ROLE OF SCN1A GENE IN CHILDHOOD EPILEPTIC ENCEPHALOPATHIES
ISCIA LOPES-CENDES (PQ)¹, MARINA C GONSALES (PQ)¹; MARILISA GUERREIRO (PQ)², MARIA AUGUSTA MONTENEGRO (PQ)², CAMILA V SOLE (IC)³, MAIARA F TERRA (IC)¹.
¹Department of Medical Genetics - UNICAMP, Campinas, SP; ²Department of Neurology - UNICAMP, Campinas, SP; and The Brazilian Institute of Neuroscience and Neurotechnology (BRAINN)

Abstract
Childhood epileptic encephalopathies (CEEs) are severe brain disorders in which epileptic electrical discharges may contribute to progressive psychomotor dysfunction in children. One of the most relevant genes in the etiology of some forms of epilepsy is SCN1A, which encodes the α1-subunit of the neuronal voltage-dependent sodium channel. Mutations in this gene can cause abnormal neuronal excitability. Therefore, our objective is to search for mutations in SCN1A in a large group of patients with different forms of CEE.

Key words: Genetic epilepsies; DNA sequencing; ion channel mutations; neurogenetics

Introduction

The epilepsies are a group of diseases in which there is a predisposition to recurrent seizures without metabolic or toxic-febrile conditions (1). These seizures are transient clinical events caused by abnormal, excessive electrical discharges of the nerve cells, as a result of abnormal ion movement across the cell membrane.

Childhood epileptic encephalopathies (CEEs) are serious brain disorders in which epileptic electrical discharges may contribute to progressive psychomotor dysfunction. It is believed that abnormal brain electrical activity during brain maturation is a major cause of cognitive and neuropsychological regression or progressive deterioration.

Currently, one of the most relevant genes in the etiology of different types of epilepsy is SCN1A, whose mutations were initially identified on the spectrum of Generalized Epilepsies with Febrile Seizures Plus (GEFS+), mainly associated with the phenotype of Dravet syndrome.

Recent studies have suggest that mutations in SCN1A may be present in patients with the phenotype outside the boundaries of typical Dravet syndrome.

The main objective of this study is to evaluate the presence of mutations SCN1A in a large group of well-characterized patients with different types of CEEs.

Results and Discussion

Overall we observed potentially deleterious changes in SCN1A in 14% of our patients (Table 1). In addition, deleterious prediction analyzes reached a consensus for most missense mutations found. Most importantly, of the eight patients with deleterious changes, seven did not show clinical feature of Dravet syndrome.

Table 1. Potentially deleterious changes identified in SCN1A gene in patients with EE and GEFS+.

<table>
<thead>
<tr>
<th>MUTATION TYPE</th>
<th>NUCLEOTIDE CHANGE</th>
<th>PROTEIN CHANGE</th>
<th>PHENOTYPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Missense</td>
<td>c.301C&gt;T</td>
<td>p.Arg101Trp</td>
<td>CEE</td>
</tr>
<tr>
<td></td>
<td>c.3830A&gt;C</td>
<td>p.Gln1277Pro</td>
<td>GEFS+</td>
</tr>
<tr>
<td></td>
<td>c.4244T&gt;C</td>
<td>p.Phe1425Ser</td>
<td>CEE</td>
</tr>
<tr>
<td></td>
<td>c.4435A&gt;T</td>
<td>p.Ile1479Phe</td>
<td>CEE</td>
</tr>
<tr>
<td></td>
<td>CM076495</td>
<td>p.Thr1658Arg</td>
<td>CEE</td>
</tr>
<tr>
<td></td>
<td>c.4915C&gt;T</td>
<td>p.Arg1639Cys</td>
<td>GEFS+</td>
</tr>
<tr>
<td>Frameshift</td>
<td>c.1693_1694insTT</td>
<td>p.Ser565PhefsX59</td>
<td>CEE</td>
</tr>
</tbody>
</table>

* unpublished changes

Conclusions

Our findings indicate the importance of studying SCN1A in patients with CEE even in the absence of typical clinical features of Dravet syndrome.

Acknowledgement

This study is developed within The Brazilian Institute of Neuroscience and Neurotechnology (BRAINN). Financial Support: PIBIC/CNPq and FAPESP

