

SCN8A-Related Epilepsy with Encephalopathy

Subjects: Genetics & Heredity

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SCN8A-related epilepsy with encephalopathy is a condition characterized by recurrent seizures (epilepsy), abnormal brain function (encephalopathy), and intellectual disability. The signs and symptoms of this condition typically begin in infancy.

Keywords: genetic conditions

1. Introduction

The seizures in SCN8A-related epilepsy with encephalopathy include involuntary muscle contractions that occur before age 1 (infantile spasms), partial or complete loss of consciousness (absence seizures), involuntary muscle twitches (myoclonic seizures), or loss of consciousness with muscle rigidity and convulsions (tonic-clonic seizures). Most people with SCN8A-related epilepsy with encephalopathy have more than one type of seizure. The frequency of seizures in different individuals with this condition ranges from hundreds per day to fewer than one per month. In many individuals, the seizures are described as refractory because they do not respond to therapy with anti-epileptic medications.

Other signs and symptoms of SCN8A-related epilepsy with encephalopathy include intellectual disability that may be mild to severe. Some affected infants have normal early development but begin to lose previously acquired skills (developmental regression) and have a gradual loss in thinking ability (cognitive decline) when epilepsy develops. Problems with movement are common, and about half of affected infants cannot perform intentional movements. Behavior disorders may also occur.

In rare cases, individuals with this condition die unexpectedly for no known reason (sudden unexpected death in epilepsy or SUDEP).

2. Frequency

There are at least 140 individuals with SCN8A-related epilepsy with encephalopathy. This condition is estimated to account for 1 percent of all cases of epilepsy with encephalopathy.

3. Causes

As its name suggests, SCN8A-related epilepsy with encephalopathy is caused by mutations in the SCN8A gene. This gene provides instructions for making one part (the alpha subunit) of a sodium channel called Na_v1.6. This channel allows positively charged sodium (Na) atoms (sodium ions) to pass into nerve cells (neurons) and plays a key role in the ability of neurons to communicate by generating and transmitting electrical signals.

SCN8A gene mutations result in altered Na_v1.6 channels that stay open longer than usual, which increases the flow of sodium ions into neurons. The persistently open channels abnormally increase electrical signals, which can lead to excess activation (excitation) of neurons in the brain. The increased neuronal activity leads to seizures in people with SCN8A-related epilepsy with encephalopathy.

It is unknown how SCN8A gene mutations lead to intellectual disability, movement problems, and the other features of SCN8A-related epilepsy with encephalopathy. Because some affected children experience developmental regression after the onset of seizures, it has been suggested that the seizures may impair brain function, but it is unclear if that is the case.

3.1. The Gene Associated with SCN8A-Related Epilepsy with Encephalopathy

- SCN8A

4. Inheritance

This condition follows an autosomal dominant pattern of inheritance, 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) 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

- early infantile epileptic encephalopathy 13
- EIEE13
- SCN8A encephalopathy

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