Glare Disability, Photostress Recovery, and Chromatic Contrast: Relation to Macular Pigment and Serum Lutein and Zeaxanthin

Billy R. Hammond Jr,[1] *Laura M. Fletcher,*[1] *and James G. Elliott*[2]

Purpose. A large body of research has linked macular lutein and zeaxanthin to reduced risk of degenerative eye disease. The earliest published hypothesis for the role of the pigments was not based on chronic protection but immediate function. Recent data on macular pigment (MP) have shown that screening the foveal cones from short-wave light does, in fact, result in improvements in photostress recovery (PR), glare disability (GD), and chromatic contrast (CC). This study examined those relations on a larger sample.

Methods. A total of 150 young healthy subjects were assessed. Plasma samples were obtained from 100 subjects for HPLC quantification of serum xanthophylls. MP density was measured using customized heterochromatic flicker photometery. GD, PR, and CC were measured in Maxwellian view using a broadband xenon light source. GD was measured by increasing the intensity of an annulus until it veiled a central target. PR was measured as the time necessary to regain sight of a central target after a 5-second exposure to an intense bleaching light. CC was measured as the amount of light necessary in a 460-nm background to lose sight of a central target.

Results. MP density was significantly related to serum lutein and zeaxanthin combined ($r = 0.31$, $P = 0.002$), GD ($r = 0.24$, $P = 0.0015$), PR ($r = -0.18$, $P = 0.01$), and CC ($r = 0.46$, $P = 0.00005$).

Conclusions. These results confirm earlier reports of a significant relation between variation in macular pigment optical density and immediate effects on visual function. As with many species, intraocular yellow filters in humans appear to improve many aspects of the visual stimulus. (ClinicalTrials.gov number, NCT00909090.) (*Invest Ophthalmol Vis Sci.* 2013;54:476–481) DOI:10.1167/iovs.12-10411

Loss of visual function is both a prognostic and the worst outcome of visual disease. This is particularly true for conditions that affect the crystalline lens and retina (like age-related cataracts [ARC] and macular degeneration [AMD]). Because treating the underlying disease is often so difficult (especially for conditions like AMD), the approach is often palliative (e.g., correcting refractive errors or magnification). The use of prescription filters, for instance, is becoming increasingly common. These filters are largely aimed at reducing glare by absorbing short-wave light.[1] This is needed because disability due to glare is a common problem for patients with even very early signs of cataract (due to increases in media scattering) and AMD. Patients with early or more severe stages of AMD, for instance, tend to recover from a photostressor 6 to 16 times more slowly, respectively, than age-matched controls.[2] For example, Sandberg and Gaudio[3] showed that when subjects with maculopathy are exposed to bright bleaching lights, visual recovery is significantly slowed despite having normal visual acuity. Disability due to glare results from increased forward light scatter originating in the cornea and lens.[4] Lens irregularities increase with age and incipient cataract.[5]

High intraocular scatter may create additional problems. For example, chromatic discrimination can be reduced due to bright light desaturating colors.[6] Color enhances the coding of images at the input stage by facilitating the detection of borders.[7] Isoluminant edges (i.e., edges defined only by chromatic differences) are common in natural scenes[8] and when viewing objects at a distance, because the distance itself tends to equalize differences in luminance that would otherwise have demarcated an edge if the object was closer. Hence, glare disability (GD), photostress recovery (PR), and chromatic contrast (CC) are all measures of visual performance that worsen with increased intraocular scatter, age, and ocular disease.

These visual variables are also united in their tendency to be strongly influenced by short-wave light, as originally noted by Walls and Judd in 1933.[9] It is likely, for instance, that many sources of glare in the environment are broad band (e.g., sunlight, as shown in Fig. 1) and contain a preponderance of Rayleigh-scattered (blue) light. Such light can degrade vision at a distance (visibility) due to the veiling effects of "blue haze."[10,11] The pernicious aspects of blue light on vision formed the basis of Walls and Judd's[9] original speculation that the ubiquity of blue-absorbing intraocular filters across species was a response to this natural evolutionary pressure. These authors noted that, based purely on filtering short-wave light, yellow intraocular filters would reduce glare discomfort and "dazzle," enhance CC (see also Mollon and Regan[12]), and extend visible range by absorbing blue haze. Like many other species, humans also possess an intraocular blue-absorbing filter in the form of macular pigment (MP). These pigments, a mixture of yellow carotenoids (lutein, zeaxanthin, and meso-zeaxanthin) are concentrated in the inner layers of the retina in and around the foveal depression. Because they are derived from the diet and influenced by numerous personal variables (e.g., sex, iris color, adiposity, tobacco usage[13]), their concentrations across individuals vary widely (greater than a factor of 10).

From the [1]Vision Sciences Laboratory, University of Georgia, Athens, Georgia; and [2]DSM Nutritional Products, Inc., Parsippany, New Jersey.

Supported by DSM Nutritional Products, Inc., and Kemin Health, LLC.

Submitted for publication June 16, 2012; revised August 24 and October 16, 2012; accepted November 23, 2012.

Disclosure: **B.R. Hammond Jr**, None; **L.M. Fletcher**, None; **J.G. Elliott**, None

Corresponding author: Billy R. Hammond Jr, Vision Sciences Laboratory, University of Georgia, Athens, GA 30602-3013; bhammond@uga.edu.

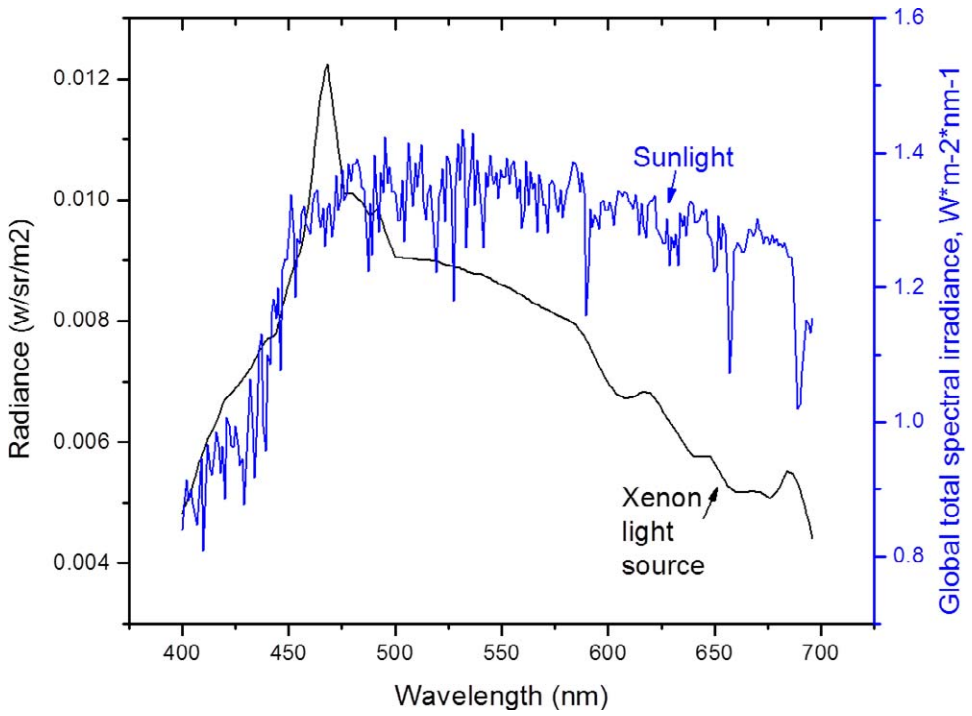

Figure 1. The relative energy of the light sources used in the GD and PR assessments compared to the spectrum of daytime sunlight. The latter was derived from the G173-03e1 Standard Tables for Reference Solar Spectral Irradiances: Direct Normal and Hemispherical on 37° Tilted Surface.[37] A copy of the complete standards may be obtained from ASTM, in the public domain, www.astm.org.

Past data have suggested that there are visual consequences for having reduced MP levels, even for young individuals. For example, empirical data have shown that increased MP density reduces glare discomfort,[14–16] GD, speeds PR,[17–19] and enhances CC.[20] Such relations make sense; the pigments are concentrated in the inner layers of the central retina where they strongly screen foveal cones but only minimally screen the more light-sensitive rods. Unlike external yellow filters, the visual system corrects for MP filtering of blue light by adjusting the gain of the S-cone system[21,22]; hence, visual performance is less likely to be reduced due to reductions in luminance as they would with external yellow filters. In this study, we further explore the link between MP density and visual performance. This was done by measuring MP and GD, as well as PR and CC in a relatively large sample of young healthy subjects.

Methods

Subjects

A total of 150 healthy subjects, 90 females and 60 males, were tested (mean age = 22.2, SD = 4.1 years); 120 subjects were white, 19 were Asian, 7 were African American, and 4 were Hispanic. All subjects were considered healthy based on a prestudy examination that included a complete medical history, physical examination, and clinical chemistry (conducted by a licensed MD at the University of Georgia [UGA] Health Center). Major inclusion criteria included the following: age range between 20 and 40 years, body mass index (BMI) between 20 and 30, and corrected visual acuity (Early Treatment Diabetic Retinopathy Study) better than 20/60. Major exclusion criteria included the following: smoking, current or history of relevant diseases (such as AMD), inability to reliably perform MP optical density (MPOD) measurements by heterochromatic flicker photometry (HFP) or any of the other ophthalmic tests of the study (only one subject was excluded based on this criterion), any condition likely to interfere with normal gastrointestinal absorption of xanthophylls or use of xanthophyll-containing supplements, participation in any other study during past 1 month, blood donation during the past 3 months, or current pregnancy or breastfeeding.

All visual measures were conducted on the right eye only. Subjects were recruited from the population (undergraduate and graduate students) at UGA. This study was approved by UGA's institutional review board and the experimental procedures were conducted in accordance with Good Clinical Practice Guidelines and the ethical principles of the Declaration of Helsinki.

Apparatus

The apparatus and procedures used to measure GD, PR, and CC are described in detail elsewhere.[13–15] Briefly, a three-channel standard Maxwellian-view optical system with a 1000-Watt xenon-arc lamp source (Thermo Oriel Instruments, Stratford, CT) was used. For the veiling glare experiment, we used a test target surrounded by an annulus. One channel of the optical system produced the target stimulus, a 570-nm 1°-diameter disk containing a black and white 100% contrast grating stimulus (note that this monochromatic target is different from the relatively broad-band target used in our previous studies[17,18]). The spatial frequency of the grating was 4 cyc/deg. During threshold testing, this stimulus was presented for 2 seconds on and 1 second off. The second channel of the optical system produced a xenon-white annulus concentric with the target stimulus, with 11° inner and 12° outer diameters (outside the range of MPOD).

For the PR assessment, the same 1° target stimulus was used (now shuttered 200 ms, on/off). The second channel of the system was used to present the 5°-diameter, xenon-white disk, which served as the photostress stimulus. The corneal irradiance of the photostress stimulus was 2.5 $\mu W/cm^2$ (5.5 log Trolands using the Westheimer method). The photostress stimulus was presented for 5 seconds using an electro-mechanical shutter (Uniblitz; Vincent Associates, Rochester, NY). Two small (5′) fixation points were used (placed at a lateral range of 6° centered on the test stimulus) to help maintain alignment during the period that the subject was recovering from the photostressor.

For the CC measure, we used a target that consisted of a 600-nm circular disk, 1° in diameter, containing a 100% contrast grating stimulus (4 cyc/deg) that was maintained at a constant energy of 2.3 $\mu W/cm^2$ (specified at the cornea). A separate channel of the optical system produced a 460-nm, 10° background (CIE/Uniform Color Stress [UCS] 1976: $u' = 0.20$, $v' = 0.077$). The absolute (i.e., unattenuated) energy in this channel at the plane of the pupil was 50.6 $\mu W/cm^3$. The wavelength composition of the target was produced by a monochromator (Model 82-410; Jewell Ash, Waltham, MA) in conjunction with blocking filters (Broadband Bandpass Interference Filters; Edmund Optics, Barrington, NJ). The target was shuttered during testing so that the target was off for 1 second and exposed for 2 seconds. The wavelength of the background was produced by an interference filter (half-power bandwidth = 8 nm; Edmund Optics).

Spatial alignment of all of the stimuli was checked every session by increasing the intensity of the light source (removing all filtration) and checking that the stimuli always projected to the same position on a wall chart that was never moved. All photometric calibrations were performed using a spectral radiometer (PR-650 Spectral Radiometer; PhotoResearch, Inc., Chatsworth, CA). Wedge and neutral density radiometric calibrations were performed using an optometer (Model 370; Graseby Optronics, Orlando, FL). A dedicated photometer (S370 Optometer; UDT Instruments, Hawthorne, CA) was used before every experimental session to ensure that the total light output of the optical system remained constant.

Procedure

Before testing, subjects were aligned to the optical system. Careful adjustments were made such that the arc image (1.5-mm diameter) was in focus and in the plane of the subject's pupil. For the veiling glare experiment, subjects first viewed the grating stimulus, and then the annulus was presented. Before each trial, the annulus was set at a level well below that which would cause the target stimulus to be veiled. The subject was then instructed to adjust, via a neutral-density wedge, the intensity of the annulus until the target stimulus was no longer visible. Often, subjects went beyond the threshold of visibility, and then adjusted the wedge to decrease the intensity of the annulus so as to pinpoint their threshold. Five thresholds were determined, and subjects were instructed to carefully maintain their criterion threshold across trials.

For the PR experiment, the same alignment procedure was used. The subject was first instructed to view the grating stimulus; after approximately 30 seconds, the subject was presented with the photostressor for 5 seconds. The photostressor was intense (2.5 $\mu W/cm^3$), and to control for reduced photopigment bleaching due to eye blinking or closure, subjects were instructed to keep their eyes open during the 5-second exposure. The subjects' eyes were monitored during the exposure (via an infrared camera [232; Watec Incorporated, Newburgh, NY] and monitor [ADEMCO AMM17; Honeywell Video Systems, Midrand, Gauteng, South Africa]), so if the experimenter observed that the test beam was occluded by blinking or eye closure, the trial was repeated. Subjects were instructed to indicate when they could first perceive the grating. The time necessary to recover central visibility of the grating stimulus was measured with a stopwatch. After PR was achieved, a 2-minute waiting period before the next stimulus presentation was observed. Three trials were obtained.

For CC, testing was initiated by setting the background at a level where the target stimulus was clearly visible. Subjects increased the intensity of the background until the target stimulus was no longer visible. Subjects were instructed to use an ascending method of limits. In other words, if subjects went past the point where the target just disappeared, subjects were asked to go back until the target was clearly visible and once again adjust the intensity of the surround until the target disappeared. Five trials were collected.

Measurement of MPOD

The apparatus and procedure used to measure MPOD has been detailed in multiple previous reports.[23,24] In brief, we used the Macular Densitometer (Macular Metrics, Rehoboth, MA), which presents stimuli in free view and uses customized HFP (cHFP).[25] MPOD was measured at 458 nm with a 570-nm reference field using stimuli with radii of 10′, 30′, 1° and 2°, with a 7° eccentric reference. Because there are large individual differences in temporal sensitivity even among young healthy subjects, we optimized the frequency settings for each subject. For HFP measures to be the most precise, it is necessary to optimize the frequency settings to achieve a relatively narrow flicker null. If, for example, the frequency settings are too high, a relatively large zone of no flicker would result and this would yield more noisy measurements. Stringham et al.[25] describe an algorithm (based on prior measurement of critical flicker thresholds) that we used to optimize our frequency settings. Subjects fixated the 7° reference point when making their parafoveal settings. Subtracting the foveal radiance measures (where MP generally is dense) from the parafoveal radiance measures (where MP is minimal) yields an OD measure of MP. Subjects made 5 null flicker settings for each locus. Several validity and reliability studies have been published on the HFP technique on young and older subjects and on patients with early and relatively advanced AMD and cataracts. In general, these studies have shown that the method is highly reliable and yields results that are consistent with the known ex vivo spectrum of lutein (L) and zeaxanthin (Z).[24]

Measurement of Serum Carotenoids

Serum data were collected on only 100 of the 150 subjects in this sample. Serum data were collected by a licensed phlebotomist who collected 10 mL of blood for quantification of xanthophylls. The samples were collected in 10-mL lithium heparin-coated blood collection tubes (BD Vacutainer; Becton, Dickinson, and Company, Franklin Lake, NJ). Plasma was separated by centrifugation at 1500*g* for 20 minutes at 4°C. After separation, the plasma was distributed into 1.5-mL light-protected vials (Safe-Lock Tubes; Eppendorf, Hamburg, Germany), 1 mL per vial. The samples were stored at −80°C until express shipment (in insulated boxes on dry ice) to DSM Nutritional Products, Inc. (Kaiseraugst, Switzerland) for analysis. Half of the total sample from each subject was kept as a backup at UGA in case any problems were encountered in shipping (no incidents occurred). For a detailed description of the serum analysis, see Hartmann et al.[26] and Thürmann et al.[27] In brief, the xanthophylls were extracted with an n-hexane/chloroform 20% (vol/vol) mixture and injected into a normal-phase HPLC system for quantification. Separation was done on a silica gel column with a mixture of n-hexane/acetone 19% (vol/vol). Detection of the xanthophylls was at a wavelength of 452 nm. Identification of the individual lutein isomers was done by comparing the HPLC elution pattern of the plasma extracts with the HPLC pattern of authentic all-E-lutein and a Z-isomer mixture of lutein obtained after heat isomerization.

Reliability of the Psychophysical Measurements

The 100 subjects who are included in the results were run over two separate experimental sessions. This allowed us to assess the reliability of all of the measures for this sample. MP (at 30′) was significantly related across sessions (Cronbach's $\alpha = 0.93$): average MP at the first session was 0.47 compared with 0.46 at the second (mean absolute difference was 0.066, approximately 3%). CC was significantly related across sessions (Cronbach's $\alpha = 0.70$): average first session CC was 0.86, the second was 0.95 (mean absolute difference was 0.16, approximately 11%); GD was significantly related across sessions (Cronbach's $\alpha = 0.69$): average first session GD was 0.89, second was 0.97 (mean absolute difference was 0.13, approximately 9%). Finally, PR was also significantly related across sessions (Cronbach's $\alpha = 0.73$): average 37 seconds for the first session and 34 seconds for the second

Table 1. Descriptive Statistics for Serum Carotenoids ($n = 100$) and the Visual Measures ($n = 150$)

Variable	Average	SD	Range
Serum L, μmol/L	0.2	0.1	0.10 to 0.67
Serum Z, μmol/L	0.072	0.03	0.02 to 0.18
MPOD* 10′	0.54	0.2	0 to 1.04
MPOD 30′	0.43	0.16	0.02 to 0.88
MPOD 1°	0.29	0.13	0 to 0.66
MPOD 2°	0.12	0.09	0 to 0.37
Glare disability, log E	1.78	0.33	0.97 to 2.49
Photostress recovery, s	34.5	18	5.4 to 85.7
Contrast enhancement, log E	0.79	0.37	0.15 to 1.75

The relation between all of the dependent measures is shown in the correlation matrix provided in Table 2. As can be seen in the table, MP density measured in one location was strongly related to measures in other locations (although the magnitude of the correlation decreases with eccentricity probably due to the reduced range of the values). Like past studies,[28] MP density (30′) was also moderately related to circulating levels of L and Z within the serum ($r = 0.31$, $P = 0.002$). GD and CC were also strongly related to one another ($r = 0.78$, $P = 0.0001$). The exception was PR, which was related only to the macular and serum carotenoids, but not the other visual measures.

* MPOD is specified by radius.

(mean absolute difference was 13.5 seconds, approximately 11%). For subjects for whom two baselines were available, the average across sessions was used in all of the following analysis under the assumption that repeated testing would yield the measure closest to the true value. We also assumed that error was random and therefore did not Winsorize the data based on repeatability.

Results

Descriptive statistics for all of the variables is provided in Table 1. As shown in the table, MPOD at 30′ ranged from 0.02 to 0.81 (mean = 0.43, SD = 0.16). The other visual measures also varied widely: GD ranged from 0.97 to 2.49 μW/cm at threshold (mean = 1.78, SD = 0.33); PR ranged from 5.4 to 85.7 seconds (mean = 34.5, SD = 18); CC ranged from 0.15 to 1.75 μW/cm at threshold (mean = 0.786, SD = 0.37). Serum lutein concentrations ranged from 0.10 to 0.67 μmol/L (mean = 0.199, SD = 0.10) and serum zeaxanthin concentrations ranged from approximately 0.02 to 0.18 μmol/L (mean = 0.07, SD = 0.03).

Discussion

The descriptive statistics for all of the variables assessed in this study are provided in Table 1. Like similar past studies[17] of this population (UGA students), average MP density was relatively high (0.43 compared with our previous study,[17] which was 0.46), when compared with other studies measuring MP density. Unlike that study, however, the range in MP density was smaller (range = 0.81, compared with the previous range of 0.96) and the distribution of values more leptokurtic (i.e., clustered around the central average). This is likely due to the sampling method. The previous smaller study screened participants and picked individuals specifically to represent a full and platykurtic range of MP density. The present study comprised a random sample having numerous exclusion criteria, which tended to bias the sample away from the extremes (e.g., nonsmokers, normal BMI). Hence, many of the relations we examined could have potentially been attenuated due to restriction in range. This would be especially true if the visual effects we studied are not linear (e.g., deficiency could cause increased loss with the effects tending to plateau at higher densities[19]) (Wong JC, et al. *IOVS* 2010;51:ARVO E-Abstract 1288).

Despite this limitation, and the relative homogeneity of this sample, we did find a reasonable range of differences in all of the variables that we tested (see Table 1). For example, when exposed to the same bright-bleaching broadband light (Fig. 1), some subjects responded in as fast as 6 seconds, others took well over a minute to recover (most of the subjects fell evenly between approximately 10 and 60 seconds). This level of variability is striking when one considers that all of the subjects were young, relatively affluent college students with good acuity and in good health. Such data emphasize that many variables are necessary to adequately characterize vision across the life span.

One factor that significantly correlates with improved GD, PR, and CC is increased MP density, primarily as measured in the central portion of the retina (Fig. 2). Such a result is consistent with past studies of these variables on smaller samples. One difference, however, is the magnitude of the correlation. Stringham et al.,[17,18] for example, testing 40 subjects, found a stronger relation between MP density (at 30′) and GD ($r = 0.79$) and PR ($r = 0.80$). Our somewhat reduced correlations may be due to the reduced range of MP (e.g., 10% of their sample was higher than our highest value),

Table 2. Pearson Product-Moment Correlations

Variable	MPOD 15″	MPOD 30″	MPOD 1°	MPOD 2°	Serum L μmol/L	Serum Z μmol/L	Glare log E	Photo Stress Recovery, s	Contrast Enhancement log E
MPOD 15″	1	0.91‡	0.71‡	0.49‡	0.28‡	0.16	0.24†	−0.12	0.47‡
MPOD 30″	0.91‡	1	0.78‡	0.60‡	0.32‡	0.20*	0.24‡	−0.18†	0.46‡
MPOD 1°	0.71‡	0.78‡	1	0.80‡	0.40‡	0.24†	0.22‡	−0.14*	0.41‡
MPOD 2°	0.49‡	0.60‡	0.80‡	1	0.38‡	0.28‡	0.12	−0.08	0.23‡
Serum L, μmol/L	0.28‡	0.32‡	0.40‡	0.38‡	1	0.77‡	−0.01	−0.20†	0.19*
Serum Z, μmol/L	0.16	0.20*	0.24†	0.28‡	0.77‡	1	−0.01	−0.21†	0.07
Glare, log E	0.24†	0.24‡	0.22‡	0.12	−0.01	−0.01	1	−0.06	0.78‡
Photo stress recovery, s	−0.12	−0.18†	−0.14*	−0.08	−0.20†	−0.21†	−0.06	1	−0.12
Contrast enhancement, log E	0.47‡	0.46‡	0.41‡	0.23‡	0.19*	0.07	0.78‡	−0.12	1

As shown in Figure 2, all of the variables were related to MP density. MP density at 30′ was related to GD ($r = 0.24$, $P = 0.0015$), PR ($r = -0.18$, $P = 0.01$), and CC ($r = 0.46$, $P = 0.00005$). The relation between serum L and Z concentrations and the visual measures was reduced (CC) or absent (GD) for all of the visual measures, except PR, which was moderately related to both L ($r = -0.2$, $P < 0.05$) and Z ($r = -0.21$, $P < 0.05$).

* $P < 0.10$.

† $P < 0.05$.

‡ $P < 0.001$.

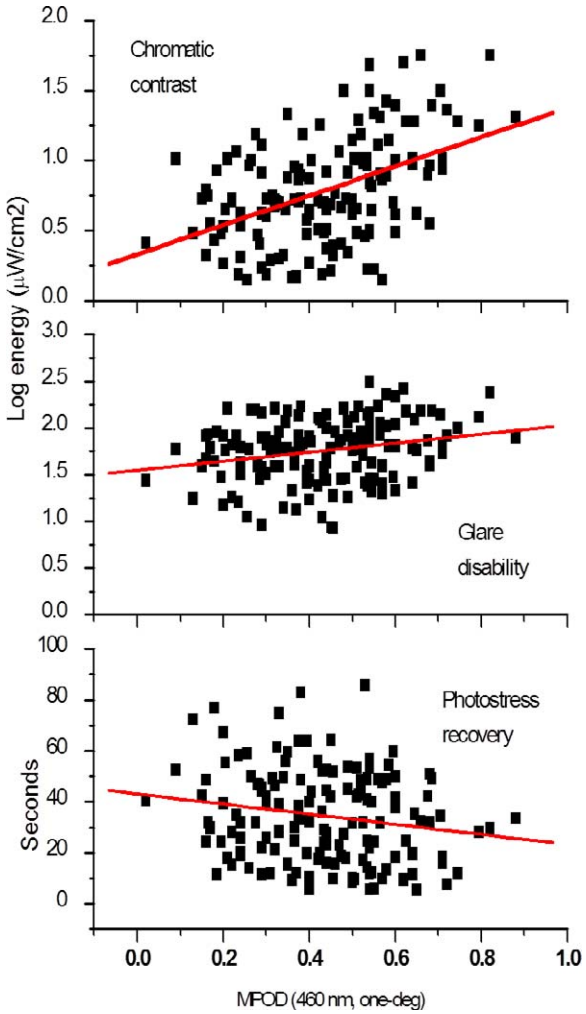

FIGURE 2. The relation between macular pigment and visual performance. *Top panel*: The CC thresholds (the amount of energy in the 460-nm background necessary to lose sight of a central 570-nm target). *Middle panel*: Glare disability thresholds (the amount of energy in an annulus necessary to veil a central target). *Bottom panel*: Photostress recovery durations (the amount of time required to regain sight of the central target after exposure to a photostressor).

and higher measurement error (reliability in our baseline GD and PR values was lower than their MP versus GD and PR correlations). Notwithstanding these limitations, the relations between MP density and our visual measures were moderately significant.

The relation between serum LZ and the visual measures was not significant for GD but was moderately related to CC ($r = 0.19$, $P < 0.05$) (Table 2). This weak relation makes sense because serum LZ is likely a proxy variable for the carotenoids in the retina. L and Z in the retina likely improve GD and CC due to simple filtration (as shown when testing wavelengths not absorbed by the pigments[17]). By absorbing scattered light at the central point of focus, individuals can see through veiling haze.

The relation between serum L and Z and PR may be more complex. The speed of visual recovery after exposure to an intense bleaching light source is a function of three factors: adaptive state, the proportion of photopigment bleached, and how rapidly the photopigment regenerates. MP could reduce the amount of bleached photopigment by simply filtering light before it is incident on the foveal cones. L and Z are found in receptoral outersegments,[29,30] but the question of whether L and Z influence photopigment regeneration has not been studied. In this data set, we found a significant relation between PR and the amount of LZ circulating within the serum ($r = -0.23$, $P < 0.01$) (Table 2). This relation was stronger than the relation to MP within the retina (when the same 100 subjects were analyzed) ($r = -0.15$, $P < 0.07$). Renzi and Hammond[31] have shown that MP is related to faster visual processing (likely a postreceptoral process). Taken together, effects of MP on visual physiology are possible and should be explored further (see, for example, the Neural Efficiency hypothesis[31]).

The stimuli that we used in this experiment were chosen to be ecologically valid. For example, the xenon-light source used in the GD and PR conditions matches quite closely the spectrum of midday sunlight (as shown in Fig. 1). Sunlight is, of course, a common source of glare. For example, there is a long history of efforts to reduce the effects of glare on the visual performance of athletes. Baseball caps and eye black (a dark grease placed under the eye), for instance, were invented to reduce glare from the overhead sun and the intense stadium lighting used to illuminate baseball fields at night (stadium lighting often uses xenon bulbs). Gray et al.[32] has shown that yellow intraocular implants (when compared to clear) improve driving performance under glare conditions. Past studies have shown that when stimuli are used that do not contain a significant short-wave component,[33,34] significant relationships between MP and such visual measures are not observed. This is likely because the ability to accumulate MP evolved under natural (e.g., sunlight), not artificial (e.g., tungsten, fluorescent), lighting sources. Based on similar logic, it is unlikely that MP would influence visual problems that were relatively uncommon throughout most of our evolutionary past, such as refractive errors.[35,36]

Finding a relation to CC thresholds also makes practical sense because such stimuli also have ecological significance. Given the neural mechanisms underlying edge detection (e.g., lateral inhibition), any alteration of an image that enhances contrast of a given target relative to its spectral surround should improve detectability of that target. Hence, under the right wavelength conditions, any chromatic filter that absorbs one side of a chromatic border more than another would improve contrast by definition. Chromatic borders (isoluminant edges) are common in the natural environment.[8] Rayleigh scatter and blue haze often create blue backgrounds when viewing objects at a distance, such as a baseball against a blue sky.

In sum, these data confirm our initial observations showing a significant relationship among MP density, GD, CC thresholds, and PR. We are currently in the process of exploring the causality of these relations through clinical intervention. The 100 subjects for whom we obtained serum are currently receiving a 12-mg LZ supplement or placebo (ClinicalTrials.gov number, NCT00909090.) for 1 year. MP density, CC, GD, and PR are being assessed at 3-month intervals throughout the year.

Acknowledgments

The authors thank Ron Forehand, MD, and Jean Chin, MD, University of Georgia Health Center, for conducting all subject blood work and physicals before enrollment. Rick Lewis provided the laboratory for collecting and processing serum samples.

References

1. Christoforidis JA, Tecce N, Dell'omo R, Mastropasqua R, Verolino M, Costagliola C. Age related macular degeneration and visual disability. *Curr Drug Targets*. 2011;12:221–233.

2. Collins MJ, Brown B. Glare recovery and age related maculopathy. *Clinical Vision Sciences*. 1989;4;145–153.
3. Sandberg MA, Gaudio AR. Slow photostress recovery and disease severity in age-related macular degeneration. *Retina*. 1995;15:407–412.
4. Aslam TM, Haider D, Murray IJ. Principles of disability glare measurement: an ophthalmological perspective. *Acta Ophthalmol Scand*. 2007;85:354–360.
5. Van Den Berg TJ, van Rijn LJ, Michael R, Heine, C, Coeckelbergh, T, Nischler, C, et al. Straylight effects with aging and lens extraction. *Am J Ophthalmol*. 2007;144:358–363.
6. Steen R, Whitaker D, Elliott DB. Age related effects of glare on luminance and color contrast sensitivity. *Optom Vis Sci*. 1994; 71:792–796.
7. Gegenfurtner KR, Rieger K. Sensory and cognitive contributions of color to the recognition of natural scenes. *Curr Biol*. 2000;10:805–808.
8. Hansen T, Gegenfurtner KR. Independence of color and luminance edges in natural scenes. *Vis Neurosci*. 2009;26:35–50.
9. Walls GL, Judd HD. The intraocular colour filters of vertebrates. *Br J Ophthalmol*. 1933;17:641–645.
10. Wooten BR, Hammond BR. Macular pigment: influences on visual acuity and visibility. *Prog Retin Eye Res*. 2002;21:225–240.
11. Hammond BR, Wooten BR, Engles M, Wong JC. The influence of filtering by the macular carotenoids on contrast sensitivity measured under simulated blue haze conditions. *Vis Res*. 2012;63:58–62.
12. Mollon JD, Regan BC. The spectral distribution of primate cones and of the macular pigment: matched to the properties of the world? *J Opt Technol*. 1999;66:847–852.
13. Hammond BR, Renzi L. *The characteristics and function of lutein and zeaxanthin within the human retina*. In: Phytochemicals: Aging and Health. Boca Raton, FL: CRC Press; 2008:89–106.
14. Stringham JM, Fuld K, Wenzel AJ. Action spectrum for photophobia. *J Opt Soc Am*. 2003;20:1852–1858.
15. Stringham JM, Fuld K, Wenzel AJ. Spatial properties of photophobia. *Invest Ophthalmol Vis Sci*. 2004;45:3838–3848.
16. Wenzel AJ, Fuld K, Stringham JM, Curran-Celantano J. Macular pigment optical density and photophobia light threshold. *Vis Res*. 2006;46:4615–4622.
17. Stringham JM, Hammond BR. The glare hypothesis for macular pigment function. *Optom Vis Sci*. 2007;84:859–864.
18. Stringham JM, Hammond BR. Macular pigment and visual performance under glare conditions. *Optom Vis Sci*. 2008;85: 82–88.
19. Stringham JM, Garcia PV, Smith PA, McLin LN, Foutch BK. Macular pigment and visual performance in glare: benefits for photostress recovery, disability glare, and visual discomfort. *Invest Ophthalmol Vis Sci*. 2011;52:7406–7415.
20. Renzi L, Hammond BR. The effect of macular pigment on heterochromatic luminance contrast. *Exp Eye Res*. 2010;91: 896–900.
21. Stringham J, Hammond BR, Wooten BR, Snodderly DM. Compensation for light loss due to filtering by macular pigment: relation to the –1 mechanism. *Optom Vis Sci*. 2006;83:887–94.
22. Stringham J, Hammond BR. Compensation for light loss due to filtering by macular pigment: relation to hue-cancellation functions. *Ophthalm Phys Opt*. 2007;27:232–237.
23. Wooten BR, Hammond BR, Land RI, Snodderly DM. A practical method for measuring macular pigment optical density. *Invest Ophthalmol Vis Sci*. 1999;40:2481–2489.
24. Hammond BR, Wooten BR, Smollon B. Assessment of the validity of in vivo methods of measuring human macular pigment optical density. *Optom Vis Sci*. 2005;82:387–404.
25. 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;87:445–453.
26. Hartmann D, Thürmann PA, Spitzer V, Schalch W, Manner B, Cohn W. Plasma kinetics of zeaxanthin and 3′-dehydro-lutein after multiple oral doses of synthetic zeaxanthin. *Am J Clin Nutr*. 2004;79:410–417.
27. Thürmann PA, Schalch W, Aebischer JC, Tenter U, Cohn W. Plasma kinetics of lutein, zeaxanthin, and 3′-dehydro-lutein after multiple oral doses of a lutein supplement. *Am J Clin Nutr*. 2005;82:88–97.
28. 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.
29. Rapp LM, Maple SS, Choi JH. Lutein and zeaxanthin concentrations in rod outer segment membranes from perifoveal and peripheral human retina. *Invest Ophthalmol Vis Sci*. 2000;41:1200–1209.
30. Bernstein PS, Khachik F, Carvalho LS, Muir GJ, Zhao D-Y, Katz NB. Identification and quantification of carotenoids and their metabolites in the tissues of the human eye. *Exp Eye Res*. 2001;72:215–223.
31. Renzi L, Hammond BR. The relation between the macular carotenoids, lutein and zeaxanthin, and temporal vision. *Ophthal Physiol Optics*. 2010;30:351–357.
32. Gray R, Perkins SA, Suryakumar R, Neuman B, Maxwell WA. Reduced effect of glare disability on driving performance in patients with blue light-filtering intraocular lenses. *J Cataract Refract Surg*. 2011;37:38–44.
33. Loughman J, Beatty S, Akkalli M, et al. The relationship between macular pigment and visual performance. *Vis Res*. 2010;50:1249–1256.
34. Nolan JM, Loughman J, Akkali MC, et al. The impact of macular pigment augmentation on visual performance in normal subjects: COMPASS. *Vis Res*. 2011;51:459–469.
35. Neelam K, Nolan J, Loane E, et al. Macular pigment and ocular biometry. *Vision Res*. 2006;46:2149–2156.
36. Engles M, Wooten B, Hammond BR. Macular pigment: a test of the acuity hypothesis. *Invest Ophthalmol Vis Sci*. 2007;48: 2922–2931.
37. ASTM standard G173-03e1 standard tables for reference solar spectral irradiances: direct normal and hemispherical on 378 tilted surface. ASTM International. Available at: http://www.astm.org/DATABASE.CART/HISTORICAL/G173-03E1.htm. Accessed July 26, 2012.