NEWS

Study links immune, metabolic theories of autism

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Rare antibodies associated with autism are unusually common among women who developed diabetes while pregnant with a child who has autism[1]. The results provide new clues to the link between immune system problems and autism.

Maternal antibodies ordinarily pass through the placenta and help to defend the fetus against pathogens. But some occasionally turn against the fetus and **attack proteins in the developing brain**. Researchers have found these antibodies in as much as **23 percent of women** who have a child with autism[2]. And prenatal exposure to these antibodies alters brain development and social behavior in **mice** and **monkeys**.

Separately, studies have shown that women who **develop diabetes while pregnant**, a condition called gestational diabetes, are at an increased risk of having a child with autism.

The new study, which appeared 17 June in *Autism Research,* ties together these two threads of research, says lead investigator **Judy Van de Water**, professor of internal medicine at the University of California, Davis. She says gestational diabetes may prompt some women to make the autism-linked antibodies.

“Gestational diabetes is an inflammatory condition,” Van de Water says. “And you have to have some sort of inflammatory dysregulation to create autoantibodies.” The details of this dysregulation and its link to autism are yet to be worked out, however.

Metabolic mystery:

Van de Water’s team screened blood from 227 women who have a child with autism, including 145 who have a child with **severe autism**, measured using scores on a standardized diagnostic

test. The researchers looked for **combinations of seven antibodies** that they had previously linked to the condition. All of the women are enrolled in the **Childhood Autism Risks from Genetics and the Environment (CHARGE)** study, and the samples were collected when their children were 2 to 5 years old.

The scientists combed medical records — or, when these were unavailable, interviewed the women — to identify those who had metabolic conditions marked by inflammation. These include diabetes (either gestational or type 2), high blood pressure and **obesity**, all of which are linked to an elevated risk of having a child with autism.

The researchers found that 56 of the women carry autism-linked antibodies. Those with either form of diabetes or high blood pressure, or who were obese, were not significantly more likely than other women to have the antibodies. But in the severe autism group, the 14 women who had gestational diabetes were more than three times as likely as those without the condition to harbor the rogue molecules.

“It was really the more severe symptoms of autism that were associated with the antibodies,” says study investigator **Paula Krakowiak**, a postdoctoral fellow at the University of California, Davis. “Among those who had a child with milder autism, there were actually very few moms who had metabolic conditions.”

Unraveling risks:

The work expands the list of maternal health conditions that track with autism-linked antibodies, says **Lior Brimberg**, assistant investigator at the Feinstein Institute for Medical Research in Manhasset, New York. Brimberg was not involved in the new study, but was part of a 2013 investigation showing that women who carry antibodies associated with autism are also at an **increased risk of developing an autoimmune disease**, in which the body attacks its own tissues.

Because the blood samples were taken after the children were born, it isn’t certain the children were exposed to the antibodies in the womb. To address this uncertainty, Van de Water’s team is repeating the analysis in pregnant women.

If the results hold up in large numbers of women, they point to a new segment of the population at risk for the antibodies. “Our hope is to better understand what the risk factors are, because you could potentially mitigate gestational diabetes,” Van de Water says.

Van de Water’s team now plans to conduct studies in mice to determine how inflammation during pregnancy might lead to the production of antibodies that attack the fetal brain.

REFERENCES:

1. Krakowiak P. *et al. Autism Res.* Epub ahead of print (2016) **PubMed**
2. Braunschweig D. *et al. Transl. Psychiatry* 3, e277 (2016) **PubMed**