Genetic Analysis of Malignant Migrating Partial Seizure in Infancy (MMPSI) Syndrome by Whole-Exome Sequencing
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Malignant migrating partial seizure in infancy (MMPSI) is a rare, severe early infantile-onset epileptic encephalopathy. The main clinical features are seizure onset in the first 6 months of life, with occurrence of almost continuous migrating polymorphous focal seizures, combined with multifocal ictal electroencephalography discharges and progressive deterioration of psychomotor development. Seizure in MMPSI are refractory to conventional treatment with antiepileptic drugs, and overall developmental prognosis is poor, with the majority of affected patients dying before the second year of age. MMPSI is a genetically heterogeneous disorder, with half the cases showing heterozygous mutations in the KCNT1 gene and few of the remaining ones displaying de novo point mutations of SCN1A, homozygous deletion of PLCB1 or duplication of 16p11.2. The majority of the patients carry a still unidentified gene lesion.

To date we collected DNA samples from 2 MMPSI probands and 5 families (3 trios and 4 quartet), all fulfilling stringent clinical criteria for diagnosis of MMPSI and their DNA were subjected to sequence capture-based enrichment and whole exome sequencing. Data were analyzed by a stepwise filtering approach, to screen the identified variants in order to select those likely to be implicated in the disorder. Data analysis identified two de novo mutations in KNCT1 genes in two probands, and other variants in new genes not previously associated to MMPSI. This approach allowed the identification of potential new candidate genes involved in the development of this syndrome, that are now being further evaluated by combining different genetic and molecular approaches.

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