Abstract

The ion channel HCN1 (hyperpolarisation-activated, cyclic nucleotide-gated channel-1) is expressed in photoreceptors of the mammalian retina. The central conclusion of the present study says that HCN1 in rods counteracts saturation of light responses by bright light stimuli.

The mammalian retina works in an intensity range that covers ten orders of magnitude. This task is achieved by two photoreceptors. The very sensitive rods are optimized for scotopic (night) vision, the less sensitive cones for photopic (day) vision. Cones relay their information via bipolar cells to the ganglion cells, the output neurons of the retina. Rods feed their signals into the cone network at multiple sites.

Using the patch-clamp technique, I recorded *in vitro* light responses of ganglion cells from retinae of normal (wild type) mice and of mice, in which the gene encoding HCN1 had been knocked out (K.O.). Recordings were performed under different states of adaptation with contribution of only rods (scotopic), only cones (photopic), or both rods and cones (mesopic) to the light responses. Flicker stimuli of different frequencies were applied and current or voltage responses were recorded.

Under scotopic and photopic conditions, no major differences were observed between light responses from wild type and from HCN1 K.O. retinae. In both retinae, ganglion cell responses followed flicker stimuli equally well. Under mesopic conditions, light intensity was chosen such that rod responses saturated. In wild type retinae, light responses of ganglion cells were similar to those under photopic conditions. In contrast, in HCN1 knock-out retinae light responses of ganglion cells could not even follow flicker stimuli of low frequencies. Cells responded as if they were saturated by bright and long lasting light stimuli.

A second mouse line was used in which in addition the gene encoding the visual pigment of rods, rhodopsin, was knocked out. These mice have no functional rods. In those retinae, despite the absence of HCN1 no saturation of light responses was observed. It is the task of HCN1 in rods to counteract saturation and thus, to enable vision under mesopic conditions. First experiments were performed to analyze the pathways that relay saturating rod responses to the retinal network.