

## What is STXBP1?

The STXBP1 gene provides instructions for a protein that allows brain cells, or neurons, to send messages to one another. Brain cells must release chemicals called neurotransmitters to send messages. The STXBP1 protein is needed for our brain cells to release the neurotransmitters. If there is a pathogenic variant in the STXBP1 gene, not enough of the STXBP1 protein is made or the STXBP1 protein works differently, which means brain cells may not send messages to one another as well. This difference in how brain cells communicate leads to epilepsy and other developmental differences seen in people with STXBP1-related disorder. People with STXBP1-related disorder have one working copy and one non-working copy of the STXBP1 gene. Many different genetic variants in the STXBP1 gene have been identified, and these genetic variants have always been found to be new, or *de novo*, in an affected person and not inherited from either parent.

Other names for STXBP1: STXBP1-epileptic encephalopathy or developmental and epileptic encephalopathy 4 [DEE4.] The STXBP1 gene is sometimes also called MUNC-18.

## What types of seizures (and epilepsies) are associated with variants in STXBP1?

Most people with STXBP1-related disorder have [epilepsy](#), though many people who have variants in the gene will never have a seizure. Seizures may start at any point in a person's life, but they most often present during the first year of life as neonatal seizures, [infantile spasms](#), or focal-onset ([aware](#) and [impaired](#)) seizures. Later in childhood or adolescence, people may present with focal-onset seizures. In most people with STXBP1-related disorder, the seizures may be managed with [anti-seizure medications](#) or other epilepsy treatments. However, about 1 in 4 people will experience [drug-resistant epilepsy](#), meaning their seizures continue despite treatment with medications.

## What non-seizure symptoms are seen with STXBP1?

Nearly all people identified with STXBP1-related disorder have developmental differences. These developmental differences may include a spectrum of global developmental delay and features of autism spectrum disorder. Most often, these developmental differences are severe, but they may range from mild to profound. People with STXBP1 may have differences with their muscles, including low muscle tone (hypotonia) and/or increased muscle tone (spasticity). Additionally, people may have problems with their movement, including ataxia (lack of coordination) or tremors (shaky movements of the

body). Because of these differences with muscle tone and movement, many people with STXBP1 need to use a wheelchair or other equipment to help them move.

## How is STXBP1 diagnosed?

STXBP1 variants may only be found using [genetic testing](#). Gene panels, which test for the most common causes of a genetic condition, may be used to diagnose STXBP1. Epilepsy gene panels, autism/ intellectual disability gene panels, or movement disorder gene panels often test for the STXBP1 gene. Whole exome sequencing, which tests for the largest number of genes that may cause a disease, is also able to diagnose STXBP1-related disorder. Often, when seizures or developmental differences are noticed, a doctor will order an MRI to see if there is anything different about how the brain looks that could cause the symptoms. Most often, the brain MRI in people with STXBP1 variants is normal. A doctor will order an [EEG](#) to diagnose seizures or abnormal brain electrical activity in a person with STXBP1. Also, an EEG may be ordered to figure out if an abnormal movement that was seen is a seizure or not.

## How is STXBP1 treated?

Today, there are no disease-specific treatments for STXBP1-related disorders. Treatment is chosen based on a person's symptoms, and due to the broad range of symptoms and severity, an individualized treatment plan should be developed.

For [seizure treatment](#), a single or combination of anti-seizure medications are used to manage seizures. No specific anti-seizure medication has been found to be more effective than others for individuals with STXBP1-related disorder. For infantile spasms, therapies may include ACTH, high dose prednisone, and vigabatrin. [Dietary therapy](#) such as the ketogenic diet may help with seizure management for some patients. [Vagal nerve stimulation \(VNS\)](#) may also help patients experiencing drug-resistant seizures. Cognitive and developmental delays are treated with physical, occupational, and speech and augmentative communication therapies.

## How common is STXBP1?

STXBP1 is a rare condition. The exact number of people who have STXBP1 variants is unknown, but the estimated incidence rate for STXBP1 disorder is ~1:30,000 (López-Rivera et al, 2020).



## What is the outlook for STXBP1?

Currently, there is no cure for people who have STXBP1-related disorders, but there are research efforts focused on finding targeted treatments for the condition.

>90% of people with STXBP1 are expected to have lifelong developmental differences that result in cognitive impairment that ranges from mild to profound.

>80% of people with STXBP1 are expected to develop seizures within their lifetime. For many people, these seizures emerge during infancy, are treated, and then do not happen again in a person's lifetime. For some people, the epilepsy associated with STXBP1 is lifelong. Treatment for people with STXBP1 focuses on treating seizures and attempting to achieve seizure-freedom in as many people as possible. Developmental therapies are recommended to maximize the potential of every person with STXBP1.

### For more information:

- [STXBP1 Foundation](#)
- [Children's Hospital of Philadelphia \(CHOP\)](#)
- [National Organization for Rare Disorders NORD](#)
- [MedlinePlus](#)
- [Simons Searchlight](#)
- [CNCR](#)

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