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Macular pigment optical density and photophobia light threshold ☆

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Abstract

Light absorption by macular pigment may attenuate visual discomfort, or photophobia, for targets composed of short-wavelength light. Macular pigment optical density (MPOD) and photophobia light thresholds were measured psychophysically in 10 subjects. The energy necessary to induce photophobia for a short-wavelength target relative to a long-wavelength target was linearly related to MPOD, as well as estimates of peak MPOD and integrated macular pigment. In four subjects who consumed lutein supplements, increases in MPOD corresponded to increases in photophobia light thresholds. Light absorption by macular pigment appears to influence the amount of short-wavelength light necessary to elicit photophobia.

Keywords: Macular pigment; Photophobia; Lutein; Psychophysics

1. Introduction

In the human eye, some short-wavelength light is absorbed by macular pigment before it reaches the photopigments in the central retina. The macular pigment, comprised primarily of two dietary carotenoids, lutein and zeaxanthin, absorbs wavelengths of light between 400 and 530 nm (Wyszecki & Stiles, 1982). The absorption of radiant energy by macular pigment may protect posterior ocular tissue from excessive exposure of potentially harmful wavelengths of light. At wavelengths of light below 450nm, for example, approximately one-hundred times less energy is needed to produce retinal insult compared to wavelengths greater than 590 nm (Ham, Mueller, & Sliney, 1976). Light absorption by macular pigment may also affect light thresholds for visual discomfort or photophobia.

Photophobia is a condition characterized by the exacerbation or generation of pain or discomfort as a consequence of normal light exposure. Although most individuals experience an acute episode of photophobia as they enter a bright environment after prolonged exposure to dark surroundings, some individuals suffer from chronic light-induced pain. Patients with neurological disorders, such as trigeminal neuralgia (Wolff, 1963), and individuals suffering from eye diseases, like retinitis pigmentosa (Gawande, Donovan, Ginsburg, & Marmor, 1989) and age-related macular degeneration (Bacotti, 2001), may report persistent hyper-sensitivity to light and periods of photophobia. Photophobia also appears to be a common symptom of migraine headaches (Drummond, 1997;Muelleners et al., 2001; Vanagaite-Vingen & Stovner, 1998). Despite its association with numerous clinical conditions, little is known about the etiology of photophobia other than the involvement of the trigeminal pupillary reflex (Lebensohn, 1951).

Most research investigating the stimulus parameters mediating visual discomfort focused on discomfort glare—a condition in which distracting, possibly discomforting, light sources are located in the peripheral field of view (Vos, 2003). Using a standardized scale (de Boer, 1967), Sivak, Flannagan, Traube, and Kojima (1999) found

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that as the duration or intensity of a light source increased, so did observers' levels of visual discomfort. Other investigators have reported that discomfort thresholds were lower for binocular, versus monocular, targets (Vanagaite et al., 1997;Vanagaite-Vingen & Stovner, 1998) and non-uniform or grating, versus uniform, stimuli (Waters, Mistrick, & Bernecker, 1995). Berman, Bullimore, Jacobs, Bailey, and Gandhi (1994) demonstrated that eye squinting magnitude, as measured by electromyography (EMG), was related to a subject's level of visual discomfort. For a glare source located at 11° retinal eccentricity, they found that muscle contraction around the eye increased as the luminance of the light source increased. Further, their subjects appeared to experience more discomfort when viewing a 2° glare source than a 1° source.

Several investigators looked at the effects of a target's spectral composition on visual discomfort. Berman and colleagues (1996), for example, reported that a light source weighted in energy toward the long-wavelength end of the spectrum induced greater discomfort (i.e., muscle contraction) compared to a light weighted in energy at the shorter wave end. In patients with migraine, Main, Vlachonikolis, and Dowson (2000) found that discomfort thresholds were lower for a short-wavelength target than for a medium or long-wavelength target. Discomfort thresholds for the short and long-wavelength targets were similar in the control group, and lower than the threshold for a medium-wavelength target. More recently, Stringham, Fuld, and Wenzel (2003) looked at the effects of monochromatic lights (with bandwidths less than 10 nm) on photophobia thresholds. Unlike other researchers, they controlled retinal illuminance (pupil size) by using Maxwellian view optics. Stringham et al., used both EMG and a rating scale to measure photophobia thresholds for wavelengths of light between 440 and 640 nm. The normalized action spectra for all of their observers showed a high degree uniformity. Between 520 and 640 nm, there was a positive relationship between wavelength and the energy needed to produce photophobia. At shorter wavelengths the spectra show a notch centered at 460 nm. Interestingly, the trough and shape of this notch roughly resemble the log transmittance spectrum of macular pigment. In fact, the difference in macular pigment optical density (MPOD) among the subjects appeared to account for their slight, but uniform, difference in photophobic sensitivity below 520 nm. Further, when the filtering effects of macular pigment, as well as the lens, were accounted for, the photophobia spectra resembled the retinal damage function reported by Ham et al. (1976). These findings suggest that macular pigment may attenuate photophobia or discomfort associated with sufficiently intense short-wavelength targets and may impact the threshold for photophobia under normal viewing conditions. The objective of the present project was to test directly the relationship between macular pigment and photophobia light threshold.

2. General methods

2.1. Measurement of macular pigment optical density

Retinal sensitivity to a short-wavelength light was measured in the fovea and parafovea with heterochromatic flicker photometry (HFP). For a given trial the subject viewed one of four centrally fixated targets or a parafoveal target. The four centrally fixated targets were two discs, with visual angles of 40′ and 60′ of arc, and two annuli, with widths of 20′ and outer diameters of 2° and 4° of arc. The parafoveal target was a 2° disc centered at 7° eccentricity by the subject's fixation of a small, long-wavelength point of light. The spatial distributions of the five targets relative to MPOD across the fovea are illustrated in Fig. 1 (top panel). Each target was superimposed on a 6°, 470 nm background (1.5 log Tds), and alternated in square-wave between a 460 nm test light and a 550 nm reference light (1.7 log Tds); the half-bandwidth of the background, reference and

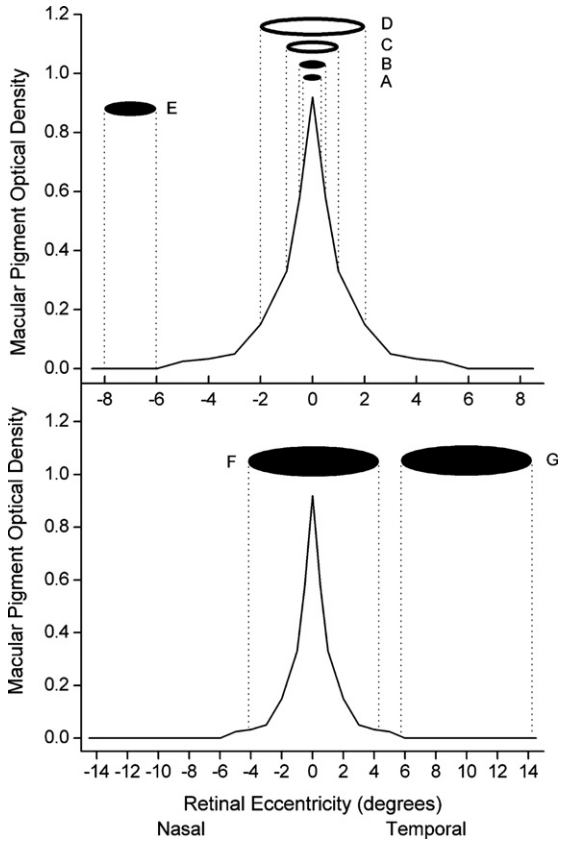

Fig. 1. Schematic of the spatial distributions of the stimuli used to measure macular pigment optical density (MPOD; top panel) and photophobia thresholds (bottom panel) relative to MPOD. In the top panel, Stimuli A and B are centrally fixated discs that subtend 40′ and 1° of visual angle, respectively. Stimuli C and D are centrally fixated annuli, with outer edges subtending 2° and 4°, respectively. The widths of the annuli subtend 20′ of visual angle. Stimulus E is a 2° disc centered at 7° eccentricity by the subject's fixating a small point of light to the left of the stimulus. Subtracting the mean log energy necessary to minimize or eliminate flicker for target E from the mean log energy necessary for the four centrally viewed targets yields measures of MPOD at 20′ (A), 30′ (B), 1° (C), and 2° (D) eccentricity. In the bottom panel, Stimuli F and G are discs subtending 8.2° of visual angle. Stimulus F is centrally fixated whereas stimulus G is centered at 10.1° eccentricity by the subject's fixation of a small point of light. Subtracting the ratio of energy necessary to induce photophobia for Stimulus G from the energy ratio necessary for Stimulus F yields a difference ratio or photophobia ratio.

test lights was approximately 20 nm. The test stimuli were produced by a Macular Metrics® (Rehoboth, MA), free-view densitometer described by Wooten, Hammond, Land, and Snodderly (1999).

The radiance of the reference light was kept constant as the subject adjusted the radiance of the test light in order to minimize or eliminate the perceived flicker of the test stimulus. The variation in combined radiance with adjustment of the test light does not effect flicker photometric measurements of this sort (Kaiser & Boynton, 1996). Likewise, the flicker frequency of the test target has little impact on the measure provided the subject can find a point of minimal or zero flicker (Werner, Donnelly, & Kliegl, 1987). Ideally, the subject should be able to adjust the intensity of the test light to observe a "zone" of flicker on both sides of a small null zone—range of radiances for which the test stimulus appears not to flicker. The subject's specific task was to find the null zone and then estimate its mid point. Typically, a subject's estimate of the mid point for a particular target varies slightly between and within testing sessions. One method to reduce such variability is to adjust the flicker frequency of the test stimulus until the null zone is small (Hammond, Wooten, & Smollon, 2005). In general, the null zone and flicker frequency are related positively, such that increasing the flicker frequency increases the null zon'e. In the current project, the flicker frequency of each target was adjusted until the subject perceived a null zone that spanned 100 radiance units according to the instrument's readout. A null zone of this size was small enough to limit subject variability, but large enough so that subjects could easily and consistently perform estimations of the null zone's mid point. The flicker frequencies used in the current project ranged between 15 and 21 Hz for the foveal targets and between 10 and 13 Hz for the parafoveal target. Regardless of the size of the null zone, subjects rarely select the exact same mid-point on successive attempts. In order to reduce the effects of such variability, eight mid-point estimations were obtained for each target. After the subject selected each mid-point by depressing a button, the radiance of the test light was offset between 100 and 300 radiance units either above or below the mid-point radiance. The mean radiance of the eight measures was used to calculate MPOD at each eccentricity. More specifically, the mean log radiance of the eight parafoveal mid-points was subtracted from the mean log radiance of each of the four foveal targets to yield measures of MPOD at the four retinal loci where the edges of the centrally fixated targets were imaged (Werner et al., 1987): 20′, 30′, 1°, and 2° eccentricity.

An estimate of aggregate light filtration by macular pigment across the fovea was estimated by taking the area under each subject's measures of MPOD, or MPOD profile. Each subject's data was plotted and fit with a Gaussian function using Origin 7.0 (Origin Lab Corporation, Northampton, MA). The area under each subject's fitted MPOD profile was taken to yield a measure of integrated macular pigment screening. The nonlinear function also provided an estimate of peak MPOD (i.e., MPOD at 0°).

2.2. Measurement of photophobia

Photophobia thresholds were measured in Maxwellian-view using a method similar to Stringham, Fuld, and Wenzel (2004). In short, a three-channel Maxwellian view optical system was used to produce the test stimuli. One channel was used to produce an 8.2°, broadband test stimulus. Light in this channel passed through either a broadband short-wavelength filter (Oriel Corp. #59830), which transmitted wavelengths of light less than 520 nm, or a broadband long-wavelength filter (Tiffen #15), which transmitted light at wavelengths above 540 nm. Thus, light transmitted by the short-wavelength filter was strongly absorbed by the macular pigment, whereas the light transmitted by the long-wavelength filter was outside the absorption spectrum of macular pigment. Another channel was used to create a mesopic (-1 log cd/m^2), xenon-white, 30.5° background. The third channel produced a small, 20′, long-wavelength fixation light.

At the beginning of each experimental session, the subject's right pupil was aligned with the exit pupil of the optical system. Throughout the experiment a dental impression and forehead rests were used by the subject to maintain this position. After the alignment procedure, subjects dark adapted for 20 min. Subjects then fixated the small long-wavelength light for 2 min. This fixation light was located either centrally, for foveal measures of photophobia, or at 10.1° temporal eccentricity for parafoveal measures of photophobia. Fig. 1 (bottom panel) shows the spatial distributions of the foveal and parafoveal test stimuli relative to MPOD. After the subject adapted to the background for 2 min, the experimenter announced that the test stimulus was to be presented. The time between the experimenter's cue and the presentation of the test target was quasi-random, between 5 and 20 s. After a 5-s presentation of the test target, subjects used a 10-point psychophysical scale, similar to the de Boer scale (de Boer, 1967) to rate their level of visual discomfort. A "1" represented no discomfort and a "10" represented photophobia—i.e., the light caused sufficient discomfort to elicit a squint and subjects' desire to divert their eye from the target. The initial test target was well below a subject's photophobia threshold. By use of the method of ascending limits, the energy of the test light was increased by subtracting neutral density from the test stimulus channel. If the subjects rated their discomfort between 5 and 9, 0.1 log units of neutral density were subtracted; otherwise 0.3 log units were removed from the channel. Random catch trials were performed in the following way to assess subject bias. After each presentation of the test stimulus, the experimenter rolled two die. If the sum of the die was 2, 0.1 log units of density were added to the test channel. If the subject correctly rated the stimulus as less intense (i.e., gave a lower number) than the previous target, the response was recorded as a "hit." Conversely, if the subject incorrectly rated the stimulus, rating it as equally or more discomforting than the previous stimulus, it was recorded as a "false alarm" (FA). Additional non-random catch trials were also performed by the experimenter to determine better subjects' photophobia thresholds. To maintain the same level of retinal sensitivity prior to each presentation of the test stimulus, subjects covered their right-eye with an eyepatch and dark adapted for 15 min between trials. This amount of time ensured that the subject was able to perceive the mesopic background. The above procedure was repeated until the subject reported that he or she experienced photophobia (i.e., a rating of 10) while viewing the test stimulus. Photophobia thresholds for the 8.2° test stimulus were measured for the short-wavelength ("blue") target in the fovea and parafovea and for the long-wavelength ("orange") target in the fovea and parafovea. All four light thresholds were measured in a single experimental session. After the experiment, the relative energy of the four test lights that induced photophobia, which ranged between 4.06 and 4.98 log Tds, was measured using a radiometer (United Detector Technology Optometer #61). The log relative energy of the orange target that induced photophobia was then subtracted from the log relative energy of the blue target that induced photophobia to yield a foveal photophobia ratio. A parafoveal photophobia ratio was calculated in the same manner. Finally, a difference ratio (PP ratio) was calculated by taking the absolute difference between the parafoveal photophobia ratio and the foveal photophobia ratio. For example, the log relative energies of the orange and blue foveal targets rated a 10 (i.e., induced photophobia) by Subject 1 were 2.158 and 2.174, respectively, yielding a fovea photophobia ratio of -0.016. The log relative energies that induced photophobia in parafovea of Subject 1 were 2.451 for the orange target and 2.238 for the blue target, yielding a parafoveal photophobia ratio of -0.673. The resulting difference ratio, or PP ratio, for Subject 1 was 0.657. The fovea and parafovea ratios used in this example are illustrated in Fig. 2 by the slashed bars (scaling technique) for Subject 1 and were obtained in the following pilot study.

2.3. Validation of scaling procedure

Prior to the initiation of the project, a pilot study was conducted to compare photophobia thresholds measured with the scaling technique to those determined with EMG. Most previous studies investigating visual discomfort asked subjects to use a scale (as was the case in the present study) to quantify their level of discomfort when viewing a light source. A few researchers, however, attempted to measure photophobia or discomfort glare using an objective, EMG procedure (Berman et al., 1994; Murray, Plainis, & Carden, 2002; Stringham et al., 2003). They recorded gross muscle potentials around the eye (EMG) while their subjects viewed a light source. Essentially, these researchers assumed that a sufficiently intense light will compel a subject to squint in order to limit the amount of light entering the eye. When the signal-to-noise ratio of the EMG trace (i.e.,

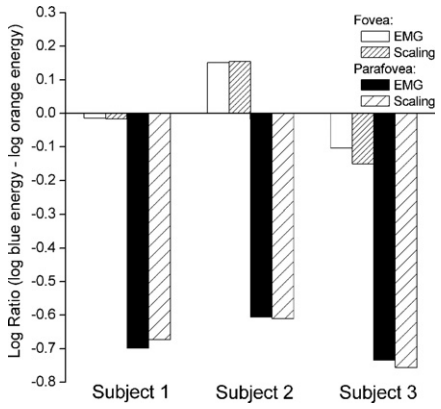

Fig. 2. Foveal and parafoveal photophobia ratios for two well trained subjects (Subjects 1 and 2) and one naïve subject (Subject 3) measured with electromyography (filled bars) and a scaling technique (slashed bars).

squint magnitude) exceeded a criterion value, the subject was defined operationally to have experienced photophobia. The subjects in these studies were also asked to rate their level of discomfort using a scale. Interestingly, the three groups of researchers noted a high degree of correspondence between squint magnitude and the subjects' subjective ratings of discomfort. In fact, Stringham et al., showed that the photophobia action spectrum obtained using EMG looked essentially identical to the spectrum based on their subjects' ratings of lights just below the photophobia threshold. Their subjects used the same 10-point psychophysical scale used in the present study. As a way to further validate the scaling procedure used in the present study, the EMG procedures described by Stringham et al. (2004) were used to measure photophobia thresholds for the blue and orange targets in two well trained subjects and one naïve subject. Three nickel-plated, surface electrodes were used to record gross potentials generated during a squint: one electrode was attached below the subject's right eye (test), another on the subject's right temple (reference), and a third on the back of the subject's neck (ground). The electrodes were connected to a Grass Instruments amplifier (#7P3B; West Warwick, RI), which sent the signal to a waveform computer program. As in Stringham et al., photophobia was defined as a signal-to-noise ratio of 4:1 on the EMG trace lasting at least 2.5 s of the 5 s duration of the test stimulus.

The fovea and parafovea ratios obtained for the two well trained subjects (Subjects 1 and 2) and one naïve subject (Subject 3) using EMG in one session and a scaling technique in a separate session are presented in Fig. 2. Each bar in the figure represents the ratio of energy necessary to induce photophobia for the orange target versus the blue target. There was a high degree of similarity within subjects using the two techniques. In Subjects 1 and 2, in particular, the fovea and parafovea ratios obtained with EMG (solid bars) were nearly identical to their respective ratios obtained using the scaling technique (slashed bars). The difference in sensitivity between the orange and blue targets was greatest in the parafovea (parafovea ratio) for all three subjects regardless of the method used to measure photophobia thresholds. The fovea ratios, in contrast to the parafovea ratios, markedly differed between subjects. In Subject 1, there was little difference in the energy that induced photophobia for the blue and orange foveal targets. On the other hand, Subject 2 had the greatest difference in threshold energy for the two targets, and unlike Subjects 1 and 3, required more energy for the blue target than the orange target to induce photophobia in the fovea (hence the positive ratio). Interestingly, Subject 1 had relatively low MPOD whereas Subject 2 had relatively high MPOD. The within-subject differences between the EMG and scaling technique measures were well within the test-retest variance observed in a previous study investigating photophobia (Stringham et al., 2003), which suggests that a scaling technique can be reliably used to determine photophobia thresholds. Further, a psychophysical scaling procedure has two primary advantages over EMG for determining photophobia thresholds. It is less invasive for the subject, and more importantly, EMG can be used only to measure squint magnitude, not the experience of visual discomfort.

2.4. Procedure

To investigate adequately the impact of macular pigment on photophobia, two experiments were performed. The objective of Experiment I was to investigate the relationship between MPOD and the energy necessary to induce photophobia for the blue target relative to the orange target. By use of the aforementioned techniques, MPOD and photophobia thresholds were measured in 10, non-smoking Caucasians: four males and six females, ages 21–33. The relationships between PP ratio and MPOD, integrated macular pigment and estimated peak MPOD were analyzed by Pearson product-moment correlations. The data are presented as means (±SEM).

The objective of the Experiment II was to increase MPOD and measure the possible changes in the energy needed to induce photophobia. Four subjects from Experiment I, two males and two females, ages 24–31, consumed 60 mg of Xangold™ (Cognis Corporation, La Grange, IL) dietary supplement daily for 12 weeks. The dosage was equal to approximately 30 mg of free lutein and 2.7 mg of free zeaxanthin per day. During the 12 weeks of intervention, subjects continued their regular diet. Photophobia thresholds and MPOD were measured at baseline and again after 6 and 12 weeks of intervention. A randomized-block design (Kirk, 1995) was used to measure the significance of changes in MPOD, integrated macular pigment, estimated peak MPOD, and PP ratio. For significant analyses ($p < 0.05$), ω^2 was calculated as a measure of effect size. The use of human subjects in this project was approved by the University of New Hampshire Institutional Review Board and adhered to the Declaration of Helsinki.

3. Results

3.1. Experiment I

Mean MPOD ($n = 10$) was 0.423 (±0.04), 0.326 (±0.04), 0.186 (±0.01), and 0.065 (±0.01) at 20′, 30′, 1°, and 2° eccentricity, respectively. There were no significant differences in MPOD between the males and females. Subjects' MPOD at 20′ ($r = 0.767$, $p = 0.009$), 30′ ($r = 0.760$, $p = 0.010$) and 1° ($r = 0.694$, $p = 0.025$) eccentricity were linearly related to PP ratio. MPOD at 2° eccentricity was not related to PP ratio ($r = -0.116$, $p = 0.750$). The relationships between MPOD at each eccentricity and PP ratio is illustrated in Fig. 3. Data points with like symbols represent each of the 10 subjects. The lines represent linear fits applied to the data points for each retinal eccentricity.

The Gaussian function appeared to describe the subjects' MPOD profiles well according to the coefficient of determination (R^2). The mean R^2 was 0.961 (±0.04), and ranged from 0.856 to 0.999. Peak MPOD estimated by the Gaussian function ranged from 0.197 to 0.730, with a mean of 0.436 (±0.05). The area under the Gaussian fit of each subject's MPOD profile, or integrated macular pigment, ranged from 7.4 to 68.3 with a mean of 48.3 (±5.9). Both estimated peak MPOD ($r = 0.776$, $p = 0.008$) and integrated macular pigment ($r = 0.830$, $p = 0.002$) were positively correlated with PP ratio.

3.2. Experiment II

The subjects' mean MPOD ($n = 4$) at baseline and after 6 and 12 weeks of lutein intervention is illustrated in Fig. 4 (error bars are SEM). Changes in MPOD significantly differed from baseline at 20′ ($F = 17.35$, $p = 0.003$, $\omega^2 = 0.73$),

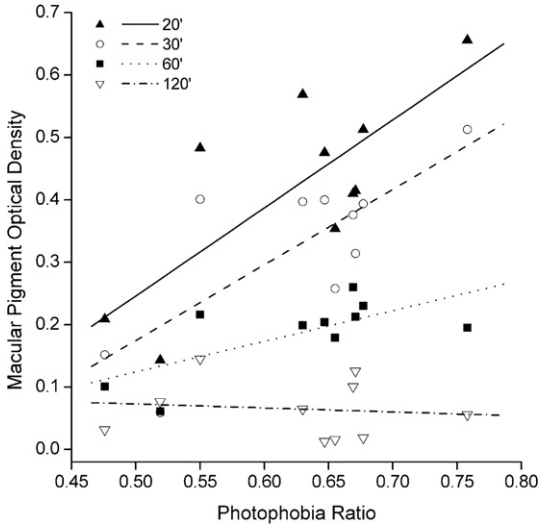

Fig. 3. The relationships between macular pigment optical density at 20′, 30′, 60′ (1°) and 120′ eccentricity and photophobia ratio in Experiment I. The lines represent a linear fit of the data at each retinal eccentricity.

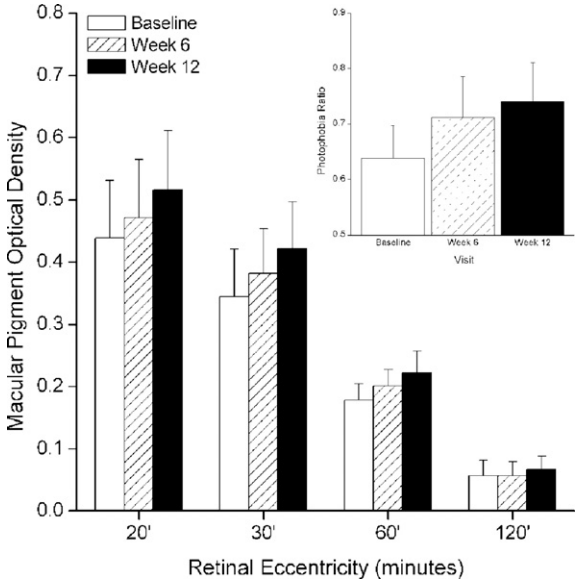

Fig. 4. Mean baseline, week 6, and week 12 macular pigment optical density (MPOD) at 20′, 30′, 60′ (1°) and 120′ eccentricity for the four subjects in Experiment II. Inset shows mean photophobia ratios at baseline, 6 and 12 weeks. Error bars represent SEM.

30′ ($F=77.00$, $p<0.001$, $\omega^2=0.92$) and 1° ($F=7.04$, $p=0.026$, $\omega^2=0.50$) eccentricity, but not at 2° eccentricity ($F=1.71$, $p=0.370$). At the three central loci, a linear trend can be used to describe the changes in MPOD (20′: $F=26.04$, $p=0.014$, $\omega^2=0.89$; 30′: $F=495.70$, $p<0.001$, $\omega^2=0.93$; 1°: $F=11.29$, $p=0.043$, $\omega^2=0.74$).

The R^2 of the Gaussian fit of the subject's MPOD profiles at baseline ranged from 0.999 to 0.950. Interestingly, the coefficient of determination increased after intervention. The mean R^2 was 0.972 at baseline and 0.983 after intervention. Mean integrated macular pigment increased from 50.86 (±9.15) at baseline to 56.10 (±8.94) after six weeks of intervention, and to 60.27 (±9.74) after 12 weeks. Integrated macular pigment significantly increased from baseline ($F=9.12$, $p=0.015$, $\omega^2=0.57$) and followed a linear trend ($F=16.74$, $p=0.026$, $\omega^2=0.75$). After 12 weeks of lutein supplementation, estimated peak MPOD increased from 0.452 (±0.11) to 0.536 (±0.11). This change significantly differed from baseline ($F=15.28$, $p=0.004$, $\omega^2=0.70$) and appeared to be linear ($F=17.03$, $p=0.003$, $\omega^2=0.94$).

In all four subjects PP ratios increased after six weeks of intervention, and in three of the four subjects, increased from 6 to 12 weeks. Mean PP ratio at baseline, 6 and 12 weeks is shown in Fig. 4 (inset), with the error bars representing SEM. Mean PP ratio significantly increased after 12 weeks of lutein intervention ($F=10.41$, $p=0.011$, $\omega^2=0.61$). As was the case for MPOD, a linear trend appears to describe the changes in PP ratio ($F=13.09$, $p=0.036$, $\omega^2=0.86$). The relationship between changes in integrated macular pigment and PP ratio observed in Experiment II appear to follow the function between these variables observed in Experiment I. Fig. 5 shows the relationships between integrated macular pigment and PP ratio obtained in Experiment I and Experiments I and II combined. The filled squares represent data for the six subjects who participated exclusively in Experiment I. The additional four symbols represent the data from the four subjects who participated in both Experiments; with the filled symbols representing baseline (or Experiment I data), the unfilled symbols week 6, and the stricken-through unfilled symbols week 12. The linear relationship between PP ratio and integrated macular pigment obtained in Experiment I

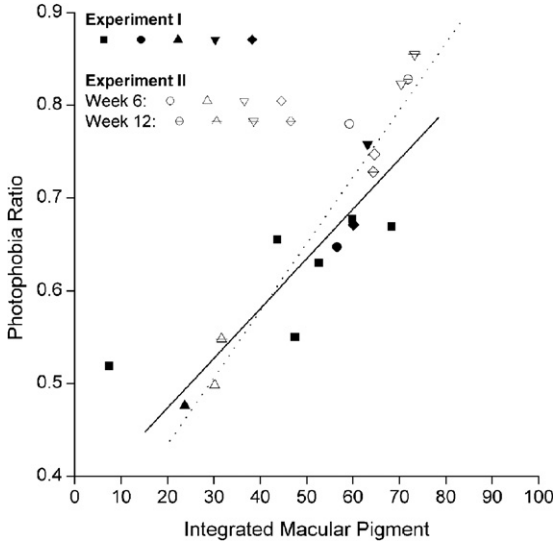

Fig. 5. Relationship between photophobia ratio (PP ratio) and integrated macular pigment observed in Experiment I and Experiments I and II combined. The data of the six subjects who participated in Experiment I are illustrated with solid squares, whereas the data of the four subjects who participated in both Experiments are illustrated with four different symbols (circle, up-triangle, down-triangle, and diamond). The solid line is a linear fit of the data from Experiment I, and the dotted line is a fit of the data from Experiments I and II combined.

($n = 10$) is illustrated by the solid line. The dotted line shows the linear relationship between integrated macular pigment and PP ratio from Experiments I and II combined ($n = 18$). The inclusion of data from Experiment II resulted in a modest change in slope of the linear fit.

Twenty-six random and 17 non-random catch trials were performed while measuring PP ratios in both Experiments. The random catch trials had a hit:FA ratio of 12:1 and the non-random catch trials had a hit:FA ratio of 7.5:1. Catch trials were not used or reported in previous investigations of photophobia; as a result, an acceptable hit:FA ratio has not been determined. However, the hit:FA ratio observed in the current study was sufficiently high to suggest that photophobia thresholds may be measured reliably using the method of ascending limits and a scaling technique.

4. Discussion

4.1. Distribution of macular pigment

The foveal distribution of macular pigment in this small sample was similar to previous studies that used HFP (e.g., Hammond, Wooten, & Snodderly, 1997, Burke et al., 2005) or reflectometry (Chen, Chang, & Wu, 2001;Robson et al., 2003) to measure MPOD. Chen et al. (2001) used a Gaussian function to describe the symmetry and distribution of macular pigment across the fovea. They reported that the Gaussian function provided a good fit for their 54 subjects' MPOD profiles, with a mean R^2 of 0.94. Hammond et al. (1997) reported a mean R^2 of 0.82 ($n = 32$) for the Gaussian fits of their subjects' MPOD profiles. The mean Gaussian R^2 for subjects in Experiment I was 0.961. If the subject with extremely low MPOD (and an uncharacteristic profile) is removed, the mean Gaussian R^2 is 0.973. Regardless, the mean Gaussian coefficient of determination in the current project was higher than those reported by Chen et al. (2001) and Hammond et al. (1997). This finding may reflect reliable subject performance or be the result of measuring a small number of subjects with similarly distributed MPOD. A few researchers have noted distinct differences among subjects' MPOD profiles. In about half of their 53 subjects, Berendschot and van Norren (2006) found a flanking MPOD peak or ring at 42′ eccentricity. Secondary MPOD peaks were also observed by Hammond et al. (1997) and Delori et al. (2006). In the current project MPOD was measured inside (20′ and 30′) and outside (60′ and 120′) the reported locus of the secondary MPOD peak. If a measure was obtained at 42′ eccentricity, the R^2 for the Gaussian function in the current study may have been lower, and more similar to those reported by Hammond et al. (1997) and Chen et al. (2001). Still, the R^2 for the Gaussian functions in those studies, as well as the current project, are sufficiently high to provide a good model of macular pigment distribution across the fovea, particularly in subjects without bimodal MPOD profiles.

The primary limitation of using HFP to measure MPOD profiles is the inability to measure MPOD at 0° eccentricity. To do so would require infinitesimally small centrally fixated targets. The smallest targets that can be used that will allow for reliable results are on the order of 12′ of visual angle. Thus, one benefit of fitting a MPOD profile with a Gaussian function is the ability to estimate a peak MPOD. A measure of MPOD close to 0° was obtained by Hammond et al. (1997). They measured MPOD using a centrally fixated 12′ target and referred to this measure as peak MPOD, although it was technically a measure of MPOD at 6′ eccentricity. They found that MPOD at 6′ was approximately 39.6% higher than MPOD at 30′ eccentricity. The authors also commented that a Gaussian fit frequently underestimated this peak. Chen et al. (2001) made the same observation. The mean estimated Gaussian peak (6′ eccentricity) of subjects in Experiment I was approximately 27.8% higher than their mean MPOD at 30′ eccentricity. Given the relationship between MPOD at 6′ and 30′ eccentricity observed by Hammond et al. (1997), it appears that the Gaussian fit also underestimated peak MPOD in the current project. Other nonlinear functions, such as the Lorentzian function (Stringham et al., 2003), may provide a better estimate of peak MPOD than the Gaussian function.

The dose of supplemental lutein used for Experiment II was based on the findings of Landrum et al. (1997), who reported that MPOD increased approximately 0.11 log units after subjects consumed 30 mg of lutein per day for 12 weeks. In Experiment II, MPOD increased approximately 0.077 log units at 20′ and 30′ eccentricity, and 0.045 and 0.010 log units at 1° and 2° eccentricity, respectively. These changes, while less than those observed by Landrum et al., at 45′ eccentricity, are similar to interventions that used 20mg of lutein per day (Aleman et al., 2001; Duncan et al., 2002). Aleman et al., for example, reported an increase of 0.07 log units at 10′ eccentricity in normal subjects and increases of 0.07, 0.07, 0.08, and 0.04 log units in patients with retinitis pigmentosa and Usher syndrome at 10′, 30′, 60′ and 120′ eccentricity, respectively. Like the current study, MPOD increased more in the central fovea than in the eccentric fovea. This may, in part, explain the increases in the coefficient of determination for the Gaussian function. It also suggests that carotenoid accumulation in the retina may be biased toward the central fovea, accumulating in a Gaussian manner.

4.2. Macular pigment optical density and photophobia

The findings of the current study suggest that macular pigment plays a role in photophobia thresholds. In Experiment I, there was a significant linear relationship between PP ratio and MPOD at 20′, 30′ and 1° eccentricity. Individuals with higher MPOD at these loci required more short-wavelength light, relative to longer wavelength light, to reach threshold for photophobia in the fovea. In other words, the amount of short-wavelength light filtered by subjects' macular pigment was directly proportional to

their PP ratios. The relationship between short-wavelength light absorption at 20′ eccentricity and PP ratio was such that a 10% change in light transmission resulted in a 0.07 change in PP ratio. The correlation between PP ratio and MPOD was strongest for the 20′ locus. Typically, individuals with high MPOD at central loci tend to have higher aggregate totals of macular pigment. This relationship was true for nine of the 10 subjects in Experiment I. The one subject who did not fit the correlation had relatively high MPOD at 1° and 2° eccentricity compared to his MPOD at 20′ eccentricity. Such individuals demonstrate that measures of MPOD at a single locus may not accurately estimate macular pigment across the fovea (Aleman et al., 2001; Robson et al., 2003), particularly if the subject has a bimodal, as opposed to Gaussian, MPOD profile. In fact, this subject's MPOD at 20′ eccentricity was the third lowest in the sample, but his integrated MPOD was approximately the same as the subject with the highest MPOD at 20′ eccentricity. Given the similarity in total macular pigment screening for these two subjects, it is not surprising that they had similar PP ratios. Stringham et al. (2004) reported a similar finding. In their study, two individuals had distinctly different MPOD profiles, but almost identical integrated macular pigment and photophobia thresholds. This finding supports the idea that photophobia thresholds are affected by the aggregate screening of macular pigment across the fovea (Stringham et al., 2003, 2004). Indeed, the correlation between PP ratio and integrated macular pigment was stronger than the relationship between PP ratio and MPOD at any single locus. This difference in the strength of the correlation would undoubtedly be larger if the sample contained more individuals with higher MPOD at 1° and 2° eccentricity relative to 20′ eccentricity.

In Experiment II, significant increases in PP ratio were observed after increasing MPOD. Although a placebo group may have unequivocally established that PP ratios did not simply increase over time or as a result of demand characteristics on the part of the subjects, the linear changes in PP ratio between baseline and week 6, and between week 6 and week 12 corresponded directly to the linear increases in MPOD. Both integrated MPOD and PP ratio increased approximately 11% between baseline and week 6. Analogous changes were observed between week 6 and week 12. Further, the function between integrated macular pigment and PP ratio observed in Experiment I predicted the changes in PP ratio observed in Experiment II, as illustrated by the similar linear fits in Fig. 5.

Numerous studies suggest that retinal lutein and zeaxanthin, or macular pigment, may protect the retina from light induced damage. The light-filtering properties of macular pigment may also influence visual comfort. Specifically, the current project demonstrated that the macular pigment increases the amount of light necessary to induce visual discomfort, or photophobia, for short-wavelength targets. Should this prove beneficial, it was demonstrated that 12 weeks of lutein supplementation can significantly increase MPOD, and as a result, photophobia light thresholds.

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