

## Publication

Adenohypophyseal and hypothalamic GABA B receptor subunits are downregulated by estradiol in adult female rats

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Keywords GABA(B) receptors, pituitary, hypothalamus, estradiol, [Ca-2]i oscillations, female rats Gamma-aminobutyric acid (GABA) participates in neuroendocrine regulation. Since steroid hormones have been shown to modulate the GABAergic system, here we evaluated the effect of chronic in vivo estradiol administration on GABA B receptor (GABA(B)R) expression. GABA(B1) and GABA(B2) subunits were analyzed by Western Blot and RT-PCR, in hypothalami and anterior pituitaries of adult female rats: a) treated for 1 week with estradiol-valerate (a single dose of 100 mug /kg: E1), b) implanted with a 10 mg pellet of estradiol-benzoate for 5 weeks (E5) or c) on proestrous (P), d) ovariectomized (OVX). Pituitary GABA(B)R levels were correlated to a biological effect: baclofen, a GABA(B)R agonist, action on intracellular calcium titers ([Ca(2+)](i)) in pituitary cells. E5 pituitaries showed a significant decrease in the expression of GABA(B1) and GABA(B2) mRNAs compared to P. The GABA(B1a) splice variant of GABA(B1) was always more abundant than GABA(B1b) in this tissue. Similar to the pituitary, hypothalamic GABA(B1) and GABA(B2) mRNAs decreased in E5; this was confirmed at the protein level. In the hypothalamus GABA(B1b) was the main variant expressed in P rats, and was the one significantly sensitive to estradiol-induced decrease, as determined by Western Blots. Castration did not modify GA-BA(B)R expression with regards to P in either tissue. In P pituitary cells baclofen induced a decrease in [Ca(2+)](i), in contrast this effect was lost in E5 cells. We conclude that chronic estradiol treatment negatively regulates the expression of the GABA(B)R subunits in the pituitary and the hypothalamus. This effect is coupled to a loss of baclofen action on intracellular calcium in pituitary cells.

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