Eur J Anat, 5 (3): 159-169 (2001)

Neuropeptides in the cat diencephalon: I. Thalamus

R. Coveñas[1], M. de León[1], M. Belda[1], P. Marcos[2], J.A. Narváez[3], J.A. Aguirre[3], G. Tramu[4] and S. González-Barón[3]

1- Instituto de Neurociencias de Castilla y León (INCYL), Laboratorio de Neuroanatomía de los Sistemas Peptidérgicos, Salamanca, Spain
2- Universidad de Castilla-La Mancha, Facultad de Medicina, Departamento de Ciencias de la Salud, Albacete, Spain
3- Universidad de Málaga, Facultad de Medicina, Departamento de Fisiología, Málaga, Spain
4- Université de Bordeaux I, Laboratoire de Neurocytochimie Fonctionelle, C.N.R.S., U.R.A. 339, Talance, France

SUMMARY

In this paper we review the distribution and functions of neuropeptides in the cat thalamus. We focus our review on the following topics: 1) the distribution of neuropeptides in the cat thalamus; 2) the coexistence of neuropeptides in the cat thalamus; 3) the anatomical relationships between neuropeptides in the cat thalamus; 4) the peptidergic pathways in the cat thalamus; 5) a comparison of the distribution of neuropeptides in the mammalian thalamus; and 6) the physiological functions of neuropeptides in the cat thalamus. Although in recent years our knowledge of the distribution of neuropeptides in the cat thalamus has increased considerably, there still remains much to do in this feline brain region in order to know the distribution of other neuropeptides, the physiological interactions among them, the afferent and efferent peptidergic pathways, and the physiological roles of such neuropeptides. In the future, other methods (e.g., in situ hybridization, tract-tracing…) in addition to immunocytochemical methods should be used in the cat thalamus to increase our knowledge of the neuropeptides in this diencephalic region.

Key Words: Neuropeptides – Thalamus – Diencephalon – Cat

Abbreviations used: AD, N. anterior dorsalis; AM, N. anterior medialis; AV, N. anterior ventralis; CL, N. centralis lateralis; CM, N. centrum medianum; GL, Corpus geniculatum laterale; GLv, Corpus geniculatum laterale (pars ventralis); GM, Corpus geniculatum mediale; Hbl, N. habenularis lateralis; Hbm, N. habenularis medialis; IAM, N. interanteromedialis; IV, N. interventricularis; LD, N. lateralis dorsalis; Lim, N. limitans; LP, N. lateralis posterior; mc, pars magnocellularis; MD, N. medialis dorsalis; NCM,: N. centralis medialis; P, N. posterior; Pc, N. paracentralis; Pf, N. parafascicularis; Prt, Praetectum; Pt, N. parataenialis; Pul, Pulvinar; PVA, N. periventricularis anterior; R, N. reticularis; RE, N. reuniens; Rh, N. rhomboidens; S, Stria medullaris; SG, N. suprageniculatus; Sm, N. submedius; Spf, N. subparafascicularis; THP, Tractus habenulo-peduncularis; VA, N. ventralis anterior; VL, N. ventralis lateralis; VM, N. ventralis medialis; VPL, N. ventralis postero-lateralis; VPM, N. ventralis postero-medialis; ZI, Zona incerta.

INTRODUCTION

The thalamus is located in the central part of the encephalon, belongs to the diencephalon, and is an important relay area between the spinal cord/brainstem and the basal ganglia/cerebral

Submitted: July 17, 2001
Accepted: October 26, 2001

Correspondence to:
Dr. R. Coveñas. Instituto de Neurociencias de Castilla y León (INCYL), Laboratorio de Neuroanatomía de los Sistemas Peptidérgicos, Facultad de Medicina, C/ Alfonso X El Sabio s/n, 37007, Salamanca, Spain.
Phone: 923-294-400 est. 1856; Fax: 923-294-549. E-Mail: covenas@usal.es

cortex. The thalamic nuclei receive somatosensorial, nociceptive, visual, auditive, vestibular, taste and olfactory inputs (see van Dongen and Nieuwenhuys, 1998). In addition, this brain region is involved in motor and speech mechanisms and is a region in which functional asymmetry has been described, since one side predominates over the other. Thus, the left side of the thalamus predominates over the right side in mechanisms involved in speech and in mechanical processes (e.g., respiration…), whereas the thalamic right side predominates over the left side in visual and spatial processes. Moreover, the thalamus has been implicated in several diseases. For example, a loss of 50% of the small neurons located in the pulvinar nucleus has been observed in schizophrenia, and a decrease in the number of neurons located in the nucleus ventralis lateralis has been described in Huntington's disease (see Ohye, 1990).

Based on topographic criteria, the thalamic nuclei have been grouped into several nuclear groups (posterior, ventral, medial, midline, intralaminar) and complexes (lateralis posterior-pulvinar, geniculate), as well as into the ephithalamus and dorsal and ventral thalamus (see Macchi, 1983; Jones and Hendry, 1989). In this review, we will follow that classification (see Table 1).

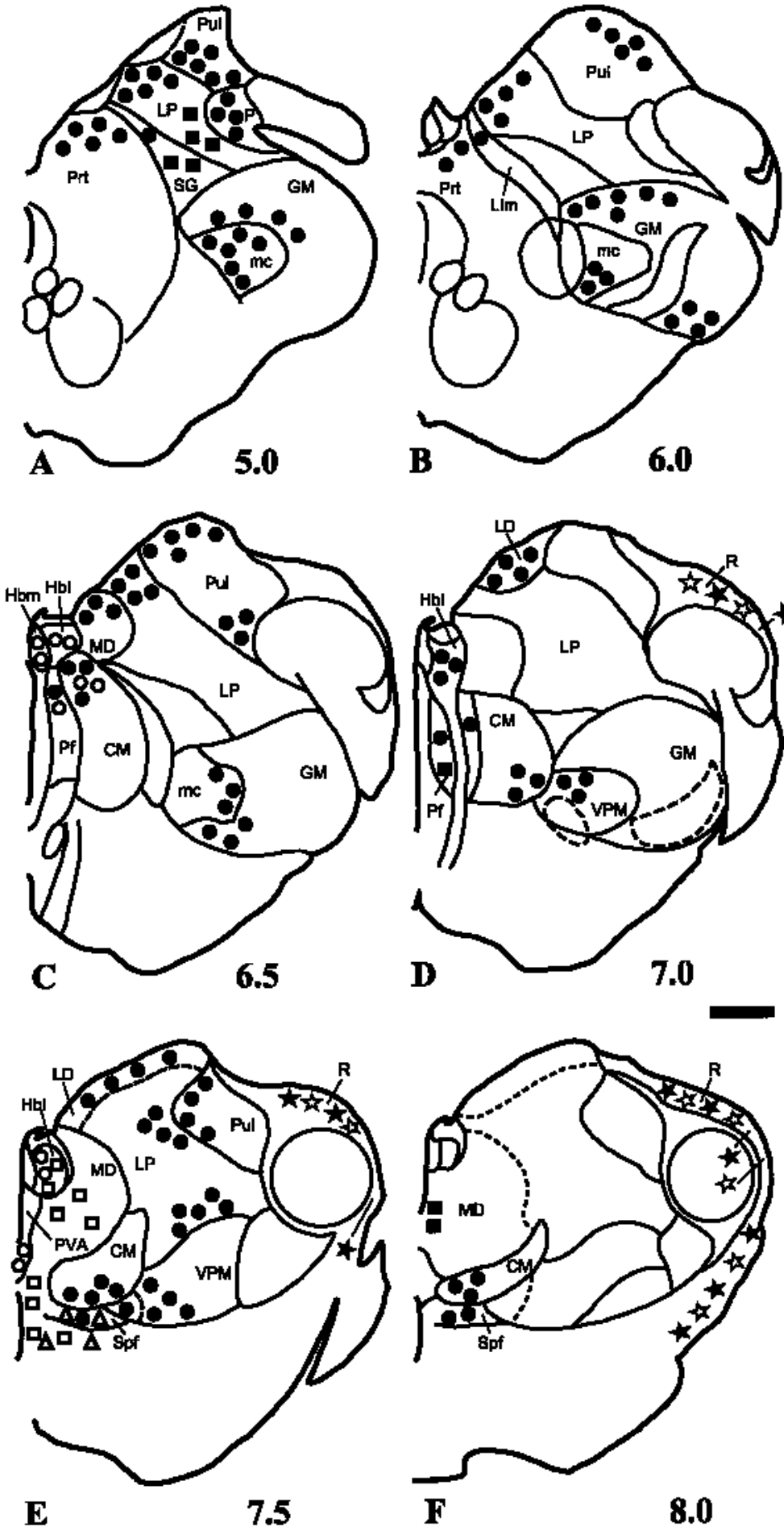
Knowledge of the distribution and functions of the neuropeptides present in the mammalian thalamus has increased considerably over the last twenty years. The distribution of many neuropeptides belonging to several peptidergic families has been studied in the rat, dog, monkey and human thalamus (see, for example, Smith et al., 1985; Palkovits, 1988; Pioro et al., 1990; Pego-Reigosa et al., 2000). The cat has been used in the laboratory as an experimental animal model in order to investigate several scientific issues related to neuroanatomy, neurophysiology, neuropharmacology and behaviour. However, until 1983 the distribution of neuropeptides in the cat central nervous system had received little attention. Over the past eighteen years, however, knowledge of their distribution has increased notably. The aim of this paper is to review, in the cat, the currently available morphological and physiological data concerning neuropeptides in one of the most complex areas of the central nervous system: the thalamus.

NEUROPEPTIDES IN THE CAT THALAMUS

Table 1 shows the presence of fibers and cell bodies containing neuropeptides in the thalamus of the cat detected using immunocytochemical methods. The table also shows a few studies in which radioimmunoassay or autoradiographic techniques were used to gain insight, respectively, into the concentration of neuropeptides and the presence of neuropeptides receptors in the cat thalamus (O'Donohue et al., 1979; Dietl et al., 1990). As can be observed, only ten neuropeptides have been studied in detail in the cat thalamus (Sugimoto et al., 1984; Conrath et al., 1986; Coveñas et al., 1986, 1990, 1996a,b,c; Rao et al., 1986, 1987; Burgos et al., 1988; de León et al., 1991a, b; Battaglia et al, 1992; Velasco et al., 1993; Belda et al., 2000), although there are partial data for another two neuropeptides (Obata-Tsuto et al., 1983; Sugimoto et al, 1985; Wahle and Albus, 1985). Moreover, scarce or very scarce data are available conceming the distribution of another four neuropeptides (not shown in Table 1): somatostatin-14, somatostatin-28, avian pancreatic polypeptide and delta sleep-inducing peptide. In the cat, immunoreactive fibers containing somatostatin-14 have been found in the nuclei habenularis lateralis, centralis medialis, reuniens, medialis dorsalis, subparafascicularis and zona incerta, and somatostatin-14-containing cell bodies have been observed in the cat nucleus reticularis (Graybiel and Elde, 1983). In this species, the same authors described immunoreactive cell bodies, but no fibers containing somatostatin-28 in the nucleus reticularis and no immunoreactive structures containing avian pancreatic polypeptide in the same thalamic nucleus (Graybiel and Elde, 1983). In addition, fibers containing delta sleep-inducing peptide have been described in the cat nuclei habenularis medialis, periventricularis anterior, reuniens and lateralis dorsalis (Charnay et al., 1990). Finally, the localization of calcitonin-binding sites has been demonstrated in the medial and intralaminar thalamus of the cat (Guidobono et al., 1987) and, with radioimmunoassay methods, a moderate level of kassinin has been described in the cat thalamus (Hunter et al., 1985).

In general, the immunoreactive fibers containing neuropeptides in the cat thalamus are located in the nuclei of the midline and in thalamic nuclei close to the midline (see Table 1), although the presence of immunoreactive fibers containing, for example, neuropeptide Y, β-endorphin or α-melanocyte-stimulating hormone has been described in thalamic nuclei located laterally, such as the corpus geniculatum mediale, corpus geniculatum laterale, pars ventralis of the corpus geniculatum laterale or lateralis posterior (Coveñas et al., 1990; 1996a,b). The distribution of cell bodies containing neuropeptides in the cat thalamus is shown in Figure 1.

The neuropeptide methionine-enkephalin (MET-E) shows the most widespread distribution, since of the 36 nuclei of the cat thalamus fibers and/or cell bodies containing MET-E have been observed in 31 of them (see Table 2). However, neurokinin A (NKA) has the lowest distrib-


Pul
LP
P
Prt
SG
GM
mc
A
5.0
Pul
LP
Prt
Lim
GM
mc
B
6.0
Hbm
Hbl
Pul
MD
LP
Pf
CM
GM
mc
C
6.5
LD
R
Hbl
LP
CM
GM
Pf
VPM
D
7.0
LD
R
Hbl
Pul
MD
LP
PVA
CM
VPM
Spf
E
7.5
R
MD
CM
Spf
F
8.0

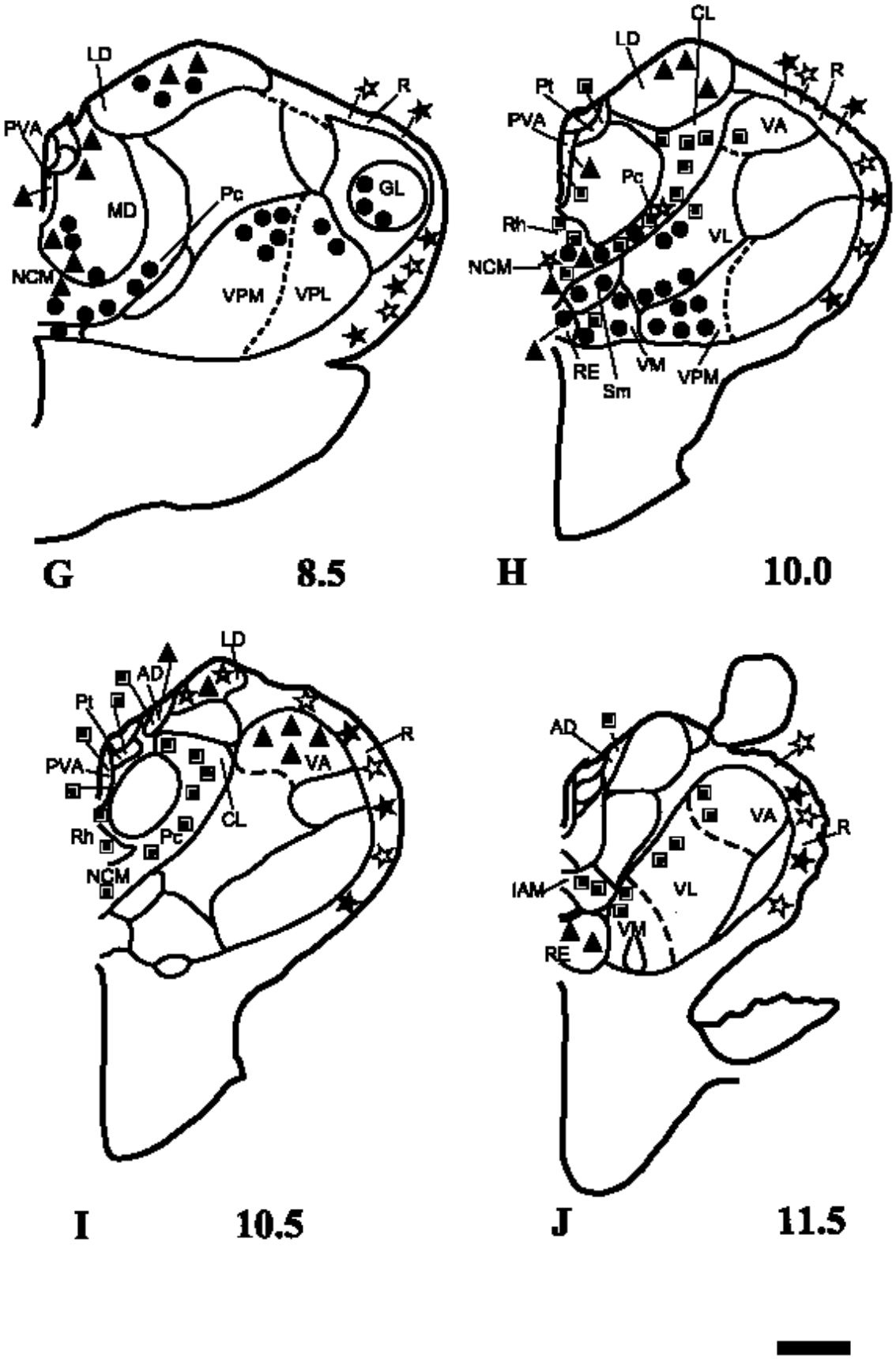


Fig. 1.- Distribution of cell bodies containing neuropeptides in frontal planes of the cat thalamus corresponding to the anteroposterior stereotaxic plane levels from anteriority 5.0 to anteriority 11.5 of the Jasper and Ajmone-Marsan (1966) stereotaxic atlas. The anteriority (A), in mm with respect to the zero stereotaxic point of each section, is indicated at the lower right. For a nomenclature of the thalamic nuclei, see list of abbreviations. Cell bodies are represented by: ◙: cholecystokinin-8; ● : methionine-enkephalin; ◘: neurokinin A; ■ : neuropeptide Y; ▲: neurotensin; ▲: somatostatin-28 (1-12); ☆: somatostatin-28; ★: somatostatin-14; ◙: substance P; ★: vasoactive intestinal peptide. Scale bar: 1.54 mm.

Table 1.- Distribution of neuropeptides in the nuclei of the cat thalamus.

	MET-E		SP		NT		SOM		NPY		β-END		α-MSH		ACTH		LH-RH		NKA		CCK-8		VIP	
	F	CB	F	CB	F	CB	F	CB	F	CB	F	CB	F	CB	F	CB	F	CB	F	CB	F	CB	F	CB
EPITHALAMUS																								
Hbl	-	+	+	+	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	+			-	
Hbm	+	-	-	+	+	-	-	-	-	-	+	-	+	-	+	-	+	-	+	-			-	
PVA	+	-	+	+	+	+	+	-	+	-	+	-	RIA +	-	+	-	+	-	+	-		+	-	
MIDLINE GROUP																								
IAM	-	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	-	-	-	-		+		
IV	+	+	-	-	+	-	-	-	-	-	+	-	+	-	+	-	+	-	+	-				
NCM	+	+	+	-	+	+	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	
RE	+	+	+	-	+	+	+	-	+	-	+	-	+	-	+	-	+	-	+	+			-	
Rh	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	-	-	+	-		+	-	
MEDIAL GROUP																								
MD	+	+	+	-	+	+	+	-	+	+	+	-	+	-	+	-	+	-	+	+			-	
Pt	+	-	-	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-	+	-		+	-	
INTRALAMINAR GROUP																								
CL	-	-	+	-	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-		+		
CM	+	+	-	+	+	-	-	-	+	-	+	-	+	-	-	-	-	-	-	-				
Pc	-	+	-	-	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-			+		+
Pf	+	+	+	+	+	-	-	-	+	+	+	-	+	-	+	-	-	-	+	+				
Spf	+	+	-	+	-	-	-	+	-	-	-	-	+	-	-	-	+	-	-	-				
VENTRAL GROUP																								
Sm	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
VA	+	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-		+		
VL	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		+		
VM	-	+	-	-	+	-	+	-	-	-	+	-	+	-	-	-	-	-	-	-		+		
VPL	+	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-		
VPM	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		-		R
POSTERIOR GROUP																								
Lim	-	+	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-				
P	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
Prt	-	+	+	-	+	-	-	-	+	-	-	-	-	-	-	-	+	-	-	-				
SG	-	+	+	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-	-	-				
LATERAL POSTERIOR PULVINAR COMPLEX																								
LP	-	+	+	-	+	-	+	-	+	+	+	-	+	-	+	-	+	-	-	-		-		
Pul	-	+	-	-	-	-	-	-	+	-	-	-	+	-	-	-	-	-	-	-		-	R	
DORSAL THALAMUS																								
AD	-	-	+	-	-	+	+	-	+	-	-	-	+	-	-	-	-	-	-	-		+		
AM	+	-	-	-	-	-	-	-	+	-	-	-	RIA -	-	-	-	+	-	-	-				
AV	-	-	-	-	-	+	-	-	+	-	-	-	RIA +	-	-	-	-	-	-	-				
LD	+	+	+	-	+	+	+	+	+	-	+	-	+	-	+	-	+	-	+	-		-		+
GENICULATE COMPLEX																								
GL	-	+	-	-	-	-	-	-	+	-	+	-	+	-	-	-	-	-	-	-		-	R	
GLv	-	-	+	-	-	-	-	-	+	+	+	-	+	-	-	-	-	-	-	-				
GM	-	+	-	-	-	-	-	-	-	-	+	-	+	-	+	-	-	-	+	-				
VENTRAL THALAMUS																								
R	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
ZI	-	-	-	-	-	-	-	-	+	-	+	-	+	-	+	-	-	-	-	-				
TRACTUS																								
S	+	-	+	-	+	-	+	-	-	-	+	-	-	-	+	-	+	-	+	-				
THP	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-	-				

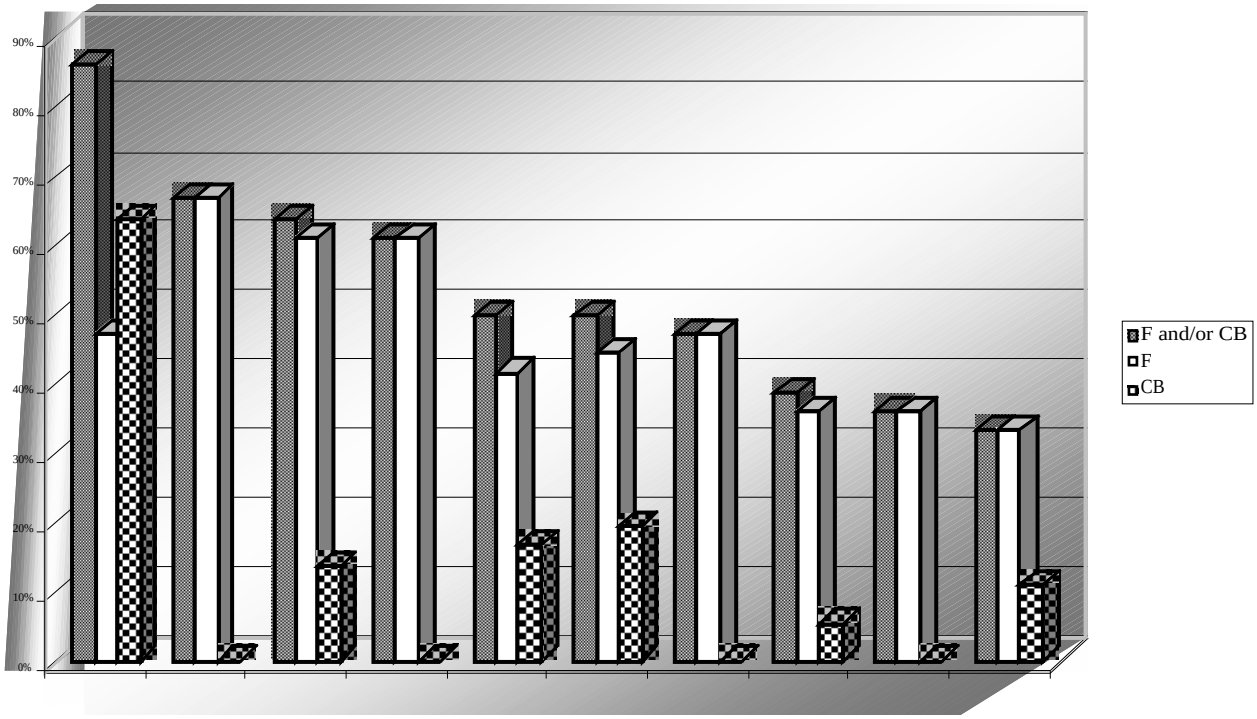
ACTH: adrenocorticotropin hormone (18-39) or (1-39); **β-END:** β-endorphin (1-27); **CCK-8:** cholecystokinin-8; **LH-RH:** luteinizing hormone-releasing hormone; **MET-E:** methionine-enkephalin; **α-MSH:** α-melanocyte-stimulating hormone; **NKA:** neurokinin A; **NPY:** neuropeptide Y; **NT:** neurotensin; **R:** receptors; **RIA:** radioimmunoassay; **SOM:** somatostatin-28 (1-12); **SP:** substance P; **VIP:** vasoactive intestinal peptide. For a nomenclature of the thalamic nuclei, see list of abbreviations. **CB:** immunoreactive cell bodies; **F:** immunorective fibers; **+:** presence; **-** : absence; **no sign:** not studied.

ution, since immunoreactive structures (fibers and/or cell bodies) are only observed in 12 nuclei of the cat thalamus. Moreover, in almost all the thalamic nuclei of the cat (except in the nuclei posterior, submedius, ventralis postero-lateralis and postero-medialis) the presence of two or more neuropeptides can be detected (see Table 3). The thalamic nucleus in which the highest number of neuropeptides (thirteen) has been observed in fibers and/or in cell bodies is the nucleus centralis medialis, whereas in other nuclei, such as the lateralis dorsalis, periventricularis anterior and reuniens, twelve neuropeptides are seen in each of them.

COEXISTENCE OF NEUROPEPTIDES IN THE CAT THALAMUS

The presence of several different neuropeptides in the same thalamic nuclei suggests the possibility that two or more neuropeptides may

Table 2.- Percentages of thalamic nuclei of the cat that contain a neuropeptide located in fibers and/or cell bodies (F and/or CB), in fibers (F) or in cell bodies (CB).



For a nomenclature of the neuropeptides, see Table 1. **CB:** immunoreactive cell bodies; **F:** immunoreactive fibers. The total number of thalamic nuclei is 36.

coexist in the same neuron. In this sense, it has been demonstrated in the cat that in the nucleus centralis medialis 70-80% of the immunoreactive neurons containing vasoactive intestinal peptide also contain cholecystokinin (Sugimoto et al., 1985). The same authors also reported the coexistence of cholecystokinin and neurotensin in cell bodies located in the nucleus anterior dorsalis, and the coexistence of vasoactive intestinal peptide and neurotensin has been also described in the rostral part of the nucleus lateralis dorsalis (Sugimoto et al., 1985).

In some cases, it has been described that the distribution in the central nervous system of neuropeptides arising from the same precursor is different. Thus, in the cat thalamus the distribution of the different forms of somatostatin (somatostatin-28, somatostatin-14 and somatostatin-28 (1-12), which originate from the precursor prosomatostatin (Fitzpatrick-McElligott et al., 1988), shows several differences (de León et al., 1991b). These discrepancies in the localization of the different forms of somatostatin could be due to intraneuronal transport of the neuropeptides (Lechan et al., 1983; Morrison et al., 1984; Lewis et al., 1986). In keeping with this, a complete intraneuronal segregation of somatostatin-28 and somatostatin-28 (1-12) has been described in the cortex of the monkey (Lewis et al., 1986), since somatostatin-28 was detected in the cell bodies and somatostatin-28 (1-12) in fibers, suggesting that somatostatin-28 is cleaved within the neuronal somata to form

Table 3.- Presence of neuropeptides in the cat thalamic nuclei.

NCM	13/13	100%
LD, PVA, RE	12/13	92,30%
Hbl, MD	11/12	91,66%
Pt, Rh	10/12	83,33%
LP	9/11	81,81%
Pf, S	8/10	80%
Hbm	9/12	75%
IAM	8/11	72,72%
IV	7/10	70%
CM	6/10	60%
AD, Spf, VM	6/11	54,54%
GM, Prt	5/10	50%
Pc	5/12	41,66%
AM, GL, GLv, SG	4/10	40%
ZI	5/13	38,46%
CL	4/11	36,36%
AV, Lim	3/10	30%
Pul, VA	3/11	27,27%
R	3/13	23,07%
THP	2/10	20%
VL	2/11	18,18%
P, Sm	1/10	10%
VPL, VPM	1/11	9,09%

For a nomenclature of the thalamic nuclei, see list of abbreviations. For example, 12/13: indicates that of 13 neuropeptides studied, 12 were found in fibers and/or cell bodies in the nucleus LD. Their percentages are also indicated.

somatostatin-28 (1-12), which is then rapidly transported into neuronal processes. In addition, it is also possible that a different kind of processing of somatostatin precursor may occur, since it has been reported that the intensity of staining for somatostatin-28 (1-12) and somatostatin-28 in the same region is quite different (see de León et al., 1991b).

ANATOMICAL RELATIONSHIPS AMONG THE NEUROPEPTIDES IN THE CAT THALAMUS

Table 4 shows the anatomical relationships among the neuropeptides in the cat thalamus. For example, in the case of substance P and β-endorphin the Table indicates that in 89.47% of the cat thalamic nuclei in which substance P-immunoreactive fibers and/or cell bodies are found, β-endorphin-immunoreactive fibers and/or cell bodies have also been observed. The percentage was calculated taking the total number of the cat thalamic nuclei in which substance P-immunoreactive fibers and/or cell bodies were visualized as 100%. The lowest percentage observed was 39.13% (neuropeptide Y/neurokinin A).

Table 4.- Anatomical relationships among the neuropeptides in the cat thalamus.

	%
SP/β-END	89.47
NPY/α-MSH	86.95
SOM/β-END; SOM/α-MSH; SOM/ ACTH; SOM/NPY	85.71
NT/α-MSH; SP/NPY; SP/α-MSH; NT/β-END	84.21
SP/NT; NT/NPY; NT/ACTH	78.94
β-END/α-MSH; β-END/ACTH	78.26
ACTH/NKA	72.22
SOM/LH-RH	71.42
NPY/β-END	69.56
NT/SOM	68.42
LH-RH/ NKA	66.66
SOM/NKA	64.28
SP/SOM; SP/ACTH; NT/LH-RH; NT/NKA	63.15
α-MSH/ACTH	62.15
ACTH/LH-RH	61.11
MET-E/β-END; MET-E/α-MSH	59.37
SP/LH-RH	57.89
β-END/NKA	56.52
MET-E/NPY	53.12
SP/NKA	52.63
NPY/ACTH	52.17
MET-E/ACTH; α-MSH/LH-RH; α-MSH/NKA	50
NPY/LH-RH; β-END/LH-RH	47.82
MET-E/NT; MET-E/LH-RH	46.87
MET-E/SP	43.75
MET-E/SOM; MET-E/ NKA	40.62
NPY/NKA	39.13

For a nomenclature of the neuropeptides, see Table 1.

POSSIBLE PEPTIDERGIC AFFERENCES TO THE CAT THALAMIC NUCLEI

Some of the results shown in Table 1 suggest that several nuclei of the cat thalamus receive peptidergic afferences. In this sense, a high or moderate density of immunoreactive fibers and no immunoreactive cell bodies have been observed in such nuclei. Table 5 shows the thalamic nuclei of the cat in which peptidergic fibers but no cell bodies have been observed. In all cases, the observation indicates that such thalamic nuclei could receive peptidergic afferences arising from neurons located inside and/or outside the thalamus.

Table 5.- Possible peptidergic afferents to the cat thalamic nuclei (F: +++/++; CB: -).

ACTH	NPY
IAM: (++)	PVA (+++)
IV: (++)	**NT**
Lim: (++)	Pf: (++)
MD: (++)	**SOM**
NCM: (++)	Hbl: (+++)
Pf: (++)	Pc: (++)
PVA: (+++)	PVA: (+++)
Rh: (+++)	**SP**
MET-E	AD: (++)
HBM: (+++)	IAM: (++)
Pt: (++)	LD: (+++)
PVA: (+++)	MD: (+++)
Rh: (++)	NCM: (+++)
α-MSH	Prt: (+++)
PVA: (++)	RE: (++)
NKA	Rh: (++)
NCM: (+++)	
PVA: (+++)	
Rh: (+++)	

For a nomenclature of the neuropeptides and the thalamic nuclei, see respectively, Table 1 and list of abbreviations. **CB:** immunoreactive cell bodies; (- : absence); **F:** immunoreactive fibers (+++: high density; ++: moderate density).

POSSIBLE PROJECTING PEPTIDERGIC THALAMIC NEURONS IN THE CAT

Unlike what has been reported above, there are thalamic nuclei in the cat in which a high or moderate density of immunoreactive cell bodies has been observed, but no immunoreactive fibers. This finding indicates that such neurons could be projecting neurons, which send projections to other thalamic nuclei and/or to other parts of the central nervous system (see Table 6).

PEPTIDERGIC PATHWAYS IN THE CAT THALAMUS

Few peptidergic pathways have been demonstrated in the cat thalamus, although the following pathways have been described:

Table 6.- Possible peptidergic projecting neurons in the cat thalamic nuclei (F: -; CB: +++/++).

MET-E	NPY
GL (+++)	SG (++)
GM (+++)	**SOM**
Hbl (+++)	Spf (+++)
LP (+++)	**SS-14**
P (+++)	Ret (+++)
Pc (+++)	**SS-28**
Pul (+++)	Ret (+++)
VL (+++)	
VM (+++)	
VPM **(+++)**	

SS-14: Somatostatin-14; **SS-28:** somatostatin-28. For a nomenclature of the other neuropeptides and the thalamic nuclei, see respectively, Table 1 and list of abbreviations: **CB:** immunoreactive cell bodies; (+++: high density; ++: moderate density); **F:** immunoreactive fibers (- : absence).

a) From the rostral region of the intralaminar nuclei to the striatum: containing cholecystokinin-8 or vasoactive intestinal peptide (Sugimoto et al., 1985; Adams and Fisher, 1990).
b) From the nuclei centralis lateralis, paracentralis and centralis medialis to the proreus gyrus: cholecystokinin (Sugimoto et al., 1985).
c) From the nucleus lateralis dorsalis to the presubiculum: neurotensin or vasoactive intestinal peptide (Sugimoto et al., 1985).
d) From the nuclei anterior dorsalis and anterior ventralis to the presubiculum: cholecystokinin or neurotensin (Sugimoto et al., 1985).
e) From the nuclei centralis medialis, centralis lateralis, paracentralis and rhomboidens to cerebral areas 5, 6, 17, 18 and 19: cholecystokinin-8 (Whale and Albus, 1985).
f) From laminae I and V of the spinal cord to the thalamus: substance P (Battaglia and Rustioni, 1992).
g) From the superior colliculus to the nuclei lateralis posterior: substance P (Hutsler and Chalupa, 1991).
h) From the nuclei centrum medianum and parafascicularis to the caudate: substance P (Sugimoto et al., 1984).
i) From the nucleus arcuatus to the nucleus periventricularis anterior: adrenocorticotropin hormone (Kitahama et al., 1986).

Other works have also indicated the possibility of peptidergic pathways. In order to demonstrate these pathways, the use of both immunocytochemical and tract-tracing techniques is required. Thus, a possible pathway containing neuropeptide Y from the pars ventralis of the corpus geniculatum laterale to the nucleus suprachiasmaticus could be proposed, since this anatomical pathway has been described in the cat (Swanson et al., 1974) and a high density of immunoreactive cell bodies containing neuropeptide Y has been found in the thalamic nucleus, and neuropeptide Y-immunoreactive fibers, but no immunoreactive cell bodies, have been observed in the hypothalamic nucleus (Ueda et al., 1986). However, some of the neuropeptide Y-immunoreactive neurons located in the pars ventralis of the corpus geniculatum laterale could be interneurons, since in that nucleus a moderate density of fibers containing neuropeptide Y has also been observed. Alternatively, that nucleus could receive afferences with neuropeptide Y from neurons located outside the pars ventralis of the corpus geniculatum laterale. Moreover, the neurons containing neuropeptide Y in this nucleus could be projecting neurons that send their axons to other thalamic nuclei such as the lateralis posterior and pulvinar (Edwards et al., 1974; Rodrigo-Angulo et al., 1988), since in the cat horseradish peroxidase-labelled cell bodies have been visualized after injections of the enzyme into the nuclei lateralis posterior and pulvinar, in the pars ventralis of the corpus geniculatum laterale; this is the same thalamic nucleus in which neuropeptide-immunoreactive cell bodies have been found (Coveñas et al., 1990).

COMPARATIVE STUDY ON THE DISTRIBUTION OF THE NEUROPEPTIDES IN THE MAMMALIAN THALAMUS

Table 7 shows that the fibers and cell bodies that contain the neuropeptides that have been most extensively studied in the mammalian thalamus show a greater or lesser degree of distribution in the species studied (rat, cat, monkey, human). Thus, in the cat thalamus, the distribution of immunoreactive fibers is widespread for neuropeptide Y and luteinizing hormone-releasing hormone in comparison with the distribution observed for these neuropeptides in the rat/mon-

Table 7.- Comparative study of the distribution of fibers and cell bodies containing neuropeptides in the thalamus of mammals.

	F	CB
MET-E	C = R > H	C = R > M > H
SP	C = R > H	C = R > H
NT	C = R = H	C > R > H
SOM	C = R = H	R > C > H
NPY	C > M > R	C > M = H
β-END	C = R	C = R
α-MSH	C = R	C = R
ACTH	C = R = H	C = R = H
LH-RH	C > R	C > R

For a nomenclature of the neuropeptides, see Table 1. **C:** cat; **CB:** distribution of immunoreactive cell bodies; **F:** distribution of immunoreactive fibers; **H:** human; **M:** monkey; **R:** rat.

key. Moreover, immunoreactive cell bodies containing neurotensin, neuropeptide Y or luteinizing hormone-releasing hormone show a more widespread distribution in the cat thalamus than that found for the same neuropeptides in the thalamus of other mammals (Hökfelt et al., 1977; Ljungdahl et al., 1978; Sar et al., 1978; Finley et al., 1981; Haber and Elde, 1982; Jennes et al., 1982; Bouras et al., 1984, 1986, 1987; Johansson et al., 1984; Barry and Dubois, 1985; Chronwall et al., 1985; Khachaturian et al., 1985; Nakagawa et al., 1985; Smith et al., 1985; Vincent et al., 1985; Bennett-Clarke and Joseph, 1986; Mai et al., 1986, 1987; Palkovits, 1988; Léger et al., 1990; Zaphiropoulos et al., 1991).

The discrepancies found as regards the distribution of fibers and/or cell bodies containing neuropeptides in the mammalian thalamus could be due to species variations and/or technical considerations (e.g., antisera used, injections of colchicine...). Accordingly, in order to know the origin of such discrepancies, additional experiments (e.g., using the same methodology in all the species studied...) should be carried out.

PHYSIOLOGICAL FUNCTIONS OF NEUROPEPTIDES IN THE CAT THALAMUS

The presence of numerous neuropeptides in the same nuclei of the cat thalamus (see Table 3) and the anatomical relationship between the neuropeptides present in the cat thalamus (see Table 4) suggest a possible interaction among them and an elaborate modulation of functions in which the thalamic nuclei are involved. Thus, for example, an interaction between enkephalins and substance P could be possible in the cat thalamus, since it is known that enkephalins inhibit the release of substance P and cholecystokinin from hypothalamic slices (Micevych et al., 1982). In addition, it has been demonstrated that methionine-enkaphalin is released by β-endorphin (Tseng, 1989) and that the neuropeptide Y could act as a melanocyte-stimulating hormone-release inhibiting factor (Verburg-Van Kemenade et al., 1987). Also, the release of luteinizing hormone-releasing hormone is modulated by neuropeptide Y (McDonald, 1990).

As shown in Table 1, the presence of the neuropeptides studied in many different sites of the cat thalamus implies that such neuropeptides serve different functions. Thus, the presence of immunoreactive fibers containing methionine-enkephalin in the thalamic midline region indicates that the neuropeptide could be involved in a motivational or affective aspect of sensory transmission (Coveñas et al., 1986), and the presence of β-endorphin and luteinizing hormone-releasing hormone in the thalamic nucleus medialis dorsalis indicates that this neuropeptide could be involved in vigilance and attentive behaviour (Bouyer et al., 1992). Moreover, the presence of immunoreactive fibers containing methionine-enkephalin in the nucleus submedius suggests the involvement of the opiate in analgesic mechanisms (Conrath et al., 1986; Miletic and Coffield, 1988). Finally, other data indicate that the thalamus is a potent source of neuropeptides (e.g., neurotensin, vasoactive intestinal peptide, cholecystokinin...) in the afferent systems to the cerebral cortex and striatum (Sugimoto et al, 1985), and that the intralaminar thalamic nuclei mediate quite sophisticated control mechanisms necessary to organize specific types of motor behaviour (Wahle and Albus, 1985).

FUTURE RESEARCH ON NEUROPEPTIDES IN THE CAT THALAMUS

In the light of the above, it is clear that there is much to be done if we are to elucidate the distribution and functions of the neuropeptides in the cat thalamus. The distribution of more neuropeptides should be studied in depth using immunocytochemical methods. In addition, radioimmunoassay and in situ hybridization techniques should be implemented in order to know the distribution and quantity of the neuropeptides in the cat thalamus, as well as the distribution of the cell bodies containing mRNAs of the neuropeptides and/or their precursors. Moreover, there are no data reporting the presence of neuropeptidases in the cat thalamus and descriptions in the same region of receptors for neuropeptides are very scarce. Both types of study must be carried out in the future. Finally, other research fields warranting development in the future are: a) demonstration of the peptidergic pathways, by combining immunocytochemical and tract-tracing methods; b) knowledge of the synaptic connections in the thalamic nuclei, using immunocytochemical and electron microscopic methods; c) coexistence of neuropeptides in the cat thalamus, using immunofluorescence methods; and d) microinjections of the neuropeptides into the cat thalamic nuclei in which the neuropeptides have been previously described in order to know the physiological functions in which such neuropeptides are involved. In sum, although in the last eighteen years our knowledge about the distribution of the neuropeptides in the cat thalamus has increased thanks to the advent of immunocytochemical methods, in the future other methodologies must be applied in order to gain further insight into the distribution and functions of neuropeptides in the cat thalamus.

ACKNOWLEDGEMENTS

This work has been supported by the D.G.I.C.Y.T. (PB 96/1467; PM 99/0159; PM 99/0160). The authors wish to thank N. Skinner for stylistic revision of the English text.

REFERENCES

ADAMS CE and FISHER RS (1990). Sources of neostriatal cholecystokinin in the cat. *J Comp Neurol,* 292: 563-574.

BARRY J and DUBOIS MP (1985). LH-RH-containing systems. In: Björklund A, Hökfelt T (eds). *Handbook of chemical neuroanatomy, vol. 4. GABA and neuropeptides in the CNS, part I.* Elsevier, Amsterdam, pp 166-215.

BATTAGLIA G and RUSTIONI A (1992). Substance P innervation of the rat and cat thalamus. II. Cells of origin in the spinal cord. *J Comp Neurol,* 22: 473-486.

BATTAGLIA G, SPREAFICO R and RUSTIONI A (1992). Substance P innervation of the rat and cat. I. Distribution and relation to ascending spinal pathways. *J Comp Neurol,* 315: 457-472.

BELDA M, COVEÑAS R, NARVÁEZ JA, AGUIRRE JA and TRAMU G (2000). Distribution of luteinizing hormone-releasing hormone in the upper brainstem and diencephalon of the cat: an immunocytochemical study. *Brain Res Bull,* 51: 281-291.

BENNETT-CLARKE C and JOSEPH SA (1986). Immunocytochemical localization of somatostatin in human brain. *Peptides,* 7: 877-884.

BOURAS C, TABAN CH and CONSTANTINIDIS J (1984). Mapping of enkephalins in human brain. An immunofluorescence study of brains from patients with senile and presenile dementia. *Neuroscience,* 12: 179-190.

BOURAS C, VALLET PG, DOBRINOV H, DE ST-HILAIRE S and CONSTANTINIDIS J (1986). Substance P neuronal cell bodies in the human brain: complete mapping by immunohistofluorescence. *Neurosci Lett,* 69: 31-36.

BOURAS C, MAGISTRETTI PJ, MORRISON JH and CONSTANTINIDIS J (1987). An immunohistochemical study of pro-somatostatin-derived peptides in the human brain. *Neuroscience,* 22: 781-800.

BOUYER JJ, MONTARON MF, BUSER P, DURAND C and ROUGEUL A (1992). Effects of mediodorsalis thalamic nucleus lesions on vigilance and attentive behaviour in cats. *Behav Brain Res,* 51: 51-60.

BURGOS C, AGUIRRE JA, ALONSO JR and COVEÑAS R (1988). Immunocytochemical study of substance P-like fibres and cell bodies in the cat diencephalon. *J Himforsch,* 29: 651-657.

CHARNAY Y, LEGER L, GOLAZ J, SALLANON M, VALLET PG, GUNTERN R, BOURAS C, CONSTANTINIDIS J, JOUVET M and TISSOT R (1990). Immunohistochemical mapping of delta sleep-inducing peptide in the cat brain and hypophysis. Relationships with the LHRH system and corticotropes. *J Chem Neuroanat*, 3: 397-412.

CONRATH M, COVEÑAS R, ROMO R, CHERAMY A, BOURGOIN S and HAMON M (1986). Distribution of Met-enkephalin immunoreactive fibres in the thalamus of the cat. *Neurosci Lett,* 65: 299-303.

COVEÑAS R, ROMO R, CHERAMY A, CESSELIN F and CONRATH M (1986). Immunocytochemical study of enkephalin-like cell bodies in the thalamus of the cat. *Brain Res,* 377: 355-361.

COVEÑAS R, AGUIRRE JA, ALONSO JR, DIOS M, LARA J and AIJON J (1990). Distribution of neuropeptide Y-like immunoreactive fibers in the cat thalamus. *Peptides,* 11: 45-50.

COVEÑAS R, DE LEÓN M, NARVÁEZ JA, TRAMU G, AGUIRRE JA and GONZÁLEZ-BARÓN S (1996a). An immunocytochemical mapping of beta-endorphin (1-27) in the cat diencephalon. *Neuropeptides,* 30: 261-271.

COVEÑAS R, DE LEÓN M, NARVÁEZ JA, TRAMU G, AGUIRRE JA and GONZÁLEZ-BARÓN S (1996b). Mapping of alpha-melanocyte-stimulating hormone-like immunoreactivity in the cat diencephalon. *Peptides*, 17: 845-852.

COVEÑAS R, DE LEÓN M, NARVÁEZ JA, TRAMU G, AGUIRRE JA and GONZÁLEZ-BARÓN S(1996c). An immunocytochemical mapping of ACTH/CLIP in the cat diencephalon. *J Chem Neuroanat*, 11: 191-197.

CRONWALL BM, DIMAGGIO DA, MASSARI VJ, PICKEL VM, RUGGIERO DA and O'DONOHUE TL (1985). The anatomy of neuropeptide Y-containing neurons in the rat brain. *Neuroscience,* 15: 1159-1181.

DE LEÓN M, COVEÑAS R, NARVÁEZ JA, TRAMU G, AGUIRRE JA and GONZÁLEZ-BARÓN S (1991a). Neurotensin-like immunoreactivity in the diencephalon of the adult male cat. *Peptides,* 12: 257-264.

DE LEÓN M, COVEÑAS R, NARVÁEZ JA, TRAMU G, AGUIRRE JA and GONZÁLEZ-BARÓN S (1991b). Somatostatin-28 (1-12)-like immunoreactivity in the cat diencephalon. *Neuropeptides,* 19: 107-117.

DIETL M, HOF PR, MARTIN JL, MAGISTRETTI P and PALACIOS JM (1990). Autoradiographic analysis of the distribution of vasoactive intestinal peptide binding sites in the vertebrate central nervous system: a phylogenetic study. *Brain Res,* 520: 14-26.

EDWARDS B, ROSENQUIST AC and PALMER LA (1974). An autoradiographic study of ventral lateral geniculate projections in the cat. *Brain Res*, 72: 282-287.

FINLEY JCW, MADERDRUT JL and PETRUSZ P (1981). The immunocytochemical localization of enkephalin in the central nervous system of the rat. *J Comp Neurol,* 198: 541-565.

FITZPATRICK-MCELLIGOTT S, CARD JP, LEWIS ME and BALDINO F (1988). Neuronal localization of prosomatostatin mRNA in the rat brain with in situ hybridization histochemistry. *J Comp Neurol,* 273: 558-572.

GUIDOBONO F, NETTI C, PECILE A, GRITTI I and MANCIA M (1987). Calcitonin binding site distribution in the cat central nervous system: a wider insight of the peptide involvement in brain functions. *Neuropeptides,* 10: 265-273.

GRAYBIEL AM and ELDE RP (1983). Somatostatin-like immunoreactivity characterizes neurons of the nucleus reticularis thalami in the cat and monkey. *J Neurosci*, 3: 1308-1321.

HABER S and ELDE R (1982). The distribution of enkephalin immunoreactive neuronal cell bodies in the monkey brain: preliminary observation. *Neurosci Lett,* 32: 247-252.

HÖKFELT T, ELDE R, JOHANSSON O, TERENIUS L and STEIN L (1977). The distribution of enkephalin-immunoreactive cell bodies in the rat central nervous system. *Neurosci Lett,* 5: 25-31.

HUNTER JC, HANNAH PA and MAGGIO JE (1985). The regional distribution of kassinin-like immunoreactivity in central and peripheral tissues of the cat. *Brain Res,* 341: 228-232.

HUTSLER JJ and CHALUPA LM (1991). Substance P immunoreactivity identifies a projection from the cat's superior colliculus to the principal tectorecipient zone of the lateral posterior nucleus. *J Comp Neurol,* 312: 379-390.

JASPER HH and AJMONE-MARSAN C (1966). A stereotaxic atlas of the diencephalon of the cat. National Research Council of Canada, Ottawa.

JENNES L, STUMPF WE and KALIVAS PW (1982). Neurotensin: Topographical distribution in rat brain by immunohistochemistry. *J Comp Neurol,* 210: 211-224.

JOHANSSON O, HÖKFELT T and ELDE RP (1984). Immunohistochemical distribution of somatostatin-like immunoreactivity in the central nervous system of the adult rat. *Neuroscience,* 13: 265-339.

JONES EG and HENDRY SH (1989). Differential calcium binding protein immunoreactivity distinguishes classes of relay neurons in monkey thalamic nuclei. *Eur J Neurosci*, 1: 222-246.

KHACHATURIAN H, LEWIS ME, TSOU K and WATSON SJ (1985). β-endorphin, α-MSH, ACTH, and related peptides. In: Björklund A, Hökfelt T (eds). *Handbook of chemical neuroanatomy, vol. 4. GABA and neuropeptides in the CNS, part I.* Elsevier, Amsterdam, pp 216-272.

KITAHAMA K, SALLANON M, BUDA C, JANIN M, DUBOIS MP and JOUVET M (1986). ACTH-immunoreactive neurons and their projections in the cat forebrain. *Peptides,* 7: 801-807.

LECHAN RM, GOODMAN RH, ROSENBLATT M, REICHLIN S and HABENER JF (1983). Prosomatostatin-specific antigen in rat brain: localization by immunocytochemical staining with an antiserum to a synthetic sequence of preprosomatostatin. *Proc Natl Acad Sci (USA),* 80: 2780-2784.

LEGER L, LEMA F, CHASTRETTE N, CHARNAY Y, CESPUGLIO R, MAZIE J and JOUVET J (1990). A monoclonal antibody directed against CLIP (ACTH 18-39). Anatomical distribution of immunoreactivity in the rat brain and hypophysis with quantification of the hypothalamic cell group. *J Chem Neuroanat,* 3: 297-308.

LEWIS DA, CAMPBELL MJ and MORRISON JH (1986). An immunohistochemical characterization of somatostatin-28 and somatostatin-28 (1-12) in monkey prefrontal cortex. *J Comp Neurol,* 248: 1-18.

LJUNGDAHL A, HÖKFELT T and NILSSON G (1978). Distribution of substance P-like immunoreactivity in the central nervous system of the rat. I. Cell bodies and nerve terminals. *Neuroscience,* 3: 861-943.

MACCHI G (1983) Old and new anatomo-functional criteria in the subdivision of the thalamic nuclei. In: Macchi G, Rustioni A, Spreafico R (eds). *Somatosensory integration in the thalamus*. Elsevier, Amsterdam, pp 3-15.

MAI JK, STEPHENS PH, HOPF A and CUELLO AC (1986). Substance P in the human brain. *Neuroscience,* 17: 709-739.

MAI JK, TRIEPEL J and METZ J (1987). Neurotensin in the human brain. *Neuroscience,* 22: 499-524.

MCDONALD JK (1990). Role of neuropeptide Y in reproductive function. *Ann NY Acad Sci,* 611: 258-272.

MICEVYCH PE, YAKSH TL and GO VLW (1982). Opiate-mediated inhibition of the release of cholecystokinin and substance P but not neurotensin from cat hypothalamic slices. *Brain Res,* 250: 283-289.

MILETIC V and COFFIELD JA (1988). Enkephalin-like immunoreactivity in the nucleus submedius of the cat and the rat thalamus. *Somatosens Res*, 5: 325-334.

MORRISON JH, BENOIT PJ, MAGISTRETI PJ, LING N and BLOOM FE (1984). Immunohistochemical distribution of prosomatostatin related peptides in hippocampus. *Neurosci Lett,* 34: 137-142.

NAKAGAWA Y, SHIOSAKA S, EMSON PC and TOHYAMA M (1985). Distribution of neuropeptide Y in the forebrain and diencephalon: an immunohistochemical analysis. *Brain Res,* 361: 52-60.

OBATA-TSUTO HL, OKAMURA H, TSUTO T, TERUBAYASHI H, FUKUI K, YANAIHARA N and IBATA Y (1983). Distribution of the VIP-like immunoreactive neurons in the cat central nervous system. *Brain Res Bull*, 10: 653-660.

O'DONOHUE TL, MASSARI VJ, TIZABI Y and JACOBOWITZ DM (1979). Identification and distribution of α-melanotropin in discrete regions of the cat brain. *Brain Res Bull,* 4: 829-832.

OHYE CH (1990) Thalamus. In: Paxinos G (ed). *The human nervous system*. Academic Press, San Diego, pp 439-468.

PALKOVITS M (1988) Neuropeptides in the brain. In: Martini L, Ganong WF (eds). *Frontiers in Neuroendocrinology, vol. 10.* Raven Press, New York, pp 1-44.

PEGO-REIGOSA R, COVEÑAS R, TRAMU G and PESINI P (2000). Distribution of met-enkephalin immunoreactivity in the diencephalon and the brainstem of the dog. *J Chem Neuroanat* 19: 243-258.

PIORO EP, MAI JK and CUELLO AC (1990) Distribution of substance P- and enkephalin-immunoreactive neurons and fibers. In: Paxinos G (ed). *The human nervous system.* Academic Press, San Diego, pp 1051-1094.

RAO JK, HU H, PRASAD CH and JAYARAMAN A (1986). The distribution pattern of adrenocorticotropin-like immunoreactivity in the cat central nervous system. *Neurosci Lett,* 71: 48-52.

RAO JK, HU H, PRASAD CH and JAYARAMAN A (1987). The distribution pattern of alpha-MSH-like immunoreactivity in the cat central nervous system. *Peptides,* 8: 327-334.

RODRIGO-ANGULO ML and REINOSO-SUAREZ F (1988). Connections to the lateral posterior-pulvinar thalamic complex from the reticular and ventral geniculate thalamic nuclei: a topographical study in the cat. *Neuroscience,* 26: 449-459.

SAR M, STUMPF WC, MILLER RJ, CHANG KJ and CUATRECASAS P (1978). Immunohistochemical localization of enkephalin in rat brain and spinal cord. *J Comp Neurol,* 182: 17-37.

SMITH Y, PARENT A, KERKÉRIAN L and PELLETIER G (1985). Distribution of neuropeptide Y immunoreactivity in the basal forebrain and upper brainstem of the Squirrel monkey *(Saimiri sciureus). J Comp Neurol,* 236: 71-89.

SUGIMOTO T, TAKADA M, TAKESHI K and MIZUNO N (1984). Substance P-positive thalamo-caudate neurons in the center median-parafascicular complex in the cat. *Brain Res,* 323: 181-184.

SUGIMOTO T, ITOH K, YASUI Y, KANEKO T and MIZUNO N (1985). Coexistence of neuropeptides in projection neurons of the thalamus of the cat. *Brain Res*, 347: 381-384.

SWANSON LW, COWAN WM and JONES EG (1974). An autoradiographic study of the efferent connections of the ventral lateral geniculate nucleus in the albino rat and the cat. *J Comp Neurol,* 156: 163-168.

TSENG LF (1989). Intracerebroventricular administration of β-endorphin releases immunoreactive met-enkephalin from the spinal cord in cats, guinea-pigs and mice. *Neuropharmacology,* 28: 1333-1339.

UEDA S, KAWATA M and SANO Y (1986). Identification of neuropeptide Y immunoreactivity in the suprachiasmatic nucleus and the lateral geniculate nucleus of some mammals. *Neurosci Lett,* 68: 7-10.

VAN DONGEN PAM and NIEUWENHUYS R (1998). Diencephalon. In: Nieuwenhuys R, Ten Donkelaar HJ, Nicholson C (eds). *The central nervous system of vertebrates, vol. 3.* Springer, Berlin, pp 1844-1871.

VELASCO A, DE LEÓN M, COVEÑAS R, MARCOS P, NARVÁEZ JA, TRAMU G, AGUIRRE JA and GONZÁLEZ-BARÓN S (1993). Distribution of neurokinin A in the cat diencephalon: an immunocytochemical study. *Brain Res Bull,* 31: 279-285.

VERBURG-VAN KEMENADE BML, JENKS BG, DANGER JM, VAUDRY H, PELLETIER G and SAINT-PIERRE S (1987). An NPY-like peptide may function as MSH-release inhibiting factor in *Xenopus laevis. Peptides,* 8: 61-67.

VINCENT SR, MCINTOSH AMJ and BROWN JC (1985). Central somatostatin systems revealed with monoclonal antibodies. *J Comp Neurol,* 238: 169-186.

WHALE P and ALBUS K (1985). Cholecystokinin octapeptide-like immunoreactive material in neurons of the intralaminar nuclei of the cat's thalamus. *Brain Res,* 327: 348-353.

ZAPHIROPOULOS A, CHARNAY Y, VALLET P, CONSTANTINIDIS J and BOURAS C (1991). Immunohistochemical distribution of corticotropin-like intermediate lobe peptide (CLIP) immunoreactivity in the human brain. *Brain Res Bull,* 26: 99-111.