Why did this happen?

When children are conceived the 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 your lifestyle or anything you did to cause a change in the *GATAD2B* gene.

In 6 out of 8 children with GATAD2B syndrome 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. One mother was found to carry the same change in the *GATAD2B* gene as her child. In another child the mother carried the change in some of the cells of her body, but not all. Doctors call this mosaicism. The mother had no developmental problems or learning difficulties herself.

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 *GATAD2B* gene. No one is to blame when they occur and nobody is at fault.

Can it happen again?

The risk of having another child affected by a rare gene disorder depends on the genetic code of the parent. If neither parent is found to carry the change in the *GATAD2B* gene, the chance of having another child with GATAD2B syndrome 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 (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 GATAD2B syndrome. If the genetic analysis of the parents of a child with GATAD2B syndrome shows that one of them carries the same variant, the chance of it happening again is much higher. Each family situation is different and a clinical geneticist can give you specific advice on the chance of recurrence in your family and, if applicable, options for testing regarding future pregnancies.

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

Rare Chromosome Disorder Support Group
The Stables, Station Road West, Oxted,
Surrey RH8 9EE, UK
Tel/Fax: +44(0)1883 723356
info@rarechromo.org | www.rarechromo.org

Facebook www.facebook.com/groups/GATAD2Bgene

This leaflet was made possible by contributions from FondsNutsOhra, Erfocentrum, VGnetwerken and VKGN in the Netherlands.

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. Unique does its best to keep abreast of changing information and to review its published guides as needed.

The text was written by Dr Laura van Dussen, MD, Erfocentrum, Netherlands and the guide was compiled by Unique. The leaflet was reviewed by Dr Marjolein Willemsen, MD, Radboud University Medical Center, Nijmegen with the participation of Marloes Brouns-van Engelen (Erfocentrum), Prof Dr C. van Ravenswaaij-Arts (UMC Groningen)and Mieke van Leeuwen (VGnetwerken). With special thanksto Annet van Betuw (VanBetuwAdvies), Marja de Kinderen (PROK Project management and training) Joyce Schaper (Chromosome Foundation) and Sarah Wynn, BSc(Hons) PhD DIC (Unique). Version 1 (LD)

Copyright © Unique 2016

Rare Chromosome Disorder Support Group
Registered in England and Wales
Charity Number 1110661
Company Number 5460413

Understanding chromosome disorders Unique

GATAD2B syndrome

rarechromo.org

What is GATAD2B syndrome and how is it caused?

GATAD2B syndrome is a condition in which children have developmental delay and/or intellectual disability. GATAD2B syndrome occurs when one of the two copies of the *GATAD2B* gene has lost its normal function. This can be caused by a spelling mistake in the gene or the loss of (a part of) one copy of the gene as a result of the deletion of the part of the chromosome on which the gene is located. GATAD2B syndrome was first described in 2013.

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 important in the development and maturation of the brain. This is why GATAD2B syndrome is primarily associated with developmental delay and/or intellectual disability.

Most children with GATAD2B syndrome have:

- Developmental delay and/or intellectual disability
- Low muscle tone (hypotonia) during childhood
- Behavioural problems.

More information on these and other features is given in this guide.

Can it be cured?

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

How many people have this condition?

Up to now, 6 children with a defect in the *GATAD2B* gene have been reported in the medical literature. This guide is based on information about 10 individuals with a defect in the *GATAD2B* gene, including 5 of the 6 children previously described in the medical literature. With the increasing use of the latest 'gene sequencing' technology, it is expected that more people will be diagnosed with this condition over the next few years.

Families say ...

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

"Maaike is forty years old and her mobility is good. She can't ride a bike by herself."

Medical concerns

Low muscle tone (hypotonia)

Six children with GATAD2B syndrome had low muscle tone. In some children muscle tone improved as they got older. Low muscle tone can result in a delay in reaching certain developmental milestones such as sitting, rolling, crawling and walking. It may also contribute to potential feeding difficulties.

Epilepsy

Three out of 10 children with GATAD2B syndrome had epilepsy. They showed 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. Doctors call this absence epilepsy. Absence epilepsy is suspected in a fourth child with GATAD2B syndrome.

Hearing and vision

Four out of 10 children had strabismus (a squint). Two children are longsighted (hypermetropic). Two other children possibly had difficulties distinguishing depth. One of these two children has difficulties seeing in the dark. Yet another child was hypersensitive to light. Hearing appears normal in most children. One child is hypersensitive to sounds and has high frequency hearing loss.

Management recommendations

Children with GATAD2B syndrome 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.

Development and behaviour

Growth and feeding

Growth appears normal in children with GATAD2B syndrome. Two out of 10 children had growth at the 5th per centile, which means they belonged to the smallest 5 per cent (out of 100 children, 95 were taller). Two children had a large head circumference (macrocephaly).

Five children have difficulties swallowing, of whom 4 dribble. One girl also had constipation. Two other children are said to have feeding difficulties. Another child suffered from gastro-oesophageal reflux (in which feeds return readily up the food passage) until she was 1½ years old.

Sitting, moving and walking

Children with GATAD2B syndrome show a delay in reaching developmental milestones such as sitting and walking. Six children who could walk, learned how to walk at a mean age of 27.5 months (range18 – 36 months).

Speech

Most children with GATAD2B syndrome have a delay in speech development. Two children did not speak and 3 children spoke only single words. Children often understand more than that they are able to express.

Learning

All children with GATAD2B syndrome have intellectual disability or learning difficulties. This is usually severe. However, there are differences. One mother of a child with GATAD2B syndrome was found to carry the change in the GATAD2B gene. She experienced learning difficulties as a child.

Behaviour

Children with GATAD2B syndrome can be happy and upbeat. But behavioural problems are common. Some children show autistic features, hyperactive behaviour, self-mutilation or aggressive behaviour. Three children had sleeping difficulties. Three children have a high threshold for pain.

Sources and references

The information in this guideis drawn from what is known about children with GATAD2B syndrome from the medical literature. Articles that have been used are: Willemsen 2013 and Hamdan 2014. In addition, a number of parents of Dutch children with GATAD2B have participated in the development of this guide by filling out a questionnaire about their child.