Glaucoma may be more than just an issue of eye pressure

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Acute angle closure glaucoma of the right eye (intraocular pressure was 42 in the right eye). Credit: James Heilman, MD/Wikipedia

A chemical known to protect nerve cells also slows glaucoma, the leading cause of irreversible blindness, results of a new study in rats show.

Led by researchers at NYU Grossman School of Medicine, the study centers on the watery fluid inside the eye on which its function depends. Fluid pressure can build up in patients with glaucoma, wearing down cells in the eye and the nerves connecting them to the brain, researchers say.

However, past studies have shown the condition to continue to worsen even after eye pressure has been controlled. The connection between pressure buildup and impaired vision remains poorly understood.

Publishing April 13 in *Neurotherapeutics*, the new study showed that ingesting the compound citicoline restored optic nerve (neural) signals between the brain and eye to near-normal levels in the study rats. Naturally produced in the brain but also available commercially, citicoline is a major source of choline, a building block in the membranes that line nerve cells and enhance nerve cell communication.

While the study results confirmed past findings that elevated eye pressure contributes to nerve damage in glaucoma, it also showed that citicoline reduced vision loss in rats without reducing fluid pressure in the eye.

"Our study suggests that citicoline protects against glaucoma through a mechanism different from that of standard treatments that reduce fluid pressure," says senior study author Kevin Chan, Ph.D., an assistant professor in the Department of Ophthalmology at NYU Langone Health. "Since glaucoma interrupts the connection between the brain and eye, we hope to strengthen it with new types of therapies."

According to the National Glaucoma Foundation, over 3 million Americans have glaucoma, but only half know they actually have it. In the US, more than 120,000 individuals are blind from the disease. In addition, the World Health Organization estimates that over 60 million individuals suffer from glaucoma worldwide.

The findings are helping scientists better understand how glaucoma works and add to past evidence that citicoline may counter the disease, says Chan, also the director of the Neuroimaging and Visual Science Laboratory at NYU Langone. Previous studies had showed that humans and rodents with glaucoma have lower than normal levels of choline in the brain. Until now, Chan says, there's been little concrete evidence of the effectiveness of choline supplements as a therapy for glaucoma or why choline occurs in lower levels in glaucoma patients.

Chan and his team tested whether increasing levels of that chemical would slow or even stop the degradation of the optic nerve and other regions of the brain involved in vision. Using a comprehensive study of the eye-brain connection in glaucoma, his team found that giving rats oral doses of citicoline over a three-week period protected nerve tissues and reduced vision loss sustainably even after the

treatment stopped for another three weeks.

For the study, the researchers simulated glaucoma in several dozen rats using a clear gel to build up eye pressure mildly without otherwise blocking their vision. Then, the team measured the structural integrity and the amount of functional and physiological activity along the visual pathway using MRI scanning. The researchers also tracked the rodents' visual behavior to test the clarity of vision of each eye.

The study showed that for rats with mildly elevated eye pressure, the tissues that connect the eye and brain, including the optic nerve, decayed for up to five weeks after the injury occurred. Meanwhile, nerve structure breakdown in the citicoline-treated rodents slowed by as much as 74 percent, which indicated that the chemical had protective effects on nerve cells, say the authors.

The researchers caution that more research is needed before turning to citicoline supplements to treat glaucoma in humans, as commercial drugs have yet to be proven fully effective in clinical trials. Moving forward, the researchers plan to investigate the origin of choline decline in people with glaucoma as well as how citicoline works to repair the damage.

More information: Yolandi van der Merwe et al, Citicoline Modulates Glaucomatous Neurodegeneration Through Intraocular Pressure-Independent Control, *Neurotherapeutics* (2021). DOI: 10.1007/s13311-021-01033-6

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