Team deciphers retina's neural code for brain communication to create novel prosthetic retinal device for blind

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(Medical Xpress) -- Two researchers at Weill Cornell Medical College have deciphered a mouse's retina's neural code and coupled this information to a novel prosthetic device to restore sight to blind mice. The researchers say they have also cracked the code for a monkey retina — which is essentially identical to that of a human — and hope to quickly design and test a device that blind humans can use.

The breakthrough, reported in the *Proceedings of the National Academy of Sciences* (*PNAS*), signals a remarkable advance in longstanding efforts to restore vision. Current prosthetics provide blind users with spots and edges of light to help them navigate. This novel device provides the code to restore normal vision. The code is so accurate that it can allow facial features to be discerned and allow animals to track moving images.

The lead researcher, Dr. Sheila Nirenberg, a computational neuroscientist at Weill Cornell, envisions a day when the blind can choose to wear a visor, similar to the one used on the television show Star Trek. The visor's camera will take in light and use a computer chip to turn it into a code that the brain can translate into an image.

"It's an exciting time. We can make blind mouse retinas see, and we're moving as fast as we can to do the same in humans," says Dr. Nirenberg, a professor in the Department of Physiology and Biophysics and in the Institute for Computational Biomedicine at Weill Cornell. The study's co-

author is Dr. Chethan Pandarinath, who was a graduate student with Dr. Nirenberg and is currently a postdoctoral researcher at Stanford University.

This new approach provides hope for the 25 million people worldwide who suffer from blindness due to diseases of the retina. Because drug therapies help only a small fraction of this population, prosthetic devices are their best option for future sight."This is the first prosthetic that has the potential to provide normal or near-normal vision because it incorporates the code," Dr. Nirenberg explains.

DISCOVERING THE CODE

Normal vision occurs when light falls on photoreceptors in the surface of the retina. The retinal circuitry then processes the signals from the photoreceptors and converts them into a code of neural impulses. These impulses are then sent up to the brain by the retina's output cells, called ganglion cells. The brain understands this code of neural pulses and can translate it into meaningful images.

Blindness is often caused by diseases of the retina that kill the photoreceptors and destroy the associated circuitry, but typically, in these diseases, the retina's output cells are spared.

Current prosthetics generally work by driving these surviving cells. Electrodes are implanted into a blind patient's eye, and they stimulate the ganglion cells with current. But this only produces rough visual fields.

Many groups are working to improve performance by placing more stimulators into the patient's eye. The hope is that with more stimulators, more ganglion cells in the damaged tissue will be activated, and image quality will improve.

Other research teams are testing use of light-sensitive proteins as an alternate way to stimulate the cells. These proteins are introduced into the retina by gene therapy. Once in the eye, they can target many ganglion cells at once.

But Dr. Nirenberg points out that there's another critical factor. "Not only is it necessary to stimulate large numbers of cells, but they also have to be stimulated with the right code — the code the retina normally uses to communicate with the brain."

This is what the authors discovered — and what they incorporated into a novel prosthetic system.

Dr. Nirenberg reasoned that any pattern of light falling on to the retina had to be converted into a general code — a set of equations — that turns light patterns into patterns of electrical pulses. "People have been trying to find the code that does this for simple stimuli, but we knew it had to be generalizable, so that it could work for anything — faces, landscapes, anything that a person sees," Dr. Nirenberg says.

VISION = CHIP PLUS GENE THERAPY

In a eureka moment, while working on the code for a different reason, Dr. Nirenberg realized that what she was doing could be directly applied to a prosthetic. She and her student, Dr. Pandarinath, immediately went to work on it. They implemented the mathematical equations on a "chip" and combined it with a mini-projector. The chip, which she calls the "encoder" converts images that come into the eye into streams of electrical impulses, and the mini-projector then converts the electrical impulses into light impulses. These light pulses then drive the light-sensitive proteins, which have been put in the ganglion cells, to send the code on up to the brain.

The entire approach was tested on the mouse. The researchers built two prosthetic systems — one with the code and one without. "Incorporating the code had a dramatic impact," Dr. Nirenberg says. "It jumped the system's performance up to near-normal levels — that is, there was enough information in the system's output to reconstruct images of faces, animals — basically anything we attempted."

In a rigorous series of experiments, the researchers found that the patterns produced by the blind retinas in mice closely matched those produced by normal mouse retinas.

"The reason this system works is two-fold," Dr. Nirenberg says. "The encoder — the set of equations — is able to mimic retinal transformations for a broad range of stimuli, including natural scenes, and thus produce normal patterns of electrical pulses, and the stimulator (the light sensitive protein) is able to send those pulses on up to the brain."

"What these findings show is that the critical ingredients for building a highly-effective retinal prosthetic — the retina's code and a high resolution stimulating method — are now, to a large extent, in place," reports Dr. Nirenberg.

Dr. Nirenberg says her retinal prosthetic will need to undergo human clinical trials, especially to test safety of the gene therapy component, which delivers the light–sensitive protein. But she anticipates it will be safe since similar gene therapy vectors have been successfully tested for other retinal diseases.

"This has all been thrilling," Dr. Nirenberg says. "I can't wait to get started on bringing this approach to patients."

The study was funded by grants from the National Institutes of Health

and Cornell University's Institute for Computational Biomedicine.

Both Drs. Nirenberg and Pandarinath have a patent application for the prosthetic system filed through Cornell University.

More information: Retinal prosthetic strategy with the capacity to restore normal vision, by Sheila Nirenberg and Chethan Pandarinath, *PNAS*, dx.doi.org/10.1073/pnas.1207035109

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