Why did this happen?

When children are conceived the parents' genetic material is copied in the egg and sperm that makes a new child. The biological copying method is not perfect and occasionally 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 anything a parent did or did not do.

In the vast majority of children with GAND who have been described and in whom the parents were investigated, the change in the *GATAD2B* gene occurred out of the blue (*de novo*) in the child.

In a few children, one parent carried the change in some (but not all) of the cells of their body. Doctors call this mosaicism. Parents of these children had no developmental problems or learning difficulties themselves.

A spontaneous change in the *GATAD2B* gene cannot be prevented. No environmental, dietary or lifestyle factors are known to cause a spontaneous change in the gene. No one is to blame when they occur and nobody is at fault.

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 neither parent is found to carry the change in the *GATAD2B* gene, the chance of having another child with GAND is very low. Nonetheless, there is a small chance that some of the egg cells of the mother or some of the sperm cells of the father carry the change in the *GATAD2B* gene (this is called germline mosaicism). This means that parents who are not found to carry the change in the *GATAD2B* gene still have a very small chance of having another child with GAND. If the genetic analysis of the parents of a child with GAND shows that one of them carries the same variant, the chance of it happening again is much higher. Each family situation is different. A clinical geneticist or genetic counsellor can give specific advice on the chance of recurrence in a particular family and, if applicable, options for testing regarding future pregnancies.

Sources and references

The information in this guide is drawn from what is known about children with GAND from medical literature. Articles that have been used are: Vera 2020; Shieh 2020; Willemsen 2013 and Hamdan 2014. In addition, a number of parents of Dutch children with GAND participated in the first version of this guide by filling out a questionnaire about their child.

Families say ...

" She is very open and honest. Her emotions are real. She shows us to live in the present and does not look back or look forward. For her, only the present counts. She teaches us to slow down." - 11 years old

Inform Network Support

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Websites and Facebook groups:
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www.facebook.com/groups/GATAD2Bcommunity
www.gatad2b.org/

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Unique lists external message boards and websites in order to be helpful to families looking for information and support. This does not imply that we endorse their content or have any responsibility for it.

This information guide is not a substitute for personal medical advice. Families should consult a medically qualified clinician in all matters relating to genetic diagnosis, management and health. Information on genetic changes is a very fast-moving field and while the information in this guide is believed to be the best available at the time of publication, some facts may later change.

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Rare Chromosome Disorder Support Group
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Understanding Chromosome & Gene Disorders

GATAD2B-associated neurodevelopmental disorder (GAND)/ *GATAD2B* syndrome

rarechromo.org

What is GAND and what causes it?

GAND (GATAD2B associated neurodevelopmental disorder), also referred to as GATAD2B syndrome, is a condition in which children have developmental delay and intellectual disability. GAND occurs when one of the two copies of the *GATAD2B* gene does not function as expected. This can be caused by a change (variant) in the gene or the loss (deletion) of one copy of the gene. The loss of the gene may occur as part of a larger deletion that affects the chromosome on which the gene is located.

Genes are instructions which have important roles in our growth and development. They are made of DNA and are incorporated into organised structures called chromosomes. Chromosomes therefore contain our genetic information. Chromosomes are located inside our cells, the building blocks of our bodies.

The *GATAD2B* gene is located in chromosome 1 in a region called 1q23.1. *GATAD2B* is important in the development and maturation of the brain. This is why GAND is primarily associated with developmental delay and intellectual disability.

Can it be cured?

There is no cure for GAND since the effects of the genetic change took place during a baby's formation and development. However, knowing the diagnosis means that appropriate monitoring and treatment can be put in place.

Most children with GAND have:

- Developmental delay and intellectual disability
- Speech delay
- Low muscle tone (hypotonia) during childhood
- Behavioural concerns

How many people have this condition?

Since it was first described in 2013, over 70 children with GAND have been reported in the medical literature. This guide is based on features described in over 100 children and adults with GAND.

Management recommendations

Children with GAND should be followed up by a general paediatrician who can oversee care so that development and behaviour can be monitored and the best help in the form of physiotherapy, occupational therapy, speech therapy and behavioural therapy can be given.

Consultation with specialists in the fields of cardiology, ophthalmology and neurology is recommended.

Families say ...

" She can't talk, but does communicate. She takes your hand and has her own language.**"** - 18 years old

" At forty years her mobility is good. She can't ride a bike by herself.**"**

Medical concerns

The number of medical concerns and the severity is highly variable in people with GAND.

Low muscle tone (hypotonia)

The majority of children with GAND have low muscle tone. In some children muscle tone improves as they get older. Low muscle tone can result in a delay in reaching certain developmental milestones such as sitting, rolling, crawling an walking. It may also contribute to potential feeding difficulties.

Epilepsy and brain anomalies

An unspecific brain anomaly(ies) was revealed in more than half the children with GAND who have been offered an MRI. Up to a quarter of children have epilepsy/seizures. Some show a type of seizure in which they lose consciousness for a brief moment (seconds). This may cause them to abruptly stop what they are doing and not respond to their surroundings. Sometimes they show automatic movements in their faces or hands.

Hearing and vision

Over half of children with GAND are reported to have sight issues. Many have strabismus (a squint) and near/long sightedness. Other children have difficulties distinguishing depth. A very small minority of children have hearing impairments but hearing is normal in most children.

Heart

A very small minority of children have been reported with heart concerns. Most often, a change in one of the heart valves (bicuspid aortic valve and aortic valve stenosis) as well as a variation in the heart muscle (cardiomyopathy) have been found. Medical treatment was required for a few of these children.

Development and behaviour

Appearance

Most children have distinctive facial features such as wide-set eyes (hypertolerism), a broad forehead, a wide nasal base and pointed chin. Some children have minor anomalies of the hands and feet.

Growth and feeding

Growth appears to be within the expected range in children with GAND; however, just under half of children have a large head circumference (macrocephaly).

Feeding issues in the new-born period are common. Low muscle tone may contribute to difficulties with swallowing. Many babies also suffer from Gastro-oesophageal reflux (GERD/GORD) (in which feeds return readily up the food passage), which may require treatment. Constipation can also be a concern.

Sitting, moving and walking

Most children with GAND show a delay in reaching developmental milestones such as sitting and walking. Many children have an unsteady or wide-based gait (variations in walking stability) and may benefit from walking aids.

Speech

Most children with GAND have a severe delay in speech development and some may remain non-verbal. Children often find it difficult to co-ordinate movement of their lips, jaw and tongue to make the right sounds (apraxia of speech) but often understand more than they are able to express. Augmentative and Alternative Communication (AAC) methods, including pointing, pictograms, gestures, simplified sign language and high-tech communication systems (aided communication) have enabled some to communicate well.

Learning

All children with GAND have intellectual disability or learning difficulties. This is usually moderate to severe but a few children have mild ID. Adults we know about with GAND enjoy partial independence.

Behaviour

Children with GAND are described as happy and often want to socialise and interact with others. Behavioural concerns are reported in half of children. These include difficulty tolerating stressful situations or unpleasant feelings (low frustration tolerance). A small number of children also show autistic features, hyperactive behaviour, self-harming or aggressive behaviour. A small minority of children also have sleep difficulties.