Petrov K., Malomouzh A., Kovyazina I., Nikitashina A. , Proskurina S., Nikolsky E.

ENDOGENEOUS REGULATION OF ACETYLCHOLINESTERASE ACTIVITY IN NEUROMUSCULAR JUNCTION BY NITRIC OXIDE

Kazan Institute of Biochemistry and Biophysics, A.E. Arbuzov Institute of Organic and Physical Chemistry, Kazan (Volga Region) Federal University, Kazan, Russia

kpetrov2005@mail.ru

Density of acetylcholinesterase (AChE) in the cholinergic synapses is not constant and can adapt to the changes in the synaptic activity. All known mechanisms of AChE regulation require dozens of hours, since synthesis, secretion and anchoring of the enzyme are required. We propose the existence of faster endogenous mechanism of regulation of synaptic AChE activity which involves the nitric oxide (NO) production. It is known that the gaseous mediator NO, in addition to many other functions in the organism, can modulate synaptic transmission. Besides, NO was shown to depress AChE activity in vitro. The question arises whether endogenous NO produced in the neuromuscular junction can influence the activity of synaptic AChE. We have shown that the exogenous NO donors induced a dose-dependent increase of miniature endplate current's amplitude and prolongation of decay time typical of AChE inhibition in rat extensor digitorum longus endplates. Considering our previously obtained experimental proofs that NMDA receptor activation resulted in the increase of NO production, we suggested the possibility of a glutamate induced NO-mediated pathway of AChE inhibition. Indeed, application of these amino acids enhanced the amplitude of miniature endplate currents, the effect being not observed after preliminary blockade of NMDA receptors and NO synthase inhibition. Thus, we suggest the existence of a previously unknown mode of regulation of cholinergic transmission based on the fine tuning of AChE activity by endogenous NO. Acknowledgement: This study was supported by RFBR grant № 11-04-12102, RFBR grant № 11-04-01188-a, grant "Leading Scientific School".

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