Case study

Translating patient priorities into objective endpoints for autonomic dysfunction in AHC

About RARE Hope

RARE Hope is a patient-centered organization dedicated to accelerating the development of therapeutics for rare neurological diseases. Adopting a unique "platform approach," the organization focuses on Alternating Hemiplegia of Childhood (AHC) as a prototype to build a scalable infrastructure for research, biomarker development, and clinical trial readiness. By leveraging common biological mechanisms and a shared scientific and clinical toolkit — and by uniting scientists, clinicians, and patient families — RARE Hope aims to incubate innovation and de-risk the therapeutic pipeline, ensuring that promising treatments can move rapidly from the lab to the patients who need them.

The opportunity

Leveraging patient experience data to target high-priority autonomic symptoms.

- Paroxysmal episodes, according to AHC patients and their caregivers, are a critical, high-burden aspect of the disease.
- Recent survey data collected by RARE Hope revealed a strong community preference: families prioritize the elimination of paroxysmal (episodic) symptoms over the improvement of chronic baseline symptoms. This insight presents a distinct opportunity to design a clinical study that specifically targets the physiological "storms" that impact quality of life, using patient priorities to define what a meaningful treatment effect looks like.
- While debilitating paroxysmal symptoms like plegia, dystonia, and seizures often dominate the clinical picture of AHC, they can be hard to evaluate in terms of severity. Episodes of autonomic dysfunction, however, may provide a useful opportunity to quantify paroxysmal episodes using a combination of mature sensors and devices used elsewhere for health or fitness monitoring.

The challenge

Developing a digital biomarker for autonomic dysfunction in AHC.

- Paroxysmal autonomic events (such as sudden changes in heart rate, skin temperature, or pallor) are unpredictable and transient.
- A major technical challenge is distinguishing a disease-driven autonomic episode from normal physiological responses to stress, excitement, or physical exertion in a pediatric population.
- Despite the range of available devices that can measure these features, validated systems with pediatric control data are less available.

The approach

Patient-driven protocol design for autonomic wearable analysis.

- RARE Hope is currently designing a pioneering study that translates patient survey insights directly into a technical protocol. Utilizing data from the RARE Hope patient survey, the team identified autonomic dysfunction metrics as a focus area due to their higher-than-anticipated frequency and their value as objectively measurable indicators within the cluster of paroxysmal symptoms that patients and caregivers have prioritized for therapeutic intervention.
- The protocol is being designed to move beyond aggregate data averages. It includes "event detection," attempting to train algorithms to recognize the specific digital signature of an AHC autonomic crash versus baseline activity.
- The study aims to deploy multi-modal wearable sensors capable of capturing a suite of autonomic signals (potentially including heart rate variability, electrodermal activity, and skin temperature) to create a holistic picture of the patient's physiological state during and between episodes.

The impact

This study represents a significant step toward Patient-Focused Drug Development (PFDD) in rare neurology aligning clinical trial endpoints with patient values.

- ✔ By focusing on the paroxysmal symptoms that families have explicitly prioritized, this research ensures that future clinical trials measure efficacy in a way that translates to real-world quality of life improvements.
- ✔ Providing a digital, objective measure for autonomic dysfunction validates a symptom set connected to paroxysmal episodes, offering a new potential secondary endpoint for candidate therapeutics.
- ✔ Demonstrating the ability to distinguish episodic events from baseline noise may provide drug developers with sensitive tools to prove a drug's specific mechanism of action.