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Macular pigment optical density is related to cognitive function in older people

Rohini Vishwanathan[1], Alessandro Iannaccone[2], Tammy M. Scott[3], Stephen B. Kritchevsky[4], Barbara J. Jennings[2], Giovannella Carboni[2,5], Gina Forma[2,5], Suzanne Satterfield[6], Tamara Harris[7], Karen C. Johnson[6], Wolfgang Schalch[8], Lisa M. Renzi[9], Caterina Rosano[10], Elizabeth J. Johnson[1]

[1]Carotenoids and Health Laboratory, Tufts University, 711 Washington St, Boston, MA 02111, USA
[2]Hamilton Eye Institute, University of Tennessee Health Sciences Center, Memphis, TN, USA
[3]Nutrition and Aging Laboratory, Tufts University, Boston, MA, USA
[4]Sticht Center on Aging, Wake Forest School of Medicine, Winston-Salem, NC, USA
[5]Universita' degli Studi di Cagliari–Istituto di Oftalmologia, Calgliari, Italy
[6]Department of Preventive Medicine, University of Tennessee Health Sciences Center, Memphis, TN, USA
[7]Geriatric Epidemiology, National Institute of Health/National Institute of Aging, Bethesda, MD, USA
[8]DSM Nutritional Products, Kaiseraugst, Switzerland
[9]Department of Psychology, University of Georgia, Athens, GA, USA
[10]Department of Epidemiology, University of Piitsburgh,130 N. Bellefield Avenue, Pittsburgh, PA 15232, USA

Address correspondence to: Elizabeth J. Johnson. Tel: 617 556 3204; Fax: 617 556 3344. Email: elizabeth.johnson@tufts.edu

Abstract

Background: the xanthophylls lutein (L) and zeaxanthin (Z) exist in relatively high concentration in multiple central nervous tissues (e.g. cortex and neural retina). L + Z in macula (i.e. macular pigment, MP) are thought to serve multiple functions, including protection and improvement of visual performance. Also, L + Z in the macula are related to L + Z in the cortex.
Objective: to determine whether macular pigment optical density (MPOD, L + Z in the macula) is related to cognitive function in older adults.
Methods: participants were older adults ($n = 108$, 77.6 ± 2.7 years) sampled from the age-related maculopathy ancillary study of the Health Aging and Body Composition Study (Memphis, TN, USA). Serum carotenoids were measured using high performance liquid chromatography. MPOD was assessed using heterochromatic flicker photometry. Eight cognitive tests designed to evaluate several cognitive domains including memory and processing speed were administered. Partial correlation coefficients were computed to determine whether cognitive measures were related to serum L + Z and MPOD.

Results: MPOD levels were significantly associated with better global cognition, verbal learning and fluency, recall, processing speed and perceptual speed, whereas serum L + Z was significantly related to only verbal fluency.
Conclusion: MPOD is related to cognitive function in older people. Its role as a potential biomarker of cognitive function deserves further study.

Keywords: *lutein, zeaxanthin, cognition, macular pigment, ageing, older people*

Introduction

Lutein and zeaxanthin (L + Z) are the only carotenoids that exclusively accumulate in the macula of the primate retina [1] forming macular pigment (MP) [2]. MP filters short-wavelength blue light and is an antioxidant protecting the retina from photo-oxidative damage [3, 4]. Macular pigment optical density (MPOD) is a non-invasive measure of L + Z concentration.

In the macula, MPOD has been associated with improved visual processing speed [5, 6]. MPOD was inversely related scotopic noise (noise associated with vision under dim light conditions) [7]. Thus, the hypothesis that L + Z may influence neural function beyond the visual system is biologically plausible.

In large epidemiological studies, older adults consuming the highest amounts of green leafy vegetables and cruciferous vegetables (rich sources of L) had slower cognitive decline than those consuming lowest amounts [8, 9]. Plasma antioxidants, particularly L + Z, were related to improved cognitive function in healthy elderly [10] and were depleted in individuals with mild cognitive impairment and Alzheimer's disease [11]. Furthermore, L supplementation improved measures of executive function, learning and short-term memory in healthy older women [12].

The objective of this investigation was to determine cross-sectional relationships of serum L + Z and MPOD with cognition in healthy older adults.

Methods

Participants

The Health Aging and Body Composition (ABC) Study is a prospective investigation of interrelationships among health conditions, body composition, social and behavioural factors and functional change in older adults. The age-related maculopathy ancillary (ARMA) study included a sample of the Memphis Health ABC cohort in Years 6 and 7 of the Health ABC study and also included non-Health ABC elderly from Memphis [13]. Participant characteristics have been previously described [13, 14]. Participants were free of visual conditions that may confound or affect MPOD measurements [13]. In Year 3 of the Health ABC study, the Cognitive Vitality Substudy was initiated, which selected the top 20% of performers on an endurance walk test in Year 2 along with a random sample of other participants for a more intensive biannual cognitive assessment. Approximately half of the ARMA participants with normal retinas were also participants of the Health ABC's Cognitive Vitality Substudy. Participants with complete data for Years 5 and 6, cognitive function measures, MPOD and serum L + Z are included in the present analysis. The studies were approved by the Institutional Review Board of the University of Tennessee Health Science Center. Informed consent was obtained from each participant. The tenets of the Declaration of Helsinki were adhered to at all times.

Serum analyses

Serum samples at Year 6 were extracted using standard lipid extraction methods, and carotenoid concentrations were determined using reverse-phase high performance liquid chromatography as previously described [15].

Macular pigment optical density

MPOD was assessed using heterochromatic flicker photometer (HFP) device (Macular Metrics Corp., Rehoboth, MA, USA) [13]. HFP has been validated in elderly subjects [13]. Details about the testing methodology and repeatability have been previously published [13]. MPOD was successfully measured in 82% of the ARMA study participants [13].

Cognitive assessments

A battery of cognitive tests was designed to evaluate several cognitive domains. All measures were taken at Year 5 except verbal fluency, which was performed at Year 7. The Teng Modified Mini-Mental State Examination is a global measure of cognition for attention, language and orientation and is similar to the Mini-Mental State Examination but has additional items in order to extend the ceiling and floor test, to sample wider range of cognitive abilities and to enhance the reliability and validity of scores [16, 17]. The Buschke selective reminding test (SRT) is a measure of verbal learning and memory [18]. In this task, the examiner presents a list of 12 written words and reads each word aloud. The number of words recalled over the first six trials (SRT-learn) and number of words recalled after a 23–30 min delay (SRT-delay) were measured. Sensory-motor, perceptual speed and reaction time were measured using a battery of tests [19, 20]. Data for the box drawing task and pattern comparison task which assess sensory-motor and perceptual speed, respectively, and simple reaction time test, which assesses reaction time are reported here. In the box drawing task, the participant is asked to complete as many boxes as possible within 30 s. In the pattern comparison task, the participant has to determine whether two patterns of lines are the same or different within 30 s. Simple reaction time was a

computerised test, where the participant is asked to press a specific key on the keyboard whenever any images appear on the screen while ignoring any numbers and words. The digit-symbol substitution task is a component of the Wechsler Adult Intelligence Scale-revised and measures speed and associative learning ability [21, 22]. In this test, participants match the digits to the appropriate symbols in four rows as per the digit-symbol combination shown at the top of their task sheet. In the verbal fluency test, which is a measure of executive function, the subject is asked to name as many items from a category as possible in 1 min [23]. Cognitive assessments were performed by trained individuals in a low-distraction environment.

Statistical analysis

Data are expressed as means ± SE unless specified differently. Statistical significance was set at $P < 0.05$. Year 5 scores on cognitive measures were used for cross-sectional analyses, since it was the closest time-point to when serum L + Z and MPOD were measured (Year 6 for serum and Years 6 or 7 for MPOD). For the verbal fluency test, Year 7 scores were used, since the test was not performed at Year 5. Age, sex and body mass index (BMI) were used as the covariates, since these variables have the strongest influence on cognitive function measures and MPOD. Partial correlation coefficients were computed to determine whether cognitive function measures were related to serum L + Z and MPOD. All statistical analyses were performed using SPSS (v19.0).

Results

Subject characteristics are described in Table 1. The mean MPOD in the study population was 0.343 (±0.018), and the mean serum concentration of L + Z was 494 (±27) nmol/l.

Cross-sectional analyses showed a negative association between serum total L + Z and verbal fluency test scores ($P < 0.05$). Of the eight measures of cognitive function, MPOD was significantly correlated to six tests ($P < 0.05$) (Table 2), including measures of global cognition, verbal learning and fluency, recall, processing speed and perceptual speed.

Discussion

The present study evaluates the relationship between L + Z and cognitive measures using a battery of tests in healthy older adults. Like in the neural retina, L + Z are detected in human brain tissue at significantly higher concentrations than other carotenoids [24]. The Health ABC cohort was an ideal population to test the hypothesis that MPOD correlates with cognition, given that these were healthy older adults with normal cognitive function for whom extensive cognitive data were available.

Associations of cognitive measures with serum L + Z were not consistent, whereas associations with MPOD were more consistent. Unlike serum, MPOD is a stable measure of L + Z that is embedded in the retina and is more representative of long-term L + Z intake. MPOD was positively related to measures of global cognitive performance and executive function. A possible explanation for this finding

Table 2. Cross-sectional relationship between cognitive function measures and serum total L + Z and MPOD for all subjects ($n = 108$). Values are partial correlation coefficients adjusted for age, BMI, education and sex

Cognitive function measures	Serum L + Z	MPOD
3MS	−0.111	0.269[a]
SRT: learn	0.067	0.263[a]
SRT: delayed recall	0.062	0.220[a]
Reaction time	0.062	−0.059
Verbal fluency	−0.2[a]	0.249[a]
Digit-symbol substitution task	−0.016	0.249[a]
Box drawing task	−0.097	0.154
Pattern comparison task	−0.127	0.195[a]

3MS, Teng Modified Mini-Mental State Examination; SRT, Buschke Selective Reminder Test.
[a]$P \leq 0.05$.

Table 1. Characteristics of Health ABC subjects participating both in ARMA and the Cognition and Vitality Substudy with complete data for serum L + Z and MPOD ($n = 108$)

Characteristic		Cognitive test[a] (means ± SE)	
Age (years) (mean ± SE)	77.6 ± 0.3	3MS	91.0 ± 7.1
Sex (female, %)	50.9	SRT: learn	47.3 ± 11.7
Black, *n* (%)	33 (30.6)	SRT: delayed recall	6.9 ± 3.0
MI (kg/m^2) (means ± SE)	26.9 ± 0.4	Reaction time	170.4 ± 184.2
Education level, *n* (%)			
Less than high school	24 (22.2)	Verbal fluency	10.0 ± 3.1
High school graduate	30 (27.8)	Digit-symbol substitution task	39.2 ± 14.2
Post secondary	54 (50.0)		
Current smoker (Year 5) *n* (%)	5 (4.6)	Box drawing task	40.3 ± 12.1
Macular pigment optical density	0.343 ± 0.018	Pattern comparison task	11.2 ± 3.1

Health ABC, Health, Aging and Body Composition study; ARMA, Age-Related Maculopathy Ancillary Study; 3MS, Teng Modified Mini-Mental State Examination; SRT, Buschke Selective Reminder Test.
[a]Estimated marginal mean scores.

could be that MPOD reflects L + Z levels in the brain. Such a relationship was indeed observed in non-human primates, whose macular L + Z levels were significantly related to their levels in the brain [25].

The advantages of using MP as a biomarker are clear. HFP is a non-invasive method that assesses of retinal L + Z concentrations *in vivo*. In contrast, blood and dietary measures are taken distally from the locus of interest (i.e. neural tissue) reflect recent dietary activity. Dietary assessments are also more prone to bias.

One limitation of the present study is that the sample size was relatively small, and that subjects were of only two ethnicities (white and black). Another limitation is that MPOD measurements were obtained cross sectionally at Years 5 and 6 of the Health ABC study, whereas cognitive function was assessed before or after the MPOD measures. Studies that prospectively measured cognition and MPOD in parallel, and/or supplementation studies that ascertained the impact of L + Z supplements on cognitive function will be necessary to better characterise the relationship between MPOD and cognitive function. Another limitation is that ARMA participants were selected based on a visual function. Therefore, our ARMA sample may have suffered from unknown selection biases and may not be representative of the cognition–MPOD relationship in older people as a whole.

Few studies to date have investigated the hypothesis that MPOD is related to cognition. Most research on L + Z in the nervous system has focused on retinal L + Z and two primary functions: antioxidant capacity and ability to filter short-wave light. These properties may not be the sole functions of L + Z. Research suggests that through a variety of mechanisms, L + Z may improve neural efficiency [6, 26]. In retinal tissue, some improved neural efficiency are reduced noise [26] and improved temporal processing speed [27, 28]. L + Z function in the cortex has not been tested. The idea that L + Z can improve neural function via similar mechanisms warrants further investigation. A significant MPOD–cognitive function relationship is crucial for the evaluation of L + Z's role in the brain.

Key points

- Serum L and Z concentrations are related to verbal fluency in older people.
- MPOD is related a battery of cognitive functions measures in older people.
- MP may be a better biomarker of cognitive function in older people than serum L and Z.

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Short-term changes in body composition after surgical repair of hip fracture

Christopher Richard D'Adamo[1], William G. Hawkes[2], Ram Ron Miller[2], Mark Jones[2], Marc Hochberg[2,3], Janet Yu-Yahiro[4], J. Richard Hebel[2], Jay Magaziner[2]

[1]Departments of Family and Community Medicine & Epidemiology and Public Health, University of Maryland School of Medicine, 520 W Lombard Street East Hall, Baltimore, MD 21201, USA
[2]Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, USA
[3]Department of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA
[4]Department of Orthopedic Surgery, Union Memorial Hospital, Baltimore, MD, USA

Address correspondence to: C. R. D'Adamo. Tel: 410-706-6165; Fax: 410-706-6210. Email: cdadamo@som.umaryland.edu

Abstract

Background: the deleterious changes in body composition that occur during the year after hip fracture are associated with increased disability, recurrent fracture, and mortality. While the majority of these unfavourable changes have been shown to occur during the first 2 months after fracture, potential changes in body composition occurring earlier than 2 months post-fracture have not been studied. Accordingly, the aim of this study was to rigorously assess short-term changes in body composition after hip fracture.
Methods: total body mass, lean mass, fat mass and total hip and femoral neck bone mineral density (BMD) were assessed via dual energy X-ray absorptiometry at 3 days, 10 days and 2 months post-fracture among 155 hip fracture patients from the Baltimore Hip Studies. Longitudinal regression analysis using mixed models was conducted to model short-term changes in body composition.
Results: no significant changes in body composition were revealed from 3- to 10 days post-fracture. However, significant decreases from 10 days to 2 months post-fracture were noted in the total body mass (−1.95 kg, $P < 0.001$), lean mass (−1.73 kg, $P < 0.001$), total hip BMD (−0.00812 g/cm^2, $P = 0.04$) and femoral neck BMD (−0.015 g/cm^2, $P = 0.03$). No meaningful changes in fat mass were uncovered.