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Prenatal Administration of Dexamethasone Causes a Violation of Glucocorticoud Feedback Associated with a Change in the Number of Corticosteroid Receptor in Extrahipotalamic Brain Structures

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Dexamethasone, like other artificial glucocorticoids, is widely used in everyday obstetric practice. Glucocorticoids can be recommended for use in cases of threatened abortion. However, there is evidence that the administration of glucocorticoids during pregnancy can lead to impaired brain development and offspring behavior, which may be due to a change in the activity of hypothalamic-pituitary-adrenal axis (HPAA). The aim of this work was to study the effect of the administration of the synthetic hormone dexamethasone on the 14–16th (DM14–16) and 17–19th (DM17–19) days of prenatal ontogenesis on the stress reactivity of HPAA in adult 3-month-old rats, as well as on the levels of gluco- (GR) and mineralocorticoid (MR) receptors in the most vulnerable areas of the brain (hippocampus and neocortex). Significant intergroup differences in the dynamics of changes in the levels of corticosterone in the blood of adult rats were revealed in response to mild stress exposure (the rapid stress reactivity test). Using the

immunohistochemical method, we have studied changes in the GR and MR expression (number of immunopositive cells) in the CA1 region and the dentate gyrus (DG) of the hippocampus, as well as in the 2nd and 5th layers of the neocortex of adult male rats. For animals of the DM14-16 group, there was a significant decrease in the number of intensively stained GR-positive cells in the CA1 field and DG of the hippocampus and the V layer of the neocortex (up to 24.5, 32.4 and 5.5% of control, respectively). The administration of dexamethasone on the 17–19th day of gestation also led to a decrease in the levels of intensely stained GR-positive cells in the CA1 field of the hippocampus and V layer of the neocortex (31.9 and 35.7% of control, respectively), but to a lesser extent than in the group DM14-16. The tendency to a decrease in the GR immunoreactive cells intensity is accompanied by an increase in the MR immunoreactive cells. Thus, the introduction of dexamethasone at different periods of prenatal ontogenesis modifies the functioning of gluco- and mineralocorticoid receptors, however, the degree, localization, and direction of these changes differ depending on the duration of exposure.

Keywords: prenatal development, brain, dexamethasone, hypothalamic-pituitary-adrenal axis, gluco- and mineralocorticoid receptors