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The Relationship Between Macular Pigment and Visual Performance

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The relationship between macular pigment and visual performance ☆

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ABSTRACT

This study was designed to assess whether macular pigment optical density (MPOD) is associated with visual performance. One hundred and forty-two young healthy subjects were recruited. Macular pigment optical density and visual performance were assessed by psychophysical tests including best corrected visual acuity (BCVA), mesopic and photopic contrast sensitivity, glare sensitivity, photostress recovery time (PRT). Measures of central visual function, including BCVA and contrast sensitivity, were positively associated with MPOD ($p < 0.05$, for all). Photostress recovery and glare sensitivity were unrelated to MPOD ($p > 0.05$). A longitudinal, placebo-controlled and randomized supplementation trial will be required to ascertain whether augmentation of MPOD can influence visual performance.

1. Introduction

The macula is a specialized part of the retina and is responsible for high spatial resolution and color vision (Hirsch & Curcio, 1989). The carotenoids lutein (L), zeaxanthin (Z) and *meso*-zeaxanthin (*meso*-Z) accumulate at the macula where they are collectively referred to as macular pigment (MP). (Bone, Landrum, Hime, Cains, & Zamor, 1993) L and Z are of dietary origin, whereas *meso*-Z is not normally found in a conventional diet, and is generated at the retina following L isomerization (Bone et al., 1993; Neuringer, Sandstrom, Johnson, & Snodderly, 2004).

Age-related macular degeneration (AMD) is a disease of the macula and results in the loss of central and color vision. AMD is the most common cause of blindness in the elderly population in the developed world (Congdon et al., 2004). It is now understood that oxidative stress (Beatty, Koh, Henson, & Boulton, 2000; Winkler, Boulton, Gottsch, & Sternberg, 1999), exacerbated in part by cumulative short-wavelength visible light exposure (Algvere, Marshall, & Seregard, 2006; Fletcher et al., 2008), is important in the aetiopathogenesis of AMD. MP is a short-wavelength (blue) light filter (Bone, Landrum, & Cains, 1992) and a powerful antioxidant (Khachik, Bernstein, & Garland, 1997), and is therefore believed to protect against AMD. This hypothesis, referred to as the "protective" hypothesis of MP, has been studied and reported on extensively (Loane, Kelliher, Beatty, & Nolan, 2008).

Beyond its "protective" hypothesis, MP's optical and anatomic properties have prompted the "optical" hypotheses of this pigment. The "optical" hypotheses of MP were originally discussed by Reading and Weale (1974) and later by Nussbaum, Pruett, & Delori (1981) and include MP's putative ability to enhance visual performance and/or comfort by attenuation of the effects of chromatic aberration and light scatter, via its light-filtering properties (Walls & Judd, 1933).

Several studies have evaluated, and reported on, the role of MP in various aspects of visual performance including visual acuity, contrast sensitivity, glare sensitivity, photostress recovery, critical flicker fusion frequency (CFF), and color vision, among others (Bartlett & Eperjesi, 2008; Engles, Wooten, & Hammond, 2007; Hammond & Wooten, 2005; Kvansakul et al., 2006; Rodriguez-Carmona et al., 2006; Stringham, Fuld, & Wenzel, 2004; Stringham & Hammond, 2007; Stringham & Hammond, 2008; Wooten & Hammond, 2002). However, the findings from these studies are inconsistent, which might be explained, at least in part, by methodological differences between studies.

In this manuscript, we present baseline data from the Collaborative Optical Macular Pigment ASsessment Study (COMPASS), and as such represents a cross-sectional evaluation of the relationship between MP optical density (MPOD) and visual performance and comfort across a broad and refined range of functional tests.

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2. Methods

2.1. Subjects

One hundred and forty-two healthy subjects volunteered to participate in this study, which was approved by the research ethics committees at both Waterford Institute of Technology (WIT) and Dublin Institute of Technology (DIT). Informed consent was obtained from each volunteer, and the experimental procedures adhered to the tenets of the Declaration of Helsinki.

The study was conducted at WIT and DIT vision science laboratories, located in the southeast and east of the Republic of Ireland, respectively. Self-selected recruitment of subjects (WIT: $n = 61$ and DIT: $n = 81$) was facilitated by poster and newsletter advertisement, and also by word of mouth, in the respective local communities. All subjects were aged between 18 and 41 years, in perfect general (self report) and ocular health, and with visual acuity of at least 20/30 in the study eye. A typical study visit lasted approximately four hours. Those aspects of visual performance assessed, and their sequence, are presented in Table 1.

All subjects recruited into the study could be classed as naïve observers to the tests carried out (with the exception of the visual acuity test, with which all subjects were familiar). To optimize performance, and also to minimize any potential learning effects on performance, all subjects underwent a defined period of pre-test training. This training consisted of careful explanation of the nature of each test, pictorial and/or video demonstration of the test requirements and procedure, and was followed by a defined session of pre-test practice.

2.2. Demographic, medical history, lifestyle and vision case history questionnaires

The following details were recorded for each volunteer by questionnaire: demographics; general health status; smoking habits (never, current or past); alcohol consumption (average unit weekly intake); exercise (minutes per week); body mass index (BMI, kg/m^2); blood pressure; ethnicity; marital status; education; occupation.

Vision case history included: time since last eye examination; spectacles or contact lens use; history of ocular treatment or surgery; history of occlusion therapy or visual training in childhood; family history of eye disease; current problems with vision; asthenopia associated with computer use; history of headaches.

Table 1
Parameters assessed and their sequence for a typical study visit.

Description	Time (min)
Information leaflet discussion and informed consent	10
Collection of blood for serum carotenoid analysis	10
Demographic, medical history, lifestyle and vision case history questionnaires	20
Spectacle refraction, visual acuity, and ocular dominance	25
Color vision	20
Glare sensitivity	10
Visual function questionnaire	10
Contrast sensitivity	25
Break	~30
Macular pigment optical density spatial profile	30
Dietary questionnaire	30
Short wavelength automated perimetry	15
Photostress recovery	15
Fundus and iris photography	10
Total time	260

2.3. Spectacle refraction, visual acuity, and ocular dominance

Each subject underwent precise spectacle refraction by an experienced optometrist to determine refractive error and best corrected visual acuity (BCVA) for each eye. A computer generated LogMAR test chart (Test Chart 2000 Pro; Thomson Software Solutions) was used to determine BCVA at a viewing distance of 4 m, using a Sloan ETDRS letterset. BCVA was determined as the average of three measurements, with letter and line changes facilitated by the software pseudo-randomization feature. Best corrected visual acuity was recorded using a letter-scoring visual acuity rating, with 20/20 visual acuity assigned a value of 100. Best corrected visual acuity was scored relative to this value, with each letter correctly identified assigned a nominal value of one, so that, for example, a BCVA of $20/20^{+1}$ equated to a score of 101, and $20/20^{-1}$ to 99. The study eye was selected on the basis of ocular dominance, determined using the Miles Test (Roth, Lora, & Heilman, 2002) with the dominant eye chosen as the study eye, except in cases of observed equidominance, in which case the right eye was selected. All subsequent tests were conducted with the subject's optimal subjective refraction in place.

2.4. Glare sensitivity

Glare sensitivity was assessed using a Functional Vision Analyzer (Hohberger, Laemmer, Adler, Juenemann, & Horn, 2007) (Stereo Optical Co., Inc., Chicago, IL) using the Functional Acuity Contrast Test (FACT) Hitchcock, Dick, & Krieg, 2004; Terzi, Buhren, Wesemann, & Kohnen, 2005) and a customized inbuilt glare source. The test comprised linear, vertically oriented, sine wave gratings presented at five different spatial frequencies including 1.5, 3, 6, 12 and 18 cycles per degree (cpd). Nine circular patches were presented at each spatial frequency, the contrast of each patch decreasing by 0.15 log units from the previous. Gratings were tilted −15°, 0° or +15° with respect to the vertical, to keep them within the orientation bandwidth of the visual channel. The background was tapered into a grey field in order to keep retinal illumination constant and avoid ghost imaging. Baseline contrast sensitivity was determined on the basis of the lowest contrast compatible with accurate determination of patch orientation across all five spatial frequencies for mesopic (3 $cd\ m^{-2}$) conditions, initially in the absence of a glare source. Subjects were asked to identify grating orientation, starting with the patch at highest contrast, and continuing until identification was no longer possible due to reducing contrast. Subjects were instructed not to guess, but to respond "don't know" if patch orientation could not be correctly identified.

Glare sensitivity was assessed using a radial glare source consisting of 12 white LED's arranged circumferentially in an oval pattern surrounding the grating charts (ranging from 4.5° to 6° from central fixation). Two customized intensity settings were used to determine the effect of different levels of glare on contrast sensitivity. Glare source settings were set at a medium intensity of 42 Lux and a higher intensity of 84 Lux. All correct responses were entered into the Eyeview software provided, and contrast sensitivity scores for no glare, medium and high glare conditions were determined for the respective spatial frequencies.

2.5. Contrast sensitivity function

A Dell Dimension 9200 computer and a Metropsis Visual Stimulus Generation device (VSG (ViSaGe S/N: 81020197), Cambridge Research Systems Ltd., Cambridge, U.K.) were used to generate and control the stimuli. The VSG provided 14-bit output resolution per phosphor. The stimuli were displayed on a 19″ ViewSonic professional series p227f color CRT flat screen monitor with a frame

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rate of 119.98 Hz. The resolution of the monitor was set to 1024 × 769 pixels. Non-linearities in the screen luminance output were eliminated by gamma correction prior to testing using a photometer system (Opti-Cal; Minolta, Japan). The Metropsis software calculated the inverse curves required to correct for the monitor's non-linearities.

The Metropsis contrast sensitivity system generated luminance modulated sine gratings (Gabor patches). The orientation of the stimuli was vertical. The Gabor patches were presented on the CRT monitor and subtended a visual angle of 4.2°. The mean luminance was used as the background luminance. The Gabor had a two-dimensional spatial Gaussian envelope and was radially symmetrical with equal standard deviations, δx and δy.

Contrast sensitivity functions were determined under both mesopic and photopic conditions. Each subject was seated at a fixed viewing distance of 1.5 m from the CRT monitor. Natural pupils were used throughout the experiment. The non-dominant eye was occluded. Testing was carried out in a light free environment. The subject was dark adapted for 5 min and a 5-min training session was given prior to testing under mesopic conditions. Subject responses were recorded using a handheld responder (CR6, Cambridge Research Systems Ltd., Cambridge, UK), which communicated with the VSG device via an infra red link. A four alternate forced choice testing system was used, with four possible target locations. The stimuli were randomly presented at 2° spatial offset from the central cross target. The subject indicated the location of the target in relation to the fixation cross using the appropriate button on the responder box. The subject's contrast sensitivity was determined for five different spatial frequencies (1.0, 4.1, 7.5, 11.8 and 20.7 cpd) under both mesopic and photopic conditions, all at a mean luminance of 3 cd m^{-2} (mesopic) and 100 cd m^{-2} (photopic).

A linear staircase method was used to determine the contrast threshold. The first Gabor at a particular location was presented at an initial contrast level where it was anticipated that the observer would be able to detect the Gabor patch for that particular spatial frequency (initial contrast settings were informed by a brief pilot study involving five young healthy subjects). Subsequently, the contrast of the Gabor patch was varied using an adaptive staircase procedure, which was computer controlled and depended upon the subject's responses. The stimulus contrast was reduced in steps of 0.3 log units until the subject did not detect the Gabor patch (first reversal). The contrast was subsequently increased by 0.15-log unit steps until the subject saw the Gabor patch and responded correctly (second reversal). The Metropsis software calculated the contrast threshold for each location and spatial frequency by taking the mid-point between the mean for peaks and troughs for 12 reversal points. The standard deviation was calculated by taking the deviations of the peak reversals from their peak means and using the average square of these deviations to calculate a peak variance. This method was repeated for the troughs. The square root of both variances were then calculated and averaged to provide the threshold standard deviation.

For each subject, the Metropsis software plotted the inverse of the contrast threshold against the range of spatial frequencies tested to provide a contrast sensitivity function under both mesopic and photopic conditions.

2.6. Photostress recovery

Photostress recovery time (PRT) was calculated using a macular automated photostress (MAP) test. (Dhalla & Fantin, 2005; Dhalla, Fantin, Blinder, & Bakal, 2007) MAP is a novel photostress method for the evaluation of macular function using the Humphrey® field analyzer (Model 745*i* Carl Zeiss Meditec Inc. Dublin, CA, USA). The foveal threshold feature of the field analyzer was used to establish baseline foveal sensitivity as the average of three consecutive foveal sensitivity measurements recorded in decibels (dB), with each dB representing a 0.1 log unit sensitivity variation.

Following baseline foveal sensitivity calculation, the subject was exposed to a photostress stimulus, which consisted of a 5-s exposure to a 300-W, 230 V tungsten lamp head from a viewing distance of one meter. The spectral irradiance in the wavelength range, 300–800 nm, was measured using a Bentham DMc 150 double monochromator scanning spectroradiometer. The input optic consisted of a very high precision cosine response diffuser (f2 error < 1%) and the measurements were performed in 1 nm intervals. Calibration was carried out with reference to a quartz-halogen lamp traceable to the UK National Physical Laboratory. The illuminance at 1 m was obtained by using the photopic weighting function. The spectral irradiance at 1 m fixation distance from the photostress lamp is presented in Fig. 1.

Immediately post-photostress, a continuous and timed cycle of foveal sensitivity measurements were conducted and recorded for each subject. The reduction in foveal sensitivity from baseline, along with the time taken to recover to baseline foveal sensitivity, was recorded.

2.7. Macular pigment optical density

We used the Macular Densitometer™, a device developed and originally described by Wooten, Hammond, Land, and Snodderly (1999) to measure MPOD, including its spatial profile across the retina (i.e. 0.25°, 0.5°, 1.0°, 1.75° and 3° of retinal eccentricity). The Macular Densitometer™ uses heterochromatic flicker photometry (HFP) to obtain a valid measure of MPOD at a given retinal location (Hammond, Wooten, & Smollon, 2005). This method has recently been refined and is now referred to as customized HFP or cHFP. For a detailed description of this protocol please see recent publications by our research group and others (Loane, Stack, Beatty, & Nolan, 2007; Nolan et al., 2009; Stringham et al., 2008). One subject (cwit2553) was excluded from analysis due to inability to use the Densitometer to obtain reliable MPOD data.

2.8. Fundus photography

Fundus photographs were obtained in both eyes using a NIDEK non-mydriatic fundus camera (AFC-230). Fundus photographs were assessed by a qualified optometrist to exclude fundoscopically evident retinal/nerve pathology.

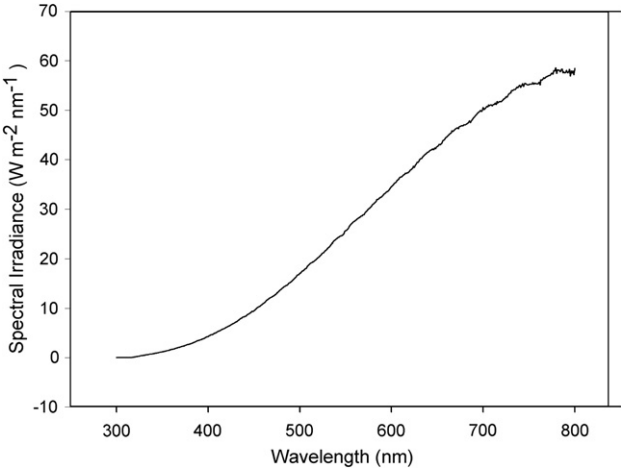

Fig. 1. Spectral Irradiance at 1 m fixation distance from Arri 300 photostress lamp.

2.8.1. Reliability testing of methods

Given that all subjects recruited into the study were classed as "naïve" to the tests carried out (with the exception of the visual acuity test), we conducted a pilot reliability study prior to the study commencing. Following pre-test training (see above), repeat testing on 10 subjects at three separate study visits (over a 10 day period) was conducted. The intraclass correlations (ICC) obtained for all methods were high and are presented in Table 2. In addition, repeat testing of radiance values obtained to compute MPOD values had previously been conducted by our research group. The data from this investigation concluded that the radiance values obtained using the Densitometer were very high (i.e. ICC in the range of 0.93–0.96; see recent publication by (Kirby et al., 2008) In addition, we conducted Bland Altman analyses of differences in MPOD at eccentricities 0.25°, 0.5°, 1° and 1.75°, measured at two separate study visits. The limits of agreement, at all eccentricities, were in the range 0.06–0.07 units away from the mean difference, which seems satisfactory. The coefficient of repeatability ranged from about 6% at the central eccentricities (0.25°, 0.5°), to 19.4% at 1.75°.

Mean differences in MPOD between study visits were 0.02, −0.01, 0.02, and 0.0 at eccentricities 0.25°, 0.5°, 1° and 1.75°, respectively. The first two of these differences were statistically significant, at the 5% level, using the paired *t*-test, suggesting bias; clinically, however, a bias of this very small magnitude is of no practical importance.

2.9. Statistical analysis

The statistical software package SPSS (version 17) was used for analysis. All variables investigated exhibited a typical normal distribution. Mean ± SD's are presented in the text. Pearson correlation coefficients were calculated to investigate bivariate relationships and partial correlation coefficients when controlling for confounding variables. We used the 5% level of significance throughout our analysis. A statistical power analysis determined a minimum sample size of 91 subjects in order to achieve 99% power with a one-tailed 5% test, with an affect size of ρ (rho) = 0.4. The 142 subjects recruited exceed these stringent statistical requirements, but more importantly, allowed for continued follow up (and standard drop-out) as part of the COMPASS lutein interventional study (ISRCTN number = 35481392), which was designed to investigate whether MPOD augmentation, following lutein supplementation, improves visual performance. Of note, this study is currently on-going.

3. Results

The demographic, medical, lifestyle, anthropometric, and vision-related data of the 142 subjects recruited into the study are summarized in Table 3. No subject was excluded from the study on the basis of fundus findings. The mean (±SD) age of the sample was 29 (±6) and ranged from 18 to 41 years. The mean (±SD) BMI was 25 (±4) and ranged from 19 to 43.

3.1. Macular pigment optical density

The mean (±SD) MPOD, at all degrees of retinal eccentricity measured, is summarized in Table 4. MPOD at peak (0.25° eccentricity) was positively and significantly correlated with MPOD at

Table 2
Reproducibility of visual performance tests used in COMPASS, assessed using intraclass correlation coefficient (ICC).

Test	Visit 1	Visit 2	Visit 3	ICC
Mesopic CSF[b] with no glare (cpd)				
1.5	1.55 (±0.21)	1.68 (±0.23)	1.62 (±0.20)	0.683
3	1.67 (±0.27)	1.74 (±0.24)	1.77 (±0.23)	0.852
6	1.51 (±0.58)	1.64 (±0.27)	1.61 (±0.25)	0.682
12	0.78 (±0.61)	0.88 (±0.52)	0.97 (±0.57)	0.867
18	0.56 (±0.45)	0.43 (±0.53)	0.39 (±0.46)	0.843
CSF under medium glare lights (cpd)				
1.5	1.47 (±0.20)	1.55 (±0.22)	1.45 (±0.21)	0.626
3	1.31 (±0.54)	1.52 (±0.34)	1.43 (±0.57)	0.533
6	1.03 (±0.77)	1.16 (±0.69)	1.18 (±0.68)	0.893
12	0.49 (±0.59)	0.60 (±0.58)	0.51 (±0.62)	0.770
18	0.19 (±0.37)	0.25 (±0.39)	0.33 (±0.41)	0.767
CSF under high glare lights (cpd)				
1.5	1.25 (±0.52)	1.34 (±0.32)	1.28 (±0.52)	0.829
3	1.26 (±0.55)	1.33 (±0.56)	1.30 (±0.51)	0.942
6	1.01 (±0.77)	0.94 (±0.71)	0.98 (±0.74)	0.978
12	0.48 (±0.57)	0.33 (±0.50)	0.36 (±0.55)	0.485
18	0.19 (±0.37)	0.07 (±0.20)	0.13 (±0.27)	0.707
CSF by metropsis mesopic (cpd)				
1	1.54 (±0.10)	1.55 (±0.15)	1.60 (±0.11)	0.432
4.1	1.73 (±0.15)	1.77 (±0.13)	1.77 (±0.17)	0.399
7.5	1.32 (±0.09)	1.31 (±0.15)	1.34 (±0.18)	0.683
11.8	0.83 (±0.14)	0.84 (±0.18)	0.82 (±0.23)	0.732
20.7	0.22 (±0.07)	0.24 (±0.09)	0.25 (±0.09)	0.746
Photopic CSF (cpd)				
1.0	1.60 (±0.17)	1.58 (±0.15)	1.59 (±0.15)	0.645
4.1	1.95 (±0.13)	1.98 (±0.13)	1.97 (±0.13)	0.662
7.5	1.75 (±0.13)	1.75 (±0.17)	1.78 (±0.18)	0.632
11.8	1.29 (±0.21)	1.34 (±0.25)	1.39 (±0.25)	0.727
20.7	0.43 (±0.24)	0.43 (±0.19)	0.41 (±0.20)	0.857
Photostress recovery test	37.41 (±1.30)	38.41 (±1.52)	38.08 (±1.68)	0.560

Q6 [a]ICC = intraclass correlation coefficient.
[b] CSF = contrast sensitivity function.

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Table 3
Demographic, medical, lifestyle, anthropometric, and ocular related data for the entire study group.

Characteristic	n[a]
Sex	
Male	74
Female	68
Medical history	
Diabetes	1
High blood pressure	4
High cholesterol	6
Angina	0
Stroke	0
Family history of eye diseases	
Unknown	3
AMD	22
Cataract	12
Glaucoma	28
Retinal problem	4
None	82
Smoking habits[b]	
Never smoked	86
Ex-smoker	25
Current smoker	31
Exposed second-hand smoke	17
BMI	
Desirable weight (BMI < 25)	83
Overweight (BMI 25–30)	42
Obese (BMI > 30)	17
Ocular dominance	
Right	86
Left	53
Equidominant	3
BCVA	
<100	1
100–105	3
>105–110	42
>110–115	79
>115–120	17

[a] n = sample size.
[b] Smoking habits: ex-smoker = smoked ⩾ 100 cigarettes in lifetime but none in last 12 months; current smoker = smoked ⩾ 100 cigarettes in lifetime and at least 1 cigarette per week in last 12 months; exposed second-hand smoke = commonly exposed to second-hand smoke at home or in the work place.

Table 4
MPOD at all measured degrees of retinal eccentricity, for the entire study group.

Retinal eccentricity[a] (°)	MPOD[b]
0.25	0.48 (±0.19)
0.5	0.39 (±0.17)
1	0.21 (±0.12)
1.75	0.09 (±0.09)
3	0.09 (±0.07)
Average	0.25 (±0.12)

n = 141.
[a] Degrees retinal eccentricity.
[b] MPOD = mean (±SD) macular pigment optical density.

all other degrees of retinal eccentricity (r = 0.472–0.919, p < 0.01 for all).

3.2. MPOD and its relationship with BCVA

The mean (±SD) BCVA of the study group was 112 (±3). There was a positive and statistically significant relationship between MPOD at each eccentricity measured and BCVA (r = 0.237–0.308, p < 0.01 for all). The relationship between MPOD at 0.25° of eccentricity and BCVA is presented in Fig. 2.

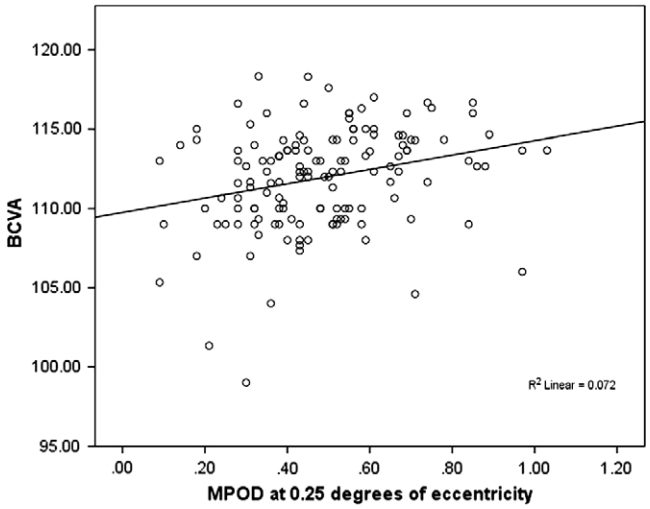

Fig. 2. The relationship between MPOD at 0.25° and BCVA.

3.3. MPOD and its relationship with contrast sensitivity

The relationships between MPOD at each eccentricity measured and log mesopic and photopic contrast sensitivity at different spatial frequencies are presented in Table 5.

The strongest relationship was seen between MPOD at 0.25° and log contrast sensitivity at 7.5 cpd for mesopic conditions (r = 0.22, p < 0.01) (Fig. 3).

3.4. MPOD and its relationship with glare sensitivity

There was no statistically significant relationship between MPOD, at any of the eccentricities measured, and mesopic contrast sensitivity observed under medium or high glare conditions for any spatial frequency (p > 0.05, for all), with the exception of the negative and statistically significant relationship between peripheral MPOD (at 1.0°, 1.75° and 3.0°) and mesopic contrast sensitivity under medium glare conditions (r = −0.178 to −0.213, p < 0.05).

3.5. MPOD and its relationship with PRT

The mean (±SD) foveal sensitivity of the study group was 38.1 (±1.4) dB. The mean (±SD) sensitivity post-photostress was 27.7 (±2.9) dB, representing a mean sensitivity reduction of 27.3% from baseline, across the entire study group. The mean (±SD) PRT

Table 5
The relationships between MPOD and mesopic and photopic contrast sensitivity at different spatial frequencies.

Spatial frequency	MPOD 0.25°	MPOD 0.50°	MPOD 1.0°	MPOD 1.75°	MPOD 3.0°
Mesopic					
1	−0.019	−0.034	−0.120	−0.200*	−0.097
4.1	0.065	0.016	−0.046	−0.080	−0.093
7.5	0.220**	0.192*	0.138	0.102	0.111
11.8	0.184*	0.183*	0.122	0.084	0.031
20.7	0.139	0.113	0.028	0.089	0.024
Photopic					
1.0	0.210*	0.159	0.108	0.160	0.081
4.1	0.124	0.100	0.007	0.067	0.053
7.5	0.176*	0.167*	0.115	0.133	0.101
11.8	0.193*	0.187*	0.135	0.131	0.114
20.7	0.153	0.153	0.082	0.132	0.117

* p < 0.05.
** p < 0.01.

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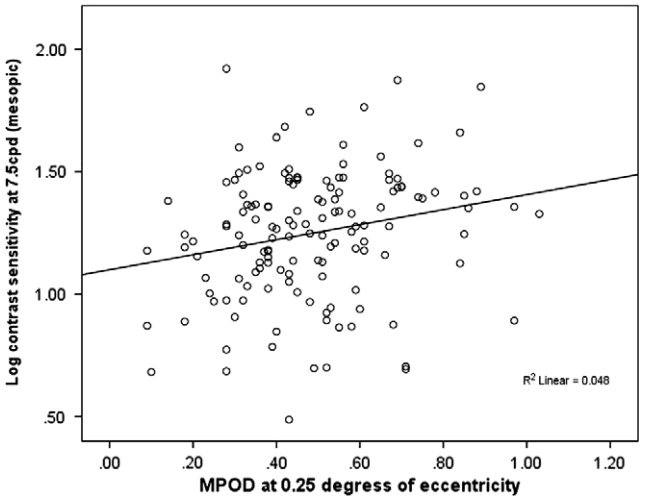

Fig. 3. The relationship between MPOD at 0.25° and log contrast sensitivity at 7.5 cpd for mesopic conditions.

(recorded as the time taken for foveal sensitivity to recover to 95%, or typically to within 2 dB, of the baseline value) was 135.8 (±63.9) s. There was no statistical relationship between MPOD at any of the eccentricities measured and either foveal sensitivity reduction (%) caused by photostress ($p > 0.05$, for all), or PRT ($p > 0.05$, for all).

4. Discussion

Given the central and pre-receptoral location (Snodderly, Auran, & Delori, 1984; Trieschmann et al., 2007) and the optical properties of MP (Bone et al., 1992), it is reasonable to hypothesize that MP would impact on visual performance, via its potential to attenuate chromatic aberration and light scatter (Nussbaum et al., 1981; Reading & Weale, 1974; Walls & Judd, 1933; Wooten & Hammond, 2002). In this study, we investigated the relationship between MPOD at various degrees of eccentricity (i.e. at 0.25°, 0.5°, 1.0°, 1.75° and 3° of retinal eccentricity) and clinically important parameters of central visual performance including BCVA, contrast sensitivity, glare sensitivity, and photostress recovery.

We report that MP (at each degree of eccentricity) is positively associated with BCVA in our study population, which suggests that MP may play a role in the optimization of visual acuity under photopic conditions; however, it is important to note that the *r* values ranged from 0.237 to 0.308 and the observed relationships can therefore only explain 5.6–9.5% of the variability. This finding is all the more provocative given that subjects in the current study were young, free from ocular pathology, and uniformly demonstrated high visual acuity. Indeed, It is somewhat intriguing to note that this statistically significant relationship was detected in a population sample where the majority of participants exhibited average to high levels of MP (at 0.25° of eccentricity). Indeed, only a very small number of subjects (~13.4%) had central MPOD of less than 0.3 in the current study. It has been previously suggested that levels above 0.3 might be superfluous to visual performance, due to the non linear nature of the effect of MP on vision (Reading & Weale, 1974).

It is important to point out that extensive efforts were made by the COMPASS study investigators to probe the limits of visual acuity, so that even the most subtle contributions of MP to visual performance might be detected. This was facilitated by customization of the vision test charts (i.e. inclusion of additional letter sizes to allow testing to a limit equivalent to 20/8) and recruitment of experienced optometrists to perform functional evaluations at both study sites (WIT and DIT). Best corrected visual acuity among the study participants ranged from a minimum of 99 (20/20^{-1}) to a maximum of 118 (20/8^{-2}). MP, it appears, could account for the theoretical refinement of acuity by up to 0.1 log units in the study sample here. This represents a substantial contribution and might be equated to the elimination of up to 0.25 dioptres of optical defocus, and appears to be consistent with previously reported limiting effects of chromatic aberration on the spatial modulation transfer function (Thibos, Bradley, & Zhang, 1991).

This finding is, however, somewhat at odds with previously reported investigations of the "acuity hypothesis" Engles et al. (2007) explored the relationship between MPOD and both gap and vernier acuity under "photopic" conditions (Engles et al., 2007). They reported that neither gap acuity nor vernier acuity was significantly related to MPOD. Their findings however are not directly comparable to the results described here, and for a number of reasons. Specifically, their adopted background luminance levels were in the low photopic range (i.e. 17 cd m^{-2} for the achromatic condition, and 15.7 cd m^{-2} for the chromatic condition. Also, gap, vernier and recognition acuity measures are not directly interchangeable, so it is entirely plausible that findings with relation to the acuity hypothesis might differ when different visual attributes are assessed. Despite the aforementioned methodological differences, the conflicting outcomes do serve to emphasize the challenges inherent in the evaluation of the role of MP on visual performance, particularly by associative means.

We also report that central MPOD (i.e. at 0.25° and at 0.5° of eccentricity) is positively and significantly related to both mesopic and photopic contrast sensitivity at intermediate spatial frequencies (i.e. 7.5 and 11.8 cpd). Central MP appears to influence sensitivity at spatial frequencies to which the visual system is highly tuned (Campbell & Robson, 1968). However, and similar to the association between MP and BCVA, it is important to note that the *r* values for MP's association with contrast sensitivity ranged from 0.167 to 0.220 and therefore the observed relationships can only explain 2.8–4.8% of the variability.

For photopic conditions, this finding might be attributable to the attenuation of the effects of chromatic aberration and light scatter, whereby image refinement potentially cause lateral inhibitory surround responses to be dampened, and the resultant ganglion cell response optimized (Kuffler, 1953). Under mesopic conditions, it is more likely that enhanced visual performance is a consequence of the selective diminution of rod mediated signals. While rod and cone photoreceptors operate interactively in the high mesopic conditions employed here (Kuffler, 1953), rods remain optimally sensitive to shorter wavelengths than cones (explaining the Purkinje shift in peak retinal spectral sensitivity towards blue under mesopic conditions). The pre-receptoral absorption of short-wavelength light by MP might, therefore, serve to attenuate rod activity and allow cone-mediated vision (which typically exhibits better contrast sensitivity (Puell, Palomo, Sanchez-Ramos, & Villena, 2004), to dominate further into the mesopic range. This theory is supported by the limited nature of the relationship observed between MP and contrast sensitivity, confined to the most central anatomic locations where MP is highest and cone activity predominates.

Of note, this is the first study to report on the association between MP and contrast sensitivity in a young healthy population (not confounded by dietary supplementation or ocular pathology). Our findings are consistent with those of Kvansakul et al. (2006) who reported that MP augmentation, via supplementation, enhances contrast acuity thresholds under mesopic conditions.

Finally, we found that MPOD was not related to either glare sensitivity or photostress recovery, as assessed here. At first glance, these findings might appear to conflict directly with a number of

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recent studies, which have reported positive and statistically significant associations between MP and several parameters of visual performance including: visual discomfort (Stringham, Fuld, & Wenzel, 2003), photophobia (Wenzel, Fuld, Stringham, & Curran-Celentano, 2006), veiling glare (Stringham & Hammond, 2007) and photostress recovery (Stringham & Hammond, 2007; Stringham & Hammond, 2008). The cited series of experimental analyses are consistent with the rationale whereby MP attenuates the effects of blue light, which is both valid and important. Fundamental methodological differences may, however, explain the differences between those reports and our observations.

Firstly, all the above studies employed a Maxwellian-view optical system to generate and present stimuli. While the rationale for doing so remains sound, in that it eliminates pupil diameter and pupil responses as a potential confounding factor, it is difficult to extrapolate their findings into a natural environment, outside of the laboratory, where changes in pupil diameter for example, are a natural consequence of the luminance changes typically observed on a daily basis, and may confer some level of protection against the deleterious effects of glare and excessive light stimulation. However, adoption of a natural pupil introduces other difficulties. Most importantly, the individual variation in pupil size, and the consequential variation in retinal illuminance, clouds the interpretation of MP's contribution to visual performance under glare conditions. It should therefore be conceded, that for a cross-sectional evaluation, the natural pupil is less appropriate for a comprehensive evaluation of the role of MP, if any, in terms of its contribution to visual comfort and glare attenuation.

Secondly, the studies cited above invariably employed stimuli containing a strong short-wavelength blue light component. Again, there is an obvious rationale for doing so, as MP predominantly absorbs blue light. However, the concept of the environmental validity of such stimuli must again be questioned. Specifically, the most common light sources employed in industrial, commercial and home lighting systems typically contain significantly less blue light than those employed in cited studies. Tungsten and tungsten–halogen filament lighting systems, in fact, contain a minimal blue light component (see Fig. 1). The absence of a strong blue light component in the photostress lamp, employed here, may partially explain the absence of any association between MP on PRT observed in our study. Our findings, therefore, in fact corroborate and extend the findings of Stringham et al. (2004) and Stringham and Hammond (2007) in that the associations between MP and glare are strongly wavelength dependent, and the influence of MP on glare disability is critically dependent on the spectral output of the source. It is worth noting, however, that the current trend for change to compact fluorescent and light emitting diode installations, which typically emit significantly more blue light (unpublished data from our laboratory suggests a twofold increase in blue light irradiance for compact fluorescent bulbs compared to tungsten), may render the role of MP for visual performance, if any, ever more important.

In conclusion, visual performance, as assessed by visual acuity and contrast sensitivity measures, appear to be weakly associated with MPOD. However, photostress recovery and visual performance under glare conditions were unrelated to this pigment. The lack of consistency between our findings and those of others possibly reflects the difficulties inherent in investigating the role of MP with respect to visual performance using a study of cross-sectional design. Fundamental experimental design issues for visual performance evaluation must also be considered. There are no gold standard techniques, no means to accurately simulate the broad range of environmental conditions experienced on a daily basis, so the selection of individual test parameters will influence both the results of the investigation, and any subsequent comparison with previous experimental results. The results of the current investigation should be interpreted with full appreciation of its design limitations, and conclusions should therefore be restricted to the specific testing conditions employed herein.

Visual acuity has been shown to relate to quality of life (Datta et al., 2008) and is important in our highly visual society, where the demands for high quality visual resolution are constant. Contrast sensitivity correlates with various functional vision tasks such as mobility orientation, balance control, driving, face perception and reading performance (Owsley & Sloane, 1987; Owsley et al., 2002), and has been established as an important measure of visual function, which is related to quality of life (Owsley & Sloane, 1987). These associations between MP and visual performance are likely to apply equally and possibly more substantially, in an older population, where, for example, the incidence of driving accidents and falls directly relate to visual performance (Owsley et al., 2002).

In summary, a placebo-controlled, randomized, L-based supplementation trial, designed to investigate if augmentation of MPOD enhances visual performance and/or comfort, is required to more adequately address this critical research question, and fully explore the proposed "optical" hypotheses of MP.

Disclosure

None.

5. Uncited reference

Sloane et al. (xxxx). Q1

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