Hereditary hyperekplexia

Description

Hereditary hyperekplexia is a condition in which affected infants have increased muscle tone (hypertonia) and an exaggerated startle reaction to unexpected stimuli, especially loud noises. Following the startle reaction, infants experience a brief period in which they are very rigid and unable to move. During these rigid periods, some infants stop breathing, which, if prolonged, can be fatal. Infants with hereditary hyperekplexia have hypertonia at all times, except when they are sleeping.

Other signs and symptoms of hereditary hyperekplexia can include muscle twitches when falling asleep (hypnagogic myoclonus) and movements of the arms or legs while asleep. Some infants, when tapped on the nose, extend their head forward and have spasms of the limb and neck muscles. Rarely, infants with hereditary hyperekplexia experience recurrent seizures (epilepsy).

The signs and symptoms of hereditary hyperekplexia typically fade by age 1. However, older individuals with hereditary hyperekplexia may still startle easily and have periods of rigidity, which can cause them to fall down. They may also continue to have hypnagogic myoclonus or movements during sleep. As they get older, individuals with this condition may have a low tolerance for crowded places and loud noises. People with hereditary hyperekplexia who have epilepsy have the seizure disorder throughout their lives.

Hereditary hyperekplexia may explain some cases of sudden infant death syndrome (SIDS), which is a major cause of unexplained death in babies younger than 1 year.

Frequency

The exact prevalence of hereditary hyperekplexia is unknown. This condition has been identified in more than 150 individuals worldwide.

Causes

Mutations in multiple genes have been found to cause hereditary hyperekplexia. Most of these genes provide instructions for producing proteins that are found in nerve cells (neurons). These proteins are involved in the response of neurons to a molecule called glycine. This molecule is an amino acid, which is a building block of proteins. Glycine also acts as a neurotransmitter, which is a chemical messenger that transmits signals in

the nervous system. Gene mutations that cause hereditary hyperekplexia disrupt normal glycine signaling in neurons in the spinal cord and the part of the brain that is connected to the spinal cord (the brainstem). Abnormal signaling in neurons in the brain and neurons that send signals to muscles throughout the body result in abnormal muscle movements, exaggerated startle reaction, and other symptoms characteristic of this disorder.

Most cases of hereditary hyperekplexia are caused by mutations in the *GLRA1* gene. The *GLRA1* gene provides instructions for making one part, the alpha (α)1 subunit, of the glycine receptor protein. When this protein attaches (binds) to glycine, signaling between cells is stopped. *GLRA1* gene mutations lead to the production of a receptor that cannot properly respond to glycine. As a result, glycine is less able to regulate signaling in the spinal cord and brainstem leading to increased cells signaling and the signs and symptoms of hereditary hyperekplexia. Mutations in other genes account for the remaining cases of hereditary hyperekplexia.

Learn more about the gene associated with Hereditary hyperekplexia

- GLRA1

Additional Information from NCBI Gene:

- GLRB
- SLC6A5

Inheritance

Hereditary hyperekplexia has different inheritance patterns.

This condition can be inherited in an autosomal dominant pattern, which means a mutation in one copy of any of the associated genes in each cell is sufficient to cause the disorder. In some cases, an affected person inherits the mutation from one affected parent. Other cases may result from new mutations in the gene. These cases occur in people with no history of the disorder in their family.

Hereditary hyperekplexia can also be inherited in an autosomal recessive pattern, which means one of the associated genes has mutations in both copies of the gene in each cell. The parents of an individual with an autosomal recessive disorder typically each carry one copy of the altered gene, but do not show signs and symptoms of the disorder.

Other Names for This Condition

- Congenital stiff-man syndrome
- Congenital stiff-person syndrome
- Familial hyperekplexia

- Hyperekplexia
- Startle syndrome
- STHE
- Stiff-baby syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Hyperekplexia (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0234166/)
- Genetic Testing Registry: Hyperekplexia 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4551954/)
- Genetic Testing Registry: Hyperekplexia 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3553291/)
- Genetic Testing Registry: Hyperekplexia 3 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3553288/)

Genetic and Rare Diseases Information Center

- Hereditary hyperekplexia (https://rarediseases.info.nih.gov/diseases/3129/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Hereditary hyperekplexia%22)

Catalog of Genes and Diseases from OMIM

- HYPEREKPLEXIA 1; HKPX1 (https://omim.org/entry/149400)
- HYPEREKPLEXIA 3; HKPX3 (https://omim.org/entry/614618)
- HYPEREKPLEXIA 2; HKPX2 (https://omim.org/entry/614619)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28hyperekplexia%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+day

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