The effects of cyclic estradiol replacement in ovariectomized rats on the response to chronic stress

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Sudden steep declines in plasma estrogen levels in women (as at postpartum and during the menopause) are typically associated with an increased risk of the occurrence of depressive symptoms and anxiety, conditions triggered by sequential life-events (i.e. chronic stress). Moreover, several studies have reported improvement of the depressive symptoms after estrogen treatment, indicating regulating effects of estrogen in the emotional system of women.
In our studies we used chronic stress, presented by daily footshocks for 3 weeks, as an animal model for stress-induced affective disorders. We treated ovariectomized rats with either vehicle or 17β-estradiol (10 µg/250 g, s.c.) once every 4 days, which imitated the normal estrus cycle, to explore the effects of estradiol on stress related systems in the brain.
The CRH mRNA expression in the PVN is decreased by estradiol treatment. In addition, estradiol-treated animals showed a reduction of 93% of the stress-induced increase in Fos protein in the PVN compared to ovariectomized rats. However, animals sacrificed when estradiol plasma concentrations are markedly lower, demonstrated a non-significant reduction in Fos protein of 37%. Chronic stress induced significant adrenal hypertrophy in the ovariectomized rats, which was alleviated by estradiol treatment. The plasma corticosterone response on stress in the estradiol-treated rats was only significantly increased on the first days of the stress protocol but returned to baseline levels after the first week, which corroborates the adrenal data and the activation pattern of the PVN.
Moreover, the expression of ERβ protein in the PVN is significantly increased in the estradiol-treated rats after chronic stress, which may indicate increased ERβ mediated processes in the PVN during chronic stress situations.
In conclusion, cyclic 17β-estradiol administration reduced the impact of chronic stress exposure on the HPA system in rats and may consequently provide a mechanism preventing the deleterious effects of chronic stress on brain function.

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