Macular Pigment Optical Density in Macular Health and Visual Function

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Abstract

Extensive research has described the biological and optical characteristics of the macular pigment (MP) and has confirmed its composition and dietary origin. Epidemiological and intervention trials support the protective role of MP in the retina as well as its positive effects on visual function in healthy individuals in addition to patients with age-related macular degeneration (AMD). The amount of MP in the macula can be assessed by measuring a surrogate optical indicator, macular pigment optical density (MPOD). New evidence from recently published clinical trials and a European consensus roundtable have confirmed that MPOD can be increased by increasing the ingestion of lutein and zeaxanthin and that MPOD increase benefits macular health and visual function. On balance, this recent evidence suggests a critical role of MP in eye health as well as the importance of assessing if adequate levels of the dietary macular carotenoids are regularly consumed in order to ensure proper availability for deposition into the macula.

Keywords

Lutein, zeaxanthin, macular pigment, MPOD, AMD, visual function

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In 1945, Wald reported that the macula lutea of humans and certain other primates contains a yellow pigment and suggested that this macular pigment (MP) was a carotenoid. By analysing the spectral sensitivity of the human foveal and peripheral photoreceptors, he estimated the light absorbed/transmitted by the macular pigment, and used the term macular pigment optical density (more recently associated with the acronym MPOD). At the same time he observed a great variation in the intensity of macula pigmentation among subjects – from foveas with no perceptible pigmentation to very intense coloured ones.[1] Research conducted in recent decades has confirmed that the MP is composed by three distinct carotenoids lutein (L), zeaxanthin (Z) and meso-zeaxanthin (MZ).[2,3] MP reaches highest concentration (per mm^2 of tissue) at the centre of the fovea decreasing rapidly with distance from the epicentre. The concentrations of L, Z and MZ also vary with eccentricity – in the adult retina, while the three macular carotenoids are present in similar concentrations at foveal centre, as the eccentricity from the fovea increases, lutein becomes the predominant pigment with a decreasing amount of Z, and with MZ, approaching undetectable levels.[3] The role of the MP in the human eye is well described and is based on the biological and optical characteristics of its main components.[4–7] It acts as an antioxidant by quenching reactive oxygen species and as a filter for damaging high energy/short-wavelengths of visible light (blue light). These functions support the protective role of the MP in the retina, a tissue particularly susceptible to oxidative stress and the more recently explored beneficial effects on visual function.

Macular Pigment Optical Density and the Diet

Studies conducted in monkeys raised on a xanthophyll-free diet from birth have shown that the macular pigment is of dietary origin and that L and Z supplementation can replenish the macular pigment. Moreover, those results indicate that, while the accumulation of L and Z in serum and retina stems from the ingestion of these two xanthophylls with the diet, MZ originates exclusively from the conversion of L in the macula. MZ is not present in serum.[8,9] Additional observations conducted in thesexanthophyll-free animals indicate the presence of drusen in the pigment epithelium.[8] A recent publication addressed the effect of acute blue-light exposure in xanthophyll-free animals lacking the macular pigment in comparison to control animals fed stock diet containing xanthophylls.[10] The presence of the macular pigment rendered control animals less susceptible to blue light-induced damage in both the fovea and parafovea although more damage was observed in the parafoveal area than in the fovea. The xanthophyll-free animals, who exhibited no MP, experienced similar damage in both the foveal and parafoveal areas resulting from blue-light exposure as well as more damage than control animals. Supplementation of the xanthophyll-free animals with L or Z increased macular pigment density and decreased foveal susceptibility to blue-light induced damage to control levels. In the author's words, "L and Z when provided in the diet and deposited as macular pigment, provided foveal protection from acute blue-light photochemical damage. It seems probable that these nutrients would also protect the macula against chronic blue-light-induced damage".

Epidemiological studies also suggest a protective role of MP in the retina. Those results show a positive association between dietary L and Z intake with their serum levels and MPOD values as well as an inverse relationship with the risk of advanced neovascular age-related macular degeneration (AMD), geographic atrophy and/or the presence and enlargement of drusen.[11–14]

A study performed in 800 healthy Irish subjects to assess MP in relation with other risk factors for age-related maculopathy (ARM) reported a statistically significant age-related decline in MPOD. It also showed a relationship between low MP levels and current and past smoking as well as with individuals presenting a family history of ARM.[15] Additional observations in healthy subjects showed that individuals presenting higher MPOD had less glare discomfort and faster recover from photo stress.[16,17] Intervention trials conducted in AMD patients or in healthy subjects have confirmed that supplementation increases MPOD and improves visual function.[18,19]

Measuring Macular Pigment Optical Density

The fact that the density of the macular pigment can be increased by increasing the consumption of L and Z coupled with the reported eye benefits associated with the intake of these xanthophylls suggest the importance of assessing whether adequate levels of these two macular carotenoids are regularly consumed and deposited in the eye.

The ability of the macular pigment to absorb blue light offers a way to determine the optical density of the MP. A consensus paper report published in 2010 addresses the role of MP and its characteristics. That report also provides a detailed review of the various methodologies for measuring MPOD.[7] In brief, MPOD is a measurement of the attenuation of blue light by macular pigment (expressed in density units [du]). It provides an indication of the amount of L and Z in the macula. Typical MPOD levels vary between 0 and 1 du. There are several non-invasive methods for measuring MPOD levels:

- subjective psychophysical techniques, such as heterochromatic flicker photometry which are perhaps the most commonly used and less expensive method, that involves the active participation and training of the subject; and
- objective optical methods, such as fundus autoflorescence and reflectometry, that do not require active participation of the individual but require more sophisticated and costly instrumentation.

Each of these methods have strengths and weaknesses but all of them are capable of detecting changes in MPOD over time as well as changes resulting from supplementation with L and Z. However, it is important to note that the imaging methodologies like autofluorescence and reflectometry have an advantage in the fact that they can also provide important details concerning the spatial distribution of MP as well as information concerning the way MP accumulates in the retina. This information may be important regarding how the MP distribution changes during ageing as well as during ocular disease development or progression.

L and Z Intake Increases Macular Pigment Optical Density and Helps Promote Macular Health and Visual Function-Evidence from Recent Studies

Additional confirmation on the benefits of the increased macular carotenoid intake in patients suffering from dry AMD originates from the findings of the three recently published clinical trials presented below. The LUTEGA trial (Long-term effects of lutein/zeaxanthin and omega-3 supplementation on optical density of AMD patients) examined the effects of daily supplementation with two fixed combination of L, Z, omega-3 fatty acids, vitamins and minerals. The one year supplementation results[20,21] showed a significant increase in

Table 1: Summary of the Main Points of Consensus Generated at the European Consensus Round Table "MPOD in Macular Health and Visual Function" (Frankfurt, Germany – 14 March 2012)

Relationship Between MPOD and AMD
• MPOD is a measure of what is going on in the tissue of interest • Low macular pigment is a risk factor for AMD. After age, genetic predisposition and smoking low MPOD is the next important, independent risk factor
Value of Measuring MPOD

• There are numbers of techniques available to measure central MPOD and all have both value and limitation. An image-based technique (providing data on spatial distribution) would be preferable
• The absolute MPOD value is not as important as the individual baseline and the changes over time. MPOD increase is usually linked to better visual performance
• The "right" MPOD can be the value where the subject has reached saturation. This level could vary among individuals, but it is important to reach and maintain it
• MPOD measurement is of value for:
  • Healthy individuals at risk for AMD
  • Patients during supplementation of lutein and other carotenoids
  • Anyone interested in good vision
  • Older population (50+ or even the entire 40+ "healthy" population) in connection with assessing visual parameter important for driving and reading

MPOD and Lutein
• MPOD can be increased by a proper diet or supplementation • Beneficial effect of supplementation with macular xanthophylls is strong   • Changes in morphology are possible: drusen may be reduced. Patients may improve visual function (visual acuity, glare disability, contrast sensitivity)
MPOD and Visual Function in Healthy Individuals

• Assessing visual function to the highest possible standard is important in healthy individuals (and AMD patients):
  • There is the need to evaluate visual performance beyond visual acuity. Contrast sensitivity at night and glare recovery have to be tested too.
• Increased MPOD-associated with a diet that is high in lutein and zeaxanthin – contributed to better visual performance
• Healthy individuals also benefit from increased MPOD:
  • Optical and antioxidant benefits: they can enhance their visual function by improving contrast sensitivity and reducing glare disability. In addition supplementation and the associated increase in MPOD levels will protect the retina for later years too

AMD = anterior macular degeneration; MPOD = macular pigment optical density.

L and Z serum levels, MPOD and visual acuity in the two active treatment groups when compared to placebo. A regression of drusen was also documented in some patients. Apart from the serum L concentration that was higher in the group administered the highest supplement dose, no additional statistically significant differences were observed in MPOD accumulation or improvement in visual acuity between the two L/Z dosages. Remarkably, the findings of a decrease in MPOD volume and plasma L concentration detected in the group administered placebo lead the authors to highlight the usefulness of supplementation in AMD patients and its protective effect on the macula. The Zeaxanthin and Visual Function (ZVF) Study[22] aimed to compare the effect of one year supplementation with similar doses of L and Z, alone or in combination, upon foveal MPOD values and visual benefits in patients with early to moderate AMD. All three supplement interventions were shown to be effective at increasing MPOD values and improving near-high contrast Visual Acuity (VA), however no statistically significant differences

between groups were observed. The L/Z combination regiment performed worse in increasing MPOD and the Z treatment alone provided greater improvement in VA. Patients supplemented with L also benefit from improvements in contrast sensitivity, glare recovery and near low-contrast VA, the last two parameters being also ameliorated with the combination of L and Z. Trends suggesting improvements in shape discrimination and in the VFQ 25 questionnaire driving subscale were observed in the group supplemented with Z only.

Finally, Piermarocchi et al. published the two year results of the Carotenoids in age-related maculopathy italian study (CARMIS)[23] which was conducted to assess the effects of a supplement containing L and Z in combination with astaxanthin, vitamins and minerals. When compared to the parallel non-treated group, the supplemented AMD patients presented significantly better visual acuity scores, contrast sensitivity and vision-related quality-of-life composite score assessed with the 25-items National Eye Institute Visual Function Questionnaire (NEI VFQ-25). The authors highlighted that their finding suggests that supplementation with carotenoids and antioxidant vitamin and minerals "not only help to delay progression to advanced stages of AMD, but may also improve some visual performances. Left untreated patients with AMD are at risk for substantial vision loss." These recent findings complemented the observation made after at the first year of this study[24] which showed that the electrophysiological abnormalities detected in subject with early AMD could be improved through supplementation.

In March 2012, an interdisciplinary panel of five international recognised experts with extensive research and/or clinical experience in retinal diseases and MP measurement, including the investigators directly involved in two of the above mentioned trials, reviewed the current science during a European Consensus Roundtable "MPOD in Macular Health and Visual Function". Specifically, the experts addressed four topics related to MPOD, 1) the relevance of MPOD as a potential biomarker for AMD, 2) the value of measuring MPOD and the reliability/objectivity of available technologies for such measurements, 3) the relationship between L consumption and MPOD, and 4) the influence of MPOD on visual function in healthy individuals. The main points of consensus generated about the importance of MPOD in the contexts of AMD, visual function/performance and healthy eyes has been published in a Continuing Medical Education (CME) publication issued in German speaking countries[25] and a summary booklet.[26] *Table 1* shows some the main point of consensus achieved.

Final Remarks

Scientific evidence supports the importance of MP in eye health. A relationship exists between MPOD and visual function. The MP is entirely of dietary origin; its optical density varies depending on the dietary intake of L and Z and can be raised by increasing consumption, via diet and/or supplementation. Considering that the average dietary intake of these two macular carotenoids in western countries[27,28] is well below the amount found to be associated with both a reduction in AMD risk and benefits in visual function, it seems important to introduce MPOD measurement into clinical practice in order to detect potentially low MPOD levels, assess age- or disease-related MPOD changes over time and induce, when needed, practitioner-recommended dietary changes in favour of a higher regular intake of L and Z. ■

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