Subthalamic deep brain stimulation for Parkinson's disease

Recent advances in methods used for deep brain stimulation (DBS) include subthalamic nucleus electrode implantation in the “asleep” patient without the traditional use of microelectrode recordings or intraoperative test stimulation.

Deep brain stimulation (DBS) + optimal drug therapy (ODT) in early PD may reduce the risk of clinically important worsening. These findings further confirm the need to determine if DBS + ODT is superior to medical therapy for managing symptoms, reducing the complications of medications, and improving quality of life. The FDA has approved the conduct of a large-scale, pivotal clinical trial of DBS in early-stage PD [1].

Asleep subthalamic deep brain stimulation for Parkinson's disease

see Asleep subthalamic deep brain stimulation for Parkinson's disease.

Targets

Subthalamic deep brain stimulation and the Globus pallidus internus are the most common surgical targets among patients with Parkinson’s disease and have equivalent beneficial effects on motor symptoms.

After subthalamic nucleus DBS, patients are able to reduce medications by 50% on average. In patients with globus pallidus interna DBS, stimulation has an anti-dyskinetic effect, although medication doses remain similar.

DBS of the subthalamic nucleus is generally avoided in patients with a history of depression or neurocognitive impairment. Thalamic DBS ameliorates tremor, but has little effect on bradykinesia or rigidity.

The pedunculopontine nucleus DBS is an emerging experimental treatment for postural and gait instability in Parkinson’s disease [2].

The efficacy of deep brain stimulation (DBS) - primarily of the subthalamic nucleus (STN) - for advanced Parkinson's disease (PD) is commonly attributed to the suppression of pathological synchronous β oscillations along the cortico-thalamo-basal ganglia network. Conventional continuous high-frequency DBS indiscriminately influences pathological and normal neural activity. The DBS protocol would therefore be more effective if stimulation was only applied when necessary (closed-

loop adaptive DBS) [3]

Subthalamic nucleus deep brain stimulation through an implanted multipolar electrode is a common treatment for advanced Parkinson's disease (PD) [4] [5] [6] [7]

Optimal targeting of STN-DBS improves function via reducing motor symptoms—tremor, bradykinesia, and rigidity—by at least 50%, allowing for a significant decrease in levodopa dosage and levodopa induced side effects [8] [9] [10].

The therapeutic benefits of deep brain stimulation are frequency-dependent, but the underlying physiological mechanisms remain unclear. To advance deep brain stimulation therapy an understanding of fundamental mechanisms is critical [11].

Patients with Parkinson's disease had similar improvement in motor function after either Pallidal Deep Brain Stimulation or subthalamic stimulation. Nonmotor factors may reasonably be included in the selection of surgical target for deep-brain stimulation [12].

In a series of 25 electrodes, best clinical results with least energy consumption were found in contacts located in the dorsolateral border zone, whereas contacts within the subthalamic white matter, e.g., zona incerta, were significantly less effective. Herzog et al. suggest that the dorsolateral STN border should be covered by STN-DBS [13].

Results suggest that the STN is involved in the abnormal oscillation between the M1 cortex and Globus pallidus GP [14].

The effect of STN DBS on working memory and attention may be much less consequential in patients with dystonia than has been reported in PD [15].

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is widely used in patients with Parkinson's disease (PD). However, which target area of this region results in the highest antiparkinsonian efficacy is still a matter of debate.

Targeting the subthalamic nucleus (STN) for deep brain stimulation (DBS) using standard stereotactic coordinates in conjunction with high-resolution magnetic resonance imaging (MRI) generally results in effective symptomatic relief for the cardinal motor features of Parkinson's disease (PD).

Data from a prospective, single blind, controlled pilot trial demonstrated that early stage PD subjects treated with STN-DBS also required less medication than those treated with optimal drug therapy (ODT).

STN-DBS in early PD reduced medication cost over the two-year study period. DBS may offer substantial long-term reduction in medication cost by maintaining a simplified, low dose medication regimen. Further study is needed to confirm these findings, and the FDA has approved a pivotal, multicenter clinical trial evaluating STN-DBS in early PD [16].

The effects of DBS depend strongly on stimulation frequency: high frequencies (>90 Hz) improve motor symptoms, while low frequencies (<50 Hz) are either ineffective or exacerbate symptoms.

The angle of approach, influences the resultant field of stimulation and can lead to undesired side effects.

Lead angle can impact outcome and should be taken into consideration [17].

Sweet spot

Sweet spot for subthalamic deep brain stimulation.

Contraindications

Although dementia is a contraindication in deep brain stimulation for Parkinson's disease, the concept is supported by little scientific evidence. Moreover, it is unclear whether PD with mild cognitive impairment (PD-MCI) or domain-specific cognitive impairments affect the outcome of DBS in non-demented PD patients.

Baseline cognitive levels of patients with PD who underwent DBS were classified into PD with dementia (PDD) (n = 15), PD-MCI (n = 210), and normal cognition (PD-NC) (n = 79). The impact of the cognitive level on key DBS outcome measures [mortality, nursing home admission, progression to Hoehn&Yahr (HY) stage 5 and progression to PDD] were analyzed using Cox regression models. Park et al. also investigated whether impairment of a specific cognitive domain could predict these outcomes in non-demented patients.

Results: Patients with PDD showed a substantially higher risk of nursing home admission and progression to HY stage 5 compared with patients with PD-MCI [hazard ratio (HR) 4.20, P = .002; HR = 5.29, P < .001] and PD-NC (HR 7.50, P < .001; HR = 7.93, P < .001). MCI did not alter the prognosis in patients without dementia, but those with visuospatial impairment showed poorer outcomes for nursing home admission (P = .015), progression to HY stage 5 (P = .027) and PDD (P = .006).

Cognitive profiles may stratify the pre-operative risk and predict long-term outcomes of DBS in PD [18].

Outcome

see Subthalamic deep brain stimulation for Parkinson's disease outcome.

Case series

Subthalamic deep brain stimulation for Parkinson's disease case series.

Case reports

A male patient with a 9-year course of PD who at 53 years of age preferred deep brain stimulation

(DBS) of the subthalamic nucleus over initial l-dopa treatment. The patient argued that he wanted to avoid the serious adverse effects of l-dopa, which would have presented within his time of full professional activity. DBS resulted in significant motor improvement lasting for 6 years without l-dopa treatment [19].

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