

First light: Scientists regenerate the optic nerve, restore some components of vision

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(Medical Xpress) -- Researchers have long tried to get the optic nerve to regenerate when injured, with some success, but no one has been able to demonstrate recovery of vision. A team at Boston Children's Hospital reports a three-pronged intervention that not only got optic nerve fibers to grow the full length of the visual pathway (from retina to the visual areas of the brain), but also restored some basic elements of vision in live mice.

Larry Benowitz, PhD, and colleagues at the F.M. Kirby Neurobiology Center at Boston Children's Hospital, showed that [mice](#) with severe [optic nerve](#) damage can regain some depth perception, the ability to detect overall movement of the visual field, and perceive light, allowing them to synchronize their sleep/wake cycles. Findings were published online by the *Proceedings of the National Academy of Sciences* during the week of May 21.

The findings hint at the possibility that patients blinded by optic nerve damage from trauma or from glaucoma, estimated to affect more than 4 million Americans, might be able to regain at least some visual function. In other forms of [vision](#) loss, such as macular degeneration, people can sometimes regain visual acuity, but there is currently no way to recover from damage to the optic nerve.

Previous studies, including many by the Benowitz lab, have demonstrated that optic nerve fibers can regenerate some distance through the optic nerve, but this is the first study to show that these

fibers can be made to grow long enough to go from eye to brain, that they are wrapped in the conducting “insulation” known as myelin, that they can navigate to the proper visual centers in the brain, and that they make connections (synapses) with other neurons, allowing visual circuits to re-form.

“Dr. Benowitz and his group have, for the first time, established proof-of-concept that a damaged optic nerve can regenerate and attain lost function,” says Nareej Agarwal, PhD, of the National Eye Institute, which supported the study. “This is an important advance in an effort to reverse vision loss in glaucoma and other neurodegenerative diseases.”

Building on their previous studies, Benowitz and colleagues combined three methods of activating the growth state of neurons in the retina, known as retinal ganglion cells: stimulating a growth-promoting compound called [oncomodulin](#), originally discovered in the Benowitz lab in 2006, elevating levels of cyclic adenosine monophosphate (cAMP) and deleting the gene that encodes the enzyme PTEN. In a [2010 paper](#), Benowitz and colleagues showed that these interventions have a synergistic effect on growth of optic nerve fibers.

“Sixteen years ago, people said it was impossible to get any regeneration in the optic nerve,” notes Benowitz, also director of the Laboratories for Neuroscience Research in Neurosurgery at Boston Children’s Hospital. “Our study regenerated only a small percentage of the total number of fibers that would normally come into the brain, but it answers questions that have been real unknowns in the field.”

Benowitz cautions, however, that the vision the mice regained was limited, and probably didn’t restore the ability to discriminate objects.

“What lies behind what we call seeing is very complicated – so many subsystems contribute to seeing,” he says. “We’re in a sense just

scratching the surface about functional recovery.”

Specifically, the study demonstrated:

- 1) *Circadian entrainment*: Whereas circadian sleep/wake cycles in mice blinded by optic-nerve injury drifted out of synch with the room’s day/night light cycle, treated mice *came back into* synch with the light cycle.
- 2) *Depth perception*: Mice were made to walk on clear plexiglass platforms above a checkerboard pattern that appeared to drop off abruptly. Untreated blind mice showed an equal probability of walking over either end, whereas mice with regeneration spent less time over the “deep” end.
- 3) *Optomotor response*: When treated mice were put on a platform surrounded by rotating vertical stripes, they moved their heads reflexively to follow the pattern.

The molecular manipulations performed in the mice would need to be adapted to create an actual treatment for patients, says Benowitz. He hopes to investigate a gene-therapy approach in the future; such an approach has been proven to work in Leber’s hereditary neuropathy, a rare genetic disease causing vision loss.

“The eye turns out to be a feasible place to do gene therapy,” says Benowitz. “The viruses used to introduce various genes into nerve cells mostly remain in the eye. Retinal ganglion cells are easily targetable.”

Silmara de Lima, of the F.M. Kirby Neurobiology Center at Boston Children’s Hospital, was first author on the study. The research was funded by the National Eye Institute, the Department of Defense, the Dr. Miriam and Sheldon G. Adelson Medical Research Foundation, and

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