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## Acetylcholine-induced inhibition of presynaptic calcium signals and transmitter release in the frog neuromuscular junction

Khaziev E., Samigullin D., Zhilyakov N., Fatikhov N., Bukharaeva E., Verkhatsky A., Nikolsky E.  
*Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia*

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### Abstract

© 2016 Khaziev, Samigullin, Zhilyakov, Fatikhov, Bukharaeva, Verkhatsky and Nikolsky. Acetylcholine (ACh), released from axonal terminals of motor neurons in neuromuscular junctions regulates the efficacy of neurotransmission through activation of presynaptic nicotinic and muscarinic autoreceptors. Receptor-mediated presynaptic regulation could reflect either direct action on exocytotic machinery or modulation of Ca<sup>2+</sup> entry and resulting intra-terminal Ca<sup>2+</sup> dynamics. We have measured free intra-terminal cytosolic Ca<sup>2+</sup> ([Ca<sup>2+</sup>]<sub>i</sub>) using Oregon-Green 488 microfluorimetry, in parallel with voltage-clamp recordings of spontaneous (mEPC) and evoked (EPC) postsynaptic currents in post-junctional skeletal muscle fiber. Activation of presynaptic muscarinic and nicotinic receptors with exogenous acetylcholine and its non-hydrolyzed analog carbachol reduced amplitude of the intra-terminal [Ca<sup>2+</sup>]<sub>i</sub> transients and decreased quantal content (calculated by dividing the area under EPC curve by the area under mEPC curve). Pharmacological analysis revealed the role of muscarinic receptors of M2 subtype as well as d-tubocurarine-sensitive nicotinic receptor in presynaptic modulation of [Ca<sup>2+</sup>]<sub>i</sub> transients. Modulation of synaptic transmission efficacy by ACh receptors was completely eliminated by pharmacological inhibition of N-type Ca<sup>2+</sup> channels. We conclude that ACh receptor-mediated reduction of Ca<sup>2+</sup> entry into the nerve terminal through N-type Ca<sup>2+</sup> channels represents one of possible mechanism of presynaptic modulation in frog neuromuscular junction.

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### Keywords

Calcium transient, Muscarinic receptors, N-type Ca channels, Neuromuscular synapse, Nicotinic receptors, Presynaptic acetylcholine receptors, Quantum secretion of acetylcholine