



Impact of macular pigment on visual performance

James Loughman, Peter Davison, John Nolan and Stephen Beatty describe the latest research into the macula and visual performance and how macular pigments may affect vision. C7230, one general CET point, suitable for optometrists and dispensing opticians

Evidence is accumulating to suggest that macular pigment (MP), composed of the dietary carotenoids lutein (L), zeaxanthin (Z) and meso-zeaxanthin (MZ), may have a protective role against macular degeneration. But does it also have a role in the visual performance of normal retinas? At the outset it should be stated that current evidence on the potential of MP to enhance, or at least affect, the quality of our visual experience is sparse, somewhat mixed and ultimately deficient. It has long been known that MP absorbs short wavelength (blue) light prior to photoreceptor stimulation. The theory that filtering such defocused blue light could enhance visual acuity (and/or contrast sensitivity) by reducing the effects of chromatic aberration goes back as far as Schülz in 1866.¹ This hypothesis, specifically in relation to MP, has, however, remained largely unexplored and unproven.

The selective accumulation of only three specific dietary carotenoids, to the exclusion of the other 40 dietary carotenoids, suggests an exquisite biological selectivity for L, Z and MZ at the site of maximum visual acuity in the human retina, and indicates a role for these carotenoids which is uniquely suited to this anatomic location. Given that Darwinian natural selection is driven by phenotypic expression of genetic background – which confers advantage before and until the period of procreation – it follows that the biological selectivity of MP's accumulation in the retina primarily represents an advantage in young and middle age. An alternative to the visual performance hypothesis is that MP protects the retina against blue light damage, but since ARM and AMD are age-related conditions, it is doubtful that this degree of biological selectivity evolved to protect against such condi-

tions. In other words, it is possible that the primary role of MP involves its contribution to visual performance.

MP most certainly affects visual experience by altering the spectral composition of the light incident upon macular photoreceptors. Whether such short wavelength absorption influences the quality of the visual experience, and whether the magnitude of such an effect correlates with MP optical density are larger questions that remain largely unaddressed, and definitely unanswered.

To address the question of whether MP may influence visual performance, one must (a) initially consider the primary factors that affect performance, (b) outline the properties of MP that make it potentially useful in enhancing visual performance in light of any such limiting factors, (c) analyse existing evidence in favour and/or against a putative role for MP in visual performance enhancement and (d) design experimental strategies that might more clearly elucidate the answers to the question of whether MP has a role to play.

Visual performance

Vision includes the capacity to detect objects against a contrasting background, to detect gaps between objects (such as in vernier tasks which provides one example of a hyperacuity), to recognise and identify objects, to perceive colour, to detect movement and to perceive depth among others. The capacity to recognise a small letter from a distance bears little relation to the capacity to differentiate colours or to detect a potential threat such as an oncoming vehicle in the peripheral field of view. Performance is critically dependent on illumination. The range of illumination we experience in the course of a day is vast. The visual system copes with the huge range of luminances by

adapting to the prevailing conditions and can function through a staggering luminance range of nearly 10 log units. Although adaptation facilitates performance over a wide range of ambient illumination levels, this does not mean that we see equally well at all levels. Under dim conditions the eyes are very sensitive and can detect subtle changes in luminance but acuity for pattern details and colour discrimination are poor.

Shaler² has explored the relationship between illumination and grating acuity. Converting his findings to Snellen equivalent, daylight (photopic) performance of 6/3 reduces to 6/90 under dim conditions, a 30-fold reduction. Threshold visibility, colour appearance and visual acuity all vary dramatically at different illumination levels, and these visual parameters change over the time-course of light and dark adaptation. No single test or testing condition can therefore define visual performance.

It is also important to remember that when describing visual processes, vision also involves the processes leading to perception. The visual system employs numerous anatomical and physiological strategies including lateral interactions between cells, specific receptive field organisation, spatial retinotopic organisation in retinal and non-retinal areas of the pathway, colour opponency and parallel visual pathways among others in order to achieve an instantaneous (stable and constant), yet coherent and highly detailed perception of the outside world and our position within it. Such image processing is not exclusive to the brain but extends throughout the visual pathway beginning at the retina. The eyes and brain are thus inextricably linked with the visual universe. The eyes actively record the form, colour and movements of the world, and the brain moulds these raw perceptions ▶



into recognisable patterns. The retina essentially acts as a spatial, temporal and spectral filter of patterns of light striking its surface. Its anatomical structure and the functional properties of individual cells determines the type of information extracted from a visual scene and delivered to the brain, namely the retina analyses and controls what information is delivered to the brain.

Specialisation of the macula

The macula, which comprises less than 4 per cent of the total retinal area, accounts for almost all of our useful photopic vision. Several distinctive anatomical and neural adaptations facilitate such high level visual performance. These include:

- Cone density reaches a peak at the centre of the macula (fovea) which intersects the line of sight. Cone density exceeds rod density only at the lower part of the foveal slope, reaching a maximum at the base of the fovea (foveola) where cone density is more than three times the density at the base of the foveal slope.³ Rods, ganglion cells and all inner nuclear layer neurons are absent from the foveola so that only here is light directly incident on photoreceptors (elsewhere light must traverse the various retinal cells and layers to reach photoreceptors).
- Midget pathways arising from these foveal cones dominate. Such parvocellular midget pathways are tuned to high spatial frequencies (allowing high acuity) and also exhibit colour opponency.
- Such midget pathways are distinctive in the absence of convergence of photoreceptor signals onto bipolar and ganglion cells. Absent or reduced convergence of information preserves the information gathered at the fovea for delivery to the visual cortex. This difference between foveal and extra-foveal processing generates a hierarchy in the importance of retinal information.
- The retinal hierarchy afforded to foveal cone-mediated vision extends back to the visual cortex where the central retinal pathways have by far the greatest representation.^{4,5}

Having outlined those anatomical and neural factors central to primates' capacity for high acuity vision, it is now important to consider the potential role of macular pigment in further enhancing visual performance. In order to do so, it is essential to characterise (a) the optical limitations that might restrict visual performance (in particular chromatic aberration and light scatter) and (b) the properties of macular pigment that might serve to lessen the effect of such limitations and thereby facilitate improved performance.

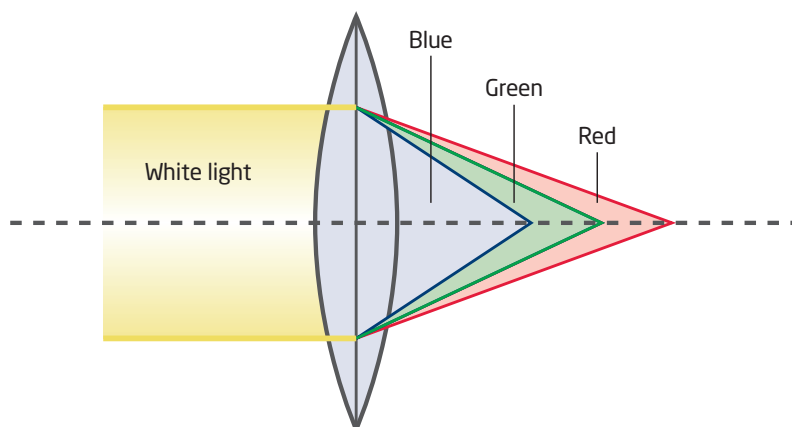


Figure 1 Longitudinal chromatic aberration - focal length for incident white light varies across wavelengths

Optical limitations of the eye

Monochromatic aberrations and diffraction limit the image quality produced by the eye so that the image is not a high quality representation of the object. While there is significant ocular and neural correction for and adaptation to such image defects, macular pigment has no role in altering their effects.

Chromatic aberration

Chromatic aberration, comprising both longitudinal (LCA) and transverse (TCA) components, has been cited as possibly the most significant aberration affecting visual quality.⁶ LCA creates up to two dioptres of wavelength-dependent optical defocus (Figure 1).

The effect of LCA across wavelength in terms of blur is non-linear – that is shorter wavelengths are significantly more blurred than longer wavelengths. For example, for a typical eye focused at 555nm, light at 460nm suffers 1.2D myopic defocus, while the equivalent long wavelength of 650nm is only 0.50D out of focus.⁶ This serves to create a purple blur circle haze around the focused 'green' component. The ultimate effect of such optical aberrations, and in particular LCA, is that capacity limits are somewhat reduced so that the anatomical limits of acuity based on foveal cone diameter (30 secs arc – equivalent to 6/3), are seldom achieved even by healthy normal individuals.

Light scatter

If one looks up to the sky on a bright, cloudless sunny day, one could be fooled into thinking that the sun's rays traverse an unobstructed path to the eye. Furthermore, one could certainly not imagine the quality of the light visible was being degraded as it traversed the seemingly clear sky, even in the most remote countryside locations far from

the smog-filled cityscapes on its way to the eye. The fact that the sky is blue is testament to the impact of the process of light scatter, whereby, particle matter including haze aerosols, fog, and cloud abstracts and re-radiates energy from light incident upon it.

Wooten and Hammond,⁷ in an excellent review of the importance of light scatter to the 'visibility' of objects, eloquently describe why light scatter, especially that induced by haze aerosols 'critically determines how far one can see and how well details can be resolved', so that, aside from the optical and neural limits, 'scatter in the haze aerosols is the primary determinant of visual discrimination and range in the outdoors'.

The question therefore arises, what effect does light scatter have on visual performance? It is a good question. On a clear day one can see for miles despite the effects of scatter. However, it has been shown that compensation for the effects of light scatter, such as could reasonably be achieved by increasing the density of macular pigment could increase the visibility and discriminability of targets in natural settings.⁷ Tackling the question from another perspective, the problems caused by scatter, while not consciously experienced by some people, do become a significant symptom of which many of our patients complain. Typical examples include those with light-coloured irides, cataract, corneal abnormalities and infections, and post-laser refractive patients among others. Scatter, therefore, does have an adverse effect on the visual experience of normals and those with ocular abnormalities alike, and therefore any means to reduce the effects of scatter can only be of benefit. So now the question arises, what are the properties of MP that might allow it to



improve visual performance in light of the limiting factors outlined above?

Optical properties of MP

The 'optical' hypotheses of MP were discussed in significant detail initially by Reading and Weale,⁸ and later by Nussbaum *et al*,⁹ and may be related to at least one of the following properties: MP may enhance visual acuity by reducing chromatic aberration; MP may reduce visual discomfort by attenuation of glare and dazzle; MP may facilitate enhancement of detail by the absorption of 'blue haze'; MP may enhance visual contrast.

MP has the capacity to achieve the above optical effects because of its optical properties and its location in the retina.

The term macula is actually derived from the presence of the xanthophyll pigments, lutein (L) and zeaxanthin (Z), at the central region of the retina, which give rise to the appearance of a yellow spot 'macula lutea' when viewed under red-free light. The yellow nature of MP is such that it selectively absorbs blue-green incident light, with maximum absorption circa 460nm and little or no absorption above 530nm.¹⁰ Given that, (a) the peak retinal spectral sensitivity lies at 555nm, (b) the percentage of blue (short wavelength sensitive) cones compared to that of red (long wavelength sensitive) and green (medium wavelength sensitive) cones is vastly reduced and (c) there is a complete absence of blue cones from the region of maximal visual performance, the foveola, MP it seems therefore removes that component of light which has least benefit from a performance perspective.

Two aspects of MP location within the retina are also central to the assumption that it has a role to play in visual performance. Firstly, although MP is diffusely distributed throughout the retina and other ocular structures,¹¹ it is mostly concentrated at the macula and remains optically undetectable elsewhere. Secondly, and importantly, MP is located at a pre-receptorial level, so such absorptions are made prior to light stimulation of underlying photoreceptors, thereby altering the spectral distribution of light incident on such photoreceptors.

Given its short wavelength absorption characteristics and central, pre-receptorial location, MP retains ideal properties to improve visual performance. Blue light absorption attenuates the more disadvantageous short wavelength component of LCA. Retinal image quality is, therefore, improved and visual performance across the full contrast range is theoretically more refined. As MP absorption overlaps with that of rhodopsin, MP may reduce

rod signal effectiveness in the mesopic range, and thus extend the usefulness of cone-mediated vision into the mesopic range.¹² In addition, blue light absorption has the benefit of improving target contrast by selectively reducing the scattered blue light in the background. Reduced LCA and reduced scatter effects associated with MP therefore have the combined potential to improve visual acuity and target visibility.⁷

The higher energy and retinal irradiance associated with shorter wavelengths also merit consideration. Bright light, which interferes with the quality of visual perception is termed glare, of which there are numerous types. Glare is a frequent complaint among persons with advanced age, retinal disease, and cataract, as well as at any age in some individuals without obvious reasons for predisposition. In high luminance or high contrast situations, where glare and dazzle are maximal, MP absorption of blue light removes the highest energy light component, reduces retinal irradiance and may therefore have the combined benefits of minimising the impact of glare on performance and increasing the threshold for photophobia under normal viewing conditions. Because of their linear structure, L and Z also exhibit dichroic properties, which facilitate glare reduction by preferential absorption of polarised light. The extent of glare reduction by preferential absorption of polarised light has not yet been quantified however.

It should hopefully now be clear, because visual performance is a highly complex issue, difficult to quantify, and dependent on numerous independent and overlapping variables, that to quantify the role of any one factor such as MP optical density (MPOD) presents numerous difficulties. It is with this thought in mind that the currently available evidence on the visual performance effects of MP will now be explored.

Experimental studies

As stated at the outset, the evidence in relation to a role for MP in visual performance is sparse and in fact is mainly associative. In terms of visual acuity and contrast sensitivity, there are no published studies of which we are aware that conclusively address this hypothesis. Instead there are numerous conflicting investigations of the effect of yellow filters on visual performance.⁸ None of these studies, however, has measured MPOD. Failure to do so clouds any reasonable interpretation of the performance effects of blue light absorption as variations in MP density between and within study populations

could fully account for conflicting results. Those with high MPOD would logically attain least benefit and those with low MPOD gain most.

Those studies that have addressed visual performance are largely confined to populations with established eye disease. As such the results, although important, must be analysed in full knowledge that their implications may not necessarily fully translate into a normal population. Studies involving normal subjects will be analysed separately.

Eye disease studies

(1) Congenital retinal degenerations
Abnormal light sensitivity, associated difficulty with glare, loss of contrast and slow dark adaptation are common symptoms of congenital and acquired retinal degenerations. It has been suggested that such symptoms could be partially attributed to the failure of MP to absorb the scattered light, resulting in reduced contrast and definition, along with excessive photoreceptor pigment bleaching by short wavelength light components. The antioxidant and protective properties of MP make it a prime candidate for use in retinal degenerations where long-term macular vision preservation has such important lifestyle implications. It is notable that there have been reports (some dating back more than 50 years) suggesting visual benefit in retinitis pigmentosa from lutein-containing medicaments.⁹

Aleman *et al*¹² analysed patients with Stargardt's disease or cone-rod dystrophy (Figure 2) and known or suspected disease-causing mutations in the ABCA4 gene to determine baseline MPOD and also response to L supplementation in terms of MPOD changes and central visual function changes. They reported that MPOD is strongly affected by the stage of ABCA4 disease leading to abnormal foveal architecture. MP could be augmented by supplemental lutein in about two-thirds of patients. However, visual function measures, including visual acuity and foveal sensitivity, showed no discernable improvement after six months of lutein supplementation. They conclude that long-term influences of L supplementation on the natural history of these macular degenerations require further study.

Dagnelie *et al*,¹³ in a primitively designed study, assessed the effect of L supplementation in patients with retinitis pigmentosa (RP). They reported moderate vision improvements in RP patients in response to short-term L supplementation. Mean visual acuity improved by 0.7dB and mean visual-



field area by 0.35dB, although the largest gains were attained by blue-eyed participants. Aleman *et al*¹⁴ explored the relationship between visual function and L supplementation in RP patients over a six-month period and despite significant increases in MPOD, could find no significant improvement in performance (measured as absolute foveal sensitivity). The dosage used in this study was lower than that in the Dagnelie report which may be of importance. Neither study, however, analysed visual function in sufficient detail to determine whether the natural history is altered by supplementation.

Duncan *et al*¹⁵ analysed MP levels and macular function in choroïderemia (a progressive degeneration of photoreceptors, RPE and choroid). Once again, despite increased MPOD after supplementation, no improvement in retinal sensitivity was seen.

(2) Age-related macular degeneration

AMD, as the leading cause of blindness in the Western world, has been the primary research focus for the effects of L and Z supplementation. Observations including relative preservation of blue cones centrally compared to perifoveally¹⁶ and geographic atrophy in AMD typically appearing initially in the perifovea where MP density is lowest, lend weight to the assertion that MP protects visual function at the fovea. Since the original findings of the Eye Disease Case-Control Study Group of a 60 per cent reduced risk of developing AMD associated with high intakes of L and Z,¹⁷ numerous investigators have explored the relationship between L and Z in the diet or blood and AMD. With a couple of exceptions (outlined below), empirical studies on the effects of L and Z supplementation on AMD progression, in terms of visual function, focus mainly (and understandably) on the capacity of L and Z supplementation to halt progression of functional loss, not on the potential to improve visual function in established AMD. Results have been somewhat variable, with some studies showing a beneficial effect of higher intakes of L or Z,^{18,19,20} while others have not.^{20,21,22}

Falsini *et al*²³ measured the effect of L supplementation on central electrophysiological function in patients with AMD and found a significant increase in focal ERG amplitude after six months' supplementation, followed by decreased amplitude back to baseline following cessation. Curiously, they did not record MPOD, so their conclusions are somewhat limited. The lutein antioxidant supplementation trial study provides the



Figure 2
Stargardt's disease

Image courtesy of J Kanski, *Clinical Ophthalmology* 4th edition, Butterworth-Heinemann

most intriguing findings in relation to visual function among AMD patients. Patients supplemented with L or L plus other antioxidants achieved improved visual function outcomes attributable to increased MPOD measures. Snellen-equivalent acuity improved by 5.4 letters in the L group and by 3.5 letters in the L plus antioxidant group.²⁴ Improvements were also seen in contrast sensitivity and subjectively on Amsler grid and glare recovery. Placebo control subjects achieved no such improvements.

(3) Other conditions

Olmedilla *et al*²⁵ explored the possibility that L supplementation might influence visual function in patients with age-related cataract. Visual performance was evaluated through visual acuity and glare sensitivity measures. This randomised, placebo-controlled study revealed significant improvements in visual acuity and glare sensitivity associated with increased blood serum L levels after supplementation. No such improvements were achieved in placebo controls or in those supplemented with α -tocopherol. The authors postulate that such improvements are not the consequence of any change in the crystalline lens, but from possibly improved retinal integrity.

Cystic fibrosis (CF) is a condition associated with deficient carotenoid absorption due to pancreatic insufficiency. Carotenoid concentrations, including the MP components, are almost uniformly low in CF patients. Beatty *et al*²⁶ have shown that ocular MP levels vary with blood serum levels and therefore MP levels can be assumed to be low in cases of CF. Schupp *et al*²⁷ assessed visual performance in 10 such CF patients. Serum L and Z concentrations, as well as MPOD in the eye were significantly reduced in CF patients to less than half the levels of control subjects. Visual performance on contrast sensitivity, colour discrimination and multifocal

ERG amplitudes, although better in the control group, were, however, not statistically significantly different between the two groups.

Normal population studies

(1) Photophobia and glare

Photophobia is a global phenomenon experienced under sudden and extreme changes of illumination from dark to light, for example turning on the bedroom lights at night. However, under normal daylight conditions, the experience of photophobia is somewhat more variable. Numerous clinical conditions cause photophobia, and even in the absence of detectable disease, clinicians are often presented with patients whose primary complaint is of periodic or persistent hyper-sensitivity to bright light. Given its absorption characteristics, MP, and in particular the density of MP may have a central role in determining the individual photophobia threshold.

Stringham *et al*²⁸ explored the effect of the spectral composition of a target on visual discomfort. They showed that while there was a positive relationship between wavelength and the energy needed to produce photophobia for wavelengths between 520nm and 640nm, at shorter wavelengths there was a notch centred at 460nm. MPOD differences among the subjects also appeared to account for differences in photophobic sensitivity below 520nm.

Such findings led to a subsequent study to test the direct relationship between MP and photophobia.²⁹ This two-part experiment explored the relationship between baseline MPOD levels and photophobia thresholds, as well as the effect of increasing MPOD on such thresholds. They found a linear relationship between baseline MPOD and photophobia – that is individuals with higher MPOD were less susceptible to photophobia.

Furthermore, increasing MPOD over a 12-week period appeared to confer a predictable improvement in photophobia threshold increasing the amount of light necessary to induce visual discomfort for short wavelength targets.

Recent data from Hammond *et al*³⁰ – presented at 'Coloured filters in the Eye' at City University in November last year – found that both photostress recovery and grating visibility under veiling conditions were strongly related to MP density, supporting the photophobia findings outlined above.

(2) Acuity and contrast sensitivity
Engles *et al*³¹ have evaluated the 'acuity hypothesis', exploring the relationship



between gap acuity, vernier acuity and MPOD under photopic conditions. They report that neither gap acuity nor vernier acuity were significantly correlated with MPOD and conclude that their 'data suggest that the predictions of the acuity hypothesis do not hold'. Numerous limitations (some recognised by the authors) in their study design, however, mean that such a conclusion goes far beyond the scope of their findings and cannot be justified. The acuity findings, however, do suggest that the contribution of MP to visual performance may be less important for the aspects of photopic vision to which the system is most highly tuned. Retinal image quality is adversely affected in mesopic conditions as a result of increased aberrations and scattered light. Visual performance is typically much more variable in the mesopic range, where the influence of rods on spatio-temporal vision pre-dominates and results in reduced contrast acuity.

As rods are sensitive to blue light (peak rod sensitivity lies around 498nm in the blue-green part of the spectrum), Kvangsakul *et al*¹² have postulated that blue light absorption may reduce rod signals and thereby extend the superior characteristics of cone-dominated vision lower into the mesopic range. They investigated the effect of increasing MPOD through L and Z supplementation on contrast acuity and found that regardless of whether groups were supplemented with L, with Z, or with a combination of the two, there was a trend towards improved performance. The improvement was statistically significant for the L group so that supplementation has now been shown to enhance visual performance at low illumination levels.

Conclusion

Visual performance in the normal human observer is less than ideal. Evidence exists that once chromatic and monochromatic aberrations are removed, visual performance improves.³² As such, numerous strategies exist which aim to improve visual performance.

Wavefront-guided laser refractive eye surgery, wavefront-guided spectacle lenses, blue-filtering IOL implants, blue-filtering contact lenses and blue-filtering spectacle lenses all attempt to improve or optimise visual performance. All such techniques, however, are designed primarily for persons with pre-existing ocular abnormality or disease.

It is generally accepted and has been shown that age results in a decline in visual function for a wide variety of

MULTIPLE-CHOICE QUESTIONS

1 What percentage of the total retinal area is the macula?

- A 1 per cent
- B 4 per cent
- C 10 per cent
- D 15 per cent

2 Relating to longitudinal chromatic aberration, which of the following is true?

- A The typical eye focused light at 460nm
- B Light of 460nm will be less blurred than that of 650nm
- C Shorter wavelengths are significantly more blurred than longer wavelengths
- D Chromatic aberration has no influence on the limit of acuity

3 What is the maximum absorption wavelength of macular pigment?

- A 460nm
- B 555nm
- C 560nm
- D 650nm

4 Which of the following is true regarding Stargardt's disease?

- A MPOD is not affected
- B Macular pigment was unaffected by supplementation
- C There is no genetic component to the disease
- D No visual function improvement is noted after six months of supplementation

5 Which of the following is true regarding retinitis pigmentosa?

- A Moderate vision improvements have been reported with short-term lutein supplementation
- B Best improvements are in dark iris patients
- C Lower dose supplementation has shown benefits in visual function
- D Mean acuity increases of 0.35 dB have been reported

6 Which of the following is true regarding cystic fibrosis?

- A It is associated with excess carotenoid levels
- B Blood serum levels of macular pigment are elevated
- C Studies have shown little change in visual function with macular pigment supplementation
- D Carotenoid level irregularity is associated with duodenal insufficiency

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reasons. MP has been shown to preserve visual function in age-related retinal disease such as AMD presumably by protecting remaining foveal cones. By preserving foveal cones and possibly crystalline lens clarity MP may thus retard functional losses into old age.

To summarise, MP has ideal properties in terms of location and spectral absorbance to have a beneficial effect on visual performance. Longer life spans, increased exposure to short wavelength blue light (ancestors had no blue light exposure after dark), increased effects of scatter from expanding smog and haze, modern visual requirements and the explosion in the incidence of AMD heightens the importance of both improving visual performance in the short term, and preserving such performance in the long term.

Definitive supporting evidence, however, has not been provided with

sufficient clarity and depth to fully describe the role of MP in vision, neither in the short term nor over time.

Interpretation of the findings in the studies cited above should therefore be approached with full appreciation of the design flaws, insufficient visual performance evaluation, and in particular the small sample sizes used. High quality emergent research with sufficient subject numbers tracked longitudinally is now required to address the issue more completely. ●

A list of references is available from william.harvey@rbi.co.uk

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