Light-induced ganglion cell responses in Ca\textsubscript{v}1.4-mutant mouse retinas

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**Background:** Mutations in the CACNA1F gene encoding for the \(\alpha_1\) subunit of Ca\textsubscript{v}1.4 channels are known to cause congenital stationary night blindness type 2 (CSNB2). Typical symptoms in CSNB2 are moderately low visual acuity, myopia, nystagmus and variable levels of night blindness or progressive photophobia. The Ca\textsubscript{v}1.4 I745T (IT) mutation is associated with this disease, and in a heterologous expression system has been shown to result in gain of Ca\textsubscript{v}1.4 channel function. How such abnormal calcium influx can affect the retinal circuits is hardly known. Using multielectrode array recordings upon visual stimulation in mesopic conditions, we have demonstrated previously that the IT mutation caused disturbances in the signal transmission of mouse retinas.

**Methods:** We used multielectrode array recordings to further examine the ganglion cell (GC) activity of IT mouse retinas under both dim light (scotopic) and bright light (photopic) conditions, and by means of multiple light stimuli aimed to detect specific GC response patterns.

**Results:** We confirmed a higher spontaneous firing rate in the absence of stimuli and a delayed response in both light conditions in IT whole-mount retinal preparations. In addition, compared to controls, IT retinas showed a diminished firing frequency within the stimulus (wild type, WT: 16 Hz, IT: 6.7 Hz, mean of 5 and 4 experiments respectively). The higher spontaneous firing rate and the decreased light-driven firing response likely account for the inability of GC to efficiently transduce visual signals. Of note, many GC previously did not respond to full-field stimulation under mesopic light conditions. In this study, the analysis of the same cell in two different light conditions showed that ON and OFF responses of IT GC are largely lost during bright light: while 275 GCs responded to dim light, only 80 GC \((n=4)\) responded using bright light stimuli. Gaussian white noise stimulus analysis instead showed a loss of GCs response also at scotopic level.

**Discussion:** These preliminary data indicate that, although scotopic and photopic pathways show similarly impaired responses, in the IT CSNB2 model the cone pathway might be more severely affected. Together, our findings reflect what is seen in electroretinographic analyses of CSNB2 patients.

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