BOYBIO RESEARCH

Phospolipids & Aging

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> There must be a difference between senior citizens and old people. We've seen seniors jitterbug to beat the band. We've also seen fortyyear-olds act like zombies at the same party. It seems that "old" is a state of mind that fills in the spaces between the physiological changes that are mandatory in humans. Where these frailties become evident, mental changes may not be so. It's not that a person awakens one day to gray hair, faulty hearing and a bucketful of wrinkles, but corporeal differences are noticeable. Cerebral changes may be subtler and far less apparent, but just might be simpler to delay, too. Memory lapses are common to everyone, even teenagers, and thus do not merit worry. And though dementia may be common with age, it need not take center stage in the absence of outright disease state, such as ALS or Parkinsonism. When asked to name their greatest fears, fewer people mention memory loss than do blindness (Giridhar, 2002).

> What is this memory of which we speak? What are its intricacies? First, it requires encoding, storage and retention, followed by recall. All this is expected to influence something happening right now. Without memory, it's difficult to adapt to new experiences. Some folks, as Samuel Clemens admitted, have such astounding talents that they can remember anything, whether it happened or not.

> Neurologically, memory is a set of encoded neural connections in the brain. For them to work the right way, the environment has to

be in good condition. That happens with a deliberate action that includes being a caretaker—fertilizing, watering, cultivating. The process of remembering is somewhat demanding. There needs to be the registration of a stimulus, meaning you must pay attention to cultivate long-term memory from short-term. That gets more detailed by distinguishing procedural from declarative function, the former requiring the recall of a skill, the latter needing recognition of a specific stimulus. Disuse of information, by the way, is a valid reason to forget, which is especially forgivable if that information is passé and now useless. Needless data can be repressed, too, when one image is replaced by another that is more pertinent.

Memory loss can be a mere annoyance or a serious impediment. In most instances, only when it interferes with everyday activities does it become a concern. Too, memory may fall to more than one gremlin, including medication, antihistamines, muscle relaxants, and pain relievers, among a few others. Sleep deprivation counts, as do substances that may deprive the brain of oxygen—alcohol, tobacco, drugs. The hormone imbalances that plague women near and at menopause may wreak havoc on memory function in varying degrees. If you find yourself increasingly forgetful, you might want to talk with your doctor to determine the cause.

Memory requires a nutritional base for its eventual expression, starting in utero. Not only is the mother's intake vital, but also is the neonate's continued intake, which directly affects brain development and results in permanent changes in cerebral function. The pure, unadulterated choline afforded by phosphatidylcholine (PC) enhances memory and learning throughout a lifetime. Conversely, deficiency delivers cognitive adversities. The bottom line of PC intake enlists DNA methylation, gene expression and alterations in stem cell proliferation and differentiation (Zeisel, 2006). Hippocampus development depends on it.

In modern times, dietary and environmental insults are more the norm than not, playing at least a small role in the burgeoning concerns of dementia incidence. Sadly, there is no reliable and promising drug to treat Alzheimer's dementia. If there be a ray of hope in this arena, it is that PC has been shown to enhance learning, memory and cognitive performance in both animals and people (Nishizakia, 2013), with an especially strong showing in the nutritionally impoverished (Teather, 2006). In laboratory animals whose senescence was accelerated by chemical interventions, those treated to a PC cocktail that included vitamin B12 exhibited stronger hippocampus and cellular energy transfer activity (via protein kinase C) than those deprived of the cocktail (Hung, 2001).

A little-heralded lipidomic approach to detecting early-onset dementia is the examination of red blood cell membrane integrity, wherein serum sphingomyelins and subsequent ceramides may offer a predictive character. Sphingomyelin may act as an insulator, effectively covering nerve fibers to maintain efficient electrical activity. As a signaling molecule it regulates muscle glucose uptake (Dobrzyn, 2004). Being hydrolyzed, sphingomyelin becomes a ceramide, then playing a role in apoptosis. At times, ceramides may signal, but are relegated to cell differentiation and proliferation, both processes important to life. Dermatologically, ceramides are components of the stratum corneum, the outermost layer of the skin, consisting of dead cells. Ceramides join with cholesterol and fatty acids on skin to make a protective layer that stops water loss by evaporation and prevents the entry of micro-organisms. In the cell membrane, however, they are not so beneficent...they portend neurological involvement and the possible incidence of Alzheimer's (Mielke, 2010, 2012). Dysregulation in PC and ceramide metabolism seem to happen in different stages of Alzheimer's progression, with deficits of PC a prominent finding associated with hippocampal atrophy (Kim, 2017).

Of late, it's been recognized that PC may gain more widespread support when ancillary fatty acids join the party. The omega-3 fat, DHA, has gathered primary interest. One of the strongest risk factors for Alzheimer's is the presence of the apolipoprotein E (APOE4) allele. Carriers of this gene have been found to respond favorably to a combination of this fatty acid and PC, despite that the mechanism is yet largely unexplained. Absolute DHA does not have the same effect as that which comes directly from fish or that which is combined with PC. This has led researchers at the U of CA to conclude that fish carry DHA in a phospholipid form, and that DHA united with PC is able to carry itself across the blood-brainbarrier (BBB) (Patrick, 2018). Of course, DHA is most commonly in the company of EPA. EPA is not to be discounted as a PC partner because it aids in the attenuation of beta-amyloid concentrations that are associated with Alzheimer's (Che, 2018).

For more than a couple decades fatty acids have been trumpeted as able to debase dementia risk. Where isolated EFA's have their place in any therapeutic application, their ratio is held to be more effective at bringing about a desirable outcome. Even in the last century, Dr. Shlomo Yehuda of Bar Ilan University in Haifa, Israel, found that an n-6:n-3 ratio of 4 to 1 yielded the most efficacious results in overall health and well-being, with defined improvements in mood, cooperation, appetite, sleep, and memory (Yehuda, 1996). Here, he named his EFA compound SR-3. Later study confirmed his initial findings, noting that dependence on the cell membrane fluidity rendered by fatty acids is the key to neuronal improvement. Rigidity of cellular membranes is but one conspicuous feature of aging (Yehuda, 2003), but is surmounted with SR-3 oils, today known as BodyBio Balance Oil, a carefully crafted blend of organic, non-GMO safflower and flaxseed oils to provide the n-6 and n-3 fatty acids, respectively. Studying pregnancy, Chinese scientists observed that ratios of n-6 to n- 3 as high as 6 to 1 benefit neurogenesis in the developing infant, and that excessive and/or isolated n-3 fats have a

negative effect on the child (Fan, 2015).

Evidence is growing that PC and fatty acids, even separated from each other, control risk for dementia. BodyBio PC and BodyBio Balance Oil provide the wherewithal. When combined, though, they present the awesome battery of a fireball pitcher and a masterful catcher.



RESOURCES

Che H, Zhou M , Zhang T , Zhang L , Ding L , Yanagita T , Xu J , Xue C , Wang Y . Comparative study of the effects of phosphatidylcholine rich in DHA and EPA on Alzheimer's disease and the possible mechanisms in CHO-APP/PS1 cells and SAMP8 mice. Food Funct. 2018 Jan 24;9(1):643-654.

Chung SY, Moriyama T, Uezu E, Uezu K, Hirata R, Yohena N, Masuda Y, Kokubu T, Yamamoto S.

Administration of phosphatidylcholine increases brain acetylcholine concentration and improves memory in mice with dementia. J Nutr. 1995 Jun;125(6):1484-9.

Cutler RG, Kelly J, Storie K, Pedersen WA, Tammara A, Hatanpaa K, Troncoso JC, Mattson MP. Involvement of oxidative stressinduced abnormalities in ceramide and cholesterol metabolism in brain aging and Alzheimer's disease. Proc Natl Acad Sci U S A. 2004 Feb 17;101(7):2070-5.

Dobrzyń A, Zendzian-Piotrowska M, Górski J. Effect of endurance training on the sphingomyelin-signalling pathway activity in the skeletal muscles of the rat. J Physiol Pharmacol. 2004 Jun;55(2):305-13.

Fan C, Sun W, Fu H, Dong H, Xia L, Lu Y, Deckelbaum RJ, Qi K. Dietary ratios of n-6/n-3 polyunsaturated fatty acids during maternal pregnancy affect hippocampal neurogenesis and apoptosis in mouse offspring. Nutr Hosp. 2015 Sep 1;32(3):1170-9

Giridhar P, Dandona R, Prasad MN, Kovai V, Dandona L. Fear of blindness and perceptions about blind people. The Andhra Pradesh Eye Disease Study. Indian J Ophthalmol. 2002 Sep;50(3):239-46.

Mei-Chu Hung, Koji Shibasakia, Riki Yoshida, Masao Sato and Katsumi Imaizumi Learning behaviour and cerebral protein kinase C, antioxidant status, lipid composition in senescenceaccelerated mouse: influence of a phosphatidylcholinevitamin B12 diet. British Journal of Nutrition. August 2001; 86(2): 163-171

Kim M, Nevado-Holgado A, Whiley L, Snowden SG, Soininen H, Kloszewska I, Mecocci P, et al. Association between Plasma Ceramides and Phosphatidylcholines and Hippocampal Brain Volume in Late Onset Alzheimer's Disease. J Alzheimers Dis. 2017;60(3):809-817

Loef M, Walach H. The omega-6/omega-3 ratio and dementia or cognitive decline: a systematic review on human studies and biological evidence. J Nutr Gerontol Geriatr. 2013;32(1):1-23.

Mielke MM, Bandaru VV, Haughey NJ, Rabins PV, Lyketsos CG, Carlson MC. Serum sphingomyelins and ceramides are early predictors of memory impairment. Neurobiol Aging. 2010 Jan;31(1):17-24.

Mielke MM, Haughey NJ, Bandaru VV, Weinberg DD, Darby E, Zaidi N, Pavlik V, Doody RS, Lyketsos CG. Plasma sphingomyelins are associated with cognitive progression in Alzheimer's disease.

J Alzheimers Dis. 2011;27(2):259-69.

Mielke MM, Bandaru VV, Haughey NJ, Xia J, Fried LP, Yasar S, Albert M, Varma V, Harris G, Schneider EB, Rabins PV, Bandeen-Roche K, Lyketsos CG, Carlson MC. Serum ceramides increase the risk of Alzheimer disease: the Women's Health and Aging Study II. Neurology. 2012 Aug 14;79(7):633-41.

Moriyama T, Uezu K, Matsumoto Y, Chung SY, Uezu E, Miyagi S, Uza M, Masuda Y, Kokubu T, Tanaka T, Yamamoto S. Effects of dietary phosphatidylcholine on memory in memory deficient mice with low brain acetylcholine concentration. Life Sci. 1996;58(6):PL111-8.

Teather LA, Wurtman RJ. Chronic administration of UMP ameliorates the impairment of hippocampal-dependent memory in impoverished rats. J Nutr. 2006 Nov;136(11):2834-7.

Tomoyuki Nishizakia, Takeshi Kannoa, Akinobu Gotohb DL-/ PO-phosphatidylcholine may shed light on the treatment of Alzheimer dementia Personalized Medicine Universe. Volume 2, July 2013, Pages 12–15

Patrick RP. Role of phosphatidylcholine-DHA in preventing APOE4-associated Alzheimer's disease. FASEB J. 2018 Oct 5:fj201801412R.

Satoi H, Tomimoto H, Ohtani R, Kitano T, Kondo T, Watanabe M, Oka N, Akiguchi I, Furuya S, Hirabayashi Y, Okazaki T. Astroglial expression of ceramide in Alzheimer's disease brains: a role during neuronal apoptosis. Neuroscience. 2005;130(3):657-66.

Yehuda S, Rabinovtz S, Carasso RL, Mostofsky DI. Essential fatty acids preparation (SR-3) improves Alzheimer's patients quality of life. Int J Neurosci. 1996 Nov;87(3-4):141-9.

Yehuda S, Rabinovitz S, Carasso RL, Mostofsky Dl. The role of polyunsaturated fatty acids in restoring the aging neuronal membrane. Neurobiol Aging. 2002 Sep-Oct;23(5):843-53.

Zeisel SH. The fetal origins of memory: the role of dietary choline in optimal brain development. J Pediatr. 2006 Nov;149(5 Suppl):S131-6.

Zhou MM, Xue Y, Sun SH, Wen M, Li ZJ, Xu J, Wang JF, Yanagita T, Wang YM, Xue CH. Effects of

different fatty acids composition of phosphatidylcholine on brain function of dementia mice induced by scopolamine. Lipids Health Dis. 2016 Aug 24;15(1):135