

Research hints at a nutritional strategy for reducing autism risk

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Quinn, an autistic boy, and the line of toys he made before falling asleep. Repeatedly stacking or lining up objects is a behavior commonly associated with autism. Credit: Wikipedia.

Folic acid has long been touted as an important supplement for women of childbearing age for its ability to prevent defects in the baby's developing brain and spinal cord. In fact, folic acid is considered so important that it is added as a supplement to breads, pastas, rice and

cereals to help ensure that women are exposed to sufficient amounts of this nutrient even before they know they're pregnant.

Soon, another prenatal supplement could protect against a certain type of autism, according to research published today in the journal *Cell Reports*. The supplement is called carnitine, and it is already available in the market.

Carnitine, which the body can manufacture itself or extract from dietary sources, is required for transport of [fatty acids](#) into mitochondria—the compartment within the cell that converts these fats into energy. Previous studies have shown that inherited mutations in a gene (called TMLHE) that is required for carnitine biosynthesis are strongly associated with risk for development of autism-spectrum disorders, but the basis for that association has been unclear—until now. The latest findings show that genetic defects in the body's ability to manufacture carnitine might be associated with an increased risk of autism because carnitine deficiency interferes with the normal processes by which [neural stem cells](#) promote and organize embryonic and fetal brain development.

The study's lead author, Zhigang Xie, Ph.D., assistant research scientist at the Texas A&M Health Science Center College of Medicine, has refined a new technology that allows him to mark, follow and analyze individual neural stem cells in their native environment in a real developing brain. "It's very difficult to study neural stem cells in their complex natural environment," Xie said. "But now we have a technology that makes such studies possible."

"Until now, this technology has not been used in this way," added Vytas A. Bankaitis, Ph.D., the E.L. Wehner-Welch Foundation Chair in Chemistry at the Texas A&M College of Medicine and Xie's collaborator. "Our application of this technology is powerful because it

allows us to identify specific neural stem cell defects that are invisible in the cell culture systems typically used by brain scientists. With regard to autism spectrum disorders, one has to consider the entire cellular environment, or niche."

Their work, which was funded by the National Institutes of Health and the Robert A. Welch Foundation, is important because some one percent of Americans are afflicted with autism, and the annual cost of autism management in the United States alone is estimated to be at least \$236 billion.

The researchers found that neural stem cells unable to produce carnitine don't behave properly and are inappropriately depleted from the developing brain, but when genetically at-risk neural stem cells are supplied with carnitine from an outside source, they don't have the same problems.

Without getting too technical, the autism-associated TMLHE gene encodes an enzyme that the body needs to manufacture carnitine. Autism risk mutations inactivate this gene and, in the absence of their own ability to produce carnitine and without adequate outside supplementation, neural stem cells become less efficient at self-renewal. That is, when they divide, neural stem cells produce two "daughter" cells, one of which should remain a neural stem cell and the other that should differentiate. Neural stem cells confronted with carnitine deficiency too often divide to produce two differentiated cells, thereby failing to resupply the developing brain with a cache of neural [stem cells](#).

"Inborn errors in carnitine production cause significant issues in a cell type one would believe has to contribute to autism risk," Bankaitis said. As the autism risk gene is located on the X chromosome and males have only one X chromosome (females have two), they are at greater risk.

Some pregnant women might absorb enough carnitine from their diet so as to make normal enzyme function less important in the context of autism risk for their babies. High levels of carnitine can be found in red meat, and one of the best vegetarian sources is whole milk. Women who don't ingest sufficient carnitine, however, might be placing their unborn child at risk.

Because the TMLHE is a recognized autism risk gene and its location on the chromosome is known, one possible first step for prevention is to test prospective mothers for TMLHE mutations before pregnancy. If a prospective mother is a carrier for the mutated autism risk gene, supplementation of her diet with carnitine before and during pregnancy could help ensure that a sufficient supply of the nutrient is available to the developing embryo and fetus, thus helping to offset the genetic defect.

"In retrospect, this preventative approach seems obvious," Bankaitis said. "But, metabolic deficiencies are complicated scenarios to interpret, and we believe these complexities obscured what will hopefully prove to be a rather simple path towards prevention."

It's important to note that this particular prevention strategy will not apply to all cases of autism. "Even if this strategy works, it will not be a panacea for reducing all autism risk," Bankaitis said. "While it could work in cases involving carnitine-deficiency, other pathways are also in play because as many as 1000 genes might ultimately be found to relate to autism risk. Still, the potential impact of even such a limited preventive strategy could be significant as mutant TMLHE alleles are surprisingly common in the human population."

"Here we have indications, at least for some types of [autism risk](#), that a dietary carnitine prevention method might be effective," Xie said. "For some individuals, this simple nutritional supplement might really help

reduce the risk of developing autism spectrum disorder. Any progress on the prevention front would be welcome given the number of people affected."

Provided by Texas A&M University

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