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Tremor and Other Hyperkinetic Movements

Video Abstracts

# Paroxysmal Exercise-induced Dyskinesias Caused by GLUT1 Deficiency Syndrome

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## Abstract

**Background:** Glucose transporter type 1 deficiency syndrome is due to *de novo* mutations in the *SLC2A1* gene encoding the glucose transporter type 1.

**Phenomenology Shown:** Paroxysmal motor manifestations induced by exercise or fasting may be the main manifestations of glucose transporter type 1 deficiency syndrome.

**Educational Value:** Proper identification of the paroxysmal events and early diagnosis is important since the disease is potentially treatable.

**Keywords:** Paroxysmal exercise-induced dyskinesia, epilepsy, GLUT1 deficiency, *SLC2A1*, dystonia

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An 18-year-old female with a history of non-febrile generalized seizures in infancy presented with paroxysmal exercise-induced dyskinesia (Video 1). Pregnancy, delivery, neonatal period and early psychomotor development were normal. Between the ages of 18 months and 3 years she had recurrent episodes of gait disturbance, lasting from a few minutes to several days. During childhood, she developed learning disability with attention deficit hyperactivity disorder (ADHD), but eventually completed high school. At age 16 years, she again began to have paroxysmal gait disturbances lasting from a few minutes to several hours. The episodes occurred several times in a month. They were triggered by prolonged exercise or fasting, and could be relieved by carbohydrate intake or rest. At the age of 18 years, interictal examination was normal. Her head circumference was 52 cm (3rd centile). Brain imaging was normal. The cerebrospinal fluid to blood glucose ratio, obtained after 10 hours of fasting, was slightly decreased (0.54, Normal>0.59). Genetic analysis found a heterozygous missense mutation in the *SLC2A1* gene (c.940G→A/pGly314Ser), which was previously found to be responsible for mild to moderate forms of glucose transporter type 1 deficiency syndrome (GLUT1-DS).

GLUT1-DS is a rare disorder mostly due to *de novo* mutations in *SLC2A1*, which encodes the type 1 glucose transporter protein.[1] Mutations in this gene limit brain glucose availability and lead to cerebral energy deficiency.[1] The consequences of energy failure on brain development and functions vary from mild motor dysfunction to severe neurological disorders, with a broad phenotypic spectrum.[1,2] Early identification of the affected patients is important for clinical practice since the disease is potentially treatable. Diagnosis should be considered in any child or adolescent with paroxysmal motor manifestations, which may occasionally be the main manifestation of the disease.[1,2,3] We provide a demonstrative video of such paroxysmal episodes, which are often difficult to capture and not always easy to recognize from history taking. The history of generalized seizures, ADHD, and learning disability may be good clues to the diagnosis in this setting.


**Video** 1. **Dystonia induced by fasting and a prolonged exercise.** The patient was asked to run as far as she could. She had no manifestation when starting to run. After 20 minutes of running, she felt discomfort that she described as "a sensation of traction" within the left thigh preventing her from walking normally. After 50 minutes of physical exercise, she had dystonic contractions resulting in flexion of her hips and knees. She had similar difficulties when walking side to side or backwards. By contrast, she was able to run normally, corresponding to an improvement, when switching the motor program.

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