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" Effect of subthalamotomy on daily life activities in idiopathic Parkinson's disease "

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ABSTRACT:

Background
Subthalamotomy, a surgical procedure targeting the subthalamic nucleus, has been shown to improve motor symptoms in Parkinson's disease patients. However, the impact of this intervention on patients' daily life activities and functional independence is an important consideration that requires further research and understanding. Evaluating the effects of subthalamotomy on the ability to perform routine tasks and maintain autonomy in daily living is crucial for assessing the overall effectiveness and benefits of this treatment approach.
The aim of the study was to determine if subthalamotomy is effective on daily life activities in Parkinson's disease patients.

Methods:
Between 2021 to 2024 in Al-Salam hospital, the general authority of healthcare, Port Said, Suez Canal University Hospital, Ismailia, and affiliated hospitals, A descriptive study was performed on fourteen patients, lesioning stereotactic surgery on the subthalamic nucleus was done. Radiofrequency thermocoagulation was employed to induce lesions, which were subsequently verified through magnetic resonance imaging. Fourteen individuals who underwent unilateral subthalamotomy were assessed over a period of up to six months, utilizing the PDQ-39 QUESTIONNAIRE, Unified Parkinson's

Results:
At six months post-operatively, during the "off" medication state, the patients demonstrated significant improvements in contralateral bradykinesia, rigidity and tremors, Schwab & England ADL scale was significantly increased six months after surgery than before from 46.0±9.21 to 84.00±7.58 during "Off" state and from 68.0±9.68 to 94.0±5.34 during "On" state. The levodopa requirement was reduced by 50.65% for the unilateral treated group. Two patients suffered hemiballismus, one was mild and resolved within two weeks through a reduction in levodopa dosage. The second patient experienced severe hemiballismus, necessitating the cessation of levodopa and the administration of valproate, ultimately recovered after two months.

Conclusion:
The results suggest that subthalamotomy can effectively manage the key symptoms of Parkinson's disease, decrease the required levodopa dosage, and enhance patients' quality of life. While deep brain stimulation of the subthalamic nucleus has been the preferred treatment approach for Parkinson's disease, ablation of the subthalamic nucleus may provide a safe, technically viable, and more cost-effective alternative

Keywords: Parkinson's disease, subthalamotomy, stereotactic ablation, motor functions, neurosurgery, surgical interventions

INTRODUCTION

Parkinson's disease is a neurodegenerative condition that develops with advancing age and can lead to substantial impairment and morbidity. It is characterized by a clinical triad of akinesia, rigidity, and tremor, which are attributed to dopaminergic neurodegeneration in the substantia nigra pars compacta. (1)

Surgical treatment for Parkinson's disease may be recommended if medical therapy fails to provide satisfactory long-term alleviation of symptoms. Ablative surgery and deep brain stimulation are two surgical approaches utilized for the management of Parkinson's disease, targeting the motor thalamus, the internal segment of the globus pallidus, and the subthalamic nucleus. (2)

Subthalamotomy has been observed to allow for a reduction in levodopa dosage, while concomitantly improving bradykinesia, rigidity, and tremor. The beneficial effects are comparable to those seen with pallidotomy and globus pallidus internus stimulation. Although the risk of hemiballismus remains a concern, its incidence is not as prevalent as initially perceived. (3)

The subthalamic nucleus (STN) is a small, almond-shaped structure situated laterally beneath the thalamus, at the junction of the diencephalon and midbrain, and is recognized as the pacemaker of the basal ganglia. Its designation as the preferred target for surgical intervention in Parkinson’s disease (PD) strongly reinforces its vital role in regulating the function of the basal ganglia in both normal and pathological states. (4)

Subthalamotomy may serve as an effective alternative to deep brain stimulation in specific circumstances. Accumulating evidence suggests that lesioning the subthalamic nucleus can induce a sustained anti-Parkinsonian benefit with a favorable risk-to-benefit ratio. (5) Nonetheless, legitimate concerns about safety, the expertise required to perform the lesioning procedure, and its irreversible nature have hindered the widespread adoption of subthalamotomy. One principal concern limiting the broader application of subthalamotomy is the risk of inducing a movement disorder characterized by involuntary, jerky movements known as hemiballism-hemichorea. (6)

This study aims to evaluate the effects of subthalamotomy in the management of idiopathic Parkinson's disease, as well as its impact on the daily life activities of affected patients. (7)

Methods

Patients and clinical assessment:

Between 2021 to 2024 in Al-Salam hospital, the general authority of healthcare, Port Said, Suez Canal University Hospital, Ismailia, and affiliated hospitals ablation of the subthalamic nucleus was carried out in fourteen patients diagnosed with Parkinson's disease.

Inclusion criteria

- Idiopathic Parkinson`s Disease.
- L-Dopa responsive at least 30% improvement in Unified Parkinson`s
- Disease Rating Score: Unified Parkinson's Disease Rating Scale (UPDRS).
- Good "on" function from medication
- Realistic expectations
- Main symptoms not adequately controlled:
- Dyskinesia or motor fluctuations
- Refractory tremors
- Frequent or severe "off" periods.
- Off period disability from: Bradykinesia, rigidity, tremors.

Exclusion criteria

- Atypical parkinsonism or Parkinson plus.
- Age>75 years.
- Lack of response to levodopa, dementia, major depression
- Levodopa-induced psychosis, severe personality disorder.
- Convulsions
- Contraindications of magnetic resonance imaging (MRI).
- Previous brain surgery for Parkinson's disease (PD)
- Presence of another central nervous system disease
- Focal abnormalities on MRI and unstable medical problems.
- Declined informed consent.

Prior to the procedures, all patients gave written informed consent after being fully briefed on the process, expected effects, potential complications, alternative treatments, and the importance of photographic documentation. (8)

A comprehensive patient history was obtained, including demographic information such as sex, age, occupation, smoking status, history of workers' compensation, and any comorbid medical conditions.

The severity of the disease was evaluated using the Parkinson's Disease Questionnaire PDQ39. Patient medical histories were documented, including any prior chronic conditions such as diabetes, hypertension, kidney/liver disease, cardiac problems, neurological issues, past trauma, or previous surgeries. Full medication histories, disease onset and diagnosis timelines, medication compliance, and medication-related complications like L-Dopa-induced dyskinesia and motor fluctuations were also recorded. (9)

Clinical assessments were performed by neurologists and neurosurgeons specializing in movement disorders. The evaluation schedule included pre-operative, immediate post-operative, 2-week post-discharge and 6-month timepoints, and encompassed neurological exams, neurosurgical evaluations, neuroimaging, and anesthesia checkups.

After Parkinson's patients were admitted, their preoperative evaluation typically commenced with an assessment by a neurologist who specialized in managing movement disorders.

- The primary role of our neurology colleagues was to ensure that the patient met our selection criteria.
- Patients underwent at least two pre-operative visits and a 6-month post-operative follow-up.
- We utilized video-recorded UPDRS Part III assessments during the 'off' state, both preoperatively and postoperatively, as well as a symptom diary in response to medical treatment, to measure disease severity. The original UPDRS comprises 42 items, with 35 rated on a 5-point scale, including 14 items in Section III.

  We also employed the Schwab and England Activities of Daily Living scale, which rates a Parkinson's patient's function on a scale from 0, indicating the worst possible function, to 100, indicating no impairment. Each 10-point increment on this scale is accompanied by a description of the patient's level of function.

The assessment team, led by a neurologist, must carefully evaluate and rule out patients who do not have idiopathic PD, as functional surgery is not indicated for atypical parkinsonism or Parkinson's plus syndromes. A positive response to levodopa is crucial, as it not only confirms the diagnosis of idiopathic PD but also suggests how well the patient may respond to surgical intervention. Additionally, preoperative neuropsychological evaluation is necessary to assess and address any signs of cognitive impairment, as dementia is a crucial factor to consider. (10)

Surgical procedures:

Pre-operative preparations: When feasible, the surgery is conducted after withholding medications overnight and without sedation, ensuring that the patient is in a relatively "off" state, facilitating the clinical assessment of the effects during the surgical procedure. A magnetic resonance imaging (MRI) scan is conducted, featuring a three-dimensional spoiled gradient-recalled volumetric sequence with a 1-mm slice thickness, which enables reconstruction in the sagittal, coronal, and axial planes. Additionally, a susceptibility-weighted imaging sequence is used to clearly outline the subthalamic nucleus. (11)

Headframe placement: After infiltration of local anesthesia at the pin insertion sites, the stereotactic frame is meticulously balanced and firmly attached to the outer surface of the skull, 3 cm above the supraorbital ridge, to avoid an artifact at the AC-PC plane. The frontal pins are inserted above the lateral third of the eyebrow, avoiding the supraorbital nerve, vessels, or the temporalis muscle. We used Zamorano–Dujovny (ZD) stereotactic frame (Inomed Instruments, Emmendingen, Germany), Cosman Roberts Wells (CRW) rigid stereotactic frame (Integra, Burlington, MA, USA) and Brown Roberts Wells (BRW) stereotactic guidance system (Radionics, Inc., Burlington, MA) all over the study. After the head frame is applied, a computed tomography (CT) scan is performed. (figure1)

Figure (1): After ZD frame application with fiducials

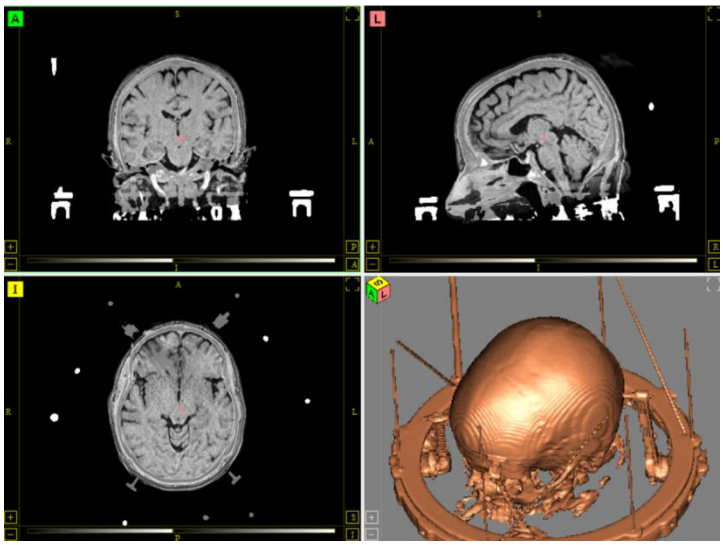

Figure (2): fused CT/MRI showing the stereotactic frame with the fiducials.

The patient is positioned with their head secured in the stereotactic frame. The entry site is marked, and a linear incision is made in the coronal direction, parting the hair along this line. The wound is prepared and draped using minimal techniques, typically involving an Ioban drape and a single craniotomy drape attached to IV poles to form a tent-like structure for easy patient assessment.

Local anesthesia is used to numb the scalp before making an incision and creating a burr hole. The dura and pia are sealed and cauterized to facilitate the gentle insertion of the electrode. Once the stereotactic frame is positioned, a guide tube is inserted into the burr hole. Gelfoam is applied to fill the space around the guide tube, and bone wax is used to seal the opening to minimize cerebrospinal fluid loss.

The subthalamic nucleus represents a challenging surgical target due to the difficulty in visualizing it on most MRI sequences utilized for targeting. As such, lesioning of the subthalamic nucleus should only be performed by experienced teams with expertise in surgical treatment for Parkinson's disease. (figure2)

However, subthalamotomy is currently considered an emerging technique rather than an established one.

The dorsolateral portion of the subthalamic nucleus was chosen as the lesion site because it is recognized as the sensorimotor area. This region receives substantial cortical motor input and projects output to the globus pallidus internus and substantia nigra pars

reticulata, making it a vital component of the basal ganglia's "motor" circuit. In contrast, the more medial regions of the subthalamic nucleus are linked to non-motor functions and are not thought to significantly influence the motor symptoms of Parkinson's disease. However, targeting the dorsolateral subthalamic nucleus poses a risk of impacting the adjacent internal capsule.

We used Microtargeting Waypoint Planner 3.0 FHC, Inc., 2009 software. The surgical technique employs a mid-sagittal T2-weighted planning scan to identify the anterior commissure-posterior commissure (AC-PC) plane. High-resolution T2-weighted axial images with a 2 mm slice thickness are then obtained parallel to this plane. Following this, coronal images orthogonal to axial images are acquired. These sequences have been shown to provide optimal delineation of the subthalamic nucleus and its surrounding structures.

Using enlarged hard copies of the MRI scans alongside the Schaltenbrand atlas, the boundaries of the subthalamic nucleus are identified. Its position is then co-registered on the coronal and axial scans to ensure precise three-dimensional target definition.

Stereotactic coordinates of the dorsolateral portion of the subthalamic nucleus are documented, with the target point typically positioned 10-12 mm lateral to the midline, 1-3 mm posterior to the midcommissural point, and 3-5 mm inferior to the AC-PC line. On T2 MRI, this target appears as a small, almond-shaped, hypointense structure located 1-2 mm anterior to the red nucleus and 2-3 mm superior and slightly lateral to the substantia nigra reticulata.

The subthalamic nucleus is externally bordered by the internal capsule and located posterior to the mammillary bodies, along which a trajectory is planned for the surgical procedure. During the operation, patients remain awake and in an "off" state, having stopped their anti-Parkinson's medications 24 hours in advance.

A 2.2-mm diameter electrode with a 6-mm exposed tip is guided to the dorsolateral subthalamic nucleus (STN). Electrical stimulation is delivered at a frequency of 100 Hz, with a pulse width of 1 millisecond and a voltage range of 0.75 to 2 volts.

The probe position is fine-tuned to attain maximal clinical improvement in the observed Parkinsonian symptoms while avoiding any adverse effects.

At the appropriate location, one or two radiofrequency lesions are generated, usually at a temperature of 72°C for 70 seconds. Following the intervention, the patient undergoes a high-resolution MRI examination to verify the lesion placement. Anti-Parkinson's medications are then reinstated as necessary. (figure3)

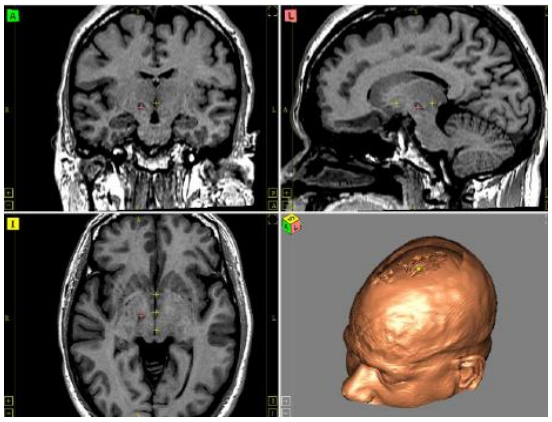

Figure (3): Post operative MRI showing right STN lesion, A case from our study

Results

Sub-thalamotomy was performed on 14 cases with male predominance representing 9 cases, ages ranged from 28 to 62 years, with a mean age of 49.1 ± 12.77 years. Subthalamotomy was performed on the left side in nine cases and on the right side in five cases. The duration of Parkinson's disease varied from 5 to 13 years, with a mean duration of 9.9 ± 3.18 years.

Schwab & England ADL scale was significantly increased 6 months after surgery than before during both "OFF and ON" states (table1)

Table 1: Schwab & England ADL scale

Schwab & England ADL	Sub-thalamotomy group (n=14)
"OFF" state	
Preoperative	46.0±9.21
Postoperative	84.00±7.58
P value (pre vs post)	**p=0.001***
"ON" state	
Preoperative	68.0±9.68
Postoperative	94.0±5.34
P value (pre vs post)	**p=0.001***

We used Levodopa Equivalent Daily Dose (LEDD) to show how much L-Dopa dose can be reduced after lesioning surgery. The results were as follows:

-Mean of LDED was 780 and 390 pre and post-operative respectively. (table2)

Table 2: mean LDED pre and post operative.

Mean LDED	Sub-thalamotomy (n=14)
Preoperative	780±10.5
Post operative	390±10.5
P Value	P<0.001*

We assessed Our patients for possible complications of surgery, we found that the complications were:

There were 2 patients 20% complicated with hemiballismus. One of them was mild and improved within 2 weeks and 1 case was severe and recovered after 2 months. No other complications were detected. (table3)

Table 3: possible complications.

	Sub-thalamotomy group (n=14)
Missed target	0
Small ICH	0
Hemiballismus	2(20.0%)
Cognitive dysfunction	0
Speech problems	0
Seizure	0
Others	0

Discussion

Patients who underwent subthalamotomy surgery demonstrated significant improvement in their motor functions after the procedure. This improved motor function was evident immediately after the surgical lesioning and was sustained throughout the monitoring period.

The subthalamotomy group demonstrated significant improvements in UPDRS III scores, with decreases from 56.60±5.04 to 28.40±6.7 in the Off period and 35.40±6.06 to 14.80±2.74 in the On period. There were dramatic improvements in rigidity, body bradykinesia, and tremors, ranging from 52%,47% and 57% respectively at 6 months post-surgery during off state. Dyskinesia was also reduced, decreasing from 6.10±1.52 to 3.40±1.07 in the On period.

Schwab & England ADL scores improved substantially, from 46.0±9.21 to 84.00±7.58 during "Off" state and from 68.0±9.68 to 94.0±5.34 in the On period. The Modified H&Y scale also decreased significantly following surgery in both Off and On states. LDED was reduced by 50.65% compared to pre-operative levels.

The differences between our study and the Su et al. study can be attributed to patient selection, unilateral versus bilateral procedures, and the timing of LDED reduction. The Alvarez et al. study showed even greater improvements, likely due to the more advanced PD in their patients and the delayed timing of LDED reduction. (12), (13)

Hanagasi et al.'s 2009 study demonstrated that subthalamotomy is an effective treatment for the motor symptoms of Parkinson's disease. Their results showed that the Unified Parkinson's Disease Rating Scale III score improved by 25% and 23% in the Off and On states, respectively. Rigidity, tremor, and bradykinesia improved dramatically, with 62%, 57%, and 38% improvements in the Off state, and 55%, 61%, and 38% improvements in the On state, respectively. The Schwab and England Activities of Daily Living score improved by 20% in both the Off and On states. Levodopa-equivalent daily dose was reduced by 27% compared to the pre-operative period. Dyskinesia improved by 50% in the On state. (14)

The discrepancy between the findings of our study and the Hanagasi et al. study may be largely explained by the notable disparity in study sample size. Our study involved a considerably larger subthalamotomy group of 10 patients, whereas Hanagasi et al. study had a much smaller sample size (4 patients).

In the subthalamotomy group, no intraoperative complications occurred. During the postoperative period, 2 patients developed contralateral hemiballismus, with 1 case being mild and resolving within 2 weeks through a reduction in levodopa dosage. The second patient experienced severe hemiballismus, requiring the cessation of levodopa and the administration of valproate, ultimately recovering after 2 months. No other complications, such as intracerebral hemorrhage, cognitive dysfunction, speech problems, seizures, or any other adverse events, were detected.

Su et al. study reported the development of hemiballismus in 3 out of 12 subthalamotomy procedures. Two cases were mild and improved within one month without specific treatment, while the third case was severe, requiring the discontinuation of levodopa and medical intervention. Sadly, this patient later succumbed to complications related to aspiration pneumonia and sepsis. Additionally, one patient experienced a small frontal intracerebral hemorrhage associated with the needle tract, which resolved without sequelae. No other complications were noted. (12)

The increased incidence of complications in the Su et al. study, compared to our findings, can be attributed to the fact that some patients underwent bilateral subthalamotomy procedures.

The L. Alvarez et al. study reported a single case of severe, persistent hemiballismus that resolved completely after the patient underwent pallidotomy 12 months later. No other complications were documented. (13)

Lastly, the Hanagasi et al. study reported one instance of hemiballismus, which recovered within one month with the use of valproate. No other complications were detected regarding the subthalamotomy group. (14)

Conclusion

This study confirms that ablation of the dorsolateral subthalamic nucleus region results in the best benefit-to-risk ratio. Subthalamotomy has a significant impact on improving daily life activities and can enhance the quality of life for patients with Parkinson's disease. It can also treat the key symptoms of Parkinson's disease and reduce the postoperative dosage of levodopa. Additionally, ablation of the dorsolateral part of the subthalamic nucleus can mitigate the risk of postoperative hemiballismus.

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