CLN3 disease

Description

CLN3 disease is an inherited disorder that primarily affects the nervous system. After 4 to 6 years of normal development, children with this condition develop vision impairment, intellectual disability, movement problems, speech difficulties, and seizures, which worsen over time.

In children with CLN3 disease, problems with vision often begin between the ages of 4 and 8 years. Vision impairment is caused by a breakdown of the light-sensitive tissue at the back of the eye (retinal degeneration), which worsens with age. People with CLN3 disease are often blind by late childhood or adolescence. Also around age 4 to 8, children with CLN3 disease start to fall behind in school. They have difficulty learning new information and lose previously acquired skills (developmental regression), usually beginning with loss of the ability to speak in complete sentences.

Seizures and movement abnormalities often develop in adolescence in people with CLN3 disease. These abnormalities include muscle rigidity or stiffness, clumsiness, slow or diminished movements (hypokinesia), and a stooped posture. Over time, affected individuals lose the ability to walk or sit independently and require wheelchair assistance. Rarely, people with CLN3 disease develop a distorted view of reality (psychosis) or false perceptions (hallucinations). Some affected individuals have an abnormal heart rhythm (arrhythmia) later in life. Most people with CLN3 disease live into early adulthood.

CLN3 disease is one of a group of disorders known as neuronal ceroid lipofuscinoses (NCLs), which may also be collectively referred to as Batten disease. All these disorders affect the nervous system and typically cause worsening problems with vision, movement, and thinking ability. The different NCLs are distinguished by their genetic cause. Each disease type is given the designation "CLN," meaning ceroid lipofuscinosis, neuronal, and then a number to indicate its subtype.

Frequency

CLN3 disease is the most common type of NCL, but its exact prevalence is unknown; more than 400 cases have been described in the scientific literature. Collectively, all forms of NCL affect an estimated 1 in 100,000 individuals worldwide.

Causes

CLN3 disease is caused by mutations in the *CLN3* gene, which provides instructions for making a protein that is found in tissues throughout the body. The CLN3 protein is part of many compartments within cells, including lysosomes, which are cellular compartments that digest and recycle different types of molecules. However, the exact function of the CLN3 protein is unclear. Research has shown that this protein is involved in many cellular processes, but it is uncertain which of them is the primary role of the protein, or if these processes instead represent downstream effects.

It is unclear how mutations in the *CLN3* gene lead to the characteristic features of CLN3 disease. One *CLN3* gene mutation, found in the vast majority of cases, leads to the production of an abnormally short protein. As a result, the abnormal CLN3 protein is broken down or may interfere with normal cellular processes. Other mutations reduce the amount of normal protein or impair its function. It is not known how loss of this protein causes the signs and symptoms of CLN3 disease.

CLN3 disease, like other NCLs, is characterized by the accumulation of proteins and other substances in lysosomes. These accumulations occur in cells throughout the body; however, nerve cells seem to be particularly vulnerable to their effects. The accumulations can cause cell damage leading to cell death. The progressive death of nerve cells in the brain and other tissues leads to the neurological signs and symptoms of CLN3 disease. However, it is unclear how mutations in the *CLN3* gene are involved in the buildup of substances in lysosomes.

Learn more about the gene associated with CLN3 disease

- CLN3

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- Batten-Mayou disease
- Batten-Spielmeyer-Vogt disease
- CLN3-related neuronal ceroid-lipofuscinosis
- Juvenile Batten disease
- Juvenile cerebroretinal degeneration
- Juvenile neuronal ceroid lipofuscinosis
- Spielmeyer-Vogt disease

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Neuronal ceroid lipofuscinosis 3 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0751383/)

Genetic and Rare Diseases Information Center

- CLN3 disease (https://rarediseases.info.nih.gov/diseases/5897/index)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22CLN3 disease%22)

Catalog of Genes and Diseases from OMIM

- CEROID LIPOFUSCINOSIS, NEURONAL, 3; CLN3 (https://omim.org/entry/204200)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Neuronal+Ceroid-Lipofuscinosis%5BMAJR%5D%29+AND+%28%28batten+disease%5BTIAB%5D%29+OR+%28juvenile+NCL%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

References

- Cotman SL, Staropoli JF. The juvenile Batten disease protein, CLN3, and itsrole in regulating anterograde and retrograde post-Golgi trafficking. ClinLipidol. 2012 Feb;7(1):79-91. doi: 10.2217/clp.11.70. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22545070) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3334816/)
- Kollmann K, Uusi-Rauva K, Scifo E, Tyynela J, Jalanko A, Braulke T. Cellbiology and function of neuronal ceroid lipofuscinosis-related proteins. BiochimBiophys Acta. 2013 Nov;1832(11):1866-81. doi: 10.1016/j.bbadis.2013.01.019. Epub2013 Feb 9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23402926)
- Licchetta L, Bisulli F, Fietz M, Valentino ML, Morbin M, Mostacci B, OliverKL,

Berkovic SF, Tinuper P. A novel mutation af Cln3 associated withdelayed-classic juvenile ceroid lipofuscinois and autophagic vacuolar myopathy.Eur J Med Genet. 2015 Oct; 58(10):540-4. doi: 10.1016/j.ejmg.2015.09.002. Epub2015 Sep 7. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/26360874)

- Mirza M, Vainshtein A, DiRonza A, Chandrachud U, Haslett LJ, Palmieri M,Storch S, Groh J, Dobzinski N, Napolitano G, Schmidtke C, Kerkovich DM. The CLN3gene and protein: What we know. Mol Genet Genomic Med. 2019 Dec;7(12):e859. doi:10.1002/mgg3.859. Epub 2019 Sep 30. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/31568712) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6900386/)
- Oetjen S, Kuhl D, Hermey G. Revisiting the neuronal localization andtrafficking of CLN3 in juvenile neuronal ceroid lipofuscinosis. J Neurochem. 2016Nov;139(3):456-470. doi: 10.1111/jnc.13744. Epub 2016 Sep 9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/27453211)
- Perez-Poyato MS, Mila Recansens M, Ferrer Abizanda I, Montero Sanchez R, Rodriguez-Revenga L, Cusi Sanchez V, Garcia Gonzalez MM, Domingo Jimenez R, Camino Leon R, Velazquez Fragua R, Martinez-Bermejo A, Pineda Marfa M. Juvenileneuronal ceroid lipofuscinosis: clinical course and genetic studies in Spanishpatients. J Inherit Metab Dis. 2011 Oct;34(5):1083-93. doi:10.1007/s10545-011-9323-7. Epub 2011 Apr 16. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21499717)
- Rakheja D, Narayan SB, Bennett MJ. Juvenile neuronal ceroid-lipofuscinosis(Batten disease): a brief review and update. Curr Mol Med. 2007 Sep;7(6):603-8.doi: 10.2174/156652407781695729. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17896996)
- Schulz A, Kohlschutter A, Mink J, Simonati A, Williams R. NCL diseases -clinical perspectives. Biochim Biophys Acta. 2013 Nov;1832(11):1801-6. doi:10.1016/j.bbadis.2013.04.008. Epub 2013 Apr 17. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23602993) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4631127/)
- Williams RE, Mole SE. New nomenclature and classification scheme for theneuronal ceroid lipofuscinoses. Neurology. 2012 Jul 10;79(2):183-91. doi:10.1212/WNL.0b013e31825f0547. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22778232)

Last updated February 16, 2021