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THE COMPARISON BETWEEN ENKEPHALIN-LIKE AND DYNORPHIN-LIKE IMMUNOREACTIVITY IN BOTH MONKEY AND HUMAN GLOBUS PALLIDUS AND SUBSTANTIA NIGRA

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Summary

The distribution of [Met]-Enkephalin and Dynorphin-like immunoreactivity were studied in the monkey and human globus pallidus and substantia nigra. These distributions were compared to those seen in these structures of the rat. Interspecies variations were observed in the substantia nigra, and in both pallidal segments. Differences between the distribution of the two opiate peptides occurred mostly in the limbic-related globus pallidus.

The efferent striatal system projects to the globus pallidus (GP) and substantia nigra (SN), structures which are rich in the opiate peptides, enkephalin (Enk) and dynorphin (Dyn) (1-7). Localization of Enk in the CNS of the rat and the monkey have revealed common patterns of distribution as well as some striking differences, particularly in the SN and the internal segment of the GP (the entopeduncular n. of the rat) (5). This study was undertaken to compare the distribution of Enk-like immunoreactivity (ELI) and Dyn-like immunoreactivity (DLI) in the GP and SN of monkey and human tissue and compare them to what has been described in the rat.

Neurons of the GP and SN are characterized by having long thick dendrites completely ensheathed in a dense plexus of thin striatal efferents (8), a unique morphological characteristic made evident with opiate peptide immunohistochemistry. These so-called woolly fibers (WF) (Fig. B) have been used as a reliable marker for the GP in the rat. Based on Enk-positive WF distribution, the GP is a more massive structure than conventionally defined, with ramifications extending into limbic-related regions. These include: the ventral pallidum and olfactory tubercle, the ventral striatum, the dorsal region of the amygdala, and a limited area invading the bed nucleus of the stria terminalis (BNST) (9). Very weak ELI is observed in the rat SN (1-3). DLI is seen in only parts of the rat GP but through most of the SN (5-7).

Materials

Anesthetized monkeys were perfused with 4% cold paraformaldehyde in phosphate buffer, post-fixed for 90 min. and stored in phosphate-buffered saline with sucrose. Human tissue was fixed by emersion for 2-3 weeks, then transferred to phosphate-buffered saline with sucrose. All tissues were sectioned serially at 50μ on a freezing microtome. Serial sections were processed for [Met]-Enk (antibodies donated by Dr. Robert Elde) and Dyn A (1-17) immunohistochemistry using the PAP technique, or stained for neuronal cell bodies with cresylviolet. Preparation and characterization of the antibodies have been described elsewhere (5,7), and under immunohistochemical conditions, do not cross-react with each other. Several sections were processed as absorption controls to show antibody specificity and to exclude cross-reactivity between the Enk and Dyn antibodies.

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Results and Conclusions

Dense ELI is found throughout the external pallidal segment in both monkey and human tissues. As in the rat GP, Enk-positive WF extend beyond the conventional pallidal borders to invade the amygdala, the ventral striatum, the lateral BNST, and the subcommissural forebrain area (Fig. A,B). In human tissue, but not in monkey, an additional large Enk-rich region is found in the central and subcommissural BNST (not shown here). Dyn-positive fibers are also found throughout the main part of the external segment in human and monkey tissue, however, it appears less intense than ELI (Fig. D,E). DLI in all three species is not found as extensively as ELI outside the conventional GP borders. Little DLI is found in the amygdala (Fig. E), BNST, or the ventral striatum. While the main part of the ventral pallidum does contain a dense plexus of fibers, they do not extend as far ventralward into the substantia innominata as do Enk-positive WF (Fig. D).

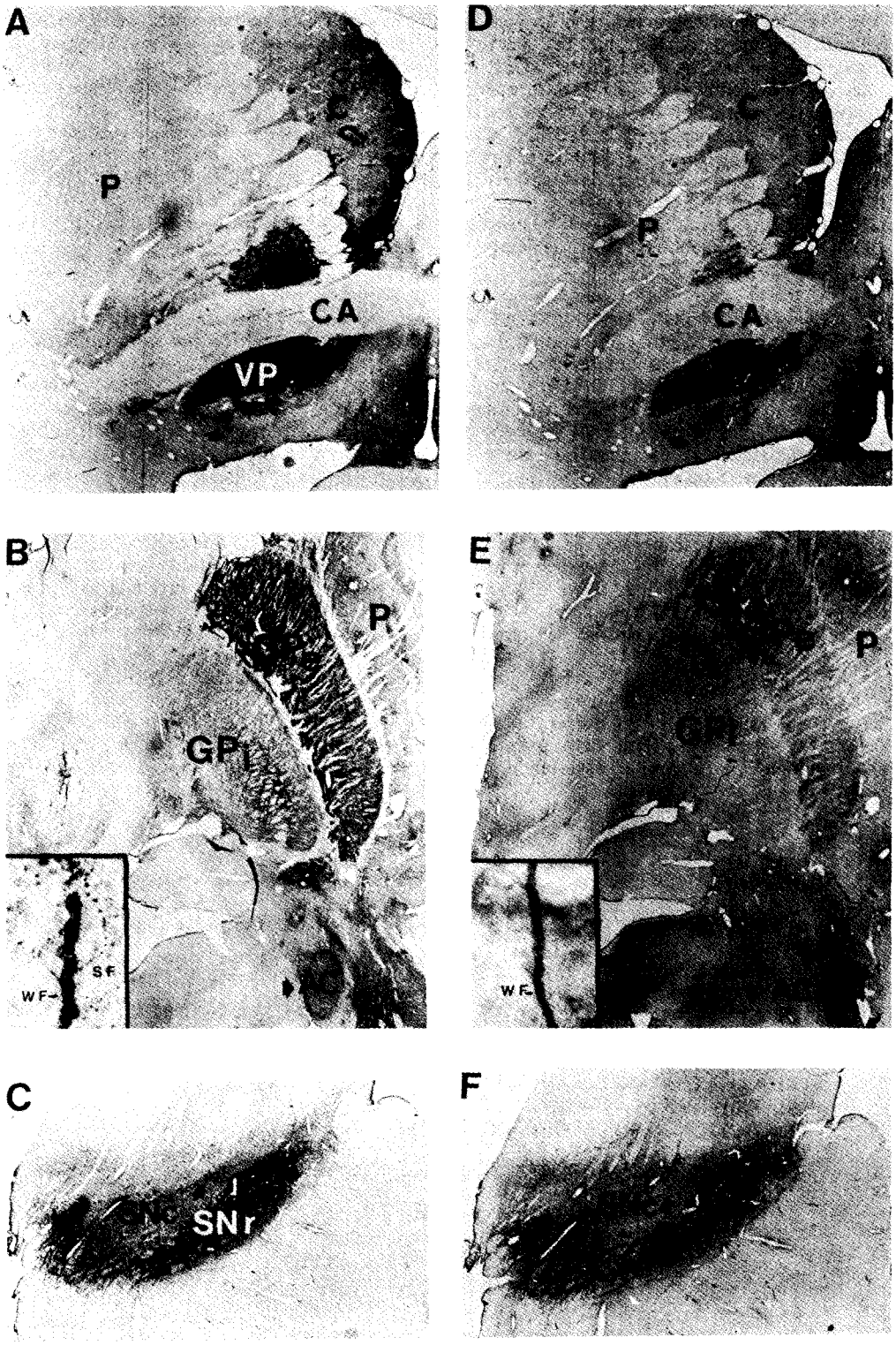
Table
Comparison between ELI and DLI in rat, monkey, and human GP and SN.

		RAT	MONKEY	HUMAN
GP-e	ELI	D	D	D
	DLI	W to M	W to M	D
GP-i outer portion	ELI	-	VW	VW
	DLI	-	VW	VW
GP-i inner portion	ELI	-	M	M
	DLI	-	W	W
Entopeduncular n.	ELI	VW	-	-
	DLI	M-D	-	-
AC	ELI	D	D	D
	DLI	VW	VW	VW
BNST	ELI	Limited Area	Limited Area	Extensive
	DLI	Limited Area	Limited Area	Limited
SN	ELI	VW	D	D
	DLI	D	D	D

ELI and DLI densities in various regions of the GP and SN of rats, monkeys and man. D = dense; M = moderate; W = weak; VW = very weak; GP-e = globus pallidus, external segment; GP-i = globus pallidus, internal segment; AC = central amygdaloid n.; BNST = bed n. of the stria terminalis; SN = substantia nigra.

Fig. 1

Photomicrographs showing ELI (A-C) and DLI (D-F) on frontal planes in monkey (A,D) and human (B,C,E,F) tissue: note WF inset in Fig. B and E. Arrows indicate differences between the opiate peptide staining. In Fig. C and F the cell body staining is nonspecific. Abbreviations: AC - central amygdaloid n.; C - caudate n.; CA - anterior commissure; GP(e) - globus pallidus (external segment); GP(i) - globus pallidus (internal segment); P - putamen; SN(c) - substantia nigra pars compacta; SN(r) - substantia nigra pars reticulata; VP - ventral pallidum; WF - woolly fiber; SF - single fiber.


A
P
CA
VP
D
P
CA
B
P
GPi
SF
WF
E
P
GPi
WF
C
SNr
F

The internal segments of both human and monkey tissue demonstrate weak staining of both peptides. Within the two portions of the internal segment, a small region of thinner portion shows more ELI and DLI than does the remainder of the internal segment. This is particularly evident in Enk preparations (Fig. B). Very little Enk staining is seen in the entopeduncular nucleus of the rat, while Dyn staining is relatively dense. Dense ELI and DLI are observed in the SN of both man and monkey. The density of peptide staining varies within the structure resulting in peptide-rich and peptide-poor regions (Fig. C,F). The distribution patterns of ELI and DLI are fairly similar here, although ELI is clearly denser. A few subtle differences, however, are apparent in the more dorsal-lateral regions (Fig. C,F, arrow). Opiate peptide staining in the rat SN is quite different; DLI is more homogenous and ELI is weak.

These results show, firstly, that the opiate peptides vary in their distribution across species, and secondly, that ELI and DLI do not always coincide within the same structure. The main discrepancies between species occur in three regions; the SN, the internal segment of the GP, and the GP extension into the BNST. The SN of the rat shows weak ELI, while in the primate Enk-positive fibers are quite dense. DLI is similar in all species in the SN but not in the internal segment of the GP. The rat entopeduncular nucleus (the homologous structure in the rat) contains a rather substantial amount of DLI, while in the internal segment of primates Dyn staining is weak. Finally, Enk-positive WF are seen widely distributed throughout the BNST of human tissue. This appears to be unique to man, for no comparable staining pattern is found there in the other species. The differential distribution between ELI and DLI is most evident in the regions of the GP which extend outside the conventional borders; that is in the amygdala, the BNST, and the substantia innominata. These forebrain regions are more associated with limbic function than somatic sensorimotor function, and therefore, differences between the opiate peptide distributions may reflect variance in limbic rather than motor circuitry.

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