Abstract

$GABA_B$ receptors play an important role in regulation of neuronal excitability and stability of neural microcircuits. It is well known that dysregulation of slow GABAergic signalisation can lead to many pathological conditions (epilepsy, anxiety etc.). Current research indicates that the imbalance in the inhibitory transfer, caused by changes in the expression of $GABA_BR$ in the auditory system could play an important role in the progression of tinnitus. The goal of the present thesis was to determine the distribution of the $GABA_B$ receptor and its auxiliary subunit KCTD12 in the mouse auditory cortex and the dorsal cochlear nucleus (DCN). Furthermore, a change in $GABA_B$ receptor localization in the DCN was observed in mice exposed to an acoustic stress.

The $GABA_B$ receptor was expressed across the entire auditory cortex, both on the body and on the neuronal fibres. On the contrary, KCTD12 was found only in a particular subgroup of neurons that includes VIP (vasoactive intestinal peptide) and cholecystokinin positive interneurons., $GABA_BR$ and KCTD12 protein were found in all layers and in all studied cells types (fusiform, cartwheel and stellate) of the DCN. Acoustic trauma of the WT mice resulted in $GABA_B$ receptor internalization specifically in fusiform cells that are the main projection neurons of the DCN. Deficiency in the KCTD12 protein led to an increase in intracellularly located receptors in the neuronal subtypes (fusiform, cartwheel and stellate cells). Acoustic trauma of the KCTD12 KO mice did not substantially increase the $GABA_B$ receptor internalization, which supports the hypothesis that KCTD12 regulates stability of the receptor on the membrane and this function could be compromised in tinnitus. These new findings could contribute to better understanding of the mechanism of $GABA_B$ receptor signalling dysregulation and could contribute to treatment of serious diseases such as tinnitus.