NEWS

Many people harbor large mutations linked to autism

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Genetic changes tied to autism crop up in people without the condition, too, according to unpublished findings presented Saturday at the **2016 American Society of Human Genetics Annual Meeting** in Vancouver, Canada.

The prevalence of these **mutations in the general population** may help to explain why some people **show subtle features** of autism without meeting the criteria for a diagnosis.

Studies suggest that spontaneous deletions or duplications of large chunks of DNA, called **copy number variations** (CNVs), appear in **2 to 4 percent** of children with autism. Some people also have inherited CNVs. But these genetic changes also occur in some **unaffected siblings**.

“Our ultimate goal is to discover why these CNVs produce such variable effects,” says **Abby Hare-Harris**, who presented the findings. Hare-Harris is a postdoctoral fellow in the laboratory of **Christa Lese Martin**, director of the Autism and Developmental Medicine Institute at Geisinger Health System in Lewisburg, Pennsylvania.

Martin’s team sequenced the coding regions of the genome, called the **exome**, of 50,000 adults. The men and women are enrolled in Geisinger’s **MyCode Community Health Initiative**, a biorepository and electronic health record database.

The researchers narrowed in on 45 regions of the exome containing genetic variants linked to neurodevelopmental conditions. They found that about 2,000 of the participants have at least one CNV associated with autism, intellectual disability or schizophrenia. But less than 5 percent of this group has received treatment for any of those conditions.

Background effects:

The most common CNVs seen in the study involve the chromosomal region 2q13, which has been associated with autism and developmental delay[1]. A total of 632 — about 1 in 150 — participants have a DNA deletion or duplication in this region. None of those individuals have an autism diagnosis, but some have received treatment for developmental delay, anxiety, depression or seizures.

The team also identified 533 people with deletions or duplications of the **15q11.2 region**, which are linked, respectively, to the autism-related conditions **Angelman** syndrome and **Prader-Willi** syndrome. Of the participants, 1 in 199 have an extra copy of this region, and 1 in 163 lack part of the region. Preliminary results from an ongoing study suggest that 15q11.2 deletions may **hinder language and math ability** among typical individuals without lowering overall intelligence.

The researchers then examined 25 CNVs present in at least three of the participants. Of these, 17 cropped up most often in individuals with a diagnosis of schizophrenia, bipolar disorder or seizures, suggesting an association between these conditions and the variants. But some people who do not have any of these conditions also carry these CNVs.

Various **other genetic factors**, along with **environmental ones**, help determine whether a CNV leads to autism in any one person, Martin says. Her team is studying the families of individuals with

these CNVs to explore how genetic background is connected to autism risk.

*For more reports from the 2016 American Society of Human Genetics Annual Meeting, please **click here**.*

REFERENCES:

1. Hladilkova E. *et al. Mol. Cytogenet*. **8**, 57 (2015) **PubMed**