FROM COMFORT TO PAIN. NEURAL BASIS OF OCULAR SURFACE SENSATIONS

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The exposed surface of the eye is richly innervated by sensory nerve fibers originated at trigeminal ganglion neurons. They reach the cornea and bulbar conjunctiva as thin myelinated or unmyelinated nerve fibers lacking of morphological terminal specialization. However, electrophysiological studies have shown that sensory neurons innervating the eye are functionally heterogeneous. Based upon their response to specific stimuli, different functional types of sensory nerve fibers have been identified in the cornea and bulbar conjunctiva. Mechanonociceptor fibers (~20% of the total) react only to mechanical forces; polymodal nociceptor fibers (~70%) respond to mechanical forces but also to heat, exogenous chemical irritants and endogenous inflammatory mediators. Cold-sensitive fibers (~10-15%) display an ongoing impulse activity at basal corneal temperatures and increase markedly their firing frequency with moderate cooling. Differences in transduction capacity among ocular sensory fibers are attributable to the variable expression of different types of transduction channels (members of the TRP superfamily, ASICs, 2P domain K channels..) HCN channels and of voltage-dependent Na^+ K^+ and Ca^{2+} channels.

Under pathological conditions (inflammation, surgical injury, dryness of the ocular surface) activity of ocular sensory nerve fibers changes markedly as the result of short-term changes in ion channel expression secondary to local release of inflammatory agents and growth factors, and of long-lasting modifications in gene expression. This leads to the development of spontaneous activity and of abnormal responsiveness to natural stimuli.

Each of the functional types of corneal sensory fibers can be stimulated selectively in humans, using an instrument (the Belmonte esthesiometer) that delivers gas pulses of variable flow at neutral temperature (mechanical stimuli), CO2 concentrations (acidic stimuli) and cooled or warmed air at subthreshold flow levels (cold and heat stimuli) onto the ocular surface. Stimulation of the different functional populations of nerve fibers of the ocular surface evokes a specific quality of sensation that includes a variable component of unpleasantness. The relationship between activation of the different classes of ocular surface sensory fibers under normal and pathological conditions and the quality of the experienced sensation is now being elucidated.

In addition to their role in the production of conscious innocuous and noxious sensations referred to the eye surface, sensory fibers appear to play a role in the maintenance of the ocular surface homeostasis, including basal and reflex modulation of tearing and trophic maintenance of corneal and conjunctival tissues.

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