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A randomized placebo-controlled study on the effects of lutein and zeaxanthin on visual processing speed in young healthy subjects

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ABSTRACT

Speed of processing is a particularly important characteristic of the visual system. Often a behavioral reaction to a visual stimulus must be faster than the conscious perception of that stimulus, as is the case with many sports (e.g., baseball). Visual psychophysics provides a relatively simple and precise means of measuring visual processing speed called the temporal contrast sensitivity function (tCSF). Past study has shown that macular pigment (a collection of xanthophylls, lutein (L), meso-zeaxanthin (MZ) and zeaxanthin (Z), found in the retina) optical density (MPOD) is positively correlated with the tCSF. In this study, we found similar correlations when testing 102 young healthy subjects. As a follow-up, we randomized 69 subjects to receive a placebo (n = 15) or one of two L and Z supplements (n = 54). MPOD and tCSF were measured psychophysically at baseline and 4 months. Neither MPOD nor tCSF changed for the placebo condition, but both improved significantly as a result of supplementation. These results show that an intervention with L and Z can increase processing speed even in young healthy subjects.

Introduction

One likely manifestation of biological thrift is that a single, typically widely available, molecule can often play many and diverse roles throughout nature. Lutein (L)[1] and zeaxanthin (Z), for instance, play a critical role in plant photosynthesis [4] and the embryonic development of chicks (giving the yellow to egg yolk; [18]). L and Z are antiatherogenic [6] but also help prevent photo-oxidative degradation of the skin [24]. L and Z are potent lipid-based antioxidants and anti-inflammatories [31] but also serve as optical filters within the macula of the eye [13]. They are ornamental [10] and yet found within human brain information processing areas such as the hippocampus [30]. Their diversity throughout nature is reflected by an equally impressive diversity within our biology.

The behavioral effects associated with L and Z seem no less encompassing. Significant relations have been reported between macular pigment optical density (MPOD; L and Z and meso-Z measured in the retina) and a large number of visual measures including glare disability and discomfort, photostress recovery, and chromatic contrast [13]. Measures of L and Z within the retina appear to be strongly linked to measures of L and Z in brain tissue [29] and MPOD has also been linked to measures that are mediated by brain such as cognition [15,9,23], auditory thresholds [33], balance time, reaction time [22], and temporal vision [11,21,2].

Taken together, L and Z seem important to biology, in general, and humans are no exception. In many cases, the basis for their functional effects has been well characterized. For example, in the eye, many effects are due simply to selective filtering. How (and really if) they influence brain function, however, is less clear. One possibility is simply protection from the accumulated effects of oxidative and inflammatory stress. Data linking reduced MPOD to dementia [19] and cognitive impairment [23] is consistent with that possibility. Another possibility, more relevant to younger individuals and palliative approaches, is a direct improvement by some type of local interaction with neural cells (the so-called neural efficiency hypothesis; [11,36,21]). Such interactions (as opposed to simply enhanced protection) would imply that supplementation over a relatively short time period (yet long enough to increase

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[1] *Abbreviations used:* tCSF, temporal contrast sensitivity function; L, lutein; MZ, meso-zeaxanthin; Z, zeaxanthin; MPOD, macular pigment optical density; LED, light-emitting diode.

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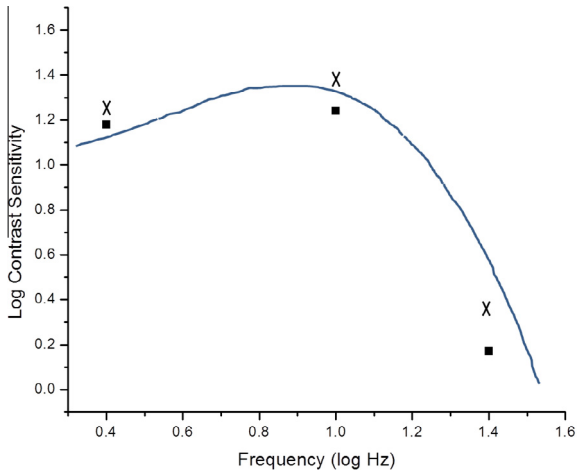

Fig. 1. The average baseline tCSF values for subjects in the placebo (*X*s) and treatment conditions (squares). The shape of the template curve depicted by the solid line was derived from Wooten et al. [35]. The similarity in shape suggests our temporal measures were a valid estimate of the general temporal contrast sensitivity function.

MPOD) in young healthy subjects would yield behavioral improvements in tasks that are generally mediated by the central nervous system.[2] To test this idea, we measured MPOD and temporal vision (specifically, the temporal contrast sensitivity function, tCSF) in a group of young healthy subjects.

We chose the tCSF because the stimuli can be designed to obviate individual differences mediated by optical effects (e.g., influence of light absorption by retinal L and Z is eliminated by using wavelengths not absorbed by MP) and because the retina is known to follow temporally varying stimuli much faster than brain, hence, high-frequency thresholds are determined by the rate limiter which, in this case, appears to be visual cortex [32]. An example of the tCSF, with the specific points we assessed, is shown in Fig. 1. Renzi and Hammond [21] originally found that MPOD was correlated with tCSF. In the first phase of our study, we correlated tCSF with MPOD in 102 subjects. In the second phase, we utilized a placebo-controlled design and randomized subjects to receive either placebo ($n = 15$) or a xanthophyll-containing supplement ($n = 54$).

Method

Subjects

Young adults (ages 18–32 years) were recruited the University of Georgia and Athens, GA community for a four-month double-blind supplementation trial. At the time of enrollment, subjects were randomly assigned (simple randomizing without replacement) to one of three treatment groups. The treatment groups were either 20 mg Z/day ($N = 29$; EyePromise Zeaxanthin, ZeaVision, LLC; Chesterfield, MO) or a "multi" condition 26 mg Z + 8 mg L + 190 mg mixed n-s fatty acids/day ($N = 25$; EyePromise vizual EDGE, ZeaVision, LLC; Chesterfield, MO). A total of 15 subjects received a placebo. Supplements were provided to subjects in an unmarked bottle, and they were instructed to follow dosage instructions listed under the cap for each day when taken with a meal.

All methods and procedures were approved by the University of Georgia's Institutional Review Board and adhered to the principles in the Declaration of Helsinki. Subjects provided written consent.

[2] Although a purely protective effect cannot be ruled out. Even young subjects can often have quite high levels of inflammatory and oxidative stress [5] and functional improvements would likely result from their amelioration.

Table 1
Baseline correlations between macular pigment and measures of temporal vision and temporal contrast sensitivity ($N = 102$).

	Macular pigment (30′ eccentricity)	
	r-Value	*p*-Value (one tailed)
Foveal temporal contrast sensitivity		
1.4 log hertz	0.29	<0.005
1.0 log hertz	0.27	<0.005
0.4 log hertz	0.26	<0.005
Parafoveal temporal contrast sensitivity		
1.4 log hertz	0.21	<0.025
1.0 log hertz	0.26	<0.005
0.4 log hertz	0.26	<0.005

MPOD and temporal visual function were measured on two separate occasions during a single week in order to determine a stable baseline value (we then used the average for the baseline correlations shown in Table 1). At the second visit, subjects received the masked pill bottles and were instructed to take the contents with a meal and to refrain from making substantial changes to their diet during the intervention. Compliance was assessed by questioning the subjects twice during and once at the conclusion of the intervention.

Assessment of macular pigment

Macular pigment optical density (MPOD) was determined at 30-min retinal eccentricity using customized heterochromatic flicker photometry with a table-top device described by [34]. In brief, a 460 nm light-emitting diode (LED) is presented in square-wave alternation with a 570 nm LED creating the perception of flicker, which is presented at an individually-customized rate. The difference in energy of the 460 nm LED required to eliminate flicker in the fovea (where macular pigment accumulates) compared to the parafovea (an area of the retinal without macular pigment) was used to derive MPOD.

Assessment of temporal contrast sensitivity

Temporal contrast sensitivity was assessed by the customized, LED-driven tabletop device described by Wooten et al. [35]. The test stimulus consisted of a 1-degree 660 nm target at the center of a 5.5-degrees 660 nm surround, separated by a 4 arc minute gap. A fixation point at the center of the target was used for foveal measurements. Unlike MP density, which was only measured in the central 1-degree, we also assessed parafoveal temporal sensitivity. To obtain these measures, subjects fixated a small red point placed at 7-degrees in the nasal visual field. Subjects viewed the stimuli through a 3 mm artificial pupil. Measurements of temporal contrast sensitivity occurred at 0.4, 1.0, and 1.4 log frequency (i.e., the LEDs were presented in sine-wave at 2.51, 10, and 25 Hz, respectively). Temporal contrast sensitivity values were derived from temporal contrast thresholds, or the depth of modulation at which the target first appeared to flicker. Depth of modulation refers to the amplitude modulation of the sine wave, or the difference between the maximum and minimum luminance of the wave. For each frequency setting, the target was initially set at 0% depth of modulation (and therefore perceptually fused) and increased until the subject reported flicker detection, for a total of five ascending trials for each frequency setting.

Statistical analyses

Results were analyzed with SPSS 17.0. The baseline relations were assessed using a Pearson product moment correlational