Regeneration of eye cells: Warning lights discovered

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Moving around in the half-light is difficult but not impossible. To help us in this undertaking we have the rods, a type of light-sensitive cells (photoreceptors) present in the retina of vertebrates, capable of detecting very low lights which allow us to move about even in poorly lit cellars or caves. These are biological wonders capable of detecting even a single

quantum of light, but they need continuous maintenance.

They are the protagonists of the new study published in *PNAS* by a team of researchers of SISSA—Scuola Internazionale Superiore di Studi Avanzati and the Istituto officina dei materiali of the National research council CNR-Iom which reveals new and essential details of how the retina works, and in particular its photoreceptors.

These consist of two segments: the outer segment (OS) and the inner segment (IS). The OS of the rods is the one where the biological machine capable of capturing the light is located, while the IS is responsible for the information to be transferred to the brain. "We have understood that the outer segment is more fragile than what was thought," comments Vincent Torre, neuroscientist of SISSA leading the team that conducted the research, who adds, "The OS consists of a stack of lipid discs containing the proteins responsible for phototransduction. New discs are generated at the base of the OS while used discs are removed at the tip of the OS. Traditionally, it was thought that in a stack of about 1000 discs there was almost perfect uniformity. However, our work shows that only the first 200 or 300 discs at the base of the OS are those effectively capable of detecting the single photon of light, characteristic from which comes the great sensitivity of the rods. The other discs positioned close to the tip gradually lose effectiveness and sensitivity and for this reason they must be disposed of and replaced with new discs in perfect condition."

It was calcium, an ion present in large numbers in biological processes that allowed the understanding of this mechanism. Its concentration in the OS is an excellent indicator of the functionality and integrity of phototransduction, the process with which the photoreceptors convert light into nerve signals. "With new optical probes we measured the concentration and the distribution of calcium in the OS. Using advanced optical microscopy instruments, we were able to study the distribution of

this metal with unprecedented resolution and accuracy," Dan Cojoc of Cnr-Iom explains "what has emerged from the analyses is that there is greater concentration of calcium at the base of the outer segment with respect to the tip, which helps to understand the structure of the rod showing its non-homogeneity, as was thought until now.

A second and no less important result is the discovery of spontaneous calcium flares, i.e. rapid increases in calcium. These flares are not evenly distributed but located in the tips of the OS, which shows the existence of a functional gradient along the OS, a fundamental property for photoreceptor transduction of all vertebrates," Cojoc concludes.

Like a warning light, the calcium flares indicate that the discs start to stop working at their best and need turnover.

Neuroscientist Gordon Fain of the University of California continues, "These differences can reflect an energy gradient that originates from the mitochondria of the inner segment. The authors of the study also make the amazing observation that calcium increases spontaneously both at the tip and at the base (but more often at the tip), as well as more rarely in the inner segment. These increases produce sudden flares, i.e. peaks of Calcium concentration, which decrease slowly for several seconds and which remain local without propagating inside the outer segment or between the inner and outer segment."

More information: Yunzhen Li et al, Calcium flares and compartmentalization in rod photoreceptors, *Proceedings of the National Academy of Sciences* (2020). DOI: 10.1073/pnas.2004909117

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