

NEWS

Study bolsters genetic link between arthritis, autism

BY SARAH DEWEERDT

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Men and women with rheumatoid arthritis are at increased risk of having a child with autism, according to a large study based on medical records from Denmark¹. By linking the risk to both parents, the new work hints that autism and arthritis share genetic roots.

Rheumatoid arthritis is a condition in which the immune system attacks the membranes around the joints.

Previous studies have linked this and other immune conditions in pregnant women to autism risk in their children. Another new study suggests that the immune environment in the womb influences autism severity².

The rheumatoid arthritis study is the first to link the condition in fathers to autism risk.

If genetic factors play a role, the increase in autism risk would be expected regardless of which parent has rheumatoid arthritis, says study investigator **Ane Lilleøre Rom**, a postdoctoral researcher at Copenhagen University Hospital, Rigshospitalet in Denmark. “If only intrauterine factors are important, we would only expect to see an association in children of mothers with rheumatoid arthritis.” The lead researcher, **Lina Steinrud Mørch**, was not available for comment.

A child’s mother and father often live in similar environments. So it’s still possible that environmental factors are at play, says **Adam Guastella**, professor of psychology at the Brain and Mind Centre at the University of Sydney in Australia, who was not involved in this study.

There is a “need for really well-controlled investigations in terms of genetic backgrounds to pull apart that question,” he says.

Guastella led the other new study, linking maternal immune conditions to autism severity in

children. His findings jibe with work showing that immune signaling molecules can cross the placenta and **alter a child's brain development**.

Relative risk:

Mørch's team gathered data from national healthcare and birth registries for nearly 2 million children born from 1977 to 2008, and their parents. Of these children, 13,556 have mothers with rheumatoid arthritis and 6,330 have fathers with the condition. (Rheumatoid arthritis is more common in women than in men.) Some parents had the condition before the child was born; others developed it later.

A total of 8,985 children in the study have autism. Of these children, 81 have a mother with rheumatoid arthritis and 39 have a father with rheumatoid arthritis. The researchers found that women and men with rheumatoid arthritis both have about a 30 percent greater risk of having a child with autism than parents without the condition. The researchers did not calculate the absolute risk for each scenario.

The results held up even when the researchers limited their analysis to parents diagnosed with rheumatoid arthritis after the birth of their child. They appeared 9 October in the *Journal of the American Academy of Child and Adolescent Psychiatry*.

The findings suggest that the risk of autism from autoimmune conditions goes beyond the intrauterine environment.

"I was a little surprised that [the risk of autism] wasn't a little more in the moms" with rheumatoid arthritis, says **Betty Diamond**, head of the Center for Autoimmune and Musculoskeletal Disorders at the Feinstein Institute for Medical Research in Manhasset, New York. "I would have thought that the immune activation in the moms would also predispose [the children]." Diamond was not involved in the work but has studied the link between maternal immune activity and autism.

Fewer than 10 children in the study have mothers who had rheumatoid arthritis before the children's birth. So the researchers were unable to study that subgroup.

Allergic reaction:

In their study, Guastella and his colleagues analyzed data for 220 children with autism and their families in an autism registry in Western Australia. They found that children with autism born to mothers with allergies or asthma have more severe social deficits than those whose mothers have no history of immune conditions. The findings were based on scores on a parent questionnaire called the Social Responsiveness Scale.

The results suggest that having certain immune conditions during pregnancy increases autism

severity. They appeared 10 October in *Molecular Psychiatry*.

But the study cannot tease apart the effects of immune activity during pregnancy and those of a shared genetic predisposition to autism and asthma or allergy. “The most critical thing we don’t know is how actively they were wheezing or itching while they were pregnant,” Diamond says.

The researchers found no link between autoimmune conditions such as rheumatoid arthritis in the mother and autism severity in the child. However, the study may have been too small to reveal a connection, Guastella says. Only 30 of the mothers have an autoimmune condition, and just 16 of them were diagnosed prior to the birth of their child with autism.

The Australian and the Danish databases don’t contain the data needed to determine how much genetics or the environment contributes to the link between autism and immune conditions. Studies that incorporate medical records with genetic tests and measures of immune activity before, during and after pregnancy could help to fill in these gaps.

REFERENCES:

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Abstract

2. Patel S. *et al. Mol. Psychiatry* Epub ahead of print (2017) **PubMed**