


The advantages of general anesthesia subthalamic deep brain stimulation for Parkinson's disease in the enhanced recovery after surgery: A randomized clinical trial

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Abstract

Background and Aims: With advancements in imaging and microelectrode recording techniques, general anesthesia (GA) has emerged as an alternative option for Parkinson's disease (PD) patients undergoing subthalamic nucleus deep brain stimulation (STN-DBS). In this study, we compared the advantages and disadvantages of using GA and local anesthesia for STN-DBS in enhanced recovery after surgery (ERAS).

Methods: Surgical outcomes of STN-DBS were evaluated using the unified PD rating scales (UPDRS). CT and magnetic resonance imaging scans are used to evaluate intracranial conditions. State-trait anxiety inventory and hospital anxiety and depression scale are used to evaluate patients' perioperative psychology.

Results: Anesthesia method does not significantly impact the accuracy of microelectrode placement or the improvement of postoperative symptoms. However, the local anesthesia group had a higher incidence of intracranial air, as well as higher rates of postoperative complications such as headache, dizziness, vomiting, and delirium. GA effectively alleviated preoperative anxiety and resulted in lower levels of perioperative anxiety and psychological stress compared to local anesthesia. Additionally, the GA group had shorter surgery duration, earlier ambulation, and a shorter average hospital stay.

Conclusion: DBS under GA is safe and effective. Due to shorter surgical duration, reduced occurrence of perioperative complications, effective reduction of preoperative anxiety, and faster postoperative recovery, DBS under GA is better aligned with the concept of ERAS.

KEYWORDS

anesthesia, ERAS, Parkinson's disease, STN-DBS

1 | INTRODUCTION

Subthalamic nucleus deep brain stimulation (STN-DBS) is a widely recognized and efficacious therapeutic modality for patients diagnosed with Parkinson's disease (PD), characterized by incapacitating motor response fluctuations despite receiving active pharmacological treatment.¹ Typically, the implantation of electrodes takes place under the administration of local anesthesia, accompanied by intraoperative observations and test to ascertain the positioning of the electrodes.^{2,3} Nevertheless, this procedure poses challenges for patients, as they frequently encounter discomfort during the placement of the stereotactic frame and throughout the surgical intervention, even with the administration of local anesthesia. Moreover, patients are subjected to a prolonged period of off-medication symptoms, leading to potential anxiety and fatigue during the clinical evaluation process.⁴ Intraoperative test stimulation constitutes a singular aspect in the process of ascertaining the optimal positioning of the electrodes within the target nucleus. Fortunately, advancements in magnetic resonance imaging (MRI) have enabled direct visualization of STN, and neurophysiological target validation through intraoperative microelectrode recording (MER) can also be performed under the general anesthesia (GA).^{5,6} These improvements offer the possibility of performing these crucial procedures while the patient is under GA, reducing the burden of pain, anxiety, and exhaustion experienced by the patients. By utilizing advanced MRI techniques and conducting neurophysiological target confirmation under GA, the overall experience for patients undergoing DBS surgery can be significantly improved. This approach provides an opportunity to reduce patient discomfort and improve the efficiency of the procedure while still ensuring accurate electrode placement within the target nucleus.

Numerous studies have demonstrated the substantial benefits of utilizing GA for DBS in enhancing the overall patient experience. However, previous research has primarily focused on comparing surgical target accuracy and symptom improvement between GA DBS and local anesthesia DBS, without conducting comprehensive quantitative analyses of the physiological and psychological states of both patients and medical staff during the perioperative period.^{2,7-9} It is crucial to extend the scope of investigation beyond the accuracy of surgical targets and symptom improvement to include a detailed assessment of the physiological and psychological factors affecting patients and medical staff throughout the perioperative period. By examining these aspects, we can gain a more comprehensive understanding of the benefits associated with GA DBS, including its impact on patient well-being and the potential reduction of stress and anxiety experienced by medical professionals involved in the procedure, which is also in line with the purpose of enhanced recovery after surgery (ERAS).¹⁰

As the medical model shifts from a doctor-centered approach to a patient-centered approach, patients have become increasingly integral to promoting their own health. Simultaneously, the pressure of medical and economic factors has led to a reduction in hospital stays, treatment costs, and the workload of medical staff, while increasing bed turnover and optimizing medical resource utilization. These factors have given rise to the development of ERAS.¹¹⁻¹³ ERAS, based on the principles of

evidence-based medicine, utilizes multidisciplinary and multimodal perioperative management to alleviate perioperative stress reactions, thereby reducing postoperative complications, shortening hospital stays, facilitating physical and psychological rehabilitation, and lowering medical costs. Surgery can induce a range of physiological and psychological stress reactions in patients.¹⁴⁻¹⁶ ERAS interventions focus on minimizing patients' stress responses and promoting recovery by addressing surgical-related stress. However, current clinical practices primarily concentrate on alleviating patients' physiological stress while paying less attention to their psychological stress.^{17,18} Perioperative psychological stress encompasses anxiety, depression, feelings of helplessness, concerns about disaster, diminished self-esteem, negative beliefs about their condition, and adverse coping styles.¹⁹ Psychological stress can significantly impact patients' postoperative recovery and overall quality of life. Despite this, the role of psychological assessment and intervention within the ERAS model has not received adequate attention thus far. Psychological interventions within ERAS often focus solely on providing psychological support and health education. While these interventions can be beneficial, they fall short of meeting the full needs of surgical patients. Regrettably, the number of studies focusing on enhancing perioperative management of patients undergoing DBS surgery from the ERAS perspective remains limited. There is a crucial need for standardized psychological assessment and intervention that go beyond simple support and education.

In summary, our study aims to conduct a thorough quantitative analysis of the physiological and psychological status of patients and medical staff during the perioperative period. This analysis will provide valuable insights into the broader advantages and improvements brought about by the use of GA in DBS. This comprehensive approach can further enhance the overall patient experience and facilitate a more favorable working environment for medical practitioners involved in DBS procedures.

2 | METHODS

2.1 | Clinical data collection

From January 2021 to 2023, 136 PD patients who underwent bilateral STN-DBS at Shandong Provincial Hospital Affiliated to Shandong First Medical University were enrolled in this comparison study. Inclusion criteria for PD patients were as follows: (1) Significant improvement with a levodopa challenge test, with a >30% improvement in the unified Parkinson's disease rating scale (UPDRS) part III scores; (2) preoperative brain MRI ruling out structural abnormalities; (3) absence of dementia or psychiatric disorders; and (4) no history of previous neurosurgical interventions for intracranial conditions. Included patients were randomly (1:1) assigned to general or local anesthesia group. All patients were followed up for 6 months. This study was approved by the Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong First Medical University (Approval No. 2021-889). All procedures performed in this study were in accordance with the Helsinki

declaration and its later amendments. Written informed consent was obtained from all of the patients.

2.2 | Local anesthesia surgery process

Preoperatively, the patient underwent the installation of a stereotactic frame under local anesthesia, followed by cranial CT scan. The CT scan was then fused with preoperative cranial MRI to reconstruct and calculate the coordinates of bilateral subthalamic nuclei targets. In the operating room, after disinfection of the head, local scalp anesthesia was achieved using lidocaine. The scalp was incised, and after drilling the cranial bone, the dura mater was coagulated and opened. Microelectrodes were implanted into the planned target points using the stereotactic frame. MER of typical STN electrophysiological signals were performed, and stimulation electrodes were implanted. Experimental stimulation was given to assess the degree of symptom relief in the PD patient, followed by an increase in stimulation voltage to confirm the absence of apparent side effects. The same procedure was repeated on the contralateral side. The stereotactic frame was then removed. Under GA, the right chest skin was disinfected, and after incising the skin, a subcutaneous pocket matching the size of the implanted pulse generator (IPG) was created. Subsequently, the electrodes were connected to the IPG through subcutaneous extension cables and buried in the subcutaneous pocket below the right clavicle.

2.3 | GA DBS process

The entire DBS surgery under GA was performed, including the electrode implantation part. Ten minutes before implanting the intracranial microelectrodes, intravenous anesthetics such as propofol were discontinued to allow the restoration of STN electrophysiological activity. After electrode implantation, only STN electrophysiological signals were recorded, as the patient was under GA, and symptom improvement and side effect assessments were not conducted. Throughout the entire surgical procedure, the cessation of propofol did not exceed 30 min, and the patient's anesthesia depth was closely monitored to prevent awakening. The electrode connection and IPG implantation parts were the same as in the local anesthesia surgery.

2.4 | Outcome analysis

At the 6-month follow-up after STN-DBS, comprehensive evaluations were performed with all patients. The assessments included the use of the UPDRS to gauge motor symptoms. Immediate postoperative cranial CT scans were conducted for all patients to assess intracranial conditions. Additionally, preoperative and 6-month postoperative evaluations of psychological status were carried out using the state-trait anxiety inventory (STAI) and the hospital anxiety and depression scale (HADS).

2.5 | Statistical analysis

Statistical analysis for the secondary outcomes between treatment groups was conducted using appropriate methods, including χ^2 test, Fisher exact test, and two-sides t-test. The significance level for the *p*-value is 0.05. The data analysis was performed using IBM SPSS statistics software, version 27.

TABLE 1 Baseline characteristic.

Characteristic	LA (n = 61)	GA (n = 64)
Age of onset (year)	55.55 ± 6.94	52.22 ± 5.21
Disease duration (year)	9.32 ± 2.48	10.12 ± 2.23
Male	42 (68.85%)	44 (68.75)
Female	19 (61.15%)	20 (31.25)
Duration of medication (year)	8.78 ± 2.12	9.23 ± 2.21
On-drug phase H&Y stage		
1	0	0
2	48 (78.69%)	49 (76.56%)
3	8 (13.11%)	9 (14.06%)
4	5 (8.20%)	6 (9.38%)
5	0	0
Average	2.30 ± 0.61	2.33 ± 0.64
Off-drug phase H&Y stage		
1	0	0
2	2 (3.28%)	3 (4.69%)
3	39 (63.93%)	38 (59.38%)
4	20 (32.79%)	23 (35.94%)
5	0	0
Average	3.29 ± 0.52	3.31 ± 0.56
Levodopa daily dose (mg)	1463.12 ± 168.38	1480.47 ± 194.18
Pre-op levodopa response (%)		
Part I	39.67 ± 9.98	38.99 ± 9.67
Part II	38.32 ± 9.94	41.01 ± 10.60
Part III	40.40 ± 12.00	42.10 ± 10.97
Brady	38.47 ± 12.23	42.95 ± 10.44
Tremor	41.56 ± 10.44	38.90 ± 9.35
Rigidity	42.68 ± 12.14	43.11 ± 11.58
Posture & gait	39.84 ± 9.36	39.28 ± 10.51
Axial	42.98 ± 10.56	41.26 ± 10.94
Part IV	40.13 ± 11.88	40.67 ± 11.26
Mattis dementia rating scale	138.82 ± 4.51	137.21 ± 5.53

Abbreviations: GA, general anesthesia; H&Y stage, Hoehn and Yahr stage; LA, local anesthesia; UPDRS, unified PD rating scales.

3 | RESULTS

A total of 132 patients were included in the study, of which 66 were randomly assigned to the local anesthesia group and 66 were randomly assigned to the GA group. The two groups maintained balance on baseline characteristic. Among them, 3 patients in the local anesthesia group and 1 patient in the GA group withdrew from

the follow-up. In addition, 2 patients in the local anesthesia group and 1 patient in the GA group did not undergo repeated neuropsychology examination 6 months later. Therefore, follow-up data is available for a total of 125 patients (Table 1).

The electrophysiological results showed typical STN signals in all patients in both groups. The discharge frequency of STN in the GA group was 33.35 ± 23.23 Hz, significantly lower than the

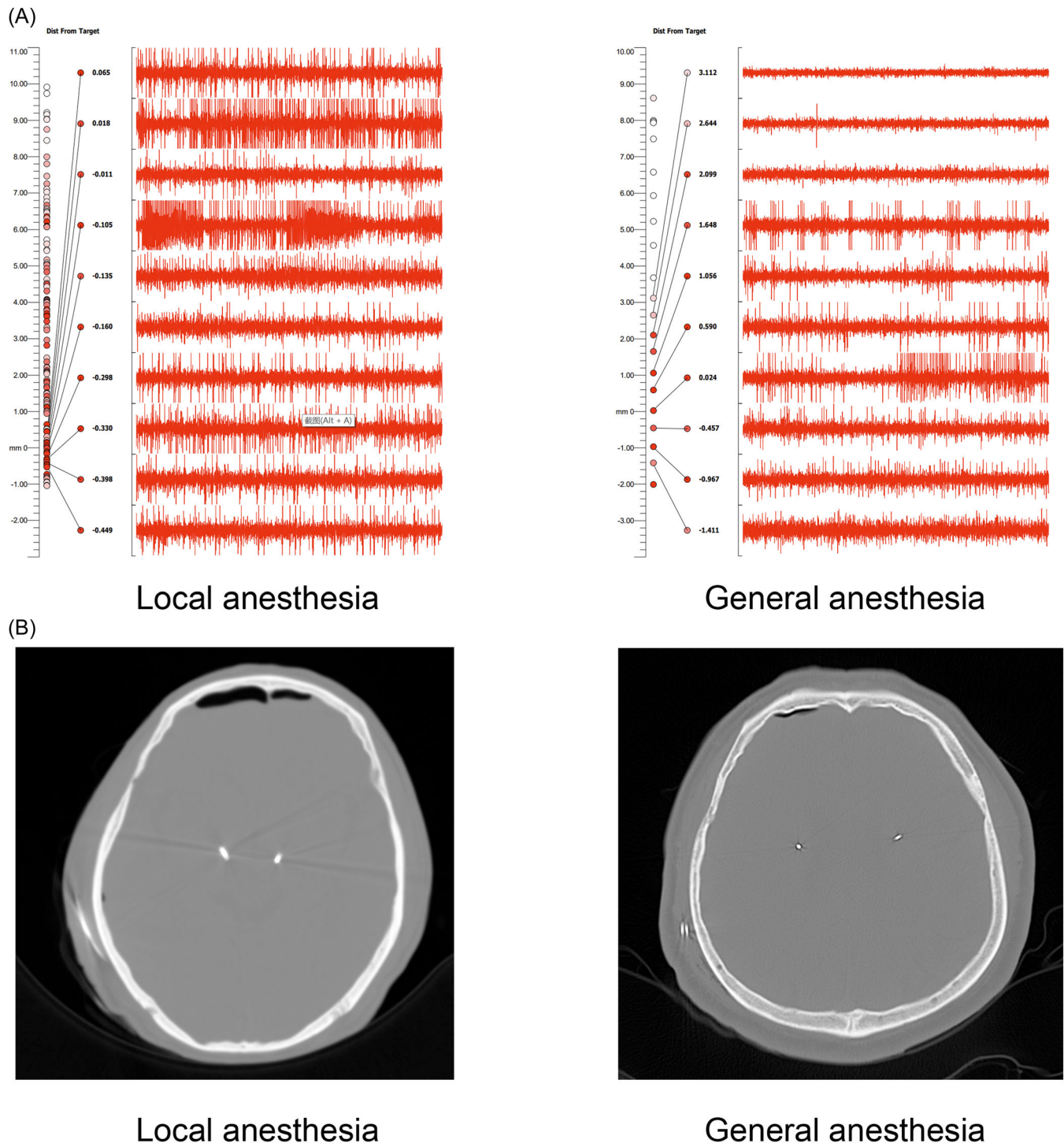


FIGURE 1 (A) Representative neuronal charges from the subthalamic nucleus in patients with Parkinson's disease (PD) under general and local anesthesia. (B) Postoperative cranial CT of PD patients under general and local anesthesia.

awake state STN discharge frequency of 43.48 ± 19.89 Hz in the local anesthesia group (Figure 1A). Immediate postoperative CT and MRI scans confirmed the accurate placement of all microelectrodes. Six months after the surgery, we conducted follow-up assessments of the improvement in Parkinson's symptoms in the patients. The postoperative electrical stimulation parameters are shown in Table 2, and the improvement in Parkinson's

symptoms in both groups was evident. The levodopa dosage in both groups was significantly reduced from 1463.12 ± 168.38 to 394.53 ± 86.23 mg and 1480.47 ± 194.18 to 414.18 ± 69.00 mg postoperatively, with no significant statistical difference between the two groups (Table 2). These results indicate that the choice of anesthesia method does not significantly affect the accuracy of microelectrode placement or the improvement of postoperative symptoms.

TABLE 2 The improvement in Parkinson's symptoms in the patients after STN-DBS.

	LA (n = 61)	GA (n = 64)	p Value
Discharge frequency of STN (Hz)	43.48 ± 19.89	33.35 ± 23.23	0.01
Efficiency of DBS (%; 6 month)			
Part I	42.34 ± 11.88	42.24 ± 9.66	0.96
Part II	38.52 ± 12.57	39.48 ± 13.59	0.68
Part III	39.62 ± 9.63	40.29 ± 11.76	0.73
Part IV	38.52 ± 12.57	42.14 ± 10.38	0.21
Levodopa daily dose (mg)	394.53 ± 86.23	414.18 ± 69.00	0.16
Stimulation parameters			
Amplitude (V)	3.20 ± 0.11 (L)	3.22 ± 0.19 (L)	0.48
	3.20 ± 0.11 (R)	3.21 ± 0.18 (R)	0.71
Pulse wide (ms)	59.92 ± 1.08 (L)	60.07 ± 1.06 (L)	0.43
	59.84 ± 1.24 (R)	60.15 ± 1.21 (R)	0.14
Frequency (Hz)	122.50 ± 13.78 (L)	122.61 ± 14.75 (L)	0.97
	122.19 ± 13.72 (R)	122.46 ± 14.82 (R)	0.92

Abbreviations: GA, general anesthesia; LA, local anesthesia; STN-DBS, subthalamic nucleus deep brain stimulation; UPDRS, unified PD rating scales.

When comparing postoperative cranial CT scans, we found that the incidence of intracranial gas in the local anesthesia group was significantly higher than that in the GA group (2952.71 ± 4240.868 vs. 479.70 ± 1480.11 mm³) (Figure 1B). Furthermore, the occurrence rates of postoperative headache, dizziness, vomiting, and delirium were significantly higher in the local anesthesia group compared to the GA group (Table 3). The occurrence of these complications was correlated with the presence of intracranial gas in postoperative patients.

To assess the impact of anesthesia method on the perioperative psychological stress level of Parkinson's patients, we used the STAI to evaluate preoperative anxiety in both groups.²⁰ The results showed no significant difference in the T-AI scores between the two groups. However, the S-AI scores in the local anesthesia group were significantly higher than those in the GA group, indicating an increased preoperative anxiety level in Parkinson's patients in the local anesthesia group despite no significant difference in long-term anxiety tendencies (T-AI) between the two groups. These results suggest that GA can effectively alleviate preoperative anxiety in Parkinson's patients. Subsequently, we used the HADS to assess patients' anxiety and depression levels before and after DBS. The results showed that patients in the GA group had lower levels of anxiety compared to the local anesthesia group. Both anxiety and depression levels were significantly improved after the surgery (Table 4). These results indicate that patients undergoing GA experience lower levels of perioperative anxiety and psychological stress compared to those undergoing local anesthesia.

TABLE 3 Complications of STN-DBS.

	LA (n = 61)	GA (n = 64)	p Value
Intracranial gas volume (mm ³)	2952.71 ± 4240.868	479.70 ± 1480.11	<0.001
Postoperative complications			
Pneumocephalus (>8000 mm ³)	12	1	<0.001
Headache	9	3	0.07
Vertigo	7	2	0.09
Delirium	6	2	0.16
Periblepsis	0	1	>0.99
Vomit	8	5	0.39
Pulmonary infection	1	1	>0.99
Urinary tract infection	0	1	>0.99

Abbreviations: GA, general anesthesia; LA, local anesthesia; STN-DBS, subthalamic nucleus deep brain stimulation.

TABLE 4 Neuropsychological assessment.

	Pre-DBS LA (n = 61)	GA (n = 64)	p Value	Sixth month LA (n = 61)	GA (n = 64)	p Value
STAI						
S-AI	66.12 ± 13.25	61.23 ± 12.43	0.03	57.15 ± 14.21	56.33 ± 10.32	0.71
T-AI	62.53 ± 16.24	63.13 ± 12.12	0.81	55.35 ± 13.35	56.35 ± 13.21	0.67
HADS						
Anxiety	9.34 ± 4.32	7.85 ± 3.22	0.03	6.12 ± 2.22	5.98 ± 2.53	0.74
Depression	8.56 ± 3.35	8.64 ± 3.23	0.89	6.32 ± 2.32	6.58 ± 2.73	0.57

Abbreviations: GA, general anesthesia; HADS, hospital anxiety and depression scale; LA, local anesthesia; STAI, state-trait anxiety inventory.

TABLE 5 STN-DBS in ERAS.

	LA (n = 61)	GA (n = 64)	p Value
Operative time (min)	195.38 ± 16.61	130.94 ± 9.39	<0.001
Out of bed (day)	1.259 ± 0.52	1.13 ± 0.33	0.04
Hospitalization time (day)	5.59 ± 0.88	5.14 ± 0.35	<0.001

Abbreviations: ERAS, enhanced recovery after surgery; GA, general anesthesia; LA, local anesthesia; STN-DBS, subthalamic nucleus deep brain stimulation.

Finally, we collected data on the duration of surgery, time to ambulation, and average length of hospital stay. The results showed that the GA group had shorter surgery duration, earlier ambulation, and shorter average hospital stay compared to the local anesthesia group (Table 5). This suggests that GA is more advantageous in reducing the surgical burden on patients and promoting postoperative recovery, aligning with the requirements of ERAS.

4 | DISCUSSION

In this study, Parkinson's patients were randomly divided into two groups: one group underwent microelectrode insertion under local anesthesia with intraoperative symptom evaluation, and the other group underwent microelectrode insertion under GA. Following microelectrode implantation, both groups underwent IPG placement under GA. The baseline characteristics of the two groups were similar without any statistical differences. Our findings indicate that STN-DBS under GA is a safe and effective approach for Parkinson's patients, and the choice of anesthesia method does not impact the long-term prognosis of PD. It is worth noting that Parkinson's patients should consider reducing their levodopa dosage after IPG stimulation to prevent dyskinesia.

While the choice of anesthesia method did not significantly affect symptom improvement in Parkinson's patients, we

observed a higher incidence of perioperative complications in the local anesthesia group, particularly with regard to intracranial air accumulation and larger intracranial gas volume compared to the GA group. Despite efforts to address this issue by tightly sealing the dura mater with physiological saline or medical adhesive during surgery, the incidence of intracranial air did not show significant improvement. This could be attributed to the need for verbal communication and limb movement during intraoperative electrophysiological testing, as well as coughing by some patients, leading to rapid changes in intracranial pressure and the entry of gas into the cranial cavity. The occurrence of intracranial air accumulation can result in postoperative symptoms such as headache, dizziness, delirium, and vomiting. It is worth mentioning that in the GA group, one patient experienced postoperative peribiosis, which was related to the inability to perform intraoperative side effect testing during the GA procedure.^{21,22} We resolved this complication by changing the stimulation contact. On the other hand, in GA surgery, patients are under anesthesia, and the surgery duration is shorter, resulting in less pronounced fluctuations in intracranial pressure. In addition, due to the prolonged surgical duration, PD patients undergoing local anesthesia DBS face higher surgical risks, including anesthesia accidents, intracranial hemorrhage, and intracranial infections. Consequently, the occurrence of such complications is effectively reduced in GA DBS, thereby promoting postoperative recovery.

Perioperative rehabilitation encompasses both physiological and psychological aspects, which are interconnected and mutually reinforcing. Physiological rehabilitation facilitates psychological recovery, and psychological rehabilitation also promotes physiological recovery. Through evaluation using the STAI scale, we found that patients informed about undergoing surgery under GA experienced a significant reduction in transient preoperative anxiety levels compared to those receiving local anesthesia. This suggests that patients' perception and expectations of local anesthesia procedures might exacerbate their anxiety. Through communication with patients, we learned that most patients perceived local anesthesia as involving more intraoperative testing

and resembling medical experimentation, while GA was seen as merely a period of sleep. This significantly increased the psychological burden on patients. Furthermore, the fixation of the stereotactic frame during the surgery restricted patients' freedom of movement, causing additional physiological discomfort. By comparing postoperative recovery, we observed that patients undergoing GA for DBS had earlier mobilization and shorter hospital stays, indicating a more proactive recovery process. Therefore, we believe that under the premise of ensuring the accuracy of electrode implantation, GA aligns better with the concept of ERAS for DBS procedures.

In summary, this study confirms the safety and effectiveness of DBS under GA. Moreover, due to the shorter surgery duration, reduced occurrence of perioperative complications, effective reduction of preoperative anxiety, and facilitation of postoperative recovery, we believe that DBS under GA is better aligned with the requirements of ERAS.

AUTHOR CONTRIBUTIONS

Cunbao Guo: Data curation. **Taihong Gao:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration. All authors have read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

[Corresponding author or manuscript guarantor] had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

TRANSPARENCY STATEMENT

The lead author Taihong Gao affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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