

Long-term outcomes of subthalamic nucleus deep brain stimulation for Parkinson's disease in Singapore

Yi Zhan Cai¹, Yilong Zheng², Wei Li^{3,4,5} MN, Saffari Seyed Ehsan^{3,5} PhD, Hwee Lan Ng^{3,4,5} BSc (Nursing), Angela Zhan^{3,4,5} MN, Zheyu Xu^{3,4,5} MB BChir, Kay Yaw Tay^{3,4,5} MBBS, Wing Lok Au^{3,4,5} MBBS, Wai Hoe Ng³ MBBS, Louis Chew Seng Tan^{3,4,5} MBBS, Wan Kai Rui^{3,4,5} FRCS, Shermyn Neo^{3,4,5} MBBS

ABSTRACT

Introduction: Subthalamic nucleus deep brain stimulation (STN-DBS) is a proven treatment modality for Parkinson's disease (PD), reducing dyskinesia and time spent in the "OFF" state. This study evaluates the long-term outcomes of STN-DBS in PD patients up to 10 years post-surgery in Singapore.

Method: We conducted a retrospective review of Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) scores, activities of daily living (ADLs), disease milestones, dopaminergic drug prescriptions, and adverse events in patients before and after STN-DBS surgery.

Results: A total of 94 PD patients who underwent bilateral STN-DBS were included. STN-DBS reduced time in the "OFF" state by 36.9% at 1 year ($P=0.034$) and 40.9% at 5 years ($P=0.006$). Time with dyskinesia did not significantly change. Levodopa equivalent daily dose was reduced by 35.1% by 5 years ($P<0.001$). MDS-UPDRS-II and III scores increased from 5 years post-DBS by 40.5% and 35.4%, respectively. Independence in ADLs decreased, though not significantly. The prevalence of frequent falls increased at 5 years. Surgery- and device-related adverse events were uncommon and generally mild.

Conclusion: STN-DBS provides sustained relief from motor complications and reduced medication requirements in PD patients in Singapore. This study highlights STN-DBS as an effective treatment option, significantly enhancing the quality of life for those with PD.

Ann Acad Med Singap 2024;53:481-9

Keywords: deep brain stimulation, neurology, neurosurgery, Parkinson's disease, subthalamic nucleus

CLINICAL IMPACT

What is New

- This is the first study examining both short-term and long-term outcomes of deep brain stimulation (DBS) in Parkinson's disease within Singapore.
- Subthalamic nucleus deep brain stimulation (STN-DBS) is shown to effectively reduce motor fluctuations and dyskinesia, even in an older cohort (mean age 60.6 years).
- The rate of adverse events related to STN-DBS in Singapore is low and comparable to global standards.

Clinical Implications

- STN-DBS is a highly effective treatment in improving clinical outcomes in patients in Singapore with Parkinson's disease, demonstrating a favourable risk profile.

INTRODUCTION

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disorder characterised by motor symptoms such as limb bradykinesia, rigidity and

resting tremor.¹ Non-motor symptoms, including mood disturbances, cognitive impairment, autonomic dysfunction and sleep disorders, are also common. Disease progression often leads to motor fluctuations and dyskinesias, along with worsening non-motor features. Deep brain stimulation (DBS) is a well-recognised surgical treatment for PD, especially for patients who respond to levodopa but experience refractory motor complications or intolerable medication side effects.² The 2 primary DBS targets in PD are the subthalamic nucleus (STN) and the internal segment of the globus pallidus (GPi).³⁻⁵ Both targets are effective in improving motor symptoms,⁵ but STN-DBS is particularly noted for significantly reducing levodopa dosage,⁶ thus lowering drug burden and costs for patients.^{7,8}

The Annals is an open access journal, allowing non-commercial use under CC BY-NC-SA 4.0.

¹ Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

² Yong Loo Lin School of Medicine, National University of Singapore, Singapore

³ National Neuroscience Institute, Singapore

⁴ Parkinson's Foundation Center of Excellence, United States of America

⁵ Duke-NUS Medical School, Singapore

Correspondence: Dr Shermyn Neo, National Neuroscience Institute, 11 Jalan Tan Tock Seng, Singapore 308433.

Email: shermyn.neo.x.m@singhealth.com.sg

This article was first published online on 20 August 2024 at annals.edu.sg

In Singapore, STN-DBS is the most frequently utilised advanced surgical therapy for PD. STN-DBS has been shown to be more effective than medical therapy alone in alleviating motor complications,⁹ with benefits potentially extending up to 10 years post-surgery.¹⁰ However, there is a lack of data on the outcomes of STN-DBS of PD patients in Singapore. Given the invasive nature of the procedure, high implant cost and the need for periodic replacement of implantable generators, further data is essential to help clinicians and patients evaluate the risks and benefits of STN-DBS. This retrospective study aims to assess the short- and long-term outcomes (up to 10 years) of STN-DBS at the largest tertiary neurological centre in Singapore, with the primary focus on the efficacy of STN-DBS in reducing motor complications associated with levodopa therapy.

METHOD

Study population

This observational study utilises data from the National Neuroscience Institute's Parkinson's Disease and Movement Disorder (PDMD) database. Since 2002, the PDMD database has prospectively collected sociodemographic and medical information of all patients diagnosed with PD based on the National Institute of Neurological Disorders and Stroke (NINDS) criteria at the National Neuroscience Institute in Singapore. We extracted and analysed data for patients who underwent STN-DBS between 2008 to 2022 from electronic health records. For our surgical protocol, all patients were awake during the procedure, and multi-electrode recording was routinely employed. Bilateral STN leads were implanted simultaneously, as it was observed that patients rarely agreed to a second procedure later. Accurate placement of electrodes was confirmed through intra-operative macrostimulation and post-operative T2-weighted MRI.¹¹ Patients with electrodes implanted outside the subthalamic nucleus or those who underwent unilateral electrode implantation were excluded from the study. In our centre, rechargeable implantable pulse generators (IPGs) were only used in 4.6% of initial insertions, typically for younger patients. Older patients often preferred non-rechargeable models to avoid the hassle of regular battery charging, and earlier rechargeable IPG models offered only a marginal advantage in lifespan. For patients without written consent for data collection, only data up to March 2019 were used, in compliance with updated regulations requiring participant consent for inclusion in retrospective databases. The study was approved

by the SingHealth Centralised Institutional Review Board (CIRB 2019/2039).

Data collection

Patient records, including Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) sub-scores and total scores, PD clinic notes, operating theatre notes, drug prescriptions, and input from relevant specialities were reviewed for the study. The MDS-UPDRS, a revision of the original UPDRS, measures PD severity across 4 domains: non-motor aspects of daily living, motor aspects of daily living, motor examination and motor complications. Each item within these domains is graded on a scale of 0 to 4, with 4 being the most severe. Our centre switched from UPDRS to MDS-UPDRS in 2014, as the latter better captures non-motor symptoms and distinguishes between slight and mild manifestations of PD.¹² The primary outcome was the difference in time spent in the "OFF" state (MDS-UPDRS item 4.3 or UPDRS item 39), and time spent with dyskinesia (MDS-UPDRS item 4.1 or UPDRS item 32), measured at the 1-year $\pm$ 6 months (1Y), 5-year $\pm$ 6 months (5Y), and 10-year $\pm$ 6 months (10Y) periods post-operation, compared to the pre-operative baseline (POB). Secondary outcomes included the impact of DBS on MDS-UPDRS motor and non-motor scores, activities of daily living (ADLs), disease milestones (frequent falls, dementia and institutionalisation), changes in dopaminergic medication dosages, and adverse events associated with DBS. MDS-UPDRS Non-Motor Aspects of Experience of Daily Living (MDS-UPDRS-I), Motor Aspects of Experience of Daily Living (MDS-UPDRS-II), and Motor Examination (MDS-UPDRS-III) scores were evaluated at the same time points. All MDS-UPDRS-III scores were assessed with patients in the "ON" state. For consistency, all UPDRS scores were converted to their corresponding MDS-UPDRS scores. Data on ADLs were obtained from PD clinic notes, covering feeding, dressing, washing, toileting, transferring and walking. Patients requiring assistance with 3 or more ADLs were classified ADL-dependent, following practice guidelines in Singapore.¹³ The percentage of ADL-dependent patients was compared pre- and post-operation. Significant disease milestones, such as frequent falls (as ≥ 2 falls within a 12-month period), dementia (identified by the prescription of cholinesterase inhibitors or memantine)¹⁴ and institutionalisation, were recorded from clinic notes. Dopaminergic medication dosages were converted to levodopa equivalent daily doses (LEDD)¹⁵ and compared from a pre-operative baseline to the 1-year, 5-year and 10-year time

points. Adverse events (AEs), defined as any undesirable outcome associated with the surgery or post-surgical DBS, were categorised into surgery-related, device-related and stimulation-related AEs. All AEs were recorded at intervals of 30 days, 6 months, 1 year, 5 years and 10 years post-operation. Stimulation-related AEs are excluded at the 30-day time point as DBS programming only began 1 month post-operatively.

For all pre-operative data, the most recent data within 18 months before the operation date were used. For post-operative follow-ups, the data entry closest to each time point was used, up to within 3 months.

Statistical analysis

For both primary and secondary outcomes, the Wilcoxon signed-rank test was used to compare follow-up with pre-operative data. All tests were two-tailed and done at the 0.05 level of significance. Continuous variables are presented as mean $\pm$ SD. Statistical analyses were performed using SPSS version 26 (IBM Corp, Armonk, US).

RESULTS

Between 2008 and 2022, our centre treated 2,490 PD patients, comprising 1,420 males (57.0%) and 1070 females (43.0%). The ethnic composition included 2038 Chinese (81.1%), 122 Malay (4.9%), 140 Indian (5.6%) and 190 from other racial backgrounds (7.6%). This demographic distribution is reflected in our study population (Table 1). Of 2,490 PD patients, 118 underwent STN-DBS. For this study, we included 94 patients with relevant primary or secondary outcome data. We excluded 23 patients due to lack of consent for data collection, and 1 patient due to missing data. The study cohort was primarily male (66%) and Chinese (76%), with a mean age at operation of 61 years, and a mean disease duration of 152 months (Table 1). The number of STN-DBS surgeries increased steadily from 2011 to 2018, peaking between 2016 and 2019. However, the number of surgeries declined from 2020 onwards due to the COVID-19 pandemic (Fig. 1). During the follow-up period, there were 13 mortalities. Pneumonia was the most common cause (8 cases), followed by cardiac arrest (1 case) and pulmonary embolism (1 case). No deaths were directly associated with the DBS surgery or implants. The cause of death was unavailable in 3 patients.

Primary outcomes

Out of the 94 patients included in the study, 79 had data relating to the primary outcomes. Compared

Table 1. Breakdown of patient demographics.

Patient demographics (n=94)	
Sex (M/F)	62/32
Ethnicity (Chinese/Malay/Indian/Others)	71/13/5/5
Age at diagnosis (years)	50.33 $\pm$ 7.75
Age at DBS operation (years)	60.62 $\pm$ 6.83
Disease duration as of DBS operation (months)	152.39 $\pm$ 62.27
Pre-op MDS-UPDRS-III score (OFF)	55.62 $\pm$ 24.42
Pre-op MDS-UPDRS-III score (ON)	25.80 $\pm$ 12.42
Levodopa responsiveness (% improvement)	51.3%

DBS: deep brain stimulation; MDS-UPDRS-III score: Movement Disorder Society-Unified Parkinson's Disease Rating Scale Motor Examination score

Age, disease duration and MDS-UPDRS-III scores are reported as mean $\pm$ SD. Levodopa responsiveness is measured as the % decrease in MDS-UPDRS-III scores after the administration of dopaminergic medications.

to baseline (1.49 ± 0.87 , $n=77$), time spent in the "OFF" state decreased significantly by 36.9% at 1 year (0.94 ± 1.00 , $n=52$; $P=0.034$) and by 40.9% at 5 years (0.88 ± 1.03 , $n=41$; $P=0.006$). However, this reduction was not maintained at 10 years (1.00 ± 1.28 , $n=12$, $P=0.44$). Similarly, compared to baseline (0.73 ± 0.87 , $n=79$), the time spent with dyskinesias decreased at 1 year (0.47 ± 0.70 , $n=51$; $P=0.10$), 5 years (0.51 ± 0.84 , $n=41$; $P=0.15$) and 10 years (0.25 ± 0.87 , $n=12$, $P=0.23$), but these reductions were not statistically significant (Fig. 2).

Secondary outcomes

Effect of STN-DBS on MDS-UPDRS

Following STN-DBS, MDS-UPDRS-I, II and III scores showed a decrease at 1 year, but these changes were not statistically significant. However, MDS-UPDRS-II and III scores significantly worsened at the 5-year and 10-year time points. Up to 5 years, there was no significant change in MDS-UPDRS-I scores. At the 10-year point, there were insufficient data to determine the effect of STN-DBS on MDS-UPDRS-I scores (Table 2).

Effect of STN-DBS on ADLs

Independence in ADLs was compared among 45 patients. There was no significant difference between ADL independence from baseline (84.4% [38/45]) to 6 months (90.9% [40/44], $P=0.727$), 1 year (87.5% [35/40], $P=1.000$), and 5 years (63.2% [12/19], $P=0.500$) after STN-DBS.

Fig. 1. Overview of patient distribution.

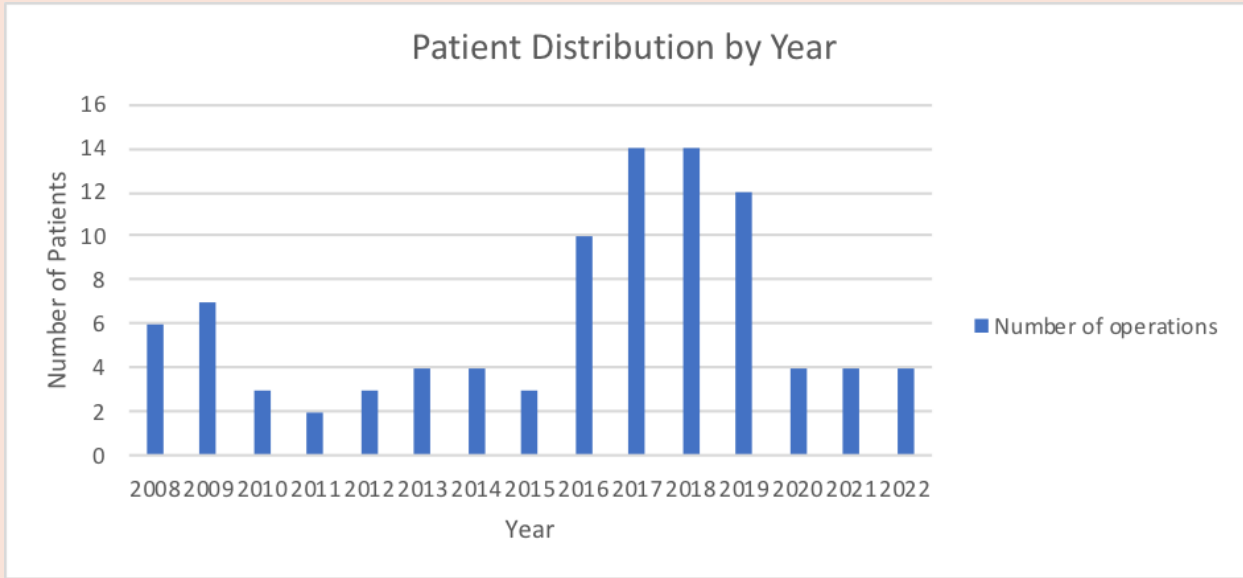
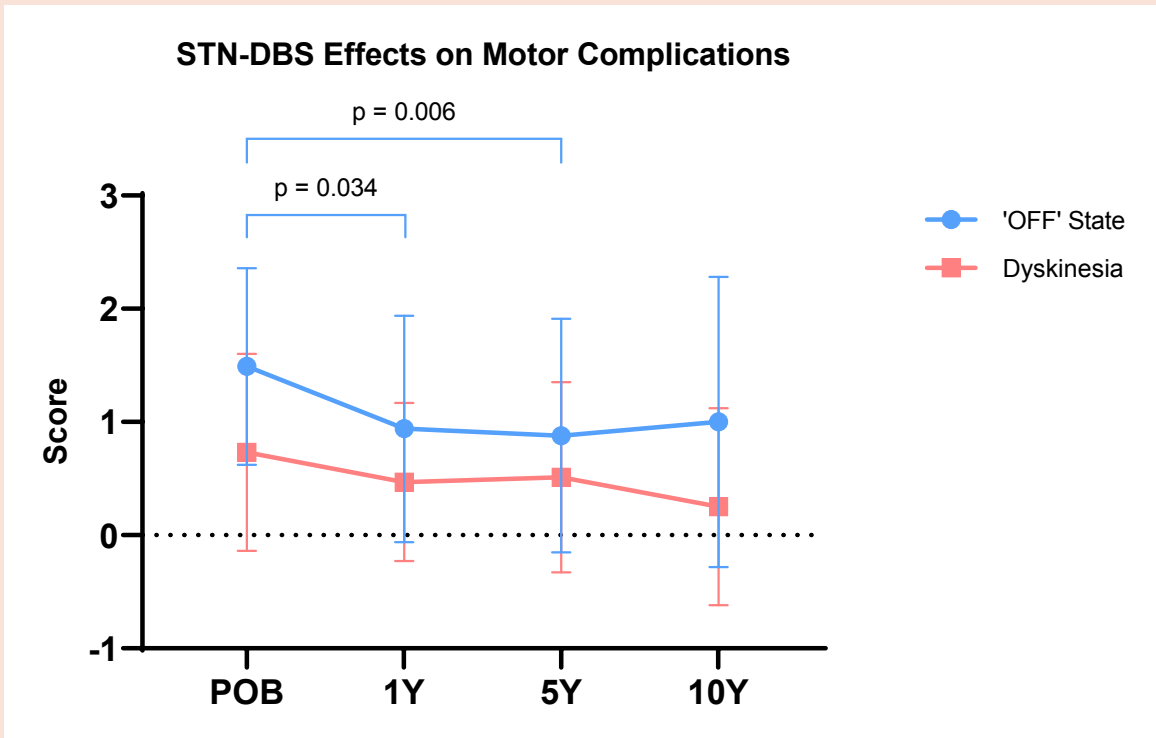


Fig. 2. Effects of subthalamic nucleus deep brain stimulation (STN-DBS) on motor complications of dopaminergic medication.



POB: pre-operative baseline
Data are presented as means with error bars for standard deviation. Statistically significant ($P<0.05$) changes are shown with significance bars. The y-axis represents the Movement Disorders Society-Unified Parkinson's Disease Rating Scale score as follows; 0: No dyskinesias/ time spent in the "OFF" state, 1: $\leq 5\%$ of waking day, 2: 26–50% of waking day, 3: 51–75% of waking day, 4: $>75\%$ of waking day.

Table 2. Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) scores at each time point.

	Time point	n	Mean	SD	P value	% change
MDS-UPDRS-I	POB	57	8.53	4.59		
	1Y	10	4.80	4.92	0.123	-43.7%
	5Y	36	8.19	4.70	0.506	-4.0%
	10Y	11	11.91	5.79	^a	^a
MDS-UPDRS-II	POB	69	15.99	8.91		
	1Y	15	8.90	4.47	0.051	-44.3%
	5Y	37	22.47	11.97	0.016	+40.5%
	10Y	11	23.36	11.62	0.028	+46.1%
MDS-UPDRS-III	POB	92	25.87	12.17		
	1Y	75	22.96	14.43	0.155	-11.2%
	5Y	43	35.03	17.94	<0.001	+35.4%
	10Y	13	46.38	20.23	0.002	+79.3%

MDS-UPDRS-I: Movement Disorder Society-Unified Parkinson's Disease Rating Scale Non-Motor Aspects of Experience of Daily Living; MDS-UPDRS-II: Movement Disorder Society-Unified Parkinson's Disease Rating Scale Motor Aspects of Experience of Daily Living; MDS-UPDRS-III: Movement Disorder Society-Unified Parkinson's Disease Rating Scale Motor Examination; POB: pre-operative baseline; SD: standard deviation

Statistically significant *P* values and % changes are in bold. All pre- and post-operative data shown were taken with patients in the "ON" state.

^a Insufficient data for statistical analysis.

Effect of STN-DBS on PD milestones

Frequent falls were observed in 30.4% (17/56) of patients before surgery, decreasing non-significantly to 19.7% (13/66, $P=0.332$) at 1 year, but significantly increasing to 60.3% (35/58, $P=0.027$) at 5 years. Dementia was present in 1.7% (1/58) of patients pre-surgery, rising non-significantly to 2.8% (2/71, $P=1.000$) at 1 year and 10.7% (6/56, $P=0.500$) at 5 years. No patients were institutionalised at the time of operation and at 1 year post-operation. However, 3 patients were institutionalised between 1 and 5 years, and 1 patient between 5 and 10 years post-operation.

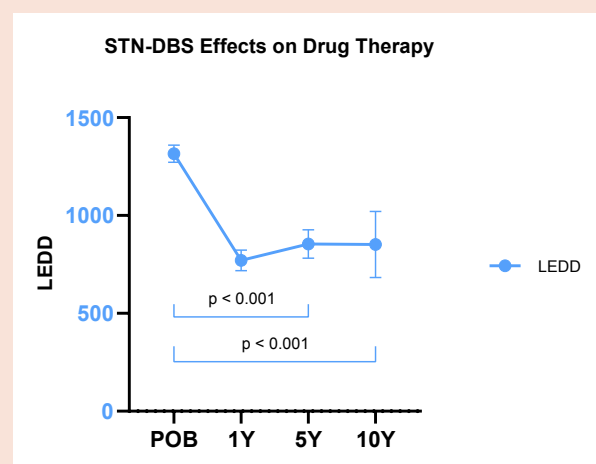
Effect of STN-DBS on drug therapy

Compared to the baseline (1315.40 ± 44.04 , $n=87$), LEDD was significantly reduced by 41.4% at 1 year (771.09 ± 52.60 mg/day, $n=80$; $P<0.001$) and by 35.1% at 5 years (854.07 ± 72.65 mg/day, $n=36$; $P<0.001$). However, there was no significant reduction at the 10-year time point (852.20 ± 168.59 mg/day, $n=10$; $P=0.139$) (Fig. 3).

Adverse events after STN-DBS

All reported adverse events (AE) are detailed in Table 3. Surgery-related AEs were observed only within the first 6 months post-operation.

Fig. 3. Effects of subthalamic nucleus deep brain stimulation (STN-DBS) on drug therapy.



LEDD: levodopa equivalent daily dose; POB: pre-operative baseline

Data are presented as means with error bars for standard deviation. Statistically significant ($P<0.05$) changes are shown with significance bars.

Device-related AEs, with infection being the most common (accounting for 50% of all device-related AEs), were observed at all time points but were most frequent between 30 days to 6 months and from 5 to 10 years post-operation. Infections led

Table 3. Adverse events associated with STN-DBS subthalamic nucleus deep brain stimulation (STN-DBS).

Adverse events		Post-op – 30 days	30 days – 6 months	6 months – 1 year	1 year – 5 years	5 years – 10 years	Total
Surgery	n	94	93	85	78	31	
	IVH	1 (1.1%)	0	0	0	0	1
	Peri- or post-operative confusion	6 (6.4%)	1 (1.1%)	0	0	0	7
	SDH	1 (1.1%)	1 (1.1%)	0	0	0	2
	Seizure	2 (2.1%)	0	0	0	0	2
	Transient neurological deficit	1 (1.1%)	0	0	0	0	1
	Total	11	2	0	0	0	
Device	n	94	93	85	78	31	
	Infection	1 (1.1%)	5 (5.3%)	0	2 (2.6%)	3 (9.7%)	11
	IPG battery failure	0	0	0	0	0	0
	Lead malfunction	1 (1.1%)	0	0	0	1 (3.2%)	2
	Lead reimplantation	1 (1.1%)	4 (4.3%)	0	1 (1.3%)	0	6
	Skin erosion	0	0	2 (2.4%)	0	0	2
	Total	3	9	3	4	4	
Stimulation	n		63	56	44	8	
	Anxiety		1 (1.6%)	0	3 (6.8%)	0	4
	Depression		0	2 (3.6%)	3 (6.8%)	0	5
	Dysarthria		0	3 (5.4%)	6 (13.6%)	2 (25.0%)	11
	Dysphagia		3 (4.8%)	7 (12.5%)	11 (25.0%)	1 (12.5%)	22
	Freezing of gait		3 (4.8%)	0	2 (4.5%)	0	5
	Hallucinations/psychosis		0	0	8 (18.1%)	1 (12.5%)	9
	Hypersalivation		7 (11.1%)	5 (8.9%)	4 (9.1%)	0	16
	ICD		2 (3.2%)	4 (7.1%)	4 (9.1%)	1 (12.5%)	11
	Incontinence		3 (4.8%)	1 (1.8%)	10 (22.7%)	0	14
	Total		19	22	51	5	

ICD: impulse control disorder; IPG: implantable pulse generator; IVH: intraventricular haemorrhage; SDH: subdural haemorrhage. Data are reported as number and percentage of patients affected by each complication. No data was collected for stimulation-related complications at the post-op to 30 days period as DBS programming was only performed 1 month after surgery.

to lead reimplantation in 4 patients. Additionally, 2 patients with lead malfunctions chose not to have their leads reimplanted, and 1 patient with lead infection had the leads explanted without replacement.

DISCUSSION

To our knowledge, this is the first study of short-term and long-term DBS outcomes in PD in Singapore. Among 2490 PD patients, 118 (4.7%) underwent DBS, a lower percentage than in other

similar high-income countries.¹⁶ This discrepancy is likely multifactorial, including the high costs of surgery,¹⁷ patient concerns about complications,¹⁸ and governmental restrictions on elective operations during the pandemic. The ethnic and gender distribution of patients who underwent DBS was representative of our PD population, indicating equal access to care. In this retrospective study at a large referral centre, we found that STN-DBS significantly reduced time spent in the "OFF" state up to 5 years post-surgery, though this effect was not maintained at 10 years, likely due to disease progression.² Compared to studies showing sustained reduction in motor fluctuations beyond 10 years,^{10,19} our cohort had poorer baseline MDS-UPDRS-III scores (in the "ON" state) and lower levodopa responsiveness. Additionally, our patients were significantly older at the time of DBS surgery, which likely contributed to their poorer motor function and levodopa responsiveness, despite similar disease durations.^{10,19}

There was no significant change in the time spent with dyskinesia. However, our patients' baseline time spent with dyskinesia was significantly shorter than in other studies (0.73 versus [vs] 1.73–2.83)^{10,20–23}, which may be partially due to a lower prevalence of dyskinesias in Asian populations.²⁴ MDS-UPDRS-I, II and III scores remained stable in the short term, up to 1 year. MDS-UPDRS-II and III scores increased at 5 and 10 years, likely due to the natural progression of the disease. The pattern of initial improvement followed by gradual worsening of UPDRS scores has been reported in other studies as well, including a seminal review by Limousin et al.^{2,20,22,23} Since all post-operative MDS-UPDRS scores were assessed with patients in the "ON" phase, significant improvement in motor symptoms beyond the effects of therapeutic drugs, even with stimulation, was not expected.²³ In this study, STN-DBS did not result in a significant change in patients' ability to perform activities of daily living, unlike previous studies that reported notable improvements in patient ADLs.^{9,25,26} This discrepancy may be due to differences in the definition of ADL independence used in our study compared to others. Additionally, cultural factors play a role; in our setting, we tend to select patients with good social support for STN-DBS, given the intensive post-operative care required. As a result, patients may continue to receive assistance with ADLs post-surgery, even if they do not need it. The poorer motor baseline and older age profile of our patients may also contribute to the lack of improvement in ADL independence. Utilising more quantitative ADL

assessment scales, such as the Katz ADL scale²⁷ and the Lawton Instrumental ADL²⁸ scale, could further clarify the effects of STN-DBS on patient ADLs.

In our study, STN-DBS did not significantly reduce the prevalence of frequent falls or prevent the long-term development of this disease milestone. This is likely due to the worsening of axial and motor symptoms, as indicated by the increase in MDS-UPDRS-III scores, a finding consistent with other studies.^{29,30} The prevalence of dementia in our patients after STN-DBS (2.8% at 1 year, 10.7% at 5 years) is comparable to that reported in another study (2.3% at 1 year, 10.9% at 5 years),³¹ despite our patients being older at the time of STN-DBS (60.6 vs 55.9 years). The same study also concluded that the prevalence and incidence are not higher than the general PD population, though this was not confirmed with a matched control group. Overall, our study did not show that STN-DBS delays late-stage milestones such as frequent falls and dementia.

STN-DBS also reduced the LEDD for at least 5 years, likely due to improvements in motor function.³² By lowering drug dosage, STN-DBS can decrease medication costs for the patient^{7,8} and alleviate the drug burden from polypharmacy, which may partially explain the improved quality of life observed with STN-DBS.¹⁰ However, based on our data, it remains unclear whether the reduction of LEDD also reduces the prevalence of certain hyperdopaminergic side effects, such as psychosis.

Adverse events associated with STN-DBS are relatively uncommon, and our results indicate a risk profile comparable to existing literature.^{10,22,33,34} No serious life-threatening complications were observed post-surgery. The most frequently observed device-related AE was infection, followed by lead reimplantation due to previous infection or unsatisfactory placement. A review of 6 randomised control trials with follow-up of 6 months to 2 years reported an infection rate of 4.49 events per 100 patients after probe implantation,³⁵ similar to our findings. The highest number of stimulation-related AEs were reported from 1 and 5 years post-surgery, likely due in part to disease progression and possibly influenced by other factors such as the development of unrelated comorbidities. It would be challenging to directly attribute stimulation-related AEs to STN-DBS because the progression of PD symptoms overlapped with some AEs associated with the treatment. All new stimulation-related AEs post-DBS surgery are thus only potentially related to STN-DBS and may be influenced by other

unconsidered factors. No suicide attempts were noted in our cohort.

The main limitation of this study is the high rate of loss to follow-up, particularly over the long term, which is typical of long-term retrospective studies. This issue is partly due to patient mortality, but also results from patients dropping out of the study and the lack of patient consent for data collection after the implementation of new regulations in March 2019. The small sample size may have led to some primary and secondary outcomes being statistically insignificant. Additionally, the study lacks a comparison with a matched control group receiving medical therapy, which would have helped to better delineate the effects of STN-DBS. Despite these limitations, our data strongly suggest that STN-DBS can sustain motor benefits over the long term while reducing the required dose of PD medications and associated side effects.

In conclusion, STN-DBS effectively reduces motor fluctuations and dyskinesia in PD patients over the long term, while also decreasing the need for dopaminergic medication. Although it does not halt disease progression, STN-DBS remains instrumental in improving outcomes with a favourable risk profile.

Declaration

No funding was received for this work. The authors declare they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

Acknowledgements

We would like to thank all our patients and their families for their support. We would like to thank Mr Aiden Wong for his logistical and data entry support.

REFERENCES

1. Jankovic J, Tan EK. Parkinson's disease: etiopathogenesis and treatment. *J Neurol Neurosurg Psychiatry* 2020;91:795-808.
2. Limousin P, Foltynie T. Long-term outcomes of deep brain stimulation in Parkinson disease. *Nat Rev Neurol* 2019;15:234-42.
3. Okun MS. Deep-brain stimulation for Parkinson's disease. *N Engl J Med* 2012;367:1529-38.
4. Moun SJ, Price CC, Limotai N, et al. Effects of STN and GPi deep brain stimulation on impulse control disorders and dopamine dysregulation syndrome. *PloS One* 2012;7:e29768.
5. Lee PS, Crammond DJ, Richardson RM. Deep Brain Stimulation of the Subthalamic Nucleus and Globus Pallidus for Parkinson's Disease. *Prog Neurol Surg* 2018;33:207-21.
6. Mansouri A, Taslimi S, Badhiwala JH, et al. Deep brain stimulation for Parkinson's disease: meta-analysis of results of randomized trials at varying lengths of follow-up. *J Neurosurg* 2018;128:1199-213.
7. Hacker M, Cannard G, Turchan M, et al. Early subthalamic nucleus deep brain stimulation in Parkinson's disease reduces long-term medication costs. *Clin Neurol Neurosurg* 2021;210:106976.
8. Hacker ML, Currie AD, Molinari AL, et al. Subthalamic Nucleus Deep Brain Stimulation May Reduce Medication Costs in Early Stage Parkinson's Disease. *J Park Dis* 2016;6:125-31.
9. Deuschl G, Schade-Brittinger C, Krack P, et al. A randomized trial of deep-brain stimulation for Parkinson's disease. *N Engl J Med* 2006;355:896-908.
10. Bove F, Mulas D, Cavallieri F, et al. Long-term Outcomes (15 Years) After Subthalamic Nucleus Deep Brain Stimulation in Patients With Parkinson Disease. *Neurology* 2021;97:e254-62.
11. Karthick PA, Wan KR, An Qi AS, et al. Automated detection of subthalamic nucleus in deep brain stimulation surgery for Parkinson's disease using microelectrode recordings and wavelet packet features. *J Neurosci Methods* 2020;343:108826.
12. Skorvanek M, Martinez-Martin P, Kovacs N, et al. Differences in MDS-UPDRS Scores Based on Hoehn and Yahr Stage and Disease Duration. *Mov Disord Clin Pract* 2017;4:536-44.
13. Agency for Integrated Care, Interim Disability Assistance Programme for the Elderly (IDAPE). <https://www.aic.sg:443/financial-assistance/interim-disability-assistance-programme-elderly>. Accessed 30 October 2023.
14. Tisher A, Salardini A. A Comprehensive Update on Treatment of Dementia. *Semin Neurol* 2019;39:167-78.
15. Schade S, Mollenhauer B, Trenkwalder C. Levodopa Equivalent Dose Conversion Factors: An Updated Proposal Including Opicapone and Safinamide. *Mov Disord Clin Pract* 2020;7:343-5.
16. Fasano A, Fung VSC, Lopiano L, et al. Characterizing advanced Parkinson's disease: OBSERVE-PD observational study results of 2615 patients. *BMC Neurol* 2019;19:50.
17. Zhang C, Ramirez-Zamora A, Meng F, et al. An International Survey of Deep Brain Stimulation Utilization in Asia and Oceania: The DBS Think Tank East. *Front Hum Neurosci* 2020;14:162.
18. Kim MR, Yun JY, Jeon B, et al. Patients' reluctance to undergo deep brain stimulation for Parkinson's disease. *Parkinsonism Relat Disord* 2016;23:91-4.
19. Park HR, Im HJ, Park J, et al. Long-Term Outcomes of Bilateral Subthalamic Nucleus Deep Brain Stimulation for Patients With Parkinson's Disease: 10 Years and Beyond. *Neurosurgery*. 2022;91:726-33.
20. Rodriguez-Oroz MC, Obeso JA, Lang AE, et al. Bilateral deep brain stimulation in Parkinson's disease: a multicentre study with 4 years follow-up. *Brain J Neurol* 2005;128:2240-9.
21. Krack P, Batir A, Van Blercom N, et al. Five-Year Follow-up of Bilateral Stimulation of the Subthalamic Nucleus in Advanced Parkinson's Disease. *N Engl J Med* 2003;349:1925-34.
22. Schüpbach WMM, Chastan N, Welter ML, et al. Stimulation of the subthalamic nucleus in Parkinson's disease: a 5 year follow up. *J Neurol Neurosurg Psychiatry* 2005;76:1640-4.
23. Moro E, Lozano AM, Pollak P, et al. Long-term results of a multicenter study on subthalamic and pallidal stimulation in Parkinson's disease. *Mov Disord Off J Mov Disord Soc* 2010;25:578-86.
24. Lim SY, Tan AH, Ahmad-Annuar A, et al. Parkinson's disease in the Western Pacific Region. *Lancet Neurol* 2019;18:865-79.
25. Gorecka-Mazur A, Furgala A, Krygowska-Wajs A, et al. Activities of Daily Living and Their Relationship to Health-Related Quality of Life in Patients with Parkinson Disease

- After Subthalamic Nucleus Deep Brain Stimulation. *World Neurosurg* 2019;125:e552-62.
26. Zibetti M, Merola A, Rizzi L, et al. Beyond nine years of continuous subthalamic nucleus deep brain stimulation in Parkinson's disease. *Mov Disord* 2011;26:2327-34.
 27. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *Gerontologist* 1970;10:20-30.
 28. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *The Gerontologist* 1969;9:179-86.
 29. Zampogna A, Cavallieri F, Bove F, et al. Axial impairment and falls in Parkinson's disease: 15 years of subthalamic deep brain stimulation. *NPJ Park Dis* 2022;8:121.
 30. Mahlknecht P, Foltynie T, Limousin P, et al. How Does Deep Brain Stimulation Change the Course of Parkinson's Disease? *Mov Disord* 2022;37:1581-92.
 31. Bove F, Fraix V, Cavallieri F, et al. Dementia and subthalamic deep brain stimulation in Parkinson disease: A long-term overview. *Neurology* 2020;95:e384-92.
 32. Nutt JG, Rufener SL, Carter JH, et al. Interactions between deep brain stimulation and levodopa in Parkinson's disease. *Neurology* 2001;57:1835-42.
 33. Buhmann C, Huckhagel T, Engel K, et al. Adverse events in deep brain stimulation: A retrospective long-term analysis of neurological, psychiatric and other occurrences. *PLoS One* 2017;12:e0178984.
 34. Falowski S, Ooi YC, Smith A, et al. An evaluation of hardware and surgical complications with deep brain stimulation based on diagnosis and lead location. *Stereotact Funct Neurosurg* 2012;90:173-80.
 35. Deuschl G, Paschen S, Witt K. Clinical outcome of deep brain stimulation for Parkinson's disease. *Handb Clin Neurol* 2013;116:107-28.