NEWS

DNA doubling on chromosome 22 shows strong ties to autism

BY **JESSICA WRIGHT**

30 MAY 2016

An extra copy of a stretch of genes on chromosome 22 may contribute to autism, according to the first study to carefully characterize a large group of individuals who carry this duplication[1]. The doubling can also lead to medical complications, such as vision or heart problems.

The region, called 22q11.2, is best known for a deletion of the same stretch of genes, which is primarily linked to schizophrenia. Some studies indicate that people with 22q11.2 deletions have an **increased risk of autism**, but in other studies, rigorous diagnostic tests have **failed to confirm** many of the autism diagnoses.

In the new study, researchers gave 20 children with 22q11.2 duplications one or both of the gold-standard diagnostic tests for autism and found that five of them have autism. The results suggest that as much as 25 percent of people with the duplication have the condition.

They also indicate that autism is more common among people with duplication than in those with the deletion. “Our study hints that duplication of genes in this region might be more specific for autism than the deletion is,” says lead researcher **Robert Schultz**, director of the Center for Autism Research at the Children’s Hospital of Philadelphia.

However, the study’s estimate for autism **prevalence** is probably inflated, says **Elliot Sherr**, professor of neurology and pediatrics at the University of California, San Francisco, who was not involved in the study. People in the general population with 22q11.2 duplication who do not have features of autism would have no reason to seek genetic testing. “These kids were only assessed because they have developmental disorders of some sort,” he says.

Chromosome clues:

For years, Schultz and his colleagues have done genetic testing on children with developmental disabilities, as well as their family members, who come to the clinic at the Children’s Hospital of Philadelphia. They have seen more than 1,000 people who turned out to have a deletion of 22q11.2. But only in the past decade have they had the technology to detect a duplication of the same region. So far, they have come across 37 people with a 22q11.2 duplication whom they were able to include in their study.

In the study, parents of 28 children filled out questionnaires that assess the children’s social and daily living skills, communication, and features of related conditions, such as attention deficit hyperactivity disorder (ADHD). The researchers found that anxiety, depression and ADHD-like symptoms are more common among children with either the deletion or the duplication than among an age- and gender-matched group of 57 controls.

The researchers then assessed 20 of the children with the duplication using an extensive parent interview called the Autism Diagnostic Interview-Revised, and, in some cases, the Autism Diagnostic Observation Schedule (ADOS), which involves clinical observation. Five children qualified for an autism diagnosis, according to these tests.

The results suggest that up to one-quarter of people with the 22q11.2 duplication have autism. Coming into the study, nearly 40 percent of the participants already had an autism diagnosis, but

the two figures are closer than the researchers had expected, based on their experiences with people who have the deletion, they say.

“We were very surprised that the majority of children who had a community diagnosis for autism also met research criteria,” says study team member **Tara Wenger**, assistant professor of pediatrics at the University of Washington.

Medical risk:

Still, the researchers used the ADOS on only eight of the children. And direct observation of the children is often needed to distinguish those who have both a 22q11.2 duplication and autism from those who just have some features of autism, says **Carrie Bearden**, professor of clinical psychology at the University of Pennsylvania, who was not involved in the study.

In support of her point, most of the 15 children with the duplication who did not receive an autism diagnosis have some features of the condition. Children who had an erroneous diagnosis of autism tend to have **repetitive behaviors**, but not social problems, the researchers found. This prominence of repetitive behaviors distinguishes children with the duplication from those with the deletion, Bearden says.

The researchers found that 9 of the 37 participants with the duplication have heart problems, 6 have hearing loss and 8 have vision problems, some of the same conditions seen in people with the deletion.

The findings show that doctors should carefully evaluate all children with autism for health issues, says Wenger. “We picked up dozens of medical problems in those children that they didn’t know they had, and some of them have potentially serious effects,” she says.

These medical problems vary from one person to the next, suggesting that other genetic variants may modify the duplication’s effect. “It seems plausible that compensatory mechanisms elsewhere in the genome, as well as environmental factors, play a role,” says **Marianne van den Bree**, professor of neuropsychiatric genetics and genomics at Cardiff University in the United Kingdom, who was not involved in the study.

Wenger and her colleagues next plan to look at children with atypical duplications of this region — those spanning fewer than the usual 40 genes — to better understand the genetic underpinnings of the various features. Some genes in the region may underlie the autism symptoms, whereas others could spawn health problems, she says.

REFERENCES:

1. Wenger T.L. *et al. Mol. Autism* **7**, 27 (2016) **PubMed**