Glut1 Deficiency Collective Voices Project

Sandra Ojeda, PhD
Glut1 Deficiency Foundation

Chantal Sanchez, BA
Columbia University Medical Center

Glenna Steele, MEd
Glut1 Deficiency Foundation

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Glut1 Deficiency Foundation
www.G1DFoundation.org

Introduction:

Glucose Transporter Type 1 Deficiency Syndrome (Glut1 Deficiency, G1D, Glut1DS) is a rare, genetic disorder that impairs brain metabolism.[1] It is caused by haploinsufficiency of the SLC2A1 gene coding for the glucose transporter type 1 (GLUT1) protein, which causes impaired glucose transport across the blood brain barrier and within the brain between astrocytes and neurons.[1,2] The failure to appropriately transport glucose to the brain causes a wide spectrum of neurological symptoms including the classical phenotype of seizures, a complex movement disorder, speech and language disorders, and cognitive disabilities.[1,3] There is currently no cure for Glut1 Deficiency; however, the recommended standard of care treatment is a medically supervised ketogenic dietary therapy (KDT), which helps improve most symptoms for most patients.

Objectives:

The Glut1 Collective Voices Project was designed to have a better understanding of the patient and family experience across a broad range of areas, including diagnosis, symptoms, the experiences with KDT and the patients and families' priorities among others. The goals of the survey were to better define the range of symptoms, identify gaps in treatment and patient care, identify gaps in knowledge and understanding of this disease, better understand disease burdens, and identify the most important components for our natural history study and our strategic research plan, our Research Compass.

Methods:

Survey content was developed through virtual focus group discussions and questionnaires in the patient community. The anonymous survey was conducted on the Qualtrics platform under Castle IRB. There were 246 questions and statistical analysis was provided by Insights Advisors Group.

Results:

We received 260 responses to the survey from 31 different countries. 95% of respondents were parents or caregivers and most of the patient population was within the 7–12 year-old range. The results indicate that on average it takes close to 3 years from the first symptom to get a diagnosis, and in most cases the diagnosis is made by a neurologist through genetic testing. Regarding symptoms, most patients experience the classical symptoms described in the literature,[1] however, many other less common symptoms were also reported. In addition, the results show that most of the patients experience changes in symptoms during puberty and adulthood. Despite the KDT being reported as at least partially helpful for most of the patients and most of the symptoms, the patients and families' top research priority is the development of new and better treatments. Furthermore, the priority outcomes that patients and families look for in new treatments are to be able to eat a normal diet, improve their cognition, and have better speech and communication skills. Finally, the results from the project helped inform the design of our natural history study as well as our Research Compass.

Conclusions:

Overall, the results from the Collective Voices Project show that there is a diverse community of patients with Glut1 Deficiency presenting a wide range of symptoms which can vary over time. The results highlight that patients and families prioritize the need for developing better treatments that improve their quality of life, emphasizing the importance they place in the social aspects, such as being able to eat a normal diet and improving their cognitive and communication skills.

Demographics:

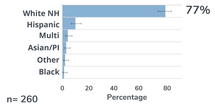
female 57% | male 43%

caregiver or parent 95% | patient 5%

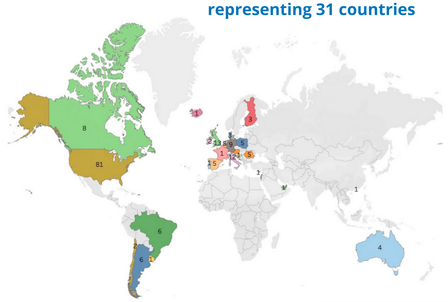
Age distribution of patients

birth to 6 years	23%
7-12 years	37%
13-17 years	17%
18-53 years	23%

Identity Group of patients



260 responses representing 31 countries

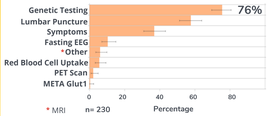


Diagnosis:

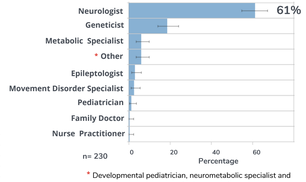
First symptom to diagnosis

shortest 1.5 weeks
longest 34 years
average 2.8 years

Diagnostic tool used?



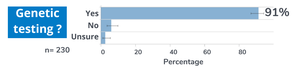
Who made the diagnosis?



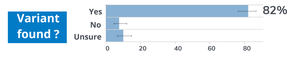
* Developmental pediatrician, neurometabolic specialist and neuropsychiatrist among others

average # of physicians seen to get diagnosis: 8

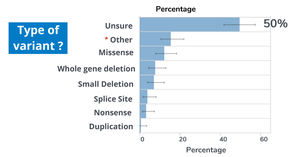
Genetic testing ?



Variant found ?



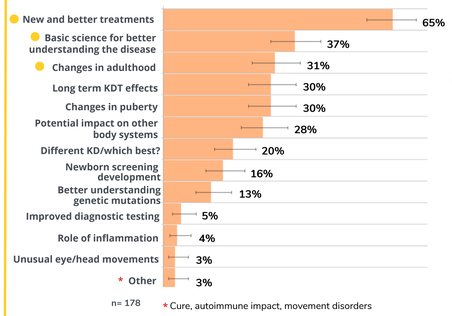
Type of variant ?



* Frameshift mutation and substitution among others

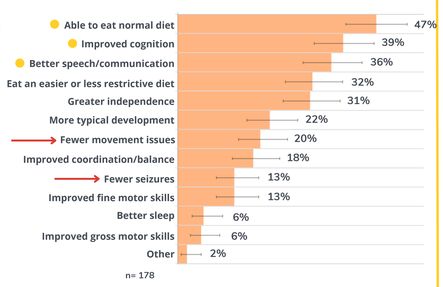
Patient and Family Priorities:

Research (choose top 3)



* Cure, autoimmune impact, movement disorders

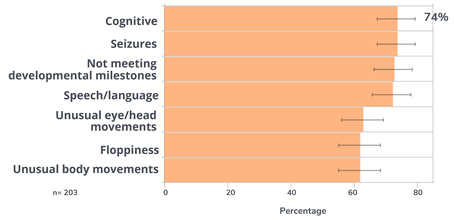
Outcomes for New Treatments



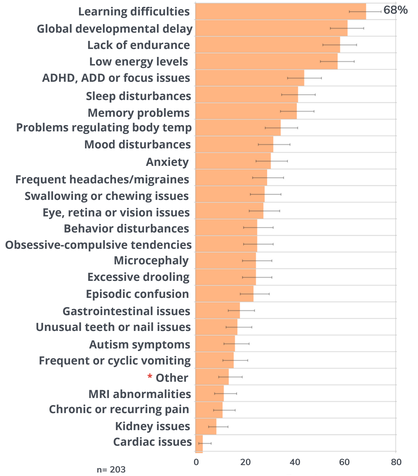
Patients and families prioritize social issues such as normal diet, cognition and speech over common symptoms

Symptoms:

Classical Check all that apply

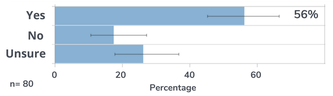


Other symptoms Check all that apply

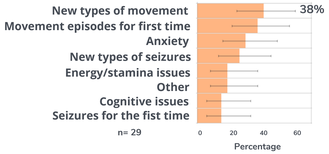


* Impulse control issues, sensory issues and hemiplegia among others

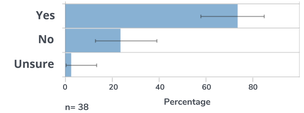
Did symptoms change with puberty?



How did symptoms change with puberty?



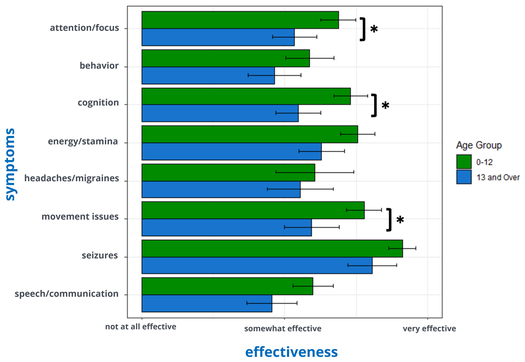
Did symptoms change in adulthood?



Which symptoms changed in adulthood?

Movement episodes and stamina/energy worsened, while seizures improved

KDT Treatment Effectiveness:



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2. Tang M, Monani UR. Glut1 deficiency syndrome: New and emerging insights into a prototypical brain energy failure disorder. Neurosci Insights. 2021;16:26331055211011507. Epub 2021/10/01. doi: 10.1177/26331055211011507. PubMed PMID: 34589708
3. Pascual J and Ronen G. Glucose Transporter Type I Deficiency (G1D) at 25 (1990-2015): Presumptions, Fact, and Lives of Persons With This Rare Disease. Pediatr. Neurol. 2015; 53:379-393. DOI:https://doi.org/10.1016/j.pediatrneurol.2015.08.001