The Relationship between Visual Performance and Macular Pigment in Non-diseased Eyes

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Vision is one of the fundamental tools with which we interact with the world around us, and good vision allows us to enjoy so many aspects of life to the full. Ophthalmologists, by virtue of their profession, are only too aware of the threat to vision that ophthalmic pathology can represent. As a consequence, however, the variability in visual performance and experience in the normal eye has been necessarily overlooked, as have measures to optimise vision in the absence of ocular pathology.

The variability in visual performance in the non-diseased eye is largely attributable to differences in visual perception which are subject to the respective and interactive influences of environment, anatomy and age. The optical (blue light filtering), anatomic (central retinal) and biochemical (antioxidant) properties of macular pigment (MP) are ideal to optimise vision in the normal eye and to maintain effective physiological functionality of the visual system into old age.

MP is composed of three carotenoids, lutein (L), zeaxanthin (Z) and *meso*-zeaxanthin (MZ), to the exclusion of all other carotenoids in the diet and serum. MZ is the dominant carotenoid in the epicentre of the macula, while Z and L are the dominant carotenoids in the mid-periphery and periphery of the macula, respectively.

Measures of visual function

Visual function, and the experience it results in for the subject, is a composite of a wide array of optical and neurophysiological processes, which are the result of an exquisitely specialised and evolved visual system, and which can be reflected in a plethora of psychophysical measures of visual performance, including object recognition, colour discrimination and depth perception (to name but a few).

Visual acuity (VA), for example, is the most commonly employed tool to assess spatial vision by eye care professionals, and is a measure of the resolving power of the eye at 100% contrast.

Contrast sensitivity (CS), on the other hand, refers to the ability of the visual system to discern the foreground from the background, and is measured at a variety of spatial frequencies (target sizes), and rests on the ability of the visual system to discern objects of differing luminance within our field of view. For example, we can easily distinguish a medium-sized object at low contrast (i.e. a grey object in front of a white background), yet smaller-sized objects require a greater degree of contrast with the background if they are to be perceived.

Contrast sensitivity declines with increasing age [1,2] and poor contrast sensitivity is associated with reduced function related to vision, and this is reflected in difficulty with everyday tasks such as reading, distinguishing traffic lights and road signage. Of note, CS, as a measure of visual performance, is more reflective of a subject's visual functioning than is VA, whether in a diseased or in a healthy eye [3].

The neurophysiological process of vision

The visual experience is created through a wide array of neurobiological processes. Photoreceptors in the inner layers of the retina, known as rod and cone cells, contain photopigments within their cellular membranes, which convert the incident light (visible electromagnetic radiation) into 'electrical' signals. Rod and cone photopigments are similar, in that they consist of retinene bound (with both ends of the molecule) to retinal proteins, or opsins. In order to produce a signal, the retinene must be activated by incident light, which converts the retinene from 11-cis-retinal to 11-trans-retinal, detaching one end of the retinene molecule from the opsin, thus initiating a nerve pulse or signal. The retinene then reverts to 11-cis-retinal and re-binds to the opsin, to begin over anew. These signals are compared and processed by retinal ganglion cells and transmitted to the occipital cortex via the optic nerve, where they are interpreted and converted into a visual experience. Visual resolution (acuity) is a measure that is a direct correlate of the strength of these signals and the sensitivity of the brain to receive them.

Rod cells, of which there are approximately 90 million in the retina, contain an opsin called rhodopsin, which is activated under conditions of low levels of incident light (as little as six photons), and these cells are therefore useful for low light conditions or nightvision. Cones are necessary for fine detailed vision, colour perception and visual resolution (acuity), and require greater amounts of incident light to be activated.The three types of cones, known as S, M and L cones, contain differing opsins, which alter the spectral absorption properties of the photopigments. S-cone cells are activated bythe shorter 'blue' wavelengths (approximately <470nm) and are thus blue light sensitive, while M-cone cells are activated by medium wavelengths (<530nm) and are green sensitive. The final type, L-cone cells, are activated by the longer wavelengths of the visual spectrum (<560nm), thereby explaining their constituent photopigments' sensitivity to red.

Beyond each cone's primary colour sensitivity, or spectrum absorption range, all three cone types are partially sensitive to the other two spectral ranges. This allows ganglion cells to compare the stimulation of the cones, which results in the visual perception of a wide spectrum of colours (and not solely red, blue and green).

Photoreceptor cell degradation / death

The ultra-structural cellular composition of photoreceptors, required for the necessarily sensitive nature of both rod and cone cells, confers a susceptibility to oxidatively-induced cell death. Reactive oxygen species (ROS) are the inevitable by-products of oxygen metabolism, and are therefore generated in large quantities in the human retina, a tissue which has the highest oxygen metabolism in the mammalian world [4]. However, ROS production in tissue is increased further when irradiated with light, especially short wavelength (high energy) light such as visible blue light. Indeed, the threshold for retinal injury is one thousand

times lower for blue light than for orange light under ambient conditions [4].

Furthermore, the photoreceptor outer segment membranes contain polyunsaturated fatty acids (PUFAs) in very high concentrations, which, because of their electron-dense molecular structures, are susceptible to oxidation. As a result, a cytotoxic chain reaction ensues, thereby damaging the photoreceptors by depletion of membrane PUFAs, in addition to perpetuating the production of ROS.

Reactive oxygen species, because of their inherent instability (free radicals, for example, contain one unpaired electron) and regardless of whether they are generated as a result of high oxygen metabolism or irradiation with blue light, damage DNA, lipids, proteins and other important components essential for cellular functions.

Optical visual benefits of macular pigment

Glare

Clinically, there are two types of glare, referred to as glare discomfort and glare disability. Discomfort glare is caused by intense environmental light sources that cause distraction and / or discomfort, such as headlights of oncoming cars.

Glare disability is the result of light scatter, where the incident light is scattered by atmospheric particles (e.g. oxygen, nitrogen, aerosols, etc) and / or by internal ocular structures (i.e. the lens and cornea). Short wavelength (blue) light scatters to a greater extent than other wavelengths, and the scattered light therefore superimposes a bluish screen or 'veil' over the retinal image, thereby increasing the increments of luminance required to discern the foreground from the background. This phenomenon, termed veiling luminance, therefore impairs CS and results in loss of visual resolution, and is perceived by the subject as a loss of fine detail and distance perception.

As a consequence of MP's pre-receptoral filtration of blue light, the adverse impact of veiling luminance on CS can be minimised, and CS therefore optimised [5,6]. Furthermore, it has recently been shown that supplementation with a formulation containing all three macular carotenoids (L, Z, and MZ; Macushield™), in normal subjects, results in enhanced CS (both mesopic and photopic) and alleviates the impact of glare disability [7].

Chromatic aberration

Chromatic aberration (CA) is the result of the differential extent to which short, medium and long wavelengths are refracted by the eye. Short wavelength (blue) light is refracted to a greater extent than the other visible wavelengths, and is therefore myopically defocused by 1.2 dioptres, resulting in a bluish tinge or edge to an image, a phenomenon known as CA andone which adversely impacts CS.

MP's pre-receptoral filtration of blue light attenuates CA by reducing the amount of defocused blue light incident upon the retina, thereby optimising CS and enhancing visual performance and experience [6,8]. Again, optimisation of visual function, in terms of CS under photopic and mesopic conditions, is best achieved following supplementation with a formulation containing all three of MP's constituent carotenoids (L, Z and MZ; Macushield™) [7].

Non-optical visual benefits of macular pigment

Neural efficiency

The functionality of the macular carotenoids is not limited to pre-receptoral light filtration or anti-oxidant capacity, nor are these compounds located exclusively in retinal tissue. Research has shown that L and Z accumulate in the occipital and frontal cortices, where they are the predominant xanthophylls [9], and where they are thought to play an important role on gap junction communication [10] and in the maintenance of neuronal membrane integrity, thereby contributing to the conditions required to optimise physiological functionality of neural tissue, sometimes referred to as neural efficiency [11]. Indeed, the observed vision-enhancing effect of supplementation with a formulation containing all three macular carotenoids (L, Z and MZ; Macushield™) precedes significant augmentation of MP, suggesting that the observed benefits are not wholly and solely attributable to the optical properties of MP, and that optimisation of neural efficiency may be playing a role [7].

Age related decline in visual function

While retinal exposure to oxygen and light is desirable, necessary and inevitable, the cumulative and adverse impact of lifelong exposure to their deleterious effects contributes to the observed age-related decline in CS and retinal sensitivity, even in the absence of disease [12].

One means of limiting such oxidative injury is through the effects of ROS-scavenging compounds, known as antioxidants, which attenuate ROS-induced cell degradation [13]. Antioxidants are known to work synergistically, and include enzymes (e.g. glutathione peroxidase) and a variety of compounds that cannot be synthesised *de novo* by mammals (e.g. vitamins C and E, lutein, zeaxanthin and meso-zeaxanthin, amongst others).

MP, composed of L, Z and MZ, accumulates at the macula to the exclusion of all other carotenoids found in serum and diet. MP's pre-receptoral filtration of blue light (thereby limiting light-induced generation of ROS) and MP's powerful ROS-neutralising capacity, suggest that it is these properties that limit age-related degradation of photoreceptors, with a consequential and parallel preservation of visual function into old age [14].

Conclusion

High levels of MP attenuate the adverse impact of CA and light scatter on visual performance, because of the optical properties of the pigment's constituent carotenoids. Further, the biochemical properties of L, Z and MZ are important for optimal physiological functionality of the neurobiological components of the visual system, and appear to be important in the maintenance of this system into old age.

Take home message

- Augmentation of macular pigment (MP), and optimisation of its spatial profile, is best achieved following supplementation with a formulation that contains all three of MP's constituent carotenoids (L, Z, and MZ; Macushield ™).
- L, Z and MZ are powerful antioxidants, and because they exert this effect synergistically, the maximum collect antioxidant activity of MP requires the presence of all three of MP's constituent carotenoids.
- MP absorbs short wavelength (blue) visible light at a prereceptoral level, thereby attenuating chromatic aberration and minimising the adverse impact of scattered (mainly blue) visible light on the retinal image (known as veiling luminance).
- Optimum contrast sensitivity, under mesopic and under photopic conditions, is achieved following supplementation with a formulation containing all three of MP's constituent carotenoids (L, Z, and MZ; Macushield ™).
- Glare disability (reduced visual performance under glare conditions) is ameliorated following supplementation with a formulation containing all three of MP's constituent carotenoids (L, Z, and MZ; Macushield ™);
- MP limits oxidatively-induced photoreceptor cell death, thereby preserving retinal sensitivity (youthful vision) into old age.
- The biochemical properties of L, Z and MZ are important for optimal physiological functionality of the neurobiological components of the visual system, and appear to be important in the maintenance of this system into old age.

References overleaf

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