



The relationship between foveal short-wavelength-sensitive visual function and macular pigment optical density in the ageing eye



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ABSTRACT

To investigate the role of macular pigment in preserving foveal short-wavelength-sensitive (SWS) visual function in the ageing eye orientation identification acuity was measured in the fovea and at 12° eccentricity (nasal visual field) under SWS-cone isolating conditions in 73 participants (aged 20–71). Macular pigment optical density (MPOD) was measured at 0.5° eccentricity from the foveal centre using a heterochromatic flicker photometry (HFP) based instrument. MPOD was not significantly related to age but reduced SWS orientation identification acuity was associated with increasing age in the fovea and at 12° eccentricity. The rate at which foveal acuity changed in relation to acuity at 12° with increasing age was not significantly related to macular pigment levels. These findings do not support the hypothesis that higher macular pigment levels protect S-cone mediated foveal visual function in the ageing eye.

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1. Introduction

Macular pigment (MP), found in the central retina of humans, consists of the carotenoids lutein (L), zeaxanthin (Z) and meso-zeaxanthin (MZ). L and Z are entirely of dietary origin, with a significant proportion coming from green leafy vegetables and egg yolk in the normal diet (Johnson et al., 2010). MZ is primarily formed in the retina following conversion from lutein (Johnson et al., 2005). Several creditable theories exist, which are not mutually exclusive to each other, as to the primary function and role of macular pigment in the human eye (for reviews see (Loane et al., 2008; Weale, 2007; Wooten & Hammond, 2002)). Of particular interest amongst this literature are those few cross-sectional studies which have suggested that higher levels of macular pigment optical density (MPOD) are associated with preserved visual function across the lifespan (Hammond & Wooten, 2005; Hammond, Wooten, & Snodderly, 1998). If increased levels of macular pigment are important in the maintenance of good vision in older years then this protective theory of macular pigment merits further investigation for a variety of different visual functions.

Psychophysical examination of the short-wavelength-sensitive (SWS) visual system can tell us much about the ageing eye and its susceptibility to disease. SWS pathway function has been shown to be significantly reduced in normal older healthy eyes for a variety of stimuli (Beirne et al., 2008; Eisner et al., 1987; Johnson et al., 1988; Werner, Bieber, & Scheffrin, 2000; Zlatkova, Coulter, & Anderson, 2003) and functional defects in age-related diseases such as age-related macular degeneration (AMD) can often present them-

selves within the short-wavelength visual system before traditional measures of visual function do (Beirne et al., 2006; Frennesson, Nilsson, & Nilsson, 1995; Remky et al., 2001). Haegerstrom-Portnoy (1988), on finding that there was less loss of foveal SWS sensitivity relative to several extrafoveal locations (out to 20° eccentricity) in an older group of individuals compared to a younger group, hypothesised that macular pigment (which was not measured) may protect the foveal area from light damage (Haegerstrom-Portnoy, 1988). Further to this Hammond, Wooten, & Snodderly, 1998 found that foveal sensitivity of the S-cones in older individuals was better preserved in those individuals with higher levels of MPOD (≥ 0.40 log units), measured by heterochromatic flicker photometry (HFP), compared to those with lower levels of MPOD (Hammond, Wooten, & Snodderly, 1998). However, Werner, Bieber, & Scheffrin, 2000 stress that the findings of these two studies were limited by the fact that one did not include cone sensitivity at more than one retinal location, (Hammond, Wooten, & Snodderly, 1998) and the other did not report MP estimates in the same observers (Haegerstrom-Portnoy, 1988). They argue that both of these previous studies findings are consistent with a gain change hypothesis whereby long-term adaptation changes in the foveal S-cones results in higher sensitivity which is directly related to the reduction in short-wavelength light that is due to MP screening (Werner, Bieber, & Scheffrin, 2000). In a study using 50 observers they showed that although a significant positive correlation was found between foveal macular pigment density and the S-cone log sensitivity difference between 2 locations (0° and 8°) specified at the retina, this result was independent of age. This age independent finding would not be expected from the MP protection hypothesis but lends weight to an alternate gain hypothesis, which the authors state should be considered in any

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study investigating the potential protective role of MP (Werner, Bieber, & Scheffrin, 2000).

This study aims to further investigate the association between S-cone function at different retinal locations and MPOD (measured using HFP) in a group of healthy individuals of increasing age to see if any protective relationship can be demonstrated. To measure S-cone function an orientation identification task with a sinusoidal grating was performed under S-cone isolating conditions in the fovea and at 12° eccentricity. Using appropriate S-cone isolating conditions this resolution acuity task is sampling limited, in the fovea and the periphery, and can provide indirect estimates of the underlying retinal ganglion cell density (Anderson, Zlatkova, & Demirel, 2002; Beirne, Zlatkova, & Anderson, 2005). Previous study has shown that the magnitude of age-related losses in sensitivity using S-cone increment thresholds can depend on the level of light adaptation (Scheffrin et al., 1992). However, the orientation identification task is not significantly affected by moderate amounts of real and simulated lens yellowing (Anderson et al., 2003; Zlatkova, Coulter, & Anderson, 2006) or by small amounts of optical blur (Anderson et al., 2003). Resolution thresholds remain sampling limited with age in healthy individuals, (Beirne et al., 2008) and do not appear to be significantly affected by an increase in prerenal filters or low sensitivity of the S-cones, (Swanson, 1989) making a S-cone isolated grating resolution acuity task an appropriate task for use in such a clinical study looking at age-related changes in visual function.

If increased levels of macular pigment are associated with preserved foveal SWS function in the ageing eye, relative to peripheral vision, this finding would have significant relevance to those individuals who have lower baseline levels of macular pigment and may benefit from interventions that may increase their MPOD such as diet alterations, lifestyle changes or food supplementation.

2. Methods

2.1. Participants

73 participants (27 males, 46 females) ranging in age from 20 to 71 years took part in the study. Participants were recruited from both poster and internet advertisement of the research study at a regional University campus and its surrounding area. All participants were Caucasian and underwent a full ophthalmic examination by an experienced optometrist with the following criteria being used for study inclusion: visual acuity of 20/20 (Snellen) or better with best correction in the study eye, refractive error between –6DS and +4DS with ≤ 2.0 DC of foveal astigmatism, intraocular pressure less than 20 mmHg as assessed by non-contact tonometry, clear ocular media assessed by slit-lamp biomicroscopy, no self-reported history of ocular disease and no history of diabetes or other systemic disease that might affect vision. Subjects were excluded if they had been taking any dietary supplements containing lutein or zeaxanthin in the 3 months preceding the study participation date.

Dilated fundus photography examination revealed no soft drusen or obvious retinal pigment epithelium changes in the macular area of any of the participants aged over 50. The eye with the best-recorded visual acuity was chosen as the study eye. If acuity and refractive error was equal in both eyes, one eye was selected to undergo testing by asking the patient which they felt was their dominant eye, and performing the testing on this eye. The study received ethical approval from the local research ethics committee and informed consent was obtained from all participants in accordance with the tenets of the Declaration of Helsinki.

2.2. Measurement of macular pigment optical density

Macular Pigment Optical Density was psychophysically estimated using a heterochromatic flicker photometry based instru-

ment from Macular Metrics (Macular Metrics, Arboath, MA). This custom-built Densitometer instrument is very similar in design to those which have been used and described in several previous studies investigating macular pigment optical density (Connolly et al., 2010; Iannaccone et al., 2007; Kirby et al., 2009; Snodderly et al., 2004). The densitometer has been shown to be an accurate (Hammond, Wooten, & Smollon, 2005; Wooten et al., 1999) and repeatable method (Gallaher et al., 2007; Loughman et al., 2012) with measurements not significantly affected by optical blur (Gallaher et al., 2007), pupil size (Wooten et al., 1999) or lens yellowing (Ciulla et al., 2001). Importantly, this instrument allows the investigator to individually adjust the optimal flicker frequency (OFF) for each of the different stimuli used, for each participant. Critical flicker fusion thresholds can vary significantly between individuals and age groups (Hammond & Wooten, 2005; Renzi & Hammond, 2010) and correct setting of the optimal flicker frequency can have a significant effect on the MPOD values obtained. This minimises the risk of over or under estimating MPOD in particular individuals in contrast to other devices which use a fixed flicker frequency (Loane et al., 2007; Loughman et al., 2012). A second advantage to this instrument is that the two different wavelengths of light (460 and 560 nm) used for the heterochromatic flicker method are inverse yoked. As the blue light becomes more intense, the green light becomes less intense keeping the brightness of the test stimulus relatively constant thus removing significant brightness change artefacts as a distraction to the participant.

All participants underwent an instruction and practice session during which the operator satisfied himself that the participant understood the nature of the task. Optimal flicker frequencies were adjusted for each individual during the instruction and practice period depending on whether it appeared that the OFF was too high (a wide no flicker zone reported) or too low (no flicker zone reported) for the individual undertaking the test. MPOD was estimated for one location of 0.5° eccentricity from the foveal centre, using a 1 degree diameter disc. Using this method it is assumed that the flicker perceived by the individual is mainly dominated by the edges of the disc-shaped stimuli being viewed. However, it should be noted that previous studies have suggested that some individuals may use other retinal locations, close to the edge of the stimuli to see the flicker (Bone, Landrum, & Gibert, 2004; van der Veen et al., 2009), and the retinal location used may depend on the shape and height of the individual's macular pigment distribution, which can show significant inter-individual variation (Berendschot & van Norren, 2006; Kirby et al., 2009).

Participants were instructed to fixate on a 5 min black fixation point in the centre of the disc which was initially set to radiance values where it would clearly flicker. The participant had to use a two option push-button response box to adjust the radiance values of the two alternating wavelengths of light (460 and 560 nm), which were superimposed on a 6.00°, 3.0 cd/m², 470-nm circular blue background, so that the stimulus appeared not to flicker or flicker minimally. This no/minimal flicker radiance was then recorded by the operator and the process was started again from a radiance where the target was clearly flickering to the observer. The reference point (where macular pigment values are assumed to be minimal) was measured using a disc of 2° diameter with a 5 min red fixation point at 7° eccentricity. Four no/minimal flicker settings were made for each of the two locations and MPOD was estimated using the formula:

$$\text{MPOD} = \text{Log}(R_{460F}/R_{460P}) - \text{Log}(R_{560F}/R_{560P})$$

where R460 is the radiance of the 460 nm light and R560 the radiance of the 560 nm light at the foveal (F) and peripheral (P) locations when no/minimal flicker is perceived.

The MPOD estimates had a mean standard deviation (SD) of 0.08 with a SD range of 0.02–0.15 log units.

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