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UNDERSTANDING GENES & CHROMOSOMES

SCN1B-related syndromes

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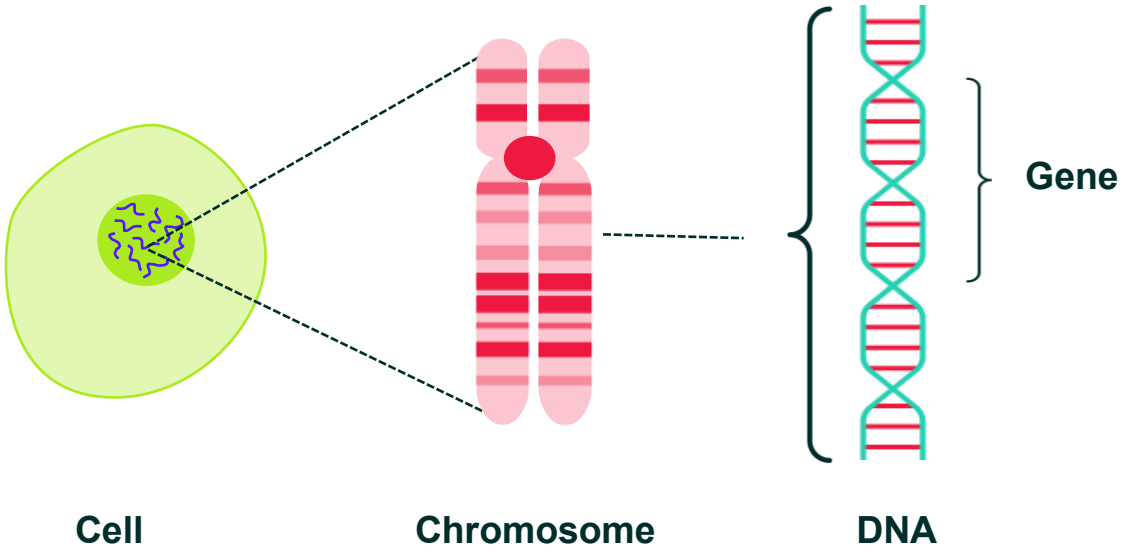
This guide is designed to help families and healthcare professionals looking after people with SCN1B-related syndromes. It contains information about the causes, the ways in which they can affect people and suggestions about the help and management that can benefit people with these conditions.

What causes SCN1B-related syndromes?

SCN1B-related syndromes are a group of rare genetic conditions caused by specific changes (pathogenic variants) in the SCN1B gene. 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 inside our cells, the building blocks of our bodies. In people with genetic conditions, one or more of their genes don't instruct the body as expected, which can lead to changes in how their body works.



The SCN1B gene codes for a protein that helps to regulate communication between brain cells (neurones) by providing the instructions for making part of brain cells called sodium channels. Sodium channels are tiny structures in nerve cells that allow electrical signals to pass from one cell to another. These electrical signals are how the brain communicates with the rest of the body to control movement, learning, memory and many other everyday functions.

When there is a variant in the DNA that carries the instructions for the SCN1B gene, the cell follows these new instructions. This can mean it makes a slightly different protein, or in some cases that it doesn't make the protein at all. This can change the balance of electrical activity in the brain. In some people, this increases the likelihood of experiencing seizures. This leads to epilepsy, which is the main health condition that is known to be linked to these variants in the SCN1B gene (see page 4).

We have two copies of the SCN1B gene in our cells, one inherited from each parent. Most people with an SCN1B-related syndrome have a causative variant in just one copy of the SCN1B gene, the other copy is unaffected. Very rarely, some people have a variant in both copies. If both copies of the gene carry a variant this can mean that the child may be more severely affected. Even then, symptoms and features vary widely between individuals. Research suggests that different types of variants can affect the SCN1B protein in different ways, which might account for the variability in symptoms and features, or their severity, in different people with SCN1B-related syndrome.

Why did this happen?

When someone is found to have a variant in their SCN1B gene it could either have been inherited from a parent, or it could be a new variant that has occurred for the first time in that person (a 'de novo' variant). Doctors can determine whether the variant is inherited or de novo by taking a blood sample from the affected child and comparing it with blood samples from both their parents.

Often in families where the genetic variant has been inherited from a parent, the parent will have a history of seizures associated with a high temperature (febrile seizures) or epilepsy (see page 4). Indeed, in several families, a parent has been found to have the same genetic variant as their child and on closer questioning reported that they had childhood epilepsy or very mild febrile seizures that completely resolved by adulthood. If a parent has no history of seizures but has the same genetic variant as their child, further evaluation will be necessary as there may be another cause for their child's epilepsy.

Another possibility when the variant is found to be inherited is a phenomenon called mosaicism, where the genetic variant is found in some, but not all, of the body's cells. If this happens, one parent, or occasionally both, carries a low level of cells with the causative variant, which might not be detectable. The level is not enough to cause disease in the parent, but it can mean they could have passed on the variant to their child, and possibly to future children.

Unique publishes a short general guide to Mosaicism

Sometimes, a genetic variant may be found in the SCN1B gene that does not cause a SCN1B-related syndrome but is instead a harmless variant and not the cause of the child's epilepsy (a benign variant). Sometimes a variant in the SCN1B gene may be found and it is unclear whether it is the cause of the child's epilepsy. These are called variants of uncertain significance (VUS).

It is also possible for a child to have a variant in both copies of the SCN1B gene, if both parents passed on a copy of the SCN1B gene containing a causative variant to their child, so one variant was inherited from the mother and one from the father.

Can it happen again?

De novo genetic variants are more likely to be the cause where a child has severe epilepsy and/or development concerns and there is no family history of seizures. If the genetic variant is de novo, then it makes it very unlikely that other children, or any future children, would be affected. There is however a small residual chance (usually less the 1 to 2 %) of recurrence due to a rare phenomenon called germline mosaicism. This is when a parent carries a genetic variant, but it is limited to some of their egg or sperm cells.

If the causative genetic variant has been inherited from one or both parents, the chance of having another affected child is higher.

A clinical geneticist or genetic counsellor can provide specific advice for each family about the chance of having further children with a SCN1B-related syndrome.

It is important to recognise that no one should be blamed for variants in their DNA and no parent is at fault when a new DNA variant occurs in their child.

Unique publishes guides to Planning your next child, Prenatal genetic testing and diagnosis, A clinical genetics appointment and Supporting siblings of children with a rare genetic condition

What features and symptoms do people with SCN1B-related syndromes have?

As is common with many genetic conditions, children and adults with SCN1B-related syndromes can have a range of features and symptoms.

The main health concern linked to causative variants in the SCN1B gene is epilepsy. Epilepsy is a condition that affects the brain and causes repeated seizures (a sudden and unexpected change in the electrical activity in the brain). However, epilepsy associated with SCN1B can present very differently from one person to another. Some individuals have only mild seizures in early childhood or when they have a high temperature (febrile seizures). Others may develop ongoing epilepsy that can be difficult to treat. Some families have multiple members with the gene variant, all of whom are affected to some extent. A number of families with different SCN1B variants also report mild learning, neurodivergence, and / or sensory processing difficulties. For children with well controlled seizures these difficulties do not often result in significant educational delay. Importantly, some people who carry a variant in the SCN1B gene never develop seizures at all.

One of the most common early features of variants in the SCN1B gene are febrile seizures. These are seizures that are typically triggered by fever and usually occur in young children (between the ages of six months and five years). Febrile seizures are common in childhood and are typically outgrown by around five or six years of age. In children with a genetic variant that causes SCN1B, however, febrile seizures may continue for longer than in other people who experience febrile seizures, or they may be accompanied by other types of seizures later in childhood (see below).

SCN1B variants are most often associated with a condition known as generalized epilepsy with febrile seizures plus (GEFS+)

GEFS+ is described as a spectrum disorder because its severity varies considerably from person to person. Some children may experience febrile seizures that continue beyond the usual age range. Others may develop additional seizure types not associated with a fever, such as generalized tonic-clonic seizures (which involve stiffening and shaking of the whole body), absence seizures (brief staring spells) or focal seizures (seizures begin in one part of the brain only). Less commonly there have been reports of SCN1B variants being linked to temporal lobe epilepsy, where seizures start in a specific area of the brain. These seizures may begin later in childhood or adolescence and can vary in frequency and severity.

There is currently no way to predict how severely someone will be affected by their genetic variant. In many cases, seizures respond well to medication, and children continue to develop as expected.

SCN1B variants can cause learning and sensory difficulties

Physical development in children with SCN1B variants typically seems to be unaffected. The majority of children with a variant in a single copy of the gene walk, talk and play in the same way as any other child and would be expected to develop in common with typically-developing children. Children with variants in both copies of the gene can have more significant delays in development or develop a physical disability. This is particularly true for children whose symptoms include significant seizure activity.

With respect to learning, the majority of children have been seen to have normal to mild learning (intellectual) disability. Development may slow down for any child when seizures are very frequent. In several cases reported in the literature, children with SCN1B variants were found to have difficulties with sensory processing and autism spectrum disorder (ASD)-like features. This appears to be independent of intellectual ability or seizure frequency. It isn't yet clear if this is directly linked to variants in the SCN1B gene, the consequence of seizures during development, or due to unrelated causes.

Are there any more serious disorders linked to SCN1B?

While many individuals with a SCN1B variant in only one copy of the gene have mild or manageable epilepsy, more severe symptoms (clinical presentations) are sometimes seen. When both copies of the SCN1B gene are altered - a situation known as homozygous inheritance - children may develop an early-onset epileptic condition, developmental encephalopathic epilepsy (DEE) or a Dravet-like syndrome. In these uncommon cases, seizures often begin in infancy, occur frequently and can be much more difficult to control. Development may also be more severely affected, with delays in speech, learning or motor skills. There are some reports of individuals with severe presentations with a SCN1B variant in only one copy of the gene, but these are the minority.

It is important to stress that these severe presentations are uncommon. Most people identified with a SCN1B variant have a much milder clinical picture, often within the GEFS+ spectrum.

As is the case for other epilepsies with a genetic cause, there is an increased risk of sudden unexpected death in epilepsy (SUDEP) in some children with SCN1B variants. It is not yet clear why this is; however, this is also seen in children with variants in other genes related to sodium channel function and research is ongoing to better understand these risks. It is possible to ask your paediatric neurologist or epilepsy nurse specialist to discuss this with you in further detail.

Can SCN1B variants affect any other organs?

There are some reports of SCN1B variants causing problems related to the heart and its ability to beat in a regular rhythm. The most evidence for these is related to Brugada syndrome (type 5) - a very rare condition that can cause fainting spells, palpitations and in some cases sudden death. It is treated with an implantable cardioverter-defibrillator, a device that shocks the heart when it detects it beating in a dangerous rhythm. There has also been an association with atrial fibrillation (familial type 13), which causes the heart to beat very quickly and irregularly but can usually be managed with medication alone.

It remains unclear which people with SCN1B-related epilepsy are at risk of these heart problems. Most individuals with epilepsy related to SCN1B who have had heart checks do not appear to have these problems. This is true in families in which the variant has been inherited, and the parent(s) also have the genetic variant. However, due to limited evidence it is advisable at present for all individuals with this genetic diagnosis to be seen for a heart check at least once. The need for ongoing monitoring, and the recommended frequency of checks, can be determined by their cardiologist. This is an area that requires further research to provide clearer evidence-based recommendations.

Why do the symptoms vary so much?

Many cells in the body contain sodium channels. Changes to the genes that control these channels can affect any or all of these cells. One of the most confusing aspects of SCN1B-related conditions is how differently they can affect people with the same genetic variant, even within the same family. A parent may carry the same genetic variant as their child who has severe seizures but may have only experienced mild febrile seizures, or no seizures at all, themselves. This is due to something called incomplete penetrance, where some people with the same variant won't develop any clinical symptoms, and variable expressivity, where the range and severity of symptoms experienced by different people can vary.

Researchers believe that other genetic factors and environmental influences also help determine whether seizures develop and how severe they become. This variability means that having an SCN1B variant increases the chance of developing symptoms, but it does not yet allow doctors to predict with certainty exactly how an individual child will be affected.

Unique publishes a short general guide to Variable Expressivity & Reduced Penetrance

What is the outlook for children who have SCN1B-related syndromes and their families?

For many families, variants in the SCN1B gene often cause mild to moderate epilepsy that can be treated successfully. Many children have typical intelligence and lead full, active lives. Regular follow-up with a neurologist is important to monitor seizures and adjust treatment if needed. Genetic counselling can also help families understand inheritance patterns and the likelihood of passing on the genetic variant.

For those children and their families who present with more severe and frequent seizures, the healthcare team looking after them will be able to provide more specific advice based on an individual's needs and symptoms.

Genetic epilepsy disorders are the subject of extensive research. Since SCN1B-related epilepsy is rare and not widely recognised outside specialist centres, this research is needed to better understand these conditions.

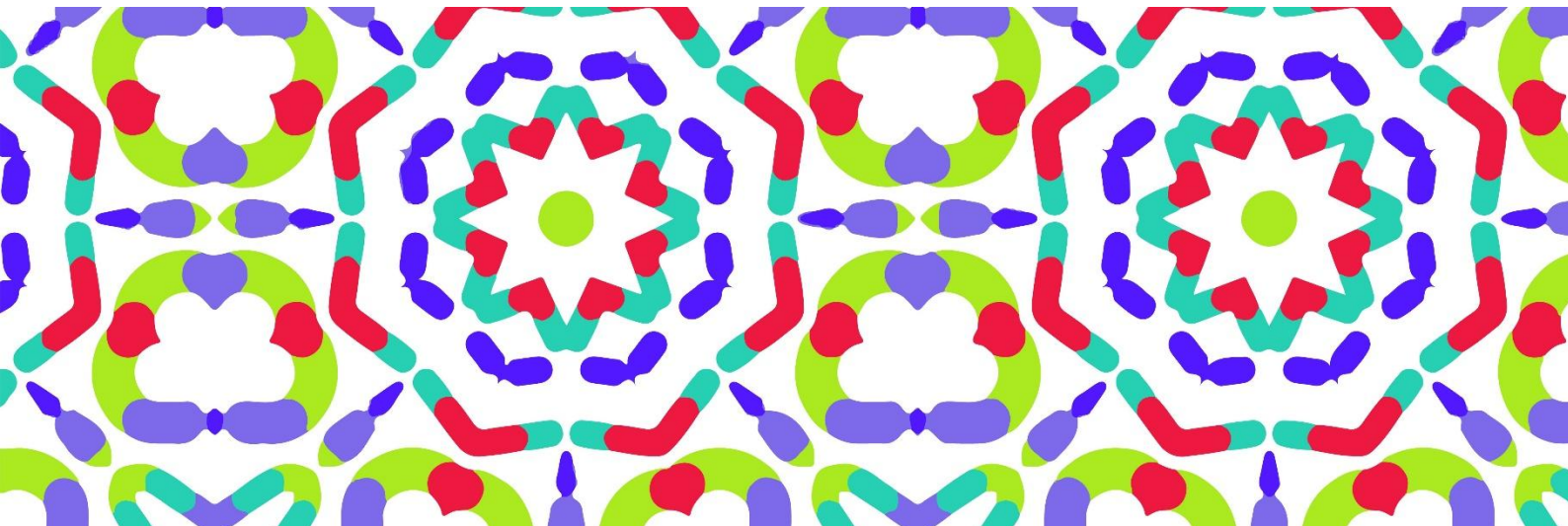
Areas of ongoing research include:

- How different genetic variants influence a child's chance of developing epilepsy
- Understanding why some variants are linked with more severe seizures
- Finding better treatment options for a child's specific genetic variant
- How to best support families and carers for children affected by SCN1B and similar conditions

Details of clinical trials related to a particular condition or gene can be found at **ClinicalTrials.gov** and **EU Clinical Trials Register**.

Recommendations for clinical care

- Ongoing neurology input for individuals with epilepsy
- Genetic counselling for affected individuals and their families should also be offered together with the provision of signposting to family support and resources
- All individuals with or without seizures should have baseline cardiac investigations (Echo and ECG). Need for surveillance thereafter to be determined by cardiology
- Assessment for ASD/ADHD where suspected
- Educational support where required



Families say ...

"Our son was a very happy healthy baby and was ahead on all his milestones for the first couple of years of his life. He had a few of febrile seizures just before his second birthday but went on to develop afebrile seizures at age two and a half years. These started with a bit of a whirlwind with him having multiple tonic-clonic seizures every day, which were resistant to medication and also associated with regression and loss of skills. We found out a couple of months after his seizures started that they were caused by a variant in the SCN1B gene.

It was a surprise to find out that I also had the gene variant but had only experienced two febrile seizures as a young child. His older sister also experienced several febrile seizures when she was little, but we have chosen not to have her tested - she can decide for herself when she is older.

We tried several different combinations of treatments for our son's seizures, including the ketogenic diet which was very helpful in gaining some level of control of the condition and regaining a more normal quality of life again, but he continued to have nocturnal tonic-clonic seizures on an almost nightly basis. Amazingly, the seventh treatment that we tried has been a good one for him and we have found a combination of three drugs and a keto diet which has allowed him to be seizure free for just under two years, which at one point we never thought would be possible!

Our son is in a mainstream school (although he was kept back a year) and is learning to read. He has recently learnt to ride his bike without stabilisers and loves swimming. He has some input from a physiotherapist as he has some struggles with his balance and coordination (likely in part due to his medications), and he needs extra help in school with his learning. He is seen every couple of years by a cardiologist as the gene variant may also cause problems with the heart but there is no sign of this at the moment for him.

Our son is a happy outgoing boy who loves to make people smile and amazes us every day with what he is capable of!"

Sources

The information in this booklet is drawn from the published medical literature and information from Unique members. In 2026, Unique had 1 member family with a SCN1B gene variant. The first-named author and publication date for articles in the medical literature are given to allow you to look for the abstracts or original articles on the internet in PubMed (**pubmed.ncbi.nlm.nih.gov/**).

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* An asterisk indicates articles which are “open access” and freely available to everyone at **https://pubmed.ncbi.nlm.nih.gov**

Inform Network Support

Rare Chromosome Disorder Support Group
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- Seizure Disorders/Epilepsy Awareness Patient's Facebook Support Group
- European Patient Advocacy Group for Epicare

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