PLASTICITY OF THE GABAERGIC TRANSMISSION IN THE RAT HIPPOCAMPUS DURING PREGNANCY

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Pregnancy is a complex physiological process that is associated with marked changes in the concentrations of hormones and steroids along with alteration in mood and anxiety level. Previous studies have shown that, in pregnant rats, augmentations of neuroactive steroid (NS) concentrations are accompanied by plastic changes of the expression of specific subunits of the $GABA_AR$ in brain. Recent studies have identified, in granule cells of the dentate gyrus (DGgcs) of the hippocampus, the presence of two different components of the GABAergic transmission, that together control the neuronal excitability of this region. A phasic component, mediated by GABA vesicularly released acting on synaptic $GABA_ARs$ composed of $\alpha_n\beta_n\gamma_2$, and a tonic component, highly sensitive to NSs, that is mediated by ambient GABA acting on extrasynaptic $GABA_ARs$ composed of $\alpha_4\beta_n\delta$. In this work we studied whether the two components of the GABAergic transmission are altered during pregnancy. Patch clamp recordings of GABAergic currents were performed in the voltage clamp mode from hippocampal slices prepared from female rats in the Estrus stage (E), at 15 (P15), 19 (P19) days of pregnancy or at 2 days after delivery (PP2). Phasic and tonic GABAergic currents were recorded from both DGgcs and CA1 pyramidal cells (CA1PCs). In DGgcs, after a baseline of 5 min, application of exogenous GABA (5 μM) induced an increase in noise variance and a current shift in the holding current. The current shift of the holding current was 12.2 pA ± 2.2 (n=64), 18.8 pA ± 5.1 (n=33), 24.6 pA ± 4.3 (n=54), 15.4 pA ± 3.8 (n=32), for E, P15, P19 and PP2, respectively. Similar results were obtained when we activated $GABA_ARs$ with allopregnanolone (1 μM) instead of GABA. In the same cell type, the basal properties of the phasic sIPSCs were not different between groups. In CA1PCs, the effect of GABA (5 μM) was not different among groups, and with respect to both phasic and tonic component. Our data clearly show that, during the final days of pregnancy, when the increase in NS brain levels reaches its maximum value, a marked increase of the GABAergic transmission in DGgcs, but not in CA1PCs, takes place. Interestingly, these changes seem to be restricted to cells expressing functional $\alpha_4\beta_n\delta$ $GABA_ARs$. Preliminary immunohistochemistry experiments to elucidate the relationship between these functional changes and parallel alteration in $GABA_ARs$ subunit gene expression indicate that, at P19, there is an increased expression of the δ subunit with respect to the animals in the estrus stage.