STXBP1 Encephalopathy

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STXBP1 encephalopathy is a condition characterized by abnormal brain function (encephalopathy) and intellectual disability. Most affected individuals also have recurrent seizures (epilepsy).

Keywords: genetic conditions

1. Introduction

The signs and symptoms of this condition typically begin in infancy but can start later in childhood or early adulthood. In many affected individuals who have epilepsy, the seizures stop after a few years, and the other neurological problems continue throughout life. However, some people with *STXBP1* encephalopathy have seizures that persist.

In people with *STXBP1* encephalopathy, intellectual disability is often severe to profound. In addition, speech and motor skills, such as sitting, crawling, and walking, can be delayed. Though they may acquire the skill late, many children with the condition can walk independently by age 5. Affected individuals usually learn their first words later than their peers, sometimes not until late childhood. Some can communicate verbally using simple sentences, while others never develop the skill.

About 85 percent of people with *STXBP1* encephalopathy develop epilepsy. The most common seizures in this condition are infantile spasms, which occur before age 1 and consist of involuntary muscle contractions. Other seizure types that can occur in people with this condition include uncontrolled muscle twitches (myoclonic seizures), sudden episodes of weak muscle tone (atonic seizures), partial or complete loss of consciousness (absence seizures), or loss of consciousness with muscle rigidity and convulsions (tonic-clonic seizures). Most people who have *STXBP1* encephalopathy have more than one type of seizure. In about one-quarter of affected individuals, the seizures are described as refractory because they do not respond to therapy with anti-epileptic medications.

Other neurological problems that occur in people with *STXBP1* encephalopathy include features of autism spectrum disorder; weak muscle tone (hypotonia); and movement problems, such as difficulty coordinating movements (ataxia), involuntary trembling (tremors), and muscle stiffness (spasticity). In some cases, areas of brain tissue loss (atrophy) have been found on medical imaging.

2. Frequency

The prevalence of *STXBP1* encephalopathy with epilepsy is unknown. More than 280 individuals with this condition have been reported in the medical literature.

3. Causes

As its name indicates, *STXBP1* encephalopathy is caused by mutations in the *STXBP1* gene. This gene provides instructions for making syntaxin-binding protein 1. In nerve cells (neurons), this protein helps regulate the release of chemical messengers called neurotransmitters from compartments known as synaptic vesicles. The release of neurotransmitters relays signals between neurons and is critical for normal brain function. Syntaxin-binding protein 1 is also thought to play a role in the positioning and growth of neurons during brain development.

STXBP1 gene mutations reduce the amount of functional protein produced from the gene, which impairs the release of neurotransmitters. A change in neurotransmitter levels can lead to uncontrolled activation (excitation) of neurons, which causes seizures. Research suggests that a shortage of syntaxin-binding protein 1 also impairs neuron development in the brain, which could underlie encephalopathy and other neurological problems characteristic of this condition.

3.1.The Gene Associated with STXBP1 encephalopathy

- STXBP1

4. Inheritance

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Most cases of this condition result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) in an affected individual's parent or in early embryonic development. These cases occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- DEE4
- developmental and epileptic encephalopathy 4
- developmental and epileptic encephalopathy, type 4
- early-infantile epileptic encephalopathy 4
- EIEE4
- STXBP1 encephalopathy with epilepsy
- STXBP1 epileptic encephalopathy
- STXBP1-related developmental and epileptic encephalopathy
- STXBP1-related early-onset encephalopathy
- STXBP1-related epileptic encephalopathy

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