

**S 13-2**

**NITRIC OXIDE ACTIONS IN THE RETINAL HORIZONTAL CELLS**

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Retinal horizontal cells (HCs) are interneurons that are extensively coupled to one other by means of gap junctions in the outer retina. These junctions provide an efficient lateral pathway to mediate the surround responses. It has been known that surround responses can be modulated by cyclic nucleotides, cAMP and cGMP, related to dopamine and nitric oxide (NO) modulators. In HCs and their axon-terminals of the fish retinas, nicotinamide adenine dinucleotide-diaphorase (NADPH-d) and neuronal nitric oxide synthase (NOS) isoforms were localized. Cone-HCs were selectively labeled by NOS isoforms among four different types of HCs in the goldfish retina. Rod-HC was not labeled by any isoforms. The different localization of NOS isoforms in cone-HCs suggests the varieties of NO effects at the outer layer in the goldfish retina. The endogenous and exogenous NO controls the  $Ca^{2+}$  concentration through the voltage-gated T- and L-type Ca channels in HCs. Intraocular injection of cyclic nucleotides, cAMP and cGMP, and carbenoxolone, gap-junction blocker, decreased the optomotor response (OMR) which is used to study the mechanism of motion vision. OMR were decreased by NO donor but increased by L-NAME in both light- and dark-adapted retinas. NO modified gap-junctions between HCs in the retina via the L-arginine:NO pathway. The modulations of gap-junction conductance by NO affect the motion perception in goldfish. These results suggest NO modulates the visual signal formation at outer layer in the goldfish retina.

**Key Word:** Nitric Oxide

**S 13-3**

**PROTON-MEDIATED FEEDBACK FROM HORIZONTAL CELLS TO CONES IN THE RETINA: A MECHANISM OF RECEPTIVE FIELD SURROUND FORMATION**

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The retina converts the image into the neural signal and, in this process, the individual photoreceptors work as pixels. But the conversion of the image is not simply pixel by pixel. An important function of the retina is to enhance the contrast of the image by lateral inhibition. As a result, a neuron in the early visual system has a concentric receptive field with a center-surround antagonism. Many vision scientists agree now that horizontal cells (HCs) contribute to the formation of the center-surround receptive field. HCs have a large receptive field due to electrical coupling. They have AMPA receptors, and a tonic glutamate release from photoreceptors keeps HCs depolarized in the dark. During surround illumination HCs are hyperpolarized. We recently found that pH of the invaginating synaptic cleft of the cone terminal is related to the membrane voltage of HCs (Hirasawa & Kaneko, 2003). It is kept acidic in the dark and is alkalized by surround illumination. The pH change we found in the retinal slices of the newt disappeared when the slice was superfused with a solution with enriched pH buffering capacity. We concluded that the surround illumination enhances the amount of L-glutamate release from the alkalized cone terminal (the effect opposite to spot illumination), resulting in the formation of the center-surround receptive field of the second- and higher-order neurons in the visual system. To examine whether depolarized HCs release protons we measured the pH of the immediate external surface (pHo) of HCs isolated from carp or goldfish retina by a fluorescent ratio imaging technique. Isolated HCs were stained by 5-hexadecanoylamino fluorescein (HAF), a pH-sensitive lipophilic dye. Depolarization by application of kainate or by high extracellular  $K^+$ , pHo acidified. The amount of pHo acidification was monotonically related to the amount of depolarization. Acidification of pHo was suppressed by 0.4  $\mu$ M bafilomycin A1, a specific inhibitor of vacuolar type  $H^+$ -ATPase, suggesting that the HC depolarization enhanced an outward proton movement by voltage-sensitive  $H^+$  pump. These results clearly indicate that depolarization of HC extrudes protons from the intracellular media to outside.

**Key Words:** retina, horizontal cell, receptive field, pH