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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.

Conclusions

$Ca_V1.3$ 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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