

Folate receptor autoimmune disorder can affect brain development and function to produce the autism phenotype.

Edward V Quadros¹, Natasha Boubrosky-Khoury², Harris Huberman³, Gabriela Mantilla-Garcia³, Daniel Mishan², and Vincent T Ramaekers⁴.

¹Dept. of Medicine, ²School of Graduate Studies, ³Division of Child Development, Pediatrics, SUNY Downstate and ⁴Univ. of Liège, Belgium.

Fetal programming in the womb and environmental influences during post-natal development are now recognized as factors that contribute significantly to how we develop and what we become during our lifetime, including neurodevelopmental disorders such as Autism Spectrum Disorder (ASD). Genetic imprinting and epigenetic control of gene expression play major roles in neuro-development and behavior that underlie most developmentally dictated disorders. Folate (vitamin B9) is a critical nutrient that influences the synthesis of DNA/RNA/amino acids/neurotransmitters and gene expression by regulating methylation. The folate receptor (FR) autoimmune disorder we have identified can profoundly block folate transport to the fetus and to the brain. The significant presence of FR autoantibodies (Ab) in autism produces cerebral folate deficiency regardless of systemic folate status. Leucovorin, a reduced form of the folate can be transported to the brain even in the presence of FRAb. Leucovorin treatment produces significant improvement in core ASD deficits such as speech, learning and social interaction. How leucovorin positively impacts language and social development at the level of brain function, mitochondrial metabolism and gene expression is the subject of ongoing research. Elucidating these mechanisms offers the potential of preventing developmental disorders by early intervention in parents and neonates.