Researchers uncover a critical early step of the visual process

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The key components of electrical connections between light receptors in the eye and the impact of these connections on the early steps of visual signal processing have been identified for the first time, according to research published today in *Science Advances* by The University of Texas Health Science Center at Houston (UTHealth).

To understand fully how the light receptors, called photoreceptors, impact the early stages of the process of vision, researchers have traditionally focused their attention on how two key sensory cells—rods and cones—convert elementary particles of light into electrical signals and how these signals are relayed to the brain through devoted circuits. Rods are used for night vision and cones are used for daytime and color vision. While it has been known for some time that electrical signals can spread between photoreceptors through cell connectors called gap junctions, the nature and function have remained poorly understood.

"This research will lead to a better understanding of how the retina processes signals from the rods and the cones in the eyes, in particular under ambient lighting conditions when both photoreceptor types are active, such as at dawn and dusk. This knowledge is currently missing and may have to be taken into consideration when designing photoreceptor or retinal implants to restore vision," said Christophe P. Ribelayga, Ph.D., co-lead author of the study and associate professor and Bernice Weingarten Chair in the Ruiz Department of Ophthalmology & Visual Science at McGovern Medical School at UTHealth.

Co-lead author Steve Massey, Ph.D., is professor, Elizabeth Morford Chair, and research director in the Ruiz Department of Ophthalmology & Visual Science at McGovern Medical School at UTHealth.

The coupling—or communication—between rods and cones in the retina is critical for understanding how the visual signaling process works.

What the researchers discovered, to their surprise, is that rods do not directly communicate with other rods and cones seldom communicate directly with other cones. Instead, the majority of signaling happens through communication between rods and cones. Researchers identified a specific protein called connexin36 (Cx36) as the main component of rod/cone gap junctions.

"We noted that every single rod has electrical access to a cone and that cone/cone gap junctions are very rare," Massey said. "We estimated that more than 95% of all gap junctions between photoreceptors are rod/cone gap junctions; they have the largest volume and the largest conductance. So, rod/cone gap junctions dominate the network of photoreceptors both in size and number."

To help researchers better understand how the photoreceptor network is organized, they developed genetic mouse strains for the work that were bred to eliminate gap junctions in either rods or cones.

"Our study has important implications," said Ribelayga. "Our data position rod/cone gap junctions as the keystone of the photoreceptor network. The rod/cone gap junction is the entry of a rod pathway through which signals of rod origin can travel across the retina. We have thus generated mice that are essentially deficient for the entry of this pathway. In future experiments, we will use these animals to determine the functional importance of the rod/cone pathway in the retinal processing of rod signals and for vision."

In 2018, researchers in the Ruiz Department of Ophthalmology & Visual Science received more than $4 million in grants from the National Institutes of Health's National Eye Institute to study photoreceptor development, function, and electrical interactions. Ribelayga and Massey led the effort to lay out the architecture of the network of electrically coupled receptors, a critical step toward a better understanding of how photoreceptors encode light signals and how the retina processes these signals.

More information: Molecular and functional architecture of the mouse photoreceptor network, *Science Advances* 08 Jul 2020: Vol. 6, no. 28, eaba7232, DOI: 10.1126/sciadv.aba7232 , advances.sciencemag.org/content/6/28/eaba7232

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