
What matters to patients?

The Patient Survey: A Systematic Investigation of Priorities



186
Respondents

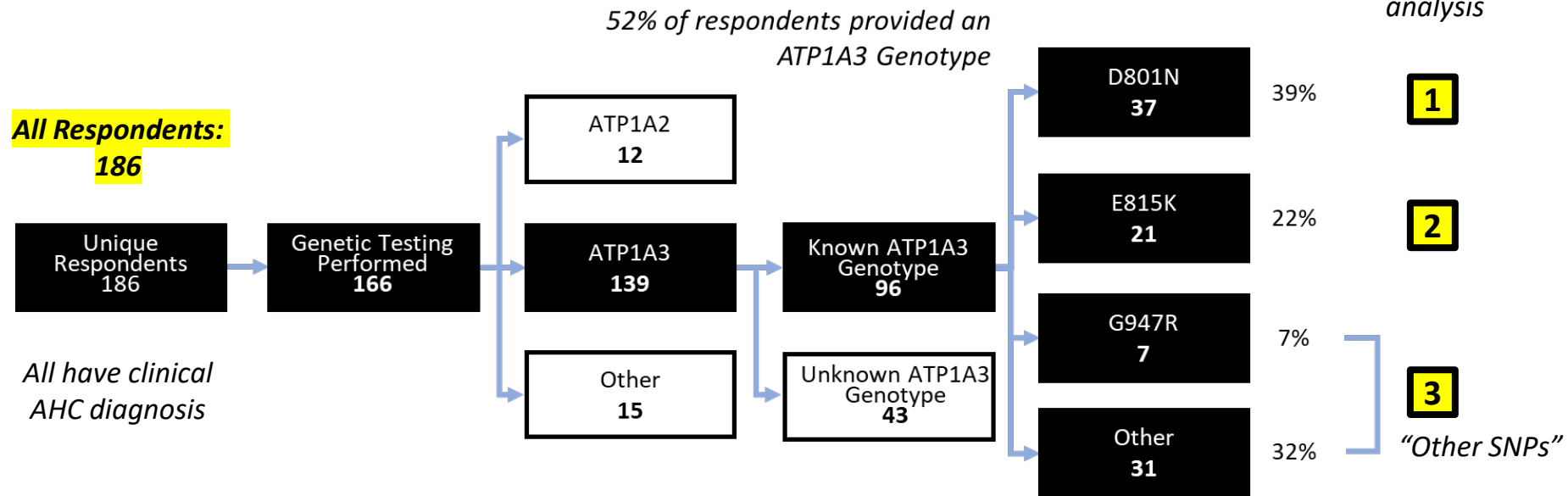
Patient survey (circulated fall 2023-winter 2024) queried AHC caregivers on:

- (1) currently experienced symptoms
- (2) the symptoms they most wanted to eliminate

Who were the survey-takers?

Survey Respondents

Patient Genotype Data As Reported by Survey Respondents

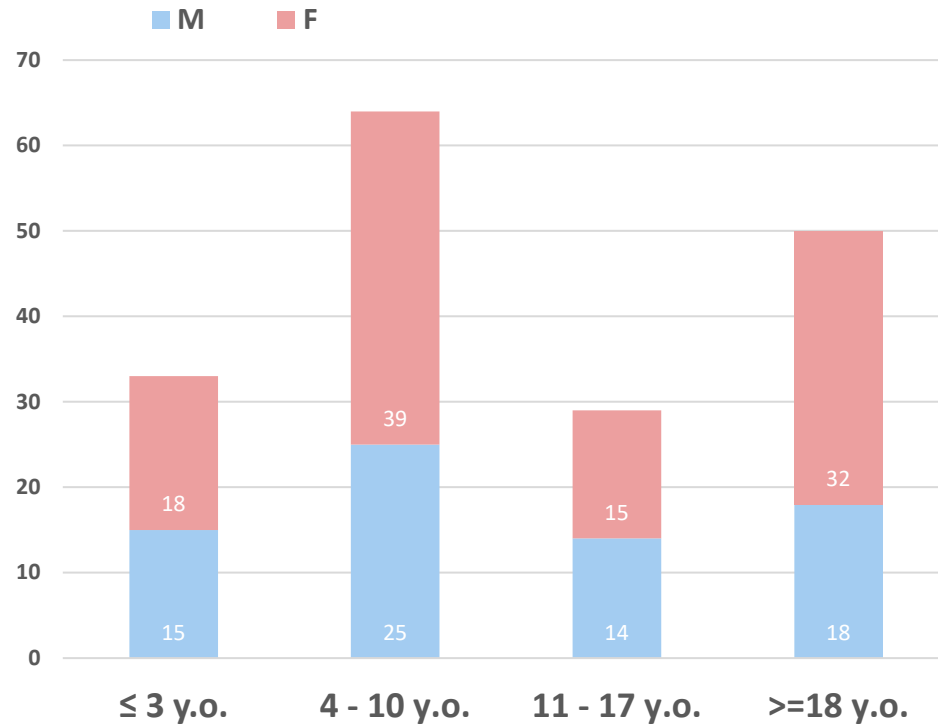


n	SNP	Location
1	Q140L	IC (post TM2)
1	V322D	TM4
1	E324Q	TM4
1	T331fs	TM4
1	C333F	IC (post TM4)
1	A338P	IC (post TM4)
1	G358S	P-site, part 1
1	T360R	P-site, part 1
1	L715P	P-site, part 2
1	K717del	P-site, part 2
1	E754fs	P-site, part 2
2	G755S	P-site, part 2
2	R756H	P-site, part 2
2	T771I	TM5
1	S772R	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

All Respondents by Age and Sex



Age	M	F	χ^2 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

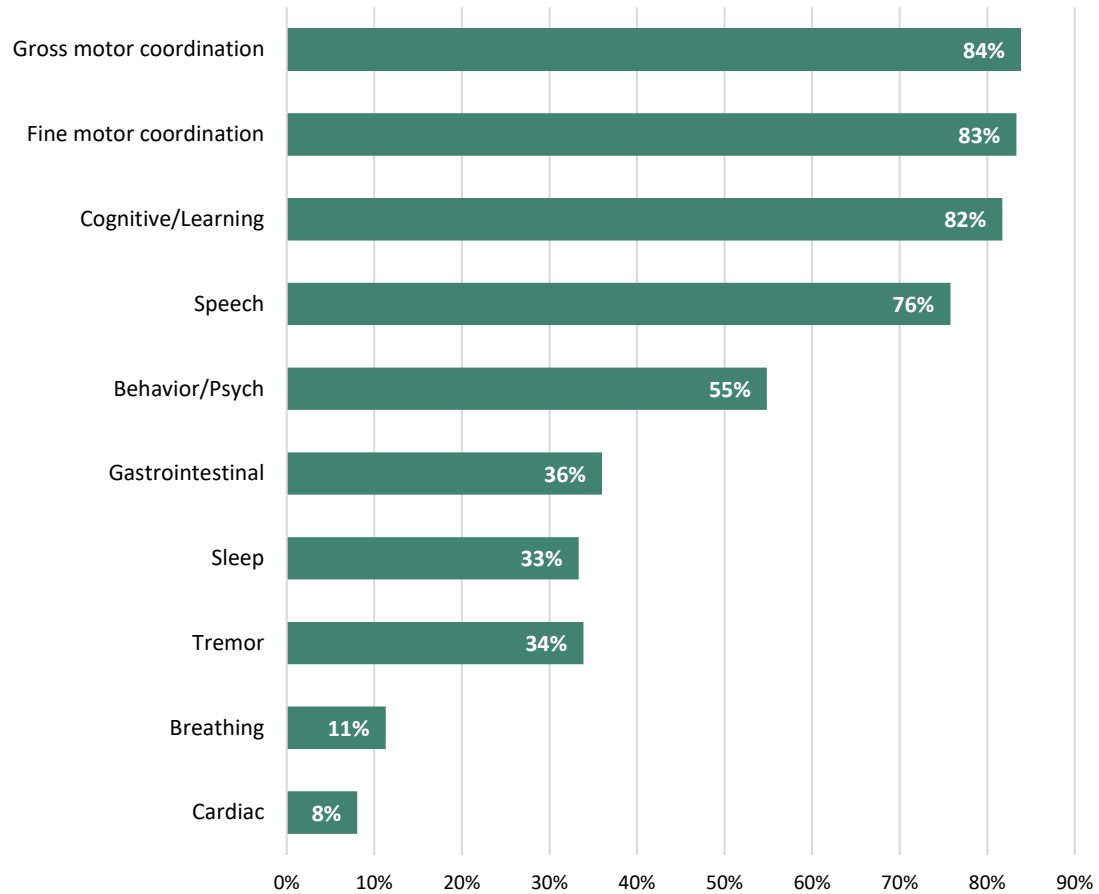
Respondents with Sex Data: 176

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

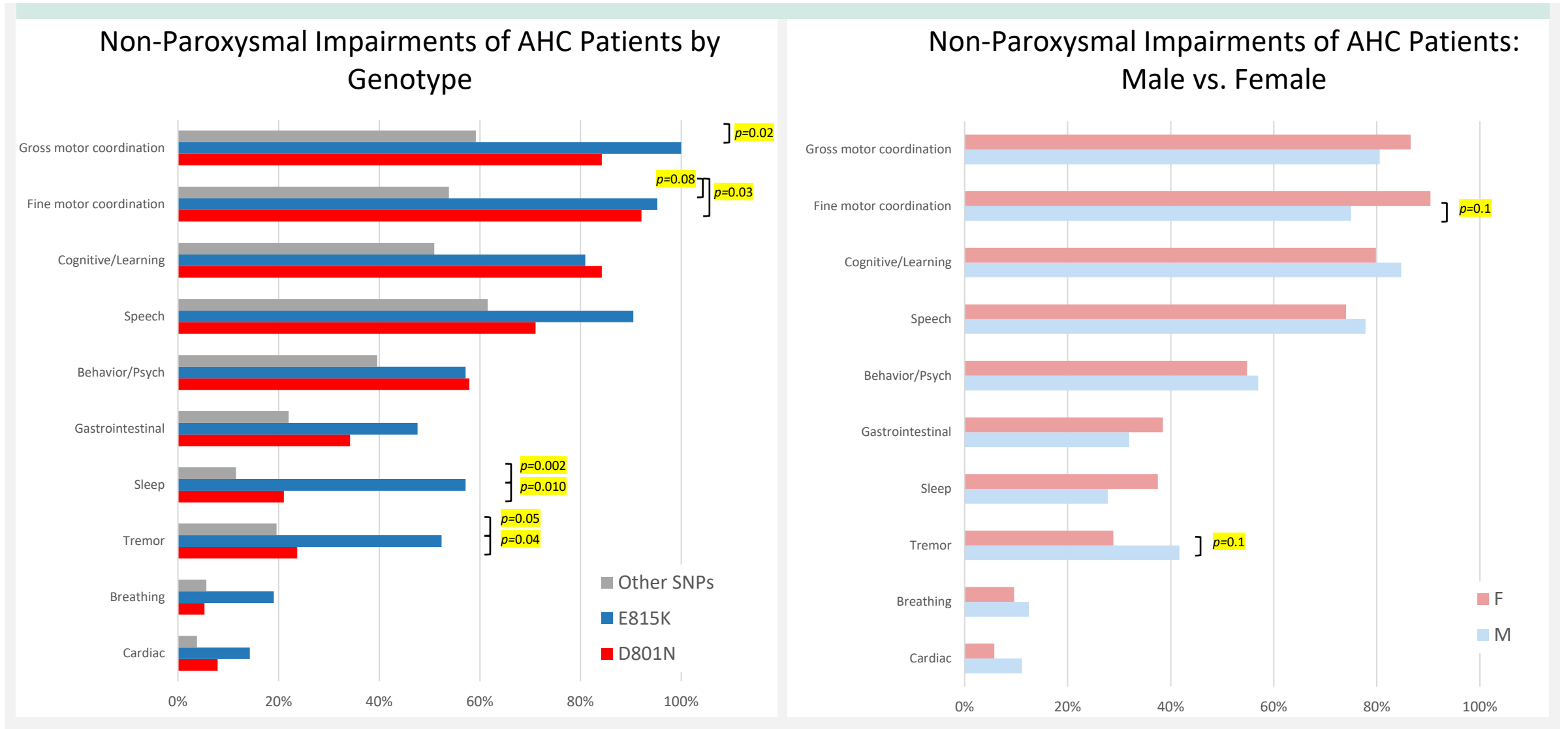


Prevalence of Non-Paroxysmal Impairments by Age



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

Understanding Patient Symptoms: Non-Paroxysmal Symptoms

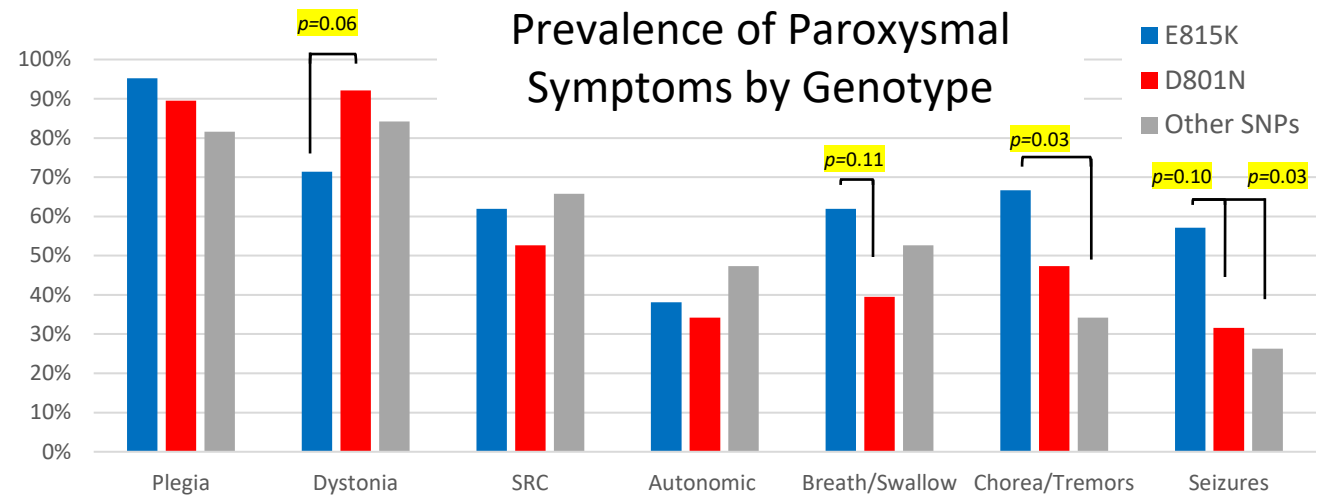
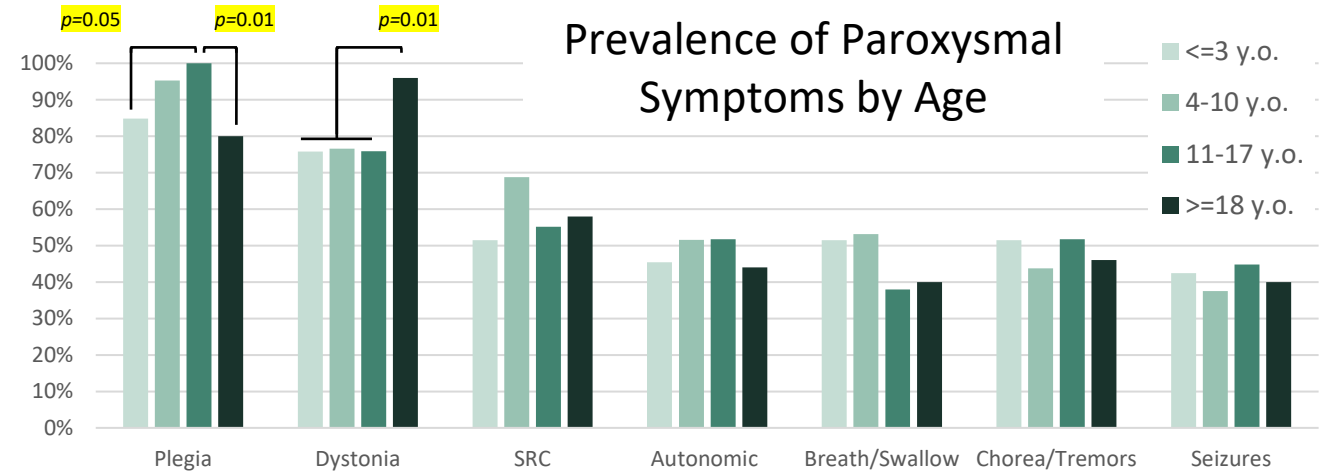
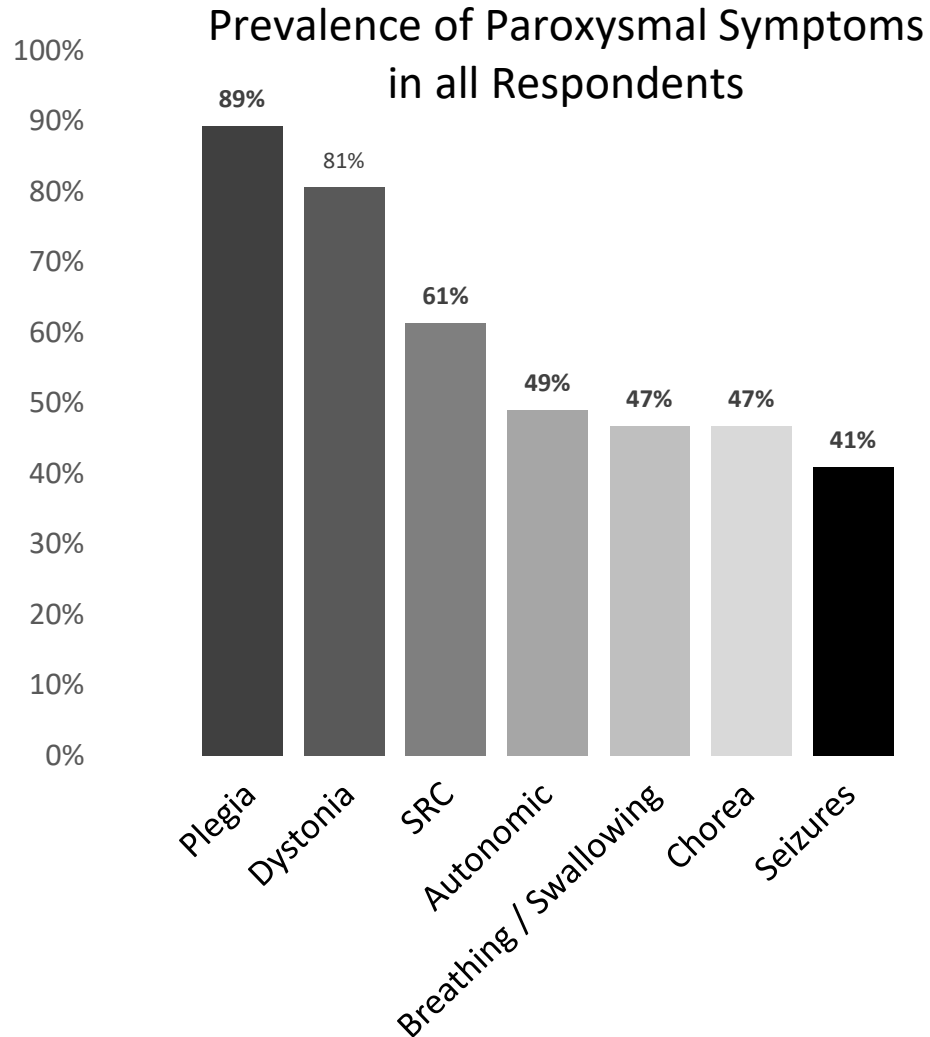


Fisher's exact test, significant results only

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.

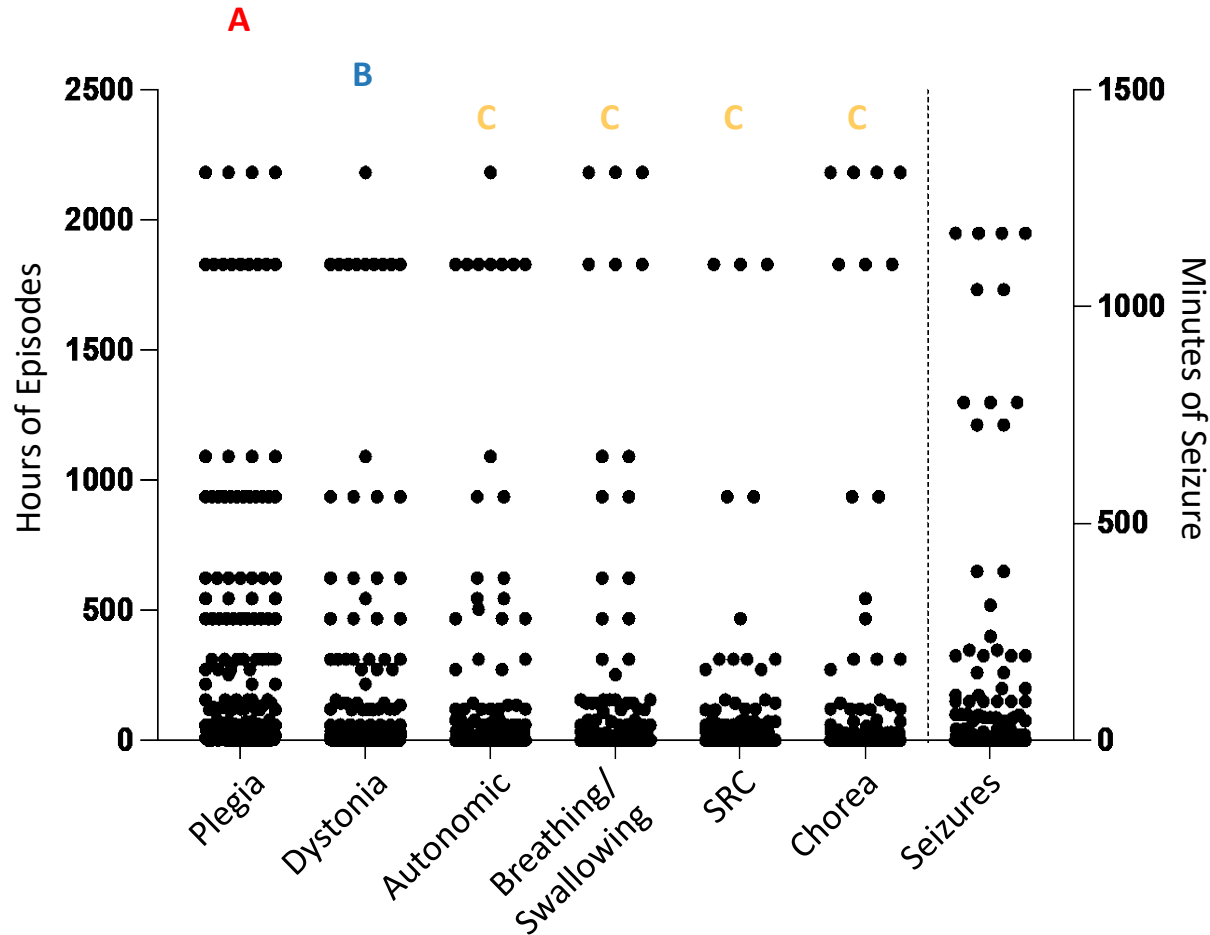
Understanding Patient Symptoms: Paroxysmal Symptoms



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

Understanding Patient Symptoms: Paroxysmal Symptoms Burden

AHC Symptom Burden in 6 Months



“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.”

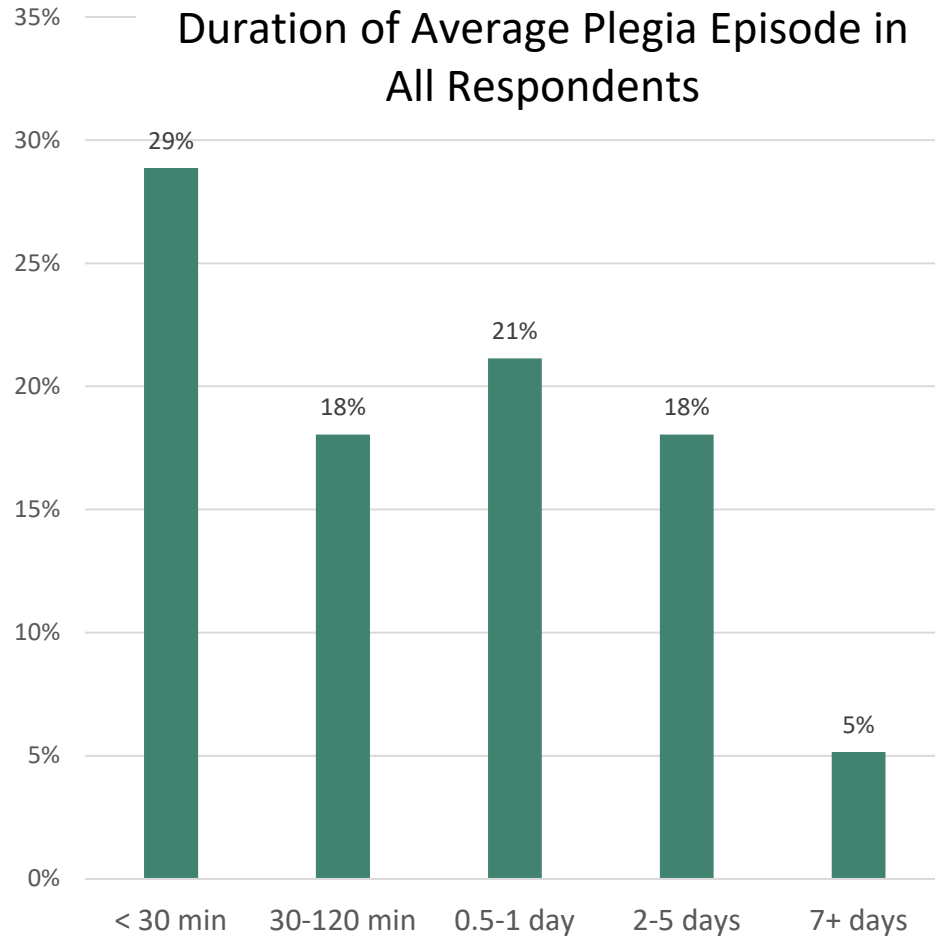
- Letters indicate the results of a statistical test for significance of difference in non-parametric data (Kruskal-Wallis test with Dunn’s multiple comparison test) at family-wise alpha threshold = 0.05.
- Scatter columns with a different letter are different from each other. Scatter columns with the 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

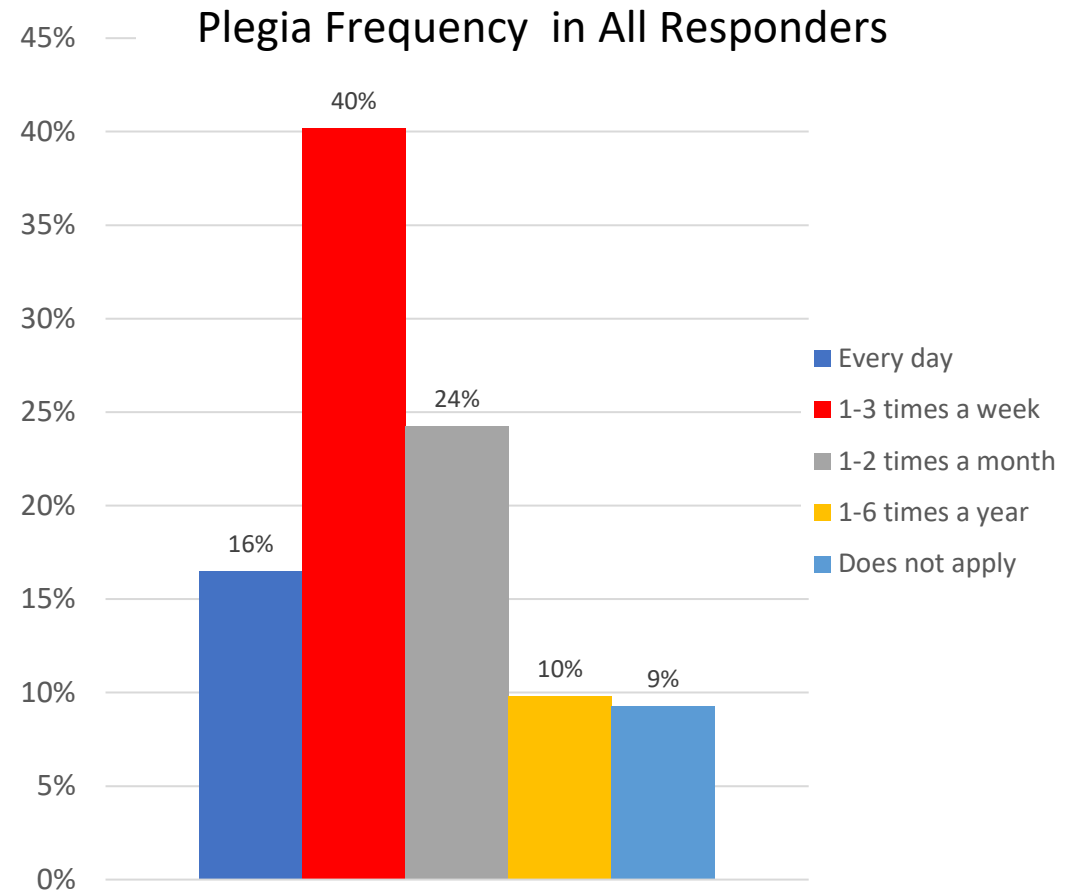
Understanding Patient Symptoms

Plegia

Understanding Patient Symptoms: Plegia



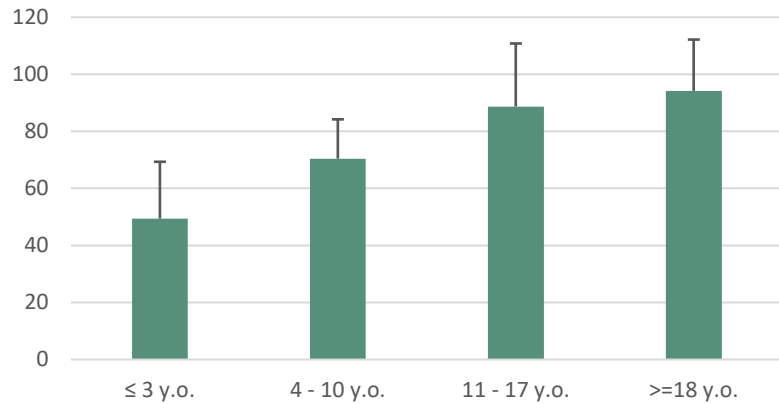
Plegia duration ranges from minutes to days at a time



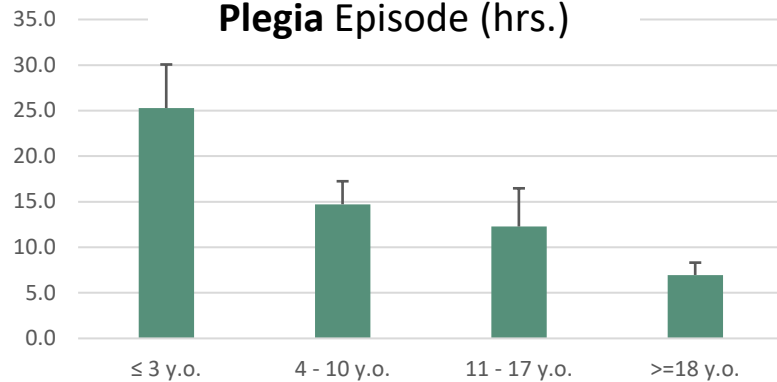
56% of responders reported plegia one or more times a week

Understanding Patient Symptoms: Plegia Burden

Number of Plegia Episodes in 6 months



Average Duration of a Plegia Episode (hrs.)



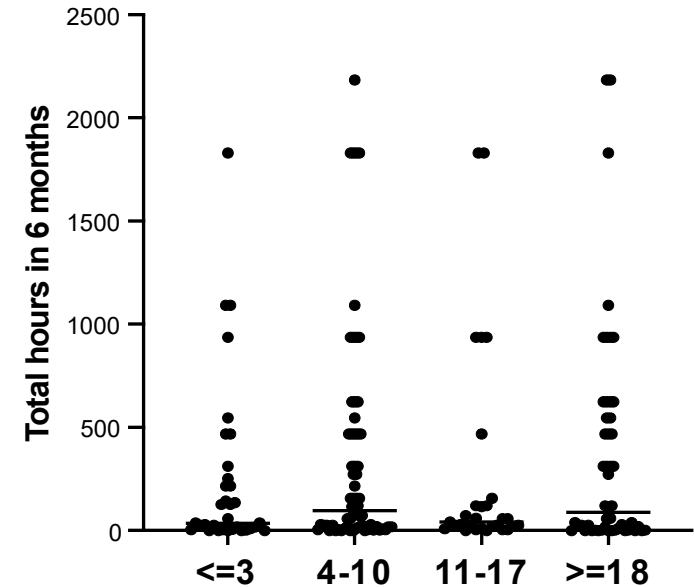
Effect of Age on Plegia

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

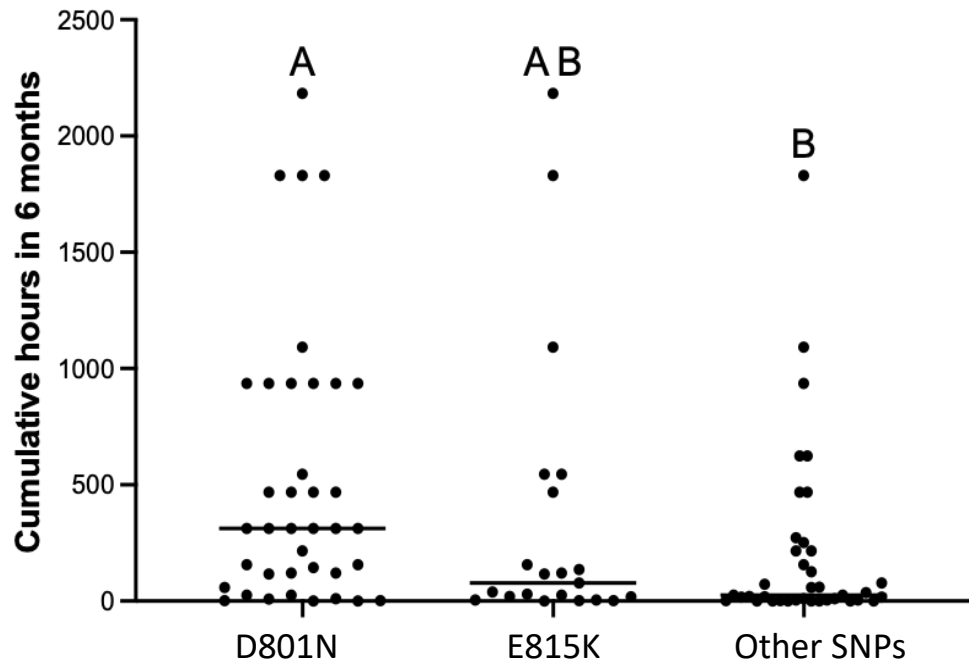


No significant difference in “burden” between the age groups

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

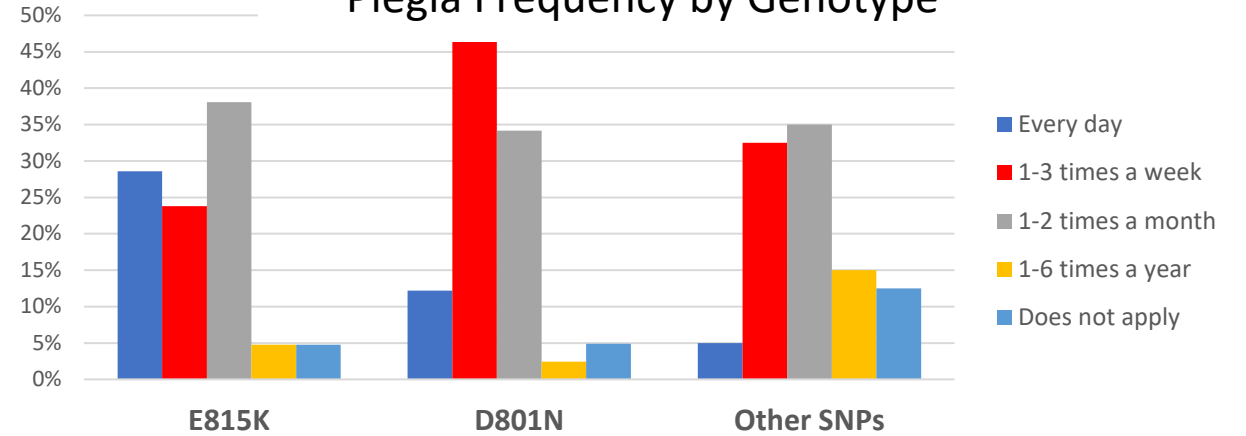
Understanding Patient Symptoms: Plegia Burden

Plegia Burden by Genotype

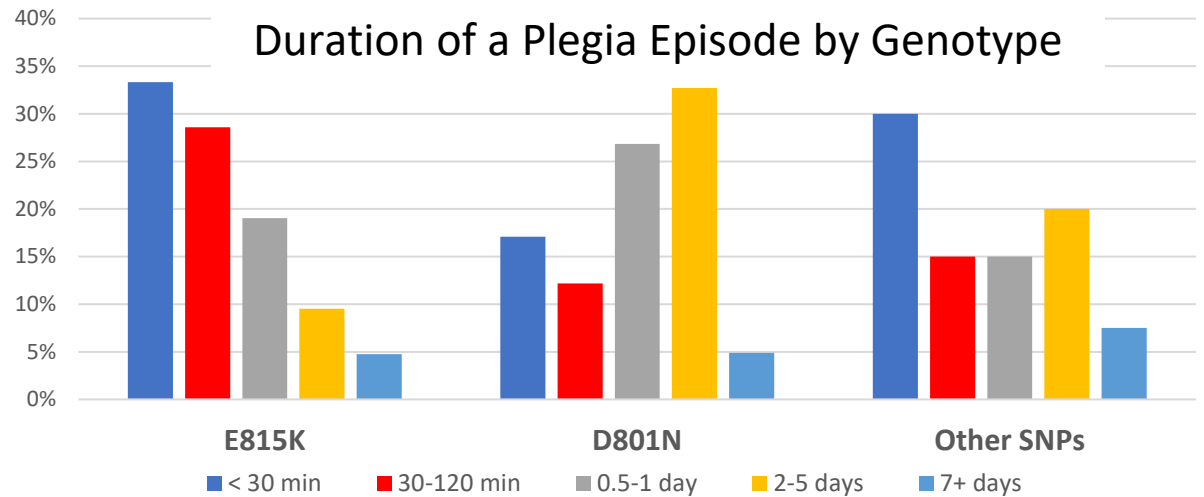


D801N patients experience higher "burden" of plegia

Plegia Frequency by Genotype



Duration of a Plegia Episode by Genotype



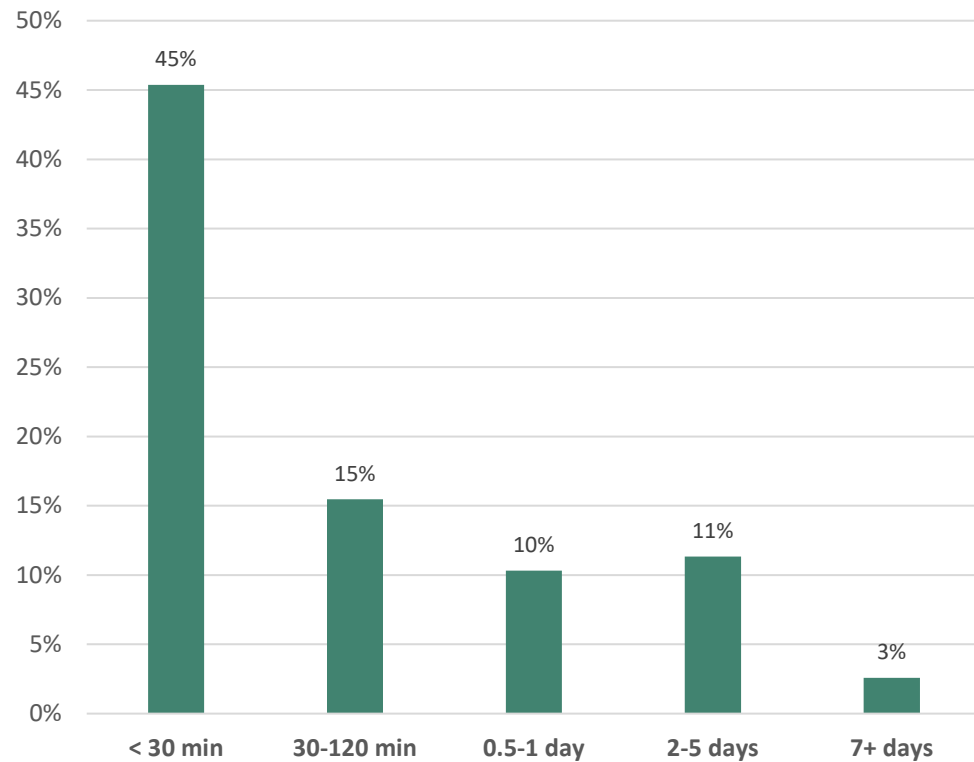
Plegia burden is higher for D801N patients than E815K patients, and significantly higher than the "other SNPs" group. Longer duration plegia drives this difference, along with lower plegia prevalence in the "Other SNPs group."

Understanding Patient Symptoms

Dystonia

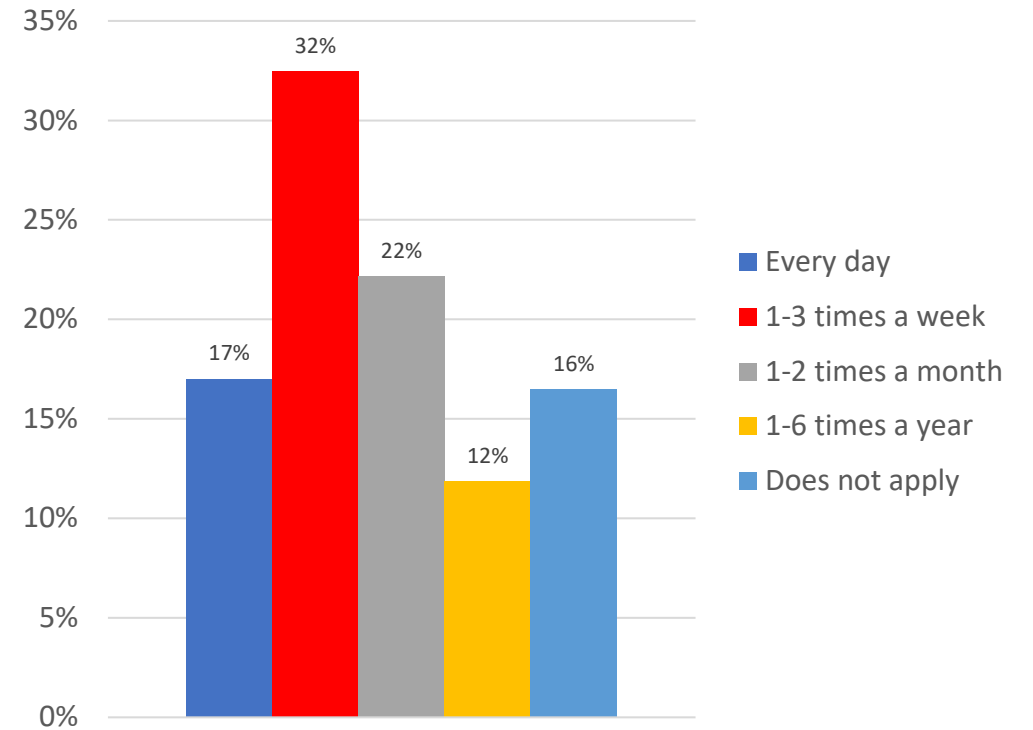
Understanding Patient Symptoms: Dystonia

Duration of Average Dystonia Episode in All Respondents



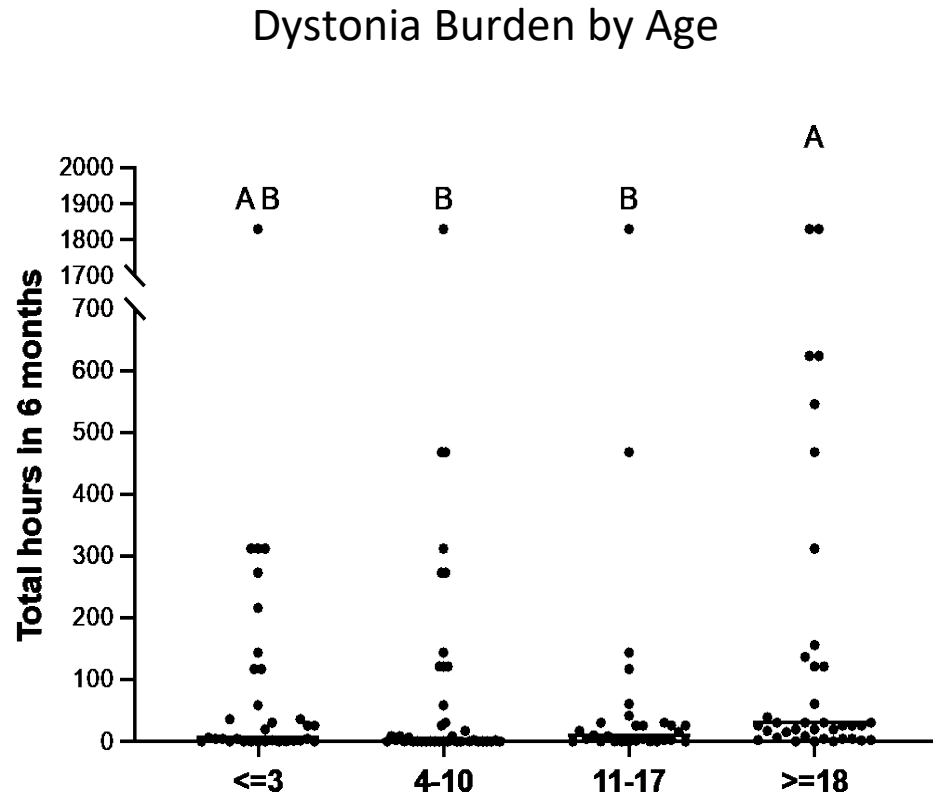
Most responders experience dystonia lasting under two hours, but 14% reported dystonia persisting over two days

Dystonia Frequency in All Responders

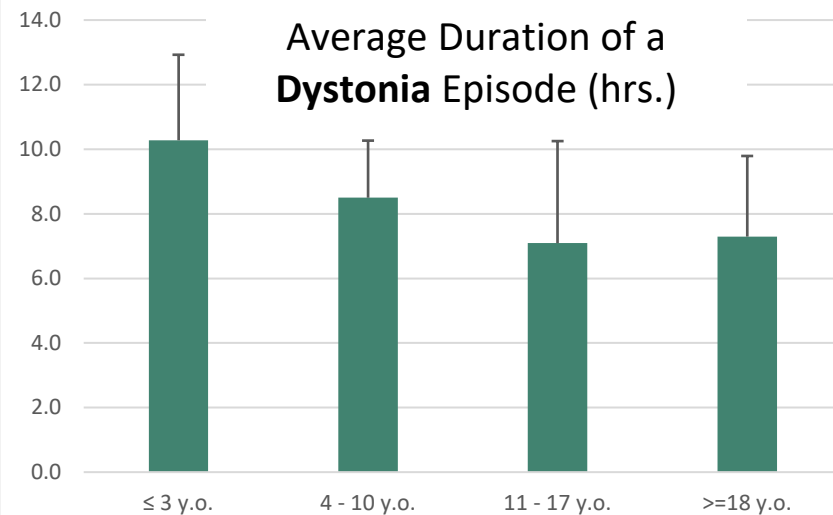
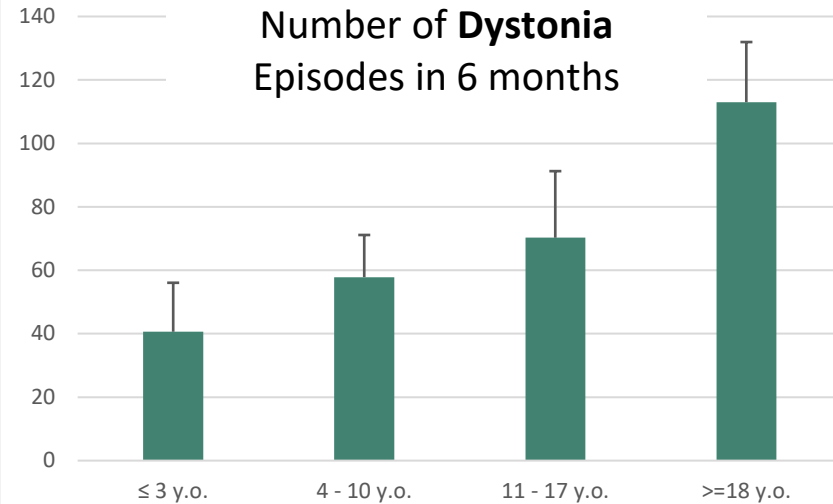


49% of respondents reported dystonia one or more times a week

Understanding Patient Symptoms: Dystonia Burden



Adults experience significantly higher "burden" of dystonia than children



Effect of Age on Dystonia

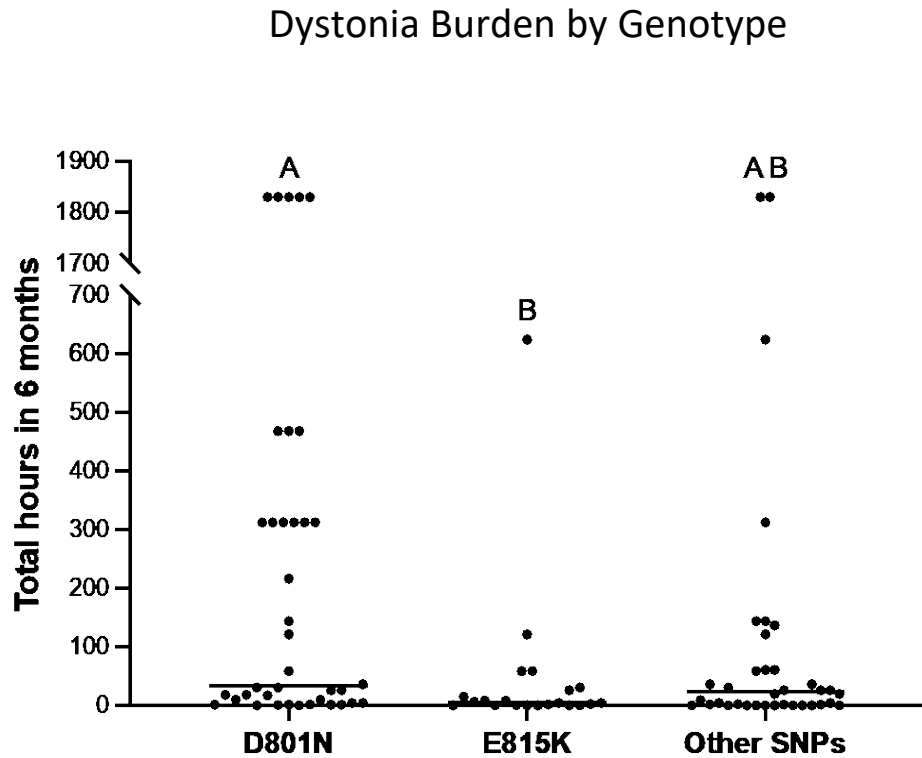
Increased dystonia frequency— and the total number of plegia episodes in 6 months— as age increases

Increased dystonia prevalence in adult patients.

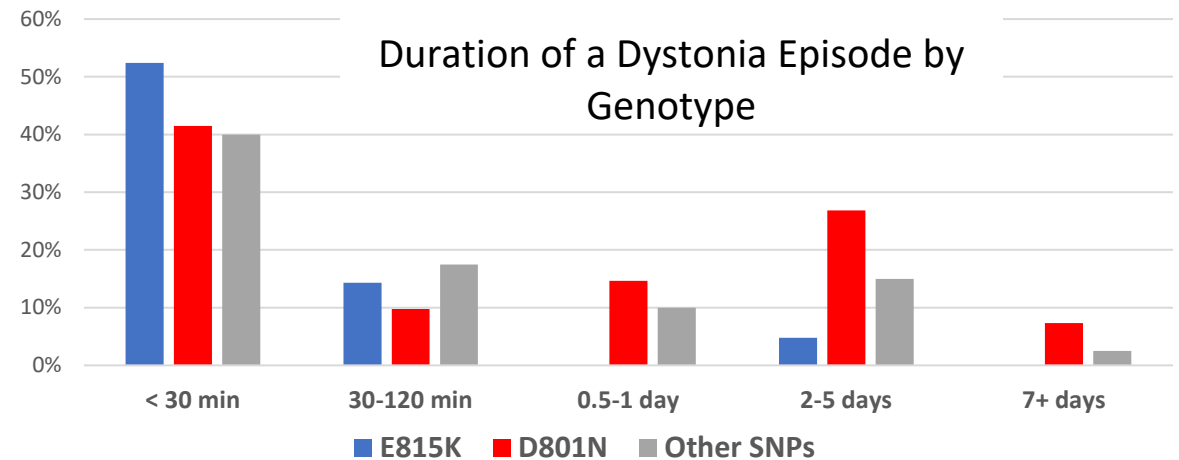
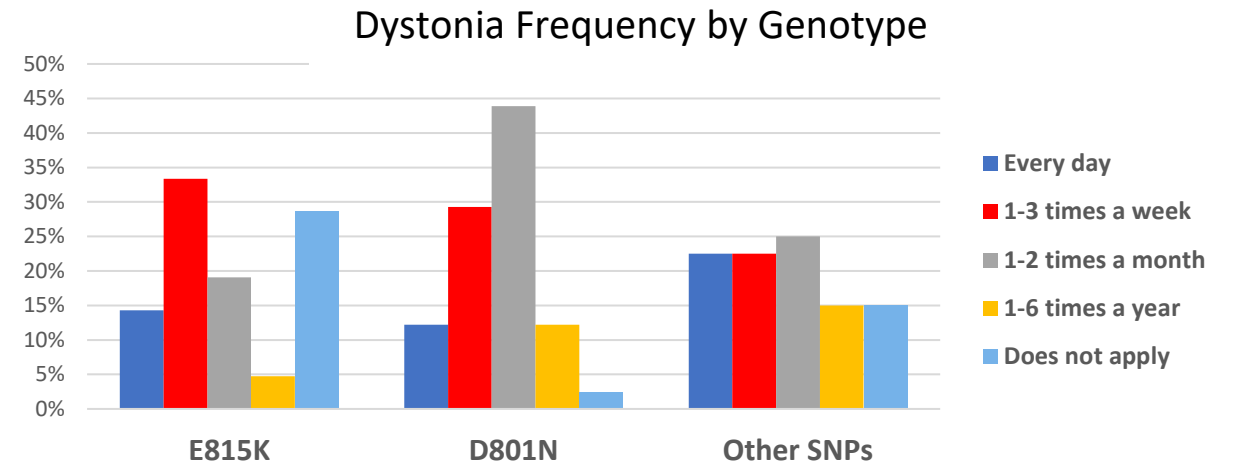
Patients experience **shorter duration** dystonia with age

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

Understanding Patient Symptoms: Dystonia Burden

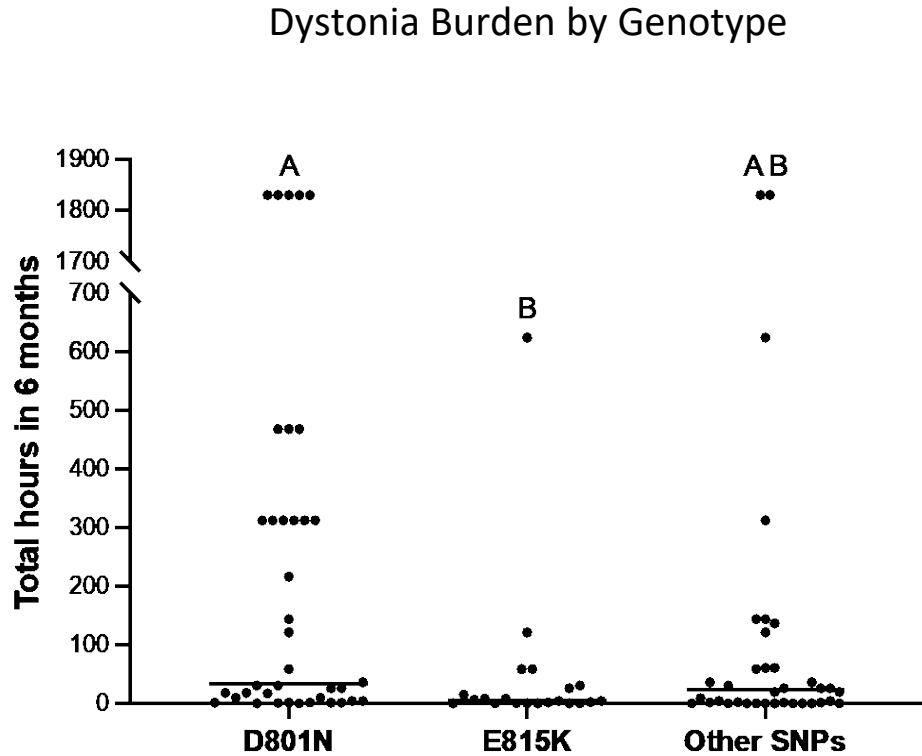


D801N patients experience significantly higher “burden” of dystonia than E815K patients

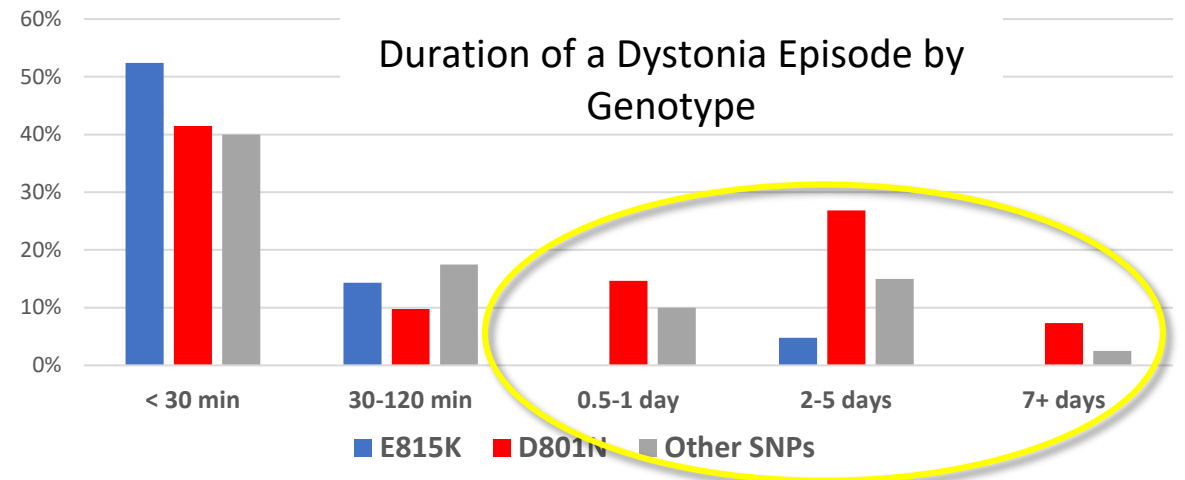
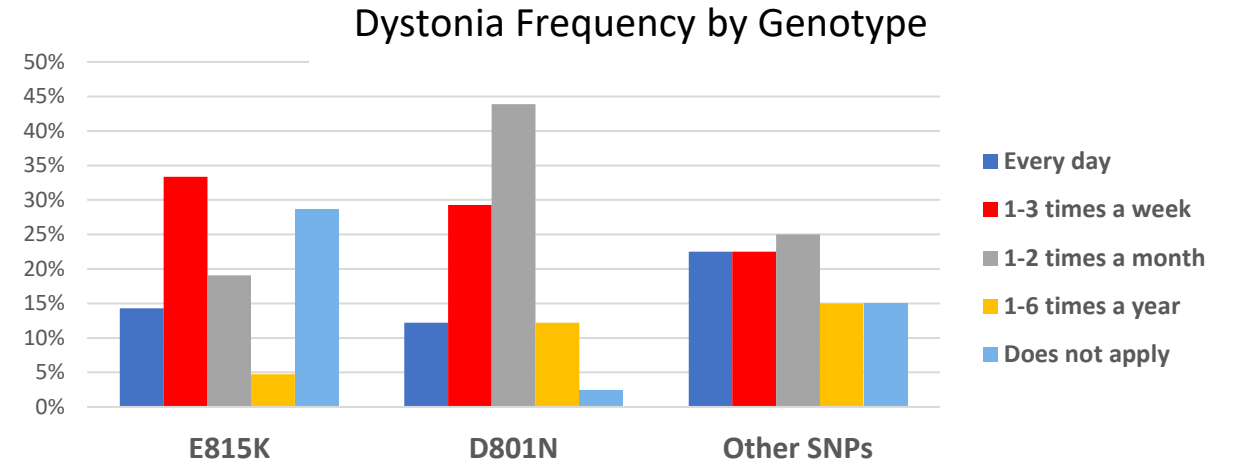


Patients with D801N genotype experience longer duration dystonia than E815K patients; increased duration and higher prevalence, not frequency, drives the increased “burden” for D801N

Understanding Patient Symptoms: Dystonia Burden



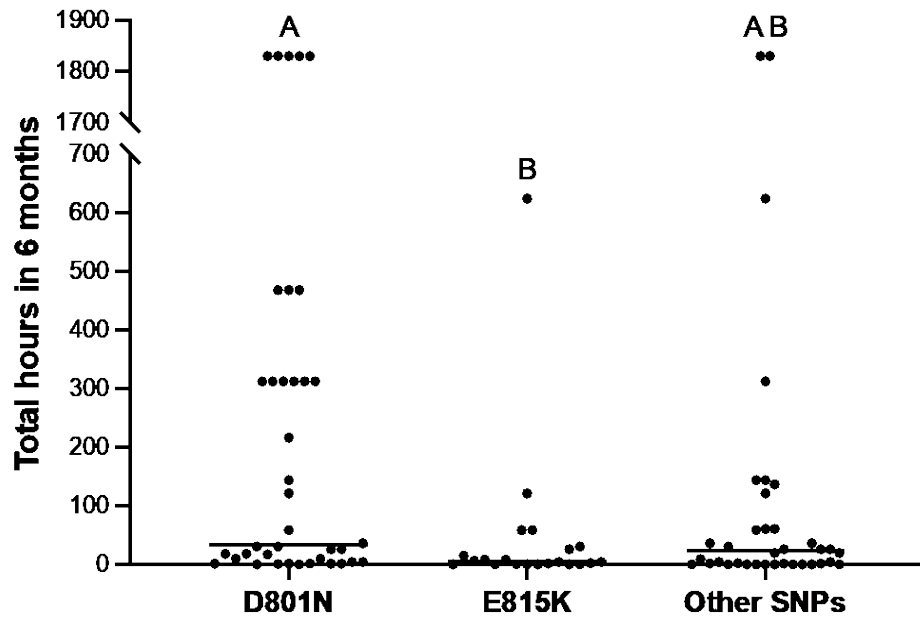
D801N patients experience significantly higher “burden” of dystonia than E815K patients



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

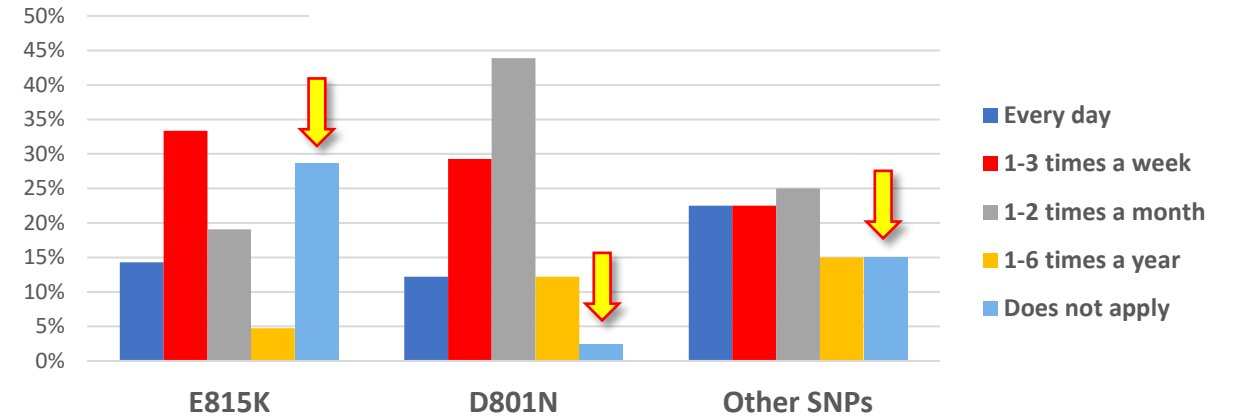
Understanding Patient Symptoms: Dystonia Burden

Dystonia Burden by Genotype

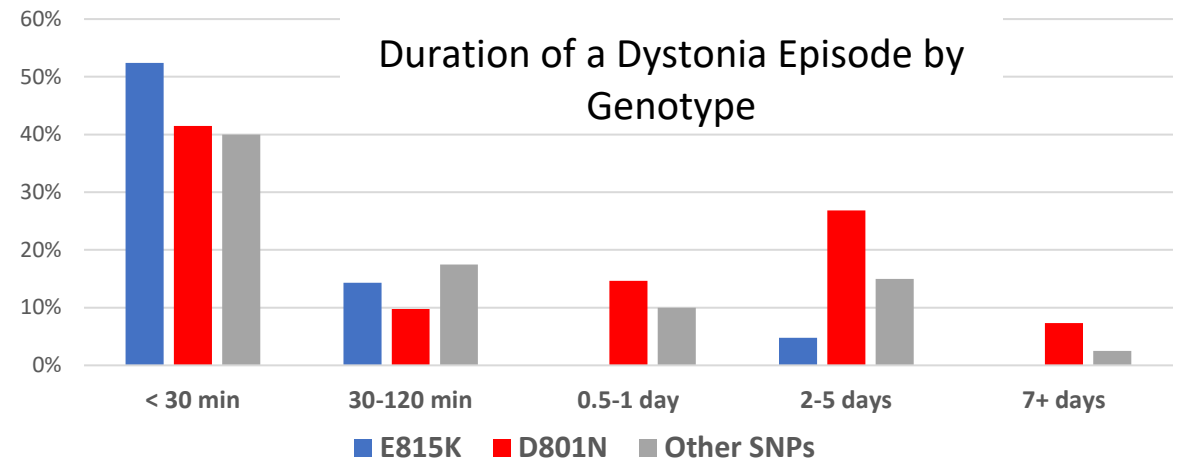


D801N patients experience significantly higher "burden" of dystonia than E815K patients

Dystonia Frequency by Genotype



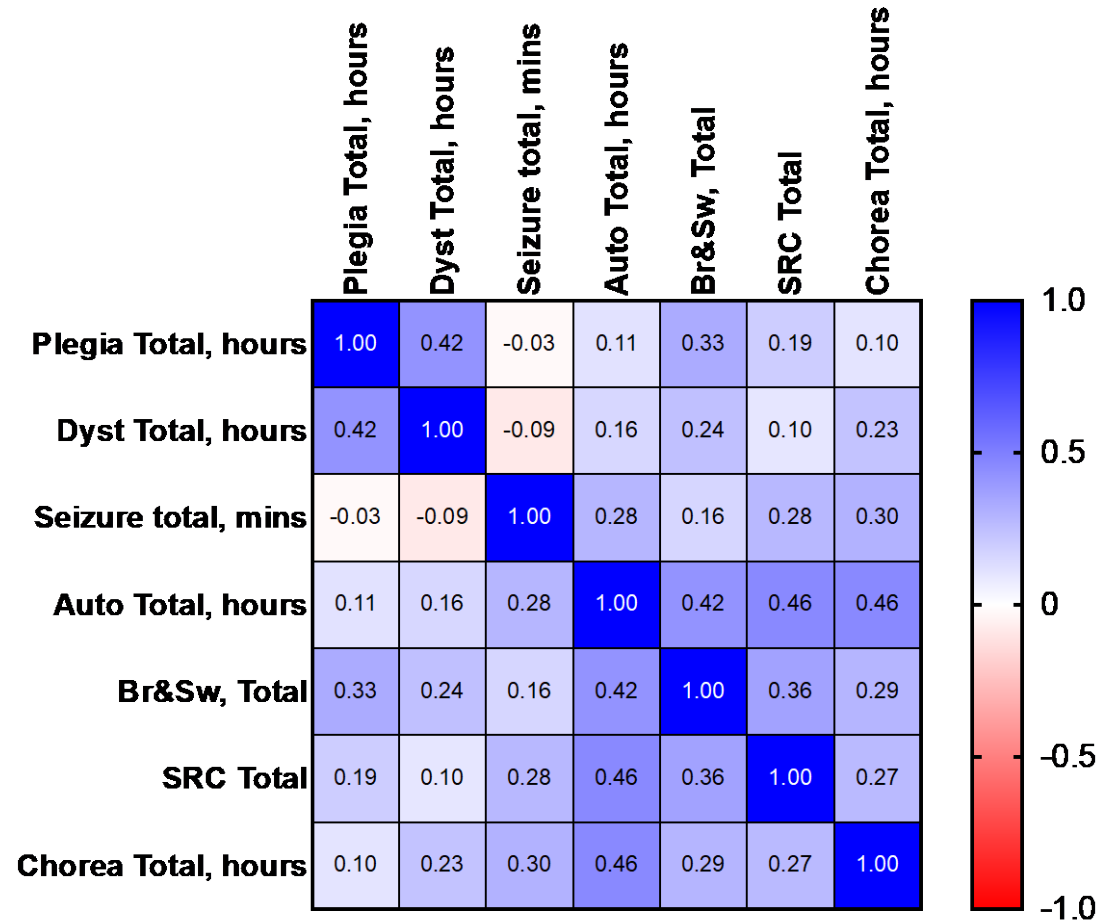
Duration of a Dystonia Episode by Genotype



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



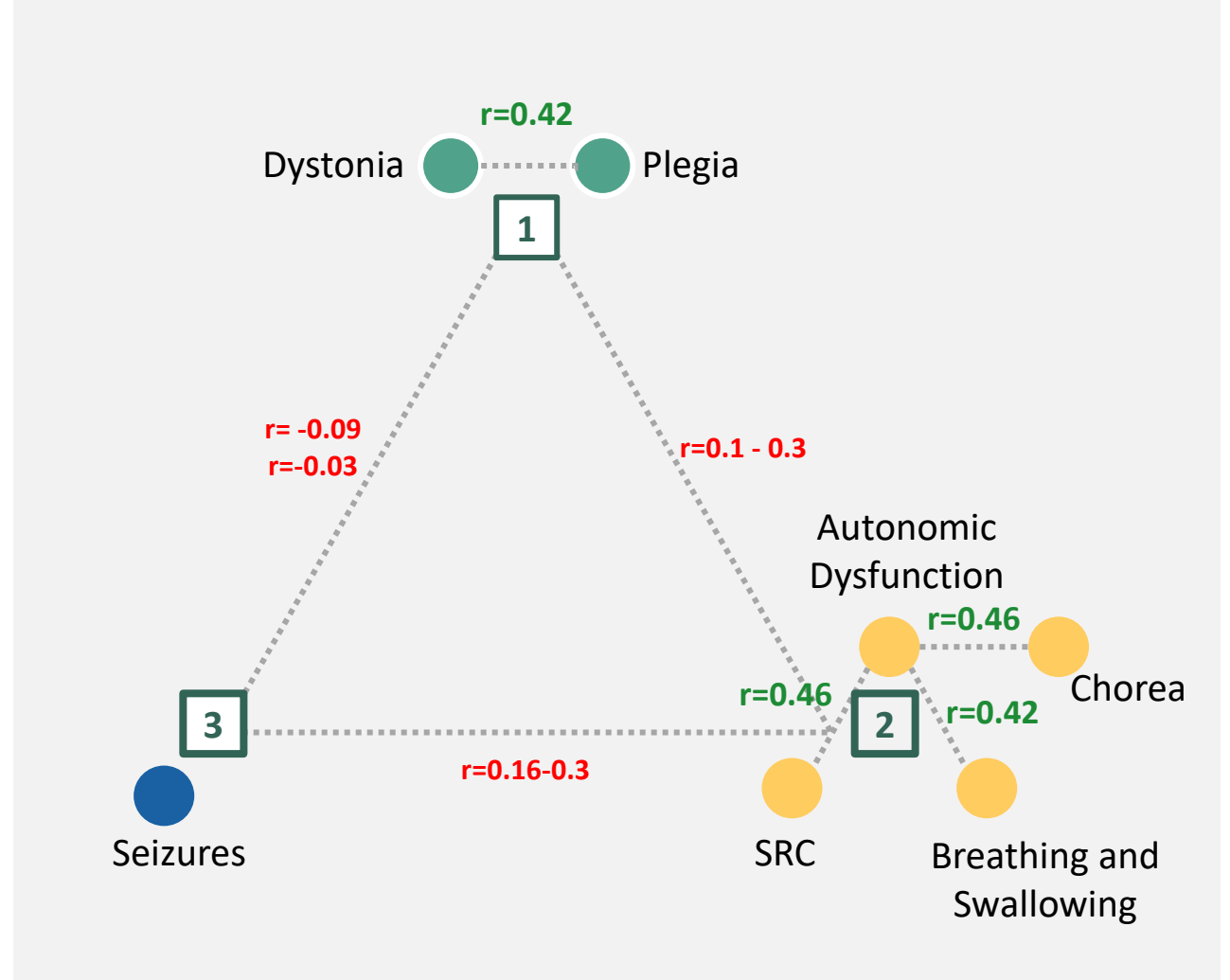
Spearman correlation in total time burden between paroxysmal symptoms

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

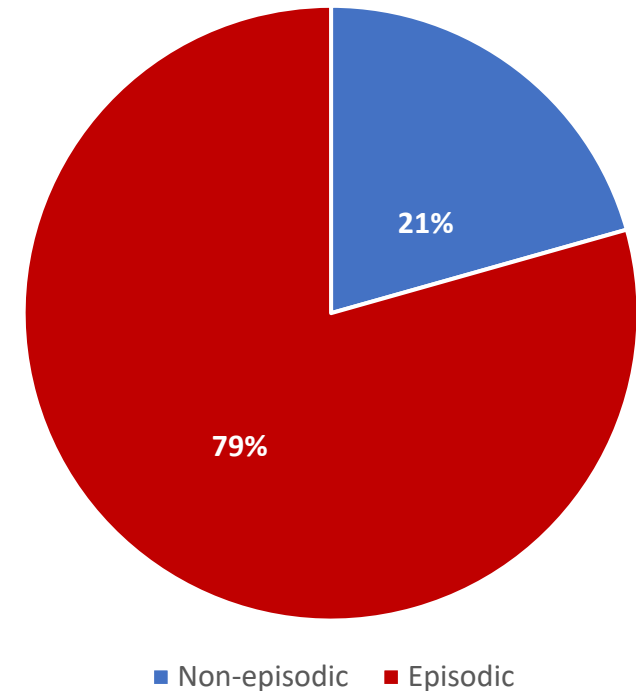
Understanding the Patient Priorities

“

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)?

”

All Responders, n=186

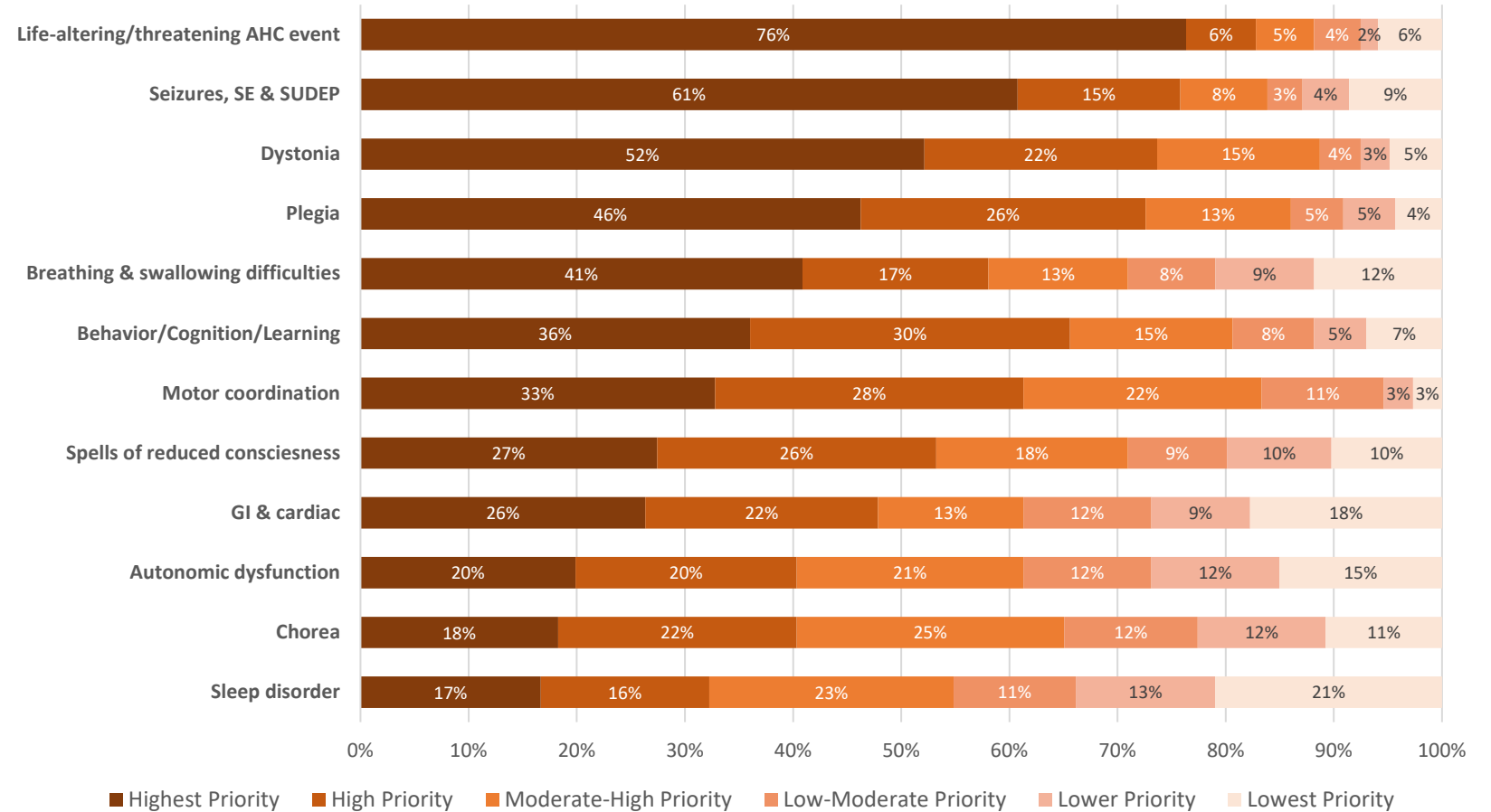


Across age, genotype, and sex groups, responders consistently prioritized the elimination of paroxysmal symptoms

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

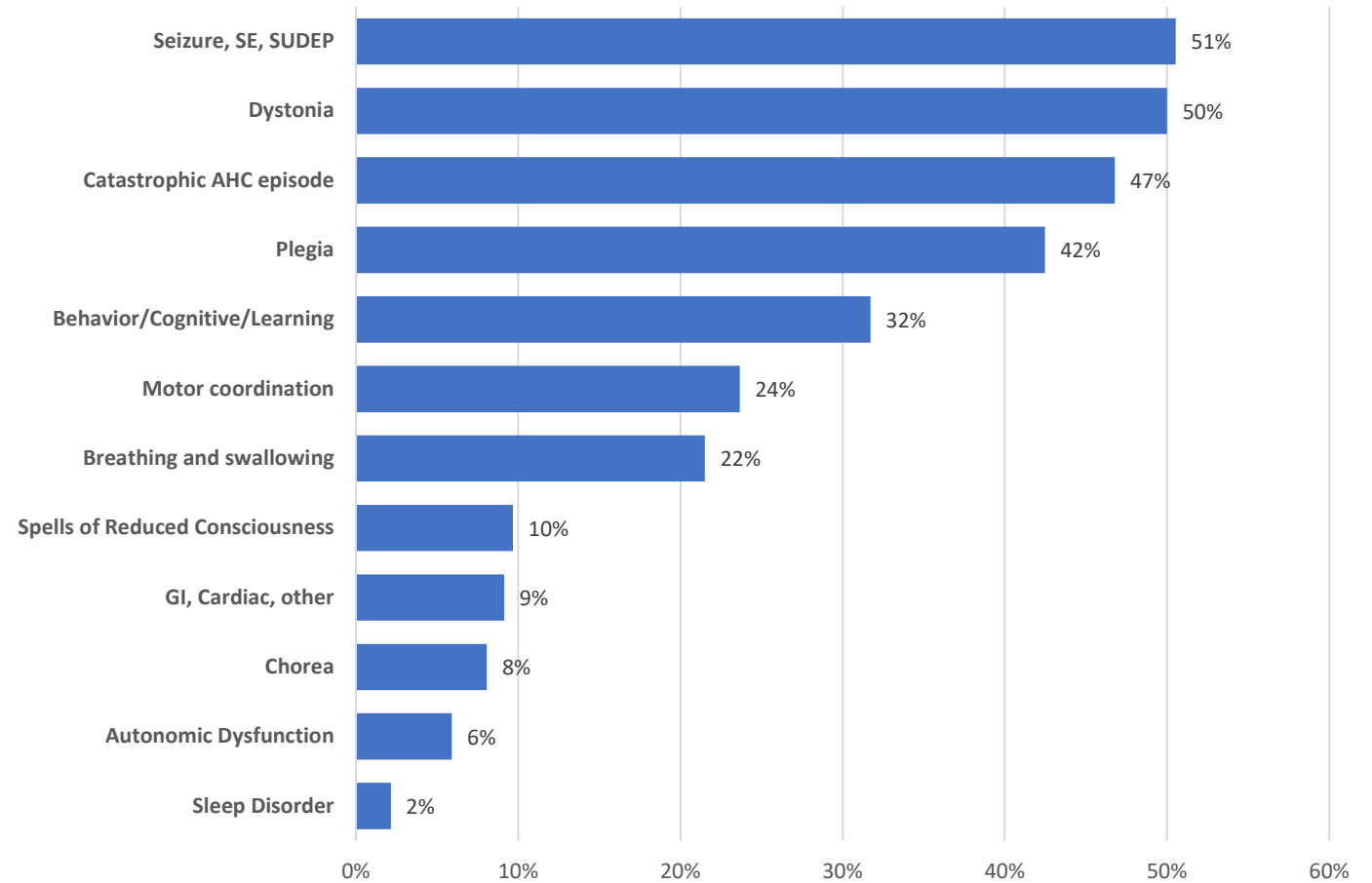
Understanding the Burden of Symptoms

“

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

Sleep

This section asks about your patient's experience with sleep. The questions refer to the last six months. This section has 16 questions.

1. Does your patient

- Always
- Often
- Rarely
- Never
- Not now, but in the past

2. Does your patient

- Always
- Often
- Rarely
- Never
- Not now, but in the past

Medications

This section asks about medications used by the patient. We will ask you to name the two medications that have had the most positive impact on the patient during their entire lifetime. We will also ask you to name the two medications that have had the most negative impact on the patient during their entire lifetime. Finally, we will ask about other medications used.

1. Which medication question refers to the patient. (Note that you will be asked to answer this question for each of the two medications you named in Question 6 below.)

Your answer

2. Which symptoms caused by the medication (Medication with the most positive impact)

- Hemiplegia or plegia
- Dystonia (painful involuntary muscle contractions)
- Seizures (patient has had seizures)
- Spells of reduced consciousness; confirmed or suspected Autonomic Dysfunction

Headaches

This section asks about the patient's experience with headaches. We understand that your patient may have difficulty communicating whether they have a headache. If you are not sure about your patient's experience, please provide your best estimate.

1. On average, approximately how often does your patient experience debilitating headaches?

- Multiple times a day
- Once a day
- Several times a week
- Once a week
- Every two weeks
- Once a month
- 6 times per year
- 3 times per year
- Once a year or less often
- My patient does not have headaches

Triggers

This section asks about your patient's experience with triggers of AHC episodes currently and over the course of their lifetime. This section has 15 questions.

1. Which triggers can cause AHC episodes in your patient, now and in the past?

Please check only those that apply and leave the others blank. If these triggers do not impact your patient, you may proceed to question 2.

	Currently (in the last six months)	In the past (more than six months ago)
Loud noise	<input type="checkbox"/>	<input type="checkbox"/>
Bright lights	<input type="checkbox"/>	<input type="checkbox"/>
Flashing lights	<input type="checkbox"/>	<input type="checkbox"/>
Hot temperatures	<input type="checkbox"/>	<input type="checkbox"/>
Cold temperatures	<input type="checkbox"/>	<input type="checkbox"/>
Humidity	<input type="checkbox"/>	<input type="checkbox"/>
Change in weather	<input type="checkbox"/>	<input type="checkbox"/>
Change in barometric pressure or change in altitude	<input type="checkbox"/>	<input type="checkbox"/>