

## Why did this happen?

Some children with GRIN2A related syndrome have inherited the mistake in the *GRIN2A* gene from one of their parents. The mistake may be present in their grandparents and earlier generations. The features of GRIN2A related syndrome can vary between family members. For instance, different forms of epilepsy as a result of GRIN2A related syndrome can occur within one family. Some family members who carry the mistake in the *GRIN2A* gene may not appear to have any symptoms or features, while other family members are affected. In some children the sequence change in *GRIN2A* occurred out of the blue (de novo). The parents were not found to carry the change in *GRIN2A*. 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 *GRIN2A* gene. A spontaneous change in the *GRIN2A* gene cannot be prevented. No environmental, dietary or lifestyle factors are known to cause a spontaneous change in the *GRIN2A* 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 parents. If neither parent is found to carry the change in the *GRIN2A* gene, the chance of having another child with GRIN2A related syndrome is very low. Nonetheless, there is a very 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 *GRIN2A* gene. This is called germline mosaicism. This means that parents who are not found to carry the same *GRIN2A* change as their child on a blood test still have a very small chance of having another child with GRIN2A related syndrome. This has not been reported in GRIN2A related syndrome in the medical literature so far. If the genetic analysis of the parents of a child with GRIN2A related syndrome showed that one of them carried the same *GRIN2A* change, the chances of it happening again are much higher. Each family situation is different and a clinical geneticist can give you specific advice on the chances of recurrence in your family and, if applicable, options for testing regarding future pregnancies.

## Families say ...

“ I have learned to be very patient. Because of this, I have become a better person. Very often she does not respond to me. You have to give without expecting anything in return. Her favourites are drills and classical music. ”

## Inform Network Support Rare Chromosome Disorder Support Group

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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 with the participation of Marloes Brouns-van Engelen (Erfocentrum), Prof Dr Conny van Ravenswaaij-Arts (UMC Groningen) and Mieke van Leeuwen (VGnetwerken). With special thanks to Annet van Betuw (VanBetuwAdvies), Marja de Kinderen (PROK Project management and training) Joyce Schaper (Chromosome Foundation) and Sarah Wynn, BSc (Hons) PhD DIC (Unique). The speech and language information in this guide was updated in 2021 by Lottie Morison and Prof. Angela Morgan, speech and language pathologists from the Murdoch Children's Research Institute and University of Melbourne, Australia.

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Understanding Chromosome & Gene Disorders

# GRIN2A related syndrome

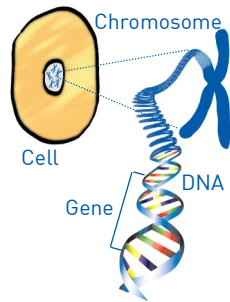


## What is GRIN2A related syndrome and how is it caused?

GRIN2A related syndrome is a condition that is associated with epilepsy as its most important feature. It occurs when one of the two copies of the GRIN2A gene has lost its normal function. This can be caused by a spelling mistake in the gene or a loss of one copy of the gene, or part of it. GRIN2A related syndrome was first described in 2010.

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 in our cells, the building blocks of our bodies.

The GRIN2A gene (on chromosome 16) plays an important role in the transmission of signals in the brain. This is why epilepsy is an important feature of GRIN2A related syndrome.



### Most children with GRIN2A related syndrome have:

- Epilepsy
  - Developmental delay and/or intellectual disability
  - Behavioural difficulties occur in a substantial proportion of children with GRIN2A related syndrome.
- 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?

More than 240 people with GRIN2A related syndrome have been described in the medical literature. Some of them were found to have GRIN2A related syndrome after the diagnosis was made in a family member. With the increasing use of the latest 'gene sequencing' technology, it is expected that many more people will be diagnosed with this condition over the next few years.

## Medical concerns

### ■ Epilepsy

Most children with GRIN2A related syndrome have epilepsy. The type and severity varies. Some children have a severe form of epilepsy in which the seizures lead to a stagnation or even decline in their development (CSWS, continuous spike and waves during slow wave sleep). Seizures may be difficult to control with medication. Some children are diagnosed with a form of epilepsy which primarily affects their speech and language development (LKS, Landau-Kleffner syndrome). Other children may show a milder form of epilepsy in which seizures do not affect their development and in which seizures spontaneously resolve during late childhood or adolescence (BECTS, benign epilepsy with centrotemporal spikes). Brain imaging by MRI is normal in most children, although in some abnormalities have been described.

## Development and behaviour

### ■ Growth

Growth in children with GRIN2A related syndrome mostly appears to be normal. Nonetheless, a number of children with short stature have been reported.

### ■ Sitting, moving and walking

Many children with GRIN2A related syndrome show delay in reaching their motor milestones. Some children do not learn to sit or walk independently. Children may have low muscle tone (hypotonia). Other children may have difficulty coordinating body movements (ataxia), jerky and stiff movements (spasticity) or involuntary jerking (chorea). Children can also have mild eating and drinking difficulties, since moving their mouth and lips is challenging.

### ■ Learning

About two-thirds of children with GRIN2A related syndrome show a degree of intellectual disability or learning difficulties, but the severity varies. For instance, some parents of children with GRIN2A related syndrome have had mild learning difficulties. These parents were found to carry the mistake in the GRIN2A gene after this diagnosis was established in their child. Intellectual disability can also be severe.

### ■ Behaviour

Behavioural difficulties are common in children with GRIN2A related syndrome. The type of behavioural difficulty is not always specified in the medical literature. Children may have autism or show autistic features, problems with concentration, self-injurious behaviour and/or aggressive behaviour.

## Speech and Language

### ■ Speech

Speech, or the sounds we make when we talk, is commonly affected in individuals with GRIN2A related syndrome. Children may have a speech disorder such as difficulties coordinating the sounds in words (speech dyspraxia) and/or voice difficulties and imprecise speech (dysarthria). These problems result in difficulty being understood.

### ■ Language

Many children with GRIN2A related syndrome have trouble understanding words and sentences (receptive language disorder) and/or using words and sentences (expressive language disorder). Other children may use single words or not talk. Speech and language difficulties can be related to a child's epilepsy. However, there are individuals with GRIN2A related syndrome who do not have epilepsy but have speech and language disorders.

## Management recommendations

Children with GRIN2A related 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 given in the form of physiotherapy, occupational therapy, speech therapy, and behavioural therapy. For the treatment and evaluation of epilepsy, it is important that a paediatrician with expertise in epilepsy is involved in care. It is very important to pay special attention to communication to support the child's development.

**Sources and references** The information in this guide is drawn from what is known about children with GRIN2A related syndrome from the medical literature. Articles that have been used include: Endele 2010; Reutlinger 2010; Hamdan 2011; Tarabeux 2011; Carvill 2012; Lemke 2012; Lesca 2012; de Ligt 2012; DeVries 2013; Dimassi 2013; Tsai 2013; Yuan 2013; Conroy 2014; Dyment 2014; Pierson 2014; Venkateswaran 2014; Allen 2015; Bramswig 2015; Turner 2015; Strehlow 2019; Lesca 2019. The first-named author and publication date are given to allow you to look for the abstracts or original articles on the internet in PubMed ([www.ncbi.nlm.nih.gov/pubmed](http://www.ncbi.nlm.nih.gov/pubmed)).