Lennox-Gastaut syndrome

Description

Lennox-Gastaut syndrome is a severe condition characterized by repeated seizures (epilepsy) that begin early in life. Affected individuals have multiple types of seizures, developmental delays, and particular patterns of brain activity measured by a test called an electroencephalogram (EEG). An EEG shows a slow spike-and-wave pattern during wakefulness and generalized paroxysmal fast activity during sleep.

In people with Lennox-Gastaut syndrome, epilepsy begins in early childhood, usually between ages 3 and 5. The most common seizure type is tonic seizures, which cause the muscles to stiffen (contract) uncontrollably. These seizures typically occur during sleep; they may also occur during wakefulness. Also common are atonic seizures, which are caused by a sudden loss of muscle tone. Tonic and atonic seizures can cause sudden falls that can result in serious or life-threatening injuries. Additionally, many affected individuals have atypical absence seizures, which cause a very brief partial or complete loss of consciousness. Other types of seizures have been reported less frequently in people with Lennox-Gastaut syndrome. Seizures associated with Lennox-Gastaut syndrome often do not respond well to therapy with anti-epileptic medications.

Although each seizure episode associated with Lennox-Gastaut syndrome is usually brief, more than two-thirds of affected individuals experience prolonged periods of seizure activity (known as status epilepticus) or episodes of many seizures that occur in a cluster.

About one-third of people with Lennox-Gastaut syndrome have normal intellectual development before seizures begin. The remainder have intellectual disability or learning problems even before seizures arise. Intellectual problems may worsen over time, particularly if seizures are very frequent or severe. Some affected children develop additional neurological abnormalities and behavioral problems. Many are also slow to develop motor skills such as sitting and crawling. As a result of their seizures and intellectual disability, most people with Lennox-Gastaut syndrome require help with daily activities. However, a small percentage of affected adults can live independently.

People with Lennox-Gastaut syndrome have a higher risk of death than their peers of the same age. Although the increased risk is not fully understood, it is partly due to poorly controlled seizures, pneumonia resulting from inhaling saliva (aspiration pneumonia) during a seizure, and injuries from falls. In addition, individuals with Lennox-

Gastaut syndrome are at risk of sudden unexpected death in epilepsy (SUDEP), which describes sudden death with no known cause in someone with epilepsy; it is not the direct result of a seizure.

Frequency

Lennox-Gastaut syndrome affects an estimated 1 to 2 per million people worldwide. This condition accounts for 3 to 4 percent of cases of epilepsy in children and 1 to 2 percent of cases in adults. For unknown reasons, it appears to be more common in males than in females.

Causes

Lennox-Gastaut syndrome can have many different causes. The disorder likely has a genetic component, although the specific genetic factors are not well understood.

Most cases of Lennox-Gastaut syndrome develop from an existing neurological abnormality. These cases maybe be caused by brain injuries that occur before or during birth, problems with blood flow in the developing brain, brain infections, or other disorders affecting the nervous system. The condition can also arise from brain malformations such as forms of cortical dysplasia, which are abnormalities in the outer surface of the brain (cerebral cortex). Many people with Lennox-Gastaut syndrome have a history of epilepsy beginning in infancy (infantile spasms) or a related condition called West syndrome before developing the features of Lennox-Gastaut syndrome. It is not clear why these neurological abnormalities evolve into Lennox-Gastaut syndrome.

In addition, variants (also called mutations) in several genes have been associated with Lennox-Gastaut syndrome, each in a small number of affected individuals. These genes are involved in the function of nerve cells in the brain, but it is unclear how changes in them contribute to the development of Lennox-Gastaut syndrome. The condition can also occur as part of a genetic disorder, such as tuberous sclerosis complex.

Learn more about the genes associated with Lennox-Gastaut syndrome

- CHD2
- FOXG1
- SCN1A
- SCN8A
- STXBP1

Additional Information from NCBI Gene:

- ALG13
- DNM1
- GABRB3

Inheritance

Most cases of Lennox-Gastaut syndrome are sporadic, which means they occur in people with no history of the disorder in their family. When Lennox-Gastaut syndrome is associated with a genetic change, the variant is usually not inherited but occurs as a random (de novo) event during the formation of reproductive cells (eggs or sperm) in an affected person's parent or during early embryonic development. However, 3 to 30 percent of people with this condition have a family history of some type of epilepsy, indicating that inherited genetic factors may play a role in some cases of Lennox-Gastaut syndrome.

Other Names for This Condition

- LGS

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Macrocephaly and epileptic encephalopathy (https://www.ncbi.nlm.nih.gov/gtr/conditions/C3807541/)

Genetic and Rare Diseases Information Center

- Lennox-Gastaut syndrome (https://rarediseases.info.nih.gov/diseases/9912/lennox-gastaut-syndrome)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Lennox-Gastaut syndrome%22)

Catalog of Genes and Diseases from OMIM

- MACROCEPHALY AND EPILEPTIC ENCEPHALOPATHY (https://omim.org/entry/606369)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Epilepsy%5BMAJR%5D%29

+AND+%28lennox-gastaut+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

References

- Arzimanoglou A, French J, Blume WT, Cross JH, Ernst JP, Feucht M, Genton P, Guerrini R, Kluger G, Pellock JM, Perucca E, Wheless JW. Lennox-Gastaut syndrome:a consensus approach on diagnosis, assessment, management, and trial methodology.Lancet Neurol. 2009 Jan;8(1):82-93. doi: 10.1016/S1474-4422(08)70292-8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19081517)
- Autry AR, Trevathan E, Van Naarden Braun K, Yeargin-Allsopp M. Increased riskof death among children with Lennox-Gastaut syndrome and infantile spasms. JChild Neurol. 2010 Apr;25(4):441-7. doi: 10.1177/0883073809348355. Epub 2009 Dec18. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20023065)
- Berg AT, Gaebler-Spira D, Wilkening G, Zelko F, Knupp K, Dixon-Salazar T,Villas N, Meskis MA, Harwell V, Thompson T, Sims S, Nesbitt G. Nonseizureconsequences of Dravet syndrome, KCNQ2-DEE, KCNB1-DEE, Lennox-Gastaut syndrome,ESES: A functional framework. Epilepsy Behav. 2020 Oct;111:107287. doi:10.1016/j.yebeh.2020.107287. Epub 2020 Aug 3. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/32759067)
- Berg AT, Kaiser K, Dixon-Salazar T, Elliot A, McNamara N, Meskis MA, GolbeckE, Tatachar P, Laux L, Raia C, Stanley J, Luna A, Rozek C. Seizure burden insevere early-life epilepsy: Perspectives from parents. Epilepsia Open. 2019 Apr14;4(2):293-301. doi: 10.1002/epi4.12319. eCollection 2019 Jun. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/31168496)
- Berg AT, Levy SR, Testa FM. Evolution and course of early life developmentalencephalopathic epilepsies: Focus on Lennox-Gastaut syndrome. Epilepsia. 2018Nov;59(11):2096-2105. doi: 10.1111/epi.14569. Epub 2018 Sep 26. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/30255934)
- Bourgeois BF, Douglass LM, Sankar R. Lennox-Gastaut syndrome: a consensusapproach to differential diagnosis. Epilepsia. 2014 Sep;55 Suppl 4:4-9. doi:10.1111/epi.12567. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/25284032)
- Camfield PR. Definition and natural history of Lennox-Gastaut syndrome.Epilepsia. 2011 Aug;52 Suppl 5:3-9. doi: 10.1111/j.1528-1167.2011.03177.x. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21790560)
- Cross JH, Auvin S, Falip M, Striano P, Arzimanoglou A. Expert Opinion on theManagement of Lennox-Gastaut Syndrome: Treatment Algorithms and PracticalConsiderations. Front Neurol. 2017 Sep 29;8:505. doi: 10.3389/fneur.2017.00505.eCollection 2017. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/29085326) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5649136/)
- Epi4K Consortium; Epilepsy Phenome/Genome Project; Allen AS, Berkovic SF, Cossette P, Delanty N, Dlugos D, Eichler EE, Epstein MP, Glauser T, Goldstein DB,

Han Y, Heinzen EL, Hitomi Y, Howell KB, Johnson MR, Kuzniecky R, Lowenstein DH, Lu YF, Madou MR, Marson AG, Mefford HC, Esmaeeli Nieh S, O'Brien TJ, Ottman R,Petrovski S, Poduri A, Ruzzo EK, Scheffer IE, Sherr EH, Yuskaitis CJ, Abou-KhalilB, Alldredge BK, Bautista JF, Berkovic SF, Boro A, Cascino GD, Consalvo D,Crumrine P, Devinsky O, Dlugos D, Epstein MP, Fiol M, Fountain NB, French J,Friedman D, Geller EB, Glauser T, Glynn S, Haut SR, Hayward J, Helmers SL, JoshiS, Kanner A, Kirsch HE, Knowlton RC, Kossoff EH, Kuperman R, Kuzniecky R,Lowenstein DH, McGuire SM, Motika PV, Novotny EJ, Ottman R, Paolicchi JM, ParentJM, Park K, Poduri A, Scheffer IE, Shellhaas RA, Sherr EH, Shih JJ, Singh R,Sirven J, Smith MC, Sullivan J, Lin Thio L, Venkat A, Vining EP, Von Allmen GK,Weisenberg JL, Widdess-Walsh P, Winawer MR. De novo mutations in epilepticencephalopathies. Nature. 2013 Sep 12;501(7466):217-21. doi: 10.1038/nature12439.Epub 2013 Aug 11. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23934111) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3773011/)

- EuroEPINOMICS-RES Consortium; Epilepsy Phenome/Genome Project; Epi4KConsortium. De novo mutations in synaptic transmission genes including DNM1 causeepileptic encephalopathies. Am J Hum Genet. 2014 Oct 2;95(4):360-70. doi:10.1016/j.ajhg.2014.08.013. Epub 2014 Sep 25. Erratum In: Am J Hum Genet. 2017Jan 5;100(1):179. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25262651) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4185114/)
- Goldsmith IL, Zupanc ML, Buchhalter JR. Long-term seizure outcome in 74patients with Lennox-Gastaut syndrome: effects of incorporating MRI head imagingin defining the cryptogenic subgroup. Epilepsia. 2000 Apr;41(4):395-9. doi:10.1111/j.1528-1157.2000.tb00179.x. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/10756403)
- Hancock EC, Cross HH. Treatment of Lennox-Gastaut syndrome. Cochrane DatabaseSyst Rev. 2009 Jul 8;(3):CD003277. doi: 10.1002/14651858.CD003277.pub2. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19588340)
- Hancock EC, Cross JH. Treatment of Lennox-Gastaut syndrome. Cochrane DatabaseSyst Rev. 2013 Feb 28;2013(2):CD003277. doi: 10.1002/14651858.CD003277.pub3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23450537) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7144815/)
- Lund C, Brodtkorb E, Oye AM, Rosby O, Selmer KK. CHD2 mutations inLennox-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://pubmed.ncbi.nlm.nih.gov/24614520)
- McTague A, Howell KB, Cross JH, Kurian MA, Scheffer IE. The genetic landscapeof the epileptic encephalopathies of infancy and childhood. Lancet Neurol. 2016Mar;15(3):304-16. doi: 10.1016/S1474-4422(15)00250-1. Epub 2015 Nov 17. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26597089)
- Nakashima M, Kouga T, Lourenco CM, Shiina M, Goto T, Tsurusaki Y, Miyatake S, Miyake N, Saitsu H, Ogata K, Osaka H, Matsumoto N. De novo DNM1 mutations in

twocases of epileptic encephalopathy. Epilepsia. 2016 Jan;57(1):e18-23. doi:10.1111/epi.13257. Epub 2015 Nov 27. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26611353)

- Nelson JA, Demarest S, Thomas J, Juarez-Colunga E, Knupp KG. Evolution ofInfantile Spasms to Lennox-Gastaut Syndrome: What Is There to Know? J ChildNeurol. 2021 Aug;36(9):752-759. doi: 10.1177/08830738211000514. Epub 2021 Mar 25. Citation on PubMed (https://www.ncbi.nlm.nih.gov/pubmed/33764203)
- Ostendorf AP, Ng YT. Treatment-resistant Lennox-Gastaut syndrome: therapeutictrends, challenges and future directions. Neuropsychiatr Dis Treat. 2017 Apr20;13:1131-1140. doi: 10.2147/NDT.S115996. eCollection 2017. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/28461749) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5404809/)
- Selmer KK, Lund C, Brandal K, Undlien DE, Brodtkorb E. SCN1A mutationscreening in adult patients with Lennox-Gastaut syndrome features. EpilepsyBehav. 2009 Nov;16(3):555-7. doi: 10.1016/j.yebeh.2009.08.021. Epub 2009 Sep 24. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19782004)
- Terrone G, Bienvenu T, Germanaud D, Barthez-Carpentier MA, Diebold B, DelanoeC, Passemard S, Auvin S. A case of Lennox-Gastaut syndrome in a patient withFOXG1-related disorder. Epilepsia. 2014 Nov;55(11):e116-9. doi:10.1111/epi.12800. Epub 2014 Sep 29. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25266269)
- Trevathan E. Infantile spasms and Lennox-Gastaut syndrome. J Child Neurol.2002 Feb;17 Suppl 2:2S9-2S22. doi: 10.1177/08830738020170021201. Erratum In: JChild Neurol. 2003 May;18(5):374. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11952036)
- Zhou P, He N, Zhang JW, Lin ZJ, Wang J, Yan LM, Meng H, Tang B, Li BM, Liu XR, Shi YW, Zhai QX, Yi YH, Liao WP. Novel mutations and phenotypes ofepilepsy-associated genes in epileptic encephalopathies. Genes Brain Behav. 2018Nov;17(8):e12456. doi: 10.1111/gbb.12456. Epub 2018 Jan 26. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/29314583)

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