OBJECTIVE and METHODS

Objective
To assess the frequency and severity of functional impairments in patients with KCNQ2-DEE and their association among key clinical features

Study Participants and Data
Data obtained from a cross-sectional survey (2018-2020) of parents of children aged ≥2 years with KCNQ2-DEE were analyzed

Four functional ability domains (communication, mobility, eating, and hand use) were assessed with classifications systems commonly utilized in the field of pediatric rehabilitation (Table 1). High scores indicate worse function for communication and eating assessments, whereas low scores indicate worse function for mobility and hand use assessment. The classification systems were assessed as follows:

- Communication was assessed using the Communication Function Classification System
- Mobility questions were adapted from the Gross Motor Functional Classification System and tailored for each child’s age
- Eating abilities were assessed based on adaptations of the Eating and Drinking Ability Classification System, with an additional item to reflect whether a child had a gastronomy tube
- Hand use was assessed focusing on the “hand grasp and purposeful manipulation of objects” item from the Manual Abilities Classification System, with an additional item to reflect whether a child had a hand prosthesis

The associations of severe functional impairment across these domains and the number of domains with severe impairment were examined to determine which, if any, impairments tended to occur in isolation or in combination with other impairments

RESULTS

Data Across Communication, Mobility, Eating, and Hand Use (Available for N=51 Afflicted Children)
- Communication impairment (n=48, 94%) and eating dependencies (n=49, 96%) were prevalent in the majority of the cohort
- Communication impairment was the most prevalent symptom (34/51, 67%) and was present regardless of the number of other domains impaired
- Severe impairment in the other domains were reported: 26/51 (51%) (mobility), 75/1 (51%) (hand use), and 22/51 (43%) (eating)

TABLE 1. Functional Ability Domains by Severity Class

<table>
<thead>
<tr>
<th>Communication</th>
<th>Mobility</th>
<th>Eating</th>
<th>Hand use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1 (mild)</td>
<td>1 (mild)</td>
<td>1 (mild)</td>
</tr>
<tr>
<td>Mild</td>
<td>2 (moderate)</td>
<td>2 (moderate)</td>
<td>2 (moderate)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (severe)</td>
<td>3 (severe)</td>
<td>3 (severe)</td>
</tr>
<tr>
<td>Severe</td>
<td>4 (extreme)</td>
<td>4 (extreme)</td>
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</tr>
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</table>

CONCLUSIONS

Among individuals with KCNQ2-associated developmental and epileptic encephalopathies (KCNQ2-DEE), there is a hierarchy of impairments wherein communication is the most sensitive domain and is often affected in isolation from others

Functional impairments are closely correlated with multiple other functional impairments

INTRODUCTION

- KCNQ2-DEE is a rare, heterogeneous condition that manifests as developmental delays combined with neurological symptoms and signs
- While recent work has described patients with KCNQ2-DEE at the group-level, more detailed information is required regarding the severity and variability of the condition within a sample of individuals
- A collection of patient experience beyond case reports and a limited case series has yet to be described in a larger sample

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Each of these aspects was considered core to KCNQ2-DEE clinical experiences and established as clinically meaningful to families

Statistical Analyses
Data were analyzed with methods appropriate for nonparametric dichotomous and ordinal data. Contingency table data were analyzed with Chi-squared tests and Chi-squared tests for trend for ordinal data when appropriate

- **Communication impairment (n=48, 94%) and eating dependencies (n=49, 96%)** were reported for the majority of the cohort; 6% and 4%, respectively, exhibited some degree of independent function in these domains (Figure 1)
- **Severe impairment in Each Domain**
  - Of the 51 children assessed, 13 reported no severely affected domains, 13 reported 1 severely affected domain, 6 reported 2 severely affected domains, 12 reported 3 severely affected domains, and 7 reported 4 severely affected domains (Figure 1)
  - Severe communication impairment was the most prevalent symptom (34/51, 67%) and was present regardless of the number of other domains impaired
  - Severe impairment in the other domains were reported: 26/51 (51%) (mobility), 75/1 (51%) (hand use), and 22/51 (43%) (eating)

- **Association among key clinical features**
  - Of the 13 participants with only one severely affected domain, communication (11/13) was most often reported as a severely affected domain (Figure 1)
  - There were 2 participants who had isolated mobility impairments (Figure 1)
  - Hand use was the likely least to be reported as impaired unless all three other domains were also severely impaired (Figure 2)
  - CVI Increased With The Number of Affected Domains
    - The presence of CVI increased with the number of affected domains from 8% for 0 domains to 71% for 4 domains (p<0.001; Figure 3)

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