REVIEW

# $Ca^{2+}$-induced Light Adaptation in Retinal ON-bipolar Cells

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**Abstract. Retinal ON-bipolar cells possess a metabotropic glutamate receptor linked to the control of a cGMP cascade, which functions to generate high synaptic amplification of rod signals under dark-adapted conditions. We report that a major component of light adaptation of the rod visual system results from a reduction in gain in synaptic transmission from rods to ON-bipolar cells, initiated by $Ca^{2+}$-loading when the cGMP-activated channels of the postsynaptic cell open with light. When intracellular $Ca^{2+}$-buffering was reduced adaptation was induced in ON-bipolar cells by background light too weak to significantly desensitize rods, a property absent in OFF-bipolar cells. Desensitization of ON-bipolar cell flash responses was induced by raising intracellular free $Ca^{2+}$.** (Keio J Med 48 (3): 140–146, September 1999)

**Key words: ON-bipolar cell, retina, mGluR6, adaptation, $Ca^{2+}$**

## Introduction

The rod visual system is extraordinary not only in its great sensitivity in the dark-adapted state, capable of the detection of a few photons, but also in its ability to operate over a range of light intensities about a million times greater than absolute threshold.[1] High sensitivity in the dark-adapted state is achieved by high gain in phototransduction in rods,[2] and in synaptic transduction in ON-bipolar cells,[3] each involving a cGMP cascade linked to rhodopsin or to a metabotropic glutamate receptor (mGluR), respectively. Psychophysical studies have indicated that the visual threshold rises at background light intensities too weak to induce significant adaptation in rod photoreceptors. The threshold doubled at backgrounds when only one out of three rods absorbed a photon, remarkable given that each rod in the human eye contains about $10^8$ rhodopsin molecules.[4] To operate over such a wide range of light intensities, there appears to be light and time-dependent control of gain, or adaptation, in both photoreceptor and ON-bipolar cell cGMP cascades.

Rod photoreceptors are relatively depolarized in the dark, releasing glutamate from their synaptic terminals at high rate. Glutamate activates the ON-bipolar cell mGluR which in turn activates a G-protein and phosphodiesterase (PDE) leading to the hydrolysis of cGMP and thus a reduction in cGMP-activated conductance. The closure of cGMP-activated cation channels results in a relatively hyperpolarized state in the dark. Light hyperpolarizes rods, shutting down glutamate release, so ON-bipolar cells depolarize due to an increase in cGMP-activated conductance.[5–7] This system inverts the rod photo-response giving rise to the ON-pathway of the visual system. The hyperpolarizing rod response is conserved on synaptic transmission to OFF-bipolar cells since these cells possess non-desensitizing ionotropic glutamate receptors.[3]

Voltage gain in synaptic transmission from rods to ON-bipolar cells is of the order of 100-fold when fully dark-adapted.[8] High gain in this system results from the coupling of single mGluRs to the control of a large number of cGMP-activated channels by the biochemical gain inherent in the cGMP cascade and the larger voltage change which results because most of these channels are closed in the dark.[3] In comparison, the voltage gain in synaptic transmission to OFF-bipolar cells is only of the order of 10-fold.[9] The problem arises, however, as to how the ON-system and hence the rod visual system as a whole, can function over a wide range of light intensities if the voltage gain in synaptic transmission was maintained at a constant high level. ON-bipolar cell responses would rapidly run into saturation with increasing light intensity. By whole-cell recording from bipolar cells in dark-adapted retinal slices in the absence and presence of $Ca^{2+}$-chelator

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