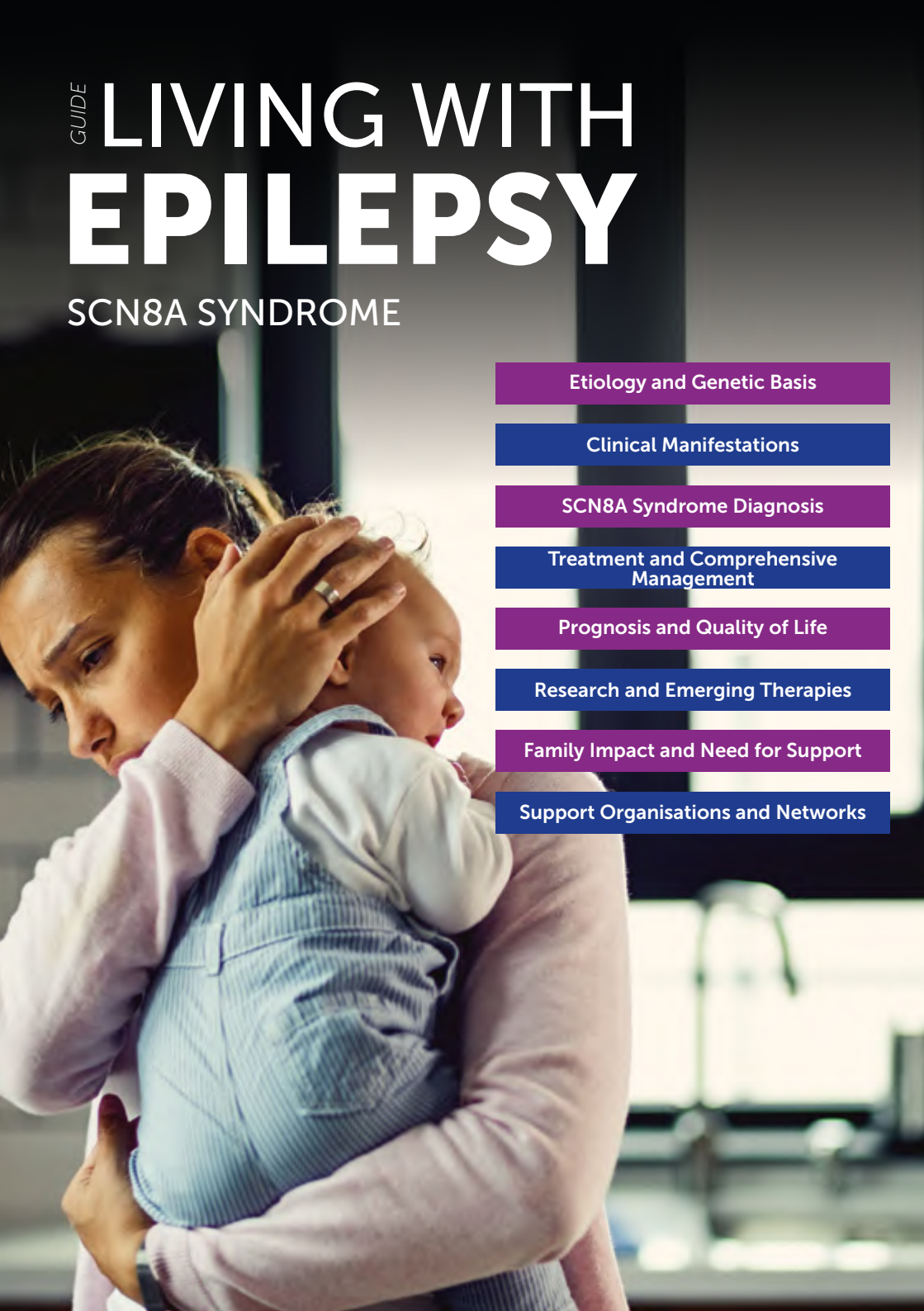
GUIDE

LIVING WITH EPILEPSY

SCN8A SYNDROME



- Etiology and Genetic Basis
- Clinical Manifestations
- SCN8A Syndrome Diagnosis
- Treatment and Comprehensive Management
- Prognosis and Quality of Life
- Research and Emerging Therapies
- Family Impact and Need for Support
- Support Organisations and Networks

TABLE OF CONTENTS

The information contained in this guide is educational and does not pretend to replace any medical advice. In case of doubt, please do seek advice with your healthcare professional.

International SCN8A ALLIANCE

Dr. Álvaro Beltrán Corbellini

Dr. Verónica Cid Izquierdo

Dr. Irene Sánchez-Miranda Román

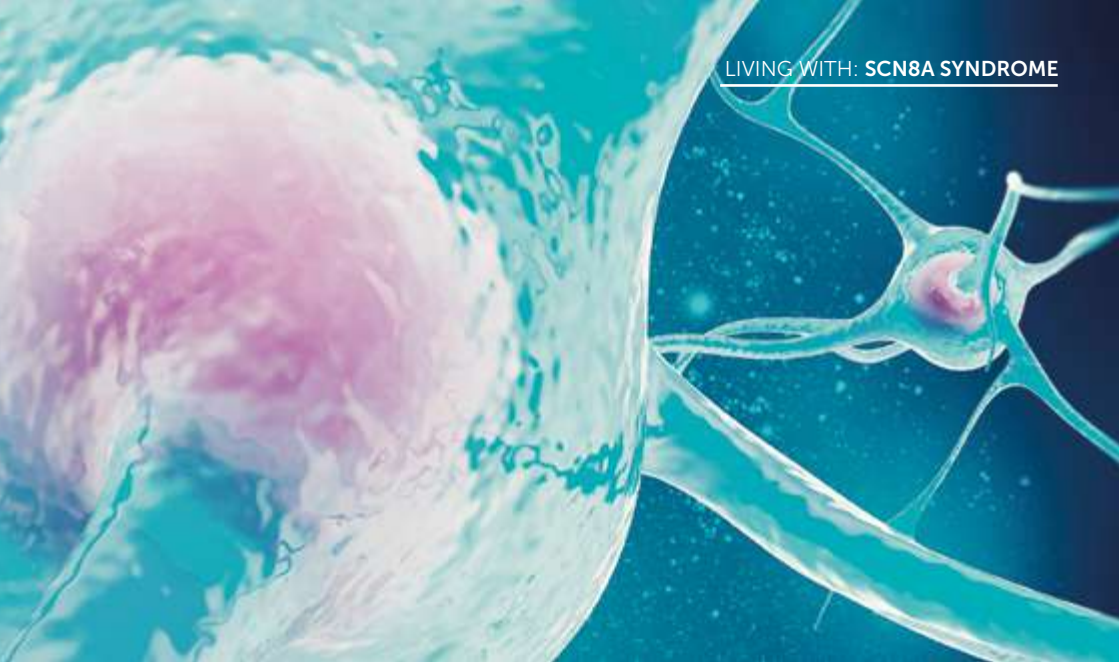
Neurologists at the Epilepsy Programme at Hospital Ruber Internacional and the Initiative for Neuroscience Foundation, Madrid

1. INTRODUCTION INTO SCN8A-RELATED DISORDERS

1.1 What are SCN8A-related disorders?

SCN8A-related disorders encompass a group of entities caused by genetic alterations in the SCN8A gene, which contains the necessary information to produce an essential protein in the brain called Nav1.6. This protein acts as a sodium channel within the neurons, allowing adequate transmission of electric signals in the brain.

When this channel is not working correctly due to certain genetic variants, the normal balance of brain activity is altered, which may cause neurons to work improperly, possibly originating epileptic seizures and difficulties in neurological development, among other manifestations.



SCN8A-related disorders encompass a wide range of clinical manifestations of different type and severity. This means that:

- Some people have milder forms with controllable epilepsy and normal or slightly altered neurological development.
- Others develop more severe forms with frequent and drug-refractory epileptic seizures and a severe impact on development (developmental and epileptic encephalopathy, DEE).
- There are also people with alteration of neurological development without epilepsy.

This variability is an important feature of the syndrome and shows how each patient can have a different development.

1.2 History and classification

SCN8A-related disorders are a relatively recent entity in medicine. Since they were first described in 2012, they have been raising great interest based on both their frequency within genetic epilepsies and the possibility of developing treatments aimed at their cause.

They are currently classified within epilepsies or developmental disorders of genetic origin. Within this spectrum, SCN8A-related disorders may manifest in different ways, which include (Figure 1):

- Severe developmental and epileptic encephalopathy (DEE).
- Mild to moderate developmental and epileptic encephalopathy.
- Self-limited familial infantile epilepsy.
- Neurodevelopmental disorder with generalised epilepsy.
- Neurodevelopmental disorder (mild to moderate) without epilepsy.

This diversity shows that the impact of the specific genetic variant may differ according to how it affects the sodium channel function. The three first groups are typically associated to sodium channel gain of function (GoF), while clinical presentations involving generalised epilepsy with neurodevelopmental disorder as well as neurodevelopmental disorders without epilepsy are associated to sodium channel loss of function (LoF).

Developmental and epileptic encephalopathies (DEE) are a group of conditions characterised by:

- Severe developmental disorder and epilepsy, typically with a common cause (which can often be genetic, but not exclusively).
- Additional impact on neurological development negatively affected by severity of epilepsy.

Key characteristics of 5 initial SCN8A phenotypes

PHENOTYPE	ONSET OF EPILEPTIC SEIZURES	DEVELOPMENTAL DELAY	TYPES OF EPILEPTIC SEIZURE	CLINICAL FEATURES	FREEDOM OF EPILEPTIC SEIZURES	PROGNOSIS WITHOUT SEIZURES
Severe DEE	0-6 months	0-6 months	Focal, generalised, infantile spasms	Limited mobility, cognitive function and functional vision, non-verbal, cannot eat by mouth	Rarely / never	Limited change to deterioration
Mild/moderate DEE	4-12 months	5-24 months	Focal, generalised	Delayed motor abilities and language, some cognitive understanding	Some of the time	Limited change to improvement
SeL(F)IE	6 months		Focal	Movement disorder	Around 1 year	Significant improvement
NDD with generalised epilepsy	24-48 months	12-60 months	Absence, generalised tonic-clonic,	Delayed language, some cognitive understanding	Some / most of the time	Limited change to improvement
NDD without epilepsy	N/A	12-36 months	N/A	Delayed motor abilities and language, some cognitive understanding, autistic features	N/A	Limited change to improvement

Figure 1: Modified from SCN8A Alliance (www.scn8aalliance.org) and based on Global modified Delphi consensus on diagnosis, phenotypes, and treatment of SCN8A-related epilepsy and/or neurodevelopmental disorders (Conecker G et al., Epilepsia, 2024). DEE: developmental and epileptic encephalopathy. SeL(F)IE: self-limited familial infantile epilepsy. NDD: neurodevelopmental disorder.

1.3 Clinical relevance

Despite being a rare disease, SCN8A-related disorders are among the most frequent causes of monogenic epilepsy during childhood. Hundreds of patients have been identified worldwide, and more undiagnosed cases are likely.

Their clinical relevance is due to several factors:

They usually start during the first months or years of life.

They are often associated to developmental alterations.

They may cause difficult to control (treatment-resistant) epileptic seizures.

They may involve severe clinical manifestations and require a specialised and multidisciplinary approach.

Knowing the genetic cause also has relevant implications:

- It allows confirming the diagnose.
- It helps guiding treatment towards more specific approaches able to modify the prognosis.
- It enables genetic advice to families.

2. ETIOLOGY AND GENETIC BASIS

2.1 Function of the SCN8A gene

Genes are DNA segments containing information to create proteins by joining smaller molecules called amino acids. Among other molecules, proteins are necessary for proper cellular function. **SCN8A is a gene codifying the synthesis of a protein called Nav 1.6.** This protein is a sodium channel expressed in the membrane of brain neurons, on which penetration of the sodium ion into the neurons relies. An adequate regulation of the sodium flow through the neuronal membrane is essential for proper brain function.

Hence **SCN8A-related disorders have a genetic origin.** In most cases, a specific genetic variant in the DNA structure of the gene leads eventually to the replacement of an amino acid by another one within the protein, thus originating a malfunction of this sodium channel and the clinical manifestations of the disease, consisting mainly of epilepsy and neurodevelopmental disorder of differing severity, among others. These genetic variants altering the channel can cause the latter's gain or loss of function. It is important to try to establish whether the genetic variant of a patient leads to channel gain or loss of function, which can be elucidated by means of the patient's symptoms or the variant features, among other methods. Depending on the type of dysfunction, symptoms, **treatments and the prognosis may vary from one patient to another**, as will be seen in subsequent sections.

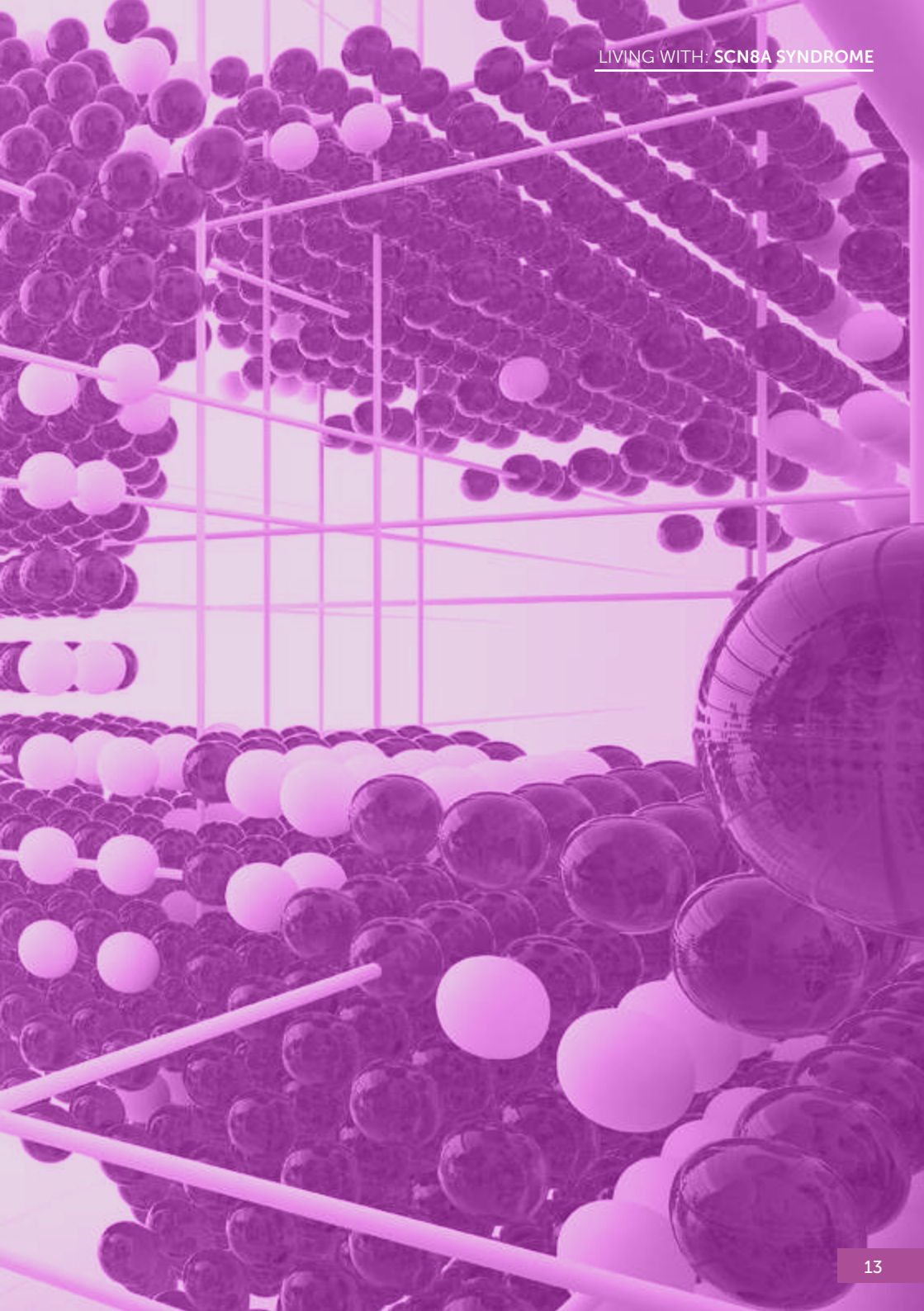
In this respect, the concept of "genetic origin" does in general not mean that the patient "has inherited the disease from their parents". Genes are DNA segments containing information to create proteins by joining smaller molecules called amino acids. Among other molecules, proteins are necessary for proper cellular function. SCN8A is a gene codifying the synthesis of a protein called Nav 1.6. This protein is a sodium channel expressed in the membrane of brain neurons, on which penetration of the sodium ion into the neurons relies. An adequate regulation of the sodium flow through the neuronal membrane is essential for proper brain function.

A variant that is present in an individual but not in their parents is called *de novo* variant, otherwise it is inherited. A specific genetic variant deemed to most likely originate a disease is generally called *pathogenic* or *probably pathogenic*. Conversely, a specific genetic variant deemed to most likely not originate a disease is called *benign* or *probably benign*. Finally, when there is not enough evidence to conclude whether a variant could cause a disease or not, the variant is called *of uncertain significance*.

Regarding the disease inheritance pattern, SCN8A-related disorders show an **autosomal dominant** Mendelian inheritance pattern. Of each gene, two copies (known as alleles) are presented, one of maternal, the other of paternal origin. The inheritance pattern described in this context means, among other considerations, that only one of both copies of the gene needs to be affected to develop the disease. A genetic variant that is present in only one of the alleles of the gene is known as *heterozygotic*.

Hence the risk for the patient's siblings to have the disease depends on the state of their parents. If one of the parents shows the same variant as the one identified in the patient, the probability of the latter's siblings inheriting it is 50%. Conversely, if the patient's variant is not identified in any of both parents (*de novo* variant), the probability to have it inherited by the patient's siblings is very low, but not zero, as there could occur more complex situations such as parental mosaicism, the detection of which is subject to technical limitations with routine methods. In this regard, family planning requires professional genetic advice.

Those described above are general considerations related to basic knowledge of the disease, which do not replace assessment by medical genetics professionals. Interpreting the results of a genetic study and genetic counselling are complex processes that require specialist care.



3. CLINICAL MANIFESTATIONS

The main clinical manifestations of SCN8A-related disorders are epileptic seizures, neurodevelopmental disorders and intellectual disability, as well as other manifestations that may involve other body regions such as the digestive system, among others. These manifestations may be shared with other epilepsies or developmental disorders of genetic origin.

However, manifestations caused by SCN8A-related disorders may present some particularities, such as age of onset and natural history, most frequent seizure types and particular triggers (change of temperature, fever or excitation, in some cases), impact of some processes regulated by the autonomic nervous system (dysautonomia) and cerebral visual impairment. Moreover, not all patients with SCN8A-related disorders feature all manifestations and their severity and development may differ considerably among each other.

Clinical manifestations ultimately appear due to genetic alteration. However, a severe epilepsy could contribute on its own to a higher severity of the developmental disorder.

3.1 Neurological symptoms

One of the main features of SCN8A-related disorders is the combination of epileptic seizures and neurodevelopmental alteration.

3.2 Epilepsy

Hence, despite not being always present, epileptic seizures are one of the most characteristic signs of SCN8A-related disorders. They can be frequent and difficult to control within a large group of patients.

Age of onset:

- Often during the first year of life, although they may also appear later
- In many cases during the first months of life

Seizures can vary in type, and even one same patient may show different types, such as:

- Focal seizures, together with different neurological symptoms according to the brain region where they originate, with or without alteration of the level of consciousness
- Bilateral tonic-clonic seizures, starting with a sudden muscle contracture (tonic phase), with shortness of breath, change of skin colour and guttural sounds, followed by convulsive movements of limbs (clonic phase)
- Epileptic spasms, characterised by sudden, very short flexion or extension of axial muscles (trunk, neck) and/or limbs, which often occur jointly when waking up

- Tonic seizures showing sustained muscle contracture causing general stiffness, without clonic movements
- Clonic seizures consisting of rhythmic jerking of limbs
- Myoclonic seizures characterised by shorter, arrhythmical and asynchronous jerks
- Absence usually showing unresponsiveness and change in facial expression for some seconds

Also, some studies show that certain types of genetic variant are associated to specific seizure patterns (e.g. earlier onset or specific epilepsy types).

3.3 Developmental disorder

In some cases, the neurological development can appear to be normal in the beginning, with difficulties appearing after the onset of epileptic seizures or progressively. In other cases, loss of previously acquired abilities can also be observed. Manifestations observed within developmental disorder are mainly cognitive, behavioural and motor.

Cognitive alterations:

- Intellectual disability of varying degree
- Attentional problems
- Language and communication difficulties
- Learning disorder

Behavioural alterations:

- Impulse control or aggressiveness problems
- Irritability or difficulties with emotional management
- Autism spectrum disorder or difficulties in social interaction

Motor alterations:

- Alterations in muscle tone
- Walking and posture problems
- Coordination problems (ataxia)
- Movement disorders (tremor, dystonia, dyskinesia and other involuntary movements)

3.4 Other associated manifestations

Apart from the manifestations described above, other equally relevant associated problems may appear, such as:

- **Sleeping disorders:** insomnia or excessive daytime sleepiness.
- **Eating problems:** difficulty to swallow with aspiration risk, underweight.
- **Gastrointestinal alterations:** constipation, diarrhea, gastroesophageal reflux.
- **Cerebral visual impairment.**
- **Respiratory pattern alterations (apnea, tachypnea) and difficulty to regulate the body temperature.**
- **Osteomuscular problems.**

4. DIAGNOSIS OF SCN8A-RELATED DISORDERS

4.1 Early clinical suspicion

The diagnostic process usually starts after identifying clinical manifestations suggesting a developmental disorder and/or an epilepsy of likely genetic origin (often different types of epileptic seizures starting in the first years of life) difficult to control with usual medication.

4.2 Diagnostic assessment process

Diagnosis requires a complete assessment including a detailed clinical history (medical interview and physical examination) plus additional exams such as:

- **Video electroencephalogram (VEEG):** allows analysing electrical brain activity and detect epileptic seizures.
- **Cerebral magnetic resonance imaging (MRI):** used to discard other structural causes, may often be normal.

Moreover, neuropsychological studies, among other additional exams, are important to characterise the development and disability profile of patients, contributing to an overall understanding of the physiopathology of the disease, more precise identification of deficient areas and a more effective therapeutic approach. All these assessments help characterising the disease, but do not confirm the diagnosis of SCN8A-related disorders as such.

4.3 Genetic study

Beyond clinical manifestations and being a disorder of specific genetic origin, the ultimate diagnosis of SCN8A-related disorders is done by means of genetic studies allowing to identify pathogenetic variants in the SCN8A gene.

The most frequently used techniques are:

- **Epilepsy gene panels.**
- **Exome sequencing.**
- **Genome sequencing.**

The two first techniques are increasingly established in common clinical practice, while genome sequencing is a technique whose routine implementation is still incipient and still rather restricted to research.

4.4 Importance of early diagnosis

Early diagnosis has a crucial impact on the patient's life and that of their family, as it allows:

- **Starting early adequate treatment with access to clinical trials.**
- **Avoiding less effective therapies.**
- **Access to early care programmes.**
- **Planning medical follow-up.**
- **Providing genetic counselling.**
- **Providing information and support to the family.**

All these actions can lead to a better functional prognosis of the patient.

5. TREATMENT AND COMPREHENSIVE MANAGEMENT

This disease can be treated in different possible ways. First, it shall be mentioned that although related research is under way (as will be seen in subsequent sections), there is currently no curative treatment correcting the genetic alteration causing the disease.

In this regard, efforts in common clinical practice are focusing on treating the above-mentioned manifestations of the disease with non-pharmacological and pharmacological strategies (symptomatic treatment). Here are some more specific approaches that are more effective for these disorders compared to others.

5.1 Pharmacological treatment of epileptic seizures

Pharmacological treatment of epileptic seizures should be individualised as it depends on the form of presentation of the epilepsy and the suspicion that the genetic alteration is leading to a gain or loss of function of the sodium channel:

- **In those patients with developmental and epileptic encephalopathy (DEE) and in those with self-limited familial infantile epilepsy with seizures since the first months of life, the likeliest suspicion is that the genetic alteration is leading to a sodium channel gain of function. Hence, in this scenario, the treatment of choice usually consists of sodium channel blockers. There are different drugs within this group that differ from each other in how the sodium channel function is reduced, among other additional mechanisms of action. Combinations of drugs from this group with additional mechanisms of action at a moderate to high dose will often be required.**
- **In those patients with a clinical presentation such as neuro-developmental disorder with generalised epilepsy, the likeliest suspicion is channel loss of function, so sodium channel blockers could worsen the epilepsy. Instead, the use of a different type of drugs would be preferrable, such as broad-spectrum drugs with multiple mechanism of action (GABAergic, inhibition of glutamate-mediated excitation) or some selective calcium channel inhibitors.**

Other drugs and therapeutic strategies could also be useful under certain circumstances. In this regard, serotoninergic or cannabinoid drugs, among others, as well as other strategies such as ketogenic diet or some neuromodulation techniques are available. It is also very important to set up an action plan for seizures, using a specific rescue treatment if necessary, to avoid any apparent triggers. All of these are general guidelines for pharmacological treatment of epilepsy. However, therapeutic decision-making is a complex, individualised process requiring assessment by specialist professionals.

5.2 Approach to developmental disorder and other manifestations

The different aspects of developmental disorder are mainly approached through optimal epilepsy management (for the reasons explained in previous sections) and non-pharmacological strategies. In certain cases, especially with severe attentional, behavioural and sleep disorders, there are also pharmacological approaches that may be beneficial.

Regarding such non-pharmacological strategies, adequate schooling, neuropsychology, logopedics, physiotherapy and occupational therapy are crucial. The final goal of all these actions is reaching maximum functional independence within each patient's possibilities and an overall improved quality of life of both the patient and their family.

Other fundamental support measures, if necessary and depending on each patient's severity, include correct constipation management, a diet adapted to swallowing problems (considering the use of a gastrostomy probe) or respiratory therapy (considering the need of respiratory support).

5.3 Multidisciplinary patient management

Hence comprehensive patient care involves multidisciplinary management by different specialists:

- **Pediatrics and family medicine.**
- **Specialist nursing.**
- **Neurology to manage epilepsy, developmental disorder and other neurological manifestations.**
- **Psychology, logopedics, physiotherapy and occupational therapy.**
- **Gastroenterology to assess and manage dysphagia, gastroesophageal reflux or bowel movement disorder.**
- **Rehabilitation and traumatology.**
- **Cardiology.**
- **Social work to provide administrative and logistic resources as well as other types of support to the patient and their family.**

5.4 Assistance and resources for relatives and caregivers

Both physicians and other specialists need to play an active role in assisting patients' relatives, clarifying doubts, offering psychological support and providing resources helping them in their care. Overload and change in the life of the main caregivers can be a frequent and severe problem, so information and counselling are necessary. As will be seen later, the role of patient associations and family advocacy groups is indispensable in this respect as well as in others.

6. PROGNOSIS AND QUALITY OF LIFE

6.1 Clinical evolution and prognostic factors

Prognosis may vary considerably depending on the clinical presentation, so managing such patients should always be on an individual basis. In most cases, it is not a progressive disease the manifestations of which worsen gradually despite treatment, although there may exist intercurrent complications. However, patients will often require follow-up and medication throughout their life.

On the one hand, regarding seizure control:

- In those patients with severe developmental and epileptic encephalopathy, it may be difficult to reach total control of all seizure types despite using high-dosage drug combinations. Sometimes, the goal should not be no seizures but avoiding as far as possible severe seizures with a higher risk of associated complications, while minimising drug side effects.
- Other forms of clinical presentation may be more effective in responding to adequate anti-seizure medication.

On the other hand, neurodevelopmental disorder involves different degrees of intellectual disability, language disorder, behavioural and motor disorder, the development of which is very heterogeneous, from severe forms manifesting even before seizure onset to mild forms with progressive improvement with adequate therapies.

Optimal control of epilepsy and developmental disorder within each patient's possibilities may contribute to reduce the risk of severe disease complications or death for different causes, such as cardiovascular events or sudden unexpected death in epilepsy (SUDEP), pneumonia or other respiratory complications or accidents. Apart from reducing the risk for complications, as has been mentioned previously, one of the main goals of treatment is reaching the highest possible degree of independence and the highest quality of life for every person.

SUDEP is sudden unexpected death of a person with epilepsy that is not related to direct, clearly identifiable causes, such as a documented cardiovascular event or trauma, among others. SUDEP is related to alterations of the respiratory rhythm and heart rhythm, especially related to highly frequent bilateral tonic-clonic seizures. This is an unusual complication, the risk of which can be significantly reduced by means of optimal control of this type of seizure in each person.

6.2 Quality of life of patients and relatives

One of the main goals of managing patients with SCN8A-related disorders is to ensure that they reach the highest possible quality of life, which requires:

- Individualising treatment, seeking a balance between effectiveness and side effects.
- Ensuring access to supportive therapies (physiotherapy, logopedics, occupational and respiratory therapy, among others).
- Fostering their autonomy within each patient's possibilities.

It is also paramount to provide support to caregivers as well as to inform about available social resources that may help.

7. RESEARCH AND EMERGING THERAPIES

As referred to in previous sections, diseases such as SCN8A-related disorders could feature two treatment options. First, there is the option of treating the cause of the disease, i.e. to correct the initial genetic alteration leading to the chain of events that eventually originate the symptoms. This type of treatment is applied with the aim of modifying the course of the disease or even with curative purposes in the future. In this regard, there is currently no available treatment of this kind to be applied in humans in daily clinical practice, nor are there any human clinical trials under way applying this type of treatment in affected patients.

Nevertheless, there are therapies aimed at modifying the course of the disease in an advanced stage of development in animals, which allows to expect their use in human clinical trials to start in the medium future. There are several research groups working along these therapeutic lines, the main being those of Michael Hammer (University of Arizona, USA), Miriam Meisler (University of Michigan, USA), Madeleine Oudin (Tufts University, Medford, USA) and Manoj Patel (University of Virginia, USA).

On the other hand, there is the option of treating the symptoms of the disease, such as epilepsy and neurodevelopmental disorder, among others. In this area there are both non-pharmacological and pharmacological approaches. Regarding pharmacological approaches, it is necessary to be able to predict if the patient's genetic variant leads to a channel gain or loss of function, as the choice of some treatments depends on this.

Drugs with a more selective profile in blocking certain sodium channels, such as Nav1.2 and Nav1.6, are currently under clinical trial (NCT05818553) in an advanced stage of development for SCN8A and SCN2A gain-of-function-related disorders at different institutes in the United States and Europe, with promising results regarding safety and efficacy.

Also, as regards treatment of disease symptoms (especially in epilepsy), there are broader clinical trials aimed at patients with developmental and epileptic encephalopathy or refractory focal epilepsy from which persons with SCN8A-related disorders could equally benefit. In this regard, it is convenient to ask the patient's referring neurologist about these options.

Finally, and equally important, there are numerous active working lines by different national and international groups related to other aspects of the disease beyond research in new therapeutic lines as a main goal. In this regard, research is conducted about how genetic alterations eventually lead to the manifestations of the disease (etiology and physiopathology, genotype-phenotype correlation), how to predict if a specific genetic variant causes channel gain or loss of function, how are the natural history of the disease up to adult age and its prognosis, or which are the main needs of patients' families and the implications for main caregivers, among other aspects. Detailed understanding of all these magnitudes shall equally contribute to a deeper knowledge of the disease and eventually to therapeutic progress.

8. CARE-RELATED, SOCIAL AND EDUCATIONAL RESOURCES

SCN8A-related disorders are a rare disease, its follow-up and treatment requiring specialisation. There are currently epilepsy units specialising in diagnosis and comprehensive management of this disease type, so it is crucial to refer patients to these institutions to ensure the best possible healthcare.

Available social, economic and educational resources include:

- Recognition of disability and dependency, allowing access to tax benefits, financial aid to adapt homes or hire personal home care as well as subsidies for reduced working time
- Early care, including actions like stimulation, physiotherapy, psychomotricity, logopedics, psychotherapy/psychology, social work and family support, from the first years of life
- Grants for pupils with specific educational support needs as well as methodological adaptations supporting school inclusion and autonomy
- Patients' associations, indispensable for certain functions as shown below

9. SUPPORT ORGANISATIONS AND NETWORKS

Patients' associations are organisations mainly made up of families with relatives affected by the disease, plus scientific and medical staff. These organisations play a crucial role regarding patient and family support and assistance, information and education on the disease, representation of patients before public and private institutions, guidance on resources and services, promoting research in the disease in collaboration with other organisations and acting as touchpoint between patients, families, healthcare professionals and researchers. Patients' associations can altogether have an impact on the development of new therapeutic options, influence health policies and eventually improve the patients' quality of life.

In connection with SCN8A-related disorders, there is the SCN8A España association (www.scn8a.es) in Spain, which includes families from Spain and different Spanish-speaking countries, being highly active in all above-mentioned main points. There are also similar associations in different European countries, including the SCN8A European Federation, The Cute Syndrome Foundation (www.thecutesyndrome.com) from the United States and the International SCN8A Alliance (www.scn8aalliance.org). The latter organisation is leading a global partnership project for patients' organisations seeking jointly disease-modifying treatments for SCN8A-related disorders.

SCN8A-related disorders were first described as a disease in 2012. There are currently established genotype-phenotype correlations, specific descriptions of clinical manifestations, information on natural history and prognosis, specialist management units, specific treatments in trial and disease-modifying treatments in preclinic development. This progress has been possible largely thanks to the work of patients' associations in collaboration with medical and research groups from different regions in the world. The joint work of the SCN8A European Federation and the US associations also originated a worldwide funding programme for SCN8A research groups, the SCN8A grants (www.scn8agrants.org).

Beyond patients' associations specifically for SCN8A-related disorders, there are also multiple epilepsy patients' organisations and associations both at national and international level with similar functions. There is a Spanish federation of these associations called Federación Española de Epilepsia (www.fedeepilepsia.com).

9.2 About SCN8A España

SCN8A España was created in February 2022. It encompasses families from Spain and Latin America.

MISSION:

- Finding families and assisting them from the diagnosis onwards
- Giving visibility to this rare disease and communicating to the families any progress in knowledge and treatment
- Promoting scientific research, putting families, healthcare professionals and researchers in contact
- Staying in touch and working collaboratively with other SCN8A associations at international level

WHAT DOES IT OFFER:

- Support among families: connecting those living the same situation
- Updated information on new pharmacological treatments, modifying therapies and clinical trials
- Guidance for treatment
- Assistance during the first steps: guides, workshops, events, meetings

SCN8A SPAIN

Scan the QR code to enter its website

On the SCN8A España website you will find information on the disease, resources for families and news from the association.

Collaborating organisations

10. REFERENCE

1. SCN8A Research Consortium. A research roadmap for SCN8A-related disorders: addressing knowledge gaps and aligning research priorities across stakeholders. Orphanet J Rare Dis. 2025 Aug 19;20(1):444. doi: 10.1186/s13023-025-03672-w. PMID: 40830973; PMCID: PMC12366098.

2. Magielski JH, Cohen S, Kaufman MC, *et al.* Deciphering the Natural History of SCN8A-Related Disorders. Neurology. 2025 May 13;104(9):e213533. doi: 10.1212/WNL.0000000000213533. Epub 2025 Apr 14. PMID: 40228184; PMCID: PMC11998016.

3. Conecker G, Hecker J, Hammer MF. Patient leadership and partnerships accelerate therapies for SCN8A and other developmental and epileptic encephalopathies. Ther Adv Rare Dis. 2025 Feb 20;6:26330040241252449. doi: 10.1177/26330040241252449.

4. Conecker G, Xia MY, Hecker J, *et al.* Global modified Delphi consensus on diagnosis, phenotypes, and treatment of SCN8A-related epilepsy and/or neurodevelopmental disorders. Epilepsia. 2024 Aug;65(8):2322-2338. doi: 10.1111/epi.17992. Epub 2024 May 27. PMID: 38802994.

5. Conecker G, Xia MY, Hecker J, *et al.* Global modified-Delphi consensus on comorbidities and prognosis of SCN8A-related epilepsy and/or neurodevelopmental disorders. Epilepsia. 2024 Aug;65(8):2308-2321. doi: 10.1111/epi.17991. Epub 2024 May 27. PMID: 38802989.

6. Hammer MF, Xia M, Schreiber JM. SCN8A-Related Epilepsy and/or Neurodevelopmental Disorders. 2016 Aug 25 [updated 2023 Apr 6]. In: GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2026.

7. Johannesen KM, Liu Y, Koko M, *et al.* Genotype-phenotype correlations in SCN8A-related disorders reveal prognostic and therapeutic implications. Brain. 2022 Sep 14;145(9):2991-3009. doi: 10.1093/brain/awab321. PMID: 34431999; PMCID: PMC10147326.

8. Talwar D, Hammer MF. SCN8A Epilepsy, Developmental Encephalopathy, and Related Disorders. Pediatr Neurol. 2021 Sep;122:76-83. doi: 10.1016/j.pediatrneurol.2021.06.011.

9. Gardella E, Møller RS. Phenotypic and genetic spectrum of SCN8A-related disorders, treatment options, and outcomes. Epilepsia. 2019 Dec;60 Suppl 3:S77-S85. doi: 10.1111/epi.16319.

10. Hammer MF, Xia M, Schreiber JM. SCN8A-Related Epilepsy and/or Neurodevelopmental Disorders. 2016 Aug 25. In: GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2026.

11. SCN8A Alliance. Apoyo para hermanos y familias [Internet]. SCN8A Alliance. Disponible en: https://scn8aalliance.org/es/family-sibling-support/.

12. International SCN8A Alliance. SCN8A care [Internet]. SCN8A Alliance; 2024. Disponible en: https://scn8aalliance.org/scn8a-care/.

GUÍA

VIVIR CON EPILEPSIA

www.vivirconepilepsia.com

UCBCares®

¿Tienes alguna duda? Llámanos
800 099 684 (Teléfono gratuito desde España)
+34 915 700 649
UCBCares.ES@ucb.com
https://ucbcares.es/

ES-DA-2600422 Julio 2026