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Criss-cross gait: A clue to glucose transporter type 1 deficiency syndrome

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Nearly 90% of patients with Glucose Transporter Type 1 Deficiency Syndrome (Glut1 DS; Figure) have paroxysmal or constant gait abnormalities, including ataxic, spastic, ataxic-spastic, and dystonic gait.[1,2] We report three cases of genetically proven Glut1 DS (Table) demonstrating a distinctive paroxysmal gait disorder triggered by exertion or fasting, herein named “criss-cross gait” (Video,http://links.lww.com/WNL/B183). It is characterized by lower-body choreo-dyskinesia causing the legs to intersect repeatedly, producing irregular, random steps combined with some loss of balance. Compensatory upper-body movements help maintain balance. In the appropriate clinical context, the criss-cross gait should prompt evaluation for the treatable Glut1 DS and not be misinterpreted as functional.

Figure. Overview of the pathogenesis, phenotypes, diagnosis, and treatment of Glut1 DS.

Legend: ATP= adenosine triphosphate; Glc = glucose; Glut= glucose transporter; KB = ketone bodies; Lac = lactate; MCT = monocarboxylic transporter; Pyr = pyruvate. Red dashed lines indicate defective pathways in Glut1 DS.

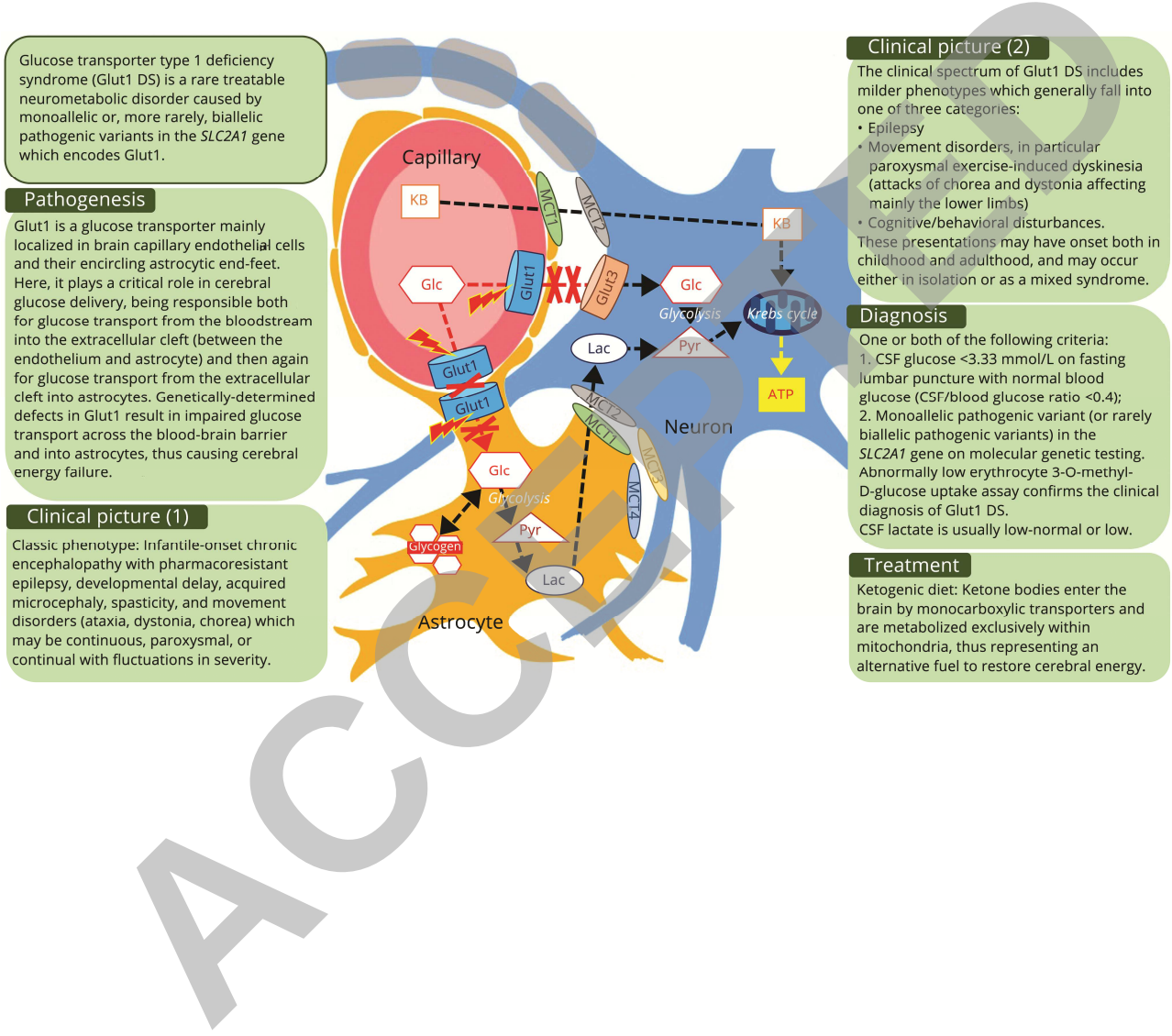

Table. Clinical and genetic features of three patients with genetically confirmed Glut1 DS showing the criss-cross gait (Video).

	Case 1	Case 2	Case 3
Current age	54	25	24
Sex	Female	Male	Female
Ethnicity	White British	White British	Germanic
Age of onset	6 years	5 years	11 months
Clinical picture	• PED (episode of toe curling, foot dystonia, limb choreoathetosis)	• PED (episodes of foot dystonia, jerky choreiform movements in his limbs) • Episodes of slurred speech	• Motor development delay • Atypical absence epilepsy • PED (episodes of "wobbly gait") Mild intellectual disability
Family history	Father: history of paroxysmal dystonic choreoathetosis, possibly affected (retrospectively); son affected.	Father affected	Negative (de novo mutation)
CSF analysis	Not performed	CSF glucose = 1.9 mmol/L (with blood glucose = 6.8 mmol/L) CSF/blood glucose ratio = 0.28	Not available
Genetic testing *SLC2A1* (ENST00000426263)	Heterozygous variant c.601T>C (p.Cys201Arg)	Heterozygous variant c.278G>A (p.Arg93Gin)	Heterozygous variant c.998G>A (p.Arg333Gin)
Treatment and follow up	Patient declined to get started on ketogenic diet. Overall reduction in the intensity and frequency of her paroxysmal symptoms with age over a 20-year follow up.	Ketogenic diet since age 6 with marked improvement of his symptoms. Episodes characterized by mild twitching in his feet, difficulty concentrating and slurred speech my occur in relation to occasional dietary indiscretions.	Ketogenic diet since age 12 with low adherence. Mild constant gait unsteadiness and occasional paroxysmal worsening of her gait disturbance over a 12-year follow up.

PED = paroxysmal exercise-induced dyskinesia.

Video. Three patients with Glut1 DS (Table) showing the “criss-cross gait”, triggered by exertion or fasting. It is characterized by attacks of lower-body choreo-dyskinesia causing the legs to intersect repeatedly, resulting in irregular, random steps with some loss of balance. Upper-body movements counteract leg dyskinesia in order to maintain balance.

Appendix 1:

Author Contributions

Name	Location	Contribution
Francesca Magrinelli, MD	Queen Square Institute of Neurology, University College London, London, UK	Design and conceptualized study; major role in the acquisition of data; analyzed the data; drafted the manuscript for intellectual content.
Eoin Mulroy, MD, FRACP	Queen Square Institute of Neurology, University College London, London, UK	Design and conceptualized study; major role in the acquisition of data; revised the manuscript for intellectual content.
Susanne A. Schneider, MD	Ludwig-Maximilians-Universität München, München, Germany	Major role in the acquisition of data; revised the manuscript for intellectual content.
Anna Latorre, MD, PhD	Queen Square Institute of Neurology, University College London, London, UK	Major role in the acquisition of data; revised the manuscript for intellectual content.
Giulia Di Lazzaro, MD	Queen Square Institute of Neurology, University College London, London, UK	Major role in the acquisition of data; revised the manuscript for intellectual content.
Anita Hennig, MD	Ludwig-Maximilians-Universität München, München, Germany	Major role in the acquisition of data; revised the manuscript for intellectual content.
Stephanie Grunewald, MD, PhD	UCL Great Ormond Street Hospital Institute of Child Health, NIHR Biomedical Research Center, London, UK	Major role in the acquisition of data; revised the manuscript for intellectual content.
Darryl C. De Vivo, MD	Columbia University Irving Medical Center, New York, NY, USA	Major role in the acquisition of data; revised the manuscript for intellectual content.
Kailash P. Bhatia, MD, DM, FRCP	Queen Square Institute of Neurology, University College London, London, UK	Design and conceptualized study; major role in the acquisition of data; revised the manuscript for intellectual content.

Video-http://links.lww.com/WNL/B183

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