Poster
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Understanding Lived Experiences with KCNQ2-Developmental and Epileptic Encephalopathy (KCNQ2-DEE)

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INTRODUCTION

- KCNQ2 developmental and epileptic encephalopathy (DEE) is a rare neurodevelopmental disorder impacting approximately six in every 100,000 live births[1,2]
- KCNQ2-DEE is caused by variants in the *KCNQ2* gene, which encodes the $K_v7.2$ subunit of the voltage-gated potassium channel[2]
- Children with KCNQ2-DEE typically present with seizures within the first few days of life and neurodevelopmental impairments[1,2]
- Prior outcomes research in the KCNQ2-DEE population has focused on characterising functional impairments and clinical outcomes in individuals with KCNQ2-DEE,[2–4] with limited qualitative interview data outlining the patient and caregiver disease-related experiences and impact of the disorder

OBJECTIVE

- Develop KCNQ2-DEE conceptual models outlining the burden of seizures, extent of neurodevelopmental delays and impact of the disease on quality of life from the perspectives of parents of children with KCNQ2-DEE

METHODS

- Semi-structured interviews were conducted via video call with United States-based parental caregivers of children (aged 1–18 years) with mild, severe and profound KCNQ2-DEE phenotypes between September and November 2023
- Eligible parents were recruited via a patient advocacy group (KCNQ2 Cure Alliance)
- Interviews consisted of three parts: collection of background information; concept elicitation to understand the signs, symptoms and impacts of KCNQ2-DEE; and descriptions of patient severity and associated developmental impacts. The most burdensome disease aspects were discussed (rated on a 0–10 scale)
- Interviews were audio recorded, transcribed, coded and analysed by ATLAS.Ti v23 software, following established methods
- Interviews were assessed for concept saturation and four conceptual models were derived – one for each KCNQ2-DEE phenotype severity and one overall model

RESULTS

Demographics

- Interviews were conducted with 53 parents of children with KCNQ2-DEE (N=54 children)
- Demographics and clinical characteristics are presented in **Table 1**
  - Most (77%) parents interviewed were mothers
  - The mean age of children with KCNQ2-DEE was 7.3 years and most were classed as having a severe KCNQ2-DEE phenotype (mild, 31.5%; severe, 50.0%; profound, 18.5%)

Table 1. Parent and child demographics and clinical characteristics

Parent demographics	N=53[a]
Age in years, mean (range)	42.3 (28–58)
Relationship with child, n (%)	
Mother	41 (77.4)
Father	13 (24.5)
Hours spent with child in last week, mean (range)	112 (20–168)
Child demographics and clinical characteristics	**N=54**
Age in years, mean (range)	7.3 (1–18)
Child sex, n (%)	
Male	25 (46.3)
Female	29 (53.7)
Diagnosis, n (%)	
Genetic test in medical record	3 (5.6)
Genetic test/panel	51 (94.4)
Severity of KCNQ2-DEE phenotype,[b] n (%)	
Mild	17 (31.5)
Severe	27 (50.0)
Profound	10 (18.5)

DEE, developmental and epileptic encephalopathy.
[a]One parent had twins with KCNQ2-DEE; [b]Severity definition based on degree of impairments across gross motor function, communication (ages 2–18 years only) and chewing ability.

Concept elicitation: signs and symptoms of KCNQ2-DEE

- Parents were asked to describe the daily limitations or difficulties related to their child with KCNQ2-DEE
- The most frequently reported signs, symptoms and functional limitations are shown in **Figure 1**
  - Overall, the most common concepts parents reported were difficulties with communication (88.9%), and gross (81.5%) and fine (63.0%) motor problems (**Figure 1**)
  - Generally, more parents of children with severe KCNQ2-DEE reported issues than parents of children with mild KCNQ2-DEE (**Figure 1**)

Most bothersome and impactful issues associated with KCNQ2-DEE

- Parents were asked to indicate the issues they considered to be particularly impactful or bothersome
  - Difficulty with communication (74.1%), behavioural disorders (37.0%) and gross motor problems (24.1%) were the most impactful and bothersome issues for parents (**Table 2**)
  - When asked about the single most bothersome concept, communication was most frequently mentioned (27.8%) (**Table 2**)

Figure 1. Frequently reported concepts from >10% of parents of children with KCNQ2-DEE

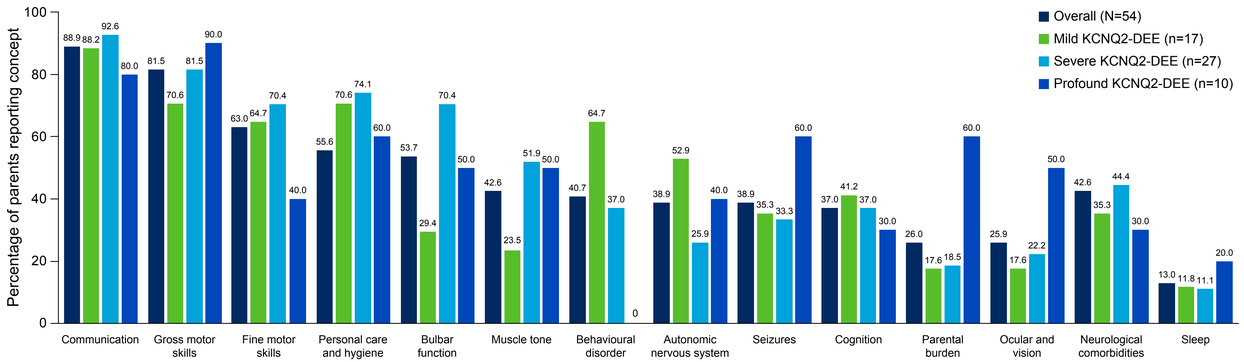


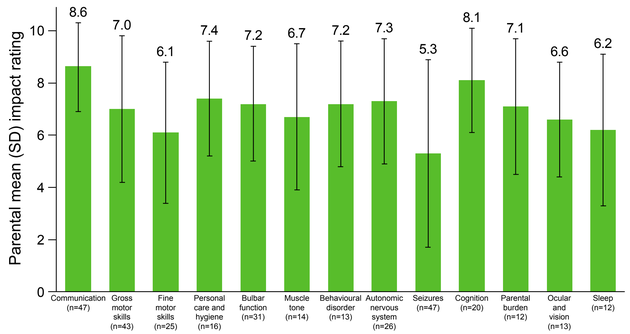
Table 2. Concepts reported as most bothersome and impactful for parents

Concept	Concepts reported as bothersome or impactful to parent,[a,b] n (%)	Most bothersome to parent, n (%)
Communication	40 (74.1)	15 (27.8)
Gross motor skills	13 (24.1)	5 (9.3)
Fine motor skills	2 (3.7)	0 (0)
Personal care and hygiene	7 (13.0)	1 (1.9)
Bulbar function	5 (9.3)	3 (5.6)
Behavioural disorder	20 (37.0)	8 (14.8)
Autonomic nervous system	4 (7.4)	5 (9.3)
Seizures	2 (3.7)	1 (1.9)
Cognition	7 (13.0)	3 (5.6)
Parental burden	6 (11.1)	3 (5.6)
Sleep	3 (5.6)	1 (1.9)

[a]Counts were not mutually exclusive; some parents reported multiple concepts; [b]One parent had twins with KCNQ2-DEE.

- Following this, parents (N=53) were asked to rate how impacted they were by each concept using a 10-point rating scale (0 = 'not impacted' to 10 = 'extremely impacted')
  - The most burdensome symptoms were difficulty with communication (mean score [SD] = 8.6 [1.7]; 87.0% parents), cognitive delays (8.1 [2.0]; 37.0% parents), and personal care and hygiene issues (7.4 [2.2]; 29.6% parents) (**Figure 2**)
  - Seizures were the least burdensome symptom (mean score [SD] = 5.3 [3.6]; 87.0% parents) (**Figure 2**); parents reported that seizure occurrence was now infrequent versus in infancy
- Together, these data informed the development of a KCNQ2-DEE conceptual model (**Supplementary Figure**)

Figure 2. Parent rating for concepts considered most impactful



CONCLUSIONS

- KCNQ2-DEE is a multi-faceted disease with wide ranging developmental and neurological impairments that impact both children and their parents
- Of concepts reported by parents of children with varying KCNQ2-DEE phenotypes, communication difficulties, cognitive delays, and issues with personal care and hygiene were the most bothersome
- Parents indicated that seizures were the least bothersome symptom post-infancy
- Together, these findings identify outcome domains important to parents and children with KCNQ2-DEE, and may inform the development of measurement tools and endpoint selection in future therapeutic trials

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Understanding Lived Experiences with KCNQ2-Developmental and Epileptic Encephalopathy (KCNQ2-DEE)
Supplementary Material

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Target population
Patients (1–18 years of age) with KCNQ2-DEE

Disease process
De novo genetic mutation characterised by seizures in the first week of life and associated with development delays

Signs, symptoms and functional limitations

Gross motor skills
Not able to walk | **Lacking mobility** | **Cannot sit independently** | **Balance issues** | **General delays** | **Poor head control** | **Requires wheelchair** | **Cannot crawl** | **Cannot walk independently** | Assistance required for walking | Cannot jump | Cannot ride a bike | Cannot roll over | Cannot scoot | Cannot transfer to a wheelchair | Difficulty rolling over to one side | Gait issues | Difficulties navigating stairs | Motor planning | Prone to falling | Requires support to stand | Standing on one leg | Uncoordinated movement | Wears leg brace

Communication
Non-verbal | **Articulation/enunciation difficulty** | **Understanding/receptive language** | Cannot read | Verbal apraxia

Autonomic nervous system
Constipation/dysmotility | **GI issues** | **Vomiting/throwing up** | **Bowel movement issues** | Fecal incontinence | GI pain | Urinary incontinence | Regulating body temperature/sensitivity to temperature | Pain experiences

Sleep
Sleep disruption | Difficulty falling asleep

Seizures/epilepsy
Intermittent breakthrough seizures | **History of seizures** | **Absence seizures** | Body jerks | Fever seizures | Neurological storming

Personal care and hygiene
Wears diaper | **Cannot dress themselves** | **Requires assistance bathing** | **Requires assistance brushing teeth** | **Cannot self-feed** | **Not toilet trained/needs support toileting**

Other
Hernia | Scoliosis | Hip dysplasia/dislocation | Pressure sores | Hearing difficulties | Immunocompromised | Weight-related issues

Fine motor skills
Weak or no grasp | **Limited finger dexterity** | **Poor hand-eye coordination** | **Limited pincer grip** | **Limited hand-eye coordination** | Cannot grasp with both hands | Cannot self-propel with wheelchair | Difficulties with AAC/iPad | Difficulty writing | General delays | Limited fine motor skills in one hand | Difficulty with utensils/cutlery

Respiratory/bulbar function
Requires preparation of food to support bulbar function/food consumption | **Dysphagia/swallowing disfunction** | **Fed and medication via g-tube/feeding tube** | **Difficulty clearing oral secretions/mucous** | Breathing difficulty | Cannot control drooling | Difficulty moving fluid in/out | No interest in food/picky | Difficulty eating orally | Pneumonia | Respiratory illness

Ocular/vision
CVI | Depth perception | Lazy eye | Nystagmus | Strabismus | Visual apraxia | Visual impairment (general)

Muscle tone
Limp/low muscle tone/hypotonia | **Stiffness/spasticity/hypertonia** | Clonus and startling | Deformed feet or foot | Dystonia | Torticollis

Behaviour/affective
Aggression | **No sense of danger or pain** | **Emotional dysregulation** | **Tantrums/mood swings** | Clonus and startling | Deformed feet or foot | Dystonia | Torticollis

Cognition
Cognitive processing | **Intellectual disability** | Auditory processing | Cognitive developmental delays | Memory issues | Motor planning

HRQoL impacts for KCNQ2-DEE children

Physical function: Lack of mobility | Unable to walk | Limited balance/coordination | Clumsiness | Difficulty running | Restrictions to play | Cannot get in and out of bed | Cannot ride a bike | Dependent on others to move

Dressing self: Unable to dress themselves | Requires assistance

Communication: Inability to communicate needs, pain or discomfort | Left out of conversations | Difficulty understanding speech

Feeding: Risk of choking | Requires food to be cut/pureed | Cannot feed themselves | Difficulty with cutlery | Challenging eating habits

Behavioural function: Autism-features | Safety concerns because of behaviour | Sensitive to light, heat and noise | Overstimulated in outdoor environments | Messy

Emotional function: Frustration | Sadness | Upset | Anger

Cognitive function: Intellectual disability limits ability to do activities, process and understand things | Difficulty learning new things | Cannot read words

General developmental delays: Limitations to daily activities and milestones due to developmental stage

Toileting: Needs assistance | Limited travel due to incontinence | Requires diaper change | Cannot change own diaper | Needs reminding to use bathroom

Personal hygiene: Inadequate hygiene | Requires assistance to wash, bathe and brush teeth

Social/relationships: Limited social skills | Bullying | Impact to family | Lack of friends | Difficult relationship with siblings | Uncomfortable meeting new people | Difficulty connecting with others | Travelling

Lack/loss of independence: General lack of autonomy; requires support for most aspects of daily life

School/activities: Difficulty with participation, activities and sports | Restrictions to playing with others | Requires specialist support at school

Medical burden on child

Parental burden
General burden | Physical (i.e., physical strain of carrying child) | Burden of medical regimen/equipment care/appointments | Constant observation | Mental health | Advocating for child | Fear about the future

Neurological/psychological comorbidities
Autism | ADHD | Hypoactive | Sensory processing disorder | Movement disorder | Cerebral palsy | Attention | CNS issues | Hyperactive | Migraine | OCD

AAC, augmentative and alternative communication, ADHD, attention-deficit hyperactivity disorder; CNS, central nervous system; CVI, cortical visual impairment; DEE, developmental and epileptic encephalopathy; GI, gastrointestinal; HRQoL, health-related quality of life; OCD, obsessive compulsive disorder.
Concepts in **bold** text were reported by >10.0% of caregivers.

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