How common is LIGOWS?

LIGOWS is very rare. Currently (2023) less than 10 children with a LIGOWS 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.

Why did this happen?

When children are conceived, the genetic material is copied in the egg and sperm that make a new child. The biological copying method is not perfect, and random rare changes occur in the genetic code of children that 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 a change affects an important gene that health and/or development are affected.

In most children diagnosed with LIGOWS so far, the change in the *KAT8* 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 *KAT8* gene has been shown to be *de novo*, that means neither parent was found to carry it, the chance of having another child with LIGOWS is low (less than 1%; there is still a very small chance if the variant is present in egg or sperm cells, this is called germline mosaicism). If a parent is found to carry the genetic variant, the chance of passing on the variant is usually 50% for each pregnancy. A clinical geneticist can give you specific advice for your family.

Can it be cured?

LIGOWS cannot be cured at the present time however, knowing the diagnosis means that appropriate monitoring and treatment can be put in place.

Inform Network Support

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Websites, Facebook groups and other links:
https://www.facebook.com/groups/1252358868437443

Join *Unique* for family links, information and support.
Unique is a charity without government funding, existing entirely on donations and grants. If you can, please make a donation via our website at www.rarechromo.org/donate Please help us to help you!

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Rare Chromosome Disorder Support Group
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Understanding Chromosome & Gene Disorders

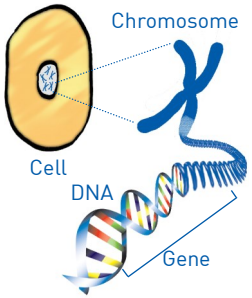
Li-Ghorbani-Weisz-Hubshman syndrome (LIGOWS) (*KAT8* gene variants)

rarechromo.org

What is Li-Ghorbani-Weisz-Hubshman syndrome?

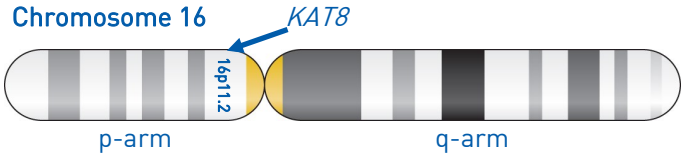
Li-Ghorbani-Weisz-Hubshman syndrome, abbreviated to LIGOWS, is a rare genetic condition that causes developmental delay and can affect a child's learning abilities and behaviour. As is common with genetic conditions, each person is affected differently. Children with LIGOWS can develop seizures that might be related to brain anomalies, but it is rare for a baby with LIGOWS to be born with other physical anomalies.

What causes LIGOWS?



LIGOWS is caused by specific changes (known as pathogenic variants) to a gene called *KAT8* (*KAT8* is an abbreviation of the gene's full name, Lysine Acetyltransferase 8).
The *KAT8* gene is located on the short 'p' arm of chromosome 16 in a region called 16p11.2 (see below).

We have two copies of chromosome 16 in our cells, so we also have two copies of the *KAT8* gene. The *KAT8* gene codes for the KAT8 protein. It is thought that the pathogenic variants that cause LIGOWS change the function of the protein.



In most people, LIGOWS occurs when only one copy of the *KAT8* gene is affected, this is known as autosomal dominant since the change occurred on an autosome (any of the chromosomes numbered 1-22) and features are apparent when only one copy of the gene is altered (this is known as dominant). So far (2023) one person has been identified with a change to both copies of their *KAT8* gene. This is known as autosomal recessive.

The KAT8 protein is part of an important group of proteins that control the activity of other genes. KAT8 has a specific pattern of activity in different parts of the brain, especially during development, so changes to its function may cause neurological difficulties such as those associated with learning and behaviour.

LIGOWS features

Most children with LIGOWS have:

- Developmental delay
- Learning difficulties/disorders or intellectual disability (ID)
- Seizures and epilepsy
- Brain anomaly identified by MRI
- Speech and language difficulties
- Motor skills delay

Other possible features include:

- Feeding difficulties in the first few months
- Unusual head shape
- Eye anomaly
- Neurodevelopmental difficulties e.g. features of ASD or ADHD

Development

Intellectual Development and Learning

Most children diagnosed with LIGOWS to date (2023) have some level of learning difficulty or intellectual disability although not all have been officially tested.

Speech and language

All children diagnosed with LIGOWS to date (2023) have some form of speech and language delay.

Physical Development

Developmental delay of gross motor function, for example balance and walking, has been reported in most children with LIGOWS so far (2023) as have difficulties with fine motor skills e.g. holding a pencil.

Behaviour

A few children with LIGOWS have been diagnosed with a neurodevelopmental disorder or difficulty. Features of ASD (autism spectrum disorder) and ADHD (attention deficit hyperactivity disorder), have been noted.

Feeding

Feeding can be problematic for some children with LIGOWS in the first few months after birth.

Height and Weight

Children with LIGOWS appear to have a height and weight within the expected range in later childhood.

Medical concerns

Seizures

Seven of the nine children described in the medical literature to date (2023) had experienced at least one seizure. Seizure types varied as did medication. Valproic acid therapy might be affective therapy but further studies are needed.

Brain anomaly

Not all children diagnosed with LIGOWS to date (2023) have had a brain MRI, but for those who have, unusual results have been found but they were different in each child.

Head shape

Children with LIGOWS have been reported to have a small head, large head or unusual head shape but no consistent findings have been reported so far.

Sight

Eye anomalies have been reported in a few children with LIGOWS but conditions vary, long-sightedness has been found in a few.

Heart anomaly

Four children with LIGOWS out of the nine reported to date (2023) had a mild heart anomaly, but each was different, and all but one self-resolved without surgery.

Unusual facial features

Some children with LIGOWS have an unusual facial feature such as eyes that slant upwards slightly, eyelid fullness, or a depressed nose bridge. Others have low set ears or unusual head shape.

Management recommendations:

Children with LIGOWS should be under the care of a multidisciplinary team including a geneticist, paediatrician, neuropaediatrician/neurologist and an epilepsy specialist if needed. Children may benefit from speech and language therapy as well as periodic evaluations by a developmental specialist.