'Little threads' coming together, doctor says

AUTISM *from page A1*

Some suffer severe cognitive impairment, others are savants. Many battle gastrointestinal problems and show a strong preference for strict routines and repetitive behaviours. But social deficits are its hallmark, impaired language, communication and the ability to interact with others.

Once considered rare, autism disorders seem to have risen dramatically over the last two decades. But Dr. Szatmari said many experts believe the increase can largely be explained by greater awareness, different diagnostic criteria and the specialized resources often made available to those with an ASD compared with another form of developmental condition.

Despite the growing awareness, autism's causes have stumped experts. Many suspect environmental triggers – prenatal hormones, toxins, food allergies and infections. But experts have long known genes play a major role. Autism disorders tend to run in families; if one identical twin has an ASD, there is a 65- to 92-per-cent chance the other will also develop the disorder. Doctors also see subtle forms of autism in parents that may not have been diagnosed.

"Still, for 99 per cent of autism cases, we don't know the underlying genes," Dr. Scherer said.

But with onetime scientific competitors sharing their families, researchers say they had enough statistical power to make connections. They also had the technology to run genome-wide scans and detect a type of genetic mutation only recently discovered.

These mutations, known as copy number variations, or CNVs, involve vast stretches of genetic code that are misplaced, repeated or deleted.

Late last year, Dr. Scherer and other colleagues reported that these quirks were far more common in the general population than expected – that people can carry extra copies of genes or be missing them completely and still be healthy.

But in this study, the scientists found certain CNVs were linked to autism – particularly if it was not seen in either parent or 500 DNA control samples and if it encompassed a genome region believed to be involved in brain function.

"These CNVs arise randomly all the time," Dr. Scherer said, "but sometimes, [depending on where they arise] they result in ASD."

Among the key findings is the involvement of a gene called Neurexin1, which researchers believe has an impact on how neurons communicate with each other. They have also found a suspicious region of Chromosome 11 that houses genes involved in the brain chemical glutamate, an important neurotransmitter.

"Nobody knew glutamate was involved in autism," Dr. Szatmari said. But it is known to be involved in epilepsy, he said, "and 20 per cent of children with autism also have epilepsy.

"All these straggly little threads are beginning to tie together into a string."

The second phase of the project, is to map the specific genes that contribute to autism.

But in uncovering "the genetic architecture" in the first phase, Dr. Scherer said autism seems much like cancer, a condition with many faces, arising from many different types of genetic mutations.

"We have to be careful," he said, "not to overinterpret the results."

Genetic counsellors at Sick Kids are already preparing for questions from parents, many of whom heard the study results at a meeting last November.

Generally, parents with one affected child are told they have a 5- to 10-per-cent chance of having another child with an ASD.

But Ms. Shuman said that's a general estimate based on population averages, and for some parents the chances could be much higher or lower.

For Ms. Jolicoeur, it is too late to consider how she and her husband, Craig Marshall, would use the information, having already had their three children, two of whom have autism. Her eldest son, Eric, 18, who read the National Geographic with his father at the age of 3, was diagnosed at age 7 with Asperger syndrome, a high-functioning form of autism, usually characterized by normal intelligence, obsessive interests in particular subjects and striking talents. But Eric's diagnosis came only after his brother Luc, 14, was diagnosed at 3 with pervasive developmental disorder, a more severe form of autism.

Still, Ms. Jolicoeur believes the discoveries, and those ahead, will be important for her youngest son, Marc, 12, who does not have a spectrum disorder and was born before Luc and Eric were diagnosed. "Marc has already said he doesn't think he would have children," she said. "But then he says, 'No, I think I would maybe have one.'"

People often ask her how she and her husband cope. "I tell them life is chaotic, busy, but it's all we have ever known," Ms. Jolicoeur said. "It is also loud and fun."

Her family has been part of Dr. Szatmari's research for more than 10 years. Ms. Jolicoeur understands that talk of screening for autism traits is controversial, since those at the mild end of the spectrum, and their advocates, see their unusual personality traits as characteristics society should accept.

But she said "it is valid" for people to have all the information they can to make their own decisions. "I didn't sign up to raise children with special needs," she said, "but they are your kids, and you love them unconditionally."

FROM KOSTERYA/THE GLOBE AND MAIL

Marie Jolicoeur and her husband, Craig Marshall, share a snack at home yesterday in Burlington, Ont., with sons, from left, Luc, Eric and Marc.