# **Parkinson's disease surgery**

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- BSCL2 and CDK5 are two genes associated with circadian rhythm disturbance in Parkinson's disease
- Boundary complexity of cortical and subcortical areas predicts deep brain stimulation outcomes in Parkinson's disease
- Gaps in the Parkinson's disease therapeutic clinical pipeline: A focus on approaches targeting disease pathobiology
- Defining cervical spondylotic myelopathy surgical endotypes using comorbidity clustering: a Quality Outcomes Database cervical spondylotic myelopathy study
- Using network toxicology and molecular docking to identify core targets and pathways underlying tacrolimus-induced tremor in organ transplant recipients
- Illness acceptance and community self-efficacy mediate the relationship between social isolation and loneliness among elderly people with parkinson's disease
- Mitochondrial alanyl-tRNA synthetase 2 mediates histone lactylation to promote ferroptosis in intestinal ischemia-reperfusion injury
- Longitudinal Analysis of the Deep Brain Stimulation Impairment Scale for Subthalamic Nucleus Stimulation in Parkinson's Disease

Before the introduction of L-dopa in the late 1960s, stereotactic thalamotomy was widely used for Parkinson's disease. The location ultimately targeted for lesioning was the ventrolateral nucleus. The procedure worked better for relieving the tremor than for the bradykinesia; however, it was the latter symptom that was most disabling. This procedure cannot be done bilaterally without significant risk to speech function. The procedure fell out of favor when more effective drugs became available <sup>1)</sup>.

Ablative techniques include pallidotomy, thalamotomy, and, more recently, subthalamotomy. Because of concern over the high incidence of side-effects associated with bilateral ablative procedures, alternative approaches were explored. Deep brain stimulation (DBS) was subsequently developed and successfully applied in the internal globus pallidus, subthalamic nucleus, and thalamus for the treatment of Parkinson's disease. Recent approaches include biological neurorestorative techniques-surgical therapies with transplantation, gene therapy, and growth factors are all being studied. Although a great deal of work remains to be done, advances in surgical therapies for the treatment of Parkinson's disease are moving forward at an unprecedented pace<sup>2)</sup>.

#### Before 1960s

Before the late 1960s, pioneers sectioned the human brain's motor pathways, and later investigators intentionally ablated many basal ganglia regions with alcohol or the application of heat; this approach met with limited success, however, partly because of inaccurate, imprecise, and inconsistent targeting. Moreover, intentionally created bilateral brain lesions frequently led to irreversible deficits in speech, swallowing, and cognition. This surgical approach faded in popularity with the discovery of levodopa (dopamine replacement).

The life for patients with Parkinson's disease was dreadful. Many were institutionalized.

#### After levodopa

After levodopa, it became routine for patients with Parkinson's disease to "awaken" from frozen states, and nearly all were able to live at home. Tremors faded, stiffness waned, and many patients regained their ability to walk. Yet important and unexpected challenges emerged. The most worrisome were dopamine-related, medication-induced complications. Patients began to report fluctuations (doses wearing off), freezing (especially when walking), and dancelike movements (chorea), later termed levodopa induced dyskinesia. Many reported tremors that did not respond to pharmacotherapy. In addition, there was a growing realization that levodopa was not a cure and that the disease progressed despite miraculous "awakenings."

### **Pallidotomy for Parkinson's Disease**

#### Pallidotomy for Parkinson's Disease

### Deep brain stimulation for Parkinson's disease

see Deep brain stimulation for Parkinson's disease

### **Current trends**

At some point, most patients will experience problematic side effects and/or resistance to treatment with antiparkinsonian drugs. This, together with recent refinements in surgical techniques resulting in improved outcomes, has produced a resurgence of interest in the operative treatment of Parkinson's disease. Tissue transplantation (e.g. with adrenal medullary tissue) has been all but abandoned in the U.S. Since 1987, a shift has taken place from lesioning to stimulation techniques. The subthalamic nucleus (STN) was an early target in PD. Deep brain stimulation (DBS) in the area of the globus pallidus pars interna (GPi) or the ventral intermediate nucleus of the thalamus (Vim) can also relieve parkinsonian symptoms without irreversibly destroying tissue. A randomized study showed similar efficacy between thalamotomy and DBS, but fewer side effects with DBS. with later interest in the and the (GPi).

### Indications for surgical treatment of PD

1. patients refractory to medical therapy (including multiple agents). However, some investigators feel the response to surgery might be better if done early

2. primary indication (based on an opinion survey): patients with levodopa-induced dyskinesias (especially those with associated painful muscle spasms). Initial results indicate that these are very responsive to pallidotomy

3. gait and postural instability, as well as falls and freezing (non-human primate data), may respond to DBS of the pedunculopontine nucleus (PPN)

4. patients primarily with rigidity or bradykinesia (unilateral or bilateral), on-off fluctuations or dystonia. Tremor may be present, but if it is the predominant symptom, then using the ventralis intermedius (VIM) nucleus of the thalamus as the target (for ablation (thalamotomy) or stimula- tion) is a better procedure. VIM stimulation is also used to treat essential tremor.

## Contraindications

1. patients with significant dementia: further cognitive impairment has been noted primarily in patients with cognitive deficits prior to treatment

2. patients with risk of intracerebral hemorrhage: those with coagulopathy, poorly controlled hypertension, those on anti-platelet drugs that cannot be withheld (may consider stereotactic radiosurgery lesions for these rare patients)

3. patients with ipsilateral hemianopsia: due to the risk of post-op contralateral hemianopsia from optic tract injury, which would make the patient blind

4. age ≥ 85 yrs

5. patients with secondary Parkinsonism, i.e. not idiopathic Parkinson's disease: respond poorly, presumably due to different pathophysiology. Look for:

a) signs of autonomic nervous system dysfunction(suggests Shy-Drager)

b) EOMabnormalities(may occur in progressive supranuclear palsy(PSNP))

c) long-tract signs

d) cerebellar findings(as in olivo-ponto-cerebellar atrophy(OPCA))

e) failure to improve with levodopa

f) MRI: lacunar infarcts in basal ganglia (as in arteriosclerotic Parkinsonism), or tumor in the region of substantia nigra

g) PETscanning(if available):decreased striatal metabolism detected by deoxyglucose PET scan (suggests striato-nigral degeneration (SND))

6. patient's with normal dopamine transport (DaT) scan which may rule out PD as the cause of a tremor

# Gamma Knife radiosurgery for Parkinson's Disease

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1)

Gildenberg PL. Whatever Happened to Stereotactic Surgery? Neurosurgery. 1987; 20:983-987

#### 2)

Walter BL, Vitek JL. Surgical treatment for Parkinson's disease. Lancet Neurol. 2004 Dec;3(12):719-28. Review. PubMed PMID: 15556804.

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