Episodic Ataxia

Subjects: Genetics & Heredity
Contributor: Nicole Yin

Episodic ataxia is a group of related conditions that affect the nervous system and cause problems with movement. People with episodic ataxia have recurrent episodes of poor coordination and balance (ataxia). During these episodes, many people also experience dizziness (vertigo), nausea and vomiting, migraine headaches, blurred or double vision, slurred speech, and ringing in the ears (tinnitus). Seizures, muscle weakness, and paralysis affecting one side of the body (hemiplegia) may also occur during attacks. Additionally, some affected individuals have a muscle abnormality called myokymia during or between episodes. This abnormality can cause muscle cramping, stiffness, and continuous, fine muscle twitching that appears as rippling under the skin.

Keywords: genetic conditions

1. Introduction

Episodes of ataxia and other symptoms can begin anytime from early childhood to adulthood. They can be triggered by environmental factors such as emotional stress, caffeine, alcohol, certain medications, physical activity, and illness. The frequency of attacks ranges from several per day to one or two per year. Between episodes, some affected individuals continue to experience ataxia, which may worsen over time, as well as involuntary eye movements called nystagmus.

Researchers have identified at least seven types of episodic ataxia, designated type 1 through type 7. The types are distinguished by their pattern of signs and symptoms, age of onset, length of attacks, and, when known, genetic cause.

2. Frequency

Episodic ataxia is uncommon, affecting less than 1 in 100,000 people. Only types 1 and 2 have been identified in more than one family, and type 2 is by far the most common form of the condition.

3. Causes

Episodic ataxia can be caused by mutations in several genes that play important roles in the nervous system. Three of these genes, *KCNA1*, *CACNA1A*, and *CACNB4*, provide instructions for making proteins that are involved in the transport of charged atoms (ions) across cell membranes. The movement of these ions is critical for normal signaling between nerve cells (neurons) in the brain and other parts of the nervous system. Mutations in the *KCNA1*, *CACNA1A*, and *CACNB4* genes are responsible for episodic ataxia types 1, 2, and 5, respectively.

Mutations in the *SLC1A3* gene have been found to cause episodic ataxia type 6. This gene provides instructions for making a protein that transports a brain chemical (neurotransmitter) called glutamate. Neurotransmitters, including glutamate, allow neurons to communicate by relaying chemical signals from one neuron to another.

Researchers believe that mutations in the *KCNA1*, *CACNA1A*, *CACNB4*, and *SLC1A3* genes alter the transport of ions and glutamate in the brain, which causes certain neurons to become overexcited and disrupts normal communication between these cells. Although changes in chemical signaling in the brain underlie the recurrent attacks seen in people with episodic ataxia, it is unclear how mutations in these genes cause the specific features of the disorder.

The genetic causes of episodic ataxia types 3, 4, and 7 have not been identified. Researchers are looking for additional genes that can cause episodic ataxia.

3.1. The Genes Associated with Episodic Ataxia

- CACNA1A
- CACNB4

- KCNA1
- SLC1A3

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.

In some cases, an affected person inherits the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- EA

References

1. Cader MZ, Steckley JL, Dyment DA, McLachlan RS, Ebers GC. A genome-wide screenand linkage mapping for a large pedigree with episodic ataxia. Neurology. 2005Jul 12;65(1):156-8.
2. Damji KF, Allingham RR, Pollock SC, Small K, Lewis KE, Stajich JM, Yamaoka LH,Vance JM, Pericak-Vance MA. Periodic vestibulocerebellar ataxia, an autosomaldominant ataxia with defective smooth pursuit, is genetically distinct from otherautosomal dominant ataxias. Arch Neurol. 1996 Apr;53(4):338-44. Review.
3. Escayg A, De Waard M, Lee DD, Bichet D, Wolf P, Mayer T, Johnston J, Baloh R, Sander T, Meisler MH. Coding and noncoding variation of the human calcium-channelbeta4-subunit gene CACNB4 in patients with idiopathic generalized epilepsy andepisodic ataxia. Am J Hum Genet. 2000 May;66(5):1531-9.
4. Jen J, Kim GW, Baloh RW. Clinical spectrum of episodic ataxia type 2.Neurology. 2004 Jan 13;62(1):17-22.
5. Jen JC, Graves TD, Hess EJ, Hanna MG, Griggs RC, Baloh RW; CINCHinvestigators. Primary episodic ataxias: diagnosis, pathogenesis and treatment.Brain. 2007 Oct;130(Pt 10):2484-93.
6. Jen JC, Wan J, Palos TP, Howard BD, Baloh RW. Mutation in the glutamatetransporter EAAT1 causes episodic ataxia, hemiplegia, and seizures. Neurology.2005 Aug 23;65(4):529-34.
7. Kerber KA, Jen JC, Lee H, Nelson SF, Baloh RW. A new episodic ataxia syndrome with linkage to chromosome 19q13. Arch Neurol. 2007 May;64(5):749-52.
8. Rajakulendran S, Schorge S, Kullmann DM, Hanna MG. Episodic ataxia type 1: aneuronal potassium channelopathy. Neurotherapeutics. 2007 Apr;4(2):258-66.Review.
9. Spacey S. Episodic Ataxia Type 2 – RETIRED CHAPTER, FOR HISTORICAL REFERENCEONLY. 2003 Feb 24 [updated 2015 Oct 15]. In: Adam MP, Ardinger HH, Pagon RA,Wallace SE, Bean LJH, Stephens K, Amemiya A, editors. GeneReviews® [Internet].Seattle (WA): University of Washington, Seattle; 1993-2020. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1501/
10. Steckley JL, Ebers GC, Cader MZ, McLachlan RS. An autosomal dominant disorder with episodic ataxia, vertigo, and tinnitus. Neurology. 2001 Oct23;57(8):1499-502.
11. Strupp M, Zwergal A, Brandt T. Episodic ataxia type 2. Neurotherapeutics. 2007Apr;4(2):267-73. Review.