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Meeting abstract

Endogenous dynorphin in emotional control and stress response

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Background

Cerebral control of stress and anxiety involves several neurotransmitter systems. Beside serotonin, noradrenaline or catecholamines, also neuropeptide systems are considered to be involved in generating symptoms of anxiety and stress. These systems act in a circuit connecting amygdaloid and hypothalamic nuclei, the pituitary and adrenal glands, regulating the physiological response via ACTH and corticosterone release.

Methods

In this study, we investigated anxiety and stress-related behaviour of germ-line prodynorphin knockout (dynKO) mice. Behavioural data were complemented by in-situ hybridization analysis of neurotransmitter expression in anxiety-related brain areas and measurement of corticosterone serum levels.

Results

Male dynKO mice exhibited about 2-fold ambulation in the open field center. DynKO mice showed also more visits (2-fold) and more time (3-fold) spent on open arms of elevated plus maze test. Significantly higher numbers of entries, distance and time spent in open lit area (ca. 30% higher values) in light-dark test were observed in dynKO as compared to wild-type mice (WT). The anxiolytic phenotype of dynKO could be mimicked by injection of the selective κ antagonists norBNI (10 mg/kg, i.p.) or GNTI (3 nmoles, i.c.) in WT. Applying the specific κ agonist U50488H (2.5 mg/kg, i.p.) entirely reversed the anxiolytic phenotype of dynKO. These data are in line with reduced CRH expression in the hypothalamic paraventricular and central amygdaloid nuclei and attenuated basal corticosteron serum levels. Stress-induced increases in corticosterone levels were also less pronounced in dynKO mice; however, they did not translate into marked differences in stress-induced immobility.

Conclusion

Taken together, our data suggest anxiogenic effects of endogenous dynorphin. These effects are mediated by κ opioid receptors, however not in an immediate manner. Therefore, we propose a higher order controlling level for the action of dynorphin, like regulating the expression of CRH and serum corticosterone levels, which in turn influence the behaviour of mice.

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