ACUPUNCTURE today

BRAIN HEALTH

A Breakthrough in the Prevention and Treatment of Neurological Disorders

DIGITAL EXCLUSIVE

Neurodegenerative diseases such as Alzheimer's disease (AD) and related dementias, Parkinson's, multiple sclerosis, and autism are reaching epidemic proportions. An estimated 25 percent of individuals older than 65 years have some form of dementia[1] Furthermore, the cumulative incidence of dementia in people living to 95 years is more than 80 percent.[2-3] Multiple sclerosis, another neurological disorder, affects 400,000 people in the United States and 2.1 million people globally.[4] It places a large burden on the patient, the patient's family and the national health care system.

A common feature of all neurodegenerative diseases is the depletion of critical membrane lipids called *plasmalogens*. Plasmalogen depletion is believed to occur due to either reduced biosynthesis associated with aging (Alzheimer's / Parkinson's) or excess degradation due to oxidative stress / inflammation (multiple sclerosis / autism).

Previously, there was no reliable way to measure an individual's plasmalogen status or to take meaningful clinical steps to restore plasmalogens to healthy levels. Fortunately, plasmalogen levels decrease years before development of dementia, so measurements of plasmalogen status can be used to guide prevention and treatment in these types of patients. Based on test results, plasmalogen levels can be replenished through supplementation with a very specific type of phospholipid.

Utilizing this type of testing and subsequent supplementation is cutting edge, novel and scientifically validated in the peer-review literature. It will help set your therapeutic offerings apart from slow adapters.

Plasmalogens: Their Role in Protecting Against AD and Dementia

Plasmalogens are a naturally occurring substance in our bodies. They are glycerophospholipids that play a critical role in the function of the brain, heart, lungs, kidneys, and eyes.[5-6] The primary species of plasmalogens that occur in the human body are plasmalogen ethanolamines (PlsEtn).[7] In fact, greater than 50 percent of the ethanolamine phospholipids in the brain are PlsEtn.[7]

Aging is not a friend to phospholipid concentrations. Plasmalogen levels in the brain increase up to approximately 30 to 40 years of age.[8] Levels then undergo a significant drop by the time an individual is about 70 years old.[8] This corresponds to the time of life when Alzheimer's disease incidence rises exponentially.[9] Brain PlsEtn levels are lower in AD patients compared with age-matched controls,[10-12] and low brain levels are associated with low serum concentrations.[11]

Research suggests plasmalogen levels decline before the development of Alzheimer's disease and dementia. For example, a study published in the *Journal of Lipid Research* found that circulating PlsEtn levels were dramatically decreased in serum from more than 400 clinically demented patients with dementia of the Alzheimer's type at all stages of the disease.[13] Additionally, the extent of the decline was associated with dementia severity. This study also determined that serum PlsEtn concentrations declined years before clinical symptoms developed.

Other studies have shown that serum and brain plasmalogen deficiencies are closely linked to the progression of age-related neurodegenerative diseases such as AD and Parkinson's disease.[5, 13-14]

Low plasmalogen levels are also associated with worse cognition in patients with AD. Wood and colleagues found that in 40 AD patients with lower plasmalogen levels (less than or equal to 75 percent of that of age-matched controls at baseline) Alzheimer Disease Assessment Scale-Cognitive (ADAS-Cog) scores increased significantly.[15] In participants with normal serum plasmalogen concentrations at baseline (greater than 75 percent), there were no declines in cognitive scores.

Plasmalogens and Beta Amyloid

The link between plasmalogen deficits and the development of β-amyloid (Aβ) plaques provides further evidence that low plasmalogens contribute to AD and dementia. Aβ deposition is a hallmark of AD. Plasmalogens act upstream of Aβ formation to stop the deposition of these damaging plaques.[7] There is an association between lower serum PlsEtn and the buildup of Aβ plaques in the central nervous system (CNS).[13] The timing of the decrease in serum PlsEtn coincides with the deposition of Aβ in humans.[13] Other evidence indicates that declining plasmalogen levels are implicated in the accumulation of Aβ plaques, which may play a role in AD pathology.[16]

Studies using human AD postmortem brains suggest optimal plasmalogen concentrations lead to a decrease in the activity of y-secretase, an enzyme that catalyzes the production of Aβ.[16] It becomes a vicious circle in which Aβ reduces plasmalogen levels, which in turn directly elevates y-secretase activity, resulting in even greater buildup of Aβ plaques.[16]

Lipoproteins to the Rescue? APOE and Plasmalogens

Apolipoprotein E (APOE) is the most abundant lipoprotein in the brain.[17] There are three common genetic variants (ε2, ε3, ε4), resulting in six possible combinations. Typically, ε2ε3 is associated with lower risk (3 percent), ε3ε3 with average / low risk (18 percent) and ε3ε4 and ε4ε4 with higher risk of AD (up to 70 percent).

The majority of the population is ε3ε3. The APOE epsilon 4 allele is the primary genetic risk factor for AD.[18] Low PlsEtn levels may determine the effects of APOE on AD and dementia.

Dr. Dayan Goodenowe, a pioneer in the plasmalogen research field, and his colleagues conducted a study in 1,205 elderly individuals to investigate the relationship between APOE genotype and serum PlsEtn on cognition and dementia.[19] They found that the ability of APOE to adversely affect cognition and the prevalence of dementia was dependent upon the plasmalogen status of the subjects.

When concentrations of the PlsEtn Biosynthesis Value (PBV, a combination of three important

PlsEtn species) were higher, the probability of dementia was close to zero, regardless of the APOE genotype. Even in elderly subjects who had an increased risk of dementia, a higher PBV index correlated with a close to zero probability of dementia, regardless of age.

These results provide evidence that PlsEtn levels can protect against dementia despite the existence of significant risk factors. The study authors wrote that the prevalence of dementia "could be reduced to at least that of the E2E3 genotype. This would result in an overall reduction in AD cases by 75% or more."

The connection between APOE and PlsEtn involves cholesterol homeostasis. Cholesterol dysregulation is linked to cognitive impairment and AD. For example, in human post-mortem brain samples, higher concentrations of free cholesterol correlated with decreased cognition.[20] The fact that both APOE and PlsEtn play a role in cholesterol homeostasis may explain the mechanism by which PlsEtn can reduce the APOE-mediated AD risk.

Editor's Note: Part 2 (October digital issue) discusses a new test for detecting plasmalogens and other biochemical indicators, and the most effective way to replenish plasmalogen levels.

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