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New genetic link to autism

Abnormalities on specific chromosome put kids at greater risk of developing disorder, massive Canadian-led study finds

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An international team of researchers led by Canadian scientists has homed in on the genetic underpinnings of autism, one of the most common and debilitating developmental disorders in children.

Previous studies have suggested between eight and 20 different genes are linked to autism, which affects an estimated one in 165 children.

"But the new data suggests there are more genes involved than we would have expected before," said Stephen Scherer, a senior scientist at the Hospital for Sick Children and co-author of the study published online yesterday in the journal *Nature Genetics*. He estimates 100 genes could be involved or work in combination to cause autism.

Scherer said it took a global effort to co-ordinate the research, a feat that could not have been accomplished by one lab alone.

The five-year collaboration, part of the Autism Genome Project, involved more than 130 scientists in 50 institutions in 19 countries, and cost $20 million.

"To make this happen is unbelievable," said Scherer, who led the Canadian team with Peter Szatmari, director of the Offord Centre for Child Studies in Hamilton.

Autism spectrum disorder can cause a range of symptoms in children, including repetitive behaviours and impaired language development and social interaction. The disorder affects

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Genetic finding opens door to early diagnosis

➤ **Autism** From A1

four times as many boys as girls.

To search for autism-susceptibility genes, the scientists collected DNA samples from 1,600 families from around the world with at least two members with autism spectrum disorder. They then scanned their entire genome to look for regions shared by people with autism.

The search led scientists to a previously unidentified area on chromosome 11, which they now believe harbours genes that increase the risk for autism.

They also used a technology pioneered at the Hospital for Sick Children, where they looked for copy number variations — long stretches of genetic material that either have missing or extra DNA. They found shared copy number variations in between 5 and 10 per cent of the families.

The analysis also uncovered a link between autism and the deletion in part of a gene known as neurexin 1, one of a family of genes important in communication between neurons in the brain.

The findings point the way for scientists to dig deeper into the genome to look for similar regions and molecular pathways that could cause autism.

James Kennedy, head of neuroscience research at the Centre for Addiction and Mental Health in Toronto, called it "a landmark study" that will have long-ranging implications for autism research.

"We expect many genes cause autism, maybe dozens," said Kennedy, who was not part of the study. "To even find one of them is a great step forward."

Szatmari said researchers have long known that autism is an inherited genetic disorder, but no one knew how it was passed on.

"We now know which haystack the needle is located in and, even more than that, we also have a better idea of where that needle is located," he said. "We really will be able to now, in the next five years, to hone in on candidate genes and candidate regions to identify those genes and DNA sequences that seem to have gone wrong or have led to autism."

The findings will help researchers come up with diagnostic methods for autism spectrum disorders, said Szatmari.

"We're still diagnosing them too late," he said. "If we can derive diagnostic tests for some forms of autism ... and lower the age of diagnosis to 24 months or 18 months, that will be really important. The earlier children get interventions, the better the outcome will be."

Every week parents of autistic children ask Wendy Roberts, a developmental pediatrician and co-director of the autism research unit at Sick Kids, whether there are prenatal tests to screen for autism. "At this point, we say that we can't."

The study won't have any immediate impact on clinical practice, said Roberts, a co-author of the study. It will take time to design a prenatal test for autism, precisely because there are so many genes involved.

Roberts collected data from Toronto-area parents, including John. He didn't want to use his last name because of the huge stigma still attached to autism spectrum disorders.

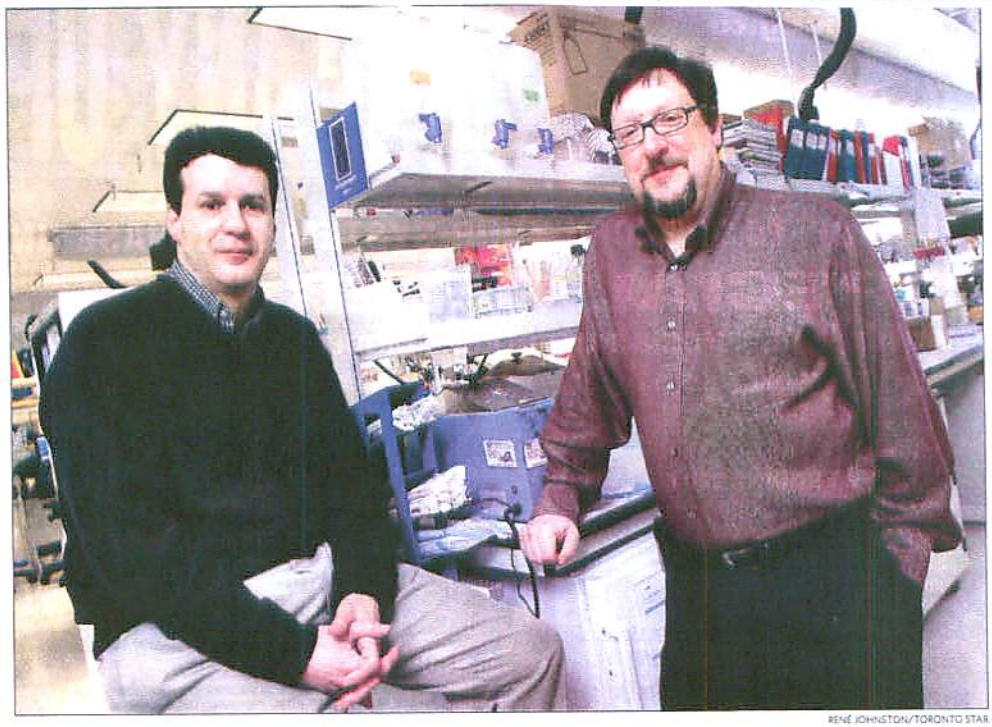
In the past, many parents blamed themselves for the onset of the disorder, looking to diet or even childhood immunizations for the cause.

John and his wife always believed there was nothing they could have done to prevent their 6-year-old son Michael's autism and the research confirms it. Now they know Michael — who has difficulty communicating with people — has a deletion in one of his chromosomes. Their older son does not have autism.

"How do you ensure that genes are passed on intact without any missing things? You can't," John said. "That's just nature. We're not going to fret about it and we encourage all parents not to fret about it, either."

They knew the study wouldn't lead to a cure for Michael or even a new treatment for his symptoms.

"But it's a start," said John. "It may help him when he's an adult. And in 10, 20 or 30 years it may lead to treatments for other children that have this type of diagnosis."



RENÉ JOHNSTON/TORONTO STAR

Stephen Scherer, left, and Peter Szatmari helped lead the international consortium of researchers looking for the genetic cause of autism.