

Basal Ganglia Organization in Amphibians: Afferent Connections to the Striatum and the Nucleus Accumbens

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ABSTRACT

As part of a research program to determine if the organization of basal ganglia (BG) of amphibians is homologous to that of amniotes, the afferent connections of the BG in the anurans *Xenopus laevis* and *Rana perezi* and the urodele *Pleurodeles waltl* were investigated with sensitive tract-tracing techniques. Hodological evidence is presented that supports a division of the amphibian BG into a nucleus accumbens and a striatum. Both structures have inputs in common from the olfactory bulb, medial pallium, striatopallial transition area, preoptic area, ventral thalamus, ventral hypothalamic nucleus, posterior tubercle, several mesencephalic and rhombencephalic reticular nuclei, locus coeruleus, raphe, and the nucleus of the solitary tract. Several nuclei that project to both subdivisions of the BG, however, show a clear preference for either the striatum (lateral amygdala, parabrachial nucleus) or the nucleus accumbens (medial amygdala, ventral midbrain tegmentum). In addition, the anterior entopeduncular nucleus, central thalamic nucleus, anterior and posteroventral divisions of the lateral thalamic nucleus, and torus semicircularis project exclusively to the striatum, whereas the anterior thalamic nucleus, anteroventral, and anterodorsal tegmental nuclei provide inputs solely to the nucleus accumbens. Apart from this subdivision of the basal forebrain, the results of the present study have revealed more elaborate patterns of afferent projections to the BG of amphibians than previously thought. Moreover, regional differences within the striatum and the nucleus accumbens were demonstrated, suggesting the existence of functional subdivisions. The present study has revealed that the organization of the afferent connections to the BG in amphibians is basically similar to that of amniotes. According to their afferent connections, the striatum and the nucleus accumbens of amphibians may play a key role in processing olfactory, visual, auditory, lateral line, and visceral information. However, contrary to the situation in amniotes, only a minor involvement of pallial structures on the BG functions is present in amphibians. *J. Comp. Neurol.* 378:16-49, 1997. © 1997 Wiley-Liss, Inc.

Indexing terms: forebrain; solitary tract nucleus; locus coeruleus; visceral; evolution

Research during the last two decades has revealed many similarities in the organization of the basal ganglia (BG) among reptiles, birds, and mammals (see, e.g., Reiner et al., 1984; González et al., 1990; Reiner and Anderson, 1990; Anderson and Reiner, 1991; Heimer et al., 1991; Smeets, 1992; Zahm and Brog, 1992). One intriguing question is whether this basic organization holds also for anamniotes, in particular amphibians. The first issue we want to address is the differentiation of the striatal complex of amphibians into a nucleus accumbens and a striatum. In mammals, the striatum is formed by two major divisions, i.e., dorsal and ventral striatum, which

share numerous cytoarchitectonical and neurochemical features but differ, to some extent, in the information preprocessed and connectivity. The dorsal striatum is consti-

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tuted by the main part of the caudate-putamen, whereas the olfactory tubercle and the nucleus accumbens represent the major components of the ventral striatum (Heimer et al., 1995). By means of cytoarchitectonic criteria, a striatum and a nucleus accumbens were already recognized in anurans at the beginning of this century (for review, see Northcutt and Kicliter, 1980; Parent, 1986). Thus, the striatum (caudado-putamen in mammals) occupies the ventrolateral portion of the telencephalic hemisphere, whereas the nucleus accumbens lies in the ventromedial portion of the telencephalic wall. Further, the amphibian striatum has been subdivided on the basis of differences in cell density and degree of cell migration into dorsal and ventral parts (Northcutt, 1974). Therefore, the terms "dorsal and ventral striatum" used for amphibians are not equivalent to those employed for mammals.

Despite the early recognition of the amphibian striatum and nucleus accumbens as two anatomically and, most likely, functionally distinct basal forebrain structures, little effort has been made to study each of these structures separately. A major reason for the lack of such information may have been the absence of sensitive neuronal tracers that can be injected at restricted sites. Thus, our current understanding of BG connections in amphibians is primarily based on the results of anterograde tracing studies by means of the degeneration technique and, less frequently, autoradiography (for reviews, see Northcutt and Kicliter, 1980; Parent, 1986), physiological studies (Vesselkin et al., 1971; Vesselkin and Kovacevic, 1973; Gruberg and Ambros, 1974; Mudry and Capranica, 1980), or retrograde tracing studies with horseradish peroxidase (Kicliter, 1979; Vesselkin et al., 1980; Wilczynski and Northcutt, 1983a; Neary, 1988; Wicht and Himstedt, 1988, 1990; Dubé et al., 1990).

Recently, a new generation of tracers has been introduced, viz. dextran amines (Glover et al., 1986; Fritzsich and Sonntag, 1991; Fritzsich, 1993). These tracers, which are transported anterogradely as well as retrogradely, can be delivered to restricted sites in the brain, and are sensitive enough to enable a selective study of the connections of the striatum and the nucleus accumbens. The main goal of the present study was to get detailed information of the afferent connections of the BG in anurans and urodeles. Although the outcome of the present study is partly confirmatory, it makes a substantial contribution to our current understanding of BG organization in amphibians for the following reasons: 1) the present study reveals differences in afferent connections between the nucleus accumbens and the striatum in both groups of amphibians; 2) it provides evidence for the existence of a nucleus accumbens in the brain of urodeles, which has remained unclear until now; 3) the results also indicate the existence of regional differences within the striatum and the nucleus accumbens; and 4) several afferents to the striatum and the nucleus accumbens are demonstrated, which were not described previously.

The present study is a first step in a research program that aims to answer the question to what extent the BG organization of amphibians is comparable to that of amniotes. To reach that goal, hodological, chemoarchitectonical, and developmental aspects of the basal forebrain in amphibians are considered. Our accompanying paper deals in detail with the sites of origin of the catecholaminergic input to the nucleus accumbens and the striatum as revealed by a combined tract-tracing/transmitter-immunohistochemical study. Further studies will provide information on the efferent connections and chemoarchitectonic

Abbreviations

A	anterior thalamic nucleus	nri	nucleus reticularis isthmi
Acc	nucleus accumbens	Nsol	nucleus of the solitary tract
Ad	nucleus anterodorsalis tegmenti	n V	nervus trigeminus
Aob	accessory olfactory bulb	n VII	nervus facialis
Apl	amygdala, pars lateralis	n VIII	nervus octavus
Apm	amygdala, pars medialis	n IX-X	glossopharyngeal and vagus nerves
Av	nucleus anteroventralis tegmenti	ob	olfactory bulb
C	central thalamic nucleus	P	posterior thalamic nucleus
Cb	cerebellum	Pb	parabrachial nucleus
cStr	caudal subdivision of the striatum	POa	anterior preoptic area
DB	diagonal band nucleus	Ra	raphe nuclei
Dp	dorsal pallium	Ri	nucleus reticularis inferior
dStr	dorsal subdivision of the striatum	Rm	nucleus reticularis medius
Ea	anterior entopeduncular nucleus	Rs	nucleus reticularis superior
epl	external plexiform layer	rStr	rostral subdivision of the striatum
gr	granule cell layer of the olfactory bulb	SC	nucleus supra-chiasmaticus
gl	glomerular layer of the olfactory bulb	SIR	superficial isthmal reticular nucleus
Hab	habenula	sol	solitary tract
Ip	nucleus interpeduncularis	spta	striatopallial transition area
La	lateral thalamic nucleus, anterior division	Str	striatum
Lc	locus coeruleus	tect	tectum mesencephali
lfb	lateral forebrain bundle	Tor	torus semicircularis
Ll	lateral line lobe	TP	tuberculum posterius
Lp	lateral pallium	v	ventricle
Lpv	lateral thalamic nucleus, posteroventral division	Vds	tractus descendens nervi trigemini
Ls	lateral septum	VH	ventral hypothalamic nucleus
m	medial tegmental area	VM	ventromedial thalamic nucleus
mfb	medial forebrain bundle	VL	ventrolateral thalamic nucleus
ml	mitral cell layer of the olfactory bulb	Vm	nucleus motoris nervi trigemini
Mp	medial pallium	vStr	ventral subdivision of the striatum
Ms	medial septum	vt	ventral thalamus
nall	anterior lateral line nerve	zav	zona anteroventralis
np11	posterior lateral line nerve	zpd	zona posterodorsalis
nPT	nucleus pretectalis	III	nucleus nervi oculomotorii

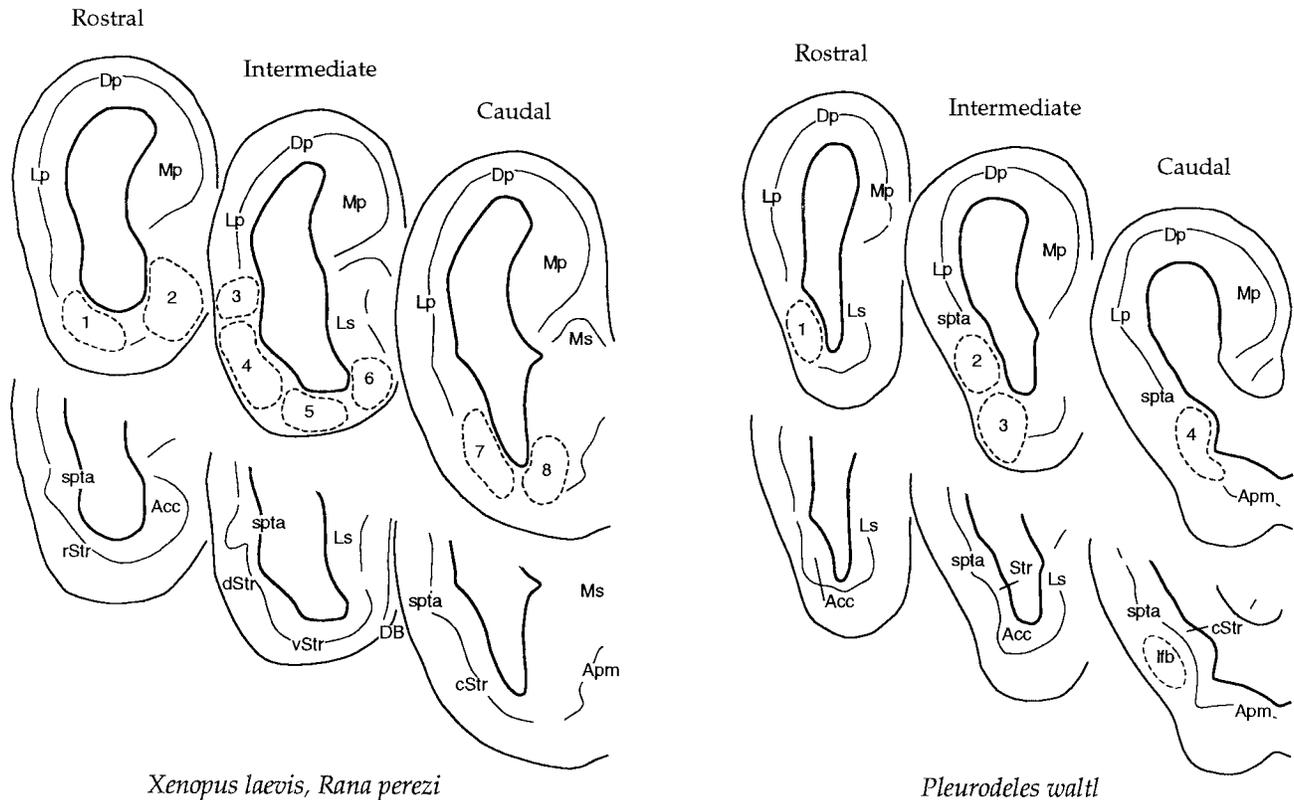


Fig. 1. Illustration of representative injection sites in the ventral telencephalon. Numbers refer to locations of injection sites as mentioned in Table 1. The lower row of drawings indicate the structures involved in the injection sites of the cases represented above. See list of abbreviations.

and developmental aspects of both basal ganglia structures in amphibians.

MATERIALS AND METHODS

For the present study, a total of 26 adult green frogs (*Rana perezi*), 23 clawed toads (*Xenopus laevis*), and 17 Iberian ribbed newts (*Pleurodeles waltl*) were used. The animals were obtained from the laboratory stocks of the Department of Cell Biology, University Complutense of Madrid (*Rana*, *Pleurodeles*), and Department of Animal Physiology, University of Nijmegen (*Xenopus*).

The animals were deeply anesthetized before surgery by immersion in a 0.3% solution of tricaine methanesulfonate (MS222, Sandoz) in distilled water, pH 7.4. In a first series of experiments, the tracers horseradish peroxidase (HRP, grade I; Boehringer, Mannheim, Germany), FluoroGold (FG; Fluorochrome, Englewood, NJ), 10 kD biotinylated dextran amine (BDA 10 kD, D-1956; Molecular Probes, Eugene, OR, USA), 3 kD biotinylated dextran amine (BDA 3 kD, D-7135; Molecular Probes), 10 kD Texas Red-conjugated dextran amine (TRDA 10 kD, D-1863; Molecular Probes), and 3 kD Texas Red-conjugated dextran amine (TRDA 3 kD, D-3328; Molecular Probes) were applied unilaterally within different subregions of the basal telencephalon. A ventral approach through the roof of the mouth was used. Table 1 and Figure 1 illustrate the level, the site, and the size of representative applications, as well as the tracers employed and the way in which they were

delivered. In an additional series of experiments, the tracer BDA 10 kD was injected into the olfactory bulb, the transition area between the lateral pallium and the striatum, the medial pallium, the dorsal thalamus, and the subcerebellar region to confirm anterogradely the projections to the striatum and the nucleus accumbens.

The tracers were applied either as a solution by means of iontophoretic injections (HRP, FG, and BDA 10 kD) or as crystals on the tip of a sharp tungsten needle (BDA, TRDA). The injections were made by applying 5–8 μ A positive pulsed current (7 seconds on/7 seconds off) to the tracer solutions (10–15% HRP in 0.1M phosphate buffer [PB], pH 7.4; 2% FG in 0.1M acetate buffer, pH 3.3; 10% BDA 10 kD in 0.01M PB) in a glass micropipette (outer tip diameter 12–20 μ m for HRP and BDA, 45–70 μ m for FG) for a period of 15–30 minutes. Cases with tracer applications as dry crystals were made by impaling the selected brain regions with a very sharp tungsten needle on the tip of which the tracer had been recrystallized from a saturated solution in distilled water. Survival times varied from 5–14 days. Following this period the animals were deeply anesthetized with an overdose of MS222, and perfused transcardially with 50 ml of a NaCl solution (0.9% in distilled water) followed by 200 ml of fixative (1% paraformaldehyde and 1.25% glutaraldehyde in 0.1 M PB for the HRP experiments or 4% paraformaldehyde in 0.1 M PB for the other cases). The brain and spinal cord were removed, postfixed in the same fixative solution for another 2–3 hours, and immersed in a solution of 30%

TABLE 1. Summary of Representative Experiments With Telencephalic Tracer Applications

Case	Tracer	Application ¹	Site of injection site ²	Location of injection site ³
Anurans				
9209	BDA 10 kD	I	S	3
9313	HRP	I	L	4 + 5
9316	BDA 10 kD	I	M	7
9331	BDA 10 kD	I	S	4
9347	HRP	I	S	2
9355	FG	I	L	1 + 4 + 5
9356	FG	I	L	4 + 5
9402	HRP	I	S	5
9475	HRP	I	S	2
9447	TRDA 10 kD	C	M	5
9506	HRP	I	S	4
9507	TRDA 3 kD	C	M	2
9510	TRDA 3 kD	C	M	8
9515	BDA 3 kD	C	M	8
9516	BDA 10 kD	I	M	1
9517	TRDA 10 kD	C	M	6
9525	TRDA 3 kD	C	L	4 + 5
9526	TRDA 3 kD	C	M	4
9528	BDA 3 kD	C	L	4 + 5
9529	BDA 10 kD	I	S	5
9532	BDA 10 kD	C	L	4 + 5
9548	BDA 3 kD	C	M	6
9560	BDA 10 kD	I	M	2
9562	BDA 10 kD	C	M	2
9598	BDA 3 kD	C	S	2
95110	TRDA 10 kD	C	L	4 + 5
Urodele				
9348	BDA 10 kD	C	L	4
9355	FG	I	L	2
9357	FG	I	L	3 + 4
9487	FG	I	L	1 + 3
9511	HRP	I	S	2
9512	BDA 3 kD	C	S	3
9564	TRDA 10 kD	C	L	2 + 3
9597	BDA 10 kD	I	S	1
95101	TRDA 10 kD	C	M	3
95102	BDA 10 kD	I	S	2
95111	TRDA 3 kD	C	L	2 + 3 + 4
95112	BDA 10 kD	C	M	3
95113	BDA 3 kD	C	S	2

¹I = iontophoretic injection; C = crystal application.

²S = small; M = medium; L = large.

³Numbers refer to location of the injection sites that are depicted in Figure 1.

sucrose in PB for 5–8 hours at 4°C. They were then blocked in a solution of 15% gelatin and 30% sucrose in PB and stored for 5 hours at 4°C in a solution containing 4% formaldehyde and 30% sucrose in PB. Sections were cut on a freezing microtome at 30–40 µm thickness in the frontal or sagittal plane and collected in cold 0.05 Tris-HCl buffer, pH 7.6 (TB).

Prior to visualization of HRP and BDA, sections were rinsed twice in 0.05 Tris-HCl buffered saline (TBS), pH 7.6, treated with 1% H₂O₂ in TBS for 10 minutes, and rinsed again three times with TBS to reduce endogenous peroxidase activity. In HRP experiments the sections were processed with heavy metal intensification of a diaminobenzidine (DAB)-based HRP reaction product (Adams, 1981). Briefly, sections were treated with a TBS solution containing 0.05% DAB, 0.04% nickel ammonium sulfate, and 0.015% H₂O₂. Thus, peroxidase activity is visualized by the blue-black reaction product. After 5–10 minutes, sections were rinsed five times in TBS, mounted on glass slides (mounting medium: 0.2% gelatin in TB), and dried overnight. After ethanol dehydration and xylene cleaning, they were coverslipped with Entellan (Merck). Some sections were counterstained with cresyl violet. For visualization of BDA, an avidin biotin complex (Vectastain, ABC Standard kit, Vector Laboratories, Burlingame, CA) was used. The sections were incubated for 1 hour in TBS with 0.5% Triton X-100 (TBS-T) and a mixture of reagents A (avidin DH)

and B (biotinylated horseradish peroxidase H complex) of the Vectastain ABC kit. The latter solution (5 µl A/5 µl B per ml TBS-T) was allowed to stand for 45 minutes prior to use. After incubation, sections were rinsed three times in TBS. Peroxidase activity was visualized as above with DAB-nickel as chromogen. Sections were also counterstained and coverslipped as above. Sections from FG and TRDA experiments were mounted immediately after sectioning (mounting medium as above) and coverslipped with Vectashield (Vector).

The distribution of retrogradely labeled cells and fibers in the brains of *Xenopus laevis*, *Rana perezi*, and *Pleurodeles waltl* was charted in representative transverse sections. In HRP and BDA cases, drawings were made by means of a camera lucida, in which the sections counterstained with cresyl violet facilitated the localization of labeled structures. Sections of FG and TRDA experiments were analyzed with a Zeiss fluorescence microscope with appropriate filter combinations. In the latter cases, the distribution of retrogradely labeled cells was charted using a computer-aided X-Y plotting system (Minnesota Datametrics, MD-2 digitizer and software). Finally, some of the sections, which were plotted, were counterstained with cresyl violet to determine cytoarchitectonic boundaries. The nomenclature is largely the same as that used in our previous studies of amphibians (González and Smeets 1991, 1994; Marín et al., 1995).

RESULTS

Methodological considerations

In the present study a variety of retrograde tracing techniques has been applied. Differences existed not only in the kind of tracer substances used, but also in the way they were delivered. Despite these differences, the resulting labeling was consistent, although some variation in the sensitivity of the different techniques was obvious. Iontophoretic injections of HRP in the striatum and the nucleus accumbens resulted in well-stained cells in the forebrain and midbrain, but failed to stain cells beyond the rostral rhombencephalon. Similar injections by means of Fluoro-Gold yielded consistently well-stained cells not only in the forebrain and midbrain, but also in the rostral and caudal brainstem. A disadvantage of the latter tracer was that the injection sites were always large. The more recently introduced dextran amine tracers were especially suited to study the inputs to the basal forebrain of amphibians. The low molecular weight (3 kD) dextran amines appeared not only to be equal in sensitivity to FluoroGold, but they could also be delivered to very restricted areas within the basal forebrain. Most injections described in the present study have, therefore, been carried out using biotinylated dextran amine (BDA) or Texas Red-conjugated dextran amine (TRDA) as retrograde tracers.

The present study has also shown that the mode of dextran amine application is an important experimental variable. In order to get an overview of all possible inputs to the basal forebrain, application of BDA or TRDA crystallized on a sharp tungsten needle were most suited. To obtain more detailed information about afferents to subregions within the basal forebrain, iontophoretic injections are favored. It should be noted that the tracers used in the present study effectively label the efferent connections of the basal forebrain. However, for clarity these will be dealt with in a separate paper. In the following sections, first the

distribution of the afferent connections to the striatum and the nucleus accumbens of anurans (*Xenopus laevis*, *Rana perezi*) is described. Subsequently, the corresponding connections in the brain of the urodele, *Pleurodeles waltl*, are dealt with. If it is not stated explicitly, the reader is referred to Table 1 and Figure 1 for details about the level, structures involved and the size of the injection sites, as well as about the tracers and the way they were delivered.

Telencephalic basal ganglia afferents in Anurans

On the basis of cytoarchitecture and chemoarchitecture, ventrolateral and ventromedial subdivisions have been identified in the ventral aspect of the anuran hemispheres. The ventrolateral portion is considered the striatum of the anuran telencephalic basal ganglia, whereas the ventromedial portion is referred to as the nucleus accumbens. A series of experiments have been carried out in which tracers were deposited in each of the two subdivisions throughout the entire rostrocaudal extent of the telencephalon. The results of these experiments are presented below.

Striatal afferent connections. The striatal afferent connections of the two anuran species are largely comparable. Only small differences were observed in the organization of the inputs from the diencephalon. Thus, for the description and the mapping of the afferent connections, *Xenopus laevis* is chosen as core species, but photomicrographs are also taken from *Rana* material, to underscore the similarities of those connections.

An overview of all possible inputs to the striatum of the two anuran species studied is shown by case 9532, in which crystallized BDA was applied to the striatum of *Xenopus* at intermediate rostrocaudal levels of the hemisphere (Fig. 2). Retrogradely labeled cell bodies were observed throughout the brain. The most rostrally located cells were found in the olfactory bulb (Fig. 2A), whereas the most caudal ones occurred in the nucleus of the solitary tract (Fig. 2N).

Telencephalic connections. A moderate number of labeled cells was observed in the mitral cell layer of the ipsilateral olfactory bulb (Fig. 2A), whereas fewer were scattered in the granular cell layer. At the level of the injection site, a small number of labeled cells was found immediately dorsal and ventral to the application site and in the ventromedial wall of the hemisphere (Fig. 2B). At the same level, additional labeling was observed in cells in the ventromedial part of the medial pallium. Slightly caudally, many labeled fibers were found within the confines of the lateral forebrain bundle.

The largest population of retrogradely labeled cells in the telencephalon was observed in the caudal ventral striatum. At a level slightly rostral to that shown in Figure 2C, large or medium cells form a rather compact group, close to the labeled fibers within the lateral forebrain bundle. In addition, a small number of fibers lies closer to the ventricle and is separated from the main bundle by an area that contains a few medium-sized cell bodies. At the same level, small-sized neurons were found in the lateral amygdala. More caudally, at the level of the rostral tip of the preoptic recess, retrogradely labeled cells were located mainly just dorsal to the lateral forebrain bundle, although neurons were also found in the lateral amygdala and in the most lateral portion of the medial amygdala (Fig. 2C). The latter cells are generally large, with round-to-piriform perikarya and one or two long apical dendrites,

which course in a lateral or dorsolateral direction. At the same level, a few cells were observed in the anterior preoptic area. The most caudal telencephalic cells that were labeled after a large striatal application were found within the lateral forebrain bundle, i.e., in the anterior entopeduncular nucleus (Fig. 2D). Except for the input from the amygdala and caudal striatum, all telencephalic projections to the striatum are ipsilateral. The contralateral afferent connections from these areas are, compared to the ipsilateral component, very restricted in number.

Diencephalic connections. After a large striatal application, labeled cells were observed bilaterally in the suprachiasmatic nucleus throughout its rostrocaudal extent (Fig. 2E). However, some variation in the exact position of those cell bodies occurred. In the rostral part of the nucleus, the cells lie in the outer lateral margin of the nucleus, predominantly in its ventrolateral part (Fig. 2E). More caudally, the neurons are less numerous and lie in the lateral portion of the nucleus. At the level of the infundibular recess, neurons were observed in the ventral hypothalamus, primarily in its dorsal part (Fig. 2F). These cells are piriform with a main process that is directed toward the lateral forebrain bundle. More caudally, a few cells were found also in the ventral part of the ventral hypothalamus.

In the dorsal thalamus, cells were located ipsilaterally in the anterior and posteroventral divisions of the lateral thalamic nucleus and in the central thalamic nucleus (Figs. 2F, 3, 4). Although the neurons in the anterior division of the lateral thalamic nucleus are distributed throughout the nucleus, they are more numerous in the caudal two-thirds. Moreover, the cells in the rostral part of the anterior division of the lateral thalamic nucleus are small and round, with no visible dendrites. On the contrary, retrogradely labeled cells at intermediate and caudal levels of the nucleus are round, fusiform, piriform or multipolar. They also possess long dendrites that enter the lateral neuropil, where they arborize. Further, neurons located in the ventral part of the anterior division of the lateral thalamic nucleus are more numerous than those in the dorsal part. A heterogeneous distribution of labeled cells was also observed in the central thalamic nucleus after striatal applications. Medium-sized round or piriform neurons with short processes lie scattered throughout the nucleus at rostral and intermediate levels, whereas a substantially larger number of cells are found in the caudal pole of the nucleus (Fig. 2G). Moreover, at the latter level, the cells are generally larger, piriform or multipolar in shape, and possess dendrites, that are directed mainly laterally. After striatal applications, a few labeled large cells were also found in the posteroventral division of the lateral thalamic nucleus. The cells are either piriform with a long process directed ventrally or, more frequently, bipolar with dorsoventrally or mediolaterally directed processes (Fig. 3). Axons of cells in the anterior and posteroventral divisions of the lateral thalamic nucleus and the central nucleus course first laterally and then ventrally to enter the dorsal aspect of the lateral forebrain bundle.

Fig. 2. A–N: Charting of the retrograde labeling following deposition of biotinylated dextran amine (BDA; case 9532) centered in the striatum (shaded area in level B) of *Xenopus laevis*. Large dots represent labeled neurons, whereas dashes and small dots represent labeled fibers. The levels of sections A–N are indicated in the upper right scheme of the *Xenopus* brain. See list of abbreviations.

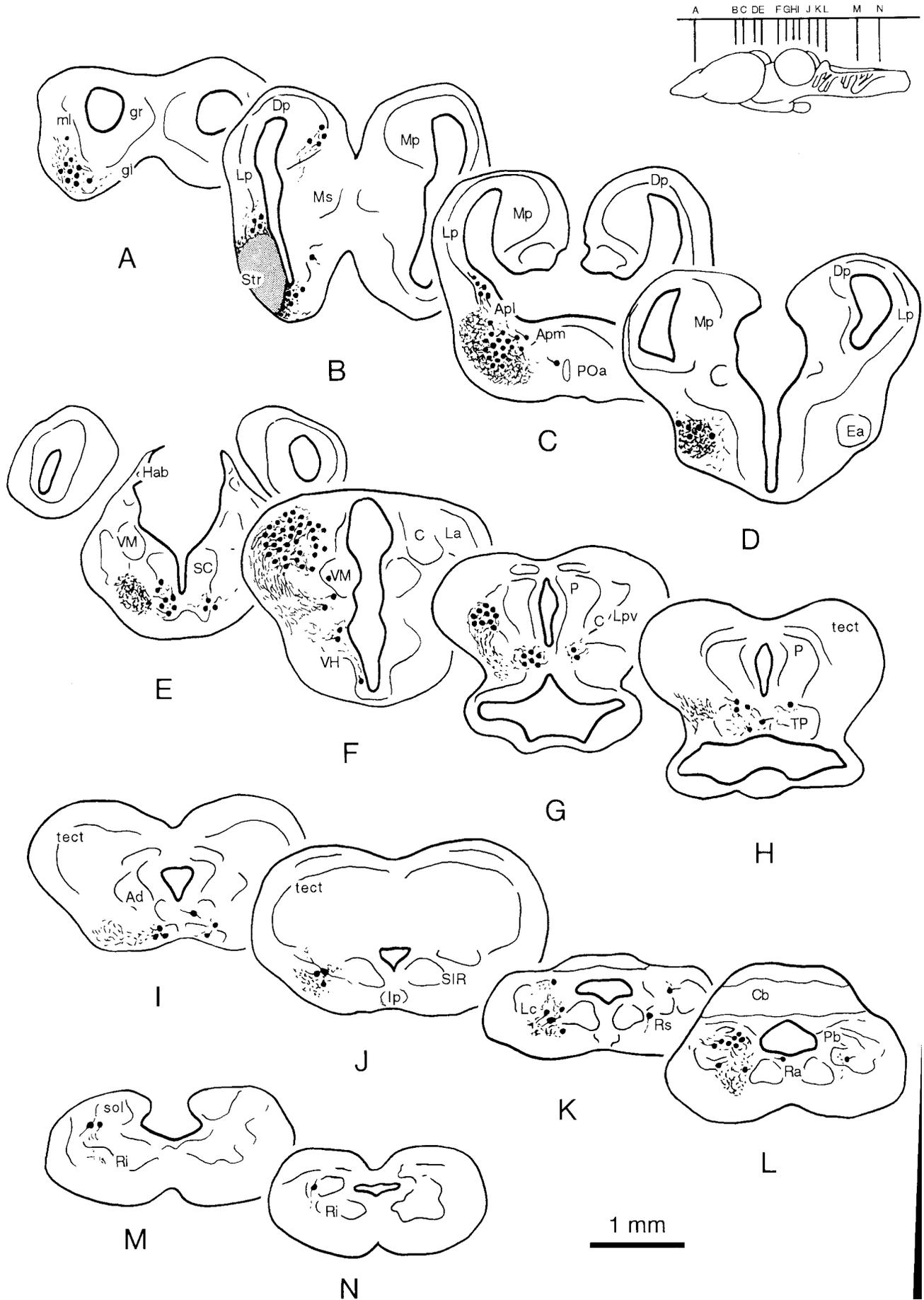
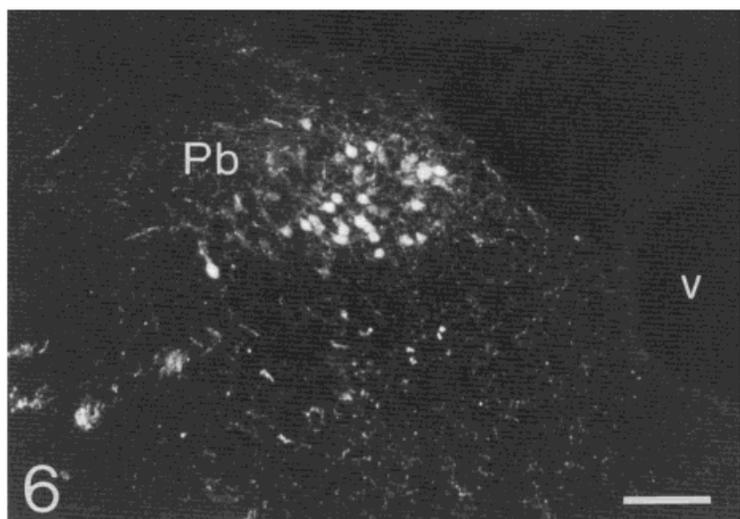
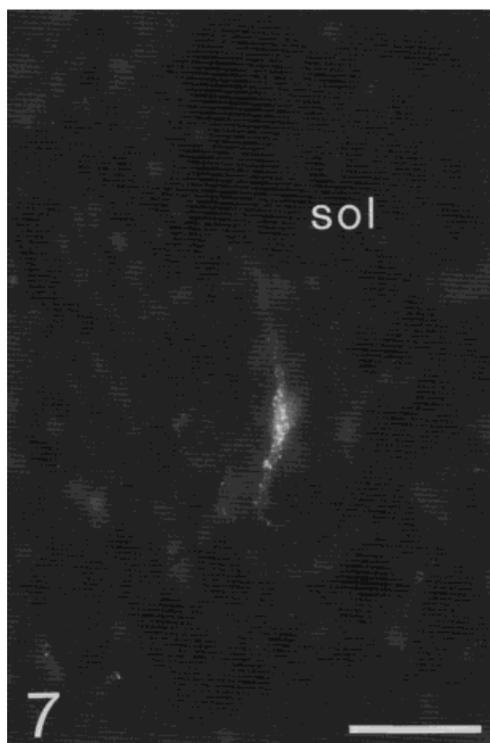
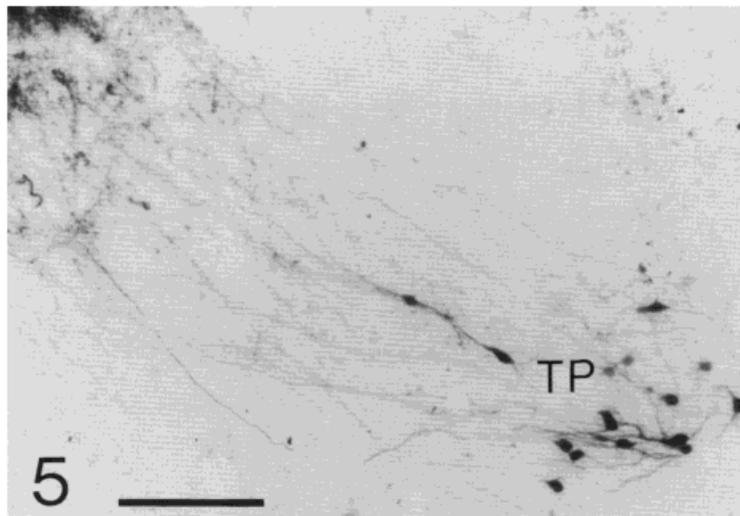
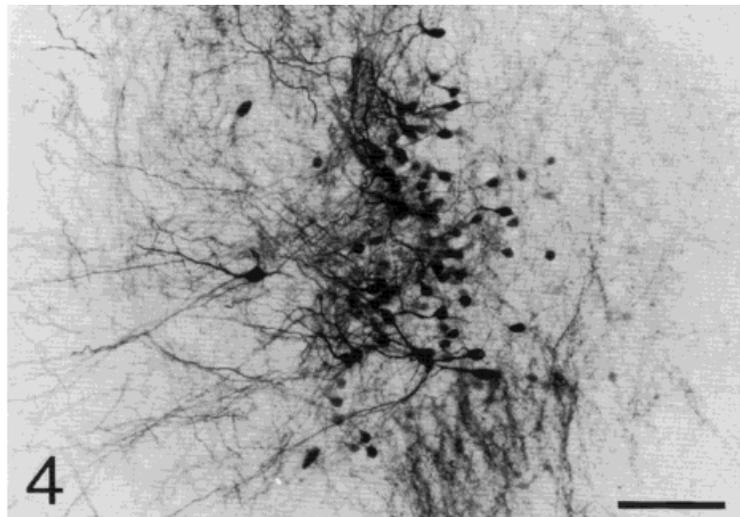
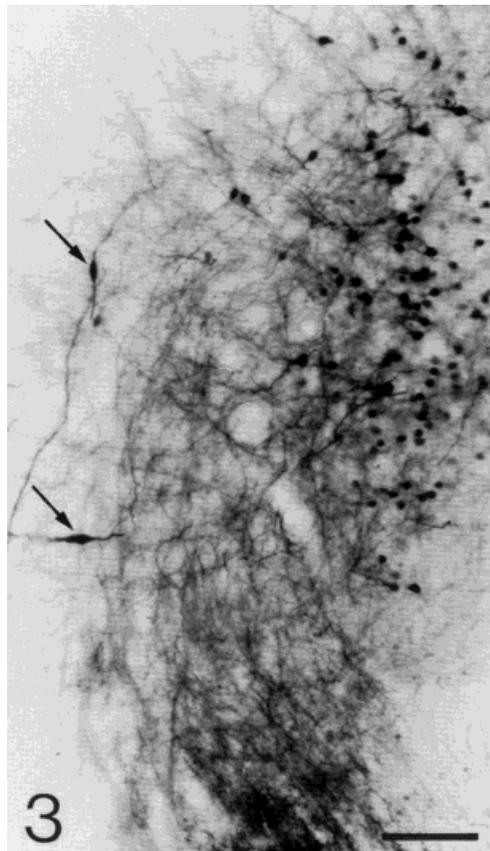


Figure 2



Figs. 3–7. Photomicrographs of retrogradely labeled cells after application of BDA (Figs. 3–5, *Rana perezi*) or Texas Red-conjugated dextran amine (TRDA) (Figs. 6, 7, *Xenopus laevis*) in the striatum of anurans. Labeled cells and fibers in the intermedio-caudal portion of the central thalamic nucleus and in the posteroventral division of the

lateral thalamic nucleus (arrows, Fig. 3); the caudal pole of the central thalamic nucleus (Fig. 4); the rostromedial portion of the posterior tubercle (Fig. 5); the parabrachial nucleus (Fig. 6); and the nucleus of the solitary tract (Fig. 7). See list of abbreviations. Scale bars = 100 μ m in Figures 3–6, 50 μ m in Figure 7.

Striatal applications always resulted in a small number of retrogradely labeled cells in the ventral thalamus. These cells occasionally lie in the ventromedial thalamic nucleus but, more often, lateral to it, within the ventral part of the ventrolateral thalamic nucleus (Fig. 2F). The cells have round or piriform perykarya with a main process that shows a mediolateral orientation.

Numerous labeled neurons were found in the posterior tubercle of both *Xenopus* and *Rana* after striatal applications, but some differences in the organization of these cells were apparent. In *Rana*, a dorsomedial and a ventrolateral subdivision of the posterior tubercle can be recognized. Even within the dorsomedial posterior tubercle, a heterogeneity is observed, since the ventral portion contains cells that are generally larger than those in the dorsal portion. Striatal applications of retrograde tracers resulted in a compact group of labeled cells ipsilaterally in the ventrolateral part of the dorsomedial posterior tubercle. In addition, some laterally displaced cells were observed (Figs. 2G, 5). The latter cells are pear-shaped with a long process directed to the lateral forebrain bundle. Another population of labeled cells occurred in the dorsal portion of the dorsomedial posterior tubercle. The latter group consists of cells that are smaller than those in the ventrolateral portion of the dorsomedial posterior tubercle and also less numerous. The dorsal portion of the dorsomedial posterior tubercle extends caudally into the midbrain tegmentum. Labeled cells, although few in number, could be found up to the level of the oculomotor nerve. In *Xenopus*, a distinction between dorsomedial and ventrolateral subdivisions of the posterior tubercle cannot be established on the basis of cytoarchitectural criteria. Also dorsal and ventral portions of the dorsomedial posterior tubercle were indistinguishable. However, it is noteworthy that in the latter species, labeled neurons were located in the dorsomedial aspect of the posterior tubercle and, more caudally, in the medial aspect of the mesencephalic tegmentum extending up to the level of the third nerve (Fig. 2G-I).

Brainstem connections. At the level of the trochlear nerve nucleus, retrogradely labeled cells were observed in the isthmic superficial reticular nucleus (Fig. 2J). These large, multipolar cells lie close to the bundle of ascending fibers. In addition, some neurons in the torus semicircularis were labeled. A few cells were observed in the ventrolateral part of the toral magnocellular nucleus; more caudally, some neurons were found within the principal nucleus of the torus.

At caudal isthmic levels, some scattered cells were found ipsilaterally in the area of the locus coeruleus (Fig. 2K). Some other labeled cells lie around the pretrigeminal nucleus or just ventral and lateral to the caudal pole of the nucleus isthmi. Labeled neurons occurred bilaterally in the nucleus reticularis superior.

At the level of the cerebellum, a large population of cells was observed in the parabrachial nucleus (Figs. 2L, 6). Some of these neurons are intermingled with the fibers of the cerebellar tracts or lie lateral to them, but the majority of the cells are located medially, close to the ventral border of the granular layer of the cerebellum. Rostrocaudally, this cell population extends from the level of the anterior medullary velum up to the caudal aspect of the cerebellum. The cells are piriform or multiform with processes that show a lateral or ventral orientation.

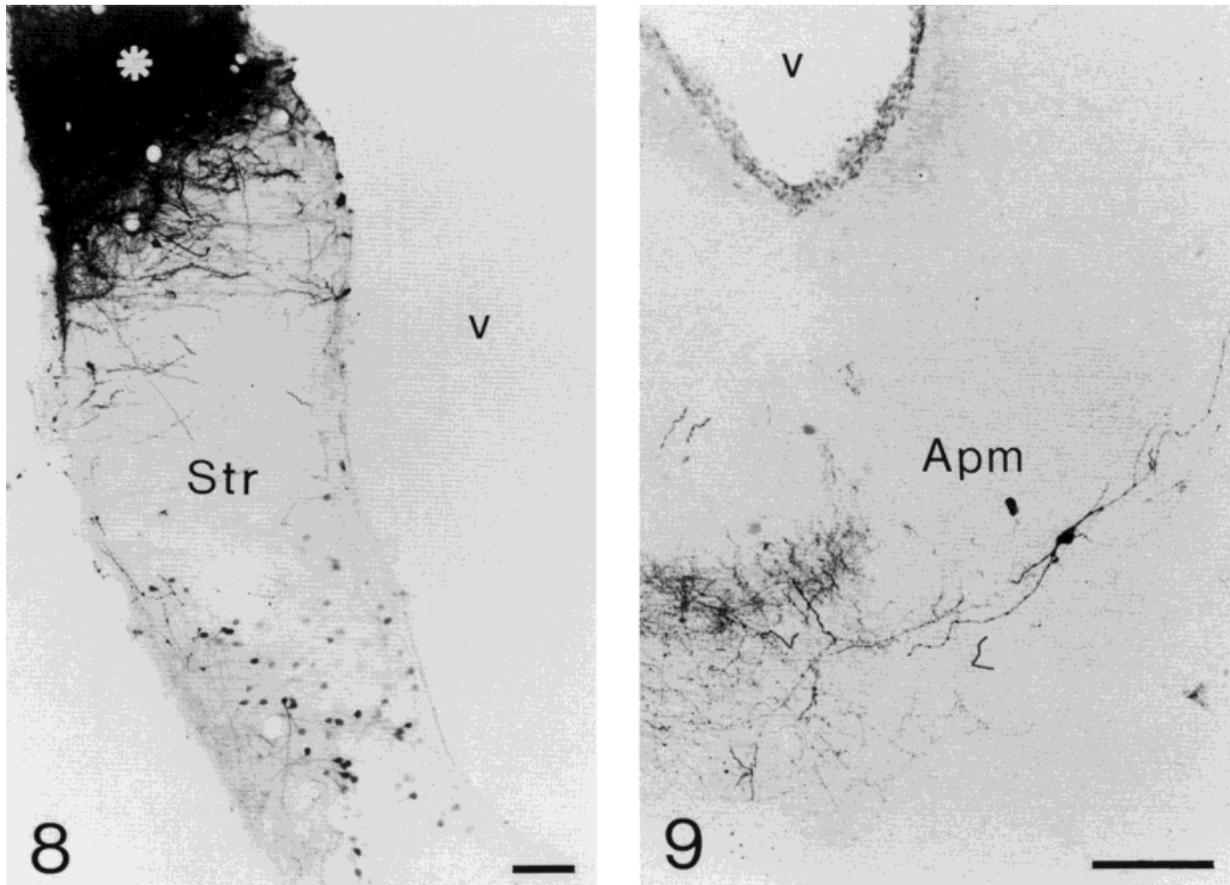
After striatal applications, labeled cells were found in the rostral raphe (Fig. 2L). The neurons are located dorsally in the midline, close to the ventricle. A few cells are bipolar, but the majority of the labeled cells in the raphe are piriform with long processes that are ventrally directed. Throughout the intermediate and caudal rhombencephalon scattered labeled cells were observed bilaterally in the reticular formation. Finally, in the caudal rhombencephalon, neurons were consistently labeled in the nucleus of the solitary tract (Figs. 2M,N, 7). Most of the labeled cells observed in the latter nucleus are located ventrally or ventrolaterally with respect to the tract. The cells are generally fusiform with two processes that have either a dorsoventral or a mediolateral orientation (Fig. 7).

Additional information on striatal afferent connections. The description of cell bodies that are retrogradely labeled after large injections of dextran amines to the striatum of anurans holds essentially for all large applications made during this study. However, in these cases it cannot be excluded that fibers of passage are also involved which could result in false positive labeling in certain nuclei. Furthermore, the striatum is a heterogeneous structure, and different inputs may reach different parts of the striatum. More restricted applications of tracers to the striatum could, therefore, provide important information not only about the true nature of retrograde labeling seen after large applications, but also about putative subregions within the striatum. For clarity, the results of these latter experiments will be discussed in relation to those obtained from the large injections in the following paragraphs.

Olfactory bulb. In experiments with injections centered in the rostral portion of the striatum (case 9516), the number of retrogradely labeled cells in the olfactory bulb was markedly high. Additional experiments by means of iontophoretic injections of BDA in the olfactory bulb, revealed that the efferent fibers of the olfactory bulb are collected within the lateral olfactory tract and, passing caudally, issue not only fibers to the lateral pallium, but also form a rostrocaudally extensive terminal field associated with a distinct cell group located at the transition zone of the lateral pallium and the striatum ("S-portion of the primordial piriform cortex," after Hoffman, 1963). Thus, most likely this area had been included in the striatal injections described above. As can be inferred, the olfactory bulb does not project to the entire striatum, but only to its dorsolateralmost portion, suggesting regional differentiation (see also below).

Medial pallium. Not only large striatal injections, but also restricted applications to the ventral aspect of the striatum (case 9529) revealed retrogradely labeled cells in the medial pallium. These cells were not seen after applications to the dorsal part of the striatum (case 9331). Additional experiments, in which injections of anterograde tracers were placed in the medial pallium, have confirmed the projection of the latter structure to the striatum. A few fibers could be traced to the dorsal aspect of the striatum, but the majority of the fibers reach its ventral aspect.

Transition zone of the lateral pallium and striatum (S-portion of the primordial piriform cortex). There are several features of afferent connections that make the dorsolateral part of the striatum distinguishable from the rest of striatum. Apart from an olfactory input, as mentioned above, this region may have reciprocal connections with the ventral part of the striatum. A small iontophoretic



Figs. 8, 9. Photomicrographs of retrogradely labeled cells in the ventral striatum (Fig. 8) and medial amygdala (Fig. 9) of *Rana perezi* after a small BDA (10 kD) injection centered in the striatopallial transition area (asterisk in Fig. 8). See list of abbreviations. Scale bars = 100 μ m.

BDA injection placed within this area at intermediate telencephalic levels (case 9209, Fig. 8), revealed anterogradely labeled fibers that course ventrally from the injection site and surround the lateral forebrain bundle. Numerous varicose fibers and terminals were observed in the neuropil adjacent to the ventromedial part of the striatum, thus confirming the efferent nature of the projection. In addition, a group of retrogradely labeled neurons was located in the dorsal aspect of the ventral striatum, suggesting a reciprocity of the connections between these two areas. The latter injection also revealed a few labeled neurons in the lateral aspect of the medial amygdala (Fig. 9). A similar result was obtained in a case in which the ventral part of the striatum was involved (case 9529). Another difference was observed in the input from the anterior entopeduncular nucleus. Whereas applications to the striatum (cases 9331, 9516, 9529) yielded retrogradely labeled cells throughout the rostrocaudal extent of the entopeduncular nucleus, a restricted application to the transition area between the lateral pallium and the striatum (case 9209) resulted in labeled cells only in its rostral part.

Thalamic input. Large applications to the dorsal thalamus demonstrated heterogeneously distributed labeled fibers in the lateral neuropil of the striatum. Whereas in the ventral striatum the fibers are mainly confined to the

lateral neuropil, in the dorsolateral portion the fibers completely overlap the periventricular cell layers of the striatum.

Parabrachial input. After restricted injections in the rostroventral striatum (case 9516), only scattered neurons were observed in the parabrachial region, whereas those experiments involving the caudal half of the ventromedial striatum (cases 9529, 9316) labeled a much larger number of neurons in this region. Some of them were located immediately rostral to the parabrachial nucleus. To define more exactly the telencephalic sites of termination of the projection from the subcerebellar region, iontophoretic BDA injections were centered in the parabrachial nucleus. As depicted in Figure 10, efferent fibers reach the caudal striatum via the lateral forebrain bundle. At caudal telencephalic level, terminals occupy an external position within the caudal striatum (Fig. 10F,G). Slightly rostrally, most terminals were found in a periventricular position (Fig. 10E), but a band of fibers, which follow a submeningeal course, reach the transition zone between the lateral pallium and the striatum (Fig. 10D,E). At rostral telencephalic levels, terminals were found only in the latter region (Fig. 10B,C).

Afferent connections of the nucleus accumbens. Tracer applications to the ventromedial wall of the telencephalic hemisphere at various rostrocaudal levels yielded

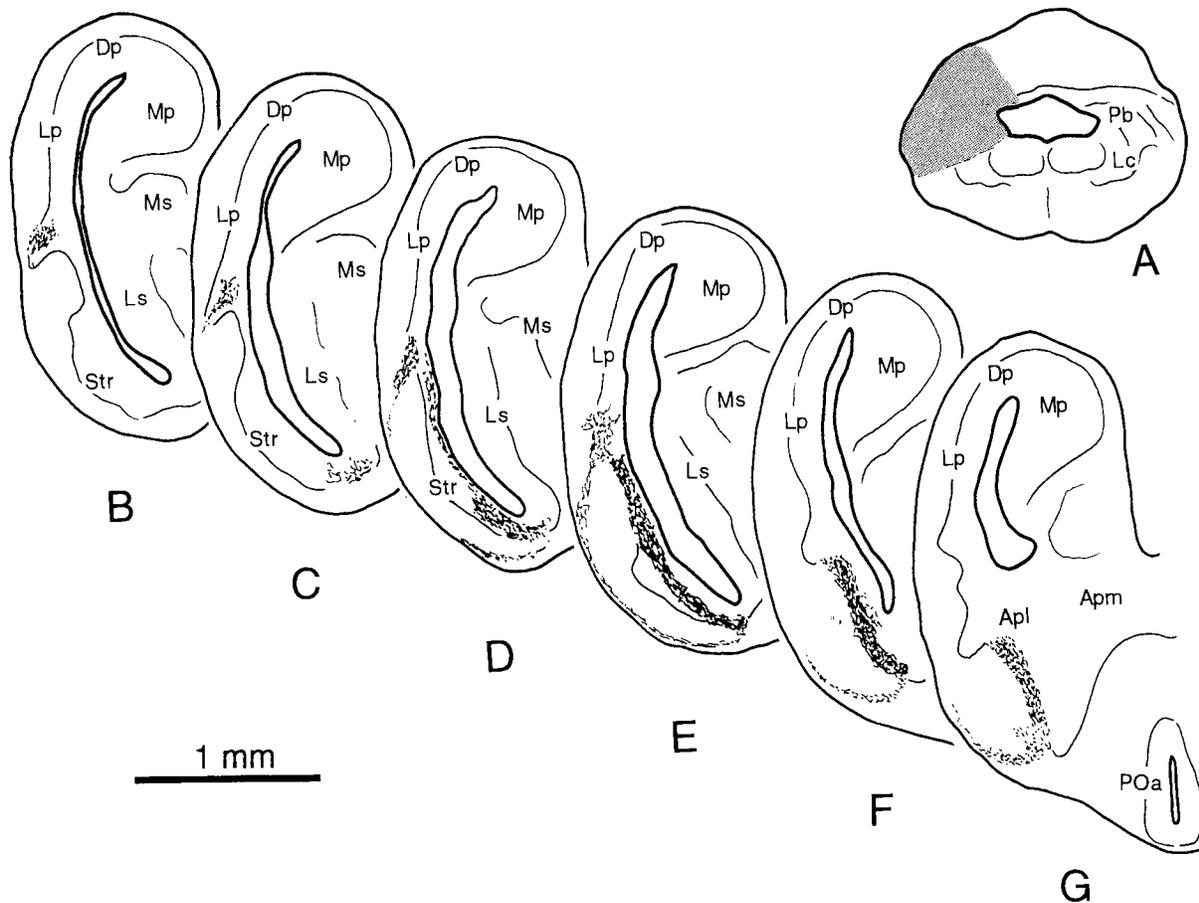


Fig. 10. A-G: Charting of anterograde labeling in the basal telencephalon of *Rana perezi* following a BDA (10 kD) injection into the subcerebellar region (shaded area in level A). See list of abbreviations.

different patterns of afferent connections. Only deposits in the rostral one-third of the ventromedial telencephalic wall resulted in a pattern that differed from that observed after striatal applications. Applications at intermediate and caudal levels may probably have involved part of the striatum and/or fibers of passage. For this reason, only the afferent connections to the rostral one-third of the ventromedial wall of the telencephalon are considered as true nucleus accumbens inputs. Even in the latter cases, it should be noted that the adjacent olfactory tubercle/diagonal band nucleus and the most ventral part of the lateral septum may be partly involved by the injection. Case 9562, in which BDA was applied to the nucleus accumbens of *Xenopus laevis*, has been selected as representative for the pattern of retrograde labeling seen after nucleus accumbens applications (Figs. 11, 12). The results are compared with those obtained from experiments in which the caudal two-thirds of the ventromedial wall were involved. If not otherwise stated, the description given for *Xenopus* holds also for *Rana perezi*.

Telencephalic connections. Application of BDA to the nucleus accumbens resulted in a considerable number of retrogradely labeled cells within the ventral part of the ipsilateral olfactory bulb (Fig. 11A). The cells are located in the mitral cell layer, although occasional scattered cells were also seen in the granular cell layer. Close to the

application site, some cells were labeled in the ventral part of the lateral septum and in the ventromedial aspect of the striatum. At this level, but also further caudally, retrogradely labeled neurons were observed in the transition zone of the lateral pallidum and the striatum (Fig. 11B,C). The axons of the latter cells form a tract superficial to the striatal neuropil that courses medially to the ventromedial aspect of the hemisphere. At the level of the application site, numerous cell bodies were labeled in the medial pallidum, mainly in its ventromedial aspect (Fig. 11B). In the caudal telencephalon, numerous neurons were located in the ipsilateral medial amygdala, intermingled with fibers of the medial forebrain bundle (Figs. 11C,D, 13). A few neurons were observed contralaterally in a corresponding position. Neurons in the lateral amygdala were restricted to the ventral and caudal portion of the nucleus. A few neurons were found immediately dorsal to the lateral forebrain bundle (Figs. 11D, 13). Some labeled cells with distinct processes are present in the preoptic area, where they lie close to the preoptic recess (Figs. 11D, 14).

Diencephalic connections. At diencephalic levels, a distinct group of labeled neurons is present in the suprachiasmatic nucleus. In the rostral portion of the nucleus, the cells were found bilaterally in the outer cell layers (Fig. 11E), whereas in its caudal portion the number of labeled

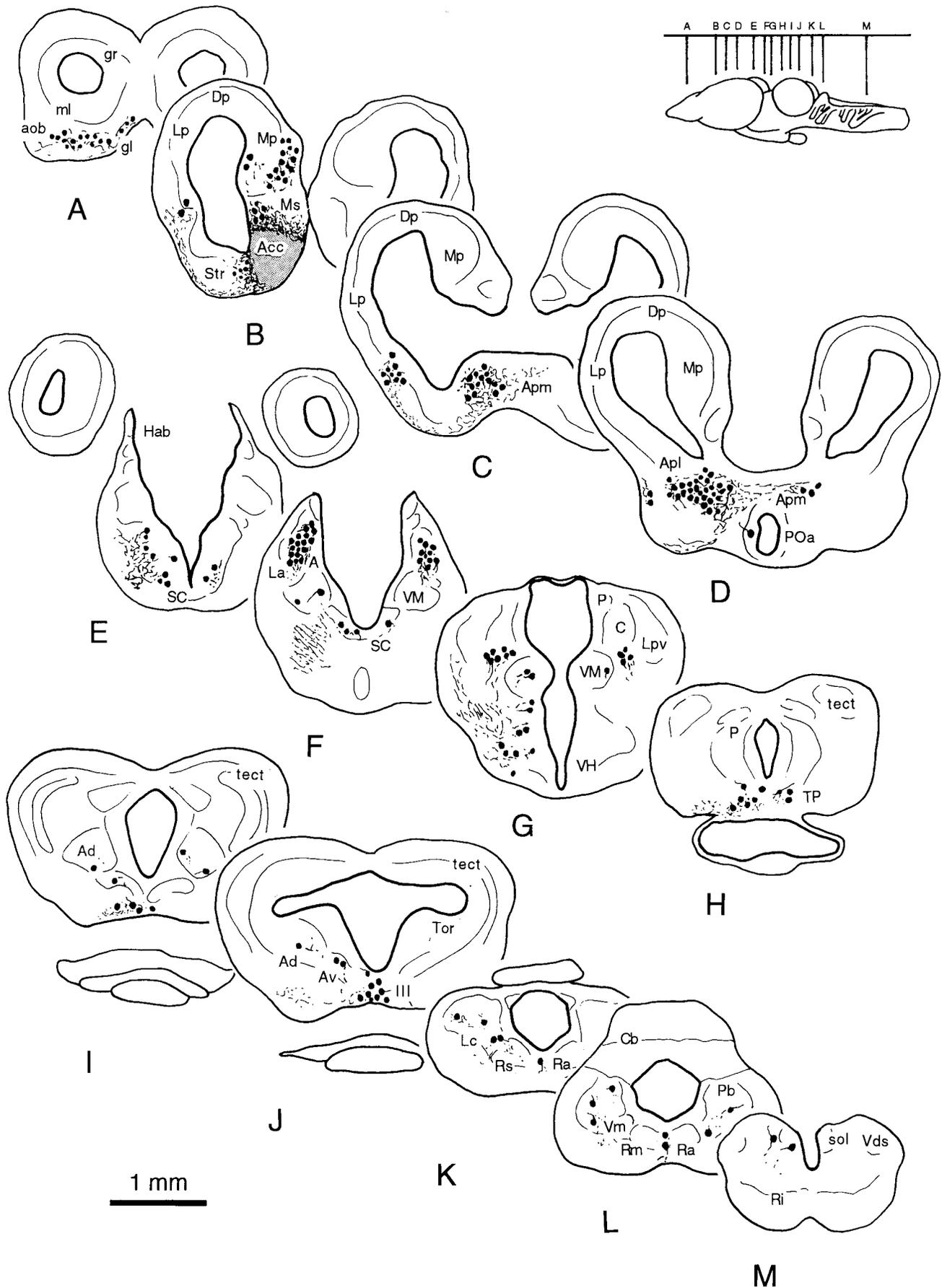
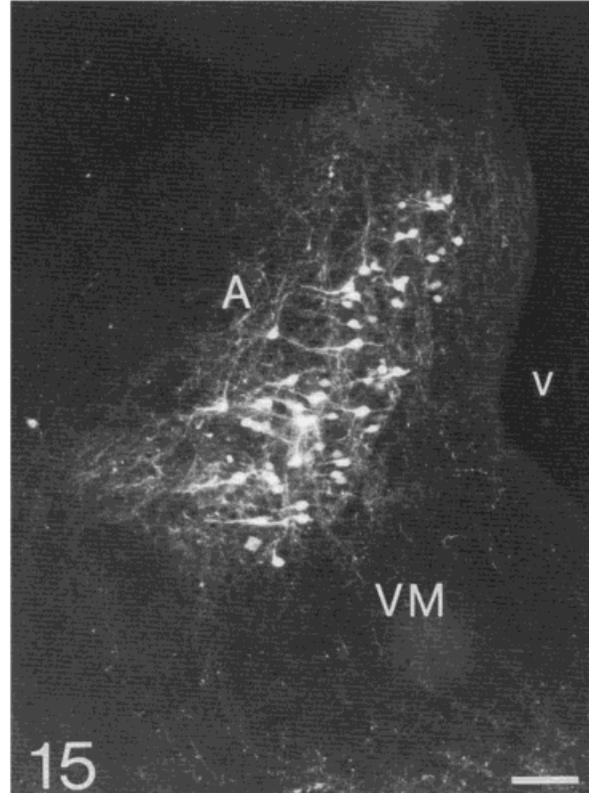
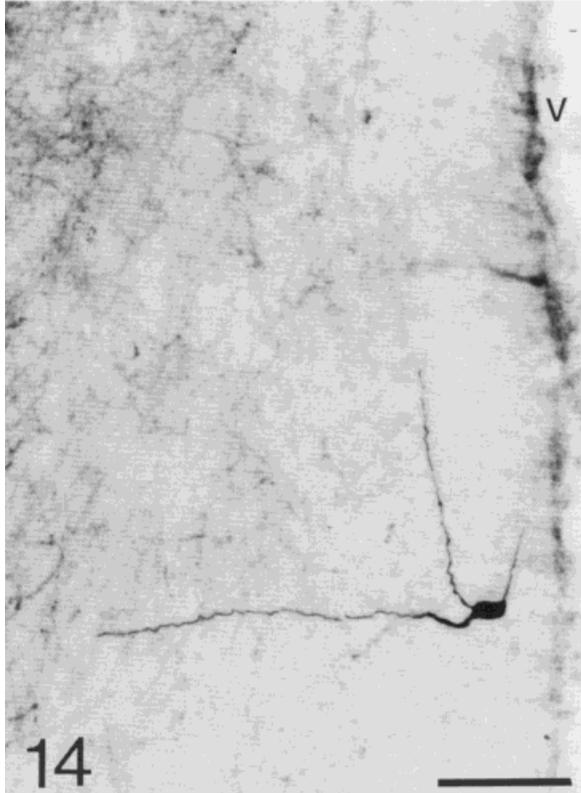
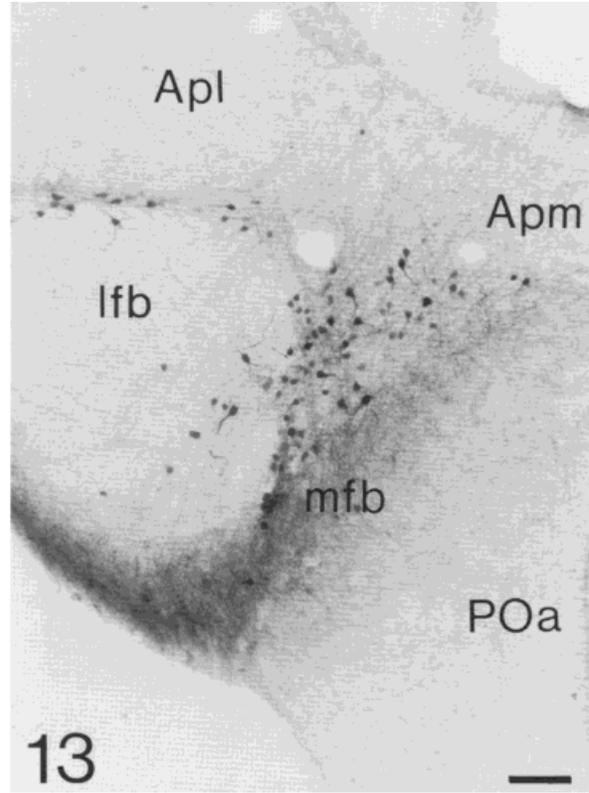
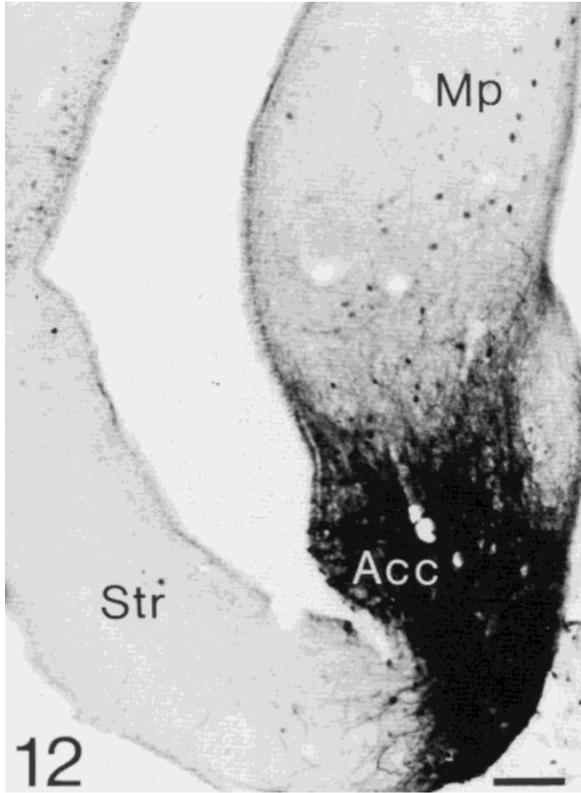


Fig. 11. A-M: Charting of retrograde labeling following a BDA (case 9562) application centered in the nucleus accumbens (shaded area in level B) of *Xenopus laevis*. Large dots represent labeled

neurons, whereas dashes and small dots represent labeled fibers. The levels of the sections A-M are indicated in the upper right scheme of the *Xenopus* brain. See list of abbreviations.



Figs. 12-15. Photomicrographs of retrograde labeling after application of BDA 10 kD (Figs. 12-14, *Rana perezii*) or TRDA (Fig. 15, *Xenopus laevis*) in the nucleus accumbens at the level of the application site (Fig. 12); around the lateral forebrain bundle and in the

medial amygdala (Fig. 13); in the anterior preoptic area (Fig. 14); and in the ipsilateral anterior thalamic nucleus (Fig. 15). See list of abbreviations. Scale bars = 200 μ m in Figure 12, 100 μ m in Figures 13-15.

cells is not only smaller, but their position also shifts from lateral to ventrolateral (Fig. 11F).

The largest diencephalic input to the nucleus accumbens arises in the dorsal thalamus. Neurons were consistently labeled bilaterally in the anterior thalamic nucleus (Fig. 11F). Within the nucleus, the labeled cells lie in a dorsal position at rostral levels, but caudally they shift to a more ventral position. These cells are fusiform or multipolar (Fig. 15), with processes that extend to the lateral neuropil. The axons of these neurons course ventrally and join the medial forebrain bundle. BDA injections in the anterior thalamic nucleus confirmed the projection of the anterior thalamic nucleus to the nucleus accumbens. Although most of the labeled fibers following such an injection were traced to septal and pallial areas, varicose fibers, and terminals were also observed in the nucleus accumbens.

A few round or piriform cells are located in the ventromedial thalamic nucleus, at the level of the caudal pole of the anterior thalamic nucleus (Fig. 11G). These cells are primarily found in the internal three cell layers. Occasionally, some neurons were observed in the contralateral ventromedial nucleus.

Hypothalamic afferents to the nucleus accumbens arise from cells in the ventral hypothalamus and the posterior tubercle. Labeled cells were consistently observed in the ventral hypothalamus (Fig. 11G), showing pear-shaped somata and a main process that courses dorsolaterally to join the bundle of ascending fibers. At the same level, the most rostrally located labeled cells within the posterior tubercle were found ventral to the ventromedial thalamic nucleus (Fig. 11G). The labeled cells in the posterior tubercle form a column that extends caudally to the level of the exit of the oculomotor nerve (Fig. 11H–J). Some differences in the topography of this projection were found between *Rana* and *Xenopus*. The rostral pole of the dorsomedial posterior tubercle in *Rana* is situated medially, whereas in *Xenopus* a more lateral position is found. Caudally, at the level where the left and right posterior tubercle fuse together, the position of the labeled cells is essentially similar in both species. In *Rana*, they were found in the caudal part of the dorsomedial posterior tubercle, whereas in *Xenopus* the cells were located mainly in the dorsal part of the posterior tubercle, where only a sparse population of cells is present. A considerable number of cells were found more caudally, extending up to the level of the third nerve (Fig. 11J).

Brainstem connections. In the midbrain tegmentum, retrogradely labeled cells were found in the anterodorsal and anteroventral tegmental nuclei and along the midline (Figs. 11J, 16, 17). The cells in the anterodorsal and anteroventral tegmental nuclei are multipolar, with processes directed ventromedially and laterally (Fig. 16). The cells along the midline, which are rostrally continuous with the labeled cells in the posterior tubercle, have processes which are mostly dorsoventrally oriented (Fig. 17). In the caudal part of the mesencephalon, a few neurons were labeled in the rostral raphe. These pear-shaped neurons have main processes, which are directed ventrally and, less frequently, laterally. This cell population continues caudally up to the level of the facial motor nucleus (Fig. 11K,L). Most cells lie close to the ventricle, but a few cells occur also in the ventral part of the raphe.

After tracer injections restricted to the nucleus accumbens, only a few labeled cells were found just rostral to or

within the parabrachial nucleus (Fig. 11K,L). However, more caudally located injections in the ventromedial telencephalon revealed a much larger number of labeled neurons in the parabrachial region. In fact, the number of labeled cells in the latter area appears to increase gradually as the injection sites is placed more caudally. Additional experiments, in which BDA was applied to the subcerebellar region, revealed varicose fibers and terminals in the ventromedial telencephalic wall at caudal and intermediate levels, but were almost absent rostrally (Fig. 10B–E).

Several other brainstem areas were found to project to the nucleus accumbens. Scattered neurons were observed in the lateral zone of the rhombencephalon at cerebellar levels and in the locus coeruleus (Fig. 11K,L). In *Xenopus*, but not in *Rana*, some cells were labeled in the area of the anterior lateral line nucleus. In both anuran species, cells were also observed in an area lateral to the pretrigeminal nucleus and, slightly caudally, lateral to the trigeminal motor nucleus. Only scattered cells were observed bilaterally in the rhombencephalic reticular formation, mainly in the nucleus reticularis superior (Fig. 11K,L). In the caudal rhombencephalon, a few cells were labeled ipsilaterally in the nucleus of the solitary tract (Fig. 11M).

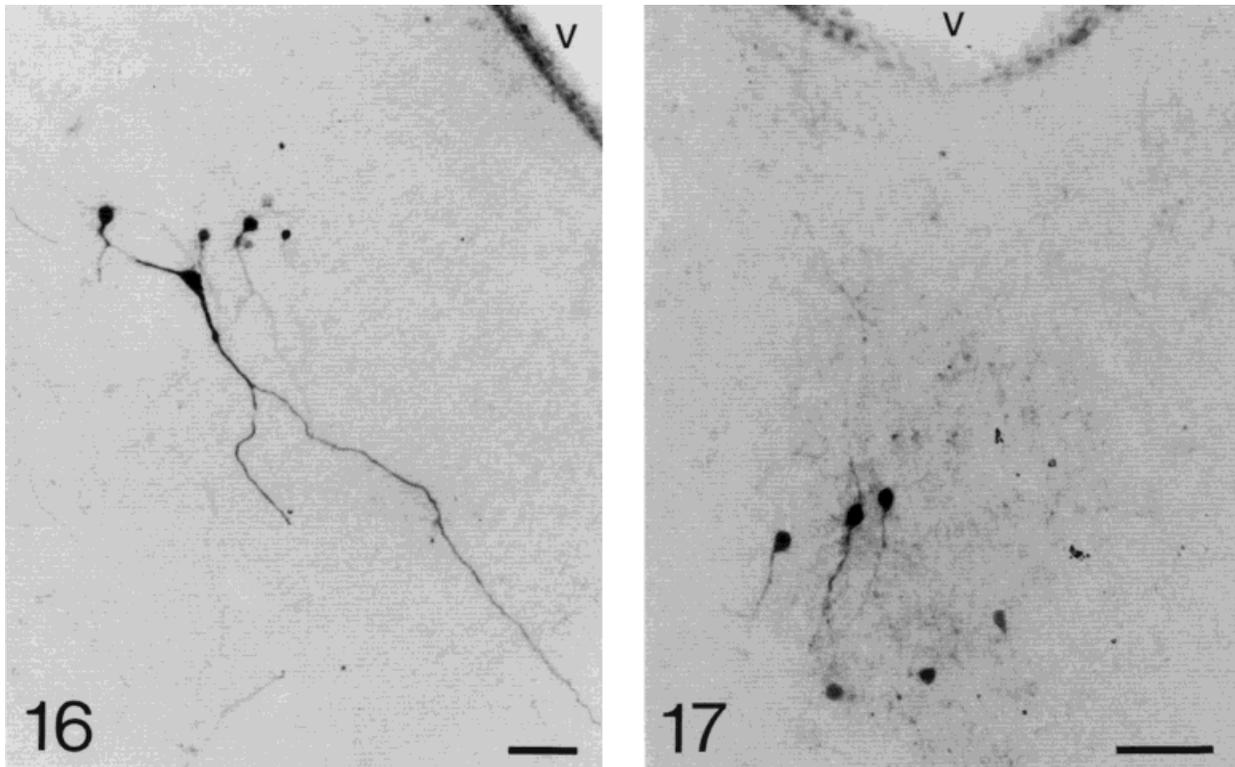
Telencephalic basal ganglia afferents in urodeles

In the urodele *Pleurodeles waltl*, small depositions of different retrograde tracers were made along the entire rostrocaudal extension of the lateral telencephalic wall, including both the striatum and the ventral cellular prominence (according to Northcutt and Kicliter, 1980). In addition, applications into the transition area between the caudal striatum and the rostral part of the lateral amygdala were made (see Fig. 1 and Table 1). Small tracer deposits located in the dorsal or in the ventral part of the ventrolateral wall of the hemisphere revealed different patterns of afferent connections. When the injection site was restricted to the striatum, the pattern of retrogradely labeled cells was similar to that obtained after striatal injections in anurans. In contrast, small injections centered in the ventral cellular prominence, revealed patterns of afferent connections that were related to those observed after nucleus accumbens injections in anurans. The position of the ventral cellular prominence, which we will refer to as the nucleus accumbens, is limited to the rostral half of the telencephalon.

Organization of striatal afferent connections. Tracer deposits in the striatum were centered in the dorsal part of the ventrolateral wall of the hemisphere. Cases with injections in the striatum not involving either the adjacent lateral pallium or the nucleus accumbens are described below. A representative series of transverse sections through the brain of *Pleurodeles* showing the distribution of retrogradely labeled cells after a striatal application of BDA is given in Figure 18 (case 95113).

Telencephalic connections. Tracer deposits made in rostral parts of the striatum resulted in labeled cells primarily in the ventral part of the ipsilateral olfactory bulb (Fig. 18A). The cells are located mainly in the mitral cell layer, although some cells are intermingled with fibers of the external plexiform layer.

At the level of the application site (Fig. 18B), a few labeled neurons were observed in the ventral aspect of the lateral pallium. Ventrally, some neurons were found inter-



Figs. 16, 17. Photomicrographs of retrogradely labeled cells after application of BDA (10 kD) into the nucleus accumbens of *Rana perezi* as observed in the anteroventral tegmental nucleus of the midbrain (Fig. 16), and in the medial tegmental area of the midbrain, at the level of the oculomotor nucleus (Fig. 17). See list of abbreviations. Scale bars = 50 μ m.

mingled with labeled fibers at the border of the application site. In the telencephalic roof, only a few neurons were observed in the medial pallium. Slightly caudal to the application site, labeled fibers course in the lateral forebrain bundle, dorsal to the nucleus accumbens.

In the caudal telencephalon, neurons were consistently labeled in the ipsilateral lateral amygdala (Fig. 18C). The cells are piriform or fusiform in shape, with a main process that intermingles with the fibers of the lateral forebrain bundle. Only a few cells were observed in the ipsilateral medial amygdala and in the contralateral lateral amygdala. Starting at the level of the rostral pole of the preoptic recess and extending caudally, labeled neurons were noted in the preoptic area (Fig. 18D). At about the same levels, labeled cells occur medial to the lateral forebrain bundle, with processes that merge into the bundle (Fig. 18D).

Diencephalic connections. Several nuclei in the diencephalon contain labeled cell bodies after striatal injections. A number of labeled cells were observed in the suprachiasmatic nucleus. The cells were found bilaterally, mainly in the dorsolateral part of the nucleus (Fig. 18E). At slightly more caudal levels, numerous neurons were seen in the posterodorsal thalamic zone (Fig. 18F). These neurons are generally large or medium-sized, piriform-shaped or round, and with a long process that extends laterally (Figs. 18F,G, 19). Axons from these cells also course first laterally and then ventrally, to enter into the dorsal aspect of the lateral forebrain bundle (Figs. 18F, 19). In a series of experiments with injection sites centered in the posterodorsal zone, the ascending efferent fibers course

within the lateral forebrain bundle and densely innervate the striatal neuropil, just external to the periventricular cell layer. Notably, this projection avoids the cells and fiber zone of the ventromedially located nucleus accumbens.

After a striatal application, a few labeled neurons were found in the ventral thalamus (Fig. 18F). Slightly more caudally, some labeled cells occurred at the border between thalamus and hypothalamus (Fig. 18G). The cells are pear-shaped with processes that laterally join the bundle of ascending fibers. Caudal to this level, labeled cells were observed bilaterally in the dorsomedial aspect of the posterior tubercle (Fig. 18H). Scattered cells were also found in a region just ventral to the ventrolateral posterior tubercle and in the ventral hypothalamus (Fig. 18H).

Brainstem connections. The labeled cells in the dorso-medial posterior tubercle extend throughout the caudal diencephalon and are caudally continuous with labeled cells in the mesencephalic tegmentum up to the level of the exit of the oculomotor nerve. In the mesencephalon, the neurons are located close to the midline and possess axons that course first ventrally and then laterodorsally to ascend in the lateral forebrain bundle (Figs. 18I, 20). At the level of the trochlear nucleus, large neurons were found in the reticular isthmus nucleus (Figs. 18J, 21).

A large population of neurons was consistently labeled in the ipsilateral subcerebellar region, i.e., the parabrachial nucleus (Fig. 18K). At the same level, large multipolar neurons were observed in the ipsilateral locus coeruleus (Fig. 18K). The latter cells possess two or three main dendrites, which are in close relationship with the longitu-

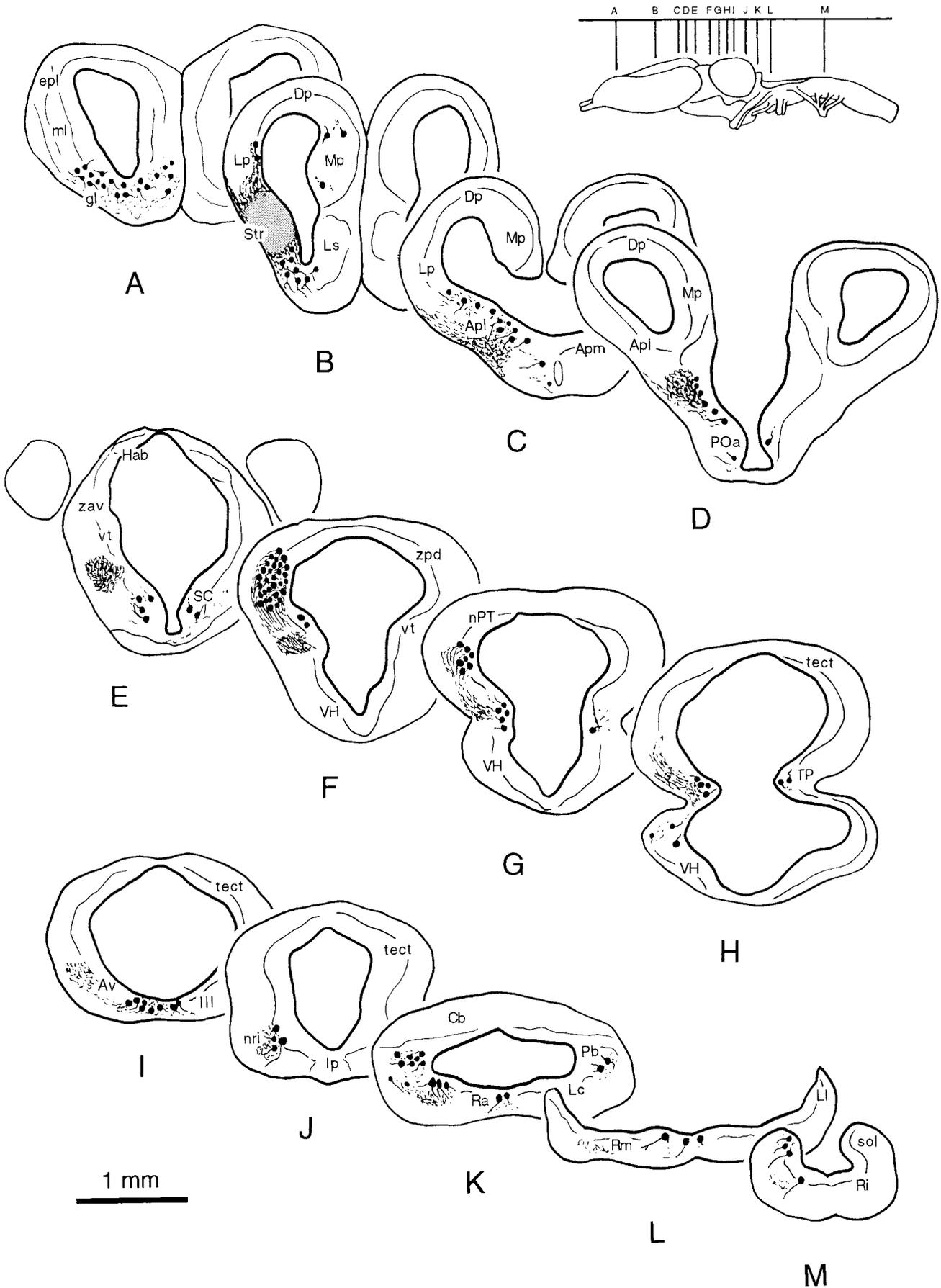
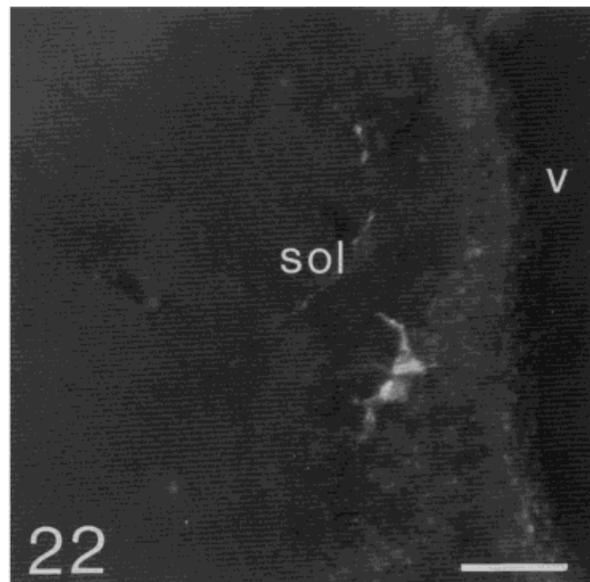
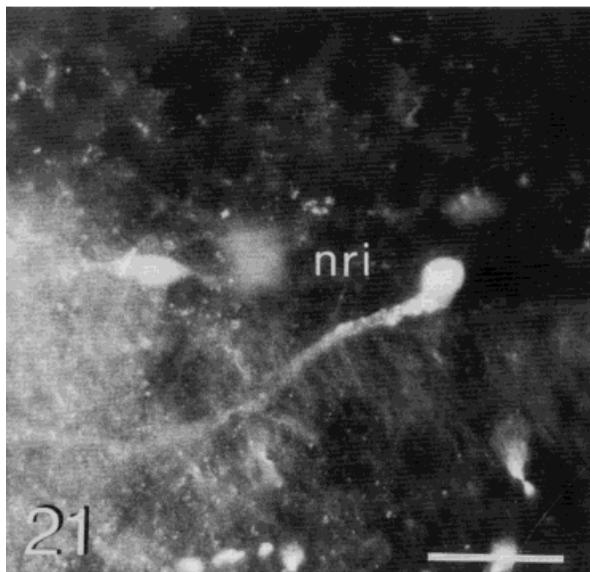
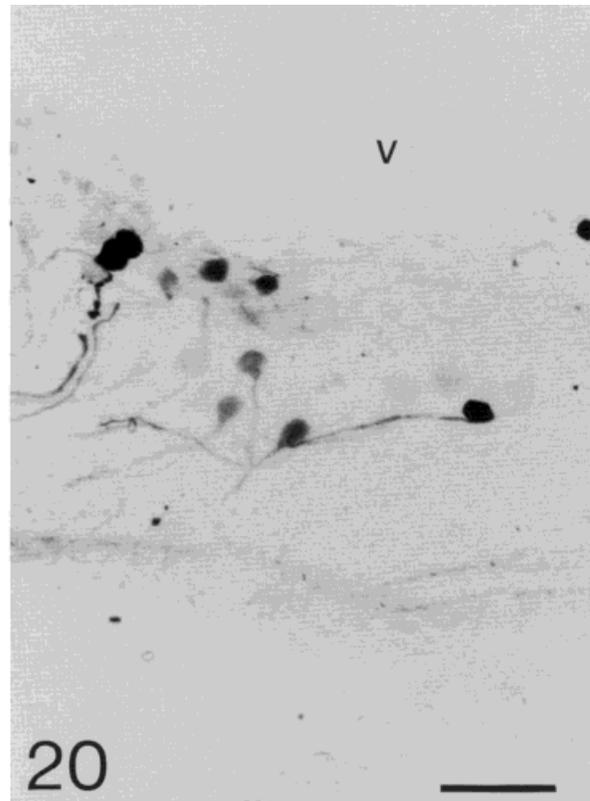
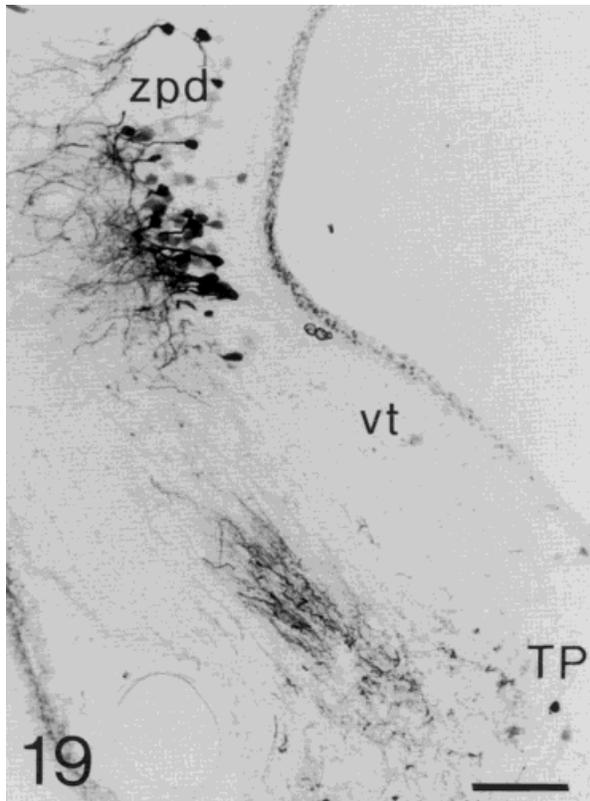


Fig. 18. A-M: Charting of retrograde labeling following a BDA (case 95113) application centered in the striatum (shaded area in level B) of *Pleurodeles waltl*. Dots represent labeled neurons whereas dashes and small dots represent labeled fibers. The levels of the sections A-M are indicated in the upper right scheme of the *Pleurodeles* brain. See list of abbreviations.



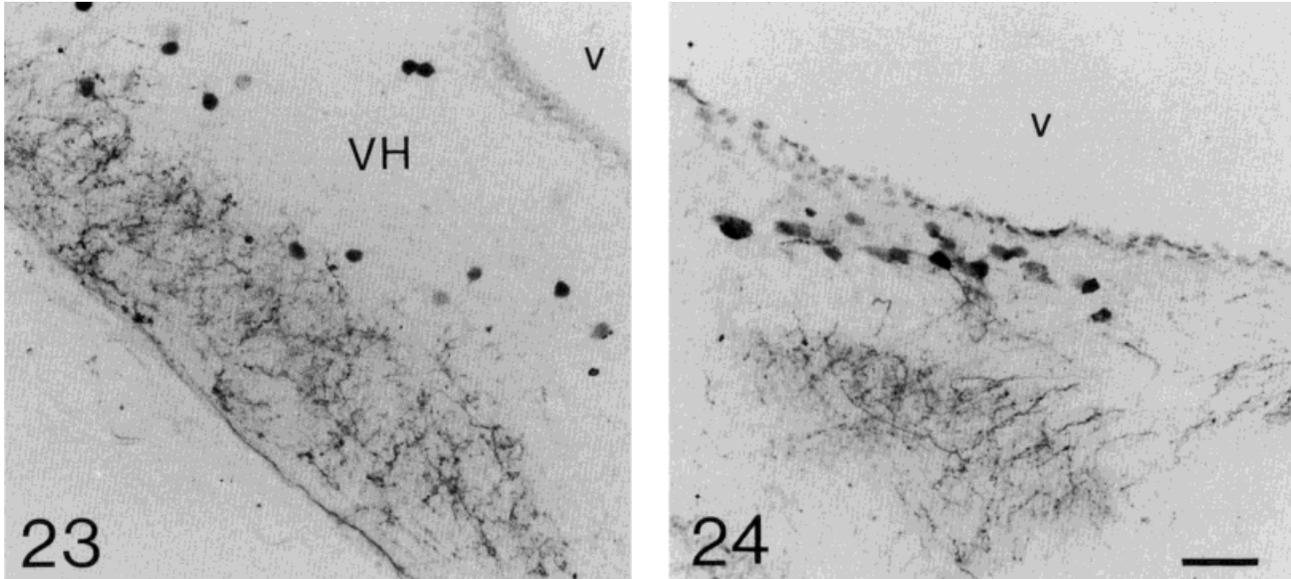
Figs. 19–22. Photomicrographs of retrogradely labeled cells after application of BDA 10 kD (Fig. 19), BDA 3 kD (Fig. 20), TRDA 3 kD (Fig. 21), and FluoroGold (Fig. 22) into the striatum of *Pleurodeles waltl* in the zona posterodorsalis of the thalamus and posterior tubercle (Fig. 19); the medial tegmental area of the midbrain, at the

level of the oculomotor nucleus (Fig. 20); the reticular isthmus (Fig. 21); and the nucleus of the solitary tract (Fig. 22). See list of abbreviations. Scale bars = 100 μ m in Figure 19, 50 μ m in Figures 20–22.

dinal bundle of labeled fibers. Medial to the locus coeruleus, some scattered reticular neurons were labeled, as well as a few large piriform cells located in the raphe (Fig. 18K,L). At caudal brainstem levels, some neurons were

labeled in the median and inferior reticular nuclei, and in the nucleus of the solitary tract (Figs. 18M, 22).

Finally, tracer applications to the caudal one-third of the lateral telencephalic wall (case 9348), labeled many more



Figs. 23, 24. Photomicrographs of retrogradely labeled cells and fibers after BDA (10 kD) application to the caudal portion of the striatum of *Pleurodeles waltl* in the ventral hypothalamus (Fig. 23), and in the anteroventral octavolateral area (Fig. 24). See list of abbreviations. Scale bar = 100 μ m.

neurons in the ventral hypothalamus (Fig. 23), the parabrachial nucleus and the solitary tract nucleus as compared to rostral injections. Furthermore, an additional population of neurons was found slightly caudal to the cerebellum, in the dorsolateral rhombencephalon within the area octavolateralis (Fig. 24).

Afferent connections of the nucleus accumbens. The following description of the afferent connections of the nucleus accumbens of *Pleurodeles waltl* is based on case 95112. The application site was restricted to the most ventral aspect of the lateral telencephalic wall (Figs. 25, 26), and did not involve the striatum, its neuropil, or the ventromedial wall of the telencephalic hemisphere.

Telencephalic connections. Rostral to the application site, labeled cells were observed in the ipsilateral olfactory bulb (Fig. 25A). They were mainly located in the ventrolateral aspect of the mitral cell layer. A few cells were present in the granular cell layer. At the level of the application, some weakly stained neurons were observed immediately dorsal to the striatum (Fig. 25B). At this level, labeled neurons in pallial areas were absent.

In the caudal telencephalon, numerous neurons were found just dorsal to the labeled fibers in the medial forebrain bundle (Fig. 25C). The majority of these cells are positioned laterally in the medial amygdala, whereas in comparison fewer labeled cells are present ventrally in the lateral amygdala. At the same level, a compact group of neurons was observed in the medial pallium (Figs. 25C, 27). The latter cells are bipolar or piriform in shape and mainly confined to the dorsolateral part of the medial pallium. In the caudolateral amygdala, only a few neurons were observed, whereas a large number of cells is present in the medial amygdala (Fig. 25D, 28). Some labeled neurons were also found contralaterally. After tracer deposition in the nucleus accumbens only a few cells were labeled in the preoptic area.

Diencephalic connections. In the dorsal thalamus, cells were observed bilaterally in the anteroventral thalamic

zone (Fig. 25F). At the same level, a few neurons are located bilaterally in the dorsolateral aspect of the supra-chiasmatic nucleus. No labeled cells were observed in the posterodorsal thalamic zone (Fig. 25G). In the ventral thalamus, round and piriform neurons were observed ipsilaterally (Fig. 25G), although occasionally cells were also found contralaterally. The number of neurons observed in the ventral thalamus was considerably higher after application in the caudal third of the ventrolateral wall of the telencephalic hemisphere. Furthermore, in such experiments, numerous neurons were labeled in the infundibular ventral hypothalamus, whereas only a few were found after tracer application in the nucleus accumbens (Fig. 25G–H).

In the posterior tubercle, neurons were labeled bilaterally, constituting a column of neurons that extends caudally into the mesencephalon (Fig. 25H,I), as is also the case after striatal injections. However, the population of cells labeled in the rostral part of this column was only observed after injections in the nucleus accumbens. The number of retrogradely labeled neurons observed in the caudal part of the diencephalon and in the mesencephalic tegmentum was approximately the same for both striatal and nucleus accumbens injections.

Brainstem connections. At the level of the oculomotor nucleus, labeled neurons were observed ipsilaterally not only adjacent to the midline (Fig. 29), i.e. the caudal continuation of the posterior tubercle group, but also in the anterodorsal and, more frequently, the anteroventral tegmental nuclei (Fig. 25I). Some cells were also present in the contralateral tegmentum. At the level of the cerebellum, a few cells were observed in the region of the parabrachial nucleus. Some scattered neurons were found ipsilaterally ventral and ventrolateral to the parabrachial nucleus, as well as bilaterally in the nucleus reticularis superior (Fig. 25J). A few large neurons were labeled in the ipsilateral locus coeruleus, mainly at a level immediately caudal to the cerebellum (Fig. 25K). At the same level,

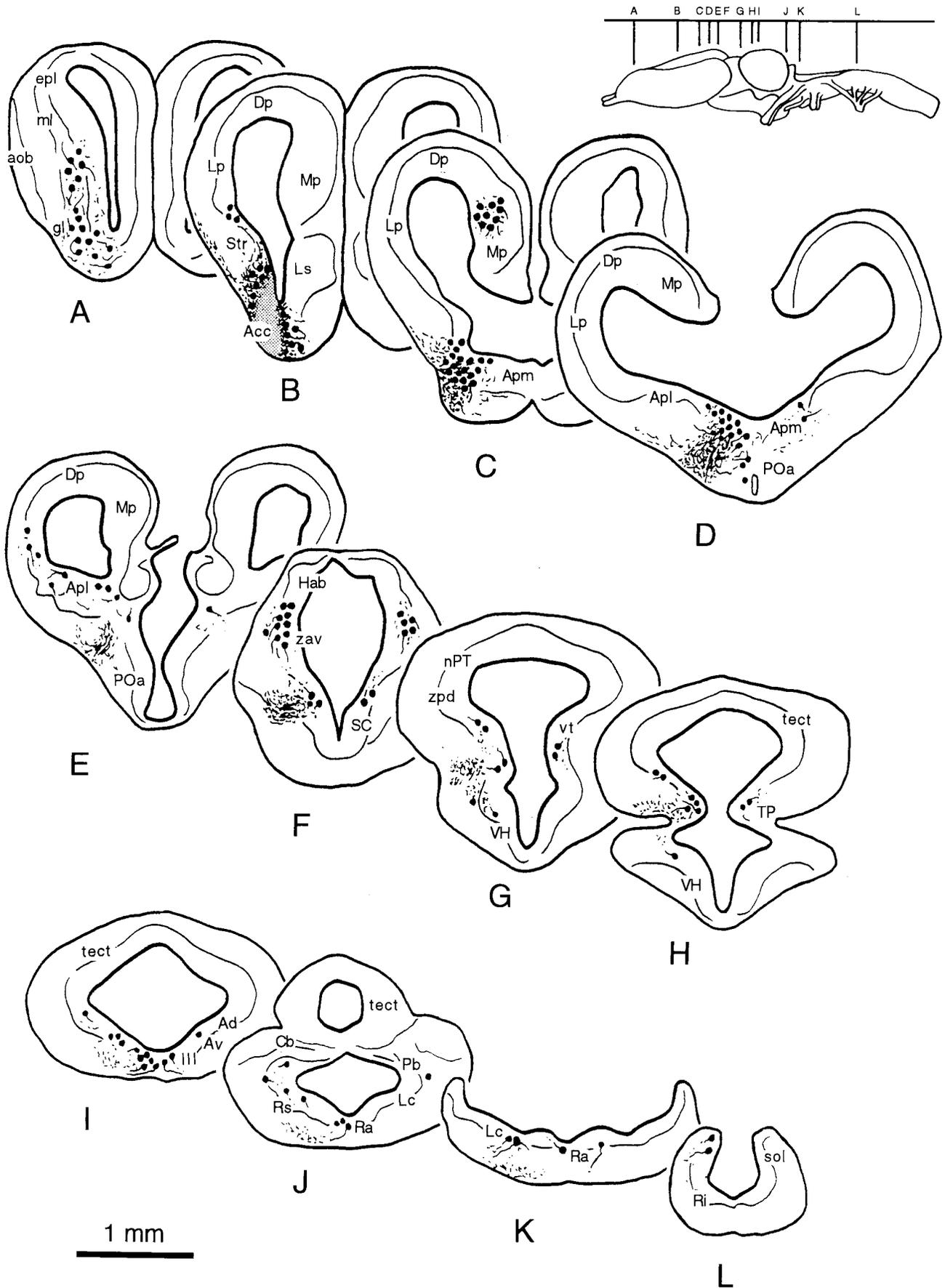
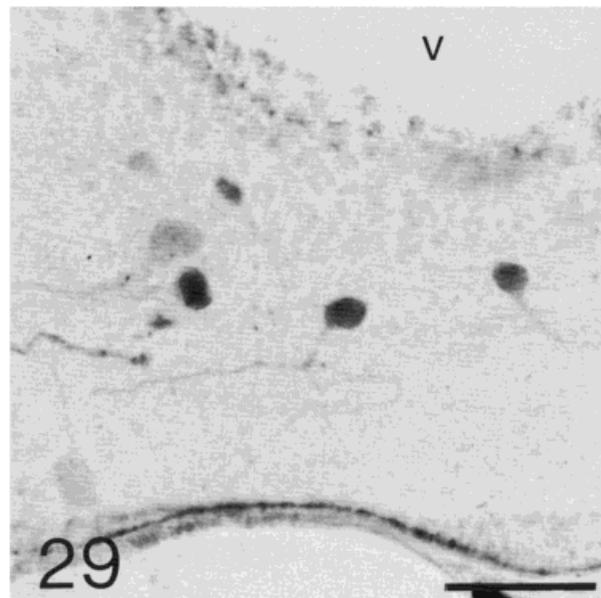
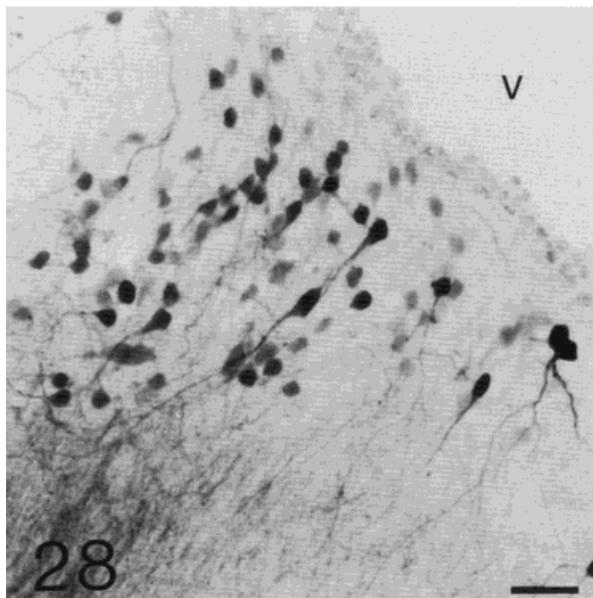
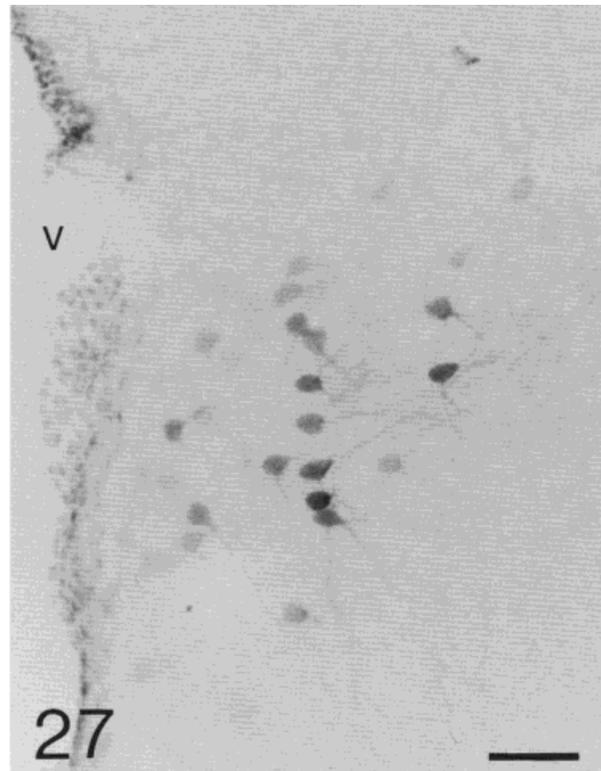
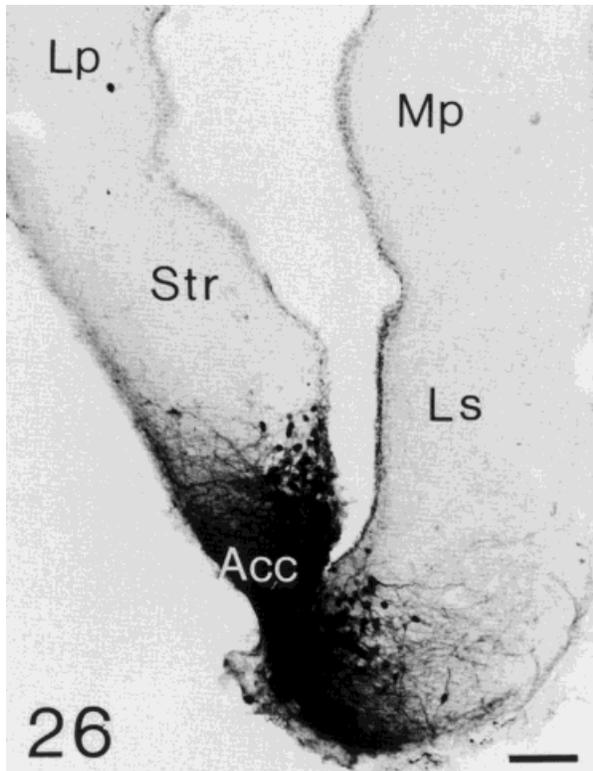


Fig. 25. A-L: Charting of the retrograde labeling following a BDA (case 95112) application centered in the nucleus accumbens (shaded area in level B) of *Pleurodeles waltl*. Large dots represent labeled

neurons; dashes and small dots represent labeled fibers. The levels of the sections A-L are indicated in the upper right scheme of the *Pleurodeles* brain. See list of abbreviations.



Figs. 26–29. Photomicrographs of retrograde labeling after tracer application of BDA 10 kD (Figs. 26–28) or BDA 3 kD (Fig. 29) into the nucleus accumbens of *Pleurodeles waltl* showing the level of the injection site (Fig. 26); the posterior region of the medial pallium (Fig.

27); the medial amygdala (Fig. 28); and the medial tegmental area of the midbrain, at the level of the oculomotor nucleus (Fig. 29). See list of abbreviations. Scale bars = 200 μ m in Figure 26, 50 μ m in Figures 27–29.

scattered cells with long ventrally oriented dendrites were observed in the nucleus reticularis medius. Numerous neurons were labeled in the raphe. They were mainly located in the dorsal aspect of the rostral raphe, at caudal mesencephalic and upper rhombencephalic levels (Fig.

25J,K). The most caudally located cells were found close to the obex in the nucleus of the solitary tract (Fig. 25L).

Tracer applications at intermediate and caudal levels of the telencephalon (e.g., cases 9348, 9512) resulted in increased numbers of labeled cells in the ventral thala-

mus, the ventral hypothalamus, and the parabrachial nucleus.

DISCUSSION

Previous immunohistochemical studies have revealed two distinct terminal fields of dopaminergic fibers in the basal forebrain of anurans and urodeles (González and Smeets, 1991, 1994; González et al. 1993), suggesting a further differentiation of this region into a nucleus accumbens and a striatum. The present study is the first attempt to provide evidence for such a differentiation on the basis of the afferent connections to the respective subdivisions. The diagrams shown in Figures 30 and 31 summarize the inputs to the striatum (A) and the nucleus accumbens (B), as demonstrated by the present study. Obviously, both structures have many inputs in common. However, there are several nuclei in the brain that project either to the striatum or to the nucleus accumbens but not to both. For example, the anterior entopeduncular nucleus, the anterior and posteroventral parts of the lateral thalamic nucleus, the central thalamic nucleus, the superficial isthmal reticular nucleus and the torus semicircularis project to the striatum but not to the nucleus accumbens. In contrast, the anterior thalamic nucleus, and the anterodorsal and the anteroventral tegmental nuclei exclusively reach the nucleus accumbens. Of note, some nuclei project to both subdivisions, but show a clear preference for the striatum (lateral amygdala, parabrachial region) or for the nucleus accumbens (medial amygdala, midbrain dopaminergic cell group). It is also clear that the projection fibers to the striatum take generally a more lateral course than those to the nucleus accumbens.

The present studies support the division of the basal forebrain into striatum and nucleus accumbens. We also confirm previous reports of basal forebrain inputs and describe several additional connections, such as those from the caudal brainstem. In the following sections, the present results are first compared with those of previous studies in amphibians. Subsequently, the expanded view on basal forebrain organization in amphibians will be discussed in relation to the basal ganglia organization in amniotes. Finally, some comments on the functional significance of basal forebrain inputs of amphibians are given.

Comparison with previous studies in amphibians

Telencephalon. In anuran as well as in urodele amphibians, telencephalic inputs to the basal forebrain arise from pallial and subpallial areas. As shown by the present study, pallial afferent projections originate primarily from the medial pallium, whereas a much weaker projection arises in the lateral pallium. A medial pallial projection to the striatum has not always been recognized. HRP studies by Vesselkin et al. (1980), Wilczynski and Northcutt (1983a) and Dubé et al. (1990) failed to retrogradely label cells in the pallium after striatal injections. On the other hand, evidence for a medial pallial projection to the striatum was provided by Neary (1988, 1990) using the wheat germ agglutinin-HRP (WGA-HRP) technique, by Northcutt and Ronan (1992) with autoradiography, and by González et al. (1994) using dextran amines and Fluoro-Gold as retrograde tracers. The present data confirm and extend the concept that medial pallial neurons project mainly to the ventromedial aspect of the striatum in

anuran amphibians. Previous studies in urodeles revealed that neurons located at anterior, but not posterior levels of the medial pallium project to the striatum (Sassoè-Pognetto et al., 1991, 1995). The present study shows that, at least in *Pleurodeles*, the nucleus accumbens receives an input from neurons located in the caudal part of the medial pallium. Since the nucleus accumbens of the latter species is located in the ventral aspect of the lateral telencephalic wall, it seems unlikely that the labeled cells are due to the interruption of fibers coursing to the medial pallium. The present study also shows that in both anurans and urodeles, more medial, as compared to lateral, pallial cells project to the nucleus accumbens.

Substantially more afferents to the striatum and the nucleus accumbens arise from several subpallial regions, viz., the lateral and medial amygdala and the caudal ventral striatum, which lies immediately dorsal to the lateral forebrain bundle. As shown by the present study, the striatum receives its input predominantly from the lateral amygdala, whereas the nucleus accumbens is the preferred target of medial amygdaloid projection fibers. In a comprehensive study of the olfactory projections in the frog, *Rana pipiens*, Scalia et al. (1991) subdivided the lateral amygdala (amygdala as originally designated by Herrick, 1921) into cortical and medial subdivisions, which are both continuous with the ventral part of the lateral pallium (Northcutt, 1974; Northcutt and Kicliter, 1980). In agreement with the studies of Scalia et al. (1991), the present study shows that neurons projecting to the striatum and the nucleus accumbens are located mainly in the cortical amygdaloid division, whereas only a few cells are found in the more caudal medial amygdaloid portion. The cortical amygdaloid subdivision receives projections from the main and the accessory olfactory bulbs, whereas the medial amygdaloid subdivision receives only projections from the accessory olfactory tract (Scalia et al., 1991). The striatum also receives a projection from the caudal extension of the ventral striatum, i.e., the anterior entopeduncular nucleus. Furthermore, cells located in the striatopallial transition area also project to lateral and medial regions of the basal telencephalon. In contrast to what has been previously suggested (Dubé et al., 1990), the telencephalic afferents to the striatum and nucleus accumbens are very similar in anuran and urodele amphibians. Although an anterior entopeduncular nucleus could not be clearly distinguished in urodeles, a number of cells were always found labeled in the caudal telencephalon in close relationship to the lateral forebrain bundle after tracer deposits in the striatum. Thus, these cells may be analogous to the anterior entopeduncular cell group of anurans.

Traditionally, the nucleus accumbens of anurans has been considered to be located in the ventromedial part of the telencephalic hemispheric wall and to extend to the level of the lamina terminalis (Northcutt, 1974; Northcutt and Kicliter, 1980; Wilczynski and Northcutt, 1983a,b; Scalia et al., 1991). However, the present study provides evidence that the nucleus in its entirety is restricted to the rostral one-third of the telencephalic hemisphere. Many cells located in the caudal two-thirds of the ventromedial telencephalic wall project to the striatum or to the nucleus accumbens. Caudally this area merges into the medial amygdala.

The striatum and, less prominently, the nucleus accumbens receive a bilateral projection from the transition area

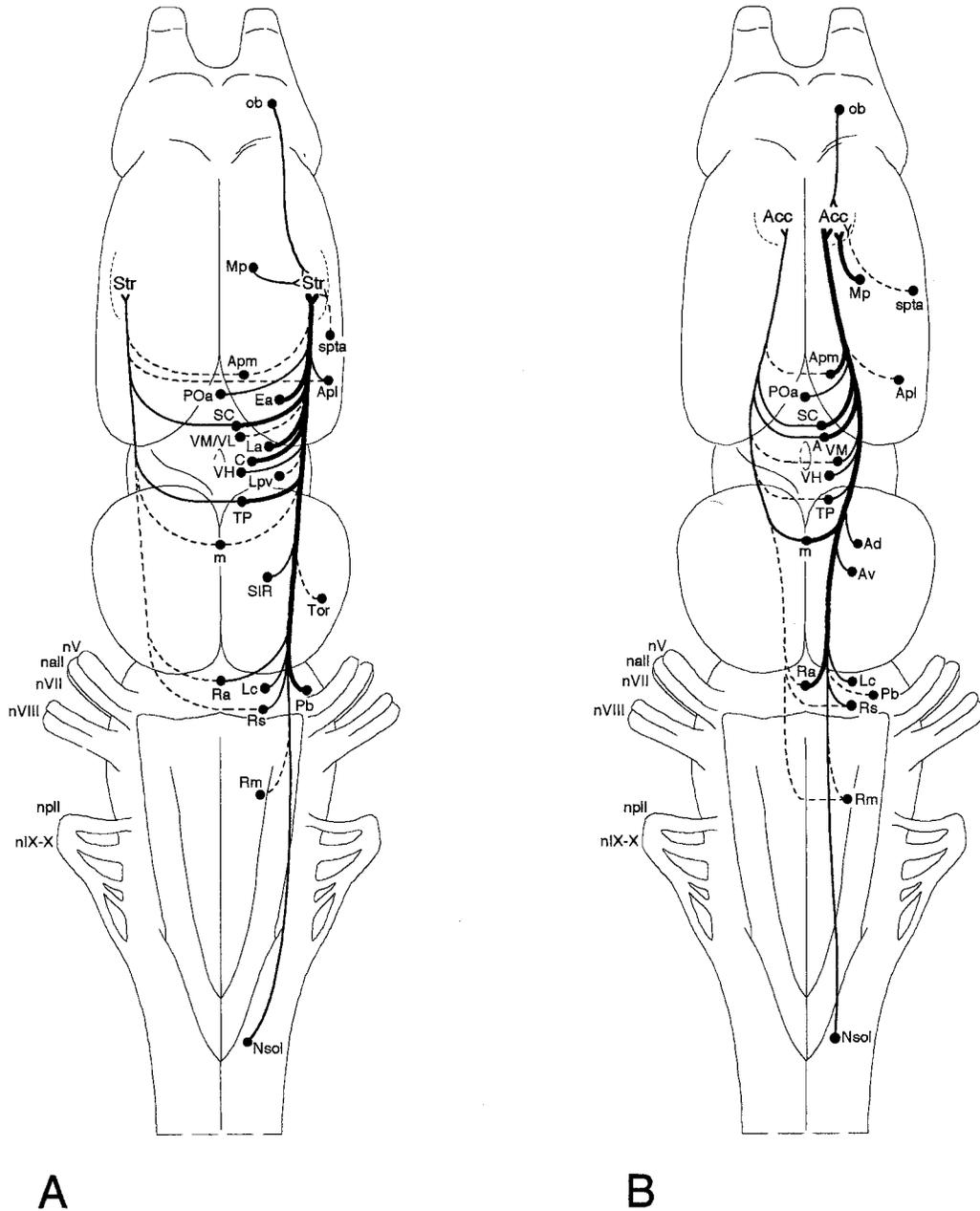


Fig. 30. Summary diagram that shows the afferent connections of the striatum (A) and the nucleus accumbens (B) in the anuran brain. See list of abbreviations.

between the caudal ventral striatum and the anterior entopeduncular nucleus. The cells of origin of this projection lie lateral to the medial amygdala, just dorsal to the lateral forebrain bundle (Fig. 13) and are reciprocally connected with more rostrally located basal ganglia regions. Reciprocal connections between the striatum of both sides were suggested for urodeles in experiments with tracer applications at very caudal telencephalic levels (Dubé et al., 1990). However, in the present study, cells were never labeled in the contralateral striatum proper after striatal applications in both anurans and urodeles.

In anurans and urodeles, vasotocinergic and mesotocinergic neurons have been demonstrated around the tip of

the lateral ventricle at caudal telencephalic levels, within the medial amygdala, the caudal ventral striatum, and the lateral amygdala (González and Smeets, 1992a,b). Since the nucleus accumbens of amphibians receives a prominent peptidergic innervation, it seems likely that the vasotocinergic and mesotocinergic innervation of the latter structure may be partly derived from these neurons. However, a combined tract-tracing and immunohistochemical study is needed to confirm this hypothesis.

Finally, some comments on the striatopallial transition area have to be made. In anurans, the striatopallial transition area extends from a level slightly caudal to the accessory olfactory bulb to preoptic levels. From rostral-to-

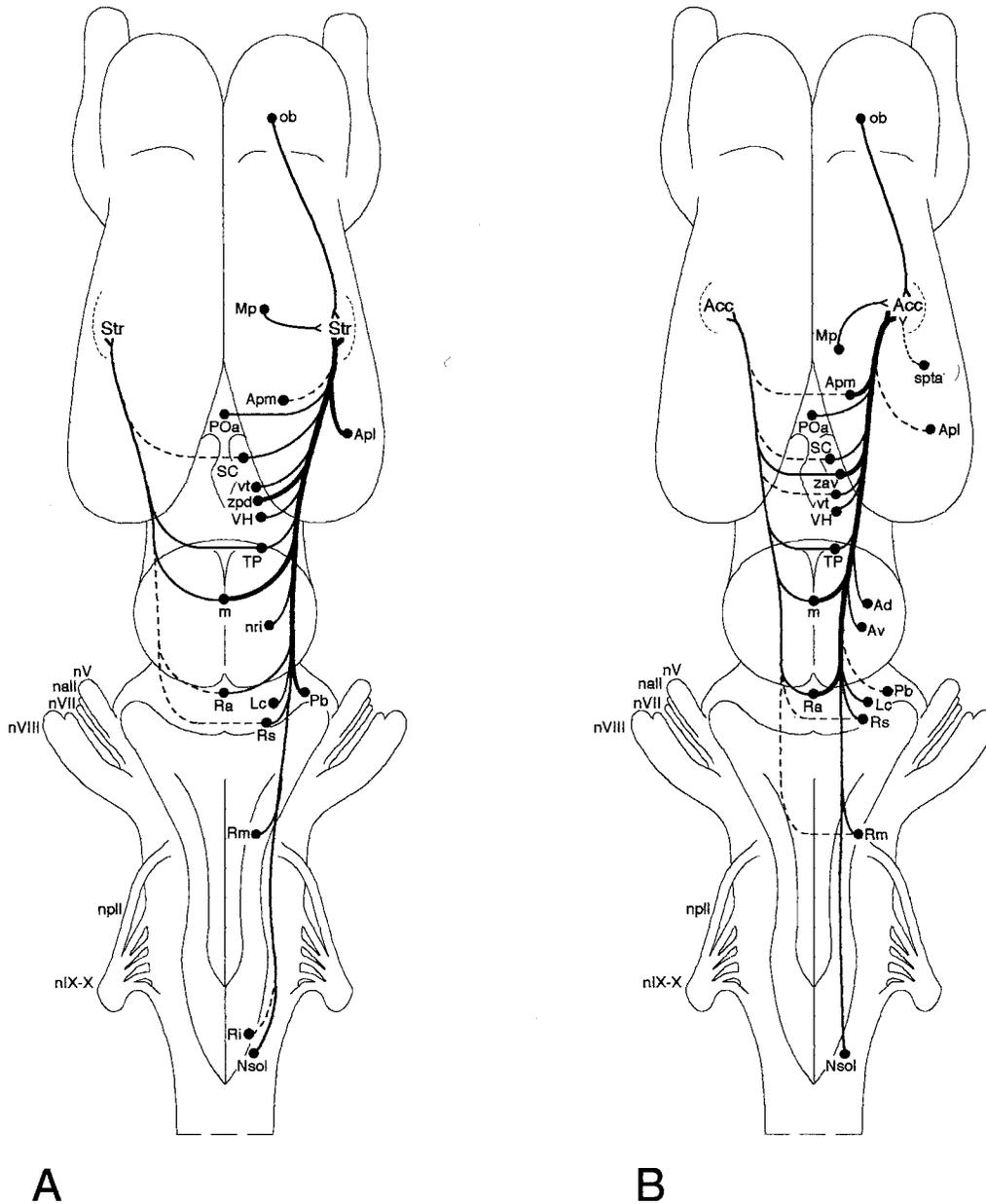


Fig. 31. Summary diagram that shows the afferent connections of the striatum (A) and the nucleus accumbens (B) in the urodele brain. See list of abbreviations.

caudal, this region is located successively ventral to the lateral pallium, the periamygdaloid area (caudal, ventral part of the lateral pallium), and the lateral amygdala (Northcutt and Kicliter, 1980; Scalia et al., 1991). Originally defined as a ventral portion of the lateral pallium (Hoffman, 1963), the histochemical and immunohistochemical pattern of this region is remarkably different from the surrounding territories (Northcutt, 1974; Inagaki et al., 1981; Taban and Cathieni, 1983; Merchenthaler et al., 1989; González and Smeets 1991, 1992a, 1992b, 1993, 1995; González et al., 1993, 1996; Muñoz et al., 1996; Tuinhof et al., 1994a). However, the chemoarchitecture of this region changes along the rostrocaudal axis. Thus, although the rostral part of the region is clearly distinct

from the lateral pallium and the striatum, its caudal aspect progressively fuses ventrally with the lateral amygdala. On the other hand, the whole rostrocaudal extent of this region receives specific projections from the hypothalamus and, most probably, the nucleus of the solitary tract (Kicliter and Northcutt, 1975; Neary and Wilczynski, 1977a; the present study). This area as a whole, and most prominently its rostral part, is reciprocally connected with the main olfactory bulb (Neary, 1990; Scalia et al., 1991; present study). In contrast, the input from the parabrachial nucleus is limited to its caudal two-thirds. Thus, some hodological data also suggest the existence of a rostrocaudal differentiation of this region. Neurons located in the striatopallial transition area project to the

striatum as well to the nucleus accumbens in anurans and urodeles.

Diencephalon. Several cell masses in the diencephalon of anuran and urodele amphibians contribute to the innervation of the basal forebrain. Retrogradely labeled cells were observed in the anterior preoptic area, the suprachiasmatic nucleus, the ventral hypothalamus, the ventral and dorsal thalamus, and the posterior tubercle.

In anurans, telencephalic basal ganglia afferents from the anterior preoptic area have not been reported by other authors. The present study has revealed that the number of preoptic area cells that project to the nucleus accumbens is larger than the number of striatal afferent neurons. Neurons in a similar position to those found in the present study in *Pleurodeles* have been described as projecting to the striatum in *Triturus cristatus* (Dubé et al., 1990). As in anurans, preoptic cells also contribute to the innervation of the nucleus accumbens.

The suprachiasmatic nucleus was found to project bilaterally to the striatum in amphibians. These findings confirm and extend the results of previous studies in other anurans (Vesselkin et al., 1980; Wilczynski and Northcutt, 1983a; Allison and Wilczynski, 1994) and urodeles (Dubé et al., 1990). Moreover, the present study demonstrates that the suprachiasmatic nucleus also contributes to the innervation of the nucleus accumbens in both amphibian orders.

Projections from the ventral hypothalamus to the striatum in anurans and urodeles have been described previously (Neary, 1988; Dubé et al., 1990). However, our findings suggest that hypothalamic neurons contribute mainly to the innervation of the caudal ventral striatum, whereas the rostral part of the striatum is only weakly innervated. In addition, the ventral hypothalamus projects massively to the striatopallial transition area. This finding may explain the numerous labeled cell bodies found in the ventral hypothalamus found after large striatal HRP injections, as reported by Neary (1988). A new finding of the present study is the demonstration of a substantial ventral hypothalamic projection to the nucleus accumbens.

In contrast to Dubé et al. (1990), we did not observe retrogradely labeled cells in the nucleus of the paraventricular organ of the urodele, *Pleurodeles waltl*, nor in that of the two anuran species studied. Dubé et al. reported that a large population of cells in the paraventricular organ region of *Triturus cristatus* was labeled after striatal HRP applications. However, a careful examination of their figures reveals that the majority of these cells are located in the ventral hypothalamus. Their position resembles that of cell bodies that project mainly to the amygdala and, less prominently, to the striatum and the nucleus accumbens, as shown by the present study. In agreement with our results, previous studies failed to show labeled, liquor-contacting cells in the nucleus of the paraventricular organ of anurans after striatal HRP injections (Vesselkin et al., 1980; Wilczynski and Northcutt, 1983a; Neary, 1988). Therefore, it seems likely that the labeled cells in the paraventricular organ of *Triturus* are false-positive staining but not a true species difference. Our recent studies on the catecholaminergic inputs to the striatum and the nucleus accumbens support this interpretation (Marín et al. 1996).

The dorsal thalamus provides the major input to the striatum in both anuran and urodele amphibians (Kicliter

and Northcutt, 1975; Northcutt and Kicliter, 1980; Vesselkin et al., 1980; Wilczynski and Northcutt, 1983a; Wicht and Himstedt, 1986, 1988; Dubé et al., 1990; present study). In anurans, the majority of the neurons that project to the striatum lies in the central thalamic nucleus. These cells are not uniformly distributed throughout the nucleus, but lie primarily in its lateral two-thirds. Previous studies had shown that most of the cells projecting to the striatum are located in the rostral half of the nucleus (Wilczynski and Northcutt, 1983a; Neary, 1988). The present study provides evidence that cell bodies in the caudal part of the central thalamic nucleus also project to the striatum. In contrast, neurons projecting to the ventral hypothalamus are concentrated in the medial part of the rostral central thalamic nucleus (Neary, 1988, 1995; Allison and Wilczynski, 1991; present study). Thus, the central thalamic nucleus appears to be a heterogeneous structure, with not only a medial to lateral, but also a rostral to caudal topography in its striatal and ventral hypothalamic thalamic projections.

In anurans, it is well established that the anterior part of the lateral thalamic nucleus projects to the striatum (Gruberg and Ambros, 1974; Kicliter, 1979; Scalia, 1976; Wilczynski and Northcutt, 1983a; present study). In contrast, striatal inputs arising from the *posteroventral part of the lateral thalamic nucleus*, as demonstrated by the present study, have not been previously described. However, Lázár and Kozicz (1990) have reported labeled cells within the posteroventral division of the lateral thalamic nucleus after prechiasmatic cobalt injections within the lateral forebrain bundle of *Rana esculenta*. Remarkably, the morphology of the cells in the latter nucleus labeled after such injections (see Fig. 21 in Lázár and Kozicz (1990) resembles that of neurons labeled retrogradely after striatal injections (present study). According to Wicht and Himstedt (1988), the dorsal thalamic area of urodeles is the presumed homologue of the anterior and posteroventral divisions of the lateral thalamic nucleus and, most probably, the central thalamic nucleus of anurans (Wicht and Himstedt, 1988). This idea is corroborated by the finding that in *Triturus* (Wicht and Himstedt, 1986, 1988; Dubé et al., 1990), as well as in *Pleurodeles* (present study), this area was found to project to the striatum.

Another notable finding of the present study was the anterior dorsal thalamus projection to the nucleus accumbens in anuran and urodele amphibians. Such a connection has never before been described in anurans, although a projection to the caudal striatum in ranid frogs has been mentioned (Neary, 1983). Dorsal thalamic neurons within the subhabenular zone of *Triturus alpestris* were found to project ipsilaterally to the nucleus accumbens (Wicht and Himstedt, 1988). In contrast, the present study revealed bilateral projections from this area and from a region located slightly caudally, which includes the anteroventral thalamic zone of Wicht and Himstedt (1988). Thus, this dorsal thalamic population probably comprises neurons from both the subhabenular and the anteroventral thalamic zones. Whether the dorsal thalamic neurons that project to the nucleus accumbens in anuran and urodeles constitute a separate entity within the anterior dorsal thalamus is a question that remains to be solved.

Projections of the ventral thalamus to the forebrain had been identified in various species of frogs (Kicliter, 1979; Vesselkin et al., 1980; Lázár and Kozicz, 1990), but details about their organization were lacking. The demonstration

of topographically organized ventral thalamic projections to the basal forebrain of anurans is one of the most striking findings of the present study. Most of the ventral thalamic cells projecting to the striatum are located in the ventral part of the ventrolateral thalamic nucleus, just medial to the lateral forebrain bundle, whereas neurons projecting to the nucleus accumbens via the medial forebrain bundle were exclusively located within the ventromedial thalamic nucleus. Recently, Puelles et al. (1996) have subdivided the ventromedial thalamic nucleus (after Neary and Northcutt, 1983) into rostral (ventromedial nucleus and intercalate nucleus) and caudal (periventricular nucleus of the zona incerta) parts. In that view, a rostral-to-caudal topography in the ventromedial-forebrain projection seems to exist. Thus, neurons projecting to the striatum are located only in the ventromedial nucleus proper, whereas cells projecting to the nucleus accumbens are located in both the ventromedial nucleus and the periventricular nucleus of the zona incerta.

Contrary to earlier reports (Wilczynski and Northcutt, 1983a; Lázár and Kozicz, 1990; Dubé et al., 1990; Wicht and Himstedt, 1990), the posterior tubercle and the ventromedial part of the mesencephalic tegmentum of amphibians provide substantial, highly organized projections to the striatum and the nucleus accumbens (González et al., 1994; Marín et al., 1995; present study). The posterior tubercle region has recently been analysed by Puelles et al. (1996) using a segmental approach. This segmental analysis has prompted us to a new interpretation of the latter region and its connections with the basal forebrain. These aspects are examined further in the accompanying paper (Marín et al., 1996).

Mesencephalon. Apart from the projection from the ventromedial part of the mesencephalic tegmentum, mid-brain inputs to the basal forebrain of anurans arise from the superficial isthmal reticular nucleus (striatum) and the anteroventral and anterodorsal tegmental nuclei (nucleus accumbens). In urodeles, neurons located in comparable positions project in a similar manner to the telencephalic basal ganglia. In addition, cells located in the anuran torus semicircularis give rise to an ascending projection that ends in the striatum (Vesselkin et al., 1980; Neary, 1988; present study). The torus semicircularis of urodeles apparently does not project to the striatum (Dubé et al., 1990; present study).

Rhombencephalon. As shown by the present study, the caudal pole of the ventral striatum, but not the anterior entopeduncular nucleus, receives a massive projection from the parabrachial region. Furthermore, this projection extends rostrally into the striatum up to mid-telencephalic levels. On the basis of these data, it seems likely that a dorsal-to-ventral topography, as well as a rostral-to-caudal topography, exists in the amphibian striatum. This suggests anatomical and possibly functional differentiation of the latter structure.

A projection from the superior raphe nucleus to the striatum has consistently been demonstrated in the present study in anurans as well as in urodeles. Comparable projections have been reported previously only for urodeles (Dubé et al., 1990; Wicht and Himstedt, 1990; González et al., 1994) and apodans (Wicht and Himstedt, 1990). The majority of these neurons are confined at isthmic levels, although some scattered cells lie slightly more rostrally, in the caudal mesencephalic tegmentum. Since serotonergic cells have been observed in a corresponding position

(Ueda et al., 1984; Fasolo et al., 1986), these cells most likely provide the serotonergic input to the amphibian striatum. This notion is supported by the observation that retrogradely labeled neurons were never found in other areas known to contain serotonergic cell bodies. The present study has also revealed a distinct projection from the raphe region to the nucleus accumbens, which is, in fact, more prominent than that to the striatum. Since raphe projections to the medial pallidum are well known (Northcutt and Ronan, 1992), it may be argued that some of the cells retrogradely labeled after nucleus accumbens applications are the result of an interruption of fibers of passage. However, cells projecting to the nucleus accumbens in *Rana perezi* and *Xenopus laevis* extend more caudally in the rhombencephalon than those projecting to the medial pallidum. Furthermore, there is no evidence that such a projection to the medial pallidum in urodeles exists (Wicht and Himstedt, 1990; Sassoè-Pognetto et al., 1991, 1995).

The locus coeruleus of amphibians is formed by noradrenergic, multipolar neurons, which lie medial and ventral to the isthmic nucleus and extend caudally to the rostral pole of the trigeminal complex (González and Smeets, 1991, 1993, 1994). Neurons projecting to the striatum and the nucleus accumbens are found in topographically corresponding positions in anurans and urodeles (Dubé et al., 1990; Lázár and Kozicz, 1990; Wicht and Himstedt, 1990; present study). However, due to the scattered distribution of the noradrenergic neurons in this region, it cannot be assumed that the cells projecting to the basal ganglia are noradrenergic, particularly since the existence of such a projection has not been supported (Tohyama et al., 1975, 1977; Yamamoto et al., 1977). The experiments in the accompanying paper, which combine tracer and immunohistochemical techniques, will address these problems further (Marín et al., 1996).

The most prominent brainstem projection to the striatum arises from a group of neurons located in the subcerebellar region. Neurons in a comparable position (namely, nucleus cerebelli) projecting to the posterior telencephalon had been reported for *Rana pipiens* (Kicliter, 1979), but not for *Rana catesbeiana* (Wilczynski and Northcutt, 1983a). More recently, similar projections were also demonstrated in the latter species by means of the WGA-HRP technique (Neary, 1988). A comparable group of cells projecting to the striatum appears to exist in urodeles and apodans (Dubé et al., 1990; Wicht and Himstedt, 1990). In the present study, we have precisely characterized the origin and targets of this projection. Thus, most of the cells projecting to the telencephalon in this region constitute a rather compact and conspicuous group located just ventral to the nucleus cerebelli (nomenclature by Opdam and Nieuwenhuys, 1976, for urodeles; Opdam et al., 1976, for ranid frogs; Nikundiwe and Nieuwenhuys, 1983, for *Xenopus*). In the present study this group of cells has been labeled as the parabrachial nucleus, mainly on the basis of its connectivity. Studies by Larsell (1923) and Barnard (1936) suggested a projection from the nucleus of the solitary tract to a region immediately ventrolateral to the nucleus cerebelli. Moreover, recent findings have confirmed the existence of such a projection to the parabrachial region from the nucleus of the solitary tract (Muñoz et al., 1995). Spinal projections have also been found to arise in the parabrachial region (see Ten Donkelaar et al., 1981). Moreover, Neary (1995) has recently described a projection

from the parabrachial nucleus to the ventral hypothalamus in frogs. Additional projections to the caudal striatum, the striatopallial transition area and the ventromedial telencephalic wall have been revealed in the present study. All these data taken together suggest that the population of isthmic cells located ventrally to the nucleus cerebelli in amphibians may be homologous to the parabrachial nuclei of amniotes.

Due to the use of very sensitive retrograde tracers in the present study, numerous cells in the rhombencephalon of anurans and urodeles were labeled after applications to the basal ganglia that were never observed in previous studies. Thus, many reticular neurons were found to project to the striatum and the nucleus accumbens. Another major difference observed is the presence of a distinct projection from the anterior lateral line region to the caudal striatum in the urodele, which is not apparent in anurans. This was the case even in *Xenopus*, an anuran in which the lateral line system is preserved throughout life. Lateral line inputs to the striatum have been established physiologically in both orders of amphibians (Northcutt and Plassmann, 1989; Birkhofer et al., 1994). In anurans the origin of this input seems to be located in the torus semicircularis or the thalamus (Plassman, 1980; Will et al., 1985; Zittlau et al., 1985; Vesselkin et al., 1980; present study), whereas in urodeles it could arise directly from the rhombencephalic alar plate, as observed in *Pleurodeles*.

In the present study, evidence for a direct projection from the nucleus of the solitary tract to the basal forebrain in anuran and urodele amphibians has been provided. In a preliminary study in ranid frogs, Neary (1983) reported a projection to the caudal striatum, but the present study revealed retrogradely labeled neurons within the nucleus of the solitary tract even after injections in rostral parts of the lateral telencephalic wall. Since anterograde tracing of this projection has not been done, the exact striatal target is not known. The present study indicates that, at least, rostral parts of the striatum and the nucleus accumbens receive an input from solitary tract neurons. In contrast to what was previously described in anurans (Neary, 1983), we found an ipsilateral predominancy in the solitary tract input to the basal forebrain in *Rana*, *Xenopus*, and *Pleurodeles*.

Comparison with amniotes

Although there are some differences, the idea is generally accepted that basal ganglia organization in reptiles, birds, and mammals is largely comparable, suggesting that a similar organization was present in the ancestors of amniotes. An intriguing question is whether such a condition may already exist in the forebrain of extant amphibians, whose ancestors are known to have given rise to reptile-like vertebrates in the Carboniferous. There are many aspects that have to be considered to answer this question. In the present study, the afferent connections of the basal forebrain of amphibians in general will be discussed in that light. The accompanying paper will deal more specifically with the catecholaminergic innervation of basal forebrain structures. The nature of efferent connections, development, and chemoarchitecture of these structures remains to be elucidated.

The present study has shown that the basal forebrain of amphibians receives inputs from all major subdivisions of the brain. Moreover, it has been demonstrated that the

basal forebrain can be subdivided into a striatum and a nucleus accumbens. In anurans, the nucleus accumbens is located in the ventromedial part of the basal forebrain, but in urodeles this structure lies more laterally. As in amniotes, fibers projecting to the nucleus accumbens course medial to those projecting to the striatum within the forebrain bundle.

Telencephalic inputs. In mammals, a hippocampal input to the ventral striatum originates primarily from the subiculum (Groenewegen et al., 1987, 1991). Similar connections have been described for birds (Veenman et al., 1995). Also the nucleus accumbens of reptiles receives a cortical input, but in contrast to birds and mammals, the cortical input of reptiles originates from the medial part of the dorsal cortex (Hoogland and Vermeulen-VanderZee, 1989; González et al., 1990). Because of this striatal projection, the dorsal cortex of *Gekko* was considered homologous to the ventral subiculum of mammals (Hoogland and Vermeulen-VanderZee, 1989).

According to several authors, the occurrence of an extensive corticostriatal projection most probably marks the anamniote-amniote evolutionary transition (Wilczynski and Northcutt, 1983a; Veenman et al., 1995). Such a projection constitutes a prominent source of sensory and motor information to striatal territories and possibly facilitates the role of basal ganglia in movement control (Veenman et al., 1995). The demonstration of medial pallial projections to the striatum and nucleus accumbens in amphibians (Neary, 1990; Northcutt and Ronan, 1992; present study) suggests that a palliostriatal system is already present in anamniotes, at least in amphibians. Moreover, on the basis of its connections, the amphibian medial pallium has been suggested to be homologous to the subicular and CA fields of mammals (Northcutt and Ronan, 1992). Thus, with respect to corticostriatal connections it can be stated that such connections are already present in amphibians, but became more elaborate in amniotes, and in particular in mammals.

Amygdaloid complex. Although it seems clear that the caudoventral part of the lateral pallium and the *striatopallial transition area (spta)* of amphibians constitute two separate cell populations on the basis of their connections and chemoarchitecture, assigning strict homologies to each component is difficult. The *spta* of amphibians is characterized by its connections with the striatum and the nucleus accumbens. In the turtle *Pseudemys scripta*, HRP injections that involved ventral striatal territories labeled a group of cells in the lateral telencephalic wall in a position that resembles that of the *spta* of amphibians (Siemen and Künzle, 1994; see their Figs. 1, 2). As in amphibians, this group of cells extends along most of the length of the telencephalic hemisphere. In amphibians, the rostral part of the *spta* lies adjacent to both the lateral and the accessory olfactory tracts. Thus, the most rostrally located cells may represent partially the nucleus of the lateral olfactory tract or the nucleus of the accessory olfactory tract of reptiles (Martínez-García et al., 1991; Bruce and Neary, 1995a). Slightly caudally, the cells of the *spta* are located in a position that is comparable to that of the external amygdala of reptiles (Lohman et al., 1988; Lohman and Smeets, 1993; Bruce and Neary, 1995a,c). The caudal part of the *spta* resembles, in position, the lateral amygdala and the caudal part of the dorsal ventricular ridge, which is also considered part of the amygdala (see Bruce and Neary, 1995a for discussion). Recently,

Bruce and Neary (1995a,c) have suggested that the caudoventral part of the lateral pallium (including our striatopallial transition area) may be homologous, as a whole, to three populations in the brain of *Gekko gecko*, viz., the centromedial dorsal ventricular ridge (equivalent to the caudal part of the dorsal ventricular ridge of *Podarcis hispanica*, as described by Font et al., [1995]), the lateral amygdala and a part of the lateral cortex. However, the present study has revealed the existence of a separate population of cells within the lateral telencephalic wall, i.e., the striatopallial transition area. As described above, this cell population is located successively ventral to the ventral part of the lateral pallium (from rostral to caudal levels) and the lateral amygdala. Thus, it seems more likely that the *stpa* correlates with a part of the amygdala of reptiles, whereas the immediately dorsally located lateral pallium resembles the lateral cortex (see also Andreu et al., 1994, for discussion). In addition, at rostral levels the cells in the *stpa* may be homologous to the external amygdala of reptiles. Along most of its rostrocaudal extent, the *spta* is reciprocally connected with the hypothalamus, which holds also for the lateral amygdala, the centromedial dorsal ventricular ridge and the external amygdala of the lizard *Gekko gecko* (Neary and Wilczynski, 1977a; Neary, 1995; Bruce and Neary, 1995a, 1995b; present study). Moreover, both the external amygdala of *Gekko* and the *spta* of amphibians are characterized by the presence of darkly stained NADPH-d cells (Muñoz et al., 1996; González et al., 1996; Smeets et al., 1996).

The dorsolateral amygdaloid region of reptiles, in turn, has been compared, as a whole, to a part of the lateral and basal amygdala of mammals (Martínez-García et al., 1993; Bruce and Neary, 1995a–c; Font et al., 1995). This comparison may now be extended to the amphibian *spta*. In the three classes of vertebrates, this region receives an input from the hypothalamus. Moreover, although the main target of the parabrachial projection in mammals is the central nucleus of the amygdala, it also reaches the basolateral nuclei (Saper and Loewy, 1980). In the lizard *Podarcis hispanica*, injections in the dorsolateral amygdala, that encompassed the caudal part of the dorsal ventricular ridge, resulted in retrograde labeling of cell bodies in the parabrachial nucleus (Martínez-García et al., 1993). In amphibians, injections of anterograde tracers into the parabrachial nucleus specifically labeled abundant terminals in the *spta*, a finding in support of the amygdaloid nature of this area. This notion is further corroborated by the efferent connections. The amygdala in mammals projects through the stria terminalis and the ventral amygdalofugal pathway (Amaral et al., 1992). A similar situation is found in reptiles (Bruce and Neary, 1995a) and, most likely, in amphibians, where fibers leave the *spta* following a subpial pathway (the stria terminalis) or along the external margin of the telencephalon (the amygdalofugal pathway, as proposed by Bruce and Neary, 1995a in *Gekko*). Interestingly, the mammalian amygdalostriatal projection originates predominantly from the basal nucleus (Groenewegen et al., 1980; Parent et al., 1983; Russchen and Price, 1984; Russchen et al., 1985; McDonald, 1991). If one considers the homologies proposed, it seems clear that the same condition is found in reptiles (González et al., 1990; Martínez-García et al., 1993) and amphibians (present study). Furthermore, the innervation of the diagonal band nucleus in reptiles and amphibians (Martínez-García et al., 1993; present study) may correlate

with the projection to the magnocellular basal forebrain nuclei, i.e., the basal nucleus of Meynert and the nucleus of the horizontal limb of the diagonal band in mammals, which also originates partly from the basal nucleus (see, e.g., Amaral et al., 1992).

The lateral amygdala in amphibians receives a massive input from the accessory olfactory bulb, and resembles in this respect the medial and posteromedial cortical amygdaloid nuclei of mammals (Scalia et al., 1991) and the proposed homologous structures in reptiles (Martínez-García et al., 1991; Bruce and Neary, 1995a–c). In that view, it seems evident that the nomenclature used by Scalia et al. (1991) i.e., the medial and cortical subdivisions of the amygdala, is appropriate to define this region of the amygdaloid complex of amphibians. A projection from the medial amygdala to the ventral striatum has been described in reptiles and mammals but, as in amphibians, does not constitute the major amygdalostriatal projection (Phillipson and Griffiths, 1985; Martínez-García, 1993).

On the basis of connections, Bruce and Neary (1995a,c) have recently suggested, that the amphibian caudal striatum and the striatoamygdalar area of reptiles may be homologous to the central amygdaloid nucleus of mammals. The central amygdaloid nucleus is reciprocally connected with the hypothalamus (Amaral et al., 1992) and is the main amygdaloid source of long descending pathways to the medulla (Krettek and Price, 1978). In turn, it receives a strong input from the parabrachial nuclei and the nucleus of the solitary tract (Norgren, 1976; Ricardo and Koh, 1978; Saper and Loewy, 1980). In amphibians, the caudal striatum is also reciprocally connected with the hypothalamus (Neary and Wilczynski, 1977a; Neary, 1995) and has long descending projections to the medulla (Ten Donkelaar et al., 1981; Wetzel et al., 1985). Moreover, the present study has revealed that the caudal striatum of amphibians is not only the main telencephalic target of the parabrachial nucleus, but also receives an input from the nucleus of the solitary tract.

The posterior part of the ventromedial telencephalic wall of amphibians was, on the basis of its chemoarchitecture, considered homologous to the basolateral amygdala of mammals (Northcutt, 1974) and was designated as the medial amygdala. However, as discussed above, the putative homologues of the mammalian basal and lateral amygdala have to be sought in the striatopallial transition area. On the other hand, the amphibian medial amygdala coincides in position with the fibers of the stria terminalis (Herrick, 1948) and has, therefore, been tentatively considered to be homologous to the bed nucleus of the stria terminalis of amniotes (González and Smeets, 1992b; Puelles et al., 1996). Moreover, vasotocinergic cells were found in the medial amygdala of amphibians (González and Smeets, 1992a,b). In reptiles and birds, vasotocinergic telencephalic cells are present in the bed nucleus of the stria terminalis (Stoll and Voorn, 1985; Kiss et al., 1987; Thepen et al., 1987; Smeets et al., 1990), whereas in mammals additional cells are found in the medial amygdaloid nucleus (Caffé and Van Leeuwen, 1983; Van Leeuwen and Caffé, 1983; Sofroniew, 1985; Caffé et al., 1989; Dubois-Dauphin et al., 1989, 1990). Furthermore, the mammalian bed nucleus of the stria terminalis is reciprocally connected with the nucleus accumbens and the basal and lateral amygdala (Russchen, 1982; Zahn and Brog, 1992; Heimer et al., 1991; Zahn and Heimer, 1993) and receives input from the parabrachial nuclei and the nucleus

of the solitary tract (Ricardo and Koh, 1978; Saper and Loewy, 1980). Therefore, it cannot be excluded that the medial amygdala, or at least part of it, is comparable to the bed nucleus of the stria terminalis of amniotes.

Diencephalic inputs. The suprachiasmatic nucleus provides a strong input to the striatum and the nucleus accumbens of urodeles and, in particular, of anurans. In addition, differential connections from the rostral and caudal subdivisions of the suprachiasmatic nucleus have been distinguished. The rostral suprachiasmatic nucleus appears to receive a direct retinal input (Montgomery and Fite, 1989; Allison and Wilczynski, 1994). On the basis of its connections, the suprachiasmatic nucleus of amphibians has been suggested to be homologous to the circadian-clock-related suprachiasmatic nucleus of mammals (Allison and Wilczynski, 1994; Tuinhouf et al., 1994b; Puelles et al., 1996). Little is known, however, about the connections of the suprachiasmatic nucleus in reptiles and birds. In mammals, only minor projections to adjacent hypothalamic nuclei were observed in early tracing studies (Swanson and Cowan, 1975; Berk and Finkelstein, 1981), but more recent evidences suggest that the suprachiasmatic projection to the basal telencephalon is extensive (Watts and Swanson, 1987; Watts et al., 1987; Kalsbeek et al., 1993; Morin et al., 1994). Thus, efferents from the suprachiasmatic nuclei and the adjacent retrochiasmatic area reach several regions that mediate the internal and external modulation of reproductive behaviors. In mammals, these regions include the preoptic area, amygdala, and bed nucleus of the stria terminalis. Similar connections appear to exist in amphibians, where the striatum has been also implicated in some aspects of the reproductive behavior (see Allison and Wilczynski, 1994, for discussion).

Dorsal thalamus. As in mammals, the amphibian dorsal thalamus represents a major source of afferent connections to the striatum. However, a clear-cut comparison with amniotes is difficult. Previous comparative considerations by Puelles et al. (1996) and the results of the present study make it unlikely that the auditory afferent innervation characterizes the entire ventrodorsal extent of the central thalamic nucleus, as suggested by Neary (1988). In reptiles, the corresponding connection is restricted to the ventral part of the dorsal thalamus (nucleus medialis/reuniens), whereas the auditory relay centers in birds and mammals are the nucleus ovoidalis and the medial geniculate nucleus, respectively (Butler, 1994). Topographically, the caudal pole of the central thalamic nucleus actually occupies a ventral position within the dorsal thalamus (Neary and Northcutt, 1983; Puelles et al., 1996), and is the only part of the nucleus that has auditory responses (Hall and Feng, 1986), equivalent to those observed in specific divisions of the medial geniculate nucleus of mammals (Calford, 1983; Takahashi et al., 1984). For example, in some mammals the ventral division of the medial geniculate body has been shown to constitute a major auditory relay station (Webster and Aitkin, 1975), which provides not only the major input to the auditory cortex, but also projects to the striatum (Jones, 1985; LeDoux et al., 1985; Price, 1995). In birds, the nucleus ovoidalis receives auditory input and projects, in turn, to the dorsal ventricular ridge as well as to the striatum (Karten, 1968; Bonke et al., 1979). Similarly, in reptiles the nucleus medialis/reuniens projects to both the dorsal ventricular ridge and the striatum (Bruce and Butler, 1984; González et al., 1990; Smeets and González, 1994).

Thus, it is likely that the caudal portion of the central thalamic nucleus of anuran amphibians is homologous to the auditory part of the nucleus medialis/reuniens of reptiles, the nucleus ovoidalis of birds and the medial geniculate nucleus of mammals. In addition, other parts of the nucleus medialis/reuniens in reptiles receive inputs from the spinal cord and dorsal column nuclei (for review, see Butler, 1994), as does the rostral portion of the anuran central thalamic nucleus (Muñoz et al., 1994a, 1995). Thus, somatosensory information may be relayed from the central thalamic nucleus to the striatum in amphibians. In mammals, the posterior thalamic complex is considered as a heterogeneous nucleus (Price, 1995), which receives somatosensory inputs from the spinothalamic tract (Cliffer et al., 1991) and auditory-related input from the inferior colliculus (LeDoux, 1987).

It is tempting to compare the projections from the anterior thalamic nucleus to the nucleus accumbens of amphibians with those of the dorsomedial thalamic nucleus and other perirhinal nuclei of reptiles and birds (Wild, 1987; González et al., 1990; Siemen and Künzle, 1994) and, to a lesser extent, with those of the intralaminar nuclei of mammals (for review, see Butler, 1994). The latter comparison seems to be reinforced by our results, since the mammalian intralaminar nuclei project to the nucleus accumbens and the striatum (Jones, 1985; Groenewegen et al., 1991), as does the anterior thalamic nucleus of amphibians.

Ventral thalamus. The anuran thalamus has been divided into dorsal and ventral nuclei and, as in all vertebrates, it was generally considered that only the dorsal thalamic nuclei project to the telencephalon (Rose, 1942; Neary and Northcutt, 1983; Jones, 1985). Our results, however, contradict this assumption, since the "topographically" described ventral thalamic nuclei of *Rana* (Neary and Northcutt, 1983; Puelles et al., 1996) have been consistently demonstrated to project to the striatum and the nucleus accumbens. In fact, ventral thalamic projections to the basal forebrain seem to be a common feature in amniotes. For example, a projection from cells located immediately medial to the lateral forebrain bundle to the basal ganglia has been identified in the lizard *Gekko gecko* (González et al., 1990, see their Figs. 3, 4) and in the turtle *Pseudemys scripta* (Siemen and Künzle, 1994, see their Fig. 4A,B). Moreover, several studies have demonstrated that the zona incerta of mammals, which is a ventral thalamic region, projects to the cortex and the basal ganglia (Ricardo, 1981; Köhler et al., 1984; Saper, 1985; Lin et al., 1990). The zona incerta receives afferents from the trigeminal complex and the dorsal column nucleus, as well as from the pretectum and the superior colliculus (Berman, 1977; Roger and Cadusseau, 1985; Shammah-Lagnado et al., 1985; Berkley et al., 1986; Appell and Behan, 1990). It sends efferents to the superior colliculus, the pretectum, the spinal cord, the basal ganglia and hypothalamus (Ricardo, 1981; Kim et al., 1992; Nicolelis et al., 1992). Similar sets of connections are recognized in reptiles (Ebbeson, 1967; Hoogland, 1982; Ten Donkelaar, 1982; Welker et al., 1983; González et al., 1990; Siemen and Künzle, 1994; Bruce and Neary, 1995a) and amphibians (Ten Donkelaar et al., 1981; Hall and Feng, 1987; Naujoks-Manteuffel and Manteuffel, 1988; Zittlau et al., 1988; Masino and Grobstein, 1990; Muñoz et al., 1995; Neary, 1995; present study). Moreover, the ventral thalamus of amphibians and reptiles contains a dopaminergic

cell group (González and Smeets, 1994; Smeets, 1994), as does the zona incerta of mammals (Tillet, 1994).

In mammals, another source of input to the basal ganglia arising from ventral thalamic regions is the subthalamic nucleus. This nucleus, located in the ventral thalamus but with a different developmental origin (Rose, 1942), receives afferents from the striatum/globus pallidus, the pedunclopontine nucleus and the cerebral cortex and projects to the striatum, the globus pallidus and the substantia nigra (Parent, 1986; Groenewegen and Berendse, 1990). Thus, on the basis of some of its connections and position within the diencephalon, the cell population located at rostral levels, immediately medial to the lateral forebrain bundle in anurans (Neary and Northcutt, 1983; Wilczynski and Northcutt, 1983b; Puelles et al., 1996; present study), would be tentatively compared to the subthalamic nucleus of mammals. A similar suggestion has been made for reptiles and birds (Northcutt, 1978; Brauth et al., 1978; Brauth and Kitt, 1980; Medina and Reiner, 1995).

Mesencephalic inputs. In amniotes, the most substantial input from the midbrain tegmentum to the basal forebrain is constituted by fibers, which originate from the dopaminergic cell groups, i.e., the ventral tegmental area, the substantia nigra and the retrorubral group. In amphibians, the dopaminergic cells in the midbrain cannot be tripartitioned making a direct comparison with amniotes difficult, although it is still possible (Marín et al., 1996).

Apart from the prominent dopaminergic projections from the midbrain, basal ganglia afferents from other mesencephalic centers are sparse in amniotes. A projection from the torus semicircularis to the basal telencephalon has been described in the turtle, *Pseudemys scripta* (Siemen and Künzle, 1994). In addition, scattered cells projecting to the rostral basal forebrain were observed in the central mesencephalic gray of reptiles (Siemen and Künzle, 1994), an area that in mammals is reciprocally interconnected with the nucleus accumbens and other medial basal telencephalic regions (Luiten et al., 1982; Groenewegen and Russchen, 1984; Heimer et al., 1991; Zahm and Heimer, 1993; Cameron et al., 1995).

Rhombencephalon. The existence of striatal serotonergic afferents from the raphe nuclei in reptiles, birds, and mammals has been consistently reported in the literature. In mammals, these fibers arise predominantly from the dorsal raphe nucleus and, to a lesser extent, from the median raphe nucleus (Azmitia and Segal, 1978). A projection from various raphe nuclei to the nucleus accumbens is also present in mammals (Groenewegen et al., 1980). At present, the raphe region in amphibians is difficult to subdivide. However, the retrogradely labeled cells observed in the dorsal aspect of the rostral raphe region after striatal injections strongly suggest a similar serotonergic input to the basal forebrain of amphibians as in mammals. As in amniotes, another monoaminergic, i.e., a noradrenergic input to the basal forebrain originates from the locus coeruleus. This projection will be dealt with in more detail in the accompanying paper (Marín et al., 1996).

Previous studies suggested that the striatal afferent projection arising from the subcerebellar region in amphibians (i.e., the parabrachial nucleus) might be homologous to the quintofrontal tract of birds (Northcutt and Kicliter, 1980; Neary, 1985). The latter tract originates from cells of the principal sensory trigeminal nucleus and projects to

the nucleus basalis of the telencephalon (Cohen and Karten, 1974; Wild et al., 1990). In amphibians, however, the cells labeled after striatal injections are not continuous with those of the principal sensory trigeminal nucleus and, most probably, do not receive direct trigeminal inputs (Matesz and Székely, 1978; González and Muñoz, 1988; Muñoz et al., 1994b). Moreover, recent hodological studies (Neary, 1995; Muñoz et al., 1995; present study) strongly suggest that this cell group is comparable to the parabrachial nucleus of amniotes. In mammals, the parabrachial nuclei form a relay in the ascending gustatory pathway (Norgren, 1976, 1978). They receive a prominent projection from the nucleus of the solitary tract (Loewy and Burton, 1978; Ricardo and Koh, 1978) and the spinal cord (see Saper, 1995) and, in turn, project to the hypothalamus, thalamus (midline, intralaminar, and ventromedial basal nuclei), amygdala, and bed nucleus of the stria terminalis (Saper and Loewy, 1980). In addition, some ascending fibers from the parabrachial nuclei project directly to the insular cortex (Krukoff et al., 1993). Similar connections have been identified in reptiles (Martínez-García et al., 1993; Siemen and Künzle, 1994; Bruce and Neary, 1995a, 1995b) and birds (Wild et al., 1990). The amphibian parabrachial nucleus receives fibers from the nucleus of the solitary tract and projects to the hypothalamus (Muñoz et al., 1995; Neary, 1995), and to the basal telencephalic areas that most probably are homologous to amniotic subdivisions of the amygdala and the bed nucleus of the stria terminalis (see above). Moreover, in *Rana perezi*, tracer applications to the subcerebellar region demonstrated direct projections to the hypothalamus and thalamus (unpublished observations). As has been suggested by Wild et al. (1990), viscerosensory projections in diverse species of vertebrates may have fundamental features in common, presumably reflecting similar basic homeostatic mechanisms. Additional isthmic-mesencephalic projections to the basal telencephalon of amniotes are also present. For example, the mammalian pedunclopontine nucleus projects to the striatum (Saper and Loewy, 1982) and is considered another key structure in the basal ganglia circuitry. A similar connection may be present in reptiles and birds (for discussion, see Siemen and Künzle, 1994; Bruce and Neary, 1995b). Thus, it could be suggested that neurons located in the posterodorsal mesencephalic tegmentum represent an amphibian counterpart of the pedunclopontine nucleus.

In mammals, the telencephalic targets of efferents of the nucleus of the solitary tract compose the central amygdaloid nucleus and the bed nucleus of the stria terminalis (Ricardo and Koh, 1978). Similar results have been obtained in birds (Arends et al., 1988) and turtles (Siemen and Künzle, 1994). In amphibians, we found a projection not only to the amygdaloid complex, but also more rostrally to the striatum and the nucleus accumbens. Though not reported by Ricardo and Koh (1978), their Figure 2A clearly shows terminal labeling in the nucleus accumbens of rats after injection of tritiated amino acids in the region of the solitary tract nucleus. More recently, Wang et al. (1992) and Zagon et al. (1994) have provided evidence that direct projections from the solitary tract nucleus to the nucleus accumbens do exist in rats. In fact, similar connections have been suggested for pigeons (Arends et al., 1988). The results of the present study, therefore, suggest that direct projections from the solitary tract nucleus to the

nucleus accumbens may be a common feature of both amphibians and amniotes.

Functional significance and concluding remarks

As suggested by Wicht and Himstedt (1986) in their elegant study of the thalamic organization in urodeles, very similar connectional patterns can be achieved with (anuran) or without (urodeles) the formation of distinct nuclei. Except for the lack of a toral input and a smaller contribution of the brainstem reticular nuclei to the basal forebrain of urodeles, no relevant differences between the two amphibian orders in basal ganglia afferent connections were observed.

The present study has not only confirmed, but also extended the notion that the striatum and nucleus accumbens receive inputs of several sensory modalities, such as olfactory, visual, auditory, somatosensory, visceral and, if present, lateral line information. The way, in which these sensory modalities reach the basal forebrain is complicated and not yet fully understood.

Olfactory and vomeronasal information may reach the striatum and the nucleus accumbens via the lateral amygdala. On the other hand, in both groups of amphibians the medial pallium appears to be an integrative center for olfactory information arising from telencephalic olfactory related centers (Scalia et al., 1968; Northcutt and Royce, 1975; Kemali and Guglielmotti, 1987; Schmidt and Roth, 1990) and auditory, somatosensory, and visual inputs. The latter modalities reach the medial pallium primarily via the anterior thalamic nucleus (Karamian et al., 1966; Vesselkin et al., 1971; Fite et al., 1977; Mudry and Capranica, 1980).

Complex, multimodal input to the basal forebrain also arises from cells in the thalamus. For example, the central thalamic nucleus receives a strong input from the torus semicircularis and the dorsal medullary tegmentum, whereas minor contributions are made by the anterior and posterior entopeduncular nuclei, the nucleus of the lateral lemniscus, the superior olivary nucleus, the dorsal column nucleus and the spinal cord (Neary, 1974, 1988; Hall and Feng, 1987; Feng and Lin, 1991; Muñoz et al., 1994a, 1995). However, these afferent fibers are not uniformly distributed in the central thalamic nucleus. Thus, most of the toral fibers distribute in its caudal portion, although a dense band of terminals is also present in the medial half of the nucleus at intermediate and rostral levels. Moreover, the central thalamic nucleus receives a dense input from both the medial and the lateral torus (Hall and Feng, 1986; Neary, 1988; Feng and Lin, 1991), which are responsive to auditory and tactile stimuli, respectively (Comer and Grobstein, 1981). It remains unclear whether both types of information are relayed separately to different subregions within the central thalamic nucleus. Neurons in the caudal region of the central thalamic nucleus are sensitive to temporal features of complex sound signals, including pulse duration and/or repetition rate (Hall and Feng, 1986, see their Fig. 3), whereas neither single nor multi-unit auditory activity could be recorded in the intermediate or rostral levels of the central thalamic nucleus (Hall and Feng, 1986). Thus, the caudal part of the central thalamic nucleus likely relays auditory information to the striatum, whereas the lateral part of the nucleus at intermediate and rostral levels may process somatosensory information. Both auditory and somatosen-

sory activities resulted in evoked potentials in the striatum (Vesselkin and Kovacevic, 1973; Mudry and Capranica, 1980). Moreover, in the anuran amphibian *Xenopus laevis*, which has a permanent lateral line system (Fritzsche et al., 1984), lateral line responses have been evoked in the striatum (Birkhofer et al., 1994). Since the torus semicircularis receives a lateral line projection (Plassmann, 1980; Will et al., 1985; Zittlau et al., 1985), lateral line information presumably reaches the striatum either directly or via the central thalamic nucleus.

Both the anterior and posteroventral divisions of the lateral thalamic nucleus receive tectal projections (Rubinson, 1968; Lázár, 1969; Scalia, 1976; Masino and Grobstein, 1990; Montgomery and Fite, 1991). In the anterior division, these projections are not topographically organized, whereas in the posterior division a distinct topographic map has been recognized (Montgomery and Fite, 1991). Thus, most likely two different types of visual information are relayed to the striatum. In addition, the lateral thalamic nucleus might relay information other than visual to the striatum (Rubinson, 1968; Lázár, 1969; Neary, 1988; Lázár and Kozicz, 1990; Feng and Lin, 1991; Muñoz et al., 1994a).

The anterior thalamic nucleus, or its homologous structure in the anterior thalamus of urodeles (Wicht and Himstedt, 1988), receives diverse inputs from sensory and limbic structures. Thus, the anterior thalamic nucleus receives visual input from the retina (Scalia and Gregory, 1970) and weak auditory input from the torus semicircularis (Neary, 1988; Feng and Lin, 1991) that may also convey somatosensory information (Comer and Grobstein, 1981). A direct projection from the dorsal column nucleus is still a matter of debate (Neary and Wilczynski, 1977b; Muñoz et al., 1995). Additionally, the anterior thalamic nucleus receives a prominent input from limbic structures, such as the medial pallium (Northcutt and Ronan, 1992), the lateral septum (Neary, 1990), the preoptic area, the suprachiasmatic nucleus and the ventral hypothalamus (Neary and Wilczynski, 1977a, 1979). Thus, the anterior thalamic nucleus has been regarded as a multimodal sensory area with strong limbic affinities (Neary, 1990). In that view, the anterior thalamus provides a pathway by which sensory activity may gain access to limbic telencephalic structures. Moreover, in addition to its projection to the nucleus accumbens, the anterior thalamic nucleus projects bilaterally to the medial pallium (Sassoè-Pognetto, 1991, 1995; Northcutt and Ronan, 1992). The medial pallium could, therefore, constitute a secondary pathway by which the anterior thalamic nucleus influences the nucleus accumbens and the striatum.

The ventromedial nucleus, the periventricular nucleus of the zona incerta, and the ventral part of the ventrolateral thalamic nucleus have generally been assigned to the ventral thalamus (Neary and Northcutt, 1983; Puelles et al., 1996). They are the major thalamic recipients of input from the dorsal column nucleus and the spinal cord (Neary and Wilczynski, 1977b; Muñoz et al., 1994a). Moreover, cells in the ventral part of the ventrolateral thalamic nucleus receive retinal afferents (Scalia and Gregory, 1970; Lázár, 1978; Levine, 1980). Therefore, somatosensory and visual information probably reach the basal ganglia also via the ventral thalamus.

The connections of the hypothalamus, the parabrachial nucleus, and the nucleus of the solitary tract with basal forebrain regions in amphibians make it likely, that the

concept of a "visceral forebrain" as defined by Van der Kooy et al. (1984) for mammals, and more recently applied to the brain of birds (Wild et al., 1990; Kuenzel and Bläher, 1993), may also hold for amphibians. The major role of the visceral forebrain is to influence cardiovascular, respiratory, and gastrointestinal functions through their reciprocal connections with the parabrachial nucleus and the nucleus of the solitary tract (Van der Kooy et al., 1984). In that context, the mammalian extended amygdala constitutes the anatomical substrate for integrating visceral afferents into the basal forebrain. The extended amygdala is defined in mammals as a cell continuum that includes the centromedial portions of the amygdaloid complex and the bed nucleus of the stria terminalis and which merges rostrally with the shell portion of the nucleus accumbens (Alheid and Heimer, 1988; see Alheid et al., 1995, for review), receives afferent projections from the nucleus of the solitary tract and the parabrachial nucleus. In addition, a part of the extended amygdala (fundus striati) rather than the caudate-putamen, receives the input from the parabrachial nucleus (Alden et al., 1994). Thus, regarding the afferent connections of the basal forebrain in amphibians in relation to this theory, the cell continuum extending from the caudal striatum into the ventromedial wall to the level of the nucleus accumbens, which is characterized by visceral afferents, may be easily compared to the mammalian extended amygdala. Further, the theory of the extended amygdala might also support the existence of a functionally core-shell dichotomy in the amphibian nucleus accumbens, since both territories of the nucleus accumbens in mammals are characterized by distinct hodological features. In conclusion, the present study has revealed that the apparently simple basal telencephalon of amphibians may contain a number of structures, that most probably have their counterparts in reptiles, birds, and mammals. Therefore, a further elaborate characterization of the hodological and chemical characteristics of the basal telencephalon is required to clarify the actual boundaries between the different parts and to identify, if they exist, subdivisions equivalent to other key components of the basal ganglia of amniotes.

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