Dynamic Chiropractic

SENIOR HEALTH

A Breakthrough in Preventing and Treating Neurodegenerative Disorders (Pt. 2)

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Editor's Note: Part 1 of this article appeared in the September issue.

Multiple Sclerosis, Autism and Plasmalogens

The relationship between multiple sclerosis, autism and plasmalogens is less straightforward. Multiple sclerosis (MS) and autism are caused by an underlying, pre-existing mitochondrial insufficiency in neuronal support cells, the glia. Due to overall changes in diet and lifestyle, mitochondrial insufficiency is increasing in our society. This increase is one of the primary reasons why MS and autism incidence also have increased.

As an inflammatory response to mitochondrial insufficiency, the body responds by activating microglia.[21] These microglia target damaged cells by exporting glutamate, which in high levels is a mitochondrial toxin. Weak or damaged cells die, while healthy surrounding cells survive. However, in MS and autism, the surrounding "healthy" cells are characterized by weak mitochondria and are not optimally healthy.[22-23] This leads to the spread of inflammation, which in turn, damages the healthy cells and further exacerbates an inflammatory response.

In events leading up to MS and autism, mitochondrial insufficiency results in the fatty acids that are supposed to be metabolized by the mitochondria being metabolized by the *peroxisome*, a tiny organelle located in the cytoplasm of most cells that is involved in the synthesis of plasmalogens. This results in higher levels of plasmalogens, very long chain fatty acids, elevated cholesterol, and higher triglycerides.[24]

However, the damaged glial cells at the MS lesion in the brain need to be repaired. To accomplish this, the local requirement for plasmalogens is much greater compared with the small increase caused by the mitochondrial insufficiency.[25] Plasmalogens are needed so the surrounding glial cells can replenish the white matter in the healthy cells at the rate the inflammation damages it. This leads to a significantly faster glial cell recovery rate, which in turn, results in a healthy inflammatory response and the inhibition of white matter loss caused by inflammation.

Once a practitioner determines the rate of inflammation and mitochondrial stress through testing of plasmalogens and other biochemical indicators, supplementation can be used to deliver and keep in reserve excess glial plasmalogen building material.

In multiple sclerosis, the immune system targets myelin, the protective coating of nerve fibers. Human research indicates myelin contains certain species of ethanolamine plasmalogens.[26] Furthermore,

supplementing with a specific plasmalogen precursor completely prevented demyelination in animal models of multiple sclerosis.[27] Autism is also associated with impaired peroxisome function and plasmalogen deficits in plasma and red blood cells.[28-30]

A New Test for Detecting Plasmalogens and Other Biochemical Indicators

In clinical practice, my motto has always been, "Test, don't guess." The same is true with plasmalogens and other biochemical risk factors for conditions like Alzheimer's, MS and autism. A new blood test can detect plasmalogen deficiencies, as well as measurements of other important biomarkers. For example, in addition to plasmalogens, the blood scan report identifies levels of anti-inflammatory gastrointestinal tract acids (GTAs).

Evidence in the medical literature supports a role of GTA deficiencies in the progression of MS.[25] GTAs may also predict the risk of colorectal cancer.[31] Approximately 90 percent of all CRC cases occur in individuals with GTA levels below the 10th percentile.[31]

The Most Effective Way to Replenish Plasmalogen Levels

After testing, the next step is to restore plasmalogen levels, or deliver and keep in reserve excess glial plasmalogen building material. Plasmalogen replenishment in both preclinical and clinical studies blocks the development and/or reduces the progression of neurodegenerative disorders, atherosclerosis, insulin resistance, and hepatosteatosis.[6] The challenge is that dietary plasmalogens are degraded by stomach acids, resulting in minimal bioavailability from food sources. Therefore, the most effective way to restore plasmalogen levels is through supplementation with 1-O-alkyl-2-acyl glycerols with DHA at the 2-acyl position.

1-O-alkyl-2-acyl glycerols are orally bioavailable. A 10 mg/kg dose leads to a twofold increase and a 50 mg/kg dose to an almost fourfold increase in blood DHA-plasmalogen concentrations. This type of plasmalogen supplement suppresses the ability of cholesterol to increase Aβ1-42 and also dose dependently decreases levels of Aβ1-42 by increasing the activity of the α-secretase pathway, which is protective against amyloid plaque formation.[27] Conversely, stearic, oleic and linoleic, three other plasmalogen precursors that exhibit other side chains, appear to have no effect.

Extensive peer-reviewed publications have found 1-O-alkyl-2-acyl glycerol oils are a highly effective natural means of resolving plasmalogen deficiencies and elevating plasmalogens to protective levels. 1-O-alkyl-2-acyl glycerol oils work with the body's natural biochemical pathways in the liver and gut, which significantly elevates blood plasmalogen levels.[32] In the gut, they release a plasmalogen precursor. This plasmalogen precursor retains its DHA sn-2 fatty acid, which allows it to be absorbed into the circulation, where it is converted to the target plasmalogen.[32]

In a mouse model of Parkinson's disease, 1-O-alkyl-2-acyl glycerols blocked neurodegeneration and may have played a role in remyelination.[27,33] Decreased myelination is implicated in AD and MS pathology. Furthermore, plasmalogens serve as myelin markers, which decline in AD.[34]

In aging and disease, peroxisomes lose their ability to produce optimal levels of plasmalogens and

DHA. Supplementation with 1-O-alkyl-2-acyl glycerols bypasses peroxisomal biosynthetic pathways,[27,35-36] thereby restoring or enhancing DHA and plasmalogen levels.[27] This is important because data indicate DHA-PlsEtn levels drop according to the severity of dementia,[34] and subjects with low, moderate and severe dementia have progressively lower concentrations of DHA-PlsEtn.[27]

As phospholipid-linked DHA, 1-O-alkyl-2-acyl glycerols oils contain an abundant amount of plasmalogens and have profound effects on cognition.[37] Conversely, triglyceride-linked DHA has only a miniscule effect.[37]

Alkylglycerols have an established safety profile and have been administered to humans at large doses for long periods. For example, Das and colleagues gave alkylglycerols to genetically compromised infants for up to four years with no adverse reactions.[38] Recently, 1-O-alkyl-2-acyl glycerol oils with either DHA or oleic acid at the 2-acyl position have become commercially available. 1-O-alkyl-2-acyl glycerol oils with oleic acid provide excess glial plasmalogen building material needed for optimal glial cell recovery rate, leading to a healthy inflammatory response and suppression of white matter loss.

Clinical Takeaway

Plasmalogens play a critical role in brain health. However, levels decline during aging, and various diseases such as Alzheimer's and dementia are characterized by low plasmalogen levels. A great deal of evidence points to the involvement of low levels of plasmalogens in AD and dementia, and research has shown that plasmalogen levels decline before the development of these disorders. Imbalanced plasmalogen levels also are involved in MS and autism.

A new blood test can now measure plasmalogen levels, as well as concentrations of other biochemical measurements of neurological disorders. Based on the results of the test, 1-O-alkyl-2-acyl glycerols can be used as a highly effective and scientifically supported means to raise plasmalogen levels.

Editor's Note: Per the author, click here to discover more about the plasmalogen blood test and to register for educational material from Dr. Goodenowe (referenced in pt. 1).

References

21. Banati RB, et al. Mitochondria in activated microglia in vitro. *J Neurocytol,* 2004;33(5):535-541.

22. Varhaug KN, et al. [Multiple sclerosis - a mitochondria-mediated disease?]. *Tidsskr Nor Laegeforen*, 2017;137(4):284-287.

23. Maes M, et al. Integrating autism spectrum disorder pathophysiology: mitochondria, vitamin A, CD38, oxytocin, serotonin and melatonergic alterations in the placenta and gut. *Curr Pharm Des*, 2019;25(41):4405-4420.

24. Salemi G, et al. Blood lipids, homocysteine, stress factors, and vitamins in clinically stable multiple sclerosis patients. *Lipids Health Dis*, 2010;9:19.

25. Senanayake VK, et al. Metabolic dysfunctions in multiple sclerosis: implications as to causation, early detection, and treatment, a case control study. *BMC Neurol*, 2015;15:154.

26. Boggs JM, et al. Comparison of two molecular species of ethanolamine plasmalogen in multiple sclerosis and normal myelin. *Neurochem Res*, 1982;7(8):953-964.

27. Wood PL KM, et al. Plasmalogen deficit: a new and testable hypothesis for the etiology of Alzheimer's disease. In: *Alzheimer's Disease Pathogenesis-Core Concepts, Shifting Paradigms and Therapeutic Targets*. London, U.K.: InTech2011.

28. Berger J, et al. Peroxisomes in brain development and function. Biochim Biophys Acta, 2016;1863(5):934-955.

29. Wiest MM, et al. Plasma fatty acid profiles in autism: a case-control study. *Prostaglandins Leukot Essent Fatty Acids,* 2009;80(4):221-227.

30. Bell JG, et al. Essential fatty acids and phospholipase A2 in autistic spectrum disorders. *Prostaglandins Leukot Essent Fatty Acids*, 2004;71(4):201-204.

31. Ritchie SA, et al. Low-serum GTA-446 anti-inflammatory fatty acid levels as a new risk factor for colon cancer. *Int J Cancer*, 2013;132(2):355-362.

32. Khan MA WP, Goodenowe D. Inventor. methods for the synthesis of plasmalogens and plasmalogen derivatives and therapeutic uses thereof. U.S. patent US 9,169,280 B2; Oct. 27, 2015.

33. Miville-Godbout E, et al. Plasmalogen augmentation reverses striatal dopamine loss in MPTP mice. *PLoS One*, 2016;11(3):e0151020.

34. Han X, et al. Plasmalogen deficiency in early Alzheimer's disease subjects and in animal models: molecular characterization using electrospray ionization mass spectrometry. *J Neurochem*, 2001;77(4):1168-1180.

35. MartÃnez M. Severe deficiency of docosahexaenoic acid in peroxisomal disorders: a defect of delta 4 desaturation? *Neurology*, 1990;40(8):1292-1298.

36. Zoeller RA, Raetz CR. Isolation of animal cell mutants deficient in plasmalogen biosynthesis and peroxisome assembly. *Proc Natl Acad Sci* (USA), 1986;83(14):5170-5174.

37. Hiratsuka S, et al. Effects of dietary docosahexaenoic acid connecting phospholipids on the learning ability and fatty acid composition of the brain. *J Nutr Sci Vitaminol*, 2009;55(4):374-380.

38. Das AK, et al. Dietary ether lipid incorporation into tissue plasmalogens of humans and rodents. *Lipids*, 1992;27(6):401-405.