Abstract

Mol Autism. 2013 Jun 3;4(1):16.

Decreased tryptophan metabolism in patients with autism spectrum disorders.

Boccuto L, Chen CF, Pittman AR, Skinner CD, McCartney HJ, Jones K, Bochner BR, Stevenson RE, Schwartz CE.

Greenwood Genetic Center, 113 Gregor Mendel Circle, Greenwood, SC 29646, USA.

BACKGROUND: Autism spectrum disorders (ASDs) are relatively common neurodevelopmental conditions whose biological basis has been incompletely determined. Several biochemical markers have been associated with ASDs, but there is still no laboratory test for these conditions.

METHODS: We analyzed the metabolic profile of lymphoblastoid cell lines from 137 patients with neurodevelopmental disorders with or without ASDs and 78 normal individuals, using Biolog Phenotype MicroArrays.

RESULTS: Metabolic profiling of lymphoblastoid cells revealed that the 87 patients with ASD as a clinical feature, as compared to the 78 controls, exhibited on average reduced generation of NADH when tryptophan was the sole energy source. The results correlated with the behavioral traits associated with either syndromal or non-syndromal autism, independent of the genetic background of the individual. The low level of NADH generation in the presence of tryptophan was not observed in cell lines from non-ASD patients with intellectual disability, schizophrenia or conditions exhibiting several similarities with syndromal autism except for the behavioral traits. Analysis of a previous small gene expression study found abnormal levels for some genes involved in tryptophan metabolic pathways in 10 patients.

CONCLUSIONS: Tryptophan is a precursor of important compounds, such as serotonin, quinolinic acid, and kynurenic acid, which are involved in neurodevelopment and synaptogenesis. In addition, quinolinic acid is the structural precursor of NAD+, a critical energy carrier in mitochondria. Also, the serotonin branch of the tryptophan metabolic pathway generates NADH. Lastly, the levels of quinolinic and kynurenic acid are strongly influenced by the activity of the immune system. Therefore, decreased tryptophan metabolism may alter brain development, neuroimmune activity and mitochondrial function. Our finding of decreased tryptophan metabolism appears to provide a unifying biochemical basis for ASDs and perhaps an initial step in the development of a diagnostic assay for ASDs.

PMID: 23731516