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Meeting abstract

Involvement of dynorphin in anxiogenic effects of estrogen

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Background

Since several years dynorphin, a member of the opioid peptide family, was suggested to play a regulatory role in numerous functional pathways of the brain, including anxiogenic effects in male mice [1]. However, emotional control and stress response depend on the hormonal state and differ between sexes, therefore we now investigated female prodynorphin-deficient (Dyn KO) mice.

Methods

Dyn KO mice were generated by replacement of the entire coding region of the prodynorphin gene [2] and backcrossed onto C57bl/6N. Age and testing experience-matched female intact and ovariectomized (OVX) Dyn KO and wildtype (WT) mice at 3-8 months age were tested in all experiments. Anxiety (open field test, OF; elevated plus maze test, EPM; light dark test, LDT) and stress-related behaviour (forced swim test, FST; tail suspension test, TST) was investigated in correlation to the estrous cycle in intact female WT and Dyn KO mice and in OVX WT and Dyn KO mice treated with the general estrogen receptor (ER) agonist 17β-estradiol (E_2), and specific agonists for ERα (PPT), ERβ (DPN) or GPER (G1) two hours before testing.

Results

In the EPM, Dyn KO mice showed a significant anxiolytic phenotype with about double time spent, distance travelled and entries in the open arm at all estrous stages compared to WT mice, while differences in the OF and LDT were less prominent than in male mice. Strikingly, the drop in ambulation observed in the OF, LDT and EPM during the proestrus phase in WT was absent in Dyn KO animals. In addition, the influence of the estrous stage on the behaviour in stress tests was abolished by the prodynorphin deficiency. Significant differences between OVX WT and Dyn KO mice were observed after DPN and G1 treatment, which both elicited anxiogenic effects in WT, but not in Dyn KO mice. In contrast, no differences were observed regarding the anxiolytic effects of PPT.

Conclusion

Our data suggest that the anxiogenic effects mediated by activation of ERβ and/or GPER may depend on the activation of κ opioid receptors. Pharmacological experiments aiming to solve this question are presently conducted.

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References

1. Wittmann W, Schunk E, Rosskothen I, Gaburro S, Singewald N, Herzog H, Schwarzer C: **Prodynorphin-derived peptides are critical modulators of anxiety and regulate neurochemistry and corticosterone.** *Neuropsychopharmacology* 2009, **34:**775-785.
2. Loacker S, Sayyah M, Wittmann W, Herzog H, Schwarzer C: **Endogenous dynorphin in epileptogenesis and epilepsy: anticonvulsant net effect via kappa opioid receptors.** *Brain* 2007, **130:**1017-1028.