

## PREGNANCY AND DELIVERY CHANGE THE GENE EXPRESSION OF SYNAPTIC AND EXTRASYNAPTIC GABA<sub>A</sub> RECEPTORS IN THE RAT HIPPOCAMPUS

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In previous studies we have shown [1] that the of gene expression of selective GABA receptor subunits ( $\alpha_{1,3,5}$ ;  $\gamma_2$ ) during pregnancy and after delivery is functionally related to fluctuations of endogenous brain concentrations of allopregnanolone, a potent and efficacious modulator of GABA receptor. We have now studied the amount of the GABA<sub>A</sub> receptor  $\delta$  and  $\alpha_4$  protein during pregnancy (15, 19, 21, day) and after delivery (2 and 7 day) in rat hippocampal slices by immunohistochemistry. The GABA<sub>A</sub> receptors containing  $\delta$  and  $\alpha_4$  subunits largely localized at the extrasynapynaptic sites, are responsible for the tonic currents, and possess an enhanced sensitivity to allopregnanolone. Moreover, we also studied the amounts of  $\alpha_1$ ,  $\alpha_2$ , and  $\gamma_2$  which are localizated in the synaptic site and are responsible for the phasic inhibition.

We found a progressive increase in the levels of the  $\delta_1$  subunit during pregnancy with a massimal value between 19-21 days. The level of this subunit significantly decressed at days 2 and 7 after delivery. On the contrary we observed an increase in the levels of the  $\alpha_4$  subunit 2 days after delivery and this effect lasted for at least 7 days. However, no significant changes were observed for this subunit during pregnancy. In addiction, the levels of the  $\alpha_1$ ,  $\alpha_2$ , and  $\gamma_2$  protein were significantly decreased and increased during pregnancy and after delivery, respectively.

Subchronic administration of finasteride, a  $5\alpha$ -reductase inhibitor able to reduce the concentration of allopregnanolone more in the brain than in plasma [1], blocked the changes in the amount of  $\delta$  and  $\gamma_2$  proteins observed during pregnancy. In contrast, the subchronic administration of clomifene a compound that blocks estrogen action, didn't abolish the changes in the same GABA<sub>A</sub> receptor subunits observed during pregnancy.

This study shows a marked alterations of  $GABA_A$  receptor plasticity localized at extrasynaptic and synaptic level induced by pregnancy and in the post-partum period. Changes in the expression of these receptors might be associate to affective disorders often present during pregnancy and after delivery.

[1] A. Concas et al., PNAS, 95: 13284-13289, 1998