Pallidal Deep Brain Stimulation for Parkinson’s Disease

- Pallidal activity in Parkinson's disease patients with intraoperative dyskinesias
- Modeling and optimizing deep brain stimulation to enhance gait in Parkinson's disease: personalized treatment with neurophysiological insights
- A Convergent Pathway for Stimulation-Induced Dyskinesia Following Deep Brain Stimulation
- Convergent mapping of a tremor treatment network
- The Persistence of Dopamine Dysregulation Syndrome after Pallidal Deep Brain Stimulation in Parkinson's Disease
- Delayed hemorrhagic complications following deep brain stimulation surgery for Parkinson's disease: Importance of comprehensive presurgical evaluation
- Motor evoked potentials as a side effect biomarker for deep brain stimulation programming
- Deep brain stimulation-entrained gamma oscillations in chronic home recordings in Parkinson's disease

---

Pallidal Deep Brain Stimulation (DBS) is a well-established neuromodulation therapy for Parkinson’s disease (PD), particularly targeting the **globus pallidus internus (GPi)**.

Mechanism of Action

DBS involves delivering continuous electrical stimulation to the GPi via implanted electrodes, modulating abnormal neuronal activity. This helps in:

- Reducing excessive oscillatory activity in the basal ganglia.

- Restoring more physiological motor function.

- Modulating neurotransmitter release (dopamine, GABA, glutamate).

Indications

GPi-DBS is mainly used in: - **Levodopa-responsive Parkinson’s disease** with motor fluctuations or dyskinesias.

- **Medication-resistant dystonia** or disabling dyskinesias.

- **Patients with prominent bradykinesia and rigidity** who may not be ideal candidates for subthalamic nucleus (STN) DBS.

GPi vs. STN DBS

- **GPi-DBS** is preferred in patients with significant dyskinesias as it has a direct antidyskinetic effect.

- **STN-DBS** often allows for greater medication reduction but may have a higher risk of worsening mood and cognitive symptoms.

- GPi-DBS generally has a **lower risk of neuropsychiatric side effects** compared to STN-DBS.

Clinical Outcomes

Studies have shown that GPi-DBS:

- Improves **motor function** (UPDRS-III scores).

- Reduces **dyskinesias** without worsening bradykinesia.

- Provides **long-term symptom control**, with sustained benefits beyond 5-10 years.

- Has **less impact on cognition and speech** compared to STN-DBS.

Limitations and Risks

- Requires **surgical expertise** and precise targeting. - Potential for **hardware-related complications** (infection, lead migration). - May not significantly reduce the need for **dopaminergic medications** as much as STN-DBS. - Limited effect on **non-motor symptoms** of PD (e.g., cognitive decline, autonomic dysfunction).

Future Directions

- **Adaptive DBS (aDBS)**: Uses real-time feedback from local field potentials (LFPs) to optimize stimulation.

- **Closed-loop DBS**: Aims to fine-tune stimulation based on patient activity and symptoms.

- **Gene therapy & neurostimulation synergy**: Exploring combined approaches to modify disease progression.

Pallidal Deep Brain Stimulation (GPi-DBS) and Subthalamic Deep Brain Stimulation (STN-DBS) for Parkinson’s disease (PD) are not the same. They target different brain structures and have distinct effects.

Key Differences

Targeted Brain Structure:

GPi-DBS: Targets the Globus Pallidus internus (GPi).

STN-DBS: Targets the Subthalamic Nucleus (STN).

Effects on Symptoms

GPi-DBS: Effective for dyskinesias, rigidity, and motor fluctuations but does not allow for as much medication reduction.

STN-DBS: More potent for tremor, bradykinesia, and rigidity, and allows for greater reduction of dopaminergic medications, which can reduce medication-induced side effects.

Cognitive and Psychiatric Considerations

GPi-DBS: Considered safer for cognition and behavior, making it preferable for patients with cognitive decline or psychiatric issues.

STN-DBS: Has a higher risk of cognitive and mood side effects, such as depression, apathy, and impulsivity.

Medication Reduction

GPi-DBS: Less reduction in levodopa is typically achieved.

STN-DBS: Can lead to significant medication reduction, which may be beneficial for patients with motor fluctuations.

Patient Selection

GPi-DBS: Often preferred for older patients or those with dyskinesias and minimal tremor.

STN-DBS: Preferred for younger patients with significant tremor and those who want to reduce medication burden.

Which One is Better?

There is no universally “better” option; it depends on the patient’s symptoms and overall profile.

If tremor is dominant → STN-DBS is often preferred.

If dyskinesias are a major issue or cognitive preservation is a priority → GPi-DBS may be better.

Subthalamic deep brain stimulation for Parkinson's disease

see Subthalamic deep brain stimulation for Parkinson's disease

Clinical research studies

The magnitude and factors associated with levodopa equivalent daily dose (LEDD) reduction in deep brain stimulation (DBS) of the Globus pallidus internus (GPi) for Parkinson's Disease (PD) remain unclear.

A consecutive cohort of 74 patients who had undergone GPi DBS was analyzed. Regression and probabilistic efficacy mapping were performed to evaluate factors predicting LEDD reduction.

32.4% of GPi individuals experienced significant LEDD reduction (>30%). Anteromedial GPi stimulation was associated with higher LEDD reduction.

Anteromedial stimulation of the GPi appears to be associated with medication reduction, challenging the idea that GPi DBS is ineffective at reducing LEDD. Further prospective study will be needed to validate these findings [1)].

The study by Di Luca et al. provides compelling evidence that GPi DBS, particularly targeting the anteromedial region, can lead to significant LEDD reduction in a subset of patients. This challenges the conventional notion that GPi DBS is ineffective for medication reduction. However, several limitations—including heterogeneity in patient profiles, lack of direct STN comparisons, and absence of long-term follow-up—necessitate caution in interpreting these findings.

Future studies should:

Conduct direct comparative analyses between GPi and STN DBS in similar patient populations. Investigate the functional impact of LEDD reduction beyond a numerical threshold. Incorporate advanced imaging techniques to refine target localization. Extend follow-up to assess durability of medication reduction over time. In summary, while the study presents an important shift in our understanding of GPi DBS, its conclusions should be validated in larger, prospective, and comparative trials before influencing clinical practice.

1)

Di Luca DG, Ramirez-Gomez C, Santyr B, Fumagalli M, Germann J, Kalia SK, Lozano AM, Fasano A. Clinical and Imaging Correlates of Medication Reduction in Globus Pallidus Stimulation for Parkinson's Disease. Mov Disord Clin Pract. 2025 Mar 18. doi: 10.1002/mdc3.70042. Epub ahead of print. PMID: 40099474.