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Effects of prenatal hyperhomocysteinemia on rat brain development during postnatal period

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Increased levels of maternal homocysteine (hyperhomocysteinemia, HHC) during pregnancy is associated with complications in fetal development. However, little is known about the effects of maternal HHC on subsequent fetal brain development. We created prenatal HHC by daily administration of methionine (0.6 mg/kg) to Wistar rats from 4th day of pregnancy until pups' delivery. The development of the HHC was confirmed by an increase in the level of homocysteine in the blood serum of rats at various stages of pregnancy. Newborns subjected to prenatal HHC have shown the increased oxidative modifications of protein and DNA in the brain, accompanied by significant reduction in the levels of superoxide dismutase and total antioxidant activity. Investigation of apoptotic markers showed activation of caspase-3 and increase of neuregulin (NRG1), exhibiting neuroprotective properties in the brain of fetuses and pups undergoing to prenatal HHC development. The signs of a disruption of short-term and long-term memory in the novel object recognition and 8-arm maze tests and decrease in biogenic amines (noradrenaline, serotonin and 5-oxyindolacetic acid) in the hippocampus in rats offspring subjected to prenatal HHC at the age of 3-4 months were demonstrated. The level of NRG1 and the activity of monoamine oxidase, regulating the metabolism of biogenic amines, in placenta of animals subjected to HHC were decreased. The data obtained show that proposed homocysteineinduced oxidative stress and apoptosis of neurons causes early developmental impairments of brain maturation, which might underlie long-term deficits in the offspring learning and memory processes. The disturbances can be a consequence of both the direct impact of homocysteine and its metabolites on the CNS of the fetus, and the result of changes of normal functional state of the placenta, including its barrier function under the HHC conditions. Supported by the Russian Foundation for Basic Research Project no. 18-015-00099.

## Biography

Yuliya Miliyutina is currently working as senior researcher at D.O. Ott Research Institute of Obstetrics, Gynecology and Reproductology, Russia. She received a PhD of Biochemistry from Research Institute of Bioregulation and Gerontology, St. Petersburg. Her research interest includes study of the disturbance of the hypothalamic regulation of reproductive function and the effect of prenatal hyperhomocysteinemia on fetal brain development.

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