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The mechanisms of inhibition of frog endplate currents with homologous derivatives of the 1,1-dimethyl-3-oxybutyl phosphonic acid

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Abstract

The mode of inhibition of endplate currents by four esters of 1,1-dimethyl-3-oxybutyl phosphonic acid with different lipophilicities and molecule lengths were estimated by mathematical modeling based on previous electrophysiological data supplemented by several experiments with rhythmic stimulation. The aim was to discriminate between their receptor and non-receptor effects. It was shown that all esters have a two-component mechanism of depression: inhibition of the receptor open channel and allosteric modulation of the receptorchannel complex. The ratio of both functional components depends on the length and lipophilicity of the esters. Short and less lipophilic esters mostly act as open channel inhibitors and the rate of inhibition substantially depends on the rate of stimulation, i. e. probability of the receptor-channel opening. As the length of the ester radicals and their lipophilicity increased, these compounds were more active as allosteric receptor inhibitors, probably hindering the function of nAChRs from the lipid annulus. © 2012 Institute of Physiology v.v.i.

Keywords

Allosteric modulation, Endplate potential, Lipophilicity and cholinergic effect, Nicotinic cholinoreceptor, Open channel block