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Abstract

Maternal Hyperhomocysteinemia Disturbs the Brain Development and Maturation in Offspring †

Dmitrii S. Vasilev [1,*], Anastasiia D. Shcherbitskaia [1,2], Natalia L. Tumanova [1], Yulia P. Milyutina [2], Anna A. Kovalenko [1], Nadezhda M. Dubrovskaya [1], Anastasiia V. Mikhel [1,2], Daria B. Inozemtseva [2], Irina V. Zalozniaia [2] and Alexander V. Arutjunyan [2]

[1] I.M. Sechenov Institute of Evolutionary Physiology and Biochemistry of the Russian Academy of Sciences, St. Petersburg 194223, Russia; nastusiq@gmail.com (A.D.S.); tuman-1946@mail.ru (N.L.T.); kovalenko_0911@mail.ru (A.A.K.); ndub@mail.ru (N.M.D.); anastasia.michel39@gmail.com (A.V.M.)
[2] D.O. Ott Institute of Obstetrics, Gynecology and Reproductive Medicine, St. Petersburg 199034, Russia; milyutina1010@mail.ru (Y.P.M.); inozemtseva400@gmail.com (D.B.I.); irinabiolog@rambler.ru (I.V.Z.); alexarutiunjan@gmail.com (A.V.A.)
* Correspondence: dvasilyev@bk.ru
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Abstract: The effect of the homocysteine toxicity on both mother and embryo is known to induce disruption of placental blood flow and disturbances of the brain formation in offspring. The mechanisms of these effects are poorly understood and should be studied. The effects of prenatal hyperhomocysteinemia (pHHC) on the expression of some neuronal genes, neural tissue maturation and neuronal migration were analyzed in this study. Hyperhomocysteinemia was induced in female rats by per os administration of 0.15% aqueous methionine solution during pregnancy. On P5–P20 some features of developmental delay were observed in both cortical and hippocampus tissue ultrastructure in pHHC pups, accompanied by a retardation in body weight and motor development. In hippocampus tissue of P20 pHHC pups of synaptic glomeruli were absence suggesting more essential tissue immaturity compared to the cortical one. In pHHC pupst was shown decreased number and disturbed positioning of the neuronal cells labeled on E14 or E18, suggesting decrease in generation of cortical neuroblasts and disturbance in their radial migration into the cortical plate. On E14 the expression of the *Kdr* gene (an angiogenesis system component) was decreased in pHHC fetus brains. The content of SEMA3E and the MMP-2 activity level was increased. On E20 the increase in proBDNF/mBDNF ratio was also shown in pHHC pups, it might affect positioning maturation and viability of neuronal cell. The activation of caspase-3 accompanied by decrease in the level of procaspase-8 in the brain tissue of E20 pHHC fetuses may suggest the presence of cell apoptosis. It can be concluded that pHHC disturbs the mechanisms of early brain development and delay in brain tissue maturation in both neocortex and hippocampus of pups during early postnatal ontogenesis.

Keywords: hyperhomocysteinemia; rat; hippocampus; brain cortex

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