Macular Pigment and Visual Performance in Low-Light Conditions

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The dietary carotenoids lutein (L) and zeaxanthin (Z), along with the zeaxanthin stereoisomer mesozeaxanthin (MZ, shown to be produced by conversion from L in the retina¹), are found in their highest concentrations in the inner layers of the central macula of the primate fovea,²⁻⁴ anterior to the photoreceptor outer segments. Here, the collective accumulation of L, Z, and MZ is referred to as macular pigment (MP). Macular pigment appears yellow in color, which affords it the ability to absorb high-energy, potentially damaging short-wavelength (SW, blue-appearing) light. In fact, MP is a relatively broadband filter, capable of absorbing light from 400 to 520 nm, with peak absorption at 460 nm.⁵,⁶ Additionally, L, Z, and MZ are potent antioxidants,⁷ a property that enables them to biochemically protect the tissue in which they are embedded. Because the fovea maintains an extremely high metabolism and concomitant oxygen tension,⁸ L and Z are optimally positioned to quench singlet oxygen species (i.e., free radicals) before they can appreciably damage retinal tissue; this is the basis for MP’s putative role in delaying the onset or retarding the progression of age-related macular degeneration (AMD).⁹ In support of this function for MP, Weale¹⁰ has suggested that the optical properties of MP are accidental, and that the biochemical properties of MP should be emphasized as the primary reason for its occurrence in the retina. This conclusion raises a few matters concerning the optical properties of MP. First, if not for optical reasons, why would MP be deposited in layers anterior to the photoreceptors, where it effectively screens high-energy SW light before it can photooxidize the vulnerable lipid-rich membranes in photoreceptor outer segments? Second, the broadband screening of photoreceptors from visible SW light must affect foveal vision in some way. From an evolutionary perspective, this effect must have promoted survival. Third, if the sole function of MP is to act as an antioxidant, then (in terms of AMD) how could human evolution select for a trait that protects against a disease that manifests well after the reproductive cycle? Clearly, the beneficial effects of MP on age-related macular disease are secondary to more immediate or acute stressors. Given this, we argue that both the optical and biochemical properties of MP are important to vision, and that neither is accidental.

Keywords: macular pigment, lutein, visual performance, visual acuity, light/dark adaptation

Purpose. By reducing rod intrusion and improving efficiency of neural signaling throughout the visual system, macular pigment (MP) could improve many aspects of visual performance in low-light level conditions. Our study examined this possibility for a variety of visual performance parameters, including spatial resolution, dark adaptation kinetics, and color detection.

Methods. Twenty-seven subjects participated in the study. Spatial profiles of MP optical density (MPOD) were determined by using heterochromatic flicker photometry. Mesopic- and scotopic-adaptation level experiments were conducted in Maxwellian view.

Results. Subjects with higher MPOD required significantly lower contrast to detect the mesopic-level resolution targets; this effect became stronger with increasing spatial frequency. Dark adaptation recovery times were significantly faster as a function of MPOD (by nearly 2 minutes for the lowest mesopic-level task [high versus low MPOD]; P < 0.001). Absolute scotopic thresholds were also significantly associated with MPOD (P < 0.001). Macular pigment optical density was inversely associated with detection of yellow (P < 0.001), and, paradoxically, approached a significant positive correlation with the detection of blue (P = 0.06).

Conclusions. Macular pigment appears to enhance visual function in low-light conditions. Based on the results of this study, it can be said that MP extends the range of foveal vision into lower light. Additionally, MP appears to enhance dark adaptation kinetics, which suggests that increased MPOD leads to more efficient photopigment regeneration. The findings of the color detection portion of the study are suggestive of an active compensatory mechanism that offsets absorption by MP in order to maintain normal color perception.
Although the fovea comprises roughly just 2% of the total retinal area,\textsuperscript{11} it is crucial to many parameters of visual performance in that it provides the highest level of the visual system’s capability. Examples of the superior performance of the fovea relative to eccentric regions of the retina include spatial resolution,\textsuperscript{12} color discrimination,\textsuperscript{13,14} and object recognition.\textsuperscript{15} With regard to visual performance, the preferential deposition of L and Z in the fovea is therefore probably not coincidental. From the evidence presented above, MP certainly has the capability to limit or prevent phototoxicative damage. Given its broadband absorption profile and location anterior to the photoreceptors in the region of the retina responsible for highest visual performance, it has been hypothesized that MP should serve to benefit some aspect(s) of visual function.\textsuperscript{16} The fact that MP absorbs poorly focused SW light has led researchers to propose a purely optical effect termed the “acuity hypothesis” of MP.\textsuperscript{17} By reducing chromatic aberration via SW light absorption, MP could, in theory, improve visual acuity. By extension, any yellow-colored filter should improve visual acuity. Many studies of this effect, however, have been inconclusive and tend to yield extremely variable results.\textsuperscript{18} Moreover, Engles et al.\textsuperscript{19} have found no effect of MP level on hyperacuity and gap acuity. Given the strong dependence of visual acuity on luminance,\textsuperscript{20} these findings could be due to the tradeoff between the benefit of SW light attenuation and the loss of luminance with this attenuation. Additionally, the spectral sensitivity of the long-and middle-wave–sensitive photoreceptors (that confer highest acuity) drops off significantly in the SW region of the visible spectrum.\textsuperscript{21} This suggests that, in terms of acuity, SW light is much less important to the visual system. An important point to add is that none of the yellow-filter studies conducted heretofore have measured the optical density of MP (MPOD) in their subjects. Because MPOD is known to vary widely among subjects,\textsuperscript{22} the variability found in the yellow-filter studies could plausibly be explained by variation in subjects’ MPOD levels.

Although MP may not prove to help people see better, it may help people see farther. Wooten and Hammond\textsuperscript{23} have modeled the effect of MP’s absorption of SW-dominant atmospheric light and concluded that a person with 1.0 log unit of MPOD could, in theory, see 26% farther through the atmosphere than someone with little or no MP. This effect has very recently been tested empirically and shown to correspond closely with modeled predictions of increased visibility in blue haze.\textsuperscript{24}

With regard to visual performance under intense lighting conditions, Stringham and Hammond\textsuperscript{25} have determined strong correlations between visual performance in glare and MPOD in young subjects. For instance, subjects with higher MPOD exhibited significantly shorter photostress recovery times and can see a target through significantly more glare. To investigate within-subject effects, Stringham and Hammond\textsuperscript{26} supplemented their subjects with L and Z for 6 months and found that visual performance increases commensurate with increases in MPOD. Both of these studies use Maxwellian-view optical systems to assess visual performance in glare. Because Maxwellian view necessitates the use of a lens system that focuses light from an optical system through the center of a subject’s pupil (thus obviating light attenuation by the iris), the visual performance in glare ostensibly afforded by MPOD could be an artifact of reducing retinal illuminance via normal pupillary function. To address this concern, Stringham et al.\textsuperscript{27} have assessed visual performance in glare in subjects with a wide range of MPOD levels, using a free-view optical system. Results from that study are similar to those of the previous studies. Additionally, they have found a significant correlation between visual discomfort ratings and MPOD, such that, overall, subjects with higher MPOD experience less visual discomfort upon exposure to an intense light source. In the year-long COMPASS study,\textsuperscript{28} visual performance in glare was examined in subjects supplemented with 12 mg L and 1 mg Z versus placebo. In general, the effects of MPOD on glare were not found to be significant. As noted by the authors, the discrepancy between theirs and previous studies may be explained by differences in stimulus conditions; namely, the COMPASS study is designed to examine conditions approximating “normal environmental experience.” Indeed, the glare conditions for COMPASS appear to more closely approximate relatively bright, indoor conditions, whereas the previous studies by Stringham et al. address the intensity of bright, outdoor conditions—there is a more than two orders of magnitude difference in glare intensity between these studies. Nevertheless, after 1 year of L and Z supplementation, subjects exhibit significantly augmented MPOD and concomitant improved mesopic contrast sensitivity for 1.5 cyc/deg under high glare conditions. Subjects in the placebo group do not experience any benefit in this regard. This within-subjects effect is similar to the between-subjects effects in the present investigation.

The available evidence suggests that MP has an appreciable impact on visual performance in sufficiently bright light conditions. The impetus for the present study, however, was provided by the other end of the light intensity scale: Can MP improve visual performance in low-light conditions? This idea has been explored by Kvansakul et al.\textsuperscript{29} They found that L supplementation improves contrast acuity thresholds in the mesopic visual range, although, ironically, the improvements are not associated with increases in MPOD or absolute MPOD level. Because the absorption spectrum of MP overlaps that of rod photoreceptors, it makes sense that an increase in MPOD would suppress rod input at mesopic light levels, thereby extending the range of cone function to lower light levels. This would, in turn, serve to improve contrast thresholds. The finding of no effect of MPOD augmentation on visual performance could be explained by a few factors, including a restriction of range effect: all but 5 of their 34 subjects appear to have had between 0.40 and 0.60 MPOD. These values do not appear to represent the normal range of values found in the population (as reported, e.g., in the study of Cuilla et al.\textsuperscript{22}) and would limit correlational power. In terms of the potential to show contrast sensitivity differences among subjects (and to show a macular carotenoid supplementation response effect), the contrast sensitivity measure at 2.5° eccentricity would have proved difficult, especially for a group of subjects with a small range of MPOD. This retinal eccentricity has substantially less MPOD than the center of the fovea. For example, someone with 0.40 MPOD at the 30° locus would have, based on a decreasing exponential function (which has been shown not to fit the data)\textsuperscript{30}, only 0.15 MPOD at the 2.5° locus. Perhaps more importantly, the 2.5° locus responds more slowly to suprathreshold than more central loci.\textsuperscript{31,32} This would make it difficult to determine a relationship between contrast acuity thresholds and changes in MPOD, because the changes in MPOD would be similar to the range of noise inherent in the measure. Using stimulus conditions that favor foveal detection of stimuli, Nolan et al.\textsuperscript{28} have examined the relationship between augmentation of MPOD and mesopic-level contrast sensitivity and found significant effects for relatively high spatial frequency (20.4 cyc/deg) contrast sensitivity performance, but for only one of their measures (Metropsis); their other measure of mesopic-level contrast sensitivity (F.A.C.T.) for a similar spatial frequency (18 cyc/deg) did not yield statistical significance. Based on the available evidence, the relationship between MPOD and mesopic-level contrast sensitivity appears to be
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In the present study, we attempted to clarify this relationship by using very carefully controlled conditions and procedures (described below).

Dark adaptation (DA) kinetics is one of the foci of the present study and relates directly to a recent investigation of the relationship between DA kinetics and MPD by Patryas et al. Their study has found modest correlations between MPD and rod-mediated recovery rates (P values of 0.07 and 0.08) and rod thresholds (P = 0.18). Additionally, Patryas et al. have found no relationship between MPD and cone-mediated DA kinetics. Although generally these data certainly trend in the direction of the present investigation’s findings, they are not statistically significant. Potential explanations for this discrepancy are offered in the Discussion section.

For the present study, we used 1° targets placed on a mesopic-level background of 0.1 cd/m² in order to assess variability in visual performance accounted for by MPD, on tasks involving luminance detection, color detection, and spatial resolution. Our hypothesis was that higher levels of MP would be related to a reduction of rod intrusion into foveal vision, thereby effectively extending cone vision further downward in the mesopic range. Presumably, on the basis of suppressing rod function via absorption of light by MP, this would benefit cone-related visual optical effects of MP. We were also interested, however, in performance parameters that MP’s neural and physiological effects could plausibly influence. It has been shown in model systems, for example, that L can improve gap junction communication between neurons. This suggests that the signaling efficiency of neurons would be improved by higher levels of L. In support of this idea, age-related declines in neuronal signal transduction have been reversed with dietary supplementation of carotenoid-rich foods (e.g., spinach) in rat models. Lutein and Z are not deposited exclusively in the foveal retina, but are found throughout retina, albeit in lower concentrations, and in neural and fatty tissues serving the visual system, including many areas in the brain. This idea is consistent with the findings of significant relationships between MPD levels and critical flicker fusion frequency, and absolute scotopic sensitivity. Because MP is deposited most densely in the fovea, a test of visual function in a retinal region outside the fovea could reveal a neural efficiency benefit of L and Z to the entire visual system. To investigate this possibility, we assessed subjects’ dark adaptation kinetics, including elapsed-time measures for detection of high-, middle-, and low-level mesopic light stimuli, and, in an attempt to replicate the findings of Hammond et al., a measure of absolute dark-adapted sensitivity.

**Methods**

**Subjects**

Twenty-five subjects, aged 22 to 50 (mean = 30.1, SD = 6.9) years participated in the luminance detection, color detection, and visual resolution aspects of the study. Twenty-seven subjects, aged 21 to 51 (mean = 31.3, SD = 7.1) years participated in the dark adaptation kinetic portion of the study. All subjects had no current or previous history of ocular pathology. Subjects were recruited from the population of active duty personnel, civilians, and contractors at Brooks City-Base Optical Radiation Branch in San Antonio, Texas, and the Tri-Service Research Laboratory, Fort Sam Houston, 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 MPOD values for use in the experiments, 48 subjects were screened. From the results of the screening, 30 subjects, with MPOD (at 0.50° eccentricity) ranging from 0.025 to 0.866, were selected to participate. Subjects’ spatial profiles of MPOD were assessed with heterochromatic flicker photometry (HFP), using a densitometer (Macular Metrics Corp., Rehoboth, MA, USA) slightly modified from the one described by Wooten et al. Macular pigment optical density 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. Briefly, 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 radiancy of the two lights until a percept of no flicker is achieved. All other factors being equal, a subject that requires more short-wave (i.e., 460 nm) relative to middle-wave (i.e., 550 nm) light to achieve null flicker has higher MP. This task is performed for the locations of interest within the fovea, which presumably contain MP, and for a reference location in the parafovea that presumably does not (approximately 7° eccentricity). To obtain a measure of MPD at a given test locus, the logarithmic ratio of short- to middle-wave radiancy (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 and light transmission of the ocular media 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, in order 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. 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 if the null zone is determined to be too wide. Twenty minutes were required to obtain a subject’s MP spatial profile.

**Apparatus**

**Luminance and Color Detection.** A two-channel Maxwellian-view optical system was used for stimulus presentation. The light source was a 75-W xenon-arc lamp with a color temperature of roughly 6500°K, the diameter of the arc image in the plane of the subject’s pupil was 2.0 mm. Stimuli were presented monocularly to the right eye. One channel of the optical system presented a 20°, 0.1 cd/m² background, onto which a 1°, monochromatic disk of light was presented. This small “target” disk was rendered monochromatic by a monochromator with a half-peak bandwidth of 4 nm. On any given trial, the target could be one of four different wavelengths: 460, 511, 575, or 620 nm, corresponding to the perceived hues blue, green, yellow, and red, respectively. Small black fixation dots were placed 2° to either side of the center of the target, which ensured a subject’s proper central fixation of the target. The intensity of the background was set by using neutral-density filters and a calibrated radiometer. The intensity...
of the test channel was adjustable by using a neutral-density wedge. The intensity required for luminance and color detection was determined by using the calibrated settings of the wedge and fixed neutral-density filters, convolved with the calibrated light output of the xenon-arc source.

**Spatial Resolution.** For the spatial resolution experiment, the same 20° background and fixation guides, as described above, were used. The test channel, however, was used to present a 1° square-wave grating of various spatial frequencies: 5.5, 7.33, 9.17, 11, and 18.33 cyc/deg. The grating was presented as a circular disk, defined by an iris aperture, and was generated by passing collimated xenon-white light through a glass filter with opaque black lines printed on it. Five filters were used; the physical frequency of the opaque lines ranged from 150 to 500 lines per inch, which corresponded to the spatial frequencies viewed by the subjects (listed above). The light passing through the filters was xenon-white, and the intensity required for threshold detection of a given spatial frequency grating was determined by subtracting the total neutral density from the energy of the light source. Although this measure is not contrast per se, the appearance of white bars (defined by the opaque black lines) made stimulus detection less subject to normal dark adaptation visual fluctuations (i.e., noise), and hence less variable. Therefore, results for the spatial resolution are presented as "white bar energy," and not contrast.

**Dark Adaptation Kinetics.** For the dark adaptation experiment, a three-channel Maxwellian-view optical system was used. A "bleaching" channel presented an intense (5.5 log troland) light in the subjects' temporal retina. The bleaching light subtended 8°, was centered 12° eccentric to fixation in the temporal retina, and appeared yellow by virtue of passing the xenon-white through a long-pass colored filter that cut off at 510 nm. This was done to ensure a 90% rod photopigment bleach, without including the high-energy and potentially uncomfortable short-wave light component. A second channel was used to present the test stimulus, a disk of 510-nm monochromatic light, 2° in angular subtense, presented 12° eccentric to fixation in the temporal retina. The third channel was used to present the fixation target, a small (10') red point of light, 12° from the center of the bleaching and test stimuli. The measurement loci for MPOD (dominant in the very center of the fovea) versus mesopic/scotopic sensitivity (12° eccentricity) are notably different, and clarification is warranted: Despite the fact that the highest density of retinal carotenoids is found in the central 2° to 3° of the retina (and generally associated with cone photoreceptors), L and Z are found throughout the retina, and it has been shown that rod photoreceptor outer segments contain up to 25% of the total retinal carotenoids. This finding suggests that, like for foveal, photopic vision, rod-mediated, scotopic vision may be influenced by the presence of retinal carotenoids.

**Procedure**

**Spatial Resolution.** For the spatial resolution experiment, the same optical system was used and the background field maintained the same characteristics (i.e., 20° angular subtense, and 0.1 cd/m² luminance). The subject's task was to adjust the intensity of the light passing through the transparent bars of the grating to the minimum level required to detect the bar pattern. The five spatial frequencies noted earlier, ranging from 5.5 to 18.33 cyc/deg, were used. The initial intensity was set by the experimenter to be below the detection threshold, and subjects adjusted the intensity upward. Often subjects would slightly exceed their threshold and then adjust the intensity downward to the just-detectable level. Three thresholds were determined for each spatial frequency tested.

**Dark Adaptation Kinetics.** Subjects initially dark adapted for 5 minutes while the experimenter provided instructions regarding the task. Once aligned to the optical system, subjects were instructed to view the fixation point. The 5.5 log troland bleaching field was then presented to the temporal retina for 60 seconds, which yielded an approximate 90% photopigment bleach. After the bleaching field was extinguished, four measures were made: three measures of elapsed time to reach threshold for the 510-nm target set at different mesopic levels (1, 0.1, and 0.05 cd/m²) of luminance, and a measure of absolute dark-adapted threshold. To determine the thresholds, the test field was flashed for 500 ms, every 5 seconds. Subjects maintained their fixation on the fixation point and attempted to detect the flash of light in the periphery. Upon two successful detections of the stimulus, the elapsed time was recorded. Subsequently, thresholds for the second (0.1 cd/m²) and third (0.05 cd/m²) mesopic-level targets were determined by using the same response criterion. Finally, after 35 minutes in the dark, the absolute dark-adapted threshold was determined by using a two-alternative forced choice procedure. Depending on subject performance, the absolute time to achieve absolute threshold ranged from 37.5 to 43.75 minutes.

**Luminance and Color Detection.** Subjects were seated in a comfortable chair and familiarized with the procedure that would ensue. A dental impression “bite bar” was made for each subject, and used in combination with forehead rests to ensure stable alignment to the optical system. Additionally, a pupil-viewing camera, coupled with a bull's-eye reticle, was incorporated to ensure that the light from the optical system was in focus and in the plane of the subject's pupil. The diameter of the arc image in the plane of the pupil was 2 mm. After initial alignment to the optical system, subjects dark adapted for 10 minutes. Subjects were then instructed to view the center of the mesopic-level background field, using the fixation points as guides, for 30 seconds. The intensity of the test stimulus was initially subthreshold; the experimenter slowly increased the intensity, via neutral-density wedge adjustment, until the subject first detected light. The rate of intensity increase was approximately 0.05 log unit per second. The experimenter noted the detection threshold wedge setting achieved, and proceeded to increase the intensity of the test light until the subject was able to correctly identify its hue. As noted in the Apparatus section, wavelengths of 460 nm (blue), 511 nm (green), 575 nm (yellow), and 620 nm (red) were used. To prevent guessing or order effects, the order of presentation of test stimulus wavelength was randomized. Three luminance and color detection thresholds were obtained from each subject. The total time elapsed for this portion of the study was 30 minutes.

**Results**

**Spatial Resolution.**

As a function of increasing MPOD, subjects required less energy for the white bars to detect the spatial gratings. This effect was found to grow stronger as the spatial frequency of the target increased (Fig. 1). The strength of association (Pearson's r value) between MPOD and the minimum white bar energy required to detect the spatial frequency grating ranged from ~0.24 (for 5.5 cyc/deg) to ~0.77 (for 18.33 cyc/deg). The two lowest spatial frequency values tested, 5.5 and 7.33 cyc/deg, failed to exhibit a statistically significant association with MPOD, although the data for 7.33 cyc/deg approached it ($P = 0.07$). Figure 1 presents the detection threshold data for 9.17, 11, and 18.33 cyc/deg, which were found to be strongly associated with MPOD. Because the
FIGURE 1. Log relative sensitivity to the various spatial frequency gratings, as a function of MPOD, averaged over the central 1° of retinal area. The spatial frequencies progress from top to bottom: 5.5, 7.33, 9.17, 11.0, and 18.33 cyc/deg. Pearson’s product-moment correlations and corresponding *P* values *inset* in each graph.
grating stimulus subtended 1° of visual angle, sensitivity data were compared to MPOD averaged over the central 15° of retinal area for each subject.

Dark Adaptation Kinetics

Significant relationships were found between MPOD and elapsed time required to detect mesopic-level targets of fixed intensity (Fig. 2), such that greater MPOD was associated with shorter elapsed time required for target detection (i.e., faster visual adaptation). To better approximate the total MP in any given subject’s retina, we averaged MPOD across the obtained spatial distribution. This was done by simply averaging the optical densities obtained at the different retinal loci assessed when measuring macular pigment (see Methods section). Similar to the spatial resolution results, as the target became more challenging (i.e., dimmer) the benefit of greater MPOD became more evident. For example, the strengths of association (Pearson’s $r$ value) between MPOD and elapsed time for the 1, 0.1, and 0.05 cd/m$^2$ conditions were $r = 0.39$ ($P = 0.041$), $r = 0.68$ ($P = 0.0001$), and $r = 0.76$ ($P < 0.0001$), respectively (see Fig. 2). Macular pigment optical density was also shown to be significantly associated with absolute dark-adapted threshold ($r = 0.79$, $P < 0.0001$; Fig. 3). Of note, although our sample had subjects who ranged in age from 22 to 50 years, the mean age of the sample was roughly 30 years, and there were only two subjects older than 40 years. No age effects were observed.

Luminance and Color Detection

The log relative sensitivities for detecting the test stimulus and for determining its color are shown in Figure 4. For all stimuli, sensitivity for luminance detection was significantly greater than for color recognition, with sensitivity differences ranging from 0.04 to 0.25 log units for the 620- and 460-nm stimuli, respectively. Results of dependent $t$-tests ranged from $t = 4.967$ (red) to $t = 9.626$ (blue) with all $P$ values $< 0.001$. Peak sensitivity for both sets of data occurred at 511 nm.

Macular pigment optical density was measured at 0.25°, 0.5°, 1°, and 2° from the fovea. The only significant association between MPOD and detection or color detection sensitivities was for color sensitivity for the yellow (575 nm) stimulus. The strongest association, $r = 0.501$, $P = 0.009$, occurred for MPOD measured at 0.5°. The results are shown in Figure 5A.
The only other relationship that approached significance was for blue detection sensitivity, which increased with increasing MPOD ($r = 0.382$, $P = 0.06$; Fig. 5B).

As a general note, dark adaptation kinetics and MPOD have been shown to be correlated with age. We statistically corrected for analyses potentially affected by these relationships and found that statistical significance was nonetheless maintained or became stronger. In fact, only one of the presented significant findings became weaker, but only mildly so (dark adaptation kinetics, 0.05 cd/m² level; $r = 0.70$; $P < 0.0001$). To be fair, our sample had only two subjects older than 40 years, and our mean subject age was roughly 30 years, so effects of age would not be expected to manifest in our data.

**DISCUSSION**

The results of the spatial resolution portion of the study appear to suggest that MPOD is associated with an enhanced ability to detect foveal targets of relatively high spatial frequency in low-light conditions. As can be seen by the progression in the plots in Figure 1, this effect appears to be directly related to spatial frequency. Because the fovea maintains the highest density of photoreceptors and is thereby capable of detecting the finest resolution, as a stimulus becomes increasingly more demanding in terms of resolution, it follows that it would be more dependent on foveal detection. Because the central 1° of the fovea is free of rods, it would seem unlikely that the mechanism for the effects presented could be explained on the basis of suppression of rod activity by MPOD. The absorption spectrum of MP does, however, overlap that of rhodopsin to a large degree and would therefore absorb an appreciable amount of light that would normally be available to rods (just outside the 1° rod-free zone), especially in those individuals with high MPOD. Despite the central fovea’s lack of rods, there may still be an effect of MPOD reducing lateral interaction between rods and foveal cones via reducing the activity of rods immediately adjacent to the central fovea. A reduction in rod activity immediately adjacent to the central cones could plausibly yield a more cone-dominated percept, and therefore confer higher spatial resolution under these conditions. Rod/cone lateral interaction has been demonstrated in psychophysical and physiological work, both at the level of the retina and lateral geniculate nucleus. An alternative explanation is that MP enhances the efficiency of the visual cycle in a manner that is directly related to MPOD. This idea is certainly consistent with our findings, and also consistent with a well-established physiological effect of visual cycle inhibition/disruption by oxidative stress. It has been shown that the retinal carotenoids serve to strongly inhibit the activity of A2E, itself the product of oxidative stress, and a potent visual cycle inhibitor. At the level of perception, a more efficient visual cycle could ultimately manifest as increased resolution. This potential enhancement effect of MPOD on the visual cycle may also explain our dark adaptation kinetics findings; this idea warrants further investigation.

The visual sensitivity data presented in Figure 1, because MP absorbs an appreciable amount of xenon light energy, it is seemingly paradoxical that those with greater MPOD, compared to those with relatively low MPOD, would require less xenon-white light to detect the gratings. This would be especially true for the central fovea, where MP is most dense. Of course, target detection was (by design) restricted to the central 1° of the fovea, and so it appears that what must be driving this visual performance effect of MP is either its screening of light for use by rods, enhancement of the visual cycle, or perhaps some other neural efficiency
mechanism. In other words, these effects do not appear to be optical in nature.

The results of the dark adaptation kinetics portion of our study addressed the possibility of visual cycle enhancement in a more direct fashion, where more efficient visual photopigment regeneration would presumably result in faster adaptation. As shown in Figure 2, subjects with higher MPOD exhibited significantly faster visual adaptation for the three levels of mesopic stimuli. In a fashion similar to the spatial resolution data, as the stimulus became more challenging (i.e., lower level), the impact of MPOD on performance appeared to become greater. One may contend that MP could not possibly have such an effect at a retinal location (12") for which its density is negligible. As noted in the Introduction and Results sections, as much as 25% of the total retinal carotenoids are accounted for by those deposited in the rod outer segments. Based on the antioxidant capability of L and Z, this makes the idea of a relationship between MPOD and enhanced visual cycle/photopigment regeneration in the parafoveal retina plausible, and may indeed be at least partly responsible for what Renzi and Hammond have termed "neural efficiency." Whatever the case, the effect is strong enough to manifest as a statistically significant performance difference for those with high MP compared to those with low MP. The recent data of Patryas et al. shows modest relationships between MPOD and rod-mediated, but not cone-mediated, dark adaptation kinetics. There are a few factors that could reconcile the discrepancies between their study and ours. As Patryas et al. note, their results may have been influenced by the large age range (15–68 years) and relatively small sample size (n = 5); nearly half of the subjects in their sample were aged 55 years or older. The rate of dark adaptation is strongly affected by age, and this effect is quite variable among people. It could be, therefore, that any potential effect of MPOD on dark adaptation kinetics was simply masked by the variability inherent in older subjects’ measures. Another potential source of variability in any dark adaptation experiment is the strength of the pretest bleach. Owing to variability in subject pupil size, Patryas et al. have achieved bleaches ranging from 50% to 98%. Given that older subjects tend to exhibit smaller resting pupil diameter (i.e., "senile miosis," as reported, e.g., in Sloane et al.), the presumably disproportionate bleach in the older subjects in the sample of Patryas et al. may have introduced systematic variation into their data. Nevertheless, their rod kinetics data very nearly achieves a statistically significant relationship with MPOD. As noted in the Methods section, we were able to achieve a 90% bleach in all of our test subjects by using Maxwellian view, whereby the subject's pupil is effectively bypassed via optics.

The results of absolute dark-adapted sensitivity portion of the study are consistent with data from Hammond et al., who have found a significant relationship between MPOD and scotopic sensitivity. Their subjects (aged 24–36 years) have a similar range in MPOD as ours, and the best-fit line to their data indicates a roughly 0.2 log unit lower scotopic threshold for subjects with high MPOD compared to low MPOD. Our data (see Fig. 3) exhibited very nearly the same sensitivity increase associated with MPOD. A similar finding has also been reported by Patryas et al. who have determined the relationship between MPOD and the scotopic threshold (after 30 minutes of dark adaptation) in their subjects. The direction and magnitude of the effect are very nearly the same as those of Hammond and colleagues and as ours, but it should be noted that the relationship was not found to be statistically significant (P = 0.10). The findings from the luminance detection and color detection portion of the study were less clear cut and exhibited slightly more variability. Unlike the contrast sensitivity and dark adaptation data, there was little evidence of improved sensitivity with increasing MPOD. However, the finding of an association between MPOD and (1) decreased sensitivity to yellow; and (2) increased sensitivity to blue (albeit approaching statistical significance) speaks to the possibility that the visual system actively compensates for MP in order to maintain stable color perception across the retina. This idea has been suggested before and has been empirically evaluated and supported by a handful of studies.

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