11 NEUROPEPTIDES IN RAT BRAIN DEVELOPMENT

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Neurohormones like vasopressin, oxytocin and the hypophysiotropic hormones LHRH, TRH, GIH were found to act not only upon the pituitary of peripheral target organs, but also within the central nervous system itself as appears from electrophysiological, biochemical and behavioral observations. Also pituitary hormones of the lipocorticotropic family (LPH, ACTH, MSH, endorphin) and prolactin were found to be present in the brain and do have central effects. The same holds for peptides originally discovered in the periphery (VIP, substance P, angiotensin). Immumocytochemistry has shown their presence in nerve fibers and endings in the brain and although specificity is far from being proven in most cases, these peptides are all regarded to be produced by nerve cells and possibly to act as peptide transmitters.

Several vasopressin and oxytocin exo-hypothalamic tracts have been described arising in supraoptic, paraventricular and suprachiasmatic (vasopressin only) nuclei, and ending with synaptic structures on dendrites and cell bodies (hippocampus, lateral septum, lateral habenula, amygdala (1) . α-MSH immunostaining was found to be most striking in the cerebellar basket cell endings and in neurons of the spinal cord and dorsal root ganglia (2).

When determined radioimmunochemically, vasopressin, oxytocin and α-MSH appeared to be present in rat brain already early in fetal development (day 16). On day 19 fetal brain immunocytochemistry showed exo-hypothalamic pathways containing neurohypophysial hormones to be present, although not fully developed.

Taking also into consideration that other (less putative) transmitters and centrally active hormones (thyroid hormone and gonadal hormones) have been found not only to be of importance in adult brain function but also in brain development, we hypothetized a role of neuropeptides in brain development, too.

The hereditary deficit for vasopressin synthesis (Brattleboro rats homozygous for diabetes insipidus) appears indeed to result postnatally in a stunted brain development which moreover persists throughout life. The lower brain weight was largely due to a suppressed outgrowth of cerebellum and medulla oblongata, of which the cell content (total DNA) appeared seriously affected. Whether this effect is a direct or indirect result of the absence of vasopressin has still to be established (3).

Subcutaneous neonatal injections of α-MSH have been described to have organizing effects on the central nervous system. Since in addition α-MSH seems of importance in the prenatal body growth spurt of rats, the effect of a single subcutaneous α-MSH antisera injection given on day 19 prenatally has also been tested upon brain development. It resulted in a reduced brain on day 21 and appears the result of a decreased cell maturation since protein and lipid content were found to decrease, while total DNA (*i.e.* cell) content remained at control levels (4).

The observations on vasopressin and α-MSH effects suggest therefore that the neuropeptides which are of importance in adult brain functioning seem also involved in normal brain development.

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