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ANTIAMYLOIDOGENIC EFFECT OF MiR-101 IN EXPERIMENTAL ALZHEIMER'S DISEASE

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Абстракт

The aim of the study was to determine the effect of miR-101 on the level of β-amyloid peptide and activation of the cytokine system in the brain regions of animals with an experimental model of Alzheimer's disease. MiR-101 is the key deactivating operator of mRNA function for the amyloid-β protein precursor. Hence, miR-101 is capable to suppress its synthesis and amyloidogenic processing. Aged male rats were injected intrahippocampally with single-dose unilaterally of β-amyloid peptide 40 aggregates (15 nmol). After 10 days, nasal administration of the liposomal form of miR-101 or empty liposomes was started. After 10 days of therapy, the level of toxic endogenous form β -amyloid peptide 42 and the activity of the cytokine system were determined by the indicators of tumor necrosis factor α, interleukin-6, and interleukin-10 in neocortex, hippocampus and olfactory bulbs.
It was found that in rats, aggregates of exogenous β -amyloid peptide 40 model the amyloidogenic and pro-inflammatory situation after 20 days in the neocortex and hippocampus (a significant increase in the concentrations of β -amyloid peptide 42 by 36% and cytokines by 16–18% in the neocortex, and β -amyloid peptide 42 by 27%, proinflammatory cytokines tumor necrosis factor α, interleukin-6 by 14% in the hippocampus), but not in olfactory bulbs. The ten-day course of nasal therapy of liposomal miR-101 normalized the level of β -amyloid peptide 42 and cytokines: in neocortex, the concentration of endogenous toxic

β
-amyloid peptide 42 decreased by 33%, in the hippocampus by 15%, and concentration of pro-inflammatory cytokines fell by 11–20%. Thus, nasal therapy of miR-101 in liposomes caused a significant anti-amyloidogenic effect in rats with the Alzheimer's disease model, whereas its anti-inflammatory effect was primarily due to a decrease in
β
-amyloid peptide 42 concentration.

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