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

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Abstract

© 2016 Khaziev, Samigullin, Zhilyakov, Fatikhov, Bukharaeva, Verkhratsky 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 Ca2+ entry and resulting intra-terminal Ca2+ dynamics. We have measured free intra-terminal cytosolic Ca2+ ([Ca2+]i) 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-hydrolized analog carbachol reduced amplitude of the intra-terminal [Ca2+]i 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 [Ca2+]i transients. Modulation of synaptic transmission efficacy by ACh receptors was completely eliminated by pharmacological inhibition of N-type Ca2+ channels. We conclude that ACh receptor-mediated reduction of Ca2+ entry into the nerve terminal through N-type Ca2+ 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