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GENE GUIDE

SETBP1 Haploinsufficiency Disorder

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. This Gene Guide was last updated in 2025. As new information comes to light with new research we will update this page. You may find it helpful to share this guide with friends and family members or doctors and teachers of the person who has ***SETBP1 Haploinsufficiency Disorder****.*

What causes SETBP1 Haploinsufficiency Disorder?

SETBP1 haploinsufficiency disorder happens when there are changes in the SETBP1 gene. These changes can keep the gene from working as it should.

Problematic genetic variants in SETBP1 can cause other conditions, including Schinzel-Giedion syndrome and SETBP1-related disorders. The information below focuses on genetic variants that lead to SETBP1 haploinsufficiency disorder.

Symptoms

Because the SETBP1 gene is important for the brain, some people may have:

- Developmental delay
- Intellectual disability
- Speech and language disorder
- Autism
- Attention deficit hyperactivity disorder (ADHD)
- Low muscle tone
- Febrile seizures
- Sleep problems
- Vision problems, often requiring glasses
- Feeding challenges
- Excessive drooling

What causes SETBP1 haploinsufficiency disorder?

SETBP1 haploinsufficiency disorder is a genetic condition, which means that it is caused by variants in genes. Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Every child gets two copies of the SETBP1 gene: one copy from their mother's egg, and one copy from their father's sperm. In most cases, parents pass on exact copies of the gene to their child. But the process of creating the egg or sperm is not perfect. A change in the genetic code can lead to physical issues, developmental issues, or both.

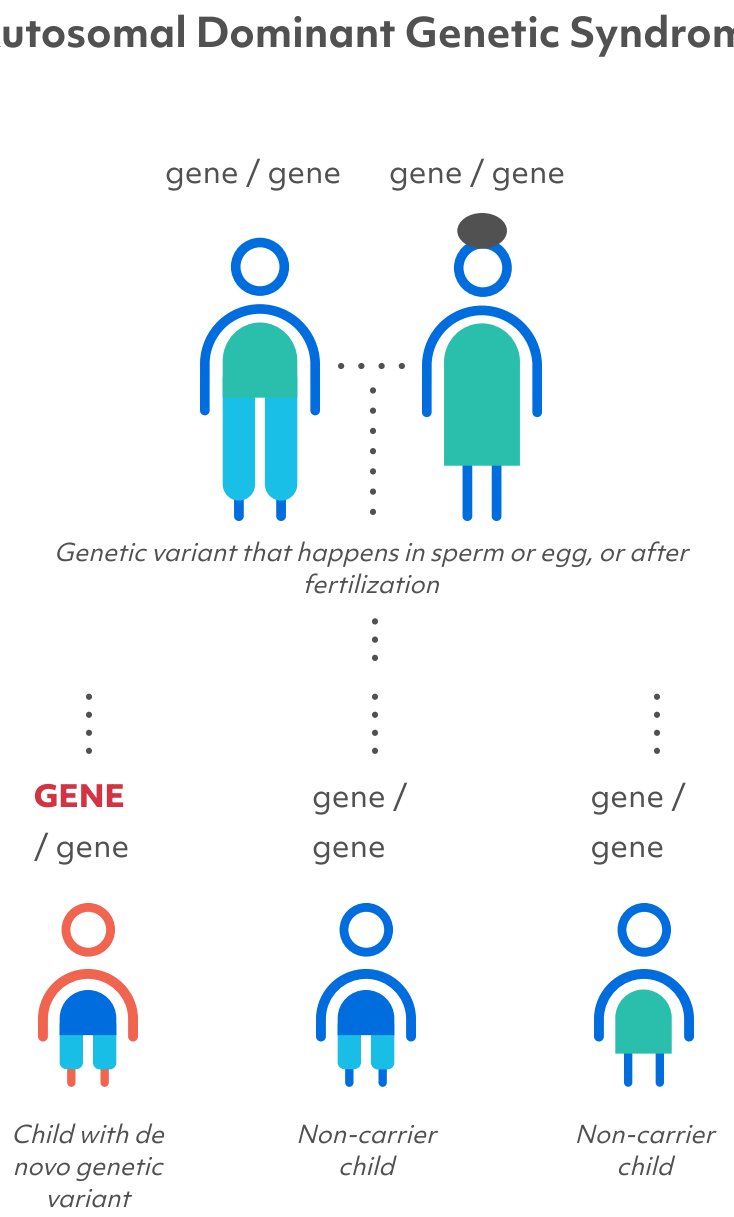
Sometimes a spontaneous variant happens in the sperm, egg or after fertilization. When a brand new genetic variant happens in the genetic code is called a 'de novo' genetic variant. The child is usually the first in the family to have the genetic variant.

De novo variants can take place in any gene. We all have some de novo variants, most of which don't affect our health. But because SETBP1 plays a key role in development, de novo variants in this gene can have a meaningful effect.

Research shows that SETBP1 haploinsufficiency disorder is often the result of a de novo variant in SETBP1. Many parents who have had their genes tested do not have the SETBP1 genetic variant found in their child who has the syndrome. In some cases, SETBP1 haploinsufficiency disorder happens because the genetic variant was passed down from a parent.

Autosomal dominant conditions

SETBP1 haploinsufficiency disorder is an autosomal dominant genetic condition. This means that when a person has the one damaging variant in SETBP1 they will likely have symptoms of SETBP1 haploinsufficiency disorder. For someone with an autosomal dominant genetic syndrome, every time they have a child there is a **50 percent** chance they pass on the same genetic variant and a **50 percent** chance they do not pass on the same genetic variant.



Why does my child have a change in the SETBP1 gene?

No parent causes their child's SETBP1 haploinsufficiency disorder. 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 SETBP1 haploinsufficiency disorder?

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 SETBP1 haploinsufficiency disorder depends on the genes of both biological parents.

- If neither biological parent has the same genetic variant 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 genetic variant.
- If one biological parent has the same genetic variant found in their child, the chance of having another child who has the syndrome is **50 percent**.

For a symptom-free brother or sister of someone who has SETBP1 haploinsufficiency disorder, the sibling's risk of having a child who has SETBP1 haploinsufficiency disorder depends on the sibling's genes and their parents' genes.

- If neither parent has the same genetic variant causing SETBP1 haploinsufficiency disorder, the symptom-free sibling has a **nearly 0 percent** chance of having a child who would inherit SETBP1 haploinsufficiency disorder.
- If one biological parent has the same genetic variant causing SETBP1 haploinsufficiency disorder, the symptom-free sibling has a **50 percent** chance of also having the same genetic variant. If the symptom-free sibling has the same genetic

variant, their chance of having a child who has the genetic variant is **50 percent.**

For a person who has SETBP1 haploinsufficiency disorder, the risk of having a child who has the syndrome is about **50 percent.**

How many people have SETBP1 haploinsufficiency disorder?

As of 2025, about 235 people with SETBP1 haploinsufficiency disorder have been identified in a medical clinic.

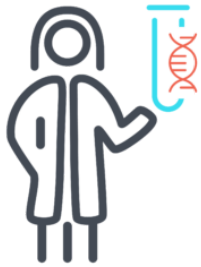
Do people who have SETBP1 haploinsufficiency disorder look different?

People with SETBP1 haploinsufficiency disorder may look different. Appearance can vary and can include some but not all of these features:

- Droopy eyelids, also called ptosis
- Narrowing of the eye opening
- Broad nasal bridge
- Widely spaced eyes
- Full tip of the nose

How is SETBP1 haploinsufficiency disorder treated?

Scientists and doctors have only just begun to study SETBP1 haploinsufficiency disorder. 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 SETBP1 haploinsufficiency disorder 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.

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 SETBP1 haploinsufficiency disorder

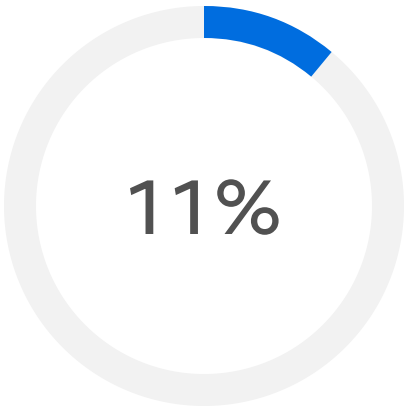
Speech and learning

Most people with SETBP1 haploinsufficiency disorder had developmental delay or intellectual disability (ID), motor delay, and speech and/or language disorders. Childhood apraxia of speech was common.

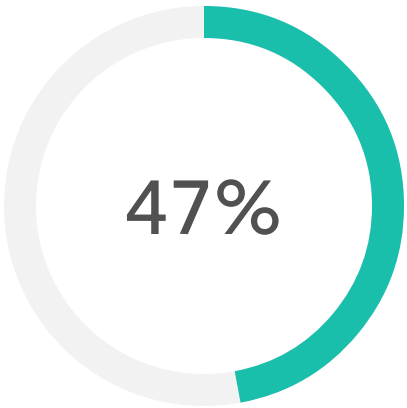
- **49 out of 51** people had developmental delay or intellectual disability (**96 percent**)
- **55 out of 56** people had speech and/or language impairment (**98 percent**)

The severity of intellectual disability (ID) varied among people:

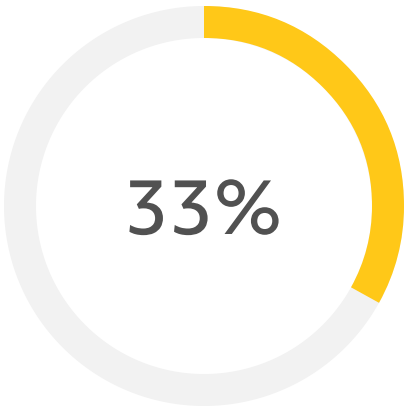
- **5 out of 45** people had no ID (**11 percent**)
- **21 out of 45** people had mild or borderline ID (**47 percent**)
- **15 out of 45** people had moderate ID (**33 percent**)
- **4 out of 45** people had severe or profound ID (**9 percent**)



5 out of 45 people had no ID.

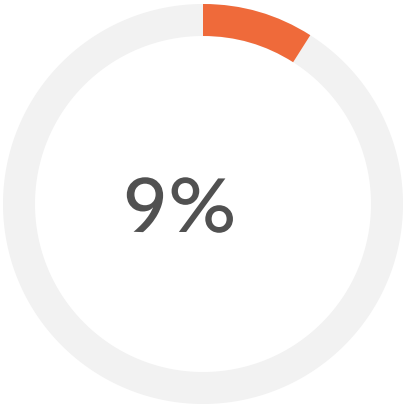


21 out of 45 people had mild or borderline ID.



15 out of 45 people had moderate ID.

4 out of 45 people had severe or profound ID.



Behavior

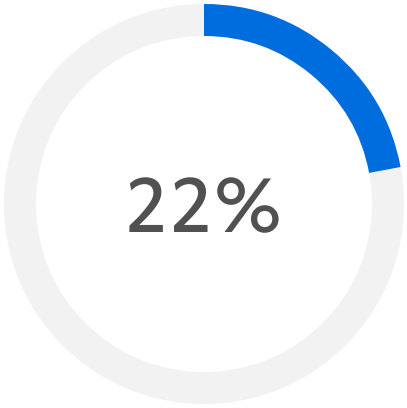
People with SETBP1 haploinsufficiency disorder had behavioral issues, such as features of autism, attention-deficit/hyperactivity disorder (ADHD), attention or concentration issues, anxiety, sleep challenges, self-injury behavior, developmental coordination disorder, and sensory integration disorder.

- **29 out of 41** people had attention or concentration issues (**71 percent**)

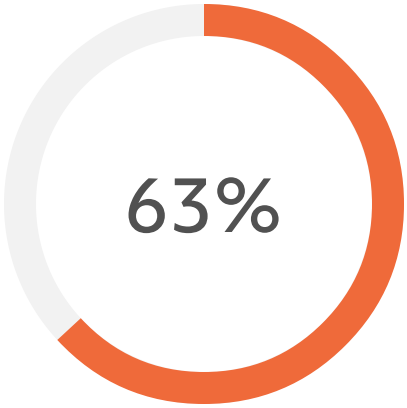
Brain

Some people with SETBP1 haploinsufficiency disorder had neurological medical issues, including seizures, most often febrile seizures, and lower than average muscle tone (hypotonia).

- **9 out of 41** people had seizures (**22 percent**)
- **19 out of 30** people had hypotonia (**63 percent**)



9 out of 41 people had seizures.



19 out of 30 people had hypotonia.

Medical and physical concerns linked to SETBP1 haploinsufficiency disorder

Vision and hearing

About one-half of people had vision issues, and some had issues with hearing. Vision issues included farsightedness (hyperopia), nearsightedness (myopia), crossed eyes (strabismus), and an imperfection of the eye that causes blurred distance and near vision (astigmatism).

- **19 out of 36** people had vision issues (**53 percent**)

Feeding and digestion issues

People with SETBP1 haploinsufficiency disorder had feeding issues, such as poor sucking or slow feeding, and digestive issues, such as diarrhea, constipation, reflux, and gastroesophageal reflux disease (GERD).

- **22 out of 42** people had feeding difficulties (**52 percent**)

Growth

Some people with SETBP1 haploinsufficiency disorder had hip joints that did not form properly (hip dysplasia), spine defects either at birth or later in life (hunched forward or deep forward curve of the lower spine), and finger defects (bent or curved fingers, fused/webbed fingers).

Where can I find support and resources?

SETBP1 Society

The SETBP1 Society aims to provide support to individuals with SETBP1 haploinsufficiency and related disorder and their families, to promote discussion and fund research, and to bring awareness and education to the public.

- https://www.setbp1.org/

Simons Searchlight

Simons Searchlight is an online international research program, building an ever growing natural history database, biorepository, and resource network of over 175 rare genetic neurodevelopmental disorders. By joining their community and sharing your experiences, you contribute to a growing database used by scientists worldwide to advance the understanding of your genetic condition. Through online surveys and optional blood sample collection, they gather valuable information to improve lives and drive scientific progress. Families like yours are the key to making meaningful progress. To register for Simons Searchlight, go to the Simons Searchlight website at www.simonssearchlight.org and click "Join Us."

- **Learn more about Simons Searchlight** – www.simonssearchlight.org/frequently-asked-questions
- **Simons Searchlight webpage with more information on SETBP1** – www.simonssearchlight.org/research/what-we-study/setbp1
- **Simons Searchlight Facebook Group –** https://www.facebook.com/groups/setbp1

Sources and References

- Jansen, N. A., Braden, R. O., Srivastava, S., Otness, E. F., Lesca, G., Rossi, M., Nizon, M., Bernier, R. A., Quelin, C., … & van Bon, B. W. (2021). Clinical delineation of SETBP1 haploinsufficiency disorder. European Journal of Human Genetics, 29(8), 1198-1205. doi:10.1038/s41431-021-00888-9
- Leonardi, E., Bettella, E., Pelizza, M. F., Aspromonte, M. C., Polli, R., Boniver, C., Sartori, S., Milani, D., & Murgia, A. (2020). Identification of SETBP1 mutations by gene panel sequencing in individuals with intellectual disability or with "developmental and epileptic encephalopathy". Frontiers in Neurology, 11, 593446. doi:10.3389/fneur.2020.593446
- Morgan, A., Srivastava, S., Duis, J., & van Bon, B. SETBP1 haploinsufficiency disorder. 2024 May 9. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK575336/
- Morgan, A., Braden, R., Wong, M. M. K., Colin, E., Amor, D., Liégeois, F., Srivastava, S., Vogel, A., Bizaoui, V., … & van Bon, B. W. (2021). Speech and language deficits are central to SETBP1 haploinsufficiency disorder. European Journal of Human Genetics, 29(8), 1216-1225. doi:10.1038/s41431-021-00894-x
- Wei, Z., Yao, L., Zhang, L., Li, S., Xu, M., Wu, D., Li, W., & Chang, Y. (2025). Prenatal diagnosis of intellectual disability, autosomal dominant 29 with a nonsense pathogenic variant in SETBP1: A case report and literature review. Frontiers in Genetics, 16, 1463485. doi:10.3389/fgene.2025.1463485