Deep Brain Stimulation of bilateral Globus Pallidus internus in a 5 year-old boy with SGCE-related myoclonus dystonia

Xiaojuan Tian[1], Changhong Ding[1], Ming Liu[1], Lifang Dai[1], Zixing Xie[2], Tie Fang[2] Email: tianxiaojuanhi2007@163.com

1.Department of Neurology, Neurological Center, Beijing Children's Hospital, Capital Medical University, National Center for Children's Health, 100045, China

2.Department of Functional Neurosurgery, Neurological Center, Beijing Children's Hospital, Capital Medical University, National Center For Children's Health, China, Beijing 100045, China

Myoclonus-dystonia syndrome (MDS) is a heritable disorder characterized by early onset subcortical myoclonic jerks and/or less prominent dystonia which is disabling and refractory to medical treatment. Deep Brain Stimulation (DBS) for treatment-refractory MDS has been effective in adults for reduction in both myoclonic jerks and dystonia. The mean age at surgery was 38.7 years old for effective use of DBS in MDS, with a significant trend toward improved myoclonus outcome with older age at onset and shorter clinical course. However, few evidence were found in pediatric patients. Here, we describe DBS in the bilateral Globus Pallidus internus (GPi) in a 5-year-old boy diagnosed with MDS.

Case Presentation

- This boy was born with an uneventful pregnancy in a non-consanguineous family . Developmental milestones were normal during the first year of life. At age 1.5 after a cold, he experienced episodes of stiffness of left lower extremity, accompanied by an abnormal walking posture, then 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 action, 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 MRI were normal. Whole exome sequencing at 2 years old revealed a novel de novo variant in the epsilon-sarcoglycan (SGCE) gene (c.1037+1G>A), which was pathogenic according to the American College of Medical Genetics and Genomics (ACMG) guidelines, finally establishing the diagnosis of MDS.
- Levodopa, valproic acid, nitrazepam, and levetiracetam were discontinued due to lack of benefit. Zonisamide was effective at first, with a reduction in falls and myoclonic jerks in arms. Later, the symptoms worsened, with abnormal posture of the left leg when walking, frequent falls accpanied by rapid leg jerks, an inability to write, shaking arms and hands when holding a pencil or chopsticks with. These symptoms seriously affected his daily life（Video 1）.
- We discussed the possibility of DBS therapy several times as for the very young age and the unknown outcome of DBS in such a young child. The boy underwent bilateral GPi-DBS surgery using a Leksell stereotactic frame finally (Fig. 2). Postoperative programming commenced 3 days after, the start-up parameters were R-Gpi C+ 2-, 2.0V, 130Hz, 60μs; L-Gpi C+ 6-, 2.0V, 130Hz, 60μs. The stimulation parameters were adjusted remotely according to the boy's symptoms and tolerance. At last follow-up (about 12 months after surgery) with parameters of R-Gpi C+ 3-, 3.4V, 150Hz, 70μs; L-Gpi C+ 7-, 3.4V, 150Hz, 70μs, 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 1）. The boy could freely perform daily activities such as dressing, eating, drinking and writing (Fig. 1). His parents described a dramatic improvement in quality of life.

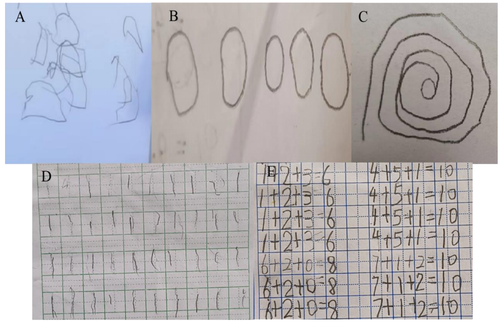


Fig. 1 The handwriting recordings of the MDS patient before and after DBS therapy. A and D before the surgery, he drew "0" and "1" hardly with frequent myoclonus of upper limbs; B and E 12 months after the surgery, he could write "0" and numbers smoothly with myoclonus significantly improved; C after the surgery, he could draw Archimedes' spiral diagram smoothly.

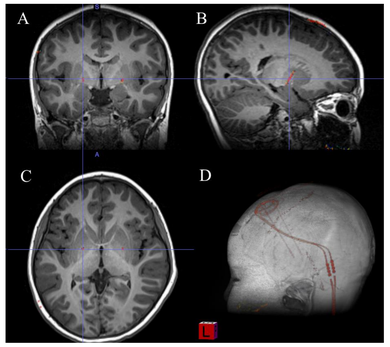
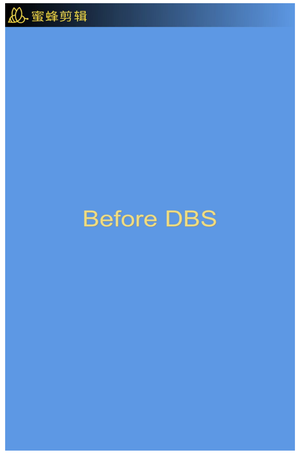


Fig. 2 Imaging of deep brain stimulation (DBS) electrode localization of globus pallidus interna(left side for example) Postoperative T1-weighted magnetic resonance images. A Coronal plane, B Sagittal plane, C Axial plane, D Electrode implantation traject.



Video 1 Pre- and Postoperative examinations for the patient Before the surgery, he wrote "0" and "1" hardly with frequent myoclonus of upper limbs, he walked unsteadily with stiffness of left leg and sudden jerks of legs (right side mainly). He had myoclonus of legs (right side mainly) in marking tine test and he walked slowly and awkwardly with stiffness of left leg. At 12 months after the GPi-DBS surgery, he could write "0" smoothly with myoclonus significantly improved and he could run normally without falls.

DISCUSSIONS AND CONCULSIONS

- MDS is a group of movement disorders with genetic heterogeneity. Mutations in SGCE are found in 30-50% of the patients with the clinical syndrome. Since the pathogenic mechanism of MDS is still unclear, it is mostly treated symptomatically.
- There is meta-analytic evidence DBS therapy resulted in remarkable and sustained improvement of myoclonus and dystonia symptoms in drug-refractory SGCE-MDS. The pathogenic mechanisms of MDS is presumed to be associated with a dysfunctional striato-pallido-thalamo-cortical pathway and cerebello-thalamo-cortical pathway. GPi stimulation is more effective and has fewer adverse events than other targets. There is a trend toward greater improvements in motor symptoms in patients at a younger age at surgery and a shorter clinical course. However, the mean age these patients underwent DBS surgery was 38.7 years (8-74 years), with the vast majority being adult patients. Our patient underwent DBS surgery at 5 years old with a satisfactory result. This case showed the efficacy and safety of DBS in pediatric patient.
- 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, A continued collaboration in pediatric neurologist, neurosurgeons and families is needed to optimize outcomes.