

## ROLE OF AN AGOUTI–RELATED PEPTIDE IN THE REGULATION OF DOPAMINE AND NOREPINEPHRINE BRAIN NEURONS

© 2020 г. А. Л. Mikhrina<sup>1,\*</sup>, Л. О. Saveleva<sup>1</sup>, and I. V. Romanova<sup>1</sup>

<sup>1</sup> *Sechenov Institute of Evolutionary Physiology and Biochemistry of the Russian Academy of Sciences, Saint Petersburg, Russia*

*\*e-mail: nastya\_mikhrina@mail.ru*

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Agouti-related peptide (AgRP – agouti gene related peptide) in the mammalian brain is expressed in neurons of the arcuate nucleus of the hypothalamus (arcuate nucleus – ARC), the processes of which are detected in various areas of the brain, in particular in the localization areas of dopamine– (ventral tegmental region – VTA) and noradrenergic (locus coeruleus – LC) brain neurons. It was shown that, in the course of post–translational changes, three fragments are formed in the ARC neurons from the precursor molecule (25–51, 54–82, and 83–132). The functional role as an antagonist of melanocortin receptors 3 and 4 (MC3R and MC4R), related to GPCR (G protein–coupled receptors), was studied only for the last fragment of AgRP 83–132. The functional significance of other fragments in the brain has not been investigated, but it has been shown that their functional activity is not associated with GPCR.

We conducted a series of experiments on C57Bl/6J mice, which were administered AgRP 25–51 bilaterally in VTA or in LC using stereotaxis instrument. The results demonstrate a decrease in the phosphorylation level of the tyrosine hydroxylase–serine 31 (dopamine bio-

synthesis's enzyme) in VTA neurons and a decrease in dopamine levels in the striatum, where projections from VTA arrive. After injections into LC a decrease in the optical density of dopamine beta–hydroxylase, an enzyme of the noradrenalin biosynthesis, is noted in noradrenergic neurons. Moreover, a decrease in the level of noradrenalin is noted in the LC projections in the striatum. The data obtained in experiments indicate the inhibitory effect of AgRP 25–51 on dopamine and noradrenergic neurons of the brain, which, obviously, is not associated with GPCR MC3R and MC4R. Double fluorescence immunolabeling and confocal microscopy show the localization of MC3R and MC4R in dopaminergic neurons in VTA, and only MC3R were detected in LC noradrenergic neurons. In VTA and LC, MC3R and MC4R were detected in GABAergic neurons. The mechanisms of action of various components of the melanocortin system on catecholaminergic brain neurons will be discussed.

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