

Familial focal epilepsy with variable foci

Description

Familial focal epilepsy with variable foci (FFEVF) is an uncommon form of recurrent seizures (epilepsy) that runs in families. Seizures associated with FFEVF can begin at any time from infancy to adulthood. The seizures are described as focal or partial, which means they begin in one region of the brain and do not cause a loss of consciousness. In more than 70 percent of affected individuals, these seizures begin in one of two areas of the brain, either the temporal lobe or the frontal lobe. The region of the brain where the seizures start tends to stay the same over time. In rare instances, seizure activity that starts in one area spreads to affect the entire brain and causes a loss of consciousness, muscle stiffening, and rhythmic jerking. Episodes that begin as partial seizures and spread throughout the brain are known as secondarily generalized seizures.

Among family members with FFEVF, individuals may not have the same brain region affected (variable foci), meaning that one person's seizures may not begin in the same part of the brain as their affected relative.

Some individuals with FFEVF also have a brain malformation called focal cortical dysplasia. Seizures in these individuals are typically not well-controlled with medication.

Most people with FFEVF are intellectually normal, and there are no problems with their brain function between seizures. However, some people with FFEVF have developed psychiatric disorders (such as schizophrenia), behavioral problems, or intellectual disability. It is unclear whether these additional features are directly related to epilepsy in these individuals.

Frequency

The prevalence of FFEVF is unknown.

Causes

Most cases of FFEVF are caused by mutations in the *DEPDC5* gene with fewer cases caused by mutations in the *NPRL2* or *NPRL3* gene. These three genes provide instructions for making proteins that attach (bind) to each other to form a protein complex called GATOR1. This complex is found in cells throughout the body, where it regulates a signaling pathway involved in cell growth and division (proliferation), the

survival of cells, and the creation (synthesis) of new proteins. The role of the GATOR1 complex is to block (inhibit) this pathway when it is not needed.

A mutation in any one of the three genes associated with FFEVF reduces GATOR1 complex formation, leading to an abnormally active signaling pathway. It is unclear how overactivity in this pathway leads to the focal seizures of FFEVF. Research suggests that increased signaling in the brain leads to changes in the development of the junctions between nerve cells (synapses) and increased activation (excitation) of nerve cells, which can cause seizures. Increased excitation of nerve cells can also cause enlargement of these cells, which is characteristic of focal cortical dysplasia.

It is unknown why some individuals with the same mutation have seizures that start in different regions of the brain. Researchers believe that other, unknown genes may influence the features of FFEVF.

Some individuals with FFEVF do not have an identified mutation in any of these three genes. The cause of the condition in these individuals is unknown.

Learn more about the genes associated with Familial focal epilepsy with variable foci

- DEPDC5
- NPRL2
- NPRL3

Inheritance

FFEVF is inherited in an autosomal dominant pattern, which means one copy of an altered gene in each cell is sufficient to cause the disorder. In most cases, an affected person inherits the mutation from one parent.

For unknown reasons, some people with FFEVF caused by a *DEPDC5* gene mutation never develop the condition, a situation known as reduced penetrance. Approximately 60 percent of individuals with *DEPDC5* gene mutations go on to develop FFEVF.

Other Names for This Condition

- Familial partial epilepsy with variable foci
- FFEVF
- Partial epilepsy with variable foci

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Epilepsy, familial focal, with variable foci 1 (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C4551983/>)

- Genetic Testing Registry: Epilepsy, familial focal, with variable foci 2 (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C4310709/>)
- Genetic Testing Registry: Epilepsy, familial focal, with variable foci 3 (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C4310708/>)

Genetic and Rare Diseases Information Center

- Familial focal epilepsy with variable foci (<https://rarediseases.info.nih.gov/diseases/13295/index>)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Catalog of Genes and Diseases from OMIM

- EPILEPSY, FAMILIAL FOCAL, WITH VARIABLE FOCI 1; FFEVF1 (<https://omim.org/entry/604364>)
- EPILEPSY, FAMILIAL FOCAL, WITH VARIABLE FOCI 2; FFEVF2 (<https://omim.org/entry/617116>)
- EPILEPSY, FAMILIAL FOCAL, WITH VARIABLE FOCI 3; FFEVF3 (<https://omim.org/entry/617118>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28familial+focal+epilepsy+with+variable+foci%5BTIAB%5D%29+OR+%28familial+partial+epilepsy+with+variable+foci%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>)

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Last updated March 1, 2017