Photosensors in Retina Revived After Death

NEW YORK (Reuters Health) - Researchers revived light signaling in human donor eyes that were removed from the body up to five hours after death, and could restore synaptic transmission within the first hour.

The findings show promise for studying the physiology of human vision and to test drugs, retinal patch transplants and other strategies to treat retinal ailments.

"We found two key factors which were needed to restore both light-signaling and synaptic transmission in the retina after death: reversing the acidification in the tissue and restoring the oxygenation," Dr. Anne Hanneken of Scripps Research in La Jolla told Reuters Health by email.

"We were surprised to learn that the loss of light signaling and neuronal communication caused by acidification was completely reversible even hours after death," she said, "whereas the loss of synaptic transmission caused by hypoxia was irreversible several hours after death."

"What was even more surprising was that the immediate loss of synaptic transmission caused by hypoxia could be restored if the eye was replenished with oxygen and nutrients within 60 minutes after circulatory death," she added. "In these situations, the retina could respond to light in the same manner as a healthy eye."

As reported in Nature, Dr. Hanneken and colleagues first confirmed the swift decline of neuronal retinal function in mice, using a method called electroretinography to track the decline in the minutes after death. They then found that if they removed the mouse eyes after death, and restored oxygen and a normal pH balance within three hours, the retinas revived, showing light-responsive electrical activity in the macular photoreceptors, and evidence of

photoreceptor signaling to bipolar and retinal ganglion cells, which constitute the next stage of visual signal processing.

They performed similar experiments in human autopsied eyes and detected retinal signaling up to five hours after death, after oxygenation and de-acidification.

Additional experiments in macaque and human donor eyes showed that although restoration of light signaling was still possible about 45 minutes after death, synaptic transmission was not.

Dr. Julia Haller, Ophthalmologist-in-Chief at the Wills Eye Hospital in Philadelphia, commented on the study in an email to Reuters Health. "Vision scientists can now use functional human patch grafts from eyes with pre-existing retinal diseases as an alternative to animal models to study defects in visual chemistry and identify new drug candidates."

"We also see this (work) as advancing the day when retinal transplantation will be possible - something that is a 'Holy Grail' for those of us in the world of eye and vision research working to help blind patients," she said.

However, she noted, "Challenges for retinal transplantation are real and substantial. Major obstacles include integration of the graft into the host retina, synaptic regeneration, controlling for rejection, lack of perfusion, dislocation, and inflammation. There are still many steps before we get to that goal, but this was a giant leap for mankind!"

"For clinicians sharing their patients' frustration and despair as they progressively lose vision, with the resultant deterioration in quality of life and independence, my take-home message is one of encouragement," she added. "Take heart - this work gives us not only more hope of a cure, but also tools to help us to that goal. This is a landmark paper in the chronicle of vision restoration research. And it has far-reaching implications for treating neurodegeneration in general, throughout the body."

Dr. Cynthia Toth, Vice Chair of Clinical Research at the Duke Eye Center in Durham also commented in email, calling the work "a major advance in the study and care of retinal disease."

She also noted challenges, "such as the time window for rescue and improvements needed in control of myriad postmortem conditions to optimize recovery and maintain phototransduction and bipolar cell signaling."

"The team also raised questions that should be pursued in the future, such as what pre-existing conditions limit the utility of tissue, and how aged and diseased human photoreceptors - as in age-related macular degeneration or inherited retinal diseases - might be tested," she added.

"However, the results of this study open a new realm of human tissue-based research methodology using donor eyes," she said. "This has great potential for identifying relevant disease pathways, advancing therapeutic discovery and paving the way to retinal cell layer transplantation. Our patients regularly ask when an eye transplant could be performed. We now are one step closer to this goal, thanks to this team."

"As a retinal surgeon who treats both adult and pediatric retinal disease, I am personally excited that my answer to retinal/eye transplant can now be, 'not yet, but eye researchers are pushing us closer to this goal,'" Dr. Toth concluded.

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