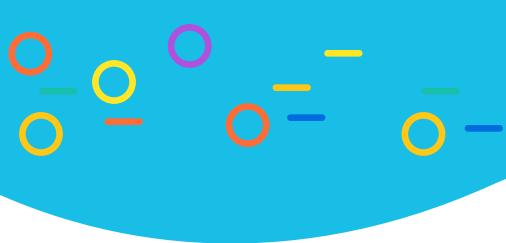




NR4A2-related syndrome





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 NR4A2-related syndrome.





What is NR4A2-related syndrome?

NR4A2-related syndrome happens when there are changes to the NR4A2 gene. These changes can keep the gene from working as it should.

Key role

NR4A2 plays a key role in the development of the brain. This gene is particularly important in brain cells that help control movement, emotion, and memory.

Symptoms

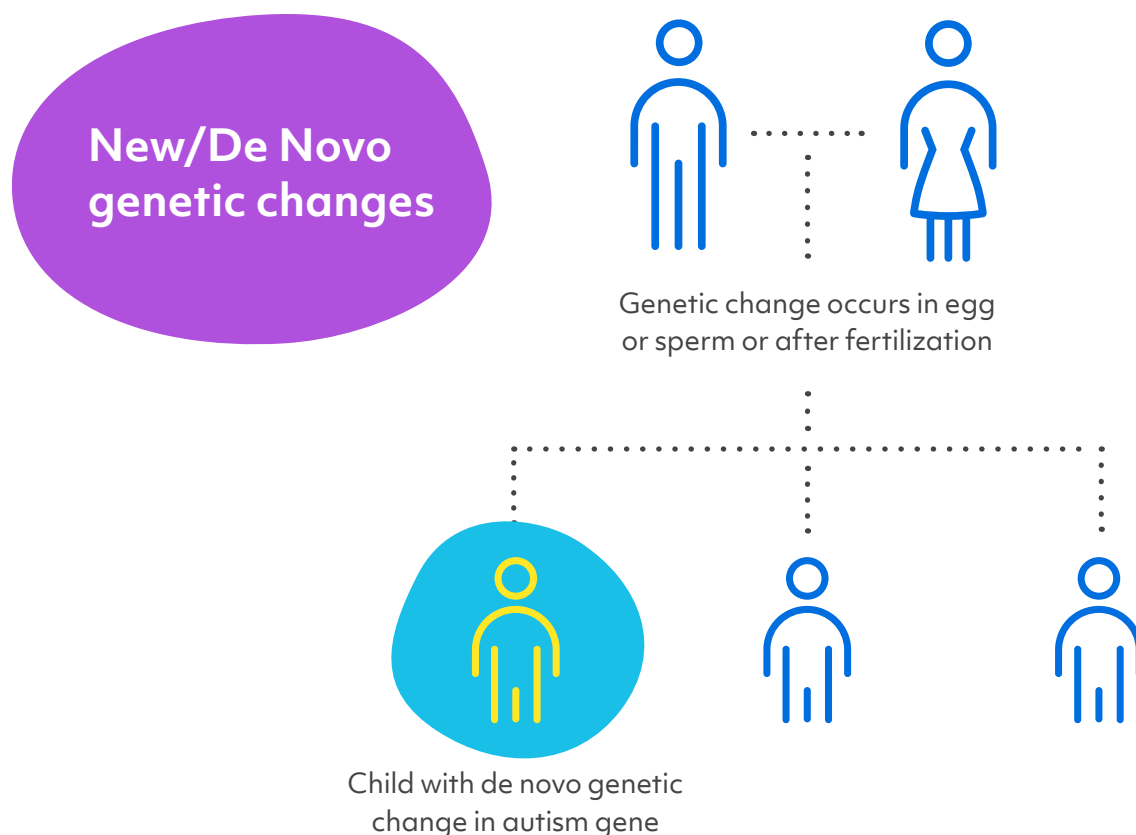
NR4A2-related syndrome can have moderate to severe effects on the development of communication skills, social skills, and learning skills. Because the NR4A2 gene is important in the development of the brain, many people who have NR4A2-related syndrome have:

- Language impairment
- Intellectual disability

What causes NR4A2-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 NR4A2 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.



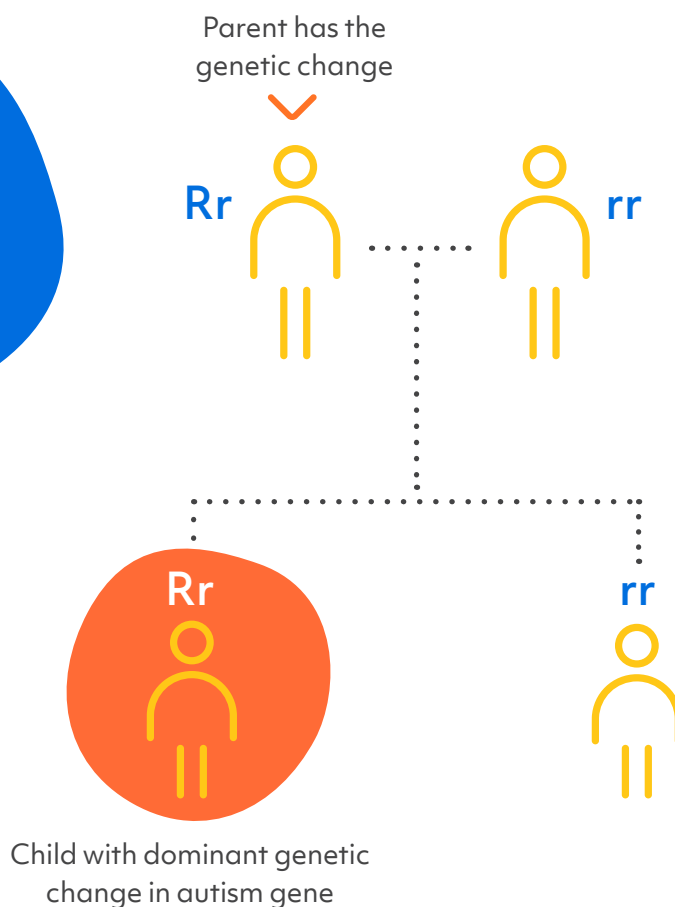
De novo changes can take place in any gene. We all have some de novo changes, most of which don't affect our health. But because NR4A2 plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that NR4A2-related syndrome is often the result of a de novo change in NR4A2. Many parents who have had their genes tested do not have the NR4A2 gene change found in their child who has the syndrome. In some cases, NR4A2-related syndrome happens because the gene change was passed down from a parent. This is called dominant inheritance.



Dominant inheritance


Children have a 50% chance of inheriting the genetic change



Why does my child have a change in the NR4A2 gene?

No parent causes their child's NR4A2-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.





What are the chances that other family members or future children will have NR4A2-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 NR4A2-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 NR4A2-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 NR4A2-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 NR4A2-related syndrome is 50 percent.

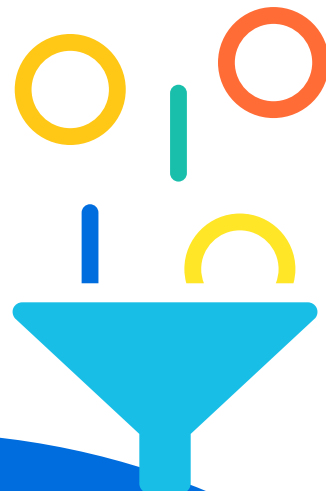
For a person who has NR4A2-related syndrome, the risk of having a child who has the syndrome is about 50 percent.


How many people have NR4A2-related syndrome?

As of 2018, fewer than 10 people in the world with changes in the NR4A2 gene had been described in the medical literature. The first case of NR4A2-related syndrome was described in 2017. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have NR4A2-related syndrome look different?

People who have NR4A2-related syndrome generally do not look different.





How is NR4A2-related syndrome treated?

Scientists and doctors have only just begun to study NR4A2-related syndrome. At this point, there are no medicines designed to treat the syndrome. 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:

- Physical exams and brain studies.
- Genetics consults.
- Development and behavior studies.
- 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 NR4A2-related syndrome should begin as early as possible, ideally before a child begins school.

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: www.epilepsy.com/learn/types-seizures.

NR4A2-related syndrome is extremely rare. Doctors and scientists have just recently begun to study it. As of 2018:

- Only three research studies on the syndrome had been published.
- The studies describe fewer than 10 people who have NR4A2-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.

Behavior and development concerns linked to NR4A2-related syndrome



In one study of four people who had NR4A2-related syndrome, all had:

- Autism
- Speech delay
- Intellectual disability, ranging from mild to severe

Medical and physical concerns linked to NR4A2-related syndrome

Scientists have not described medical and physical concerns related to changes in the NR4A2 gene.



Where can I find support and resources?

Simons Searchlight is another research program sponsored and run by the Simons Foundation Autism Research Initiative, also known as SFARI. As part of the next step in your research journey, Simons Searchlight offers you the opportunity to partner with scientists and other families who have the same gene change. Simons Searchlight is a registry for more than 200 genetic changes that are associated with neurodevelopmental conditions, including autism spectrum disorder. Simons Searchlight makes it easier for researchers to access the information they need to advance research on a condition.

To register for Simons Searchlight, go to the Simons Searchlight website at www.simonssearchlight.org and click “Join Us Today”.

- **Learn more about Simons Searchlight**
www.simonssearchlight.org/frequently-asked-questions
- **Simons Searchlight webpage with more information on NR4A2**
www.simonssearchlight.org/research/what-we-study/slc6a1
- **Simons Searchlight NR4A2 Facebook community**
www.facebook.com/groups/411122836052533

Sources and References

The content in this guide comes from published studies about NR4A2-related syndrome. Below you can find details about each study, as well as links to summaries.

- Reuter MS. *et al. American Journal of Medical Genetics Part A*, **173**, 2231-2234, (2017). Haploinsufficiency of NR4A2 is associated with a neurodevelopmental phenotype with prominent language impairment
www.ncbi.nlm.nih.gov/pubmed/28544326
- Lévy J. *et al. Clinical Genetics*, **94**, 264-268, (2018). NR4A2 haploinsufficiency is associated with intellectual disability and autism spectrum disorder
www.ncbi.nlm.nih.gov/pubmed/29770430



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