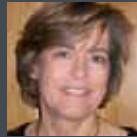


PHOTOSENSITIVITY AND BLUE LIGHT



BRIGITTE GIRARD
Associate Professor at the Paris
Hospitals College of Medicine
Tenon Hospital, France

__ **PHOTOPHOBIA IS THE PAINFUL SENSATION** felt by a patient on exposure to light. It is responsible for the reflex closing of the eyelids, which protects the retina from too much exposure to light rays, and particularly the sun's rays, due to the phototoxicity of light on the chorioretinal layers.

Photosensitivity occurs only within the spectrum of visible light. This sensorial information can be exacerbated and in this case we then refer to it as photophobia. Some diseases cause photophobia and it is seen as one of the symptoms. The most common diseases of this type affect the integrity of the eye or vision paths, such as corneal lesions, traumatic corneal ulcers, corneal abscesses or superficial punctate keratitis, which are common in all dry eye syndromes. Uveitis may also be mentioned here, along with retrobulbar neuropathy or extra-ocular conditions such as migraine or meningitis.

__ SPECIALISED GANGLION CELLS

Photophobia originates in specialised ganglion cells known as "ipRGCs" (intrinsically photosensitive retinal ganglion cells). At the current stage of research we do not yet know whether these cells sub-divide according to the wavelength presented. These ipRGCs are located in the retina's layer of ganglion cells. At the outset their axons take the same path as all the retinal nerve fibres and head towards the optic nerve. Their specific path has only recently been discovered, and is called the *non-visual path* of the optic nerve, which arrives at the posterior section of the thalamus or pulvinar^[6]. These *non-visual paths*, individualised using the techniques of Diffusion MR tractography provide an anatomo-physiological basis for the pain engendered by light. There are also nerve connections between the pulvinar and the nucleus of the trigeminal nerve which can explain photophobia in all ocular lesions that stimulate the ophthalmic branch of the trigeminal nerve. After direct connection by the optic nerve to the pulvinar, the route of the *non-visual path* connects the cortex, both visual (Brodmann occipital areas 18, 19, 20), parietal (association area, Brodmann area 7), frontal and pre-frontal. The connections of this *non-visual path* interact with motor and sensorial paths (olfactive). This *non-visual path*, activated by photic stimulation, acts on the excitation limit of the trigeminal neurones in the lateral posterior and posterior nucleus of the thalamus (rat) increasing the feeling of pain to light exposure in migraine. A functional IRM study^[8] has also shown an increase in pulvinar activity during central cerebral sensitisation (migraine), thus explaining photophobia. The pulvinar is divided into four areas, three of which (medial, superior and inferior) concentrate visual information^[3]. The pulvinar is therefore a major centre for the integration

and modulation of sensorial inputs, particularly those conveyed by the ipRGCs and the *non-visual path* which itself has connections with the suprachiasmatic nucleus (SCN), the habenula, the pineal gland, the intergeniculate leaflet (IGL) and the olivary pretectal nucleus (OPN). The latter is connected to the ciliary ganglion and to the Edinger-Westfal nucleus which is involved in photo-dependent pupil reflexes.

__ THE TOXICITY OF BLUE LIGHT

To protect itself from the harmful effects of high energy light radiation, nature has established numerous filters. A, B and some C ultraviolet rays, which have even higher energy than blue light, do not reach the retina because they are halted by the ozone layer, then the cornea and the crystalline lens. On the other hand, the various radiations of the visible spectrum of light do reach photoreceptors. The blue light wavelength has the most high-energy. It is located at between 400 and 510nm. It includes violets, indigo-blue and cyan (*fig. 1*). Blue light is absorbed by the yellow pigments of the crystalline lens (*fig. 2*), which gradually appear as age progresses (*fig. 3*) and in the retina by pigments, rhodopsin, lipofuscin and the macular pigments (lutein, zeaxanthin, meso-zeaxanthin). The photochemical reaction is responsible not only for phototransduction but also for the formation of free radicals during

Light energy:
 $E \text{ (eV)} = h \square$
 $\square \text{ (Hertz)} = 1 / \square \text{ (nm)}$

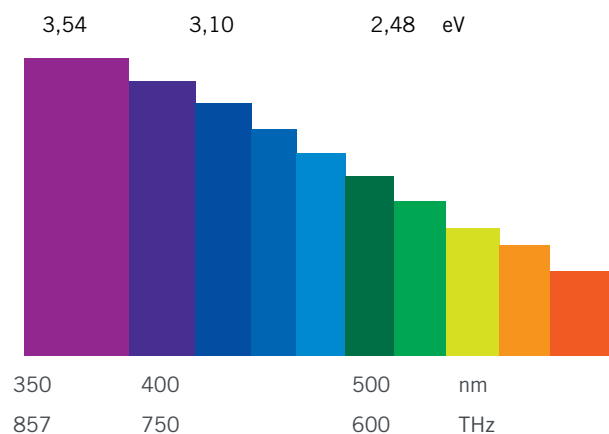


FIG. 1 | Photon energy depending on wavelength, within the visible light spectrum.

→ oxidative phenomena. These free radicals, which are ionic unstable, are toxic directly on cellular membranes and intracellular metabolites, causing a slow-down in retinal metabolism, non-renewal of the external articles of photoreceptors and their apoptosis. Photophobia is the retina's final protection against their oxidative phenomena, blocking the input of light by means of a blepharospasm (blinking) reflex.

Results in literature are still contradictory in stating the trigger role played by blue light in the genesis of AMD (fig. 4) and cataract, but a certain number of articles come down in favour of this hypothesis. The generations of yellow crystalline lens implants, which block out blue light, are the results of these scientific hypotheses. The debate is still open, but optical filters which block both UV and blue light are still more efficient. Blue light is however of major importance to the body, in addition to better scotopic perception by means of stimulation of the rods, there is also regulation of the circadian cycle and mood regulation^[5]. Melanopsin, the retinal pigment that absorbs blue, with an absorption peak of 480nm, controls the diurnal cycle via the *non-visual path* that stimulates the pineal gland directly as well as the secretion of melatonin^[7]. Changes in serum melatonin levels are responsible for sleep cycles and mood (photodependent or seasonal depression).

Photosensitivity is a natural phenomenon that gives humans their diurnal behaviour, with regulation of the internal biological clock. The ipRGCs mediated by the *non-visual path* control hormonal circadian cycles, sleep and mood. Photophobia triggers retinal protection against light energy and more particularly blue light, which has the most high-energy and is responsible for irreversible cellular lesions with apoptosis of the photoreceptors during photochemical mechanisms that release toxic oxidative residues. •

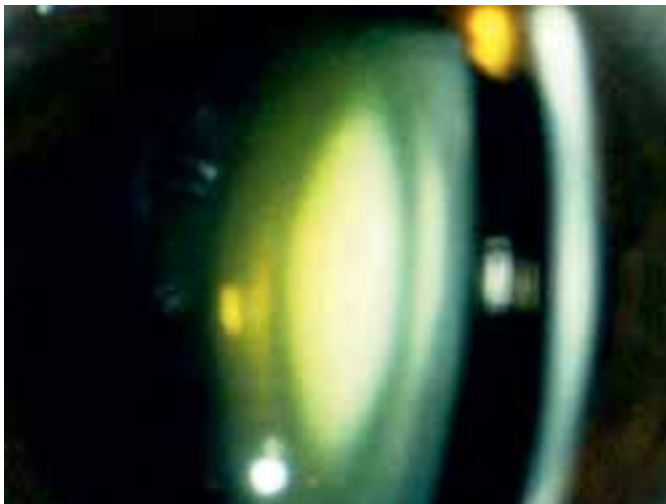


FIG. 2 | Natural ageing of the crystalline lens; cortical nuclear cataract.

Transparent at birth, the crystalline lens is gradually loaded with yellow pigments through the product of oxidation of the tryptophan and protein glycosylation; cataractogenic role of short wavelengths in the case of nuclear cataract: attenuation, followed by non perception of blues and violets. Protective role of the retina?

FIG. 3 | Light absorption in a phakic or pseudophakic patient.

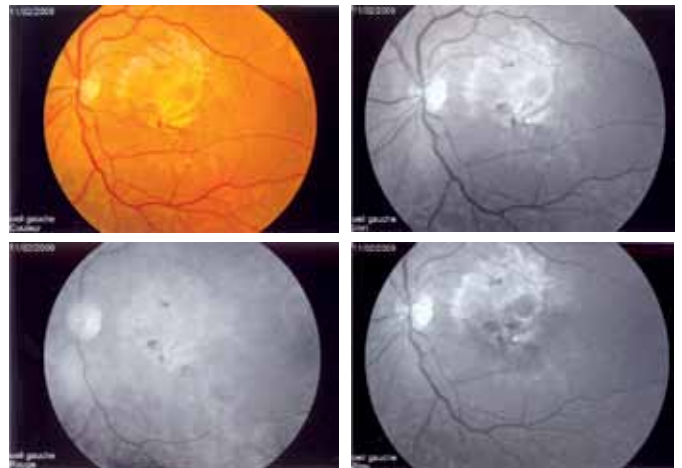
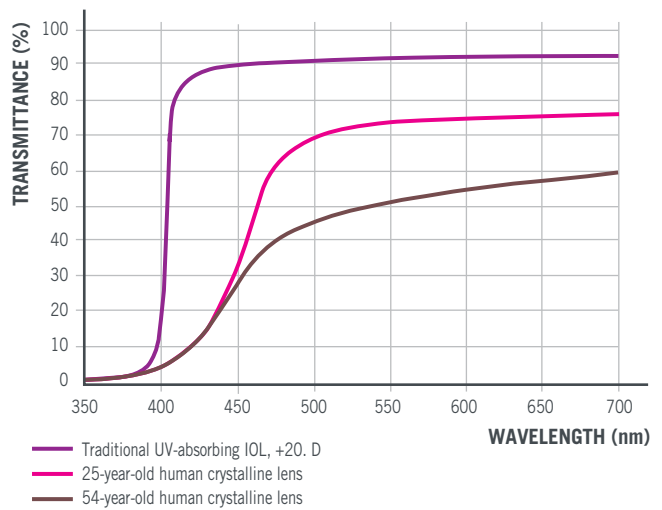


FIG. 4 | AMD.

Change in the pigmentary epithelium; cicatricial fibroglial appearance. Atrophy of the photoreceptors. Accumulation of lipofuscin and cellular deterioration products caused by the oxidative mechanisms of phototransduction.

REFERENCES

- Dillon J, Zheng L, Merriam J, Gaillard E.: Transmission of light to the aging human retina: possible implications for ARMD. *Exp Eye Res* 2004 Dec; 79(6): 753-9.
- Glazer-Hockstein C, Dunaief J.: Could blue light-blocking lenses decrease the risk of ARMD. *Retina* 2006; 26(1): 1-4.
- Grieve KL, Acuna C, Cudeiro J.: The primate pulvinar nuclei/Vision and action. *Trends Neurosci.* 2000;23: 35-39.
- Lane N.: To block or not to block-is blue light the enemy? *ESCRS-Eurotimes*, July 2007;12: 7.
- Mainster MA, Turner PL: Blue light : to block or not to block. *J Cataract Refract Surg today Europe* 1, May 2007;1-5.
- Maleki N, Beccera L, Upadhyay J, Burstein R, Borsook D.: Direct optic nerve pulvinar connections defined by diffusion MR tractography in humans: implications for photophobia. *Human brain mapping.* 2012; 33: 75-88.
- Munch M., Kobiakka S., Steiner R., Oelhafen P., Wirz-Justice A., Cajochen C.: Wavelength-dependent effects of evening light exposure on sleep architecture and sleep EEG power density in men. *Am J Physiol Regul Integr Comp Physiol*, 2006; 290: 1421-1428.
- Nosedá R, Kainz V, Jakubowski M, Gooley JJ, Saper CB, Digre K, Burstein R.: A neural mechanism for exacerbation of headache by light. *Nat Neurosci*, 2010;13: 239-245.