
ABSTRACT

BACKGROUND: Creatine Deficiency Syndromes (CDSs) can present with developmental delays, autistic symptoms, and seizures. The prevalence and phenotypic variation of CDS has not been well studied in autism spectrum disorder (ASD). Genetic variation in creatine metabolism may be a factor in the neurobiology of autism.

PURPOSE: A pilot study to identify the prevalence of CDS in children with autism spectrum disorder and to assess the interaction of genotypic variability of the 3 known genes involved in creatine metabolism (GAMT, AGTM, and CRT) with the autism phenotype

METHODS: Subjects will be recruited prospectively at 3 sites in the ATN (Autism Treatment Network), a multicentre ASD registry. 1) CDSs will be screened for using urine tandem mass spectrometry. 24 hour urine collection performed for guanidino compound analysis will be performed in positive cases. A diagnosis of CDS will be confirmed by gene sequencing and magnetic resonance spectroscopy of the brain. 2) High-throughput DNA sequencing of three genes (GAMT, AGAT and CRT) involved in creatine metabolism will be completed in subjects with autism previously recruited in a multisite genetics study and in ancestrally matched controls.

SIGNIFICANCE: CDSs may be an undiagnosed but treatable cause of ASD and if so, future screening and treatment may lead to prevention of ASD. Genetic variation in the genes controlling creatine metabolism may contribute to the phenotype of ASD. Early recognition of these variants may allow intervention to ameliorate the symptoms of autism.