

News from Seattle and the Northwest

Autism researchers zeroing in on a genetic cause

by KEITH SEINFELD

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Scientists have been pretty sure autism must begin very early in development, possibly even at the moment a sperm meets an egg. New research, conducted partially in Seattle, supports two interesting theories:

- In families with no history of autism, it may take just one or two genetic mutations to trigger autism. But if you sampled 500 autistic children, it's possible that no two would have the exact same mutations. Each one is slightly different.
- Many autism cases start with a father's mutated sperm, as opposed to something in the mother's egg, and the chances of that happening go up as fathers get older.

To understand this first point better, imagine a room that has 400-1,000 light switches. If any one or two of those gets switched on, the brain won't develop quite right, and you've got autism (or some developmental delay).

This might be why symptoms and behaviors of autism seem to vary so much, says [Evan Eichler, a geneticist at the University of Washington](#) and lead author for one of three studies published together in the journal *Nature*. There are hundreds of different paths leading to the disorder, and each one could lead to different symptoms.

The good news is scientists are getting closer to knowing where each of those genetic switches is located, which would enable them to test for each one.

Knowing the genetic type of autism could be useful to parents.

Parents often get frustrated talking to other families with autistic children, since children with autism can be so different with respect to each other, says Eichler.

But that changes if they can get connected with others who share the same mutation:

"They say, 'My child was never like those other children. Johnny was totally different. And now that we are part of this group, we understand there are a lots of people that have similar problems as Johnny has and we are working on finding some real-life solutions.'"

Families can focus on improving day-to-day living, by sharing what works for their children with same type of autism.

Eichler's team used the sheer muscle of powerful computers to look for those rare genes. They looked at 209 children with autism—plus their parents and siblings—and then scanned the entire genomes from everyone,

looking for mutations. About a quarter of those families were recruited through the U.W. All are part of a [unique autism database called the Simons Simplex Collection](#). The other two related studies were based at Yale (which also used the Simons database) and Harvard.

The scientists found a big variety of genes, but Eichler says even if it turns out there are a thousand different mutations that can each trigger autism, it's a manageable number. "It's not infinite, just large," he says.

That opens the door to a future where parents could use a genetic test to see if their child has autism and what type.

Dad's piece of the puzzle

As for the role of aging fathers, Eichler likes to minimize its importance.

"I guess I was surprised to see so many new mutations come from dad," he says. "But, if I were a 50-year-old father, I would not be concerned."

In his study, Eichler was able to quantify the risk in a way that's not been possible before. He says a 50-year-old father is twice as likely to have an autistic child as a 30-year-old father. The reason he's not concerned: Even at age 50, it's still rare and unlikely.

The risk relative to aging is different from the risk for women who get pregnant after age 35 of having a child with down syndrome. That risk goes up exponentially, year by year. The risk of mutated sperm goes up a tiny bit every year.

The mutations are a natural part of aging; all of our cells start to have errors when they copy themselves, and those errors add up over time.