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Molecular pathways of serotoninergic neurons regulation in murine brain in metabolic syndrome of various etiologies

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Abstract. Serotonin system participates in control of feeding behavior and energy balance jointly with hypothalamic neurohormonal systems. Tryptophan hydroxylase-2 (TPH2) is a key enzyme in serotonin biosynthesis in CNS. We compared TPH2 level in the hypothalamus and the midbrain and to evaluate neuroprotective mechanisms activated in metabolic syndrome.

Key words: serotonin, serotonin system, hypothalamus, obesity, metabolic syndrome.

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Serotonin system participates in control of feeding behavior and energy balance jointly with hypothalamic neurohormonal systems. Tryptophan hydroxylase-2 (TPH2) is a key enzyme in serotonin biosynthesis in CNS [1]. Midbrain dorsal raphe nucleus (DRN) is a main serotonin source for the hypothalamus. The aim of the study: to compare TPH2 level in the hypothalamus and the midbrain and to evaluate neuroprotective mechanisms activated in metabolic syndrome of various etiologies. Results: In C57Bl/6J mice, after 16 weeks keeping on a high-calorie diet, diet-induced obesity (DIO) developed [3], and decreased TPH2 level was detected immunohistochemically in DRN neurons [2;4]. With real-time PCR in DIO was shown decreased TPH2 mRNA level in the midbrain ($p<0.05$) and no changes in the hypothalamus [3]. In mice with genetically determined melanocortine obesity any changes in TPH2 level in DRN neurons were not detected [2], but with high-performance liquid chromatography was shown increased level of serotonin in hypothalamus and detected increased TPH2 gene expression in the hypothalamus with real-time PCR [3]. It can indicate the existence of alternative serotonin biosynthesis sources. The data of double immunolabeling indicates the possibility of TPH2 expression in hypothalamic neurons, which can be aimed to increase brain serotonin level in metabolic syndrome [3]. In DIO decreased Akt1-kinase mRNA level revealed in the midbrain, but it was detected decreased level of immunopositive-Akt1 in serotonin DRN neurons and increased phospho(serine-473)Akt1 level, as well as increased level of phospho(serine-19)TPH2 ($p<0.05$) and increased level of the neurotrophic factor (BDNF) ($p<0.05$). Thus, in DIO activates compensatory mechanisms aimed to maintain the serotonergic neurons vitality and their functional activity. Conclusions: obesity of various etiology differ in compensatory mechanisms aimed to increase of serotonin level in the hypothalamus.

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