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Meeting abstract

Behavioural characterization of prodynorphin knockout mice

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Dynorphin, with a high selectivity for kappa opioid receptors, is a member of the opioid peptide family. Application of opioid agonists and antagonists revealed crucial effects of the opioid system in numerous physiological functions. However, data obtained are often contradictive, reflecting the complex situation of the cross-activation of 3 receptors through a peptide derived from 3 different precursors. Therefore we investigated prodynorphin knockout mice (DynKO) to establish the effect of prodynorphin deficiency on explorative behaviour in mice. DynKO exhibited higher ambulation in the open field test. Thus, center distance, center time and number of center entries were increased about 2-fold, and number of center rearings about 3-fold. DynKO mice showed also more visits (~2-fold) and more time (~3-fold) spent on open arms of the elevated plus maze test. Significantly higher numbers of entries, distance and time spent in open lit area (ca. 30% higher values) in the light-dark test were observed in DynKO as compared to wild type mice (WT). In contrast to increased explorative behaviour of DynKO under aversive conditions, no differences in motor activity or circadian rhythms were observed in the home cage. The anxiolytic phenotype of DynKO could be mimicked by injection of the selective kappa antagonists norBNI (10 mg/kg, i.p.) or GNTI (3 nmol, i.c.) in WT. Applying the specific kappa agonist U50488 H (2.5 mg/kg, i.p.) entirely reversed the anxiolytic phenotype of DynKO. Taken together our data clearly show an anxiolytic phenotype of male DynKO mice. These data are in line with reduced CRH expression in the PVN and attenuated corticosteron serum levels.