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ORIGINAL ARTICLE - FUNCTIONAL NEUROSURGERY - MOVEMENT DISORDERS

Early detection of cerebral ischemic events on intraoperative magnetic resonance imaging during surgical procedures for deep brain stimulation

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Abstract

Background Although intracerebral hemorrhage is the most feared complication of deep brain stimulation (DBS) surgery, cerebral ischemic events in association with DBS surgery have only rarely been described. We therefore evaluated the role of intraoperative MRI (iMRI) for early identification of cerebral ischemic events during DBS procedures and determined how ischemic infarctions affect patients over acute and long-term periods.

Methods Between January 2010 and December 2017, 1160 DBS electrodes were implanted in 595 patients at Chinese People's Liberation Army General Hospital, with the help of iMRI. The iMRI was performed in all patients after implantation, to define the accuracy of lead placement and detect complications. A CT scan was performed on postoperative days 1 to 7.

Results The iMRI showed that cerebral ischemic changes happened in nine (1.51% of patients, 0.78% of leads) patients. Only two (0.34%) of nine patients had an ischemic infarction in the basal ganglia, while seven (1.18%) had cortical ischemia. Six (67%) of the nine patients had long-term complications, two with mild hemiparesis, two with seizures, one with language dysfunction, and one with memory loss. Of those with a cortical ischemic infarction, only three (42.86%) of seven patients had no long-term complications. Long-term follow-up imaging showed that not all the patients recovered normal morphological structure in the area of ischemic foci. The factors of sex, age, target, and anesthesia were not related to ischemic events. In six (66.7%) cases, the entry point on the cortex or the path was not ideal.

Conclusions Intraoperative ischemic events are not uncommon in DBS surgery. Ischemia can cause serious permanent complications, and regions subject to severe ischemia cannot be restored; it is therefore necessary to pay careful attention to any signs of ischemia. iMRI objectively provides the basis for early diagnosis of intraoperative ischemic infarction, providing guidance for follow-up treatment. The deviation in the entry point on the cortex or in the path resulted in vascular injury; it may be the key cause of ischemic events during DBS procedures.

Keywords Intraoperative magnetic resonance imaging (iMRI) · Deep brain stimulation (DBS) · Ischemic infarction

Introduction

Deep brain stimulation (DBS) is generally a safe and effective method for alleviating motor impairment in movement disorder patients. However, adverse events during surgery have been noted, including hemorrhage, infection, seizures, and device failure, with cerebral vascular events (intracerebral hemorrhage) being the most feared complications of DBS surgery. Reports of the estimated risk of intracerebral hemorrhage in DBS surgery vary from 0.2 to 5.6% [1, 2, 10, 18, 26]. Although several reports have substantiated the risk of cerebral ischemic events following neurosurgical procedures, [6, 17, 20, 21, 23] cerebral ischemic events in association with DBS surgery have rarely been described in detail (only 14 cases) [9, 11, 13, 15, 16, 27]. Other reports have mentioned infarction as a complication in DBS surgery, but have not provided detailed information on the cases [3–5, 14, 24]. It may be that little attention is paid to infarction as a complication of DBS surgery, because the symptoms may not be

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immediately apparent, and those caused by ischemic infarction in the punctured cortex may be mild.

Postoperative MRI following DBS lead placement can help to determine the anatomical position of electrodes, as well as identifying acute complications [7, 13, 22, 25]. Intraoperative magnetic resonance imaging (iMRI) during DBS surgery offers immediate confirmation of precise lead placement and screening for complications. In the present study, we evaluated the role of iMRI for early detection of cerebral ischemic events during the DBS procedure and investigated how ischemic infarction affected patients over acute and long-term periods.

Methods

This study was approved by the ethics committee of the Chinese People's Liberation Army General Hospital.

Patients

Between January 2010 and December 2017, 1160 DBS electrodes were implanted in 595 patients at People's Liberation Army General Hospital with the help of iMRI. The patients' diagnoses included Parkinson's disease, Meige's syndrome, spasmodic torticollis, essential tremor, Tourette's syndrome, generalized dystonia, obsessive-compulsive disorder, and epilepsy. iMRI was performed to define the accuracy of lead placement and to detect any complications such as hematoma, ischemia, and pneumocephalus. A CT scan was performed on the first day after surgery. Imaging was repeated if the iMRI or CT showed signs of ischemic change.

Surgical procedure

One or two days prior to surgery, MRI was performed on all patients using a 1.5- or 3.0-T scanner (MAGNETOM Espree; Siemens Healthineers, Erlangen, Germany). On the day of surgery, a model F stereotactic head frame (Leksell; Elekta, Stockholm, Sweden) was positioned on the patient, they underwent a computed tomography (CT) scan, the CT images were fused with the pre-surgical MRI, and planning was performed to determine the entry points for a safe electrode trajectory and avoidance of blood vessels (especially the blood vessels within the sulcus) and ventricles. Upon completion of imaging and acquisition of the target coordinates, the patient was returned to the operating room under sterile conditions and local anesthesia. A Robotic Stereotactic Assistance (ROSA, MedTech Surgical, Inc) device was used to guide the surgical procedure in a minority of patients. To reduce cerebrospinal fluid (CSF) leakage, the neck was flexed to raise the head as far as possible while maintaining airway patency. A scalp incision and bur holes were created according to the entry points of the planned trajectory coordinates. Intraoperative microelectrode recording (MER) was routinely performed in most patients. Single-channel MER or multi-channel MER was generally performed using intraoperative microelectrodes (Medtronic Inc., Minneapolis, MN, USA) and the Leadpoint Neural Activity Monitoring System (Medtronic Inc.), although an Alpha Omega recording system (Alpha Omega, Nazareth, Israel) was used in a minority of patients. The electrodes were advanced to 8 mm above the target using a clinical microdrive (microTargeting Drive; FHC Inc., Bowdoin, ME, USA). During MER, fibrin sealant was used to cover the bur holes to reduce the loss of CSF. After MER and placement of the DBS electrodes (Medtronic Inc. and Beijing PINS Medical Co.), a test stimulation was conducted. The patient remained awake through this procedure, so that the temporary efficacy could be observed and verbal feedback could be obtained to ensure that unwanted adverse effects did not occur. Some patients, such as those with dystonia, epilepsy, and Parkinson's disease, were deemed to be unable to cooperate with the surgical procedure under local anesthesia; in these patients, general anesthesia was used for the whole of the surgical procedure.

Intraoperative MRI

After implantation of the bilateral intracerebral electrodes, an iMRI scan was immediately performed. The MR scanner (Siemens Espree, 1.5 T) entered the operating room via a sliding door and a short track attached to the ceiling. Before the iMRI scans, an open MR indicator was fixed in the stereotactic head frame. The MRI sequences and parameters included: T1-weighted 3D magnetization-prepared rapid gradient echo (MP-RAGE) with TE 3.02 ms, TR 1650 ms, matrix size 256 × 256, FOV 260 × 260 mm, FOV phase 100%, slice thickness 1 mm, 16-cm slab; and T2-weighted imaging with TE 93 ms, TR 5500 ms, matrix size 512 × 512, FOV 260 × 260 mm, FOV phase 100%, and slice thickness 3 mm. All patients underwent an intraoperative T1-weighted sequence; however, T2-weighted, FLAIR, and diffusion-weighted sequences, which are sensitive to hematoma and infarction, were generally not performed, to shorten the scan time. The purpose of the iMRI was mainly to determine the accuracy of the electrode positioning, with this accuracy being fully determined according to a fused image of the intraoperative 3D T1-weighted sequence and the preoperative plan.

A CT scan was performed on postoperative days 1 to 7 (a routine cerebral CT scan on post-operative day 1, or in some cases, a repeat CT when imaging findings or symptoms had changed).

Criteria for cerebral ischemia

As pre-surgical MRI (1–2 days before surgery) and CT (day of surgery) imaging data were available for all patients, the diagnosis of ischemia on comparative imaging was not difficult. Patients who met the following criteria were diagnosed with cerebral ischemia. The iMRI T1-weighted sequence showed low signal along the electrode trajectory; yet, the preoperative MRI showed no lesion, and post-operative CT confirmed the presence of low-density areas. Ischemia could also be diagnosed if the patient had obvious ischemic symptoms such as unilateral face weakness or hemiparesis; yet, the iMRI was ambiguous.

Statistical analysis

Statistical analysis was performed using SPSS 18.0 for Windows (version 18; IBM Corp., Armonk, NY, USA). Variables are expressed as mean ± standard deviation or number (%) of patients.

Results

The intraoperative and postoperative imaging showed that cerebral ischemic changes happened in nine (1.51%) patients, resulting in an ischemic stroke rate of 0.78% per implanted lead. Only two (0.34%) of nine patients showed ischemia in the basal ganglia or target area, while seven (1.18%) of nine patients showed signs of cortical ischemia. The mean age of the patients with cerebral ischemia at the time of surgery was 56.33 ± 17.45(19–83) years, and the mean duration of disease 6.89 ± 3.37 (1–11) years. The mean follow-up duration was 27.44 ± 11.16 (12–44) months. General anesthesia was performed in five of these patients, and local anesthesia (implanted the lead), then general anesthesia (implanted the pulse generator) in four of them (Table 1).

Two patients immediately showed severe hemiplegia after recovery from general anesthesia, with the other seven patients showing different symptoms after surgery, such as seizures, headache, nausea, language dysfunction, apathy, hallucinations, lethargy, mild mental symptoms, and urinary incontinence. In regard to long-term complications, patients 2 and 4 suffered from mild hemiparesis during 12 months of follow-up, patients 3 and 7 suffered from seizures and took antiepileptic drugs for more than 1.5 years, patient 5 suffered from language dysfunction for 3 years, and patient 6 suffered from memory loss for almost 4 years. Six (67%) of nine patients had long-term complications (more than 1 year), with only three patients (33.3%) showing no permanent neurological deficit. Although the ischemic infarctions in the cortex did not cause hemiparesis, four patients suffered from seizure, language dysfunction, or memory loss, and only three (42.86%) of seven patients had no long-term complications (Table 2).

IMRI was performed in all patients, and the images of all nine patients were positive. Two patients showed cerebral ischemia in the basal ganglia (Figs. 2 and 4) and seven patients showed cerebral ischemia in the frontal lobe, around or partially adjacent to the electrodes (Figs. 1, 2, 3, 4, 5, 6, 7, 8, and 9). T1-weighted imaging showed low signal and T2-weighted images showed high signal. The time from the initial placement of the first electrode to the iMRI scanning was around 2–4 h. The CT scan on the first day post-surgery was considered necessary to exclude delayed complications, and the ischemic foci seen on the CT scans were identical to those on the MRI scans in all patients. Some patients underwent more than one MRI or CT scan, to observe changes in ischemic foci. The long-term MRI follow-up showed that not all patients recovered a normal morphological structure in the area of the ischemic foci.

Ischemic events were unrelated to sex, age, implant target location, or anesthesia ($\chi^2 = 0.219$, $P = 0640$; $\chi^2 = -$, $P > 0.999$; $\chi^2 = 1.888$, $P = 0.393$; and $\chi^2 = 0.665$, $P = 0.415$, respectively). However, the GPI targets showed the highest incidence of ischemic events at 2.4%, while general anesthesia had the lowest incidence of ischemic events at only 1.1% (Table 3).

With respect to the entry point on the cortex or the path of the electrode, intraoperative MRI and postoperative CT showed that in five cases of cortical ischemia, the electrode entry point was in the superior frontal sulcus (patients 1, 5, 6, 8, and 9), and that in two cases (patients 3 and 7), it was in the convex of the middle frontal gyrus. In patient 4, the electrode was biased to the right, passing through the insular cortex. Examination of the positional relationship between the ischemic foci and the electrode revealed that the electrodes were in the center of the ischemic foci in four cases (patients 3, 7, 8, and 9), and at the edge of the ischemic foci in five cases (patients 1, 2, 4, 5, and 6) (Table 2).

With respect to the relationship between the ischemic events and the expected efficacy, in seven cases with cortical ischemia, the postoperative improvement rates varied from 64 to 85%, which we consider as good results that basically achieved the expected effect. The improvement rates in two cases with deep ischemic foci were 52% (patient 2, Parkinson's disease) and 55% (patient 4, generalized dystonia), and the desired results were not achieved (Table 2).

Discussion

Cerebral ischemic events during the DBS procedure

The incidence and location of cerebral ischemic events

Although much attention has been given to the risk factors for intracerebral hemorrhage in DBS surgery, not much is known

Table 1 Characteristics of the patients experiencing an ischemic event during a DBS procedure

No.	Age (years)/sex	Diagnosis	Anesthesia	Lead model	Stereotactic instrument	DBS target	Coordinate of anatomical target	Angle of entry point on cortex (°)	Track/MER
1	50/F	ST	GA	PINSL302	leksell	GPI	L:X = 19, Y = 3, Z = -4.5	Arc = 100, Ring = 62	1/MLNAMS
2	83/M	PD	GA	Medt3389	leksell	STN	R:X = 11.5, Y = -2, Z = -5	Arc = 85, Ring = 58	3/AORS
3	19/M	TS	GA	Medt3387	ROSA	GPI	L:X = 20, Y = 2, Z = -5	Arc = 99, Ring = 68	1/MLNAMS
4	63/M	GD	GA	PINSL302	leksell	GPI	R:X = 18,Y = 3, Z = -5	Arc = 78, Ring = 68	3/AORS
5	50/M	PD	LA+ GA	PINSL301	leksell	STN	L:X = 13, Y = -1.5, Z = -5	Arc = 108, Ring = 55	1/MLNAMS
6	64/F	MS	GA	PINSL301	leksell	STN	L:X = 12, Y = -2, Z = -4.5	Arc = 105, Ring = 57	4/AORS
7	68/F	PD	LA+ GA	PINSL301	leksell	STN	L:X = 12, Y = -1, Z = -5	Arc = 107, Ring = 58	1/MLNAMS
8	53/F	ET	LA+ GA	Medt3387	leksell	VIM	R:X = 14, Y = -6, Z = 0	Arc = 79, Ring = 55	4/AORS
9	57/F	PD	LA+ GA	PINSL301	leksell	STN	R:X = 12.5, Y = -1.5, Z = -5	Arc = 74, Ring = 60	1/MLNAMS

GPi globus pallidus internus, *STN* subthalamic nucleus, *VIM* ventral intermediate nucleus, *ST* spasmodic torticollis, *PD* Parkinson's disease, *TS* Tourette's syndrome, *MS* Meige's syndrome, *GD* generalized dystonia, *ET* essential tremor, *GA* general anesthesia, *LA* local anesthesia, *MER* microelectrode recording, *AORS* Alpha Omega recording system (Alpha Omega, Nazareth, Israel), *MLNAMS* Medtronic Leadpoint neural activity monitoring system (intraoperative microelectrode, Medtronic Ltd.); Medt 3389,3387 electrodes (Medtronic, Ltd.); PINSL302,301 electrodes (Beijing PINS Medical Co.)

about the frequency, clinical significance, prognostic outcome, and risk factors of ischemic infarction. Only a few cases of cerebral ischemic events in association with DBS surgery have been reported in detail (Table 4) [9, 11, 13, 15, 16, 27]. Cerebral ischemic events may develop at two sites, depending on the puncture tract: (1) in the basal ganglia or target area or (2) in the punctured cortex area. Morishita et al. [15] reported that four patients (0.8% per lead, 1.3% per patient) had a symptomatic cerebral venous infarction of 500 DBS lead (301 patients) implantation procedures; all of these infarctions happened in the cortical area around the lead, and no patient suffered an infarct in the basal ganglia or target area. In contrast, Downes et al. [9] reported that 5 (2.14% per lead, 3.88% per patient) of 129 patients (234 leads) showed ischemic strokes during implantation, with the ischemic infarctions all being located in the basal ganglia or target area, and there being no cortical ischemic infarctions. Novak et al. [12] reported that 2 (4.88% per patient, 2.30% per lead) of 41 patients (87 leads) had an unusual adverse ischemic event associated with subthalamic nucleus stimulator implantation, with both of these occurring in the thalamus. Kang et al. and Larson and Cheung both reported one ischemic case during a DBS surgical procedure, both of which were in the basal ganglia [11, 13], and there is also one report of a case of delayed and recurrent cerebral ischemia occurring 6 and 9 months after DBS surgery [27].

Our findings included both cortical infarction and basal ganglia infarction. In our patient cohort, 7 (1.18%) of 595 patients were revealed to have cortical ischemia; an incidence of ischemic infarction very similar to that reported by Morishita et al. (1.3% per patient) [15]. Only two of 595 patients (0.34%) revealed ischemic infarction in the target or basal ganglia; an incidence rate for subcortical ischemia that is obviously lower than reported in two other studies [9, 12]. In our group, 9 (1.51%) of 595 patients suffered ischemic infarction, resulting in a 0.78% rate of ischemic stroke per lead implanted. As all patients underwent iMRI and postoperative CT, we can feel confident that our incidence rates for ischemic events are accurate and real representations of the true situation for ischemic events during the DBS procedure, avoiding any floor or ceiling effects.

In summary, reviewing these previous articles, we found that the incidence of ischemic infarction during DBS surgery ranges from 1.3 to 4.88%. The true rates of cortical infarction may actually be higher, as patients may have experienced intraoperative or perioperative ischemic events that went unrecognized because of delayed clinical manifestation and inconsistent follow-up with imaging data.

Symptoms and prognostic outcomes of cerebral ischemic events

If a patient is under local anesthesia and a cerebrovascular accident happens in the basal ganglia or target area, the patient will immediately show symptoms such as hemiplegia, facial weakness, and slurred speech. The location of bleeding or infarction can be inferred from these signs occurring during the DBS procedure, with bleeding often being inferred first, because bleeding is more common in DBS complications. However, despite these early signs, the diagnosis ultimately

Table 2 Characteristics of the patients experiencing an ischemic event during a DBS procedure

No.	Symptoms of ischemia	Site of ischemia	Entry point on cortex or path	Site of damaged blood vessels	FU (month)	Improvement rate (%)	Long-term complications
1	Headache, nausea, partial aphasia, mental symptoms, hallucinations	L, Cortex of middle frontal gyrus; lead at the edge of the ischemia	Superior frontal sulci	Superior frontal sulci	44	69	No
2	Left hemiplegia, weakness of left face light coma, lethargy, dysarthria	R, Thalamus; lead at the edge of the ischemia	Anterior thalamus	Basal ganglia	23	55	L, Mild hemiparesis
3	Seizures, headache, nausea, hallucinations	L, Cortex of middle frontal gyrus; lead in the center of the ischemia	Superior frontal gyrus	Convex of superior frontal gyrus	32	72	Seizure,3–6 times/year
4	Lethargy, left hemiplegia, weakness of left face dysarthria	R, White matter under insular; lead at the edge of the ischemia	Insular cortex	Insular cortex	12	52	L, Moderate hemiparesis
5	Headache, nausea, slow speech, apathy, hallucinations, lethargy, urinary incontinence	L, Cortex of middle frontal gyrus; lead at the edge of the ischemia	Superior frontal sulci	Superior frontal sulci	38	75	Slow speech
6	Lethargy, headache, nausea, mental symptoms	L, Cortex of middle frontal gyrus; lead at the edge of the ischemia	Superior frontal sulci	Superior frontal sulci	39	64	Memory loss
7	Seizure, headache, nausea, mild mental symptoms	L, Cortex of middle frontal gyrus; lead in the center of the ischemia	Middle frontal gyrus	Convex of middle frontal gyrus	18	80	Seizures total of 5 times
8	Mild headache	R, Cortex of superior frontal sulci; lead in the center of the ischemia	Superior frontal sulci	Superior frontal sulci	23	85	No
9	Headache, urinary incontinence	R, Cortex of superior frontal sulci; lead in the center of the ischemia	Superior frontal sulci	Superior frontal sulci	18	78	No

FU follow-up, *L* left, *R* right

depends on imaging. Downes et al. reported [9] that all five patients with ischemic strokes during implantation showed clear positioning signs. In two patients in our cohort, ischemic infarctions were not immediately found or diagnosed because the patients were under general anesthesia; however, the iMRI identified the ischemic regions. Compared with ischemia in the basal ganglia or target area, cortical infarction often has no specific manifestations during surgery, and it can easily be confused with the reactions to withdrawal of levodopa. In the report of Morishita et al. [15], four patients were finally diagnosed with cortical ischemia on the first post-operative day; however, because of the iMRI in our study, the seven patients with cortical infarction (patients 1, 3, 5–9) received an objective and clear diagnosis during surgery.

With respect to long-term complications, ischemic infarctions in basal ganglia or target areas will have different levels of complications. However, cortical ischemia always showed slightly better results. Morishita et al. [15] reported that all four patients completely recovered, while in our group only three (42.86%) of seven patients had no long-term complications. Seizure is one of the complications that can occur after DBS surgery, because of cortical damage. Although we immediately administered intravenous antiepileptic drugs when cortical ischemia was found on iMRI, and then continued oral antiepileptic drugs for 3 months after discharge, two patients still suffered from seizure for a long time. In short, of the 12 previously reported cases of ischemic infarction after DBS surgery, only five (41.67%) patients fully recovered without permanent dysfunction, a rate consistent with our report.

Rughani et al. reported 14 deaths in 4961 patients undergoing DBS, giving an in-hospital mortality rate of 0.26%. The cause of death of each of these 14 patients was further analyzed according to the ICD-9 codes, revealing that in eight (0.15%) patients, the death appeared to be directly related to the procedure, while in the remaining six patients, the cause was either cardiac or multifactorial. [19] So far, there have been no reports of death caused by an intraoperative or postoperative cerebral ischemic event.

In our group of patients with ischemic events after DBS (a group involving a variety of diseases), ischemia in the superficial cortex generally did not result in any significant differences between the expected and achieved effects, with only two patients with deep ischemia not achieving the expected results, with improvement rates of only 52% and 55%. Downes et al. [9] reported a poor postoperative stimulation effect in only one out of five cases with deep ischemia. Assessment of the postoperative efficacy of DBS complicated by target and basal ganglia ischemia is complex and should include the type of disease, site of ischemia, size of ischemic foci, and function loss because of ischemia. There are very few reports in this area, and therefore, no specific conclusion can be drawn.

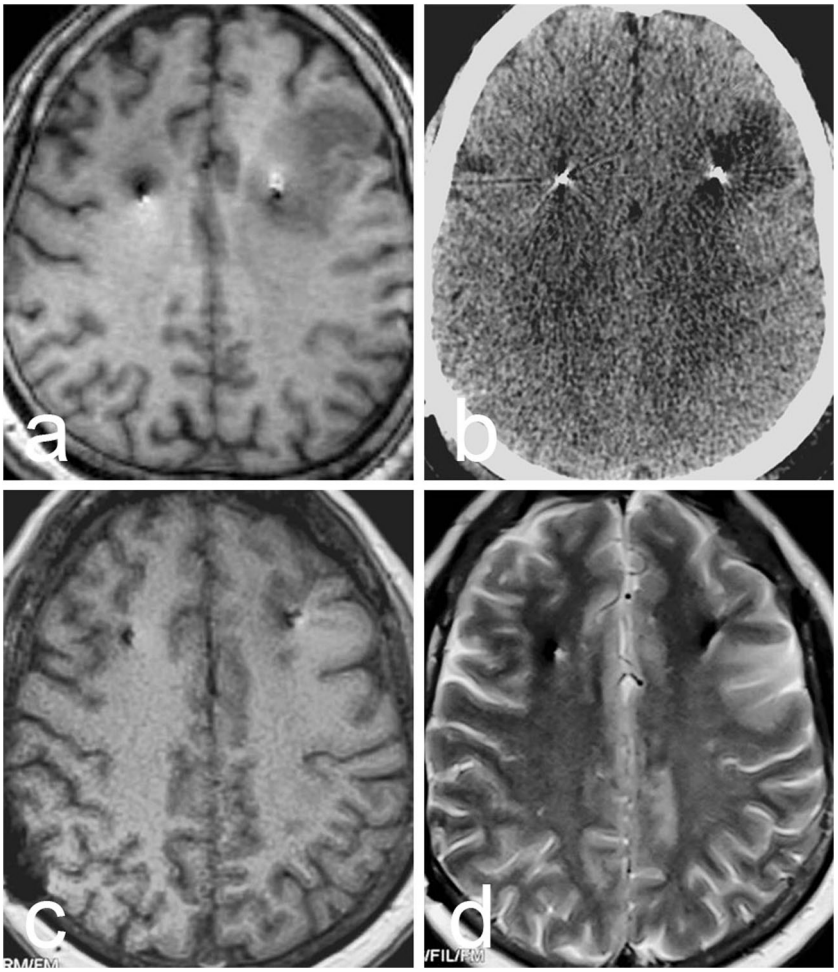

Fig. 1 Case 1: **a** the intraoperative 3D T1-weighted image shows low signal around the left electrode. **b** The CT scan on day 1 post-operation shows the ischemic infarct was low density. **c**, **d** T1 and T2-weighted MRI images at 9 months post-operation show a slight abnormality around the leads

Imaging of cerebral ischemic events

Although we can infer a cerebrovascular accident by the positioning signs, imaging is an objective method of diagnosing ischemic infarction. The iMRI images in all nine patients with ischemia were positive, and the results for ischemic foci on the CT scan acquired on the first day after surgery were identical to those on the iMRI scans in all patients. The long-term MRI

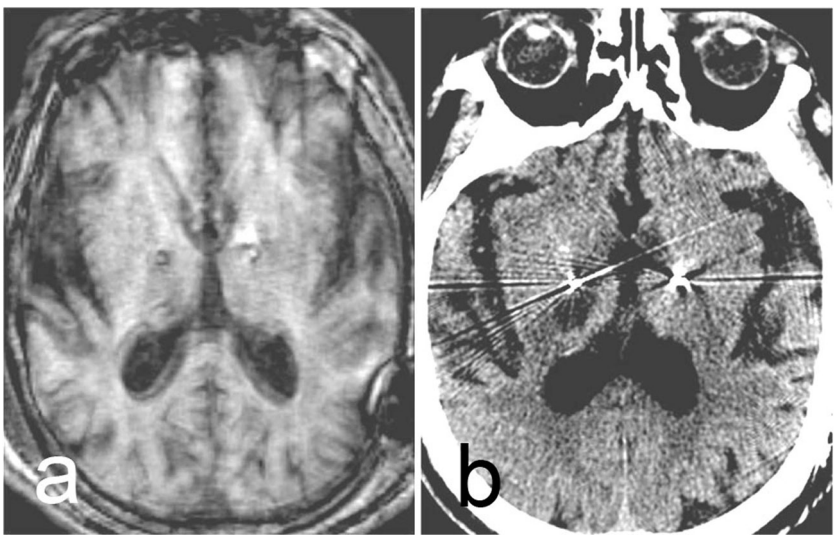

Fig. 2 Case 2: **a** the intraoperative T1-weighted image shows low signal in the right thalamus. **b** The CT scan on day 1 post-operation shows a low-density ischemic infarct

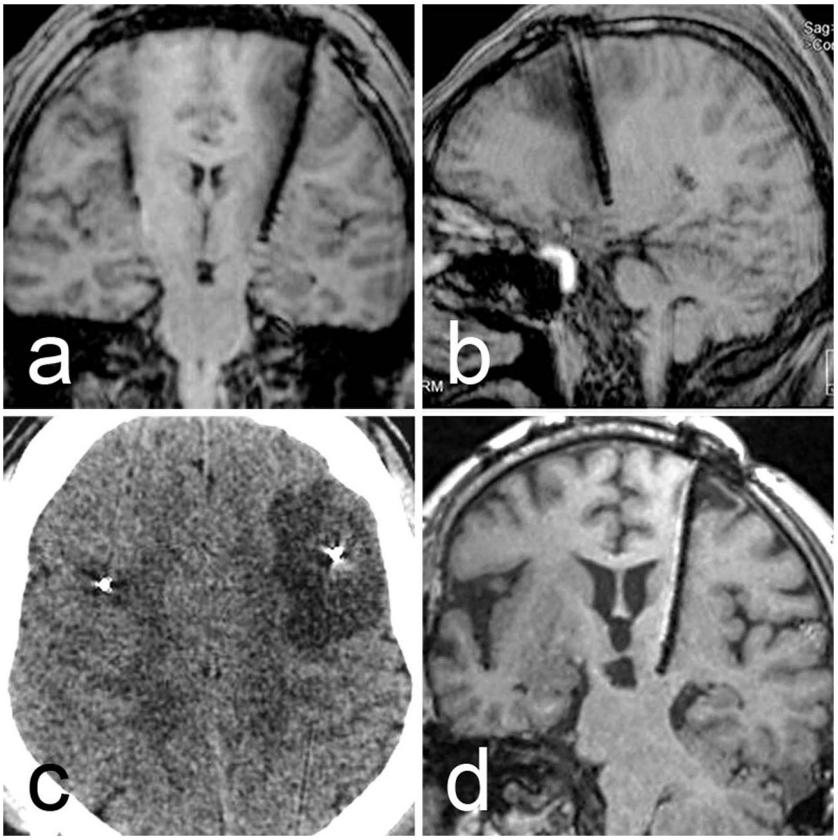

Fig. 3 Case 3: **a**, **b** the intraoperative 3D T1-weighted image shows a large area of low signal in the left frontal cortex around the left electrode. **c** The CT scan on day 1 post-operation shows the ischemic infarct was low density. **d** T1-weighted MRI images at 13 months post-operation show an encephalomalacia in the left frontal cortex

follow-up showed that not all patients recovered their normal morphological structure in the area of the ischemic foci, indicating that cortical or deep ischemic infarctions caused by DBS surgery are sometimes irreversible. Most of the previous studies did not report long-term imaging outcomes [9, 11, 13, 15, 16, 27].

Cause of cerebral ischemic events

The mechanism of the post-DBS bleeding is clear; however, the causes and pathological mechanisms behind DBS-related ischemia remain unclear. From our cases, we conclude that deviation in the entry point on the cortex or in the path was the key factor causing vascular injury (compression, contusion, or vasospasm). In six (66.7%) cases (five with an electrode entry point in the superior frontal sulci, one with the electrode passing through the insular cortex), the path was not ideal. The cerebral sulcus and insular cortex are rich in blood vessels, and dural incision, coagulation of the cortex, and the passage of ducts through sulci can lead to its injury. In Morishita's cases [15], the ischemic infarctions all happened in cortical areas, and they concluded that the puncturing of the cortex injured venous structures, which resulted in cerebral venous infarction. However, in our series, it is difficult to fully confirm that all cases of ischemia were a result of venous infarction. In Downes' cases [9], all ischemia happened in subcortical areas, and Jeff Arle in his comment inferred that their higher rate of ischemia may have been related to the general trajectory for the globus pallidus internus, which was slightly posterior in their cases. Our results show that the GPI targets have the highest incidence of ischemic events, with a rate of 2.4%. In our patient 4, the electrode was biased to the right and passed through the insular cortex, and both Downes' cases and ours indicate that deviation in the path is the main cause of vascular injury.

We tried to analyze other factors (sex, age, target, and anesthesia) related to ischemic events during the operation, but unfortunately, no significant results were found, which may well be because of the small number of cases; the true mechanism of ischemic infarction remains unclear and is still under investigation. Therefore, it is important to pay attention to infarction after DBS and to strengthen intraoperative and post-operative imaging examinations so as not to miss asymptomatic ischemic infarction; this will thereby provide more information on the causes and pathogenesis of ischemic infarction in DBS surgery.

Early findings of cerebral ischemic events on iMRI

With the development of neuroimaging, iMRI during DBS surgery offers immediate confirmation of precise lead placement and screening for complications. In our previous study,

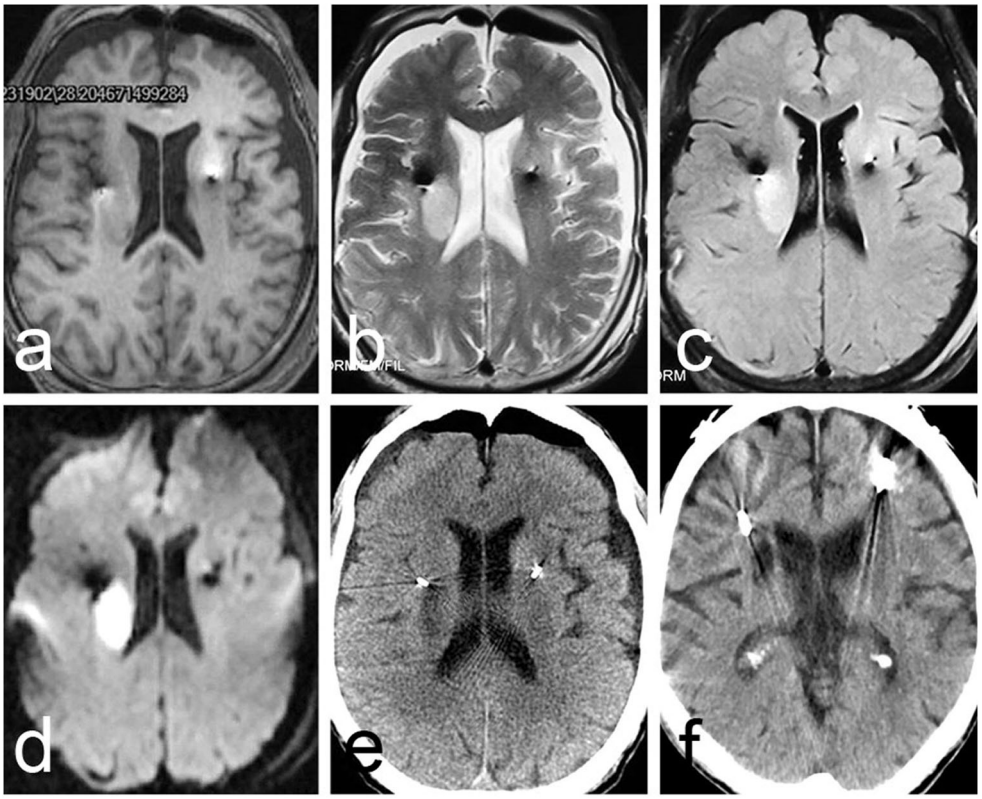

Fig. 4 Case 4: **a** the intraoperative 3D T1-weighted image shows low signal in the right basal ganglia behind the electrode. **b**–**d** The axial T2-weighted, FLAIR, and diffusion images on day 1 post-operation show an ischemic infarct in the right basal ganglia. **e** The CT scan on day 7 post-operation shows the ischemic infarct was low density. **f** The CT scan at 3 months post-operation shows that recovery from the ischemic infarct had not been made

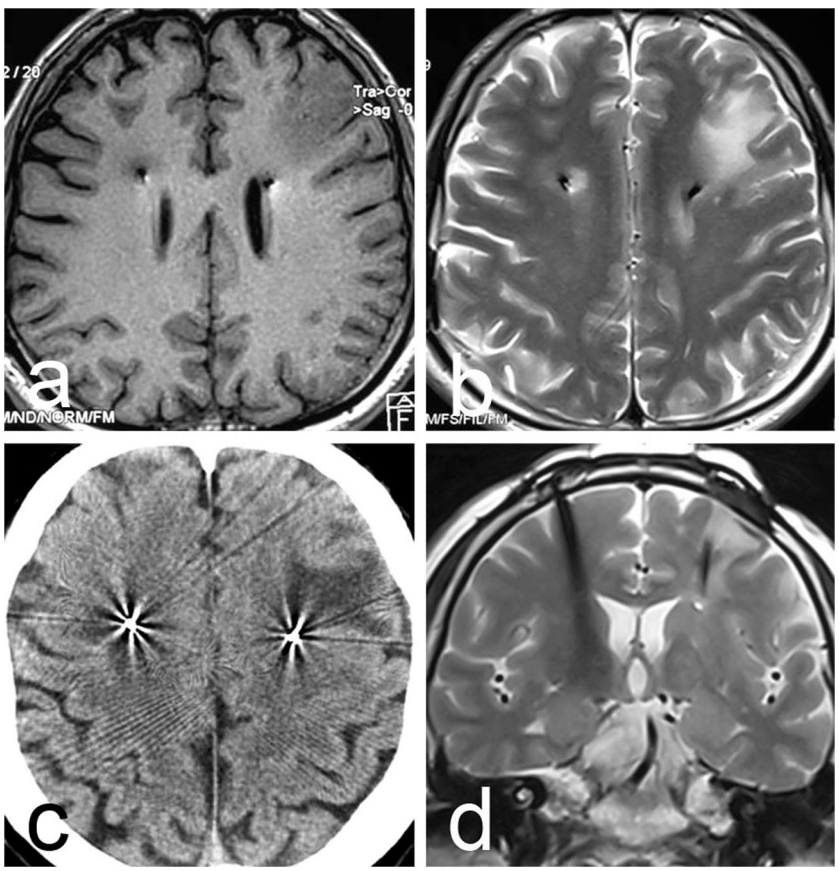

Fig. 5 Case 5: **a**, **b** the intraoperative 3D T1-weighted and T2-weighted images show an ischemic infarction in the left frontal lobe. **c** The CT scan on day 1 post-operation shows the ischemic infarct was low density. **d** The T2-weighted image at 4 months post-operation shows that recovery from the ischemic infarct had not been made

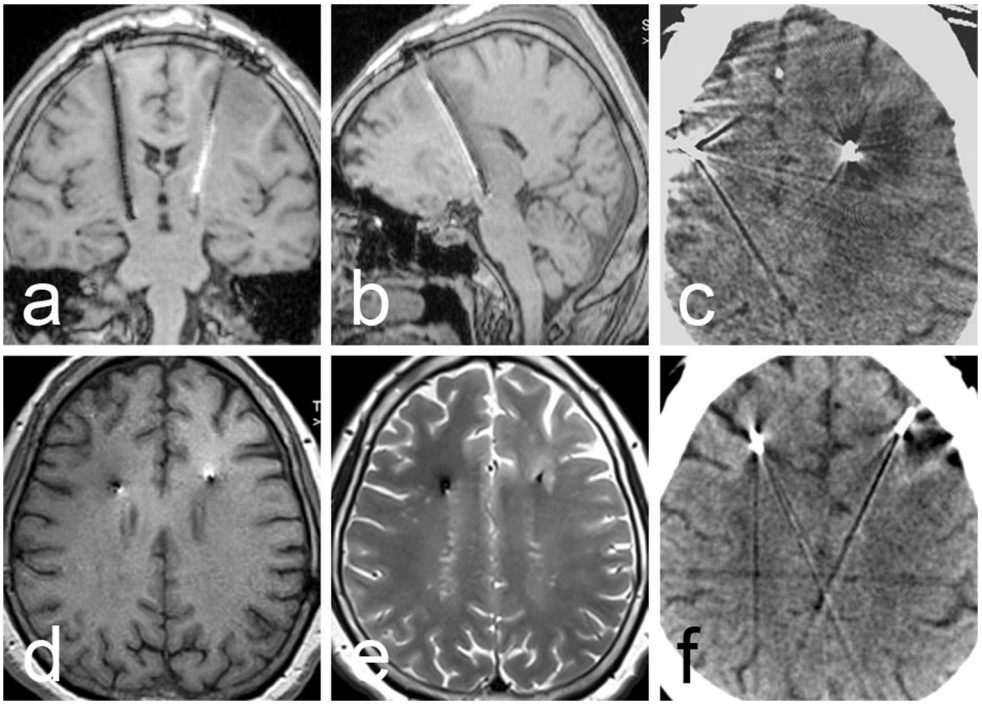

Fig. 6 Case 6: **a**, **b** the intraoperative 3D T1-weighted image shows an ischemic infarction in the left frontal lobe. **c** The CT scan on day 1 post-operation shows the ischemic infarct was low density. **d**, **e** The T1-weighted and T2-weighted images at 3 months post-operation show that recovery from the ischemic infarct had not been made (compared with the contralateral side, the left frontal white matter is abnormal). **f** The CT scan at 22 months post-operation shows an encephalomalacia in the left cortex

we used iMRI to not only confirm accurate electrode placement and repositioning, but also to find intraoperative hemorrhage and brain shift caused by intracranial air [8].

CT scans are sensitive to hematoma and intraoperative early hemorrhage, but for early ischemia, which always shows a low density 1–2 days after ischemia, a very early CT scan

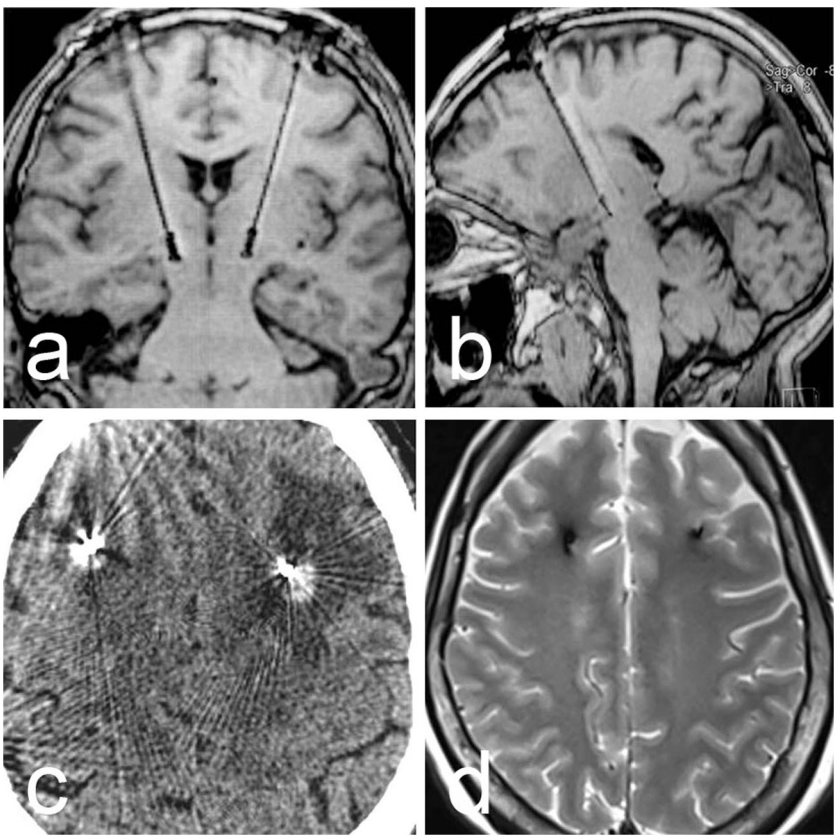

Fig. 7 Case 7: **a**, **b** the intraoperative MRI 3D T1-weighted image shows slightly low signal in the left frontal lobe. **c** The CT scan on day 1 post-operation shows the ischemic infarct was low density. **d** The T2-weighted image at 3 months post-operation shows a slight abnormality in the left frontal lobe

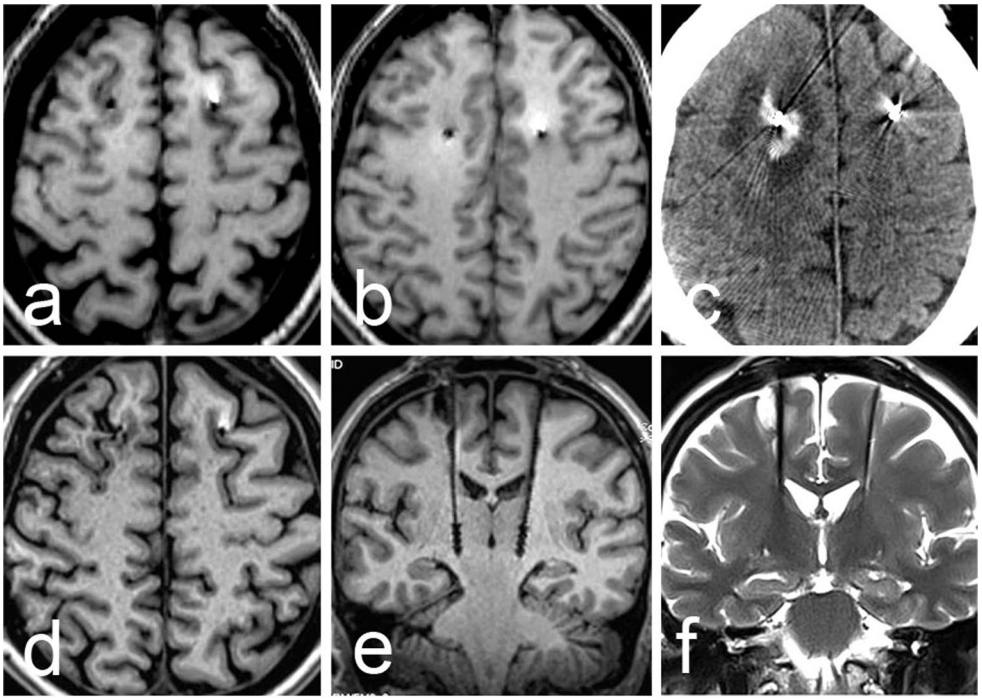

Fig. 8 Case 8: **a**, **b** the intraoperative 3D T1-weighted image shows a slight ischemic infarct in the right frontal cortex. **c** The CT scan on day 1 post-operation shows the ischemic infarct with a small amount of hematoma. **d**–**f** The T1-weighted image at 5 months post-operation shows that recovery from the ischemic infarct had not been made (the right frontal cortex is abnormal)

always shows normality. iMRI can detect cerebral ischemic events early during the DBS surgical procedure; in our group, nine patients all showed image change around the electrodes, with the T1-weighted images showing low signal. When compared with the preoperative image for determining implant location, the T1-weighted image is sufficient to diagnose

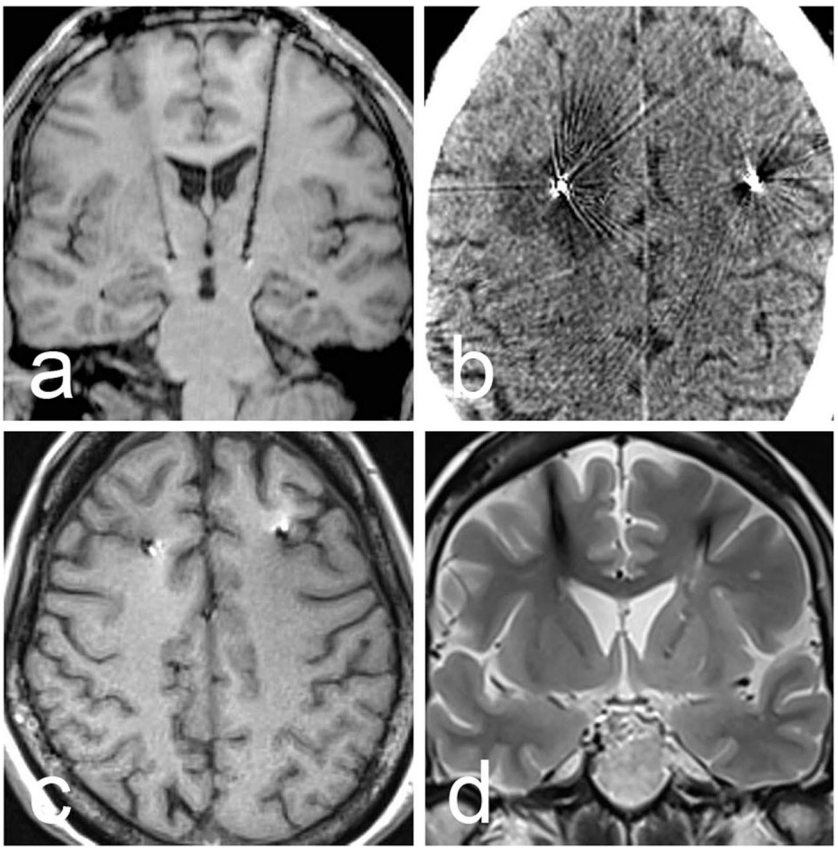

Fig. 9 Case 9: **a** The intraoperative 3D T1-weighted image shows an ischemic infarction in the right frontal lobe. **b** The CT scan on day 1 post-operation shows the ischemic infarct was low density. **c**, **d** The T1-weighted and T2-weighted images at 3 months post-operation show the right frontal lobe is slightly abnormal

Table 3 Risk factors for ischemic events during the deep brain stimulation

Factor		Ischemic cases	No ischemic cases	Total number	χ^2	*P* value
Gender	F	4(1.2%)	339(98.8%)	343	0.219	0.640#
	M	5(2.0%)	247(98.0%)	252		
Age (years)	< 60	5(1.6%)	312(98.4%)	317	–	> 0.999*
	≥ 60	4(1.4%)	274(98.6%)	278		
Target	STN	5(1.2%)	421(98.8%)	426	1.888	0.393*
	GPI	3(2.4%)	121(97.6%)	124		
	VIM	1(2.2)	44(97.8%)	45		
Anesthesia	LA+ GA	5(2.3%)	215(97.7%)	220	0.665	0.415#
	GA	4(1.1%)	371(98.9%)	375		

Note: # indicates the use of the continuity correction, * denotes the use of Fisher's exact

GPi globus pallidus internus, *STN* subthalamic nucleus, *VIM* ventral intermediate nucleus, *GA* general anesthesia, *LA* local anesthesia

ischemic infarction. Of course, for very early ischemia, FLAIR, T2-weighted, and especially diffusion-weighted images, can reveal some very early characteristic changes. Considering the special circumstances of iMRI, if patients are under local anesthesia they may suffer from discomfort or mental symptoms because of levodopa drug withdrawal, while if they are under general anesthesia with tracheal intubation and no medical staff are present in the surgical operative room during the iMRI acquisition, there is an increased chance of the patients suffering unexpected events. A longer scanning protocol with more sequences may be of benefit for diagnosing ischemia; however, it would increase other risks to the patient, so the scan time must be kept short. Therefore, in our group, all patients underwent the T1-weighted sequence, but only a small number of patients underwent the T2-weighted sequence. A CT scan was also performed on postoperative days 1 to 7 (a routine cerebral CT scan on day 1 postoperation, or a repeat CT in some cases where the imaging or symptoms had changed).

Patient 4, who was diagnosed with generalized dystonia, would have been unable to cooperate during the operation because the whole body was twisted, and immediate observation of symptom improvement would not be possible, unlike in the Parkinson's disease patients. Therefore, general anesthesia was adopted for this procedure. Patient 2, an 83-year-old male, was diagnosed with Parkinson's disease, and because of the patient's old age, long disease history, and brain atrophy, he was also given general anesthesia. Ischemic infarction occurred in both of these patients, which was confirmed by the iMRI, and both immediately showed severe hemiplegia after recovery from general anesthesia. Downes et al. and Novak et al. report [9, 16] that patients on local anesthesia all showed anatomical localization signs for cerebrovascular accidents, and all were intraoperatively inferred; however, cortical ischemia may have a lack of anatomical localization signs, and iMRI is helpful in its diagnosis.

iMRI can detect ischemia early, which has an absolute guiding significance for postoperative treatment and is beneficial for recovery. If the diagnosis of ischemic infarction is made intraoperatively, its management should include control of blood pressure, monitoring of blood coagulation series and thromboelastogram, vascular dilation, avoidance of dehydration, application of neutral neurotrophic drugs, elevation of the head of the bed, and early initiation of rehabilitation. If the ischemic infarction happened in the cortex, antiepileptic drugs should be applied by intravenous medication after surgery. A repeat CT or MRI should be performed. Intraoperative MRI can detect almost all ischemic events, but transient cerebral ischemia without imaging-noted change in brain structure during the operation needs further study. This method is reproducible and generalizable, although a specific scan protocol designed for infarct detection is required. Intraoperative MRI is expensive, which is one of its shortcomings, but this can be compensated for by using postoperative CT instead, especially 3–7 days after surgery.

Limitations iMRI scans are mainly performed to determine the accuracy of the electrode placement, and there is no specific scan series designed for infarct detection in this study; therefore, the iMRI scan sequence can be considered incomplete, with only T1-weighted imaging being performed in most patients, and T2-weighted imaging being reserved for special cases. Diffusion-weighted imaging, which is sensitive to infarction, is not generally performed, and infarction was an accidental finding in this non- prospective study.

Conclusion

Although there are few reports, intraoperative ischemic events during surgical procedures for deep brain stimulation are not uncommon. Ischemia can cause serious permanent

Table 4 Summary of the previously described cases of cerebral ischemia after DBS

Reference	Age (years)/sex	DBS target	Diagnosis	Onset time	Symptoms of ischemia	Location of ischemia	Follow-up	Long-term complications
Novak et al. [16], 2006	53/M	STN	PD	Intraoperation	Slurred speech, mild weakness	Thalamus	6 weeks	Persisted mild dysarthria
	67/M	STN	PD	3 days post-operation	Confusion, short-term memory loss, epileptiform attack	Periventricular and subcortical white matter, thalamus	9 months	Short-term memory problems
Kang et al. [11], 2011	34/M	GPI	CD	Intraoperation	Slurred speech, motor and facial weakness	Internal capsule	3 months	Almost full recovery
Larson et al. [13], 2013	56/F	STN	PD	1 day post-operation	Hearing loss	Anterior body of the caudat	18 months	Hearing loss
Morishita et al. [15], 2013	67/F	STN	PD	1 day post-operation	Word-finding difficulties, confusion	Cortex around the lead	Several weeks	Full recovery
	50/M	STN	PD	1 day post-operation	Somnolent and confused	Cortex around the lead	3 days	Full recovery
	60/M	GPI	PD	1 day post-operation	Weakness, lethargy, confusion	Cortex around the lead	Several days	Full recovery
	58/M	GPI	PD	1 day post-operation	Word-finding difficulty, confusion	Cortex around the lead	Four months	Full recovery
Downes et al. [9], 2016	64/F	GPI	PD	Intraoperation	Dysarthria, weakness of right face, arm, leg	Left PLIC and lateral putamen	6 months	Mild left hemiparesis
	54/F	GPI	PD	Intraoperation	Somnolence, dysarthria, weakness of left face and arm	Right PLIC	6 months	Mild left facial weakness and dysarthria
	52/M	GPI	PD	Intraoperation	Somnolence, dysarthria, left face weakness, resolution of tremor	Right PLIC	6 months	Left facial weakness
	51/F	GPI	PD	Intraoperation	Left gaze preference, dysarthria, right arm and leg weakness	Left GPi and PLIC	3 months	Dysarthria and mild right hemiparesis
	52/F	GPI	TD	Intraoperation	Somnolence, resolution of right-sided dyskinesias	Left GPi and PLIC	3 months	Slightly dysarthric
Wang et al. [27], 2016	40/F	STN	PD	Six and 9 months post-operation	Seizure	Right basal ganglia	7 days	Full recovery

STN subthalamic nucleus, *GPi* globus pallidus internus, *PD* Parkinson's disease, *TD* tardive dystonia, *CD* cervical dystonia, *PLIC* posterior limb of internal capsule

complications, and damage from severe ischemia cannot be restored. iMRI objectively provides a basis for the early diagnosis of intraoperative ischemic infarction, and is instructive for follow-up treatment.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Informed consent Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

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