SCN8A-related epilepsy with encephalopathy

Description

SCN8A-related epilepsy with encephalopathy is a condition characterized by recurrent seizures (epilepsy), abnormal brain function (encephalopathy), and intellectual disability. The signs and symptoms of this condition typically begin in infancy.

The seizures in *SCN8A*-related epilepsy with encephalopathy include involuntary muscle contractions that occur before age 1 (infantile spasms), partial or complete loss of consciousness (absence seizures), involuntary muscle twitches (myoclonic seizures), or loss of consciousness with muscle rigidity and convulsions (tonic-clonic seizures). Most people with *SCN8A*-related epilepsy with encephalopathy have more than one type of seizure. The frequency of seizures in different individuals with this condition ranges from hundreds per day to fewer than one per month. In many individuals, the seizures are described as refractory because they do not respond to therapy with anti-epileptic medications.

Other signs and symptoms of *SCN8A*-related epilepsy with encephalopathy include intellectual disability that may be mild to severe. Some affected infants have normal early development but begin to lose previously acquired skills (developmental regression) and have a gradual loss in thinking ability (cognitive decline) when epilepsy develops. Problems with movement are common, and about half of affected infants cannot perform intentional movements. Behavior disorders may also occur.

In rare cases, individuals with this condition die unexpectedly for no known reason (sudden unexpected death in epilepsy or SUDEP).

Frequency

There are at least 140 individuals with *SCN8A*-related epilepsy with encephalopathy. This condition is estimated to account for 1 percent of all cases of epilepsy with encephalopathy.

Causes

As its name suggests, *SCN8A*-related epilepsy with encephalopathy is caused by mutations in the *SCN8A* gene. This gene provides instructions for making one part (the alpha subunit) of a sodium channel called $Na_v1.6$. This channel allows positively charged sodium (Na) atoms (sodium ions) to pass into nerve cells (neurons) and plays

a key role in the ability of neurons to communicate by generating and transmitting electrical signals.

SCN8A gene mutations result in altered $Na_v1.6$ channels that stay open longer than usual, which increases the flow of sodium ions into neurons. The persistently open channels abnormally increase electrical signals, which can lead to excess activation (excitation) of neurons in the brain. The increased neuronal activity leads to seizures in people with *SCN8A*-related epilepsy with encephalopathy.

It is unknown how *SCN8A* gene mutations lead to intellectual disability, movement problems, and the other features of *SCN8A*-related epilepsy with encephalopathy. Because some affected children experience developmental regression after the onset of seizures, it has been suggested that the seizures may impair brain function, but it is unclear if that is the case.

Learn more about the gene associated with SCN8A-related epilepsy with encephalopathy

- SCN8A

Inheritance

This condition follows an autosomal dominant pattern of inheritance, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Most cases of this condition result from new (de novo) mutations in the gene that occur during the formation of reproductive cells (eggs or sperm) or in early embryonic development. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- Early infantile epileptic encephalopathy 13
- EIEE13
- SCN8A encephalopathy

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Developmental and epileptic encephalopathy, 13 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3281191/)

Genetic and Rare Diseases Information Center

- Developmental and epileptic encephalopathy 13 (https://rarediseases.info.nih.gov/di

seases/13085/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22SCN8A-related epilepsy with encephalopathy%22)

Catalog of Genes and Diseases from OMIM

- DEVELOPMENTAL AND EPILEPTIC ENCEPHALOPATHY 13; DEE13 (https://omim.org/entry/614558)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28SCN8A-related+epilepsy+with+encephalopathy%5BTIAB%5D%29+OR+%28SCN8A+encephalopathy%5BTIAB%5D%29+OR+%28early+infantile+epileptic+encephalopathy+13%5BTIAB%5D%29+OR+%28SCN8A%5BTI%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

References

- Butler KM, da Silva C, Shafir Y, Weisfeld-Adams JD, Alexander JJ, Hegde M, Escayg A. De novo and inherited SCN8A epilepsy mutations detected by gene panelanalysis. Epilepsy Res. 2017 Jan;129:17-25. doi:10.1016/j.eplepsyres.2016.11.002. Epub 2016 Nov 6. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/27875746) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5321682/)
- Hammer MF, Xia M, Schreiber JM. SCN8A-Related Epilepsy and/ orNeurodevelopmental Disorders. 2016 Aug 25 [updated 2023 Apr 6]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors.GeneReviews(R) [Internet]. Seattle (WA): University of Washington,Seattle; 1993-2025. Available from http://www.ncbi.nlm.nih.gov/books/NBK379665/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/27559564)
- Larsen J, Carvill GL, Gardella E, Kluger G, Schmiedel G, Barisic N, DepienneC, Brilstra E, Mang Y, Nielsen JE, Kirkpatrick M, Goudie D, Goldman R, Jahn JA, Jepsen B, Gill D, Docker M, Biskup S, McMahon JM, Koeleman B, Harris M, Braun K,de Kovel CG, Marini C, Specchio N, Djemie T, Weckhuysen S, Tommerup N, TroncosoM, Troncoso L, Bevot A, Wolff M, Hjalgrim H, Guerrini R, Scheffer IE,

Mefford HC,Moller RS; EuroEPINOMICS RES Consortium CRP. The phenotypic spectrum of SCN8Aencephalopathy. Neurology. 2015 Feb 3;84(5):480-9. doi:10.1212/WNL.0000000000001211. Epub 2015 Jan 7. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25568300) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4336074/)

- Meisler MH, Helman G, Hammer MF, Fureman BE, Gaillard WD, Goldin AL, Hirose S,Ishii A, Kroner BL, Lossin C, Mefford HC, Parent JM, Patel M, Schreiber J,Stewart R, Whittemore V, Wilcox K, Wagnon JL, Pearl PL, Vanderver A, Scheffer IE.SCN8A encephalopathy: Research progress and prospects. Epilepsia. 2016Jul;57(7):1027-35. doi: 10.1111/epi.13422. Epub 2016 Jun 8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/27270488) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5495462/)
- Wagnon JL, Barker BS, Hounshell JA, Haaxma CA, Shealy A, Moss T, Parikh S, Messer RD, Patel MK, Meisler MH. Pathogenic mechanism of recurrent mutations ofSCN8A in epileptic encephalopathy. Ann Clin Transl Neurol. 2015 Dec21;3(2):114-23. doi: 10.1002/acn3.276. eCollection 2016 Feb. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26900580) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4748308/)

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