

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 some 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 - the symptom that responds most to this therapy in GLUT1 Deficiency. There are reported benefits in also improving movements and cognitive function, and the earlier ketogenic therapy is implemented the better the outcomes.

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 for 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.

For a subset of people with GLUT1 Deficiency, a ketogenic diet proves ineffective despite adequate levels of ketosis. Medications to address the lingering symptoms 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 can 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.

E74.810
ICD-10 CODE

Estimated Prevalence

A few thousand people are thought to be 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 fundamental understanding of this disease, especially the idea that it 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 find easier and more effective treatments for the future.



Our Mission

The GLUT1 Deficiency Foundation is a parent-led nonprofit patient advocacy organization dedicated to bringing help and hope to the GLUT1 Deficiency community as we work together to improve lives through awareness, education, advocacy, and research.

Our Vision

We are building a brighter future where GLUT1 Deficiency will be easy to diagnose early, treat effectively, and one day cure completely.



shining a *light* on
GLUT1 DEFICIENCY

**GLUCOSE TRANSPORTER TYPE 1
DEFICIENCY SYNDROME**



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, all playing critical roles in multiple metabolic pathways.

Individuals who have 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 variants in the *SLC2A1* gene, which is responsible for encoding the glucose transporter protein type 1 (GLUT1). This is an autosomal dominant condition, which means just one altered copy of the gene (out of two total) can cause disease. These variants most often arise spontaneously and are not inherited, but individuals with GLUT1 Deficiency do have a 50% chance of passing the same variant on to each of their children.

Understanding Symptoms

Since GLUT1 is so important for brain function, individuals 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 loss of movement 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 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.

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, illness, hunger, weather and temperature changes, hormones, stress, fatigue, anxiety, excitement, and other strong emotional reactions.



Diagnostic Protocol

Early diagnosis is critical for initiating treatment, which can help relieve symptoms, support optimal brain growth and development, and enhance quality of life. The presence of at least 2 of the following 3 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



LOW: CSF glucose
LOW to LOW-NORMAL: CSF lactate



NORMAL: blood glucose, cell counts, CSF protein

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

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 a genetic variant.

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



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