Østergaard J, Hannibal J, Fahrenkrug J. Synaptic contact between melanopsin-containing retinal ganglion cells and rod bipolar cells. Invest Ophthalmol Vis Sci. 2007 Aug;48(8):3812-20. Departments of Ophthalmology, Rigshospitalet, Copenhagen, Denmark.

PURPOSE: Evidence indicates that the melanopsin-containing intrinsically photosensitive retinal ganglion cells (ipRGCs) receive input from rods and cones, which are thought to modulate the irradiance detecting system driving entrainment of the circadian system and pupillomotor control. This study was performed to identify retinal cells that have synaptic contact with ipRGCs. METHODS: Immunohistochemistry and high-power confocal microscopy were used to generate stacks of digital images of sections stained with antibodies against melanopsin, protein kinase C (PKCalpha), tyrosine hydroxylase (TH), presynaptic terminal markers (C-terminal binding protein 2 [CtBP2], vesicular monoamine transporter 2 [VMAT2] and postsynaptic marker (glutamate receptor subunit 4 [GluR4]). Results were analyzed in a computer-based three-dimensional reconstruction program for cellular contacts. RESULTS: Markers and melanopsin rod bipolar processes were found to have axosomatic and axodendritic contact with melanopsin-containing RGCs. Typically, three to four contacts were found on the soma of the melanopsin-containing RGCs, together with contacts on proximal dendrites. Contacts visualized by only CtBP2 immunoreactivity could also be demonstrated on melanopsin cell bodies and processes representing contacts with other types of bipolar cells. At the border of the inner plexiform layer (IPL) and inner nuclear layer (INL), where melanopsin processes stratify, contacts between melanopsin and TH or VMAT2 immunoreactivity processes were observed. CONCLUSIONS: Through confocal microscopy and computer-based three-dimensional analyses, this study demonstrates that **melanopsin-containing RGCs have synaptic contact with PKC/CtBP2-containing rod bipolar cells and TH/VMAT2-immunoreactive amacrine cells through axodendritic and axosomatic contact, supporting electrophysiological observations that rods and cones signal to the melanopsin-containing intrinsically photosensitive RGCs.**

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