Study provides first anatomical, functional representation of the ocular surface in the central nervous system

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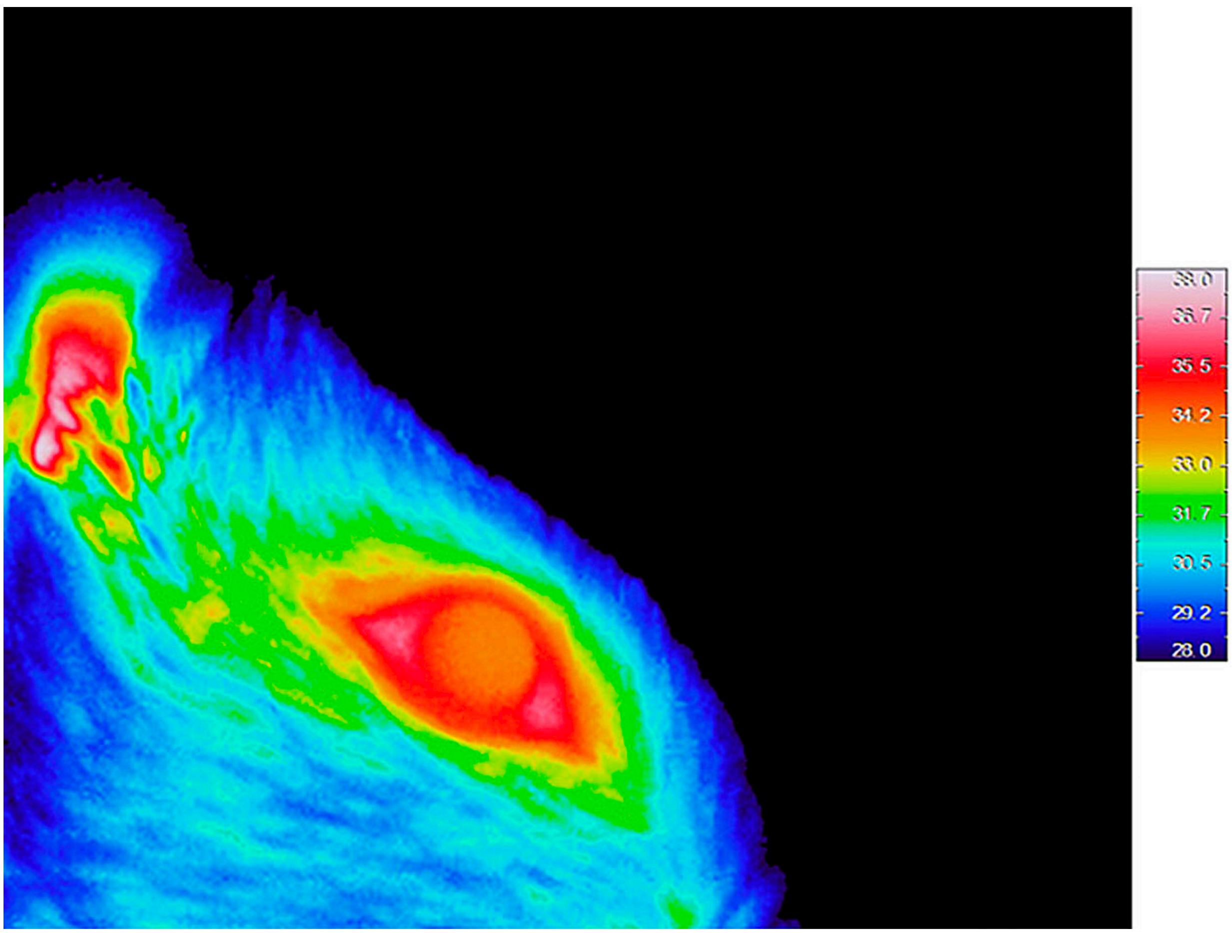

Infrared thermography image in an awake rat. The average temperature in the center of the cornea is 34°C. Credit: IN-CSIC-UMH.

Nerve fibers on the eye surface are involved in many relevant physiological processes, from detecting and transmitting external stimuli to maintaining the integrity of the cornea. However, research on the sensory system of the ocular surface has focused mainly on the peripheral axons of the trigeminal ganglia neurons, leaving information processing in the central nervous system unknown.

Now, a new study carried out by the Institute for Neurosciences (IN), a joint center of the Miguel Hernández University (UMH) of Elche and the Spanish National Research Council (CSIC), together with the National Hospital for Paraplegics-SESCAM of Toledo, has characterized, for the first time, the neurons of the thalamus and cerebral cortex that respond to stimulation of the ocular surface.

The work, published in *The Journal of Physiology*, reveals that along the somatosensory pathway, there are neurons capable of responding to different types of stimuli applied to the eye surface and that their functional diversity increases as progress from the peripheral system to higher levels of the central nervous system.

The eye surface is sensitive to external stimuli that cause discomfort, such as irritation, dryness, or a feeling of sand in the eyes. Although these are the most relevant symptoms of many ocular pathologies, little is currently known about the central nervous system circuits involved in these perceptions.

"Until relatively recently, ocular sensitivity and pain had not been the subject of attention because these symptoms barely existed in the field of ophthalmology," explains Juana Gallar, co-director of the Ocular Neurobiology Laboratory at the IN together with Mª Carmen Acosta, who also has participated in the study.

"It has been the arrival of some social changes such as the habitual presence of air conditioning in many places, the high levels of environmental pollution or the introduction of refractive surgery, which has led to focusing on this issue," says the researcher.

The study shows the precise location of the thalamic and cortical neurons that receive information from the ocular surface and analyzes how the activity caused by stimuli of different types is integrated, which is transmitted from the trigeminal sensory neurons to the thalamus and, subsequently, the cerebral cortex.

"Until now, the primary sensory neurons have been characterized, which are those in the trigeminal ganglion, but this is the first time that it has been analyzed which stimuli activate the neurons of the thalamus and the cerebral cortex," says researcher Enrique Velasco, first author of the article.

Multimodal neurons

The peripheral nerves found on the ocular surface are composed of axons of unimodal neurons, which respond to a single stimulus modality, and polymodal neurons, which respond to stimuli from several modalities. As the authors describe, there are different degrees of sensory multimodality, so there are neurons that activate in response to multiple modalities of stimuli and others that respond to a smaller number.

Researchers have discovered that, although in the peripheral nervous system, some sensory nerves act as detectors of a single class of stimuli, this unimodality is practically non-existent in the brain.

"In the detectors of our eye, cold, heat and touch are totally separate," says Velasco. "However, in the central nervous system we find neurons that respond to various stimuli, which tells us that information from the periphery converges as it progresses through the nervous system and is compared one with another to give rise to conscious sensations that we perceive when we are exposed to a stimulus."

Furthermore, investigators have observed that both the degree of multimodality of neurons and the percentage of highly multimodal neurons increase along the somatosensory pathway: it is lowest in the trigeminal, intermediate in the thalamus, and maximum in the cerebral cortex.

This distribution implies that different stimuli can activate the same neuron, and conversely, the same stimulus can activate many different neurons, so the perceptions they produce are intermixed.

"In the case of the skin, we can clearly distinguish between a cold, hot, mechanical, or other type of stimulus. However, in the case of the cornea, we are not able to describe the sensations with that precision. This happens because most neurons that are part of the somatosensory pathway of the ocular surface are multimodal and, therefore, the information collected by these receptors on the eye surface converges and is intermixed along the pathway," explains Gallar.

To carry out this study, the researchers used electrophysiology techniques, which allowed them to explore the physiology of tissues and synaptic connections in living beings. To observe trigeminal, thalamic, and cortical activity in response to different stimulation modalities, the authors took recordings of rats while they administered eye drops of different temperatures, which allowed them to test five sensory modalities: intense cold, light cold, neutral temperature, light heat, and intense heat, the later capable of causing a sensation of pain.

Regarding the evolutionary significance of these results, experts consider that "the high functional diversity of these ocular neurons in the cerebral cortex guarantees that any kind of stimulus that we receive in the eyes produces a conscious perception," says Gallar.

"This allows us to be alert regarding our eyes to be able to react quickly in the case of harmful stimuli and, in addition, launch fundamental mechanisms to protect vision, such as increased tear production and blinking itself. The flip side is that we can not differentiate the types of stimuli with precision, or define their exact location on the ocular surface."

Along these lines, Gallar explains that this diversity of neurons constitutes the basis of the very characteristic sensations that are perceived on the surface of the eye.

"When we feel discomfort on the ocular surface we usually say that we have 'something' in the eye (the so-called foreign body sensation), grittiness, dryness, etc., but generally we do not use the word pain, although in reality what we are doing is using different terms to describe the different kinds of discomfort and pain that the neurons on our ocular surface are capable of processing," says the researcher.

More information: Enrique Velasco et al, Ocular surface information seen from the somatosensory thalamus and cortex, *The Journal of Physiology* (2024). DOI: 10.1113/JP285008

Provided by Miguel Hernandez University of Elche