Abstract

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Brain carnitine deficiency causes nonsyndromic autism with an extreme male bias: A hypothesis.

Beaudet AL.

Departments of Molecular and Human Genetics and Pediatrics, Baylor College of Medicine, Texas Children's Hospital, Houston, TX, USA.

BACKGROUND: Could 10-20% of autism be prevented? We hypothesize that nonsyndromic or "essential" autism involves extreme male bias in infants who are genetically normal, but they develop deficiency of carnitine and perhaps other nutrients in the brain causing autism that may be amenable to early reversal and prevention. That brain carnitine deficiency might cause autism is suggested by reports of severe carnitine deficiency in autism and by evidence that TMLHE deficiency - a defect in carnitine biosynthesis - is a risk factor for autism.

FINDINGS: A gene on the X chromosome (SLC6A14) likely escapes random X-inactivation (a mixed epigenetic and genetic regulation) and could limit carnitine transport across the blood-brain barrier in boys compared to girls. A mixed, common gene variant-environment hypothesis is proposed with diet, minor illnesses, microbiome, and drugs as possible risk modifiers. The hypothesis can be tested using animal models and by a trial of carnitine supplementation in siblings of probands.

CONCLUSION: Perhaps the lack of any Recommended Dietary Allowance for carnitine in infants should be reviewed.

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