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Tremor and Other Hyperkinetic Movements

Case Report

A Case of Myoclonus–Dystonia Responding to Low-frequency Pallidal Stimulation

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Abstract

Background: High-frequency pallidal stimulation has been shown to improve various types of dystonia, including myoclonus-dystonia.

Case Report: We report a case of epsilon sarcoglycan mutation-negative myoclonus–dystonia with response to low-frequency bilateral pallidal stimulation.

Discussion: Low-frequency pallidal stimulation provides an effective means of treating various dystonias, regardless of genetic status, as in our case, as it provides increased programming options with fewer adverse effects.

Keywords: Myoclonus–dystonia, deep brain stimulation, low-frequency stimulation

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Introduction

Myoclonus–dystonia (MD) is a genetically and phenotypically heterogenous condition, which presents with myoclonus of proximal muscles and dystonia, typically of the neck and arm.[1] Most commonly, mutations in the epsilon sarcoglycan (*SGCE*) gene are found but approximately 50% of cases do not have mutations in this gene.[2] Deep brain stimulation (DBS) can be effective in the treatment of MD, with most cases reporting positive effects of pallidal stimulation.[2] Although several reports demonstrated improvement with high-frequency pallidal stimulation, we report a case of *SGCE* mutation-negative MD whose myoclonus and dystonia responded to low-frequency bilateral pallidal stimulation.

Case report

The patient is a 36-year-old female without any significant medical or family history who presented to our movement disorders center after 7 years of difficulty walking and myoclonus. Her family reported that her walking difficulty began at the age of 14 years. Her symptoms continued to progress, and she developed severe alcohol- responsive myoclonus of the trunk and limbs, particularly of the right arm, hyperextension of the legs, and bilateral foot drag and plantar flexion. In addition, she developed adductor spasmodic dysphonia, tongue protrusion, jaw-opening dystonia, and retro- and laterocollis. Dystonia impaired ambulation, and negative myoclonus caused falls, resulting in her use of a motorized wheelchair. The myoclonus interfered with her right-hand movements, and she relied on her left for getting dressed and eating. Failed medication trials included sodium oxybate (1.5 grams (GM) orally twice a day), topiramate (200 mg orally three times a day), levetiracetam (500 mg orally twice a day), and clonazepam (2 mg orally three times a day). Botulinum toxin injections of the lateral pterygoids for jaw opening, genioglossus for tongue protrusion, and laryngeal injections for spasmodic dysphonia (SD) temporarily improved speech.

Pre-surgical mental status examination demonstrated normal language, attention, and memory, and general neurologic examination was likewise normal. On movement examination, she had a hoarse voice, constant low-amplitude myoclonic jerks of the trunk and pelvis

worsening with action and stress, no bradykinesia, mild bilateral intention tremor, and slight right laterocollis of about 5 degrees with superimposed jerky retrocollis. She was able to stand with her arms crossed. While walking, she had right plantarflexion and dragged the right leg. The left leg was internally rotated. While pouring water, she had right limb, truncal, and pelvic myoclonus. Both hands had myoclonic jerks while using utensils, but the jerks were more prominent on the right. However, she was able to bring a fork to her mouth. Writing triggered severe myoclonus of the right hand and both legs. There was also a tight gripping of the pen while writing. Her pre-surgical Burke–Fahn–Marsden Dystonia Rating Scale (BFMDS) was 76. The Unified Myoclonus Scale was not performed but her initial Clinical Global Improvement Scale (CGI) was 7. Genetic testing did not reveal an *SGCE* mutation.

She underwent bilateral globus pallidus interna (GPi) DBS surgery. The postoperative BFMDS 1 month after surgery was 26 and decreased to 3 within 1 year. Her current CGI is 1. At 4 years postoperatively, her BFMDS remains at 3, and her current settings are left GPi, 3.6 V/180 pulse width (PW)/60 Hz/1-2-C+; and right GPi, 3.6 V/180 PW/65 Hz/1-2-C+.

Discussion

DBS improves MD with reductions in BFMDS scores from approximately 14% to 97%, typically using high-frequency pallidal stimulation.[1–12] Improvements in the Unified Myoclonus Rating Scale also improved from 11% to 100%.[1–12] Our patient had a reduction in her BFMDS by 96% with low-frequency, high pulse width pallidal stimulation, similar to two recent cases of MD that responded to 60 Hz pallidal stimulation.[13] Unlike these recent cases, however, our case was not positive for the *SGCE* gene, yet demonstrated a robust reduction in clinical severity, as seen in the reduction of her CGI from 7 to 1. Thus, ours is the first report of a sarcoglycan mutation-negative case to respond well to low-frequency, high pulse width pallidal stimulation.

Despite the presence of epsilon sarcoglycan in the basal ganglia, cerebellum, and hippocampi of animals, the role of a mutation in this gene in the development of MD is unknown. In addition, the pathomechanisms of newly discovered gene loci in disease development are also unknown.[1,2] Thus, despite the presence of this gene mutation in many previously reported DBS cases, the positive response in both cases with and without this mutation,[1,2] like ours, and the small number of total MD cases with DBS suggest that, at this time, it is difficult to utilize gene status in predicting surgical outcomes, unlike in those with *DYT-1* or *DYT-6* mutations.[14] It is possible, however, that those without the mutation may have only a moderate reduction in myoclonus compared with those with positive mutation status,[1] but as seen in our report the myoclonus may respond in mutation-negative patients with low-frequency stimulation.

We did not attempt high-frequency stimulation in our case. We base our programming paradigm on our center's extensive experience with low-frequency stimulation in *DYT-1*-positive patients.[15,16] The lower frequency allows more posteriorventral contacts to be used, providing more programming options and fewer side effects. Our case responded robustly to low frequency from the beginning without significant adverse effects, mitigating any need to attempt high frequency stimulation. Also, the low-frequency stimulation may approximate the intraoperative firing rate of the target neurons.[15] Thus, a frequency higher than what is recorded intraoperatively may not be necessary in treating dystonia. Apart from *DYT-1*, we have also shown that low-frequency stimulation can provide relief in other dystonia syndromes, including X-linked dystonia Parkinsonism[17] and ADCY5-related hyperkinetic movement disorder syndrome with dystonia, myoclonus, and chorea.[18]

Thus, our case further supports the utility of low-frequency GPi DBS for MD as an effective therapeutic option not only in epsilon sarcoglycan-positive cases but in those without the mutation. Further study is needed to determine the role of mutation status in predicting DBS response as in other dystonia syndromes, such as DYT-1.

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