The Influence of Dietary Lutein and Zeaxanthin on Visual Performance

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ABSTRACT: The idea that normal constituents of the diet can influence visual function is not new. As early as 1782, Buzzi identified the yellow of the macula and Schulze (1866) specifically postulated that the yellow pigments led to improvements in human vision. These pigments were later found to be derived from dietary lutein and zeaxanthin that are known to be oxygenated carotenoids (xanthophylls). Walls and Judd (1933) postulated that these yellow intraocular pigments could improve visual performance by absorbing light scattered both within (for example, glare) and outside of the eye (increasing visual range by absorbing blue light scattered in the atmosphere), and by improving spatial vision through enhancing contrast and reducing chromatic blur. In this article, evidence for these ideas is reviewed with particular emphasis towards more recent data on glare effects.

Keywords: acuity, carotenoids, lutein, macular pigment, visual performance, zeaxanthin

Introduction

Carotenoids are a group of pigments (carotenes and xanthophylls) that are found primarily in green leafy vegetables and colored fruits. Of the many carotenoids (approximately 600) that can be identified in nature, only a fraction are absorbed by humans. Additional specificity is indicated by the highly selective manner with which these circulating carotenoids are deposited into different tissues. For example, lycopene (found richly in tomatoes) is concentrated in the prostate, beta-carotene (found, for example, in sweet potatoes and carrots) in the corpus luteum, and lutein and zeaxanthin (L and Z, found, for example, in kale and spinach) in the retina. Although it is clear that some carotenoids (about 10%) serve as precursors of Vitamin A (for example, beta-carotene), specific roles for most carotenoids found within human blood and tissues have only recently begun to emerge. These roles include functions such as intercellular communication (for example, Sies and Stahl 1997), cell differentiation (for example, Gross and others 1997), the inhibition of mutagenesis and transformation (for example, Bertram and Bortkiewicz 1995), enhancement of immune function (for example, Hughes 1999), anti-inflammatories (for example, Hozawa and others 2007), and lipid-based antioxidants (for example, Agamey and others 2004). Of the 20 or so carotenoids found in human serum, the fact that only L and Z are found in the visual system has suggested that these pigments play a special role in human vision.

In the anterior portion of the eye is a set of lenses (the cornea and crystalline lens) that focus light back toward the neural tissue lining the back. This neural tissue, the most metabolically active tissue in the body, is the retina. See Figure 1. The retina is composed of photoreceptive cells (rods and cones) that transduce light into a neural signal. This signal is then further processed by the brain (ultimately leading to perception). Before that light is converted, it passes through the inner layers of the retina that contains the oxygenated carotenoids, L and Z. These pigments give the central retina its clinical designation, the macula lutea (latin, yellow spot) because they give the central retina or macula a yellow appearance (also termed macular pigment, MP). Because light must traverse L and Z before being processed by the photoreceptors, it is also absorbed by the pigments according to their spectral absorbance profile (see Figure 2). This absorbance is quite specific and significant. The pigments absorb a full third of the visible spectrum and it is not uncommon to find peak absorbance as high as 1.3 optical density units (meaning only about 5% of the "blue" or short-wave light is transmitted on to the photoreceptors). The optical density is not always so high, however, and the extent to which L and Z filter light varies largely according to individual differences in the dietary intake of L and Z (none of the carotenoids are synthesized *de novo*). Curran-Celentano and others (2001), for example, measured retinal L and Z in a relatively large sample ($n = 280$) tested in the midwestern United States. They found that average levels of MP were quite low (a peak OD of 0.21) due, likely, to low average intake of L and Z (about 1.1 mg/d; analogous to about what could be obtained in a couple of tablespoons of spinach). If the amounts of MP in the eye vary so dramatically, it follows that any function these pigments might serve would vary equally dramatically. Furthermore, due to poor dietary habits, many individuals have low levels; whatever function the pigments serve might be deficient in these individuals. This, of course, begs the question of what function these pigments serve in the human visual system.

The fact that we possess internal yellow filters is conspicuous. Yellow filters have long been known to have distinct optical effects upon visual performance. Visual performance, of course, means more than simply a good refractive state and high Snellen acuity (high contrast letters on an eye chart). After all, only about 15% of the population has refractive errors (about 98.4% of the population still has better than 20/25 best-corrected acuity into their 60s; Kahn 1976). Rather, vision is often reduced due to other optical factors (intrinsic and extrinsic) that can be influenced by colored filters like the MP. These effects have been generally categorized as follows (see Walls and Judd 1933; Nussbaum and others 1981): (1) The reduction of glare disability and discomfort by the absorption of intraocular scattered light. (2) Improvement in visibility (that is,

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doi: 10.1111/j.1750-3841.2009.01447.x

THE Society for Food Science & Technology

Journal of Food Science

A Publication of the Institute of Food Technologists

visual range) by the absorption of veiling illumination arising from atmospheric scatter and "blue haze." (3) Contrast enhancement resulting from the differential absorbance of light across chromatic borders. (4) The improvement of resolution acuity by delimiting the effects of longitudinal chromatic aberration.

The glare hypothesis

The idea that retinal lutein and zeaxanthin can improve glare is based, largely, on a basic filtering mechanism. When intense light enters the eye it can cause discomfort, disability, and temporary blindness due to photopigment bleaching. The latter two, in particular, are reduced by simple filtering of scattered light.

Visual discomfort. Visual discomfort, also referred to as discomfort glare or photophobia, is defined as a subjective experience of discomfort upon exposure to sufficiently intense light. The experience of discomfort is marked by behavioral responses such as squinting or averting the eyes. Nearly everyone experiences visual discomfort on a daily basis. For example, bright sunlight, either directly viewed or reflected off of objects, usually produces acute visual discomfort. Oncoming automobile headlights, particularly high-intensity discharge lamps (for example, xenon), often cause aversive visual reactions due to discomfort, and even intense interior lighting can result in visual discomfort. Although visual discomfort is usually associated with intense lighting conditions, there are circumstances that can produce discomfort in relatively mild lighting conditions: if a person has spent an appreciable length of time in a dark environment, and then abruptly enters a moderately bright environment (for example, kitchen lighting) discomfort often occurs due to insufficient visual adaptation. Results from empirical investigations offer evidence for a protective role of MP in attenuating visual discomfort (for example, Stringham and others 2003, 2004; Wenzel and others 2006).

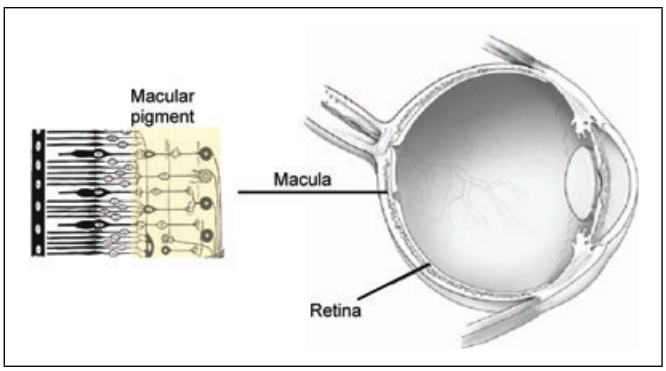

Figure 1—A schematic of the eye showing a blown up cross section of the retina with the yellow macular pigments highlighted.

Visual discomfort can be measured using subjective ratings (for example, the Boer visual analog scale; de Boer 1968) or objective methods such as electromyography (EMG). The EMG technique measures muscle activity associated with a squinting response. Stringham and others (2003) used a subjective rating scale in conjunction with EMG recordings in response to wavelengths of light ranging from 440 to 640 nm. Prior to this, evidence regarding the effects of wavelength on visual discomfort was limited, and sensitivity was assumed to be similar to standard spectral sensitivity, where people are most sensitive visually to green lights, and less sensitive to blues and reds. The results of Stringham and others' investigation of visual discomfort, however, showed that discomfort thresholds decreased with decreasing wavelength. In other words, the subjects were most sensitive to blue lights, followed by greens, yellows, and reds. It should be noted that this trend was observed after correcting for ocular media and absorption by MP. Given that less energy is required to induce retinal damage at shorter wavelengths (for example, Ham and others 1976), the authors suggested that a greater photophobia response to these wavelengths is indicative of a protective function. An influence of MP was hypothesized based on an observed minimum sensitivity point in the photophobia function at 460 nm (that is, the peak absorption of MP). In fact, because MP acts as a relatively broadband filter of blue light, visual discomfort was strongly attenuated for much of the blue region of the visible spectrum. This suggests that the filtering properties of MP serve to reduce the visual discomfort associated with central viewing of any light containing short wavelengths. With regard to off-axis lights (not filtered by MP), subsequent investigations of visual discomfort have shown that visual discomfort sensitivity linearly increases in the blue region of the visible spectrum (for example, Stringham and Snodderly 2009).

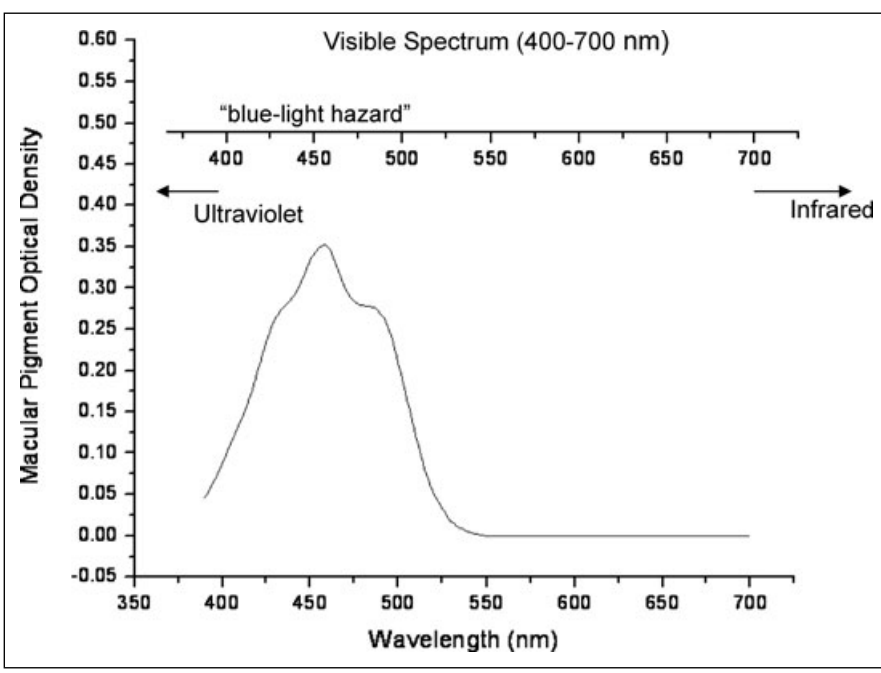

Figure 2—The absorbance spectrum of retinal lutein and zeaxanthin (from Bone and others 1992) compared to the visible spectrum.

Stringham and others (2004) determined the extent to which MP mediates photophobia thresholds by establishing the relationship between the spatial properties of photophobia and the distribution of MP across the retina. Photophobia responses, measured by EMG, were determined for stimuli presented in the central retina, where MP accumulates, and the peripheral retina. Measurements of MP at different eccentricities were made and plotted to determine the spatial distribution of MP. Results indicated a greater photophobia response in the central retina for stimuli composed of a wavelength outside of the absorption spectrum of MP. For xenon-white light, which contains short-wavelength light (filtered by MP), however, differences in responses to central compared with peripheral conditions were mediated by individual differences in MP. For example, subjects with higher MP tolerated more white light in the central condition, most likely due to the filtering of discomforting short-wavelength light. In fact, for the 2 subjects with high MP, the intensity of white light needed to induce photophobia was nearly equivalent in both central and peripheral conditions. The results suggest that MP is able to reduce visual discomfort by acting as a spatially integrated filter, which means that even a low level of MP, integrated across the fovea, can provide a meaningful benefit in terms of visual discomfort reduction.

Wenzel and others (2006) directly tested the relationship between MP across the retina and photophobia thresholds in 2 experiments. Photophobia thresholds were determined in the fovea and the parafovea using a short-wavelength (blue) light and a long-wavelength (orange) light. The energy of the long-wavelength target that induced photophobia was subtracted from the energy that induced photophobia for the short-wavelength target. A photophobia ratio was determined by taking the difference between the foveal and parafoveal photophobia thresholds for short- and long-wavelength lights. In the 1st experiment, results revealed a significant linear relationship between MP and photophobia ratios for 10 subjects. Integrated macular pigment, an estimate of aggregate light filtration across the retina by MP, also positively correlated with photophobia ratios. This relationship was stronger than the relation between photophobia ratio and MP at any one retinal eccentricity. In fact, the authors argue that an integrated MP value is more accurate than a single measure of MP at one eccentricity. In general, the results support an aggregate screening of MP across the central retina that would, as noted by Stringham and others (2004), benefit a person with even a small amount of MP. Furthermore, this finding suggests that small increases in MP (through dietary modification or L + Z supplementation) could potentially have disproportionately positive benefits in terms of visual discomfort.

The 2nd experiment conducted by Wenzel and others measured changes in photophobia thresholds and MP following supplementation with L and Z. The dietary intervention was equivalent to 30 mg/d of lutein and 2.7 mg/d of zeaxanthin for 12 wk. Significant linear increases in MP corresponded with linear changes in photophobia ratios. In other words, the amount of light necessary to induce photophobia for short-wavelength targets increased as a function of increased MP across the retina. These findings demonstrate a direct relationship between MP and photophobia thresholds. Furthermore, the results support the use of a dietary intervention to reduce visual discomfort. This information could be useful for clinical populations, specifically as a means of reducing symptoms of photophobia.

Disability glare. Whereas the aforementioned studies tested the role of MP in discomfort glare, another aspect of glare that affects visual performance is disability glare, or the ability to see "through" glare. As light passes through the eye, the various structures it encounters serve to scatter it as it approaches the retina. In glare conditions, this forward scattering of light can be very conspicuous, and results in the reduction of an image's contrast, thereby reducing visibility. This is a common visual deficit experienced in situations such as night driving due to exposure to bright headlights. The elderly are especially vulnerable to impaired vision in these situations, as structural changes in the crystalline lens lead to greater light scatter. MP could, in theory, help absorb scattered light, thereby improving visibility in glare for 3 reasons: (1) MP is located in the fovea, the region of the retina crucial to visibility. (2) The absorption spectrum of MP covers roughly one-third of the visible spectrum, so MP is capable of absorbing a visually meaningful amount of scattered light. (3) The "kind" of light that MP absorbs (short wavelengths) is relatively less important to the visual system in terms of luminance, or brightness than middle- or long-wavelength light. In most cases, therefore, MP would not negatively impact the visual detection of a target.

Stringham and Hammond (2007) investigated the role of MP in improving visibility, as opposed to simply reducing discomfort, in the presence of a glare source. Thirty-six subjects with a wide range of MP values (from 0.08 to 1.04 log optical density) participated in their study. Visual performance was assessed as the ability to detect a 100% contrast grating stimulus (a black and white striped pattern) under intense glare conditions. The glare stimulus was an annulus (concentric with the target stimulus) that consisted of either broadband (that is, "white") light or monochromatic light ranging from 460 to 620 nm. The subjects' task was to increase the glare intensity of the annulus to the point when the grating target just disappeared. As expected, for subjects with high levels of MP, the scatter effect was greatly reduced for the short-wavelength monochromatic lights. Interestingly, for the broadband white light, an even stronger effect of scatter reduction was found. Subjects with higher MP were able to withstand much more of the white light glare before losing sight of the target ($P < 0.001$). This finding suggests that the filtering effect of MP integrates across wavelengths, and thus MP is apparently very effective at relieving disability glare under broadband illumination. The authors suggested that a filtering mechanism, specific to MP's absorption spectrum, is responsible for the relation between MP and disability glare in such conditions, as no relation was found between MP and glare sources composed of wavelengths outside the absorption spectrum of MP (for example, 620 nm). In an attempt to extend these cross-sectional findings and determine a possible causal relationship between MP and disability glare, Stringham and Hammond (2008) measured changes in MP and disability glare following a 6-mo, daily supplementation regimen of 10 mg of lutein and 2 mg of zeaxanthin. In a linear fashion, subjects' MP levels increased during the supplementation trial (average increase of 0.16 log optical density after 6 mo of supplementation), and a reduction in disability glare commensurate with MP increases was also found. These results confirmed a causal relation between MP and disability glare. In fact, improved visual performance corresponded to subjects' ability to withstand an average of 58% greater intensity of the glare source before losing sight of the target.

Photostress recovery. A 3rd parameter of visual performance impacted by glare is the time necessary to recover vision following exposure to a bright light source. Because this effect is related to stressing the photoreceptors via bleaching of photopigments with intense light, this phenomenon is termed photostress recovery. In the case of glare, a bright light source that reaches the retina leads to the bleaching of photopigments, which need to regenerate in order to regain visual function. Generally speaking, the higher the intensity of the glare source, the greater the length of time it takes to recover visual function. There are numerous everyday situations

involving glare that produce noticeable photostress recovery. For example, briefly viewing strong reflections of the sun (for example, off of a windshield or automobile mirror) often results in a ghostly afterimage through which objects with low contrast, or in low light, cannot be seen. Additionally (as with disability glare), photostress recovery is important to visual performance in night driving situations, where intense oncoming headlights can result in debilitating afterimages that can temporarily blind a driver. In most situations, photostress recovery lasts for less than 10 to 15 s, whereupon normal vision is restored. In extreme circumstances, however, photostress recovery can endure for over 1 min. This is commonly experienced by people who enter a dark room after being outside in a sunny environment (without sunglasses).

To test the hypothesis that MP can reduce photostress recovery time by absorbing light before it reaches the photoreceptors, Stringham and Hammond (2007) presented intense monochromatic (440 to 620 nm) and white-light bleaching stimuli to 36 subjects with a wide range of MP levels, and then measured the time elapsed before the subjects reacquired visually a high contrast grating target. For the white-light condition, results indicated a significant inverse relation between photostress recovery and MP. In other words, higher MP values led to shorter photostress recovery times. For the monochromatic light condition, a ratio of photostress recovery in the fovea (where MP is dense) and parafovea (where there is little or no MP) was plotted as a function of wavelength, revealing a peak at 460 nm, consistent with the maximum absorbance by macular pigment. This suggests that MP acts as a filter to improve photostress recovery by preferentially screening the photoreceptors of short-wavelength light. This screening, of course, simply reduces photopigment bleaching. Interestingly, the subjects with the lowest MP levels (less than 0.10 log optical density) had recovery times (approximately 45 s) that were twice that (approximately 22 s) of the subjects with the highest MP levels (over 0.90 log optical density). It is evident, therefore, that this is not a trivial effect. In a follow-up study, Stringham and Hammond (2008) conducted an L and Z supplementation trial (described earlier) to determine within-subject effects. As was found with disability glare, improvement was found in photostress recovery times following L and Z supplementation. Subjects' photostress recovery times decreased in a fashion commensurate with increases in MP level. For the sample of 40 subjects, the average increase in MP level was 0.16 log optical density, and the average decrease in photostress recovery time for the white-light condition was found to be 5 s. This finding is potentially very significant. For example, a car traveling at 60 miles/h covers 440 feet in 5 s. If a driver is impacted by glare (especially at night), then visual performance would be compromised. If photostress recovery time could be improved by just 1 s, then (given the example above) vision could be restored nearly 100 feet sooner. Based on the results of Stringham and Hammond (2008), augmentation of MP could provide this kind of improvement. These findings are consistent with other dietary interventions with clinical populations that lead to improvements in glare sensitivity. Richer and others (2004), studying Veterans with early AMD, and Olmedilla and others (2002), studying cataract patients, tested the effects of L on glare sensitivity using a randomized double-blind placebo-controlled design. These authors found that L and Z reduced glare sensitivity in the treated groups.

The visibility hypothesis

In addition to blur and scatter arising from within the eye, image degradation also occurs due to external optical sources. It may not be a coincidence that the peak absorbance of MP is 460 nm, which is also the peak wavelength of sky light. Of course, the reason that the sky appears blue is that the more highly energetic short-wave component of white sunlight is more easily scattered by molecules in the atmosphere (for example, oxygen and nitrogen, termed Rayleigh scatter). In addition, haze aerosols, which are composed primarily of dust, volcanic ash, pollution particles, sea salt, and exudates from foliage, more easily scatter short-wave light. Wooten and Hammond (2002) originally proposed that this preponderance of short-wave light in the atmosphere results in a bluish veiling luminance that degrades visibility, that is, how well and how far we can see targets in the outdoors. MP may improve vision through the atmosphere by preferentially absorbing the SW energy produced by "blue" haze and, thereby, increasing both the contrast within the objects that we view and the contrast of those objects with respect to their backgrounds. Wooten and Hammond (2002) mathematically modeled these effects and argued that MP would improve vision in the atmosphere by about 30% (that is, one could see about 30% farther distance) when comparing subjects with low and high MP. For example, when viewing a series of parallel ridges covered with vegetation, ridges nearby will appear green. With each successive ridge, however, air light reduces contrast, until distant ridges are lost in a milky bluish haze, even on a clear day (for example, Green River Area, Wyoming, average visual range in June = 108 miles). The visibility hypothesis predicts that an individual with high MP would be able to distinguish such ridges up to 27 miles further than individuals with little or no MP, but equal Snellen acuity.

Recently, Wong and others (2009) examined the visibility hypothesis by using a variable path length filter that contained a solution that closely approximates the spectral absorbance of MP. By creating a filter cell with an adjustable path length, optical density could be adjusted on a continuous scale. Optical density is a function of both chemical concentration and path length (how far light travels through the solution). This external and artificial MP filter added linearly to a subjects' measured MP. Hence, changes in MP could be simulated as if a person was supplemented with L and Z and had MP increases (without waiting months for the natural increases). This variable path length filter was placed within an optical system that used broadband light (xenon-white) that approximated sunlight. A system of colored filters was used to match the spectral conditions of atmospheric haze. Subjects viewed a target stimulus at 8 cycles/degree through the artificial MP solution and contrast sensitivity levels were measured. This preliminary study, using 5 healthy young subjects, found that addition of about 0.50 OD units of artificial MP to subjects with average MP levels resulted in about a 40% increase in contrast sensitivity thresholds. These initial data were consistent with the predictions of Wooten and Hammond (2002).

Contrast enhancement

Walls and Judd also argued that yellow filters enhance contrast. Enhancing contrast is an important aspect of spatial vision, particularly as they apply to edges. Edges define the boundaries of objects and are therefore necessary to segment, register, and ultimately identify objects in a scene. Lateral inhibition at the level of the retina accentuates visual discontinuities and the exact nature of these edges (length, orientation, movement, and so on) are coded by specific cells (simple, complex, and hypercomplex) within the visual cortex. Anything that accentuates edges would be expected to improve spatial vision and the detection of objects against a background. Luminance differences are certainly one way an edge can be defined. Of course, in the real world, things are rarely achromatic. Consequently, other differences, such as wavelength composition (chromaticity), are also used to define edges (for

example, Hansen and Gegenfurtner 2009). This is one reason that colored filters can make objects appear more "crisp." Yellow filters, for instance, will make a yellow target with a blue surround (like the sky) more visible by selectively reducing the surround relative to the central target. This simple optical effect enhances the contrast between a mid-or long-wave target and a background with more short-wave energy. Both Luria (1972) and Wolffsohn and others (2000) have shown that the visibility of such stimuli is improved when viewed through yellow lenses. Renzi and others (2009) has recently shown that contrast thresholds for such stimuli are strongly related to individual differences in MP density.

The acuity hypothesis

The acuity hypothesis has been touted more in the literature than any other optical hypothesis of macular pigment function. It was originally postulated by Schulze (1866) but has been supported by such luminaries as the Nobel Laureate George Wald. Paradoxically, it was not until 1974 that Reading and Weale 1st created a quantitative model of the effects of MP on acuity. They started with the basic premise of the hypothesis: acuity is improved by reducing the deleterious effects of chromatic aberration. Chromatic aberration is based on the fact that lenses will refract (or bend) light of varying wavelength differently. Short-wave light (the blue light absorbed by MP) is refracted the most and is considerably out-of-focus at the plane of the retina (mid-wave or green light is brought to focus right at the retina and long-wave or red light is slightly behind the retina) under normal conditions. Hence, if a white disc was imaged on the retina, a blue or purple halo (or penumbra) would be seen surrounding the disc. Reading and Weale (1974) calculated that an average amount of MP would remove this bluish penumbra (according to their calculations, any additional amount of MP would be superfluous). Of course, it is not clear that this would necessarily make the white disc easier to see per se but it would accentuate the edges. Engles and others (2007) empirically evaluated the hypothesis with 40 subjects. They found that MP density did not correlate significantly with either gap or hyper acuity measured in yellow light (not absorbed by MP) or white light conditions (absorbed by MP). A very careful psychophysical procedure was used (a criterion-free, 2-alternative forced-choice task) but the full contrast sensitivity function was not measured. Nonetheless, these data, like others (McLellan and others 2002), and the modeling done by the authors (showing that one would not expect much spatial improvement based on the spectral sensitivity function, s-cone contributions to spatial vision, and so on) suggest that, even if true, the beneficial effects of delimiting chromatic aberration on spatial vision are small (see also Bradley and others 1988) and of questionable significance.

Conclusions

It seems clear that MP does influence visual performance through, at least, a few optical mechanisms. The most robust effects appear to be related to its actions as an optical filter. Results showing that retinal L and Z reduce glare disability and discomfort, reduce photostress recovery times, and enhance contrast are significant. MP improves glare performance through absorption of forward scattered short-wave (blue) light. There is also data (albeit preliminary) to support the idea that MP increases visual range by absorbing short-wave scattered light in the atmosphere. MP also appears to enhance contrast by improving the visibility of colored edges through differential absorption across a color border.

One advantage to testing optical theories of MP function is that they can be specifically evaluated by carefully manipulating the optical characteristics of the stimuli. All of the optical effects of MP are related to its spectral absorption. This is important because it is also clear that lutein and zeaxanthin could potentially improve vision through purely biological means as well. For example, a large body of literature (see Hammond and Renzi 2008) suggests that the pigments protect the retina and lens, and perhaps even help to prevent age-related eye diseases such as macular degeneration (see Carpentier and others 2009) and cataract. It is likely that a healthier retina and lens, especially in the elderly, is related to improved visual performance.

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