Genetic Epilepsies

WHAT IS GENETIC EPILEPSY?

According to the International League Against Epilepsy (ILAE), genetics is one of the leading causes of epilepsy, alongside structural, infections, metabolic, immune and unknown factors. (1) It is estimated that about 70% of epilepsy cases are associated with a genetic cause.(2) In total, 76 epilepsy genes have been identified.(3) Depending on the genes impacted, the seizure types, and the complexity of the seizures can vary significantly for each person living with a genetic epilepsy. Genetic epilepsies are strongly associated with developmental epileptic encephalopathy (DEE), which is a sub-group of genetic epilepsies that are known to be rare, more severe, and harder to treat, because seizures at times can be drug-resistant against anti-seizure medications (ASMs). DEEs usually begin during early life and are associated with developmental delay, poor motor skills, respiratory problems, digestive and heart issues and other comorbidities.(4)

CAUSES

Genetic epilepsies are strongly associated with a person's genes. Abnormal changes to a single or group of genes can cause the brain to become under or overactive, resulting in people with genetic epilepsy having seizures. Genetic epilepsy can either be inherited from a parent or occur spontaneously without any prior family history. Maternal smoking and other environmental factors can also cause genetic epilepsy.(5) In some cases, the cause of genetic epilepsy is idiopathic.

DIAGNOSIS

Genetic epilepsies, at times, can be misdiagnosed because they are rare, complex and harder to understand. As a result, it can take time to get to an accurate diagnosis.

In most cases, genetic testing will be conducted to help examine and identify the underlying cause of epilepsy. There are many types of genetic tests, each that looks at different genes. It is important to remember that no single genetic test can diagnose all genetic epilepsies. The diagnosis process can also include:

- Blood tests
- Electrocardiogram (ECG)
- Magnetic resonance imaging (MRI)
- Electroencephalogram (EEG)
- EEG/Video monitoring
- Ambulatory EEG (aEEG)
- Computerized tomography (CT) scan

You can read more about diagnosis in diagnosing epilepsy and test and investigation sections.

SEIZURES TYPES

The types of seizures for a person living with genetic epilepsy will vary significantly depending on the gene or group of genes that are affected. To learn more about the different types of seizures, go to seizure types.

SEIZURES SYNDROMES

The unique symptoms and features associated with genetic epilepsy can also form a specific syndrome. Go to the epilepsy syndromes section to learn more.

TYPES OF GENETIC EPILEPSIES

The ILAE has reported that 76 epilepsy genes in total have been associated with different age groups.(3) With some are more common in infants (0-12 months), children (13 months to 12 years), adolescents (13 years to 28 years) and adults (18 years and over).(6)

Genetic epilepsies that have been studied the most include:

- CACNA1A
- CDKL5
- CHD2
- KCNQ2
- PCDH19
- SCN1A
- SCN2A
- SCN8A
- SYNGAP1

TREATMENT

Treatment options for genetic epilepsy will vary from person to person depending on the frequency, type of seizures, comorbidities and other challenges experienced. For most people living with genetic epilepsy, multiple treatment options may be required depending on the complexity and difficulties associated with their condition. Treatment options include:

- Anti-seizure medications (ASMs) Genetic counselling
- Genetic counselling
- Dietary management
- Surgery
- Seizure monitor and devices

MANAGING GENETIC EPILEPSY?

Managing the seizures and comorbidities associated with a rare and complex type of epilepsy and DEE can be difficult. Most often, this is because seizures can be frequent and drug-resistant. Strategies for the management of genetic epilepsies may include:

- Complementary therapies
- Vagus nerve stimulation (VNS)

REFERENCES

1. Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017;58(4):512-21.
2. Hildebrand M, Myers C, Carvill G, Regan B, Damiano J, Mullen S, et al. A targeted resequencing gene panel for focal epilepsy. Neurology. 2016;86.
3. Martin JB, Sameer MZ, Ingrid ES, Robert SF. The 2017 ILAE classification of seizure types and the epilepsies: what do people with epilepsy and their caregivers need to know? Epileptic Disorders. 2018;20(2):77-87.
4. Noebels JL. Single-Gene Determinants of Epilepsy Comorbidity. Cold Spring Harb Perspect Med. 2015;5(11):a022756.
5. Shi X-Y, Wang G, Li T, Li Z, Leo P, Liu Z, et al. Identification of susceptibility variants to benign childhood epilepsy with centro-temporal spikes (BECTS) in Chinese Han population. eBioMedicine. 2020;57.
6. Oluwayemi J, Bamikole, Olufeagba M-D, Soge T, Bukoye N, Olajide T, et al. Genetics of Epilepsy. 2019.