



GLAUCOMA

Connecting glaucoma and circadian rhythms

by Matt Young EyeWorld Contributing Editor

Disruption linked to reduction of light transmission

How melanopsin, in retinal ganglion cells, affects light perception (and as a result, circadian rhythm)

- They encode ambient light intensity.
- They receive synaptic inputs from rod and cone photoreceptors, and photic input is only eliminated when both melanopsin cells and rod/cone photoreceptors don't work.

Source:
Girardin Jean-Louis, Ph.D.

Glaucoma, by way of disrupting circadian rhythms, could interfere with sleep or cause depression, a new study suggests.

"We propose that glaucoma may be the primary ocular disease that directly compromises photic input to the circadian time-keeping system because of inherent ganglion cell death,"

according to lead study author Girardin Jean-Louis, Ph.D., clinical assistant professor, Department of Ophthalmology, SUNY Downstate Medical Center, Brooklyn, N.Y. The work was published in the January 2008 issue of the *Journal of Circadian Rhythms*.

While the study did not perform a randomized trial, it hypothesized that ocular diseases—and most especially glaucoma—can disturb sleep by reducing light transmission. This reduction, in addition to inadequate exposure to the light-dark cycle, can cause circadian misalignment and sleep disturbances.

How disease could affect sleep

Dr. Jean-Louis noted that ophthalmic diseases that could affect "photopic input to the circadian system" include cataract, diabetic retinopathy, macular degeneration, retinitis pigmentosa, optic nerve atrophy, and glaucoma.

"Plausibly, cataract, defined as opacity of the crystalline lens of the eye, does not diminish light input significantly unless the disease is far advanced," Dr. Jean-Louis wrote.

Meanwhile, diabetic retinal diseases vary in their severity, consequently affecting light input to various degrees. Other diseases also have a varying impact on light levels.

Glaucoma would have a twofold impact, Dr. Jean-Louis wrote, including, "1) a direct impact through degeneration of retinal ganglion cells and/or ocular ischemia and reperfusion damage and 2) an indirect impact through social isolation due to blindness."

He continued, "Glaucoma is an ocular degenerative disease that affects ganglion cells, eventually causing optic nerve dysfunction by way of axonal loss. Reduced axonal stimulation to the central visual pathways likely diminishes light input to the circadian system. This is supported by recent evidence that melanopsin, which is found in retinal ganglion cells,



is a major photopigment involved in circadian entrainment.” So while a disease like retinitis pigmentosa would cause progressive degeneration of rods, glaucoma affects ganglion cells, which may have more of a direct link to maintaining normal circadian rhythm. “Light-regulated functions—entrainment of the circadian pacemaker, suppression of activity and melatonin rhythms, and modulation of the papillary reflex—involve special signal transduction mechanisms of intrinsically photosensitive retinal ganglion cells,” Dr. Jean-Louis wrote. “These cells are believed to harbor melanopsin, the primary photopigment in the synchronization of circadian rhythms.” Already, research analyzing patients aged 12 to 20 years old from the Missouri School for the Blind found that patients with optic diseases showed greater circadian dysfunction, such as more napping during daytime hours and variable time of awakening compared to those without disease.

Who is affected

If Dr. Jean-Louis’s hypothesis is correct, glaucoma patients—and in particular African-Americans—could be at higher risk for depression and sleep disturbances.

“Glaucoma, for instance, is more prevalent among African-Americans, and ambient light data have shown reduced illumination among African-American men and women, compared to their Caucasian counterparts,” Dr. Jean-Louis noted.

Dr. Jean-Louis’s hypothesis also offers further compelling reasons for glaucoma patients to take their eye drops. Not only would they potentially be preserving vision, they would also help preserve sleep and good moods.

Meanwhile, Mark Packer, M.D., clinical associate professor, ophthalmology, Casey Eye Institute, Oregon Health & Science University, Portland, said it makes sense that glaucoma could affect circadian rhythm.

“There is a subcortical connection between the retina and melatonin, which establishes circadian rhythm,” Dr. Packer said. “There are subcortical pathways by which I mean neural pathways from the eye that do not come to the visual cortex. These are pathways that go from the eye and eventually get to the pineal gland, where melatonin release is mediated. So you could imagine that someone who has glaucoma—if you’ve lost half of your neurons, the input to those areas that mediate melatonin release may be reduced as well.”

Melatonin, meanwhile, acts on the release of cortisol, “which is kind of what gets you up in the morning,” Dr. Packer said. Cortisol “is the mediator of your sympathetic response, it’s what is released when you get palpitations, sweaty palms, blood pressure and arousal levels.”

All this could get messed up “in people who have reduced input from eyes due to atrophy of the nerve fiber layer,” Dr. Packer said.

He said he hasn’t noticed that glaucoma patients have disturbed sleep, but then again, he said his clinic up until now hasn’t asked that question. The study’s hypothesis was interesting enough, however, for Dr. Packer to say he might start asking this question to patients.

Editors’ note: Dr. Jean-Louis has no financial interests related to this study. Dr. Packer has no financial interests related to his comments.

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