

# SCN2A related conditions



## What is the SCN2A gene and what does it do?

SCN2A is the name of a gene that codes for part of the sodium or salt channel. This is an electrically activated gate in the brain which allows sodium in and out of neurones [cells that conduct nerve impulses], affecting the excitability of the brain.

## What is a mutation in the SCN2A gene?

DNA is the material that genes are made of. It can be thought of as individual letters which make up sentences (genes). A mutation is like a spelling mistake which leads to sentences not making sense. For each gene, everybody has two copies: one inherited from the father and one from the mother. With SCN2A, a 'spelling mistake' - a mutation - in one copy of the gene is enough to cause problems.

The SCN2A gene is found on chromosome 2 in the band called 2q24.3.

## What are the disorders of SCN2A?

Changes (mutations) in SCN2A cause a range of conditions, from less to more severe. The mildest type is Benign Familial Neonatal/Infantile Seizures (BFNIS). This is a condition that runs in families where babies will have seizures that they normally grow out of by the end of the first year of life, and usually have normal development. SCN2A mutations can also cause more severe epilepsy and developmental delay. They can even cause learning difficulties or autistic spectrum disorder without epilepsy.

### Mutations in SCN2A can cause:

- Benign familial neonatal /infantile seizures (BFNIS)
- A more severe epilepsy which may be given a name such as Ohtahara syndrome, West syndrome, or epilepsy of infancy with migrating focal seizures (see box on page 4)
- Autistic Spectrum disorder (ASD) without epilepsy
- Learning difficulties without epilepsy

“ A is a delightful, loving boy who contributes to our life by his incredibly warm personality. We love him dearly, though the future is uncertain as we do not know any adults with SCN2A to compare with. ” - 4 years

“ E has brought people into our lives we would likely have never met. She brings pure joy to anyone who meets her and loves everyone unconditionally. She has taught us to be better people and parents and has taught us patience. We love her just the way she is! ” - 11 years

## Why did this happen? Can it happen again?

When a SCN2A mutation is found in your child, the doctors will test the DNA from both parents to find out if the mutation is inherited, or if it is **de novo** which means it has arisen for the first time in your child. If a parent who is unaffected with epilepsy does have the mutation, then further careful evaluation of the mutation will be necessary, because in this situation, the mutation may not be the cause of the child's epilepsy. For most families, where their child has severe epilepsy and/ or developmental problems but no family history of epilepsy, the SCN2A mutation is more likely to be **de novo** rather than **inherited** from a parent.

### A new gene change?

A **de novo** mutation is a spelling mistake that has happened in your child's DNA for the first time. This makes it very unlikely that your other children or future children will be affected. There is however a very low risk that the mutation, while not present in the parent's body, is carried in their sperm or eggs and could then be passed on to another child. Empirically, this risk is about 1-2%.

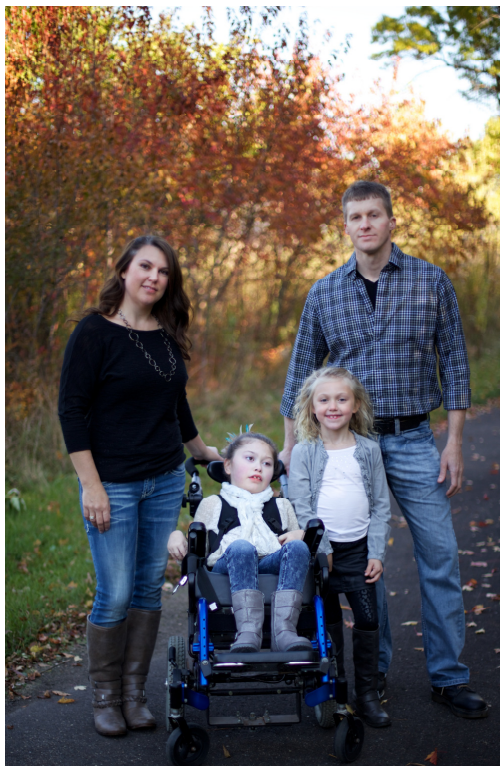
### An inherited gene change?

There is a mild form of SCN2A related disorder where the gene mutation is commonly found to be inherited from one of the child's parents.

Another possibility when the change is found to be inherited is that you or your partner carry a low level of the mutated gene in your blood. The level is not enough to cause disease in you or your partner, but it can mean you could have passed on the mutation to your child, and possibly to future children. This is called mosaicism.

A third explanation for an inherited change is that the mutation found in SCN2A is not a disease causing mutation but is a harmless familial inherited alteration and not the cause of your child's epilepsy.

Your genetic counsellor or genetics consultant will discuss all of these issues with you in detail and will explain what the SCN2A mutation means for your child, you and your family.



## Medical concerns

### ■ Seizures

Most (but not all) children with mutations in SCN2A will have seizures which usually start in the first few weeks of life. More rarely the seizures can start in later childhood and may then be less severe.

In the benign familial form, short-lasting jerky (clonic) seizures are seen. They may not necessarily need treatment as often the epilepsy is self-resolving and children grow out of it by the end of the first year of life.

In the more severe SCN2A epilepsies such as Ohtahara syndrome or EIMFS, the seizures may involve stiffening (tonic) or jerking (clonic or myoclonic) seizures and are very frequent. Unfortunately, they can be quite difficult to treat with medications. In the severe forms of SCN2A epilepsy, using high therapeutic levels of medicines that block the sodium channel such as carbamazepine or phenytoin may be helpful.

As in other severe epilepsies, there is an increased risk of sudden unexplained death, known as SUDEP. Although it is not clear why, this has been seen in some children with SCN2A mutations. It is also seen in children with mutations in a different, related gene called SCN1A, so may relate to sodium channel function in general. Your paediatric neurologist or epilepsy nurse specialist can discuss this in further detail.

### Epilepsy syndromes caused by SCN2A mutations

#### ■ Ohtahara syndrome

A severe neurological condition where seizures start in the first few weeks of life. Frequent, brief stiffening of arms or legs occurs and a typical electroencephalogram (EEG) or brain wave test appearance is seen.

#### ■ Epilepsy of infancy with migrating focal seizures (EIMFS)

This starts within the first 6 months of life with frequent focal seizures where one limb or part of the body is affected. Often there is head and eye turning to one side and facial flushing or breathing abnormalities with the seizures. The seizures are very frequent and are difficult to treat. There is a typical EEG appearance which helps to make the diagnosis.

#### ■ West syndrome

This starts later, usually after 3 months of age, and babies have frequent seizures in clusters called infantile spasms, where the head nods forward and there is a sudden stiffening and bending forward of the body, or the arms and legs are thrown outwards. Again, there is a typical EEG appearance and specific medications that are useful for this type of epilepsy.

## ■ Feeding

Many children have severe constipation, gastro-oesophageal reflux or diarrhoea. This could be because the gut is also controlled by its own nervous system which is affected by the mutation. The symptoms can be very severe, in which case they may be called gastrointestinal dysmotility. Children with severe problems can be referred to a paediatric gastroenterologist. They may recommend specific medications or procedures such as gastrostomy (feeding button insertion) or fundoplication (a procedure to tighten the junction between the gullet and the stomach to help severe reflux).

## ■ Cardiac

Although SCN2A mutations have not been associated with heart problems, it is a good idea in all severe epilepsies to have a baseline ECG, a test of heart function.

## ■ Movement disorder

Abnormal and rapid movements with flailing or writhing of the arms and legs (called dyskinesia or chorea) or holding an abnormal posture (dystonia) is frequent and can sometimes be mistaken for seizures. In fact these are involuntary movements or a movement disorder and there are specific treatments which may be prescribed by a paediatric neurologist.

“ A has two mutations in the gene but his condition is milder than some. ”

“ Even though SCN2A is considered rare and so much is unknown about it, we are grateful to have a known cause for E’s neurological complexities. The diagnosis helped give me closure and I have joined other families whose children have SCN2A and we are searching for answers, effective treatments and ultimately a cure. ”  
- 11 years

### Most children severely affected by an SCN2A mutation have:

- Epilepsy
- Developmental delay
- Movement disorder
- Hypotonia (floppiness of the body)
- Gastrointestinal problems

## Development

*The following details do not apply to children with BFNIS.*

### ■ Physical development

Many children will have delayed development of their movement skills which may be exacerbated by the floppiness of their muscles. A wide range of abilities is seen, with some children achieving independent walking but many unable to sit independently.

“ He can walk and run etc but his co-ordination is weak. ” - 4 years

### ■ Learning

The majority of children have moderate to severe learning difficulties and will require substantial additional support in school. Development may slow down when seizures are very frequent. More rarely the intellectual impairment can be mild.

“ He can read and loves nursery rhymes. ”  
- 4 years

“ Although E is non-verbal and completely dependent on an adult for all daily cares she is able to use a DynaVox Eyegaze computer to communicate with us. She attends 5<sup>th</sup> grade and spends most of her time in the classroom with children who do not have special needs. When tested on reading comprehension and math, she scores above average for her age. She is very smart, but it frustrates her that she is trapped inside a body that cannot move or speak. ” - 11 years

### ■ Speech

Many children will have severe language delay and may communicate using gestures, Makaton or vocalisations. Less commonly the speech impairment can be mild.

## ■ Behaviour

As for many children with severe epilepsy, behavioural problems may occur and can be exacerbated by seizures or medication. Some children may show autistic features.

“ A has been diagnosed as autistic and displays some symptoms such as not making conversation etc. Friendships are challenging for him as he does not seem to see other kids and doesn't know how to act around them. He is often in his own little world but he is happy. ”

- 4 years

“ As a part of the SCN2A gene mutation, E also carries a diagnosis of autism. This explains all of her sensory issues, self-stimulation and need for a consistent schedule. ”

- 11 years





## Support and Information



### Rare Chromosome Disorder Support Group,

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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.

### FamilieSCN2a Foundation

[www.scn2a.org](http://www.scn2a.org)

### Facebook

FamilieSCN2a Community Discussion Group

[www.facebook.com/groups/504056566376771](https://www.facebook.com/groups/504056566376771)

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.

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