"She has truly changed our lives for the better. Because of her, we have learned to be more patient and have learned not to sweat the small stuff. She has also opened us up to the whole wide world of disability. Through support groups and playgroups and therapies, we have made so many wonderful new friends that we probably never would have made before any of this. We are far more compassionate and less judgmental because of our daughter’s rare diagnosis."

Support and Information

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

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.

Facebook groups
https://www.facebook.com/grin2b/
https://www.facebook.com/groups/grin2bfamilysupport/
https://www.facebook.com/groups/GRIN2B/
Foundation
www.grin2b.com

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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. 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.

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What is GRIN2B-related syndrome and how is it caused?

GRIN2B-related syndrome is a condition that causes developmental delay and intellectual disability. GRIN2B is the name of a gene that plays an important role in the transmission of signals in the brain. This is why developmental delay/intellectual disability is an important feature of GRIN2B-related syndrome.

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 GRIN2B gene is found on chromosome 12. People have two chromosome 12s, and so two copies of the GRIN2B gene. The syndrome occurs when one of the two copies of the GRIN2B gene loses its normal function. This can be caused by a 'spelling mistake' in the gene or by the loss of one copy of the gene, or part of it.

GRIN2B-related syndrome was first described in 2010.

Most children with GRIN2B-related syndrome have:

- developmental delay and/or intellectual disability

They may also have:

- low muscle tone (hypotonia)
- epilepsy
- behaviour problems, including autism or autistic features.

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

Sources and references


The first-named author and publication date are given to allow you to look for articles on the internet in PubMed (www.ncbi.nlm.nih.gov/pubmed). If you wish, you can obtain most articles from Unique. In addition, a number of members from Unique with GRIN2B-related syndrome helped in the development of this guide by filling out a questionnaire about their child.

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 GRIN2B gene.

In almost all the children with GRIN2B-related syndrome who have been described in the medical literature, the change occurred out of the blue (de novo). A spontaneous change in the GRIN2B gene cannot be prevented. No environmental, dietary or lifestyle factors are known to cause any spontaneous gene change in the GRIN2B gene. No one is to blame when they occur and nobody is at fault.

Can it happen again?

The chances of having another child affected by a rare gene disorder depend on the genetic code of the parents. At present, only one parent has been found to carry the same change in the GRIN2B gene as their child. In the others, the change was spontaneous (de novo) and neither parent carried it. If neither parent is found to carry the change in the GRIN2B gene, the chances of having another child with GRIN2B-related syndrome are 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 do carry the same change in the GRIN2B gene. This rare finding is called germline mosaicism. It means that parents who are not found to carry the same GRIN2B change as their child when they have a blood test do still have a very small chance of having another child with GRIN2B-related syndrome. We know that this can happen, but it has never been reported for GRIN2B related syndrome in the medical literature so far.

If the genetic analysis of the parents of a child with GRIN2B-related syndrome shows that one of them has the same change in the gene, 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.
Can this 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.

Management recommendations
Children with GRIN2B-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, if needed, behavioural therapy.

How many people have this condition?
Approximately 20 children with a change in the GRIN2B gene have been described in the medical literature (2016). 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
Approximately 30-40% (3-4 in 10) of the children with GRIN2B-related syndrome have epilepsy. Some children have a severe form of epilepsy in which the seizures lead to a stagnation or even decline in their development (West syndrome or Lennox-Gastaut syndrome).

- Low muscle tone (hypotonia)
Approximately 30% (3 in 10) of the children with GRIN2B-related syndrome have low muscle tone (hypotonia). This can result in a delay in reaching certain developmental milestones such as rolling, sitting, crawling and walking. It may also contribute to the feeding difficulties seen in some children.
Development and behaviour

Growth and feeding

Growth in children with GRIN2B-related syndrome mostly appears to be normal. Feeding problems and/or constipation have been reported in some children. Among 20 children reported in the medical literature, one child showed failure to thrive, meaning that s/he failed to grow and gain weight at the expected rate. Three of the 20 children had a small head circumference (microcephaly).

Sitting, moving and walking

Many children with GRIN2B-related syndrome show a delay in reaching motor milestones. Some children do learn to sit and walk independently, but this is not possible for all. Out of 12 children with GRIN2B-related syndrome, seven learned to walk independently, at a mean age of 24 months. The youngest reported age of learning to walk without support was 19 months, and the oldest was 36 months. Five children were not able to walk.

Speech

A delay in speech and language development is common in GRIN2B-related syndrome. A few children do not speak or use only single meaningful words. Out of 12 children described in the medical literature on whom information is available, five were able to talk, or say more than one word. They spoke their first words at a mean age of 17 months. The youngest age at which they spoke first words was 10 months, and the oldest was 2 years and 4 months. Six other children did not talk or could say only one word.

Learning

Children with GRIN2B-related syndrome show some degree of intellectual disability. The degree can range from mild to severe.

Behaviour

Behaviour problems are common in children with GRIN2B-related syndrome. Some children have autism or show autistic traits. Hyperactivity, problems with attention or concentration, aggressive behaviour and sleeping problems have also been described.

Families say ...

“Non-verbal, but can do 3 signs and understands several others. We think she may be trying to repeat the word hi.” - 3 years
“Likes to shout and occasionally babble a little.” - 8 years
“laughs a lot at my voice, squeals and cries and likes to blow raspberries!” - 8 years