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Effect of galantamine on muscular nicotinic receptors desensitization – a patch-clamp study

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Galantamine is an acetylcholine-esterase inhibitor, which has also been reported to act by allosterically potentiating the binding of acetylcholine (ACh) to the nicotinic receptor (Santos 2002, Akk 2005). Here we report, for the first time to our knowledge, an effect of galantamine on the desensitization of the muscular nicotinic receptor. These receptors are naturally expressed by the TE671LH cell line, which was used here for the whole-cell patch-clamp characterization of ACh+galantamine elicited ionic currents, under voltage-clamp conditions. In order to investigate the receptor short-time desensitization, ACh and/or ACh+galantamine have been applied with a fast perfusion system in trains of pulses at 5 seconds intervals, at different concentrations of ACh (10-50 uM) and galantamine (0.1-5 uM). Receptor desensitization has been evaluated from the decrease of the peak-current amplitude in a train of elicited responses. Different responses can be obtained in the presence of ACh and galantamine, depending on their relative concentrations: (i) a less significant decrease of the amplitude of the peak currents in a train of elicited responses as compared to the application of ACh alone (control), (ii) no alteration of the peak currents, or (iii) an increase of nicotinic currents, after initial desensitization. Our data suggest that the pattern of response is less dependent on the absolute values of ACh and galantamine concentration and influenced more by the balance between the two drugs and the number of available nicotinic receptors.