# Evolution of the basal ganglia in tetrapods: a new perspective based on recent studies in amphibians

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**It has been postulated frequently that the fundamental organization of the basal ganglia (BG) in vertebrates arose with the appearance of amniotes during evolution. An alternative hypothesis, however, is that such a condition was already present in early anamniotic tetrapods and, therefore, characterizes the acquisition of the tetrapod phenotype rather than the anamniotic–amniotic transition. Re-examination of the BG organization in tetrapods in the light of recent findings in amphibians strongly supports the notion that elementary BG structures were present in the brain of ancestral tetrapods and that they were organized according to a general plan shared today by all extant tetrapods.**

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THE BASAL GANGLIA (BG) constitute key brain structures that play a prominent role in motor functions, in particular in the planning, initiation and execution of movement[1]. Most of our current knowledge about the involvement of the BG in motor functions has been derived from the study of human disorders, in particular Parkinson's and Huntington's diseases, and from animal (mammalian) models mimicking these diseases[2–5]. In addition, it is now generally accepted that the BG are involved in a variety of non-motor functions, including those related to incentive and motivated behaviors[6].

Research during the past two decades has led to the conclusion that numerous similarities exist in the organization of the BG of extant reptiles, birds and mammals (that is, amniotic vertebrates), suggesting that a comparable organization was already present in the ancestors of amniotes[7–11]. On the contrary, it has been pointed out that major differences in the organization of the BG between living amniotes and anamniotes (that is, fish and amphibians) might exist, suggesting that well-developed BG evolved only at the anamniote–amniote transition during evolution[9]. However, recent studies have shown that fundamental features of BG organization, as seen in amniotes, already exist in the brain of extant amphibians, whose ancestors are known to have given rise to the reptile-like vertebrates in the Carboniferous period. This article summarizes recent findings on the BG of tetrapods that provide a new perspective to the evolution of the BG in vertebrates.

## Dorsal and ventral striatopallidal systems

In a restrictive sense, the term basal ganglia refers to the striatal and pallidal components of the basal telencephalon that develop from the lateral and medial ganglionic eminences, respectively. The term, however, frequently includes the substantia nigra (SN), the ventral tegmental area (VTA) and the subthalamic nucleus (STN), because of their close anatomical and functional relationship with the striatum and the pallidum[12]. In mammals, the BG are subdivided into two distinct components, both comprising striatal and pallidal structures, that is, the dorsal and the ventral striatopallidal systems[13]. The dorsal striatopallidal system consists of the dorsal striatum or striatum proper (caudate nucleus and putamen in felines and primates, caudate–putamen in other mammals) and the dorsal pallidum (Fig. 1). The dorsal pallidum is subdivided into two parts with distinct chemoarchitecture and connectivity, as regards the external segment of the globus pallidus (GPe; primates) or merely the globus pallidus (GP; non-primates), and the internal segment of the globus pallidus (GPi; primates) or entopeduncular nucleus (EP; non-primates)[4,5,9,13]. The ventral striatopallidal system is constituted by the ventral striatum (the nucleus accumbens and part of the olfactory tubercle) and the ventral pallidum (Fig. 1)[13,14]. The striatal nature of the nucleus accumbens and the medium-sized cell portion of the olfactory tubercle has been established on the basis of their development, connections and chemoarchitecture[15–19]. The ventral pallidum, on the other hand, shares some features with both segments of the dorsal pallidum[13].

Comparative studies have provided substantial evidence for a conservative structural plan in the basal telencephalon of tetrapods. Thus, the BG in birds and reptiles (sauropsids) also consist of dorsal and ventral striatopallidal systems (Fig. 1)[20–22]. Furthermore, recent studies have demonstrated a similar BG organization in amphibians (Fig. 1)[23]. Of note is the fact that the dorsal pallidum in non-mammalian tetrapods does not possess anatomical subdivisions. As in mammals, the dorsal and ventral striatopallidal systems of sauropsids and amphibians have distinct connections with the forebrain, midbrain and isthmus, suggesting that both systems are involved in partially segregated circuits in all tetrapods (Fig. 2).

The existence of dorsal and ventral striatopallidal systems in the brain of all tetrapods has a major implication for the understanding of the organization of the basal telencephalon. Since the ventral striatum

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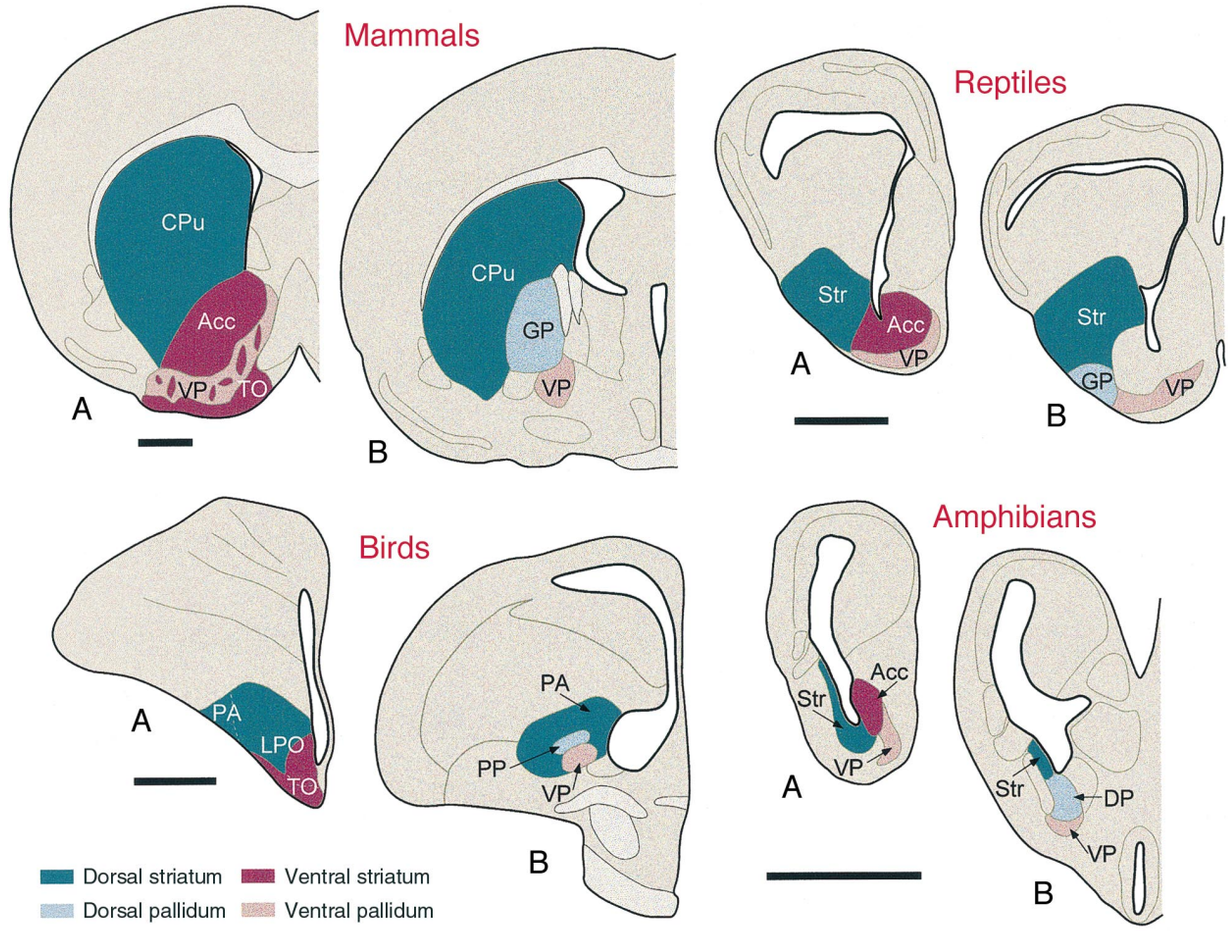
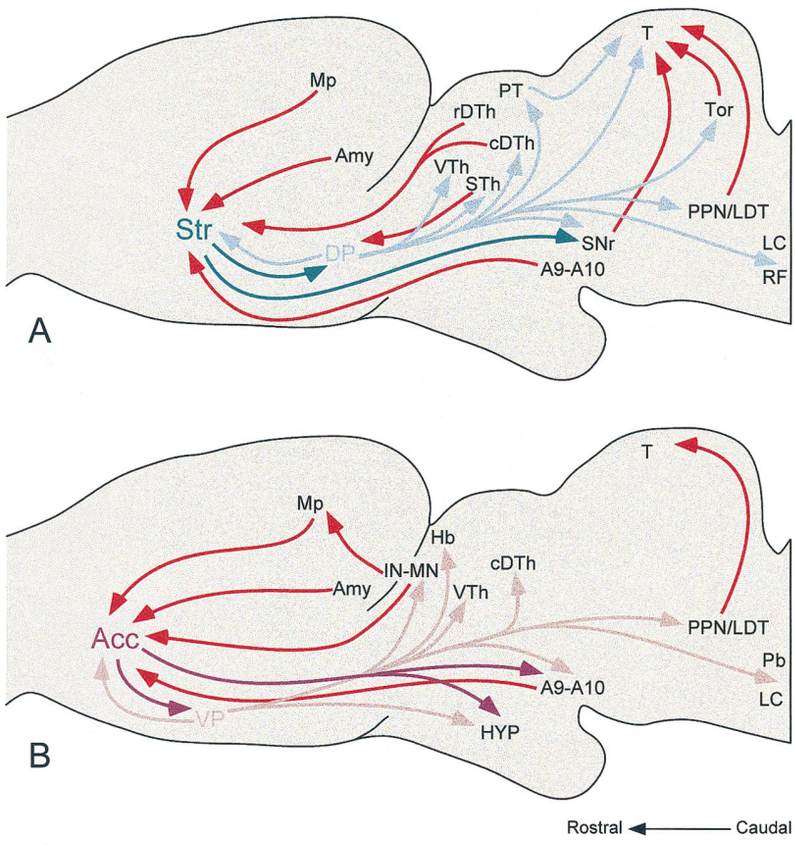



**Fig. 1.** ***The dorsal and ventral striatopallidal systems.*** *The basal ganglia are organized into dorsal and ventral striatopallidal systems in all tetrapods. For each vertebrate class, two representative transverse brain sections (***A****, rostral;* ***B****, caudal) illustrate the relative position of striatal and pallidal structures. Although in the literature different names have been given to homologous structures, the same colors have been used for comparable regions in each tetrapod, to simplify identification. Scale bars, 1 mm. See Box 1 for abbreviations.*




and the ventral pallidum constitute the extension of the dorsal striatum and the dorsal pallidum to the surface of the brain, the striatal and pallidal components of the BG comprise two distinct rostro-caudally adjacent compartments in the basal telencephalon. The existence of such compartments in all tetrapods is supported by the pattern of expression of different sets of homeobox genes, which appear to play an important role in the regional specification of the telencephalon. For example, genes of the *dlx* class delineate the BG anlage during the early development of the basal telencephalon in mammals, birds and amphibians (Refs 24,25 and J. Rubenstein, pers. commun.), and are essential for the differentiation of the striatum[26]. In addition, the expression of the *nkx-2.1* gene specifically demarcates the medial ganglionic eminence, which is thought to give rise to the globus pallidus, among other structures[27].

## Neuronal cell types in the striatum

The dorsal and ventral striatum share numerous cytoarchitectural and neurochemical features. The spiny projection neuron is the most abundant neuronal type

**Fig. 2.** ***Basal ganglia connections in ancestral tetrapods.*** *The putative connections of the dorsal* **(A)** *and ventral* **(B)** *striatopallidal systems in ancestral tetrapods can be inferred from a comparative analysis of the basal ganglia organization in extant tetrapods. See Box 1 for abbreviations.*

in the striatum and contains the inhibitory neurotransmitter GABA (Refs 11,28). Two distinct populations of projection neurons are distinguished in the amniotic striatum: (1) GABAergic cells containing the preprotachynin peptides substance P (SP) and dynorphin (DYN); and (2) GABAergic cells containing the preproenkephalin neuropeptide enkephalin (ENK)[11,28]. Distinct sets of SP and ENK striatal neurons have been demonstrated in the striatum of amphibians[29], suggesting that the existence of two largely segregated populations of striatal projection neurons is a primitive feature of the BG in tetrapods. The striatum of amniotes also contains different classes of local circuit neurons, including cholinergic and GABAergic interneurons. The existence of striatal cholinergic interneurons seems to be a primitive feature of the BG in tetrapods[30]. On the other hand, distinct cell populations of GABAergic interneurons are present in the striatum of amniotes, which are distinguished on the basis of their chemical content in calcium binding proteins (parvalbumin, calretinin), neuropeptides (somatostatin, neuropeptide Y), or nitric oxide synthase[31–35]. Since most of the chemical markers of the striatal GABAergic interneurons of amniotes are present in extant amphibians[23], it can be hypothesized that at least some of those subtypes of local circuit neurons could have been already present in the brain of ancestral tetrapods.

### Cortical and thalamic inputs to the striatum

The striatum is the major receptive structure of the BG in all tetrapods and receives its main inputs from the cortex (or pallium), the thalamus and the dopaminergic neurons of the VTA–SN complex. Afferents from the cortex (or pallium) and the thalamus provide the striatum with a direct access to diverse and multimodal information, although substantial differences exist in the extent and degree of organization of these projections among tetrapods.

In mammals, virtually all cortical areas contribute to the innervation of the striatal territories, giving rise to a complex representation of the functional cortical map at the striatal level[4,9]. Cortical afferents to the dorsal striatum arise primarily from the isocortex, whereas those to the ventral striatum have their origin mainly in the allo-, periallo- and proisocortical areas, and in the cortical-like basolateral amygdaloid complex[13]. In contrast, the dorsal ventricular ridge (DVR), a telencephalic structure that is embryologically derived from the pallium, is the major source of projections to the striatum in sauropsids[36,37]. The nature of this telencephalic structure is still a matter of debate. Alternatively, the DVR has been compared, to some extent, to the mammalian isocortex, basolateral amygdaloid complex, or claustrum (see Ref. 38 for a review). In addition, the striatum of birds and reptiles receives projections from other pallial regions, such as the Wulst and the dorsal cortex, respectively[36,37]. Thus, the existence of striatal afferents from the telencephalic mantle is a feature shared by all amniotes, although a dramatic increase in the number and complexity of the corticostriatal projections characterizes the transition from non-mammalian to mammalian amniotes. In contrast to early hypotheses[9,39], recent studies have demonstrated the existence of palliostriatal connections in living amphibians[40].

The evolution of thalamic afferents to the striatum has been related to the expansion of the cortex and, consequently, to the elaboration of the corticostriatal system. In mammals, direct thalamic afferents to the striatum originate primarily in the midline and intralaminar nuclear complex that relays diverse multimodal information to specific parts of the striatum and the cortex[41]. Specific sensory information, on the contrary, reaches the BG primarily via thalamo–corticostriatal connections, although striatal afferents from certain specific relay nuclei in the thalamus do exist[13]. In sharp contrast, projections from specific sensory thalamic nuclei are the main afferents of the striatum in living amphibians[40] and, therefore, sensory information of different modalities is essentially relayed to the amphibian BG without involvement of the telencephalic pallium.

## Box 1. Abbreviations

| | |
|---|---|
| III | nucleus nervi oculomotorii |
| A9 | substantia nigra pars compacta |
| A10 | ventral tegmental area |
| Acc | nucleus accumbens |
| Ad | anterodorsal tegmental nucleus |
| Amy | amygdala |
| Av | anteroventral tegmental nucleus |
| BG | basal ganglia |
| cDTh | caudal dorsal thalamic nuclei |
| CPu | caudate–putamen |
| DP | dorsal pallidum |
| DVR | dorsal ventricular ridge |
| EP | entopeduncular nucleus |
| GP | globus pallidus |
| Hb | habenula |
| HYP | hypothalamus |
| IN/M | intralaminar midline-like nuclei |
| Ist | isthmic segment |
| Jc | juxtacommissural pretectal nucleus |
| LC | locus coeruleus |
| LDT | laterodorsal tegmental nucleus |
| LPO | lobus parolfactorius |
| M | mesencephalic segment |
| Mp | medial pallium |
| Ncp | nucleus of the posterior commissure |
| nPT | nucleus pretectalis |
| oc | optic chiasm |
| p1 | prosomere 1 |
| p2 | prosomere 2 |
| p3 | prosomere 3 |
| PA | paleostriatum augmentatum |
| Pb | parabrachial nucleus |
| PP | paleostriatum primitivum |
| PPN | pedunculopontine nucleus |
| PT | pretectal region |
| rDTh | relay dorsal thalamic nuclei |
| RF | raphé nuclei |
| SC | superior colliculus |
| SN | substantia nigra |
| SNL | substantia nigra lateralis |
| SNr | substantia nigra pars reticulata |
| SpL | nucleus spiriformis lateralis |
| SPr | secondary prosencephalon |
| STh | subthalamus |
| Str | striatum |
| T | tectum mesencephali |
| TO | olfactory tubercle |
| Tor | torus semicircularis |
| VP | ventral pallidum |
| VTh | ventral thalamus |

## Box 2. The segmental concurrence of the A9–A10 cell groups in tetrapods

The dopaminergic innervation of the striatum constitutes one of the most important features of the organization of the basal ganglia in tetrapods (BG)[a–c]. However, essential differences in the localization and development of the dopaminergic cell groups that project to the basal telencephalon have been thought to exist in amphibians and amniotes (reptiles, birds and mammals)[b]. In amniotes, the BG receive a strong dopaminergic input primarily from the substantia nigra pars compacta (A9) and the ventral tegmental area (A10). The ventromedially located A10 cell group as well as the dorsolaterally extending A9 cell group are considered classically to be located in the mesencephalic tegmentum[a,b]. In contrast, the dopaminergic neurons projecting to the basal telencephalon in amphibians constitute a continuous field along the rostrocaudal axis of the diencephalic–mesencephalic basal plate, extending from the retromammillary region to the level of the exit of the oculomotor nerve[c,d]. The apparent differences in topography of these cell groups in amniotes and amphibians have traditionally constituted a strong argument against their homology. However, when a segmental approach is applied to the localization of the dopaminergic cell groups in the brain of vertebrates, a different conclusion can be reached (Fig. A). Recent developmental studies have provided evidence that the brains of all vertebrates possess equivalent units or segments and, thus, the segmental paradigm constitutes a suitable tool to study evolutionary variation in forebrain organization among tetrapods[e,f]. In that respect, the A9–A10 cell groups of amniotes are not restricted to the mesencephalic tegmentum but extend into diencephalic (prosomeres p1–p3) and isthmic segments[g–i]. In mammals, the A9 cell group consists of at least three different segments (p2, p1 and midbrain), whereas the A10 cell population comprises distinct p3, p2, p1, mesencephalic and isthmic portions. In amphibians, the dopaminergic cell field corresponding to the paramedian A9–A10 cell complex of amniotes is almost completely present, although they lack a laterally migrated

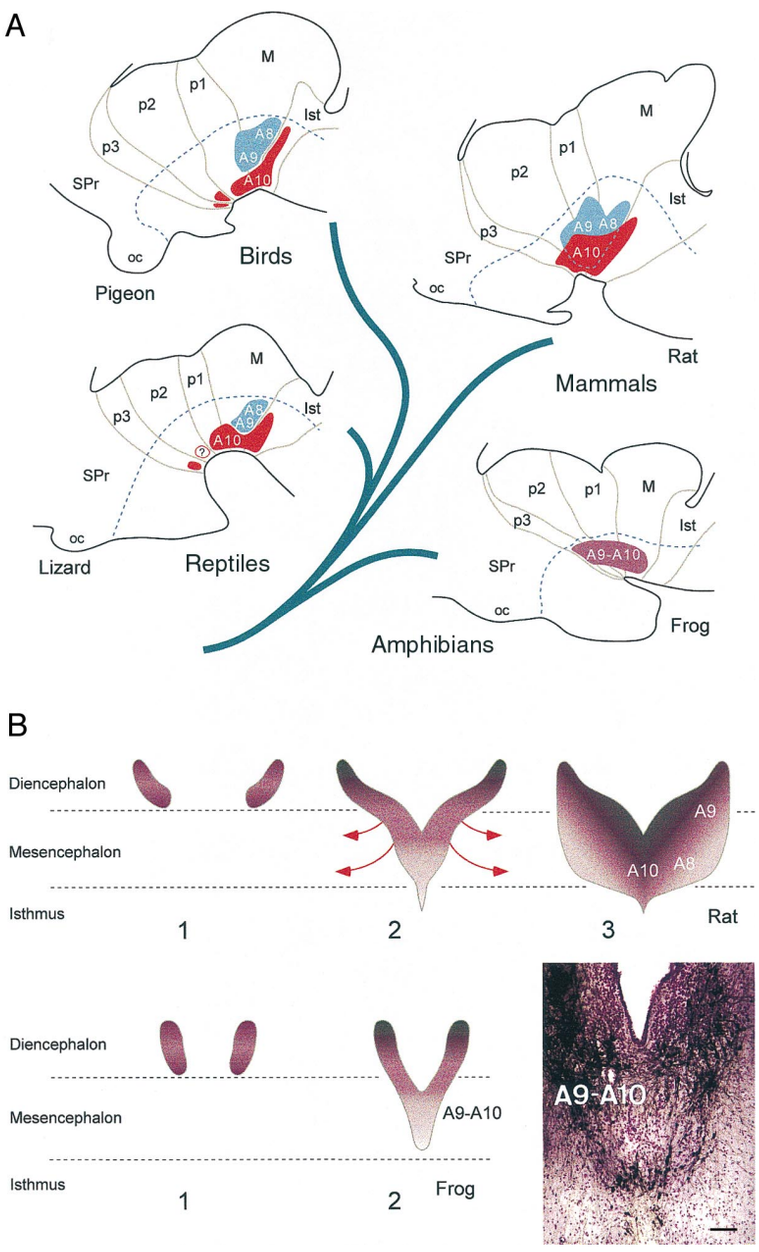



**Fig.** ***Localization and development of the dopaminergic A8–A10 cell groups in tetrapods.*** **(A)** *A comparative segmental approach is applied to the study of the distribution of the dopaminergic cells in the ventral tegmental area (A10), substantia nigra pars compacta (A9) and retrorubral field (A8) in tetrapods. The localization of these cell groups, with special reference to neuromeric boundaries, is depicted in schematic drawings of midsagittal sections of representative brains belonging to the four classes of vertebrate tetrapods. The segmental boundaries are marked by solid lines, whereas the interrupted line indicates the boundary between basal and alar plates. In all tetrapods, a continuous paramedian population of dopaminergic cells extends across several diencephalic and mesencephalic segments.* **(B)** *Comparison of the development of the A9–A10 cell groups in mammals and amphibians suggests a common process for the generation of the dopaminergic neurons along the rostrocaudal brain axis (steps 1 and 2). In the drawings, the more intense color within the limits of the cell group corresponds to the position of older cells. On the other hand, the gradual migration of cells into the lateral zone of the A8–A9 cell groups, as observed in mammals (red arrows), does not occur in amphibians (step 3). The photomicrograph illustrates the localization of the A9–A10 cell group in a horizontal section through the brain of the adult frog, which resembles the situation in mammals before the lateral migration (step 2). See Box 1 for abbreviations. Scale bar, 100 μm.* Modified after Refs g,h,l and n.

Multimodal sensory and limbic information is relayed to the amphibian striatum and pallium by the anterior thalamic region. An intermediate condition is found in sauropsids, where specific sensory thalamic nuclei project to the dorsal cortex and the DVR, but also to the striatal components of the BG (Refs 37,42). Furthermore, a region of the dorsal thalamus of sauropsids appears to be largely comparable to the entire intralaminar, mediodorsal and midline thalamic nuclear complex of mammals, providing widespread projections to the striatum and the pallium[43]. In conclusion, the existence of direct sensory inputs from the thalamus to the striatum seems to be a primitive feature of the BG in tetrapods (Fig. 2). A major evolutionary trend is, however, the progressive involvement of the cortex in the processing of the thalamic sensory information relayed to the BG of tetrapods. It also seems likely that the striatum of the common ancestors of tetrapods has been the target of the projections of a dorsal thalamic nuclear complex that receives inputs of diverse and multimodal nature (Fig. 2). In contrast to the specific sensory thalamic nuclei, the midline intralaminar

substantia nigra and retrorubral field, as well as the isthmic portion of the A10 complex (Fig. A)[d]. Developmental studies using the segmental approach have demonstrated that the dopaminergic cells of the diencephalic prosomeres (p1–p3) of amphibians, like the corresponding cell groups in birds and mammals, develop earlier than those in the midbrain and isthmic segments (Fig. B)[g,j–n]. Accordingly, the first dopaminergic cells projecting to the basal telencephalon are found in the rostrolateral portions of the developing A9–A10 complex and reach the striatum before the nucleus accumbens[g,h,j–m]. As in the adult brain, however, misunderstanding of the boundaries between the diencephalon, mesencephalon and isthmus during development has led traditionally to the erroneous conclusion that the mammalian A9–A10 cell groups originate from the isthmic region (see Refs g and n for discussion and references). The segmental approach of the development of the A9–A10 cell groups gives further support to the notion that the organization of the dopaminergic innervation of the BG of tetrapods is highly conservative. The amphibian homologs of the A9–A10 cell groups might, therefore, exemplify an early stage in the evolution of these structures in tetrapods, which most probably have evolved further in amniotes by increasing their number of cells and expanding caudally and laterally, in parallel with the increase of the striatal territories (see Fig. 1).

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nuclei are involved in non-discriminative or affective aspects of the information, which might be required to prevent the organism from potentially dangerous situations and, therefore, possess an obvious adaptative value[41].

## The dopaminergic innervation of the striatum

The dopaminergic innervation of the dorsal and ventral components of the striatum is one of the most conservative features of the BG in tetrapods[44]. The question of whether the dopaminergic innervation of the basal telencephalon of amniotes is similar to that of amphibians has been puzzling for a long time (Box 2). Recent evidence, however, supports the hypothesis that ancestral tetrapods already possessed dopaminergic cell groups that could be considered to be homologous to both the substantia nigra pars compacta (SNc, A9 group) and the VTA (A10 group) of amniotes (Fig. 2). The presence of highly organized dopaminergic projections to the dorsal and ventral striatum in all tetrapods points to a remarkably conserved modulatory mechanism of the striatal function. In mammals, one of the main functions of the dopaminergic innervation is to modulate the cortical or thalamic inputs directly on the striatal projection neurons[45]. It seems conceivable that, independently of the origin and nature of other striatal afferents, the dopaminergic input to the striatum might play a similar role in other tetrapods. Depletion of dopaminergic input to the BG modifies the normal motor behavior in all tetrapods[46–50], suggesting that dopamine can have a fundamental effect on striatal function.

## The substantia nigra: a phylogenetically dual structure

The mammalian SN is a highly heterogeneous structure that comprises at least two distinct components, the pars compacta (SNc) and the pars reticulata (SNr). The SNc is a major source of dopamine in the striatum, whereas the SNr contains GABAergic neurons and is the main recipient of the striato–nigral pathway[51]. Despite the close topographical relationship of both components, it is clear that the mammalian SN is a functionally dual structure[9]. The mesencephalic tegmentum of sauropsids and amphibians also contains a population of GABAergic neurons in the place where striatal projections form a conspicuous network, which is, therefore, considered homologous to the mammalian SNr (Refs 21,52–54). However, the topographical relationship between the SNc and the SNr varies greatly among tetrapods (Fig. 3). In amphibians and lizards the striato–nigral pathway terminates primarily lateral to the SNc (Refs 53–55), whereas in turtles and rats the terminal field of striatal fibers lies primarily ventral to the SNc (Refs 51,55). In sharp contrast, extensive overlap between the striato–nigral fibers and the SNc occurs in crocodiles, snakes, pigeons and primates, including humans[9,55,56]. The close topographical relationship between the SNr and the SNc reached in some tetrapods might confer a number of advantages. For example, it allows a simultaneous influence of the striato–nigral projections on both components of the SN, as well as a dopaminergic control of the striatal inputs to the SNr through dendritically released dopamine from the SNc (Ref. 51). On the basis of these data, it seems likely that the SN is not only a functionally dual structure in all tetrapods, but also that both components of the SN have evolved separately, converging only in some tetrapods. Recent data about the development of the SNr in humans support the latter hypothesis[57]. Remarkably, the GABAergic neurons of the SNr in humans appear to be generated in the region of the alar plate contiguous to the basal plate, resembling the condition found in embryonic and adult amphibians and lizards (Fig. 3). Later in development, they migrate ventromedially, invade the basal plate and partially overlap with the SNc. These observations suggest that the SN

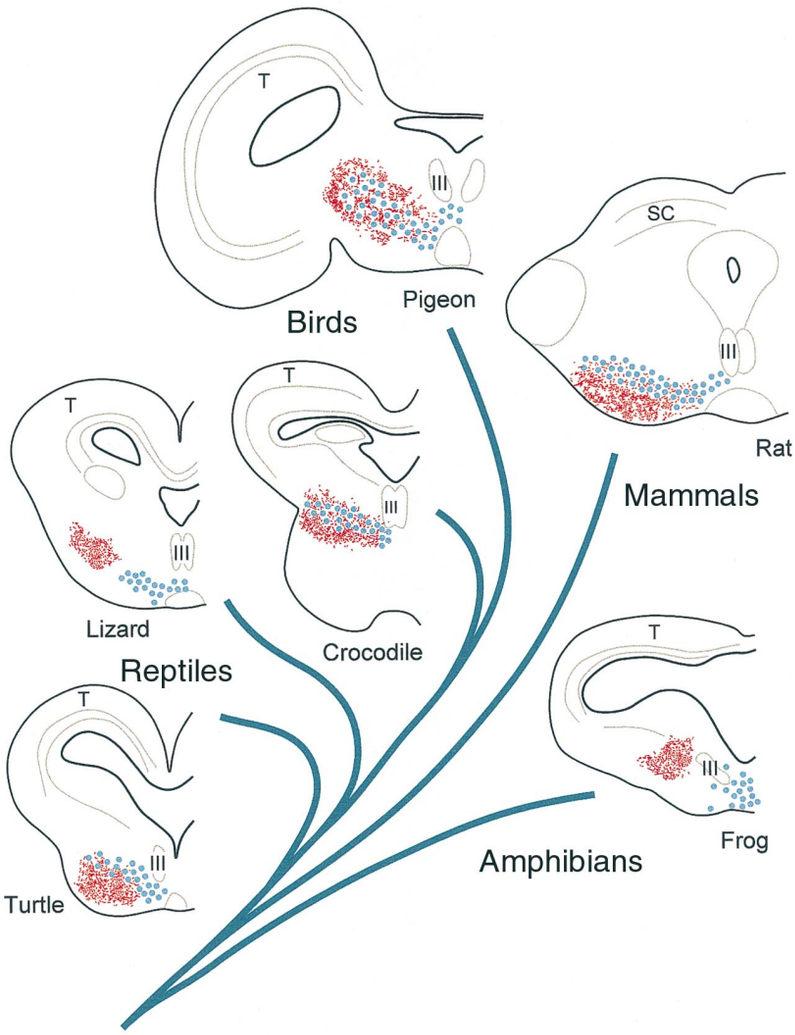


**Fig. 3.** ***Evolution of the striato–nigral pathway in tetrapods.*** *Different conditions can be recognized among tetrapods in the topographical relationship between the terminal field of the striato–nigral projection (red dashes and small dots) and the dopaminergic cell bodies of the substantia nigra pars compacta and the ventral tegmental area (blue large dots). As shown in the phylogenetic tree of transverse sections of representatives of the four classes of tetrapods, complete separation, partial or total overlapping of both components occurs. See Box 1 for abbreviations.*

in all tetrapods might consist of a floor- or basal-plate-derived cell group (SNc) and an alar-plate-derived cell group (SNr). In that perspective, the differences found in the pattern of organization of the SN among tetrapods could be attributed to the degree of migration of each component. As suggested for other brain regions, the modifications of the general plan of organization of homologous structures are most probably generated by a limited set of developmental mechanisms.

## Re-entrant circuits versus output pathways

In mammals, the pallidum (GPi or EP and VP) and the SNr give rise to prominent projections that terminate in several nuclei of the dorsal thalamus, which in turn project to the cerebral cortex[1,4,58]. The ventral tier nuclei of the dorsal thalamus represent the link between the dorsal striatopallidal system and the cortex, whereas the mediodorsal thalamic nucleus constitutes the thalamic relay of the ventral striatopallidal projections towards the cortex[4,13]. Thus, cortical activity in mammals is influenced via BG–thalamocortical re-entrant circuits. In birds, the existence of a pallido–thalamocortical pathway comparable to the loop mediated by the motor part of the mammalian ventral tier nuclei has been suggested recently[59]. In addition, ventral striatopallidal projections reach the proposed homologue of the mammalian mediodorsal nucleus of birds[22,43]. However, it is not clear yet whether the cortical regions that receive the thalamic input in birds are fully comparable to the mammalian cortical areas under BG influence[59]. Dorsal pallidal projections to a region comparable to the motor component of the ventral tier of the mammalian dorsal thalamus appear to be sparse or absent in extant reptiles and amphibians. It is, therefore, difficult to determine whether the observed similarities between birds and mammals are due to common inheritance from ancestral reptiles. In contrast, the ventral striatopallidal system of both reptiles and amphibians projects to a thalamic region comparable to the midline nuclei of the dorsal thalamus[53,60], suggesting that a rudimentary BG–thalamocortical circuit involving the ventral component of the BG might have been present in the ancestors of tetrapods (Fig. 2).

Apart from the BG–thalamocortical circuits, a considerable number of efferent fibers arising from the pallidum and SNr project directly to brainstem areas, including the superior colliculus or tectum and the reticular formation. In contrast to the re-entrant circuits, these output pathways are largely comparable among tetrapods, suggesting that they constitute a highly conserved feature of BG organization (Fig. 2). All tetrapods possess several routes by which the BG reach the tectum and, thus, influence a variety of motor behaviors (Box 3). Moreover, projections from the pallidum and the SNr reach the reticular formation, providing the BG with additional routes to participate in central motor pathways[13,21,23,54,61]. The divergence of the mammalian BG outputs into re-entrant circuits and brainstem pathways, and the conditions found in other tetrapod vertebrates, could reflect distinct phylogenetic origins of both output systems.

## The 'indirect pathway' of tetrapods

In mammals, the GPe and the STN have been viewed classically as control structures within the BG circuitry, as part of the so-called 'indirect pathway'[5]. This pathway conveys striatal information to the output structures of the BG (GPi or SNr) through a relay in the STN. Because the STN contains excitatory (glutamatergic) projection neurons, the effect of the indirect pathway appears to serve as a balance of the inhibitory drive of the striatum to the output structures of the BG. Evidence is increasing, however, that the GPe is likely to produce a much more widespread effect on the BG output than by simply controlling the activity of the GPi and the SNr throughout the STN (Refs 5,12). Interestingly, recent observations suggest that the avian subthalamus contains glutamatergic neurons that share much of the connections of the mammalian STN, including reciprocal connections with the pallidum[62]. Moreover, the pallidum and the subthalamus are reciprocally connected in reptiles and amphibians[30,37,52,53], suggesting that the existence of a subthalamic structure involved in the processing of output from the BG might be a common primitive feature shared by all tetrapods (Fig. 2).

## Concluding comments

The mammalian BG are highly complex and many aspects of their functional organization are unique to

## Box 3. Basal ganglia influence on tectal function: multiple strategies in tetrapods give clues to evolution

The basal ganglia (BG) in tetrapods accomplish one of their main functions by means of connections to the mesencephalic tectum (superior colliculus in mammals). Tectal efferent projections reach several midbrain and medullary centers, as well as the spinal cord. Through these pathways, the BG possess a direct access to specific motor functions such as orientation and defensive behaviors, gaze shifting and fixation, and saccadic movements. In mammals, these pathways represent additional routes to lower motor centers besides the well-established striato-pallidal–thalamo–cortical pathway. In non-mammalian tetrapods, on the other hand, the BG–tectal pathways constitute the main anatomical basis for the involvement of the BG in motor control. Classically, two major BG pathways to the tectum have been recognized in tetrapods, that is, a ventral route via the substantia nigra pars reticulata (SNr) and a dorsal route via a pretectal relay nucleus[a]. However, recent findings have demonstrated several additional BG–tectal connections. In fact, comparison of the BG projections to the tectum in extant amniotes and amphibians suggests that the existence of multiple pathways is the primitive condition in tetrapods. The ventral route, that is, the striato–nigro–tectal pathway, is present in all tetrapods (Fig.). Since both the striato–nigral and nigro–tectal neurons contain the inhibitory neurotransmitter GABA, activation of this pathway results in disinhibition of tectofugal neurons[b]. The striatum can also modulate the activity of nigro-tectal neurons via the globus pallidus (Fig.). Pallidal inputs to the SNr are GABAergic and, therefore, stimulation of a particular set of dorsal striatal neurons can cause either inhibition or excitation (or a combination of both effects) on nigro–tectal neurons and, ultimately, on tectal projection neurons[c]. The striato–pallido–pretecto–tectal pathway forms the second major route by which the BG influence tectal function, but this route is not equally developed in all tetrapods. It is well developed in anurans, some lizards (for example, *Podarcis*), crocodiles, turtles and birds, but weak or absent in urodeles, other lizards (for example, *Gekko*), snakes and mammals (Fig.)[a,d]. Striatal stimulation would lead to inhibition of tectofugal neurons through this pathway, because both pallidal and pretectal neurons are inhibitory. The final outcome is, however, further complicated by the existence of direct striato–pretectal (amphibians, birds) and pallido–tectal (amphibians, reptiles, mammals) pathways[d–f], which would result in disinhibition of tectofugal neurons. On the other hand, in amphibians direct striato–tectal connections have also been demonstrated[d], which would account for a direct inhibition.

The presence of multiple routes that relate the BG and tectal neurons in all tetrapods reflects a complicated system by which the motor behavior elicited by the tectum can be influenced. This seems to hold true in particular for amphibians, which is in sharp contrast with previous views[g]. It is still unknown, however, how the different BG–tectal pathways modulate the output of tectal neurons. It is possible that different BG–tectal routes control distinct sets of movements or, alternatively, that the BG could modulate the temporal coding of movements elicited in the tectum by convergence of the multiple pathways on a particular set of tectofugal neurons.

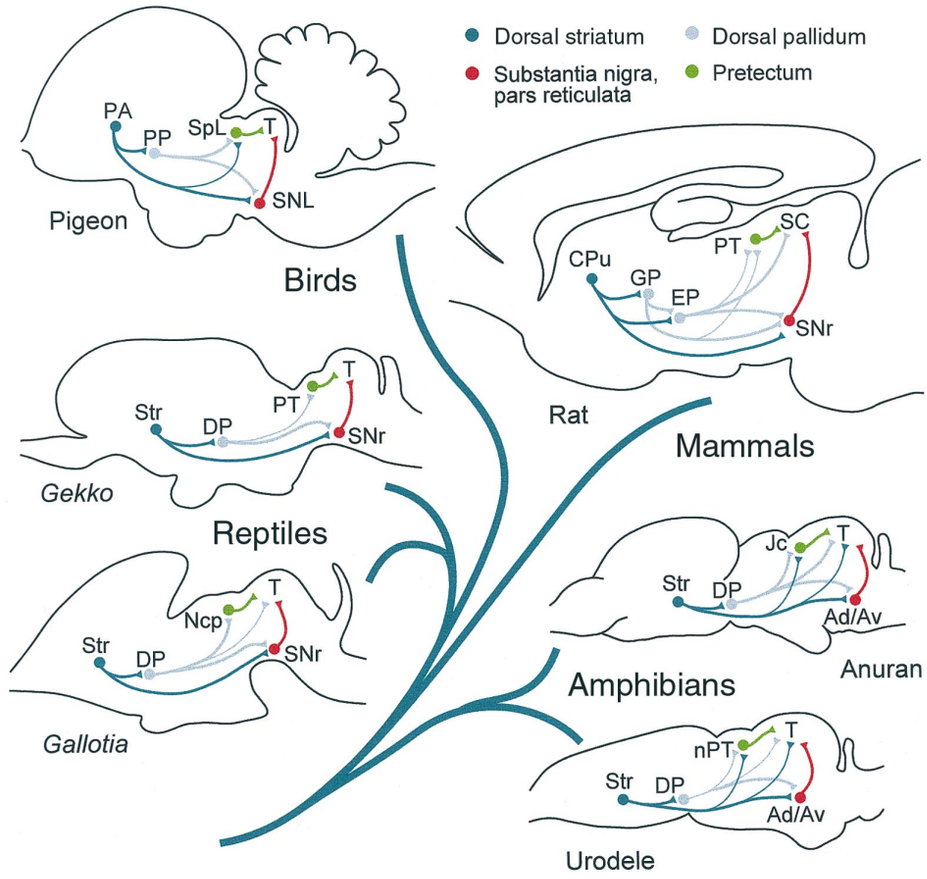


**Fig.** ***Basal ganglia–tectal connections in tetrapods.*** *Phylogenetic tree showing schematic drawings of the various ways by which the striatopallidal system can influence the superior colliculus or tectum of tetrapods. Predominant pathways are indicated by thick lines, whereas less prominent projections are represented by thin lines. In the light of recent anatomical findings, the basal ganglia involvement in visuomotor behavior in tetrapods appears to be far more complex than previously thought. Diverse descending pathways from the basal ganglia to the midbrain tectum have been documented in amphibians and amniotes, suggesting that the existence of several basal ganglia–tectal pathways is the primitive condition in tetrapods. See Box 1 for abbreviations.*

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this class of vertebrates. However, a comparative analysis of the BG organization in birds, reptiles and, very recently, in amphibians has revealed that evolution of the BG in tetrapods has been much more conservative than previously thought. The main conclusion that can be drawn from these studies is that living amphibians possess a pattern of BG organization largely similar to that of modern reptiles, birds and

mammals. It is suggested that BG structures were probably present in the brain of ancestral tetrapods and that their organization shared many features with that of extant tetrapods. The intriguing question that arises now is whether the basal forebrain organization of non-tetrapods differs essentially from that observed in tetrapods. A similar approach to that recently made for amphibians might provide a more definitive answer.

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