NEWS

Autism, fragile X follow different developmental paths

BY **ANN GRISWOLD**

1 FEBRUARY 2017

Autism and **fragile X syndrome** have distinct trajectories during childhood, according to a study that tracked children with the conditions for more than two years. In particular, children with autism show an increase in restricted interests in their preteen years that is not apparent in those with fragile X syndrome[1].

Fragile X syndrome is an inherited form of intellectual disability caused by mutations in the **FMR1** gene. About one-third of children with the syndrome also have an autism diagnosis. These children show a narrower set of **repetitive behaviors** and more interest in social interactions than children with autism alone.

The new study found that features such as social difficulties and restricted interests change more quickly and dramatically in children with autism alone than in those who have both autism and fragile X.

“People have started to recognize that the phenotypic overlap between fragile X and autism isn’t quite as clear-cut as we once thought,” says lead investigator **Molly Losh**, chair of learning disabilities, communication sciences and disorders at Northwestern University in Evanston, Illinois. The work appeared 30 December in the *Journal of Neurodevelopmental Disorders.*

The findings hint that an autism diagnosis may often arrive late in boys with fragile X syndrome: More of these boys meet the criteria for autism at age 11 than they did at age 9. Children with autism alone are often diagnosed **by age 4**.

The new study suggests separate mechanisms give rise to the divergent features of fragile X and autism, says **Leonard Abbeduto**, director of the MIND Institute at the University of California, Davis, who was not involved in the study. Understanding the biology behind the similarities and differences between the two groups could lead to targeted treatments, he says.

Parsing profiles:

Losh and her colleagues assessed the cognitive ability, language skills and behavior of 31 boys and 34 girls with fragile X, as well as 19 boys who have idiopathic autism — that of unknown origin. Clinicians assessed the children at two time points — ages 9 and 11, on average — using the **Autism Diagnostic Observation Schedule** (ADOS).

In addition, parents rated their children's social skills, repetitive behaviors and restricted interests using the **Autism Diagnostic Interview-Revised (ADI-R)**. And standardized tests measured the children's language and cognitive abilities.

About 42 percent of the children with fragile X met the ADOS and ADI-R cutoffs for autism at age 9. But by age 11, 60 percent of the children fit the criteria for autism — including many more boys than girls. About 81 percent of the boys met autism cutoffs at age 11, compared with 41 percent of the girls.

These numbers are higher than previous estimates, suggesting that many more children with fragile X have autism than are diagnosed with it. Previous estimates are based on studies in younger children with fragile X syndrome.

Boys with fragile X syndrome who had an autism diagnosis by age 9 had nearly identical features to boys with other forms of autism. These features included problems with social communication, sensory sensitivity and restricted interests.

By age 11, however, differences emerged. All of the boys made fewer attempts to engage other people socially over time, but this decline was more dramatic in boys with idiopathic autism than in those who have fragile X and autism. Although speech and eye contact similarly worsened in both groups, boys with idiopathic autism were much more likely to use stereotyped speech and showed much less eye contact than those with fragile X.

Restricted interests also increased in boys with idiopathic autism, but remained stable in boys who have both fragile X and autism.

The study suggests that autism features associated with FMR1 mutations differ from the features that stem from other genetic causes. But it is small, making it difficult to draw firm conclusions, says **Scott Hall**, associate professor of psychiatry and behavioral sciences at Stanford University in California, who was not involved in the study.

Larger studies would allow researchers to better parse the spectrum of autism features in children with fragile X syndrome, he says.

REFERENCES:

1. Lee M. *et al. J. Neurodev. Disord.* **8**, 47 (2016) **PubMed**