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

Citation: Sarva H, Miravite J, Swan MC, et al. A case of myoclonus-dystonia responding to low-frequency pallidal stimulation. Tremor Other Hyperkinet Mov. 2017; 7. doi: 10.7916/D82Z1BS4

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Editor: Elan D. Louis, Yale University, USA

Received: March 5, 2017 Accepted: April 17, 2017 Published: May 5, 2017

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Funding: None.

Financial Disclosures: None.

Conflict of Interest: The authors report no conflict of interest.

Ethics Statement: This study was reviewed by the authors' institutional ethics committee and was considered exempted from further review.

Introduction

Myoclonus–dystonia (MD) is a genetically and phenotypically heterogeneous 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 drop 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 laterocollics 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 hippocampus 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.17 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 Parkinsonism17 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.

References

1. Sidiroplou C, Mestre T, Hutchison W, et al. Bilateral pallidal stimulation for sarcoglycan epsilon negative myoclonus. Parkinsonism Relat Disord 2014;20:915–918. doi: 10.1016/j.parkreldis.2014.04.017

2. Ramdhan RA, Frucht SJ, Behnagar A, Kopell BH. Improvement of isolated myoclonus phenotype in myoclonus dystonia after pallidal deep brain stimulation. Tremor Other Hyperkinet Mov 2016;6:10.7916/D8F47POC

3. Papac E, Obzanska K, Rejdak K, Stelmasiak Z, Trojanowski J. Atypical symptomatology of myoclonus dystonia (DYT-11) with positive response to bilateral pallidal deep brain stimulation. Mov Disord 2014;29:E3. doi: 10.1002/mds.23783

4. Uruha A, Kimura K, Okiyama R. An Asian patient with myoclonus–dystonia (DYT11) responsive to deep brain stimulation of the globus pallidus internus. Case Rep Neurol Med 2014;2014:937095. doi: 10.1155/2014/937095

5. Kurtis MM, San Luciano M, Yu Q, et al. Clinical and neurophysiological improvement of SGCE myoclonus–dystonia with GPi deep brain stimulation. Clin Neurol Neurosurg 2010;112:149–152. doi: 10.1016/j.clineuro.2009.10.001

6. Kuhn AA, Krause P, Lauritsch K, Zeuner C, Brucke C, Schneider GH. Early surgical treatment in a case of myoclonus dystonia syndrome. J Child Neurol 2014;29:NP149–150. doi: 10.1177/0883073813513071

7. Cif L, Valente EM, Henn M, et al. Deep brain stimulation in myoclonus–dystonia syndrome. Mov Disord 2004;19:724–727. doi: 10.1002/mds.20030

8. Azoulay-Zysa J, Roze E, Welter ML, et al. Bilateral deep brain stimulation of the pallidum for myoclonus–dystonia due to epsilon-sarcoglycan mutations: a pilot study. Arch Neurol 2011;68:1087–1088. doi: 10.1001/archneurol.2011.338

9. Contarino MF, Foncke EM, Schuurman PR, Speelman JD, Tijssen MA. Effect of pallidal deep brain stimulation on psychiatric symptoms in patients with dystonia. J Child Neurol 2014;29:E3. doi: 10.1177/0883073813513071

10. Beukers RJ, Contarino MF, Speelman JD, Schuurman PR, Booc J, Tijssen MA. Deep brain stimulation of the pallidum is effective and might stabilize striatal D2 receptor binding in myoclonus–dystonia. Front Neurol 2012;3:22. doi: 10.3389/fneur.2012.00022

11. Roze E, Vidaillhet M, Hubsch C, Navarro S, Grabl H. Pallidal stimulation for myoclonus–dystonia: ten years’ outcome in two patients. Mov Disord 2015;30:871–872. doi: 10.1002/mds.26215

12. Kim JH, Na YC, Lee WH, Chang WS, Jung HH, Chang JW. Bilateral globus pallidus interna deep-brain stimulation in a patient with...
13. Fernandez-Pajarin G, Sesar A, Relova JL, et al. Bilateral pallidal deep brain stimulation in myoclonus–dystonia: our experience in three cases and their follow-up. *Acta Neurochir* 2016;158:2023–2028. doi: 10.1007/s00701-016-2904-3

14. Jinnah HA, Alterman R, Klein C, et al. Deep brain stimulation for dystonia: a novel perspective on the value of genetic testing. *J Neural Transm* 2017. doi: 10.1007/s00702-016-1656-9

15. Alterman RL, Miravite J, Weisz D, Shils JL, Bressman SB, Tagliati M. Sixty hertz pallidal deep brain stimulation for primary torsion dystonia. *Neurology* 2007;69:681–688. doi: 10.1212/01.wnl.0000267430.95106.ff

16. Alterman RL, Shils JL, Miravite J, Tagliati M. Lower stimulation frequency can enhance tolerability and efficacy of pallidal deep brain stimulation for dystonia. *Mov Disord* 2007;22:366–368. doi: 10.1002/mds.21274

17. Miravite J, Deik A, Swan M, Sarva H, Kopell BH, Severt WL. Parkinsonism and dystonia in Lubag disease respond well to high pulse width/low-frequency globus pallidus interna deep brain stimulation. *Neuror Clin Pract* 2015;5:267–269. doi: 10.1212/CPJ.0000000000000130

18. Meijer IA, Miravite J, Kopell BH, Lubarr N. Deep brain stimulation in an additional patient with ADCY5-related movement disorder. *J Child Neurol* 2017;32:438–439. doi: 10.1177/0883073816681353