

NUTRITION FOR THE YOUNG AND NOT SO YOUNG

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DISCLOSURE

- Sanofi Speaker
- EyePromise Employee

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WHILE ~750 CAROTENOIDS ARE FOUND IN NATURE, ONLY TWO ARE CONCENTRATED IN THE RETINA



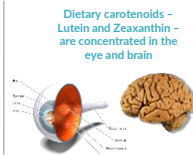
~750
Carotenoids



<50 Primary
Carotenoids



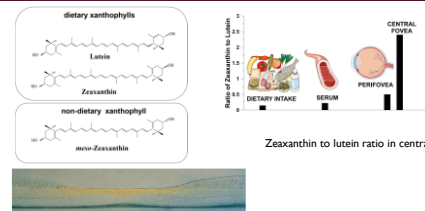
~20 Carotenoids



≈ 75 % of carotenoids in
infant's brain is lutein and
zeaxanthin

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CAROTENOIDS IN RETINA-XANTHOPHYLLS



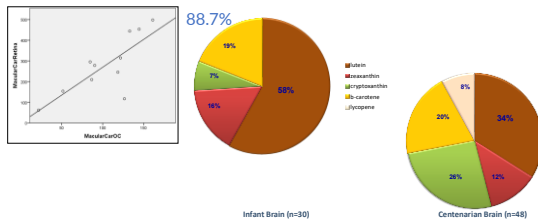
Zeaxanthin to lutein ratio in central retina is 2.5:1

Photomicrograph courtesy of Dr. Joanne Curran-Celestino.

Nutrients 2020, 12, 1333; doi:10.3390/nu12051333

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MPOD is a neural biomarker



Vishwanathan R, Schach W, Johnson E. J Nutr Neurosci. 2016;19(3):95-101

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IMPORTANCE OF CAROTENOIDS IN DEVELOPMENTAL YEARS

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REVIEW

Possible influences of lutein and zeaxanthin on the developing retina

J Paul Zimmer¹Billy R Hammond, Jr²¹Vivint Nutrition, Clinical Nutrition Research, Collegeville, PA, USA
²Vivint Science Laboratory, University of Georgia, Athens, GA, USA

Abstract: The carotenoids lutein and zeaxanthin (LZ) are found throughout the central nervous system but reach their highest concentration within the macular region of the primate retina where they are commonly referred to as the macular pigments. Although LZ are a major integral feature of the central fovea, no information currently exists regarding the effects of variability in the concentration of these pigments on the developing retina. In particular, the long-term effects of very low levels of macular pigment are not known and potentially meaningful. Macular pigment levels depend upon dietary intake since LZ cannot be synthesized *de novo*. **Low intake of LZ (eg, infants receiving unfortified infant formula or breast milk from mothers with low carotenoid diets) would be expected to have considerably lower macular pigment compared with infants with high LZ intake (eg, breast-fed infants with mothers on carotenoid-rich diets).** In this paper we discuss possible **implications** of this difference and the available evidence suggesting that **LZ could influence the developing visual system.**

Keywords: lutein and zeaxanthin, carotenoids, macular pigment, infant



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JN THE JOURNAL OF NUTRITION

journal homepage: <https://jn.nutrition.org/>

Nutrient Physiology, Metabolism, and Nutrient-Nutrient Interactions

Systemic Effects of Prenatal Carotenoid Supplementation in the Mother and her Child: The Lutein and Zeaxanthin in Pregnancy (L-ZIP) Randomized Trial—Report Number 1

Emmanuel K. Addo^{1,2}, Susan J. Allman¹, Ranganathan Arunkumar¹, Joanna E. Gorka¹, Deborah Y. Harrison¹, Michael W. Varner³, Paul S. Bernstein^{1,2,*}

Conclusion: Prenatal carotenoid supplementation significantly increased maternal and infant systemic (skin and serum) carotenoid status, which may benefit pregnant women and their infants' health. This trial was registered at clinicaltrials.gov as NCT03750968.

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Ocular Effects of Prenatal Carotenoid Supplementation in the Mother and Her Child: The Lutein and Zeaxanthin in Pregnancy (L-ZIP) Randomized Trial - Report Number 2

Emmanuel K. Addo, OD,^{1,2} Joanna E. Gorka, BS,¹ Susan J. Allman, CCRC,¹ Deborah Y. Harrison, MSc,¹ Mohsen Sharifzadeh, PhD,¹ Robert O. Hoffman, MD,¹ M. Elizabeth Hartnett, MD,¹ Michael W. Varner, MD,³ Paul S. Bernstein, MD, PhD^{1,2,*}

Conclusion: Prenatal carotenoid supplementation significantly increased maternal and infant systemic carotenoids and caused a pattern of increased infant ocular carotenoid status, which may benefit both mothers and their infants' ocular development and function. This study provides important data to design and power a future multicenter study of prenatal carotenoid supplementation in higher-risk pregnancies.

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The Journal of Nutrition
Nutritional Epidemiology

Maternal Intake of Lutein and Zeaxanthin during Pregnancy Is Positively Associated with Offspring Verbal Intelligence and Behavior Regulation in Mid-Childhood in the Project Viva Cohort

Hira A. Mahdian,¹ Karri M. Swickowski,² Tammy M. Kuo,³ Elizabeth J. Johnson,⁴ Sheri L. Rifkin-Shimizu,⁵ Emily Olson,⁶ and Paul J. Jacques^{1*}¹Division of Endocrinology, Diabetes, and Metabolic Diseases, National Institutes of Health, Bethesda, MD, USA; ²Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, USA; ³Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA; ⁴Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA; ⁵Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA; ⁶Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA

Conclusions: Higher maternal L-Z intake during pregnancy was associated with better offspring verbal intelligence and behavior regulation ability in mid-childhood, suggesting a potential benefit during prenatal development. We did not find a benefit of higher maternal LZ intake on other child cognitive or behavioral outcomes. Project Viva is registered at clinicaltrials.gov as NCT02820402. *J Nutr* 2021;00:1–13.

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Macular pigment optical density is positively associated with academic performance among preadolescent children

Sasha M. Barnett, Nathan A. Khan, Anne M. Wolf, Lauren B. Rame, Christopher M. Hetherington, Neal J. Cohen

Original Article
Published online 22 May 2017

Results: The regression analyses revealed that MPD improved the model, beyond the covariates, for overall academic achievement ($\Delta R^2 = 0.10$, $P < 0.01$), mathematics ($\Delta R^2 = 0.07$, $P = 0.02$), and written language composite standard scores ($\Delta R^2 = 0.15$, $P < 0.01$).

Discussion: This is the first study to demonstrate that retinal L and Z, measured as MPD, is positively related to academic achievement in children, even after accounting for the robust effects of IQ and other demographic factors. These findings extend the positive associations observed between MPD and cognitive abilities to a pediatric population.

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Review

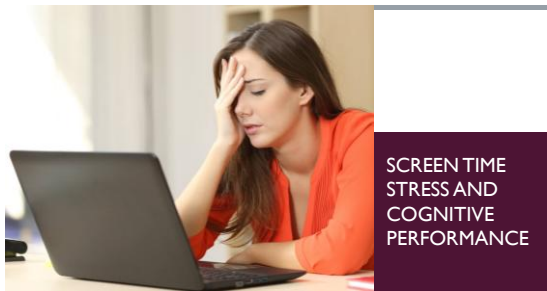
Associations Between Carotenoid Status, Visual Outcomes and Cognitive Metrics in Children: A Scoping Review

Fayal Sangani¹ and Pankaj Gargava Dary^{1*}

1. Carotenoids—especially lutein, zeaxanthin, and β -carotene—are concentrated in the developing retina and brain and likely support visual and cognitive development in children.
2. Higher carotenoid status (diet, serum, skin, or MPD) is consistently associated with better cognitive performance, including memory, executive function, reasoning, and academic achievement.
3. Human milk provides carotenoids that are more bioavailable than those from most fortified infant formulas, leading to greater delivery to the infant eye and brain.
4. Macular Pigment Optical Density (MPD) is a promising, noninvasive biomarker of retinal and possibly brain carotenoid status, with links to visual and cognitive outcomes.
5. Current evidence is encouraging but largely observational; more long-term randomized controlled trials are needed to establish causation, optimal dosages, and clinical recommendations for children.



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FRONTIERS IN NUTRITION

A Machine Learning Based Dose Prediction of Lutein Supplements for Individuals With Eye Fatigue

Juntao Kan^{1†}, Ao Li^{2†}, Hong Zou², Liang Chen¹ and Jun Du^{1*}

¹ Nutrilite Health Institute, Shanghai, China, ² Department of Bioinformatics, WuXi NextCODE Genomics, Shanghai, China

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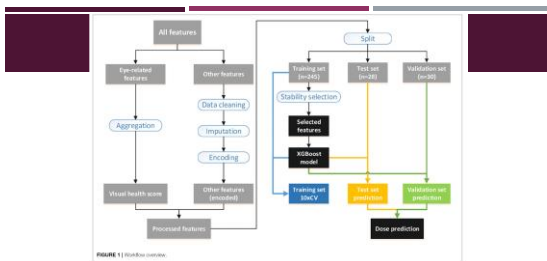


FIGURE 1 | Workflow overview.

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- Visual health score (VHS) was a composite score developed from 4 most correlated/predictive parameters

 1. Total score of eye fatigue,
 2. Visuosignosis persistence,
 3. **Macular pigment optical density (most predictive)**
 4. Schirmer's test

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SCREEN TIME ISSUES- PREDICTION AND PRECISION NUTRITION

Most individuals
67.24% need high
dose of carotenoids –
14 mg lutein
equivalent

29.31% may take a
lower dose – 10 mg
lutein equivalent

3.45% cannot be
helped

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MANAGEMENT OF DIGITAL EYE STRAIN

- Refraction
- Dry eye issue
- Accommodation / convergence
- Ergonomics
 - Regular break
 - Blinking
 - Working distance
 - Light levels

- MPD is low
- Need at least 13 mg of carotenoids probably 24 mg/day for 6 months to year
- Increase it to 0.5 du or higher
- If at 0.5 increase 0.15 du



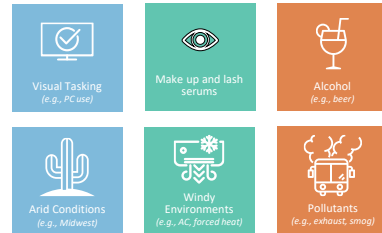
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CAN NUTRITION PROVIDE SIGNIFICANT DRY EYE RELIEF



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Identify Environmental Factors that may exacerbate DED



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Identify Systemic and Medication Factors that may exacerbate Dry Eye Disease

Other underlying high-risk diseases or medications?

- Thorough medication history
 - Antihistamines, decongestants, antidepressants
- Eyedrops – GLAUCOMA!
- Systemic history
 - Sjogren's
 - Rheumatoid
 - Rosacea
 - Thyroid dysfunction
 - Lupus
 - Hormonal changes



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MILD TO MODERATE DRY EYE TREATMENT



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Systematic Review Efficacy of Omega-3 Intake in Managing Dry Eye Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Wei-Xiang Wang¹ and Mei-Lan Ko^{2,3,*}

Based on the evidence, omega-3 FAs effectively reduce DED symptoms, especially in high doses, for a long duration, and with increased EPA levels. However, given the heterogeneity in study results and diverse patient characteristics, caution is needed in generalizing these findings. In conclusion, omega-3 FA supplementation is still recommended for DED management in clinical settings.

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CAN WE MEASURE BLOOD OMEGA -3? ABSOLUTELY



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What role do Omega 3 fatty acids play in dry eye ?

- Decrease inflammation; increase quality of tear film¹
- Reduction of dry eye symptoms¹
- Faster epithelial healing & visual recovery ²
- Regeneration of corneal nerves³



1. Saperstein, David T. (2004). "Omega-3 fatty acids: A review of the literature." *Journal of the American Academy of Ophthalmology*. 10: 149-156.
2. Saperstein, David T. (2004). "Omega-3 fatty acids: A review of the literature." *Journal of the American Academy of Ophthalmology*. 10: 149-156.
3. Saperstein, David T. (2004). "Omega-3 fatty acids: A review of the literature." *Journal of the American Academy of Ophthalmology*. 10: 149-156.

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Meibum Expression and Analysis before and after Omega 3 supplementation

S. Gregory Smith MD, Assistant Professor, Toledo Eye Institute, Presented at 2011 Contact Lens/EBAAA Fall Educational Symposium

Meibum expressed and analyzed before and after supplementation with Omega-3 fatty acids (1680mg EPA/560mg DHA).
Results after 8 weeks supplementation:

- 82% of patients treated showed the EPA and DHA in the meibum
- 70% of patients became completely asymptomatic! 100% felt better!
- Significant improvement in TBUT, staining, and osmolality!

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Blind Randomized Placebo Controlled Research

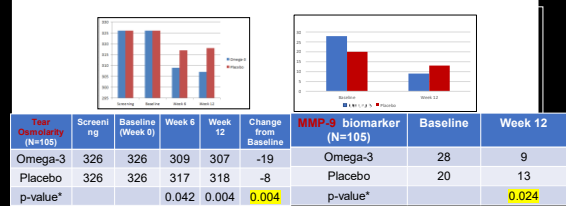


- Study Design**
- Multicenter
 - Randomized
 - Prospective
 - Double-Masked
 - Interventional
 - Placebo Controlled

- Subjects**
- 105 completed study
 - 54 in treatment group (received 2 grams re-esterified Omega-3)
 - 51 in placebo group
 - Average Age: 56.8 Years
 - Gender: 71.4% Female

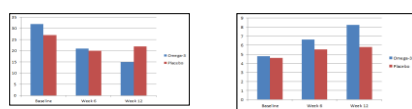
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Tear Osmolarity & MMP-9 Change from Baseline

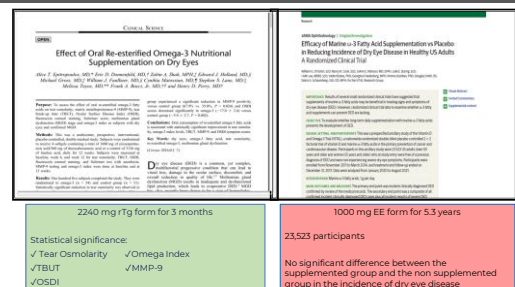


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OSDI & TBUT Change from Baseline by Visit



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IS HIGH OMEGA -3 OUR ONLY OPTION?

- Omega -3 important anti inflammatory, Vitamin E along side works synergistically
- Vitamin A is crucial for epithelial integrity and mucin
- Turmeric is an excellent anti inflammatory inhibits MMPs
- Systemic inflammation can also be an important issue
 - Green tea
 - Vitamin D
 - Mixed Tocotrienols/Tocopherols

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NUTRITION AND DRY EYE

The Ocular Nutrition Impact on Tear Film (ONIT) Study

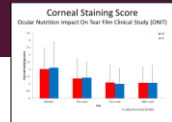
Advances in Ophthalmology and Visual System

- 8 weeks
- Dry eye confirmed by diagnostic markers and symptoms

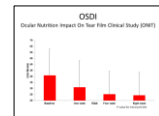
45% Improvement



Muliyilum SP, Davis HL, Townsend WB, et al. The ONIT study—ocular nutrition impact on tear film. *Adv Ophthalmol Vis Syst*. 2013;2(2):55-61. DOI: 10.1515/adv.2013.02.000.00



33% Improvement



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NIGHT VISION AND CAROTENOIDS



Communication

Night Vision and Carotenoids (NVC): A Randomized Placebo Controlled Clinical Trial on Effects of Carotenoid Supplementation on Night Vision in Older Adults

Stuart Richer ^{1,2,*}, Steven Novak ¹, Taylor Gullett ², Armi Dervishi ², Sherwin Nassiri ², Co Duong ², Robert Davis ³ and Pinakin Gnanvart Davey ¹

Aim:

Can carotenoid improve night vision and comfort in driving in individuals that complain of nighttime driving issues?

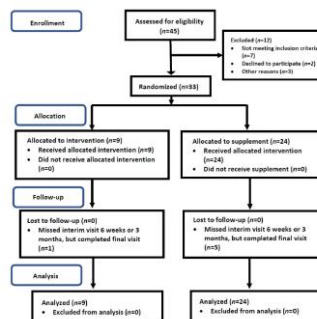


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Active Ingredients	Amount per Serving
Zeaxanthin	14 mg
Lutein	7 mg
Vitamin A	2500 IU
Vitamin C	60 mg
Vitamin D	1000 IU
Vitamin E	60 IU
Vitamin B6	2 mg
Folic Acid	400 mcg
Vitamin B12	6 mcg
Zinc	15 mg
Selenium	70 mcg
Manganese	2 mg
Fish Oil	150 mg
Coenzyme Q10	15 mg
Bilberry	15 mg
Berry Anthocyanin Extract	15 mg
Alpha Lipoic Acid	10 mg
Mixed Tocopherols	6 mg

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RESULTS

- Improvements in contrast sensitivity with glare in both eyes
- Monocularly tested glare recovery time improved 2.76 and 2.54 s, respectively, ($p = 0.008$ and $p = 0.02$),
- decreased preferred luminance required to complete visual tasks
- Improvements in UFOV scores of divided attention ($p < 0.001$) and improved composite crash risk score ($p = 0.004$) were seen in the supplemented group.
- The placebo group remained unchanged.

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Dietary carotenoids related to risk of incident Alzheimer dementia (AD) and brain AD neuropathology: a community-based cohort of older adults

Changcheng Yuan,^{1,2,3} Hai Chen,¹ Yimin Wang,⁴ Julie A Schneider,⁵ Walter C Willett,^{2,5,6} and Martha Clare Morris⁴

¹Department of Big Data and Health Science, Zhejiang University School of Public Health, Hangzhou, Zhejiang, China; ²Department of Nutrition, Harvard TH Chan School of Public Health, Boston, MA, USA; ³Channing Division of Network Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA; ⁴Rush Institute for Healthy Aging, Rush University Medical Center, Chicago, IL, USA; ⁵Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL, USA; and ⁶Department of Epidemiology, Harvard TH Chan School of Public Health, Boston, MA, USA

927 participants (No AD) were followed up for 7 years- Rush Memory and Ageing project
AD neuropathy was assessed in 508 deceased participants

Results were controlled for Age, sex, education, cognitively stimulating activities, physical activities, Apolipoprotein

Conclusions: Our findings support a beneficial role of total carotenoid consumption, in particular lutein/zeaxanthin, on AD incidence that may be related to the inhibition of brain β -amyloid deposition and fibril formation.

Am J Clin Nutr 2021;113:200–208.

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