recommended *treatment*

There is currently no cure for Glut1 Deficiency. The recommended standard of care treatment is a medically supervised ketogenic diet, which can help improve most symptoms for most patients. A ketogenic diet is a high fat, moderate protein, and low carbohydrate diet that causes the body to produce ketones which can be used as a fuel source for cells and can alter brain metabolism. Ketogenic diets have been used for more than 100 years to treat seizures, and studies show 4 out of 5 people who have epilepsy caused by Glut1 Deficiency will become seizure-free on a ketogenic diet. There are reported benefits in also improving movements and cognitive function, and the earlier ketogenic therapy is implemented the better the outcomes seem to be.

A classical 3:1 or 4:1 ketogenic diet is recommended in infancy and early childhood to ensure optimal benefits during critical stages of brain growth and development. Although it is also recommended to continue the classical version as long as tolerated, alternative versions such as Modified Ketogenic (2:1 and 1:1 ratios) or Modified Atkins Diet may be more feasible for quality of life and compliance considerations as people with Glut1 Deficiency get older.

For a subset of people with Glut1 Deficiency, a ketogenic diet proves ineffective despite adequate levels of ketosis. Medications to address the lingering symptoms of seizures, movement disorders, attention, and mood issues may provide some benefit, although there is currently no clear basis for specific recommendations, and there can be concerns to consider regarding potential harmful interactions with ketogenic diets.

other *therapies*

Occupational, physical, and speech and language therapies are often recommended for supporting optimal development in children and remain beneficial into adulthood. Families also report benefits from additional forms of regular therapy and exercise, particularly hippotherapy, aquatic therapy, martial arts classes, and mindfulness activities.

Many adults with Glut1 Deficiency have reported that regular physical exercise can help reduce movement disorder symptoms.

estimated *prevalence*

It is believed that two to three thousand people are currently diagnosed with Glut1 Deficiency worldwide. Recent studies have estimated prevalence to be at least 1:24,000, so the vast majority remain undiagnosed. There's no known susceptibility for gender or race.

current *research*

Recent research developments have changed the way we understand the fundamentals of this disease, especially the idea that this isn't just a brain energy defect. Ongoing research aims to better understand the mechanisms of Glut1 Deficiency in the brain and throughout the body, develop better diagnostic tools, and identify easier and more effective treatments for the future.

research *compass*

scan to learn more about PATIENT-LED RESEARCH PRIORITIES

our *mission*

The Glut1 Deficiency Foundation is a nonprofit patient advocacy organization dedicted to improving lives in the Glut1 Deficiency community through:

- increased awareness
- improved education
- advocacy for patients and families
- support and funding for research

natural history STUDY — Glut1 Deficiency

The Glut1 Deficiency Foundation has developed a natural history study to help understand individual experiences of people who have this disease so researchers can better understand its impact on patients and how that may change over time. These insights will be critical for developing new and better ways to diagnose and treat Glut1 Deficiency.

Learn how you can participate at www.G1DFoundation.org.

Reaching for a Brighter Future! — Glut1 Deficiency Foundation — www.G1DFoundation.org

new code
ICD-10
glucose transporter protein type 1 deficiency syndrome
E74.810
effective October 1, 2020

A GUIDE TO *understanding* Glut1 Deficiency

GLUCOSE TRANSPORTER TYPE 1 DEFICIENCY SYNDROME

Glut1 Deficiency Foundation

www.G1DFoundation.org

disease *definition*

Glut1 Deficiency is a rare genetic disorder that impairs brain metabolism. Glut1 is the only transporter of glucose across the blood brain barrier, but it also moves other necessary sugars into the brain as well, and these all play critical roles in multiple metabolic pathways.

People with Glut1 Deficiency don't have enough of these transporters or they don't work properly, so their brains are not getting all the necessary components for normal brain metabolism, which can cause a wide range of neurological symptoms.

genetic *cause*

Glut1 Deficiency is caused by mutations or variants in the SLC2A1 gene, located on chromosome 1. This gene is responsible for providing the instruction code to produce the glucose transporter protein type 1 *(Glut1)*. It only takes one faulty copy of this gene *(out of two)* to cause disease in an individual. These variants most often occur spontaneously and are not inherited, but people with Glut1 Deficiency do have a 50% chance of passing the same variant on to each child.

understanding *symptoms*

Since Glut1 is so important for brain function, people who have Glut1 Deficiency can have a number of symptoms in a variety of combinations. These symptoms and their severity may look different from person to person and can fluctuate daily and change over time as they grow and age. Puberty often brings changes in symptoms and treatment response.

SEIZURES

Seizures are common but not always present, and multiple seizure types can occur within the same individual. Typically, seizures begin in infancy or early childhood and tend to stabilize, decrease, or sometimes eventually stop in adulthood for some people. Most seizures in Glut1 Deficiency are not easily treated with medications.

MOVEMENT DISORDERS

The majority of people with Glut1 Deficiency experience some type of complex movement disorder that can cause ongoing difficulties with tone, gait, balance, coordination, and fine and gross motor skills. Temporary episodes of a wide range of unusual and involuntary body movements or paralysis can occur as well, including those that are triggered by exercise or other factors. Movement disturbances tend to become the dominant feature in adolescence and adulthood, and new types of movement episodes may appear.

UNUSUAL EYE-HEAD MOVEMENTS

Many patients experience episodes of unusual eye-head movements, which are often the first symptom to appear in infancy and represent an important diagnostic clue. These resemble opsoclonus but are distinct in that the eyes and head move together in multiple directions. They tend to resolve by early childhood even without treatment.

scan to watch an UNUSUAL EYE-HEAD MOVEMENT VIDEO

SPEECH AND LANGUAGE DISORDERS

Communication challenges are common for people with Glut1 Deficiency, including difficulties producing clear and fluent speech and also with processing and expressing language.

COGNITION AND LEARNING

Most people with Glut1 Deficiency experience some degree of cognitive impairment ranging from subtle learning and memory difficulties to severe intellectual disabilities.

DEVELOPMENTAL DELAYS

Due to the many symptoms that people with Glut1 Deficiency experience, global developmental delays are common. In childhood, this may mean milestones take longer to reach, and in adulthood these disabilities can have a substantial impact on independence.

BEHAVIORAL CHALLENGES

Behavioral symptoms may include a short attention span and delays in achieving age-appropriate behaviors. Some people with Glut1 Deficiency have been additionally diagnosed with attention deficit and/or autism spectrum disorders. Anxiety, obsessive-compulsive tendencies, and mood and behavior disorders are also reported. Sociability, however, is often reported as a strength.

ADDITIONAL POSSIBLE SYMPTOMS

- migraines
- hemiplegia
- episodic confusion
- low energy and stamina
- sleep disturbances
- cyclic vomiting
- smaller than normal head size
- temperature regulation issues

TRIGGERS

Symptoms can be triggered or worsened by excessive exercise, fever and illness, hunger, weather and temperature changes, hormones, fatigue, changes in routine and sleep patterns, anxiety, excitement, and other strong emotional reactions.

diagnostic *protocols*

Early diagnosis is critical in order to initiate treatment so symptoms can be alleviated, brain growth and development may be optimized, and quality of life can be improved. The presence of at least two of the following three criteria warrants a Glut1 Deficiency diagnosis:

- ✓ suggestive symptoms
- ✓ lumbar puncture results
- ✓ genetic testing results

LUMBAR PUNCTURE

When Glut1 Deficiency is suspected, glucose should be measured in the spinal fluid (CSF) and in the blood after a 4-6 hour fast. Blood samples should be drawn first to avoid any stress-related elevations in blood glucose, and a lumbar puncture should quickly follow.

METABOLIC HALLMARKS

- ✓ FASTING CSF GLUCOSE: below 3.0 mmol/L or 53 mg/dl
- ✓ FASTING CSF TO BLOOD GLUCOSE RATIO: below 60%

LOW: CSF glucose

NORMAL: blood glucose cell counts CSF protein

LOW NORMAL: CSF lactate

GENETIC ANALYSIS

Genetic testing can also help confirm the diagnosis by detecting a variant in the SLC2A1 gene, although current testing does not identify a variant in 10 to 15% of cases. The combination of suggestive clinical symptoms and the characteristic CSF findings indicate a Glut1 Deficiency diagnosis, even in the absence of an SLC2A1 variant.

Dystonia 9 and 18 are also associated with variants in the SLC2A1 gene.

scan the consensus GUIDELINES