Poster 2.451

Functional Impairments in Patients With KCNQ2-DEE: Associations Among Key Clinical Features

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CONCLUSIONS

1. 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
2. Gross and fine motor skill impairments tend to be correlated
3. Hand use impairment is closely correlated with multiple other functional impairments

INTRODUCTION

- KCNQ2-DEE is a rare, heterogenous condition that manifests as developmental delays combined with neurological comorbid signs and symptoms[1,2]
- While seminal work has described patients with KCNQ2-DEE at the group-level,[3,4] relatively little information is available regarding the severity and variability of the condition within a sample of individuals
- A collation of patient experience beyond case reports and a limited case series has yet to be described in a larger sample

References: **1.** Weckhuysen S, et al. *Neurology*. 2013;81(19):1697-1703. **2.** Berg AT, et al. *Ann Clin Transl Neurol*. 2021;8(3):666-676. **3.** Berg AT, et al. *Epilepsy Behav*. 2020;111:107287. **4.** Cossu A, et al. *Epilepsy Behav*. 2023;142:109153. **5.** Hidecker MJ, et al. *Dev Med Child Neurol*. 2011;53(8):704-710. **6.** Palisano R, et al. E & R Gross Motor Function Classification System expanded and revised. 2007. www.canchild.ca. Accessed October 24, 2023. **7.** Sellers D, et al. *Dev Med Child Neurol*. 2014;56(3):245-251. **8.** Morris C, et al. *Dev Med Child Neurol*. 2004;46(7):455-460.

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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[3]
- 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[5]
  - *Mobility* questions were adapted from the Gross Motor Functional Classification System and tailored for each child's age[6]
  - *Eating* abilities were assessed based on adaptations of the Eating and Drinking Ability Classification System,[7] 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[8]
- 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
- Cortical visual impairment (CVI) is a decreased or abnormal visual response caused by a neurological problem, rather than an ocular disorder, and was also considered as another marker of disease severity in this study
- Each of these aspects was considered core to KCNQ2-DEE clinical experiences and established as clinically meaningful to families[3]

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

Table 1. Functional Ability Domains by Severity Class

Classification system and severity level for each domain	
Communication (Communication Function Classification System)	
1	"My child effectively communicates back and forth with both people she/he knows as well as new people as appropriate for age"
2	"My child effectively communicates back and forth with both people she/he knows as well as new people but at a slower pace or with some greater difficulty than others of the same age"
3	"My child effectively communicates back and forth with both people she/he knows, but not so much with unfamiliar people"
4	**"My child inconsistently communicates even with people she/he knows"**
5	**"My child seldom communicates effectively even with people she/he knows"**
Mobility (Gross Motor Functional Classification System)	
1	**"Has difficulty sitting independently and controlling head and body posture in most positions -AND- has difficulty achieving any voluntary control of movement -AND- needs a specialty supportive chair to sit comfortably -AND- has to be lifted or hoisted by another person to move"**
2	**"Sits independently but does not stand or walk without significant support -AND- therefore relies mostly on wheelchair at home, school and in the community -AND- and often needs extra body/trunk support to improve arm and hand function and may achieve self-mobility using a powered wheelchair"**
3	"Stands independently and in the home generally walks using a walking aid (such as a walker, rollator, crutches, canes, etc) -AND- finds it difficult to climb stairs"
4	"Walks independently in the home without using walking aids but needs to hold the handrail when going up or down stairs"
5	"Walks independently in the home without using walking aids and can go up or down stairs without needing to hold the handrail -AND- can run and jump (speed and balance may be limited)"
Eating (the Eating and Drinking Ability Classification System)	
1	"Completely independent"
2	"Requires some assistance or supervision"
3	"Requires considerable assistance"
4	**"Is completely dependent on someone else"**
5	**(Added for gastronomy tube exclusively)**
Hand use (Manual Abilities Classification System) – "Does your child have any functional use of his or her hands?"	
0	**"No, does not use hands at all"**
1	**"No, may flap or wave hands, but hands are not used purposefully"**
2	"No, may bat at objects, but no functional grasp with fist or fingers"
3	"Yes, uses hands purposefully to manipulate objects (to any extent)"

[a]Color gradients correspond to severity level. For each domain, bolded/underlined levels are considered severe.

RESULTS

Data Across Communication, Mobility, Eating, and Hand Use (Available for N=51 Affected Children)

- 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**)

Severity of 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 comorbidity (34/51, 67%) and was present regardless of the number of other domains impacted
- Severe impairment in the other domains were reported: 26/51 (51%) (mobility), 7/51 (14%) (hand use), and 22/51 (43%) (eating)

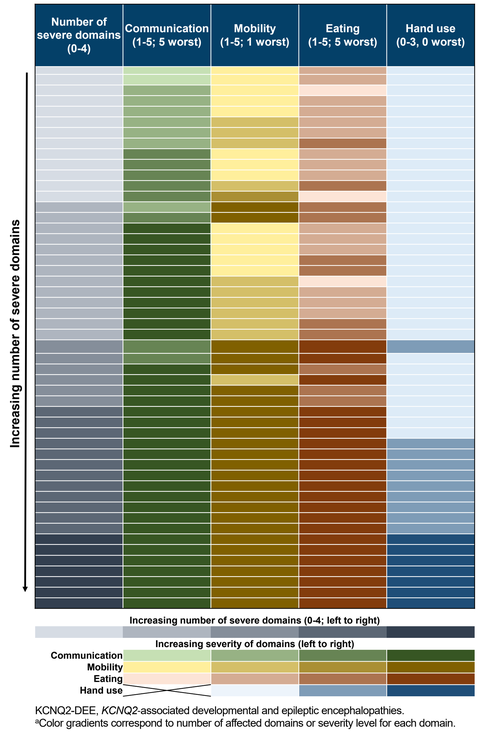
Examination of Isolated Impairments

- 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 least likely 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 ($p<0.0001$; **Figure 3**)

Figure 1. Summary of Data Across Key Domains Assessed in Individuals With KCNQ2-DEE[a]



KCNQ2-DEE, *KCNQ2*-associated developmental and epileptic encephalopathies.
[a]Color gradients correspond to number of affected domains or severity level for each domain.

Figure 2. Proportion of Patients Severely Impacted in 0 to 3 Domains, When Impaired by the Fourth Domain

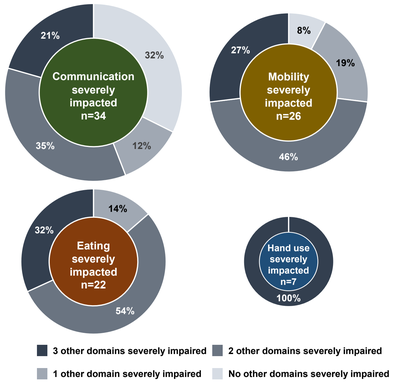
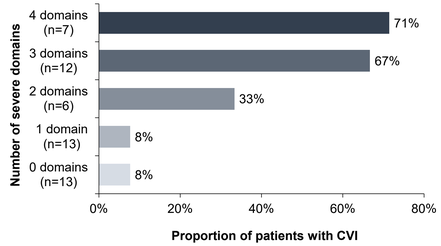


Figure 3. Presence of CVI by Number of Severe Domains in Individuals With KCNQ2-DEE



CVI, cortical visual impairment; KCNQ2-DEE, *KCNQ2*-associated developmental and epileptic encephalopathies.