

Developmental and Epileptic Encephalopathy 1

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Developmental and epileptic encephalopathy 1 (DEE1) is a seizure disorder characterized by a type of seizure known as infantile spasms. The spasms usually appear before the age of 1.

Keywords: genetic conditions

1. Introduction

Several types of spasms have been described, but the most commonly reported type involves bending at the waist and neck and extending the arms and legs (sometimes called a jackknife spasm). Each spasm lasts only seconds, but they occur in clusters several minutes long. Although individuals do not usually have spasms while they are sleeping, the spasms commonly occur just after awakening. Infantile spasms usually stop by age 5, but many children then develop other types of seizures that recur throughout their lives.

Most babies with DEE1 have characteristic results on an electroencephalogram (EEG), a test used to measure the electrical activity of the brain. The EEG of these individuals typically shows an irregular pattern known as hypsarrhythmia, and this finding can help differentiate infantile spasms from other types of seizures.

Early in life, babies with DEE1 stop developing normally and begin to lose skills they have acquired (developmental regression), such as sitting, rolling over, and babbling. Most affected individuals also have intellectual disability throughout their lives.

2. Frequency

Infantile spasms are estimated to affect 1 to 1.6 in 100,000 individuals. This estimate includes DEE1 as well as infantile spasms that have other causes.

3. Causes

DEE1 is caused by mutations in the *ARX* gene. The protein produced from this gene plays a role in the normal functioning of the brain by regulating other genes that contribute to brain development. Research suggests that mutations in the *ARX* gene reduce the amount or function of the *ARX* protein. A shortage of *ARX* function is thought to disrupt normal brain development, leading to seizures and intellectual disability.

It is likely that mutations in other genes that have not been identified cause rare cases of DEE1. Infantile spasms can also have nongenetic causes, such as brain malformations, other disorders that affect brain function, or brain damage. In addition, changes in genes that are not located on the X chromosome cause infantile spasms in rare cases.

3.1. The Gene Associated with Developmental and Epileptic Encephalopathy 1

- *ARX*

4. Inheritance

DEE1 is inherited in an X-linked recessive pattern. The *ARX* gene is located on the X chromosome, which is one of the two sex chromosomes. In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), a mutation would usually have to occur in both copies of the gene to cause the disorder. However, in some instances, one altered copy of the *ARX* gene is sufficient because the X chromosome with the normal copy of the *ARX* gene is turned off through a process called X-inactivation.

Early in embryonic development in females, one of the two X chromosomes is permanently inactivated in somatic cells (cells other than egg and sperm cells). X-inactivation ensures that females, like males, have only one active copy of the X chromosome in each body cell.

Usually X-inactivation occurs randomly, such that each X chromosome is active in about half of the body cells. Sometimes X-inactivation is not random, and one X chromosome is active in more than half of cells. When X-inactivation does not occur randomly, it is called skewed X-inactivation. Some *ARX* gene mutations may be associated with skewed X-inactivation, which results in the inactivation of the X chromosome with the normal copy of the *ARX* gene in most cells of the body. This skewed X-inactivation causes the chromosome with the mutated *ARX* gene to be expressed in more than half of cells, causing DEE1.

A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

5. Other Names for This Condition

- early infantile epileptic encephalopathy-1
- EIEE1
- epileptic encephalopathy, early infantile, 1
- infantile epileptic-dyskinetic encephalopathy
- ISSX
- ISSX1
- X-linked infantile spasm syndrome
- X-linked infantile spasm syndrome 1
- X-linked Ohtahara syndrome
- X-linked West syndrome

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