

What are GATOR1-related epilepsies?

The DEPDC5, NPRL2, and NPRL3 genes provide instructions for making proteins that comprise a complex (a group of proteins) called GATOR1. The GATOR1 complex is found in cells throughout the body. It regulates a signaling pathway called the mTOR pathway. The mTOR pathway is involved in cell growth and division (proliferation), the survival of cells, and the creation (synthesis) of new proteins. The role of the GATOR1 complex is to block this pathway by inhibiting (stopping) the activity of a complex called mTOR complex 1 (mTORC1) that is integral to the mTOR pathway. In the brain, the mTOR pathway regulates many processes, including the growth and development of nerve cells. Loss of GATOR1 function results in increased mTORC1 activity, which may be the underlying cause for epilepsy in these conditions.

Other names for GATOR1-related epilepsies: DEPDC5, NPRL2, and NPRL3 are collectively referred to as the GATOR1-related epilepsies.

What types of seizures (and epilepsies) are associated with GATOR1-related epilepsies?

The GATOR1-related epilepsies are associated with a variety of focal epilepsy types. The most common association is [Sleep-Related Hypermotor Epilepsy \(SHE\)](#). SHE seizures tend to occur at night and look like brief (usually less than one minute) abrupt onset of excessive movements often with an agitated appearance. Other types of focal seizures ([aware](#) and [impaired](#)) have also been reported. Seizures may present at any time between birth and adolescence but typically start in early childhood. Over half of the individuals will have drug-resistant epilepsy. GATOR1-related epilepsy causes a [broad range of seizures](#), however focal seizures are the most common seizure type. Simple febrile seizures, genetic epilepsy with febrile seizures plus epilepsy (GEFS+), and infantile spasms (West Syndrome) have all been reported in children with GATOR1-related epilepsy.

What non-seizure symptoms are seen in GATOR1-related epilepsies?

Some individuals with GATOR1-related epilepsy also have structural changes to the brain (i.e., malformations of cortical development). These structural changes in the brain may range from a small area called a focal cortical dysplasia to changes affecting an entire hemisphere, referred to as hemimegalencephaly. Most people with milder epilepsy types associated with GATOR1-related epilepsy do not have any learning problems. More severe epilepsy types and early-onset epilepsies may be associated with variable degrees of learning and behavior challenges.

How are GATOR1-related epilepsies diagnosed?

DEPDC5, NPRL2, and NPRL3 variants may only be identified by [genetic testing](#). Targeted testing of the GATOR1-related genes specifically is the most direct method of testing an individual when there is a high degree of confidence that a variant in one of the GATOR1 complex genes is likely to be the underlying cause. Epilepsy gene panels, which involve testing of multiple epilepsy-associated genes, and whole exome sequencing (WES) will also detect DEPDC5, NPRL2, and NPRL3 variants.

How are GATOR1-related epilepsies treated?

[Treatment of GATOR1-related epilepsy](#) depends on the seizure type. Rescue medication may be provided to be used if a seizure is prolonged. Daily anti-seizure medication is usually considered for people who have recurrent, unprovoked seizures. [Epilepsy surgery](#) may be considered in individuals with focal seizures that are drug-resistant. Individuals with complete resection of a brain malformation associated with focal epilepsy have more favorable outcomes.

Investigative treatments that target the mTOR pathway are being considered for GATOR1-related epilepsy. Drugs that inhibit the mTOR pathway reduce seizures in animal models of GATOR1-related epilepsy. A few case reports have shown that Everolimus, an mTOR inhibitor, reduced seizures in individuals with GATOR1-related epilepsy but sustained response has not been clearly demonstrated.

How common are GATOR1-related epilepsies?

We do not have adequate data to be able to report on how common GATOR1-related epilepsies may be.

What is the outlook for are GATOR1-related epilepsies?

The prognosis for GATOR1-related epilepsies depends on the type of epilepsy present. Some persons in families with GEFS+ will outgrow their seizure disorder. People with severe, early-onset epilepsy most commonly have life-long seizures. Individuals with the same genetic change, even within the same family, may not have the same symptoms. Variable penetrance of the genetic change means that some individuals that inherit a change in a GATOR1-related gene may not have any symptoms.



For more information:

- [NPRL3 gene](#)
- [NPRL2 gene](#)
- [DEPDC5 gene](#)

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