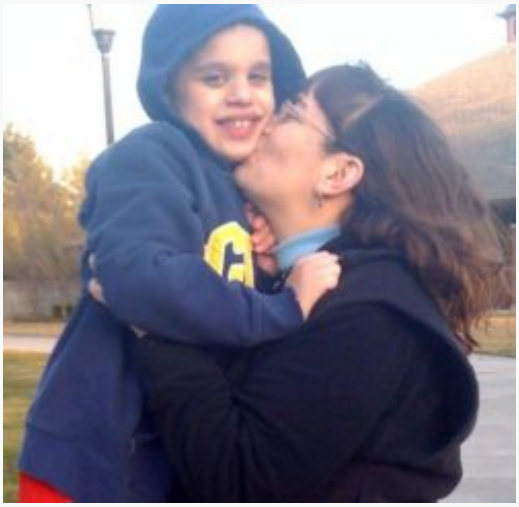
Autism Spectrum Disorder and Fragile X Syndrome

Fragile X syndrome is the most common known single gene cause of ASD

What Is Autism Spectrum Disorder?

Autism spectrum disorder (ASD) is a behavioral diagnosis. The range of symptoms in ASD vary and are generally characterized by an impaired ability to communicate and interact socially with other people. Sometimes children will not meet the diagnostic criteria for ASD but will have autistic-like features.



Read my Story

The diagnosis of ASD is usually made by a developmental or general pediatrician, neurologist, psychologist, psychiatrist, or other specialist. A clinician may make a diagnosis of ASD after observing the behavior and language of a child and using the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria for their evaluation. In addition, the diagnosis may be made after evaluating the child using a number of testing instruments, such as the Autism Diagnostic Observation Schedule – 2nd edition (ADOS-2) or the Autism Diagnostic Interview – Revised (ADI-R). These instruments are considered the gold standard – the most accurate instruments available – for a diagnosis and are often used in research.There is no blood test for ASD, and imaging studies such as MRIs don't diagnose the condition – it is purely a behavioral diagnosis similar to Attention Deficit Hyperactivity Disorder (ADHD).

What Causes ASD?

Much remains unknown about the condition—including what causes it in many individual cases. However, when a child is diagnosed with ASD, blood tests are often ordered to rule out the known genetic causes. Fragile X syndrome (FXS) is the most common known single gene cause of ASD. Other genetic causes of ASD include deletions of chromosome 15q, tuberous sclerosis and other rare genetic conditions.

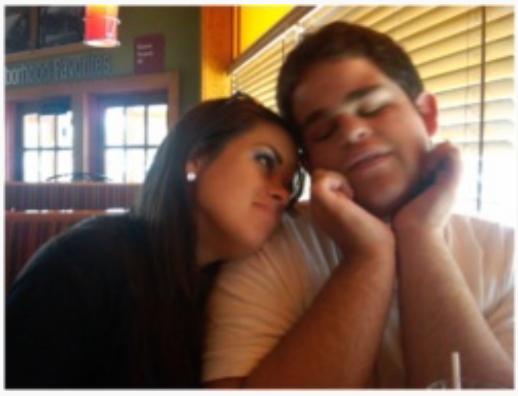
Many times a child with ASD will be tested or evaluated for all the known genetic causes of autism but no cause will be found. However, family studies have shown that in families with one child with ASD there is an increased risk for another child to have the condition. This risk is not as high as in those families with an identified single gene cause, such as FXS. It is more in line with multifactorial risks, similar to heart defects or cleft lip. This leads experts to believe there is a genetic component even in those without a single gene identified cause.

Many researchers are trying to determine both the genetic and non-genetic factors that contribute to ASD.

Relationship Between ASD and FXS

Whereas ASD is a behavioral diagnosis, FXS is a medical, or more accurately, a genetic diagnosis. When associated with FXS, ASD is caused by the genetic change or mutation in the Fragile X gene. If a child is diagnosed with ASD and then diagnosed with FXS, he or she still has ASD, it is just that the cause of their ASD is known. It is no different than someone with FXS also having ADHD or any other behavioral symptom of FXS.

The article FXS and ASD: Similar But Different highlights a well-attended panel discussion at the 13th International Fragile X Conference that addresses the topic: FXS and ASD: Clinical Insights into the Similarities and Differences for Diagnosis and Treatment.



Read my Story

How Many Children With FXS Have ASD?

Many studies have evaluated the FXS-ASD link over the past decade. Since many children with FXS are interested in social interactions, they may not meet the diagnostic criteria for ASD, even though they exhibit some features of ASD such as poor eye contact, shyness, social anxiety, hand-flapping and sensory issues. Autism is much more common in boys with FXS than in girls with FXS. According to the CDC, a national parent survey found that 46 percent of males and 16 percent of females with FXS have been diagnosed or treated for ASD. The FORWARD Registry and Database tells us that 40 percent of individuals with FXS are diagnosed with ASD by their doctor in the clinics of the Fragile X Clinical and Research Consortium (FXCRC).

How Many Children With ASD Have FXS?

About 10 percent of children with ASD are identified as having another genetic and chromosomal disorder, such as Fragile X syndrome. Given the possibility of a link, it is recommended that all children with ASD, both male and female, be referred for genetic evaluation and testing for FXS and any other genetic cause of ASD.

ASD's Effect on Children With FXS

Studies show that individuals with FXS who have autism can have a more significant intellectual disability (lower IQ) than those with FXS who do not have autism.

For further reading on the relationship between autism and Fragile X syndrome, see:

- CDC's Fragile X-related concerns page
- FXCRC Consensus Document titled "Autism Spectrum Disorder in Fragile X Syndrome"
- The Fragile X Family of Disorders: A Model for Autism and Targeted Treatments
  Abstract
  CGC-repeat expansion mutations of the Fragile X mental retardation 1 (FMR1) gene are the leading known cause of autism and autism spectrum disorders (ASD). Full mutation expansions (>200 CGC repeats) of the gene are generally silenced, resulting in the absence of the FMR1 protein and Fragile X syndrome. By contrast, smaller expansions in the premutation range (55-200 CGC repeats) results in excess gene activity and RNA toxicity, which is responsible for the neurodegenerative disorder, Fragile X-associated tremor/ataxia syndrome (FXTAS), and likely additional cases of developmental delay and autism. Thus, the FMR1 gene is causative of a common (autism) phenotype via two entirely different pathogenic mechanisms, RNA toxicity and gene silencing. The study of this gene and its pathogenic mechanisms therefore represents a paradigm for understanding gene-brain relationship and the means by which diverse genetic mechanisms can give rise to a common behavioral phenotype.
- The Fragile X Syndrome–Autism Comorbidity: What do We Really Know?
  Abstract
  Autism spectrum disorder (ASD) is a common comorbid condition in people with Fragile X syndrome (FXS). It has been assumed that ASD symptoms reflect the same underlying psychological and neurobiological impairments in both FXS and non-syndromic ASD, which has led to the claim that targeted pharmaceutical

treatments that are efficacious for core symptoms of FXS are likely to be beneficial for non-syndromic ASD as well. In contrast, we present evidence from a variety of sources suggesting that there are important differences in ASD symptoms, behavioral and psychiatric correlates, and developmental trajectories between individuals with comorbid FXS and ASD and those with non-syndromic ASD. We also present evidence suggesting that social impairments may not distinguish individuals with FXS with and without ASD. Finally, we present data that demonstrate that the neurobiological substrates of the behavioral impairments, including those reflecting core ASD symptoms, are different in FXS and non-syndromic ASD. Together, these data suggest that there are clinically important differences between FXS and non-syndromic ASD that are masked by reliance on the categorical diagnosis of ASD. We argue for use of a symptom-based approach in future research, including studies designed to evaluate treatment efficacy.

Keywords: Fragile X syndrome, autism spectrum disorder, comorbid conditions, language and communication impairments, psychiatric conditions