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Genetic finding paves way for controversial autism testing

An autistic child peers from between curtains at the Consulting Centre for Autism in Amman, March 30, 2010. REUTERS/Ali Jarekji

Canadian discovery makes prenatal scan possible, giving parents opportunity for early behaviour therapy

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An international effort led by Canadian scientists has uncovered the complex genetic architecture of autism, revealing brand new targets for treatment and making it possible to predict with a DNA test at birth, or even before, about 10 per cent of those who will develop the condition.

But precisely how or when people should have access to such a test could prove to be nearly as tricky as the disorder itself, now seen as the most common serious developmental condition of childhood.

After sifting through the DNA of 1,500 families, members of the Autism Genome Project, a consortium of 120 researchers in 11 countries, have made the humbling discovery that the genetic risk factors for autism are different for each person who suffers from it.

“I highly doubt you will find two families with the same combination of genetic variants,” said study leader Stephen Scherer, senior scientist at the Hospital for Sick Children in Toronto.

Autism encompasses a spectrum of lifelong neurological disorders that can vary widely in severity and symptoms. Researchers agree an early diagnostic test could be crucial to countering the condition’s worst effects, but also acknowledge it could be used in family planning, or as a prenatal test in which parents may opt to terminate a pregnancy.

Researchers however caution it is too early to use a genome scan to routinely diagnose autism until they can figure out how the genetic glitches they have discovered play out in real life. Their paper, released Wednesday in an online edition of Nature, says that the roots of autism involve dozens of genes fouled up by long stretches of missing or duplicated pieces of DNA. But which genes and which stretches differ from person to person.

To learn more about the genetic quirks they have found, Dr. Scherer, director of the Centre for Applied Genomics, has received $8-million from the Ontario government to run a DNA scan on nearly every child diagnosed with autism in the province over the next three years, expected to be more than 5,000 children. Researchers in the United States and Britain have similar plans, all of it with an eye to developing diagnostic tests.

But in the direct-to-consumer age, the market rarely waits for more research. Dr. Scherer expects people will be able to buy a mail-order genetic test that scans for autism-related genes in the near future – even if the information they can glean from it is dubious at best.

“I get e-mails from U.S. companies every month, start-ups and diagnostic companies, looking for markers for autism,” he said, noting the findings for this study are not protected by patent.

In this study, approximately 10 per cent of the 1,000 people with autism tested had mutations in genes known to disrupt brain function. For this reason, Dr. Scherer believes certain variations within these genes are predictive of an autism disorder.

Still, if families came for testing now, “in the majority of cases we won’t be able to tell them anything,” he said. What’s more, the results from such tests can be so nuanced they ought to be delivered by a genetic counsellor, he added. “In many ways delivering the information is in and of itself a science.”

Study co-author Peter Szatmari, director of the Offord Centre for Child Studies at McMaster Children’s Hospital in Hamilton, said the prospect of a commercial test “makes me nervous. I don’t think we have the science yet to nail it down. … This isn’t one gene, but a profile of genes, a pattern of susceptibility, not cause.”

Autism spectrum disorders (ASD) strike one in every 110 children. Some suffer such severe cognitive impairment they’re unable to speak. Others are savants. Most show a preference for rigid routines and repetitive behaviours. But common to all are social deficits that hamper the ability to interact with others.

Currently, children generally aren’t diagnosed until age 4 or 5, after a battery of psychological tests. A genetic test could allow parents to intervene with behavioural therapies in infancy. It could also shed light on their chances of having another child with autism, and their children’s chances of having an affected child.

Lisa Bond, a single mother of two in Campbellford, Ont., waited years to learn both her children had autism spectrum disorders. When a developmental specialist tried to assess

her younger son Joshua when he was three, he refused to co-operate. Ms. Bond was told to bring him back in six months. Her son, now 14, was 6 when he was diagnosed.

“It was a nightmare for me, constantly going to doctors,” she said. “Now they realize the quicker we get to these kids the better. … There’s that critical time between the ages of 2 and 5.”

A genetic test, she said, could also tell parents about the specific problems their child is likely to encounter. As part of the study, Ms. Bond learned her son has a region of chromosome 16 deleted, which helps to explain why he also has trouble with his spine, walking and swallowing.

“Now we know this chromosome affects so many systems,” she said. “Hopefully someday parents will be able to hear when their child has autism that he might need a speech therapist, but also a heart specialist.”

Ms. Bond’s eldest child Rebecca, now 17, was diagnosed at 12 with Asperger syndrome, a high-functioning form of autism characterized by normal intelligence, striking talents and obsessive interests (in Rebecca’s case, dinosaur teeth). But she does not carry the same genetic mutation as her younger brother.

Some experts believe the increased prevalence reflects better detection and the trend to diagnose autism over other developmental disorders. Others suspect environmental triggers, such as toxins or food allergies. But no one doubts the major role genes play, or that environmental forces influence them. Autism disorders run in families, and if one identical twin develops an ASD the chances are as high as 92 per cent the other twin will as well.

For some people at the mild end of the autism spectrum, and their advocates, who see their unusual traits as characteristics that enrich society, the notion of screening for autism is highly controversial.

Dr. Szatmari said the genetic research is not geared “to eradicate the disorder, to get rid of it, but to ease the suffering earlier, when the brain is developing, and give [children] the skills to cope as they grow up.”

Still, he acknowledged the findings “can have big effects on family planning.”

Scientists used the latest microchip tools to scan the DNA of nearly 1,000 people with autism and 1,200 controls. Such scans are not designed to pick up specific mutations, but rather cover the whole genome and highlight areas where large chunks of DNA are deleted or repeated like a record skipping.

These types of hiccup mutations are known as copy-number variants, or CNVs. Researchers found that people with autism have more CNVs in their genes than controls.

In all, the study, spearheaded by post-doctoral research fellow Dalila Pinto at Sick Kids, identified more than 100 genes affected in the people with autism, many of them forming part of a network that governs how brain cells grow and talk to each other.

Some of these genes include those that overlap other forms of intellectual disabilities and certain drugs already exist to treat them.

But where researchers expected to find that a common set of CNVs would explain autism disorders, they instead found unique patterns of CNVs in each case. Most had been inherited, but some are new mutations that sprung up during conception. Researchers are now investigating whether the age of the parents increases the risk of these glitches.

Dr. Scherer said these types of mutations are rare because people with autism do not tend to have children who will go on to spread it through a population. In cases where one parent has passed down a CNV, it may be that something in the environment has transformed it from a mild trait to full blown autism. Or, he said, it could be another inherited trait has combined to result in the disorder.

Scientists suspect the genetic pattern found in autism, similar to the model uncovered in schizophrenia, will also be detected in most other neuro-psychiatric conditions.