Macular Pigment and Visual Performance in Glare: Benefits for Photostress Recovery, Disability Glare, and Visual Discomfort

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Purpose. One theory of macular pigment's (MP) presence in the fovea is to improve visual performance in glare. This study sought to determine the effect of MP level on three aspects of visual performance in glare: photostress recovery, disability glare, and visual discomfort.

Methods. Twenty-six subjects participated in the study. Spatial profiles of MP optical density were assessed with heterochromatic flicker photometry. Glare was delivered via high-bright-white LEDs. For the disability glare and photostress recovery portions of the experiment, the visual task consisted of correct identification of a 1° Gabor patch's orientation. Visual discomfort during the glare presentation was assessed with a visual discomfort rating scale. Pupil diameter was monitored with an infrared (IR) camera.

Results. MP level correlated significantly with all the outcome measures. Higher MP optical densities (MPODs) resulted in faster photostress recovery times (average $P < 0.003$), lower disability glare contrast thresholds (average $P < 0.004$), and lower visual discomfort ($P = 0.002$). Smaller pupil diameter during glare presentation significantly correlated with higher visual discomfort ratings ($P = 0.037$).

Conclusions. MP correlates with three aspects of visual performance in glare. Unlike previous studies of MP and glare, the present study used free-viewing conditions, in which effects of iris pigmentation and pupil size could be accounted for. The effects described, therefore, can be extended more confidently to real-world, practical visual performance benefits. Greater iris constriction resulted (paradoxically) in greater visual discomfort. This finding may be attributable to the neurobiologic mechanism that mediates the pain elicited by light. (*Invest Ophthalmol Vis Sci.* 2011;52:7406–7415) DOI:10.1167/iovs.10-6699

Visual performance can be greatly compromised when glaring light enters the visual field. This is especially true of central vision, where intense light imaged onto the fovea tends to cause the most discomfort and disability, compared with the para- and perifoveal regions of the retina.[1–3] Intense, glaring lights in the periphery, however, can be strongly scattered by the ocular media over the fovea, which results in reduced contrast for objects viewed centrally.[2] This phenomenon is referred to as disability glare and is often experienced while viewing oncoming automobile headlights. Because the fovea yields the highest visual performance for nearly all parameters of vision, any factor that negatively impacts its function (i.e., glare) will result in noticeable decrements in visual performance. Conversely, any factor that promotes or protects foveal function would seemingly have noticeable visual performance benefits. Based on recent empiric evidence, it appears that the macular pigment (MP) could be such a factor.

The MP is a yellow, diet-derived pigment that is deposited anterior to the sensory retina, in the photoreceptor axon layer of the Henle and inner plexiform layers of the macula.[4] MP is distributed in a radially symmetric fashion about the center of the fovea, and, in most subjects, its optical density (MPOD) decreases exponentially with increasing eccentricity from the center of the fovea.[5,6] There are, however, exceptions.[7] MP is composed primarily of two dietary carotenoids: lutein (L) and zeaxanthin (Z).[8] In addition, meso-zeaxanthin (MZ), a stereoisomer of zeaxanthin that is converted from L in the retina,[9] makes up roughly 25% of the MP.[10] The molecular structures of L, Z, and MZ enable them to effectively protect biological tissue in two ways. First, by virtue of their carbon-conjugated double bonds, these carotenoids can quench the energy of damaging singlet oxygen and other free radical oxygen species.[11] Second, L, Z, and MZ (which are yellowish) selectively absorb high-energy, potentially damaging short-wavelength (blue) light.[12] On absorption, the energy is dissipated as heat. From the available data, the two roles (antioxidant and short-wave light filter) played by the retinal carotenoids appear to protect the macula from acute damage,[13] protect against cumulative damage resulting in age-related macular disease,[14] and maintain visual sensitivity over a lifetime.[15] L and Z are found in many colored fruits and vegetables, but tend to be most dense within leafy green vegetables such as spinach and kale.[16] Because of its exclusive dietary origin, MP density varies significantly among subjects: Those with diets rich in foods containing high amounts of L and Z tend to have higher densities of MP than do those with L- and Z-deficient diets.[17] The variation found among subjects in MP optical density (MPOD) is not trivial. Many studies have characterized samples in which subjects range from 0 to well over 1 log unit of MPOD.[5,18,19] Of the 20 or so carotenoids found circulating in human serum, only L and Z are found in the retina, and their concentration there is the highest level of carotenoid in any tissue in the body. In fact, the concentration of L and Z in the fovea is roughly 10,000 times greater than that of the blood,[10] which is indicative of active, continuous transport and deposition in retinal tissue.

The specificity of the location of L and Z in the fovea is conspicuous. As noted above, the fovea is critical for optimal visual performance, and so it makes sense that a substance

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with beneficial biochemical and absorptive properties would be present there to protect the retina and potentially improve performance. Until recently, the dominant hypothesis regarding MP's existence in the fovea involved its potential to reduce the blurring effects of chromatic aberration via absorption of short-wave light.[20–24] Although the spectral absorption properties of MP are well suited for this purpose, a recent study determined no relationship between MP levels and gap or hyperacuity.[25] It appears that any acuity advantage gained by higher levels of MP is offset by a commensurate reduction in luminance (which correlates positively with acuity[26]). It has also been suggested that MP could enhance the contrast of objects on a background via color filtering.[21,27] This hypothesis was recently tested and found to be tenable (Renzi L, et al. *IOVS* 2009;50:ARVO E-Abstract 1703).

An alternative hypothesis, first proposed by Schultze in 1866,[20] is that MP serves the function of reducing the adverse visual symptoms associated with glare (e.g., visual discomfort). Previous work has demonstrated that subjects with higher MP levels tend to experience less visual discomfort on exposure to intense light,[3,28,29] are less affected by disability glare,[29] and recover visual sensitivity faster after exposure to intense light (i.e., photostress recovery).[29] In addition, Stringham and Hammond[19] supplemented their subjects with 12 mg of L+Z over 6 months' time and showed within-subject increases in MPOD and commensurate improvements in disability glare and photostress recovery. Recently, however, Loughman et al.[30] found no relationship between MP and disability glare and photostress recovery, probably because of the glare conditions used in their study. For example, the glare source for the photostress recovery test was a tungsten lamp, which contains very little short-wavelength energy. In fact, the spectrum of the source published by Loughman et al. indicates that less than 10% of the energy of the lamp was accounted for by the wavelength range from 400 to 500 nm (most strongly absorbed by MP). Therefore, differences in subjects' MP levels should not have been expected to yield significant differences in photostress recovery times.

Many of the aforementioned studies produced convincing, convergent data. Most of the studies, however, used Maxwellian-view optics, and therefore ecological validity was limited. In Maxwellian view all the light from the optical system is typically focused to a small point (usually a 1 to 3 mm in diameter) in the plane of the pupil. This effectively disables the ability of the iris to modulate the amount of light reaching the retina. Because the study of visual performance in glare is strongly dependent on the amount of light reaching the retina, accounting for the effects of pupil size is vital, especially in consideration of real-world glare effects. To address this concern, we used a free-view stimulus delivery system to assess the effects of MP on visual performance in glare, in subjects with a wide range of MPOD.

Methods

Subjects

Twenty-six subjects, aged 23 to 50 years (mean, 31.7 ± 7.3 [SD]) participated in the study. Twenty-one of the subjects were men. Twenty-one were white, two were African-American, two were Latino, and one was of Asian descent. All subjects had uncorrected or contact lens-corrected binocular visual acuity of 20/25 or better and had no current or previous history of ocular disease. The subjects' iris pigmentation density was graded according to Seddon et al.[31] Pupil diameter was assessed for three viewing conditions: while viewing low- and moderate-brightness backgrounds, and during glare source presentation. Pupil diameter was determined with a calibrated infrared (IR) pupil-viewing camera. Each of the subjects participated in the three experimental sessions, detailed below. They were recruited from the population of active duty personnel, civilians, and contractors at Brooks City-Base Optical Radiation Branch in San Antonio, Texas. Informed consent was obtained from each subject, and the study adhered to the tenets of the Declaration of Helsinki. The study was approved by the Institutional Review Board of the Air Force Research Laboratory.

Measurement of Macular Pigment

To obtain subjects with a wide range of MPODs for use in the glare experiments, 52 candidates were screened. Based on the results of the screening, 26 with MPOD (at 0.50° eccentricity) ranging from 0.07 to 0.94 were selected to participate in the glare experiments. Before glare testing, spatial profiles of MPOD were assessed with heterochromatic flicker photometry (HFP), using a densitometer (Macular Metrics Corp., Rehoboth, MA) slightly modified from the one described by Wooten et al.[32] MPOD at 0.25°, 0.50°, 1°, and 2° retinal eccentricity was measured in the right eye of each subject. The modified instrument, measurement procedures, and the principle of HFP have been fully described in earlier publications.[33,34] Briefly, the subjects are presented with two superimposed lights that are temporally alternated in square-wave counterphase. One of the lights is chosen to bypass the absorption of MP (e.g., 550 nm), and the other is strongly absorbed by MP (e.g., 460 nm). The subject's task is to adjust the relative radiance of the two lights until a percept of no flicker is achieved. All other factors being equal, a subject who requires more short-wave (i.e., 460 nm) relative to middle-wave (i.e., 550 nm) light to achieve null flicker has higher MPOD. This task is performed for desired locations (e.g., those listed above) within the fovea, which presumably contain MP, and for a reference location in the parafovea (usually ~7° eccentricity). To obtain a measure of MPOD at a given test locus, the logarithmic ratio of short- to middle-wave radiance (for null flicker) at the reference location is subtracted from the corresponding logarithmic ratio found at the test locus. Because individual differences in temporal sensitivity[35] and light transmission of the ocular media[36] can influence the variability of subject responses during HFP, best results are achieved by customizing the HFP task for each subject. The primary means of customization is adjusting the frequency of the flicker, to obtain a narrow perceptual null zone (where the stimulus does not appear to flicker), and thereby a more accurate and less variable estimate of null flicker. Stringham et al.[37] describe this procedure in detail. In short, a subject's critical flicker fusion threshold is used to determine the flicker frequency for the HFP task. Furthermore, fine frequency adjustments can be made to compensate for situations involving a lack of a perceptual null or a null zone that is determined to be too wide. Twenty minutes were necessary to obtain a subject's MP spatial profile. MP spatial profile measurement was conducted before the photostress recovery/visual discomfort session (described below).

Glare System Apparatus

The subjects were seated 6 feet from a projection screen (DA-Lite, Warsaw, IN) on which the background and target stimuli were presented. They viewed the background and target fields through a beam splitter, which served to reflect the glare sources: two high-bright-white LEDs (Model LXHL LW6C; Luxeon Corp., Randoph, VT) mounted in 1-in. optical tubes. These LEDs have a color temperature of 6500°K, roughly equivalent to sunlight. Relevant to MP absorption, the emission spectrum for the LEDs exhibits a large peak centered at approximately 440 nm (strongly absorbed by MP), along with a broader emission band in the mid- to long-wavelength region of the visible spectrum. The LEDs appear white, with a tinge of blue (similar to xenon lamps). Each LED was mounted in the bottom of a 6-in. tube, along with three other optical components: (1) a 10° holographic diffuser, which served to make the glare image homogenous; (2) an adjustable circular iris, which defined the glare source size of 5°; and (3) a positive lens, which served to focus the glare light such that it was the same optical distance from the subject as the projection screen.

This reduced the probability of accommodation problems when the subjects were presented with both the target and glare fields. The two tubes were mounted in front of and below the subject's eyes, pointing straight upward and, as mentioned above, reflected off of a beam splitter onto the subject's eyes. The diameter of the light beam was 1.5 in. in the plane of the eyes and completely filled the subject's eye socket area. The LEDs were driven at 700 mA with a stable DC power source (Model HY3010E; Mastech, San Jose, CA). Coupled with the optics, each glare field produced a luminance of 10,000 cd/m^2.

The background and target stimuli were projected onto the aforementioned screen (XGA Powerlite 1716; Epson, Long Beach, CA). A Cambridge Research Systems visual stimulus generator (Rochester, UK) was used (via LabView software; National Instruments Corporation, Austin, TX), to present the background and target stimuli. The background field was an achromatic gray, and the target stimulus was a circular Gabor patch. The Gabor patch was configured such that the average luminance of the spatial sine wave pattern was equivalent to the background luminance level. This ensured that the Gabor "blended" into the background and eliminated edge effects. There were two background luminance levels used in these experiments, 5 cd/m^2 (low) and 27 cd/m^2 (moderate). The background field and Gabor patch target subtended 40° and 1° of visual angle, respectively. The subjects were tested with two Gabor patch spatial frequencies, 4 cyc/deg, which is near the peak of the human contrast sensitivity function, and 10 cyc/deg (roughly half the sensitivity of that found at 4 cyc/deg). The background luminance levels used correspond roughly to dawn/dusk and low daytime intensity levels, respectively.

Procedure, Visual Discomfort, and Photostress Recovery

The assessments of visual discomfort and photostress recovery were combined into one session. First, a subject's visual acuity was tested, to ensure an uncorrected or contact lens-corrected binocular Snellen acuity of 20/25 or better. Because the placement of the glare sources was dependent on the position of the subject's eyes, the subject's interpupillary distance (IPD) was determined. Next, the subject was aligned to the optical system. A chin- and forehead-rest assembly served to maintain subject stability during the trials. For the visual discomfort and photostress recovery portions of the study, the optical tubes were separated by the subject's IPD. The subjects were adjusted precisely to create a binocularly fused, single percept of a central white disc of light. To enable fine position adjustments of the glare sources the aforementioned optical tubes were mounted on *X*–*Y* stages and versa mounts, which allowed side-to-side and front-to-back angular adjustments of the tubes. These fine adjustments were often needed to obtain the perception of sharply focused edges, which was indicative of good subject alignment. To ensure the consistency of subject alignment and fixation, the subject's left pupil was monitored, via an infrared (IR) pupil viewer (Arrington Research, Scottsdale, AZ). If the subjects blinked more than once or averted their gaze during the 5-second glare exposure, the trial was repeated. Pupil diameter was recorded for each subject for three conditions: low background, moderate background, and glare. Before the photostress recovery experiment was initiated, the subjects were familiarized with a visual discomfort rating scale, which ranged from 1 to 10, 1 being no noticeable discomfort, 10 being unbearable, and 5 being mildly irritating. This kind of scale has been successfully used in previous studies of visual discomfort.[28,38] The subjects were then asked to view the low background for 1 minute. They were then warned that the glare light would be presented shortly, and they were asked to keep their eyes open (attempting not to blink) during the exposure and look straight ahead into the glare. The glare light was then introduced for 5 seconds. After the glare light was terminated, a Gabor patch, tilted either 45° to the left or right, at a contrast of 4%, 8%, or 16%, was presented. The subject's task was to correctly indicate, via a left or right computer mouse button press, the orientation of the Gabor patch. Because of the strong dependence on foveal fixation for threshold detection of the Gabor patch target, the subject's fixation was aided by two laterally placed fixation guides during the recovery period. These were 2° high-contrast black discs located 4° to the left and right of the center of the Gabor patch. Because the Gabor patch was located in the center of the discs, the subjects were instructed to fixate the bisection of the imaginary line between the discs. The discs' angular distance from the Gabor patch target placed them outside the temporary scotoma caused by the glare. Also, because the scotoma was much larger than the Gabor target, minor deviations in fixation would not result in making the target stimulus visible. The elapsed time for each trial was recorded to a spreadsheet (Excel; Microsoft Corporation, Redmond, WA). After the first trial ended, the subjects were asked to rate their experiences of visual discomfort, using the rating scale described above. Although discomfort ratings were obtained only for the first trial on the low background, the subjects indicated that their discomfort level for subsequent exposures remained consistent. All other trials in this session were used to assess photostress recovery. After recovering from the glare, the subjects were given a 1-minute rest period between trials. To generate an average recovery time for each background/target contrast condition, three measures were made at each combination of background (low/moderate) and target contrast (4%, 8%, and 16%). Repeated trials due to blinking or fixation issues notwithstanding, the subjects completed a total of 18 trials for the visual discomfort/photostress recovery portion of the study. The duration of the experimental session was approximately 45 minutes.

Procedure, Disability Glare

The disability glare session sought to determine the subject's threshold for detection of Gabor patch orientation while under duress from glare located outside the central fovea. The same glare level, backgrounds, and spatial frequencies as those used in the photostress recovery experiment were used for the disability glare experiment. In addition, to determine potential cumulative effects of glare exposures, pre- and post-experiment contrast thresholds (with no glare) for both 4- and 10-cyc/deg Gabor targets presented on the low and moderate backgrounds were determined. The 5° glare sources were moved laterally so that each was centered 5° from the center of the 1° Gabor patch target. Therefore, the edges of the glare sources and center of the Gabor patch were separated by 2.5° of visual angle. The perception of the glare stimuli was that of two bright discs of light separated horizontally (inner edge-to-inner edge) by 5° of visual angle. By the use of subject feedback, an alignment procedure ensured that the glare sources were precisely located the proper distance from the center of the Gabor patch. To ensure consistent subject alignment (as with the photostress recovery experiment), we monitored the position of the subject's left pupil. The subjects were presented simultaneously with the glare sources and the Gabor patch for 2 seconds. The subject's task was to indicate the orientation (left/right) of the Gabor patch within the 2 seconds. A two-alternative, forced-choice staircase procedure was implemented to determine the subjects' disability glare contrast thresholds. If there was no response, it was recorded as incorrect. Twenty-five stimulus presentations were used to determine a threshold, and trials always started with the Gabor set to maximum contrast (90% Michelson contrast). On correct responses, the contrast of the Gabor was decreased 27% of its previous value. Incorrect responses resulted in an increase of 21% of the previous Gabor's contrast value. Based on the results of an ideal observer model, these values most accurately predicted actual contrast thresholds for a trial consisting of 25 stimulus presentations, averaging the last three reversals. The subjects typically produced five or more reversals; actual thresholds were determined by computing the average of the last three reversals. For each stimulus condition, two thresholds were determined. A 1-minute rest period was allowed between each trial. The subjects therefore completed 16 trials, and the session lasted approximately 30 minutes.

Statistical Analysis

Because of the potential of factors such as iris pigmentation and pupil diameter during glare exposure to uniquely influence the visual per-

formance data, partial correlation coefficients were determined for the effects of MP. This method allowed for determination of the unique contribution of MP to visual performance and statistically controlled for the subjects' iris pigmentation density and pupil diameter while viewing the glare sources. Iris pigmentation data were analyzed by using ANOVA with Tukey's post hoc test (SPSS, Chicago, IL). For all analyses, the significance level was set at 0.05.

Results

Macular Pigment Spatial Profiles

The subjects' MPOD spatial profiles exhibited three distinct shapes (Fig. 1). First, a decreasing exponential function (Fig. 1A) sufficiently described 17 of our 26 subjects. Second, a distribution with a prominent shoulder (Fig. 1B) was found in six of our subjects. Last, a distribution with a secondary peak either equivalent to or exceeding the central peak was found in three of our subjects (Fig. 1C). This is sometimes called a trimodal distribution, because if the full horizontal profile (e.g., from nasal to temporal retina) were to be assessed, three distinct peaks would be evident. A decreasing exponential function for the MPOD spatial profile has been characterized by several groups.[5,6,39] Hammond et al.[5] discovered that a small number of their subjects exhibited a secondary peak or shoulder, similar to the subjects in our study, exemplified in Figures 1B and 1C. Snodderly et al.[40] noted that, in monkeys, the MPOD spatial profile is often found to exhibit shoulders or to be trimodal. In addition, Berendschot and van Norren[7] found that half of their subjects had these types of MPOD spatial distributions, which they termed "ring-like." Although intriguing, individual differences in MPOD spatial profiles are not the focus of the present paper. Rather, the spatial profiles were used to generate estimates of total screening over the 1° Gabor patch target area and 5° glare source area, by fitting a first-degree decreasing exponential function to each subject's MPOD spatial profile and averaging the optical density over the relevant area. This method assumes MPOD symmetry about the center of the fovea, which has been shown to hold.[5] The decaying exponential fit accounted for nearly all the variance in the subjects' spatial profiles ($r^2 = 0.984$).

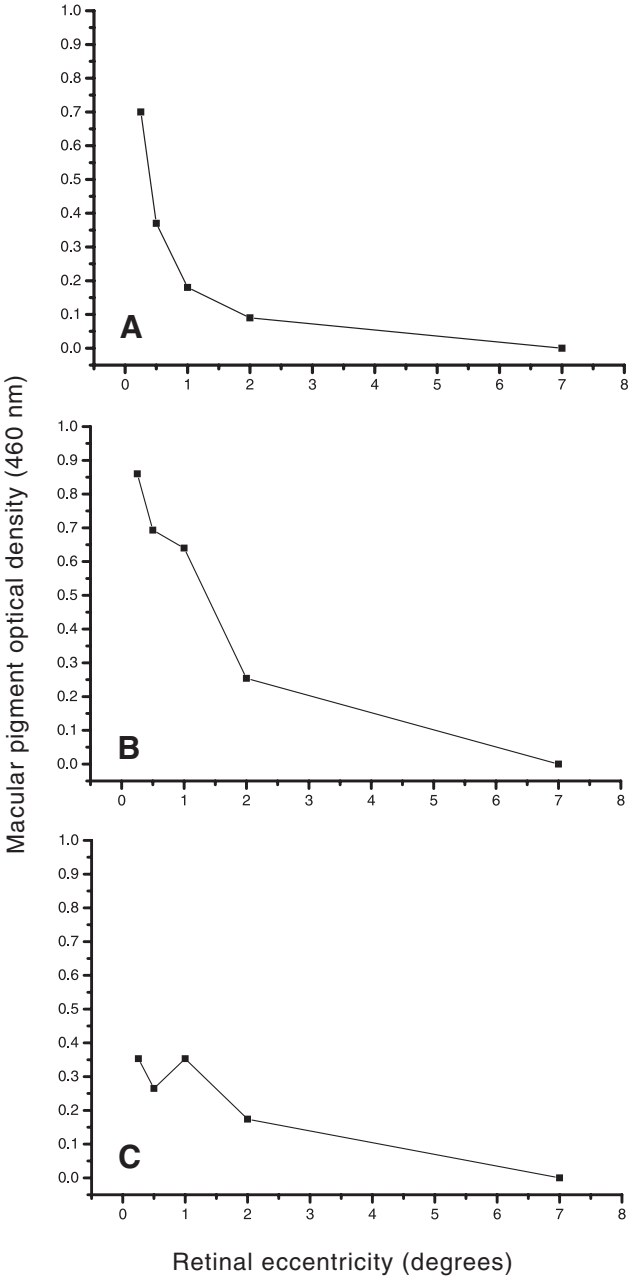

Figure 1. Variations of MPOD spatial profiles found in the present study. (**A**) Decreasing exponential function, (**B**) prominent shoulder at 1° retinal eccentricity, and (**C**) trimodal distribution.

Photostress Recovery

Photostress recovery time (PRT) was significantly reduced as a function of subjects' central 1° area-averaged MPOD level. For example, with the low background coupled with a 4-cyc/deg Gabor set to 4% contrast, there was a significant inverse relationship between PRT and MPOD level ($r = -0.66$; $P < 0.001$; Fig. 2, top). In fact, for all combinations of Gabor patch spatial frequency and contrast level on the low background, similar results were determined, with partial Pearson's r ranging from -0.429 ($P = 0.046$; for the 10-cyc/deg, 8% contrast condition) to -0.736 ($P < 0.001$; for the 4-cyc/deg, 8% contrast condition). There was, however, one exception: With the 10-cyc/deg, 4% contrast condition, the best-fit line to the data was essentially flat ($r = 0.06$; $P = 0.82$). Of all the PRT trials, this was the most demanding for the subjects; 12 of 26 were not able to recover after 2 minutes. For those subjects who were able to recover within the 2-minute period, the average PRT was 37.7 seconds. Data for the moderate background level produced similar results. As can be seen in Figure 2 (bottom), PRT has a significant inverse correlation with MPOD. The figure depicts the subjects' data for the 4-cyc/deg, 4% contrast Gabor, but the same relationship was found for the other spatial frequency/contrast combinations presented on the moderate background: Strength of association (partial r values) ranged from -0.406 ($P = 0.049$; for the 10-cyc/deg, 8% contrast condition) to -0.614 ($P = 0.003$; for the 10-cyc/deg, 4% contrast condition). As with the low-background data, there was one exception to this trend with the moderate background. In the 4-cyc/deg, 16% contrast condition, the strength of association between PRT and MPOD was determined to be -0.334 ($P = 0.110$). The conditions for this trial were the easiest for the subjects, producing the lowest average PRT of 1.62 seconds.

Disability Glare

Baseline contrast thresholds (without glare) were consistent before and after glare testing, as indicated by the nonsignificant, paired-sample t-test results (aggregate $P = 0.965$). For the low background conditions, the subjects' average Michelson contrast threshold was 1.48% (SD 1.01%) for 4 cyc/deg and

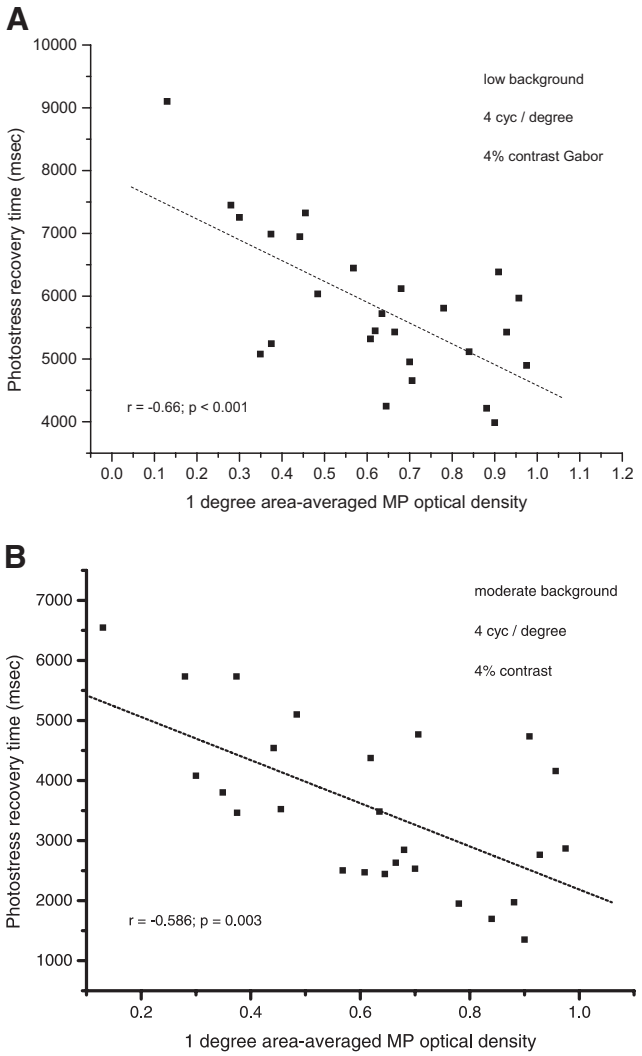

FIGURE 2. *Top*: subjects' photostress recovery time as a function of MPOD. Partial correlation coefficient (adjusted for iris pigmentation and pupil constriction) = 0.66; $P < 0.001$. *Bottom*: Same as *top*, but for different conditions; $r = 0.586$, $P = 0.003$.

5.94% (SD 5.51%) for 10 cyc/deg. For the moderate background conditions, the subjects' average Michelson contrast threshold was 1.2% (SD 0.61%) for 4 cyc/deg and 3.28% (SD 2.5%) for 10 cyc/deg. With regard to trials involving glare exposure, a surprisingly wide range of disability glare thresholds was evident. For example, in the low-background, 10-cyc/deg condition (the most difficult disability glare condition), contrast thresholds ranged from 2.6% to 49.95%. MPOD accounted for a significant proportion of the variance in contrast thresholds in all disability glare conditions (partial $r = -0.434$ to -0.685; corresponding $P < 0.001$ to 0.005; see Fig. 3, top panel, for an example). In addition, MPOD was significantly related to 10-cyc/deg baseline contrast thresholds with both low and moderate backgrounds ($P = 0.005$ and 0.006, respectively; see Fig. 3, bottom, for moderate background data).

Visual Discomfort

Visual discomfort showed a significant inverse correlation with the subjects' central 5° area-averaged MPOD level (partial $r = -0.607$; $P = 0.002$; Fig. 4). Although this relationship was significant for individual loci in the MPOD spatial distribution, the MPOD in the central 5° was averaged because Stringham et al.[3] showed a strong dependence of visual discomfort on glare stimulus area (Recall that the glare source covered the central 5° of the subject's retina.) All other factors being equal, subjects with broader spatial distributions would, in theory, be afforded a greater reduction in discomfort than would those with narrower distributions. This kind of relationship was evident in our data; an example can be seen in Figure 5. Although a trend was evident, iris pigmentation was not determined to be significantly related to visual discomfort ($P = 0.18$). A significant correlation, however, was found between pupil diameter during glare exposure and visual discomfort (see below).

Iris Constriction and Pigmentation

A seemingly paradoxical, yet significant, inverse correlation was determined between visual discomfort ratings and pupil diameters obtained during glare presentation (partial $r = -0.429$; $P = 0.037$, after adjustment for central 5° area-averaged MPOD level and iris pigmentation; Fig. 6). In other words, on average, the smaller a subject's pupils during the glare

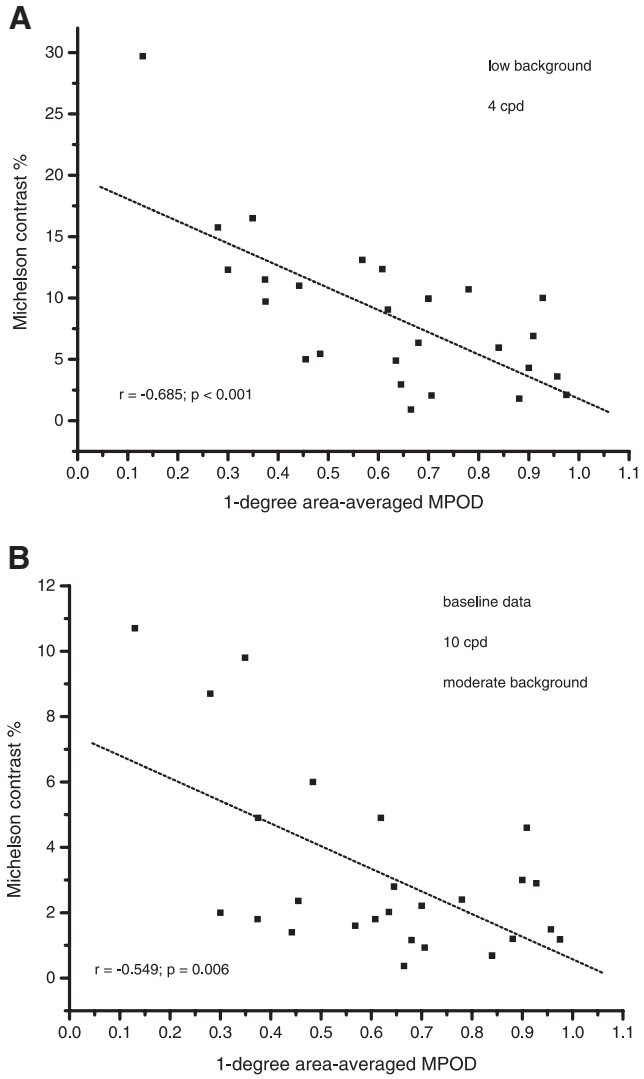

FIGURE 3. *Top*: subjects' disability glare thresholds as a function of 1° area-averaged MPOD for the low background, 4-cyc/deg condition. Partial correlation coefficient (controlling for iris pigmentation and pupil constriction) = -0.685; $P < 0.001$. *Bottom*: same as *top*, but for baseline (no-glare) condition; $r = 0.549$, $P = 0.006$.

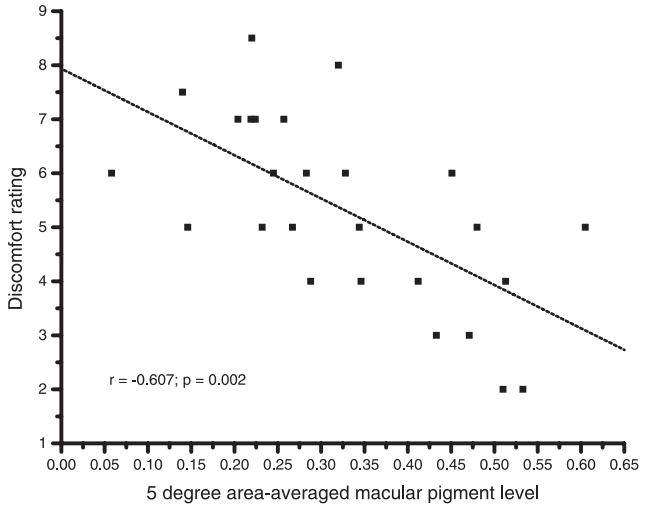

FIGURE 4. Subjects' visual discomfort ratings as a function of central 5° area-averaged MPOD. Partial correlation coefficient (adjusted for effects of iris pigmentation and pupil constriction) = −0.607; P = 0.002.

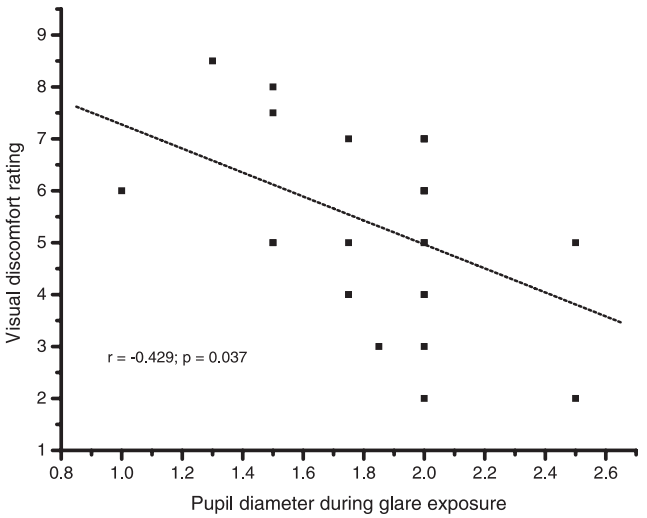

FIGURE 6. Visual discomfort ratings as a function of pupil diameter during glare exposure. Partial correlation coefficient (with adjustment for effects of central 5° area-averaged MPOD level and iris pigmentation) = −0.429; P = 0.037.

exposure, the higher the discomfort rating for that subject, despite less light reaching the retina. Although a minor positive trend was evident (larger pupils with higher MP), the correlation between MP level and pupil diameter at full iris constriction was not significant (P = 0.36). Iris pigmentation was graded on a scale from 1 (light) to 5 (dark) according to the scale of Seddon et al.,[31] and found to correlate positively with MPOD at the 0.5° locus (r = 0.40; P = 0.045; Fig. 7), such that subjects with darker irides tended to have higher MPOD levels. This finding is consistent with those in previous work.[41] Whereas most data shown in the figures in this article are presented in terms of averaged MP over the area corresponding to the stimulus or glare source area, Figure 7 is plotted in terms of MP level at the 0.5° locus; this is the generally recognized standard, and we used it to facilitate direct comparison to the paper by Hammond et al.[41] on the relationship between iris pigmentation and MP. To determine which specific iris pigmentation groups were significantly different in terms of MPOD, we conducted a one-way ANOVA with Tukey's post hoc test. The overall ANOVA was significant (F = 3.23; P = 0.032), and groups 1 (lightest pigmentation) and 5 (darkest) were determined to have significantly different MPOD (0.31 vs. 0.81) levels.

DISCUSSION

The results of the present study suggest that MP significantly improves three aspects of visual performance in glare: (1) photostress recovery, (2) disability glare, and (3) visual discomfort. Previous studies of these phenomena[3,19,28,29] used Maxwellian-view optical systems, in which the action of the iris in modulating the amount of light entering the eye is bypassed. In addition, the ability of dark-pigmented irides to absorb more incident light than light-pigmented irides[42] is also discounted by Maxwellian view. The results of the previous studies indicated that visual performance in glare was strongly associated with MP level. However, given that the deleterious effects of glare are strongly dependent on the amount of light reaching the retina, Maxwellian view is a rather artificial situation. In

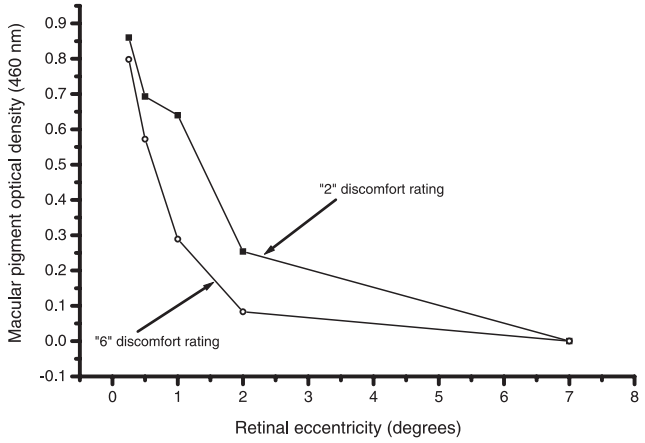

FIGURE 5. Discomfort ratings for two subjects with similar peak MPODs, but different central 5° area-averaged MPODs (0.52, ■; 0.33, ○).

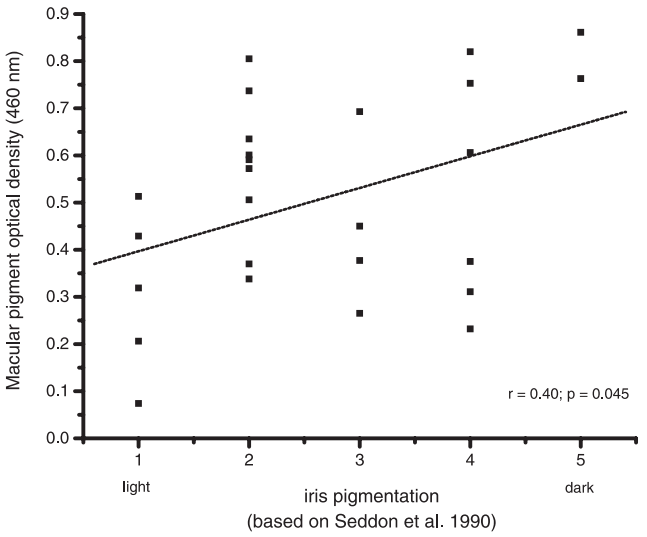

FIGURE 7. Subjects' MPOD (at 0.5° retinal eccentricity) as a function of iris pigmentation (light→dark; after Seddon et al.[31]); r = 0.40, P = 0.045.

fact, the data from our subjects show that iris constriction diameter during glare exposure ranged from 1.0 to 2.5 mm. This represents a more than sixfold difference in the amount of light reaching the retina. To account for the effects of iris constriction and pigmentation on visual performance in glare, we used a free-view optical system. Interestingly, our study produced results similar to the Maxwellian-view–based studies, although the magnitude of the relationships was not quite as high in the present study as in previous studies. For example, in the PRT tasks, the average strength of association (Pearson's r) in the present study was determined to be -0.53. Stringham and Hammond[29] produced PRT versus MPOD data that yielded a Pearson's r of -0.785. For the disability glare portion of the study, the average strength of association in the present study was determined to be -0.60, whereas Stringham and Hammond produced a correlation of -0.76. With regard to visual discomfort, our data indicate that an increase in 5° area-averaged MPOD of 0.15 results in a rank reduction of 1 on the visual discomfort rating scale (Fig. 4). Wenzel et al.[28] noted a nearly linear relationship between increases in MPOD and the amount of light necessary to produce visual discomfort. The differences between the results in the present study and previous studies could be explained by the use of Maxwellian- versus free-view optical systems. In addition, these differences could be partially accounted for by between-study differences in experimental design, stimulus conditions, such as square-wave gratings versus Gabor patch, or perhaps glare source intensity. For example, in previous studies, visual discomfort thresholds were determined by increasing the intensity of glare lights between trials to reach a discomfort threshold. This is fundamentally different from the approach used in the present study, in which the glare stimulus intensity was held constant, and subjects were simply asked to rate their experience of discomfort. Despite the slightly weaker relationships determined in our study compared with others, the findings are statistically significant and are suggestive of real-world, practical benefits of relatively high levels of MP. For example, the results of the PRT portion of the present study indicate that, averaging across conditions, an increase of 0.3 MPOD in the central 1° of the fovea results in a 3.5-second decrease in PRT. In a situation involving intense oncoming headlights, for example, this kind of improvement is substantial and could reduce the risk of vehicle accidents, property damage, and loss of life. In our experiments, the highest performance gain with respect to MP level on the PRT tasks was found in trials that challenged the subjects—namely, those that involved low background luminance and low-contrast targets. As an example, for the low background, 4-cyc/deg, 8% contrast condition, subject PRTs ranged from roughly 5 seconds, for those with relatively low MP, down to roughly 2 seconds (for those with relatively high MP). Out of the 12 PRT conditions, two were found to be unrelated to MPOD. Of note, these were, respectively, the most difficult and easiest PRT tasks for subjects. The data for the most difficult PRT condition (low background, 10-cyc/deg, 4% contrast) appear to reveal a floor effect; as reported in the Results section, many subjects were unable to recover in less than 2 minutes. Similarly, the data for the easiest condition (moderate background, 4-cyc/deg, 16% contrast) are indicative of a floor effect. We believe this may explain why these two conditions were not related to MPOD.

For disability glare, the effects of MP were quite dramatic. As noted above, the range of disability glare thresholds spanned, in some cases, one order of magnitude (e.g., 2.6% to 49.95% in the low background, 10-cyc/deg condition). Based on the -0.56 correlation between MP and disability glare thresholds in this condition, MPOD accounts for 31.6% of the variance in disability glare thresholds. Such visual improvement with increased MPOD would presumably translate to real-world conditions. In the case of oncoming headlights, the ability to "see through" glare would greatly benefit a driver (e.g., seeing pedestrians in the presence of headlights or sunlight). Perhaps tasks such as reading signs at long distances on particularly bright, sunny days would be made easier with higher MPOD.

The finding that MPOD was significantly related to baseline 10-cyc/deg contrast thresholds in both low and moderate background conditions was somewhat surprising. Given the relatively demanding nature of the 10-cyc/deg visual task, good performance would have been highly dependent on the use of the central fovea, where MP is most dense. MP's rich deposition in the central fovea may have enabled good performance for those subjects with relatively high levels of MPOD, via mechanisms of contrast enhancement (Renzi L, et al. *IOVS* 2009;50:ARVO E-Abstract 1703). The most plausible explanation for this effect is that MP enhances contrast by reducing intraretinal and intraocular scatter, albeit minimal, for the baseline task. Those with relatively low MPOD would presumably not have derived this benefit. An alternative explanation involves improvement of neural efficiency in the visual system by L and Z. This improved efficiency could aid spatial vision by serving to enhance the edges of stimuli, thereby increasing the detectability of low-contrast objects. For temporal vision, Hammond and Wooten[43] noted a significant positive correlation between critical flicker fusion thresholds and MP level. Moreover, Craft et al.[44] discovered a rich deposition of L and Z in the occipital lobe (primary visual cortex) of donor brains. Both of these findings point to a visual function for L and Z that goes beyond acting purely as an optical filter. It appears that, given their optical and biochemical properties along with their conspicuous placement in anatomic locations specific to vision, the primary function of L and Z is to protect and enhance visual function.

There is much evidence in the results of this and previous studies to suggest that MP is the optimal filter for attenuating visual discomfort, thereby increasing the bandwidth of comfortable visual operation. First, we consider the characteristics of visual discomfort. The threshold for visual discomfort is much lower with centrally viewed lights than with lights viewed eccentrically.[3] In addition, the action spectrum for visual discomfort (when MP is accounted for) exhibits increasing sensitivity with decreasing wavelength[45] (i.e., we have greater visual discomfort sensitivity to short-wavelength, blue light). Because of its relatively high density in the fovea and spectral absorption properties, MP would therefore appear to be ideally suited to reducing the discomfort induced by centrally viewed lights. This functional role of MP would increase visual performance by increasing the bandwidth of comfortable visual operation, which would allow a person with relatively high MP to tolerate intense lights without taking aversive action (i.e., squinting, blinking, or looking away). Wenzel et al.[28] found a significant, positive correlation between MPOD and visual discomfort thresholds. To investigate the possibility of within-subject effects, they then supplemented their subjects with 30 mg/L+ 3 mg Z for 12 weeks, and found that increases in MPOD corresponded to nearly linear increases in discomfort thresholds. As noted previously, their study was conducted using Maxwellian view. To extend these findings with improved ecological validity, we plan to conduct a within-subject, L+Z supplementation study of these effects, using our current, free-view optical system.

Our finding that iris pigmentation is significantly related to MPOD is not new,[41] but an intriguing relationship between iris pigmentation and visual discomfort ratings, although not statistically significant, was produced in our study. Recall that the present study selected subjects on the basis of MPOD level, to achieve a wide range. Perhaps a study with subjects specifically

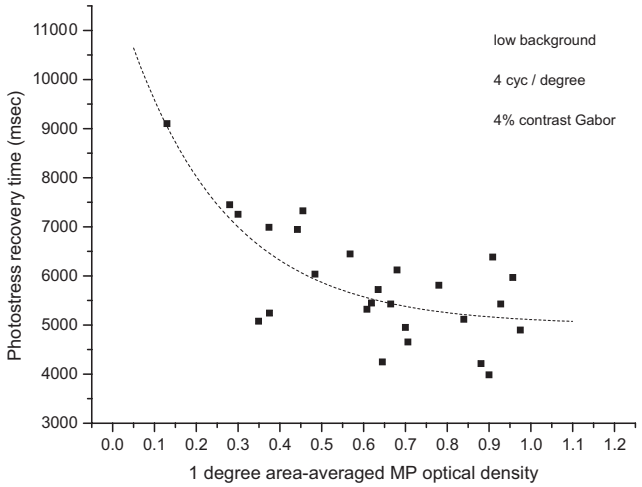

FIGURE 8. Data from Figure 2, fit with a first-order decreasing exponential function to reveal the asymptote of MPOD benefit.

selected on the basis of iris pigmentation would reveal a significant effect on visual discomfort ratings. Anecdotal evidence has shown that individuals with darker irides generally have less trouble with intense light than do those with light irides. Because iris pigmentation correlates significantly with MPOD, if a significant relationship were to be established between iris pigmentation and visual discomfort, the unique contribution of MPOD and iris pigmentation to visual discomfort would be an important determination. The results of our study indicate that MPOD accounts for more of the variance in discomfort ratings, but, as noted above, a random sample of subjects, who would presumably contain normally distributed levels of MP and iris pigmentation, might produce different results. Nevertheless, it appears that MP makes a significant, unique contribution to the reduction of visual discomfort.

With regard to iris constriction and visual discomfort, the paradoxical finding of a significant inverse relationship between pupil diameter during glare exposure and visual discomfort rating is intriguing. It stands to reason that increased light reaching the retina would produce more visual discomfort, but this clearly was not the case for the subjects in our sample. Given our result, it appears that the iris plays a significant role in the genesis of discomfort from bright light. Neurophysiological and clinical evidence and some previous work are supportive of this idea. Because pain-signaling fibers of the trigeminal nerve innervate the dilator and constrictor muscles of the iris, it has been suggested that the pupillary light reaction gives rise to visual discomfort under lighting conditions that cause intense stretching and maximum constriction of the irides.[46] Indeed, it has been demonstrated that an intact trigeminal nerve is necessary to experience visual discomfort.[47] More recently, however, Howarth et al.[48] showed that hippus (an irregular oscillation of iris constriction and dilation under intense illumination) is not consistently associated with subjective reports of visual discomfort. However, they assessed the relationship between hippus and visual discomfort in only one subject. We observed the irregular pupillary oscillation, characteristic of hippus, in only three of our subjects. Interestingly, those subjects tended to rate the glare stimulus generally higher (average rating, 6.5, roughly equivalent to "irritating") on the visual discomfort scale, compared with the other subjects (average rating, 5.19, roughly equivalent to "somewhat irritating"). Given the visual discomfort rating results of our study, the light level used for the glare sources, although quite intense, was perhaps below the level that would, on average, produce pupillary hippus in normal human subjects. Moreover, other investigators[3,28,45] have sought to determine visual discomfort thresholds by modifying the intensity of the glare source. This approach may have limited the ability to analyze the range of individual responses to single glare sources. Our use of fixed-intensity, moderately discomforting glare stimuli may have serendipitously revealed a clue to the relationship between iris constriction and visual discomfort. In the clinic, it is not uncommon for subjects to experience extreme visual discomfort on billowing or prolapse of the iris during cataract surgery. This is referred to as floppy iris syndrome[49] and further supports the idea that the genesis of pain from light involves the iris.

Although our sample of subjects was reasonably homogeneous, there were clear interindividual differences in iris constriction under glare-viewing conditions. There are many potential explanations for this, including individual differences in retinal sensitivity or perhaps genetic factors that affect iris function. The data available from our study suggest that MPOD ($P = 0.38$) and iris pigmentation ($P = 0.52$) did not account for a significant proportion of the variance in pupil constriction in our subjects.

One pressing question regarding the relationship between MPOD and visual performance in glare remains: How much MP is enough…or too much? Although we used linear fits to the data for our analyses, from visual inspection of some of the graphs it appears that the effect of MP may asymptote in some cases. Take, for example, the PRT data originally presented in Figure 2. If the data are fit with a first-order decreasing exponential function, the beneficial effect of MPOD appears to level off at approximately 0.6 or 0.7 (Fig. 8). In addition, for the baseline contrast threshold data originally presented in Figure 3 (bottom panel), the downward slope of the data appears to level off sharply near 0.6 MPOD. To examine this more closely, we fit the data below and above 0.6 MPOD with separate linear functions (Fig. 9). Similar to the data in Figure 8, the results in Figure 9 are indicative of a leveling off of MP benefit at approximately 0.6. Figures 8 and 9 illustrate the idea that, beyond a certain level of MP, additional MP is probably superfluous for some aspects of visual performance in glare. Furthermore, and perhaps more importantly, Figures 8 and 9 indicate that, below some critical level of MP, severe deficits in visual performance in glare may be experienced. In the examples of photostress recovery and baseline contrast sensitivity presented in Figures

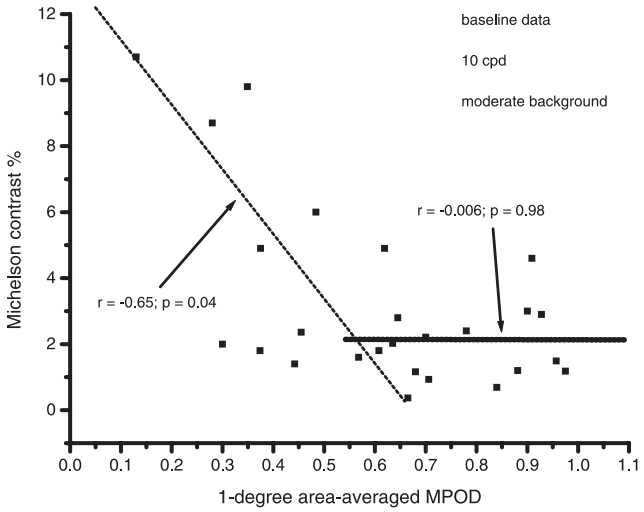

FIGURE 9. Same as data presented in Figure 3 (*bottom*), data fit linearly below and above, respectively, the 0.6 MPOD level. Subjects' disability glare thresholds as a function of 1° area-averaged MPOD for the baseline (no-glare), 10-cyc-deg, moderate background condition.

8 and 9, above some critical level of MPOD (despite the glare sources being attenuated more strongly), the detectability of the target may have been compromised via reduced luminance. This effect may be limited to specific performance parameters or stimulus conditions. In the case of visual discomfort, for example, more MP would translate to increased attenuation of glare. Based purely on light absorption, additional MP would presumably reduce visual discomfort. In support of this idea, the data in Figure 4 indicate a linear relationship between MPOD and visual discomfort.

Last, an important point should be made regarding the effect of the spectral composition of the glare source. Because glare-related visual performance enhancements afforded by MP are assumed largely to be filter-based, effects would presumably be obtained only when using a glare source with a relatively strong short-wavelength component. The effects characterized in the present study and previous studies of visual performance in glare and MP (with the exception of Loughman et al.[30]) are based on lights with a strong short-wavelength component (e.g., xenon-arc lamp). This approach also lends ecological validity to the results, especially in consideration of visual performance outdoors, where solar radiation (with much short-wave energy) is present. With that said, the reader is reminded that the spectral emission of the LEDs used in the present study is somewhat unnatural, in that it is not continuous (like solar or xenon spectra), but rather is composed of two distinct short- and mid-wavelength lobes (as noted in the Methods section). The strong blue component, coupled with the close correspondence with previous results using a xenon-arc source, however, suggests that the results from the present study can be extended to real-world conditions.

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References

1. Holladay LL. Action of a light-source in the field of view in lowering visibility. *J Opt Soc Am.* 1927;14:1–9.
2. Vos JJ. On the cause of disability glare and its dependence on glare angle, age and ocular pigmentation. *Clin Exp Optom.* 2003;86(6):363–370.
3. Stringham JS, Fuld K, Wenzel AJ. Spatial properties of photophobia. *Invest Ophthalmol Vis Sci.* 2004;45(10):3848–3858.
4. Snodderly DM, Auran JD, Delori FC. The macular pigment, II: spatial distribution in primate retinas. *Invest Ophthalmol Vis Sci.* 1984;25(6):674–685.
5. Hammond BR Jr, Wooten BR, Snodderly DM. Individual variations in the spatial profile of human macular pigment. *J Opt Soc Am A Opt Image Sci Vis.* 1997;14(6):1187–1196.
6. Stabell U, Stabell B. Variation in density of macular pigmentation and in short-wave cone sensitivity with eccentricity. *J Opt Soc Am A Opt Image Sci Vis.* 1980;70(6):706–711.
7. Berendschot TT, van Norren D. Macular pigment shows ringlike structures. *Invest Ophthalmol Vis Sci.* 2006;47(2):709–714.
8. Bone RA, Landrum JT, Tarsis SL. Preliminary identification of the human macular pigment. *Vision Res.* 1985;25(11):1531–1535.
9. Neuringer M, Sandstrom MM, Johnson EJ, Snodderly DM. Nutritional manipulation of primate retinas, I: effects of lutein or zeaxanthin supplements on serum and macular pigment in xanthophyll-free rhesus monkeys. *Invest Ophthalmol Vis Sci.* 2004;45(9):3234–3243.
10. Bone RA, Landrum JT Hime GW, Cains A, Zamor J. Stereochemistry of the human macular carotenoids. *Invest Ophthalmol Vis Sci.* 1993;34:2033–2040.
11. Krinsky NI, Landrum JT, Bone RA. Biologic mechanisms of the protective role of lutein and zeaxanthin in the eye. *Ann Rev Nutr.* 2003;23:171–201.
12. Snodderly DM, Brown PK, Delori FC, Auran JD. The macular pigment, I: absorbance spectra, localization, and discrimination from other yellow pigments in primate retinas. *Invest Ophthalmol Vis Sci.* 1984;25(6):660–673.
13. Ham WT, Ruffolo JJ, Mueller HA, Clarke AM, Moon ME. Histologic analysis of photochemical lesions produced in rhesus retina by short-wavelength light. *Invest Ophthalmol Vis Sci.* 1978;17(10):1029–1035.
14. Snodderly DM. Evidence for protection against age-related macular degeneration by carotenoids and antioxidant vitamins. *Am J Clin Nutr.* 1995;62(6 suppl):1448S–1461S.
15. Hammond BR Jr, Wooten BR, Snodderly DM. Preservation of visual sensitivity of older subjects: association with macular pigment density. *Invest Ophthalmol Vis Sci.* 1998;39(2):397–406.
16. Humphries JM, Khacik F. Distribution of lutein, zeaxanthin, and related geometrical isomers in fruit, vegetables, wheat, and pasta products. *J Agric Food Chem.* 2003;51:1322–1327.
17. Curran-Celentano J, Hammond BR, Ciulla TA, Cooper DA, Pratt LM, Danis RB. Relation between dietary intake, serum concentrations, and retinal concentrations of lutein and zeaxanthin in adults in a midwest population. *Am J Clin Nutr.* 2001;74:796–802.
18. Nolan JM, Stack J, O'connell E, Beatty S. The relationships between macular pigment optical density and its constituent carotenoids in diet and serum. *Invest Ophthalmol Vis Sci.* 2007;48(2):571–582.
19. Stringham JM, Hammond BR Jr. Macular pigment and visual performance under glare conditions. *Optom Vis Sci.* 2008;85(2):82–88.
20. Schulze M. *Ueber den gelben Fleck der Retina, setnen Einfluss auf normales Seben und auf Farbenblindbeit.* Bonn, Germany: VonMax Cohen and Sohn; 1866.
21. Walls GL, Judd HD. The intraocular colour filters of vertebrates. *Br J Ophthalmol.* 1933;17:641–75,705–725.
22. Wald G. The photochemistry of vision. *Doc Ophthalmol.* 1949;3:94–137.
23. Ruddock KH. Light transmission through the ocular media and macular pigment and its significance for psychophysical investigation. In: Jameson D, Hurvich LM, eds. *Handbook of Sensory Psychology.* Vol. VII/4,*Visual Psychophysics*. Berlin: Springer-Verlag; 1972.
24. Reading VM, Weale RA. Macular pigment and chromatic aberration. *J Opt Soc Am.* 1974;64:231–234.
25. Engles M, Wooten B, Hammond BR. Macular pigment: a test of the acuity hypothesis. *Invest Ophthalmol Vis Sci.* 2007;48(6):2922–31.
26. Shlaer S. The relation between visual acuity and illumination. *J Gen Physiol.* 1937;21:165–188.
27. Wooten BR, Hammond BR. Macular pigment: influences on visual acuity and visibility. *Prog Retin Eye Res.* 2002;21(2):225–240.
28. Wenzel AJ, Fuld K, Stringham JM, Curran-Celentano J. Macular pigment optical density and photophobia light threshold. *Vision Res.* 2006;46(28):4615–4622.
29. Stringham JM, Hammond BR Jr. The glare hypothesis of macular pigment function. *Optom Vis Sci.* 2007;84(9):859–864.
30. Loughman J, Akkali MC, Beatty S, et al. The relationship between macular pigment and visual performance. *Vision Res.* 2010;50:1249–1256.
31. Seddon JM, Sahagian CR, Glynn RJ, Sperduto RD, Gragoudas ES, and the Eye Disorders Case-Control Study Group. Evaluation of an iris classification system. *Invest Ophthalmol Vis Sci*. 1990;31(8):1592–1598.
32. Wooten BR, Hammond BR, Land R, Snodderly DM. A practical method of measuring macular pigment optical density. *Invest Ophthalmol Vis Sci.* 1999;40:2481–2489.
33. Snodderly DM, Hammond BR. In vivo psychophysical assessment of nutritional and environmental influences on human ocular tissues: lens and macular pigment. In: Taylor AJ, ed. *Nutritional and Environmental Influences on Vision*. Boca Raton, FL: CRC Press; 1999;251–273.
34. Snodderly DM, Mares-Perlman JA, Wooten BR, Oxton L, Gruber M, Ficek T. for the CAREDS Macular Pigment Study Group. Macular pigment measurement by heterochromatic flicker photometry in older subjects: the Carotenoids and Age-related Eye Disease Study. *Invest Ophthalmol Vis Sci*. 2004;45:531–538.
35. Tyler CW. Two processes control variations in flicker sensitivity over the life span. *J Opt Soc Am A Opt Image Sci Vis.* 1989;6(4):481–490.

36. Norren DV, Vos JJ. Spectral transmission of the human ocular media. *Vision Res.* 1974;14(11):1237–1244.
37. Stringham JM, Hammond BR, Nolan JM, et al. The utility of using customized heterochromatic flicker photometry (cHFP) to measure macular pigment in patients with age-related macular degeneration. *Exp Eye Res.* 2008;87(5):445–453.
38. de Boer JB. Visual perception in road traffic and the field of vision of the motorist. In: de Boer JB, ed. *Public Lighting*. Eindhoven, The Netherlands: Philips Technical Library; 1967;11–96.
39. Werner JS, Donnelly SK, Kliegl R. Aging and human macular pigment density (appended with translations from the work of Max Schultze and Ewald Hering). *Vision Res.* 1987;27:257–268.
40. Snodderly DM, Handelman GJ, Adler AJ. Distribution of individual macular pigment carotenoids in central retina of macaque and squirrel monkeys. *Invest Ophthalmol Vis Sci.* 1991;32:268–279.
41. Hammond BR Jr, Fuld K, Snodderly DM. Iris color and macular pigment optical density. *Exp Eye Res.* 1996;62(3):293–297.
42. Cumming RG, Mitchell P, Lim R. Iris color and cataract: The Blue Mountains Eye Study. *Am J Ophthalmol.* 2000;130:237–238.
43. Hammond BR Jr, Wooten BR. CFF thresholds: relation to macular pigment optical density. *Ophthalmic Physiol Opt*. 2005;25(4):315–319.
44. Craft NE, Haitema TB, Garnett KM, Fitch KA, Dorey CK. Carotenoid, tocopherol, and retinol concentrations in elderly human brain. *J Nutr Health Aging.* 2004;8(3):156–162.
45. Stringham JM, Fuld K, Wenzel AJ. Action spectrum for photophobia. *J Opt Soc Am A.* 2003;20(10):1852–1858.
46. Hopkinson RG. Glare discomfort and pupil diameter. *J Opt Soc Am.* 1956;46(8):649–656.
47. Lebensohn JE. The nature of photophobia. *Arch Ophthalmol.* 1934;12:380–390.
48. Howarth P, Heron G, Greenhouse D, Bailey I, Berman S. Discomfort from glare: the role of pupillary hippus. *J Illum Eng.* 1993;25:37–42.
49. Chang DF, Braga-Mele R, Mamalis N, et al. ASCRS Cataract Clinical Committee. ASCRS White Paper: Clinical review of intraoperative floppy-iris syndrome. *J Cataract Refract Surg*. 2008;34(12):2153–2162.