

Vitamins and Brain Health

Celeste A de Jager*

OPTIMA, Nuffield Department of Medicine, University of Oxford, UK

Brain shrinkage occurs with ageing and has been shown to predict the decline of mental functions such as memory, executive function and speed of information processing [1]. Cognitive impairment resulting from loss of brain tissue and loss of neuronal excitation can progress to Alzheimer's disease (AD) and dementia. Thus there is a challenge to find ways to maintain brain health before these processes affect cognitive function and functional independence. Certain vitamins have gained attention in the promise of protecting neuronal integrity and slowing brain shrinkage including omega-3, vitamin B12, folic acid, vitamin D and anti-oxidants such as vitamins C and E. A recent study in an ageing cohort showed that a nutrient biomarker profile high in plasma marine ω -3 fatty acids was associated with positive cognitive and MRI outcomes [2]. Another biomarker profile high in plasma vitamins B (B1, B2, B6, folate, and B12), C, D, and E was also associated with more favourable cognitive and MRI measures, while a profile characterised by high trans-fats was less favourable.

Docosahexanoic acid (DHA) and eicoso-pentanoic acid (EPA) are important long chain omega-3 polyunsaturated fatty acids (PUFAs), found in fish, seafood and breast milk and have been shown to be essential for healthy brain development. The brain contains about 60% essential fatty acids and together with arachidonic acid these are essential constituents of cell membranes in the brain and vascular system [3]. Unfortunately the western diet is becoming depleted of PUFAs as seafood is becoming too scarce to support the world's needs and DHA in meat from farm-reared animals and battery-fed chickens is being markedly reduced by the high amount of saturated fats in the animals' diets [4]. This is suggested to contribute to the growing population of young and older people with mental health illnesses such as depression and dementia [5] as well as obesity [4]. Children born to mothers' deficient in DHA [6] have been shown to be compromised in cognitive performance at school age. Intervention studies with DHA with or without EPA have had variable results in various life stages Karr et al. [7]. Studies with DHA supplementation have been successful in children under 2 years of age [5], but not convincingly so after age 2 or in children of school going age. Omega-3 supplements during pregnancy were associated with higher birth weight, body length and increased gestational age of offspring [7]. Elderly with age related cognitive decline (ARCD) were shown to improve in memory performance after 6 months intervention with DHA alone [8], while a trial with patients with AD showed no improvement [9]. But in an AD subgroup negative for the ApoE4 allele, less cognitive decline was seen for those on DHA than those on placebo.

B vitamins (6, 9 [folic acid] and 12) are known to be involved in the metabolism of dietary proteins into useful amino acids such as glutathione. But when these vitamins are in short supply the levels of another amino acid, homocysteine (tHcy), will rise. Elevated levels of tHcy are toxic and are associated with increased risk of stroke, cardiovascular disease, cognitive impairment and Alzheimer's disease. A study on vitamin B12 and brain shrinkage showed that older people who had higher vitamin B12 levels were six times less likely to experience brain shrinkage compared with those who had lower blood levels of the vitamin [10]. Children whose mothers had low levels of B12 during gestation had poor cognitive performance [11].

B vitamin intervention trials have shown variable success in

different patient populations and with differing treatment regimes. A trial with folic acid supplementation showed improved episodic memory for those with baseline plasma homocysteine above 13 μ mol/L [12]. In the VITAL trial, participants with mild AD, but not those with moderately severe AD, showed some improvement upon B-vitamin treatment [13], suggesting that once brain atrophy is advanced there is less likelihood of intervention being successful. A trial with cognitively normal participants showed no cognitive benefit of B vitamins [14]. By contrast, the Oxford Project to Investigate Memory and Ageing (OPTIMA) conducted a B vitamin study with elderly with Mild Cognitive Impairment (MCI). After 2 years of intervention with high doses of vitamin B6, B12 and folic acid there was significantly less brain shrinkage in the treated group compared with the placebo group and this was related to the concentration of tHcy at baseline [15]. Furthermore, for those with plasma tHcy above the median (11.3 μ mol/L) at baseline, the treated group showed significantly less cognitive and clinical decline [16].

Thus, although there seem to be some promising results for the benefits of certain vitamin supplements on mental health, these benefits so far seem confined to certain neuro-developmental and -degenerative stages in the lifespan such as very early developmental years and in older age without moderately advanced Alzheimer's disease. There also appear to be subgroups of people more likely to benefit from some supplements, eg, non-carriers of the ApoE4 allele and elderly with elevated plasma tHcy. The question is are these vitamins more necessary at certain times in the lifespan or are the intervention trial designs at fault? Does maternal health need more priority to avoid poor neuro-development in children? Also, is it too late to intervene with vitamins when brain shrinkage in the elderly has reached a critical level and symptoms of dementia are already detectable? Better design in intervention trials might include attention to understanding mechanisms of action of nutrients, choice of study populations, length of intervention and dosage, outcome measures to be used, as well as baseline status or plasma nutrient profile.

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*Corresponding author: Celeste A de Jager, Senior Research Associate, OPTIMA, Nuffield Department of Medicine, University of Oxford, UK, Tel: +44 1865 231460; E-mail: celeste.de-jager@ndm.ox.ac.uk

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