GRIN2A related syndrome

https://pubmed.ncbi.nlm.nih.gov/27683935/

Clinical characteristics:

GRIN2A

-related speech disorders and epilepsy are characterized by speech disorders in all affected individuals and a range of epilepsy syndromes present in about 90%. Severe speech disorders observed can include dysarthria and speech dyspraxia, and both receptive and expressive language delay/regression; more mildly affected individuals may display subtly impaired intelligibility of conversational speech. Epilepsy features include seizure onset usually between ages three and six years, focal epilepsy with language and/or global developmental regression, and electroencephalogram (EEG) showing continuous spike-and-wave discharges in sleep or very active centrotemporal discharges. Seizure types include seizures associated with aura of perioral paresthesia, focal or focal motor seizures (often evolving to generalized tonic-clonic), and atypical absence seizures. Epilepsy syndromes can include: Landau-Kleffner syndrome (LKS), epileptic encephalopathy with continuous spike-and-wave during sleep (ECSWS), childhood epilepsy with centrotemporal spikes (CECTS), atypical childhood epilepsy with centrotemporal spikes (ACECTS), autosomal dominant rolandic epilepsy with speech dyspraxia (ADRESD), and infantile-onset epileptic encephalopathy.

Diagnosis/testing:

The diagnosis of a

GRIN2A

-related speech disorder and epilepsy is established in a proband by the identification of a

GRIN2A

heterozygous pathogenic variant on molecular genetic testing.

Management:

Treatment of manifestations:

Significant speech/language deficits require therapy from a speech pathologist. Seizures should be treated with anti-seizure medication (ASM). Many different ASMs may be effective, and no one medication has been demonstrated to be effective specifically for these disorders.

Prevention of secondary complications:

Monitoring for possible adverse effects of ASMs.

Surveillance:

Developmental surveillance in all affected children; routine monitoring of speech and language by a speech pathologist should be considered for all children, particularly those diagnosed before reaching school age.

Agents/circumstances to avoid:

In individuals with ECSWS, phenytoin, barbiturates and carbamazepine should be avoided as they are rarely effective, may worsen the EEG, and have negative effects on neuropsychological outcomes.

Evaluation of relatives at risk:

It is appropriate to clarify the genetic status of apparently asymptomatic at-risk relatives in order to identify as early as possible those who would benefit from prompt evaluation for speech disorders and/or seizures and institution of treatment.

Genetic counseling:

GRIN2A

-related speech disorders and epilepsy are inherited in an autosomal dominant manner. The proportion of

GRIN2A

-related speech disorders and epilepsy caused by a

de novo

pathogenic variant is unknown. Each child of an individual with a

GRIN2A

-related speech disorder and epilepsy has a 50% chance of inheriting the

GRIN2A

pathogenic variant. Once the

GRIN2A

pathogenic variant has been identified in an affected family member, prenatal testing for a

pregnancy at increased risk and preimplantation genetic testing are possible.