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PLASTICITY OF BRAIN CORTICOSTEROID RECEPTOR SYSTEMS: ACTION OF NEUROPEPTIDES.

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Receptor sites for corticosteroids in rat brain are heterogeneous. The binding characteristics and the effects indicate classification in three types:glucocorticoid receptors (GR), mineralocorticoid receptors (MR) and corticosterone (CORT) preferring receptors (CR). GR is widely distributed in neurons and glial cells.Highest density of GR occurs in cortical,limbic and hypothalamic subregions including the CRF producing neurons in paraventricular nucleus.$K_D$ CORT to GR $\sim$ 5 nM.GR is thought to mediate the feedback action of CORT on stress-activated brain processes.CR has its predominant localization in limbic neurons,in particular those of the hippocampus.$K_D$ CORT to CR$\sim$ 0,5 nM.CR is thought to have a tonic influence on hippocampus-associated expressions in behaviour and neuroendocrinology. MR mediates the mineralocorticoid effect on salt and water balance. CR an MR may represent the same receptor type, which is differentially expressed depending on the presence of corticosteroid binding globulin (CBG).Corticosteroid receptors display plasticity under a number of environmental,metabolic and genetic determined conditions.Reduced receptor number was observed after exposure to a stressful environment,in senescent rats and in animals homozygous for diabetes insipidus, that lack vasopressin.Reduced receptor number of the senescent rat is restored towards the level observed in young control animals after chronic treatment with an analog of neurotropic $ACTH_{4-9}$, which is a neuropeptide that improves mental performance and mood of the elderly. Similar observations were made after treatment of the diabetes insipidus rats with vasopressin related peptides.CR and GR respond differentially after treatment with these neuropeptides Prominent is the receptor plasticity in hippocampus,which is a brain structure involved in cognitive processes,emotional state and regulation of pituitary-adrenal activity.

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Interactions between Brain Peptides and Sex Steroids in the Control of Pituitary Function.

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Sex steroid concentrating neurons are distributed extensively in the rat brain. Under the influence of changing steroid milieu these neurons may modulate the functions of hypothalamic peptidergic neurons involved in the control of pituitary gonadotropin secretion. We have studied the effects of sex steroids on secretory activities of luteinizing hormone releasing hormone (LHRH) and neuropeptide Y (NPY)-containing neurons. Castration resulted in decreased hypothalamic LHRH levels, while treatment with testosterone, 5α- dihydrotestosterone or estradiol 17β raised LHRH levels in the median eminence. A close monitoring of circulating levels of testosterone and estradiol indicated that small concentrations of these steroids which do not suppress LH release were highly effective in promoting LHRH levels in the basal hypothalamus. Further, castration also decreased the hypothalamic LHRH output in vitro while priming with testosterone augmented LHRH release. In female rats, ovarian steroids exerted a similar dual effect on hypothalamic LHRH accumulation and release. Progesterone augmented LHRH concentrations in the basal hypothalamus prior to LH hypersecretion in estrogen-primed ovariectomized rats. Ovarian steroid treatment also increased the in vitro LHRH release from the hypothalamus. Similarly, the effects of intraventricular administration of NPY on LH release were affected by ovarian steroids. In ovariectomized rats NPY decreased LH release, however, in steroid-primed ovariectomized rats similar NPY treatment stimulated LH release. Additionally, we have found that estradiol treatment decreased NPY concentrations in the median eminence in association with suppression of LH release. However, NPY concentrations in the median eminence were raised by progesterone in conjunction with stimulation of LH release in estrogen-primed rats. Collectively, these observations demonstrate that sex steroids may facilitate the accumulation and release of those hypothalamic neuropeptides which are normally involved in the regulation of pituitary gonadotropin secretion. (Supported by NIH grants HD 08634, 14006 and 11362).