

Meeting abstract

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Ca_v1.3 L-type calcium channels modulate depression-like behavior in mice independent of deaf phenotype

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Background

Mounting evidence suggests that neuronal voltage-gated Ca_v1.2 and Ca_v1.3 L-type calcium channels (LTCCs) can modulate mood and anxiety behaviors. In Ca_v1.2 dihydropyridine (DHP)-insensitive mice (Ca_v1.2DHP^{-/-} mice), systemic application of the DHP channel activator BAYK 8644 induced pro-depression-like behavior providing evidence for a possible role of Ca_v1.3 channels in mood behavior. We therefore explored the role of Ca_v1.3 LTCCs in depression- and anxiety-like behaviors using Ca_v1.3-deficient mice (Ca_v1.3^{-/-}). However, Ca_v1.3^{-/-} mice are congenitally deaf and it is so far unclear how deafness affects emotional behavior in mice. We therefore used another mouse model suffering from congenital deafness, claudin 14-deficient mice (Cldn14^{-/-}) as a control to address this question. As Ca_v1.3 channels are expressed in the retina we also investigated Ca_v1.3^{-/-} mice for possible disturbances in retinal morphology and visual function that could interfere with behavioral analysis.

Methods

Depression-like behavior was assessed using forced swim and tail suspension tests (FST and TST) whereas elevated

plus maze (EPM) and stress-induced hyperthermia (SIH) were performed to test anxiety-like behavior. Morris water maze, electroretinography and immunofluorescence stainings were performed to evaluate the consequence on visual acuity and retinal morphology of Ca_v1.3 deletion in Ca_v1.3^{-/-} mice.

Results

We showed that Ca_v1.3^{-/-} mice displayed less immobility in the FST as well as in the TST, indicating an antidepressant-like phenotype. In the EPM, Ca_v1.3^{-/-} mice entered the open arms more frequently and spent more time there indicating an anxiolytic-like phenotype which was, however not supported in the SIH test. By performing parallel experiments in Cldn14^{-/-} mice, an influence of deafness on the antidepressant-like phenotype could be ruled out. On the other hand, a similar EPM behavior indicative of an anxiolytic phenotype was also found in the Cldn14^{-/-} animals. Using electroretinography and visual behavioral tasks we demonstrated that in mice, Ca_v1.3 channels do not significantly contribute to visual function. However, distinct morphological changes were revealed in synaptic ribbons in the outer plexiform layer of Ca_v1.3^{-/-} retinas by

immunohistochemistry. Although these changes have no major effects on visual function, they indicate a possible role of this channel type in structural plasticity at the ribbon synapse.

Conclusion

Ca_v1.3 LTCCs modulate depression-like behavior but are not essential for visual function. The findings raise the possibility that selective modulation of Ca_v1.3 channels could be a promising new therapeutic concept for the treatment of mood disorders.

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