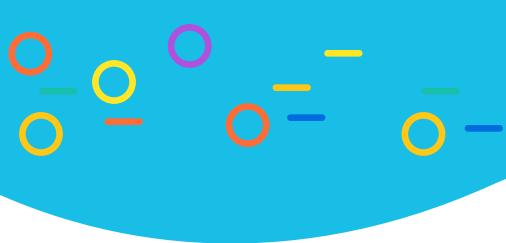




# SCN2A-Related Syndrome





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This guide is not meant to take the place of medical advice.

Please consult with your doctor about your genetic results and health care choices. The information in this guide was up to date at the time it was written in 2019. But new information may come to light with new research. You may find it helpful to share this guide with friends and family members or doctors and teachers of the person who has SCN2A-related syndrome.



# What is SCN2A-related syndrome?

SCN2A-related syndrome happens when there are changes to the SCN2A gene. These changes can keep the gene from working as it should.



## Key role

The SCN2A gene produces a protein that sits on the surface of brain cells and allows sodium to enter the cell. This protein is important for brain cells to make and transmit signals between cells. The protein is essential for these brain cells to work properly.

## Symptoms

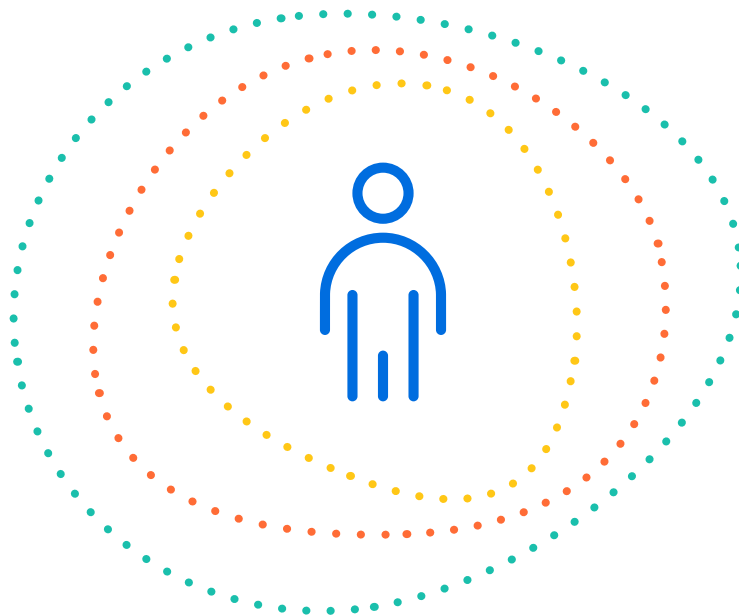
Because the SCN2A gene is important in the development and function of brain cells, many people who have SCN2A-related syndrome have:

- Seizures
- Developmental delay, or intellectual disability, or both
- Autism or features of autism
- Movement problems
- Low muscle tone
- Gastrointestinal problems

## Changes in the SCN2A gene may be associated with any of three different disorders:

1. Infantile epileptic encephalopathy, or IEE: This condition is defined by seizures that begin before 1 year of age. There is also neurodevelopmental delay.
2. Benign infantile familial seizures, or BIFS: In this condition, seizures begin before 1 year of age but usually stop by 2 years of age. Usually, the person has no long-term neuropsychiatric problems. This is the least common disorder associated with changes in the SCN2A gene.
3. Autism and developmental delay: Up to one-third of people who have autism and developmental delay also develop late-onset seizures. Development concerns may increase over time.

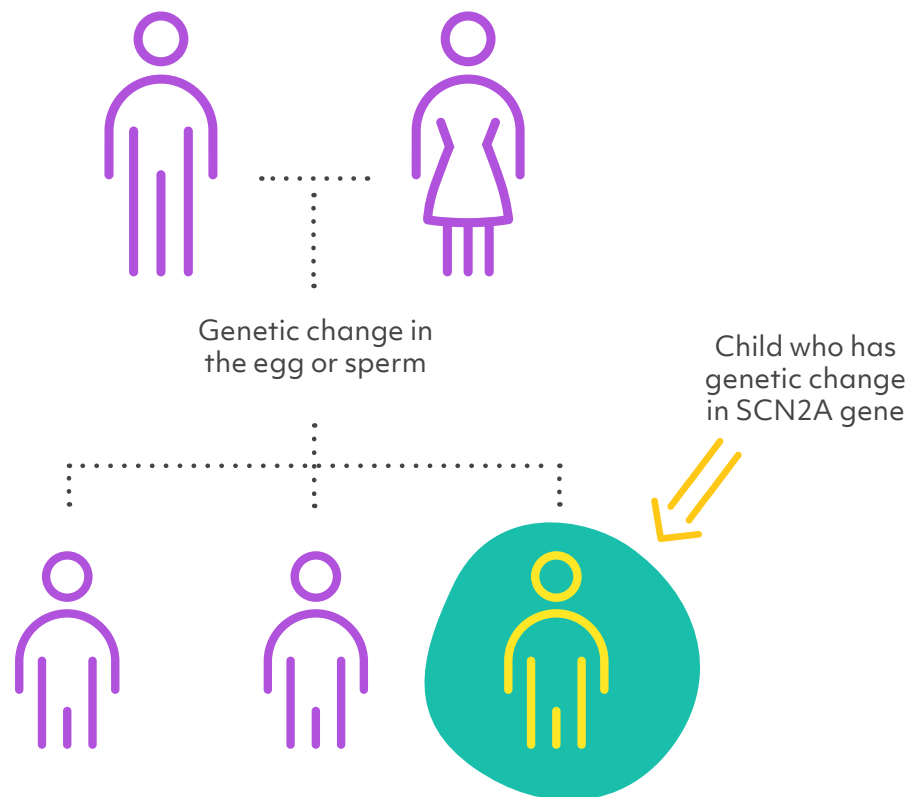
Most but not all children who have SCN2A-related syndrome fit into one of these categories. Related conditions include schizophrenia, a movement disorder called late-onset episodic ataxia, and a seizure disorder called childhood-onset epileptic encephalopathy.



# What causes SCN2A-related syndrome?

Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Every child gets two copies of the SCN2A gene: one copy from their mother, from the egg, and one copy from their father, from the sperm. In most cases, parents pass on exact copies of the gene to their child. But the process of copying genes is not perfect. A change in the genetic code can lead to physical issues, developmental issues, or both.

Sometimes a random change happens in the sperm or egg. This change to the genetic code is called a 'de novo', or new, change. The child can be the first in the family to have the gene change.



De novo changes can take place in any gene. We all have some de novo changes, most of which don't affect our health. But because SCN2A plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that SCN2A-related syndrome is often the result of a de novo change in SCN2A. Many parents who have had their genes tested do not have the SCN2A gene change found in their child who has the syndrome. In some cases, SCN2A-related syndrome happens because the gene change was passed down from a parent.



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## Why does my child have a change in the SCN2A gene?

No parent causes their child's SCN2A-related syndrome. We know this because no parent has any control over the gene changes that they do or do not pass on to their children. Please keep in mind that nothing a parent does before or during the pregnancy causes this to happen. The gene change takes place on its own and cannot be predicted or stopped.

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## What are the chances that other family members or future children will have SCN2A-related syndrome?

Each family is different. A geneticist or genetic counselor can give you advice on the chance that this will happen again in your family.

The risk of having another child who has SCN2A-related syndrome depends on the genes of both birth parents.

- If neither birth parent has the same gene change found in their child, the chance of having another child who has the syndrome is on average 1 percent. This 1 percent chance is higher than the chance of the general population. The increase in risk is due to the very unlikely chance that more of the mother's egg cells or the father's sperm cells carry the same change in the gene.
- If one birth parent has the same gene change found in their child, the chance of having another child who has the syndrome is 50 percent.

For a symptom-free sibling, a brother or sister, of someone who has SCN2A-related syndrome, the risk of having a child who has the syndrome depends on the symptom-free sibling's genes and their parents' genes.

- If neither parent has the same gene change found in their child who has the syndrome, the symptom-free sibling has a nearly 0 percent chance of having a child who has SCN2A-related syndrome.
- If one birth parent has the same gene change found in their child who has the syndrome, the symptom-free sibling has a small chance of also having the same gene change. If the symptom-free sibling has the same gene change as their sibling who has the syndrome, the symptom-free sibling's chance of having a child who has SCN2A-related syndrome is 50 percent.

For a person who has SCN2A-related syndrome, the risk of having a child who has the syndrome is about 50 percent.

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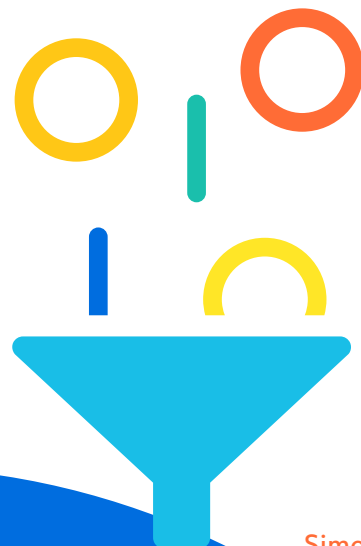
## How many people have SCN2A-related syndrome?

As of 2019, doctors had found about 200 people in the world with changes in the SCN2A gene. The first case of SCN2A-related syndrome was described in 2002. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

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## Do people who have SCN2A-related syndrome look different?

People who have SCN2A-related syndrome generally don't look different.





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## How is SCN2A-related syndrome treated?

Epilepsy is common in people who have SCN2A-related syndrome. In some cases, seizures that are linked to SCN2A-related conditions cannot be controlled. But, for infants whose seizures begin before 3 months of age, a class of medication known as sodium channel blockers, such as phenytoin and carbamazepine, may be helpful (Wolff *et al.*, 2017). Note that this is the opposite of best practice guidelines for neonatal seizures.

Children who have autism and developmental delay whose seizures begin after 12 months of age respond best to a different set of medications, including levetiracetam, benzodiazepines, and valproate.


Little information is available on how to best treat infants whose seizures begin between 3 and 12 months of age. Some studies suggest that sodium channel blockers are the best option. Other studies have found improvement with medications including lidocaine (Foster *et al.*, 2017; Ogiwara *et al.*, 2009), ethosuximide (Wolff *et al.*, 2017), and acetazolamide (Leach *et al.*, 2016; Liao *et al.*, 2010). There is not enough data on these medications to give specific advice.

If seizures happen, consult a neurologist. There are many types of seizures, and not all types are easy to spot. To learn more, you can refer to resources such as the Epilepsy Foundation's website: [epilepsy.com/learn/types-seizures](https://www.epilepsy.com/learn/types-seizures).

It is important to seek care and therapies to help the person's brain and nervous system develop and operate as well as it can. Soon after diagnosis, this can include:

- Physical exams and brain studies. An electroencephalogram, also called an EEG, measures the brain's electrical activity and may show the overall electrical disturbances in the brain. This may lead to the use of antiepileptic medications.





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At present, there is no specific advice about how to treat other symptoms. A genetic diagnosis can help people decide on the best way to track the condition and manage therapies. Doctors can refer people to specialists for:

- Genetics consults.
- Development and behavior studies.
- Gastrointestinal issues. Many children who have SCN2A-related syndrome have constipation, gastroesophageal reflux, or diarrhea.
- Other issues, as needed.

A developmental pediatrician, neurologist, or psychologist can follow progress over time and can help:

- Suggest the right therapies. This can include physical, occupational, speech, or behavioral therapy.
- Guide individualized education plans (IEPs).

Specialists advise that therapies for SCN2A-related syndrome should begin as early as possible, ideally before a child begins school.

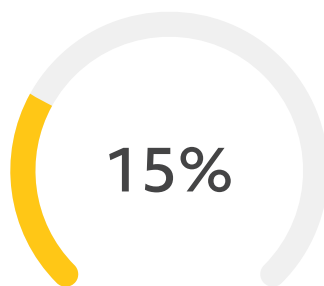
SCN2A-related syndrome is very rare. Doctors and scientists have just recently begun to study it. As of 2019, studies found around 200 people who have SCN2A-related syndrome.

This section includes a summary of information from major published articles. It highlights how many people have different symptoms. To learn more about the articles, see the [Sources and references](#) section of this guide.

## Medical, behavior, and development concerns linked to SCN2A-related syndrome

### Brain

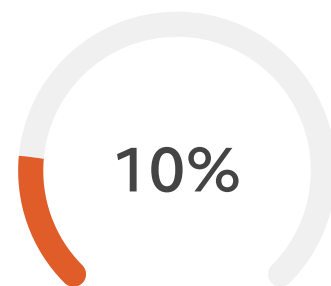
Seizures are common in people who have SCN2A-related syndrome. The seizures fall into different categories:



About 15 percent of people who have the syndrome have benign infantile seizures.



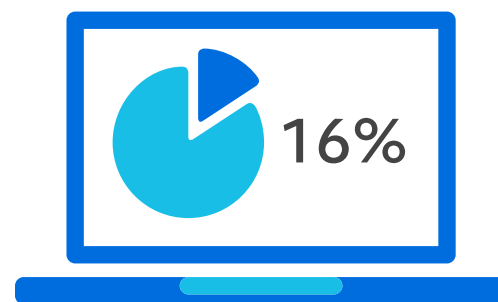
More than one-third have early infantile onset epilepsy.



Less than 10 percent have epilepsy with unknown age of onset.

### Development and behavior

Sixteen percent of people who have the syndrome have autism or intellectual disability without seizures.





**Where can I  
find support  
and resources?**

- **Simons Searchlight Community SCN2A Facebook group**  
[www.facebook.com/groups/SCN2A](http://www.facebook.com/groups/SCN2A)
- **FamilieSCN2A Foundation**  
[www.scn2a.org](http://www.scn2a.org)
- **FamilieSCN2A Community Discussion Group**  
[www.facebook.com/groups/504056566376771](http://www.facebook.com/groups/504056566376771)

## Sources and References

The content in this guide comes from published studies about SCN2A-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.

- Ogiwara I. *et al. Neurology*, **73**, 1046-1053, (2009). De novo mutations of voltage-gated sodium channel alpha1 gene SCN2A in intractable epilepsies [www.ncbi.nlm.nih.gov/pubmed/19786696](http://www.ncbi.nlm.nih.gov/pubmed/19786696)
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- Ben-Shalom R. *et al. Biological Psychiatry*, **82**, 224-232, (2017). Opposing effects on NaV1.2 function underlie differences between SCN2A variants observed in individuals with autism spectrum disorder or infantile seizures [www.ncbi.nlm.nih.gov/pubmed/28256214](http://www.ncbi.nlm.nih.gov/pubmed/28256214)
- Foster LA. *et al. Pediatric Neurology*, **66**, 108-111, (2017). Infantile epileptic encephalopathy associated with SCN2A mutation responsive to oral mexiletine [www.ncbi.nlm.nih.gov/pubmed/27867041](http://www.ncbi.nlm.nih.gov/pubmed/27867041)
- Wolff M. *et al. Brain*, **140**, 1316-1336, (2017). Genetic and phenotypic heterogeneity suggest therapeutic implications in SCN2A-related disorders [www.ncbi.nlm.nih.gov/pubmed/28379373](http://www.ncbi.nlm.nih.gov/pubmed/28379373)



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