MedicalXpress

Researchers visualize the retina's function at the cellular level

September 10 2020, by Bobbi Nodell

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While there is no cure for blindness and macular degeneration, scientists have accelerated the process to find a cure by visualizing the inner workings of the eye and its diseases at the cellular level.

In an effort led by UW Medicine, researchers successfully modified the standard process of optical coherence tomography (OCT) to detect minute changes in response to light in individual photoreceptors in the living eye.

The results were published Sept. 9 in *Science Advances*.

"We have now accelerated the life cycle of vision restoration," said lead author Vimal Prabhu Pandiyan, a ophthalmology researcher at the University of Washington School of Medicine.

The study was funded in part by the National Eye Institute's Audacious Goals Initiative, which embraces bold ideas in helping people to see better.

The OCT modifications outlined in the study will help researchers who want to test therapies such as stem cells or gene therapy to treat retinal disease. They now have the tools to zoom in on the retina to evaluate whether the therapy is working.

Corresponding author Ramkumar Sabesan, a UW assistant research professor of ophthalmology, said the only way to objectively measure the eye currently is to look at a wide retinal area. Sabesan said researchers currently can attach electrodes on the cornea but it captures a large area with around 1 million cells. Now they are talking about nanometers, or one billionth of a meter—a small fraction of the size of a cell, providing orders of magnitude improvement.

"Since photoreceptors are the primary cells affected in retinal generation and the target cells of many treatments, noninvasive visualization of their physiology at high resolution is invaluable," the researchers wrote.

Cone photoreceptors are the building blocks of sight, capturing light and

funneling information to the other retinal neurons. They are a key ingredient in how we process images and patterns of light falling on the retina.

Optical coherence tomography has been around since the 1990s. In this study, researchers used OCT with adaptive optics, line-scanning and phase-resolved acquisition to deliver the concept of Thomas Young's interference to the human eye. With the ability to zoom in on the retina at high speeds, they found that cone photoreceptors deform at the scale of nanometers when they first capture light and begin the process of seeing.

As Sabesan explained: "You can imagine a picture that looks visually and structurally normal. But when we interrogate the inner working of the retina at a cellular scale, we may detect a dysfunction sooner than what other modalities can do. A doctor then can prescribe medication to intervene early or follow the time-course of its repair via gene therapy or stem cell therapy in the future."

"We will now have a way to see if these therapies are acting in the way they should," Sabesan said.

More information: Vimal Prabhu Pandiyan et al, The optoretinogram reveals the primary steps of phototransduction in the living human eye, *Science Advances* (2020). DOI: 10.1126/sciadv.abc1124

Provided by University of Washington