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The role of the melanocortin system in the regulation of the functional activity of dopamine and norepinephrine neurons in the brain

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Abstract. In the mammalian brain AgRP is expressed in the neurons of the hypothalamic arcuate nucleus (ARC). The obtained data indicate the inhibitory effect of AGRP on the DA- and NE- brain neurons, which can effect through GPCR asossiated MCR3/4 signaling and through GPCR uncoupled.

Key words: brain, dopamine, melanocortin system.

Conflict of interest. The authors declare the absence of obvious and potential conflicts of interest associated with the publication of this article.

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The melanocortin system includes: melanortin peptides, melanocortine receptors (1, 3, 4) types and AgRP (agouti gene related protein) [3]. In the mammalian brain AgRP is expressed in the neurons of the hypothalamic arcuate nucleus (ARC). During processing three fragments (25-51, 54-82, 83-132) are formed from the AgRP-precursor. The role of AgRP83-132 in the brain is associated with the blockade of GPCR melanocortin receptors 3 and 4. The functions of other AgRP-fragments are not known, but it has been shown that their functions are not associated with GPCR. Processes of AgRP-neurons have been identified in the ventral tegmental area (VTA) and locus coeruleus (LC), where dopamine- and norepinephrine-ergic neurons are located[2]. It was shown that the injections of AgRP83-132 into these brain areas in C57BL/6J mice leads to a decrease in the neurons the level and phosphorylation of tyrosine hydroxylase (TH), a key enzyme in the biosynthesis of catecholamines, as well as a decrease in the level of dopamine (DA) and norepinephrine (NE) in the striatum, where the processes from the VTA and LC come [1]. The aim of this study was to evaluate the role of melanocortin system in the regulation of functional activity of DA and NE system in the VTA and LC at brain mice. The results. The melanocortin receptors 3/4 were detected on dopamine neurons of VTA, and only MCR3 were shown in LC. After administration of AgRP 25-51 into midbrain mice and into LC using immunohistochemistry in brain sections showed no changes in the level of phospho-(serine-40) TH in VTA and LC neurons. However, they showed a decrease in the level of phospho (serine-31) TH and a decrease in the level of dopamine-beta-hydroxylase in LC-neurons. By real-time PCR in the LC region a decrease in the mRNA level of the NE-membrane transporter was shown. The results of HPLC show a decrease in the level of DA and NE in the striatum. Conclusions. The obtained data indicate the inhibitory effect of AGRP on the DA- and NE- brain neurons, which can effect through GPCR-associated MCR3/4 signaling and through GPCR uncoupled MCR. The study was supported by state budget.

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