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Journal
Annals of Clinical and Translational Neurology, 2(6)

ISSN
2328-9503

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Publication Date
2015-06-01

DOI
10.1002/acn3.206

Peer reviewed

ANNALS of Clinical and Translational Neurology
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BRIEF COMMUNICATION

Intraoperative neurophysiology in deep brain surgery for psychogenic dystonia

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Funding Information
This work was supported by the NINDS Intramural Program.

Received: 23 March 2015; Accepted: 30 March 2015

Annals of Clinical and Translational Neurology **2015; 2(6): 707–710**

doi: 10.1002/acn3.206

Abstract

Psychogenic dystonia is a challenging entity to diagnose and treat because little is known about its pathophysiology. We describe two cases of psychogenic dystonia who underwent deep brain stimulation when thought to have organic dystonia. The intraoperative microelectrode recordings in globus pallidus internus were retrospectively compared with those of five patients with known DYT1 dystonia using spontaneous discharge parameters of rate and bursting, as well as movement-related discharges. Our data suggest that simple intraoperative neurophysiology measures in single subjects do not differentiate psychogenic dystonia from DYT1 dystonia.

Introduction

Psychogenic dystonia is a challenging entity to diagnose and treat, because its pathophysiology is little understood, and separation from organic dystonia has been difficult. Deep brain stimulation (DBS) in the globus pallidus internus (GPi) is an established therapy for generalized dystonia, where better outcomes are associated with earlier treatment.[1,2]

Methods

We describe two patients with psychogenic dystonia who were originally thought to have organic dystonia. Intraoperative microelectrode recordings in GPi in these patients (ages 18 and 23) were retrospectively compared with those from five patients with known DYT1 dystonia (ages 15, 17, 23, 24, and 27) using spontaneous discharge parameters of rate and bursting, as well as movement-related discharges, similar to previous reports.[3] Single unit recordings in the GPi were obtained from patients undergoing physiologic mapping for placement of DBS electrodes. All patients received propofol for frame placement and drilling but stopped 30 min prior to recording. Neurons were screened for movement-related activity based on audible changes in action potential discharge evoked by passive (investigator-initiated) limb movements around the shoulder, elbow, wrist, hip, knee, and ankle joints). Two-tailed independent *t*-test analysis was used to explore the differences.

Case 1: PSY-DYS 1

A woman had sudden onset of left hand tremor while on a camping trip at age 16. Tremor spontaneously resolved after several months. One year later, she had intermittent stuttering that also went away after a few months, followed by left leg shaking. Two weeks later, she developed painful, symmetric, fairly fixed bilateral inward turning of both feet with toe curling; present when supine or sitting, but worse when standing. She became wheelchair-bound in a few months. She also had a mild symmetric bilateral

hand postural tremor. Magnetic resonance imaging brain and whole spine, electroencephalogram, electromyography, DYT1, autoimmune and mitochondrial disease work-up were normal. Botulinum toxin and levodopa gave minimum benefit. At age 18, she was implanted with bilateral GPi DBS. Six weeks postop, on the day of initial programming, she had remarkable improvement in her dystonia and tremor and was able to walk. Improvement persisted and she was able to walk across the stage for her high school graduation and dance at her wedding. Occasionally, she would experience pain and foot inversion that responded to increasing DBS voltage. She remained well for ~4 years, until she had sudden onset cramping and inward turning of her left foot while attending a crowded concert. The next day, her feet turned inward with toe curling, forcing her to stop driving. Despite adjustment of DBS settings, her symptoms worsened, and she began needing the wheelchair again. She was unable to continue at her job as a perinatal technician. Her programming neurologist noted that blinded changes in her stimulator (including turning the stimulator on and off) did not alter her symptoms. She was diagnosed with psychogenic dystonia, underwent intensive cognitive, and behavioral therapy, and physical therapy. She was successfully explanted and remains symptom-free at age 23.

Case 2: PSY-DYS2

A woman, at age 12, had sudden onset tightness in shoulders and neck, more on the right, after being hit by a car and knocked briefly unconscious. She then developed right jaw pulling, right shoulder elevation, and truncal dystonia. Symptoms worsened with not only writing and typing tasks but also progressively worsened with trouble breathing and slurred speech. Magnetic resonance imaging brain and cervical spine, DYT1, and PNKD gene testing were normal. Symptoms were initially controlled by trihexiphenidyl, but could not be continued because of worsening eczema with concern for drug rash. She tried valproate, baclofen, clonazepam, botulinum toxin, and levodopa with no benefit. At age 23, she was implanted with bilateral GPi DBS. Six weeks after initial programming, her torso was much straighter and she had less neck and jaw pulling. After a brief initial improvement, her symptoms worsened with no effect after multiple adjustments to her stimulation parameters. She then developed laryngeal-spasm-like symptoms that were not seen on fiberoptic laryngoscopy. She began having choreiform movements in hands and toe curling with heel tapping. She was hospitalized for depression and suicide attempts with conversion disorder. At age 25, she was diagnosed with psychogenic dystonia and her DBS was turned off. Her symptoms did not worsen. She began to improve with intensive psychiatric, cognitive behavioral, and physical therapy. She was explanted at age 27, being treated with quetiapine and trihexiphenidyl, and she remains symptom-free with occasional flares with stressful situations.

Results

The number of units recorded in each condition was five at rest and 11 with movement for the first psychogenic patient, and three at rest and three with movement for the second psychogenic patient. For the DYT1 dystonia patients, the first patient had 20 units at rest and five with movement, the second had 10 units at rest and five with movement, the third had four units at rest and seven with movement, the fourth had six units at rest, and five with movement, and the fifth had one unit at rest and 13 with movement. Mean rate of firing for the two psychogenic patients were 54.62 and 39.96 Hz, respectively, at rest, and 60.00 and 51.91 Hz, respectively, with passive movement. These were not different from those of the DYT1 patients, with a mean of 56.95 (range: 39.07–81.52) Hz at rest and 56.42 (range 48.52–59.53) with movement (Table 1). Bursting properties for the psychogenic patients showed burst indices[4] (2.76 and 6.63 at rest, 2.62 and 1.61 with movement), and proportion of spikes in burst[5] (0.07 and 0.36 at rest, 0.06 and 0.02 with movement). These also did not differ significantly from DYT1 patients (burst index mean 3.64 at rest, and 3.17 with movement, mean proportion of spikes in burst 0.11 at rest and 0.07 with movement). Two-tailed independent *t*-tests showed no significant differences. These results are comparatively illustrated in Figure 1.

Discussion

Similar to a prior study examining thalamic activity, GPi single unit discharge characteristics do not appear to separate psychogenic dystonia and organic dystonia.[6] Previous studies showed lower firing rates for GPi neurons in dystonia versus Parkinson's disease patients.[3,7,8] More recently, analysis of pallidal firing rates showed no significant difference between hemidystonia and generalized dystonia patients and Parkinson's disease patients. The study also showed GPi firing rates did not correlate with dystonia severity.[4,9] For our cohort, all patients underwent surgery at the same institution with the same surgeon. Recordings were obtained uniformly. Microelectrode recordings may be affected by anesthetics,[4,9,10] but all our patients were studied in the awake state at least 30 min after stopping propofol. Age at the time of surgery and recording was also similar between the DYT1 and psychogenic patients in our study.

Table 1. Electrophysiological characteristics of globus pallidus internus neurons in psychogenic versus DYT-1 dystonia.

Patient	Mean firing rate, Hz, at rest (with movement)	Interspike interval mean, msec, at rest (with movement)	Interspike interval standard deviation, msec, at rest (with movement)	Burst index at rest (with movement)	Mean firing rate in burst, Hz, at rest (with movement)	Mean proportion of spikes in burst at rest (with movement)
PSY-DYS1	54.62 (60)	19 (18.83)	19.33 (18.11)	2.76 (2.62)	179.10 (187.74)	0.07 (0.06)
PSY-DYS2	39.96 (51.91)	40.05 (19.29)	67.45 (16.91)	6.63 (1.61)	115.44 (126.29)	0.36 (0.02)
DYT 1	56.95 (56.42)	20.97 (19.54)	21.66 (20.32)	3.64 (3.17)	187.24 (191.77)	0.11 (0.07)
t-test PSY-DYS versus DYT1	0.41 (0.93)	0.56 (0.64)	0.53 (0.2)	0.68 (0.24)	0.43 (0.46)	0.58 (0.26)

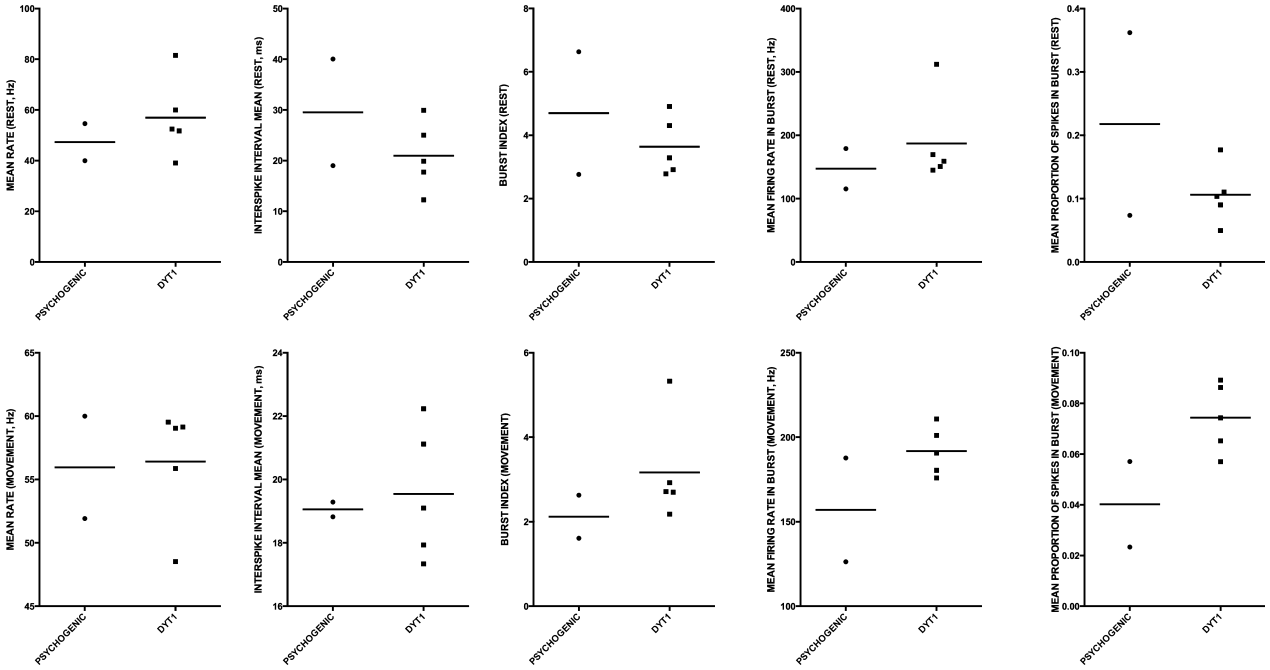

Figure 1. Comparative illustration of electrophysiological characteristics of globus pallidus internus (GPi) neurons in psychogenic versus DYT-1 dystonia.

As previously suggested, baseline rates and patterns of neuronal activity need to be compared across fairly large numbers of dystonia cases to draw conclusions concerning the relationship between mean firing rates, response to somatosensory input, or patterns of neural activity in GPi, and the phenotype, or etiology of dystonia.[10] However, opportunities to study such cases are not common. Based on our results, spontaneous single unit discharge characteristics in single subjects do not seem to be sensitive markers to help differentiate organic dystonia from DYT1 dystonia. Although caution must be exercised in interpreting our results, it does highlight that there is still no neurophysiologic parameter, and thus no reliable diagnostic test, capable of differentiating between organic and psychogenic dystonia. As such, the diagnosis remains clinical and can be challenging for complex cases. Other features for future investigation, which may be more helpful, include synchronization of discharges across multiple units, power spectrum analysis, or measures of EMG-coherence. Unfortunately, as this study is performed retrospectively, data for these analyses were not available for our patients.

Acknowledgment

This study was supported by the NINDS Intramural Program. The authors would like to thank Traian Popa, Leslie Markun, Elena Ryapolova, Salman Qasim, and Nathan Ziman for their valuable assistance in the preparation of this manuscript.

Author Contributions

Dr. Ramos – study conception and design, data gathering, data analysis, drafting, and editing the manuscript. Dr. Pillai – study conception and design, data analysis, drafting, and editing the manuscript. Dr. Lungu – study conception and design, data gathering, data analysis, drafting, and editing the manuscript. Dr. Ostrem – study conception and design, data gathering, data analysis, and editing the manuscript. Dr. Starr – study conception and design, data gathering, data analysis, editing the manuscript. Dr. Hallett – study conception and design, data analysis, drafting, and editing the manuscript. All authors approved the final draft of the paper being submitted.

Conflict of Interest

Dr. Ramos is a federal government employee, working for the National Institutes of Health. This study was undertaken as part of her official duty. Her research at the NIH is supported by the NIH Intramural Program. She was also under a fellowship support grant from the Dystonia Medical Research Foundation. Dr. Pillai is a federal government employee, working for the National Institutes of Health. This study was undertaken as part of his official duty. Dr. Lungu is a federal government employee, working for the National Institutes of Health. This study was undertaken as part of his official duty. Dr. Lungu's research at the NIH is supported by the NIH Intramural Program. Dr. Ostrem reports receiving compensation from Medtronic Consulting and Educational grant support, MRI Interventions grant support, Abbvie consulting, Merz Educational grant support, and Allergan Speakers Program. Dr. Starr receives compensation from Medtronic Consulting and Educational grant support. Dr. Hallett is a federal government employee, working for the National Institutes of Health. This work was undertaken as part of his official duty. Dr. Hallett's research at the NIH is largely supported by the NIH Intramural Program. Dr. Hallett serves as Chair of the Medical Advisory Board for and receives honoraria and funding for travel from the Neurotoxin Institute. He may accrue revenue on U.S. Patent #6,780,413 B2 (Issued: 24 August 2004): Immunotoxin (MAB-Ricin) for the treatment of focal movement disorders, and U.S. Patent #7,407,478 (Issued: 5 August 2008): Coil for Magnetic Stimulation and methods for using the same (H-coil); in relation to the latter, he has received license fee payments from the NIH (from Brainsway) for licensing of this patent. He is on the Editorial Board of 22 journals, and received royalties from publishing from Cambridge University Press, Oxford University Press, John Wiley and Sons, Wolters Kluwer, and Elsevier. He has received honoraria for lecturing from Columbia. Supplemental research funds have been granted by the Kinetics Foundation for studies of instrumental methods to monitor Parkinson's disease, BCN Peptides, S.A. for treatment studies of blepharospasm, Medtronics, Inc., for studies of deep brain stimulation, Parkinson Alliance for studies of eye movements in Parkinson's disease, Merz for treatment studies of focal hand dystonia, and Allergan for studies of methods to inject botulinum toxins.

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