Are Sialic Acid Levels Altered in Human GM3 Synthase Deficiency?: Comparison to Ganglioside GM3 Levels in Amish Infantile-Onset Epilepsy Syndrome

Eurich, Jenny

Over 65 million people worldwide are affected by epilepsy, and there is no known cause for 60% of these cases. GM3 Synthase Deficiency is due to the loss of function of an enzyme at the head of the metabolic cascade responsible for synthesizing most complex gangliosides from lactosylceramide; gangliosides are sialylated glycosphingolipids and carry the majority of the sialic acid within the central nervous system. The result is a severe infantile seizure disorder, with onset of generalized tonic-clonic seizures as well as other types of seizures within the first year of life that are poorly controlled; most cases have been identified in the Old Order Amish population. It is unknown if the clinical disease is due to a lack of downstream gangliosides or the toxic effect of increased levels of lactosylceramide and alternate overproduction of its derivatives. This study investigated the relationship between plasma ganglioside GM3 and sialic acid levels. Sialic acid levels in plasma from GM3 Synthase Deficient homozygotes, heterozygotes and control subjects were measured and compared to published GM3 values. Control total plasma sialic acid levels were 13.12 +/- 4.68 uM, heterozygotes were 50.46 +/- 9.17 uM and homozygotes were 132.8 +/- 45.28 uM of sialic acid. Free (unbound) sialic acids were 15%, 40% and 61% of total sialic acids for control, heterozygote and homozygotes, respectively. Control sialic acid levels were comparable to published data of sialic acid levels in normal plasma. When compared to known plasma GM3 levels, there was an inverse correlation between the concentrations of sialic acid and GM3. Sialic acid levels have been suggested to be an indicator of epilepsy, and this study suggests that regulation of sialic acid levels may be a key to seizure control.

Awards Won: