

# Comparison of the distribution of calcium-binding proteins and intrinsic connectivity in the lateral nucleus of the rat, monkey, and human amygdala

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## Abstract

A large amount of anatomic, electrophysiologic, pharmacologic, and behavioral data published over the past decade has provided novel insight into the function of the amygdala in the rat. An important question remains as to how well the data obtained in the rat amygdala can be extrapolated to primates. To address this issue from a functional neuroanatomic point of view, we compared the recently published data on the distribution of calcium-binding proteins (parvalbumin, calbindin-D<sub>28k</sub>, calretinin) and intrinsic connectivity in the rat, monkey, and human amygdala. The aim of our ongoing analysis is twofold: (1) to determine whether the nuclei with the “same name” in the three species are chemoarchitecturally similar and (2) to determine whether the intradivisional, interdivisional, and internuclear connectivity is similarly organized in the rat and monkey. We focused on the lateral nucleus, which is the major recipient of thalamic and cortical sensory information directed to the amygdala and provides the most widespread intraamygdaloid connections. Our analysis suggests many similarities in the organization of chemoarchitectonics and intrinsic connectivity of the different subdivisions of the lateral nucleus of the rat, monkey, and human amygdala. There are also dissimilarities, however, which might relate to differences in the function of the amygdala in rodents and primates. © 2002 Elsevier Science Inc. All rights reserved.

**Keywords:** Amygdaloid complex; Anterograde tracer; Calbindin-D<sub>28k</sub>; Calretinin; Parvalbumin

## 1. Introduction

The amygdaloid complex is an anatomically heterogeneous structure that comprises more than 10 nuclei and cortical areas and their subdivisions, each of which have unique cytoarchitectonic, chemoarchitectonic, and connective characteristics (Pitkänen, 2000). Consistent with the anatomic data, the function of the different amygdaloid nuclei varies substantially (Aggleton, 2000). Understanding the function of the amygdala in greater detail will require a more targeted pharmacologic manipulation or lesioning of each of the amygdaloid nuclei and nuclear subdivisions.

In the laboratory, it is often cumbersome to interpret amygdala data obtained from several different studies. This

is partially due to the use of different nomenclatures for the different nuclei and nuclear subdivisions of the amygdala (Paxinos and Watson, 1986; Price et al., 1987; Swanson, 1992). Comparison of data obtained in different species provides an even a greater challenge because there has not been a comprehensive interspecies analysis of the anatomy of the amygdala since the classical work of Price et al. (1987). Such a comparison, however, would provide a starting point for unified nomenclature in different species. Further, an understanding of the interspecies similarities and differences in the connectivity of the homologous amygdaloid nuclei and nuclear subdivisions might also provide a tool to predict the similarities and differences in amygdala function in various species.

The present study is a review of the published data on the distribution of three calcium-binding proteins, parvalbumin, calbindin-D<sub>28k</sub>, and calretinin, in the rat, monkey, and human amygdala to address the question: “How similar is the chemoarchitecture of the amygdala between

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different species?" In addition, the organization of intrinsic connectivity in the rat and monkey amygdala is compared to further elaborate the anatomic similarities and/or differences of the amygdala in rodents and primates. We focus on the lateral nucleus, first, for methodologic reasons. Much of the immunohistochemical data on calcium-binding proteins from the lateral nucleus in the rat, monkey, and human have been obtained using the same antibodies in different species, which facilitate the comparison. In addition,

intraamygdaloid projections of the lateral nucleus were recently described in the rat and monkey using small *Phaseolus vulgaris*-leucoagglutinin (PHA-L) tracer injections that were restricted to only one subdivision. Second, the lateral nucleus is the major input region for sensory-related thalamic and cortical inputs directed to the amygdala and provides the most extensive intraamygdaloid projections. Therefore, it is in a key position to guide the formation of behavioral responses evoked by sensory

Table 1

Partitioning of the amygdaloid complex into different nuclei and nuclear subdivisions in the rat, monkey, and human

	Rat subdivisions	Monkey subdivisions	Human subdivisions
<i>Deep nuclei</i>			
Lateral nucleus	dorsolateral <sup>a</sup> ventrolateral <sup>a</sup> medial	dorsal <sup>b</sup> dorsal intermediate <sup>b</sup> ventral intermediate <sup>b</sup> ventral <sup>b</sup>	lateral <sup>c</sup> medial <sup>c</sup>
Basal nucleus	magnocellular intermediate <sup>d</sup> parvicellular	magnocellular intermediate <sup>c</sup> parvicellular	magnocellular <sup>c</sup> intermediate <sup>c</sup> parvicellular <sup>c</sup>
Accessory basal nucleus	magnocellular <sup>f</sup> parvicellular <sup>f</sup>	magnocellular parvicellular ventromedial <sup>c</sup>	magnocellular <sup>c</sup> parvicellular <sup>c</sup> ventromedial <sup>c</sup>
Paralamina nucleus		paralamina nucleus	medial <sup>c</sup> lateral <sup>c</sup>
<i>Superficial areas</i>			
Bed nucleus of the accessory olfactory tract	Bed nucleus of the accessory olfactory tract	–	–
Nucleus of the lateral olfactory tract	Nucleus of the lateral olfactory tract	Nucleus of the lateral olfactory tract	Nucleus of the lateral olfactory tract <sup>c</sup>
Anterior cortical nucleus	Anterior cortical nucleus	Anterior cortical nucleus	Anterior cortical nucleus <sup>c</sup>
Periamygdaloid cortex	PAC PACm <sup>a</sup> PACs	PACo <sup>b</sup> PAC1 PAC2 PAC3 PACs	PACo <sup>c</sup> PAC1 <sup>c</sup> PAC3 <sup>c</sup> PACs <sup>c</sup>
Medial nucleus	rostral <sup>a</sup> central (dorsal and ventral parts) <sup>a</sup> caudal <sup>a</sup>	medial nucleus	medial nucleus <sup>c</sup>
Posterior cortical nucleus	Posterior cortical nucleus	Posterior cortical nucleus	Posterior cortical nucleus <sup>c</sup>
<i>Remaining areas</i>			
Anterior amygdaloid area	Anterior amygdaloid area	Anterior amygdaloid area	Anterior amygdaloid area <sup>c</sup>
Central nucleus	capsular <sup>g,h</sup> lateral <sup>g,h</sup> intermediate <sup>g,h</sup> medial <sup>g,h</sup>	lateral medial	lateral <sup>c</sup> medial <sup>c</sup>
Amygdalahippocampal area	lateral <sup>a</sup> medial <sup>a</sup>	dorsal ventral	lateral <sup>c</sup> medial <sup>c</sup>
Intercalated nuclei	Intercalated nuclei	Intercalated nuclei	Intercalated nuclei <sup>c</sup>
Lateral capsular nuclei	–	Lateral capsular nuclei	–

The nomenclatures have been derived to all three species from the original description of Price et al. (1987) for the rat and monkey amygdala. References describing the modification of the original nomenclature are indicated in the table notes.

Location of each amygdaloid area is schematically presented in Fig. 2

<sup>a</sup> Pitkänen et al., 1995.

<sup>b</sup> Pitkänen and Amaral, 1998.

<sup>c</sup> Sorvari et al., 1995.

<sup>d</sup> Savander et al. 1995.

<sup>e</sup> Amaral and Bassett, 1989.

<sup>f</sup> Savander et al., 1996.

<sup>g</sup> McDonald, 1982a.

<sup>h</sup> Jolkkonen and Pitkänen, 1998.

stimuli in different species, and it provides an attractive target for interspecies comparisons.

## 2. Lateral nucleus

Since the description of the cytoarchitectonic and chemoarchitectonic parcellation of the rat, cat, and monkey amygdala by Price et al. (1987), there have been some modifications of the nomenclature of the lateral nucleus, both in the rat and monkey (Table 1; Fig. 1). Further, this nomenclature was also adopted to partition the human amygdala (Table 1).

Based on cytoarchitectonic criteria, the lateral nucleus can be partitioned into three subdivisions in the rat (dorsolateral, ventrolateral, medial), four subdivisions in the monkey (dorsal, dorsal intermediate, ventral intermediate, ventral) and two subdivisions in the human (medial, lateral; Table 1; see Fig. 2). This parcellation is used in the present analysis.

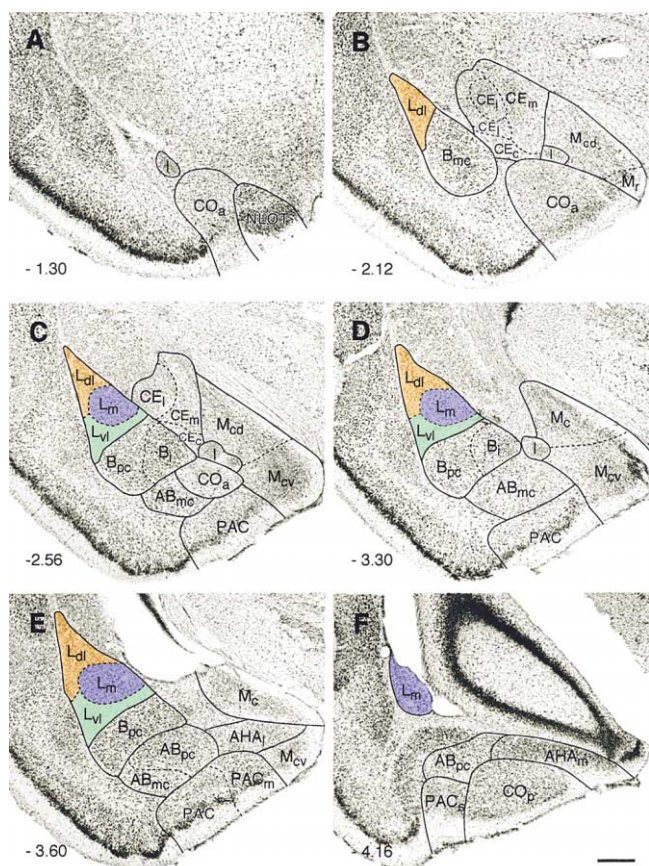


Fig. 1. The amygdaloid complex in the rat. The six rostrocaudal levels are arranged from rostral (panel A) to caudal (panel F). The dorsolateral (orange), ventrolateral (blue-green), and medial (blue) subdivisions of the lateral nucleus along the rostrocaudal extent of the amygdala are shown with different colors. The numbers in the lower left corner correspond to the distance from bregma according to rat brain atlas of Paxinos and Watson (1986). Scale bar equals 0.5 mm.

It should be noted that in the rat, the rostral and caudal aspects of the medial subdivision differ both cytoarchitectonically, chemoarchitectonically, and connectionally, and it might become necessary to partition the medial subdivision into two further subdivisions when more data become available (Kemppainen and Pitkänen, 2000). In the monkey, the cytoarchitectonic analysis of the dorsal intermediate subdivision suggests that it contains more than one independent subdivision (Pitkänen and Amaral, 1998). In addition, in the human, the lateral subdivision of the lateral nucleus will probably become partitioned into more subdivisions after additional detailed data become available (see Sorvari et al., 1995).

### 2.1. Distribution of calcium-binding proteins in the lateral nucleus

#### 2.1.1. Morphology of immunopositive cells

Parvalbumin, calbindin-D<sub>28k</sub>, and calretinin are calcium-binding proteins that label neuronal subpopulations in the rat, monkey, and human lateral nucleus of the amygdala [Figs. 2 and 3; Tables 2 and 3; Pitkänen and Amaral, 1993a,b (monkey); McDonald, 1994 (rat and monkey); McDonald, 1997 (rat); Sorvari et al., 1995, 1996a,b (human); Kemppainen and Pitkänen, 2000 (rat)]. There are several similarities in the morphology of immunopositive cells in all three species. First, the dendrites of all parvalbumin-immunoreactive (ir) neurons and a proportion of calbindin-D<sub>28k</sub>-ir and calretinin-ir neurons are smooth, nonspiny, or sparsely spiny. Second, based on the morphology of the somata and dendritic trees, smooth neurons are classified into small spherical or small multipolar (Type 1), large multipolar (Type 2), or fusiform (Type 3) categories (Table 3) in the rat, monkey, and human lateral nucleus. Such morphology resembles that of the local circuit neurons demonstrated by Golgi techniques in rats (McDonald, 1982b, 1984; Millhouse and DeOlmos, 1983) and humans (Braak and Braak, 1983). Consistent with the morphologic analysis, colocalization studies of calcium-binding proteins with GABA in the rat lateral nucleus indicate that parvalbumin-ir neurons are GABAergic, whereas calbindin-D<sub>28k</sub> and calretinin colocalize with GABA only in a subpopulation of amygdaloid neurons (Kemppainen and Pitkänen, 2000). Finally, in the rat, monkey, and human, subpopulations of calbindin-D<sub>28k</sub>-ir neurons have lightly stained pyramidal-shaped somata (Type 4), and are considered to be excitatory cells [Pitkänen and Amaral, 1993a (monkey); Sorvari et al., 1996a (human); McDonald, 1997 (rat); Kemppainen and Pitkänen, 2000 (rat)].

There are also several interspecies differences in the morphology of neurons immunopositive for calcium-binding proteins. For example, unlike in the rat lateral nucleus, the human lateral nucleus does not contain calretinin-positive pyramidal-shaped neurons (Sorvari et al., 1996b; Kemppainen and Pitkänen, 2000). Analysis of densities of



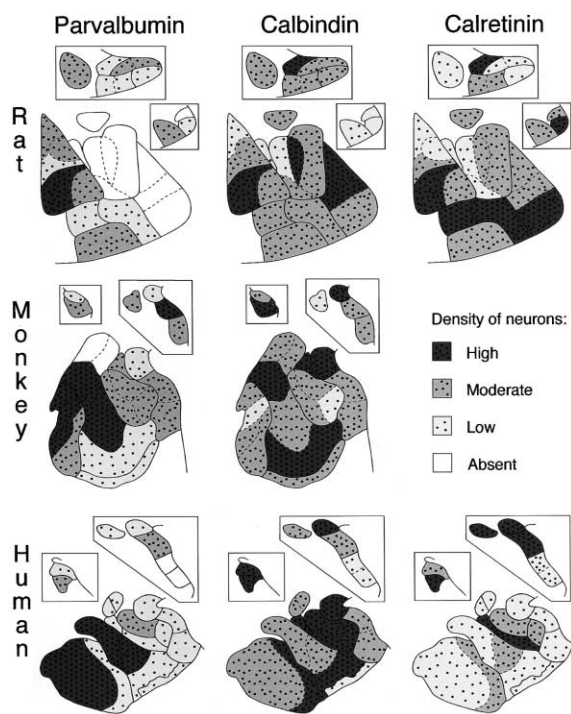


Fig. 3. Schematic representation of the distribution of parvalbumin, calbindin- $D_{28k}$ , and calretinin-ir neurons in the rat, monkey, and human amygdala. The density of dots indicates the variability in the neuronal density within the species and should not be considered to indicate differences between the species. For references, see legend to Fig. 2.

### 2.1.2. Parvalbumin

In the rat lateral nucleus, the density of neurons is similar in various subdivisions. The highest density of terminals is observed in the dorsolateral and ventrolateral subdivisions, whereas in the medial subdivision, the terminal labeling is

lighter (Fig. 2). In the dorsolateral and ventrolateral subdivisions, terminals form pericellular basket-like plexus and axo-axonic cartridges. Some basket-like plexus are also observed in the medial subdivision (Kemppainen and Pitkänen, 2000).

In the monkey, the highest density of parvalbumin-ir neurons and terminals is observed in the dorsal, dorsal intermediate, and ventral intermediate subdivisions (Pitkänen and Amaral, 1993b, 1998). However, the ventral subdivision contains relatively few cells and terminals. Like in the rat, basket-like plexus are present in the monkey lateral nucleus. Unfortunately, there are no data on the distribution of basket-like plexus in different subdivisions. The cartridges are most prevalent in the ventrolateral subdivision (Pitkänen and Amaral, 1993a,b), which largely corresponds to the ventral intermediate subdivision in a recent parcellation of the lateral nucleus (Pitkänen and Amaral, 1998).

In the human, the density of parvalbumin-ir neurons is substantially (20-fold, Table 2) higher in the lateral subdivision than in the medial subdivision. Accordingly, the density of terminals is higher in the lateral subdivision than in the medial subdivision. A high density of cartridges and basket-like plexus is observed in the lateral subdivision (Sorvari et al., 1995).

### 2.1.3. Calbindin- $D_{28k}$

In the rat lateral nucleus, the density of calbindin- $D_{28k}$ -ir cells, terminals, and neuropil varies more at different rostrocaudal levels than between the different subdivisions (McDonald, 1997; Kemppainen and Pitkänen, 2000). The highest neuronal density is observed in the caudal aspect of the medial and ventrolateral subdivisions. Accordingly, the neuropil and terminal labeling is also high caudally. Unlike

Table 2

Density of parvalbumin, calbindin- $D_{28k}$ , and calretinin-ir cells in the rat, monkey and human amygdala<sup>a</sup>

Species	Calcium binding protein	Lateral nucleus (total)	Subdivision of the lateral nucleus	
			Lateral <sup>b</sup>	Medial <sup>c</sup>
Rat <sup>d</sup>	Parvalbumin	–	87 ± 5	82 ± 25
	Calbindin- $D_{28k}$	–	98 ± 29	99 ± 19
	Calretinin	–	47 ± 8	81 ± 6
Monkey	Parvalbumin <sup>e</sup>	65		
	Calbindin- $D_{28k}$ <sup>f</sup>	115		
Human	Parvalbumin <sup>g</sup>	14	20	1
	Calbindin- $D_{28k}$ <sup>h</sup>	43	42	64
	Calretinin <sup>i</sup>	–	67	103

Abbreviations: –, data not available.

<sup>a</sup> Table shows the density of neurons/mm<sup>2</sup> (± standard deviation; when available). Note that human data are obtained from 50- $\mu$ m-thick sections, whereas data from the rat and monkey is obtained from 30- $\mu$ m-thick sections. Therefore, data presented here should be considered relative rather than absolute regarding the various sources of bias present in different studies.

<sup>b</sup> Corresponds to dorsolateral subdivision in the rat.

<sup>c</sup> Corresponds to medial and ventrolateral subdivisions in the rat.

<sup>d</sup> Unpublished observations (Kemppainen and Pitkänen).

<sup>e</sup> Pitkänen and Amaral, 1993a.

<sup>f</sup> Pitkänen and Amaral, 1993b.

<sup>g</sup> Sorvari et al., 1995.

<sup>h</sup> Sorvari et al., 1996a.

<sup>i</sup> Sorvari et al., 1996b.

Table 3

Mean cross-sectional areas and proportions of different morphologic cell types in the lateral nucleus of the amygdala in the rat, monkey, and human

CaBP	Cell type	Rat <sup>a</sup>		Monkey <sup>b,c</sup>		Human <sup>d,e,f</sup>	
		Mean size ± S.D. (μm <sup>2</sup> )	%	Mean size ± S.D. (μm <sup>2</sup> )	%	Mean size ± S.D. (μm <sup>2</sup> )	%
PV	Spherical	95 ± 30	25	95 ± 28	54	121 ± 43	16
	Multipolar	137 ± 58	71	158 ± 64	21	205 ± 85	72
	Fusiform	93 ± 44	2	133 ± 49	11	172 ± 77	2
	Unclassified	n.a.	1	86 ± 30	14		10
CB	Spherical	78 ± 24		102 ± 40	40		46
	Multipolar	123 ± 38		178 ± 59	3		40
	Fusiform	103 ± 36		156 ± 55	7		5
	Pyramidal	183 ± 38		202 ± 52	30		
	Unclassified	n.a.		146 ± 56	20		9
CR	Spherical	72 ± 16				93 ± 27	66
	Multipolar	117 ± 29				199 ± 82	15
	Fusiform	82 ± 31				118 ± 42	12
	Pyramidal	193 ± 45					
	Unclassified	n.a.					7

Note that spherical cells correspond to Type 1 cells, multipolar cells correspond to Type 2 cells, fusiform cells correspond to Type 3 cells, and pyramidal cells correspond to Type 4 cells in original publications. Abbreviations: CaBP, calcium-binding protein; CB, calbindin-D<sub>28k</sub>; CR, calretinin; n.a., not analyzed; PV, parvalbumin.

<sup>a</sup> Unpublished observations (Kemppainen and Pitkänen).

<sup>b</sup> Pitkänen and Amaral, 1993a.

<sup>c</sup> Pitkänen and Amaral, 1993b.

<sup>d</sup> Sorvari et al., 1995.

<sup>e</sup> Sorvari et al., 1996a.

<sup>f</sup> Sorvari et al., 1996b.

in other species, calbindin-D<sub>28k</sub>-ir terminal-like puncta form pericellular clusters around the unstained somata (McDonald, 1997; Kemppainen and Pitkänen, 2000) that resemble the basket-like plexus observed in parvalbumin staining.

In the monkey, the highest density of calbindin-D<sub>28k</sub>-ir neurons and terminal labeling is observed in the dorsal and ventral subdivisions. The lowest density of neurons is in the dorsal intermediate subdivision (Pitkänen and Amaral, 1998). Unlike in the rat or human lateral nucleus, in the monkey, the dorsal subdivision contains bundle-like formations that are immunoreactive for calbindin-D<sub>28k</sub> and resemble the bundles formed by axons and dendrites of double-bouquet cells in the neocortex (DeFelipe et al., 1989).

In the human lateral nucleus, the density of calbindin-D<sub>28k</sub>-immunopositive cells is higher in the medial subdivision than in the lateral subdivision. Consistent with the neuronal density, the most intense neuropil and terminal labeling is in the medial subdivision (Sorvari et al., 1996a).

#### 2.1.4. Calretinin

In the rat lateral nucleus, the density of immunopositive neurons decreases in the following order: ventrolateral > medial > dorsolateral (Kemppainen and Pitkänen, 2000; Woodson et al., 2000). The terminal and neuropil labeling, however, is moderate in all subdivisions.

In the monkey, the density of calretinin-ir neurons varies in the different portions of the lateral nucleus, being the lowest in “the dorsomedial portion” (Lam et al., 1994). Another study reported that the ventral part of the lateral

nucleus (which corresponds approximately to the ventral subdivision) contains numerous large moderately stained neurons (McDonald, 1994). To our knowledge, there are no detailed studies on the distribution of calretinin immunoreactivity in the monkey amygdala.

In the human, the medial subdivision of the lateral nucleus contains a higher density of calretinin-ir neurons than the lateral subdivision (Table 2; Sorvari et al., 1996b). Accordingly, the density of fibers and terminals is higher in the medial subdivision.

#### 2.2. Intraamygdaloid connectivity of the lateral nucleus

As recent tract tracing studies indicate, three levels of intraamygdaloid connectivity can be differentiated in the rat and monkey: intradivisional, interdivisional, and intraamygdaloid. This connectivity is compared in the rat and monkey lateral nucleus.

##### 2.2.1. Intradivisional connectivity

In the rat, various subdivisions of the lateral nucleus do not initiate substantial intradivisional projections. Rather, each rostrocaudal level projects only a short distance within the subdivision (Pitkänen et al., 1997).

In the monkey, the intradivisional projections appear somewhat more extensive. In the dorsolateral subdivision, the intradivisional projection is heavy at the injection site and rostral to it. In the dorsal intermediate subdivision, the intradivisional labeling is light. In the ventral intermediate subdivision, there is some labeling that is both rostral and caudal to the injection site. Finally, in the ventral subdivi-



sion, a heavy intradivisional projection extends caudally from the injection site (Pitkänen and Amaral, 1998).

2.2.2. *Interdivisional connectivity*

In the rat, each rostrocaudal level of the dorsolateral subdivision projects heavily to the ventrolateral and medial subdivisions of the lateral nucleus (Pitkänen et al., 1997). This allows information entering any part of the dorsolateral subdivision to activate the other subdivisions. Information flow between these subdivisions is unidirectional, as the ventrolateral and medial subdivisions do not project back to the dorsolateral subdivision. Further, interconnections between the ventrolateral and medial subdivisions are meager (Pitkänen et al., 1995, 1997).

In the monkey, information flow between the dorsal and ventral aspects of the lateral nucleus is rather unidirectional (see Fig. 4, Pitkänen and Amaral, 1998). The dorsal, dorsal intermediate, and ventral intermediate subdivisions project heavily to the ventral subdivision. Like in the rat, there is relatively little interconnectivity between these subdivisions. In addition, the ventral subdivision does not project back to

other more dorsally located subdivisions (Pitkänen and Amaral, 1998).

2.2.3. *Intraamygdaloid connectivity*

In the rat, each of the subdivisions of the lateral nucleus provides a unique set of projections to other amygdaloid regions. The dorsolateral subdivision innervates the parvicellular subdivision of the basal nucleus, the magnocellular and parvicellular subdivisions of the accessory basal nucleus, the nucleus of the lateral olfactory tract, the periamygdaloid cortex (PAC subdivision), and the capsular subdivision of the central nucleus. Projections from the ventrolateral subdivision terminate in the intermediate subdivision of the basal nucleus, the magnocellular and parvicellular subdivisions of the accessory basal nucleus, the dorsal part of the central subdivision of the medial nucleus, all three subdivisions of the periamygdaloid cortex (PAC, PACm, PACs), the posterior cortical nucleus, and the capsular subdivision of the central nucleus. The medial subdivision provides substantial input to the intermediate and parvicellular subdivisions of the basal nucleus, the parvicellular subdivision of the accessory basal nucleus, the lateral and medial subdivisions of the amygdalohippocampal area, and the posterior cortical nucleus (Pitkänen et al., 1995, 1997).

In the monkey, the dorsal subdivision projects to the magnocellular, parvicellular, and ventromedial subdivisions of the accessory basal nucleus, to the periamygdaloid cortex (PAC3), the nucleus of the lateral olfactory tract, the dorsal subdivision of the amygdalohippocampal area, and the lateral capsular nuclei. The dorsal intermediate subdivision projects to the intermediate and parvicellular subdivisions of the basal nucleus, the parvicellular subdivision of the accessory basal nucleus and to the periamygdaloid cortex (PACo, PAC3). The ventral intermediate subdivision projects to the magnocellular subdivision of the accessory basal nucleus and to the parvicellular subdivision of the basal nucleus. The major projections from the ventral subdivision are directed to the parvicellular subdivision of the basal nucleus, the parvicellular subdivision of the accessory basal nucleus, the medial nucleus, and the periamygdaloid cortex (PACo, PAC3). Projections from all portions of the lateral nucleus to the central nucleus are generally very light (Pitkänen and Amaral, 1998).

2.3. *How similar is the anatomy of the lateral nucleus of the amygdala in the rat, monkey, and human?*

Cytoarchitectonic analysis of the amygdala in the rat, monkey, and human indicates that the size of the lateral nucleus relative to other amygdaloid regions grows in the following order: rat < monkey < human (Price et al., 1987; De Olmos, 1990). Particularly, the dorsal aspect of the lateral nucleus becomes larger and cytoarchitectonically more complicated. In the rat, the dorsolateral subdivision includes 40% (24 000 of 60 000 neurons) of the lateral

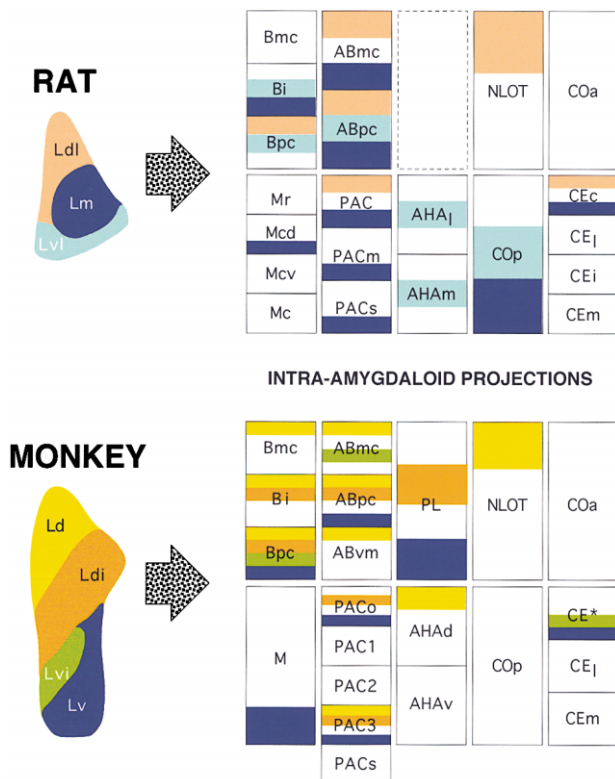


Fig. 4. Intra-amygdaloid projections originating in the different subdivisions of the lateral nucleus in rat (upper part) and monkey (lower part). Different subdivisions of the lateral nucleus on the left and corresponding intra-amygdaloid projections on the right are labeled with different color codes. Notes that there are some indications that the medial subdivision in the rat shares some anatomic similarities with the ventral subdivision in monkey, however the homology between the other subfields is poorly understood.

nucleus), ventrolateral 23% (14000), and medial subdivision 37% (22000) of the neurons in the lateral nucleus (Tuunanen and Pitkänen, 2000). To our knowledge, no such analysis of the other species is available.

Comparison of the distribution of calcium-binding proteins in the lateral nucleus of the rat, monkey, and human amygdala suggests that there are some similarities between the medial subdivision of the lateral nucleus in the rat, the ventral subdivision in the monkey, and the medial subdivision in the human. For example, in all three species, the density of parvalbumin-ir terminals is the lowest in these regions. On the other hand, the density of calbindin-D<sub>28k</sub>-ir lightly stained pyramidal-shaped cells and neuropil staining is high. There are similarities also in the organization of intranuclear information flow. Intranuclear inputs of the lateral nucleus converge in the medial (rat) and ventral (monkey) subdivision.

The more widespread intradivisional connectivity in the primate lateral nucleus compared to that in rodents suggests that the primate amygdala can associate information entering different parts of one subdivision more extensively than the rodent amygdala. The meagerness of interdivisional connectivity and unidirectional information flow within the lateral nucleus, however, suggests that the information entering one subdivision remains segregated from the data processed by other subdivisions until it reaches the medial or the ventral subdivision in rodents and in primates, respectively.

The medial subdivision of the lateral nucleus in the rat and the ventral subdivision in the monkey stain rather similarly to different calcium-binding proteins relative to other subdivisions. In both species, these subdivisions converge interdivisional inputs. Further, both in the rat and monkey, the medial subdivision/ventral subdivision converge polymodal information from sensory-related cortices (Stefanacci and Amaral, 2000; Pitkänen, 2000) and provide substantial inputs to the entorhinal cortex (Pitkänen and Amaral, unpublished; Pikkarainen et al., 1999). In the rat, the medial subdivision innervates six other amygdaloid regions, including the basal nucleus, accessory basal nucleus, medial nucleus, periamygdaloid cortex, posterior cortical nucleus, and central nucleus. In the monkey, the six innervated amygdaloid nuclei are the basal nucleus, the accessory basal nucleus, the paralamina nucleus, the medial nucleus, the periamygdaloid cortex, and the region recently proposed to be part of the central nucleus, CE\* (a region lateral to the central nucleus in the monkey that is proposed to correspond to the capsular subdivision of the central nucleus in the rat; see Pitkänen and Amaral, 1998). Therefore, the projections originating in the medial (rat)/ventral (monkey) subdivisions are similar, rather than different, in the two species. There are, however, differences in the distribution of intraamygdaloid projections at the subdivisional level. For example, in the rat, the projections to the basal nucleus terminate in the intermediate subdivision, whereas in the monkey, they innervate the parvicellular

subdivision. Unlike in the monkey, the posterior cortical nucleus receives a substantial input from the medial subdivision of the lateral nucleus in the rat. This suggests the importance of the association of auditory and visual information entering the amygdala via the lateral nucleus with the olfactory and pheromonal information entering the amygdala via the posterior cortical nucleus in rodents.

### 3. Concluding remarks

Comparison of cytoarchitectonics and chemoarchitectonics is a useful tool when trying to assess which amygdaloid regions might be anatomically homologous in rodents and primates. When such analysis is combined with the comparison of connectivity, we can start to predict similarities and differences in the function of the amygdala, amygdaloid subnuclei, and nuclear subdivisions in different species. The present analysis of the lateral nucleus of the rodent and primate amygdala indicates that there are interspecies similarities in the chemoarchitectonic organization of various subdivisions. The connective analysis, however, demonstrates that the connectivity of the presumed homologous subdivisions of the lateral nucleus in the rat and monkey does not completely overlap, even when assessed in regions that are chemoarchitectonically similar, such as the medial division of the lateral nucleus in the rat and the ventral division in the monkey. Whether this is related to the parcellation of the amygdala or whether such mismatch predicts true differences in the function of the amygdala in rodents and primates remains a testable hypothesis.

### 4. Abbreviations

AAA	anterior amygdaloid area
AB <sub>mc</sub>	accessory basal nucleus, magnocellular subdivision
AB <sub>pc</sub>	accessory basal nucleus, parvicellular subdivision
AB <sub>vm</sub>	accessory basal nucleus, ventromedial subdivision
AHA	amygdalohippocampal area
AHA <sub>d</sub>	amygdalohippocampal area, dorsal subdivision
AHA <sub>l</sub>	amygdalohippocampal area, lateral subdivision
AHA <sub>m</sub>	amygdalohippocampal area, medial subdivision
AHA <sub>v</sub>	amygdalohippocampal area, ventral subdivision
BAOT	bed nucleus of accessory olfactory tract
B <sub>i</sub>	basal nucleus, intermediate subdivision
B <sub>mc</sub>	basal nucleus, magnocellular subdivision
B <sub>pc</sub>	basal nucleus, parvicellular subdivision
CE*	central nucleus, capsular subdivision (proposed)
CE <sub>c</sub>	central nucleus, capsular subdivision
CE <sub>i</sub>	central nucleus, intermediate subdivision
CE <sub>l</sub>	central nucleus, lateral subdivision
CE <sub>m</sub>	central nucleus, medial subdivision
CO <sub>a</sub>	anterior cortical nucleus
CO <sub>p</sub>	posterior cortical nucleus
I	intercalated nucleus



L <sub>d</sub>	lateral nucleus, dorsal subdivision
L <sub>di</sub>	lateral nucleus, dorsal intermediate subdivision
L <sub>dl</sub>	lateral nucleus, dorsolateral subdivision
L <sub>l</sub>	lateral nucleus, lateral subdivision
L <sub>m</sub>	lateral nucleus, medial subdivision
L <sub>v</sub>	lateral nucleus, ventral subdivision
L <sub>vi</sub>	lateral nucleus, ventral intermediate subdivision
L <sub>vl</sub>	lateral nucleus, ventrolateral subdivision
M	medial nucleus
M <sub>c</sub>	medial nucleus, caudal subdivision
M <sub>cd</sub>	medial nucleus, central subdivision, dorsal part
M <sub>cv</sub>	medial nucleus, central subdivision, ventral part
M <sub>r</sub>	medial nucleus, rostral subdivision
NLOT	nucleus of the lateral olfactory tract
PAC	periamygdaloid cortex
PAC <sub>m</sub>	periamygdaloid cortex, medial subfield
PAC <sub>o</sub>	periamygdaloid cortex, oral subfield
PAC <sub>s</sub>	periamygdaloid cortex, sulcal subfield
PAC <sub>1</sub>	periamygdaloid cortex 1
PAC <sub>2</sub>	periamygdaloid cortex 2
PAC <sub>3</sub>	periamygdaloid cortex 3
PL	paralamina nucleus

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