**Therapeutic Brief**

**Title: Difference in the effectiveness of subthalamic nucleus and globus pallidus deep brain stimulation in Parkinson's disease**

**Hushyar Azari MD.** Urmia University of Medical Sciences, Urmia, Iran

ORCID: 0000-0002-4340-2830

Phone: +989188811447 - +98 44 3223 4897

Fax: +98 44 322 290 59

Postal code: 571478334

Email: [hushyarazari@hotmail.com](mailto:hushyarazari@hotmail.com)

Adress: Orjhans Street, Resalat Blvd, Urmia, Iran (Postal Code:571478334)

**Abstract**

Deep brain stimulation (DBS) is considered a viable therapeutic strategy for Parkinson's disease (PD). The subthalamic nucleus (STN) and globus pallidus (GPi) are the two most common sites for DBS. Studies that evaluated the Unified PD Rating Scale (UPDRS) III were selected if they met the following criteria: (1) had at least three months of follow-up periods; (2) compared both GPi and STN DBS; (3)had at least five participants in each group; (4)were conducted after 2010. The majority of studies reported no statistically significant between-group difference for improvements in UPDRS ш scores. Although there were some promising results regarding action tremor, rigidity, and urinary symptoms, which indicated that STN DBS might be a better choice; however, regarding the adverse effects, GPi seemed better; but it cannot be concluded that one target is superior. Other larger randomized clinical trials with longer follow-up periods and control groups are needed to decide which target is more efficient for stimulation and imposes fewer adverse effects on the patients.

**Keywords:** deep brain stimulation, globus pallidus, Parkinson's disease, subthalamic nucleus, UPDRS

**Main Text**

PD is the most common movement disorder, the second common progressive, disabling, and neurodegenerative disease, which is expected to be as prevalent as 12.9million cases by 2040 [[1-4](#_ENREF_1)]. PD is characterized by slow movements, rigidity, and low amplitude movements without the previous automaticity. Levodopa, a dopamine precursor, was developed for the first time in 1911[[5](#_ENREF_5)]. It has been used as an efficacious drug for PD treatment for over 50 years, but it has been shown that its efficacy declines as the disease progresses [[6](#_ENREF_6), [7](#_ENREF_7)]. Surgical treatment of movement disorders started in 1987 by targeting the ventral intermediate nucleus of the thalamus [[8](#_ENREF_8), [9](#_ENREF_9)] by the DBS technique. DBS is a common and effective surgical treatment option that alleviates motor symptoms. It was introduced about three decades ago and is recently performed on several new targets in the brain, including the STN and GPi [[10-12](#_ENREF_10)]. The efficacy of these two targets has been different according to studies. It has been offered that there is a persistent coordination of beta band oscilation in PD, and short-term bursts of these oscilations shows normal sensory and motor processing. DBS can shorten the bursts and result in improved movement in PD[[13](#_ENREF_13)].

Potentially relevant English-language articles, published from 2010 to 2021, were recognized by searching in Embase, Cochrane Library, and PubMed databases. We searched for studies including both targets (GPi and STN) and their related aspects. Search terms were deep brain stimulation (DBS) [MeSH term] or in combination with the following keywords: Controlled Clinical Trial [Publication Category],Randomized Controlled Trial [Publication Category],Globus Pallidus internus [MeSH term],Globus Pallidus [MeSH term], GPi [MeSH term], Subthalamic nucleus [MeSH term], STN [MeSH term], and Parkinson’s disease [MeSH term].

For this research, we included the clinical studies that (1) contained evaluated unified PD rating scale (UPDRS) III before and after deep brain stimulation ;(2) compared GPi-DBS and STN-DBS for PD; (3) recruiting more than five subjects in GPi and STN groups ;(5) had a description of adverse events; (5) had more than three months of follow-up period; (6) Availability of English full text (7).

Odekerken et al. demonstrated that the change in UPDRS score during the off drug phase was lower in the GPi group than in the STN group, and during the on-phase, dyskinesia was less in the GPi group compared to the STN group. In both phases, the reduction in time was similar, but it was significant only in the off-phase (*p* = 0.02) [[14](#_ENREF_14)]. Troche et al. showed there was a significant improvement in UPDRS score in the off-medication state before and after surgery for both groups (*p* < 0.001) [[15](#_ENREF_15)]. In another study conducted by Odekerken et al., more improvements were reported the off-drug phase UPDRS-ME score after three years in the STN group (*p* = 0.04 while no between-group differences were shown in the on-drug phase [[16](#_ENREF_16)]. In the study of Gong et al., four months after DBS, all patients experienced improvement (≥ 30% ) in UPDRS score in off-period, and pain symptoms improvement rate was 79±27% and 75%± 27% in STN and GPi groups, respectively [[17](#_ENREF_17)]. Fan et al. demonstrated that in the drug off-phase, the mean improvement of UPDRS was 41.50% and 43.56% in STN and GPi groups, respectively, with no significant difference between the group (*p* = 0.609). Additionally, GPi DBS had direct anti-dyskinesia effects [[18](#_ENREF_18)]. Wong et al. proved that STN DBS was related to a statistically significant decrease in bradykinesia and rigidity after six months compared with GPi DBS (*p* < 0.001 and *p* = 0.025, respectively). However, there was no significant between-group difference in terms of tremor outcomes. [[19](#_ENREF_19)]. Celiker et al. reported that on-phase UPDRS motor scores were significantly declined in both STN and GPi groups (*p* < 0.05), while STN DBS was better in improving bladder symptoms. In addition, both groups had fewer sleep problems after the surgery [31]. Okun et al. investigated the effect of unilateral and staged bilateral STN and GPI DBS. They found that off-phase UPDRS motor scores, in both unilateral and staged bilateral modes, improved significantly after four and 12 months of follow-up [[20](#_ENREF_20)]. Odekerken et al. reported no statistically significant difference between groups in terms of adverse events (*p* > 0.05) [[14](#_ENREF_14)]. Troche et al. showed that mean penetration-aspiration (PA) scores did not change significantly for participants who received GPi surgery ( *p* = 0.857) but significantly worsened for participants who received STN DBS ( *p* = 0.007) and STN DBS has an adverse effect on swallowing function. In contrast, unilateral GPi DBS does not have this deleterious effect [[15](#_ENREF_15)]. Fifty percent of patients in the STN group in the study of Fan et al. had dyskinesia caused by stimulation. In ten of these patients, the direct anti-dyskinesia effect of STN DBS was also noticed [[18](#_ENREF_18)]. Okun et al. reported only minor mood and apathy effects which were not significant [[20](#_ENREF_20)]. In another study carried out by Odekerken et al., no significant differences were reported in terms of adverse events for the two groups; only minor events were reported [[16](#_ENREF_16)]. Wong et al. found that the most common adverse events were problems with DBS lead hardware and hemorrhage, which were minor and controlled easily [[19](#_ENREF_19)].

Odekerken et al. reported no statistically significant difference between groups in terms of adverse events (p>0.05) [[14](#_ENREF_14)]. Troche et al. showed that mean penetration-aspiration (PA) scores did not change significantly for participants who received GPi surgery ( p = .857) but significantly worsened for participants who received STN DBS ( p = .007) and STN DBS have an adverse effect on swallowing function. In contrast, unilateral GPi DBS does not have this deleterious effect [[15](#_ENREF_15)]. Fifty percent of patients in the STN group in the study of Fan et al. had dyskinesia caused by stimulation. In ten of these patients, the direct anti-dyskinesia effect of STN DBS was also noticed [[18](#_ENREF_18)]. Okun et al. reported only minor mood and apathy effects which were not significant [[20](#_ENREF_20)]. In another study carried out by Odekerken et al., no significant differences were reported in terms of adverse events for the two groups; only minor events were reported [[16](#_ENREF_16)]. Wong et al. found that the most common adverse events were problems with DBS lead hardware and hemorrhage, which were minor and controlled easily [[21](#_ENREF_21)]. The findings of this study must be interpreted cautiously. It can be can generally hypothesized, but not definitely stated, that STN-DBS and GPi-DBS are both suitable stimulation sites. However, STN had better outcomes regarding urinary symptoms, pain, dyskinesia, and action tremor.

**Conclusion**

Although STN was better in terms of improving action tremor, and GPi was related to fewer adverse events, it cannot prove the superiority of any of the two targets. More and more clinical trials with large sample sizes, longer follow-up periods, and more specific outcome assessments are needed to conclude which target is definitely better.

Table 1 Main characteristics of studies

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | reference | target | age | Sample size | UPDRS on-period- baseline | UPDRS off-period- baseline | Follow up period  [[22](#_ENREF_22)] | Location |
| 1 | Odekerken[[14](#_ENREF_14)] | GPi  STN | 59·1± 7.8  60.9± 7.6 | 62  63 | 16±8  17±9.9 | 43.8±13.5  44.4±15.5 | 12 | Europe |
| 2 | Troche[[15](#_ENREF_15)] | GPi  STN | 64.26±8.79  66.5±7.02 | 19  14 | 23.13±6.73  23.43±10.64 | 39.89±11.06  35.93±8.98 | 6 | Asia |
| 3 | Odekerken[[16](#_ENREF_16)] | GPi  STN | 59.1±7.8  60.9±7.6 | 43  47 | NA | 43  41 | 36 | Europe |
| 4 | Gong[[17](#_ENREF_17)] | GPi  STN | 63.2±9.1  62.3±10.4 | 28  36 | 26.2±7.5  29.0±10.0 | NA | 4 | Asia |
| 5 | Fan[[18](#_ENREF_18)] | GPi  STN | 60.43±8.44  59.65±9.11 | 23  20 | NA | 50.68±15.36  47.85±14.95 | 18.26±8.38 and  21.60±8.79 | Asia |
| 6 | Celiker[[23](#_ENREF_23)] | GPi  STN | 54±4.51  56.16±9.6 | 6  6 | 22.50±6.65  22.16±6.55 | 49.00±13.57  47.00±14.01 | 24 | Asia |
| 7 | Okun[[20](#_ENREF_20)] | GPi  STN | 60.1±5.5  58.0±10.7 | 14  16 | 20.8±8.68  21.3±7.56 | 40.5±11.2  41.2±9.32 | 12 | USA |
| 8 | Wong[[19](#_ENREF_19)] | GPi  STN | 63±8.12  61±10.33 | 31  57 | NA | 47.32±11.79  44.12±10.45 | 12 | USA |

Data presented as Mean±SD

**DECLARATIONS**

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**Authors’ contributions**

The author contributed solely to the article

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Not applicable

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Single author - None

**Ethical approval and consent to participate**

Not applicable.

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