Avoidance and Management of Surgical and Hardware-Related Complications of Deep Brain Stimulation

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Key Words
Deep brain stimulation, complications • Parkinson’s disease • Subthalamic nucleus

Abstract
Objective: Although deep brain stimulation (DBS) is nonablative, it may give rise to many complications. In order to identify and reduce factors contributing to the complications, we performed a retrospective analysis of patients who received DBS in our institution over a 9-year period from March 2000 to December 2008. Methods: Included in this study were 161 patients (85 male and 76 female). Data from these patients were collected and analyzed with respect to the complications and factors potentially related to these complications. Results: A total of 25 surgical and hardware-related complications occurred in 24 patients, including confusion in 11 cases (6.83%), asymptomatic intracranial hemorrhage in 1 case (0.62%), electrode misplacement in 2 cases (1.24%), infection of the subcutaneous pocket receiving the pulse generator in 1 case (0.62%), skin erosion in 2 cases (1.24%), pulse generator seroma formation in 6 cases (3.72%), and device malfunction in 1 case (0.62%). There was no permanent neurological deficit. Conclusion: Confusion is the most common complication in simultaneous bilateral DBS targeting the subthalamic nucleus, especially in patients with severe Parkinson’s disease. With increasing experience of surgeons, complete obedience to intraoperative surgical routines and reasonable application of the microelectrode recording technique, other complications could also be reduced.

Introduction
Since deep brain stimulation (DBS) was first reported in 1987 by Benabid et al. [1] to treat Parkinson’s disease (PD) by targeting the ventral intermediate nucleus of the thalamus, it has gradually replaced ablative procedures for the treatment of PD, essential tremor and dystonia. New applications of DBS are rapidly emerging and being refined for conditions such as epilepsy, psychiatric disorders, Tourette syndrome and chronic pain [2–6]. These expansions will result in an increasing number of patients and implanted electrodes.

DBS conveys several advantages over lesioning: it is nonablative and its effects can be modified or reversed. However, the stimulators require surgical procedures to implant them, which may be accompanied with intracranial hemorrhage (ICH), infection, erosion, electrode migration and/or dislodgment, electrode fracture, electrical...
short circuit or open circuit, and component malfunction [7–15]. Such complications may require additional operations to remove or revise the DBS, leading to extra hospitalizations, long-term use of antibiotics, increased medical expenses and loss of the benefits of stimulation. Therefore, complications of DBS surgery have received much attention [7, 9–19]. However, reports about avoidance and management of DBS complications are limited.

In order to identify and potentially reduce factors contributing to DBS complications, we performed a retrospective analysis of 161 patients who received DBS treatment in our institution over a 9-year period, hoping to maximize the benefits of DBS therapy.

**Patients and Methods**

**Patients**

Included in this study were 161 patients (85 male and 76 female) who received DBS treatment by the same surgeon in a single institution from March 2000 to December 2008. Of them, 153 patients suffered from idiopathic PD, 2 from essential tremor, and 6 from dystonia (table 1), and of the 153 PD patients, 9 patients had received DBS treatment with previous pallidotomy on the contralateral side, and 2 patients had received DBS treatment while performing contralateral pallidotomy. The patients ranged in age from 16 to 80 years with a mean of 63.5 ± 8.7 years. The course of disease was 3–20 years (mean, 5.7 ± 3.3 years). The number of DBS targets was 259 including the subthalamic nucleus (STN) (n = 241), ventral intermediate nucleus (n = 8) and globus pallidus internus (GPI) (n = 10). All the procedures were examined and approved by the Academic Board of the Second Military Medical University (Shanghai, China).

**Surgical Procedures**

The patient was placed in a Cosman-Robert-Wells frame that was oriented parallel to the infraorbitomeatal line under local infiltrative anesthesia. The target was located by 1.5-tesla magnetic resonance imaging (MRI) (Siemens, Erlangen, Germany). The targeting images were 2 mm thick. No overlap slices were obtained in axial, sagittal and coronal planes. The tentative target coordinates were based on the anterior commissure-posterior commissure line and direct visualization of MRI.

After induction of local anesthesia, a hole was drilled over the coronal suture and the dura was opened adequately for direct cortical exposure. Microelectrode recording (MER) (Fred Haer Corporation) was performed in all cases targeting the GPIs, and part of the cases targeting the STN. According to the signal record of the microelectrodes, the number of trajectories (1–4 trajectories) was recorded.

A guide tube for the DBS electrode (Medtronic Model 3389 for STN and ventral intermediate nucleus, and Model 3387 for GPI) with a blunt tip stylet was then introduced into the brain parenchyma to a point 10 mm proximal to the target. Test stimulation was performed to record voltage thresholds for stimulation and adverse effects. The DBS electrode was anchored to the burr hole ring (a plastic ring designed to fit the 14-mm burr hole) by wedging the electrode into one of its two grooves. An additional plastic burr hole cap further locked the DBS electrode into the burr hole ring.

In 96 of our more recent patients who did not undergo MER, the target position was confirmed by a second MRI scan in the department of radiology with the Cosman-Robert-Wells stereotactic frame. The actual target was modified in 21 cases in subsequent operations after intraoperative MRI, of which 19 cases were adjusted by 2.0–3.5 mm in depth, and the other 2 cases by 1.5–2.0 mm on the x-axis and y-axis of the coordinate.

In 89 patients whose therapeutic effect was satisfactory at a low voltage (<3.5 V) without causing significant adverse effects and complications such as ICH as shown on intraoperative MRI scan, an internal pulse generator (IPG) was implanted under general anesthesia. A small retromastoid curvilinear incision was made to facilitate pulling the extension (Model 7495 or 7482; Medtronic Inc.) from the chest to the scalp through a subcutaneous tunnel. One or two bone grooves were made on the occipital bone under the incision for Itrel II, Soletra or Kinetra IPG (fig. 1). The connector was placed into the bone groove and fixed. An IPG was placed in the infraclavicular fossa subcutaneously. A hole was drilled on the clavicular bone to facilitate fixation of the IPG by a silk thread and subsequently prevent stretch of the connector by a sagged IPG (fig. 2).

In the other 72 patients with major motor symptoms in posture, balance or gait and/or without achieving the expected surgical therapeutic outcome, staged procedures were employed by using a temporary pulse generator for 4–14 days first, and then the IPG was implanted instead when the symptoms were relieved. Only 1 patient was not implanted with a permanent IPG due to poor stimulating results through externalized lead.

Intraoperative and postoperative antibiotics were administered for 3–5 days. Preventive anticonvulsant treatment was initiated 3–5 days before surgery and discontinued 2–3 weeks after surgery. Postoperative CT scan was performed in all patients within 24 h after electrode implantation. Hemorrhage was scored as symptomatic (associated with any new neurological deficit last-
ing for longer than 24 h) or asymptomatic [10]. All patients were clinically followed up for 6–84 months (mean 14 months).

Data Collection and Statistical Analysis
Demographic information on the 161 patients was reviewed and collected, including age, sex, diagnosis, preoperative off-phase Hoehn and Yahr stage for PD, the presence of systemic illness, target, unilateral and simultaneous or staged bilateral treatment, application of MER, intraoperative adjustment of the electrode, simultaneous or staged IPG implantation and routine battery change. All procedure-related complications were recorded in detail.

Potential risk factors related to postoperative confusion were categorized and analyzed between the subgroups of confusion and nonconfusion. Odds ratio and p value were calculated for each risk factor. The level of statistical significance was set at 0.05.

Results
A total of 25 surgical and hardware-related complications occurred in 24 of the 161 patients, of which 7 complications occurred in recent 3 years from 2006 to 2008 including 6 confusions and 1 severe pneumonia (fig. 3).

Confusion and Pneumonia
Of the 161 patients, 11 (6.83%) experienced an episode of postoperative confusion after simultaneous bilateral DBS targeting the STN, which was relieved completely after 2–5 days of conservative treatment in 10 patients. The remaining 65-year-old female patient with preoperative off-phase Hoehn and Yahr stage V progressed to ‘coma’ (a Glasgow Coma Scale score of 8–9), which was further complicated by severe pneumonia. No ICH or migration of the microelectrode was seen on repeated MRI and CT scan. After anti-infection and ventilator-assisted breathing therapies, the patient recovered without new development of permanent neurological deficits but needed a permanent tracheotomy. This was the only patient in our series in whom IPG implantation was aborted.
Intracranial Hemorrhage
Postoperative CT imaging identified a case of asymptomatic ICH in the trajectory tract. The patient was treated conservatively and recovered well without any neurological deficit.

Electrode Misplacement
Electrode misplacement occurred in 2 cases (1.24%) in our early days of DBS surgery, when no intraoperative C-arm or MRI was available for confirmation. Although the target position was confirmed by MER and intraoperative test stimulation showed good results, postoperative stimulation was ineffective with increased adverse effects. Subsequent MRI showed that the electrodes were placed 4 mm deeper than the desired position. After proper adjustment of the electrodes under local anesthesia, good stimulation effects were achieved in the 2 patients.

Table 2. Potential risk factors related to postoperative confusion

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Confusion</th>
<th>Non-confusion</th>
<th>OR</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simultaneous bilateral STN DBS</td>
<td>11/11</td>
<td>63/150</td>
<td>NA</td>
<td>0.0006*</td>
</tr>
<tr>
<td>Off-phase Hoehn and Yahr stage ≥IV</td>
<td>9/11</td>
<td>44/150</td>
<td>10.8</td>
<td>0.0012*</td>
</tr>
<tr>
<td>Age ≥65 years</td>
<td>6/11</td>
<td>73/150</td>
<td>1.3</td>
<td>0.7066</td>
</tr>
<tr>
<td>Female</td>
<td>6/11</td>
<td>76/150</td>
<td>1.2</td>
<td>0.8038</td>
</tr>
<tr>
<td>Trajectories of MER ≥2</td>
<td>2/11</td>
<td>32/150</td>
<td>0.8</td>
<td>0.8922</td>
</tr>
<tr>
<td>Repeated puncture</td>
<td>1/11</td>
<td>5/150</td>
<td>2.9</td>
<td>0.8819</td>
</tr>
</tbody>
</table>

NA = Not applicable. * Statistical significance.

Infection
There was a 56-year-old male patient who underwent DBS treatment for PD targeting the right STN on April 26, 2004. An IPG (Itrel II 7424) was implanted simultaneously. Three weeks later, subcutaneous empyema was found around the location of the IPG, which was surgically evacuated. After 3 months, the ethylene-oxide-sterilized original IPG was implanted subcutaneously into the contralateral (left) chest. However, 1.5 years later, subcutaneous suppurative fluid appeared around the IPG with the trend of skin erosion, and the IPG was subsequently translocated to the right chest. In May 2009, subcutaneous suppurative fluid appeared again around the IPG with obvious skin erosion and exposure of IPG (fig. 4). The skin infection did not heal after simple removal of the IPG. We therefore further removed the electrode-extension connector and the wire in June 2009, with only the brain electrode preserved. As a result, the skin infection healed properly. We planned to implant the IPG for this patient in October 2009.

Skin Erosion
Skin erosion occurred in 2 patients (1.24%). One 16-year-old skinny boy who presented with primary dystonia underwent bilateral DBS targeting STN with simultaneous IPG implantation. Five months later, signs of skin erosion were noticed at the right bottom of the IPG location. The IPG was removed under local anesthesia, with the electrode-extension wire preserved. Three months later, the ethylene-oxide-sterilized original IPG was implanted subcutaneously into the contralateral (left) chest. The other case of retromastoid skin erosion occurred in the patient who underwent DBS treatment without occipital bone grooves and in whom the elec-
trode-extension connector was implanted right under-neath the skin. One year later, skin erosion occurred over the electrode-extension connector site. We therefore moved the connector medially to a newly made occipital bone groove. The skin erosion healed over time, without removing the electrode and the extension wire.

Formation of Seroma
Seroma formation was observed around the IPG location in 6 patients. There were 3 patients who experienced formation of seroma around the IPG location, in whom subcutaneous bloody fluid was grained 3–5 days after surgery. They were cured after puncture drainage. In the other 3 patients, the seroma was cerebrospinal fluid leaking through the burr hole ring and cap along the electrode-extension wire to the chest where the IPG was located. After bandaging the patients’ head with pressure, the subcutaneous fluid was stopped.

Device Malfunction or Electrode Migration
Device malfunction occurred in 1 case during a 6-month clinical follow-up. In a home visit, we found that the IPG (Kinetra) did not respond to the controller, although the symptoms were well controlled. We replaced the IPG at the patient’s request. The removed IPG was tested in Medtronic, Inc., and it was shown that it worked well. During the 1-month follow-up after replacement, the IPG failed to respond to the controller again in his home, but responded well in a nearby hotel. We therefore presumed that the device malfunction in this patient may be related to his living environment. There was no electrode migration or fracture of the electrodes in our series.

Discussion
Complications of DBS can be classified as those related to the surgical procedure such as ICH, infection, postoperative seizure and procedure abortion, and those related to the hardware such as electrode fracture or dislocation and device malfunction [8, 15, 18, 20, 21]. The postoperative mortality of DBS treatment was reported to be 0–1.8%, and the incidence of postoperative permanent neurological deficits was 0.6–6% [1, 15, 21–24]. The occurrence of complications in our series is summed up and discussed as follows.

Confusion and Pneumonia
Data in this series show that confusion is the most common and unpreventable complication for simultane-ous bilateral DBS targeting the STN, especially in patients with severe PD. The incidence of confusion in this series was 6.83%, similar to 5.5% reported by Kenney et al. [25] and 6.12% reported by Seijo et al. [21]. However, the reasons for confusion remain elusive, presumably related to puncture injury to basal ganglia, postoperative pneumocephalus, irregular administration of anti-PD medications, and administration of narcotic drugs. Generally, patients would recover in 3–4 days spontaneously, even those with severe symptoms such as lethargy or light coma. Nevertheless, these patients are susceptible to aspiration pneumonia (a clinical challenge for cure), because of poor swallowing and decreased cough reflex. There was 1 patient with a permanent tracheotomy for treating severe pneumonia, the most severe DBS complication occurring in this series. Therefore, more attention should be paid to confusion.

Since simultaneous bilateral DBS targeting the STN and off-phase Hoehn and Yahr stage ≥IV were statistically related to postoperative confusion, staged bilateral DBS treatment may be recommended for patients with severe PD. The incidence of postoperative confusion should be further decreased with the availability of electrodes smaller than 1.27 mm (Medtronic). In addition, Seijo et al. [21] reported that dexamethasone could decrease cerebral edema arising from surgical manipulation of DBS, thus relieving the reversible cerebral injury leading to confusion. However, its effect has not been finally confirmed. Nasal feeding and intensified respiratory tract nursing care are important to prevent pneumonia from occurring after a swallowing assessment in patients who have developed confusion.

Intracranial Hemorrhage
ICH is a severe complication of stereotactic surgery including DBS. The incidence of ICH in our series was 0.39% (1/259 electrodes), and varied from 1.7 to 3.3% in the literature with a symptomatic ICH rate of 0–2.6% [7, 9, 21, 23, 26, 27]. Risk factors contributing to ICH in PD DBS procedures include age, sex, blood pressure, selection of anatomical targets and utilization of MER [28]. The ICH incidence in this series was lower than that reported previously [9, 10, 21, 23, 24, 29], which may have been attributed to our experience accumulated from 450 cases of ablation before DBS surgery, careful perioperative treatment of coagulation dysfunction and hypertension, incision of the arachnoid and pia mater under direct vision, cautious and proper insertion of the electrode in the gyrus avoiding the vascular surface of the brain, and application of intraoperative MRI scan with a stereotac-
tic frame instead of MER to avoid MER-related cerebral hemorrhage.

**Electrode Misplacement**

The electrodes require adjustment from time to time postoperatively due to unsatisfactory stimulation effects or adverse effects even with the use of MER during the procedure [16, 27, 30, 31]. The rate of electrode misplacement was 9% according to Lyons et al. [16], and 2.2% according to Seijo et al. [21]. In the early stage of our study, MER was routinely used in DBS. Nevertheless, the more recent 96 patients who did not receive MER were checked by intraoperative MRI scan with a stereotactic frame and the adjustment was made accordingly during surgery. The only 2 cases of electrode misplacement in this series occurred in our early stage. We therefore think that intraoperative MRI scan with the stereotactic frame may reduce the incidence of electrode misplacement.

**Skin Infection, Erosion, Seroma and Device Malfunction**

Many published series documented that the incidence of infection after device implantation varied from 1.2 to 23% [8, 22, 26, 32–36]. In the current series, infection occurred in only 1 case with an incidence of 0.62%. However, we have learned a lesson from this case. We reimplanted the infected IPG after ethylene oxide sterilization, which resulted in 2 additional infections and IPG removals. This reminded us that an infected unit should not be implanted, because the IPG must have been colonized with bacteria.

Skin erosion usually occurs over the connector site [14]. Therefore, connectors with a lower profile such as model 7482 (Medtronic), and placing the connectors into the bone grooves may help reduce skin erosion. For thin patients, the IPG is recommended to be placed directly onto or underneath the well-vascularized pectoralis fascia rather than into subcutaneous fat in order to prevent skin erosion on the chest. The IPG should be implanted medially in case of friction between the upper arm and skin over the IPG.

Formation of seroma in the subcutaneous pocket receiving the IPG may occur if the pocket was made too large [14] and a cerebrospinal fluid leak existed through the burr hole ring and cap, which may be prevented by the application of glue over the cap. Device malfunction occurred only in 1 patient in this series, and may be related to the interference from his living environment.

**Electrode Migration, Fracture and Seizures**

No electrode migration, fracture or postoperative seizure occurred in this series. The incidence of electrode migration ranges from 0 to 5.1% [12, 19]. The main reason may be due to poor attachment of the electrode to the burr hole. To prevent this from occurring, we used a silicone burr hole ring and a plastic cap (Medtronic Inc.) to

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**Fig. 5.** a Plain film radiography showed that 2 connectors had slipped to the neck with 1 electrode fractured. b Plain film radiography after replacement of the fractured electrode showed that the connectors were adjusted and embedded into the retromastoid occipital bone grooves.
lock the DBS electrode in the burr hole ring. No electrode migration occurred in our series, probably because we strictly controlled the diameter of the skull hole within 14 mm so that the silicone burr hole ring was firmly embedded into the skull hole. Should any looseness occur, Baiyun medical glue (octyl-alpha-cyanoacrylate; Xiang-xue Biomedical Engineering Co. Ltd., Guangzhou, China) can be used to fix the ring firmly.

The incidence of electrode fracture or malfunction ranges from 0.76 to 14.2% per patient [12, 14, 17, 21, 22, 25, 37, 38]. The wires in the electrode are made of platinum and can easily be crushed by the screws. Any point of the electrode subjected to stretching or crushing is susceptible to this complication, but most fractures occur in the electrode near the connection between the electrode and extension, especially if the connection is placed in the upper area of the neck [14]. Mohit et al. [17] reported 7 fractures in 35 cases, with 6 sites of breakage in the neck and 1 in the paramastoid area over the skull. No electrode fracture occurred in our series, probably because the connectors were embedded into the occipital bone grooves, thus preventing the connection from moving to the supraclavicle. We treated a patient with electrode fracture who received treatment in another hospital 4 years ago, whose diagnosis was confirmed by plain film radiography showing that 2 connectors had slipped to the neck with 1 electrode fractured (fig. 5a). After replacement of the fractured electrode, proper adjustment of the connectors and embedment into the retromastoid occipital bone grooves, the symptoms were well controlled (fig. 5b).

Coley et al. [11] summarized the results of 32 papers concerning DBS, 16 of which mentioned seizures as a complication in 42 patients (2.7%) out of 1,555 patients who received 2,101 electrode placements. They also pointed out that 74% of the seizures occurred in the early postoperative period, and most of these patients had ICH. There was no postoperative seizure in our series, probably due to our preventive anticonvulsant treatment and the low incidence of ICH.

**Conclusion**

Confusion is the most common complication that is difficult to prevent in simultaneous bilateral DBS targeting the STN, especially in patients with severe PD. Mild confusion can recover spontaneously within days, but severe confusion may be complicated by secondary pulmonary infection. For patients with severe PD, staged electrode implantation is an option for preventing confusion. With increasing experience of neurosurgeons, complete obedience to intraoperative surgical routines and a relatively fixed surgical team, the other DBS complications could be further reduced.

**References**


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