LETTER TO THE EDITOR

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Bilateral globus pallidus internus-deep brain stimulation in a 5-year-old boy with *SGCE*-related myoclonus dystonia syndrome

To the editor:

Myoclonus-dystonia syndrome (MDS) (OMIM15990) is a heritable disorder characterized by early onset subcortical myoclonic jerks and/or less prominent dystonia. This leads to disability and is often refractory to medical treatment.[1] Deep brain stimulation (DBS) for the treatment of refractory MDS has been proven effective in adults for reducing both myoclonic jerks and dystonia.[1–3] Here, we describe the application of bilateral globus pallidus internus (GPi) DBS in a 5-year-old boy diagnosed with MDS.

This boy was born with an uneventful pregnancy in a non-consanguineous family. The developmental milestones were normal during the first year of life. However, at the age of 1.5 years old, following a cold, he experienced episodes of stiffness in the left lower extremity, accompanied by an abnormal walking posture. Subsequently, he began to fall repeatedly, with sudden muscle jerks in the legs while walking. The jerks initiated in the legs progressively intensified and spread to the trunk, neck, and arms. These involuntary movements were exacerbated by actions, stress, and fatigue. Due to the severe impact on the upper limbs, he was unable to feed himself and draw.

Conventional blood examinations, electroencephalogram, and cerebral magnetic resonance imaging results were normal. At the age of 2 years old, whole exome sequencing revealed a novel *de novo* variant in the epsilon-sarcoglycan (*SGCE*) gene (c.1037+1G>A, Figure S1), which was pathogenic according to the American College of Medical Genetics and Genomics guidelines, finally establishing the diagnosis of MDS.

Levodopa, valproic acid, nitrazepam, and levetiracetam were discontinued due to a lack of benefit. Zonisamide was effective at first, leading to a reduction in falls and myoclonic jerks in the arms. However, the symptoms worsened, including an abnormal posture of the left leg during walking, frequent falls accompanied by rapid leg jerks, an inability to write, and shaking arms and hands when holding pencils or chopsticks. These symptoms significantly affected his daily life (Video S1).

After several formal meetings with the functional neurosurgery team and the patient's family at our neurological center, the boy underwent bilateral GPi-DBS surgery using a Leksell stereotactic frame finally (Figure S2). Postoperative programming commenced 3 days later, the start-up parameters were R-Gpi C+ 2−, 2.0 V, 130 Hz, 60 μs; L-Gpi C+ 6−, 2.0 V, 130 Hz, 60 μs. The stimulation parameters were adjusted remotely based on the boy's symptoms and tolerance. In the last follow-up (about 12 months after surgery), with parameters set at R-Gpi C+ 3−, 3.4 V, 150 Hz, 70 μs; L-Gpi C+ 7−, 3.4 V, 150 Hz, 70 μs, the boy exhibited normal walking, no longer experienced falls, could run and jump, and demonstrated significantly improved abilities to hold a pencil for writing and use chopsticks (Video S1). He could freely perform daily activities such as dressing, eating, drinking, and writing (Figure 1). His parents described a dramatic improvement in his quality of life.

MDS is a group of movement disorders with genetic heterogeneity. Mutations in the *SGCE* gene are detected in 30%–50% of the patients with the clinical syndrome, while other genes including *ADCY5*, *CACNA1B*, *KCTD17*, and *RELN*, can also contribute to the MDS phenotype.[1,2] Myoclonus, the most prominent and disabling feature, manifests as brief, rapid, lightning-like, involuntary, and uncontrollable muscle contractions. The contractions mostly involve the neck, trunk, and upper limbs, with less frequent involvement of the legs. Dystonia is found in approximately 50% of affected individuals, which is more common in the cervical muscles and upper extremities. In children, it may also extend to the lower extremities. Since the pathogenic mechanism of MDS

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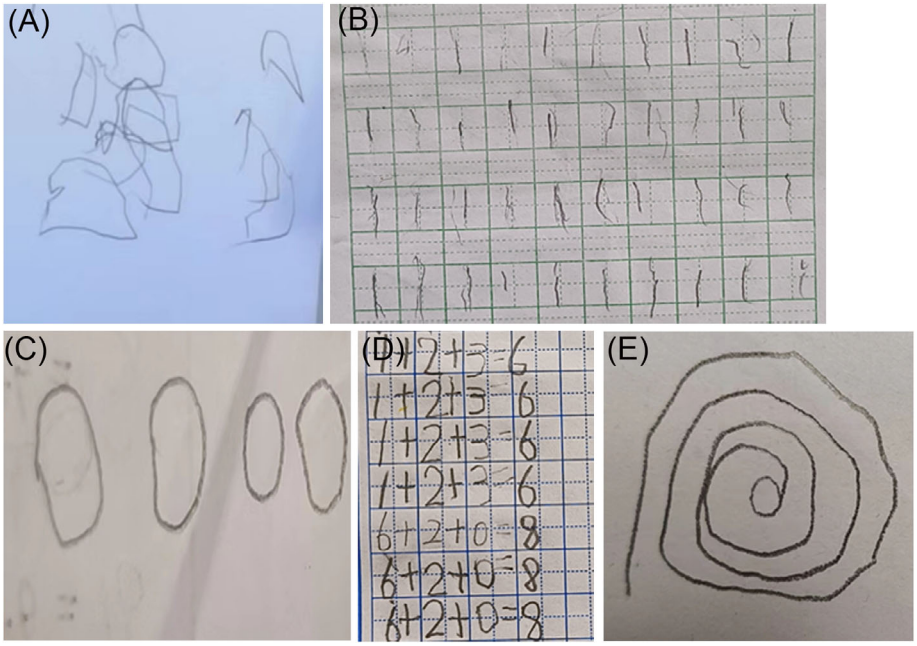

FIGURE 1 Handwriting recordings of the boy with myoclonus-dystonia syndrome before and after deep brain stimulation therapy. (A, B) Before the surgery, the patient struggled to draw "0" and "1" due to frequent myoclonus in the upper limbs. (C, D) Twelve months after the surgery, he could write "0" and numbers smoothly, with a significant improvement in myoclonus. (E) After the surgery, he could draw Archimedes' spiral diagram smoothly.

remains unclear, it is mostly treated symptomatically.[4] This patient had an early onset age (around 1.5 years old) and presented with episodic lower limb dystonia as the first manifestation, which is rare in MDS and was poorly treated with drugs.

In recent years, DBS has shown significant promise in pediatric neurological disorders such as primary and secondary dystonia, refractory epilepsy, Tourette syndrome, and cerebral palsy,[5,6] despite pediatric patients often have altered anatomy and challenging relationships between diseased and eloquent structures. There is meta-analytic evidence DBS therapy resulted in remarkable and sustained improvement of myoclonus and dystonia symptoms in drug-refractory SGCE-MDS.[3,7–11] The pathogenic mechanisms of MDS are presumed to be associated with a dysfunctional striato-pallido-thalamo-cortical pathway and cerebello-thalamo-cortical pathway.[2,4] GPi stimulation is more effective and has fewer adverse events than other targets.[3,4] There is a trend toward greater improvements in motor symptoms among patients who undergo surgery at a younger age and have a shorter clinical course.[3] However, the mean age of the patients who underwent DBS surgery was 38.7 years (8–74 years), with the vast majority being adult patients.[3,10] Our patient underwent DBS surgery at 5 years old with a satisfactory result. This case implied the efficacy and safety of DBS in pediatric patients.

To our knowledge, this case is the youngest child with SGCE-MDS reported to have undergone bilateral GPi-DBS. This case underscores the potential of early-stage DBS in pediatric cases, paving the way for further research to refine treatment protocols and explore the broader applicability of this intervention in diverse pediatric movement disorders. Moreover, continued collaborations with pediatric neurologists, neurosurgeons, and families are needed to optimize outcomes.

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CONSENT FOR PUBLICATION

The family provided informed consent on the publication of this case.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

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