The Dragonfly Study

A Longitudinal Natural History Registry of Individuals with SCN2A-Related Disorders

FamilieSCN2A Foundation and the SCN2A Community

Rationale: SCN2A-related disorders are rare neurodevelopmental conditions caused by pathogenic variants in the SCN2A gene. While seizure control has historically served as a common therapeutic endpoint, emerging evidence suggests a broader phenotypic spectrum requiring deeper understanding. The Dragonfly Study was launched in 2024 by the FamilieSCN2A Foundation in collaboration with the National Organization for Rare Disorders to longitudinally capture real-world data from individuals with SCN2A variants. This registry aims to identify evolving clinical features, assess treatment effectiveness, and support the development of novel therapeutics.

Methods. The Dragonfly Registry is a global, patient-reported, longitudinal natural history study hosted on the IAmRare platform. Caregivers of individuals with confirmed SCN2A variants complete structured survey modules covering demographics, genetic findings, clinical milestones, comorbidities, medication use, and treatment outcomes. Participants are encouraged to update data every six months.

Results. Initial analyses of the first 150 enrollees reveal:

- Median age of SCN2A diagnosis is ~2 years, ranging from infancy to adulthood.
- Communication and learning challenges are the most prevalent features, surpassing seizures in frequency.
- Fewer than half of participants report seizures.
- Milestone data across motor, cognitive, social, and communication domains demonstrate a wide but continuous distribution of developmental capabilities.
- Early findings indicate that areas like GI symptoms and motor deficits may merit more clinical and research attention.

Conclusions. The Dragonfly Study is a family-powered longitudinal registry capturing the diverse phenotypes and treatment experiences of individuals with SCN2A-related disorders. Preliminary data highlight the need for broader clinical outcome measures and suggest that a shift beyond seizure-centric measures is warranted. Ongoing data collection and future analyses—especially those stratified by variant function—are expected to inform clinical practice, guide therapeutic development, and support more individualized treatment strategies.

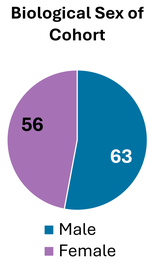

FIGURE 1: Participants in the **Dragonfly Study**—SCN2A families and caregivers—were recruited through the FamilieSCN2A Foundation's contact registry, social media, and newsletters between July 2024 and June 2025. Of the 154 who consented, 121 participants completed one or more surveys capturing demographics, genetic variant information, medical history, and developmental milestones. Shown in this figure are the Dragonfly Study recruitment logo and a breakdown of the cohort's biological sex.

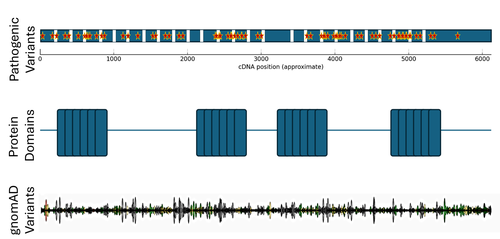

FIGURE 2. Schematic alignment of canonical SCN2A cDNA and approximate location 95 variants reported from participants in the Dragonfly Study. Additionally shown are the corresponding SCN2A proteins domains (transmembrane ion channels depicted in blue blocks) and known single nucleotide polymorphisms (SNPs) identified through population-scale sequencing data (gnomAD). This visualization allows comparison of variant distribution relative to transcript structure and highlights regions of interest for functional and clinical relevance.

Country of Residence	Count
United States	85
Australia	4
Canada	4
Netherlands	4
United Kingdom	4
South Korea	3
Spain	3
Poland	2
Austria	1
Colombia	1
Georgia	1
Germany	1
Italy	1
Latvia	1
Mexico	1
Romania	1
Russia	1
Ukraine	1

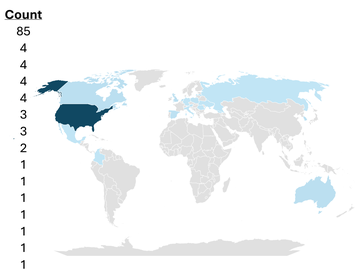

FIGURE 3: Country of residence for Dragonfly Study participants. The figure displays the geographic distribution of enrolled participants across 18 countries.

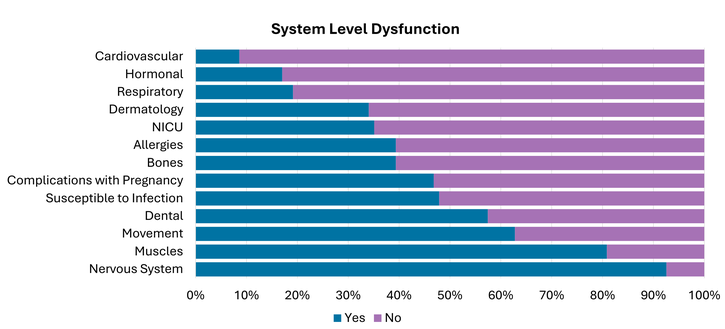

FIGURE 4: Respondents reported whether their affected loved one experienced medical challenges or dysfunctions across various biological systems, as well as any complications during pregnancy or the neonatal period.

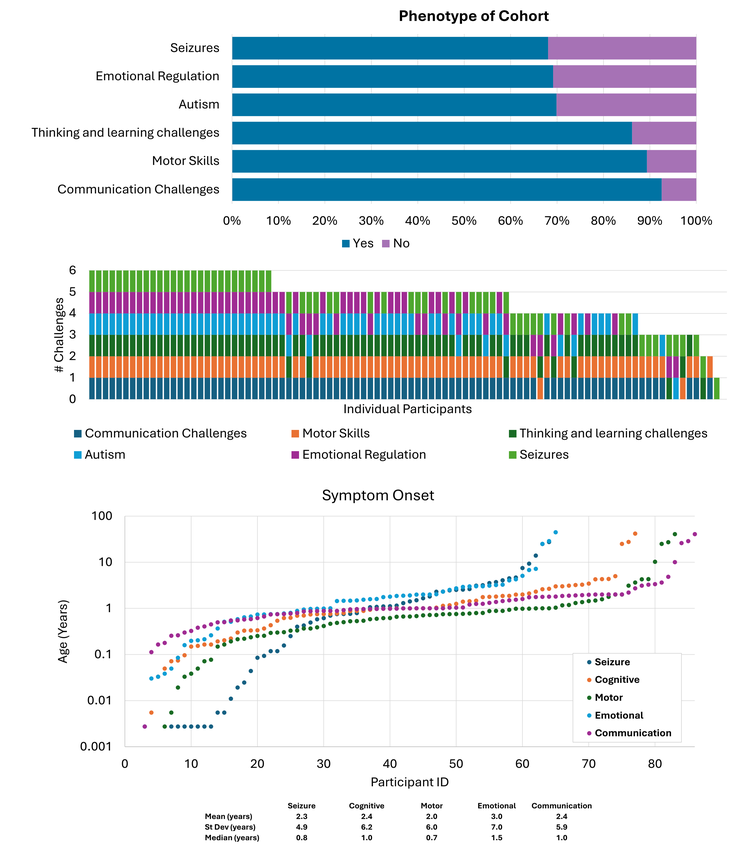

FIGURE 5: Respondents were asked to report the phenotypes exhibited by their loved ones with SCN2A variants, including seizures, emotional regulation challenges, autism, thinking and learning challenges, motor skill challenges, and communication challenges. Plots display: **(A)** the percentage of the cohort affected by each challenge, **(B)** individual-level data showing the number of challenges experienced per participant, and **(C)** the age of onset for each symptom, including mean ± SD and median values.

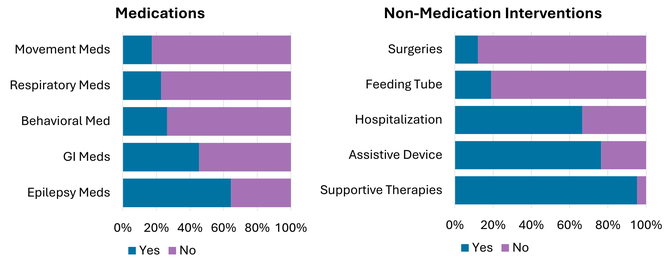

FIGURE 6: Respondents were asked to report both **(A)** medications (for movement, respiratory, behavioral, gastrointestinal, and epilepsy-related issues) and **(B)** non-medicative interventions, including surgeries, hospitalizations, feeding tubes, assistive devices (for mobility and communication), and supportive therapies (physical, occupational, and communication therapies).

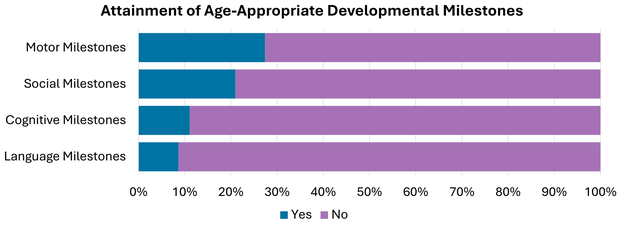

FIGURE 7: Respondents with children aged 5 years and under were asked 162 questions aligned with CDC developmental milestone guidelines. Questions spanned four categories: motor, social, language, and cognitive milestones. Age-adjusted scores were calculated for each participant to assess whether age-appropriate developmental milestones had been attained.

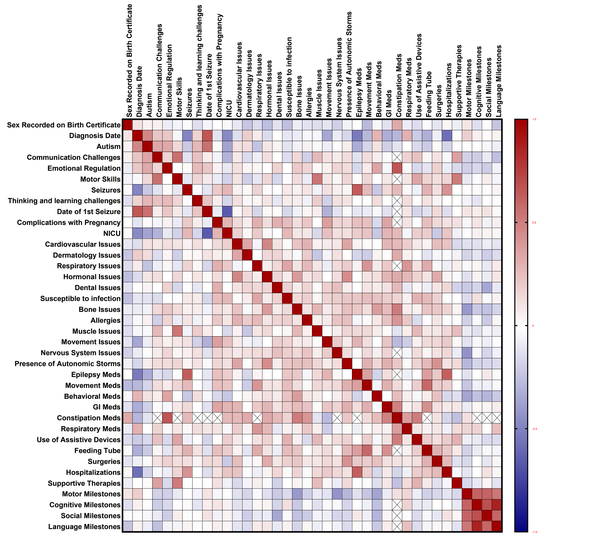

FIGURE 8: To explore relationships among all categories of questions in the survey, we generated a correlation matrix. This approach helps identify patterns of co-occurrence across different clinical features and interventions. Strong positive correlations (dark red) suggest that certain traits or outcomes tend to appear together, while strong negative correlations (dark blue) indicate traits that are inversely related.

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