Abstract

The aim of the current study was to elucidate the function of HCN1-channels (hyperpolarisation-activated and cyclic nucleotide-gated) in retinal information processing. A transgenic mouse strain was employed, in which the gene encoding HCN1 had been knocked-out by targeted deletion (HCN1-knock-out).

The expression of HCN-channels was studied by immunocytochemistry in retinae of both HCN1-knock-out-mice and wildtype-mice. Analysis revealed that HCN1 is the predominant isoform in wildtype-retinae. Isoforms HCN-2, HCN3 and HCN4 are expressed to a lesser extend. No noticeable differences are observed in the expression patterns and level of expression for these three isoforms between retinae of wildtype-mice and knock-out-mice.

Retinal light responses recorded by two different methods were compared between wildtype-mice and HCN1-knock-out-mice. Electroretinograms (ERGs) were recorded from anesthetized mice. The analysis focused on the length of the b-wave and on the frequency response during repetitive stimulation. In both scotopic (rod ERG) and photopic (cone ERG) conditions at low intensities neither the duration of the b-wave nor the frequency response of the HCN1-knock-out were significantly affected. At higher intensities, a lengthening of the b-wave and a pronounced deficit in the frequency response was observed in the HCN1-knock-out.

In a second approach, light responses of retinal ganglion cells were recorded *in vitro* in the whole-cell-mode of the patch clamp-technique. First results show that the deficit observed in the ERG´s frequency response is also present on the level of individual ganglion cells. Frequency transmission is reduced in both ON- and OFF-ganglion cells of the HCN1-knock-out-mouse.

Vertebrate photoreceptors show a hyperpolarising light response. In wildtype, HCN-channels become activated during hyperpolarisation. The depolarisation induced by HCN-channel activation counteracts the saturation of the photoreceptor light response in bright light. In contrast, in the knock-out light responses in the rod-system might saturate. This saturation might block signal transmission in both ON- and OFF-pathway. These results point towards a new function for HCN1-channels in retinal signal processing.