PRENATAL STRESS DIFFERENTIALLY AFFECTS NEURONAL PLASTICITY IN ADULT MALE AND FEMALE RATS

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Prenatal Stress (PS) in rats is a well-documented model of early stress known to induce neurobiological and behavioural alterations (i.e., altered circadian rhythms, "anxiety", decreased feedback mechanisms of the HPA axis) (1). Recently, we found that PS rats prefer an active coping strategy when exposed to an anxiogenic environment, whereas they show less interest towards a more reassuring environment. This negatively correlated with Fos expression in limbic brain regions. The influence of PS on neuronal plasticity has been studied in male rats, where PS reduces hippocampal neurogenesis (2) and increases the expression of PSA-NCAM and BDNF. PSA-NCAM and neurogenesis are reversed by chronic treatment with agomelatine (a melatonergic agonist and 5HT2c antagonist). PS also reduces the expression and activity of type-5 metabotropic glutamate receptors (mGlu5 receptors) in the hippocampus of male rats. This is relevant because mGlu5 receptors are implicated in the regulation of both synaptic plasticity and neurogenesis. We now report a series of data indicating that PS differentially affects neuronal plasticity in adult female rats. Female rats exposed to PS did not show significant changes in the number of putative neuroprogenitor cells labelled with BrdU in the hippocampal dentate gyrus, but they showed a higher percentage of BrdU-positive cells differentiated into astrocytes. In addition, PS female rats showed an increased activity of mGlu5 receptors in the hippocampus, as assessed by measurements of agonist-stimulated polyphosphoinositide hydrolysis in hippocampal slices, as compared to their age-matched controls. We are currently studying whether adult male and female rats previously exposed to PS differ in their learning capacity and in long-lasting forms of hippocampal synaptic plasticity in the hippocampus. Mechanisms underlying the PS effects on the offspring remain largely unknown. However, previous works demonstrated that maternal glucocorticoids during pregnancy may play an important role in the HPA disturbances reported (3). Recently, we reported that PS leads to a decrease of the placental 11beta-HSD2 activity and consequently an increase in maternal corticosterone that reach the foetus (4). Finally, gestational stress has long lasting effects on HPA axis and behaviour in female dams (5). Thus, it could be postulated that high maternal corticosterone levels and altered maternal behaviour may also contribute to the long-term effect described in the offspring after PS.

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