Biallelic CACNA1A variants: Review of literature and report of a child with drug-resistant epilepsy and developmental delay.


**What did we do?**

- CACNA1A variants have been associated with a wide range of neurodevelopmental and neurological difficulties.
- We all have two copies of the CACNA1A gene. Most people with a CACNA1A-related disorder have one CACNA1A variant and one normal copy of the gene.
- Much more rarely, variants are present in both copies, and this is called biallelic.
- We wanted to understand more about the range of characteristics present in individuals with biallelic CACNA1A variants to address the challenges highlighted in genetic counselling and clinical management.
- To do this, we summarised previous research literature and reported a new case of a child with biallelic CACNA1A variants.

**What did we find?**

- Biallelic CACNA1A variants are associated with different forms of epilepsies, including developmental and epileptic encephalopathy, status epilepticus and tonic-clonic seizures.
- Most individuals display motor, visual and communication difficulties as well as changes in brain structure.
- There is also variability in the characteristics present in parents carrying one of the two variants, with parents displaying none to severe neurodevelopmental difficulties.

**How can this research help?**

- The variability in individuals with biallelic CACNA1A variants, and family members who may carry one of the two variants, complicates genetic counselling.
- Recognition of the range of difficulties experienced by these patients and families can improve care after diagnosis.

**What is next?**

- Research is trying to bridge the gap between CACNA1A variants and the variability in neurodevelopmental and neurological characteristics present.
- We hope that this will improve symptom management and long-term outcomes for these rare children and families.

**Resources**

- You can read the full paper [here](#).
- CACNA1A-specific resources:
  - [CACNA1A-related disorders guide](#)
  - [CACNA1A foundation](#)