Blind patient regains partial vision with help from new gene-therapy techniques

By Miles Martin
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After four decades of blindness, a 58-year-old patient suffering from a rare genetic disorder that degrades the cells of the retina has now regained part of his vision, thanks to a groundbreaking new treatment.

After receiving a gene-therapy injection to deliver light-sensitive proteins to the retina, then donning specially engineered goggles, the patient was able to perceive, locate and count different objects. The case study, published Monday in *Nature Medicine,* is the first peer-reviewed example of vision restoration in a blind patient, bringing researchers one step closer to a holy grail of medical research: reversing blindness.

"I think there's a new scientific field getting born here. Namely, visual rehabilitation," said senior author Botond Roska, an ophthalmology professor at the University of Basel. "In blind patients so far, there are no successful rehabilitations to restore their vision."

Retinitis pigmentosa affects one in 3,500 people in the United States and causes the cells of the retina, the light-

sensitive region on the back wall of the eye, to slowly deteriorate, leading to permanent and severe vision loss. The only approved treatment available for retinitis pigmentosa is a type of gene therapy that only works on the early stages of the disease. For those whose disease has progressed further, their vision loss is lifelong.

The retina is composed of several layers: a light-sensitive layer closest to the interior of the eye, a series of light-processing middle layers and a final ganglion cell layer at the very back, which is responsible for transmitting all this information to the optic nerve so it can be read by the brain.

Because retinitis pigmentosa only targets the upper, light-sensitive region of the retina, the researchers hypothesized that they could help restore vision using optogenetics, a relatively new medical technique that uses genetically modified neurons to improve light sensitivity.

"In optogenetic therapy, what we're using in this paper, we create an artificial photosensitive layer in this blind retina," Roska said. "We do this by taking light sensors from microbes and [delivering them] to the blind retina using gene therapy by an injection."

While optogenetics, which emerged in the mid-2000s, has proven useful for studying the biology of the brain and eyes, it poses a lot of challenges for clinical applications. Current optogenetic techniques involve the use of implantable electronic devices to provide light stimulation. This usually means an invasive surgery.

While the method the researchers employed is not completely noninvasive, as it does require an injection into the eye, the specialized goggles eliminate the need for an implanted device. This means a much easier procedure for the patient, compared with past techniques.

"I'm convinced that patients are going to use it because it's very simple surgery," said first author José Sahel, an ophthalmology professor at the University of Pittsburgh and Sorbonne Université.

For this trial, the researchers injected a harmless virus into one eye of the patient. The virus carried a gene encoding ChrimsonR, a light-sensitive protein, allowing the virus to implant this gene into the cells of the retina. After several months, giving the cells time to express the protein, the patient returned to the lab and put on the engineered goggles, which use cameras to translate the surroundings into light signals that ChrimsonR can receive.

After training him on the use of the goggles, the researchers put the patient through a series of tests to see if he could detect objects. When the patient had only one eye open — the eye that had received the injection — he perceived and counted objects in 63% of the trials, and was able to locate the objects by pointing in 58%. When the non-treated eye was tested, he was unable to perceive any objects, so could not even attempt to count or locate them.

"You can imagine that he was very excited," Sahel said, "maybe as much as we were. Everyone was excited!"

While the findings are a breakthrough in vision restoration, the researchers warn that it will be a long time before they are able to restore patients' vision entirely. The team explained that even with the treatment, this patient would not be able to read or recognize faces.

"For recognizing a face, you need a very high resolution," Roska said. "That is not yet possible using the approach we are using."

As the present study was a phase 1b/2a clinical trial, intended mostly to establish safety at effective doses, it could be years before the treatment is ready for widespread availability. However, the results are promising enough that the researchers are proceeding quickly to the next phase of trials, where they will work on validating the treatment in more patients.

"I would say in the next five years, potentially, this could be something that could be provided to many more patients," Sahel said. "The level of vision we are going to reach is impossible to predict at this stage … This is something which is early but going in the right direction."

The study, "Partial recovery of visual function in a blind patient after optogenetic therapy," published May 24 in Nature Medicine, was authored by José-Alain Sahel, Sorbonne Université, University of Pittsburgh, Centre

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