondary simplification through a paedomorphic reduction of anatomical differentiation.

Number of Optic Nerve Fibers

Salamanders have very few optic nerve fibers, ranging among bolitoglossines from 25,000 in *Batrachoseps attenuatus* to 33,500 in *Hydromantes italicus* [Linke and Roth, 1990], with 75,000 in the salamandrid *Notophthalmus viridescens* [Ball and Dickson, 1983].

The reduced eye of the caecilian *Ichthyophis kohtaoensis* has about 4,000 optic nerve fibers [Fritzsche et al., 1985a]. In anurans, the number of optic nerve fibers ranges from 68–80,000 in *Xenopus laevis* [Dunlop and Beazley, 1984] to 470,000 in *Rana pipiens* [Maturana, 1959].

Turtles possess from 213,000 optic nerve fibers in *Testudo* to 483,000 in *Emys* [Peterson and Ulinski, 1979; Davydova et al., 1982; Geri et al., 1982]. The snake *Vipera aspis* has 65,000 fibers [Ward et al., 1987]. Birds possess from 1,500,000 RGCs in *Anas platyrhynchos* [O’Flaherty, 1971] to 2,380,000 in the pigeon *Columba livia* [Binggeli and Paule, 1969]. In mammals, marsupials possess from 74,000 in *Didelphis* [Hokoc and Oswaldo-Cruz, 1978] to 230,000 in *Trichosaurus* [Freeman and Watson, 1978] and placental mammals range from 106,200 in the golden hamster [Rhoades et al., 1979] to 1,410,000 RGCs in the macaque *Macaca mulatta* [Ogden and Miller, 1966], with rats [Hughes, 1977], rabbits [Vaney and Hughes, 1976] and cats [Hughes and Wässle, 1976] in between.

Lepidosirenid lungfishes (*Protopterus* and *Lepidosiren*) possess about 1,500 RGCs [Northcutt, 1977]. The number of optic nerve fibers is unknown in *Neoceratodus* and *Latimeria*. Among actinopterygians, goldfish have 120,000–200,000 fibers [Meek, 1983] and the percomorphs *Eugerres* [Tapp, 1974], *Sebastiscus* and *Navodon* [Ito and Murakami, 1984] possess 200,000–700,000 optic nerve fibers. There are 210,500 optic nerve fibers in the chondrichthyan *Rhinobatos battilium* [Collin, 1988]. The lamprey *Lampetra fluviatilis* possesses 35,000 optic nerve fibers [Öhman, 1977] and the hagfish *Eptatretus stouti* possesses 100–1,500 [Wicht, pers. comm.].

One might expect a positive correlation between eye or retina size and the number of optic nerve fibers present both within and among taxa. However, this correlation exists only among taxa in which the size of RGCs and the diameter and degree of myelination of RGC axons remains

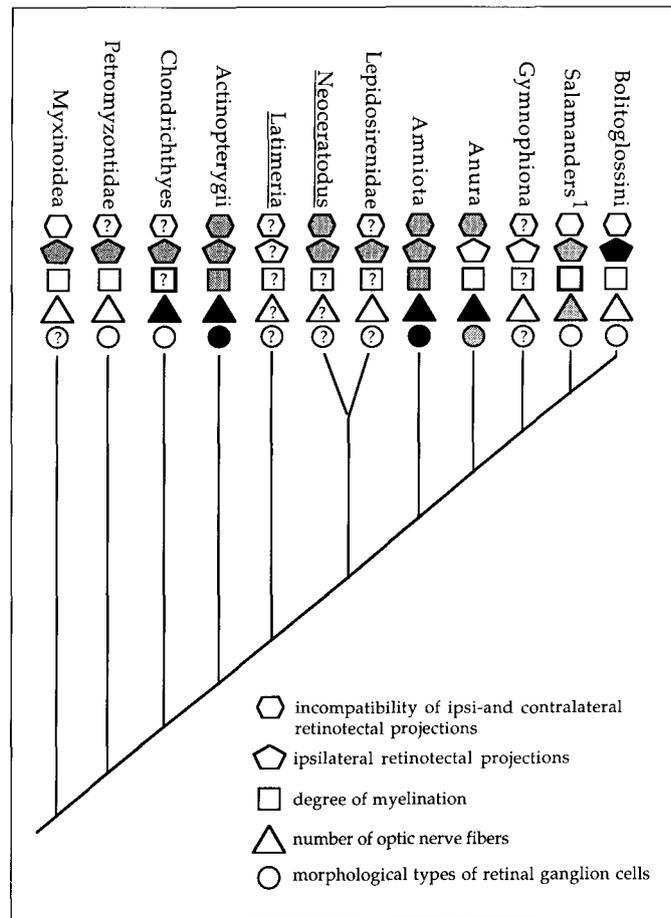


Fig. 4. A cladogram showing the states of each taxon for five characters of the visual system. Open symbols represent the simplest character state, hatched symbols are intermediate in complexity, and black symbols represent the most complex character state. Bolitoglossine salamanders exhibit the simplest morphology for all characters, except ipsilateral retinotectal projections, which are more extensive in bolitoglossines than in most other vertebrates. Character coding and polarity are given in table 1. Footnote is the same as in figure 1.

relatively constant. The size of RGCs varies widely among vertebrates, as a function of genome size (see Discussion). Thus, species with identical eye/retina sizes may have very different numbers of optic nerve fibers. This is clearly demonstrated by plethodontid salamanders, in which *Desmognathus ochrophaeus* (with small genome size and small RGCs) has more optic nerve fibers than *Bolitoglossa subpalmata* (with large genome size and small RGCs), although *D. ochrophaeus* has much smaller eyes and retinas [Linke and Roth, 1990; Roth et al., 1990a].

In summary, salamanders have fewer optic nerves than any other vertebrates that depend heavily on vision for survival. All vertebrates except for hagfishes, lampreys, lepi-

dosirenid lungfishes and caecilians have more optic nerve fibers than salamanders (fig.4). The hypothesis that the number of optic nerve fibers has been secondarily reduced in salamanders is more parsimonious than the hypothesis that salamanders have retained the plesiomorphic condition. Reduced numbers of optic nerve fibers in salamanders may result from reduced rates of cell division. While differences in body size within and among taxa make it difficult to estimate the exact number of optic nerve fibers that represents the primitive condition for vertebrates, we believe that the evidence supports the hypothesis that the number of optic nerve fibers has been reduced in salamanders.

Myelination of the Optic Nerve

The degree of myelination of the optic nerve ranges from 0–7% in salamanders [Roth, 1987; Linke and Roth, 1990], with plethodontids generally having less myelination (*Desmognathus ochrophaeus* and *Bolitoglossa subpalmata*, about 4%; *Hydromantes italicus*, about 2%; *Batrachoseps attenuatus*, 0–0.24%) [Linke and Roth, 1989, 1990]. The degree of myelination is unknown in caecilians. Among anurans, *Xenopus laevis* has 12–14% myelination of the optic nerve, and *Rana pipiens* has 7% myelination [Maturation, 1959; Wilson, 1971; Dunlop and Beazley, 1984].

In turtles, the degree of myelination of optic nerve fibers ranges from 10% in *Agrionemys* to 80% in *Pseudemys* [Geri et al., 1982]. In the snake *Vipera aspis*, 83% of the fibers are myelinated [Ward et al., 1987]. In birds [Binggeli and Paule, 1969] and mammals [Ogden and Miller, 1966; Forrester and Peters, 1967], almost all of the optic fibers possess a myelin sheath.

In teleost fishes, 74–97.5% of optic nerve fibers are myelinated [Tapp, 1973, 1974; Easter et al., 1981; Collin and Collin, 1988]. The degree of myelination is unknown in dipnoans, *Latimeria* and chondrichthyans [Collin, pers. comm.]. Among vertebrates other than bolitoglossine salamanders, only the lamprey *Lampetra fluviatilis* [Öhman, 1977] and the hagfish *Eptatretus stouti* [Wicht and Northcutt, 1990] have unmyelinated optic nerves.

In summary, salamanders have fewer myelinated optic nerve fibers than all other vertebrates except hagfishes and lampreys (fig.4). Myelination is a late ontogenetic event and depends on the differentiation of embryonic glial cells into astrocytes and oligodendrocytes (which form myelin sheaths in the central nervous system) within the optic nerve. Astrocytes and oligodendrocytes are found in the optic nerves of all salamanders investigated, although often in an undifferentiated form [Linke and Roth, 1990]. In the bolitoglossine salamander *Batrachoseps*, the glial cells of

the optic nerve show features of both astrocytes and oligodendrocytes [Linke and Roth, 1990], as do the common progenitor cells of type-II astrocytes and oligodendrocytes of mammalian optic nerves in tissue culture [Raff et al., 1983].

Ipsilateral Retinotectal Projections

Salamanders exhibit a well developed system of retinofugal projections. There are three thalamic (geniculate thalamic neuropil, neuropil Bellonci pars lateralis and pars medialis) and two pretectal projections (posterior thalamic neuropil and area uncinata), as well as a projection to the mesencephalic tectum and tegmentum (basal optic neuropil) [Fritsch, 1980; Rettig and Roth, 1982, 1986; Compoint and Clairambault, 1986]. Most of the projections, including those to the lateral optic tectum, are supplied by the marginal optic tract, whereas the neuropil Bellonci pars medialis, the area uncinata and the medial portion of the optic tectum are supplied by the medial optic tract.

In salamanders, projections to the optic tectum are generally bilateral. The ipsilateral projections are usually much weaker than the contralateral ones. Among plethodontids, ipsilateral projections to the tectum are most extensive in the bolitoglossines [Rettig and Roth, 1986], in which a deep layer of ipsilateral retinofugal fibers extends throughout the tectal hemispheres and a superficial layer covers the rostral third of the tectum. In *Ambystoma mexicanum* [Stirling and Brändle, 1982] and *Triturus alpestris* [Rettig et al., 1981], the earliest ipsilateral retinotectal projections are found in embryos. During metamorphosis, the number of ipsilateral fibers increases. All ipsilateral projection fields found in adults are present three months after metamorphosis. In contrast, ipsilateral projections develop very early in bolitoglossines, and by late embryonic stages are more pronounced than those found in adults of other salamander groups [Rettig, Roth and Wake, unpubl. obs.; Roth, 1987].

In the caecilians *Typhlonectes* and *Ichthyophis*, ipsilateral projections to the optic tectum are restricted to the medial optic tract, which is related to phototaxis [Himstedt and Manteuffel, 1985]. The lateral optic tract is absent [Clairambault et al., 1980; Fritsch et al., 1985a; Himstedt and Manteuffel, 1985].

The pattern of termination of retinofugal projections in anurans is generally similar to that of salamanders [Lázár and Székely, 1969; Fite and Scalia, 1976; Levine, 1980], with the exception of the neuropil Bellonci pars medialis, which appears to be absent in anurans [Fritsch, 1980]. While ipsilateral projections to thalamic and pretectal sites are comparable to those of salamanders, ipsilateral projec-

tions to the optic tectum are sparse in *Rana pipiens* [Singman and Scalia, 1990] and in *Xenopus laevis* [Degen, pers. comm.]. Earlier reports of extensive ipsilateral retinotectal fibers in *Xenopus* [Levine, 1980; Tóth et al., 1980] are apparently an artifact of transsynaptic transport.

Ipsilateral fibers to the tectum are found in the night lizard *Xantusia* [Butler, 1974] and in geckos [Northcutt and Butler, 1974a]. In snakes [Northcutt and Butler, 1974b] and adult birds [O'Leary et al., 1983; Takasugi et al., 1983; Weidner et al., 1985], no ipsilateral retinotectal fibers are present. Ipsilateral retinotectal projections vary in size among mammals, being sparse in rodents and microchiropterans, but extensive in primates and flying foxes [Pettigrew, 1986]. Most ipsilateral fibers are restricted to the rostral part of the optic tectum.

Lepidosirenid lungfishes also possess ipsilateral retinotectal projections [Northcutt, pers. comm.]. The Australian lungfish *Neoceratodus* possesses substantial ipsilateral projections to the optic tectum [Northcutt, 1980]. These projections do not form a dense continuous sheet, as in salamanders. Instead, they form distinct puffs similar to those of mammals. However, unlike those of mammals, the retinotectal projections extend throughout the entire tectum [Northcutt, 1980]. It is unknown whether *Latimeria* possesses ipsilateral retinotectal projections.

The holostean fish *Lepisosteus osseus* possesses ipsilateral retinotectal projections [Northcutt and Butler, 1976]. For teleosts, the presence of some ipsilateral fibers is plesiomorphic, and the presence of few or no ipsilateral retinotectal fibers represents the derived condition [von Bartheld and Meyer, 1987]. Bazer and Ebbesson [1987] report 'extremely rare fibers' in the ipsilateral optic tectum of *Esox*. The piranha, *Serrasalmus niger*, has more ipsilateral projections to most visual centers, including the optic tectum, and these projections are restricted to a narrow band within the deep white matter [Ebbesson and Ito, 1980]. Ipsilateral retinotectal fibers also are reported in the catfish *Ictalurus* [Dunn-Meynell et al., 1983] and the goldfish *Carassius auratus* [Springer and Gaffney, 1981].

Like teleosts, sharks generally have relatively few ipsilateral fibers to the optic tectum [Northcutt, 1979, 1990; Repérant et al., 1986], with the exceptions of *Hemiscyllium plagiosum* and *Platyrrhinoides triseriata*, in which ipsilateral projections to the rostral optic tectum are found [Northcutt and Wathey, 1980; Jen et al., 1983]. The hagfish *Eptatretus stouti* [Wicht and Northcutt, 1990] and the lamprey *Lamprolaima fluviatilis* [Vesselkin et al., 1980] have substantial ipsilateral retinotectal projections.

In summary, ipsilateral retinofugal projections to the optic tectum are widespread among vertebrates, occurring

in some members of all classes (fig. 4). Retention of some ipsilateral projections in salamanders (except bolitoglossines) appears to be plesiomorphic. Loss or reduction of these projections has occurred independently in some sharks, some teleosts, birds, mammals, anurans, and caecilians, while primates, flying foxes and bolitoglossine salamanders have increased the size of this projection independently.

Incompatibility of Ipsilateral and Contralateral Retinotectal Fibers

Two patterns of retinotectal topology are common among vertebrates. In frogs [Constantine-Paton, 1988], birds [O'Leary et al., 1983] and bony fishes [Collin, pers. comm.], ipsilateral fibers occur early in ontogeny, but are eliminated progressively through competition with contralateral fibers. In mammals [Huerta and Harting, 1984] and *Neoceratodus* [Northcutt, 1980], ipsilateral fibers are retained, but the terminals from the two eyes segregate into puffs or columns, and do not intermingle within the tectal hemispheres. Both elimination of ipsilateral projections and segregation of terminals within the tectum suggest that there is an incompatibility between ipsilateral and contralateral fibers in the tectum. Nothing is known about tectal incompatibility in caecilians, lepidosirenid lungfishes, *Latimeria*, sharks or lampreys. In hagfishes [Wicht, pers. comm.] and salamanders [Rettig and Roth, 1986], ipsi- and contralateral retinotectal fibers intermingle in the tectum. Thus, it appears that incompatibility fails to develop in salamanders. Evidence for this conclusion comes from a variety of experiments and observations which we briefly review.

In anurans, projections from a transplanted supernumerary eye to one tectal hemisphere lead to the formation of stripes or patches. These consist of terminals of alternating groups of afferent fibers from the normal contralateral and the supernumerary eye [Constantine-Paton, 1981; Reh and Constantine-Paton, 1985]. The hypothesized mechanism underlying the formation of these stripes is that activity-dependent competition leads to the segregation of terminals from the two eyes. Terminals from neighboring retinal ganglion cells within one retina that show synchronized activity tend to cluster, and to separate from fibers of the other retina that have different patterns of activity [Constantine-Paton, 1988].

In the chicken, numerous ipsilateral projections appear transiently during development [O'Leary et al., 1983]. Only a small number of ipsilateral fibers survive to adulthood. However, a substantial number of ipsilateral fibers survive if one eye is removed during the first few days of

incubation, which suggests that an incompatibility between ipsilateral and contralateral fibers develops during ontogeny.

Segregation of terminals from the two eyes also arises during the normal development of the mammalian optic tectum and visual cortex, and leads to the appearance of alternating puffs or stripes of fibers from the two eyes [Huerta and Harting, 1984]. Early in development, the ipsi- and contralateral fiber systems are intermingled, and they segregate later in ontogeny in both anurans [Constantine-Paton and Reh, 1988] and mammals [Hubel et al., 1977]. The presence of alternating puffs of ipsi- and contralateral fibers in the tectum of *Neoceratodus* suggests incompatibility of these fibers as well [Northcutt, 1980].

Experiments on teleosts suggest that the incompatibility of ipsi- and contralateral fibers in anurans and mammals may be plesiomorphic for osteichthyans plus tetrapods. When one optic nerve of cichlid teleosts is crushed, ipsilateral fibers grow into the denervated optic tectum from the intact optic nerve [Wilm and Fritsch, 1989, 1990]. These fibers are eliminated when contralateral fibers from the regenerating optic nerve enter the tectal hemisphere, but survive if regeneration of the contralateral optic nerve is prevented. An increase in number of ipsilateral retinotectal fibers also has been reported for mammals as a consequence of enucleation [Fawcett et al., 1984]. These results indicate that in teleosts, anurans and mammals, and probably in *Neoceratodus* and birds as well, an incompatibility exists between contralateral and ipsilateral fibers in the tectum.

In contrast to experimental results in frogs, birds, mammals and teleosts, transplantation of a supernumerary eye in salamanders results in an intermingling of the two fiber tracts [Harris, 1980], indicating that there is no incompatibility between retinotectal fibers from different eyes in the tectum of salamanders (fig. 4). The absence of incompatibility between ipsilateral and contralateral retinotectal projections is most parsimoniously interpreted as a derived characteristic of salamanders.

Segregation of fibers in frogs (and in goldfish as well) is believed to be dependent on the activity of N-methyl-D-aspartate (NMDA) glutamate receptors, because blocking these receptors results in complete, reversible desegregation of tectal stripes in frogs [Cline and Constantine-Paton, 1987; Constantine-Paton, 1988]. The lack of incompatibility in salamanders could result from the failure of specific receptors, or classes of receptors, to mature, and thus it, too, may be a paedomorphic trait.

Auditory System

Salamanders long were considered to be nearly or completely deaf, and accordingly their auditory system was believed to be very simple [Herrick, 1948]. They were supposed to lack a primary auditory nucleus within the brainstem, a superior olive and a torus semicircularis involved in processing auditory signals [Herrick, 1948; Fritsch, 1988a]. However, a functional auditory system must be present in salamanders, because they can detect both substrate vibration and airborne sounds [Hetherington, 1988; Manteuffel and Naujoks-Manteuffel, 1990].

The peripheral auditory system of salamanders is highly reduced compared to that of most other tetrapods. Salamanders lack an external ear, a tympanum, a middle ear cavity and Eustachian tubes. One or two small middle ear bones (operculum, columella/stapes) are fused to each other or to the otic capsule, or are lost [Hetherington, 1988; Jaslow et al., 1988]. Loss of the columellar rod within the family Plethodontidae has been interpreted as paedomorphic [Wake, 1966]. A trend toward reduction of the periotic canal has been identified in plethodontids, with the extreme of reduction occurring in the bolitoglossines. This reductionary trend and other features of the inner ear of plethodontids (particularly bolitoglossines) have been identified by Lombard [1977] as paedomorphic.

A relatively simple auditory periphery is also found in caecilians which, like salamanders, lack a tympanum and a middle ear cavity. Most caecilians have a single middle ear bone, the stapes, but in the Scolecomorphidae even the stapes is absent [de Villiers, 1938; Taylor, 1969].

Most frogs have a well-developed auditory periphery with a tympanum and two middle ear bones (operculum and columella). The tympanum is absent in some species of several families, and some species (e.g., *Bombina*) exhibit a reduction of the middle ear [Stadtmüller, 1931; Smirnov, 1989] or lack it entirely [Duellman and Trueb, 1986; Jaslow et al., 1988].

Amniotes have a well-developed auditory periphery, with one (primitively) to three (in mammals) middle ear bones. Dipnoans, *Latimeria*, actinopterygians, chondrichthyans and lampreys lack external and middle ears, and middle ear bones [Lewis et al., 1985].

In summary, the presence of a columella is the plesiomorphic condition for the Lissamphibia. The reduced nature of the peripheral auditory system of salamanders in general, and of bolitoglossine plethodontids in particular, can be attributed to paedomorphosis. The ear of caecilians probably has been reduced independently [Lombard and Bolt, 1979, 1988]. It is likely that salamanders evolved from

an ancestral stock that had an ear more similar to that of modern frogs than to that of modern salamanders [Bolt and Lombard, 1985; Lombard and Bolt, 1988].

Papilla basilaris

The inner ear of amphibians follows the general tetrapod plan in possessing three semicircular canals, a sacculus, utriculus, lagena, and papilla basilaris. In addition, amphibians have a papilla amphibiorum, a structure unique to the inner ear of amphibians. The papilla amphibiorum is considered to be a specialized derivative of the papilla neglecta, which is widespread in vertebrates [Fritsch and Wake, 1988]. In frogs, acoustic sensitivity has been demonstrated for sensory epithelia located in the sacculus, the lagena, the papilla basilaris (sensitive to sound frequencies between 1000 and 5000 Hz) and the papilla amphibiorum (sensitive to sound frequencies below 1000 Hz) [Lewis and Lombard, 1988].

The papilla basilaris is reduced in a number of salamander genera, and is completely absent in some salamandrids and all members of the families Plethodontidae, Sirenidae and Proteidae [Lombard, 1977; Lewis and Lombard, 1988]. The papilla amphibiorum is also reduced in plethodontids [Lombard, 1977].

All caecilians have a papilla amphibiorum and papilla neglecta, but some lack a papilla basilaris and a lagena [Fritsch and Wake, 1988]. The papilla amphibiorum of caecilians arises from a part of the papilla neglecta which moves into the sacculus [Fritsch and Wake, 1988]. A well-developed inner ear with a papilla basilaris and a papilla amphibiorum is present in most frogs [Lewis and Lombard, 1988].

Amniotes possess a papilla basilaris, which is usually highly elaborated [Lewis et al., 1985]. However, Lewis and Lombard [1988] have suggested that the papilla basilaris of amniotes is not homologous to the papilla basilaris of amphibians. The inner ear of *Latimeria*, dipnoans, actinopterygians and chondrichthyans is well developed and consists of otolith-bearing sacculus, lagena and utriculus. The lamprey *Petromyzon* possesses two canals, but only one end organ [Popper and Hoxter, 1987]. *Latimeria* is the only nontetrapod that has a papilla basilaris in the same relative position as amphibians and a comparable pattern of innervation [Fritsch, 1987, 1991].

In summary, a papilla basilaris is present in all sarcopterygians (including tetrapods) except dipnoans, some caecilians and bolitoglossine salamanders (fig. 5). Whether the papilla basilaris of amphibians is homologous or convergent, it is more parsimonious to assume that bolitoglossine salamanders have lost the papilla basilaris than that they never possessed one [see also Fritsch, 1991].

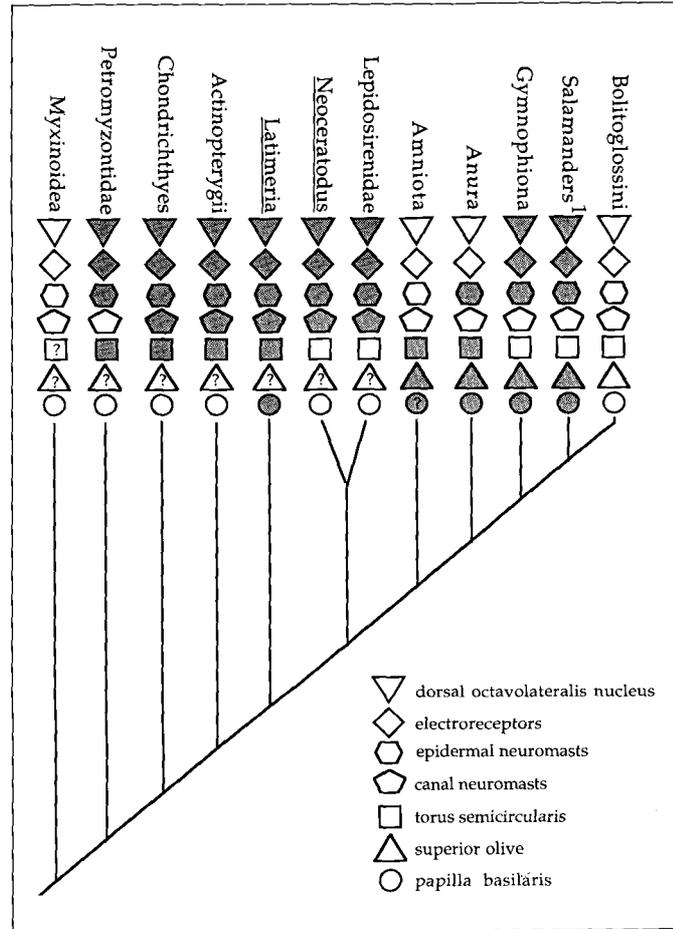


Fig. 5. A cladogram showing the states of each taxon for three characters of the auditory system and four characters of the lateral line system. Symbols and footnote are the same as in figure 1. Character coding and polarity are given in table 1. The papilla basilaris may not be homologous in amniotes and amphibians (see text). Bolitoglossine salamanders exhibit the simplest morphology for all seven characters.

Superior Olive

The superior olive, an important secondary auditory center in most vertebrates, long was thought to be absent in salamanders. However, it recently has been identified in this group based on retrograde tracing techniques and electrophysiology [Naujoks-Manteuffel and Manteuffel, 1987; Manteuffel and Naujoks-Manteuffel, 1990]. In juvenile salamandrids, superior olivary neurons occur in the periventricular gray matter. In adult *Salamandra*, these neurons are found in a partially migrated position outside the periventricular gray matter. No such migration of superior olivary neurons takes place in plethodontids [unpubl. obs.].

A migrated cell group tentatively named 'superior olive' has been distinguished on cytoarchitectural grounds

in caecilians, but not in *Latimeria* or dipnoans [Kuhlenbeck, 1975]. In frogs [Nieuwenhuys and Opdam, 1976; Pettigrew, 1981; Wilczynski, 1981] and amniotes [Ariens-Kappers et al., 1936], a migrated superior olive is present.

The superior olive is commonly defined as a group of neurons that receives second order auditory input and projects to the torus semicircularis. In the carp [Echteler, 1984] and the catfish [Finger and Tong, 1984], the medial auditory nucleus (MAN) appears to be homologous with the superior olive. The MAN is migrated in carp [Echteler, 1984]. In catfish, both saccular and lagenar fibers also project to the MAN [Bleckmann et al., 1991]. Because the MAN receives primary auditory afferents, it also resembles the cochlear nuclei of tetrapods. However, saccular and lagenar afferents also project to the superior olive in ranid frogs [Matesz, 1979; Will and Fritsch, 1988], which indicates that primary auditory input to the superior olive may be present in some tetrapods as well.

In chondrichthyans, three migrated cell groups (nucleus X and nuclei C1 and C2) receive second order auditory input and project to auditory midbrain areas [Barry, 1987; Corwin and Northcutt, 1982]. Thus, these nuclei may be homologous to the superior olive. It is unknown whether hagfishes or lampreys possess a superior olive.

In summary, the presence of a superior olive in nontetrapods is problematic due to the uncertain homology of the second and third order auditory nuclei of these groups to the superior olive of tetrapods. All tetrapod species that have been examined, except bolitoglossine salamanders, possess a migrated superior olive (fig. 5). We conclude that a migrated superior olive represents the ancestral tetrapod condition, and the nonmigrated superior olive of bolitoglossine salamanders is most parsimoniously interpreted as secondary and paedomorphic.

Torus semicircularis

In 19 species of salamanders studied to date [Manteuffel and Naujoks-Manteuffel, 1987, 1990; Naujoks-Manteuffel and Manteuffel, 1987; Roth et al., unpubl. data], the caudal intermediate nucleus and the superior olive project to the morphologically indistinct, unlaminated torus semicircularis, which consists mostly of densely packed, periventricular neurons [Manteuffel and Naujoks-Manteuffel, 1987, 1990; Naujoks-Manteuffel and Manteuffel, 1987].

In caecilians, there is no clear distinction between the tectum proper and the torus [Schmidt, unpubl. obs.]. There are more migrated neurons than in the salamander torus, but like that of salamanders, the caecilian torus is unlaminated [Schmidt, unpubl. obs.].

In 23 species of anurans representing all major families [Potter, 1965; Feng, 1983; Blanke and Roth, unpubl. data], an anatomically distinct, laminated torus semicircularis is present and consists of five subnuclei with extensive cell migration and lamination. Exceptions are members of the genus *Bombina* [Walkowiak, pers. comm.] and *Arenophryne rotunda* [Roth et al., in prep.], in which the torus is nearly unlaminated.

Amniotes possess a laminated torus [Ariens-Kappers et al., 1936; Kuhlenbeck, 1975]. The torus is migrated and laminated in *Latimeria* [Nieuwenhuys, pers. comm.], but not in *Neoceratodus* [Holmgren and Van der Horst, 1925] or in lepidosirenids [Northcutt, 1987]. Teleosts [Senn, 1976; Knudsen, 1977; Nieuwenhuys, 1982; Echteler, 1984] and chondrichthyans [Smeets et al., 1983; Northcutt, 1989a] have a torus with migrated cells and several clearly definable subnuclei. The torus is partly migrated and laminated in lampreys and is entirely absent in hagfishes [Wicht, pers. comm.].

In summary, a laminated torus semicircularis with several anatomically distinct nuclei is found in all gnathostomes except dipnoans, some frogs, some caecilians and all salamanders (fig. 5). In salamanders, the unlaminated and morphologically indistinct torus semicircularis is most parsimoniously interpreted as the result of secondary simplification.

Lateral Line System (Mechano- and Electrorception)

The peripheral lateral line system of salamanders includes both electroreceptors and mechanoreceptors. Electroreceptors (ampullary organs) project via the anterior lateral line nerve to the dorsal octavolateralis nucleus of the medulla oblongata and they do not receive efferent fibers. Mechanoreceptors (epidermal neuromasts) project via the anterior (head neuromasts) and posterior (trunk neuromasts) lateral line nerves to the intermediate nucleus. The mechanoreceptive system possesses efferent fibers whose cell bodies are found in the ventral medulla oblongata close to the roots of the VIIth and IXth nerves [Fritsch et al., 1984].

With respect to the degree of development of the lateral line system, salamanders can be grouped as follows [Fritsch, 1981; Roth and Wake, 1985a]:

(1) Species with aquatic larvae and aquatic to semiaquatic adults retain epidermal neuromasts and ampullary organs throughout life (Cryptobranchidae, Hynobiidae, Proteidae, Amphiumidae, and some isolated representatives of other families such as *Ambystoma mexicanum*,

Rhyacotriton, *Pleurodeles*, *Leurognathus*, and *Typhlomolge*) [Fritzschn, 1981; Wright, 1951], or have organs that regress periodically, such as *Siren*, *Notophthalmus*, *Triturus* and *Taricha* [Wright, 1951; Reno and Middleton, 1973].

(2) Species with aquatic larvae and a postmetamorphic terrestrial stage either retain neuromasts and ampullary organs throughout life (*Ambystoma*, *Eurycea*, *Gyrinophilus*, *Desmognathus*, *Pseudotriton*), or lose both at metamorphosis (*Stereochilus*, *Hemidactylum*, *Salamandra salamandra*, *Dicamptodon*) [Hilton, 1947; Wright, 1951; Fritzschn, 1981].

(3) Species with direct development (including live-bearers), which are strictly terrestrial throughout life, either transiently possess neuromasts and ampullary organs (*Salamandra atra*) [Escher, 1925], or never possess them (plethodontid tribes Plethodontini and Bolitoglossini) [Dent, 1942; unpubl. obs.]. Anterior lateral line nerves are found in two direct-developing desmognathine species that appear to lack both neuromasts and ampullary organs [Wake et al., 1987].

The lateral line system of caecilians contains both electroreceptors and neuromasts [Hetherington and Wake, 1979; Fritzschn and Wake, 1986]. In species with aquatic to semiaquatic larvae and terrestrial adults (*Ichthyophis*, *Epicrionops* and *Sylvacaecilia*), epidermal neuromasts and ampullary organs are lost at metamorphosis. Species that are viviparous and have an aquatic adult (*Typhlonectes*) never develop neuromasts, but they retain ampullary organs throughout life [Fritzschn and Wake, 1986]. Viviparous species that are strictly terrestrial (*Geotrypetes* and *Dermophis*) develop neither neuromasts nor ampullary organs [Fritzschn and Wake, 1986]. At least one species with direct development and terrestrial adults retains both neuromasts and ampullary organs [*Hypogeophis*; Fritzschn and Wake, 1986].

Anurans lack ampullary organs, and the lateral line system is represented only by epidermal neuromasts [Fritzschn, 1989]. Neuromasts persist throughout life in some species with aquatic larvae and adults (*Xenopus*), or are lost at metamorphosis (*Pseudis*) [Fritzschn et al., 1987]. Neuromasts are retained in some species with aquatic larvae and terrestrial adults (*Bombina*), or are lost at metamorphosis (most species) [Will, 1982]. Neuromasts are retained throughout life in species with direct development and aquatic adults (*Pipa*). Neuromasts are transiently present in some species with direct development and terrestrial adults (*Arthroleptella*) [de Villiers, 1929] or are absent throughout development (*Eleutherodactylus*) [Lynn, 1942].

No sign of a lateral line system, neither end organs nor central components, has been found in reptiles or mammals [Northcutt, 1991]. Birds possess a paratympanic organ that contains baroreceptive hair cells which may be derived from the lateral line [von Bartheld, 1990].

In addition to ampullary organs and epidermal neuromasts, *Neoceratodus* and *Latimeria* possess canal neuromasts. In lepidosirenid lungfishes, canal neuromasts are either strongly reduced (*Protopterus*) or completely absent (*Lepidosiren*) [Northcutt, 1987].

The lateral line system of actinopterygians includes electroreceptive organs and mechanoreceptive canal and epidermal neuromasts. Many species have lost the electroreceptive organs, the canal neuromasts, or both, but all species possess epidermal neuromasts [Northcutt, 1989b]. There is evidence for convergent evolution of novel electroreceptors in teleosts [Bullock et al., 1983]. Reduction in the canal system of the head and trunk in miniaturized teleosts has been attributed to paedomorphosis [Webb, 1989]. Chondrichthyans possess canal and epidermal neuromasts and ampullary organs [Northcutt, 1984a]. Lampreys possess only epidermal neuromasts and electroreceptors [Ronan, 1986], and hagfishes appear to lack the lateral line system entirely [Northcutt, 1991]. However, canal neuromasts were present in extinct agnathans [Jarvik, 1980].

The ancestral condition for vertebrates is the presence of electroreceptive organs and mechanoreceptive epidermal and canal neuromasts [Northcutt, 1985] (fig. 5). Losses and re-inventions of the electroreceptive system and parts of the mechanoreceptive system have occurred repeatedly in different groups [Bullock et al., 1983; Northcutt, 1984a]. Thus, we interpret the general absence of canal neuromasts in amphibians and the absence of electroreceptive organs and epidermal neuromasts in some groups of all three amphibian orders as a result of secondary simplification. In a parallel fashion, lepidosirenid lungfishes have lost or reduced canal neuromasts which are present in *Neoceratodus* and *Latimeria* [Northcutt, 1987].

If loss of components of the peripheral lateral line system in amphibians is to be attributed to paedomorphosis [Fritzschn, 1989], one would expect late-developing structures to be lost first during phylogenesis. The most complete lateral line systems develop as follows. The first step is the formation of the sensory ganglia, first of the anterior and then of the posterior lateral line, followed by the formation of the respective lateral line nerves. The next step is the induction of epidermal neuromasts. Finally, canals are formed [Northcutt, 1991]. Thus, the canal system would be the first to disappear, as is found in lepidosirenid lung-

fishes and all amphibians. The next components to disappear would be the neuromasts, while the lateral line ganglia and nerves would be retained. This has occurred in miniaturized desmognathine plethodontids [Wake et al., 1987]. The final event would be the disappearance of the lateral line nerve, which has occurred in plethodontine and bolitoglossine plethodontids. Apart from amniotes, which have lost the entire system, the strongest reduction of the lateral line system is found in terrestrial, direct-developing salamanders [Dent, 1942] and frogs [Lynn, 1942].

The alar plate of the medulla oblongata of salamanders, like that of most other anamniotes, consists of three longitudinally arranged, functionally distinct columns of cells: (1) the dorsal octavolateralis nucleus receives afferents from electroreceptive ampullary organs; (2) the intermediate or medial nucleus receives afferents from mechanoreceptive neuromasts and from auditory inner ear afferents; and (3) the ventral nucleus receives vestibular inner ear afferents [Nieuwenhuys, 1974; McCormick, 1982, 1988; Fritzschn, 1988b].

The dorsal nucleus is present in all salamanders except the direct developing plethodontines and bolitoglossines, which lack both electroreceptors and mechanoreceptors [Fritzschn, 1988b]. The intermediate nucleus of salamanders receives lateral line afferents when present, and its caudal part is considered to be the auditory nucleus [Will, 1988; Manteuffel and Naujoks-Manteuffel, 1990]. The rostral intermediate nucleus is also absent in bolitoglossines [Fritzschn, 1988b; Will and Fritzschn, 1988].

In caecilians, dorsal, intermediate and ventral nuclei are present. The dorsal nucleus is reduced in fossorial species. The intermediate nucleus is partially migrated in some species, and the unmigrated condition is thought to be more derived [Fritzschn et al., 1985b; Fritzschn 1988b].

In frogs, the dorsal nucleus is absent [Northcutt, 1984a]. In adult frogs that lack neuromasts, the rostral intermediate nucleus is also absent, whereas the caudal intermediate nucleus is present and represents the plesiomorphic auditory pathway [Fritzschn et al., 1984; Will, 1988]. Frogs have a unique dorsolateral nucleus which receives afferents from the papilla amphibiorum and the papilla basilaris, and serves as the main primary auditory center. The origin of this nucleus is unknown, but it is thought to derive at least in part from the dorsal alar plate and the ventral nucleus [Fritzschn, 1988b].

Dorsal and intermediate nuclei are absent in amniotes, although the ventral nucleus is present [Northcutt, 1984a]. In dipnoans, *Latimeria*, chondrosteans, chondrichthyans and lampreys, a dorsal octavolateralis nucleus is present [Northcutt, 1984a]. This nucleus has been lost in teleost

fishes [Northcutt, 1984a] and in hagfishes [Wicht, pers. comm.].

In summary, the presence of dorsal, intermediate and ventral nuclei receiving mechanoreceptive, auditory and vestibular afferents, respectively, is the plesiomorphic vertebrate condition [Boord and McCormick, 1984; Will, 1988] (fig. 5). In salamanders, loss of the dorsal nucleus and (in bolitoglossines) the rostral intermediate nucleus are most parsimoniously interpreted as secondary simplification.

Olfactory System

Salamanders possess a dual olfactory system: the olfactory system proper, contained in the olfactory bulb, and the accessory or vomeronasal system, situated caudal to the bulb. Primary olfactory projections enter the bulb laterally and form an oval terminal area. The termination sites of the accessory olfactory nerve lie caudal to the main olfactory terminal sites.

Vomeronasal Organ

Salamanders generally possess the simplest vomeronasal organs found among tetrapods [Bertmar, 1981]. However, the vomeronasal system is more fully developed in species with a biphasic life history and aquatic larvae than in direct developing species [Schmidt et al., 1988]. In species with aquatic larvae, the olfactory and accessory olfactory bulbs are confluent, and the termination sites of the accessory olfactory system are multi-lobed. In direct-developing species of plethodontids, the termination sites are separate, the pattern of termination of the accessory olfactory nerve is single- or double-lobed, and the accessory olfactory system is simpler than in salamanders with a biphasic life history [Schmidt et al., 1988]. The vomeronasal organ is completely absent in *Proteus* [Seydel, 1895].

In caecilians, primary olfactory projections enter the olfactory bulb both dorsally and ventrally, and primary accessory projections have a single-lobed termination pattern [Schmidt and Wake, 1990]. The vomeronasal organ is well developed and the terminal field of primary accessory projections is large in aquatic species, whereas terrestrial species have reduced vomeronasal organs and smaller terminal fields [Schmidt and Wake, 1990]. In frogs, the vomeronasal organ is well developed, although the accessory olfactory projections have a relatively simple organization [Weiss, pers. comm.]. Primary olfactory fibers enter the bulb ventrally [Northcutt and Kicliter, 1980].

Among adult amniotes, aquatic turtles, arboreal lizards, crocodylians, birds, cetaceans and some primates (including man) lack vomeronasal organs [Bertmar, 1981]. Rhynchocephalians have a small vomeronasal organ, located dorso-medially. Non-arboreal lizards and snakes have a medial, well developed, vomeronasal organ with a separate opening into the oral cavity [Parsons, 1959, 1969]. In mammals, a small digitiform vomeronasal organ is generally present [Parsons, 1969].

All living fishes, including chondrichthyans, actinopterygians, *Latimeria* and dipnoans lack vomeronasal organs [Millot and Anthony, 1965; Nieuwenhuys, 1965; Northcutt, 1987], although the nasal diverticulae of lungfishes are considered to be primordial vomeronasal organs [Bertmar, 1969, 1981]. Lampreys possess accessory olfactory organs that are not homologous to those of gnathostomes [Bertmar, 1969], and accessory olfactory organs are absent in hagfishes [Wicht, pers. comm.].

In vertebrates possessing a dual olfactory system, the accessory olfactory system develops later than the primary one [Parsons, 1969]. The reduction of the accessory olfactory system in direct-developing salamanders may be paeodomorphic (fig. 6).

Brain

The salamander brain has been considered primitive because: (1) the optic tecta do not bulge as in teleosts, frogs and birds; (2) the cerebellum is very small; (3) there are few anatomically distinct, migrated nuclei in the diencephalon, synencephalon and mesencephalon; (4) the optic tectum is unlaminate; and (5) the neurons appear relatively immature and undifferentiated [Herrick, 1948; Leghissa, 1962]. However, it has been suggested previously that the salamander brain is secondarily simplified rather than primitive [Senn and Farner, 1977; Northcutt, 1987], and even Herrick [1948] suspected this, at least with respect to the auditory system.

Telencephalon

Although the salamander telencephalon appears simple, it contains all of the basic components of the tetrapod telencephalon. Pallial regions include the lateral, dorsal and medial pallium and the pars lateralis amygdalae. Subpallial regions consist of the septum, striatum, nucleus accumbens and pars medialis amygdalae [Kicliter and Northcutt, 1975]. Subpallial areas develop earlier than pallial areas. Substantial cell migration takes place during development in the medial pallium (fig. 6). However, this

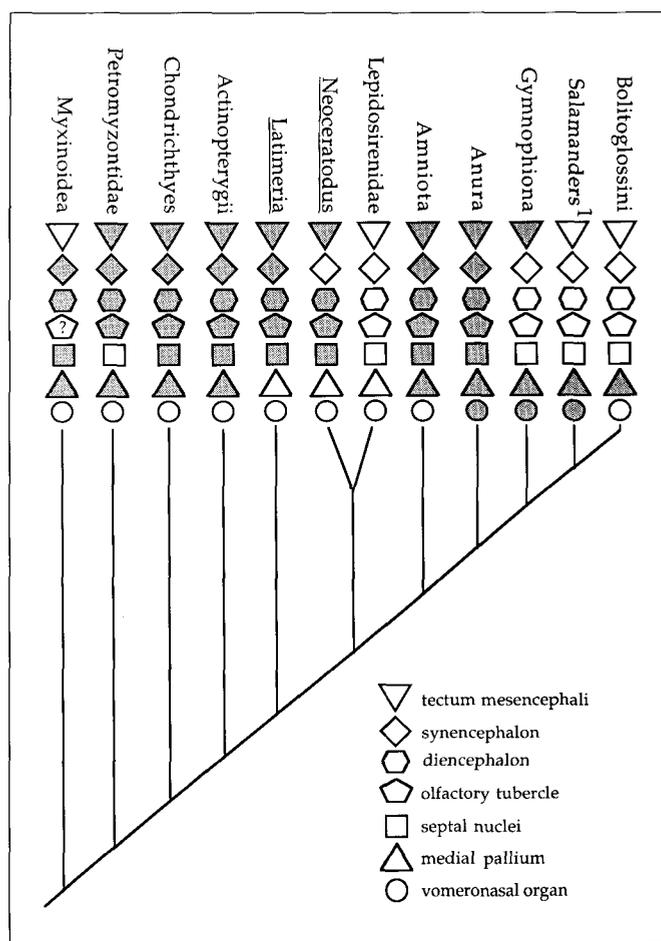


Fig. 6. A cladogram showing the states of each taxon for characters of the olfactory system, forebrain and midbrain. Symbols and footnote are the same as in figure 1. Character coding and polarity are given in table 1. Bolitoglossine salamanders exhibit the simplest morphology for all seven characters except migration of cells in the medial pallium.

migration does not lead to the formation of distinct laminae [Kicliter and Northcutt, 1975; Schmidt, unpubl. obs.]. Instead, the cells are loosely scattered in the white matter. There is little cell migration in the septal area. Lateral and medial septal nuclei have been recognized, but are not nearly as well migrated as in anurans [Kicliter and Northcutt, 1975]. Salamanders lack an olfactory tubercle and a postolfactory eminence [Northcutt and Kicliter, 1980].

Some caecilians have almost no cell migration in the medial pallium [Leutenegger, 1972; Kicliter and Northcutt, 1975], while others show substantial cell migration [Schmidt and Wake, unpubl. obs.]. As in salamanders, however, cell migration does not lead to the formation of distinct laminae [Leutenegger, 1972]. Although the rostral

septal area is several times the size of the medial pallium, it is also unmigrated in caecilians, so that lateral and medial septal nuclei cannot be distinguished [Northcutt and Kicliter, 1980]. The olfactory tubercle is absent in caecilians [Northcutt and Kicliter, 1980].

In ranid frogs, extensive cell migration is found in the medial pallium [Kicliter and Northcutt, 1975]. Distinct septal nuclei are present, and the medial nucleus is laminated at mid-hemispheric levels [Kicliter and Northcutt, 1975]. Both a postolfactory eminence and an olfactory tubercle are found [Northcutt and Kicliter, 1980].

In the teiid lizard *Tupinambis nigropunctatus*, pallial cells migrate into four distinct layers, and the telencephalon is usually regarded as a true cortex [Ebbesson and Voneida, 1969]. An autapomorphy of the reptilian telencephalon is the dorsal ventricular ridge, a marked dorsal enlargement of the lateral telencephalic wall which is of pallial origin [Reiner et al., 1984]. The pallial regions of the avian telencephalon have been termed paleostriatum, archistriatum, neostriatum, ectostriatum and hyperstriatum. The neostriatum and hyperstriatum are the largest cell masses in the avian telencephalon, and both have complex subdivisions. They are assumed to be of pallial origin and comparable to the neocortex of mammals [Reiner et al., 1984]. In mammals, the cortex in general, and the neocortex in particular, have undergone a dramatic enlargement and differentiation [Ariens-Kappers et al., 1936; Creutzfeldt, 1983]. However, the striatal or basal ganglia complex has also undergone a substantial structural and functional differentiation [Reiner et al., 1984; Alexander and Crutcher, 1990]. Differentiated septal nuclei [Kuhlenbeck, 1977] and a well developed olfactory tubercle composed of several subdivisions [Källén, 1951] are present in amniotes.

The telencephalon of the lungfish *Protopterus* is very similar to that of amphibians, with a thickening of the dorsomedial telencephalon [Schnitzlein and Crosby, 1965]. In *Protopterus*, most of the neurons of the medial pallium are periventricular, with only a few islets of migrated neurons in a superficial location [Reiner and Northcutt, 1987]. The dorsomedial telencephalon may not be homologous to the medial pallium of amphibians, but instead may represent a septal area [von Bartheld et al., 1990]. Septal neurons are mostly unmigrated, and olfactory tubercles are absent in *Protopterus* [Reiner and Northcutt, 1987].

In *Neoceratodus* and *Latimeria*, there is no thickening of the medial pallium, and few cells are migrated [Nieuwenhuys, 1965; Northcutt, 1987]. Both *Neoceratodus* [Nieuwenhuys and Hickey, 1965; Northcutt, 1987] and *Latimeria* [Nieuwenhuys, 1965] possess differentiated septal nuclei and olfactory tubercles.

The organization of the telencephalon of teleosts is not directly comparable to that of tetrapods, because it shows evagination of the pallial parts rather than invagination found in tetrapods [Northcutt and Braford, 1980]. During the evolution of teleosts, the dorsal striatum and the medial pallium have become hypertrophied and more differentiated, as has the ventral striatum. The dorsal pallium remains small, and the lateral pallium is reduced in size and complexity. Actinopterygians have differentiated septal nuclei and olfactory tubercles [Northcutt and Braford, 1980; Northcutt, 1981; Northcutt and Davis, 1983].

Chondrichthyans possess a specialized portion of the dorsal pallium, the central nucleus, which is small in squalomorph and large in galacomorph sharks [Northcutt, 1989a]. There is extensive cell migration in the medial pallium of chondrichthyans [Northcutt, 1989a], the septal nuclei are differentiated, and olfactory tubercles are present [Northcutt, 1981; Smeets et al., 1983].

Lampreys possess a laminated dorsal telencephalon [Northcutt, 1981], differentiated septal nuclei [Northcutt, 1981], and olfactory tubercles [Northcutt and Puzdrowski, 1988]. Myxinooids possess a laminated dorsal telencephalon [Northcutt, 1981; Wicht and Northcutt, 1990], but the septal nuclei are undifferentiated [Northcutt, 1981]. Olfactory tubercles are unknown in myxinooids.

In summary, the telencephalon of amphibians shows the simplest organization among gnathostome vertebrates. This is particularly true for pallial areas, which are more specialized in all other vertebrates. However, there are differences in the morphology of the telencephalon among living amphibians. Frogs have more migrated cells in the medial pallium than other amphibians, and possess an olfactory tubercle (which is absent in both salamanders and caecilians) and distinct septal nuclei (fig. 6). Reduction of the telencephalon in salamanders and caecilians compared to anurans, and in amphibians compared to other gnathostome vertebrates, appears to be due to secondary simplification.

Diencephalon

The diencephalon of salamanders consists of the epithalamus, including the large habenular nuclei, eminentia thalami, dorsal thalamus, ventral thalamus, hypothalamus and preoptic nucleus [Herrick, 1948]. No clear cytoarchitectural subdivisions of the periventricular gray and very few migrated nuclei are found in the diencephalon of salamanders. The zona subhabenularis of the anterior dorsal thalamus of *Triturus alpestris* contains very few migrated neurons [Wicht and Himstedt, 1988], and the same condition is found in *Pleurodeles waltl* and in plethodontid salamanders [Roth, 1987].

The diencephalon of caecilians is largely unmigrated [Wicht, 1988]. In anurans, the diencephalon is complex, with a large number of migrated, and some partly migrated nuclei. The epithalamus contains the dorsal and ventral habenular nuclei, both formed of densely packed cells. The dorsal thalamus of *Rana catesbeiana* consists of anterior, central and posterior nuclei, all of which are partially migrated [Neary and Northcutt, 1983]. A complex of migrated nuclei also is found in the ventral thalamus, which consists of the ventrolateral nucleus, the nucleus Bellonci, the corpus geniculatum thalamicum and the superficial ventral nucleus. The ventromedial nucleus is unmigrated.

The diencephalon of reptiles, birds and mammals is differentiated to a much higher degree anatomically than in amphibians. In primates, more than one hundred nuclei and subnuclei are present in the dorsal thalamus alone [Creutzfeldt, 1983; Jones, 1985].

In lepidosirenid lungfishes, all of the diencephalic nuclei are periventricular [Northcutt, 1987]. In contrast, *Neoceratodus* [Holmgren and Van der Horst, 1925] and *Latimeria* [Nieuwenhuys, pers. comm.] have migrated diencephalic nuclei. Actinopterygians have highly migrated diencephalic nuclei [Braford and Northcutt, 1983]. All chondrichthyans possess migrated diencephalic nuclei, but the degree of migration is higher in galaeomorph sharks, batoids and heterodontids, and lower in holocephalimorphs, squalomorphs and squatinomorphs [Smeets et al., 1983; Northcutt, 1989a]. Diencephalic nuclei are also migrated in myxinooids [Wicht and Northcutt, 1990] and lampreys [Northcutt and Puzdrowski, 1988].

In summary, only lepidosirenid lungfishes, caecilians and salamanders have unmigrated diencephalic nuclei (fig. 6) and the hypothesis of secondary simplification is more parsimonious than the hypothesis that these groups have retained the primitive condition.

Synencephalon

The synencephalon of vertebrates consists of the junctional area between the diencephalon and mesencephalon. It includes the praetectum dorsally and the accessory optic system ventrally, both involved in visual and optomotor reflexes [Manteuffel, 1985].

The praetectum of salamanders is similar to the diencephalon in that most neurons are unmigrated. Three nuclei can be identified: the nucleus praetectalis profundus, the nucleus Darkschewitsch (both involved in optomotor reflexes), and the nucleus praetectalis superficialis (of unknown function) [Manteuffel, 1985; Naujoks-Manteuffel and Manteuffel, 1988]. The name 'nucleus Darkschewitsch' was chosen after Herrick [1948], although the sala-

mander nucleus Darkschewitsch is not homologous to the mammalian nucleus Darkschewitsch. In most salamanders, the nucleus Darkschewitsch is only partly migrated. The number of migrated neurons varies from about 20 in *Salamandra* to 4 in *Batrachoseps* [Naujoks-Manteuffel, unpubl. obs.]. Due to differences in connectivity, the homology of the superficial pretectal nucleus of salamanders to that of other vertebrates is unclear [Naujoks-Manteuffel and Manteuffel, 1988].

The caecilian praetectum is generally unmigrated, and no migrated superficial pretectal nucleus is present [Kuhlenbeck, 1975; Naujoks-Manteuffel et al., 1988a; and unpubl. obs.].

The praetectum of most anurans, like the diencephalon, is highly differentiated anatomically. It contains three migrated nuclei: the pretectal gray, the nucleus lentiformis mesencephali, and the nucleus commissurae posterioris [Neary and Northcutt, 1983]. The n. lentiformis mesencephali is found in the same position as the n. superficialis praetectalis of salamanders. However, the homology between these two nuclei is unclear because of differences in connectivity [Montgomery et al., 1981, 1985; Finkenstädt et al., 1983; Rettig, 1984; Naujoks-Manteuffel and Manteuffel, 1986].

In reptiles and birds, three migrated, primary visual nuclei are found in the synencephalon: the nucleus lentiformis mesencephali (=nucleus superficialis synencephali), the nucleus geniculatus praetectalis, and the area optica praetectalis (nucleus posterodorsalis in reptiles) [Northcutt and Butler, 1974a; Repérant et al., 1977]. In mammals, four migrated, primary visual pretectal nuclei are present: the nucleus of the optic tract, the nucleus praetectalis olivaris, and the nuclei praetectales anterior and posterior [Scalia, 1972].

Migrated synencephalic nuclei are present in *Latimeria* [Northcutt, pers. comm.; Nieuwenhuys, pers. comm.], but not in dipnoans [Northcutt, 1980; Fite, 1985]. In teleosts, several primary and secondary migrated visual nuclei are found: (1) the pars parvocellularis of the superficial pretectal nucleus (=nucleus geniculatus lateralis of earlier authors), which is the most superficial; (2) the pars magnocellularis of the superficial pretectal nucleus (=nucleus rotundus of Schnitzlein); (3) the central pretectal nucleus, the nucleus corticalis; and (4) the periventricular pretectal nucleus (=nucleus commissurae posterior of earlier authors) [Northcutt and Wullimann, 1988; Wullimann and Meyer, 1990]. Chondrichthyans [Northcutt, 1979, 1989a], lampreys [Northcutt and Puzdrowski, 1988] and myxinooids [Wicht and Northcutt, 1990] possess migrated synencephalic nuclei.

In her review of pretectal and accessory optic visual nuclei, Fite [1985] reports that in all classes discussed, three pretectal visual nuclei are present (superficial, central and deep). In dipnoans, caecilians and salamanders, these pretectal subdivisions are not migrated (fig.6), and thus can only be found using tracing techniques. The low level of anatomical differentiation and the weak development of distinct nuclei in salamanders, caecilians and dipnoans is more parsimoniously interpreted as secondarily simplified than as primitively simple.

Tectum mesencephali

The tectum of salamanders has an essentially unlaminate, bipartite morphological organization, consisting of a periventricular zone of cell bodies, and a superficial zone containing dendrites of neurons and afferent and efferent fibers. Very few neurons migrate into the superficial zone [Roth, 1987; Roth et al., 1990b].

The tectum of derived caecilians (i.e., *Typhlonectes*) resembles that of salamanders, with a bipartite organization and only a few neurons located in the superficial zone [Himstedt and Manteuffel, 1985; Schmidt and M. Wake, pers. obs.]. However, basal taxa (i.e., *Epicrionops*) have a laminated tectum that contains more migrated neurons than salamanders, but fewer than frogs [Schmidt and Wake, pers. obs.].

The tectum of anurans is distinctly laminated, although the degree of lamination varies among species. In all neobatrachians studied so far (e.g., *Rana Bufo*, *Eleutherodactylus*, *Dendrobates*) and in some archaeobatrachians (e.g., *Discoglossus*), there is a periventricular layer of ependymal cells (layer 1 of Potter, 1969), followed by migrated cellular layers 2, 4, and 6. The cellular layers are separated by fiber (plexiform) layers 3 and 5. Above layer 6, efferent fibers are found (layer 7), with a few cell bodies scattered in between. Layer 8 consists of loosely arranged cell bodies intermingled with retinal afferent fibers. Layer 9 occupies the most superficial one-third of the tectum. It contains a few cell bodies and several fiber laminae, including the laminae of retinal afferents [Potter, 1969]. The degree of lamination is less pronounced in *Bombina* [Walkowiak and Roth, unpubl. obs.] and in *Arenophryne* [Roth et al., in prep.].

Among amniotes, reptiles [Ulinski, 1977; Schroeder, 1981; Northcutt, 1984b] and birds [Hunt and Brecha, 1984] have a highly complex optic tectum, with many alternating layers of cells and fibers, and many morphologically distinct types of tectal neurons. The mammalian optic tectum (colliculus superior) is strikingly less elaborated than that of other amniotes, and is considered to be secondarily simplified [Huerta and Harting, 1984].

Among dipnoans, the tectum of *Neoceratodus* has alternating cell and fiber layers and substantial migration of cells into the superficial zone [Northcutt, 1980]. In contrast to *Neoceratodus* the lepidosirenid lungfishes possess a relatively small tectum similar to salamanders and caecilians with a minimum of cell migration into the superficial zone [Northcutt, 1977, 1987]. The tectum of *Latimeria* resembles that of *Neoceratodus* [Northcutt and Neary, 1975; Northcutt et al., 1978; Kremers and Nieuwenhuys, 1979].

Holostean and teleost fishes have a highly differentiated optic tectum with many alternating cell and fiber layers and at least 15 different morphological types of tectal cells [Meek and Schellart, 1978; Vanegas et al., 1984]. Autapomorphies of the teleostean dorsal mesencephalon are the stratum marginale, which is the most superficial layer of the optic tectum, but is not a primary visual layer, and the torus longitudinalis, which extends rostrocaudally along the medial part of the tectum. A multi-laminated tectum is also found in elasmobranchs [Smeets et al., 1983; Northcutt, 1989a] and lampreys [Kennedy and Rubinson, 1984; Northcutt, 1985]. Although myxinoids have many migrated neurons, the tectum is unlaminate [Wicht, pers. comm.]

According to our phylogenetic hypothesis, the most parsimonious interpretation of these data is that: (1) a multi-laminated tectum is the primitive vertebrate condition [Roth et al., 1990b]; and (2) secondary simplification of the tectum has occurred independently in the lepidosirenid lineage and twice in the Lissamphibia (fig.6) [see also Northcutt, 1987].

We next present a detailed comparison of the morphological types, projection patterns, electrophysiological properties and neurotransmitters of tectal neurons in salamanders and frogs. This comparison shows that the same basic functional organization is found in these taxa, despite the profound difference in tectal lamination that results from the failure of cell migration in salamanders.

In salamanders, there are three morphological types of tectal neurons and several subtypes. There is a correlation between morphological type and projection site. Pear-shaped neurons with flat, symmetric or asymmetric dendritic trees are located superficially (type 2c) or sometimes deeper (type 1) in layer 6. The axons of these neurons constitute the bulk of the uncrossed tectobulbosplinal tract [Roth et al., 1990b].

Pear-shaped cells situated superficially (type 2a, *Salamandra* and *Bolitoglossa*) or somewhat deeper (type 2b, *Bolitoglossa*) in the periventricular gray have narrow to medium-wide dendritic trees and substantial arborization within the layers of retinal afferents. Axons of these cells

constitute the majority of crossed tectobulbospinal fibers. In salamandrids, large, migrated, spindle-shaped cells, found at the border between layers 4 and 5, also give rise to crossed tectobulbospinal fibers [Roth et al., 1990b].

A third type of tectal cell possesses slender dendritic arbors that reach the upper tectal layers containing retinal afferents (type 3). Their somata are dispersed throughout the periventricular gray. These interneurons apparently are the main targets of retinal afferents. This group consists of local interneurons, as well as neurons that project via the commissura postoptica to contralateral thalamic and isthmic termination sites and the ipsilateral praetectum [Naujoks-Manteuffel and Manteuffel, 1986; Roth et al., 1990b].

Morphological types of neurons in the optic tectum of ranid and bufonid anurans include: (1) large pear-shaped cells with relatively small dendritic trees that arborize within superficial fiber layers (the main elements of layers 2, 4, and 6); (2) small pear-shaped cells with smaller somata and narrower dendritic trees that are found only in layers 8 and 9; (3) pyramidal cells located in deeper cellular layers (mainly layer 6); and (4) large ganglionic cells situated in layers 6 and 7, with extremely wide dendritic arborization and spindle-shaped perikarya [Székely and Lázár, 1976; Lázár, 1984]. A recent reinvestigation of tectal cell morphology has suggested that a continuum exists between small and large pear-shaped cells in size and location [Antal et al., 1986].

In frogs, tectal projections to the diencephalon via the commissura postoptica originate mainly from pear-shaped cells situated in layer 8, less frequently from pear-shaped and pyramidal cells located in layers 4 and 6, and from large ganglionic cells in layer 7. Large ganglionic cells give rise to the descending tectobulbospinal tracts. The uncrossed tract originates mainly from cells located in layer 7, with dendrites arborizing predominantly in deep layers of retinal afferents, whereas the contralateral tract originates from cells found mostly in layer 6, with dendrites terminating primarily in the upper layer of retinal afferents [Lázár et al., 1983; Tóth et al., 1985].

Projection patterns of tectal neurons are similar in anurans and salamanders. Type-1 cells of salamanders (including the large, migrated, spindle-shaped cells of *Salamandra*) correspond closely with the large ganglionic cells of anurans. In both taxa, these cells are situated immediately below or within the main efferent fiber layer (layer 7 in anurans, layers 4–5 in urodeles). They have wide dendritic trees with only a few slender processes extending to the surface. The main morphological difference is that the large ganglionic cells of anurans possess several major den-

drites that originate immediately from the soma, whereas in salamanders the widespread arborization is constituted by thick secondary dendrites (except for the spindle-shaped cells of *Salamandra*) [Roth et al., 1990b].

The crossed and uncrossed tectobulbospinal tracts originate from the same types of cells in anurans and urodeles. Cells constituting the uncrossed tract have extremely wide dendritic arborization in the deeper fiber layers of the tectum, whereas those constituting the crossed tract possess dendrites extending into the superficial tectal fiber layers. The two types of cells apparently receive different kinds of visual and/or non-visual input, which is relevant to the differences in function of the descending tracts [Roth, 1987; Naujoks-Manteuffel and Manteuffel, 1988; Roth et al., 1990b].

Type-2 cells of salamanders resemble large pear-shaped and pyramidal cells of frogs. Both are found mostly in deeper cellular layers of the tectum. Their arborization is narrower than that of the previous type, and varies from rather small to wide. As in frogs, they are involved in both descending and ascending pathways. Type-3 cells of urodeles and small pear-shaped cells of anurans are comparable in that both have narrow dendritic trees and give rise to the tectopretectal, tecto-thalamic and tecto-isthmic tracts, or are intrinsic neurons.

The same basic visual response properties of tectal neurons (with respect to prey recognition and localization) are found in salamanders and frogs [Ewert, 1984; Roth, 1986]. In fact, there are more similarities in tectal response types between frogs and salamanders showing the same behavioral prey preferences than between members of either group having different prey preferences [Roth, 1986, 1987].

The distribution of neuropeptides and neurotransmitters in the tectum is as complex in salamanders as in anurans [Kuljis and Karten, 1982; Schmidt et al., 1989]. The laminae in which dendrites of type-2a and type-3 cells of urodeles arborize express the same neuropeptides as those layers that contain dendritic arborization of small and large pear-shaped cells of anurans.

One major difference between the taxa is that frogs have many more tectal neurons than do salamanders. In *Rana esculenta*, there are about 114,000 cells in the superficial layers 7, 8, and 9, with a total of 400,000 tectal cells per hemisphere [Székely and Lázár, 1976]. A relatively large salamander, *Salamandra salamandra* has about 280,000 tectal cells, and a miniaturized salamander, *Desmognathus aeneus*, has only about 51,000. Hatchlings of a small plethodontid salamander, *Batrachoseps attenuatus*, have only about 43,000 tectal cells [Roth et al., in prep.].

Tectal neurons of salamanders are also less differentiated in morphology than those of frogs, and the differences between the morphologically and functionally defined cell types are smaller. For example, the somata are mostly pear-shaped in salamanders (with the marked exception of some large spindle-shaped cells in *Salamandra*), whereas frogs have pear-shaped, pyramidal and spindle-shaped somata. Also, the pattern of dendritic arborization is more elaborate in frogs than in salamanders.

Frogs also have many more migrated tectal neurons than salamanders. In the tectum of *Rana* roughly 30% of the neurons migrate above the periventricular cellular layers. In contrast, the percentage of migrated neurons is 5% in *Salamandra* and 3.3% in *Pleurodeles*. In the bolitoglossine plethodontids, the percentage of migrated neurons ranges from 0.7% in the smallest (*Thorius narisovalis*) to 1.6% in the largest (*Hydromantes italicus*) species studied [Roth et al., 1990b].

Recent experiments using bromodeoxyuridine (BRDU) to mark mitotic cells show that cell proliferation and migration patterns are similar in salamanders and frogs [Schmidt and Roth, submitted]. However, there are differences in the proliferation rate and time course of development. The cell proliferation rate is much lower in salamanders than in frogs, which results in a slow-down of development.

Despite the differences in tectal lamination which are so apparent in histological sections of the brains of frogs and salamanders, the main differences between the tecta of the two groups are quantitative, relating to number, differentiation and migration of different cell types. The fact that fewer, less differentiated and less migrated cells are present in the tecta of salamanders supports the hypothesis that the appearance of the salamander tectum is a result of a general retardation of development [see also Senn and Farner, 1977].

Mesencephalic Tegmentum

Several nuclei can be distinguished in the mesencephalic tegmentum of salamanders [Naujoks-Manteuffel and Manteuffel, 1986, 1988]. Most of these are located within the periventricular gray matter. Because they lack clear boundaries, they are detectable only by retrograde tracing.

In all vertebrates examined, the nuclei associated with the basal optic system are found in a migrated position [Fite, 1985]. In salamanders, the migrated nucleus of the basal optic neuropil (nBON) receives direct visual input from the basal optic neuropil and projects to the praetectum [Naujoks-Manteuffel and Manteuffel, 1986]. The migrated nucleus of the basal optic neuropil of salamanders

is apparently homologous to the nucleus of the basal optic root (nBOR) of frogs [Montgomery et al., 1981] and birds [Gioanni et al., 1983], the nucleus basalis tegmenti of reptiles [Northcutt and Butler, 1974a] and the medial terminal nucleus of mammals [Giolli et al., 1984].

Montgomery et al. [1981] observed as many as six cell types in the nucleus of the BOR and in the peri-nBOR of frogs. No such differentiation has been observed in the nBON of salamanders [Naujoks-Manteuffel and Manteuffel, 1986].

Nucleus ruber

Neurons of the nucleus ruber are found in the ventral or ventrolateral tegmentum and project to the spinal cord via the contralateral dorsolateral funiculus in tetrapods [ten Donkelaar, 1988]. The magnocellular part of the nucleus ruber is believed to be associated with premotor control of limbs and limb-like structures [ten Donkelaar, 1982].

In many salamanders, including *Salamandra* and *Pleurodeles*, the nucleus ruber is partly migrated. Some nucleus ruber neurons migrate into the neuropil of the lateral tegmentum, but remain within the confines of the dendrites of unmigrated rubral neurons [Naujoks-Manteuffel and Manteuffel, 1988]. In plethodontid salamanders, however, all rubral neurons are unmigrated [Naujoks-Manteuffel, unpubl. obs.].

Caecilians apparently lack a nucleus ruber [Manteuffel et al., 1986; Naujoks-Manteuffel et al., 1988]. In frogs, an unmigrated, periventricular nucleus ruber is stained by labeling from the caudal medulla or spinal cord [ten Donkelaar et al., 1981; Tóth et al., 1985]. However, migrated neurons are stained in the contralateral nucleus ruber by labeling from a level immediately rostral to the VII/VIIIth roots [unpublished results]. In amniotes except snakes [ten Donkelaar et al., 1981], a migrated nucleus ruber is present [Kuhlenbeck, 1977; Kuypers, 1981; ten Donkelaar, 1982]. Lepidosirenid lungfishes also possess a migrated nucleus ruber [Ronan and Northcutt, 1985]. Nothing is known about the nucleus ruber in *Neoceratodus* or *Latimeria*.

A migrated nucleus ruber with a strong contralateral cerebellar input and a strong ipsilateral projection to the spinal cord is present in some teleosts [Hlavacek et al., 1984; Sloan and Demski, 1985; Oka et al., 1986; Wullmann and Northcutt, 1988; Behrend and Donicht, 1990]. The nucleus ruber is migrated in chondrichthyans [ten Donkelaar, 1982; Smeets et al., 1983]. It remains unknown whether a nucleus ruber is present in hagfishes and lampreys.

In the tegmentum, plethodontid salamanders and particularly bolitoglossines show little cell migration and mor-

phological differentiation. We hypothesize that migrated tegmental nuclei are a synapomorphy of sarcopterygians (including tetrapods), and that the relatively unmigrated state, or absence, of tegmental nuclei in salamanders is a derived condition arising from secondary simplification (fig. 7). Cell migration and the development of the projections of the nucleus ruber take place late in ontogeny in *Pleurodeles* [Naujoks-Manteuffel, unpubl. obs.].

Cerebellum

The cerebellum of salamanders is small and inconspicuous [Herrick, 1948]. It consists of lateral auricles with large recesses (supposed homologues of the mammalian flocculus and paraflocculus), a simply organized medial corpus cerebelli (homologue of the vermis of mammals) and a deep nucleus cerebelli (homologue of the deep cerebellar nuclei of mammals). There is no pons. Histologically, no cortical structure is observable. In *Ambystoma*, the gray of the corpus and auricles contains neurons resembling Purkinje cells, while other smaller cells are thought to represent granular cells [Herrick, 1948]. In *Necturus*, there is virtually no corpus cerebelli, and a reduced type of Purkinje cell is found, but there are no granular cells [Herrick, 1948]. Among salamanders, the least conspicuous cerebellum is found in bolitoglossines, in which it is very small and has partly retreated under the tectum [Roth, 1987]. There is no detailed modern study on the cerebellum of salamanders.

The cerebellum of caecilians is so poorly developed that recent workers have suggested it is absent altogether [Fritsch and Sonntag, 1987]. Frogs also have a small cerebellum, although it is larger than that of salamanders and caecilians, mostly due to a larger corpus cerebelli [Larsell, 1967]. This increase in size is accompanied by an increase in morphological differentiation.

It long has been recognized that while the anuran cerebellum is far more elaborated than that of caecilians and salamanders, the cerebellum of amphibians as a group is small and little differentiated in relation to other vertebrates [Larsell, 1967; Kuhlenbeck, 1975]. The degree of differentiation has been considered greater than that of lampreys and lepidosirenid lungfishes on one hand, and less than that of chondrichthyans, teleosts, *Neoceratodus* and amniotes on the other [Gerlach, 1933].

The amniote cerebellum is generally much larger than in anurans. The cerebellum of reptiles is evaginated (turtles, crocodylians), or everted (lizards, rhynchocephalians), and foliated [Starck, 1982]. Birds resemble crocodylians in general organization of the cerebellum, but have a much more highly developed structure with a massive corpus [Larsell,

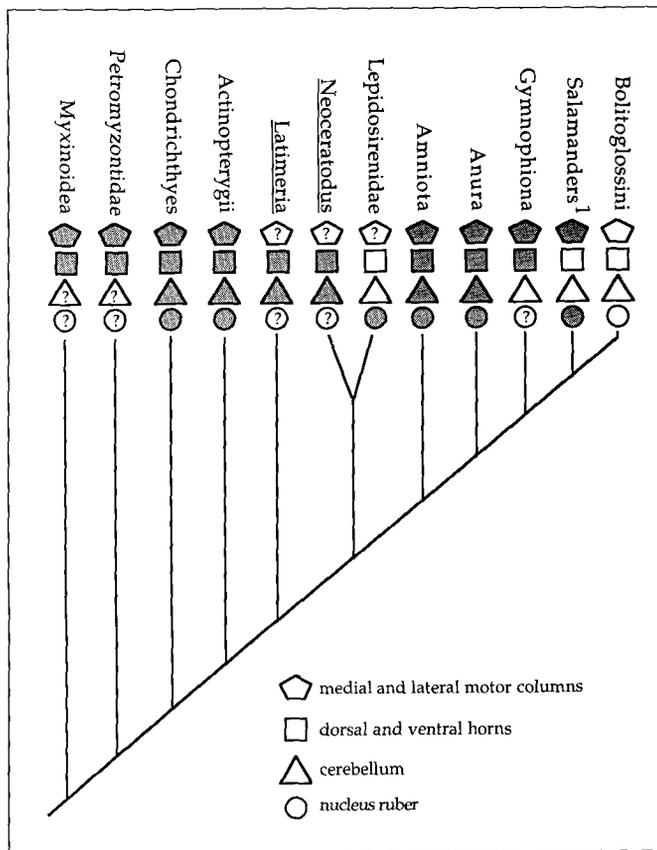


Fig. 7. A cladogram showing the states of each taxon for characters of the hindbrain and spinal cord. Symbols and footnote are the same as in figure 1. Character coding and polarity are given in table 1. Bolitoglossine salamanders exhibit the simplest morphology for all four characters.

1967]. In mammals, the cerebellum is greatly expanded, and is increased in complexity by the addition of folia and the neocerebellum [Kuhlenbeck, 1975].

Latimeria and *Neoceratodus* have large cerebella, with clearly separated corpus cerebelli and auricles [Kremers and Nieuwenhuys, 1979; Northcutt, 1987]. Both have extensive vestibulolateral lobes divided into distinct upper and lower leaves. This appears to be the plesiomorphic condition based on fish outgroups [Northcutt, 1987]. The lobes are very reduced in lepidosirenids, in which the cerebellum is similar to that of lissamphibians [Northcutt, 1987].

The cerebellum of most teleosts is highly elaborated, often specialized (e.g., in mormyrids, where it covers nearly the whole brain) and variable in size and differentiation [Kuhlenbeck, 1975]. The cerebellum is large but simply organized in most chondrichthyans [Northcutt, 1978b;

Smeets et al., 1983]. Sawfishes, guitarfishes, skates and galaeomorph sharks possess a highly elaborated cerebellum [Northcutt, 1989a]. Hagfishes [Wicht and Northcutt, 1990] and lampreys [Wicht and Northcutt, pers. comm.] appear to lack a cerebellum.

In all vertebrates, the cerebellum is the last major part of the brain to develop. Herrick [1914] pointed out that the cerebellum of salamanders resembles early developmental stages of the mammalian cerebellum. On the basis of the above comparative analysis, we conclude that the small and rather undifferentiated cerebella found in amphibians and in lepidosirenid lungfishes are independently derived pedomorphic traits [fig. 7; Northcutt, 1987], and that the small size and simplicity of the amphibian and lepidosirenid cerebellum result from retardation of brain development.

Medulla oblongata

The medulla oblongata of salamanders conforms to the basic vertebrate bauplan, and consists of four longitudinal columns (i.e., somatosensory, viscerosensory, visceromotor and somatomotor) [Herrick, 1948]. As in most other parts of the brain, the neurons are arranged in a densely packed periventricular layer, with little indication of subdivision. The motor nuclei and efferent neurons of the 5th, 7th, 9th and 10th nerves are located at the ventrolateral edge of the periventricular gray, and there is a substantial overlap in the rostrocaudal extent of the 7th, 9th and 10th motor nuclei [Roth and Wake, 1985a; Roth et al., 1988a].

Efferent neurons of the 8th nerve are situated ventrolaterally at the same level as the motor nucleus of the 7th nerve. This nucleus arises late in development as neurons migrate from medial positions. In bolitoglossines, these neurons fail to migrate and remain in a medial position [Fritsch, pers. comm.].

Nuclei of the ventral alar plate column are unmigrated in salamanders [Opdam and Nieuwenhuys, 1976]. Anterior, lateral and medial vestibular nuclei are similar in salamanders, frogs and amniotes [Will et al., 1985; McCormick, 1988; Naujoks-Manteuffel and Manteuffel, 1988; Manteuffel and Naujoks-Manteuffel, 1990]. The caudal intermediate nucleus of amphibians that receives saccular afferents may be homologous to the descending nucleus of mammals, and may be involved in mediating auditory information. A locus coeruleus, containing noradrenergic cells as in amniotes [Dubé and Parent, 1982] and projecting to the spinal cord, is lacking in salamanders [Naujoks-Manteuffel and Manteuffel, 1988].

The reticular formation of salamanders is subdivided into the nucleus reticularis superior, medius and inferior, with medial and lateral components [Opdam and Nieuwen-

huys, 1976]. The medial and lateral parts of the reticular formation differ in the laterality of their projections.

The medulla oblongata of caecilians is more complex morphologically than that of salamanders [unpublished data]. Anteriorly, the medullary nuclei are more clearly separated than in salamanders. In salamanders, the IXth and Xth motor nuclei overlap, whereas they are separate in caecilians. Caecilians are the only amphibians in which the nucleus intermedius is located subpially.

In frogs, the medullary nuclei are more discretely bounded and more separated rostrocaudally than in salamanders. They are found in a partially migrated position, and their neurons have a more complex morphology, with a dorsomedial dendritic projection [Matesz and Székely, 1977] that is absent in salamanders. Anurans also possess a fifth, migrated, ventral column nucleus (the dorsolateral nucleus), which receives auditory input and is an autapomorphy of anurans. A well migrated superior olive is present, and an inferior olive is present at least in *Xenopus* [Gonzales et al., 1984; Grover and Grüsser-Cornehls, 1984]. The presence of a locus coeruleus is debated [ten Donkelaar et al., 1981].

The medulla oblongata of amniotes shows a high degree of migration, differentiation and separation of motor nuclei, including the division of motor nuclei into morphologically and functionally distinct, migrated subnuclei [Ariens-Kappers et al., 1936; Matesz and Székely, 1977]. Information is absent for dipnoans, *Latimeria*, lampreys and hagfishes. The organization of the vestibular complex of teleosts is more complex than that of amphibians because a fifth nucleus, the nucleus tangentialis, is present [Ariens-Kappers et al., 1936]. Chondrichthyans possess four vestibular nuclei [McCormick, 1988].

Spinal Cord

The spinal cord of salamanders differs from that of most other gnathostomes in lacking dorsal and ventral horns [Roth and Wake, 1985a; Fetcho, 1986a]. In cross sections, the gray matter has an oval, rather than the characteristic butterfly, shape. Within the spinal cord, there are two motor columns. The medial column contains small, pear-shaped cells, and the lateral column contains large, spindle-shaped cells [Wake et al., 1988]. In salamanders with aquatic larvae, the latter originate medially and migrate laterally at or shortly after hatching. In direct-developing salamanders (except the bolitoglossine plethodontids), the lateral motor column is already present at hatching [Nishikawa et al., 1991]. In contrast, all bolitoglossine salaman-

ders lack a lateral motor column at all stages of development [Roth and Wake, 1985a; Wake et al., 1988; Nishikawa et al., 1991]. In these salamanders, migration of neurons out of the gray matter and differentiation into spindle-shaped cells is suppressed.

The spinal cord of caecilians varies among taxa, with some genera possessing ventral horns and others lacking them [unpublished observations]. Unlike bolitoglossine salamanders, however, caecilians possess lateral motor columns [unpublished observations].

The spinal cord of anurans is similar to that of most other vertebrates in having distinct dorsal and ventral horns, and lateral and medial motor columns [Fetcho, 1987]. It shows a higher degree of cellular differentiation and migration than that of salamanders [Székely, 1976].

The spinal cord of amniotes is more complex than that of amphibians. There are prominent dorsal and ventral horns, an increase in fasciculation of ascending and descending fibers, and an increase in segregation of the gray matter into distinct nuclei [Ariens-Kappers et al., 1936]. Medial and lateral motor columns are always present except in limbless reptiles [Fetcho, 1986b, 1987].

Lepidosirenid lungfishes lack dorsal and ventral horns, whereas *Neoceratodus* and *Latimeria* have dorsal and ventral horns [Northcutt, 1987]. Nothing is known concerning the migration of motor neurons into the lateral motor column in lungfishes and *Latimeria*. The spinal cords of teleosts, chondrichthyans, lampreys and hagfishes have distinct dorsal and ventral horns and two motor columns [Smeets et al., 1983; Fetcho, 1986a, 1987].

In summary, the absence of dorsal and ventral horns in the spinal cord of salamanders is most parsimoniously interpreted as secondarily simplified (fig. 7). Lepidosirenid lungfishes and some caecilians also have lost the dorsal and ventral horns during phylogenesis. The bolitoglossines are unique among vertebrates in lacking a lateral motor column (fig. 7). The absence of a lateral motor column in bolitoglossine salamanders is also a secondary simplification. Both of these characteristics are most probably the result of paedomorphosis.

Descending Pathways to the Medulla oblongata and Spinal Cord

In amphibians, the only telencephalic projection to the medulla is the ipsilateral striatobulbar pathway. This pathway extends to spinal levels in *Ambystoma* [Kokoros and Northcutt, 1977] but not in *Salamandra* [Naujoks-Manteuffel and Manteuffel, 1988]. A bilateral striatobulbar projec-

tion is found in *Rana* [Tóth et al., 1985] and a striatospinal projection is found in *Xenopus* [ten Donkelaar et al., 1981]. A striatospinal projection has been reported in lizards as well [Northcutt, 1984a]. Striatospinal projections are absent in mammals and birds and have probably been replaced by circuits that feed back striatal output to the thalamus and pretectal areas [Reiner et al., 1984]. The corticospinal tract present in mammals apparently is autapomorphic. Its elaboration is associated with the capacity for precise finger movements, especially in primates [Kuypers, 1982]. The nucleus ruber system is responsible for moving the proximal parts of the extremities which may not need to be tuned as precisely. Thus, the nucleus ruber may suffice to guide limb movements in other vertebrates. Telencephalic projections to the caudal medulla have been described in nurse sharks [Ebbesson, 1972], but not in *Raja* or *Scyliorhinus* [Smeets and Timerick, 1981]. Because the latter species are generally considered to be primitive, it is likely that descending projections from the telencephalon to the medulla have evolved independently in sharks and tetrapods [Northcutt, 1984a].

Telencephalic projections to the midbrain tegmentum characterize all vertebrate species [Northcutt, 1984a] and thus are probably plesiomorphic. Striatotectal projections are presumed to occur in salamanders [Rettig, 1988]. In frogs, the tectum [Wilczynski and Northcutt, 1983a,b] and the torus [Wilczynski, 1981] receive projections from the anterior entopeduncular nucleus, which is described as a caudal continuation of the striatum.

Descending hypothalamic pathways, such as the descending projections of the preoptic and periventricular hypothalamic nuclei of salamanders and frogs, are common to all vertebrates [ten Donkelaar et al., 1981; Tóth et al., 1985; Naujoks-Manteuffel and Manteuffel, 1988]. Hypothalamospinal projections are absent in lepidosirenid lungfishes [Ronan and Northcutt, 1985] and some teleosts [Hlavacek et al., 1984; Oka et al., 1986]. In *Lepisosteus*, a holostean fish, [Northcutt, 1982] and in chondrichthyans [Smeets and Timerick, 1981], these projections are present. Thus, the descending diencephalic projections of salamanders appear to be plesiomorphic.

Tectobulbar and tectospinal projections are common to all vertebrates. They relay visual input to brainstem motor neurons to control saccadic orientation of the head or eyes for object identification and localization.

In all vertebrates, the nucleus of the medial longitudinal fasciculus projects to the spinal cord. The probable homologue in mammals is the nucleus interstitialis of Cajal. Contralateral rubrospinal projections are found in vertebrates with limbs and limb-like structures and are absent in caeci-

lians [Naujoks-Manteuffel et al., 1988], snakes [ten Donkelaar, 1988] and teleosts [Hlavacek et al., 1984].

In salamanders and lepidosirenid lungfishes, a bilateral spinal projection originates in the cerebellar nucleus [Ronan and Northcutt, 1985; Naujoks-Manteuffel and Manteuffel, 1988]. Spinocerebellar projections are common to all gnathostomes, even to those with very small cerebella.

In salamanders, reticulospinal pathways are subdivided into a medial ipsilateral and a lateral contralateral descending pathway similar to lepidosirenid lungfishes [Ronan and Northcutt, 1985]. In all vertebrates, vestibulospinal projections originate in the magnocellular vestibular nucleus, and one or more subnuclei contribute to this projection.

We conclude that the descending pathways to medullary and spinal centers of salamanders are similar to those of other vertebrates. Pathways in terrestrial vertebrates that exert supraspinal control (i.e., interstitiospinal, reticulospinal and vestibulospinal) [ten Donkelaar, 1982] arise early in ontogeny [van Mier and ten Donkelaar, 1984]. Systems that arise somewhat later include basic supraspinal systems as well as hypothalamospinal, rubrospinal, cerebellospinal and solitariospinal systems. Secondary simplification of the central nervous system in salamanders apparently has not affected the descending pathways.

Ascending Pathways

The vertebrate brainstem contains ascending pathways to the telencephalon which are relayed in thalamic nuclei. These pathways are directed to cortical sites in mammals, to the anterior dorsal ventricular ridge in reptiles and to the striatum in frogs [ten Donkelaar, 1990]. In anamniotes, a substantial ascending input to the thalamus originates in the reticular formation [ten Donkelaar, 1990; Naujoks-Manteuffel, unpubl. obs.]. Spinothalamic pathways occur in mammals [Jones et al., 1987] and are primarily involved in nociception. Spinoreticular, spinocerebellar and spino-tectal tracts are common to all vertebrates [ten Donkelaar, 1990].

The salamander brain possesses all of the major ascending and descending pathways that are characteristic of the brains of tetrapods or vertebrates in general. This shows that paedomorphosis has not affected the bauplan of the salamander brain, but rather has affected only relatively late-occurring processes that determine the degree of differentiation and migration of neurons, but not their basic connections or functions.

Discussion

This paper summarizes data on the morphology and organization of four special sensory systems (visual, auditory, lateral line and olfactory systems) and the central nervous system of vertebrates. Most of these neural characters display a morphocline from more simple to more complex (i.e., from few cells to many, from a low to a high degree of morphological differentiation, lamination, formation of nuclei, cell migration, and myelination). Although a few traits appear to be either present or absent (e.g., canal neuromasts, basilar papilla and dorsal electroreceptive nucleus), a more detailed comparison might reveal morphoclines in these traits as well. In almost all cases, the end of the morphocline displaying the greatest simplicity occurs in salamanders. Frequently, this simple state is shared with other groups, most commonly with caecilians and lepidosirenid lungfishes. Furthermore, for those characters that display morphoclines within the salamander lineage, the simplest end of the morphocline almost invariably occurs in the bolitoglossine plethodontids.

The observed simplicity of the salamander brain raises four important questions about its evolution: (1) Is the simple morphology primary (i.e., primitive in a phylogenetic sense), or secondary, in which case it has been derived from a more complex ancestral state? (2) If the salamander brain is indeed derived, what are the developmental mechanisms for its simplification? (3) What are the functional consequences of simplification? and (4) Is there any evidence that salamanders may compensate for the negative consequences of simplification?

Phylogenetic Analysis

Phylogenetic analysis uses outgroup comparisons to determine whether a character state in the taxon under study is primitive or derived [Hennig, 1966; Wiley, 1981]. In every part of the brain that we have investigated, phylogenetic analysis shows that taxa which are believed to be more primitive than salamanders (based on non-neural characters) have more complex brains than salamanders. For example, lampreys, chondrichthyans and all osteichthyans except lepidosirenid lungfishes (which are also believed to be secondarily simplified [Northcutt, 1987]), possess a laminated optic tectum. The derivation of salamanders from an ancestor with an unlaminated tectum, under the hypothesis that salamanders have retained the primitive condition during their evolution, requires that multiple lamination has evolved 8 times independently in vertebrates (fig. 6) [see also Roth et al., 1990c]. The alternative hypothesis, that salamanders are derived from

ancestors with more complex brains through the process of secondary simplification, requires only three evolutionary events: independent reduction of tectal lamination in hagfishes, lepidosirenid lungfishes and salamanders.

In order to test whether the simple morphology of the salamander brain is primitive or secondary, it is necessary to examine the complexity of each character in the relevant outgroups of salamanders. These are caecilians, anurans, amniotes, lungfishes (i.e., lepidosirenids and *Neoceratodus*), *Latimeria*, Actinopterygii, Chondrichthyes, lampreys and hagfishes respectively.

For each of the 23 characters listed in table 1, we calculated the number of evolutionary steps required to explain the evolution of that character under two alternative hypotheses: (1) that salamanders have retained a primitively simple organization during their evolution; or (2) that the simple organization of salamanders is derived secondarily from a more complex ancestral state.

Of all of the characters we analyzed, only the presence of migrated cells in the medial pallium is most parsimoniously interpreted as plesiomorphically simple in salamanders (table 1). In only one character are the brains of bolitoglossine salamanders more elaborated than those of most other vertebrates. Like primates and flying foxes, bolitoglossines have evolved well developed ipsilateral retinotectal projections. Of the 21 remaining characters, only the number of morphological types of retinal ganglion cells and the degree of myelination of the optic nerve require the same number of evolutionary steps under both hypotheses. The remaining 19 characters are most parsimoniously interpreted as secondary reversal to the primitive character state (5 characters) or as a derived loss from a more complex ancestral character state (14 characters). The hypothesis that salamanders have retained the primitive state for all 23 characters during their evolution requires 128 evolutionary events during vertebrate phylogenesis, whereas the hypothesis that salamanders are secondarily simplified from a more complex ancestral state requires only 56 events (table 1).

Furthermore, species of the plethodontid tribe Bolitoglossini have the simplest brains found among salamanders. The hypothesis that bolitoglossine salamanders have primitively simple brains requires the assumption that lamination and cell migration have increased many times independently within the order Caudata, and several more times within the family Plethodontidae. We conclude that many sensory systems as well as the central nervous system of salamanders, especially those of bolitoglossines, are secondarily simplified rather than plesiomorphically simple.

It is important to note that data are missing for many taxa, and much neuroanatomical work remains to be done before we can be sure that character states in different taxa truly represent homologous structures. It is possible that the addition of new data may change the polarity of a few characteristics, but it is unlikely to change the overall interpretation of our results.

Paedomorphosis and Secondary Simplification

Paedomorphosis is a state in which the adults of a taxon possess a morphology that characterizes juveniles of outgroups or postulated ancestors [Alberch et al., 1979]. Paedomorphosis results from heterochronic processes, such as progenesis and neoteny [Gould, 1977; Alberch et al., 1979]. These heterochronic processes give rise to differences between taxa in the degree of development along a shared ontogenetic trajectory, so that one taxon will have a more abbreviated and the other a more extended ontogeny. Thus, the idea of a phylogenetically conserved, stable ontogeny is implicit in the concept of paedomorphosis [Rieppel, 1988].

When a derived taxon has a truncated or abbreviated version of a plesiomorphic ontogenetic trajectory, the resulting simplicity represents a reversal to the primitive condition, and thus is phylogenetically secondary. Secondary simplification appears to be a phylogenetic regression, which may restore or approximate an ancestral condition (i.e., reverse recapitulation) [Alberch et al., 1979]. Paedomorphosis reverses the expected parallelism between ontogeny and phylogeny, and has been viewed as significant for the introduction of evolutionary novelties in most major taxa of the animal kingdom [Gould, 1977; Matsuda, 1987]. Paedomorphosis may result from heterochronic processes that affect the whole organism (i.e., global heterochrony) [Raff and Wray, 1989]. Thus, secondary simplification may come, not trait by trait, but as a package. Cases of extreme or pure paedomorphosis (in essence reproductively mature embryos) are rare [Gould, 1977]. In general, the descendants of a common paedomorphic ancestor will exhibit a combination of secondarily simplified traits and their own specialized apomorphies.

It is widely believed that all living amphibians (Lissamphibia) are paedomorphic compared with their hypothesized sister taxon, the Palaeozoic temnospondyls. Traits believed to be paedomorphic include miniaturization, juvenilized cranial proportions including relative enlargement of the orbits, a single vertebral centrum, absence of labyrinthine infolding of the teeth, pattern of distribution of teeth, loss of palatal fangs, and bicuspid, pedicellate teeth [Bolt, 1977; Carroll, 1986; Milner, 1988].

Table 1. Raw data for phylogenetic analysis of the 23 characters used in this study

	P	C	A		L				G	S	B
	e	h	c		e						
	r	o	t		p						
	m	n	n		i						
	y	d	o		d						
	x	r			o						
	i	i	p		s						
	n	c	t		i						
	o	t	r		r						
	i	t	e		r						
	d	h	y		e						
	e	d	g		r						
	a	a	i		i						
	e	e	s		a						
1 Types of RGCs (0=<5; 1=5–10; 2=>10)	–	0	0	1, <u>2</u>	–	–	–	2	1	–	0
2 Optic nerve fibers (0=<50,000; 1=50–100,000; 2=>100,000)	0	0	2	2	–	–	0	1, <u>2</u>	1, <u>2</u>	0	1
3 Degree of myelination (0=<25%; 1=>25%)	0	0	–	1	–	–	–	0, <u>1</u>	0	–	0
4 Ipsilateral retinotectal fibers (0=present; 1A=few, if any; 1B=well developed)	0	0	<u>0</u> , 1A	<u>0</u> , 1A	–	0	0	<u>0</u> , 1A, 1B	1A	1A	0
5 Incompatibility of retinotectal fibers (0=incompatible; 1=compatible)	1	–	–	0	–	0	–	0	0	–	1
6 Papilla basilaris (0=absent; 1=present)	0	0	0	0	1	0	0	1*	1	0, <u>1</u>	0, <u>1</u>
7 Superior olive (0=migrated; 1=unmigrated)	–	–	–	–	–	–	–	0	0	0	<u>0</u> , 1
8 Torus semicircularis (0=laminated; 1=unlaminated)	–	0	0	0	0	1	1	0	<u>0</u> , 1	1	1
9 Canal neuromasts (0=present; 1=absent)	1	1	0	<u>0</u> , 1	0	0	<u>0</u> , 1	1	1	1	1
10 Epidermal neuromasts (0=present; 1=absent)	1	0	0	0	0	0	0	1	<u>0</u> , 1	<u>0</u> , 1	<u>0</u> , 1
11 Electrorceptors (0=present; 1=absent)	1	0	0	<u>0</u> , 1	0	0	0	1	1	<u>0</u> , 1	<u>0</u> , 1
12 Dorsal octavolateralis nucleus (0=present; 1=absent)	1	0	0	<u>0</u> , 1	0	0	0	1	1	0	<u>0</u> , 1
13 Vomeronasal organ (0=absent; 1=present)	0	0	0	0	0	0	0	0, <u>1</u>	1	1	0, <u>1</u>
14 Medial pallium (0=migrated; 1=unmigrated)	0	0	0	0	1	1	1	0	0	<u>0</u> , 1	0
15 Septal nuclei (0=differentiated; 1=undifferentiated)	0	1	0	0	0	0	1	0	0	1	1
16 Olfactory tubercle (0=present; 1=absent)	–	0	0	0	0	0	1	0	0	1	1
17 Diencephalon (0=migrated nuclei; 1=unmigrated nuclei)	0	0	0	0	0	0	1	0	0	1	1
18 Synencephalon (0=migrated; 1=unmigrated)	0	0	0	0	0	1	1	0	0	1	1
19 Tectum mesencephali (0=laminated; 1=unlaminated)	1	0	0	0	0	0	1	<u>0</u> , 1	<u>0</u> , 1	<u>0</u> , 1	1
20 Nucleus ruber (0=migrated; 1=unmigrated)	–	–	0	0	–	–	0	0	0	–	<u>0</u> , 1
21 Cerebellum (0=large; 1=small)	–	–	0	0	0	0	1	<u>0</u> , 1	<u>0</u> , 1	1	1
22 Dorsal and ventral horns (0=present; 1=absent)	0	0	0	0	0	0	1	0	0	<u>0</u> , 1	1
23 Lateral motor column (0=present; 1=absent)	0	0	0	–	–	–	<u>0</u> , 1	0	0	0	0

Some taxa possess multiple character states. For these taxa, the character state that is assumed to be primitive is underlined, and the underlined state was used in the analysis.

¹ The sister group of bolitoglossines varies among the characters. For some characters, families of salamanders other than the Plethodontidae were used. For other characters, tribes of the Phlethodontidae other than Bolitoglossini were used. For each character, the outgroup taxon is given in the text.

* Indicates uncertain homologies.

Paedomorphosis is often invoked to explain aspects of salamander evolution. A well-known example is perennibranchiation, a type of paedomorphosis in which sexual maturity is attained at the ancestral chronological time, but metamorphosis is delayed [Gould, 1977]. Perennibranchiate genera include *Proteus*, *Necturus*, *Siren*, *Typhlomolge* and the axolotl (*Ambystoma mexicanum*), a species whose closest congeneric relatives metamorphose before sexual maturation. Although perennibranchiation is a type of paedomorphosis, it is not the most extreme type of paedomorphosis exhibited by salamanders. Perennibranchiate species of *Ambystoma* differ from their metamorphosing relatives only in relatively few traits (i.e., the retention of gills and an unlayered epidermis, and the absence of eyelids), and have essentially fully developed nervous systems. In contrast to the axolotl, many taxa, such as the bolitoglossine plethodontids, exhibit a more profound paedomorphosis, in which many parts of both the central nervous system and special sensory systems never develop beyond embryonic stages.

Genome Size, Cell Size and Paedomorphosis

We hypothesize that secondary simplification in the salamander nervous system results principally from enlarged genome size. Differences in genome size among vertebrates are due not only to polyploidy (which occurs in some populations of ambystomatids as well as in some fishes) but also to an increase in middle-to-highly repetitive DNA sequences [Horner and MacGregor, 1983]. There is no universal agreement on the origin and significance of increased genome size in vertebrates. Apparently, genome size tends to increase until the tendency is halted by countervailing selection (i.e., the selfish DNA hypothesis) [Orgel and Crick, 1980].

Genome size varies enormously among vertebrates [Olmo, 1983]. The smallest genome is found in teleost fishes, with less than 1 pg DNA per haploid nucleus. Some salamanders and all lungfishes have haploid genome sizes between 70 and 142 pg, the largest genomes found in any animals. Average genome sizes for amniotes are 2.5 pg for reptiles, 1.5 pg for birds, and 3.3 pg for mammals [Olmo, 1983]. (Note: only haploid genome sizes are reported here, although some authors, including Olmo, report diploid genome sizes.)

In salamanders, the smallest genome (13.7 pg) is found in the plethodontid *Desmognathus wrighti* [Hally et al., 1986; Sessions and Larson, 1987], and the largest (83 pg) is found in the neotenic (perennibranchiate) *Necturus maculosus* [Olmo, 1983]. The plethodontid salamander *Hydromantes italicus* (77 pg) appears to have the largest genome

of any terrestrial animal, although several tropical bolitoglossine plethodontids (e.g., *Bolitoglossa subpalmata*, 64 pg) approach this value [Sessions and Larson, 1987]. Species of the Bolitoglossini, on average, have larger genome sizes than other plethodontids and than other salamander families, except for the perennibranchiate species [Olmo, 1983; Sessions and Larson, 1987].

Among plethodontid salamanders, genome size appears to have increased many times independently, especially in the tribes Plethodontini and Bolitoglossini [Sessions and Larson, 1987]. However, a recent phylogenetic analysis concludes that several terrestrial plethodontid species have undergone a secondary reduction of genome size, which counteracts the general increase in genome size seen in terrestrial plethodontids. In *Thorius*, for example, the decrease is about 27% from the postulated ancestral bolitoglossine genome size of 34.5 pg [Sessions and Larson, 1987].

Frogs generally have the smallest genomes found among amphibians. Among anurans, the mean genome size is 3.3 pg [Olmo, 1983]. The smallest (about 1 pg) is found in *Limnodynastes ornatus*, and the largest is found in *Arenophryne rotunda* (19 pg) [Mahony, 1986]. *Arenophryne rotunda* has the largest neurons and the least differentiated brain found among anurans [Roth et al., in prep.]. *Bombina* has a relatively large genome (10 pg) [Olmo, 1983], and also shows clear signs of secondary simplification in neural (e.g., reduction of lamination of the tectum and torus) as well as non-neural characters (e.g., reduction of middle and inner ear structures) [Smirnov, 1989, 1990].

Caecilians have genome sizes intermediate between those of salamanders and anurans. The largest known caecilian genome is 13.2 pg per haploid nucleus [M. Wake, pers. comm.]. Like salamanders, caecilians have many secondarily reduced neural and non-neural characters. Of the 19 characteristics that are most parsimoniously interpreted as secondarily simplified in salamanders, 7 are also secondarily simplified in caecilians (table 1). From the few characters studied in detail, the degree of simplification of caecilians appears to lie between that of anurans and salamanders.

Increase in genome size has many important morphological correlates, including: (1) increase in cell size; (2) decrease in cell metabolic rate; (3) decrease in cell division rate; and (4) decrease in cell differentiation rate [Sessions and Larson, 1987]. Compared to other vertebrates, salamanders in general, and bolitoglossines in particular, have large to very large cells, very low metabolic rates [Feder, 1983], and slow to extremely slow developmental rates [Sessions and Larson, 1987]. The ova of plethodontine and

bolitoglossine salamanders are large to very large (up to 9 mm in diameter), and they develop very slowly [Collazo, 1990]. *Bolitoglossa* may take 10 or more months to hatch [Hanken, 1979; Houck, 1982; Collazo, 1988].

In salamanders, there is a negative association between genome size and degree of morphological differentiation of the nervous system. Species with small genomes have more, smaller nerve cells per volume of gray matter, their neurons are more differentiated morphologically, and the number and degree of lamination of migrated nuclei (e.g., within the tectum) are higher than in species with larger genomes [Roth et al., 1988b, 1990b]. Although the causal relationship between genome size and retardation of brain development remains unknown, we suggest that there may be both general effects of low metabolic rate on brain development and more specific effects, such as retarded expression of developmental genes or disturbance of epigenetic tissue interactions. For example, migration of neural crest cells depends on the synchronous maturation of extracellular matrix components and cell surface molecules, and is blocked by temporal dissociation of these processes in the axolotl [Löfberg et al., 1989; Newgreen, 1989].

The hypothesis of a causal relationship between secondary simplification and an increase in genome size is corroborated by the fact that simplification of the brain and sense organs is observed in both salamanders and lungfishes, the two vertebrate groups with the largest genomes. Among dipnoans, the genome size is 80 pg per haploid nucleus in *Neoceratodus*, 111 pg in *Lepidosiren*, and 142 pg in *Protopterus* [Olmo, 1983]. *Protopterus* possesses the largest known genome of any living vertebrate. Of the 19 characters that are secondarily simplified in salamanders, four are also secondarily simplified in dipnoans, and 11 are secondarily simplified in lepidosirenid lungfishes. Because lungfishes and amphibians are more closely related to relatively less paedomorphic species (i.e., *Latimeria* and frogs, respectively) than they are to each other, simplification must have occurred independently in these taxa.

Compensation for Morphological Simplification

The simplification of the salamander nervous system would be adaptive if it were the result of natural selection for a specific functional role. At present, it remains unclear whether simplification of the salamander brain is the result of natural selection, of a selfish DNA mechanism, of developmental constraints, or some combination of these factors. However, evolution toward more specialized sense organs or toward a more complex nervous system usually is

viewed as resulting from adaptive processes. An adaptive explanation is problematic in the case of loss or reduction of sensory and brain structures in salamanders, because these same structures appear to be advantageous in other vertebrates. Evolutionary reduction is not necessarily maladaptive, however, as is demonstrated by the hyoid apparatus of some bolitoglossine salamanders. Because of incomplete chondrification, salamanders of the genus *Thorius* are able to protract their tongues more efficiently than related taxa [Lombard and Wake, 1977; Wake, 1982].

In virtually every respect, bolitoglossine salamanders exhibit the most extreme simplification of the nervous system found among vertebrates. Yet, this lineage appears to be the most 'progressive' among salamanders. Bolitoglossines are speciose (constituting about 50% of living salamander species), and have undergone an extensive adaptive radiation in the Neotropics (they are the only tropical salamanders). They lack larvae and have direct development, they have diverse locomotor specializations, including acrobatic ability for life in three-dimensional environments (e.g., walls of caves, trees, bromeliads, etc.), and they have highly developed and extremely specialized feeding and visual systems [Wake, 1966, 1987; Wake and Lynch, 1976; Lombard and Wake, 1977, 1986; Roth, 1987]. In fact, bolitoglossines have the most effective visually-guided feeding systems found among salamanders. For example, *Hydromantes*, using a tongue that is projected up to 70% of head plus body length, virtually never misses prey (small insects), even when the prey is moving rapidly. These salamanders are able to catch prey with their tongues not only at substantial distance, but also at a wide angle from the mouth and from a variety of head and body positions.

The bolitoglossine retina contains the fewest photoreceptors and retinal ganglion cells, the simplest cell morphology and the lowest degree of myelination of optic nerve fibers found among salamanders that depend on vision. Yet, electrophysiological studies demonstrate a high level of visual resolution power of retinotectal fibers among bolitoglossines [Wiggers and Roth, in prep.].

The bolitoglossine tectum has the fewest cells and the lowest degree of cell migration and morphological differentiation among salamanders with good vision. Yet, electrophysiological recordings from bolitoglossines show that the visual response characteristics of tectal neurons are essentially indistinguishable from those of anurans, which have highly developed visual systems with 10 to 20 times as many neurons and a much higher degree of morphological differentiation and cell migration [Roth, 1987].

We believe that the functional integrity of the brain can be maintained, despite profound paedomorphosis, by the process of ontogenetic repatterning [Roth and Wake, 1985b; Wake and Roth, 1989]. Ontogenetic repatterning refers to non-terminal changes in the temporal sequence of ontogenetic processes, including the loss or incomplete formation of traits that develop in non-terminal stages (e.g., the embryonic or larval branchial apparatus) and the re-ordering of developmental events (e.g., precocious formation of ipsilateral visual neuropils in bolitoglossine embryos, see below). Ontogenetic repatterning establishes new sources of variation by uncoupling processes that previously were organized in particular ontogenetic sequences. Such uncoupling may offer an escape from specialization [Lauder, 1981; Roth and Wake, 1989]. Dramatic ontogenetic changes, such as loss of the larval stage, establish a framework of embryonization [Matsuda, 1987] in which ontogenetic repatterning is most profound. In the bolitoglossine salamanders, embryonization has contributed importantly to ontogenetic repatterning by slowing embryogenesis and providing an opportunity for re-ordering.

Despite profound simplification, the visual system of bolitoglossines remains effective because of: (1) an increase in cell packing density; (2) a ratio of about 1:1 between photoreceptors and retinal ganglion cells, which makes the whole retina a functional fovea [Linke et al., 1986]; and (3) enlargement of the projection areas of retinofugal fibers from the temporal retina (corresponding to the central binocular visual field) onto the tectal surface, which increases visual resolution power in the binocular visual field at the expense of monocular peripheral vision [Roth, 1987; Wiggers and Roth, in prep.].

The clearest example of how functional integrity has been maintained by ontogenetic repatterning despite profound simplification comes from the visual system of bolitoglossine salamanders. We believe that bolitoglossines owe the functional integrity of their visual systems to the precocial development of ipsilateral retinotectal fibers and to an increase in the number of these fibers. In bolitoglossines, these fibers cover the whole tectum in a deep layer, and the rostral tectum (corresponding to the temporal retina and the central, binocular visual field) in a superficial layer [Rettig and Roth, 1986]. Their presence increases the resolution power of the retina, but their main function seems to be enhancement of stereopsis [Roth, 1987; Wiggers and Roth, 1991].

Depth perception in amphibians appears to be based on the disparity between the tectal images of an object coming from the two eyes. In most amphibians, stereopsis is based

on disparities between direct contralateral and indirect (via nucleus isthmi) ipsilateral retinal inputs to each tectal hemisphere. The indirect ipsilateral input is characterized by a delay of 30 ms, which slows the process of depth perception and decreases its accuracy. In bolitoglossines with substantial direct ipsilateral input to the tectum, the comparison between information coming from the two eyes can be made directly in each tectal hemisphere, with virtually no time delay between the two images (in addition to the 'conventional' indirect system, which also is present) [Wiggers and Roth, 1991]. Direct ipsilateral retinotectal projections are always present in amphibians, but these seem to play little, if any, role in depth perception in frogs or salamanders other than plethodontids.

We believe the evolutionary increase in number of ipsilateral fibers and in the size of their projection fields in plethodontids, especially bolitoglossines, is an outcome of both secondary simplification and ontogenetic repatterning. The development of incompatibility between contralateral and ipsilateral retinotectal fibers is a plesiomorphic character for vertebrates, which results in elimination of most ipsilateral fibers early in development. Paedomorphosis has resulted in loss of this incompatibility, and consequent retention of ipsilateral fibers.

However, paedomorphosis alone cannot explain why there are more ipsilateral fibers in the bolitoglossine tectum than in the tecta of other amphibians at any stage of development, or why these fibers develop so much earlier than in outgroups. Accordingly, we must incorporate into our hypothesis an additional, adaptive, repatterning mechanism to explain the substantial increase in numbers of ipsilateral fibers, their precocious development and the increased acuity of vision and depth perception that result from their presence in the bolitoglossine salamanders.

Conclusions

Phylogenetic analysis shows that, of the 23 characters we analyzed, 19 are most parsimoniously interpreted as secondarily simplified from a more complex ancestral condition. Among vertebrates, lepidosirenid lungfishes and caecilians also frequently exhibit secondary simplification. Simplification of the brain and sense organs of salamanders is likely the result of the retention of an undifferentiated, embryonic morphology into adulthood (i.e., an evolutionary pattern of paedomorphosis). We hypothesize that paedomorphosis results from increased genome size, which is positively correlated with cell size, and negatively correlated with cell proliferation and differentiation rates. This

hypothesis is supported by the fact that salamanders, caecilians and dipnoans, especially the lepidosirenids, share both a large genome size and a pattern of paedomorphic reduction of the brain and sense organs. Finally, although large genome size and paedomorphosis tend to compromise the functional integrity of the salamander brain, compensating mechanisms have evolved that restore or even enhance brain function.

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