

Bilateral DBS of the Antero-Medial GPi and GPe for the Treatment of Tourette Syndrome. Case Report

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Abstract

Tourette Syndrome is a childhood neurobehavioral disorder defined by one year of persistent waxing and waning motor and vocal tics.

More than 90% of patients have co-morbid psychiatric conditions including Obsessive Compulsive Disorder, and Attention Deficit Hyperactivity Disorder.

Many targets have been used in the treatment of the Tourette Syndrome. It is well known that, when placing a target in the GPi, the electrode is spread lengthwise or in part in the GPe.

Our objective was to delimit these nuclei, and identify contacts in GPi and GPe, activate them bilaterally in both leads and determine results.

We report a 25-year-old male, with severe and medically intractable Tourette Syndrome who started with the disease in the early childhood, at the age of 5.

A Saint Jude multi-programmable quadripolar deep brain stimulation system was implanted under general anesthesia in a combined antero-medial GPi-central GPe target.

Targets were localized by images and semi-microelectrode intraoperative recording.

We present the follow up results until one year after DBS surgery.

We have obtained an improvement (36%) in motor tics and (20%) in phonic tics.

The qualitative Y-BOCS and GTS-QOL scales showed improvement in the quality of life, with patient satisfaction that has grown from 74 to 95 points according to the postoperative GTS-QOL scale, and the assessment of mood, an improvement was found through the Hamilton scale from severe depression (21 points) to minor depression as a result of having stimulated both nuclei.

Keywords: Tourette Syndrome; Bilateral DBS; Combined Antero-Medial GPi; Central GPe Target Selection

Abbreviations

GPi: Globus Pallidus Internus; GPe: Globus Pallidus Externus; YGTSS: The Yale Global Tic Severity; GTS-QOL: Gilles de la Tourette Quality of Life Scale; Y-BOCS: The Yale Brown Obsessive Compulsive Scale; HDRS: Hamilton Depression Rating Scale; AC/PC: Anterior commissure/Posterior commissure; ICP: Inter commissural Point; DBS: Deep Brain Stimulation; OCD: Obsessive Compulsive Disorder; MNPS: Stereotactic Planning System; NDRS: Neurosurgical Deep Recording System

Introduction and Case Report

All information was entered into data registry. The surgery and follow up was done at the Franchin Hospital, Buenos Aires, Argentina.

A 25-year-old male with severe disabling, and medically resistant Tourette Syndrome was recruited.

The patient was treated with different drugs, including risperidone, tetrabenazine [1] and guanfacine [2].

Prior to surgery, different scales were performed, including Yale Global Tic Severity Scale (YGTSS) [3], Yale-Brown obsessive-compulsive Scale (Y-BOCS) [4], Gilles de la Tourette Quality of Life Scale (GTS-QOL) [5], Global Assessment of Functioning (GAF) [6] and Hamilton Depression Rating Scale (HDRS) [7].

Surgery was performed by a team comprising a psychiatrist, neurologists, bio-engineer and neurosurgeons, on the basis of clinical indication.

A Saint Jude multiprogrammable quadripolar deep brain stimulation system, model Brio was implanted under general anesthesia using stereotactic procedure, Micromar Stereotactic Frame, and the stereotactic planning system MNPS (Mevis Ltd, Brazil) [8] was used.

To perform coordinates planning, Stereotactic CT SCAN was done, and then fused with MRI T1 and T2 sequences performed 48 hours prior surgery.

In reference to the anterior commissure/posterior commissure, (AC/PC), we relied on the classical location of the ventro-lateral portion of the GPi using 21 mm lateral to midline, (just 2 mm upper from optical nerve), 3 mm anterior to the Inter Commissural Point (ICP) and 3 mm ventral to it. From this planning, we move the target 4 mm anterior and 4 mm medial to locate our final target, remaining the same at 18 mm lateral, 7 mm anterior and 3mm ventral with reference to our basal system (ICP). Trajectories were angled 62 degrees in the sagittal plane, and 22 degrees in the coronal plane. The planning software includes a digitalized version of the Morel and Schaltenbrand and Wahren atlas, which adjusts to the anatomy of the patient and were used as a guide to show the spatial orientation of the nuclei (Figure 1 and 2).

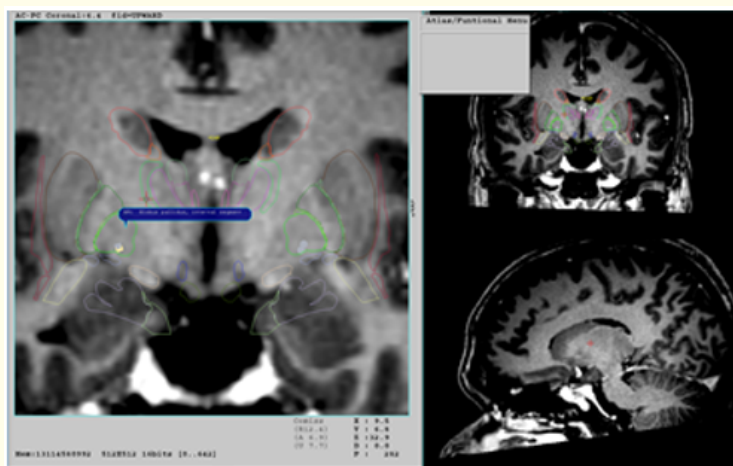


Figure 1: Coronal view of the GPi.

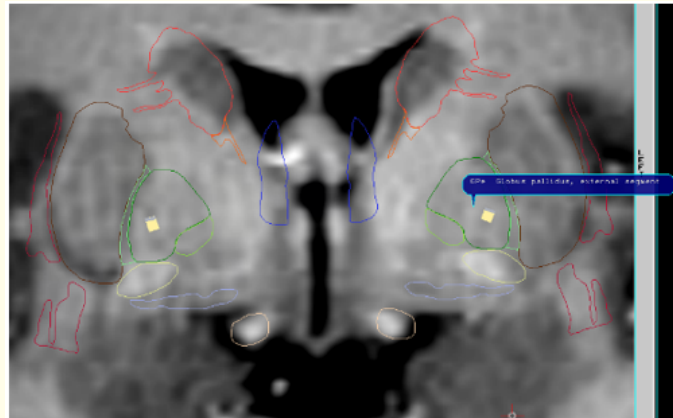


Figure 2: Coronal view of the GPe.

A trephine hole (14 mm) was made with local anesthesia in the precoronal region, and then a cannula was introduced with a concentric bipolar semi-microelectrode -Unique Medical Co. Ltd, Tokyo, Japan- (\varnothing 0.3-0.4 mm, distance interpolate 0.2-0.3 mm, 100 K Ω). The multi-unit neuronal activity is recorded and visualized with the help of the NDRS digital recording and processing software (Neurosurgical Deep Recording System, CIREN, Havana, Cuba) [9,10].

It was advanced carefully under vision and listening the multi-unit electrical activity from a point (25 mm) superior to target, trying to recognize with the help of the micro-driver the different structures before arriving to it.

The recognition of the structures using the multi-unit register is based on different frequency patterns that are emitted by the Striatum, and Globus Pallidus. This strategy enables us to recognize audible and graphic changes of the electrical physiological signal based on differential analysis. The striatum has a low frequency electrical signal, which increases significantly at the beginning of the Globus Pallidus Externus (GPe) whose pattern is a high frequency signal, this change allows to differentiate both nuclei. (Striatum and Globus Pallidus Externus). Subsequently, the signal shows a marked decrease at the beginning of the Internal Medullary Lamina to finally increase again at the start of the Globus Pallidus Internus (GPi). It is also possible to identify the optical tract through visual evoked responses. This information finally gives us the exact location of the electrode between different regions of the same structure (GPe-GPi) (See figure 3 and 4).

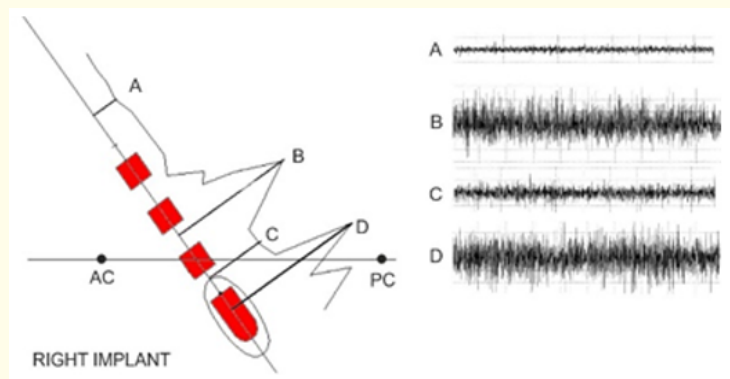


Figure 3: Electrical electrode recording and final position of the right lead. AC anterior commissure, PC, posterior commissure, A Striatum, B GPe (maximum activity), C internal medullary lamina, D GPi (maximum activity).

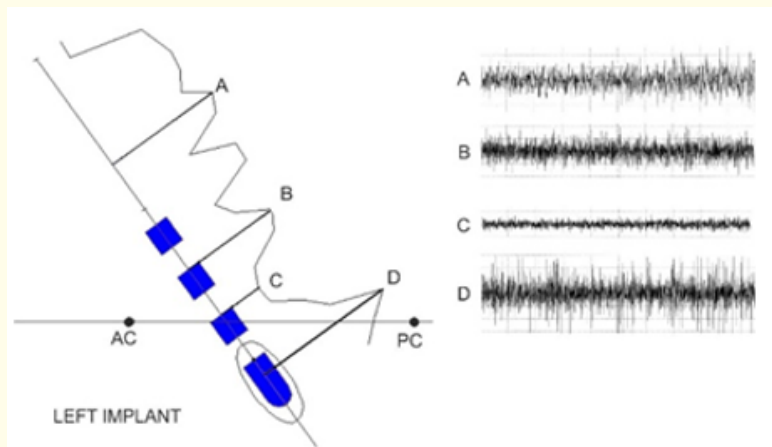


Figure 4: Electrical electrode recording and final position of the left lead. AC anterior commissure, PC, posterior commissure, A Striatum, B GPe (maximum activity), C internal medullary lamina, D GPi (maximum activity).

It is well known that, when placing a target in the GPi, the electrode is spread lengthwise or in part in the GPe. Our objective was to delimit these nuclei, and identify contacts in each of them, activate them bilaterally in both leads and determine result.

The impulse generator was placed in the subclavicular region.

A postoperative brain CT SCAN was undertaken and fused to the preoperative MRI to confirm the correct lead position.

Deep Brain Stimulation (DBS), began in the immediate postoperative period, after the patient recovered from the anesthesia.

The activation of the contacts of the leads were carried out on the basis of an electrical simulation performed with our stereotaxic planning system in order to activate contacts in both nuclei (Figure 5 and 6).

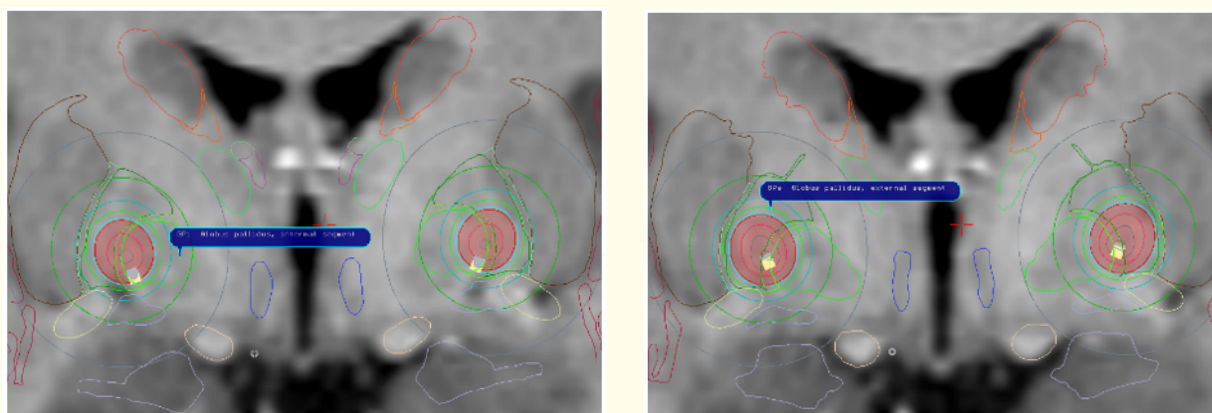


Figure 5: Simulation activation GPi-GPe on coronal view.

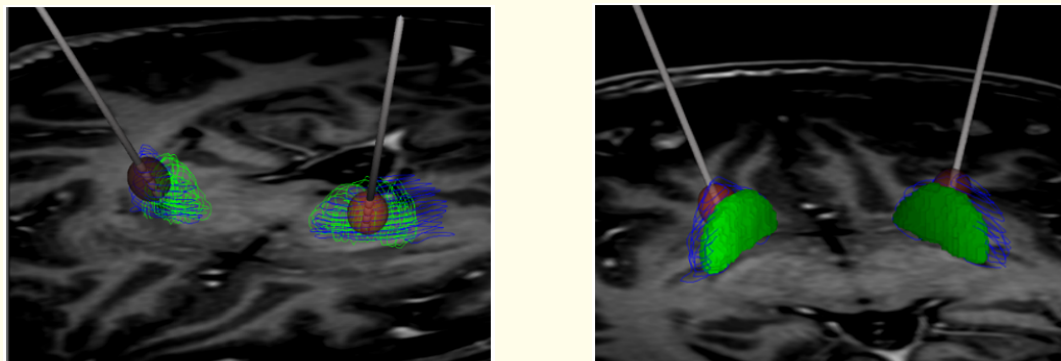


Figure 6: 3D image simulation of electrical activity in GPi (green) and GPe (blue).

The active contacts were numbers 2 and 3 during the current follow up.

Initial stimulations parameters were bilateral 1 milliampere, pulse width 62 milliseconds, and frequency 130 hertz with monopolar activation.

During the first month, the patient was followed up weekly. Afterwards, every 3 months approximately. Rating scales were repeated every 3 months, and the last at one year follow up.

Throughout the postoperative controls, the stimulation parameters were gradually increased and the patient developed progressive improvement including motor and Obsessive Compulsive symptoms.

Last change on stimulation was made 4 months after surgery, bilateral 1.5 milliampere, pulse width 62 milliseconds, frequency 140 Hertz, monopolar activation on contacts number 2 and 3 in the GPi and in the GPe.

Result

According to the patient’s neurological examination and using pre and post-surgical scales validated for the evaluation of symptoms of motor and phonic tics, obsessive-compulsive behaviors and their implication of the previously expressed in terms of their quality of daily life, improvement was observed after DBS in target combining GPi-GPe nuclei.

For this purpose, the YGTSS, GAF, Y-BOCS, GTS-QOL and HDRS were performed prior to the procedure and after surgery, until one year off follow-up.

After one year of the DBS, an initial total improvement of 8 points (16%) was observed in the YGTSS scale, with equal improvement within both the motor and phonic tics (4 points each), reaching an improvement of 14 points (28%),9 (36%) in motor tics and 5 (20%) in phonic tics. Through this scale there is evidence of an improvement of the global disability assessment from severe to mild (Table 1).

| DATE | | 4/19/2018 | 4/21/2018 | 4/21/2018 | 90 days after | 7/13/2018 | 150 days after | 8/31/2018 | 180 days after | 360 days after |
|-------|------------|-------------------|-----------|--------------------|-------------------------|---------------------|-------------------------|---------------------|-------------------------|-------------------------|
| YGTSS | | Preoperative exam | Surgery | Initial Parameters | Neurological Evaluation | Stimulation control | Neurological evaluacion | Stimulation control | Neurological Evaluation | Neurological Evaluation |
| | Motor | 21 | | 1 mA | 17 | 1.5 mA | 14 | 1.5 mA | 12 | 12 |
| | Fonic | 23 | | 62ms | 19 | 62ms | 18 | 62 ms | 18 | 18 |
| | Subtotal | 44/50 | | 130 Hz | 36/50 | 130 Hz | 32/50 | 140 Hz | 30/50 | 30/50 |
| | Disability | 40 | | | 20 | | 20 | | 20 | 20 |
| | Total | 84 | | | 56 | | 52 | | 50 | 50 |

The qualitative Y-BOCS (Table 2) and GTS-QOL (Table 3) scales showed improvement in the quality of life with patient satisfaction, that grew up from 74 to 95 points according to the last item of the GTS-QOL scale.

| DATE | | 4/19/2018 | 4/21/2018 | 4/21/2018 | 90 days after | 7/13/2018 | 150 days after | 8/31/2018 | 180 days after | 360 days after |
|--------|----|-------------------|-----------|--------------------|---------------|---------------------|----------------|---------------------|----------------|----------------|
| Y-BOCS | | Preoperative exam | Surgery | Initial Parameters | Evaluation | Stimulation control | evaluacion | Stimulation control | Evaluation | Evaluation |
| | 1 | C | | | B | | B | | B | B |
| | 2 | C | | | A | | A | | A | A |
| | 3 | C | | 1 mA | B | 1.5 mA | B | 1.5 mA | B | C |
| | 4 | E | | 62ms | A | 62ms | A | 62 ms | A | A |
| | 5 | B | | 130 Hz | A | 130 Hz | A | 140 Hz | A | A |
| | 6 | C | | | A | | B | | A | A |
| | 7 | C | | | B | | A | | A | A |
| | 8 | C | | | D | | C | | C | D |
| | 9 | A | | | C | | D | | D | D |
| | 10 | B | | | C | | C | | C | C |

Table 2

The GAF scale showed a moderate improvement in comparison to the usual daily functioning (Table 3).

| DATE | | 4/19/2018 | 4/21/2018 | 4/21/2018 | 90 days after | 7/13/2018 | 150 days after | 8/31/2018 | 180 days after | 360 days after |
|---------|---------|-------------------|-----------|--------------------|---------------|---------------------|----------------|---------------------|----------------|----------------|
| GTS-QOL | | Preoperative exam | Surgery | Initial Parameters | Evaluation | Stimulation control | Evaluation | Stimulation control | Evalutaion | Evaluation |
| | 1 | 4 | | | 1 | | 3 | | 2 | 2 |
| | 2 | 2 | | | 0 | | 0 | | 0 | 0 |
| | 3 | 4 | | 1 mA | 1 | 1.5 mA | 0 | 1.5 mA | 0 | 0 |
| | 4 | 4 | | 62ms | 0 | 62ms | 0 | 62 ms | 0 | 0 |
| | 5 | 3 | | 130 Hz | 0 | 130 Hz | 1 | 140 Hz | 1 | 1 |
| | 6 | 0 | | | 0 | | 0 | | 0 | 0 |
| | 7 | 1 | | | 0 | | 1 | | 1 | 0 |
| | 8 | 0 | | | 0 | | 0 | | 0 | 0 |
| | 9 | 2 | | | 0 | | 1 | | 1 | 0 |
| | 10 | 2 | | | 0 | | 0 | | 0 | 0 |
| | 11 | 4 | | | 0 | | 1 | | 1 | 0 |
| | 12 | 0 | | | 1 | | 1 | | 1 | 1 |
| | 13 | 4 | | | 1 | | 0 | | 0 | 0 |
| | 14 | 0 | | | 0 | | 0 | | 0 | 0 |
| | 15 | 2 | | | 0 | | 0 | | 0 | 0 |
| | 16 | 3 | | | 0 | | 0 | | 0 | 0 |
| | 17 | 4 | | | 4 | | 2 | | 1 | 0 |
| | 18 | 4 | | | 4 | | 4 | | 2 | 1 |
| | 19 | 4 | | | 4 | | 4 | | 4 | 4 |
| | 20 | 2 | | | 0 | | 4 | | 4 | 4 |
| | 21 | 4 | | | 2 | | 1 | | 1 | 1 |
| | 22 | 1 | | | 0 | | 0 | | 0 | 0 |
| | 23 | 4 | | | 0 | | 0 | | 0 | 0 |
| | 24 | 0 | | | 0 | | 0 | | 0 | 0 |
| | 25 | 0 | | | 0 | | 0 | | 0 | 0 |
| | 26 | 4 | | | 2 | | 4 | | 3 | 3 |
| | 27 | 0 | | | 0 | | 0 | | 0 | 0 |
| | Overall | 74 | | | 95 | | 95 | | 95 | 95 |
| GAF | | 51 | | | 61 | | 61 | | 61 | 65 |

Table 3

Regarding the assessment of mood, an improvement was found through the Hamilton scale of a severe depression (21 points) to a minor depression (10 points) (Table 4).

Discussion

Different targets have been used for the treatment of Gilles de la Tourette Syndrome.

Van der Linden., *et al.* [11], published the first report on the efficacy of pallidal stimulation (both electrodes in posteroventral GPi) in a patient with TS.

| DATE | | 4/19/2018 | 4/21/2018 | 4/21/2018 | 90 days after | 7/13/2018 | 150 days after | 8/31/2018 | 180 days after | 360 days after |
|----------|--------|-------------------|-----------|--------------------|---------------|---------------------|------------------|---------------------|------------------|------------------|
| HAMILTON | | Preoperative exam | Surgery | Initial Parameters | Evaluation | Stimulation control | Evaluation | Stimulation control | Evalutaion | Evaluation |
| | 1 | 3 | | | 3 | | 1 | | 1 | 1 |
| | 2 | 2 | | | 2 | | 0 | | 0 | 0 |
| | 3 | 2 | | 1 mA | 1 | 1.5 mA | 0 | 1.5 mA | 0 | 0 |
| | 4 | 1 | | 62ms | 1 | 62ms | 0 | 62 ms | 0 | 0 |
| | 5 | 1 | | 130 Hz | 1 | 130 Hz | 1 | 140 Hz | 1 | 1 |
| | 6 | 2 | | | 1 | | 1 | | 1 | 1 |
| | 7 | 1 | | | 0 | | 0 | | 0 | 0 |
| | 8 | 0 | | | 0 | | 0 | | 0 | 0 |
| | 9 | 1 | | | 1 | | 0 | | 0 | 0 |
| | 10 | 3 | | | 4 | | 3 | | 3 | 3 |
| | 11 | 2 | | | 2 | | 2 | | 2 | 2 |
| | 12 | 0 | | | 0 | | 0 | | 0 | 0 |
| | 13 | 0 | | | 0 | | 1 | | 1 | 1 |
| | 14 | 0 | | | 0 | | 0 | | 0 | 0 |
| | 15 | 1 | | | 1 | | 1 | | 1 | 1 |
| | 16 | 0 | | | 0 | | 0 | | 0 | 0 |
| | 17 | 2 | | | 2 | | 0 | | 0 | 0 |
| | Total | 21 | | | 19 | | 10 | | 10 | 10 |
| | Result | Severe | | | Severe | | Minor depression | | Minor depression | Minor depression |

Table 4

Stimulation of the GPe has also been proposed. In 2007 Filho., *et al.* [12], reported an implantation on the GPe in the treatment of TS.

The reason for targeting the antero-medial GPI is based on the associative-limbic connections that may impact the underlying urge driving the expression of motor and phonic tics.

In our case report, we have used a combined target, antero-medial GPI and central GPe.

We have considered that the changes produced with Deep Brain Stimulation in our patient have been progressive.

One of the objectives of this procedure in patients with Tourette Syndrome should be social integration, not only by reduction of tics, but also by the reduction of co-morbidities of the syndrome, and we have fulfilled it.

Taking into account the Obsessive-Compulsive Disorder, we have tried that the tics and obsessive-compulsive behaviors also decrease progressively. Since they are part of the patient’s personality, the abrupt disappearance of these rituals would cause them feeling of emptiness and in extreme cases, it could cause even depersonalization [13].

Conclusion

In all the scales we have performed, the results were better than de preoperative baseline.

Establishing an optimal target has been controversial as the precise pathophysiology of Tourette Syndrome in not yet elucidated and stimulated structures have high interconnectivity.

The results are not definitive, and the discussion is open respect how the stimulation has worked in our patient.

It is not possible to clarify if the improvement has been due to stimulate the GPI, the GPe, or both of them at the same time working together synergistically.

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