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МАТЕРИАЛЫ КОНФЕРЕНЦИИ И ШКОЛЫ

INVESTIGATION OF MECHANISMS AIMED ON SEROTONIN BIOSYNTHESIS INCREASING IN THE BRAIN AT THE DORSAL RAPHE NUCLEUS NEURONS DYSFUNCTION

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Raphe nucleus (RN) neurons are the main source of serotonin in the brain that sends projections to the hypothalamus and innervate, in particular, the hypothalamic arcuate nucleus neurons involved in the regulation of eating behavior and energy balance of the body. After 16 weeks of diet-induced obesity (DIO) in C57Bl/6J mice was detected decrease in the level of tryptophan hydroxylase-2 (TPG2), a key enzyme of serotonin biosynthesis, in the dorsal RN (dRN) neurons. **The aim of the study** was to compare the level of *Tph2* gene expression in the midbrain and hypothalamus, as well as to evaluate the pathways affecting the activity of this enzyme. Real-time PCR results demonstrate a decrease in the level of TPH2 mRNA in the midbrain ($p < 0.05$) and the absence of changes in the hypothalamus in DIO, which indicates the existence of additional sources of serotonin biosynthesis in hypothalamus. Data about the possibility of TPH2 expression in hypothalamic neurons, in particular in proopiomelanocortin-immunopositive neurons, and about an increase level of TPH2 in them in DIO were obtained with double immunolabeling and confocal microscopy. A decrease in Akt1 kinase mRNA was detected in midbrain in DIO. Moreover, a decrease of Akt1-immunoreactivity and an increase in the phosphor-Akt1 (ser-473) as well as an increase of the phosphor-TPH2 (serine-19) level ($p < 0.05$), were detected in dRN in DIO, which indicates an increase in TPH2 activity. At the same time in dRN neurons an increase in the immunoreactivity of neurotrophic factor BDNF ($p < 0.05$) and the respiratory chain enzyme SDH(B) ($p < 0.05$) were detected. Thus, an increase in the level of phosphorylated forms of TPH2 and Akt1, BDNF and SDH(B) can be considered as compensatory mechanisms aimed at maintaining the activity and viability of serotonergic neurons in obesity. The immuno-expression of TPH2 in the hypothalamic neurons is obviously aimed at increasing serotonin in the brain in this pathology.

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