Clinical predictors of positive genetic investigation in Developmental and Epileptic Encephalopathies

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Developmental and epileptic encephalopathies (DEE) are diseases where there is developmental impairment related to both the underlying etiology independent of epileptiform activity and the epileptic encephalopathy [1]. The improvement of genetic tests optimized the etiology diagnosis, and, presently, a genetic factor is identified in approximately 40% of children with DEE [2]. Genetic tests expanded the landscape of DEEs, making essential the rational genetic investigation [2-3]

OBJECTIVES

The present study evaluated the clinical predictors of positive genetic investigation in DEE.

METHODS

66 patients with DEE followed in the Clinical Hospital of Campinas University (UNICAMP) were submitted to Sanger sequencing of *SCN1A* gene, chromosomal microarray analysis, and whole exome sequencing. The association of clinical, electroencephalogram (EEG) and neuroimaging data with a positive genetic test was investigated using univariate and multivariate analysis.

RESULTS

The genetic etiology was defined in 34 (51.1%) patients with DEE. Clinical characteristics associated with a positive or negative genetic investigation are presented in Table 1.

Table 1. Clinical variables associated with genetic investigation among patients with DEE

	Crude OR (CI 95%)	*P* level
Univariate analysis		
Positive genetic investigation		
Female sex	3.0 (1.06 – 8.53)	0.03
First febrile seizure	19.2 (2.22 – 157.97)	< 0.01
Focal seizures	3.6 (1.2 – 10.04)	0.01
Negative genetic investigation		
Generalized discharges on the EEG	0.4 (0.13 – 0.98)	0.04
Epilepsy with myoclonic-atonic seizures	0.1 (0.01 – 0.48)	< 0.01
Lennox-Gastaut syndrome	0.2 (0.04 – 0.64)	< 0.01
Multivariate analysis		
Negative genetic investigation		
Epilepsy with myoclonic-atonic seizures	0.1 (0.01 – 0.64)	0.02
Lennox-Gastaut syndrome	0.1 (0.03 – 0.78)	0.03

CONCLUSIONS

In this cohort of DEE, female sex, first febrile seizure and focal seizures increased the chances of a positive genetic test; whereas generalized discharges on the EEG, and a diagnosis of epilepsy with myoclonic-atonic seizures or Lennox-Gastaut syndrome decreased the chances.

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