Hereditary sensory and autonomic neuropathy type II

Description

Hereditary sensory and autonomic neuropathy type II (HSAN2) is a condition that primarily affects the sensory nerve cells (sensory neurons), which transmit information about sensations such as pain, temperature, and touch to the brain. These sensations are impaired in people with HSAN2. In some affected people, the condition may also cause mild abnormalities of the autonomic neurons, which control involuntary body functions such as heart rate, digestion, and breathing. The sensory and autonomic neurons are part of the body's peripheral nervous system, which comprises the nerves outside the brain and spinal cord. HSAN2 is considered a form of peripheral neuropathy.

The signs and symptoms of HSAN2 typically begin in infancy or early childhood. The first sign of the condition is usually numbness in the hands and feet. Soon after, affected individuals lose the ability to feel pain or sense hot and cold. In people with HSAN2, unnoticed injuries often lead to open sores (ulcers) on the hands and feet. Because affected individuals cannot feel the pain of these sores, they may not seek treatment right away. Without treatment, the ulcers can become infected and may require amputation of the affected area. People with HSAN2 often injure themselves unintentionally, typically by biting the tongue, lips, or fingers. These injuries may lead to loss of the affected areas, such as the tip of the tongue. Affected individuals often have injuries and fractures in their hands, feet, limbs, and joints that go untreated because of the inability to feel pain. Repeated injury can lead to a condition called Charcot joints, in which the bones and tissue surrounding joints are damaged.

The effects of HSAN2 on the autonomic nervous system are more variable. Some infants with HSAN2 have digestive problems such as the backflow of stomach acids into the esophagus (gastroesophageal reflux) or slow eye-blink or gag reflexes. Affected individuals may also have weak deep-tendon reflexes, such as the reflex being tested when a doctor taps the knee with a hammer.

Some people with HSAN2 lose a type of taste bud on the tip of the tongue called lingual fungiform papillae and have a diminished sense of taste.

Frequency

HSAN2 is a rare disease; however, the prevalence is unknown.

Causes

There are several types of HSAN2, each caused by mutations in a different gene. HSAN2A is caused by mutations in the *WNK1* gene, and HSAN2B is caused by mutations in the *RETREG1* gene. Additional types caused by mutations in other genes are rare. Although different genes are involved, all types of HSAN2 have similar signs and symptoms.

The *WNK1* gene provides instructions for making multiple versions (isoforms) of the WNK1 protein. HSAN2A is caused by mutations that affect a particular isoform called the WNK1/HSN2 protein. This protein is found in the cells of the nervous system, including sensory neurons. The mutations involved in HSAN2A result in an abnormally short WNK1/HSN2 protein. Although the function of this protein is not well understood, it is likely that the abnormally short version cannot function properly or is broken down. People with HSAN2A have a reduction in the number of sensory neurons; however, the role that WNK1/HSN2 protein changes play in that loss is unclear.

HSAN2B is caused by mutations in the *RETREG1* gene. These mutations lead to an abnormally short and nonfunctional protein. The RETREG1 protein is normally found in sensory and autonomic neurons. It is involved in the recycling of worn-out cell parts (autophagy), specifically a cell structure called the endoplasmic reticulum. When the RETREG1 protein is nonfunctional, recycling of the endoplasmic reticulum is impaired. The buildup of these structures likely results in death of the neurons.

The loss of neurons leads to the inability to feel pain, temperature, and touch sensations and to the impairment of the autonomic nervous system seen in people with HSAN2.

Learn more about the genes associated with Hereditary sensory and autonomic neuropathy type II

- RETREG1
- SCN9A
- WNK1

Additional Information from NCBI Gene:

- KIF1A

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Congenital sensory neuropathy
- Hereditary sensory and autonomic neuropathy type 2
- HSAN type II
- HSAN2
- HSAN2A
- HSAN2B
- HSAN2C
- HSAN2D
- HSANII
- HSN type II
- Morvan disease

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Neuropathy, hereditary sensory and autonomic, type 2A (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2752089/)
- Genetic Testing Registry: Neuropathy, hereditary sensory and autonomic, type 2B (https://www.ncbi.nlm.nih.gov/gtr/conditions/C2751092/)

Genetic and Rare Diseases Information Center

- Hereditary sensory and autonomic neuropathy type 2 (https://rarediseases.info.nih.gov/diseases/3976/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 sensory and autonomic neuropathy type II%22)

Catalog of Genes and Diseases from OMIM

- NEUROPATHY, HEREDITARY SENSORY AND AUTONOMIC, TYPE IIA; HSAN2A (https://omim.org/entry/201300)

- NEUROPATHY, HEREDITARY SENSORY AND AUTONOMIC, TYPE IIB; HSAN2B (https://omim.org/entry/613115)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28hereditary+sensory+and+autonomic+neuropathy+type+ii%5BTIAB%5D%29+OR+%28HSAN2%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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