



**Translational Medicine** 

Editorial

## Concocting the Right Diet for Brain Health

## Cara J Westmark

University of Wisconsin, Waisman Center for Developmental Disabilities, 1500 Highland Avenue, Madison, WI 53705, USA

The old adage, "Starve a fever, feed a cold," infers that nutritional status modulates the immune system. The digestive enzymes work less efficiently as body temperature rises, so reducing caloric intake during a fever puts less stress on the body, while increasing caloric intake for a cold provides additional energy to fight the infection. There are also well-established roles for diet in diabetes (sugar), heart disease (cholesterol), bone density (calcium and vitamin D3), phenylketonuria (phenylalanine) and Celiac disease (gluten). But what about the brain? Does nutrition affect normal brain function and is there a diet that can curb the development of neurological disorders such as autism and Alzheimer's disease? How do nutritional supplements, such as vitamins and herbs affect brain biochemistry? The most recent statistics published by Centers for Disease Control estimate that autism spectrum disorders affect as many as 1 in every 110 children in the U.S while the Alzheimer's Association calculates that 5.4 million Americans have Alzheimer's disease. Finding dietary interventions that prevent or slow down the progression of these devastating disorders will have immense implications for caregivers, our healthcare system and the economy.

There is ample evidence in the literature that nutritional deficiencies exacerbate pathological processes; yet, there have been very few intervention studies assessing the effects of specific nutrients on the prevention of cognitive decline [1]. There is anecdotal evidence that a gluten- and casein-free diet improves autism symptoms, and recent studies suggest that medical foods can significantly retard the progression of Alzheimer's disease. A medical food cocktail consisting of the dietary supplements curcumin, piperine, epigallocatechin gallate, a-lipoic acid, N-acetylcysteine, B vitamins, vitamin C and folate improved cognitive function while decreasing the neuropathology associated with Alzheimer's disease in a mouse model of the disorder [2]. Another medical drink that was developed by Danone Research (Souvenaid) contains omega-3 fatty acid docosahexaenoic acid (DHA), uridine monophosphate (UMP) and choline, and was designed to stimulate neuronal cell membrane formation. A randomized, double-blind controlled clinical trial with 225 drug-naïve patients demonstrated that Souvenaid taken once-daily for 12 weeks significantly improved delayed verbal recall in individuals with mild Alzheimer's disease [3]. Nutritional supplements derived from plants, such as Huperzine A, have also shown efficacy in treating dementia. Huperzine A is found naturally in the dried herb of Huperzia serrata and is a potent, reversible, competitive inhibitor of the enzyme acetylcholinesterase. Clinical trials indicate that Huperzine A is as potent as the pharmaceutical acetylcholinesterase inhibitors tacrine, donepezil and rivastigmine in improving cognition [4]. Other natural compounds such as antioxidants and vitamin C have produced mixed results in regards to improved cognitive performance.

Natural compounds are widely marketed at promoting good health, but for many of these substances, we know very little regarding their physiological effects. Even for supplements that have beneficial health effects, it is possible to digest too much of a good thing particularly for individuals with genetic predispositions to certain conditions. In 1987, there was a large-scale U.S. anti-narcotics campaign sponsored by the Partnership for a Drug-Free America. Their television commercials entitled, "This is Your Brain on Drugs," compared your brain to an egg and narcotics to a hot frying pan, and poignantly illustrated the harmful effects of using illegal drugs. Due to these types of public service announcements, the general population today understands the harmful health effects of cigarette smoking, alcohol abuse and narcotics, as well as the beneficial effects of prenatal vitamins, calcium and vitamin  $D_3$ . But do we stop and consider how dietary supplements or even prescription medications can affect our health? For example, OcyContin and Vicodin are opiate-type prescription drugs used for chronic pain relief. Their use during pregnancy has recently resulted in a large increase in neonatal abstinence syndrome. Prescription drugs cause drug addiction in the fetus during pregnancy just as well as alcohol, cocaine and heroin resulting in severe withdrawal symptoms after birth.

A natural compound that may be detrimental to healthy infant development is soy. Soy products such as soymilk, tofu, tempeh and soy infant formula are widely used. There are many health benefits for adults that are associated with the consumption of soy in terms of prevention of age-related cardiovascular disease, osteoporosis and peri- and postmenopausal symptoms; however, this natural product holds potential danger for infants. Soy products are rich in phytoestrogens, ie. Natural plant chemicals that are structurally similar to estrogen and thus are potential endocrine disruptors. There is a paucity of studies on the effects of phytoestrogens on fetal and early childhood development; yet, twenty-five percent of infant formulas are based on soy protein [5, 6]. Considering body weight, these infants are getting 6-11 times the dose of phytoestrogens necessary to exert hormone-like effects in adults [5]. There are epigenetic changes associated with a soy-based diet in monkeys suggesting the potential to greatly alter gene expression [7]. We have observed significantly elevated seizure rates in mouse models of Alzheimer's disease, Fragile X syndrome and Down syndrome when juvenile mice are fed a soybased diet. Our data suggests that soy-based infant formulas may lower seizure threshold particularly in babies genetically predisposed to developmental disorders. Thus, understanding the negative effects of soy phytoestrogens and modulating intake during pregnancy and infancy could prevent neurological damage during critical periods of sensory development. The prevailing view is that soy products are healthy, but much remains to be learned regarding its effects on brain development and function.

Dietary supplements and medical foods do not require FDA approval before they are marketed to consumers whereas drug products must be proven safe and effective for their intended use. Yet, supplements can potentially interfere with the same signal transduction pathways in the brain that are affected by both legal and illegal drugs. There is emerging evidence that medical diets delay the onset and

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**Corresponding author:** Cara J. Westmark, Waisman Center for Developmental Disabilities, University of Wisconsin, 1500 Highland Avenue , Madison, WI 53705, USA, Tel: (608) 262-9730; E-mail: westmark@wisc.edu

progression of Alzheimer's disease if the treatments commence before pathology is too advanced. As the focus of Alzheimer's disease and other brain disorder research widens from a solely treatment approach to prevention strategies, lifestyle factors such as diet will undergo more intense investigation. It is important for all of us to weigh the potential benefits versus harm of the dietary supplements and medications that we consume as the jury and the FDA are still out regarding the safety and effectiveness of these compounds making the law of the land 'caveat emptor'.

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