C13

Daniel Mishan B.S.

Advisor(s): Harris Huberman M.D.

Co-author(s): -

Investigation of L-leucovorin treatment on language impaired ASD children through behavior, folate receptor autoantibody status and biomarkers of blood brain barrier efficacy.

Autism Spectrum Disorder (ASD) is a neurodevelopmental disability, affecting approximately 1 in 36 individuals in the USA (Maenner 2023). Core symptoms of ASD include impairments in social communication and restrictive repetitive behaviors (RRBs) (APA 2013), leading to difficulties in daily functioning. Early diagnosis and intervention are critical for achieving optimal outcomes, yet the average age of diagnosis in the US remains around 54 months. Currently, behavioral and speech therapies are the mainstays of treatment, with no FDA-approved pharmacological interventions targeting core symptoms.

Research has shown a strong association between Folate Receptor Autoantibodies (FRAA) and ASD, with FRAAs blocking folate transport across the blood-brain barrier (BBB) and contributing to CNS folate deficiency (a.k.a. vitamin B deficiency) in a majority of ASD-diagnosed children. Leucovorin, a derivative of vitamin B9, has shown promise in alleviating some core symptoms, particularly in language and RRBs, in older children (3 to 15 years, median age 7.2yrs) with ASD (Frye 2018).

The project encompasses three aims: assessment of treatment efficacy, exploring FRAA status and treatment response, and lastly investigating whether FRAA status is associated with biomarkers of blood brain barrier (BBB) damage and/or neuroinflammation.

The expected outcomes of this project are 1) to determine the efficacy of l-leucovorin in treating core ASD symptoms; 2) to establish links between FRAA positivity, symptom severity, and treatment response; and 3) to explore changes in biomarkers of BBB efficacy and neuroinflammation. This research holds the potential to significantly impact early interventions for ASD, paving the way for targeted pharmacological approaches to improve outcomes for affected children.