# *What matters to patients?*

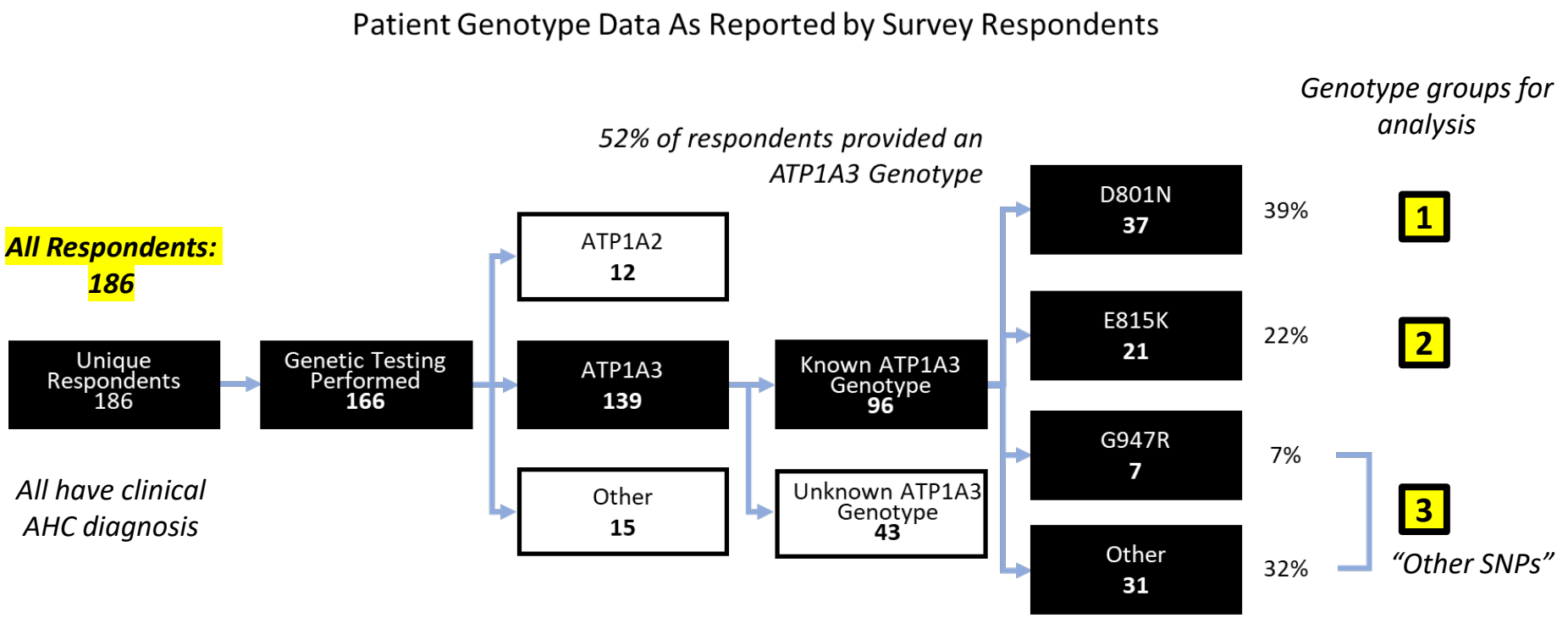
The Patient Survey: A Systematic Investigation of Priorities

**186 Respondents**

Patient survey (circulated fall 2023-winter 2024) queried AHC caregivers on:
(1) currently experienced symptoms
(2) the symptoms they most wanted to eliminate

***Who were the survey-takers?***

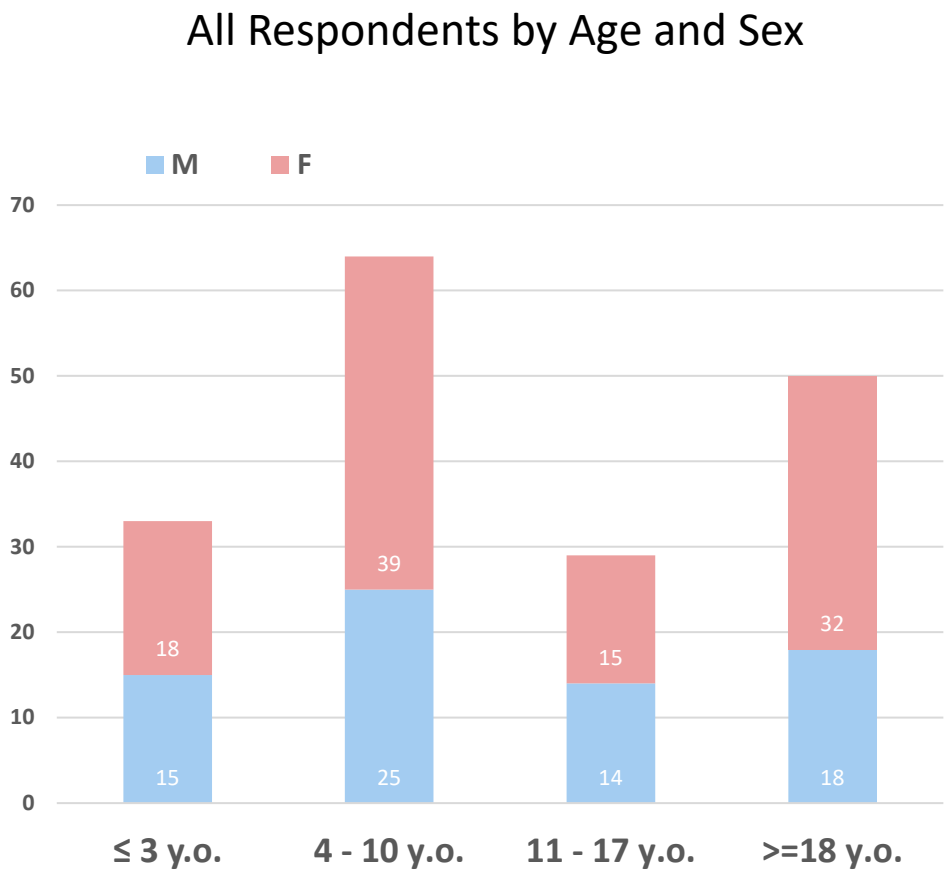
# Survey Respondents




| n | SNP | Location |
|---|---|---|
| 1 | Q140L | IC (post TM2) |
| 1 | V322D | TM4 |
| 1 | E324Q | TM4 |
| 1 | T331fs | TM4 |
| 1 | C333F | IC (post TM4) |
| 1 | A338P | IC (post TM4) |
| 1 | G358S | P-site, part 1 |
| 1 | T360R | P-site, part 1 |
| 1 | L715P | P-site, part 2 |
| 1 | K717del | P-site, part 2 |
| 1 | E754fs | P-site, part 2 |
| 2 | G755S | P-site, part 2 |
| 2 | R756H | P-site, part 2 |
| 2 | T771I | TM5 |
| 1 | S772R | TM5 |
| 1 | N773I | TM5 |
| 1 | N773S | TM5 |
| 37 | D801N | TM6 |
| 1 | D801V | TM6 |
| 1 | G803D | TM6 |
| 1 | T804I | TM6 |
| 1 | D805H | TM6 |
| 21 | E815K | IC (post TM6) |
| 2 | L839P | TM7 |
| 1 | Q851R | TM7 |
| 1 | V919del | TM8 |
| 2 | D923N | TM8 |
| 7 | G947R | TM9 |
| 1 | K996Y | TM10 |

*Expected ratios of most frequent alleles among respondents who knew patient's ATP1A3 genotype*

# Survey Respondents




| Age | M | F | χ2 Test |
|---|---|---|---|
| **≤3 y.o.** | 15 | 18 | 0.60 |
| **4 – 10 y.o.** | 25 | 39 | 0.08 |
| **11 – 17 y.o.** | 14 | 15 | 0.85 |
| **≥18 y.o.** | 18 | 32 | 0.05 |
| **Total** | 72 | 104 | 0.02 |

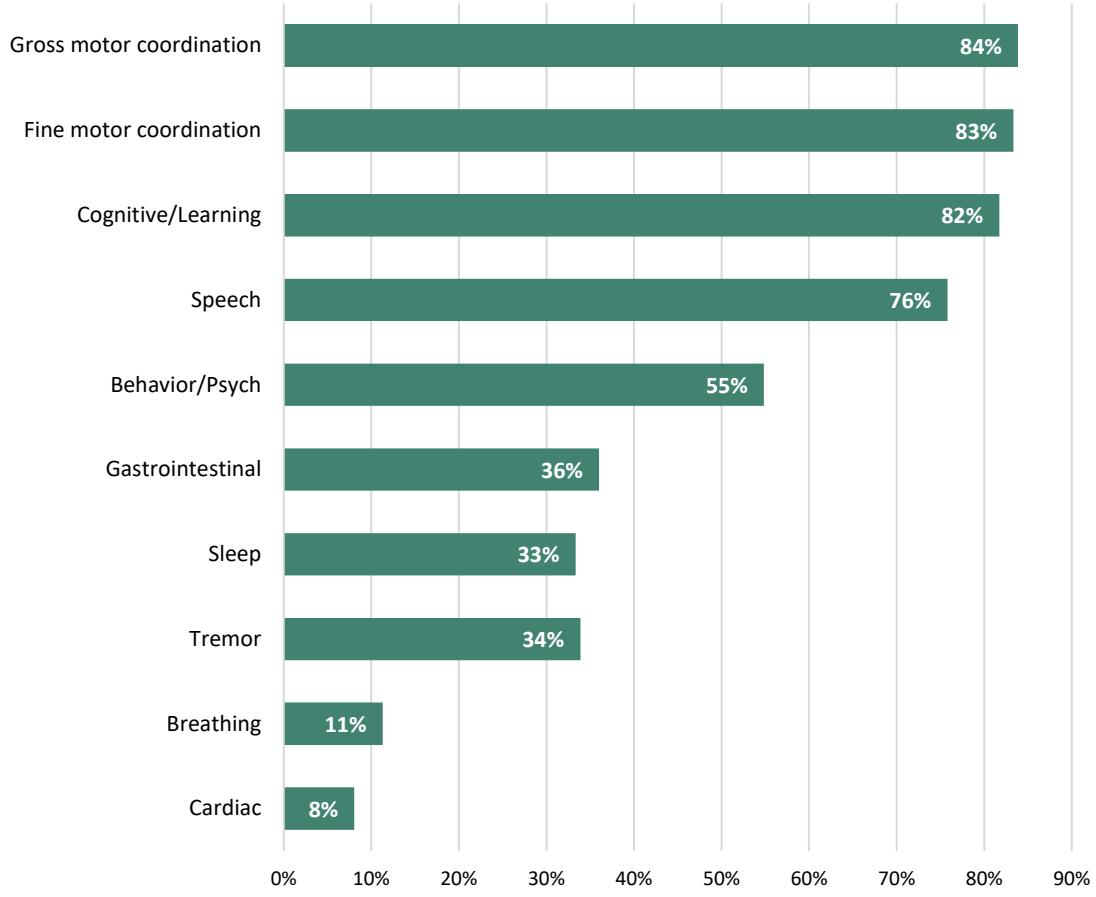
Respondents with Sex Data: 176

*Significantly fewer survey responses for male patients (41%) than female patients (59%)*

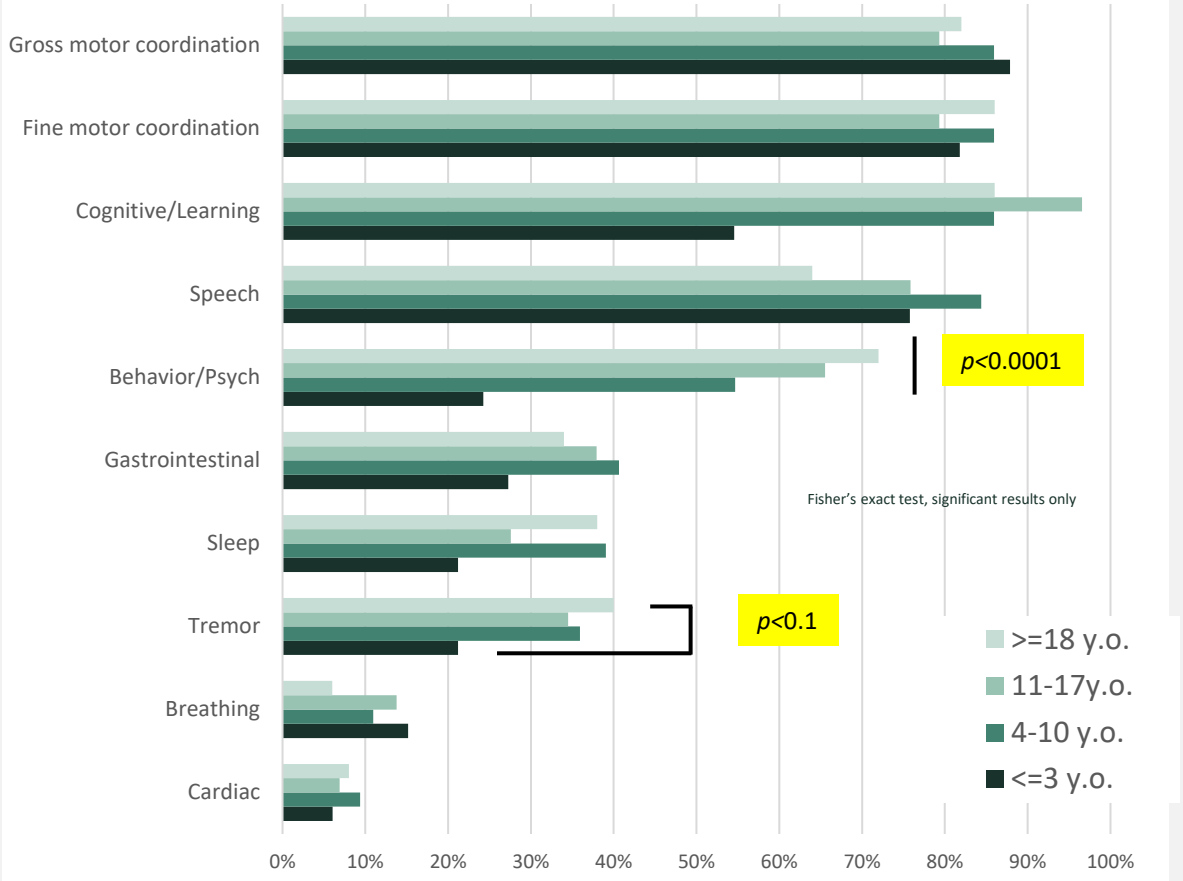
***What is the symptom profile of AHC patients?***

# Understanding Patient Symptoms: Non-Paroxysmal Symptoms

## Non-Paroxysmal Impairments of all AHC Patients



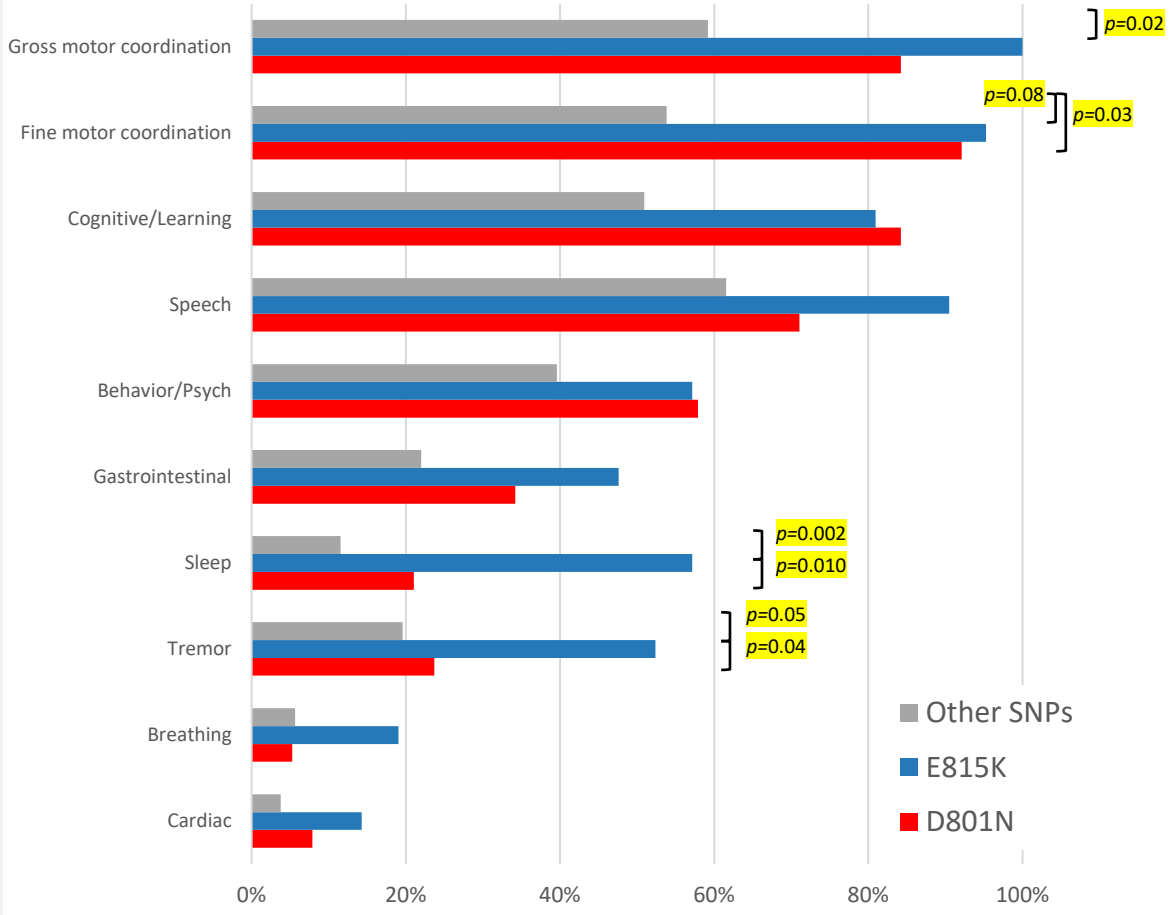

## Prevalence of Non-Paroxysmal Impairments by Age



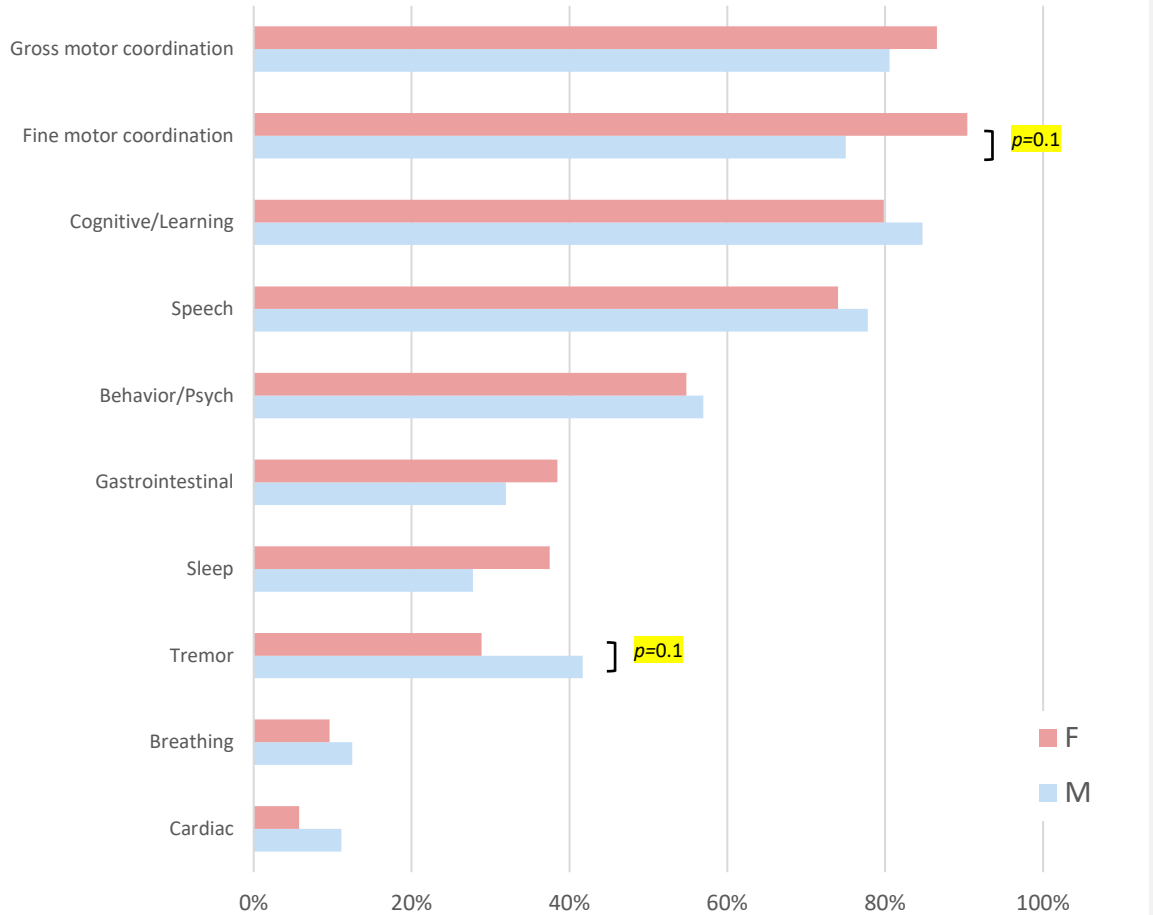

*Non-paroxysmal symptoms are consistent across age groups, except in the prevalence of behavioral/psychological symptoms and tremor*

# Understanding Patient Symptoms: Non-Paroxysmal Symptoms

## Non-Paroxysmal Impairments of AHC Patients by Genotype




## Non-Paroxysmal Impairments of AHC Patients: Male vs. Female

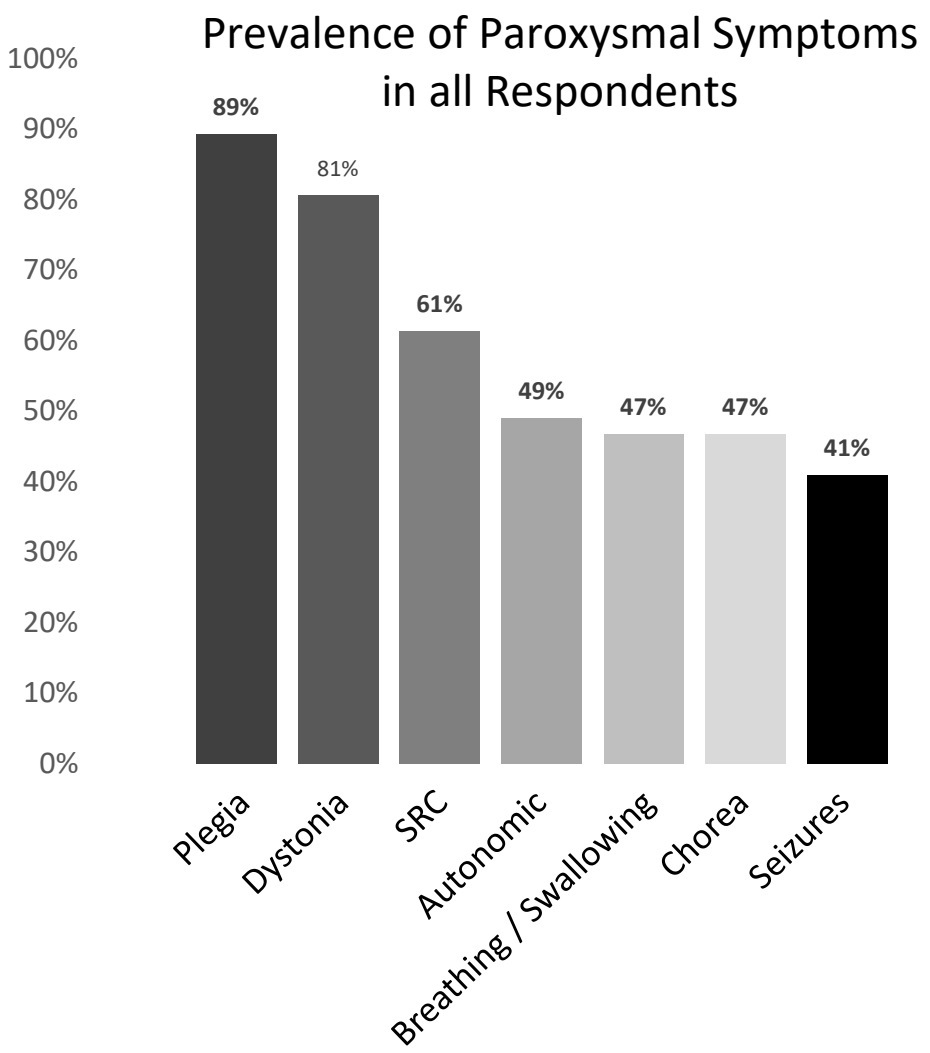


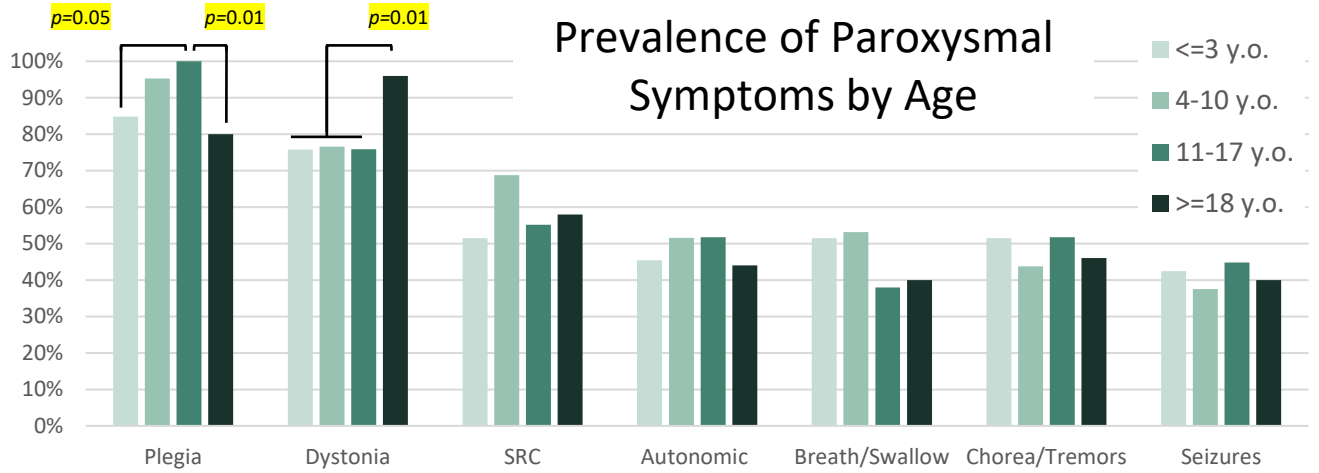

Fisher's exact test, significant results only

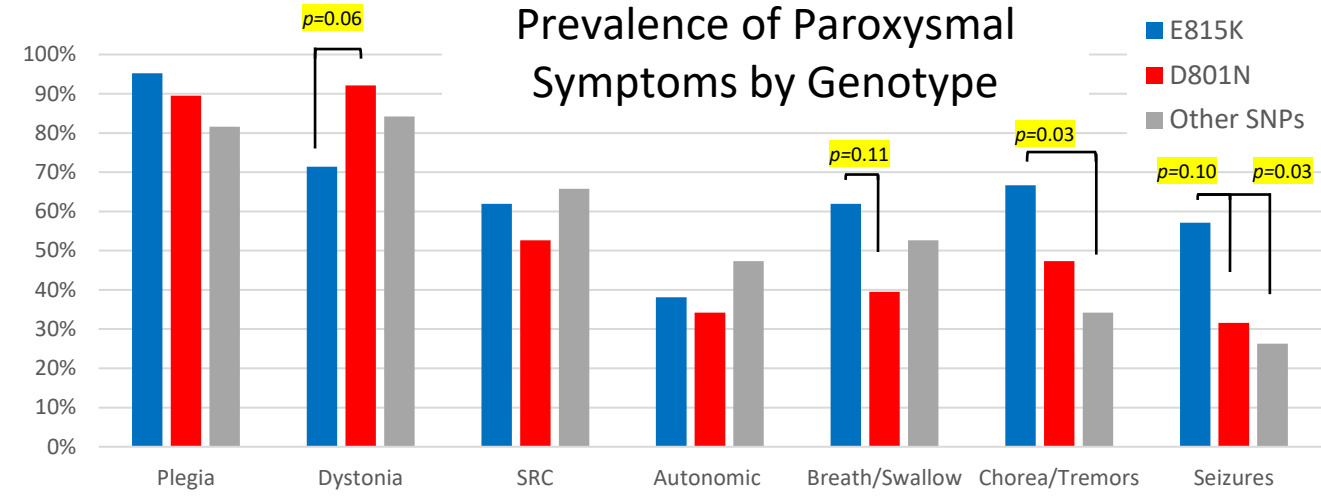
*Prevalence of gross/fine motor challenges is lower for the "Other SNPs" group. Prevalence of sleep issues, tremor are higher in E815K patients.*

*None of the differences in non-paroxysmal symptoms by sex reach statistical significance.*

# Understanding Patient Symptoms: Paroxysmal Symptoms

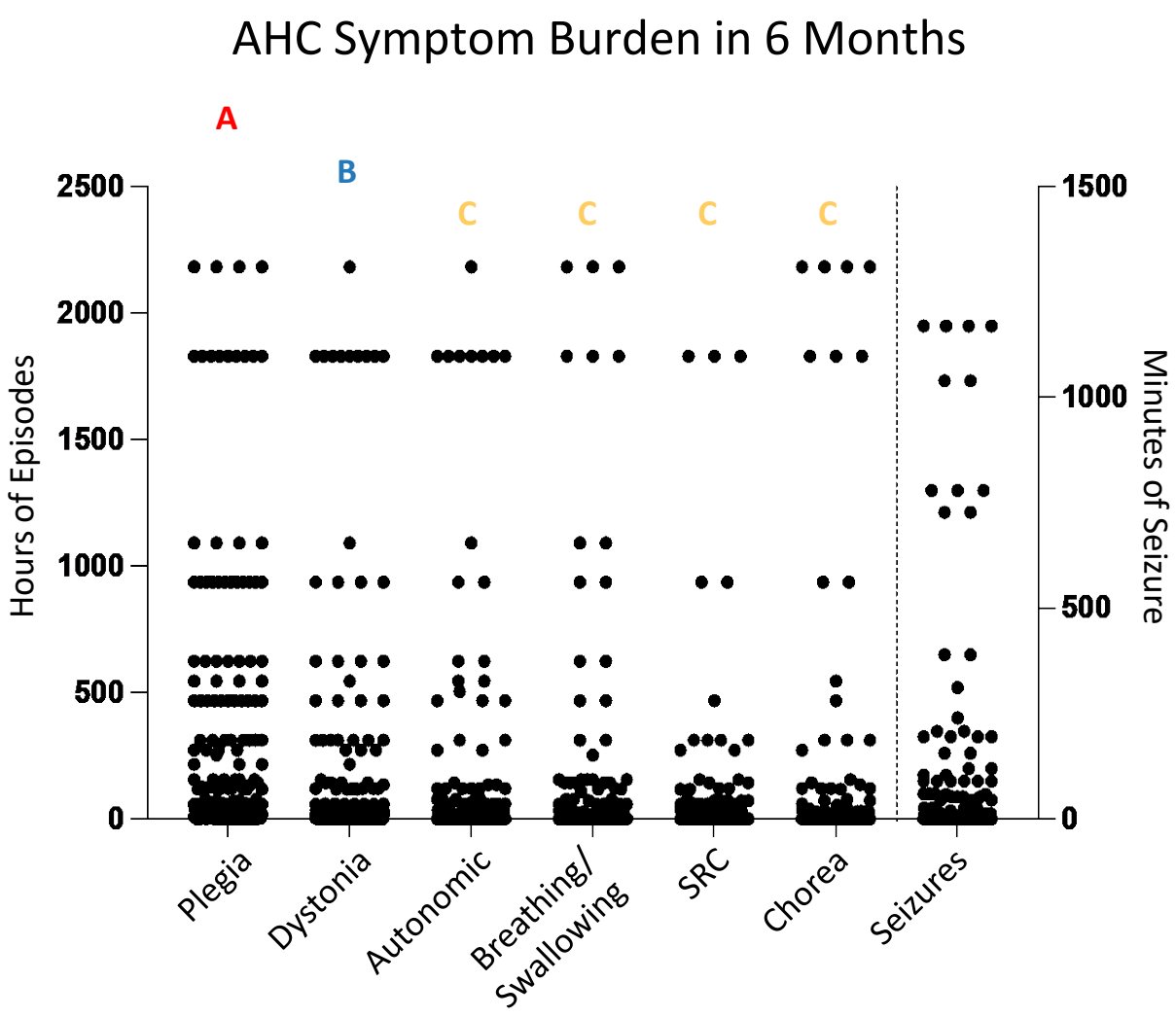



*The prevalence of some paroxysmal AHC symptoms varies by age and genotype.*

# Understanding Patient Symptoms: Paroxysmal Symptoms Burden




"Burden" is the total time spent experiencing a particular symptom within 6 months.

We converted patient responses on the frequency and duration of episodes into a single value to represent "burden."

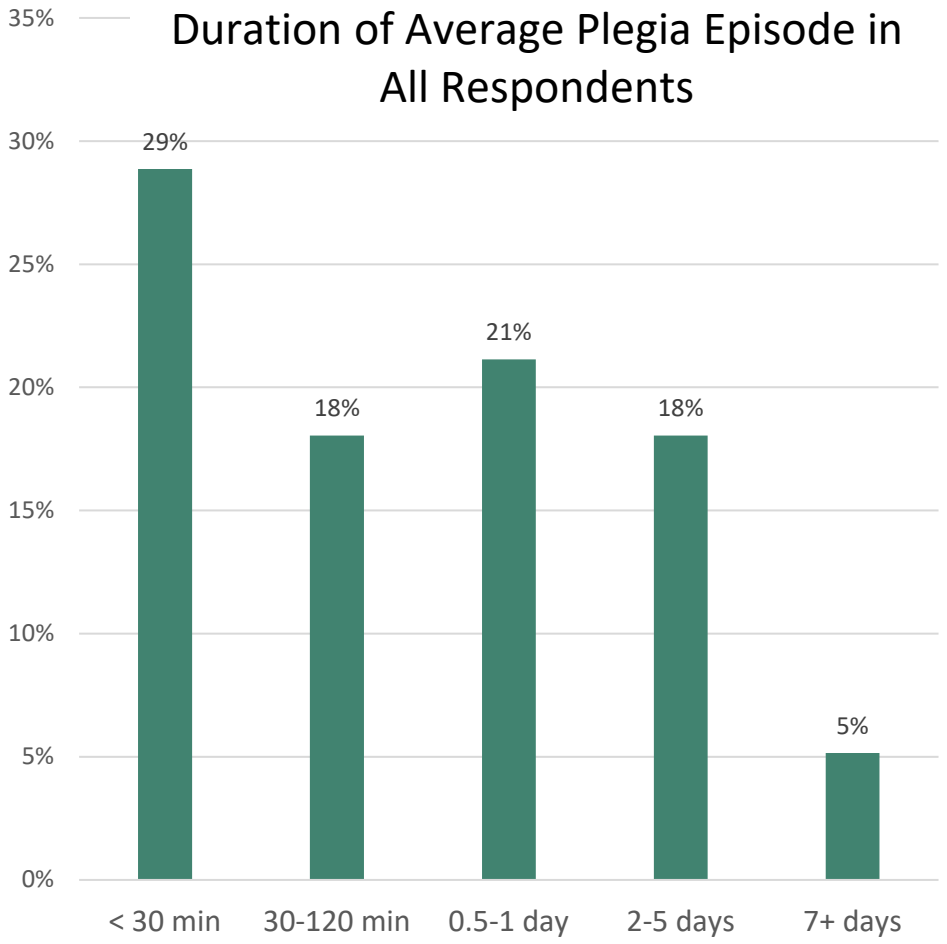
- Letters indicate the results of a statistical test for significance of difference in non-parametric data (Kruskal-Wallis test with Dunn's multiple comparison test) at family-wise alpha threshold = 0.05.
- Scatter columns with a different letter are different from each other. Scatter columns with the same letter are not different from each other.
- Note the different units of the seizure burden

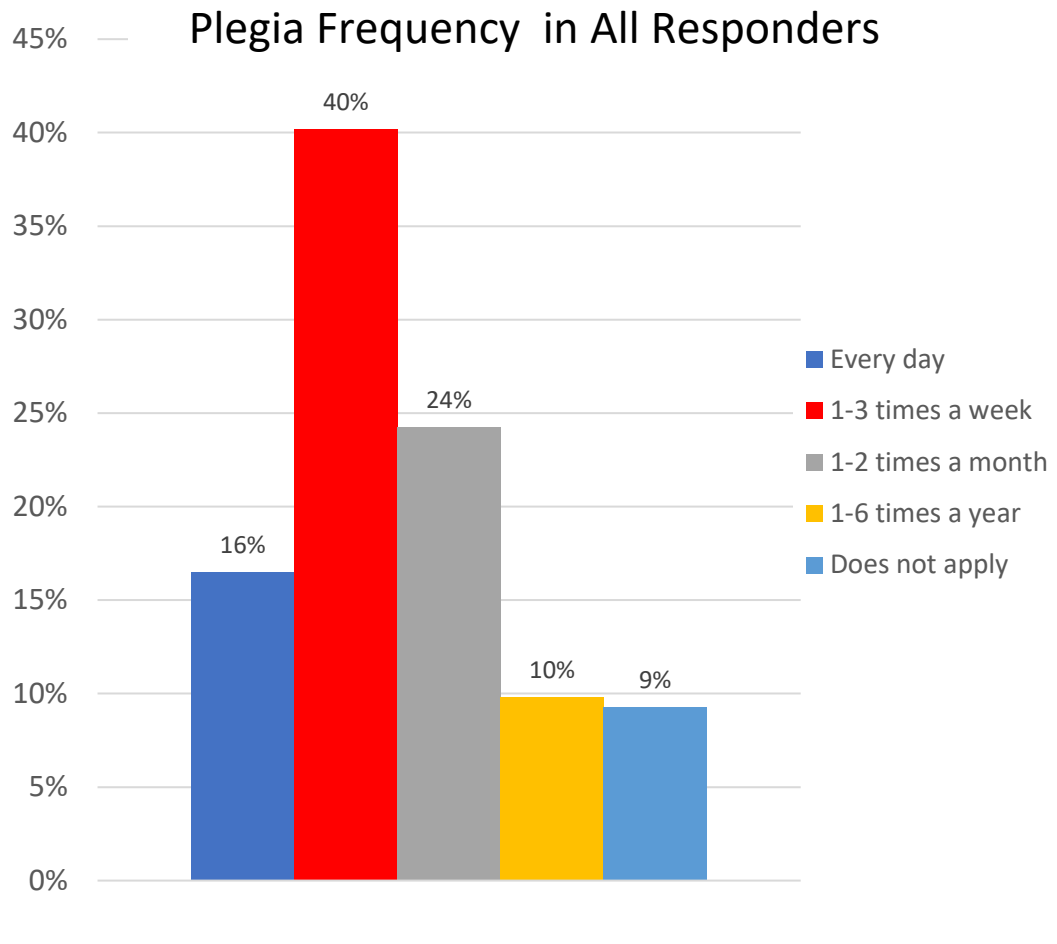
*In terms of hours, the symptoms that present the highest burden across all patients are: (1) plegia; (2) dystonia; and (3) "the rest," excluding seizure*

# Understanding Patient Symptoms

***Plegia***

# Understanding Patient Symptoms: Plegia



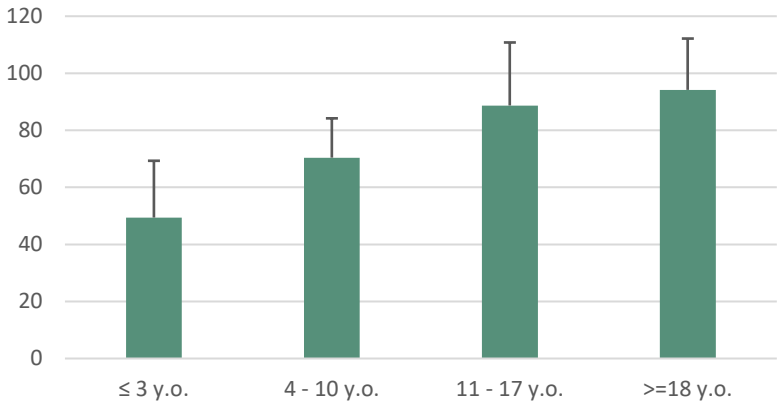




*Plegia duration ranges from minutes to days at a time*

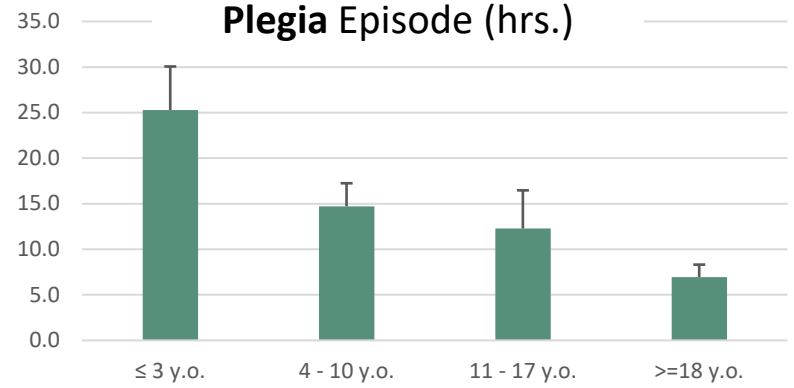
*56% of responders reported plegia one or more times a week*

# Understanding Patient Symptoms: Plegia Burden

Number of **Plegia** Episodes in 6 months




Average Duration of a **Plegia** Episode (hrs.)



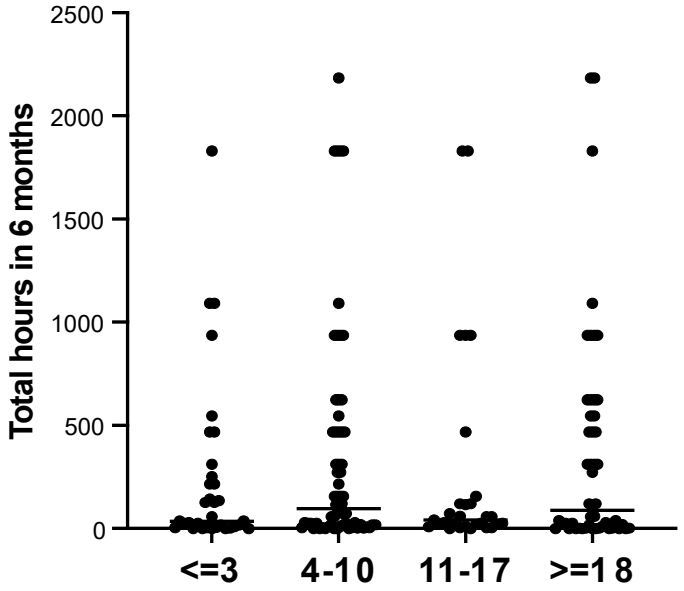

Effect of Age on Plegia

**Increased plegia frequency**– and the total number of plegia episodes in 6 months–with age for AHC patients.

**Shorter duration plegia** for patients as age increases

**Decreased plegia prevalence** in adult patients.

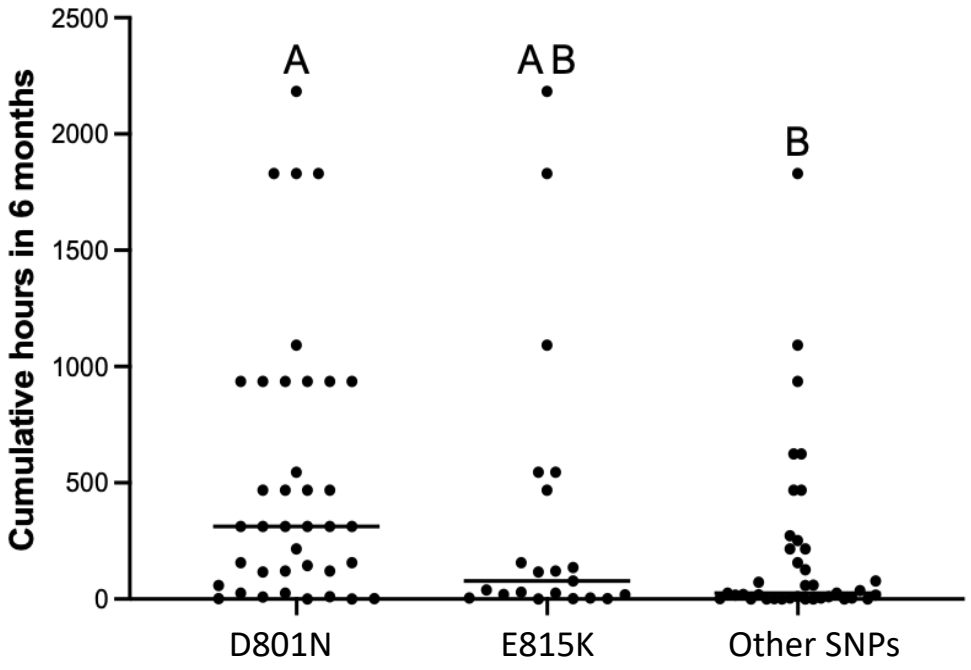
Plegia Burden by Age



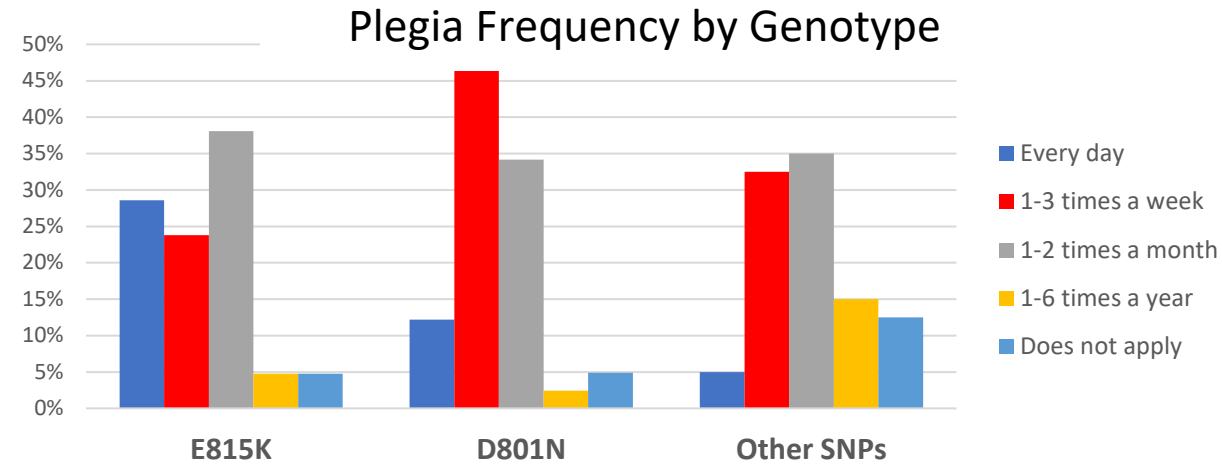

No significant difference in "burden" between the age groups

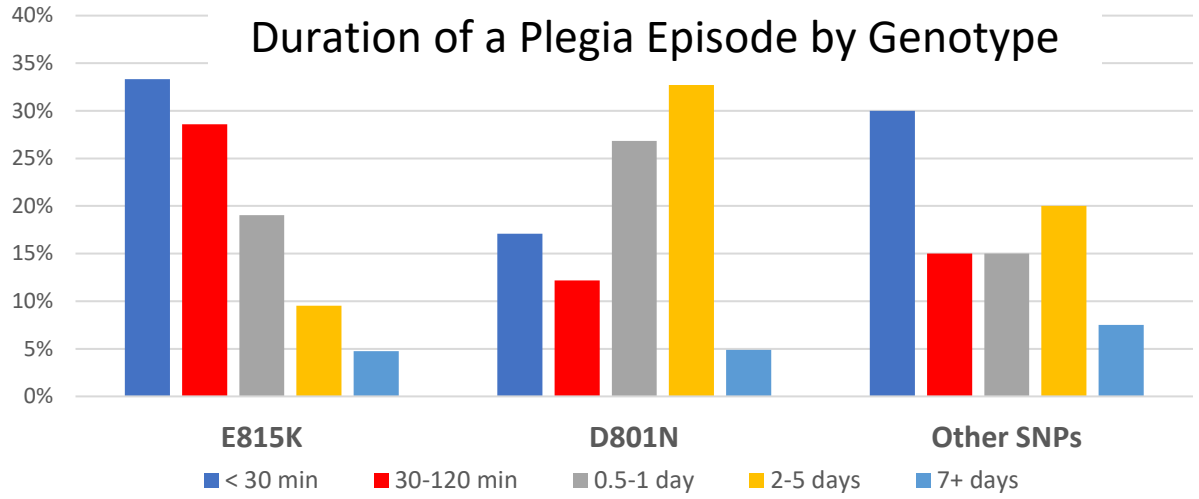
*While the burden of plegia is consistent between age groups, plegia presents differently at different ages*

# Understanding Patient Symptoms: Plegia Burden




D801N patients experience higher "burden" of plegia



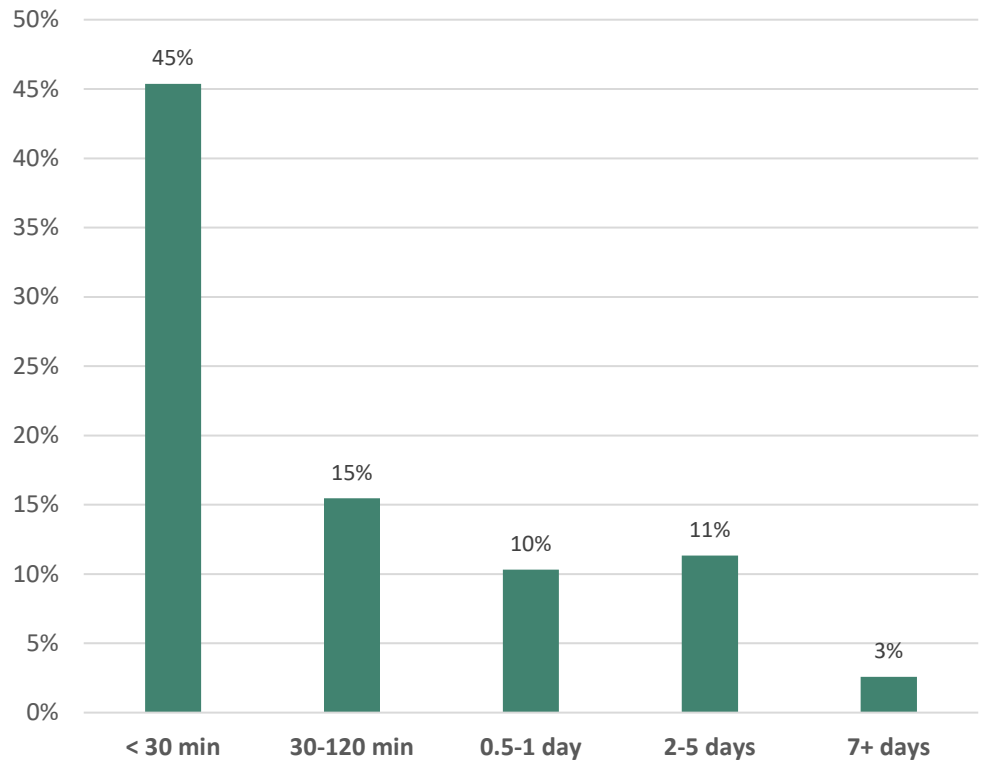




*Plegia burden is higher for D801N patients than E815K patients, and significantly higher than the "other SNPs" group. Longer duration plegia drives this difference, along with lower plegia prevalence in the "Other SNPs group."*

***Dystonia***

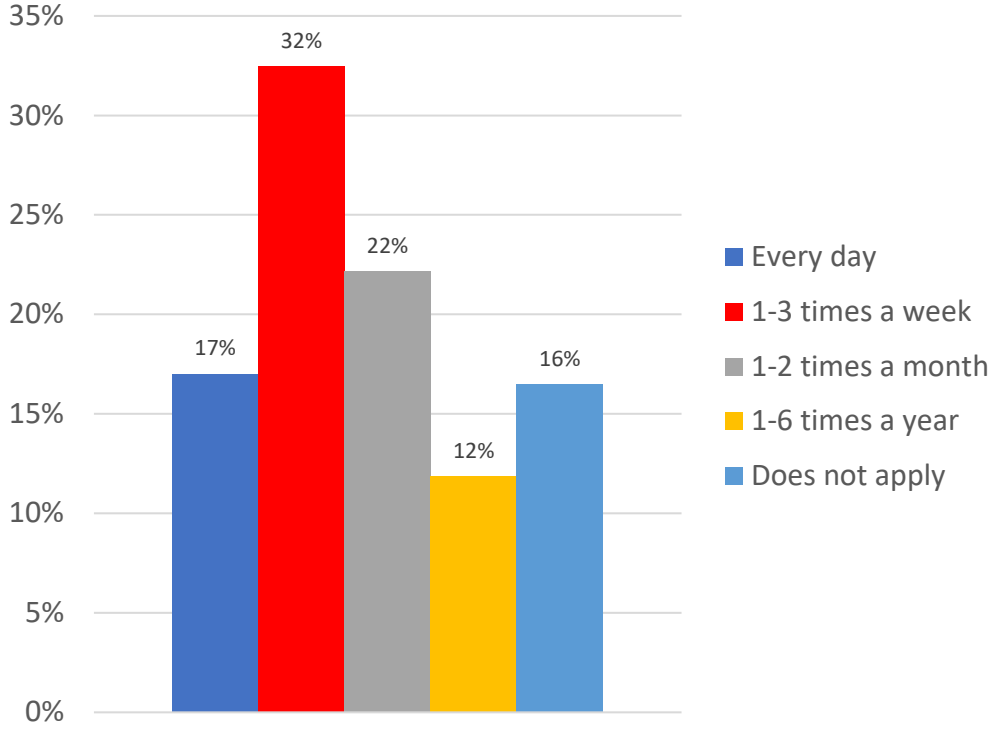
# Understanding Patient Symptoms: Dystonia

## Duration of Average Dystonia Episode in All Respondents



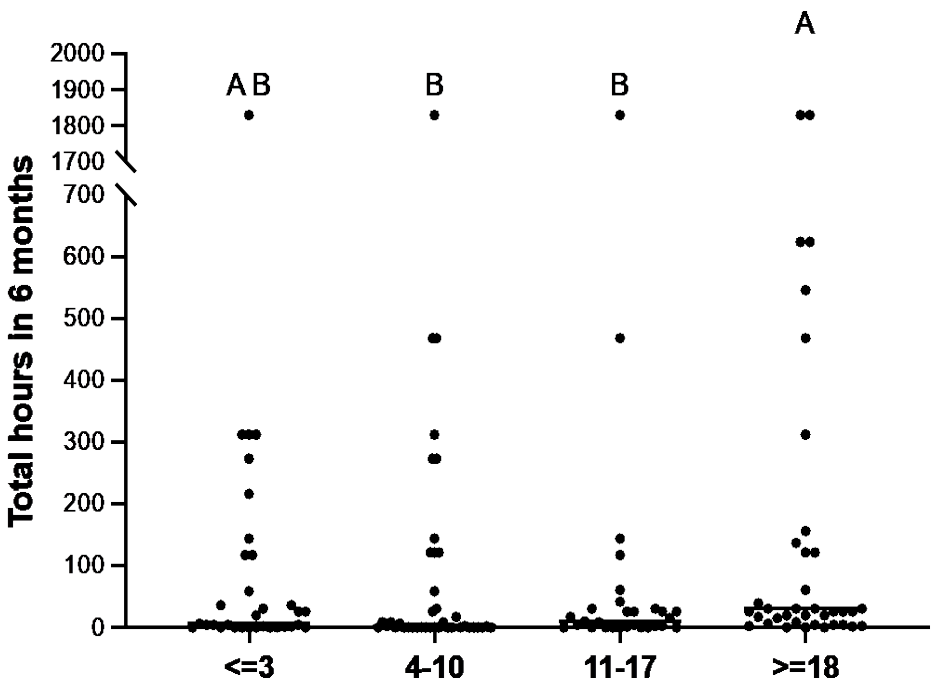

*Most responders experience dystonia lasting under two hours, but 14% reported dystonia persisting over two days*

## Dystonia Frequency in All Responders

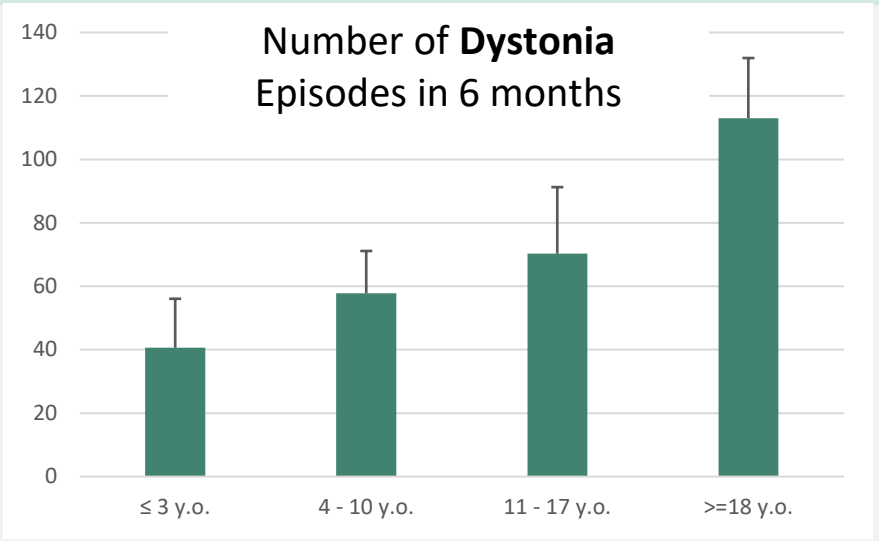


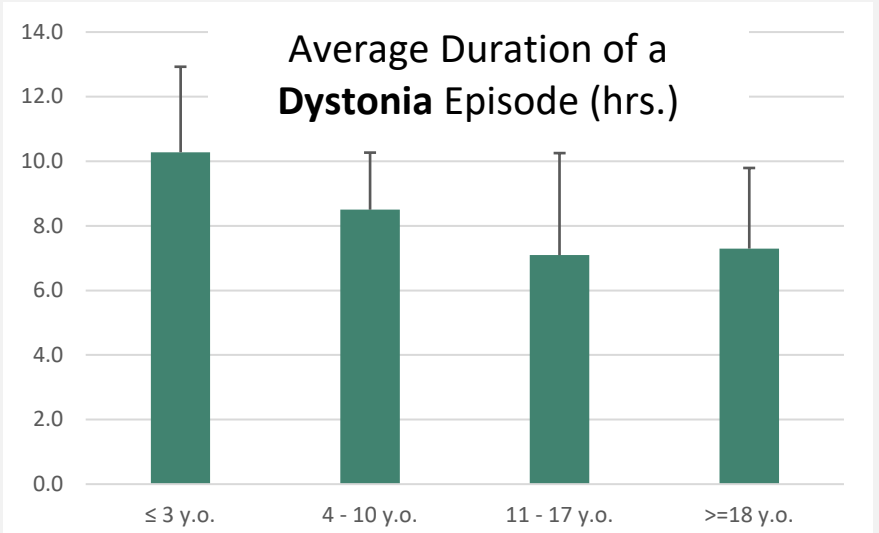

*49% of respondents reported dystonia one or more times a week*

# Understanding Patient Symptoms: Dystonia Burden




Adults experience significantly higher "burden" of dystonia than children




**Effect of Age on Dystonia**

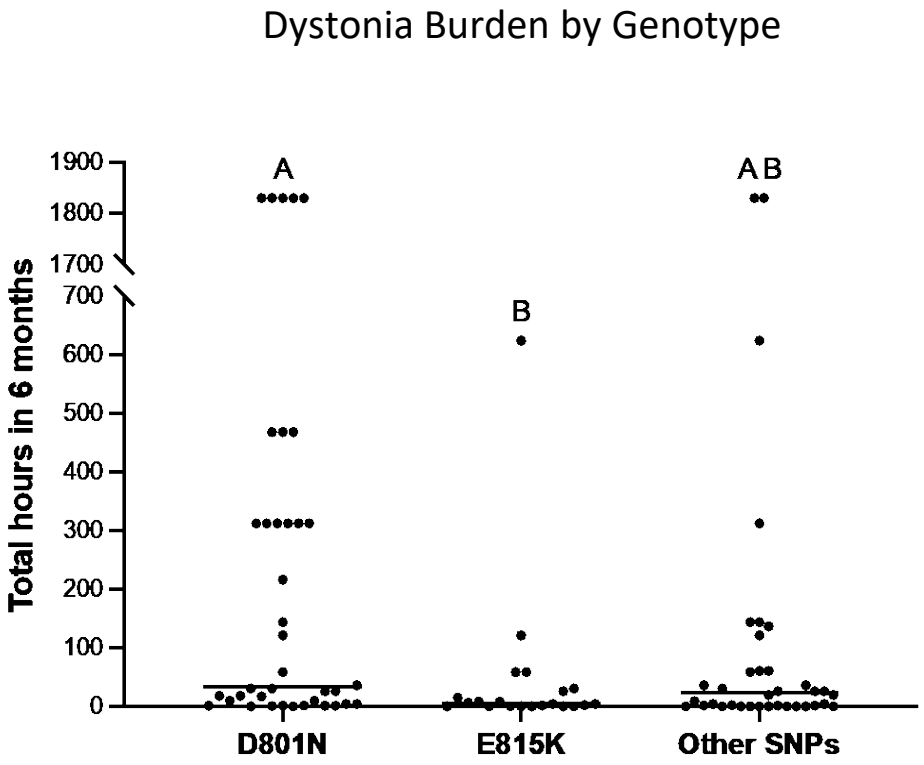
**Increased dystonia frequency**– and the total number of plegia episodes in 6 months– as age increases

**Increased dystonia prevalence** in adult patients.

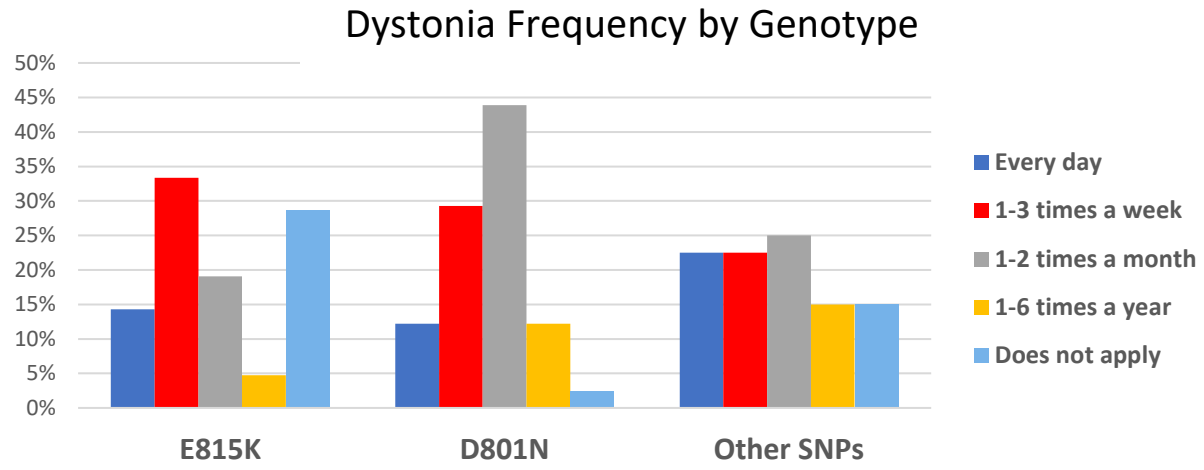
Patients experience **shorter duration** dystonia with age

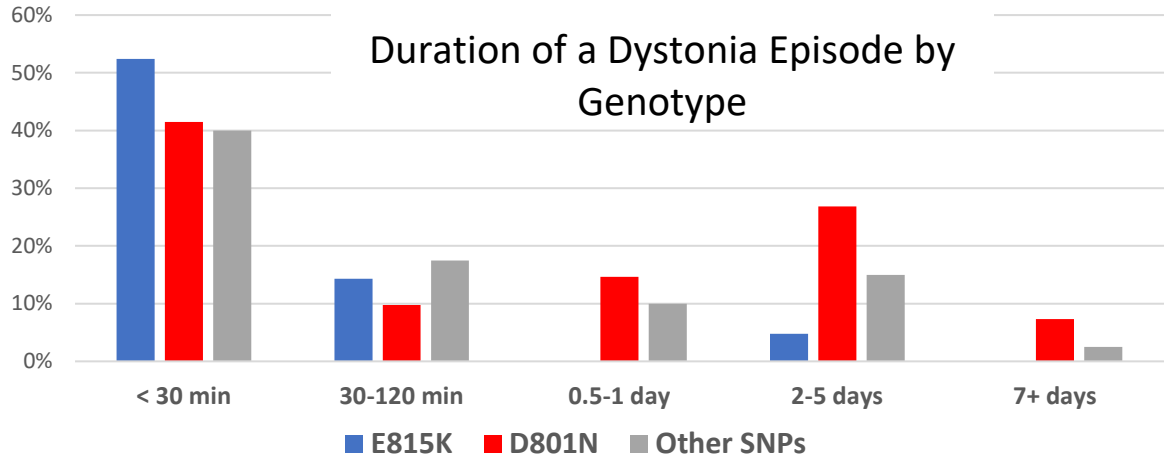
*Dystonia frequency increases and duration decreases as age increases; older patients experience a greater burden of dystonia*

# Understanding Patient Symptoms: Dystonia Burden



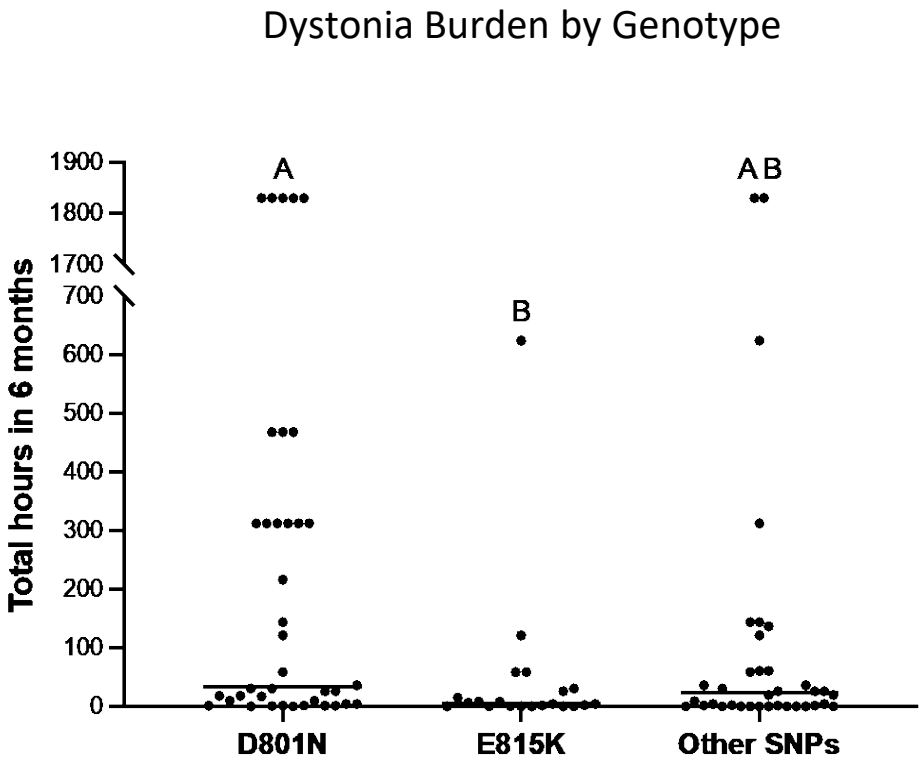

D801N patients experience significantly higher "burden" of dystonia than E815K patients



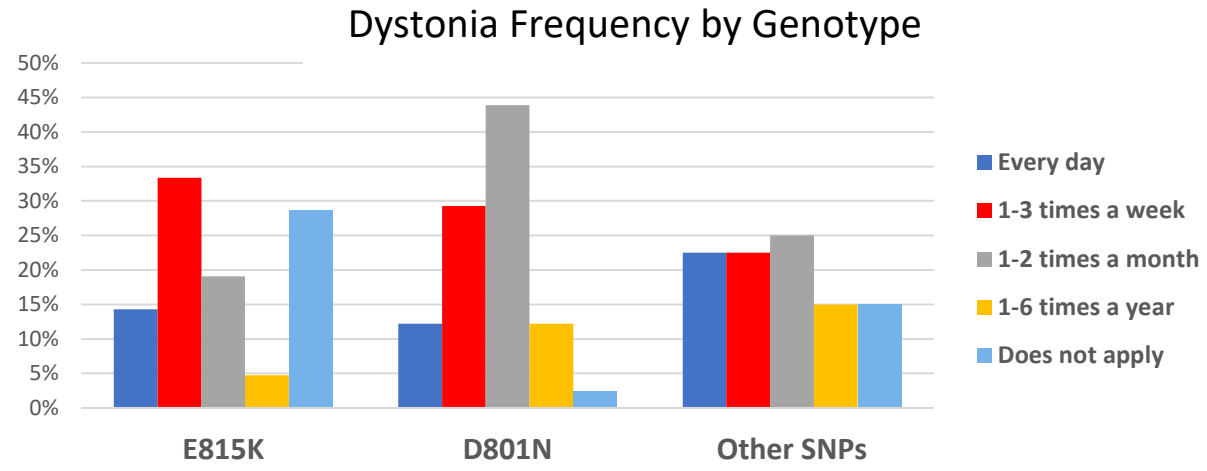



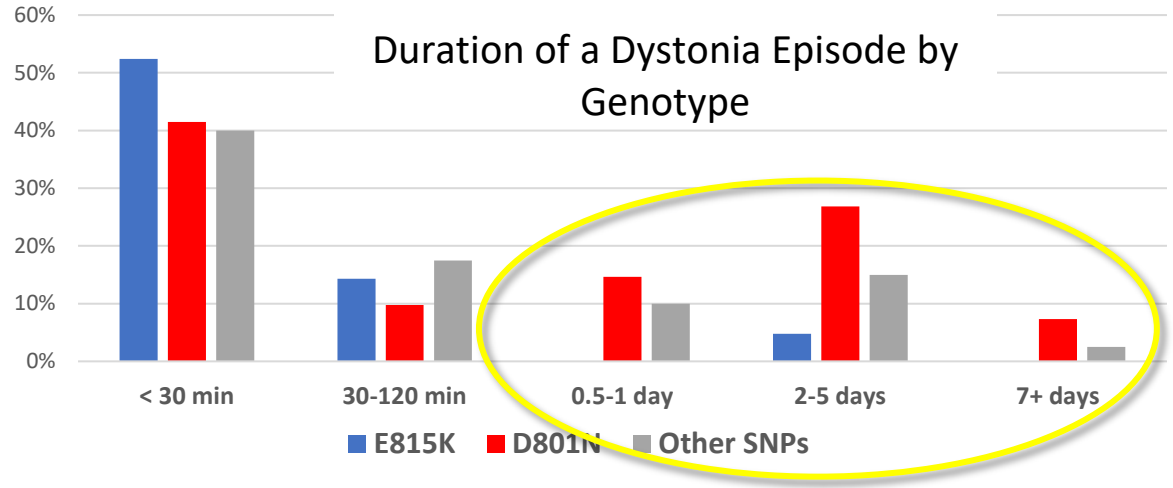

*Patients with D801N genotype experience longer duration dystonia than E815K patients; increased duration and higher prevalence, not frequency, drives the increased "burden" for D801N*

# Understanding Patient Symptoms: Dystonia Burden



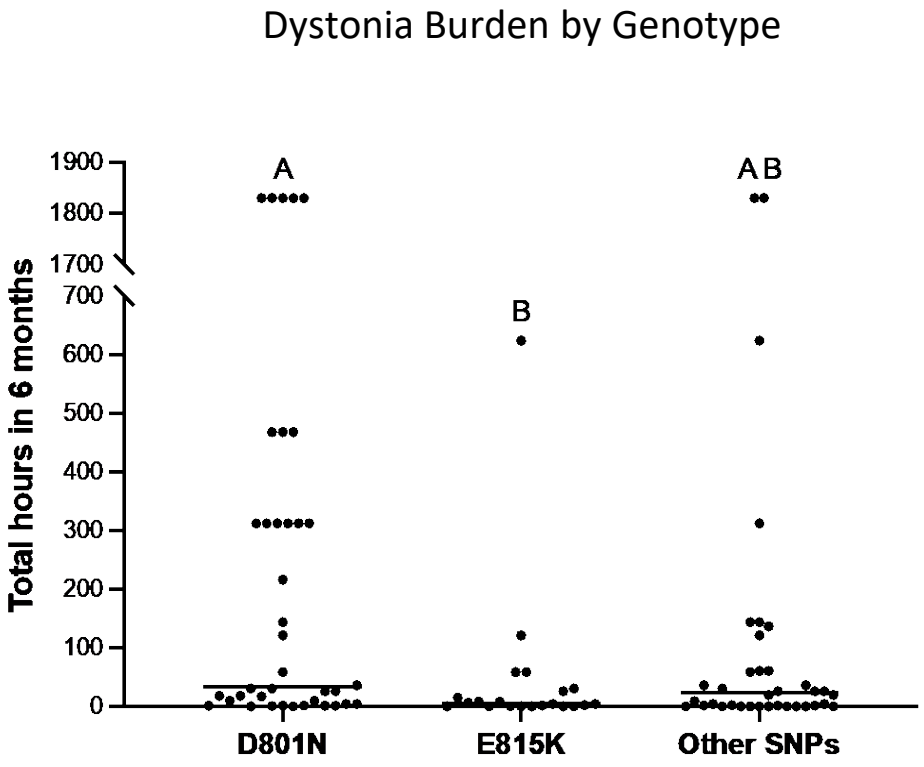

D801N patients experience significantly higher "burden" of dystonia than E815K patients



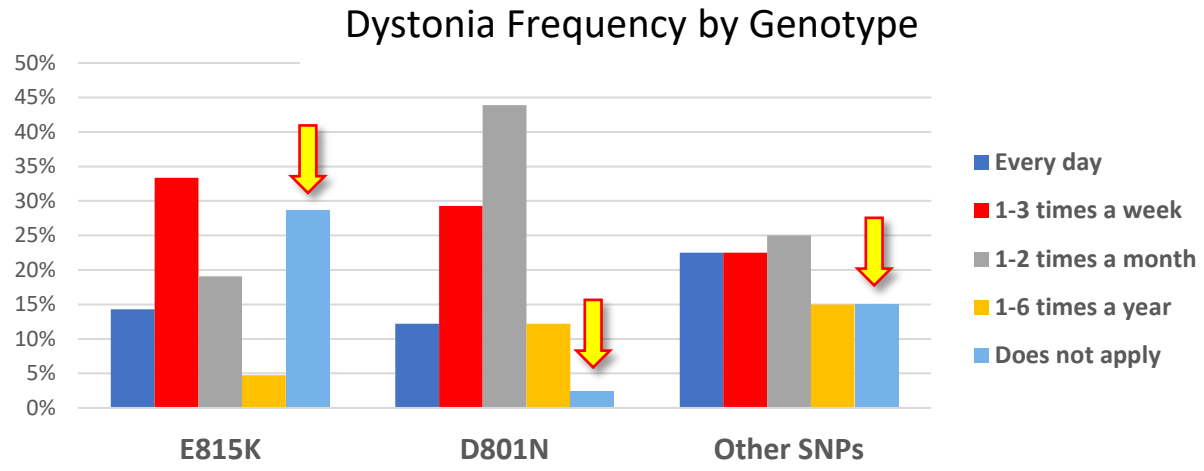



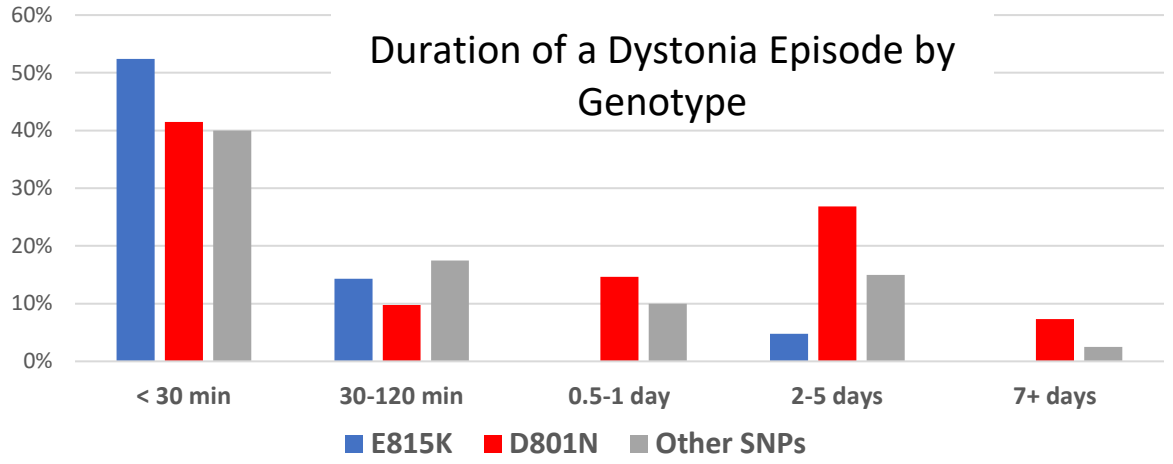

*Patients with D801N genotype experience longer duration dystonia than E815K patients; increased duration and higher prevalence, not frequency, drives the increased "burden" for D801N*

# Understanding Patient Symptoms: Dystonia Burden




D801N patients experience significantly higher "burden" of dystonia than E815K patients

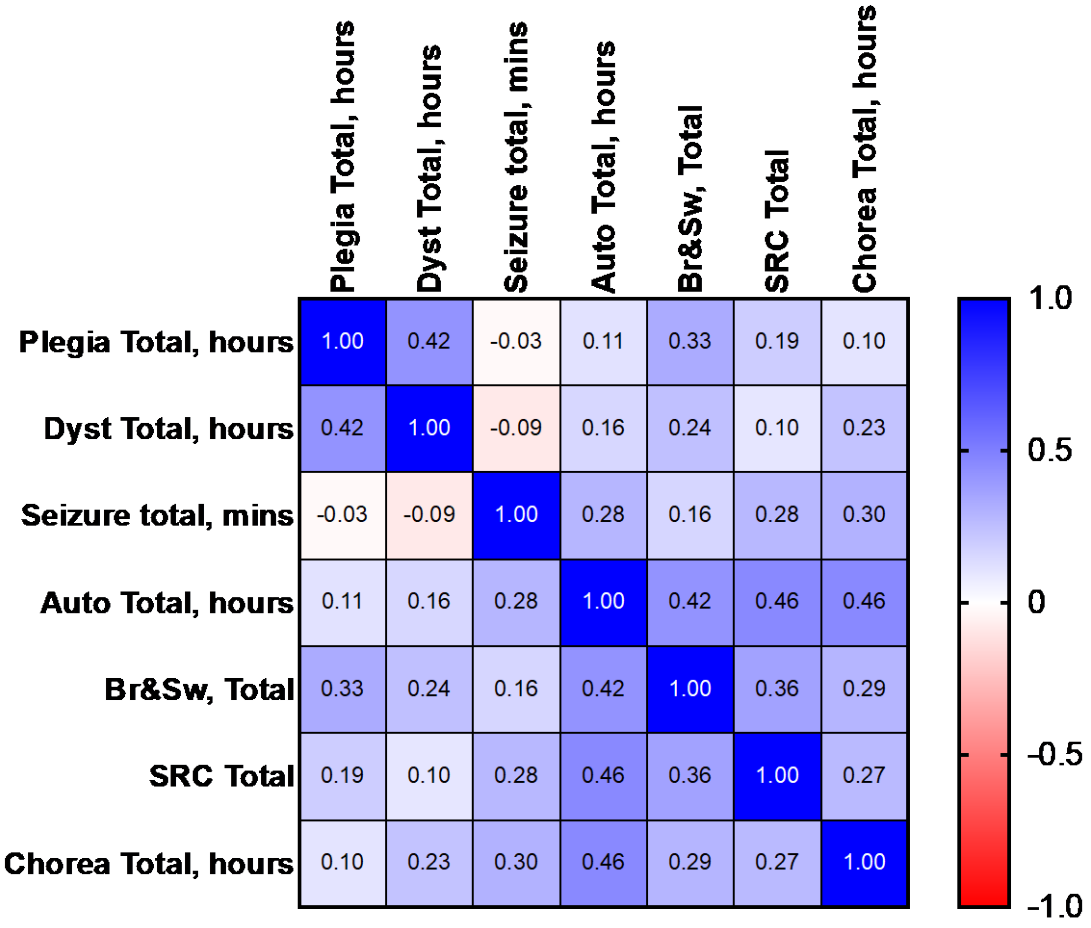



*Patients with D801N genotype experience a significantly greater burden of dystonia than E815K patients; increased duration and higher prevalence drives the increased "burden" for D801N*

***Correlations between Symptoms?***

# Understanding Patient Priorities




Spearman correlation in total time burden between paroxysmal symptoms

# Understanding the Burden of Symptoms

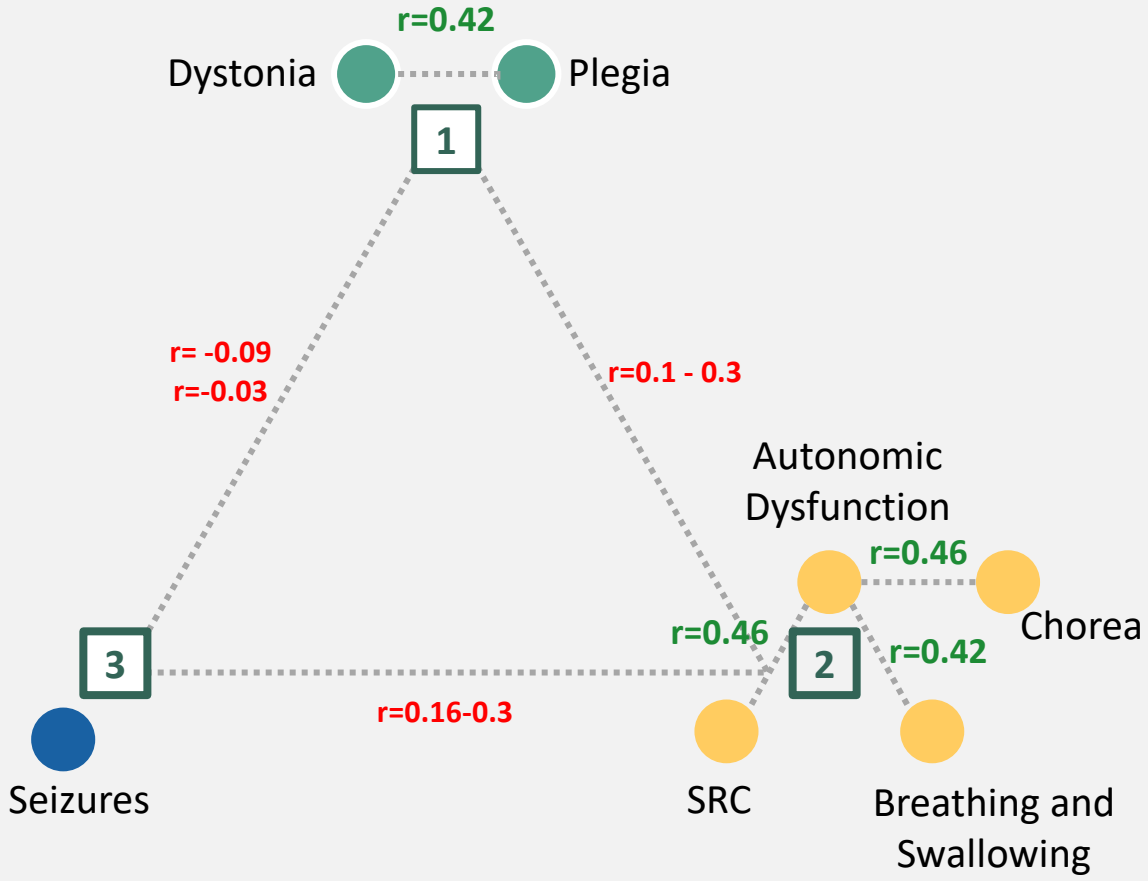
## *Three Clusters of Moderate Correlation*

**1** Moderate correlation between total burden of plegia and dystonia

**2** Moderate correlation between Autonomic Dysfunction, Breathing and Swallowing Difficulties, SRC, and Chorea

**3** No correlation, or weak correlation, between seizures and other symptoms

*No correlation between* **1** *,* **2** *and* **3**

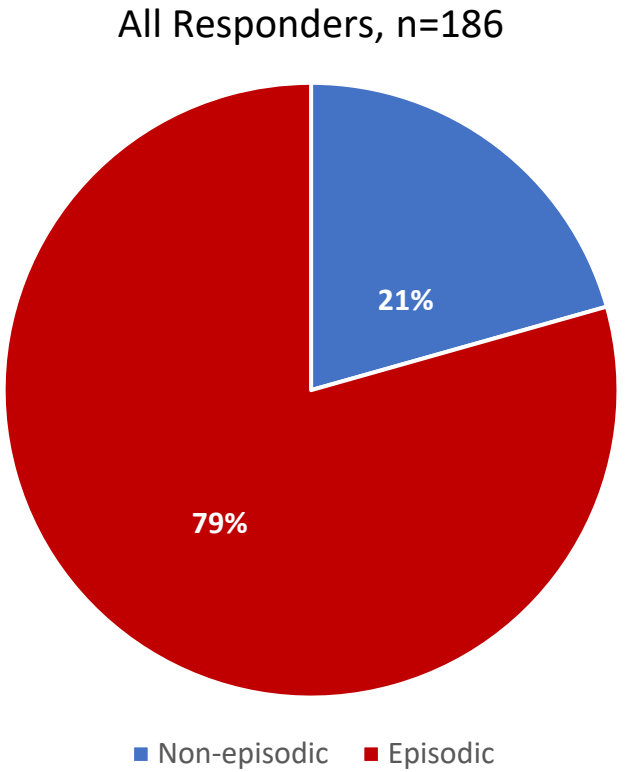



*Clusters of similarly-experienced symptoms from correlation analysis*

***Patient Priorities***

# Understanding the Patient Priorities

“Would you prefer to eliminate the episodic symptoms of AHC (such as hemiplegia, dystonia and seizures) OR the constant or non-episodic daily symptoms experienced by your patient (such as motor and speech difficulties)?”

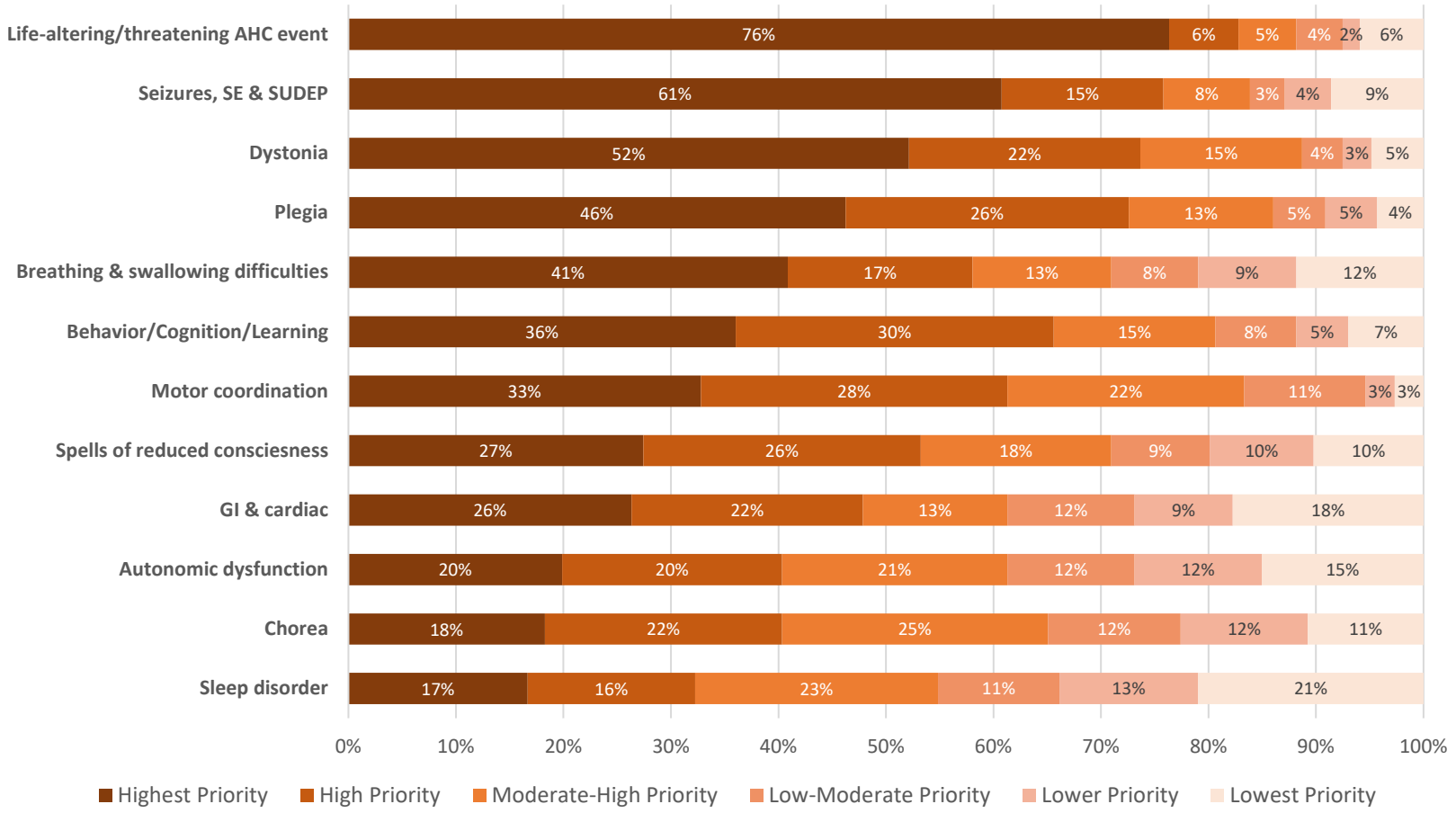



*Across age, genotype, and sex groups, responders consistently prioritized the elimination of paroxysmal symptoms*

# Understanding Patient Priorities

“Please prioritize which AHC symptoms you would like to eliminate from your patient's experience, now and in the future.”

Priorities for Symptom Elimination, All Responders, n=186

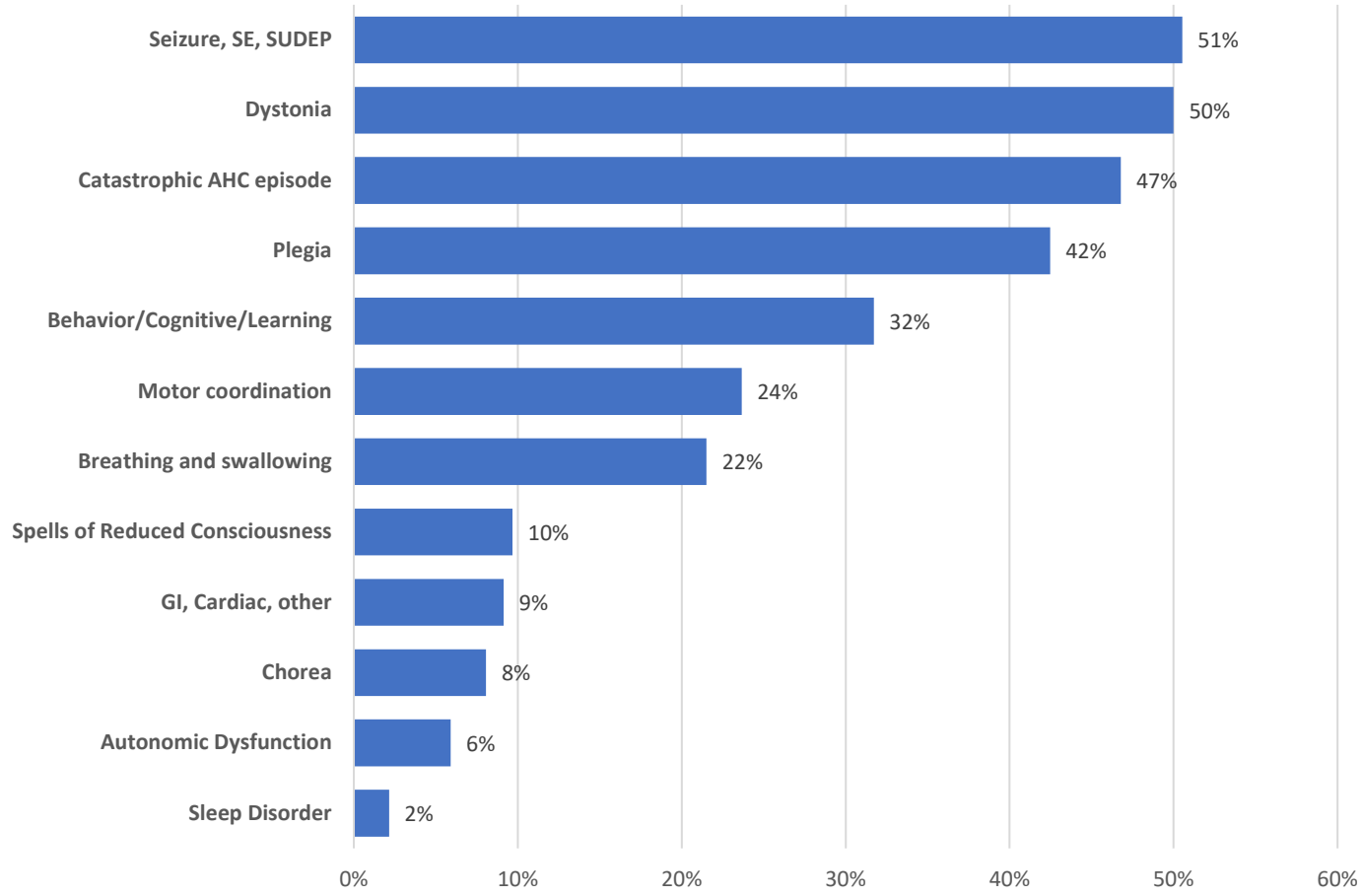



*The most severe paroxysmal symptoms were prioritized most highly for elimination*

# Understanding the Burden of Symptoms

“Of the following symptoms that your patient may be experiencing now or in the future, please identify the TOP THREE that you would like to eliminate. Please check ONLY 3 options.”

Top Three Symptoms to Eliminate, All Responders, n=186




*Responders had a consistent preference for eliminating the most severe paroxysmal symptoms*

# Contextualizing Phenotypes: New Patient Survey

1. **Sleep**
2. **Triggers**
3. **Medications**
4. **Headache**