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Genetic epilepsy with febrile seizures plus

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Description

Genetic epilepsy with febrile seizures plus (GEFS+) is a spectrum of seizure disorders of varying severity. GEFS+ is usually diagnosed in families whose members have a combination of febrile seizures, which are triggered by a high fever, and recurrent seizures (epilepsy) of other types, including seizures that are not related to fevers (afebrile seizures). The additional seizure types usually involve both sides of the brain (generalized seizures); however, seizures that involve only one side of the brain (partial seizures) occur in some affected individuals. The most common types of seizure in people with GEFS+ include myoclonic seizures, which cause involuntary muscle twitches; atonic seizures, which involve sudden episodes of weak muscle tone; and absence seizures, which cause loss of consciousness for short periods that appear as staring spells. The most common and mildest feature of the GEFS+ spectrum is simple febrile seizures, which begin in infancy and usually stop by age 5. When the febrile seizures continue after age 5 or other types of seizure develop, the condition is called febrile seizures plus (FS+). Seizures in FS+ usually end in

early adolescence. A condition called Dravet syndrome (also known as severe myoclonic epilepsy of infancy or SMEI) is often considered part of the GEFS+ spectrum and is the most severe disorder in this group. Affected infants typically have prolonged seizures lasting several minutes (status epilepticus), which are triggered by fever. Other seizure types, including afebrile seizures, begin in early childhood. These types can include myoclonic or absence seizures. In Dravet syndrome, these seizures are difficult to control with medication, and they can worsen over time. A decline in brain function is also common in Dravet syndrome. Affected individuals usually develop normally in the first year of life, but then development stalls, and some affected children lose already-acquired skills (developmental regression). Many people with Dravet syndrome have difficulty coordinating movements (ataxia) and intellectual disability. Some people with GEFS+ have seizure disorders of intermediate severity that may not fit into the classical diagnosis of simple febrile seizures, FS+, or Dravet syndrome. Family members with GEFS+ may have different combinations of febrile seizures and epilepsy. For example, one affected family member may have only febrile seizures, while another also has myoclonic epilepsy. While GEFS+ is usually diagnosed in families, it can occur in individuals with no history of the condition in their family.

Frequency

GEFS+ is a rare condition. Its prevalence is unknown.

Causes

Mutations in several genes, including some that have not been identified, can cause GEFS+. The most commonly associated gene is SCN1A. More than 80 percent of Dravet syndrome cases and about 10 percent of other GEFS+ cases are caused by changes in this gene. Mutations in other

genes have been found in only a small number of affected individuals or families. The SCN1A gene and others associated with GEFS+ provide instructions for making pieces (subunits) of channels that transport positively charged sodium atoms (sodium ions) into cells. The transport of these ions helps generate and transmit electrical signals between nerve cells (neurons). Proteins produced from other genes involved in GEFS+ are subunits of another type of ion channel called the GABAA receptor. GABAA receptor channels block (inhibit) signaling between neurons. Still other GEFS+-associated genes are also involved in nerve signaling. Mutations in the SCN1A gene have a variety of effects on sodium channels. Many mutations that cause Dravet syndrome reduce the number of functional channels in each cell. Mutations that cause the milder GEFS+ disorders likely alter the channel's structure. All of these genetic changes affect the ability of the channels to transport sodium ions into neurons. Some mutations are thought to reduce channel activity while others may increase it. It is unclear, however, how these changes underlie the development of seizures. Some studies show that certain SCN1A gene mutations cause signaling between neurons to be constantly turned on (stimulated). Researchers believe that overstimulation of certain neurons in the brain triggers the abnormal brain activity associated with seizures. It is not known if all SCN1A gene mutations have the same effect. Changes in GABAA receptor subunit genes impair the channel's function, causing uncontrolled signaling between neurons, which likely leads to seizures. Researchers do not understand how changes in any one of the genes associated with GEFS+ can lead to a range of seizure disorders. Because the disorders are so varied, even among family members, researchers believe that other genes and environmental factors help determine the severity of the condition.

Learn more about the genes associated with Genetic epilepsy with febrile seizures plus

SCN1A

SCN9A

Additional Information from NCBI Gene:

GABRD

GABRG2

SCN1B

SCN2A

STX1B

Inheritance

GEFS+ is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In some cases, an affected person inherits the mutation from one affected parent. Other cases result from new (de novo) mutations in the gene and occur in people with no history of the disorder in their family. Dravet syndrome is almost always caused by de novo mutations, although it can be inherited from a parent who has a milder form of GEFS+. Other forms of GEFS+ are usually inherited from an affected parent. Rarely, Dravet syndrome or other forms of GEFS+ are inherited from a parent with somatic mosaicism. Somatic mosaicism means that some of the body's cells have the gene mutation, and others do not. A parent with mosaicism may be less severely affected or not show any signs or symptoms of GEFS+.

Other Names for This Condition

GEFS+ Generalized epilepsy with febrile seizures plus

Additional Information & Resources

Genetic Testing Information

Genetic Testing Registry: Generalized epilepsy with febrile seizures plus

Genetic Testing Registry: Generalized epilepsy with febrile seizures plus 3

Genetic Testing Registry: Generalized epilepsy with febrile seizures plus, type 1

Genetic Testing Registry: Generalized epilepsy with febrile seizures plus, type 2

Genetic Testing Registry: Generalized epilepsy with febrile seizures plus, type 9

Genetic Testing Registry: SCN2A-related generalized epilepsy with febrile seizures plus

Genetic and Rare Diseases Information Center

Dravet syndrome

Myoclonic-astatic epilepsy

Patient Support and Advocacy Resources

National Organization for Rare Disorders (NORD)

Catalog of Genes and Diseases from OMIM

GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS, TYPE 2; GEFSP2

GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS, TYPE 1; GEFSP1

FEBRILE SEIZURES, FAMILIAL, 8; FEB8

GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS, TYPE 9; GEFSP9

EPILEPSY, IDIOPATHIC GENERALIZED, SUSCEPTIBILITY TO, 10; EIG10

GENERALIZED EPILEPSY WITH FEBRILE SEIZURES PLUS, TYPE 7; GEFSP7

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