



Nutrition | Brain | Cognition

powered by



# Nutrition and brain development

(DHA, choline & lutein)

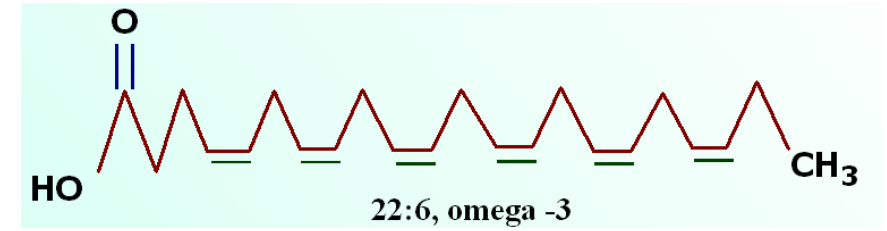
October 2019

GM

# Presentation overview

- DHA, lutein and Choline
  - In breast milk
  - In brain and eye
  - Scientific evidence

# DHA in breast milk



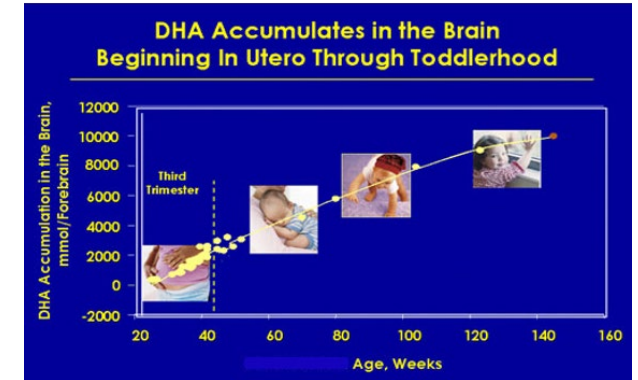
- An omega-3 long-chain polyunsaturated fatty acid, DHA is found in human milk at levels ranging between 0.17% to 0.99% of the total fatty acids (FAs)<sup>(1)</sup>
- It been estimated that the global mean DHA levels in human milk is ~0.32% of total FAs<sup>(2)</sup>

Breastfed infants DHA intake varies, given that the levels in the human milk are dependent on the mother's diet<sup>(1)</sup>

1. Yuhas et al., 2006;  
2. Brenna et al., 2007

# DHA and brain

- Accumulation is high during the 3rd trimester and by birth, it's the predominant fatty acid in brain
  - The accumulation acceleration continues through to 2nd year of life<sup>(1, 2)</sup>

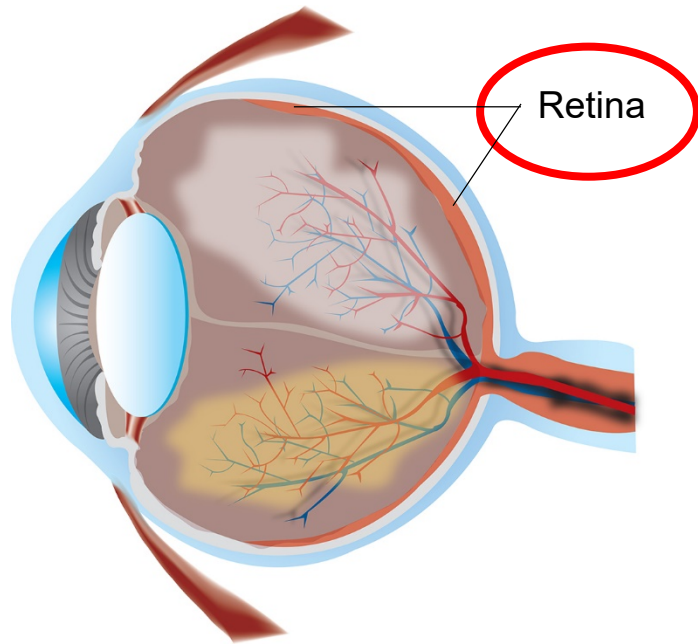


- DHA is a structural building block of cell membranes in the brain
  - The accumulation acceleration continues through to 2nd year of life<sup>(1, 2)</sup>

1. Martinez M., 1992  
2. Clandinin et al., 1980  
3. McCormick D., 1993  
4. FAO 2010

# DHA and eye

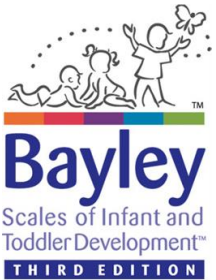
- DHA is a predominant fatty acid in the retina<sup>(1)</sup>



- ~50% of all fatty acids in retina - photoreceptor cells is DHA<sup>(2)</sup>
- In the retina DHA accumulation is essential for maturation & optimal visual function<sup>(1)</sup>

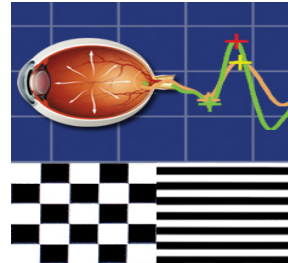
1. Lien & Hammond 2011  
2. Anderson et al., 1974

# Scientific evidence on DHA



- Clinically DHA has been demonstrated to impact both brain and visual functions<sup>(1-7)</sup>

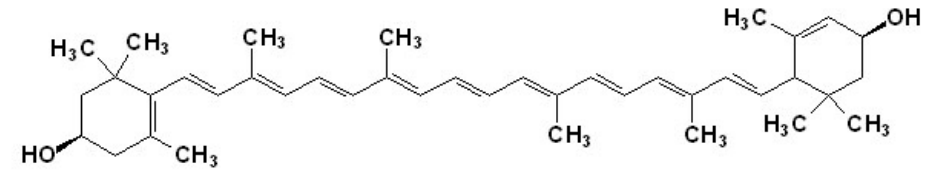
**Visual Evoked Potential**  
measures the activity of the  
visual system



DHA is regarded as conditionally essential, especially early in life, due to the low ability in humans to convert it's precursor alpha-linolenic acid to DHA<sup>(8, 9)</sup>

1. Hoffman et al., 2000; 2. Guesnet et al., 2011; 3. EFSA 2009; 4. Birch et al., 2010; 5. Birch et al., 2011; 6. Drover et al., 2011; 7. Birch et al., 2000; 8. FAO 2010; 9. Pawlosky et al., 2001 .

# Lutein in breast milk



- Breast milk levels have been shown to be dependent on maternal dietary intake<sup>(1)</sup>

Country	Breast milk levels ug/L
Mexico	36.1 ± 17.6
Philippines	15.4 ± 14.6
Oman	29.0 ± 18.9
All countries	25.2 ± 18.9

- Lutein is a carotenoid that plays an important role as an antioxidant<sup>(2-4)</sup>

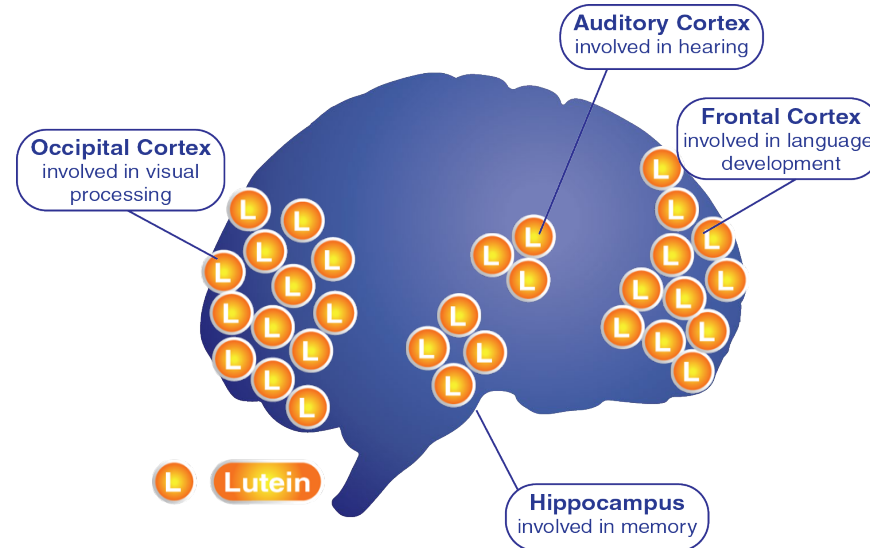
1. Pramuk et al., 2010

2. Johnson E., 2002

3. Winkler et al., 1999

4. Alves-Rodrigues &amp; Shao 2004

# Lutein and brain

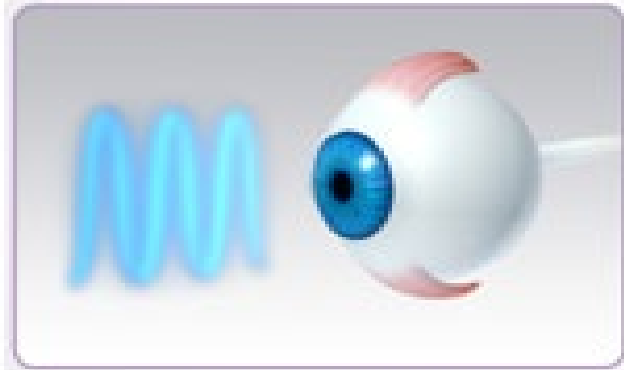


- Lutein is a major carotenoid found in the brain<sup>(1)</sup>
- In infants its been isolated from brain regions associated with cognition<sup>(2, 3)</sup>

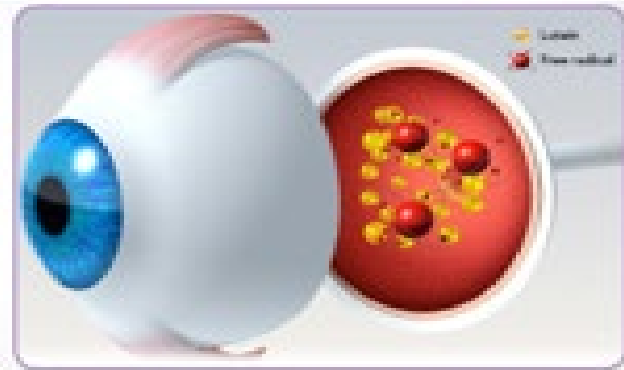
1. Craft et al., 2004  
2. Vishwanathan et al., 2011  
3. Vishwanathan et al., 2014



# Lutein and eye



Absorb potential damaging light



Lutein protect against oxidation

- Highly accumulated in the inner retina known to protect the eye from harmful light<sup>(1)</sup>
- Found in these high lipids areas, as an antioxidant it's been suggested to protect these areas against oxidative stress<sup>(1)</sup>

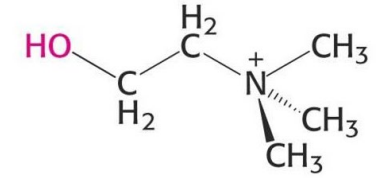
1. Snodderly D., 1995

# Scientific evidence on lutein

- Early in life mode of feeding may influence lutein bioavailability, whereby at least about ~4 times more lutein has to be in formula as compared to mean levels in breast milk to support similar infant plasma levels<sup>(1)</sup>
- In young adults 18-25yrs lutein mix supplementation resulted in increased macular pigment optical density and visual performance<sup>(2)</sup>
- In subjects  $\geq 50$  yrs, lutein composition in neural tissue and macular pigment had a positively correlated with cognitive function<sup>(3-6)</sup>

1. Bettelr et al., 2010; 2. Stringham et al., 2017; 3. Johnson et al., 2013.; 4. Vishwanathan et al., 2014; 5. Feeney et al., 2013; 6. Renzi et al., 2014;

# Choline in breast milk



- Human milk levels have been reported to range with a mean estimated to be 160 mg/L<sup>(1, 2)</sup>

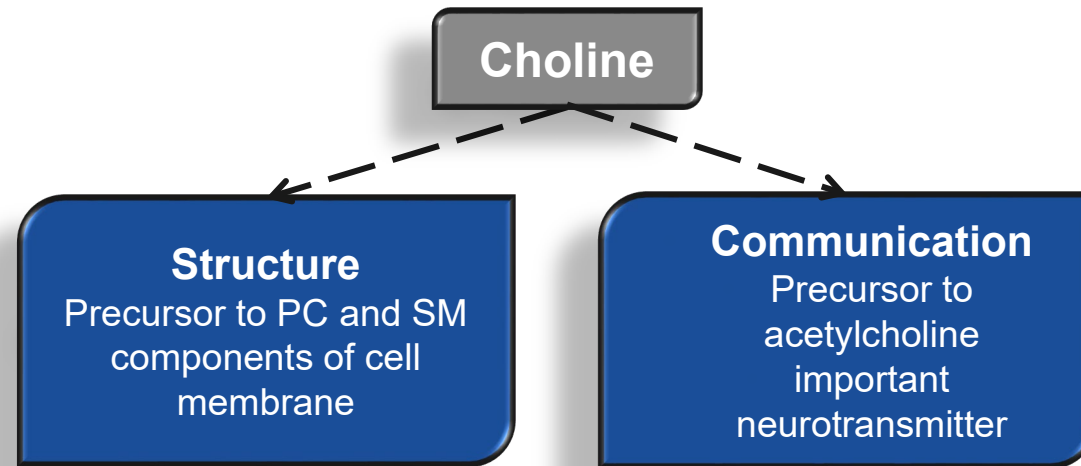
Human milk Sample	n	Total Choline $\mu\text{mol/L}$	Total Choline mg/L
Colostrum (0- 2 days)	21	676 $\pm$ 35	70.42 $\pm$ 3.64
Mature milk			
12 – 180 days	95	1476 $\pm$ 48	153.75 $\pm$ 5
12 – 28 days	14	1595 $\pm$ 82	166.15 $\pm$ 8.54
75 – 90 days	12	1441 $\pm$ 84	150.12 $\pm$ 8.75
165 – 180 days	11	1349 $\pm$ 105	140.53 $\pm$ 10.94

- A water soluble vitamin with 3 main physiological functions, cell structure integrity, signaling role and a major methyl donor for methylation one of the key driver for biological reactions in the body<sup>(3, 4)</sup>

1. IOM 1998; 2. Ilcol et al., 2005; 3. Zeisel S., 2000; 4. Glier et al., 2014

# Choline and brain

- Within the brain choline can be found incorporated into phosphatidylcholine (PC) and sphingomyelin (SM) which are components of cell membranes
- Choline is a precursor to acetylcholine a neurotransmitter, that travels across the synapse transmitting signals between neurons



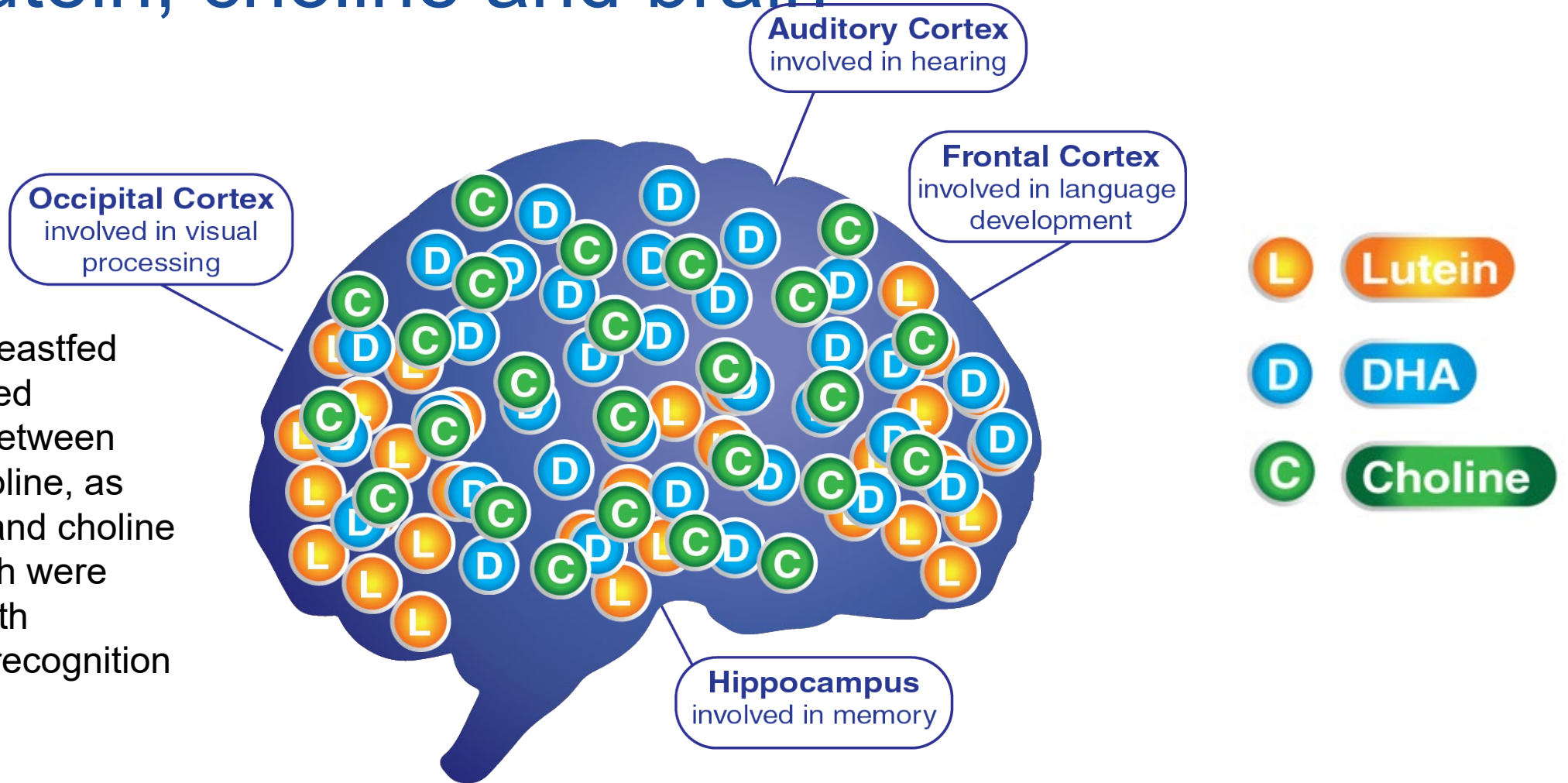
# Scientific evidence on choline

- Maternal choline status in the first half of pregnancy has been associated with later cognitive development in healthy term-born infants<sup>(1)</sup>
- In toddlers, plasma betaine concentration (a product of choline oxidation) was positively associated with better visual-motor development<sup>(2)</sup>
- In adult and aged population cohort choline intake was related to better cognitive performance<sup>(3,4)</sup>

1. Wu et al., 2012  
2. Wiedeman et al., 2018  
3. Poly et al., 2011  
4. Nurk et al., 2013

# DHA, lutein, choline and brain

- A cohort of breastfed babies reported interactions between lutein and choline, as well as DHA and choline - both of which were associated with measures of recognition memory <sup>(1)</sup>



1. Cheatham & Sheppard 2015.

Adequate & balanced nutrition is critical to support rapid brain growth, development and long term cognitive abilities

DHA support brain/eye development and functional outcomes

Lutein an antioxidant protects both the brain and the eye

Choline a component of PLs vital for cell membrane and has a role in cell signaling, facilitating memory

**DHA, lutein, and choline are found in the brain and may work in complement/together to support its development and function, both of which are vital for learning**

# References

- Alves-Rodrigues A, Shao A. The science behind lutein. *Toxicology Letters*. 2004;150:57–83.
- Anderson RE, Benolken RM, et al. Proceedings: Polyunsaturated fatty acids of photoreceptor membranes. *Exp Eye Res*. 1974;18(3):205-213
- Birch E, Carlson S, Hoffman D, et al. The DIAMOND (DHA Intake And Measurement Of Neural Development) Study: a double-masked, randomized controlled clinical trial of the maturation of infant visual acuity as a function of the dietary level of docosahexaenoic acid. *Am J Clin Nutr*. 2010;91(4):848-859.
- Birch E, Castañeda Y, Wheaton D, et al. Visual maturation of term infants fed long chain polyunsaturated fatty acid supplemented or control formula for 12 mo. *Am J Clin Nutr*. 2005;81(4):871-879.
- Birch E, Garfield S, Hoffman D, et al. A randomized controlled trial of early dietary supply of long chain polyunsaturated fatty acids and mental development in term infants. *Dev Med Child Neurol*. 2000;42(3):174-181.
- Birch E, Hoffman D, Uauy R, et al. Visual acuity and the essentiality of docosahexaenoic acid and arachidonic acid in the diet of term infants. *Pediatr Res*. 1998;44(2):201-209.
- Birch E, Garfield S, Castañeda Y, et al. "Visual acuity and cognitive outcomes at 4 years of age in a double-blind, randomized trial of long-chain polyunsaturated fatty acid-supplemented infant formula. *Early Hum Dev*. 2007;83(5):279-284.
- Blokland A. Acetylcholine: a neurotransmitter for learning and memory? *Brain Research Reviews*. 1996;21:285-300
- Brenna J, Varamini B, Jensen R., et al. Docosahexaenoic and arachidonic acid concentrations in human breast milk worldwide. *Am J Clin Nutr*. 2007;85:1457–64.
- Carlson SE. Docosahexaenoic acid supplementation in pregnancy and lactation. *Am J Clin Nutr*. 2009;89(suppl):678S-84S.
- Cheatham C, Sheppard K, Synergistic Effects of Human Milk Nutrients in the Support of Infant Recognition Memory: An Observational Study. *Nutrients*. 2015;7:9079–9095.
- Clandinin MT, Chappell JE, Leong S, Heim T, Swyer PR, Chance GW. Extrauterine fatty acid accretion in infant brain: implications for fatty acid requirements. *Early Hum Dev*. 1980;4(2):131-138.
- Craft N, Haitema T, Garnett K, et al. Carotenoid, tocopherol, and retinol concentrations in elderly human brain. *J Nutr Health Aging*. 2004;8(3):156-62.
- Drover J, Hoffman D, Castañeda Y, et al. Cognitive function in 18-month-old term infants of the DIAMOND study: a randomized, controlled clinical trial with multiple dietary levels of docosahexaenoic acid. *Early Hum Dev*. 2011;87(3):223-230.
- EFSA. DHA and ARA and visual development. Scientific substantiation of a health claim related to docosahexaenoic acid (DHA) and arachidonic acid (ARA) and visual development pursuant to Article 14 of Regulation (EC) No 1924/2006. *The EFSA Journal*. 2009;941:1-14.
- EFSA. Scientific Opinion on Dietary Reference Values for fats, including saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, trans fatty acids, and cholesterol. *EFSA Journal*. 2010;8:1461-1568.
- FAO. Fats and Fatty Acids in Human Nutrition. Rome. Food and Agriculture Organization, WHO. 2010;ISSN 0254-4725.
- Feeney J, Finucane C, Savva G, et al. Low macular pigment optical density is associated with lower cognitive performance in a large, population-based sample of older adults. *Neurobiol Aging*. 2013;34:2449–2456
- Glier M, Green T, Devlin A. Methyl nutrients, DNA methylation, and cardiovascular disease. *Mol Nutr Food Res*. 2013;00:1–11.
- Guesnet P, Alessandri J. Docosahexaenoic acid (DHA) and the developing central nervous system (CNS) e Implications for dietary recommendations. *Biochimie*. 2011;93:7-12.
- Hoffman DR1, Birch EE, Birch DG, et al. Impact of early dietary intake and blood lipid composition of long-chain polyunsaturated fatty acids on later visual development. *JPGN*. 2000;31(5):540-553.
- Ilcol Y, Ozbek R, Hamurtekin E, Ulus I. Choline status in newborns, infants, children, breast-feeding women, breast-fed infants and human breast milk. *J Nutr Biochem*. 2005;16(8):489-499..
- Innis SM. Dietary (n-3) Fatty Acids and Brain Development. *J Nutr*. 2007;137:855-9.



# References

- IOM. Choline. Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline Washington DC, National Academy Press: 1998;390-422.
- Johnson E. The Role of Carotenoids in Human Health. *Nutrition in Clin Care*. 2002;5(2):56-65.
- Johnson E, Vishwanathan R, Johnson M, et al. Relationship between serum and brain carotenoids,  $\alpha$ -tocopherol, and retinol concentrations and cognitive performance in the oldest old from the Georgia Centenarian Study. *J Aging Res*. 2013;2013:951786
- Lien EL, Hammond BR. Nutritional influences on visual development and function. *Prog Retin Eye Res*. 2011;30(3):188-203.
- Martinez M. Tissue levels of polyunsaturated fatty acids during early human development. *J Pediatr*. 1992;120(4 Pt 2):S129-138.
- McCormick D. The Meaning of Nutritional Essentiality in Today's Context of Health and Disease. *Nutritional Essentiality: A Changing Paradigm*. Columbus, Abbott Laboratories. 1993;12:11-15.
- Nurk E, Refsum H, Bjelland I, et al. Plasma free choline, betaine and cognitive performance: The Hordaland health study. *Br J Nutr*. 2013;109:511–519.
- Pawlosky RJ, Hibbeln JR, et al. Physiological compartmental analysis of alpha-linolenic acid metabolism in adult humans. *J Lipid Res*. 2001;42(8):1257-1265;
- Poly C, Massaro JM, Seshadri S, et al. The relation of dietary choline to cognitive performance and white-matter hyperintensity in the Framingham Offspring Cohort.. *Am J Clin Nutr*. 2011;94(6):1584-91
- Pramuk K, Burgher A, Ramirez-Mayans JA, Montijo-Barrios E, Sablan B, Trabulsi J, Wali Y, DeRusso PA. Lutein concentrations in maternal diet, human milk and infant plasma in mothers-infant pairs: A multinational study. *Journal Compilation 2010 Blackwell Publishing Ltd, Child: care, health and development*. 2010;36 (Suppl. 1):87.
- Renzi L, Dengler M, Puente A, et al. Relationships between macular pigment optical density and cognitive function in unimpaired and mildly cognitively impaired older adults. *Neurobiol Aging*. 2014;35:1695–1699
- Snodderly D: Evidence for protection against age-related macular degeneration by carotenoids and antioxidant vitamins. *Am J Clin Nutr*. 1995;62(6 suppl.):1448S-1461S.
- Stringham JM, Stringham NT, O'Brien KJ. Macular Carotenoid Supplementation Improves Visual Performance, Sleep Quality, and Adverse Physical Symptoms in Those with High Screen Time Exposure. *Foods*. 2017;6(7). pii: E47.
- Vishwanathan R, Kuchan M, Johnson E. Lutein is the predominant carotenoid in the infant brain. 16th International Symposium on Carotenoids. 2011. Krakow, Poland. [http://www.ib.uj.edu.pl/abc/pdf/suppl53\\_1/sup\\_53\\_s1.pdf](http://www.ib.uj.edu.pl/abc/pdf/suppl53_1/sup_53_s1.pdf).
- Vishwanathan R, Kuchan MJ, Sen S, Johnson EJ. Lutein and preterm infants with decreased concentrations of brain carotenoids. *J Pediatr Gastroenterol Nutr*. 2014;59(5):659-65.
- Renzi L, Dengler M, Puente A, et al. Relationships between macular pigment optical density and cognitive function in unimpaired and mildly cognitively impaired older adults. *Neurobiol Aging*. 2014;35:1695–1699
- Wiedeman AM, Chau CMY, Grunau RE et al. Plasma Betaine Is Positively Associated with Developmental Outcomes in Healthy Toddlers at Age 2 Years Who Are Not Meeting the Recommended Adequate Intake for Dietary Choline.. *J Nutr*. 2018;148(8):1309-1314.
- Winkler BS, Boulton ME, Gottsch JD, Sternberg P. Oxidative damage and age-related macular degeneration. *Mol Vis*. 1999;5:32.
- Yuhas R, Pramuk K et al. Human milk fatty acid composition from nine countries varies most in DHA. *Lipids*. 2006;41(9):851-858.
- Zeisel S. Choline: Needed for Normal Development of Memory. *Journal of the American College of Nutrition*. 2000;19(5):528S–531S.
- Zeisel S. The fetal origins of memory: The role of dietary choline in optimal brain development. *The Journal of Pediatrics*. 2006;149(5):S131-S136.

A doctor in a white coat with a stethoscope, holding a smartphone and a pen, with a network overlay.

THANK YOU