What is SLC6A1?

The gene SLC6A1 encodes the GABA transporter protein type 1 (GAT1). The primary function of GABA transporters, such as GAT1, is to lower the concentration of GABA in the extracellular space between neurons and other cell types. The activity of GAT1 is dependent upon concentrations of sodium and chloride ions within as well as outside the cell.

Other names for SLC6A1 include SLC6A1, GABATR, and GAT1.

What types of seizures (and epilepsies) are associated with variants in SLC6A1?

Variants in SLC6A1 are most commonly associated with myoclonic atonic seizures, which occur in approximately 25% of patients. Patients may also present as genetic generalized epilepsy (22% of patients) or non-acquired focal epilepsy (~10% of patients). Other types of generalized seizures, including absence, atonic, and myoclonic seizures, may also be seen. The average age of seizure onset is 2.5 years. EEGs reveal common characteristics in children with SLC6A1 disorder and may be used to assist with diagnosis.

What non-seizure symptoms are seen in individuals with variants in SLC6A1?

Developmental delay, cognitive impairment, and symptoms of autism spectrum disorder are the most common clinical features reported in the literature. Many children also have impairments in motor coordination and function. Musculoskeletal, gastrointestinal, sleep disturbances, and visual impairments are also reported. There are some reports that select variants result in regression in some children. For instance, cognitive skills such as verbal communication skills gained during infancy may be lost with age in some children. There is currently no evidence to support a connection between seizures and cognitive performance.

How are variants in SLC6A1 diagnosed?

SLC6A1 variants can only be identified by genetic testing. Targeted testing of the SLC6A1 gene specifically would be the most direct method of testing an individual when there is a high degree of confidence that a variant in the SLC6A1 gene is likely to be the underlying cause. However, single gene testing is performed infrequently in most clinical practice settings. Epilepsy gene panels, which involve testing of multiple epilepsy-associated genes, and exome sequencing (ES) are the most common tests that are in use to detect SLC6A1 variants.

Genetic counseling prior to genetic testing is an important step in making sure that the best testing strategy is selected, and that patients and families understand the risks, benefits, limitations, and possible outcomes of testing.

How is SLC6A1 treated?

Current treatments for epilepsy associated with SLC6A1 disorder include anti-seizure medications, including valproic acid, lamotrigine, and benzodiazepines. These medications are effective at reducing and/or eliminating seizures in some individuals. Ketogenic diets have also been utilized to manage seizures with some degree of success.

How common are SLC6A1-related disorders?

The current incidence estimate is 1 in 38,000 births. The vast majority of variants in SLC6A1 appear to have occurred *de novo* (presenting for the first time in the individual diagnosed due to a variant in the egg or sperm that gave rise to the individual, rather than inherited from a family member). There are currently more than 20 pathogenic variants reported and a wide range in symptoms.

What is the outlook for SLC6A1-related disorders?

The outlook for children affected by SLC6A1 variants remains promising. As we speak, there are scientists around the world studying the impact of these variants and how they lead to clinical symptoms. Our understanding of this genetic condition increases daily, and we now understand that children with variants in SLC6A1 may regress as well as improve in respect to select clinical symptoms. The field is rapidly evolving, and the first SLC6A1-specific clinical trials began in 2021.

For more information

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