SUMMARY

We have reviewed the distribution and functions of neuropeptides in the cat hypothalamus. Our review focuses in the cat hypothalamus on the following points: 1) the distribution and coexistence of neuropeptides; 2) the anatomical relationships among the different neuropeptides; 3) the peptidergic pathways (afferences and efferences); 4) comparison of the distribution of neuropeptides in the mammalian hypothalamus; and 5) the physiological functions of neuropeptides. Although at present the distribution of many neuropeptides in the hypothalamus of the cat is known, there is little information about other aspects of neuropeptides in the same diencephalic region. Thus, in order to know more the distribution and functions of neuropeptides in the cat hypothalamus in detail, in the future appropriate methodologies must be applied in order to determine, for example, the distribution of the neuropeptide receptors, the distribution of neuropeptidases, the peptidergic synaptic connections, the coexistence of neuropeptides and the physiological actions of the neuropeptides in the cat hypothalamus.

Key Words: Neuropeptides – Hypothalamus – Diencephalon – Cat

INTRODUCTION

The hypothalamus is part of the diencephalon. Along the animal scale, it is one of the most preserved zones of the central nervous system (CNS). This shows that the findings observed in the hypothalamus of animals used for experimental research can be extrapolated to humans. It is a centre that is connected with the limbic system, which is involved in autonomic and homeostasis functions. In this sense, the hypothalamus has been considered as the “great ganglion” of the autonomic nervous system, since it integrates autonomic function at central level (Kupfermann, 1981). In addition, the hypothalamus has been implicated in a large number of very important functions, such as drinking, food intake, thermoregulation, neuroendocrine control of the hypophysis (by means of releasing and inhibiting factors), defence (immunoregulation), circadian rhythms, blood pressure, emotions, stress, reproduction, aggressive behaviour, sexual orientation, as well as in the production of neurohormones (vasopressin, oxytocin,...) (see Swaab, 1997). In sum, it is a small centre in the CNS, but is involved in very important functions. Thus, it has been indicated that lesions in the hypothalamus could elicit several diseases/alterations: depression, anorexia nervosa, bulim-
ia, changes in sexual orientation, diabetes insipidus, Cushing’s disease, alterations in sleep and temperature, sudden-infant-death-syndrome, Wolfram’s syndrome, Prader-Willi’s syndrome, malignant syndrome, aggressive behaviour, alterations in the emotions, as well as alterations in the release of hormones into the hypophysis. Moreover, hypothalamic modifications have been reported in neurodegenerative diseases, such as Alzheimer’s, Parkinson’s, Huntington’s, multiple sclerosis,... (see Swaab, 1997).

Moreover, the hypothalamus is connected to a large number of other CNS centres (Carpenter; 1980; Saper, 1990). Thus, the hypothalamus receives inputs from the hippocampus, the amygdala, the cerebral cortex, the retina, the spinal cord, the ventrolateral medulla, the nucleus of the solitary tract, the parabrachial nucleus, the locus coeruleus and the raphe, whereas hypothalamic neurons send projections into the amygdala, the periaqueductal gray, the reticular formation of the mesencephalon, the thalamus, the hypothysis, the nucleus of the solitary tract, the parabrachial nucleus, the locus coeruleus, the nucleus ambiguus, the area postrema, the spinal cord, the nucleus accumbens and the median eminence.

As mentioned in a previous article (Part I: Thalamus) (Coveñas et al., 2001), a large number of neuroanatomical, neurophysiological, neuropharmacological and behavioural data have been reported for the cat. However, until the eighties research on the distribution of neuropeptides in the cat diencephalon has received little attention. Here, our aim is to review, in the current available morphological and physiological data concerning neuropeptides that have emerged over the past eighteen-twenty years concerning one of the most important functional areas of the CNS: the hypothalamus. We also compare the results obtained on neuropeptides in the cat hypothalamus with those found in the same diencephalic area of others mammalian species (e.g., rat, monkey, human).

NEUROPEPTIDES IN THE CAT HYPOTHALAMUS

The hypothalamus can be divided according to topographic criteria into several regions (Kupfermann, 1981): mamillary, periventricular, medial, lateral and preoptic (see Table 1). In this review, we use the terminology of the hypothalamic nuclei according to the stereotaxic atlas of the diencephalon of the cat carried out by Jasper and Ajmone-Marsan (1966). Table 1 shows the distribution of fibers and cell bodies containing neuropeptides in the cat hypothalamus, using immunocytochemical methods. In general, as can be seen in the table, the immunoreactive structures (fibers and cell bodies) containing the neuropeptides studied showed a widespread distribution throughout the cat hypothalamus. At present, the distribution of thirteen neuropeptides has been fully studied in the cat hypothalamus. In this sense, the distribution has been studied of methionine-enkephalin (Micevych and Elde, 1980; Coveñas et al., 1988; Yoshimoto et al., 1989), substance P (Burgos et al., 1988; Yoshimoto et al., 1989), neurotensin (Hu et al., 1988; Yoshimoto et al., 1989; de León et al., 1991a), somatostatin-28 (1-12) (de León et al., 1991b), neuropeptide Y (Ueda et al., 1986; Hu et al., 1987; Léger et al., 1987), β-endorphin (1-27) (Coveñas et al., 1996a), β-endorphin (1-31) (Micevych and Elde, 1982), α-melanocyte-stimulating hormone (Micevych and Elde, 1982; Rao et al., 1987; Coveñas et al., 1996b), adrenocorticotropin hormone (Kitahama et al., 1984, 1986; Rao et al., 1986; Coveñas et al., 1996c), luteinizing hormone-releasing hormone (Barry and Dubois, 1975; Belda et al., 2000), neurokinin A (Velasco et al., 1993), delta sleep-inducing peptide (Chamay et al., 1990) and vasactive intestinal polypeptide (Obata-Tsuto et al., 1983, 1984) (see Figure 1). Also, there are very few data concerning the distribution of another seven neuropeptides (not shown in Table 1): galanin, corticotropin-releasing factor, somatostatin-14, vasopressin, oxytocin, cholecystokinin octapeptide and thyrotropin-releasing hormone (Micevych and Elde, 1980; Kawata et al., 1982; Graybiel and Elde, 1983; Wahle and Albus, 1985; Caverson et al., 1987; Yoshimoto et al., 1989). Thus, immunoreactive cell bodies containing galanin were observed in the hypothalamus ventromedialis and in the regio preoptica; those containing corticotropin-releasing factor in the hypothalamus posterior, hypothalamus lateralis, nucleus supraopticus, nucleus periventricularis hypothalami and in the regio preoptica; those containing thyrotropin-releasing hormone in the regio preoptica and around the anterior hypothalamic nucleus; those containing vasopressin in the nuclei periventricularis hypothalami, suprachiasmaticus and supraopticus, hypothalami lateralis and in the regio preoptica; those containing oxytocin in the hypothalamus dorsomedialis, hypothalamicus lateralis, regio preoptica and in the nuclei periventricularis hypothalami and supraopticus, and those containing cholecystokinin in the nuclei arcuatus and periventricularis hypothalami, as well as in the hypothalamus lateralis. In addition, somatostatin-14-, galanin-, corticotropin-releasing factor-, and thyrotropin-releasing hormone-immunoreactive fibers were observed in the hypothalamus posterior, whereas fibers containing vasopressin and oxytocin have been described in the nuclei periventricularis hypothalami and supraopticus.

Furthermore, using a microdissection technique combined with radioimmunoassay the...
concentration of α-melanocyte-stimulating hormone has been measured in several regions of the cat hypothalamus (O’donohue et al., 1979), and the concentration of neurotensin and kassinin in the whole cat hypothalamus has also been measured (Goedert and Emson, 1983; Hunter et al., 1985). Finally, the localization of calcitonin- and neurokinin-1 binding sites has been demonstrated in the cat hypothalamus (Guidobono et al., 1987; Yao et al., 1999). Except for β-endorphin (1-31) and vasoactive intestinal polypeptide, the other neuropeptides studied (eleven) in the cat hypothalamus showed a widespread distribution in this diencephalic region (see Table 2). Thus, in all the hypothalamic nuclei of the cat, immunoreactive fibers and/or cell bodies containing methionine-enkephalin, neuropeptide Y, β-endorphin (1-27) and α-melanocyte-stimulating hormone were observed, whereas substance P, luteinizing hormone-releasing hormone- and neurokinin A-immunoreactive fibers and/or cell bodies were found in twelve of the thirteen hypothalamic nuclei and in eleven of the thirteen nuclei fibers and/or cell bodies containing neuropeptin, somatostatin-28 (1-12), adrenocorticotropic hormone and delta sleep-inducing peptide.

Finally, in all the hypothalamic nuclei of the cat, seven or more neuropeptides were described (Table 3). The hypothalamic nucleus in which the highest number of neuropeptides (thirteen) was observed in fibers and/or cell bodies was the nucleus arcuatus, whereas in other nuclei, such as the hypothalamus ventromedialis, periventricularis hypothalami, suprachiasmaticus, hypothalamus lateralis and supraopticus, twelve neuropeptides were seen in each of them.

**Coexistence of neuropeptides in the cat hypothalamus**

As indicated in the previous chapter, the presence of at least seven neuropeptides in each of the hypothalamic nuclei has been reported. This indicates a possible interaction among such neuropeptides and an elaborate modulation of functions in which the hypothalamic nuclei are involved. In addition, the localization of several different neuropeptides in the same hypothalamic nuclei indicates the possibility that two or more of them may coexist in the same neuron. This research line must be developed in the future, since only a few data showing the coexistence of neuropeptides in the neurons of the cat hypothalamus are available. Thus, Micevych and Elde (1982) reported that α-melanocyte-stimulating hormone and β-endorphin coexist in neurons located in the cat nucleus arcuatus, whereas the coexistence of delta sleep-inducing peptide and luteinizing hormone-releasing hor-

**Table 1. Distribution of neuropeptides in the nuclei of the cat hypothalamus.**

<table>
<thead>
<tr>
<th>Neuropeptide</th>
<th>Mammilar Region</th>
<th>Periventricular Region</th>
<th>Medial Region</th>
<th>Lateral Region</th>
<th>Preoptic Region</th>
<th>Tracts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>β-END</strong></td>
<td>+ + - +</td>
<td>+ + + + + + + +</td>
<td>+ + - + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + +</td>
<td>+ + + + + + + + +</td>
</tr>
<tr>
<td><strong>α-MSH</strong></td>
<td>+ + + + + + + +</td>
<td>+ + - + - - - -</td>
<td>+ + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
</tr>
<tr>
<td><strong>ACTH</strong></td>
<td>+ + + + + + + +</td>
<td>+ + - + - - - -</td>
<td>+ + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
</tr>
<tr>
<td><strong>LH-RH</strong></td>
<td>+ + + + + + + +</td>
<td>+ + - + - - - -</td>
<td>+ + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
</tr>
<tr>
<td><strong>NKA</strong></td>
<td>+ + + + + + + +</td>
<td>+ + - + - - - -</td>
<td>+ + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
</tr>
<tr>
<td><strong>ΔMEL</strong></td>
<td>+ + + + + + + +</td>
<td>+ + - + - - - -</td>
<td>+ + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
</tr>
<tr>
<td><strong>GOMP</strong></td>
<td>+ + + + + + + +</td>
<td>+ + - + - - - -</td>
<td>+ + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
<td>+ + + + + + + + +</td>
</tr>
</tbody>
</table>

ACTH: adrenocorticotropic hormone (18-39); DSIP: delta sleep-inducing peptide; β-END: β-endorphin (1-27); β-END (1-31): β-endorphin (1-31); LH-RH: luteinizing hormone-releasing hormone; MET-E: methionine-enkephalin; α-MSH: α-melanocyte-stimulating hormone; NKA: neurokinin A; NPY: neuropeptide Y; NT: neurotensin; RIA: radioimmunoassay; SOM: somatostatin-28 (1-12); SP: substance P; VIP: vasoactive intestinal peptide. For the nomenclature of the hypothalamic nuclei, see list of abbreviations. CB: immunoreactive cell bodies; F: fibres; +: presence; -: absence; no sign: no studied.
mone has also been described in the cat hypothalamus (Chamay et al., 1990). Moreover, the possible coexistence of neurotensin and α-melanocyte-stimulating hormone can be suggested for cell bodies located in the nucleus arcuatus because the morphological characteristics of perikarya containing α-melanocyte-stimulating hormone are similar to the neuronal population containing neurotensin (de León et al., 1991a; Coveñas et al., 1996b). By contrast, in the cat nucleus arcuatus, the existence of cell bodies containing substance P, neuropeptide Y and neurotensin has been described (Léger et al., 1987; Burgos et al., 1988; de León et al., 1991a). However, although there is an identical localization of immunoreactive perikarya containing such neuropeptides and β-endorphin (1-27)-immunoreactive cell bodies in the nucleus arcuatus of the cat (Coveñas et al., 1996a), the possible coexistence of β-endorphin (1-27) with some of the three above-mentioned neuropeptides cannot be suggested in this nucleus since the morphological characteristics of β-endorphin (1-27)-immunoreactive perikarya are quite different from those shown by the neuronal populations containing substance P, neuropeptide Y or neurotensin.

ANATOMICAL RELATIONSHIPS AMONG NEUROPEPTIDES IN THE CAT HYPOTHALAMUS

There is a close anatomical relationship among the neuropeptides in the cat hypothalamus, since as shown in Table 4, the lowest level found was 76.92%. This value indicates that in 76.92% of the cat hypothalamic nuclei, for example, substance P-immunoreactive fibers and/or cell bodies and neurotensin-immunoreactive fibers and/or cell bodies have been observed. The percentage was calculated taking the total number of the cat hypothalamic nuclei (thirteen) as 100%. In addition, this Table also indicates that in all the hypothalamic nuclei of the cat (100%) methionine-enkephalin and neuropeptide Y-immunoreactive structures were observed, and this was also the case for methionine-enkephalin and β-endorphin, methionine-enkephalin and α-melanocyte-stimulating hormone, neuropeptide Y and β-endorphin, neuropeptide Y and α-melanocyte-stimulating hormone and β-endorphin and α-melanocyte-stimulating hormone.

PEPTIDERGIC PATHWAYS IN THE CAT HYPOTHALAMUS

Yoshimoto et al. (1989) have reported the following afferent peptidergic pathways to the cat posterior hypothalamus:

1. From the medial preoptic area, medial amygdaloid nucleus and nucleus of the stria terminalis to the ventrolateral/dorsolateral posterior hypothalamus: containing galanin.
2. From the anterior hypothalamus and medi-
al preoptic area to the posterior hypothal-
amus: containing corticotropin-releasing factor.

3. From the medial preoptic area, dorsal hypothalamic nucleus and ventrolateral posterior hypothalamus to the posterior hypothalamus: containing neuropeptide Y.

4. From the medial preoptic area and the mamillary region to the posterior hypothalamus: containing methionine-enkephalin.

5. From the medial amygdaloid nucleus, medial preoptic area and lateral/dorsal and posterior hypothalamic areas to the posterior hypothalamus: containing substance P.

6. From the medial preoptic area and around the anterior hypothalamic nucleus to the posterior hypothalamus: containing thyrotrpin-releasing hormone.

7. From the nucleus of the stria terminalis to the posterior hypothalamus: containing substance P or methionine-enkephalin.

In addition, in the cat Yanagihara and Niimi (1989) have described a projection containing substance P from the posterior hypothalamus to the hippocampal formation. Kitahama et al.
(1984, 1986) have demonstrated that several peptidergic pathways come from the nucleus arcuatus of the cat. The peptidergic projections described, containing adrenocorticotropic hormone, coursed from the nucleus arcuatus to the midline of the thalamus, the nucleus periventricularis anterior, the locus coeruleus, the paraventricular hypothalami. These authors also indicated that all the peptidergic fibers and terminals containing adrenocorticotropic hormone observed in the cat central nervous system come from the cell bodies located in the nucleus arcuatus. In addition, Kitahama et al. (1986) showed that all the fibers and terminals containing adrenocorticotropic hormone in the cat nucleus ventromedialis hypothalami come from cell bodies located in the nucleus arcuatus. These data suggest that the adrenocorticotropic hormone-immunoreactive cell bodies observed later in the nucleus ventromedialis hypothalami of the cat (Coveñas et al., 1996c) would be projecting neurons. At present, in the cat central nervous system the only sites in which cell bodies containing adrenocorticotropic hormone have been described are the nucleus arcuatus (Kitahama et al., 1986; Rao et al., 1986; Coveñas et al., 1996c) and the nucleus ventromedialis hypothalami (Coveñas et al., 1996c).

Tables 5 and 6 show the nuclei of the cat hypothalami in which peptidergic fibers but no cell bodies have been observed (Table 5), as well as the nuclei in which a moderate/high density of immunoreactive cell bodies has been found, but no immunoreactive fibers (Table 6).

These data indicate that the hypothalamic nuclei shown in Table 5 could receive peptidergic afferents arising from neurons located inside and/or outside the hypothalamus, whereas the nuclei included in Table 6 could contain projecting neurons, which could send projections to other hypothalamic nuclei and/or other parts of the central nervous system. According to these data, the following peptidergic pathways can be suggested in the cat (in order to demonstrate these pathways, the use of both immunocytochemical and tract-tracing techniques is required):

1. From the hypothalamus lateralis to the parabrachial nuclei, the locus coeruleus, the nucleus of the solitary tract, the nucleus medialis dorsalis, and to the nucleus habenularis lateralis: containing α-melanocyte-stimulating hormone. This pathway could be possible, since in the brainstem and thalamic nuclei referred to, fibers containing α-melanocyte-stimulating hormone were observed but no immunoreactive cell bodies were found in the hypothalamic nuclei of the cat (Coveñas et al., 1996b, 2000), whereas in the hypothalamus lateralis a high density of cell bodies containing α-melanocyte-stimulating hormone was described (Coveñas et al., 1996b). Moreover, this observation is in agreement with previous works carried out in the cat, in which, using horseradish and autoradiographic techniques, researchers have described pathways from the hypothalamus lateralis to the five brain areas mentioned above (Ono and Niimi, 1985; Holstege, 1987).

2. From the pars ventralis of the corpus geniculatum laterale to the nucleus suprachiasmaticus: containing neuropeptide Y. In this case, a moderate density of immunoreactive cell bodies containing neuropeptide Y was found in the hypothalamic nucleus (Coveñas et al., 1990), whereas in the hypothalamic nucleus neuropeptide Y-immunoreactive fibers, but no cell body

---

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

<table>
<thead>
<tr>
<th>Neuropeptide</th>
<th>ACTH</th>
<th>β-END</th>
<th>NPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-MSH</td>
<td>Sch</td>
<td>PVH</td>
<td></td>
</tr>
<tr>
<td>HA</td>
<td>NKA</td>
<td>SOM</td>
<td></td>
</tr>
<tr>
<td>HP</td>
<td>RPO</td>
<td>Hvm</td>
<td></td>
</tr>
<tr>
<td>PVH</td>
<td>So</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

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

<table>
<thead>
<tr>
<th>Neuropeptide</th>
<th>MET-E</th>
<th>NT</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTH</td>
<td>Hdm</td>
<td>RPO</td>
</tr>
<tr>
<td>β-END(1-31)</td>
<td>Mn</td>
<td>SP</td>
</tr>
<tr>
<td>β-END(1-31)</td>
<td>PVH</td>
<td>Ml</td>
</tr>
<tr>
<td>β-END(1-31)</td>
<td>Hm</td>
<td>Ma</td>
</tr>
<tr>
<td>β-END(1-31)</td>
<td>Ha</td>
<td>RPO</td>
</tr>
<tr>
<td>β-END(1-31)</td>
<td>Hvm</td>
<td></td>
</tr>
</tbody>
</table>

For nomenclature of the neuropeptides and the hypothalamic nuclei, see respectively, Table 1 and list of abbreviations. CB: immunoreactive cell bodies (++++: high density; ++: moderate density); F: immunoreactive fibers (-: absence).
Neuropeptides in the cat diencephalon: II. Hypothalamus

Comparative study of the distribution of fibers and cell bodies containing neuropeptides in the hypothalamus of mammals.

<table>
<thead>
<tr>
<th>Neuropeptide</th>
<th>C</th>
<th>R</th>
<th>M</th>
<th>H</th>
<th>F</th>
<th>CB</th>
</tr>
</thead>
<tbody>
<tr>
<td>MET-E</td>
<td>C = R &gt; H</td>
<td>C = R &gt; M &gt; H</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SP</td>
<td>C = R &gt; H = M</td>
<td>C = R &gt; H = M</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT</td>
<td>C = R = H</td>
<td>C = R = H</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOM</td>
<td>C = R = H</td>
<td>R = H = C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NPY</td>
<td>C = R = M = H</td>
<td>C = R = M = H</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>β-END</td>
<td>C = R</td>
<td>C = R</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>α-MSH</td>
<td>C = R</td>
<td>C = R</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACTH</td>
<td>C = R = H</td>
<td>C = R = H</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LH-RH</td>
<td>C &gt; R</td>
<td>M = H &gt; C = R</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For 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.

containing this neuropeptide was observed (Hu et al., 1987). This possible pathway containing neuropeptide Y is in agreement with the results obtained by Swanson et al. (1974), since these authors demonstrated an anatomical projection from the pars ventralis of the corpus geniculatum laterale to the nucleus suprachiasmaticus.

3. From the hypothalamus lateralis to the superior colliculus: containing α-melanocyte stimulating hormone. This anatomical pathway has been demonstrated previously in the cat (Rieck et al., 1986). The peptidergic pathway could be possible, since a high density of immunoreactive cell bodies and a low density of fibers containing α-melanocyte-stimulating hormone has been observed in the hypothalamus lateralis (Coveñas et al., 1996b), whereas immunoreactive fibers containing the neuropeptide were only found in the superior colliculus (Coveñas et al., 2000).

Comparative study of the distribution of neuropeptides in the mammalian hypothalamus

The distribution of the neuropeptides in the mammalian hypothalamus has mainly been studied in humans, the monkey, cat and rat. Table 7 compares the distribution of fibers and cell bodies containing neuropeptides in the four species studied, and depicts the neuropeptides that have been most extensively studied in the hypothalamus of mammals (Barry and Carette, 1975; Hökfelt et al., 1977; Ljungdahl et al., 1978; Sar et al., 1978; Bennet-Clark et al., 1980; Finley et al., 1981a, b; Haber and Elde, 1982; Jennes et al., 1982; Micevych and Elde, 1982; Bouras et al., 1984; Johanson et al., 1984; Krukoff and Calare-
an elaborate modulation of functions in which these nuclei are involved, and that in these hypothalamic nuclei a possible interaction between the neuropeptides localized in them could occur. In this sense (see Table 4), it is known that enkephalins inhibit the release of substance P from hypothalamic slices (Micevych et al., 1982) and that the opiate receptors mediate the inhibition of cholecystokinin and substance P release in the cat hypothalamus (Micevych et al., 1984). The release of methionine-enkephalin by β-endorphin has also been demonstrated (Tseng, 1989). In addition, the regulation of pro-opiomelanocortin gene expression by neuropeptide Y has been described and that neuropeptide Y may act as a melanocyte-stimulating hormone-release inhibiting factor and that neuropeptide Y modulates the release of luteinizing hormone-releasing hormone from the hypothalamus. This suggests that neuropeptide Y could be a component of the luteinizing hormone-releasing hormone pulse-generating system (Verburg-Van Kemenade et al., 1987; McDonald, 1990; de Yébenes et al., 1995).

The presence of cell bodies containing methionine-enkephalin in the nuclei periventricularis hypothalami and supraopticus suggests that such neurons could project to the median eminence and posterior pituitary, where they might regulate the release of oxytocin and vasopressin in the neurohypophysis and probably participate in cardiovascular control (Micevych and Elde, 1980). Moreover, the presence of methionine-enkephalin in the nucleus suprachiasmaticus, as well as the localization of cell bodies containing the neuropeptide in the hypothalamus dorsomedialis and in the regio praepoptica indicates that the neuropeptide could be involved in the control of circadian rhythms and/or in visual processes, as well as in controlling somatostatin release into the blood of the portal plexus (Tramu et al., 1981; Pickard, 1985; Swaab et al., 1985).

The presence of substance P in the nuclei periventricularis hypothalami, supraopticus, hypothalami ventromedialis and in the suprachiasmaticus indicates that the neuropeptide could play a role, respectively, in synaptic control of the vasopressinergic neurons of the nucleus periventricularis hypothalami, in increasing the firing frequency of neurons located in the nucleus supraopticus, in feeding behavior, and in visual processes (Clarke et al., 1980; Heike et al., 1986). In addition, the localization of immunoreactive structures containing β-endorphin and α-melanocyte-stimulating hormone in the nuclei hypothalami ventromedialis, periventricularis hypothalami and suprachiasmaticus indicates that both neuropeptides could be involved in feeding, affective defense behavior, the regulation of thermogenesis, circadian rhythms, and in visual and stress mechanisms (Fuchs et al., 1985; Pickard, 1985; Gray et al., 1989; Preston et al., 1989). Also, the presence of immunoreactive structures containing luteinizing hormone-releasing hormone in the nuclei arcuatus, regio praepoptica, hypothalami ventromedialis, suprachiasmaticus and in the median eminence indicates that the neuropeptide could play a role in regulating the release of luteinizing hormone and follicle-stimulating hormone from the anterior pituitary, in sexual behavior, in circadian rhythms, in visual mechanisms and in the regulation of thermogenesis (Kow and Pfaff, 1988; Pan et al., 1988; Merchenthaler et al., 1989).

Moreover, in the cat, it has been described that hypothalamic vasopressin and oxytocin immunoreactive neurons are activated during the pressor reflex exercise and that vasopressin is involved in the regulation of evaporative water loss and body temperature, and it is known that the release of cholecystokinin in the cat hypothalamus is involved in nutrient and volume loading (Doris, 1982; Schick et al., 1989; Li et al., 1997).

Finally, it is known that the destruction of the preoptic area, in which cell bodies containing delta sleep-inducing peptide have been found in the cat (Chamay et al., 1990), result in a strong decrease or disappearance of both paradoxical sleep and deep slow-wave sleep (Scyzmusiak and McGinty, 1986; Sallanon et al., 1989). This suggests that the neuropeptide could be involved in the hypothalamic control of sleep.

**Future research on neuropeptides in the cat hypothalamus**

As we have indicated in a previous work on the neuropeptides in the cat thalamus (Coveñas et al., 2001), in the hypothalamus there is also much to be done in order to know the distribution and the physiological functions of the neuropeptides in this diencephalic region of the cat. Thus, in addition to studying the distribution of other neuropeptides that, at the present, have not been studied in detail in the cat hypothalamus, in the future radioimmunoassay and in situ hybridization techniques should be carried out in order to compare the results obtained after using both techniques in the cat hypothalamus with those described for the distribution of neuropeptides in the same diencephalic area of the cat. In addition, however, in the future the following aspects should be explored in greater depth in the cat hypothalamus, since they have not received sufficient attention: 1) The distribution of the receptors of the neuropeptides; 2) The distribution of the neuropeptidases; 3) The location of the cell bodies that originate peptidergic afferences to the hypothalamus; 4) The
projections of the peptidergic neurons observed in the hypothalamus; 5) Knowledge of the synaptic connections; 6) The existence of neuropeptides and 7) The physiological functions of the neuropeptides. In sum, the application of other methodologies (combining immunocytochemical and tract-tracing methods, immunocytochemical and electron microscopic methods, immunofluorescence methods, microinjections of neuropeptides...) is required in order to gain further insight into the distribution and functions of the neuropeptides in the cat hypothalamus.

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.

ABBREVIATIONS USED

- aHd: Area hypothalamiica dorsalis
- Arc: Nucleus arcuatus
- Fx: Fornix
- Ha: Hypothalamus anterior
- HL: Hypothalamus lateralis
- Hdm: Hypothalamus dorsomedialis
- Hp: Hypothalamus posterior
- Hvm: Hypothalamus ventromedialis
- MFB: Median forebrain bundle
- MI: Nucleus mammillaris lateralis
- Mn: Corpus mammillare
- PVH: Nucleus periventricularis hypothalami
- RPO: Regio praeoptica
- Sch: Nucleus suprachiasmaticus
- So: Nucleus supraopticus
- TMT: Tractus mamillo-thalamicus

REFERENCES


DE YEBENES EG, SOONGUEN L, FOURNIER A, ST-PIERRE S and PELLETER G (1995). Regulation of proopiomelanocortin...


Neuropeptides in the cat diencephalon: II. Hypothalamus


