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Photophobia or thermophobia in dry eye

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The sensory nerves that are accountable for the sensation of the cornea originate from the ophthalmic division of the trigeminal ganglion. Around 20% of the nociceptors present in the cornea serve a vital function in transmitting intense and sharp pain sensations when there is mechanical contact with the ocular surface. Roughly 70 percent of the nociceptors present in the cornea respond to different chemical stimuli, such as acetylcholine, prostaglandins, and bradykinin, as well as heat and mechanical irritants. The rest of the receptors are sensitive to temperature. Most of the patients who have cornea pathological conditions complain of photophobia as one of the clinical signs. Photophobia is characterized by an elevated sensitivity of the eye to light in contrast to its usual reaction. Given that light is composed of various wavelengths, each containing a certain amount of thermal radiation energy, the term "thermophobia" might be a more suitable descriptor than photophobia. This paper presents novel findings on the perception of photophobia in cornea inflammatory conditions. It thoroughly explores the proposed neural pathway of photophobia in various neurological and eye medical conditions, shedding light on the potential underlying causes for patients experiencing photophobia, even when the exact cause remains undetermined.

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Фотофобия или термофобия при синдроме сухого глаза

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Резюме. *Чувствительные нервы, которые отвечают за чувствительность роговицы, берут начало в глазном отделе тройничного ганглия. Около 20% ноцицепторов, присутствующих в роговице, выполняют жизненно важную функцию по передаче интенсивных и острых болевых ощущений при механическом контакте с поверхностью глаза. Примерно 70% ноцицепторов, присутствующих в роговице, реагируют на различные химические раздражители, такие как ацетилхолин, простагландины и брадикинин, а также на тепло и механические раздражители. Остальные рецепторы чувствительны к температуре. Одним из клинических признаков у большинства пациентов с патологическими состояниями роговицы являются жалобы на светобоязнь. Светобоязнь характеризуется повышенной (по сравнению с обычной) чувствительностью глаза к свету. Учитывая, что свет включает спектр излучений с различной длиной волны, каждое из которых содержит определенное количество тепловой энергии, термин «термофобия» может быть более подходящим описанием, чем светобоязнь. В статье представлены новые результаты, касающиеся светобоязни при воспалительных состояниях роговицы. В ней подробно описывается предполагаемый нейронный путь светобоязни при различных неврологических и глазных заболеваниях, указываются основные потенциальные причины светобоязни у пациентов, даже если точная причина остается неопределенной.*

Ключевые слова: роговица, синдром сухого глаза, фотофобия, термофобия, воспаление
Конфликт интересов: отсутствует.
Прозрачность финансовой деятельности: автор не имеет финансовой заинтересованности в представленных материалах или методах.
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Pain information from the eye is transmitted by afferent fibers stemming from the ophthalmic (V1) segment of the trigeminal ganglion. The conjunctiva, cornea, sclera, and uvea are extensively innervated by trigeminal nerves and display a remarkable susceptibility to pain. Discomfort associated with orbital myositis is attributed to the nociceptive afferents that course through cranial nerves (CN) III, IV, and VI, originating from the extraocular muscles. The painful stimulus associated with optic neuritis is attributed to 5th cranial nerve afferents present in blood vessels and dura that surround the optic nerve. Sensory innervation from the trigeminal nerve to the blood vessels in the orbit contributes to the pain experienced during idiopathic orbital inflammation syndrome. Autonomic effectors densely innervate the orbital structures primarily utilizing the branches of the trigeminal nerve for their course. Activation of the trigeminal ganglion results in the release of mediators that trigger the trigeminovascular reflex, causing the dilation of cranial vessels innervated by the trigeminal nerve after exposure to a nociceptive stimulus. Another multisynaptic reflex, the trigeminoautonomic reflex is characterized by the activation of superior salivatory and Edinger — Westphal nuclei through collaterals originating from the trigeminal nucleus caudalis (TNC). The TNC mediates painful stimulus from head. Superior salivatory outputs activate lacrimation and pupillary constriction is regulated through the output signals originating from the Edinger — Westphal nucleus during occurring of a painful stimulus.

Within the human body, the cornea stands out as an exceptionally sensitive and richly innervated tissue. The preservation of the cornea and conjunctiva relies on the corneal nerves, which are responsible for generating reflex tears, blinking, and the secretion of neurotrophic factors. These combined actions are vital for maintaining the integrity of the ocular surface. As a result, reduced corneal sensitivity, corneal surface abnormalities, and potential vision loss can arise from damage to the corneal nerves caused by corneal diseases, injury, or surgery.

Sensory nerves responsible for the cornea's sensation have their origin in the ophthalmic division of the trigeminal ganglion. These nerves follow the course of the nasociliary nerve and long ciliary nerve, eventually dividing into nerve fibers that penetrate the cornea [1].The overlying corneal epithelium is supplied by the subbasal nerve plexus (SBNP), which is formed by the division and parallel arrangement of these branches between the basal epithelium and Bowman's layer on the superficial surface of the cornea [2]. Each sensory axon is associated with a considerable receptive field owing to the extensive branching of the corneal nerve fibers.

Due to the overlapping receptive fields, this organizational structure results in a reduced ability to accurately localize or discern stimuli. Nonetheless, it compensates for this deficiency by demonstrating an extraordinary level of sensitivity toward external stimuli [3].

Ocular dryness, discomfort, or pain can be perceived by the cornea due to its wide sensory nerve supply, which enables it to transduce different temperature, mechanical, and chemical stimuli [4].

The mechanoreceptors form about 20 percent of the cornea nociceptors that play a significant role in transmitting intense and sharp pain when there is mechanical contact with the ocular surface via the thinly myelinated Aδ type corneal nerves [5].

The majority, approximately 70 percent, of nociceptors in the cornea are polymodal in nature. These nociceptors utilize slow-conducting unmyelinated C type nerves to convey sharp and sustained pain responses. They are activated by various chemical stimuli, such as acetylcholine, prostaglandins, and bradykinin, as well as heat and mechanical irritants [6]. Aδ and C fiber cold receptors make up the remaining 10%. These receptors activate when the cornea is exposed to cold fluid or air after dryness of the cornea [7].

The condition of photophobia is defined as an increased sensitivity of the eye to light compared to its regular response. Is there a shared pathophysiological pathway of photophobia between iritis or ocular albinism and corneal inflammatory conditions?

The presence of photophobia in anterior uveitis can be attributed to the irritation of the trigeminal nerve caused by ciliary spasm. Conversely, light sensitivity in ocular albinism arises from the deficiency of melanin in the retinal pigment epithelium, leading to the internal reflection of light.

Most patients who seek medical attention for cornea pathology, such as dry eye or cornea ulcer, commonly report photophobia as a notable symptom.

On the other hand, a condition known as photo-oculodynia is an idiopathic chronic eye pain syndrome that presents with hypersensitivity and pain in response to light such as ambient illumination, despite the absence of any inflammation.

Remarkably, there have been documented instances of photophobia occurring in blind patients, despite their inability to form visual images [8].

The electromagnetic spectrum is a classification system that categorizes and organizes electromagnetic waves based on their different wavelengths and frequencies. This spectrum encompasses all the various types of electromagnetic radiation present in our universe, as illustrated in the figure below (Fig. 1).

Within the electromagnetic spectrum, the visible light range occupies a position between the wavelengths of infrared and ultraviolet. This range extends from 380 nm to 740 nm. Ultraviolet light is found below 380 nm, whereas infrared waves are situated above the 700 nm.

It is very important to distinguish between thermal and infrared radiation; thermal radiation encompasses electromagnetic radiation of all frequencies produced by the thermal emission process, whereas infrared radiation specifically refers to electromagnetic radiation within the frequency range of 0.3 THz to 400 THz, regardless of its origin.

The Venn diagram, conceptualized by the scientist John Venn, serves as a graphical tool to depict the emission of thermal radiation (Fig. 1). This diagram showcases the relationship between

visible light, ultraviolet light, and infrared light, highlighting the fact that all three types of light emit thermal radiation. Through this visual representation, Venn effectively conveys the interconnectedness and shared characteristics of these different forms of light. The presence of thermal energy can be observed in all wavelengths, each exhibiting a distinct percentage.

The incandescent bulb's brightness is predominantly in the infrared spectrum, with only a small fraction of its light falling within the visible range and minimal ultraviolet radiation. In the figure below (Fig. 2), the infrared carries the highest thermal energy.

Proposed neural pathways associated with photophobia. Several articles tried to explain the neural pathway of photophobia in corneal conditions such as dry eye. Photophobia and dry eye can be linked to the trigeminal nerve and its nuclei, particularly the nucleus caudalis [9].

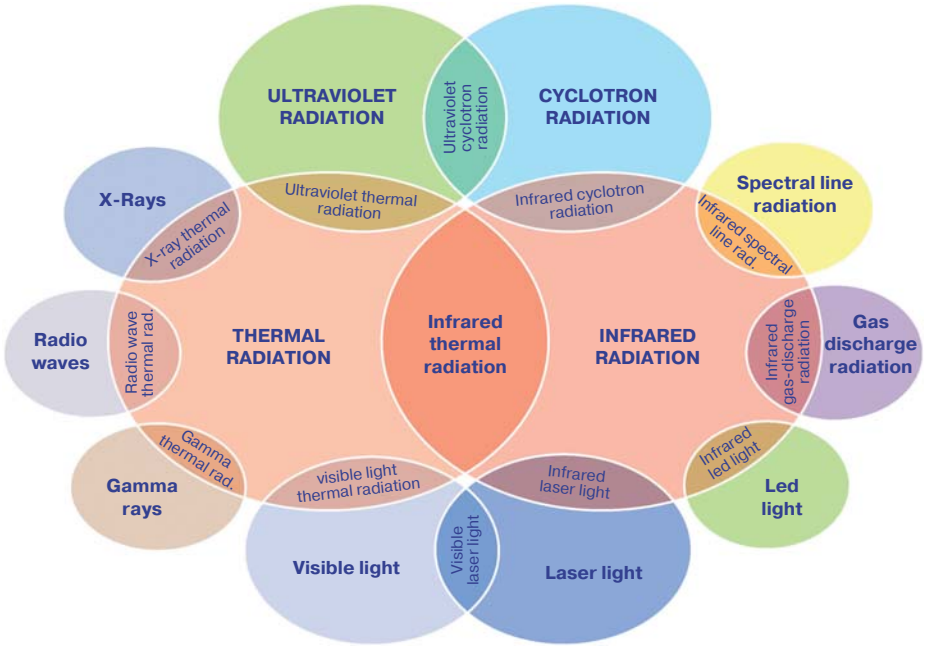

Fig. 1. Venn diagram
Рис. 1. Диаграмма Венна

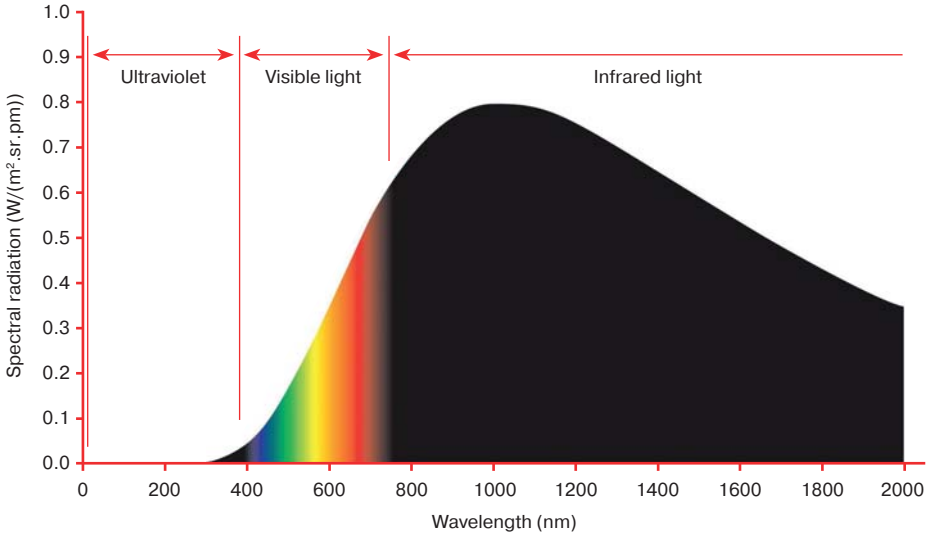

Fig. 2. Thermal radiation spectrum
Рис. 2. Спектр теплового излучения

1) The sensory input from the primary afferents in the ophthalmic division is consolidated in the trigeminal nucleus caudalis, which subsequently transmits this information to the central nervous system. From there, nociceptive sensation is projected through the parabrachial and thalamic nuclei, ultimately reaching the cortex and subcortical centers responsible for processing pain perception [10].

2) The investigation conducted by Noseda and colleagues identified a distinct second neural pathway, showing that a subset of intrinsically photosensitive retinal ganglion cells (IPRGCs) establish direct connections with thalamic nuclei that are not typically associated with vision. These specific nuclei are involved in somatosensation and pain [11].

3) The author proposes a neural pathway that incorporates the heat cornea receptors through the 5th cranial nerve. These receptors play a crucial role in transmitting the heat properties of electromagnetic wavelength as it is important to not ignore the other physical properties of light. It is suggested that this proposed pathway might overlap with the two pre-existing neural pathways. This might explain the cause of photophobia in blind individuals as reported before or the children and individuals in which specific diagnosis was not determined and complained of photophobia [12].

Dry eye is a multifaceted disease, wherein the tear film is persistently unstable and/or inadequate, resulting in discomfort and/or visual disturbances. This is further accompanied by variable degrees of damage to the surface of the eye, inflammation, and abnormalities in the sensory nerves. Various tests are accessible for evaluating dry eye, with fluorescein staining being the most prevalent method.

The composition of cornea stromal nerve trunks involves a multitude of axons, encompassing both myelinated and unmyelinated types. These axons, numbering between 900 and 1200, possess diameters that span from 0.5 to 5 μm [13].

The oblate nature of fluorescein molecules was deduced by examining their structure, revealing semi-axes of 7 angstrom and 2 angstrom. These dimensions were estimated based on bond length and van der Waals radii [14].

The limitation in the magnification capability of the slit-lamp may result in the failure to detect cornea staining, owing to the extremely small size of fluorescein molecules and the micrometer diameter of cornea nerve fibers. It is feasible for the patient to present with symptoms of dry eye, even if there are no apparent clinical manifestations such as cornea staining.

In a clinical setting, patients experiencing inflammatory cornea conditions, such as dry eye, often have a low tolerance for the intense white light emitted by the slit lamp. However, when a blue filter is introduced into the light pathway, the examiner can observe that

the patients exhibit a higher pain tolerance towards blue light compared to white light.

Regarding inflammatory conditions that affect the cornea, the author suggests that the patient complains of thermophobia which is an intolerance towards temperature rather than photophobia. Due to the cornea's temperature-sensitive nociceptors, thermophobia might be a more fitting term than photophobia in cornea inflammatory conditions. Additional investigation is needed to explore filters that block wavelengths associated with high levels of thermal radiation.

References/Литература

1. Marfurt CF, Kingsley RE, Echtenkamp SE. Sensory and sympathetic innervation of the mammalian cornea. A retrograde tracing study. *Invest Ophthalmol Vis Sci*. 1989 Mar; 30 (3): 461–72. PMID: 2494126.
2. Cruzat A, Qazi Y, Hamrah P. In vivo confocal microscopy of corneal nerves in health and disease. *Ocul Surf*. 2017; 15 (1): 15–47. doi: 10.1016/j.jtos.2016.09.004
3. Belmonte C, Acosta MC, Gallar J. Neural basis of sensation in intact and injured corneas. *Exp Eye Res*. 2004 Mar; 78 (3): 513–25. doi: 10.1016/j.exer.2003.09.023
4. Belmonte C. Eye dryness sensations after refractive surgery: impaired tear secretion or "phantom" cornea? *J Refract Surg*. 2007 Jun; 23 (6): 598–602. doi: 10.1016/j.exer.2003.09.023
5. Belmonte C, Giraldez F. Responses of cat corneal sensory receptors to mechanical and thermal stimulation. *J Physiol*. 1981 Dec 1; 321 (1): 355–68. doi: 10.1113/jphysiol.1981.sp013989
6. Steen KH, Reeh PW. Sustained graded pain and hyperalgesia from harmless experimental tissue acidosis in human skin. *Neurosci Lett*. 1993 May; 154 (1–2): 113–6. doi: 10.1016/0304-3940(93)90184-m
7. Acosta MC, Tan ME, Belmonte C, et al. Sensations evoked by selective mechanical, chemical, and thermal stimulation of the conjunctiva and cornea. *Invest Ophthalmol Vis Sci*. 2001 Aug 1; 42 (9): 2063–7.
8. Amini A, Digre K, Couldwell WT. Photophobia in a blind patient: an alternate visual pathway. Case report. *J Neurosurg*. 2006 Nov; 105 (5): 765–8. doi: 10.3171/jns.2006.105.5.765
9. Okamoto K, Thompson R, Tashiro A, Chang Z, Bereiter DA. Bright light produces Fos-positive neurons in caudal trigeminal brainstem. *Neuroscience*. 2009 Jun 1; 160 (4): 858–64. doi: 10.1016/j.neuroscience.2009.03.003
10. Digre KB, Brennan KC. Shedding light on photophobia. *Journal of neuro-ophthalmology: the official journal of the North American Neuro-Ophthalmology Society*. 2012 Mar; 32 (1): 68–81. doi: 10.1097/WNO.0b013e3182474548
11. Noseda R, Constandil L, Bourgeais L, Chalus M, Villanueva L. Changes of meningeal excitability mediated by corticotrigeminal networks: a link for the endogenous modulation of migraine pain. *J Neurosci*. 2010 Oct 27; 30 (43): 14420–9. doi: 10.1523/JNEUROSCI.3025-10.2010
12 Buchanan T, Digre KB, Warner JE. The unmet challenge of diagnosing and treating photophobia. *Journal of Neuro-Ophthalmology*. 2022 Mar 25; 42 (3): 372–7. doi: 10.1097/WNO.0000000000001556
13. Murphy PJ, Patel S, Kong N, Ryder RE, Marshall J. Noninvasive assessment of corneal sensitivity in young and elderly diabetic and nondiabetic subjects. *Invest Ophthalmol Vis Sci*. 2004 Jun 1; 45 (6): 1737–7. doi: 10.1167/iovs.03-0689
14. Pu Y, Wang W, Dorshow RB, Alfano RR. Picosecond polarization spectroscopy of fluorescein attached to different molecular volume polymer influenced by rotational motion. In: Proc. SPIE 8258. Organic photonic materials and devices XIV. 2012 Feb. 825818 (20). https://doi.org/10.1117/12.904692

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