Exploring simplified screening cut-offs: classification of KCNQ2-DEE patients into age-adjusted disease phenotypes

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Background

- KCNQ2 Developmental and Epileptic Encephalopathy (KCNQ2-DEE) is a rare, early onset condition that involves seizures in infancy and a range of developmental impairments throughout life.
- The heterogeneity of signs, symptoms, and impacts across age groups makes assigning severity based on phenotypic presentation challenging.
- Cossu et al. (2023) defined three phenotypic categories (mild, severe, and profound), based on neurodevelopmental features and symptoms.
- This criterion was developed to derive phenotype classifications in a KCNQ2-DEE interview study.

Methods

- 53 parents of children with KCQN2-DEE, 1-18 years of age, were recruited for a concept elicitation study.
- The preliminary screening interview included questions about gross motor function (e.g., walking) and communication abilities (e.g., speaking) to categorize the children as either mild, severe, or profound.
- Children were further categorized by age (in years) into five groups (1-2, 3-5, 6-8, 9-11, 12-18).
- Participants were classified by phenotypic severity and age so that a representative sample could be recruited.
- KCNQ2-DEE expert input (n=3) was obtained mid-study to review the domains and abilities by age, and the phenotypic classifications were updated to help better reflect all age ranges.

Figure 1: Approach to KCNQ-2 phenotype screening

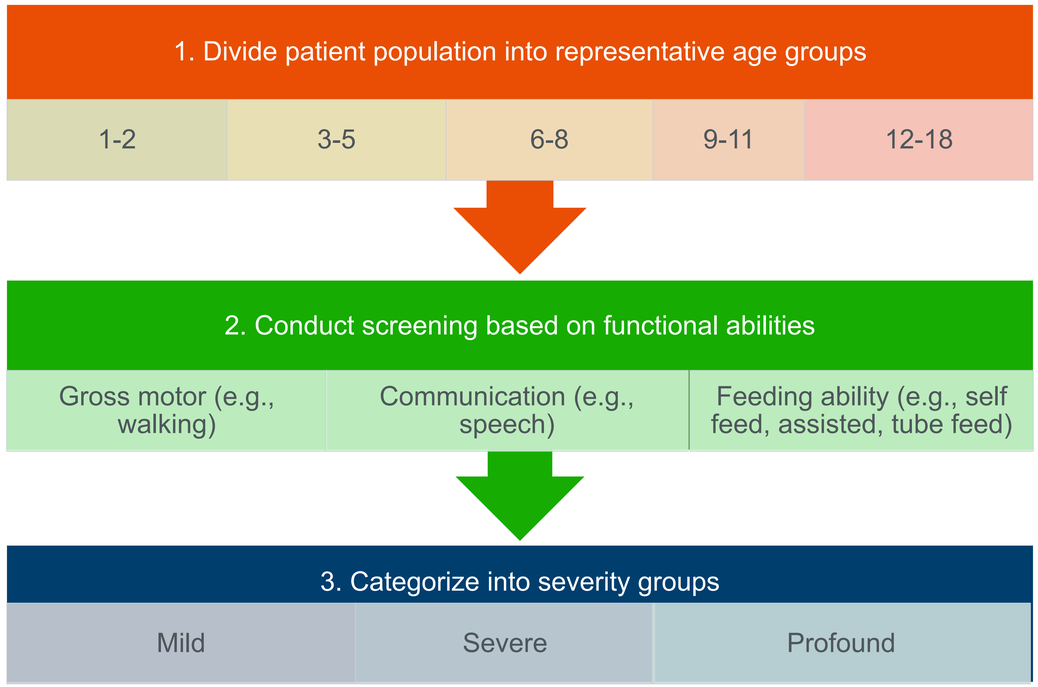
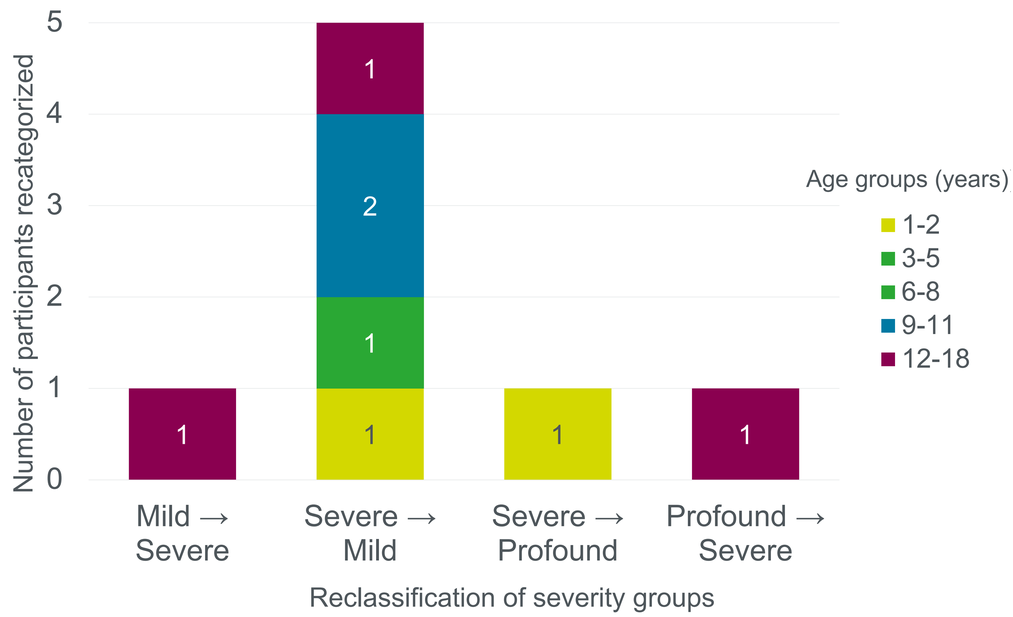


Figure 2. Participants reclassified across age groups and severity levels



Results

- We identified that the criteria and the neurodevelopmental variance due to age led to the potential for misclassification.
- Using only gross motor and communication as a classification of severity in the youngest age groups (1-2; 3-5) resulted in skewed effects, as it led to children being overcategorized into the profound phenotype group.
- Phenotypic categorization was updated (Figure 1), with consideration to Cossu et al, to include feeding ability (self-fed, assisted, or tube feeding), resulting in the re-classification of n=8 participants (Figure 2).

Conclusions

- Reclassifying with closer consideration of their developmental milestones and delays this population faces, increased data quality and the representativeness of the study sample recruited.
- For highly heterogenous populations, appropriate classifications based on age and severity is critical.

REFERENCES

Cossu, A., Barco, T.L., Proietti, J., Dalla Bernardina, B., Cantalupo, G., Ghobert, L., Brambilla, I., Giarola, E., Costa, A., De Benito, T. and Bethge, S., 2023. Clinical characteristics of 80 subjects with KCNQ2-related encephalopathy: results from a family-driven survey. *Epilepsy & Behavior*, *142*, p.109153.