GRIN2B-related neurodevelopmental disorder

GRIN2B-related neurodevelopmental disorder is a condition that affects the nervous system. Neurodevelopmental disorders result from impaired growth and development of the central nervous system, which includes the brain and spinal cord, and the nerves connecting them. These disorders often affect learning ability, memory, and behavior and can be associated with other neurological problems.

Individuals with *GRIN2B*-related neurodevelopmental disorder have mild to profound intellectual disability and delayed development of speech and motor skills, such as sitting and walking. Some affected individuals never develop speech or the ability to walk on their own. Many people with this condition have weak muscle tone (hypotonia), which can contribute to the problems developing motor skills and lead to difficulty eating. Some affected individuals have abnormal muscle stiffness (spasticity), which can also cause problems with movement.

Recurrent seizures (epilepsy) occur in about half of people with *GRIN2B*-related neurodevelopmental disorder. About one-quarter of affected individuals have features of autism spectrum disorder, which is characterized by impaired communication and social interaction. Other behavioral problems are also possible. These individuals may be hyperactive, impulsive, or easily distractible, and some are described as being overly friendly. Sleeping difficulties can also occur in this condition.

Less common features of *GRIN2B*-related neurodevelopmental disorder include structural brain abnormalities, an unusually small head size (microcephaly), impaired vision, and involuntary muscle movements.

Frequency

The prevalence of *GRIN2B*-related neurodevelopmental disorder is unknown. Fewer than 100 cases have been reported in the medical literature.

Causes

GRIN2B-related neurodevelopmental disorder is caused by mutations in a gene called *GRIN2B*. This gene provides instructions for making a protein called GluN2B, which is found in nerve cells (neurons) in the brain primarily during development before birth. This protein is a part of specialized protein structures called NMDA receptors, which are involved in normal brain development, changes in the brain in response to experience (synaptic plasticity), learning, and memory.

Some *GRIN2B* gene mutations lead to production of a nonfunctional GluN2B protein or prevent the production of any GluN2B protein from one copy of the gene in each cell. A shortage of this protein may reduce the number of functional NMDA

receptors, which would decrease receptor activity in cells. Other mutations lead to production of abnormal GluN2B proteins that likely alter how the NMDA receptors function; some mutations reduce NMDA receptor signaling while others increase it. Researchers are unsure how abnormal activity of NMDA receptors prevents normal growth and development of the brain or why too much or too little activity lead to similar neurological problems in people with *GRIN2B*-related neurodevelopmental disorder.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, 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) in an affected individual's parent or in early embryonic development. These cases occur in people with no history of the disorder in their family.

Other Names for This Condition

- EIEE27
- epileptic encephalopathy, early infantile, 27
- GRIN2B encephalopathy
- GRIN2B related syndrome

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Epileptic encephalopathy, early infantile, 27
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C4015316/
- Genetic Testing Registry: Mental retardation, autosomal dominant 6
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C3151411/

Other Diagnosis and Management Resources

- GeneReview: GRIN2B-Related Neurodevelopmental Disorder
  https://www.ncbi.nlm.nih.gov/books/NBK501979
- GRIN2B Foundation: Treatments
  http://grin2b.com/treatments/

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Epilepsy
  https://medlineplus.gov/ency/article/000694.htm
- Encyclopedia: Intellectual Disability
  https://medlineplus.gov/ency/article/001523.htm
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html

Additional NIH Resources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development: Intellectual and Developmental Disabilities
  https://www.nichd.nih.gov/health/topics/idds
- National Institute on Deafness and Other Communication Disorders: Speech and Language Developmental Milestones
  https://www.nidcd.nih.gov/health/speech-and-language

Educational Resources

- Centers for Disease Control and Prevention: Facts About Intellectual Disability
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- KidsHealth from Nemours: Delayed Speech or Language Development
  https://kidshealth.org/en/parents/not-talk.html
- MalaCards: epileptic encephalopathy, early infantile, 27
  https://www.malacards.org/card/epileptic_encephalopathy_early_infantile_27
- MalaCards: mental retardation, autosomal dominant 6, with or without seizures
  https://www.malacards.org/card/mental_retardation_autosomal_dominant_6_with_or_without_seizures

Patient Support and Advocacy Resources

- American Association on Intellectual and Developmental Disabilities
  https://www.aaidd.org/
- GRIN2B Foundation
  http://grin2b.com/
- Resource List from the University of Kansas Medical Center: Developmental Delay
  http://www.kumc.edu/gec/support/devdelay.html
- Unique: The Rare Chromosome Disorder Support Group (UK): GRIN2B Related Syndrome
  https://www.rarechromo.org/media/information/Chromosome%2012/GRIN2B%20related%20syndrome%20FTNW.pdf

Clinical Information from GeneReviews

- GRIN2B-Related Neurodevelopmental Disorder
  https://www.ncbi.nlm.nih.gov/books/NBK501979

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28GRIN2B%5BTIAB%5D%29+AND+%28%28encephalopathy%29+OR+%28neurodevelopment%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- EPILEPTIC ENCEPHALOPATHY, EARLY INFANTILE, 27
  http://omim.org/entry/616139
- MENTAL RETARDATION, AUTOSOMAL DOMINANT 6, WITH OR WITHOUT SEIZURES
  http://omim.org/entry/613970

Medical Genetics Database from MedGen

- Epileptic encephalopathy, early infantile, 27
  https://www.ncbi.nlm.nih.gov/medgen/863753
- Mental retardation, autosomal dominant 6
  https://www.ncbi.nlm.nih.gov/medgen/462761

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https://ghr.nlm.nih.gov/condition/grin2b-related-neurodevelopmental-disorder

Reviewed: September 2018
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