

Cerebral Folate Deficiency in ASD

Folate is essential for a wide range of important metabolic processes, including oxidative pathways, homocysteine metabolism, and gene methylation. Autism Spectrum Disorder (ASD) is associated with several gene polymorphisms (gene variations) that can decrease the production of **5-methyltetrahydrofolate (5-MTHF)**, an active form of folate. This can impair the transport of folate across the blood-brain barrier and into neurons in the brain.

There can also be impairment of the transport of folate across the blood-brain barrier due to dysfunction in the folate receptor (**folate-receptor alpha [FR α]**) at the blood-brain barrier. This dysfunction may be due to **mitochondrial dysfunction**. This impairment may also be due to the production of an antibody to the FR α receptor, effectively blocking the binding of folate to the folate-receptor. This FR α autoantibody appears to be present in the majority of ASD children. Of importance is that **a milk-free diet** has also been shown to reduce serum FR α autoantibody titers in a controlled study. The milk-free diet has been shown to decrease serum concentrations of the FR α autoantibody and improve irritability in ASD in a controlled study.



A number of studies have demonstrated that folinic-acid treatment in ASD children with the FR α autoantibody can result in either partial improvements in **communication, social interaction, attention, and stereotypical behaviour**, to complete recovery of ASD symptoms. Two case reports have noted improvement in seizures in children with ASD and cerebral folate abnormalities, with folinic acid treatment.

Individuals with the FR α autoantibody are typically treated with mg/kg/day doses of folinic acid, while individuals with mitochondrial disease may require considerably higher levels of folinic acid.

Clinical Observation

In clinic I have certainly seen some very beneficial effects of using the active forms of folate in ASD children. The most significant benefits seem to be in the improvement of speech. Mitochondrial dysfunction may need to be treated first.

Recommended Testing

This is where an **Organic Acid Test** may be beneficial in detecting mitochondrial dysfunction. A blood test for **folate** may also indicate the need for the active form of folate, especially if the levels of folate are relatively high.

References

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