ATP11A: Hypomyelinating Leukodystrophy 24 (HLD24)

UNDERSTANDING GENES & CHROMOSOMES

What is HLD24?

Hypomyelinating leukodystrophies are a group of disorders that affect the central nervous system. More specifically, the formation of myelin is disrupted. Myelin is the protective layer of insulation around our nerves that is important for their activity, including the activity of neurons in the brain.

There are a number of different HLDs that are caused by changes to different genes. HLD24 is caused by changes to a gene called ATP11A.

Less than 10 people to date (2025) with HLD24 have been reported in the medical literature. With the information available so far, it is thought that people with HLD24 are likely to have developmental delay and learning difficulties (or intellectual disability) and speech and language difficulties. Children with this condition may also have seizures and other nerve-related symptoms (neuropathies). ATP11A variants have also been found in a few people who have seizures but no other symptoms or features.

Different changes to the ATP11A gene can cause different conditions that are not covered in this guide, e.g. Autosomal Dominant Deafness 84 (DFNA84) and Autosomal Dominant Auditory Neuropathy 2 (AUNA2).

What causes HLD24?

The genetic information in the ATP11A gene is used to make a protein called phospholipid-transporting ATPase IH. Specific variants in the gene sequence (known as pathogenic missense variants) cause this protein to be made with a slightly altered function. The protein's usual function aids the transport of a specific set of molecules called phospholipids. The protein made using the information in the gene with the missense variant allows the transport of an additional and different phospholipid. This means the usual balance of phospholipids in the outer layers of some nerve cells (the cell membrane) of people with HLD24 is altered, and this disrupts formation of the myelin sheath.

ATP11A is widely expressed in our brains, and expression is thought to increases over time. It is possible that this condition may worsen over time. The position of the variant within the gene, and the corresponding change to the ATPase protein, is likely to be related to the severity and number of symptoms. Gene variants located on or near specific parts of the protein (called transmembrane regions) are expected to result in more severe and multiple symptoms, whereas those located in other regions of the protein might result in relatively mild and single symptoms, such as seizures.

Features and symptoms

As is common with many genetic conditions, children and adults with HLD24 are likely to have a range of symptoms and features. As more people are diagnosed, and information is shared, this range of symptoms and features, and the likelihood of a person having a specific feature, will become clearer.

The following developmental and medical concerns have been reported in people with HLD24, but it's unlikely that a person will have all the features listed and each person with this condition can have different developmental and medical concerns.

Possible features

- Learning difficulties or intellectual disability: challenges in school and with everyday tasks
- Speech and language delay: speech may be slow to develop or absent
- Structural brain anomaly and/or reduced neuron myelination (hypomyelination)
- Numbness/tingling/pain in extremities: peripheral polyneuropathy
- Seizures: unexpected electrical activity in the brain
- Balance and coordination issues: taxic gait

Other features have been identified in people with an ATP11A variant but with so few people reported in the medical literature to date (2025) it is not yet known how common these features are expected to be. Very little information is currently available, so the list of concerns and abilities are likely to change.

Therapies and support

The care of a person with HLD24 is likely to require regular follow-ups and coordinated care by a multidisciplinary team of specialists, which may include a paediatrician, neurologist and geneticist, together with the following therapy and support:

- Speech and language therapy (can also help with swallowing difficulties)
- Occupational therapy (to help with daily tasks like eating, dressing, and play)
- Physical therapy (to help with strength, balance, and coordination)
- ABA therapy (applied behaviour analysis, to help with behaviour and learning)
- AAC tools (augmentative and alternative communication tools for non-verbal children)
- Education plans/tailored support in mainstream or special educational needs (SEN) schools
- Medication to help manage focus, anxiety, mood, or seizures

How common is HLD24?

HLD24 is ultra-rare. Currently (in 2025) less than 10 people with this diagnosis have been reported in the medical literature. It is expected that more people will be diagnosed with this condition as awareness increases and genetic testing becomes more routine. It is important to know that the most severely affected children are likely to be the first identified so initial findings may not represent the possible spectrum of abilities or symptom severity.

Why did this happen?

When children are conceived, random rare changes occur in the genetic material of the egg and/or sperm that make a new child. Such changes are part of the child's genome but they are not seen in the DNA of their parents. This happens naturally and is not due to any lifestyle, dietary or environmental factors. No one is to blame and nobody is at fault. Such changes happen to everyone but it's only when particular genes or specific parts of a chromosome are affected that there is an impact on health and/or development.

In all people diagnosed with HLD24 so far, the change in the *ATP11A* gene occurred by chance in that child (this is known as de novo) and was not found in their parents.

Can it happen again?

The chance of having another child affected by a rare gene disorder depends on the genetic code of the parents. If the change in the *ATP11A* gene has been shown to be *de novo*, meaning neither parent was found to carry it, the chance of having another child with HLD24 is very low. The reason there is still a small chance is due to something called germline mosaicism, which is where the gene variant can be found in a few eggs or sperm, but is not found in the rest of the body's cells. A clinical geneticist or genetic counsellor can give specific advice for each individual family.

Can it be cured?

HLD24 cannot be cured at the present time; however, knowing the diagnosis means that appropriate monitoring and treatment can be put in place, especially for features of medical, behavioural and educational concerns.

Inform Network Support

Join Unique for family links, information and support: Unique is a charity without government funding, existing

Become a member

entirely on donations and grants. If you can, please make a donation:

Donate via our website

Rare Chromosome Disorder Support Group,
The Stables, Station Road West,
Oxted, Surrey. RH8 9EE. UK.
Tel +44(0)1883 723356
help@rarechromo.org I rarechromo.org

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