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Light damage to the retina: an historical approach

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Abstract

A brief review of retinal light damage is presented. Thermal damage requires a local rise in temperature of at least 10 °C, causing an instant denaturation of proteins. The primary absorber is melanin. Photochemical damage occurs at body temperature and involves cellular damage by reactive forms of oxygen. The photosensitizers are photoproducts of the visual pigments. First indications that non-thermal damage might exist, in particular in the case of eclipse blindness, was presented by Vos in 1962. Attribution thereof to photochemical action was presented in 1966 by Noell *et al* who also measured the first action spectrum, in rat. It turned out to be identical to the absorption spectrum of rhodopsin. However, in 1976 and 1982 Ham *et al* found a quite different spectrum in monkeys, peaking at short wavelengths. The latter spectrum, but not the former, was confirmed since in numerous publications with animal models including rat. In ophthalmological practice a 'sunburn' was at first the only complaint caused by light damage. To avoid this, patients with dilated pupils should always be advised to wear sunglasses. Since the invention of the laser accidents have been reported, the most recent development is youth playfully pointing a strong laser pen in their eyes with marked consequences. The operation microscope and endoilluminators should always be used as brief as possible to avoid photochemical damage. Arguments for implant lenses that block not only the UV but also part of the visible spectrum seem too weak to justify extra costs.
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Two main types of damage

Children might, on a sunny day, use a magnifying glass to burn a hole in a newspaper or to set fire to shoelaces. When grown up they naturally take it that people who lose their eye sight after prolonged staring in the sun have burned their retina. This concept, around since ancient times, survived until the 1960s. Vos[1] then calculated that the local rise in temperature of a human retina exposed to direct sunlight is only some 2°C , far too low to cause thermal damage. This rather restricted rise in temperature should be attributed to the pupil being fully constricted. With a dilated pupil the damage would indeed be thermal in nature and develop in a matter of seconds.[2] Protecting the retina against thermal damage is a very important, often overlooked, property of the pupil. An additional reason for the moderate rise of the local temperature is the significant cooling effect of the large blood flow in the choroid. Vos speculated about a 'metabolic overload' as the real cause for eclipse blindness. Extensive research on this topic started in 1966 after Noell published a breakthrough paper.[3] He exposed albino rats to long-lasting (>12 h) fluorescent light. Even without calculations, it is immediately clear that in such a condition the retina cannot be burned. A few years later it was shown that other species, including monkey, could also suffer from light exposures below the thermal threshold.[4,5] From that time on two main types of retinal light damage are distinguished, thermal and photochemical. In thermal damage the structure of proteins is corrupted by strong oscillations that break bonds between molecules. When boiling an egg, the change in protein from transparent to opaque is all too familiar. Photochemical damage involves cellular damage by supercharged molecules. The most familiar human photochemical damage is a 'sunburn' of the skin. Table 1 summarizes the main properties of the two types of retinal damage.[6,7]

For the sake of completeness a third type of light damage to the retina is mentioned here, photodisruption. This requires a pulsed laser often operating in the infrared. In ophthalmological practice a 1064-nm Nd-Yag

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Table 1 Properties of thermal and photochemical damage of the retina

Property	*Thermal damage*	*Photochemical damage*
Required rise in local temperature	>10 °C	None
Visibility of fundus change	Nearly immediate	Might take >12 h
Size	Larger than exposed spot and fuzzy edges by diffusion of heat	Confined to exposed spot, sharp edges
Exposure time in practice	<10 s	>10 s
Damage mechanism	Denaturation of proteins	Cellular damage by reactive forms of oxygen
Primary absorber	Melanin	Photoproducts of visual pigments
Threshold set by	Exposure time, spectrally weighted irradiance, field size	Dose: product of spectrally weighted irradiance and exposure time
Action spectrum	More or less flat	Peaking in the blue part of the spectrum

laser is used for surgery of the posterior lens capsule, the iris, vitreous strands, and occasionally, for retinal embolysis.[8]

History of action spectra

The action spectrum of retinal damage is first of all influenced by the spectral transmission of the eye media, with a window from 400 to 1200 nm.[9] At the short-wavelength side the cutoff wavelength shifts to longer wavelengths with increasing age, thereby offering increased protection. The thermal action spectrum set by absorption of light by melanin is nearly flat in the visible range. For photochemical damage the situation is quite different. Noell found in 1966 an action spectrum for albino rats identical to the absorption spectrum of rhodopsin. Harwerth and Sperling[4] succeeded in selectively damaging short-wavelength-sensitive (SWS) and middle-wavelength-sensitive (MWS) cone receptors by repetitive narrow band exposures close to the maximum sensitivity of the respective cone system. With these data an action spectrum cannot be calculated, but they suggest that the absorption spectrum of the cones has an important role. Ham *et al*[10] found, with exposures of up to 1000 s, that in monkey the action spectrum strongly peaked in the blue part of the spectrum, and with the lens removed, in the UV.[11] This photic damage is therefore often called the 'blue light hazard'. International standards for protection against light damage, drawn up in the 1980s, ignored Noell's spectrum, arguing that data on rhesus macaque were more relevant (personal communication with David Sliney). Yet, it later turned out that rats could also exhibited an action spectrum peaking in the short wavelengths.[12] Kremers and van Norren[13] tried to reconcile both spectra by distinguishing two classes of damage: one for relatively low level, long-lasting (>12 h) exposures and free running animals, with the Noell type spectrum, and one for relatively short, intense exposures, measured under anesthesia, with the Ham-type spectrum. What they overlooked at that time was that Noell measured his spectrum in the 'Ham conditions', relatively short (1.5–3 h) exposures and anesthetized rats. Recently, an exhaustive literature search covering the period 1966–2010 failed to find any data confirming the Noell spectrum, except one 1983 publication[14] of somewhat questionable quality.[15] Support for Ham's spectrum was found in 16 sources. An additional search in summer 2015 did not change that conclusion. Dose data for the earlier mentioned 1971 monkey experiments by Harwerth and Sperling[4] were not presented in the aforementioned literature search. Yet, these are interesting because the conditions were a mixture of those of Noell and Ham. Permanent SWS cone damage was achieved with 169 J/cm^2 at 463 nm (assuming a media transmission of 0.43) obtained in three series with 6-week intervals. A series consisted of 80-min exposures on 7 consecutive days. Temporary MWS damage was obtained by 520-nm exposures in 10 consecutive days with a total dose of 153 J/cm^2, and in another series in 6 consecutive days with a dose of 865 J/cm^2 (transmission 0.54). These data are in line with the mean single-session doses (thus without any repair during intervals) of the Ham-type spectra for monkeys/rabbits read from Figure 1b in the review, viz. 40 J/cm^2 for 460 nm and 500 J/cm^2 for 520 nm. Mean dose data for the two Noell type rat spectra as read from Figure 1a are two to three orders of magnitude lower.[15]

Thus, at the fiftieth anniversary of research on the photochemical action spectrum, we conclude that there exists only one consistently reproduced action spectrum for photochemical damage, viz. the one peaking at short wavelengths. It should be noted, though, that Noell's early conclusion that rhodopsin has a crucial role in photochemical light damage was right on target. Photoreceptors lacking rhodopsin in genetically modified mice are completely protected against light-induced cell death.[16]

Retinal light damage in ophthalmological practice

Retinal radiation damage must have been known since times immemorial, since prolonged staring at solar eclipses must have occurred time and again. Actually, in

Plato's Phaedo (99 d4–99 e1) Socrates is reported to have warned against eclipse blindness by advising to only look at the sun via reflection against water. Until World War II, the sun was virtually the only light source reported to produce retinal burn. The marked nuclear explosions above Hiroshima and Nagasaki not only produced inconceivable damage but also a 'nuclear flash' even more capable to produce retinal damage than the sun. It actually was this 'side effect' that brought Ham to start his lifelong study of retinal radiation damage.

The real impulse toward continued extensive research, however, came from the invention of the laser. It was immediately realized that a new branch of radiation protection was needed. The present ICNIRP internationally adopted guidelines are an example.[17] We presented more theory-founded alternative guidelines.[18,19] As its invention laser accidents have been occasionally reported, but the newest development are reports about children who expose themselves to their interesting new 'toy', a laser pen. A few decennia ago the output of red laser pointers was generally limited to a few not dangerous mW. Nowadays, pointers with outputs exceeding 100 mW are, unfortunately, easily purchased through the internet, or, for example, on a beach resort in the Mediterranean; the consequences might be disastrous.[20,21]

The newly developed light sources and techniques evidently should be of great concern to ophthalmologists. Traditionally, their task of course was to warn against solar blindness—not only at solar eclipses but also after conventional widening of the pupil, to wear sunglasses. A scientific basis for this advisory task can be found in our guest editorial in *Ophthalmic and Physiological Optics*.[22] A further task in this field did not fall on the ophthalmological profession, as curing retinal radiation damage was—and still is—no successful ophthalmological activity.

However, newly developed optical instruments and technology should ask the ophthalmologists' continuous attention to protect their patients against (additional) retinal damage. For instance, long exposures to the operating microscope might result into photochemical retinal damage to the patient, a phenomenon recognized since the eighties of the previous century.[23] The endoscope is potentially dangerous too, in particular due to the hardly accurately adjustable distance to the retina. The maximum exposure time, as defined by ICNIRP, is reached within a minute.[24] A filter that blocks the short wavelengths lengthens the maximum permissible exposure time but hampers color vision. A more extensive treatment of the subject is given by Wolffe.[25]

Implant lenses have since long a filter that blocks the UV part of the spectrum,[26] generally approaching the one in the crystalline lens of a newborn.[27] Ophthalmologists are presently confronted with the question whether this filter should be extended toward longer wavelengths, available in 'blue blocker' lenses. Proponents argue that it might provide, for example, extra protection against age-related retinal disease and improves chromatic aberration.[28] Opponents point out that positive effects are unproven that 'blue blockers' cause loss in scotopic vision and might have adverse effects on the circadian physiology by reducing the input to nonvisual photoreception.[29] A meta-analysis showed no advantages for visual performance.[30] At the moment blue blockers are more expensive in most countries. It therefore seems prudent to avoid the extra costs for filters extending into the blue until firm scientific evidence for advantages is available.

Prolonged staring in halogen lamps or in point source white or blue LEDs might lead to photochemical damage,[31] but the chance of a patient entering the clinic with such an anamnesis will probably be extremely low. Patients suffering from diseases affecting the visual cycle, such as Stargardt's dystrophy, Best disease, or Oguchi disease, should require extra care as they might suffer increased susceptibility to light damage, as was found in animal models.[7,32]

Continued research on photochemical damage is relevant because many open questions remain, only some of them treated in this limited review. An action spectrum for freely moving animals exposed to continuous light for one or more natural days, thus in the 'Noell conditions', is still lacking, and the search for the photosensitizers underlying the Ham-type action spectrum is far from complete. Peculiarly, an action spectrum for mice, about the most frequently used animal model, is not available.[15] New questions are risen after discovery of unexpected changes in images of the pigment epithelium after long exposures to yellow light,[7] and recently even after exposures to infrared radiation, argued to be photochemical in nature.[33] Moreover, photochemical damage can be used as a model for aging mechanisms. Prevention or repair of photochemical light damage might therefore lead to prevention or cure of damage by aging.[7]

Conflict of interest

The authors declare no conflict of interest.

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