Treatment Consultants

John M. Schreiber, MD

Child Neurologist, Neurophysiologist, and Epileptologist

Director, Epilepsy Genetics
Medical Director, EEG
Children's National Hospital

Associate Professor, Neurology and Pediatrics
The George Washington University
School of Medicine

111 Michigan Ave NW
Dept of Neurology
Washington, DC 20010
Phone: 202-476-2120
Fax: 202-476-2864

Patient & Family Support Group Information

Shelley Frappier

Executive Assistant,
The Cute Syndrome Foundation

Administrator, SCN8A Families Support Group

shelley@thecutesyndrome.com

Support Group Referrals

supportgroup@thecutesyndrome.com

Clinician & Researcher Information

Visit scn8a.net

Disclaimer

The wisdom provided in this clinical reference guide is for informational purposes only. The purpose of this guide is to promote a broad understanding and knowledge of SCN8A in an effort to support clinicians in the care of patients with this rare genetic disorder. It is not intended to be a substitute for published data, clinical practice guidelines, professional medical expertise, diagnosis, or treatment and is useful when corresponding published data are not otherwise available. Always seek the guidance of the contributing physicians with any questions you may have regarding treatment and before beginning a new health care regimen for your patient(s).

Due diligence in research for updates in SCN8A related clinical information is expected before changing treatment course. Never disregard professional medical advice because of something you have read within this reference guide.

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Foundation Information & Partnership Opportunities

Kacie Craig, M.Ed.

Executive Director,
The Cute Syndrome Foundation

executivedirector@thecutesyndrome.com

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The Cute Syndrome© FOUNDATION
www.TheCuteSyndrome.com

Discover clinical wisdom about SCN8A from physicians with experience treating this rare disorder.

Learn more about the resources available for your patients with SCN8A.

SCN8A
Clinician Information & Reference Guide

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John Schreiber, MD
Michael Hammer, PhD
Juliann Bradish, PharmD
Manoj Patel, PhD

thecutesyndrome.com

General Information

SCN8A Mutation Pathology

- Most concentrated in neural tissue but also found in cardiac tissue
- SCN8A variants associated with epilepsy usually produce a gain-of-function in the voltage-gated channel Nav1.6. In contrast, some loss-of-function variants have been observed and more commonly result in intellectual disability ***without*** seizures.

SCN8A Mutation Onset

- Age: mean 4 months (Range: birth to >10 years, N=127) [1]
- Seizure type varies
- EEG findings vary from normal or baseline slowing to infantile spasms with or without hypsarrhythmia
- Symptoms range from mild behavioral or movement disorders to severe developmental and cognitive delays

Symptomatic Treatments

Drugs of Choice

Sodium-channel blockers

- Patients take 2.4 anti-epileptic drugs on average [2]
- Monitor for drug-efficacy ***AND*** toxicity
- SCN8A epilepsy is commonly drug resistant but has shown a positive response to sodium channel blockers, usually at ***supratherapeutic*** doses [3]
- Seizure control may be related to prognosis
- Those with the best success rates at high dose:

Oxcarbazepine	Lacosamide
Carbamazepine	Eslicarbazepine
Lamotrigine	Benzodiazepines
Phenytoin	

Additional Treatments

- Vitamin D and calcium supplementation—use for Osteopenia prevention
- VNS Therapy—Vagus Nerve Stimulation
- Ketogenic Diet

Drugs to avoid

Levetiracetam (Keppra) has been shown to ***increase seizure severity*** or ***has no effect*** in up to 90% of SCN8A patients. Failure rate = 82%*2 (makes seizures worse, or no effect) *N=83.

Comorbities

Consider the following referrals:

- **Gastroenterology**
  G-tube dependency, Constipation
- **Pulmonary**
  Sleep apnea, Laryngomalacia, Pneumonia
- **Orthopedic**
  Scoliosis
- **Ophthalmology**
  Cortical Visual Impairment
- **Cardiology (with experience in channelopathies)**
  Arrhythmias, Bradycardia
- **Physical/Occupational Therapy**
  Hypotonia, Ataxia, Dyskinesias/Movement disorders
- **Speech and Language Pathology**
  Flaccid Dysarthria, Unsafe swallow, Non-verbal
- **Behavior/Neuropsychology**
  Autism Spectrum Disorder, ADHD
- **Endocrinology**
  Osteopenia, Frequent fractures

Most common comorbidities include constipation, hypotonia, movement disorders/ ataxia, high pain tolerance, sleep difficulties, osteopenia and frequent fractures

Monitoring

SUDEP

Genetic epilepsies have a higher risk of Sudden Unexpected/Unexplained Death in Epilepsy (SUDEP). SCN8A specifically may increase the risk of SUDEP possibly due to increased susceptibility of arrhythmias. [4]

- **Consider a seizure monitoring device, pulse oximetry, video/audio monitoring, movement monitors, and antisuffocation pillows in these patients**
- **Seizures may also cause apnea and prominent autonomic symptoms**
- **Counsel parents to use on child during sleep**
- **Encourage parents/caregivers to receive CPR certification**

The presence of either sleep apnea or a bradycardia diagnosis (or both) will aid in insurance approval

Genetic Testing

- Consider testing for genetic epilepsy (namely SCN8A) in any patients who have shown an adverse response to levetiracetam, refractory seizures without a known cause, and/or early seizure onset
- Consider SCN8A testing for biological parents to determine if a variant is inherited or de novo
- Refer for genetic counseling if the diagnosis is uncertain or for variants of unknown significance

Patients with SCN8A mutations should *NOT* be treated like those with SCN1A mutation or Dravet Syndrome

Genetic Counseling

Most useful when the diagnosis is uncertain, for variants of unknown significance, and for questions regarding family planning, particularly if a variant is found to be inherited.

References

1. SCN8A Families Support Group. Survey of SCN8A parents. SCN8A Registry data. <www.scn8a.net>

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3. Møller RS, Johannesen KM. Precision Medicine: SCN8A Encephalopathy Treated with Sodium Channel Blockers. Neurotherapeutics. 2016;13(1):190-191. doi:10.1007/s13311-015-0403-5

4. American Epilepsy Society. "Unraveling the Genetic Basis of Sudden Unexpected Death in Epilepsy." https://www.aesnet.org/about_aes/press_releases/unravelinggeneticbasissudep