Disease Stabilization of DYT1-Positive Primary Generalized Dystonia with DBS of the Globus Pallidus Interna: a 15-year Follow-Up

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Introduction

Primary generalized dystonia (PGD) is a genetic form of dystonia that frequently displays resistance to pharmacotherapy and progresses quickly within the first few years after onset. In particular, PGD has been shown to more consistently respond to deep brain stimulation (DBS) than the secondary type. DBS has been used successfully in the treatment of refractory dystonia targeting the Globus Pallidus Interna (GPi) for patients with DYT1-positive PGD. Long-term follow-up of the safety and efficacy falls short of the longevity seen in other diseases treated with DBS.

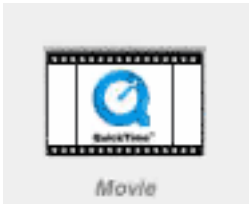
Methods

Case report and long term follow-up of a patient with disabling DYT1-positive dystonia treated with bilateral GPi DBS.

Results

A male patient presented for neurosurgical evaluation with scapular winging, hand contractures, and violent truncal spasms which were debilitating to the point where he was bedridden. After failing conservative therapy, the patient was implanted with bilateral GPi-DBS at the age of 18. DBS parameter adjustments were made primarily within the first three years after implantation, with nominal changes in the ensuing years. Initial settings were contact of 3+0-, amplitude of 4.9 V, frequency of 185 Hz, and pulse width of 270 μsec on the left and 3+0-, 2.8 V, 185 Hz, and 120 μsec on the right. Current settings are 3+2+1-, 5.2 V, 130 Hz, 330 μsec on the left and 3+0-, 3.5 V, 185 Hz, and 180 μsec on the right and have been relatively unchanged in the past four years.

Prior to DBS



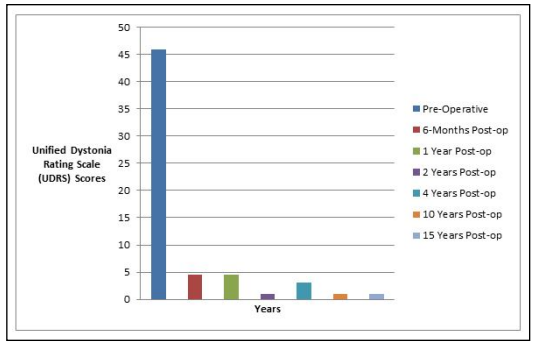
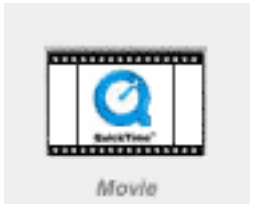


Figure 1. Unified Dystonia Rating Scale from Pre-operative Assessment to Fifteen Years After DBS Implantation. This plot shows the unified dystonia rating scale score at varying time periods during this patient's DBS treatment course for dystonia. It conveys the drastic reduction in symptoms in the first year following DBS implantation and importantly, the maintenance of a relatively symptom-free state for the following 15 years.

15 Years After DBS Implantation



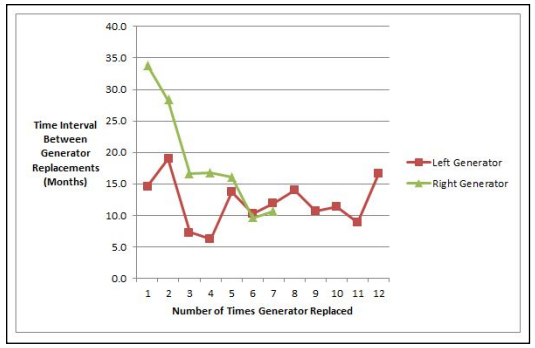


Figure 2. Internal Pulse Generator Battery Replacements. Depicted here is the number of battery replacements the patient underwent since initial DBS implantation in 2000, along with the time interval between replacements. The last replacement, which featured a transition to the rechargeable IPG, was in Feb. 2012 on the left side in June 2011 on the right side.

Table 1: Stimulation parameters during the 15-year period after implantation of the DBS device

Left Hemisphere					Right Hemisphere				
Date	Contact	Amp (V)	Frequency (Hz)	Pulse Width (μsec)	Date	Contact	Amp (V)	Frequency (Hz)	Pulse Width (μsec)
4/4/00	3+0-	4.9	185	270	8/8/00	3+0-	2.8	185	120
1/23/01	2+0-	4.0	185	330	1/23/01	3+0-	3.2	185	120
4/3/01	2+1+	4.5	185	330	4/3/01	3+0-	3.7	185	120
8/28/01	3+1-	5.5	185	330	8/28/01	3+0-	4.1	185	120
3/24/03	3+2+1-	6.0	130	330	1/8/02	3+0-	4.1	185	150
5/4/04	3+2+1-	5.8	130	330	5/4/04	3+0-	4.1	185	180
1/5/05	3+2+1-	5.8	130	330	1/5/05	3+0-	4.1	185	180
2/19/10	3+2+1-	5.8	130	330	2/19/10	3+0-	4.1	185	180
7/28/15	3+2+1-	5.2	130	330	7/28/15	3+0-	3.5	185	180

Results (ct'd)

Unified Dystonia Rating Scale (UDRS) scores reveal a significant decrease in dystonic symptoms. The patient was able to function independently at three months after the initial GPi electrode implantation and resumed his prior activities of daily living. Improvement in the UDRS has persisted over 15 years. In addition, the patient has not had any dystonic symptoms while being maintained on a stable medication regimen consisting of Artane and Klonopin. Aside from subtle dysarthria and mild rigidity while walking, the patient is employed, independent and leads an active lifestyle.

Conclusions

While prior reports have shown that GPi-DBS is effective for dystonia, this is the first with 15 years of long-term follow up showing disease stabilization, suggesting that stimulation is not only efficacious for symptom control but also prevents disease progression. This report affirms the validity of previous reports which recommend early surgical intervention prior to the onset of permanent neuromusculoskeletal deficits. Bilateral DBS of the GPi is a safe, effective and durable long-term treatment for PGD.