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Review

Electrical synapses between AII amacrine cells in the retina: Function and modulation

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ABSTRACT

Adaptation enables the visual system to operate across a large range of background light intensities. There is evidence that one component of this adaptation is mediated by modulation of gap junctions functioning as electrical synapses, thereby tuning and functionally optimizing specific retinal microcircuits and pathways. The AII amacrine cell is an interneuron found in most mammalian retinas and plays a crucial role for processing visual signals in starlight, twilight and daylight. AII amacrine cells are connected to each other by gap junctions, potentially serving as a substrate for signal averaging and noise reduction, and there is evidence that the strength of electrical coupling is modulated by the level of background light. Whereas there is extensive knowledge concerning the retinal microcircuits that involve the AII amacrine cell, it is less clear which signaling pathways and intracellular transduction mechanisms are involved in modulating the junctional conductance between electrically coupled AII amacrine cells. Here we review the current state of knowledge, with a focus on the recent evidence that suggests that the modulatory control involves activity-dependent changes in the phosphorylation of the gap junction channels between AII amacrine cells, potentially linked to their intracellular Ca^{2+} dynamics.

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1. Introduction

The performance of rod vision is quite remarkable (Hecht et al., 1942). The absorption of a single photon, in just one of the several thousand rod photoreceptors within the receptive field of a ganglion cell, leads to a change in the firing rate of that ganglion cell (Mastronarde, 1983). This sensitivity is made possible by the amplification of visual signals in rods and further amplification and convergence within the downstream pathway. The ability of the visual system to operate across a large range of background light intensities, from starlight to bright sunlight, represents a cardinal example of sensory adaptation. This adaptation takes place not only at the level of photoreceptors, but also involves functional optimization of multi-purpose retinal microcircuits. There is evidence that such optimization can correspond to the modulation of gap junction coupling, thereby functionally tuning the circuits for the changing light intensity, with the gap junctions functioning as electrical synapses (Bloomfield and Völgyi, 2009; Massey, 2009). While such tuning is thought to take place both in the outer and inner retina, corresponding to electrical synapses located in the outer and inner plexiform layers (OPL and IPL), respectively, particular focus has been directed toward elucidating the cellular and molecular mechanisms that mediate the tuning of the gap junction coupled network of AII amacrine cells, how this tuning might be related to activity-dependent synaptic input and how such tuning modifies synaptic integration. Activity-dependent plasticity of electrical synapses is an increasingly important theme in neuroscience (Haas et al., 2011; Hestrin, 2011; Landisman and Connors, 2005; Pereda et al., 2004; Zsiros and Maccaferri, 2008) and it is important to increase our understanding of how modulating the strength of electrical synapses can optimize the signal processing in the CNS. The gap junction coupling between neurons (and many other cells) is mediated by specialized channel proteins termed connexins (reviewed by Söhl et al., 2005) where post-translational modification by phosphorylation can modulate important functional properties (reviewed by Moreno and Lau, 2007). As with other areas of the CNS, progress in our understanding of electrical synaptic transmission in the retina is to a large extent hampered by the difficulties associated with investigating the structure and function of intact neural circuits under natural conditions. Here we focus on the electrical coupling of the AII amacrine cell, a retinal interneuron that plays a central role in visual signal processing in starlight, twilight and daylight and that seems to be found in the retina of all mammals.

2. Neuronal networks in the retina and visual coding

During a 24 h day and night cycle, our eyes are exposed to intensities of light that vary by a factor of $\sim 10^{12}$ (Valberg, 2005). Our vision is fully operative throughout this range, even though the spike rate of retinal ganglion cells varies by only a factor of 10^2 (reviewed by Demb, 2010). The ability of the ganglion cells to cover this range is made possible through a series of mechanisms, both at the level of photoreceptors and at post-receptoral levels. First, phototransduction is mediated by two types of photoreceptors, rods and cones, each with a different sensitivity to light (Fig. 1). At the lowest light intensities (starlight, corresponding to scotopic vision), each rod will capture only a single photon perhaps once a minute, while at the highest intensities (daylight, corresponding to photopic vision), each cone may capture hundreds or even thousands of photons every second. Second, the sensitivity of the transduction process itself can be adjusted in response to changes in the ambient light intensity (reviewed by Fain et al., 2001). Third, rod and cone photoreceptors connect to two fundamentally different