CHD2 myoclonic encephalopathy

CHD2 myoclonic encephalopathy is a condition characterized by recurrent seizures (epilepsy), abnormal brain function (encephalopathy), and intellectual disability. Epilepsy begins in childhood, typically between ages 6 months and 4 years. Each individual may experience a variety of seizure types. The most common are myoclonic seizures, which involve involuntary muscle twitches. Other seizure types include sudden episodes of weak muscle tone (atonic seizures); partial or complete loss of consciousness (absence seizures); seizures brought on by high body temperature (febrile seizure); or tonic-clonic seizures, which involve loss of consciousness, muscle rigidity, and convulsions. Some people with *CHD2* myoclonic encephalopathy have photosensitive epilepsy, in which seizures are triggered by flashing lights. Some people with *CHD2* myoclonic encephalopathy experience a type of seizure called atonic-myoclonic-absence seizure, which begins with a drop of the head, followed by loss of consciousness, then rigid movements of the arms. Epilepsy can worsen, causing prolonged episodes of seizure activity that last several minutes, known as status epilepticus. The seizures associated with *CHD2* myoclonic encephalopathy are called refractory because they usually do not respond to therapy with anti-epileptic medications.

Other signs and symptoms of *CHD2* myoclonic encephalopathy include intellectual disability that ranges from mild to severe and delayed development of speech. Rarely, individuals can have a loss of acquired skills (developmental regression) following the onset of epilepsy. Some people with *CHD2* myoclonic encephalopathy have autism spectrum disorders, which are conditions characterized by impaired communication and social interaction. In some instances, areas with a loss of brain tissue (atrophy) have been found with medical imaging.

Frequency

The prevalence of *CHD2* myoclonic encephalopathy is unknown; at least 32 cases have been described in the scientific literature.

Causes

As its name suggests, *CHD2* myoclonic encephalopathy is caused by mutations in the *CHD2* gene. This gene provides instructions for making a protein called chromodomain DNA helicase protein 2. This protein is found in cells throughout the body and regulates gene activity (expression) through a process known as chromatin remodeling. Chromatin is the complex of DNA and proteins that packages DNA into chromosomes. The structure of chromatin can be changed (remodeled) to alter how tightly DNA is packaged. The role of chromodomain DNA helicase protein 2 in the brain is unknown.

Researchers suspect that the protein may be involved in regulating the development and functioning of nerve cells.

CHD2 gene mutations either prevent the production of any chromodomain DNA helicase protein 2 or lead to the production of a nonfunctional version of the protein. As a result, chromatin remodeling and gene expression normally regulated by chromodomain DNA helicase protein 2 are disrupted. It is unclear why *CHD2* gene mutations seem to only affect nerve cells in the brain or how they lead to the signs and symptoms of *CHD2* myoclonic encephalopathy.

Inheritance Pattern

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

This condition results 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

- CHD2 encephalopathy
- CHD2-related neurodevelopmental disorders

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Epileptic encephalopathy, childhood-onset
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3809278/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22CHD2+myoclonic+encephalopathy%22+OR+%22Epilepsies%2C+Myoclonic%22

Other Diagnosis and Management Resources

- GeneReview: CHD2-Related Neurodevelopmental Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK333201

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Epilepsy
  https://medlineplus.gov/epilepsy.html
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Encephalopathy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Encephalopathy-Information-Page
- National Institute of Neurological Disorders and Stroke: Epilepsy Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Epilepsy-Information-Page

Educational Resources

- Boston Children's Hospital: Pediatric Epilepsy and Seizure Disorder in Children
  https://www.childrenshospital.org/Conditions-and-Treatments/Conditions/E/Epilepsy
- Centers for Disease Control and Prevention: Epilepsy
  https://www.cdc.gov/epilepsy/index.html
- Centers for Disease Control and Prevention: Facts About Developmental Disabilities
  https://www.cdc.gov/ncbddd/developmentaldisabilities/facts.html
- MalaCards: chd2-related neurodevelopmental disorders
  https://www.malacards.org/card/chd2_related_neurodevelopmental_disorders

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities (AAIDD)
  https://www.aaidd.org/
- American Epilepsy Society
  https://www.aesnet.org/
- CURE: Citizens United for Research in Epilepsy
  https://www.cureepilepsy.org/

Clinical Information from GeneReviews

- CHD2-Related Neurodevelopmental Disorders
  https://www.ncbi.nlm.nih.gov/books/NBK333201

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CHD2%5BTIAB%5D%29+AND+%28epilepsy%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

Catalog of Genes and Diseases from OMIM

- EPILEPTIC ENCEPHALOPATHY, CHILDHOOD-ONSET
  http://omim.org/entry/615369

Sources for This Summary

- Lund C, Brodtkorb E, Øye AM, Røsby O, Selmer KK. CHD2 mutations in Lennox-Gastaut syndrome. Epilepsy Behav. 2014 Apr;33:18-21. doi: 10.1016/j.yebeh.2014.02.005. Epub 2014 Mar 12.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24614520
- Suls A, Jaehn JA, Kecskés A, Weber Y, Weckhuysen S, Craiu DC, Siekierska A, Djémié T, Afrikanova T, Gormley P, von Spiczak S, Kluger G, Iliescu CM, Talvik T, Talvik I, Meral C, Caglayan HS, Giraldez BG, Serratosa J, Lemke JR, Hoffman-Zacharska D, Szczepanik E, Barisic N, Komarek V, Hjalgrim H, Møller RS, Linnankivi T, Dimova P, Striano P, Zara F, Marini C, Guerrini R, Depienne C, Baulac S, Kuhlenbäumer G, Crawford AD, Lehesjoki AE, de Witte PA, Palotie A, Lerche H, Esguerra CV, De Jonghe P, Helbig I; EuroEPINOMICS RES Consortium. De novo loss-of-function mutations in CHD2 cause a fever-sensitive myoclonic epileptic encephalopathy sharing features with Dravet syndrome. Am J Hum Genet. 2013 Nov 7;93(5):967-75. doi: 10.1016/j.ajhg.2013.09.017. Epub 2013 Oct 24.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24207121
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3824114/
- Thomas RH, Zhang LM, Carvill GL, Archer JS, Heavin SB, Mandelstam SA, Craiu D, Berkovic SF, Gill DS, Mefford HC, Scheffer IE; EuroEPINOMICS RES Consortium. CHD2 myoclonic encephalopathy is frequently associated with self-induced seizures. Neurology. 2015 Mar 3;84(9):951-8. doi: 10.1212/WNL.0000000000001305. Epub 2015 Feb 11.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25672921
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4351660/
- Trivisano M, Striano P, Sartorelli J, Giordano L, Traverso M, Accorsi P, Cappelletti S, Claps DJ, Vigevano F, Zara F, Specchio N. CHD2 mutations are a rare cause of generalized epilepsy with myoclonic-atonic seizures. Epilepsy Behav. 2015 Oct;51:53-6. doi: 10.1016/j.yebeh.2015.06.029. Epub 2015 Aug 7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26262932

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/condition/chd2-myoclonic-encephalopathy

Reviewed: December 2016
Published: November 12, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services