

Hereditary Sensory Neuropathy Type IA

Subjects: Genetics & Heredity

Contributor: Camila Xu

Hereditary sensory neuropathy type IA is a condition characterized by nerve abnormalities in the legs and feet (peripheral neuropathy).

Keywords: genetic conditions

1. Introduction

Many people with this condition experience prickling or tingling sensations (paresthesias), numbness, and a reduced ability to feel pain and sense hot and cold. Some affected individuals do not lose sensation, but instead feel shooting pains in their legs and feet. As the disorder progresses, the sensory abnormalities can affect the hands, arms, shoulders, joints, and abdomen. Affected individuals may also experience muscle wasting and weakness as they get older. Weakness in the ankle muscles can make walking difficult. As the condition progresses, some people with hereditary sensory neuropathy type IA require wheelchair assistance.

Individuals with hereditary sensory neuropathy type IA typically get open sores (ulcers) on their feet or hands or infections of the soft tissue of the fingertips (whitlows) that are slow to heal. Because affected individuals cannot feel the pain of these sores, they may not seek immediate treatment. Without treatment, the ulcers can become infected and may require amputation of the surrounding area or limb.

Some people with hereditary sensory neuropathy type IA develop hearing loss caused by abnormalities of the inner ear (sensorineural hearing loss). Hearing loss typically develops in middle to late adulthood.

The signs and symptoms of hereditary sensory neuropathy type IA can begin anytime between adolescence and late adulthood. While the features of this condition tend to worsen over time, affected individuals have a normal life expectancy if signs and symptoms are properly treated.

2. Frequency

Hereditary sensory neuropathy type IA is a rare condition; its prevalence is estimated to be 1 to 2 per 100,000 individuals.

3. Causes

Mutations in the *SPTLC1* gene cause hereditary sensory neuropathy type IA. The *SPTLC1* gene provides instructions for making one part (subunit) of an enzyme called serine palmitoyltransferase (SPT). The SPT enzyme is involved in making certain fats called sphingolipids. Sphingolipids are important components of cell membranes and play a role in many cell functions.

SPTLC1 gene mutations reduce the amount of functional SPTLC1 subunit that is produced, which results in an SPT enzyme with altered activity. This altered enzyme makes molecules called deoxysphingoid bases, which it does not normally produce. Because of this new function, the SPT enzyme's production of sphingolipid is reduced. Overall, there does not seem to be a decrease in sphingolipid production because the body is able to compensate for the SPT enzyme's reduced production. When accumulated, deoxysphingoid bases are toxic to nerve cells (neurons). The gradual destruction of neurons caused by the buildup of these toxic molecules results in loss of sensation and muscle weakness in people with hereditary sensory neuropathy type IA. Although the SPT enzyme does not produce a normal amount of sphingolipids, the body is able to compensate, and there does not seem to be an overall reduction of these fats in the body.

3.1. The gene associated with Hereditary sensory neuropathy type IA

- SPTLC1

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.

5. Other Names for This Condition

- autosomal dominant hereditary sensory radicular neuropathy, type 1A
- hereditary sensory and autonomic neuropathy, type IA
- HSN IA
- HSN1A
- HSN IA
- HSN1A

References

1. Bejaoui K, Wu C, Scheffler MD, Haan G, Ashby P, Wu L, de Jong P, Brown RH Jr. SPTLC1 is mutated in hereditary sensory neuropathy, type 1. *Nat Genet.* 2001Mar;27(3):261-2.
2. Dawkins JL, Hulme DJ, Brahmabhatt SB, Auer-Grumbach M, Nicholson GA. Mutations in SPTLC1, encoding serine palmitoyltransferase, long chain base subunit-1, cause hereditary sensory neuropathy type I. *Nat Genet.* 2001 Mar;27(3):309-12.
3. Houlden H, King R, Blake J, Groves M, Love S, Woodward C, Hammans S, Nicoll J, Lennox G, O'Donovan DG, Gabriel C, Thomas PK, Reilly MM. Clinical, pathological and genetic characterization of hereditary sensory and autonomic neuropathy type 1 (HSAN I). *Brain.* 2006 Feb;129(Pt 2):411-25.
4. Penno A, Reilly MM, Houlden H, Laurá M, Rentsch K, Niederkofler V, Stoeckli ET, Nicholson G, Eichler F, Brown RH Jr, von Eckardstein A, Hornemann T. Hereditary sensory neuropathy type 1 is caused by the accumulation of two neurotoxic sphingolipids. *J Biol Chem.* 2010 Apr 9;285(15):11178-87. doi:10.1074/jbc.M109.092973.
5. Rotthier A, Penno A, Rautenstrauss B, Auer-Grumbach M, Stettner GM, Asselbergh B, Van Hoof K, Sticht H, Lévy N, Timmerman V, Hornemann T, Janssens K. Characterization of two mutations in the SPTLC1 subunit of serine palmitoyltransferase associated with hereditary sensory and autonomic neuropathy type I. *Hum Mutat.* 2011 Jun;32(6):E2211-25. doi: 10.1002/humu.21481.

Retrieved from <https://encyclopedia.pub/entry/history/show/11556>