Unpredictable Seizures and Disruptive Behavior in Developmental and Epileptic Encephalopathies: Interim Results of a Caregiver Survey

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Disclosures

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MAM: Employee, Dravet Syndrome Foundation.

DLO: Honoraria, Gene DX; Illumina. Member, ACMG secondary findings working group. Board member, CACNA1A Foundation.

LR: Founder, SLC6A1 Connect UK-AQ. Member, SLC6A1 Europe. Pediatric practice development nurse, NHS. Steering committee member, UKRET.

CSR: President and cofounder, STXBP1 Foundation. CEO, Global Genes. Shareholder, Fabric Genomics; Chrysalis Genetics.

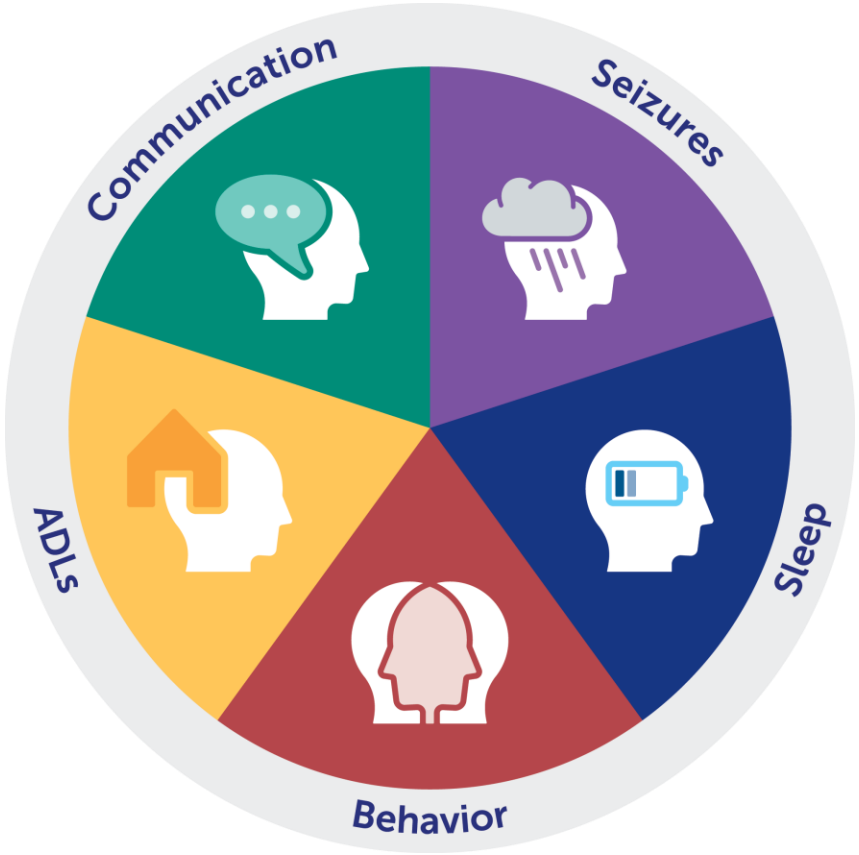
Background

- Developmental and epileptic encephalopathies (DEEs) are characterized by high seizure burden and developmental disability, and can cause behavioral difficulties
- DEEs have a profound impact on patients, their primary caregivers, and their siblings
- Caregiver definitions of "normal" and "disruptive" have not been extensively explored

Domain	Description
Seizures	Frequency, clustering, and average length of seizure; duration of seizure freedom; rescue medication/device use
Sleep	Number of >30 min awakenings, hours of total sleep per night; number of awakenings with inability to return to sleep per week
Behaviors, disruptive	Any of the following behaviors – hitting, biting, kicking, shouting, hair pulling, swearing, harsh language, throwing objects, refusal to cooperate, destruction of property, threatening physical harm, invading a person's personal space, anger
Activities of daily living (ADLs)	Feeding; toileting; bathing/personal hygiene; dressing
Communication	Basic methods, tools, or devices used to exchange information

Objectives & Methods

Define patterns of typical and disruptive seizures and disruptive behaviors in people with DEEs and explore their relationships with ADLs and communication



- Internet-based anonymous survey (63 questions, English only) developed in consultation with DS and LGS communities
- Distributed via US patient advocacy websites, social media, and patient community events
- Respondent eligibility criterion: primary caregiver to, or helps care for, a person diagnosed with DEE

The survey was distributed for 7 weeks beginning in March 2024.
ADLs, activities of daily living; DEE, developmental and epileptic encephalopathy; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome; US, United States.

Normal and Disruptive Seizures

Normal: the typical daily experience during the current phase of the DEE journey

- Out of 489 respondents, 86 (17.6%) individuals reported that the person with DEE was **seizure-free** for 6 months prior to the survey
- 198 (40.5%) reported **multiple seizures per day**

Disruptive: a deviation from the normal daily experience

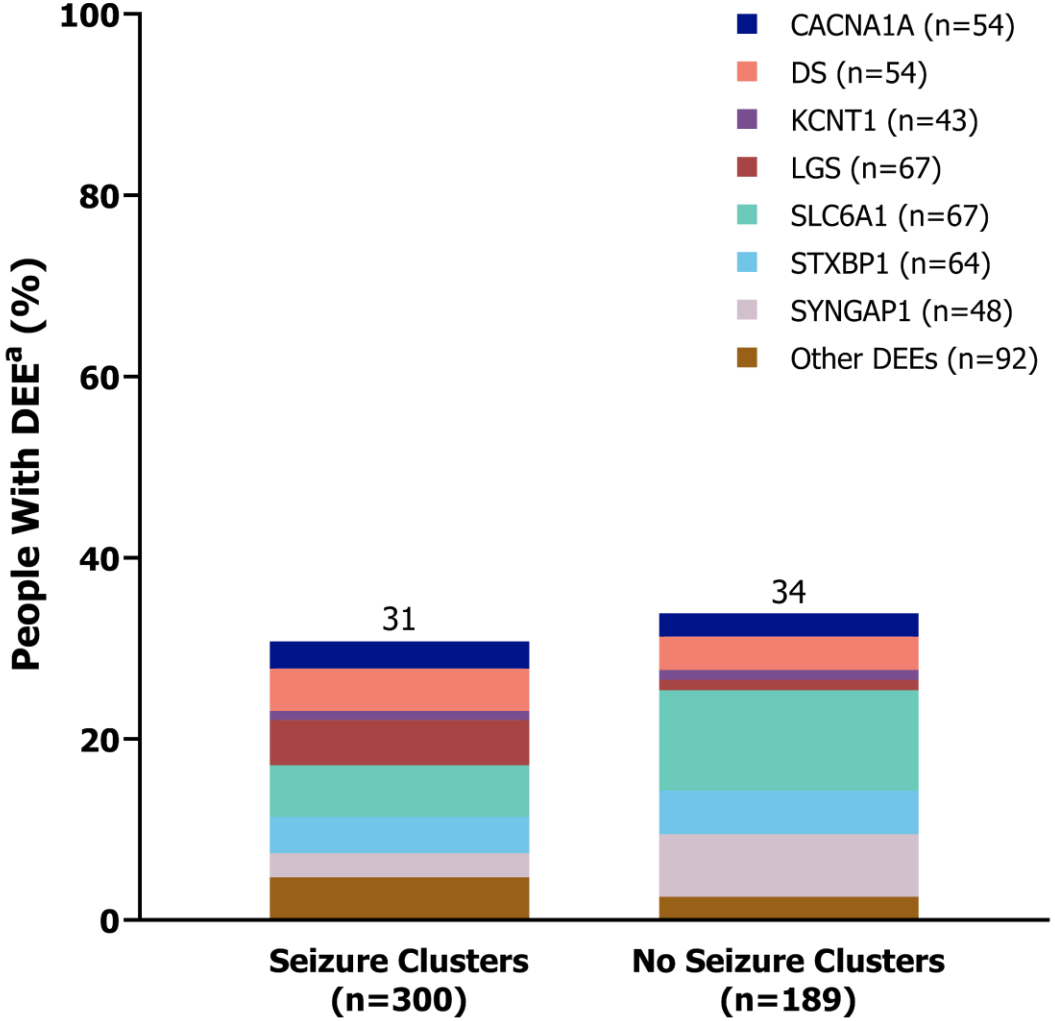
104 (21.3%) reported **no disruptive seizures** in the 6 months prior to the survey

Always disruptive: no pattern or distinguishable "typical" experience

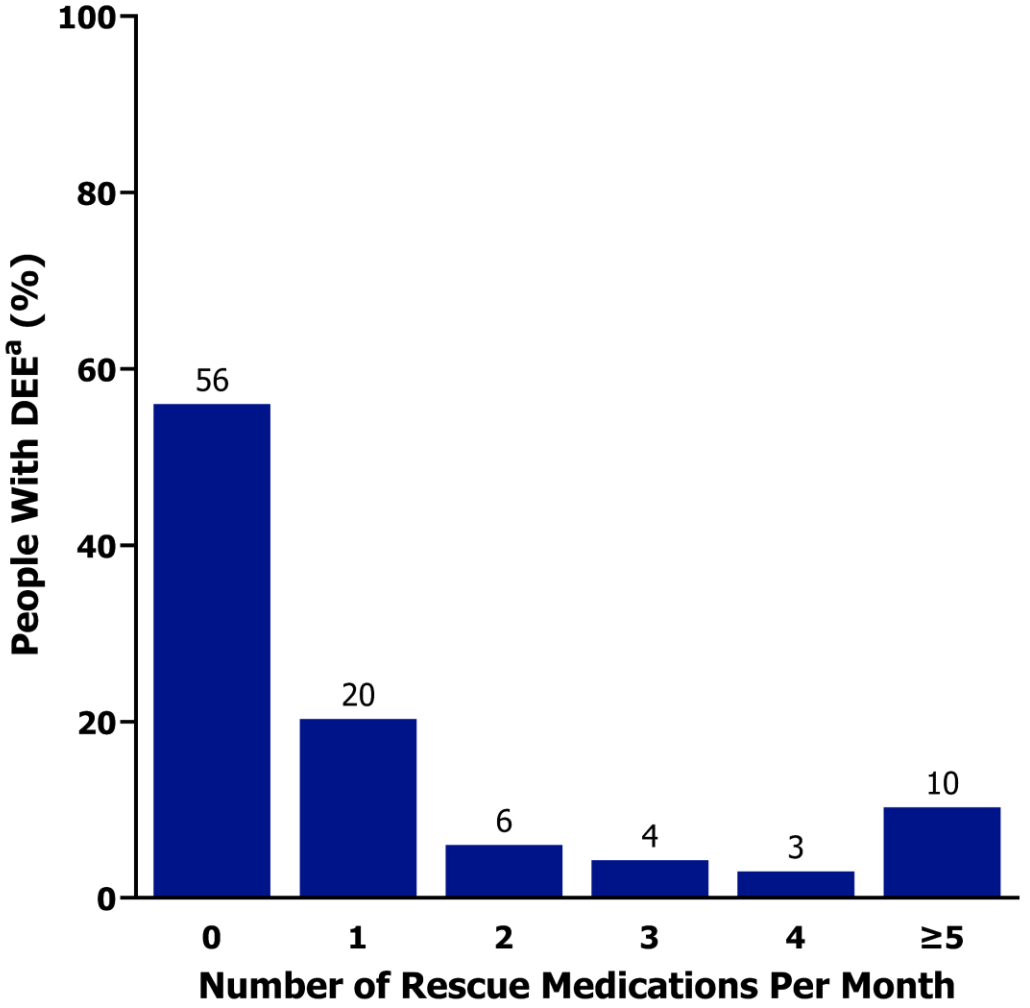
110 (22.5%) reported that the person with DEE had **seizures that were always disruptive**

DEE, developmental and epileptic encephalopathy; DS, Dravet syndrome; LGS, Lennox-Gastaut syndrome.

Always Disruptive Behavior With and Without Seizure Clusters by DEE (n=489)

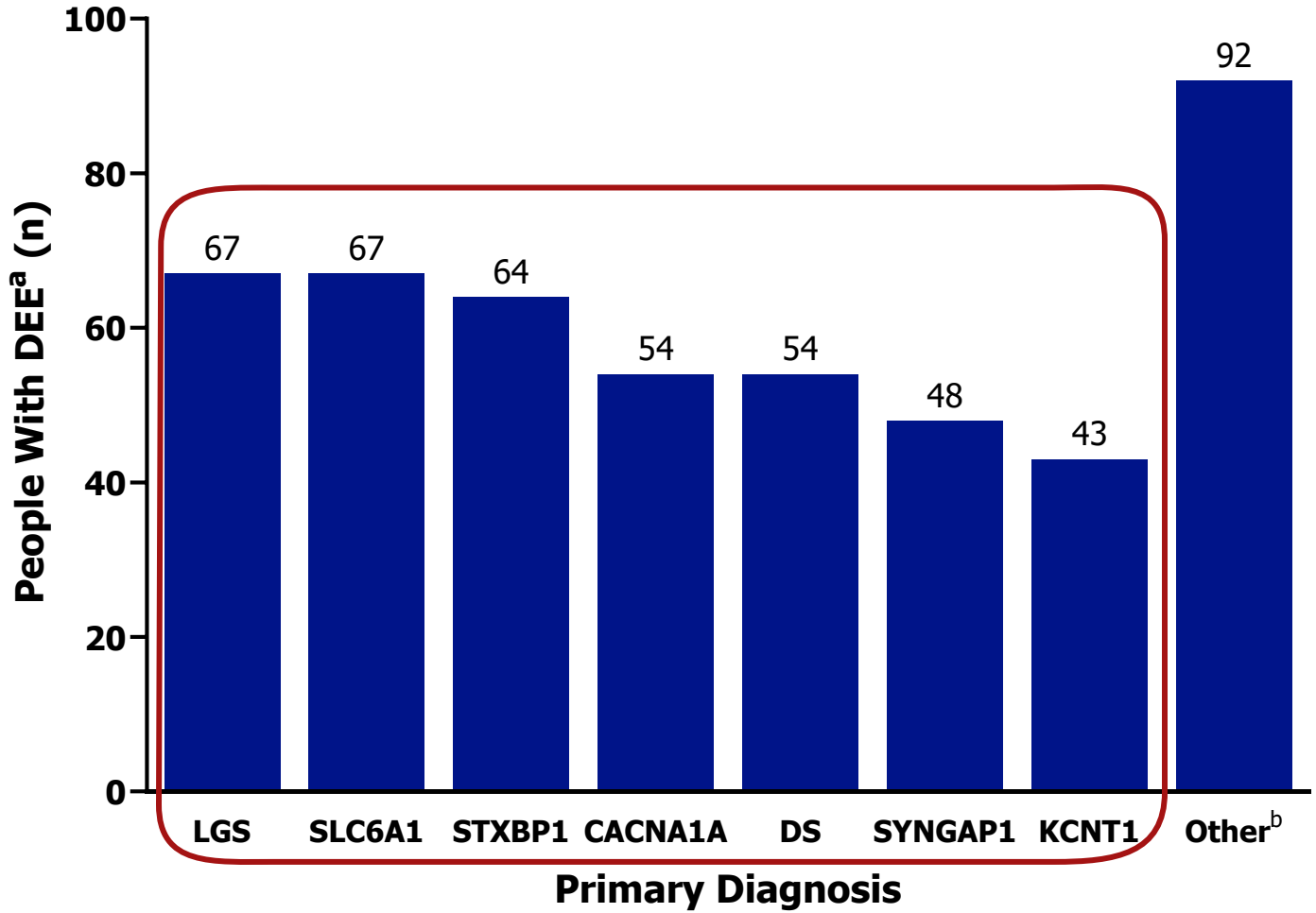


Rescue Medication Use in People With Seizure Clusters (n=300)



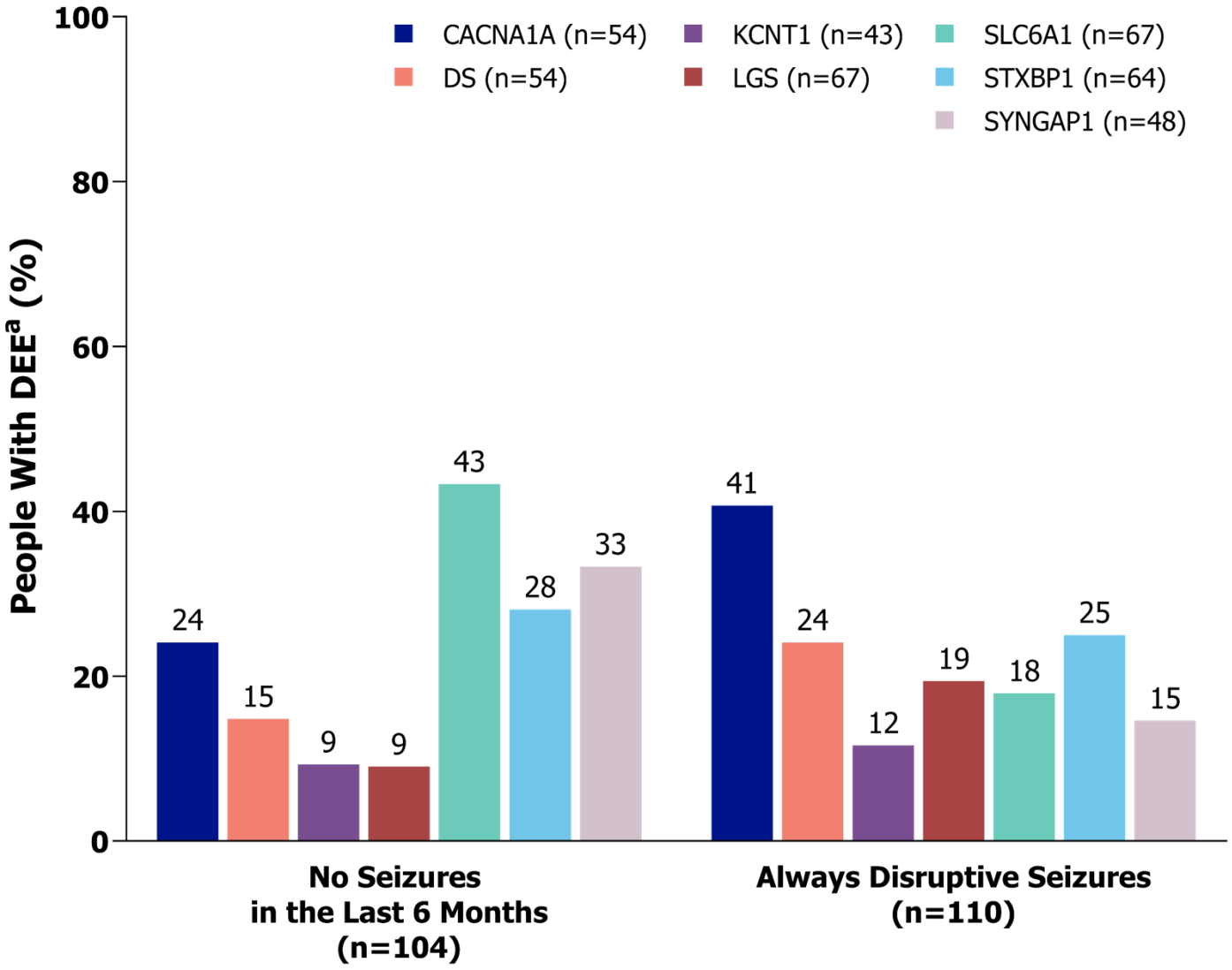
Disruptive behavior: "any of the following – hitting, biting, kicking, shouting, hair pulling, swearing, harsh language, throwing objects, refusal to cooperate, destruction of property, threatening physical harm, invading a person's personal space, anger". [a]As reported by caregivers.
Wilson score binomial interval (lower, upper): With seizure clusters (28%, 40%); Without seizure clusters (29%, 43%).
CACNA1A, CACNA1A-related disorder; DEE, developmental and epileptic encephalopathy; DS, Dravet syndrome; KCNT1, KCNT1-DEE; LGS, Lennox-Gastaut syndrome; SLC6A1, SLC6A1-related neurodevelopmental disorder; STXBP1, STXBP1-DEE; SYNGAP1, SYNGAP1-DEE.

397 (81.2%) of 489 Total Responses Were Included In Analyses That Were Stratified by DEE



[a]As reported by caregivers. [b]Other DEEs: 22q11.2 deletion syndrome, Aicardi syndrome, CDD, CHD2-related neurodevelopmental disorders, CRELD1-related disorder, Doose syndrome, Dup15Q syndrome, HNRNPU-related neurodevelopmental disorder, infantile spasms, lissencephaly, Malan syndrome (NFIX), PCDH19-DEE, Pura syndrome, Rolandique épilepsie (Rolandic epilepsy), SCN1A-related disorders, SCN2A-DEE, SCN1A-related epilepsy (non-Dravet, GEFS+), Set1b-related neurodevelopmental disorder, Sunflower syndrome, and TSC.
CACNA1A, CACNA1A-related disorder; CDD, CDKL5 deficiency disorder; DEE, developmental and epileptic encephalopathy; DS, Dravet syndrome; GEFS+, generalized epilepsy with febrile seizures plus; KCNT1, KCNT1-DEE; LGS, Lennox-Gastaut syndrome; SLC6A1, SLC6A1-related neurodevelopmental disorder; STXBP1, STXBP1-DEE; SYNGAP1, SYNGAP1-DEE; TSC, tuberous sclerosis complex.

Disruptive Seizures by DEE (n=397)



[a]As reported by caregivers.
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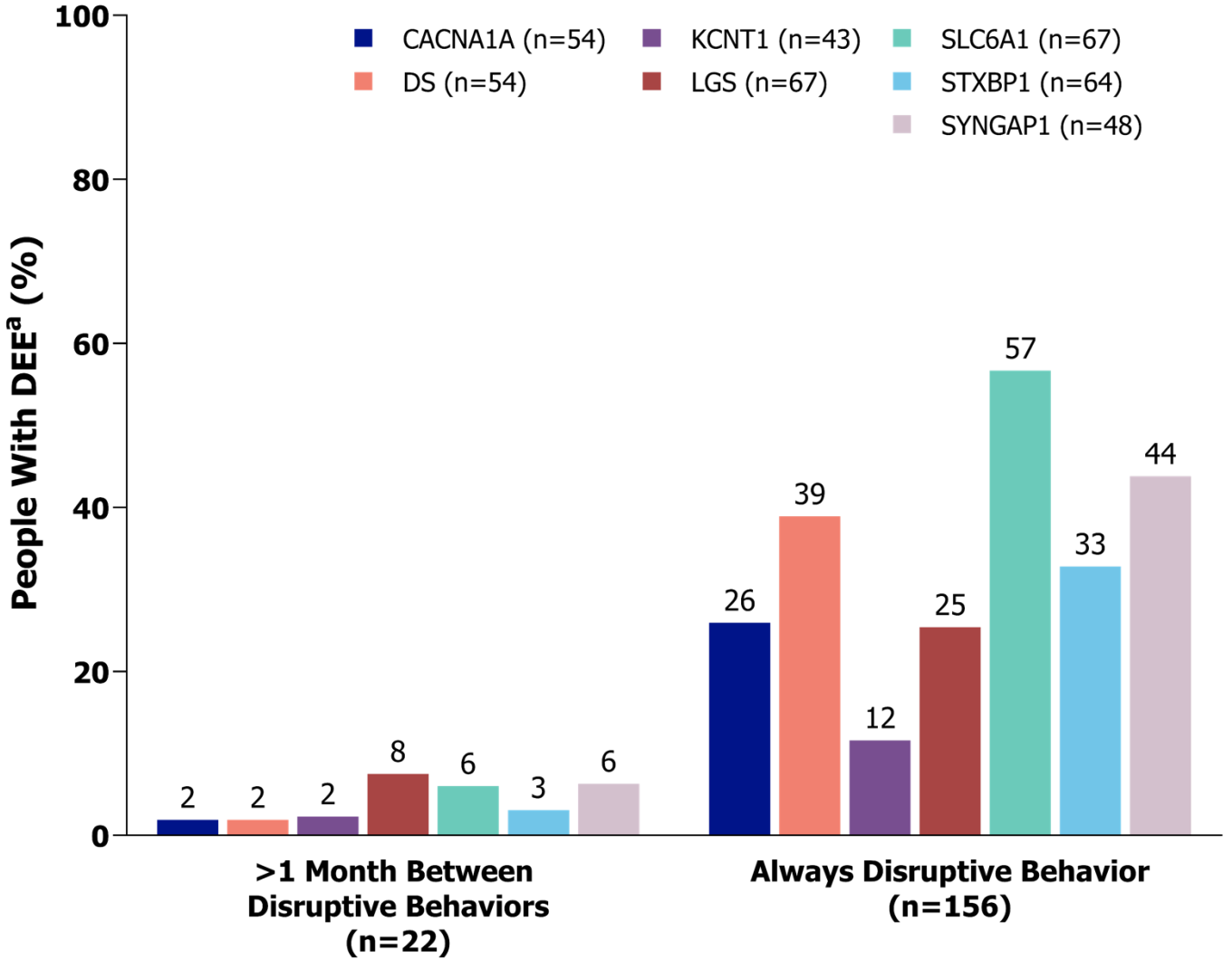
Disruptive Behaviors by DEE (n=397)



Disruptive behavior was defined in the survey as "any of the following – hitting, biting, kicking, shouting, hair pulling, swearing, harsh language, throwing objects, refusal to cooperate, destruction of property, threatening physical harm, invading a person's personal space, anger".

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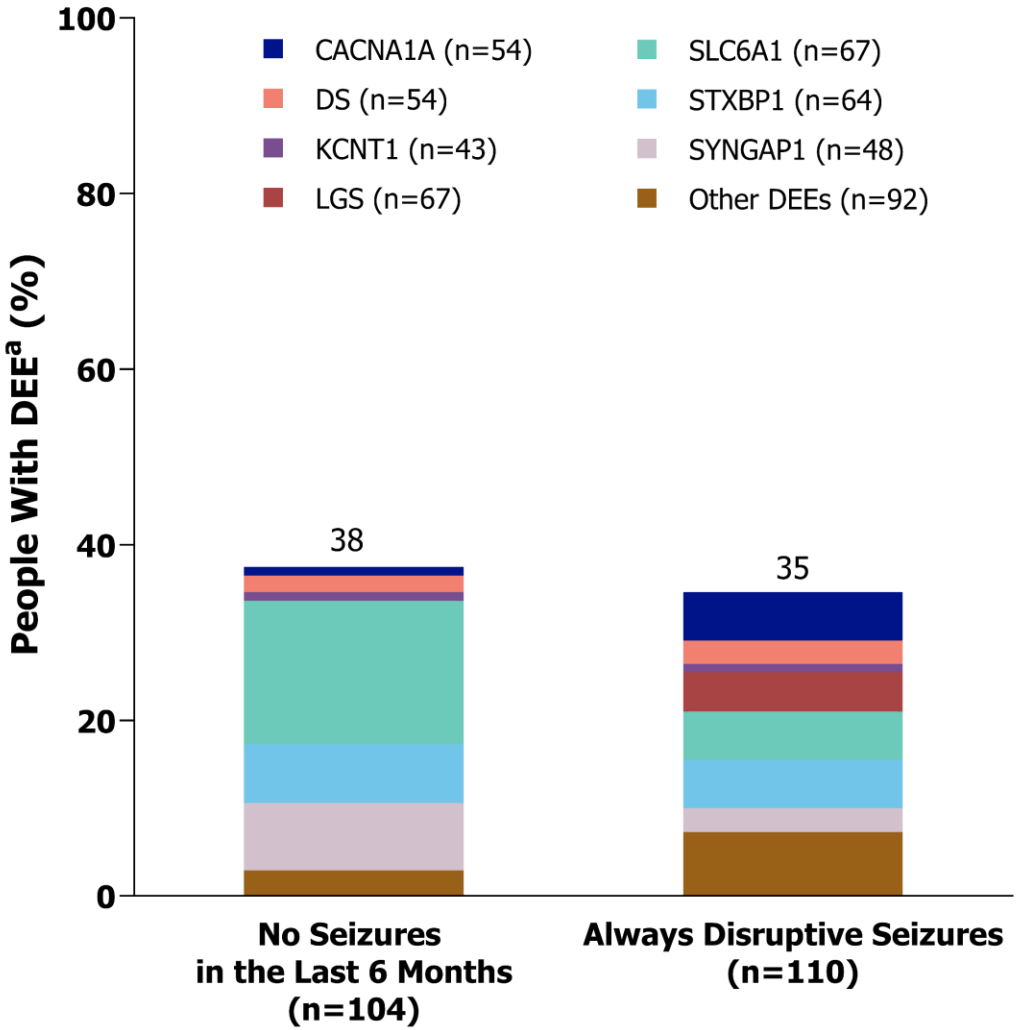
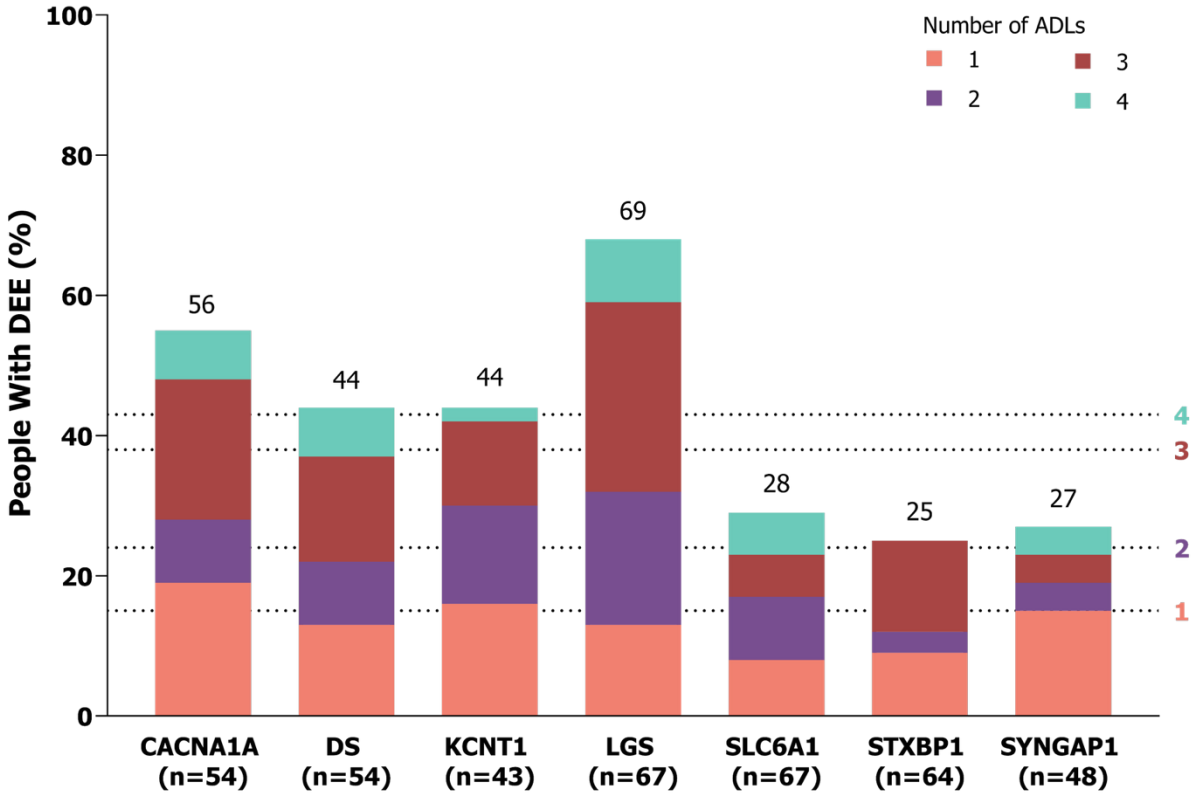
Always Disruptive Behavior by Disruptive Seizure Frequency and DEE (N=489)



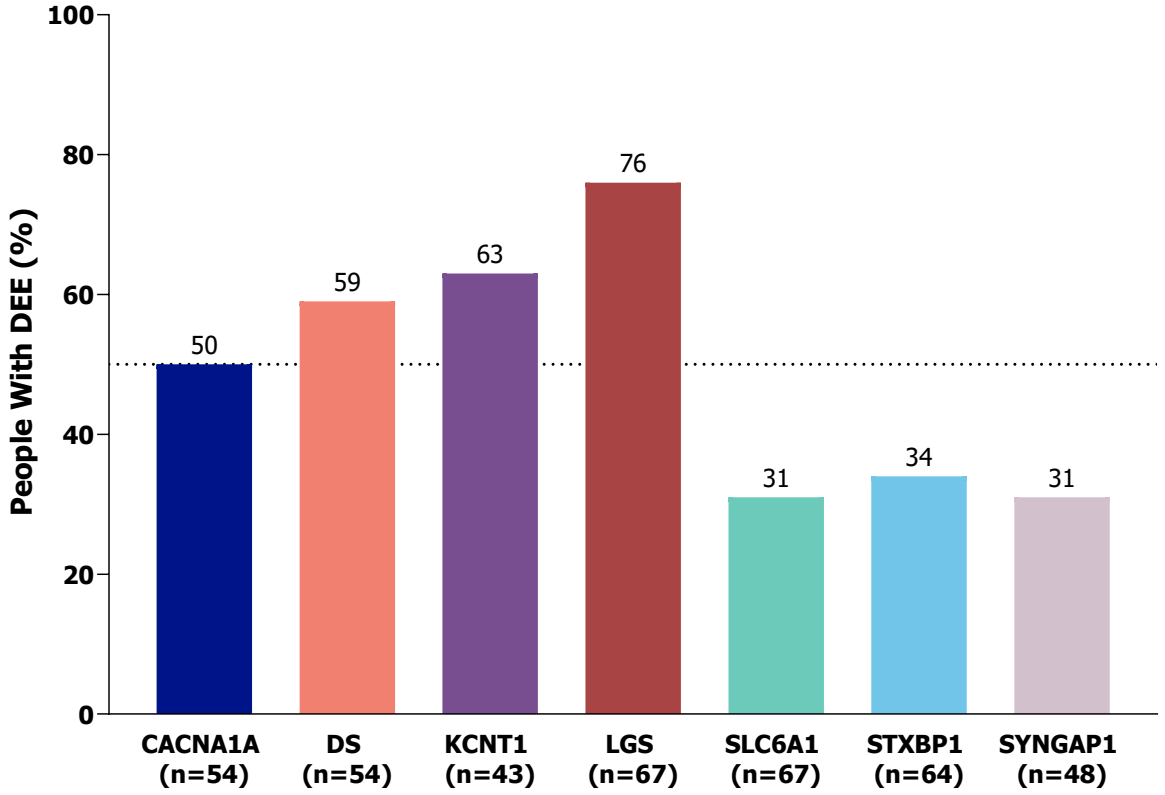
[a]As reported by caregivers.
Wilson score binomial interval (lower, upper): No seizures in the last 6 months (29%, 47%); Always disruptive seizures (26%, 44%).
CACNA1A, CACNA1A-related disorder; DEE, developmental and epileptic encephalopathy; DS, Dravet syndrome; KCNT1, KCNT1-DEE; LGS, Lennox-Gastaut syndrome; SLC6A1, SLC6A1-related neurodevelopmental disorder; STXBP1, STXBP1-DEE; SYNGAP1, SYNGAP1-DEE.

Temporary Loss of Abilities Due to Disruptive Seizures by DEE (N=489)

ADLs



Communication



ADLs: feeding, toileting, bathing/personal hygiene, and dressing.
The horizontal dashed lines represent the percentage of respondents across all primary DEE diagnoses (N=489).
ADLs, activities of daily living; CACNA1A, CACNA1A-related disorder; DEE, developmental and epileptic encephalopathy; DS, Dravet syndrome; KCNT1, KCNT1-DEE; LGS, Lennox-Gastaut syndrome; SLC6A1, SLC6A1-related neurodevelopmental disorder; STXBP1, STXBP1-DEE; SYNGAP1, SYNGAP1-DEE.

Conclusions

- Disruptions to daily life in individuals with DEE are interconnected and complex
- Multiple daily disruptive behaviors were reported at similar rates (31%–38%) in people with always disruptive seizures, no disruptive seizures for >6 months, and with or without seizure clusters
- Nearly half of caregivers reported that disruptive seizures/behavior led to temporary loss in abilities
  - Impairments in ADLs have previously been associated with reduced quality of life in other patient populations[1]
- Continued examinations of typical and disruptive experiences and their relationships with loss of abilities in people with DEE are warranted

1. Wu Y, et al. *Front Public Health*. 2024;12:1398361.
ADLs, activities of daily living; DEE, developmental and epileptic encephalopathy.

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PCDH19 Alliance

SLC6A1 Connect

STXBP1 Foundation

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