

Studying the effect of the cholinergic modulation in giant cells and astrocytes of the rat cochlear nucleus

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Summary

Earlier findings indicated that cholinergic modulation might influence the signal processing taking place in the cochlear nucleus (CN). It has not been studied, however, how this neuromodulatory effect influences the synaptic connections of the neurones. Considering the fact that in the last decades the active role of the glial cells in the functioning of the neuronal networks has been proven, it is necessary to address the question whether the astrocytes in the CN might be targets of the cholinergic neuromodulation.

In the work presented here, the cholinergic effects targeting the giant cells in the dorsal part of the CN were investigated in slice preparations using the patch-clamp technique. It was found that the application of the acetylcholine agonist carbachol (CCh) increased the firing activity of the giant cells. This effect was mediated by the M3 and M4 type muscarinic receptors. Moreover, it was shown that in the presence of CCh the amplitude of the excitatory postsynaptic currents (EPSCs) evoked by electrical stimulation of either the superficial or the deep layer of the CN decreased and the character of the short-term depression (STD) was modified, too. The effect on the EPSCs evoked by superficial stimulation was mediated solely by M3 receptors while M2, M3 and M4 receptors were responsible for influencing the EPSCs following deep layer stimulation. Inhibitory postsynaptic currents (IPSCs) evoked by superficial stimulation were not modified by CCh but the amplitude of the IPSCs evoked by deep layer stimulation was decreased via M3 receptors and the STD was also changed. Evaluation of the findings revealed that both pre- and postsynaptic muscarinic receptors might play roles in the cholinergic modulation.

Sensitivity of the astrocytes towards cholinergic modulation was investigated on astrocyte cell cultures prepared from the CN. Ca^{2+} transients were evoked by CCh application and recorded using the fluorescent indicator dye Fluo-4. It was shown that 36.3 % of the cells responded to the cholinergic stimulation. 45 % of the CCh-sensitive astrocytes produced transients possessing fast time-course while in 50.5 % of the CCh-sensitive cells the fast component was followed by a slow, plateau-like phase. The role of the M1 and M3 receptors in evoking the Ca^{2+} transients was proven by applying muscarinic agonists (CCh, muscarine) and antagonists (atropine, pirenzepine, 4-DAMP, hexamethonium) and the presence of these receptors was shown at both RNA and protein levels. The results unequivocally indicate the CCh-sensitivity of a population of the astrocytes in the CN. It can be assumed, consequently, that these cells may play some roles in mediating cholinergic modulation of the CN.

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