# Combined subthalamic nucleus and globus pallidus internus deep brain stimulation in Parkinson's disease

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**Introduction.** Subthalamic nucleus (STN) and globus pallidus internus (GPi) deep brain stimulation (DBS) are the main surgical approaches for advanced Parkinson's disease. Stimulation is usually applied bilaterally in the same brain structure. However, when various motor symptoms concomitantly present in the same patient, simultaneous modulation of different brain structures may be a suitable alternative.

**Case report.** We present a patient with advanced Parkinson's disease with a combined DBS neurosurgery. Left STN DBS optimally controlled the off right hemibody symptomatology while left side troublesome dyskinesias were successfully relieved by right GPi stimulation.

**Discussion.** Combined STN/GPi stimulation can be considered a suitable approach when challenging motor symptomatology arises in advanced Parkinson's disease patients.

**Key words.** Combined. Deep brain stimulation. Globus pallidus internus. Neuromodulation. Parkinson's disease. Subthalamic nucleus.

## Introduction

Deep brain stimulation (DBS) has been proved as an effective treatment for medication-refractory motor fluctuations and dyskinesias in advanced Parkinson's disease [1]. Due to the implication of the basal ganglia-thalamocortical circuity in this disease, different brain structures have been targeted. Subthalamic nucleus (STN) and globus pallidus internus (GPi) have been positioned as the main targets in DBS for movement disorders. Although there is still controversy about the best target for Parkinson's disease, STN DBS is usually preferred over GPi DBS when tremor, bradykinesia or rigidity are the main complains. However, GPi stimulation has shown a higher anti-dyskinetic effect [2]. Thus, selection of the ideal surgical target should be individualized, based on motor symptoms profile and patient's preferences. Adverse events associated with DBS surgery are usually infrequent and include from hardware failure to infections and intracranial hemorrhages. Overall, incidence of brain hemorrhage is 5%, being asymptomatic in 1.9%, symptomatic in 2.1% and with permanent deficit in 1.1% [3]. On the other hand, dyskinesias in STN post-operative period are indicative of an accurate lead placement within the nucleus and tend to resolve either spontaneously or with medication and/or stimulation adjustment [4]. Whilst post-operative stimulation-induced dyskinesias generally habituate, basal ganglia vascular lesions can induce dyskinesias that tend to persist over time and might be a major cause of disability [5], as this clinical case reflects.

## Case report

A 50-year-old right-handed white woman presented with an 8-year history of Parkinson's disease that had started with right-side clumsiness and rigidity initially responsive to levodopa/carbidopa. As the disease progressed, rasagiline and ropinirole were successively added. Six years later, motor fluctuations appeared in the form of disabling wearing-off dystonic postures in the right foot and slight on-state right-side dyskinesias. Continuous apomorphine infusion was poorly tolerated and levodopa/carbidopa intestinal gel infusion was started. The patient reported no other medical conditions. The main disabling symptom at the baseline visit was painful right foot off dystonia insufficiently controlled by optimized pharmacological treatment. Bilateral STN-DBS was then considered.

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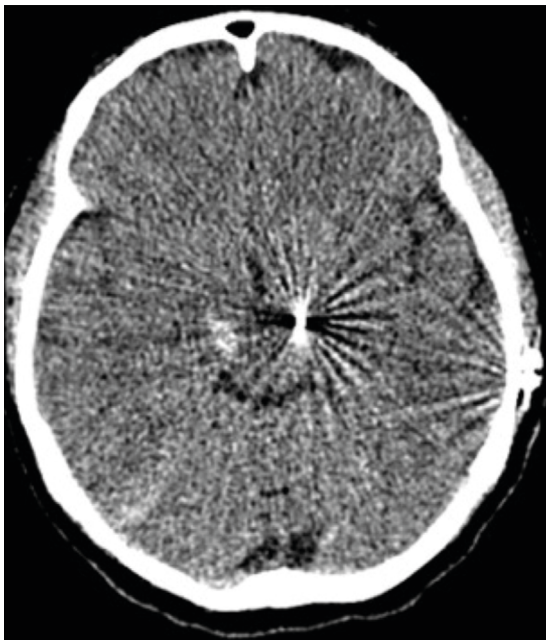
**Figure 1.** Postoperative neuronavigational computed tomography scan showing a 1.5 cm diameter small hemorrhage located in the inferior part of right subthalamic nucleus (STN). Left STN electrode artifact.



STN target planning was assessed by 3 T magnetic resonance imaging-guided neuronavigation (StealthStation S7; Medtronic, Minneapolis, Minnesota, United States) and bilateral STN-DBS 3389 quadripolar lead implantation (Medtronic) was performed under general anesthesia. Intraoperative imaged-guided placement was checked using O-arm images fused with preoperative magnetic resonance imaging. Microelectrode recording was performed following a standard protocol using one track for the left STN and another for the right. The leads were attached intraoperatively to an implantable pulse generator (Activa RC; Medtronic).

The postoperative neuronavigation computed tomography scan showed a small hemorrhage (diameter, 1.5 cm) in the right inferior STN (Fig. 1). Patient reported mild headache and displayed mild dysarthria and left upper limb dysmetria but no signs of intracranial hypertension. DBS was not switched on and levodopa/carbidopa intestinal gel infusion was restarted. Twenty days later, the focal neurological signs resolved and a computed tomography scan confirmed resolution of the hemorrhage. However, the patient initiated with choreo-dyskinetic movements in the left lower limb. She reported that these were usually absent on waking up but grew in intensity during the day, making it difficult to walk unaided. The patient was admitted for further evaluation. In the off medication/off stimulation state, she experienced disabling left-side dyskinesia that increased in severity on levodopa treatment.

Analysis of electrode placement showed that the two most rostral contacts (C2 and C3) of the left DBS electrode were optimally situated inside the superior segment and tip of the STN, respectively. The right electrode ran adjacent to the posteromedial border, with C2 and C3 adjacent to the superior part of the STN. Neurostimulation for the left electrode was performed with monopolar C2 stimulation at 60 μs, 130 Hz, and progressive increases in voltage up to 1.6 V with optimal control of the right-side symptomatology. Stimulation of the more rostral contact for the right electrode was also analyzed. The aim was to reach the pallidothalamic fibers, known to have an anti-dyskinetic effect. Screening was performed with monopolar C3 stimulation at 60 μs, 130 Hz, and gradual increases in voltage up to 3.5 V without dyskinesia control. Higher voltages stimulated the internal capsule (eyelid twitching). Various pharmacological strategies (reduction in oral medication, introduction of amantadine, restarting of levodopa/carbidopa intestinal gel infusion with a low continuous dose) were also attempted without benefit.

Finally, four months later, the right STN electrode was removed and right GPi DBS was performed. The postoperative computed tomography scan fused with preoperative magnetic resonance imaging showed optimal placement of the right GPi electrode (C0 and C1 inside the posteroventral GPi) (Fig. 2). The parameters were progressively adjusted to C2-, 1.6 V, 60 μs, 130 Hz for the left STN electrode and C0, 2 V, 60 μs, 130 Hz for the right GPi electrode. Optimal control of symptoms was achieved on both sides of the body. The benefit of this combined STN and GPI bilateral stimulation persisted one year after the implantation.

## Discussion

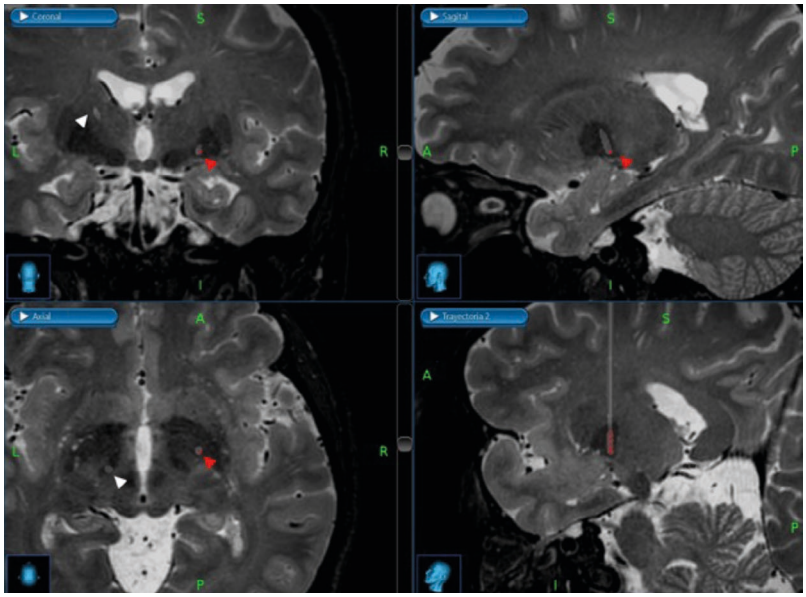
STN DBS has been successfully used to treat different types of involuntary movements [6]. In Parkinson's disease, it has demonstrated to improve levodopa-induced dyskinesia, mainly by reducing the need for dopaminergic medication. STN DBS can also improve dyskinesia by stimulating the rostral subthalamic area comprising the pallidothalamic

fibers [7]. Nevertheless, this approach was not successful in our patient, probably due to the slightly medial and insufficiently rostral placement of the right STN electrode. Additionally, loss of STN DBS efficacy over time leading to a successful second-stage GPi implantation has also been previously described in the literature. Several case reports have shown improvement in dystonic/dyskinetic symptoms with additional GPi DBS in Parkinson's disease patients where STN stimulation turns out to be insufficient. However, scarce publications are available specifically assessing DBS as a rescue therapeutic opportunity in patients with intracranial hemorrhage related complications. In 2014 Oyama et al reported a case of a rescue GPi DBS after a stroke-associated hemiballism [8] and in 2015 Xie et al demonstrated that GPi DBS was able to reduce hemichorea due to arteriovenous malformation STN microbleeding [9].

On the other hand, combined stimulation of different brain areas is reaching interest in the literature as novel stimulation strategies are emerging. It is known that GPi and STN targets complement each other within the spectrum of therapeutic options for patients with Parkinson's disease. Recently, a pilot study in eight patients has shown that combined and contralateral stimulation of different brain targets is a plausible approach [10]. The authors also speculated that modulating structures with distinct risk profile could minimize stimulation-induced adverse effects.

Modulation of diverse brain structures within the same patient can be a plausible neurofunctional surgery approach in order to specifically address different motor symptomatology. Selecting a different target in each hemisphere might also reduce morbidity associated with bilateral lesions, an important consideration given the current re-emergence of ablative procedures. This strategy could be interesting for patients in whom a higher risk, especially for axial symptoms, may be foreseen preoperatively. This case report provides a valuable insight into how individualized modulation of diverse brain structures can be applied within the same patient in order to specifically address different motor symptomatology.

**Figure 2.** Postoperative neuronavigation 3 T magnetic resonance imaging (StealthStation S7; Medtronic) in axial, sagittal and coronal views. Left deep brain stimulation electrode located inside the superior segment and tip of the subthalamic nucleus (white arrow) and right electrode inside the posteroventral globus pallidus internus (red arrow).

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## Estimulación cerebral profunda combinada del núcleo subtalámico y el globo pálido interno en la enfermedad de Parkinson

**Introducción.** La estimulación cerebral profunda (ECP) del núcleo subtalámico (NST) y el globo pálido interno (GPi) son los principales abordajes quirúrgicos en la enfermedad de Parkinson avanzada. La estimulación suele aplicarse de forma bilateral en la misma estructura cerebral. Sin embargo, cuando diferentes síntomas motores se presentan concomitantemente en el mismo paciente, la modulación simultánea de diferentes estructuras cerebrales puede ser una alternativa eficaz.

**Caso clínico.** Presentamos un paciente con enfermedad de Parkinson avanzada en el que se realizó ECP combinada en NST y el GPi. La ECP del NST izquierdo controló de manera óptima la sintomatología del hemicuerpo derecho, mientras que las discinesias problemáticas que presentaba en el hemicuerpo izquierdo se redujeron con éxito mediante la estimulación del GPi derecho.

**Discusión.** La estimulación combinada del NST/GPi puede considerarse un enfoque neuroquirúrgico adecuado cuando surge una sintomatología motora desafiante en pacientes con enfermedad de Parkinson avanzada.

**Palabras clave.** Combinada. Enfermedad de Parkinson. Estimulación cerebral profunda. Globo pálido interno. Neuromodulación. Núcleo subtalámico.