NEWS

Study links dietary supplement to brain development

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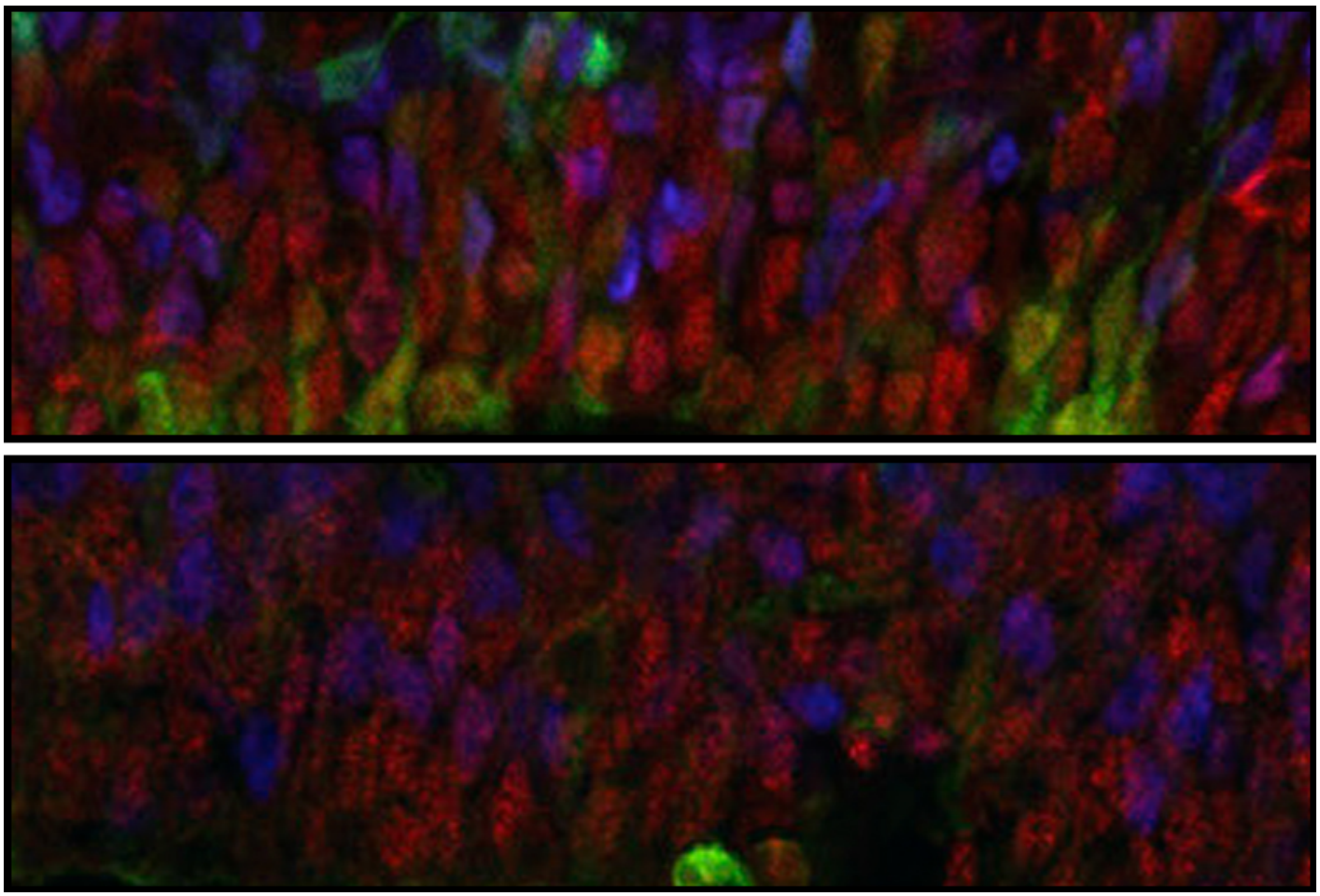

For some pregnant women, taking the nutritional supplement carnitine may lower the risk of having a child with autism, a new mouse study suggests.

Previous studies have hinted at a link between autism and a common genetic defect that prevents the body from synthesizing carnitine. The new findings, published 9 February in *Cell Reports*, suggest that the molecule, a nutrient found in meat and dairy products, plays a crucial role in brain development[1].

“The take-home lesson is that carnitine is important,” says **Vytas Bankaitis**, professor of molecular and cellular medicine at Texas A&M University. “It’s important, and it’s important way earlier than many people feel are the stages at which autism is hardwired.”

In the body, carnitine helps to transform dietary fats into energy. Most people both make it naturally and absorb it from food. But nearly 1 in 400 boys and men have a mutation in the enzyme trimethyllysine dioxygenase (TMLHE), which is necessary for the body to synthesize carnitine. Low levels of carnitine — whether from genetic causes or a dietary lack of the nutrient — can cause confusion, muscle weakness and low blood sugar.

Until now, no one knew how a mutation in the enzyme might affect brain development. To test the effects of the mutations in the developing brain, the researchers blocked the TMLHE gene’s expression in embryonic mice. They found that having low levels of the gene’s expression diminishes the brain’s pool of neural stem cells, the precursors to neurons.

Subtle link:

A 2012 paper first hinted at a possible link between carnitine and autism. That study, led by **Arthur Beaudet**, reported that mutations in TMLHE are more common in boys with autism whose families have a history of the condition than they are in controls[2].

Last year, Beaudet’s team at Baylor College of Medicine in Houston, Texas, published the case of a 4-year-old boy with a TMLHE mutation who had lost language skills and developed other features of autism[3]. After taking a carnitine supplement for three months, the boy improved dramatically, regaining the ability to speak and other skills.

The link between TMLHE mutations and autism risk is weak, however. The 2012 study did not find any relationship between the two in families that have only one child with autism. The new study gives some credence to the association by showing how these glitches may affect brain development.

“The publication draws more attention to this general issue of carnitine in autism,” says Beaudet, who is collaborating with the researchers to follow up on their new findings.

The researchers injected RNA that blocks production of TMLHE into the brains of 12.5-day-old mouse embryos. They then returned these embryos to the womb and examined their brains three days later.

Neural stem cells typically divide before turning into neurons so that the brain always has a pool of available stem cells. But lack of the enzyme somehow spurs both daughter cells to become neurons, diminishing the brain's stem cell stockpile, the study found. Bathing brain slices from the carnitine-deprived embryos in the nutrient almost completely restores their pool of neural stem cells after 18 hours.

Brain food:

The findings show for the first time that neural stem cells need carnitine to function normally, Bankaitis says.

Still, the study does not bolster the genetic link between TMLHE mutations and autism, which is "tenuous at best," says **Cecilia Giulivi**, professor of redox biology at the University of California, Davis, who was not involved in the study.

If lack of carnitine contributes to autism risk, it is not yet clear when its absence is most problematic. But by tying the nutrient to brain development, the new study suggests that it may be crucial *in utero*.

If so, some women might be wise to take carnitine during pregnancy, says Bankaitis. A pregnant woman who is vegan, for example, may get little carnitine in her diet and so might want to take supplements of the nutrient to buttress brain development in her child. Infants with TMHLE mutations might also benefit from carnitine supplements as they transition to eating solid foods low in carnitine, says Beaudet.

Beaudet's team has engineered multiple strains of mice that cannot synthesize carnitine, including one strain missing the TMLHE gene. The next step would be to look at how diminished levels of TMLHE influence behavior in the mice, and then test the effects of carnitine supplementation at different ages.

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