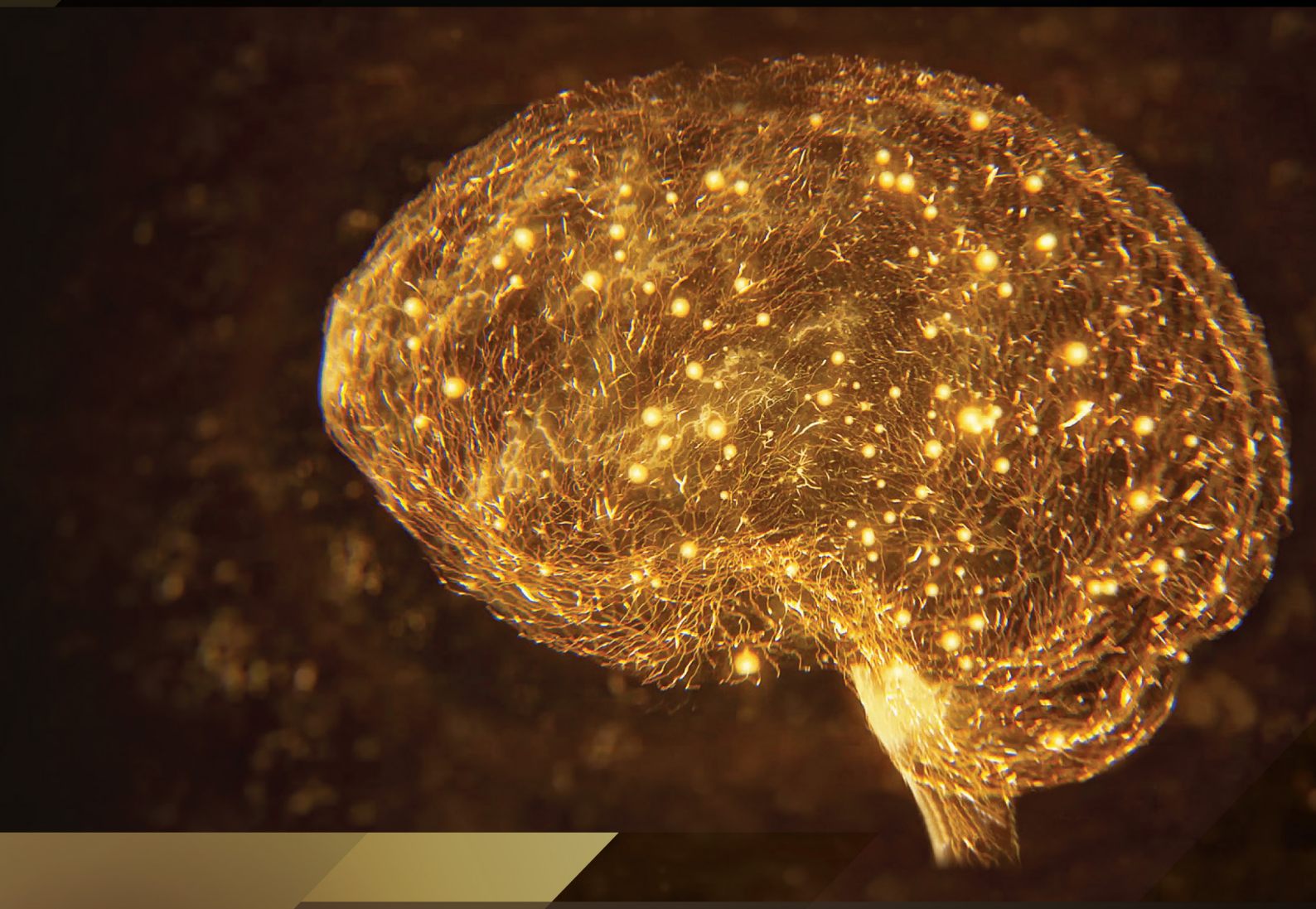
Wyeth® | Nutrition
SCIENCE CENTER



BRIDGING THE GAP:
Optimizing Early Neurodevelopment Through Nutrition

The first 1,000 days of life is a period regarded to be a unique opportunity in child development when foundations of optimum health, cognitive function, emotional health, and lifelong trajectories are set.[1] This window of time, spanning from conception to the second year of life, is particularly sensitive to the influence of nutrition, with early nutrient deficiencies potentially leading to lasting adverse outcomes, including cognitive impairments and increased susceptibility to chronic diseases later in life. Understanding the intricate ways by which specific nutrients influence brain development in young children offers a valuable opportunity to optimize these complex processes through targeted and informed nutritional strategies.[2] Three specific nutrients that have been well-studied for their role in brain development are docosahexaenoic acid (DHA), choline, and lutein. Each plays a distinct role in shaping brain architecture, cognitive function, and visual acuity, highlighting the intricate and multifaceted nature of nutrient influences on early neurodevelopment.

DHA

This omega-3 fatty acid plays a major role in the development of the brain and retina during fetal development and the first two years of life.[3] It accumulates in the grey matter of the brain and in the rod outer segments of the retina.[4] Research suggests that DHA supplementation of infant formula at 0.32% of total fatty acids is optimum, leading to enhanced cognitive development at 18 months of age and improved visual acuity.[5,6]

Choline

This vital precursor plays a central role in the function and structure of membranes, including their signaling, transport, and repair.[7]

Choline is required for the synthesis of acetylcholine, a brain neurotransmitter that fuels learning, memory and information processing speed in infants.[8,9] Evidence suggests that choline supplementation during pregnancy improves infant attention and information processing speed.[9,10]

Lutein

This potent carotenoid is an important nutrient for eye development and function. It protects developing eyes by reducing oxidative stress and inflammation.[11]

Its accumulation in key brain regions critical for cognitive functions, such as the hippocampus, suggests a potential role in enhancing memory, learning, and overall processing abilities.[12] Moreover, lutein is also concentrated in the occipital cortex, the brain region dedicated to visual processing.[13]

Real-world evidence: Synergy in action

Studies demonstrate that these nutrients work synergistically to support and optimize early brain development. For instance, evidence from an observational study of breastfed infants suggests that interactions between DHA, choline, and lutein impact infant cognition.[14] Milk samples obtained three to four months postpartum were analyzed for fatty acids, lutein, and choline. At six months, participants underwent an electrophysiology session that tested recognition memory with a 70–30 oddball paradigm in a high-density 128-lead event-related potential (ERP) paradigm. Data on the latency to peak, peak amplitude, and mean amplitude were measured on six different areas of the brain: frontal right, frontal central, frontal left, central, midline, and parietal. Results showed that associations between nutrient combinations, i.e., higher choline levels with higher lutein levels (**Figure 1**), as well as higher choline with higher DHA choline levels (**Figure 2**), were associated with better recognition memory at six months.

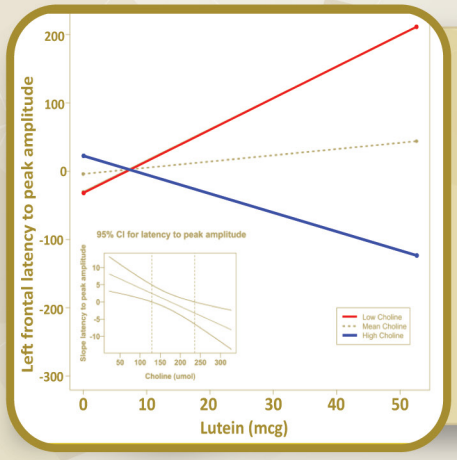


Figure 1. Simple slopes model of **lutein by choline** interaction for **latency to peak amplitude** at the **left frontal area**. The figure depicts the effect of lutein at high, mean and low levels of choline. The figures depict the effect of lutein and DHA at high, mean and low levels of choline. Low choline was defined as 1 SD below the mean, and high choline was defined as 1 SD above the mean. Sample sizes for each group were as follows: low choline, n = 9; mean choline, n = 41; and high choline, n = 10.

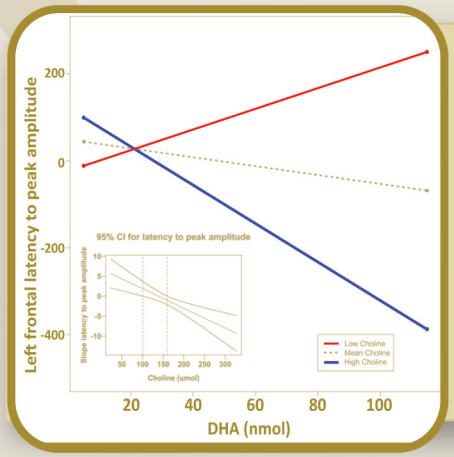


Figure 2. Simple slopes model of **DHA by choline** interaction for **latency to peak amplitude** at the **left frontal area**. The figure depicts the effect of DHA at high, mean, and low levels of choline. Low choline was defined as 1 SD below the mean, and high choline was defined as 1 SD above the mean. Sample sizes for each group were as follows: low choline, n = 9; mean choline, n = 41; and high choline, n = 10.

The embedded graphs show the 95% CIs for the slope of the latency to peak amplitude at left frontal sensors. Latency to peak amplitude is interpreted as a measure of sustained attention. The slope outside the dotted lines is significant. Negative numbers are indicative of better recognition.

CI: Confidence Interval; DHA: Docosahexaenoic Acid; SD: Standard Deviation. Adapted from Cheatham CL, Sheppard KW. 2015

Similarly, the benefits of higher concurrent intakes of DHA, choline and lutein in optimizing cognitive development were also demonstrated in an observational study of school-aged children (median age, 5.8 years).[15] The study showed that children who consumed higher levels of all three nutrients (DHA, choline, and lutein) had better short-term memory and general mental processing abilities compared with children with lower intakes of all three nutrients. The study also found that children who consumed higher levels of DHA and choline had better general mental processing abilities. These findings provide evidence that dietary intake of DHA, choline, and lutein is associated with better cognitive function in children.

The table below shows the current dietary recommendations for these nutrients in young children.

Nutrient	Recommended dietary intake (RDI)
DHA[16]	6-24 months: 10-12 mg/kg body weight 2-4 years old: 100-150 mg/day* 4-6 years old: 150-200 mg/day* 6-10 years old: 200-250 mg/day*
Choline[17]	7-12 months: 150 mg/day 1-3 years old: 200 mg/day 4-8 years old: 250 mg/day
Lutein	No recommended daily intake for lutein**

**DHA+EPA*

*****There are currently no RDIs for lutein specifically for children. However, studies suggest intakes of 200-600 mcg/-day for children aged 4-10 years may be beneficial for cognitive development and visual health.[11,14]***

Bridging the Gap

Despite compelling evidence, average intakes of these vital nutrients often fall short of recommended levels in children.[18,19,20,21] Empowering families by equipping parents and caregivers with knowledge about nutrient-rich foods and appropriate supplementation strategies, particularly during critical periods (pregnancy, infancy, and early childhood), can create a supportive environment for optimal early nutrition.

Conclusions

Establishing optimal nutrition in the critical early years of life lays the groundwork for unlocking children's future cognitive potential. Understanding the profound impact of nutrition on early neurodevelopment empowers healthcare professionals, parents, and caregivers to advocate for and adopt effective nutritional interventions. By communicating the intricate interplay between nutrition and developmental processes during this crucial "window of opportunity", professionals can guide parents and caregivers toward informed choices that can positively influence their child's cognitive development and overall well-being.

What is new? Take Home Message

Understanding the intricate ways by which specific nutrients influence brain development in young children offers a valuable opportunity to optimize these complex processes through targeted and informed nutritional strategies.[2]

- **Three specific nutrients – docosahexaenoic acid (DHA), choline, and lutein – have been well-studied for their role in brain development. Each plays a distinct role in shaping brain architecture, cognitive function, and visual acuity.**

- **Studies demonstrate that these nutrients synergistically support and optimize early brain development. Evidence from an observational study of breastfed infants suggests that associations between nutrient combinations, i.e., higher choline levels with higher lutein levels, as well as higher choline with higher DHA choline levels, were associated with better recognition memory at 6 months.[14]**

- **The benefits of higher concurrent intakes of DHA, choline and lutein in optimizing cognitive development were also demonstrated in school-aged children (median age, 5.8 years).[15] Children who consumed higher levels of all three nutrients (DHA, choline, and lutein) had better short-term memory and general mental processing abilities compared with children with lower intakes of all three nutrients.**

References

1. UNICEF. The first 1,000 days of life: The brain's window of opportunity. Available at: https://www.unicef-irc.org/article/958-the-first-1000-days-of-life-the-brains-window-of-opportunity.html. Accessed February 2024.
2. Georgieff MK, Ramel SE, Cusick SE. Nutritional influences on brain development. Acta Paediatr. 2018;107(8):1310-1321.
3. Martinez M. Tissue levels of polyunsaturated fatty acids during early human development. J Pediatr. 1992;120(4 Pt 2):S129-S138.
4. Calder PC. Docosahexaenoic Acid. Ann Nutr Metab. 2016;69 Suppl 1:7-21.
5. Birch EE, Carlson SE, Hoffman DR, 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.
6. Drover JR, Hoffman DR, Castañeda YS, 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.
7. Derbyshire E, Obeid R. Choline, Neurological Development and Brain Function: A Systematic Review Focusing on the First 1000 Days. Nutrients. 2020;12(6):1731.
8. Zeisel SH, Niculescu MD. Perinatal choline influences brain structure and function. Nutr Rev. 2006;64(4):197-203.
9. Caudill MA, Strupp BJ, Muscalu L, Nevins JEH, Canfield RL. Maternal choline supplementation during the third trimester of pregnancy improves infant information processing speed: a randomized, double-blind, controlled feeding study. FASEB J. 2018;32(4):2172-2180.
10. Bahnfleth CL, Strupp BJ, Caudill MA, Canfield RL. Prenatal choline supplementation improves child sustained attention: A 7-year follow-up of a randomized controlled feeding trial. FASEB J. 2022;36(1):e22054.
11. Alves-Rodrigues A, Shao A. The science behind lutein. Toxicol Lett. 2004;150(1):57-83.
12. 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):659-665.
13. Gazzolo D, Picone S, Gaiero A, et al. Early Pediatric Benefit of Lutein for Maturing Eyes and Brain-An Overview. Nutrients. 2021;13(9):3239.
14. Cheatham CL, Sheppard KW. Synergistic Effects of Human Milk Nutrients in the Support of Infant Recognition Memory: An Observational Study. Nutrients. 2015;7(11):9079-9095.
15. Mulder K, Wiedeman A, Yan J, et al. Docosahexaenoic Acid, Choline and Lutein Intakes are Associated with Cognitive Performance in School-aged Children. In: Excellence in Pediatrics (2016) 8th Excellence in Pediatrics Conference - 2016 Book of Abstracts, Cogent Medicine, 3:1. ID: 116 / OP4: 1
16. Food and Agriculture Organization of the United Nations (2010). Fats and fatty acids in human nutrition: Report of an expert consultation. FAO Food and Nutrition Paper 91. Rome. Available at: http://www.fao.org/docrep/013/i1953e/i1953e00.pdf. Accessed January 2024.
17. Institute of Medicine. Food and Nutrition Board. Dietary Reference Intakes: Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline. Washington, DC: National Academy Press; 1998.
18. Forsyth S, Gautier S, Salem N. Estimated Dietary Intakes of Arachidonic Acid and Docosahexaenoic Acid in Infants and Young Children Living in Developing Countries. Annals of Nutrition and Metabolism. 2016;69(1):64-74.
19. Vennemann FB, Ioannidou S, Valsta LM, et al. Dietary intake and food sources of choline in European populations. Br J Nutr. 2015;114(12):2046-55.
20. Wallace TC, Fulgoni VL. Assessment of Total Choline Intakes in the United States. J Am Coll Nutr. 2016;35(2):108-12
21. Stringham JM, Johnson EJ, Hammond BR. Lutein across the Lifespan: From Childhood Cognitive Performance to the Aging Eye and Brain. Curr Dev Nutr. 2019;3(7):nzz066.

Wyeth® | Nutrition
SCIENCE CENTER

To learn more about the
Wyeth Nutrition resources, visit:
www.singapore.wyethnutritionsc.org

This material is for medical professionals only
Wyeth Nutrition (Singapore) Pte Ltd
15A Changi Business Park Central 1
#05-02/03 Eightrium @ Changi Business Park, Singapore 486035