Morphologic Comparisons Between Rhodopsin-Mediated and Short-Wavelength Classes of Retinal Light Damage

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The histologic manifestations of rhodopsin-mediated versus short-wavelength classes of retinal phototoxicity were compared after spectral exposures of the albino rat retina. Animals were exposed to wave-bands of light centered at the peak of rhodopsin absorbance (green, 500 nm) or in the ultraviolet A (UVA; 360 nm). Intensity-damage curves generated for each wave-band indicated that UVA light was 50–80 times more effective than green light at causing photoreceptor cell losses. Examination of early ultrastructural changes in rod inner segments, outer segments, and retinal pigment epithelium revealed a remarkable degree of similarity between UVA and green light-induced damage. Furthermore, the two classes of damage were indistinguishable in terms of post-exposure recovery from threshold damage and regional distribution of photoreceptor cell loss along the vertical meridian. The finding of essentially identical histologic manifestations for the two classes of damage raises the possibility that they share a common biochemical etiology or pathway of cell destruction. Invest Ophthalmol Vis Sci 33:3367–3377, 1992

Photochemical retinal damage refers to the degenerative changes in photoreceptor cells and retinal pigment epithelium (RPE) resulting from light exposures below the threshold for thermal injury. Two classes of photochemical retinal damage have been described, based on the chromophores thought to be mediating and the wavelengths of light they absorb. In one class, damage is initiated by rod and cone visual pigment absorption of visible light. In rats, the rod visual pigment rhodopsin has been implicated because the action spectrum of photoreceptor cell death and electroretinogram deficits closely corresponded to rhodopsin absorbance. Furthermore, numerous studies have shown that varied rhodopsin levels, because of experimental manipulation or inherent factors, are associated with differing susceptibility to light-induced degeneration in rats. In primates, evidence for cone visual pigment mediation of light damage was obtained by studies that documented selective sensitivity loss of two classes of monkey cones caused by exposure to narrow-band light.

The second class of photochemical damage is distinguished by an action spectrum peaking in the near ultraviolet. Originally, this type of phototoxicity was referred to as the “blue-light” effect because studies on rhesus monkeys showed the short-wavelength end of the visible spectrum to most effectively cause retinal damage. Blue light damage to the RPE actually may be an independent phenomenon. However, studies that used aphakic monkeys revealed that the wavelength of peak effectiveness at causing retinal damage extended into the near ultraviolet. Retinal damage by near-ultraviolet light also has been documented in subprimate species. Exposure to ultraviolet A has been shown to cause photoreceptor cell damage in mice, rats, and squirrels. Recently, a question of interest has been whether or not near-ultraviolet and rhodopsin-mediated light damage could be distinguished as separate mechanisms in a single animal species. Using funduscopic or histologic evaluation, retinal damage in pigmented rats was shown to occur at irradiance levels 50–100 times less for ultraviolet A (UVA) than for mid-visible (green) light. The UVA light used to cause damage was relatively ineffective at bleaching rhodopsin, indicating that mediation by this visual pigment was not involved. A subsequent study showed that albino and pigmented rats were equally susceptible to retinal damage by near-ultraviolet light. Considering the extensive documentation of rhodopsin-mediated damage in albino rats, these studies suggest that both of the two classes of damage can occur in the albino strain.

Only a limited number of studies have provided
information concerning the histologic distinctions, if any, between near-ultraviolet and visual pigment-mediated retinal light damage. Preliminary ultrastructural findings from our laboratory suggested that the two classes of damage differ regarding their site of initial insult. In the present study, UVA and mid-visible exposures were matched in terms of their ability to cause photoreceptor cell death and their histologic features were compared at different levels of damage severity. In contrast to expectations based on earlier studies, we report here that the two classes of light damage in rats have strikingly similar histologic characteristics in terms of post-exposure progression and recovery, initial sites of damage at the ultrastructural level, and regional distribution of photoreceptor cell loss along the vertical meridian.

Methods and Materials

Animals

Six- to seven-week-old female albino rats of the Sprague-Dawley strain were obtained from Charles River Breeding Laboratories (Wilmington, MA). They were housed in temperature-controlled rooms with a 12 hr light, 12 hr dark lighting cycle. The luminance inside their cages ranged from 1-30 lux with an average of 5 lux. The animals were acclimated to this environment for at least 1 wk, after which they were used for experimentation. All experimental procedures in this study conformed to the ARVO Resolution on the Use of Animals in Research.

Light Exposure

The light source used was a 300 W xenon arc with a stabilized voltage supply. All optical components of the light delivery system were made of fused silica to allow for maximal visible and ultraviolet light transmission. A collimated beam from the arc was modified with an infrared filter to eliminate heat and was modified with the appropriate combination of neutral density and bandpass filters to produce the desired intensity and spectral distribution of the exposure light, respectively. The filters used for spectral exposure were Oriel (Stratford, CT) 57560 interference filters (λ max = 500 nm, 70 nm bandwidth at 50% peak) for green light and a Schott (Oriel) UG1 colored glass filter (λ max = 355 nm, 80 nm bandwidth at 50% peak) for UVA. After it passed through the filters, the light was focused onto a 1.6 mm diameter fiber optic bundle, which was used to deliver light to the rat’s eye.

To prepare for exposure, the animal was dark-adapted overnight and anesthetized in dim red light by intraperitoneal injection of sodium pentobarbital (Abbott Laboratories, Chicago, IL) 50 mg/kg body weight. Drops of 0.25% scopolamine hydrobromide and 10% phenylephrine hydrochloride to dilate the pupil and 0.5% proparacaine hydrochloride for local anesthesia were applied to the corneal surface. The animal’s right eye was retracted with a speculum and the tip of the fiber optic bundle was positioned close (<1 mm) to the corneal surface of the eye. The bundle was aligned at a slight angle (approximately 10%) to the optical axis to direct the beam to the retinal region just inferior to the optic nerve head. The exposed (right) eye was regularly moistened during the exposure with a synthetic tears solution (Tears Renewed; Akorn, Inc., Abbott Springs, LA). A patch of black darkroom cloth was used to block light from reaching the left (nonexposed control) eye during the exposure. All exposures lasted for 30 min. After exposure, the animal was allowed to recover from the anesthesia and was returned to the 5 lux cyclic light environment. The irradiance of exposure light that fell on the corneal surface was measured with a United Detector Technology (Hawthorne, CA) model S370 radiometer calibrated from 200–1100 nm.

Light exposures also were performed on some animals to evaluate regional distribution of retinal damage. For these experiments, light from the xenon source was delivered to the animal’s eye via an Oriel model 70481 integrating sphere. The animal was prepared as described above, and its right eye was positioned in the plane of the 2° diameter exit port of the integrating sphere. Typical irradiance uniformity is within 1–2% of the average over this port. The interior of the sphere was coated with thorium sulfate, which provided a spectrally flat (±5%) reflective surface between 280–1500 nm. Light intensity and spectral bandwidth were modified with the same filters used for the fiber optic exposures. The duration of exposures with the integrating sphere ranged from 3–5 hr.

Light and Electron Microscopy

At post-exposure times ranging from 1–14 days, animals were given an overdose of sodium pentobarbital, and, after enucleation, whole eyes were immersed in 2.5% glutaraldehyde and 1% paraformaldehyde in 0.125 mol/l sodium cacodylate buffer, pH 7.35. All enucleations took place at 1.5 hr after the onset of the animal’s light cycle. The cornea and lens were dissected free and the superior half of the eye cup was trimmed off and discarded. For some eyes used to examine regional distribution of light damage, the peripheral one-third of the nasal retina was trimmed off instead so the sections along the vertical meridian could be obtained. The remaining tissue was fixed overnight at 4°C and post-fixed the next day in 1% osmium tetroxide in the same buffer for 1 hr at room temperature. After dehydration in a graded eth-
anol series and clearing in propylene oxide, the tissue was infiltrated with an Embed 812-Araldite plastic mixture (Electron Microscopy Sciences, Fort Washington, PA) and polymerized for 2 days at 65°C. For light microscopy, 0.5 μm sections were cut, dried on glass slides, and stained with 1% toluidine blue. For electron microscopy, 80–90 nm sections were floated onto copper mesh grids, stained with 5% uranyl acetate and 2% lead citrate, and examined on a JEOL (Tokyo, Japan) 100 CX electron microscope. All ultrastructural comparisons were made on groups with a sample size of three or more animals.

Morphometry

To estimate the amount of photoreceptor cell loss caused by light, outer nuclear layer (ONL) thickness was measured in the inferior retina tissue blocks. Sections for light microscopy were taken at the inferior edge of the optic nerve in the nasotemporal plane, thereafter at 200 μm intervals, moving through the block in the direction of the inferior ora serrata. Measurements were made using a Zeiss (Thornwood, NY) Videoplan computer in conjunction with a magnetically operated digitizing table and camera lucida. ONL thickness was measured at 20 loci, 240 μm apart, along the central 4.8 mm of each tissue section. This area made up more than two-thirds of the total retinal length and always included the damaged area, which was empirically found to cover 1.2–1.6 mm of the central inferior retina. To further ensure targeting of the damaged area (which varied slightly in retinal position), the 10 lowest of the 20 total values were selected for each section, averaged, and used for comparison among groups. For each exposure, the inferior retina section that exhibited the greatest decrease in ONL thickness and always included the damaged area, which was empirically found to cover 1.2–1.6 mm of the central inferior retina. To further ensure targeting of the damaged area (which varied slightly in retinal position), the 10 lowest of the 20 total values were selected for each section, averaged, and used for comparison among groups. For each exposure, the inferior retina section that exhibited the greatest decrease in ONL thickness also was used to determine the retinal expanse that exhibited complete photoreceptor and RPE cell loss. For each cell type independently, the number of fields without cells was measured using an eyepiece micrometer at 100×.

To determine the light intensities that would cause comparable levels of cell loss by green and UVA light, intensity-damage curves were generated. For each wave-band, animals were exposed to intensities empirically determined to range in effect from no change in retinal structure (as measured by ONL morphometry or ultrastructural observation) to those found to cause a greater than 60% decrease in ONL thickness. Regression lines fit to the data differed markedly in slope for the two wave-bands (P < 0.001: also see legend of Fig. 1). Based on extrapolation from the regression lines, light intensities that caused a 1% decrease in ONL thickness (i.e., threshold damage) were 100 μW/cm² and 5,000 μW/cm² for the UVA and green exposures, respectively.

At the lower end of the intensity range that caused damage, photoreceptor loss at 7 days post-exposure

Results

Intensity-Damage Relationships

At 7 days post-exposure, the percent decrease in ONL thickness was linearly related to intensity for 30 min exposures to UVA and green light (Fig. 1). However, the intensity range that caused ONL loss was 50–80 times higher for green than UVA exposures. Regression lines fit to the data differed markedly in slope for the two wave-bands (P < 0.001: also see legend of Fig. 1). Based on extrapolation from the regression lines, light intensities that caused a 1% decrease in ONL thickness (i.e., threshold damage) were 100 μW/cm² and 5,000 μW/cm² for the UVA and green exposures, respectively.

At the lower end of the intensity range that caused damage, photoreceptor loss at 7 days post-exposure

Fig. 1. Semilogarithmic plot of intensity–damage relationship for UVA (triangles) and green (circles) exposures. The index of retinal damage was percent decrease in ONL thickness, which reflects photoreceptor cell loss. The data were best fit by linear regression curves (dotted lines) representing the equations y = -93.28 + 0.29x: r = 0.93 for UVA and y = -18.22 + 0.0037x: r = 0.86 for green. The semilogarithmic plotting results in a curved shape for the fitted lines. Moreover, it shows that on a proportional basis, intensity–damage relationships are similar for UVA and green exposures.
Table 1. Retinal expanse at 7 days post-exposure showing complete loss of photoreceptor and RPE cells as a function of light intensity

<table>
<thead>
<tr>
<th>Wave-band</th>
<th>Light intensity (μW/cm²)</th>
<th>Retinal expanse showing complete cell loss (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UVA</td>
<td></td>
<td>ONL</td>
</tr>
<tr>
<td>200</td>
<td></td>
<td>180 ± 172</td>
</tr>
<tr>
<td>256</td>
<td></td>
<td>1101 ±322</td>
</tr>
<tr>
<td>320</td>
<td></td>
<td>1535 ±226</td>
</tr>
<tr>
<td>Green</td>
<td></td>
<td>RPE</td>
</tr>
<tr>
<td>12,500</td>
<td></td>
<td>359 ±311</td>
</tr>
<tr>
<td>16,000</td>
<td></td>
<td>490 ± 49</td>
</tr>
<tr>
<td>20,000</td>
<td></td>
<td>996 ± 102</td>
</tr>
</tbody>
</table>

Values shown are mean ± SD for a sample size of three animals.

was seen as a thinning of the ONL for both wavebands. With increasing intensity, a complete loss of photoreceptor and RPE cells occurred near the center of the exposed retinal area. This region of maximal damage increased progressively in size as a function of light intensity (Table 1). Three-way analysis of variance indicated that for both wave-bands, retinal lesion size depended on light intensity \( F(4,35) = 16.75; P = 0.001 \) but was unrelated to cell type \( F(1,35) = 0.0; P = 1.0 \). Thus, for all exposures, retinal expanse that exhibited complete cell loss was the same for RPE and photoreceptors. Ad hoc analysis revealed that lesions that resulted from 256 μW/cm² UVA and 20,000 μW/cm² green exposures were not significantly different in size \( P > 0.6 \), the combined group mean being equal to 1069 ± 208 μm. Likewise, percent decrease in ONL thickness was not significantly different between these two intensities \( P > 0.3 \), the combined group mean being equal to 57.11 ± 6.4%. This degree of damage was used to represent the severe level for comparing early ultrastructural changes from UVA and green light.

Recovery from Threshold Damage

Threshold exposures to green and UVA light caused damage to rod inner and outer segments that...
recovered over time. The characteristics of the damage and sequence of recovery were virtually the same for green and UVA exposures (Fig. 2). Relative to control retinas (Figs. 2A and G), damage at 1 day post-exposure included rod outer segment disc separation and rod inner segment vacuolization (Figs. 2B and H; also see Figs. 3 and 4). After 4 days, outer segments were shortened and disorganized, and an excessive number of phagosomes were present (Figs. 2C and I). Outer segments underwent further shortening at 6 days (Figs. 2D and J), but outer segment disorganization and inner segment vacuolizations mostly had recovered. Localized regions with unusually high numbers of phagosomes still were seen at this time.

Fig. 3. Electron micrographs of distal rod outer segments damaged by green (A, B) and UVA (C, D) exposures. Disc alterations at two levels of damage severity, that is, threshold (A, B) and severe (B, D) were indistinguishable between the two wave-bands (original magnifications, ×8000).
By 2 wk, most exposed retinas showed complete recovery of rod structure and were indistinguishable from controls (Figs. 2E and K). Even retinas that exhibited incompletely recovered damage after 2 wk (i.e., mild disorganization or pyknosis) resembled control morphology to a greater extent than any of the earlier time points (Figs. 2F and L).

Early Ultrastructural Changes in Photoreceptors and RPE

Figure 3 compares early (1 day) changes in rod outer segments resulting from 30 min green and UVA exposures at two levels of damage severity. Threshold damage was similar for both wave-bands and was seen as rod outer segment disc separation and vesiculation (Figs. 3A and C). Likewise, there was striking similarity between the green and UVA exposures in terms of the early rod outer segment changes of severely damaged retinas. For both wave-bands, rod outer segments were swollen and tortuous (Figs. 3B and D). Rod outer segment disks showed an unusual configuration of wave-like patterns and irregular spacing.

Similar characteristics of damage to rod inner segments were seen for green and UVA exposures (Fig. 4). Threshold damage for both wave-bands resulted in...
increased intercellular spacing (Figs. 4A and C) but no change in mitochondrial structure. Severe damage was characterized by rounding and inner membrane vesiculation of mitochondria. Large vacuoles and increased intercellular spacing also was observed (Figs. 4B and D).

No damage to RPE from the threshold exposures was observed, except for occasional vacuole formation (Figs. 5A and C). In severely damaged cells, numerous phagosomes, residual bodies, and vacuoles were observed (Figs. 5B and D). Some of the mitochondria had a rounded appearance. As was found for the photoreceptor cells, ultrastructural changes in the RPE could not be distinguished between green and UVA light damage.

Regional Distribution of Damage

Photoreceptor cell loss, as reflected by ONL thickness measurements, occurred nonuniformly along the vertical meridian for green and UVA exposures (Fig. 6). With 5 hr green light exposure, ONL thickness was reduced by as much as 85% relative to nonexposed controls in the central superior region of the retina. In contrast, there was no more than a 20% decrease in ONL thickness at any point along the inferior retina. UVA exposures produced a regional distribution of damage similar to that for green light. With 3 hr UVA exposure, reduction in ONL thickness was nearly twice as great at the retinal locus 960 μm superior to the optic nerve compared to a corre-

Fig. 5. Electron micrographs of basal RPE damaged by green (A, B) and UVA (C, D) exposures. As for rod inner segments, mitochondrial alterations (arrows) occurred with severe (B, D) but not threshold (A, C) damage with both wavebands (original magnification, ×17,300).
The corresponding region of the central inferior retina. With 5 hr UVA exposure, the retinal region that extended 480-1680 μm superior to the optic nerve incurred maximal damage (ie, complete loss of photoreceptor cells).

Discussion

Historically, classification schemes for photic retinal damage have used characteristics such as morphologic manifestations and action spectra to provide a meaningful basis for distinguishing damage types. In 1980, Noell18 described two kinds of light damage based on his rat studies. The "first" kind occurred in older animals, which were rendered relatively more vulnerable to damage by their higher body temperature during exposure and dark rearing. Morphologically, this kind of damage resulted in the destruction of photoreceptor and RPE cells. In contrast, damage of the "second" kind was observed in animals afforded some protection against light damage, such as rearing in weak cyclic light and exposure at a younger age. In this case, damage appeared as the selective loss of photoreceptor cells with the pigment epithelium spared. Exposure intensity also was a factor that influenced damage type, with RPE involvement being more prominent with brighter light. Experimental evidence from Noell's and other laboratories supported the idea that both kinds of light damage in the rat were mediated by rhodopsin absorption. In particular, the action spectrum for electrophysiologic changes and photoreceptor cell death corresponded to the absorbance curve for rhodopsin.2–4

Subsequent classification schemes that took into account the primate studies recognized a different type of damage produced most effectively by short-wavelength light.1–9 A number of studies have attempted to identify the distinguishing histologic characteristics of short-wavelength light damage. Ham et al12 compared structural changes in the retina after exposure of aphakic monkeys to blue (441 nm) or near-ultraviolet (325–350 nm) light that caused minimal fundusscopic lesions. At 2 and 5 days after near-ultraviolet exposure, there was evidence of severe damage to photoreceptor cells ranging from outer segment organization and ONL thinning to the focal eradication of photoreceptor cells. The RPE became hypopigmented but remained intact. Blue light caused the same RPE changes, but photoreceptors were only minimally affected and recovered over time. Schmidt and Zudich13 found that the photoreceptor cells were the primary site of damage from near-ultraviolet exposures with 325 nm laser light. In contrast, Li et al21 recently found that repeated exposure of aphakic or pseudophakic monkeys to low intensity, near-ultraviolet radiation damaged the RPE primarily. Using narrow-band exposure to visible wavelengths, Lawwill19 found that light damage consisting of mitochondrial swelling occurred to a similar extent in all retinal layers, with inner retina changes more prominent when shorter wavelengths were used.

Regarding comparison of rhodopsin-mediated and
short-wavelength classes of damage. These studies have at least two important disadvantages. First, differences in exposure parameters such as intensity, duration, and size of exposed retinal field likely play a role in determining the nature of resulting damage. Second, the two classes of damage typically were studied in widely divergent species: rhodopsin-mediated mechanisms in rats and short-wavelength in primates. Ham et al.\cite{12} did match all other aspects of exposure when they compared blue and near-UV light. However, whether or not the spectrally specific damage they observed represented different classes of damage could not be ascertained (except by ad hoc reasoning).

Recently, our laboratory developed a model for comparing rhodopsin-mediated and short-wavelength classes of light damage in a single animal species, the Long Evans rat.\cite{14} Anesthetized animals were exposed to wave-bands of light centered at the peak of rhodopsin absorbance (500 nm) or in the UVA (360 nm) to cause retinal damage. When the intensity of these lights was adjusted to cause equal photoreceptor cell loss, the rhodopsin bleaching efficacy of the green was more than two orders of magnitude higher than for the UVA, both in vitro and in vivo. This suggested that rhodopsin bleaching was not involved in the mechanism of UVA damage and that separate classes of damage were represented. A preliminary ultrastructural examination at 1 day post-exposure indicated that the outer segment disks were the initial site of green light damage, whereas UVA primarily affected the mitochondria. Unfortunately, the intensities of exposure light used for this comparison were not equated in terms of permanent retinal damage. With 4 hr exposures, the UVA intensity caused a 53% loss in ONL thickness compared to only a 10% loss for green.\cite{14}

The present study was an in-depth examination of the morphologic characteristics of green and UVA damage to the albino rat retina as a function of light intensity and damage severity. In accord with previous findings on Long Evans rats, the retina was exquisitely susceptible to damage by UVA light, requiring irradiances 50–80 times lower to cause permanent photoreceptor cell damage with this wave-band compared to green light. Measurements of cell loss at 7 days post-exposure indicated that the susceptibility of photoreceptors versus RPE did not depend on wave-band. For green and UVA light, a region of complete photoreceptor and RPE cell loss progressively increased with exposure intensity. Furthermore, at all intensities examined and for both wave-bands, the expanse of the lesioned area was nearly identical for photoreceptors and RPE. These findings suggest that, in terms of cell death, light damage to photoreceptors and RPE are closely linked for the rhodopsin-mediated and short-wavelength classes of phototoxicity in the rat.

The findings on intensity-damage relationships may be relevant to the classification scheme of Noell.\cite{18} Based on his criteria of RPE involvement, both UVA and green exposures used in the present study resulted in the first kind of damage with higher intensities and the second kind of damage with lower intensities. Because light history and body temperature during exposure were the same in all animals, both kinds of damage occurred independently of the influence of these predisposing factors. Thus, light intensity (and therefore damage severity) may be the primary determinants of damage "type." This concept is consistent with the fact that all factors that favored Noell's first kind of damage also were related to higher damage vulnerability.

To facilitate comparison of early post-exposure changes for green and UVA light, criteria for severity of permanent retinal damage were established. Threshold changes were defined as a 1% loss of photoreceptor cells at 7 days post-exposure, whereas a sizable (1069 μm) retinal lesion was chosen to represent severe damage. For threshold and severe levels, early (1 day post-exposure) ultrastructural damage to inner segments, outer segments, and the RPE was strikingly similar for green and UVA exposures. Particularly significant were the changes in outer segment disks and mitochondria. With threshold exposures to both wave-bands, outer segments showed disk separations, but mitochondria were unaffected. Severe damage was seen as marked disk disorganization and mitochondrial rounding and vesiculation. This mitochondrial change previously was attributed to UVA exposures specifically. However, when damage severity was equated for UVA and green exposures, there was no qualitative differences between wave-bands in the observed ultrastructural changes. Because the criterion for severe damage (measured at 7 days) represented complete cell loss in most of the region examined, the rounding of mitochondria at 1 day probably indicated a lethal change in the photoreceptor and RPE cells for both wave-bands.

Several studies have documented the capability of photoreceptors to recover from light damage.\cite{22-24} In general, damage to photoreceptor inner and outer segments that did not result in cell death was repaired over time. Accordingly, the present study found that damage caused by threshold exposures typically was repaired in a 2 wk period. Corresponding to the other histologic characteristics of light damage examined in this study, the sequence of recovery was found to be
remarkably similar for green and UVA exposures. Common features of recovery for both wave-bands included shortening of outer segments with excessive RPE phagocytosis between 4 and 6 days, and return of normal outer segment length and orientation by 2 weeks.

Previous work has shown that photoreceptor cell loss after exposure to diffuse “white” or green light occurs to the greatest extent in the central superior region of the retina. Using an integrating light sphere in the present study to produce exposures of uniform irradiance, decrease in ONL thickness caused by green exposures was most pronounced in a region centered at 960 μm superior to the optic nerve along the vertical meridian. This region of high susceptibility to light damage was located very close to, but slightly more central than that previously reported. When the integrating sphere was used to deliver UVA light, the region most severely damaged corresponded precisely to that found for green light. Thus, there appears to be no difference between rhodopsin-mediated and short-wavelength classes of light damage in terms of the regional susceptibility of photoreceptor cells.

The finding of essentially identical histologic manifestations for retinal damage caused by UVA and green light is somewhat difficult to understand considering the accepted evidence for separate damage mechanisms. Assuming that different chromophores mediate short-wavelength and mid-visible light damage, the initial site of insult should correspond to the cell compartment that contains the respective chromophores. Primary localization of green threshold damage to rod outer segments is consistent with the concept of rhodopsin mediation. Mitochondrial enzymes and rhodopsin bleaching products have been postulated to mediate short-wavelength retinal damage, but only the latter would be consistent with the early involvement of outer segments with UVA damage to the rat retina. If, however, mitochondrial enzymes located in rod inner segments are mediating UVA damage, the present observations suggest that a common histologic pathway of cellular damage exists for the two classes of damage that originates from two different cellular locations.

Is it possible that common histologic manifestations of the two light damage classes indicate a shared biochemical etiology? One possibility is that the mechanism of both UVA and rhodopsin-mediated retinal light damage is linked to lowered steady-state rhodopsin levels. Although UVA light is relatively ineffective at bleaching rat rhodopsin in vitro, recent findings showed that after a 45 min threshold damaging exposure, rhodopsin levels were lowered to less than 10% of their dark-adapted level. Because this decrease in rhodopsin preceded any observable morphologic retinal damage, it may have been a causative factor. A second possibility is that both classes of damage are mediated by the same chromophore. The action spectra for funduscopically induced damage to the monkey and rat retina show a steadily rising susceptibility to damage as a function of decreasing wavelength throughout the visible and near ultraviolet. This suggests that if a single pigment were involved, its maximal absorbance would be in the ultraviolet. However, the idea of single pigment involvement contradicts an abundance of experimental evidence that suggests at least one kind of light damage to the rat retina is rhodopsin-mediated. Further investigation will be required to sort out the mechanisms responsible for the spectral dependence of photic retinal damage.

Key words: photoreceptor cell, retinal light damage, retinal pigment epithelium, rhodopsin, short-wavelength, ultraviolet

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References