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# Specific breast milk nutrients may work together to influence cognitive abilities of 6-month-old infants

*Possible mechanism of action based on literature data is also explored*

**A research team led by Professor Carol Cheatham from the University of North Carolina at Chapel Hill's Nutrition Research Institute conducted an observational cohort study of breastfeeding dyads.**

Breast milk concentrations of DHA, choline, and lutein were analyzed when infants were 3-4 months of age. Recognition memory was measured by event-related potential (ERP)^ test when infants were 6 months of age. Key preliminary findings were (i) higher DHA levels with higher choline levels in breast milk were related to better recognition memory, and (ii) higher choline levels with higher lutein levels in breast milk were related to better recognition memory. The authors concluded that "interactions between human milk nutrients appear important in predicting infant cognition, and there may be benefit associated with specific nutrient combinations". (*See citation on page 2*)

These preliminary results are thought to be the first of its kind to indicate specific breast milk nutrients may work together to influence cognitive abilities of young infants. Although the observational nature of the study could not establish causality, existing literature data support these findings.

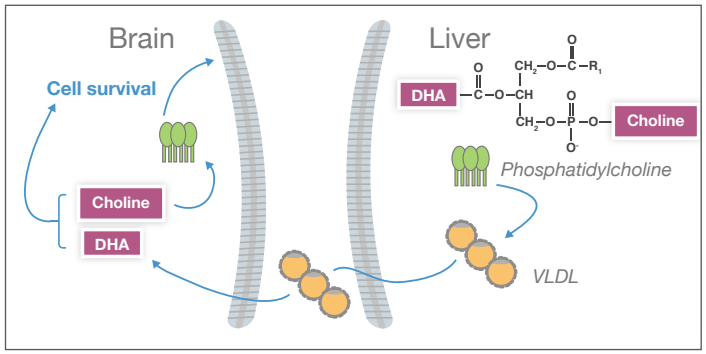
## Existing data on DHA, choline and lutein in relation to brain development

- **DHA**, an omega-3 long-chain polyunsaturated fatty acid that is found in high concentrations in fetal and infant eye and brain[1], plays a critical role in normal retinal and brain development in infants and toddlers[2]. Research has demonstrated that DHA has a positive impact on visual acuity[3] and improves cognitive outcomes[4] during early stages of development.
- **Choline**, an essential nutrient found in breast milk, is a precursor to acetylcholine, an important brain neurotransmitter[5] and a constituent of metabolites (phosphatidylcholine) needed for cell division and cell growth for the structural integrity and cell signaling function of cell membranes[6].
- **Lutein**, a predominant carotenoid in the brain and eye, has antioxidant roles that protect the retina from oxidative stress and shields the eye from blue light damage through the accumulation of yellow pigment in the macula[7]. More recently, lutein has been found to be present in 5 regions of the infant brain relating to learning and memory[8].

^ERP is a painless method using a net of electrodes to read the electrical impulses in the brain while the child looks at a series of familiar and novel pictures. It is a method to determine recognition memory, how well children remember a picture, by monitoring brain activity.

## Possible mechanisms underlying cohort study findings based on literature data

**Figure 1: Possible mechanism for how DHA and choline may work together†**




† Figure 1 is for illustration purposes and is not part of the findings from the cohort study.

Choline may facilitate brain uptake of DHA. Specifically, phosphatidylcholine is a choline metabolite containing choline and fatty acids, such as DHA[9]. In the liver, phosphatidylcholine is needed in the synthesis of very-low-density lipoprotein (VLDL), which transports lipids out of the liver. Thus, phosphatidylcholine facilitates the hepatic export of DHA and choline so that they become available for extra-hepatic tissues such as the brain[10-13]. In the brain, DHA and choline may further work together to impact brain function because (i) they are components of cell membrane, and (ii) they influence neuron survival and death[14-16].

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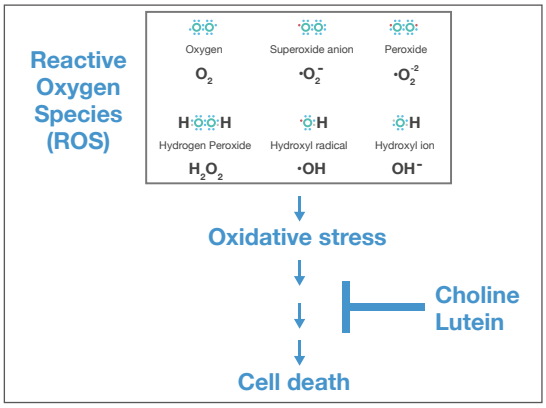
**Figure 2: Possible mechanism for how choline and lutein may work together†**




† Figure 2 is for illustration purposes and is not part of the findings from the cohort study.

Both choline and lutein have anti-oxidant properties. Reactive oxygen species (ROS) are active chemicals produced during oxygen metabolism in metabolic active tissues such as the brain. Too much of ROS would lead to Oxidative Stress which is harmful to neurons and has been linked to neural degeneration[17]. Choline and lutein have anti-oxidant properties and could influence oxidative stress as well as cell survival and death[7,15,18-20]. Therefore, choline and lutein may work together to impact brain functions via their combined anti-oxidant effects.

## KEY TAKEAWAYS

- There is scientific evidence suggesting that DHA, choline and lutein play important roles in the infant's brain development.
- In an observational study of breast milk nutrients, the results report that specific breast milk nutrients work together to positively influence cognitive abilities of young infants. More data is needed to better understand these findings.
- Possible mechanisms based on literature data may explain the influence of specific nutrient combinations on cognitive performance from the cohort study.

**Citation: Cheatham CL, Sheppard KW. Synergistic Effects of Human Milk Nutrients in the Support of Infant Recognition Memory: An Observational Study. Nutrients 2015, 7, 9079-9095; doi10,3390.nu7115452.**

**References: 1.** Martinez. Tissue levels of polyunsaturated fatty acids during early human development. J Pediatr.1992;120 (4Pt 2):S129-38. **2.** Food and Agriculture Organization of the United Nations. Fats and fatty acids in human nutrition: report of an expert consultation. *Food and Nutrition Paper* 91, 2010. Accessed September 11, 2015 at http://www.fao.org/3/a-i1953e.pdf. **3.** Birch, et al. The DIAMOND Study: a double-masked, randomized controlled clinical trial of the maturation of infant visual acuity as a function of the dietary level of DHA. *AJCN.* 2010;91(4):848-859. **4.** Drover, et al. Cognitive function in 18-month-old term infants of the DIAMOND study: a randomized, controlled clinical trial with multiple dietary levels of DHA. *Early Hum Dev.* 2011;87(3):223-230. **5.** Anderson, et al. Proceedings: Polyunsaturated fatty acids of photo receptor membranes. *Exp Eye Res.* 1974;18(3):205-213. **6.** Zeisel. Nutritional importance of choline for brain development. *AJCN.* 2004;23(6):S621-S626. **7.** Alves-Rodrigues, et al. The science behind lutein. HYPERLINK "http://www.ncbi.nlm.nih.gov/pubmed/15068825" Toxicol Lett. 2004;150(1): 57-83. **8.** Vishwanathan et al. Lutein and preterm infants with decreased concentration of brain carotenoids. *JPGN.* 2014;59:659-665. **9.** DeLong, et al. Molecular distinction of phosphatidylcholine synthesis between the CDP-choline pathway and phosphatidylethanolamine methylation pathway. *J Biol Chem.* 1999;274:29683–29688. **10.** Watkins, et al. Phosphatidylethanolamine-N-methyltransferase activity and dietary choline regulate liver-plasma lipid flux and essential fatty acid metabolism in mice. *J Nutr.* 2003;133:3386–3391. **11.** Li, et al. Choline redistribution during adaptation to choline deprivation. *J Biol Chem.* 2007;282:10283–10289. **12.** West, et al. Choline intake influences phosphatidylcholine DHA enrichment in nonpregnant women but not in pregnant women in the third trimester. *AJCN.* 2013;97(4):718-727. **13.** Yan, et al. Maternal choline supplementation programs greater activity of the phosphatidylethanolamine N-methyltransferase (PEMT) pathway in adult Ts65Dn trisomic mice. *The FASEB J.* 2014;28(10):4312-4323. **14.** Wurtman. Synapse formation and cognitive brain development: effect of docosahexaenoic acid and other dietary constituents. *Metabolism.* 2008;57:S6–S10. **15.** Craciunescu, et al. Choline availability during embryonic development alters progenitor cell mitosis in developing mouse hippocampus. *J Nutr.* 2003;133(11):3614-3618. **16.** Bazan, et al. Docosahexaenoic acid signalolipidomics in nutrition: significance in aging, neuroinflammation, macular degeneration, alzheimer's, and other neurodegenerative diseases. *Annu Rev Nutr.* 2011;31:321–51. **17.** Götz, et al. Oxidative stress: free radical production in neural degeneration. HYPERLINK "http://www.ncbi.nlm.nih.gov/pubmed/7972344" *Pharmacol Ther.* 1994;63(1):37-122. **18.** Arnal, et al. Lutein and docosahexaenoic acid prevent cortex lipid peroxidation in streptozotocin-induced diabetic rat cerebral cortex." *Neuroscience.* 2010;166(1):271-278. **19.** Sachan, et al. Decreasing oxidative stress with choline and carnitine in women. *AJCN.* 2005;24(3):172-176. **20.** Jiang, et al. Choline inadequacy impairs trophoblast function and vascularization in cultured human placental trophoblasts. HYPERLINK "http://www.ncbi.nlm.nih.gov/pubmed/?term=Choline+inadequacy+impairs+trophoblast+function+and+vascularization+in+cultured+human+placental+trophoblasts" *J Cell Physiol.* 2014; 229(8):1016-1027.