

MEDLINE Abstract

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Developmental and epileptic encephalopathies are genetic disorders in which both the developmental disability and the frequent epileptic activity are the effect of a specific gene variant. While heterozygous variants in SCN1B have been described in families with generalized epilepsy with febrile seizures plus, Type 1, only three cases of homozygous, missense variants in SCN1B have been reported in association with autosomal recessive inheritance of a severe developmental and epileptic encephalopathy. We present two siblings who are homozygous for a novel, missense variant in SCN1B, c.265C>T, predicting p.Arg89Cys. The proband is an 11-year-old female with infantile-onset, fever-induced, intractable generalized tonic-clonic seizures, myoclonic seizures, and developmental slowing and autism spectrum disorder occurring later in the course of the disease. Her 4-year-old brother had a similar epilepsy phenotype, but still displays normal development. This variant has not been previously reported in the homozygous state in control databases. The variant was predicted to be damaging and occurred in the vicinity of other epileptic encephalopathy-associated missense variants that are biallelic and located in the extracellular immunoglobulin loop domain of the protein, which mediates interaction of the beta-1 subunit with cellular adhesion molecules. Our report is the first set of siblings with homozygosity for the p.Arg89Cys variant in SCN1B and further implicates biallelic mutations in this gene as a cause of epileptic encephalopathy mimicking Dravet syndrome. Interestingly, the phenotype we observed was milder compared to that previously described in patients with recessive SCN1B mutations.

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