Recurrent Infections Leading to DBS Removal but Reimplantation Achieving a Good Outcome: a Case Report

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Case Report

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Abstract

Background: Deep brain stimulation (DBS) is an established treatment for patients with medical refractory Parkinson's disease (PD). DBS systems are implanted with the aim of providing permanent treatment, but infections, several early and late hardware related complications, suboptimal outcomes ,which might require revision operations with partial or even complete hardware removal. Here we described a surgical procedure with complete implants removal due to infections but reimplantation of a new DBS system achieved a good outcome in a patient with PD for over 20 years.

Case presentation: A 70-year-old male with idiopathic PD for 22 years who underwent bilateral subthalamic nucleus (STN) DBS surgery with a non-rechargeable implantable pulse generator (IPG) when he was diagnosed PD for 8 years. His past history included hypertension and type 2 diabetes mellitus (DM). He underwent IPG replacement surgery in his 4th and 9th year after his initial DBS implantation. Four years after his latest IPG replacement surgery, he developed recurrent skin erosion around the DBS system. He underwent a total of four local incisions debridements (including two times of dissociated flap transplantation) and several sessions of antibiotic therapy before the final removal of the hardware. Fortunately after completion of antibiotic treatment, he underwent implantation of a new DBS system nine months later. No further complications appeared at the ninth months follow-up after reimplantation. The patient's symptoms had improved to a great extent, and he could take care of himself and his quality of life had improved significantly, which met the needs of the patient and his family.

Conclusions: Infection is one of the most serious and difficult complications to manage after DBS implantation. Treatment of this complication can take a long time and lead to additional hospitalization, surgery and partial or total removal of the DBS system. However as long as the indications are met in any case, the reimplantation procedure can be reconsidered later, despite having had an infection and the electrode being removed.

Background

Deep brain stimulation (DBS) is an established treatment for patients with medical refractory Parkinson's disease (PD). The procedure brings good results for properly selected patients. DBS systems are implanted with the aim of providing permanent treatment, but infections, several early and late hardware related complications, suboptimal outcomes ,which might require revision operations with partial or even complete hardware removal. Hardware infection remains a common complication with a reported incidence of 1-15%, which may lead to additional interventions and loss of efficacy [1]. Infection management can be challenging, potentially resulting in multiple surgical wound incisions and drainage procedures for hardware salvage, additional hospitalization, prolonged courses of antibiotics, loss of stimulation benefits, and increased health care costs. As the number of DBS procedure increases, so does the number of lead removal procedure performed due to infection, erosion, lead breakage and suboptimal placement [2]. There are currently no standardised recommendations for the management of complications following DBS surgery and for the reimplantation of hardware after its removal due to

complications [3]. Here we described a surgical procedure with complete implants removal due to infections but reimplantation of a new DBS system achieved a good outcome in a patient with PD for over 20 years.

Case Presentation

A 70-year-old male with idiopathic PD for 22 years who underwent bilateral subthalamic nucleus (STN) DBS surgery with a non-rechargeable implantable pulse generator (IPG) (Medtronic Activa PC, USA) in other hospital when he was diagnosed PD for 8 years. The intracranial leads and IPG implantation had been completed in a single operation with an uncomplicated perioperative procedure. His past history included hypertension and type 2 diabetes mellitus (DM). He underwent IPG replacement surgery in his 4th and 9th year after his initial DBS implantation. The second IPG replacement surgery was performed in our hospital. Medtronic 3389 leads (USA) were implanted initially and rechargeable IPG (Medtronic Activa RC, USA) was applicated in the latest replacement surgery. From then on, the next four years were peaceful and uneventful.

Four years after his latest IPG replacement surgery, he developed skin erosion around his bilateral parietal surgical wounds, which had been treated with oral antibiotics by his general practitioner for a fortnight, but to no avail, and he came back to our neuromodulation clinic. On assessment, there were a few millimeters of erosion of the skin around bilateral parietal incisions with sense of fluctuation but no other signs of active infections. Then he underwent urgent wound debridement and irrigation. Meanwhile intraoperative microbiology samples cultured Staphylococcus aureus. After that, he received 24 hours of postoperative intravenous antibiotics (cefoperazone) followed by a seven-day course orally (cefdinir capsules) and his wounds gradually healed. However, one year later, recurrent skin erosion appeared in the same areas. His wounds were surgically debrided and irrigated again. Meanwhile intraoperative swabs were re-cultured for Staphylococcus aureus and irrigated with moxifloxacin, followed by completion of a 20-day course of intravenous cefoperazone and then oral cefdinir capsules. But one month later, he was found to have a discharging sinus at the medial edge of the left parietal incision. The wounds were surgically explored, flushed with vancomycin and iodine solution. Then the necrotic tissue was cleared and the dissociated flap transplantation was performed by a plastic surgeon. Staphylococcus aureus was again isolated and he was treated with intravenous vancomycin for two weeks. One month later, there were a few millimeters of erosion of the skin around bilateral parietal incisions from which purulent discharge can be withdrawn with sense of fluctuation around the whole DBS systems, including the parietal incisions, the retro-auricular extension cable and the right chest wall, which show signs of infections (Fig. 1). We speculated that bacterial colonization of the cranial elements of the system is likely and high risk of intracranial infection in this patient. He underwent a total of four local incisions debridements (including two times of dissociated flap transplantation) before the final removal of the hardware. Unfortunately, in the 13th year of DBS treatment, he dismantled his entire DBS system, leaving no remaining hardware, and since then levodopa equivalent (LED) had increased dramatically, his symptoms had worsened and his quality of life in a bedridden state has been very poor.

Fortunately after completion of antibiotic treatment, he underwent implantation of a new DBS system nine months later at the age of 70. His symptoms were dominated by tremor, stiffness and bradykinesia, without dyskinesia, so the target was again identified as bilateral STN. The problem was that brain atrophy leading to ventricular dilatation, gliosis of previous electrode paths, and atrophy of the nucleus, which makes the target localisation and trajectory selection difficult (Fig. 2). Using the Leksell SurgiPlan system software (Elekta, Stockholm, Sweden), the data of the 3.0 T head MRI scan (3-dimensional T1, axial position T2 and coronal position T2), before the operation, and the CT scan of the head with Leksell stereotactic frame (Elekta, Stockholm, Sweden) were combined. Furthermore, the cartesian stereo coordinate system was established using the midpoint of the AC-PC (anterior commissure-posterior commissure) as the origin, and then we designed a transcranial approach, avoiding blood vessels on the surface of the brain, the sulci of the brain, and the lateral ventricle. After a careful targeting and intraoperative microelectrode recording (MER) (Fig. 3), the range (7 mm of bilateral STN) met the length of the implantation despite the intermittent electrophysiological signals and the efficiency of intraoperative test was satisfactory. The surgical phase consisted of bilateral leads (Medtronic 3389, USA) and IPG (Medtronic Activa RC, USA) implantation under local and general anaesthesia, respectively, with the IPG implanted in the left chest wall. Slight postoperative intracranial edema was identified by magnetic resonance imaging (MRI) (Fig. 4). No further complications appeared at the ninth months follow-up after reimplantation. The patient's symptoms had improved to a great extent, and he could take care of himself and his quality of life had improved significantly, which met the needs of the patient and his family. And LED also significantly declined. (Supplementary material: Table 1. Patient History and Course of Treatment)

Discussion

The clinical definition of infection due to hardware of DBS system was purulence or erythema identified from any DBS incision site (cranial, retro-auricular, or IPG), which was subsequently confirmed with a positive culture [1]. In neurosurgery and other surgical areas, DM has been noted as an independent risk factor for the development of postoperative surgical infection [4, 5]. To diagnose an infection, at least one of the following is required: (1) purulent drainage, (2) organisms isolated from an aseptically-obtained culture, (3) at least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, erythema or heat, fever (>38°C), or spontaneous dehiscence, (4) an abscess or other evidence of infection that is detected on gross anatomical or histopathological exam or on an imaging test, (5) diagnosis of an surgical site infection(SSI) by a surgeon, attending physician, or other designee [6, 7]. Our patient met all criteria other than fever. The main differential diagnosis is allergic reactions with symptom onset usually occurred between eight days and three years after implantation. The most commonly reported presentation of hypersensitivity was skin changes over the site of the IPG. Although hypersensitivity reactions are rare, implanting physicians should remember the distinguishing features of an allergic reaction, such as a normothermic body temperature, blood tests (white blood cell count, erythrocyte sedimentation rate and inflammatory markers such as C-reactive protein) within normal limits, negative bacterial cultures, and no response to antibiotics [8].

The sites of infection tend to be around the IPG, connector in retro-auricular site or cranial burr hole, while intracerebral infection seems to be rare. A study retrospectively analysed complications after the first month postoperatively in 249 patients treated with DBS for a period of 16 years. The results showed that infection was the most common delayed complication, while IPG was the most common involving location [9]. Most infections seemed to arise from the IPG within 2 months of implantation, with the majority caused by Staphylococcus species. Each patient underwent 1–5 salvage procedures. Another study involved 13 patients who underwent a total of 32 incisions and drainage procedures for the hardware salvage prior to the final resection. Of the cranial and connecting site infection, more than half occur in the retro-auricular connector site [10]. Staphylococcus species are the most common offending organism. Obtaining intraoperative cultures in all cases of infection in order to dictate appropriate antibiotic management was recommended [11].

In cases of infection all attempt should be made to salvage the DBS leads. Infection at the IPG site and/or extension lead connector would likely necessitate hardware removal of everything except for the DBS leads and treatment with a six weeks course of intravenous antibiotics. Skin erosion or infection at the cranial wound would be treated with debridement, change of stimlock base plates and six weeks of intravenous antibiotics. Exposed lead wire without infection would require wound revision, antibiotic irrigation, and isolation of the lead from the skin incision [12]. Fortunately, most of the infections responded to antibiotic therapy and/or surgical debridement. Only a fraction of these patients had intractable infection or inflammation that made removal of hardware components inevitable [13]. In DBS related SSI, there has been a policy to try a conservative approach to avoid unnecessary hardware removal. Our case suggests prompt local hardware removal and long-term antibiotic treatment when an infection caused by Staphylococcus aureus was suspected. Decolonization has been shown to be effective in reducing the risk of intracranial infection, especially for the deep SSI.

If infection recur, then most experience is that complete removal of the hardware is inevitable even after prolonged antibiotic treatment, although we acknowledge that others had reported success with partial removal of the hardware and prolonged (up to six weeks) intravenous antibiotics. A total of 362 patients underwent 530 electrode placements by three neurosurgeons in a study period. Of these, 16 (4.4%) underwent ≥ 1 DBS revision surgical procedures due to infection. Despite hardware salvage attempts, 15 of the 16 infected patients (93.8%) subsequently underwent complete device explantation due to recurrent infection. Seven patients (53.8%) underwent DBS reimplantation after explantation and resolution of infection. The mean length of time between explantation and reimplantation was 5.7 ± 3.0 months. Rates of complete and partial hardware salvage success are estimated to be only 30% and 21% respectively, and complete DBS system explantation is frequently needed [1]. The clinical benefits provided by DBS are significant, while hardware explantation may lead to loss of efficacy and exacerbation of symptoms [10]. This is particularly problematic for PD patients, who are at significant risk of developing life-threatening DBS withdrawal syndrome when stimulation continues for several years [14, 15].

In a cross-sectional study using individual-level data provided by the Australian Government, they evaluated 1849 patients identified as having PD and implanted with DBS over a 15-year period. 51.4% of patients required repeat hardware surgery. 11.3% of patients had repeat intracranial electrode surgery. 47.6% of patients had repeat IPG/extension-cable surgery including for presumed battery depletion. Repeated hardware procedures, including those for intracranial leads, are therefore common [14]. A retrospective, single-centre analysis of 123 consecutive patients treated with DBS was conducted. Four patients (3.3%) had their IPG removed due to infection [16].

In one study, researchers present there outcomes after revision or reimplantation surgery in patients with infections, device failure, or unsatisfactory results after DBS surgery for PD. Reimplantation after surgical infection seems feasible and overall safe [17]. When they analyzed patients who had the device removed and reimplanted due to infection, they did not notice significant differences in outcome, suggesting that reimplantation after infection can be successfully accomplished. Although management of infection is costly, it seems possible to recapture the initial benefit of DBS after reimplantation [18].

The problem in our case was that brain atrophy led to ventricular dilatation, gliosis of former electrode pathways, and atrophy of the nucleus, which made target localization and trajectory selection difficult. These changes are consistent with moderate degradation, particularly in the medial-edge portion of the STN. One study compared the lateral parts of STN of patients treated with DBS with that of nine non-DBS treated PD patients, the former showing moderate astrogliosis, microglial activation, thickening of neuronal processes, and changes in neuronal shape, size and density around the STN. In contrast to short-duration DBS, chronic DBS may elicit moderate degeneration of the stimulated target neuronal tissue after up to 16 years of stimulation. It remains unclear whether these changes are related to chronic depolarization block or an alteration of the synaptic conduction or other causes including the mere physical proximity of a foreign body, which is a matter of speculation [19]. Typical findings include fibrous sheaths of 5-25 mm surrounding the electrode track, a chronic inflammation with reactive astrocytes, multinucleated giant cells, macrophages, mononuclear leucocytes and T-lymphocytes, fibrillary gliosis and Rosenthal fibers [20]. Glial scarring around DBS leads in the brain has been described previously and this is thought to be the result of an inflammatory response of microglia to the leads [3]. Our case and similar results suggest that positive clinical outcomes can be reproduced following extraction and reimplantation of bilateral DBS leads by adjacent trajectories within the STN [21].

Reasons for not re-placing the lead include cognitive decline after the original surgery, patient choice, comorbidities, and the threat of hardware erosion in patients with compromised skin integrity at the surgical site. When complete explantation is eventually performed, the experience of failed salvage attempts may contribute to the decision by these patients to not undergo DBS system reimplantation, leading to permanent loss of stimulation benefit. The cost of new IPG type accounted for about 80% of the cost of the whole DBS system and it was higher than that of earlier non-rechargeable models. All of these highlighted the need for long-term follow-up and ongoing patient/carer education, especially for patients with rechargeable IPG implants [22].

Conclusions

In conclusion, infection is one of the most serious and difficult complications to manage after DBS implantation. Studies showed that the infection risk was increasing as it related to poor health conditions, such as poor personal hygiene habits, and low cultural background, which would cause more serious infection risk particularly in advanced PD patients. Treatment of this complication can take a long time and lead to additional hospitalization, surgery and partial or total removal of the DBS system. Hardware explantation may lead to a loss of efficacy of therapy and exacerbate of symptoms throughout the period of time that elapses before the system can be replaced. In our opinion, therefore, as long as the above indications are met in any case, the reimplantation procedure can be reconsidered later, despite having had an infection and the electrode being removed.

List Of Abbreviations

DBS, Deep brain stimulation

PD, Parkinson's disease

STN, Subthalamic nucleus

IPG, Implantable pulse generator

DM, Diabetes mellitus

LED, Levodopa equivalent dose

AC-PC, Anterior commissure-posterior commissure

MER, Microelectrode recording

MRI, Magnetic resonance imaging

SSI, Surgical site infection

Declarations

- Ethics approval and consent to participate

According to local ethical regulations (Ethics committee of the First Affiliated Hospital of Dalian Medical University, Dalian, China) “case reports are not prospectively planned research projects on or with people, but retrospective case descriptions of medical actions. Therefore, the ethics committee is not responsible for evaluating case reports” and consequently is waiving the necessity of an ethical approval for case reports.

- Consent for publication

We have obtained written informed consent for this publication from the patient’s family.

- Availability of data and materials

Not applicable.

- Competing interests

The authors declare they have no competing interests.

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- Authors' contributions

TL and XW: are the co-first authors who write the manuscript. CS, LR and XY: work for the treatment of the patient and draft preparation. LP and ZL: work for the review and critique of the article. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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Table

Table 1 is available in the Supplementary Files section.

Figures

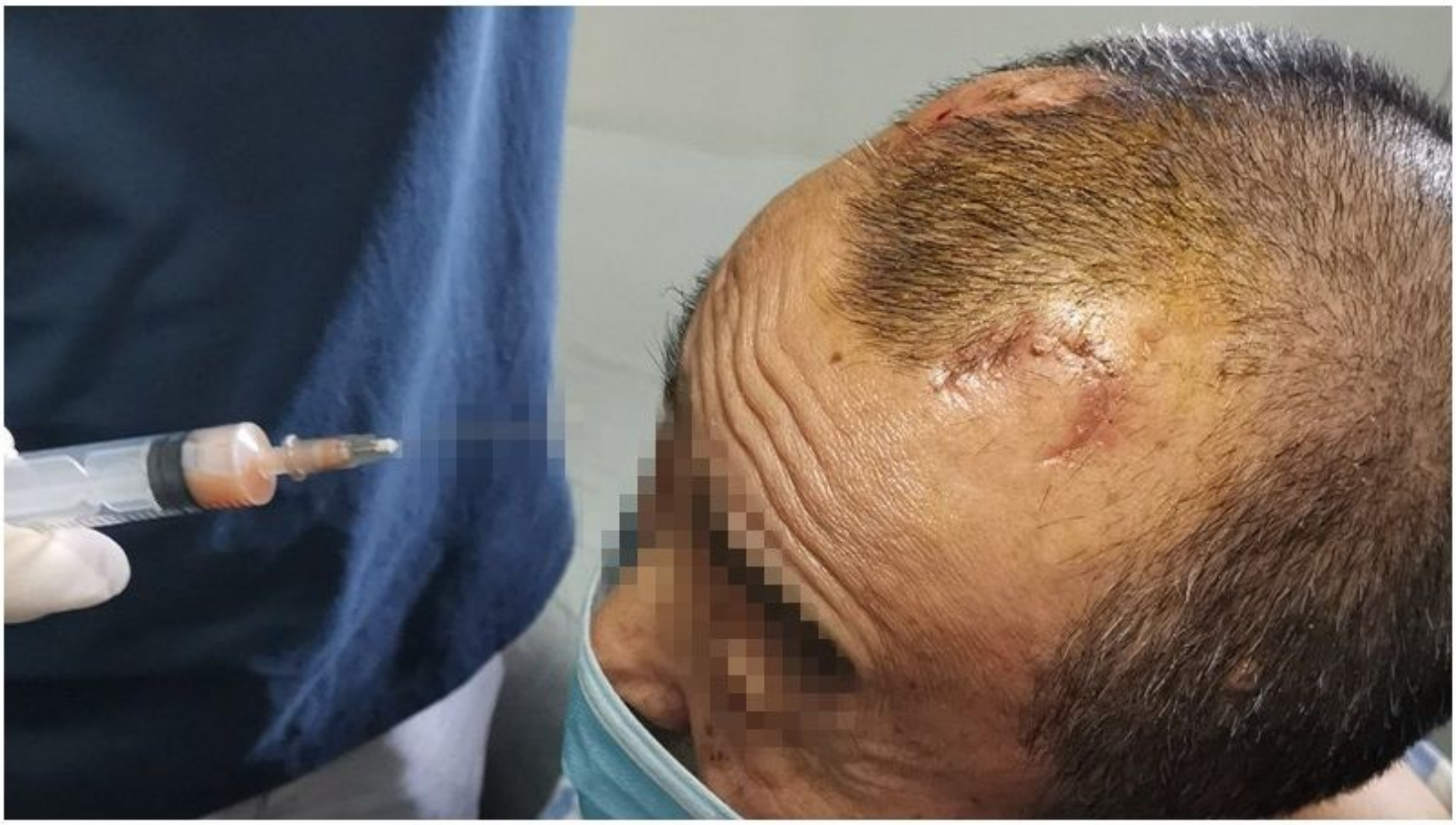

Figure 1

There were a few millimeters of erosion of the skin around bilateral parietal incisions with sense of fluctuation and with syringe drawn out purulent secretion before the final removal of the hardware.

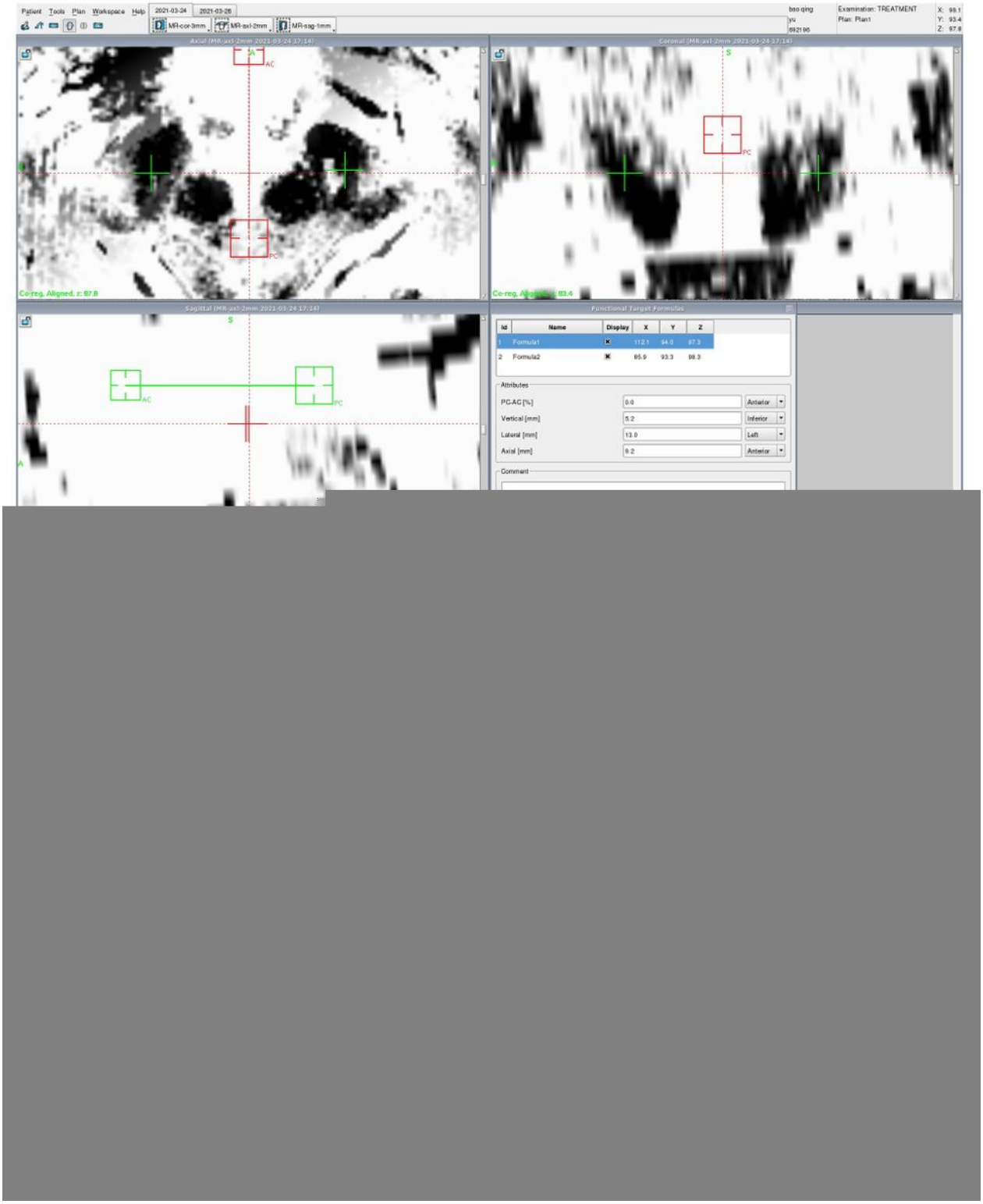

Figure 2

Stereotactic planning of electrode reimplantation. Brain atrophy led to ventricular dilatation, gliosis of previous electrode pathways, and atrophy of STN, which made target localization and trajectories selection difficult. The target (coordinates of the planned target on the left side were as follows: x=112.1, y=94, z=97.3, arc=109, and ring=67; coordinates of the planned target on the right side were as follows: x=85.9, y=93.3, z=98.3, arc=67, and ring=65) and the electrode implantation path were set according to

the actual anatomy of the patient's brain. Left and right electrode trajectory views showing the stereotactic planning for the second surgery on T2-weighted MRI. The burr holes and hyperintense electrode trajectories from the first surgery were still visible. A Leksell model frame (Elekta, Stockholm, Sweden) was placed on the head under local anesthesia. The patient was in the operation room for surgery.

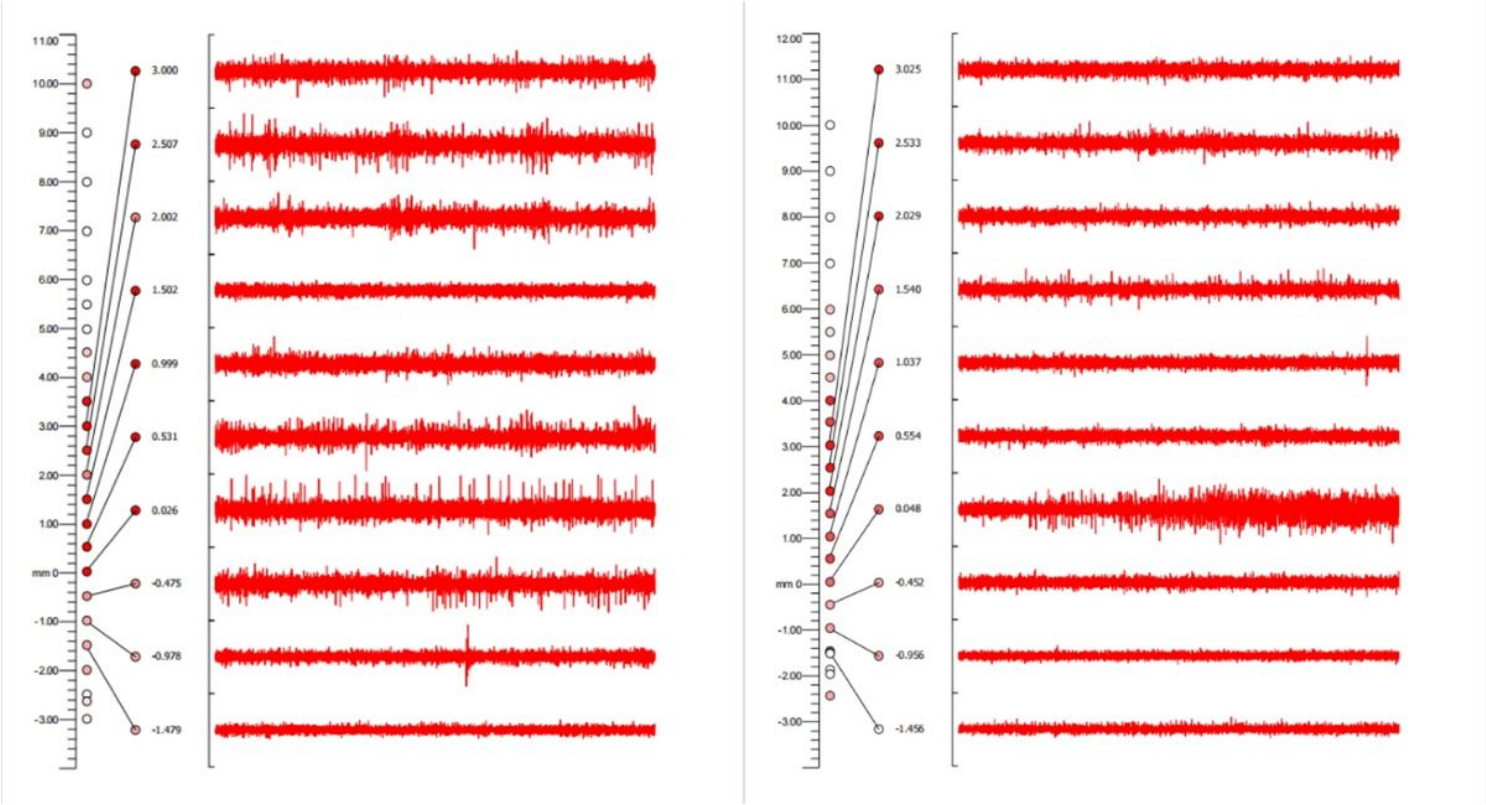

Figure 3

During local anesthesia, an OMEGA electrophysiologic instrument (Alpha Omega Engineering Inc., Nazareth, Israel) was used to record the single-cell discharge waveform of the bilateral STN nuclei. Intraoperative microelectrode recording of left and right trajectories were obtained. The subthalamic nucleus discharge waveform range on both sides was 4.5mm above to 2.5 mm below the target point on the left side and 5.5mm above to 1.5 mm below the target point on the right side.

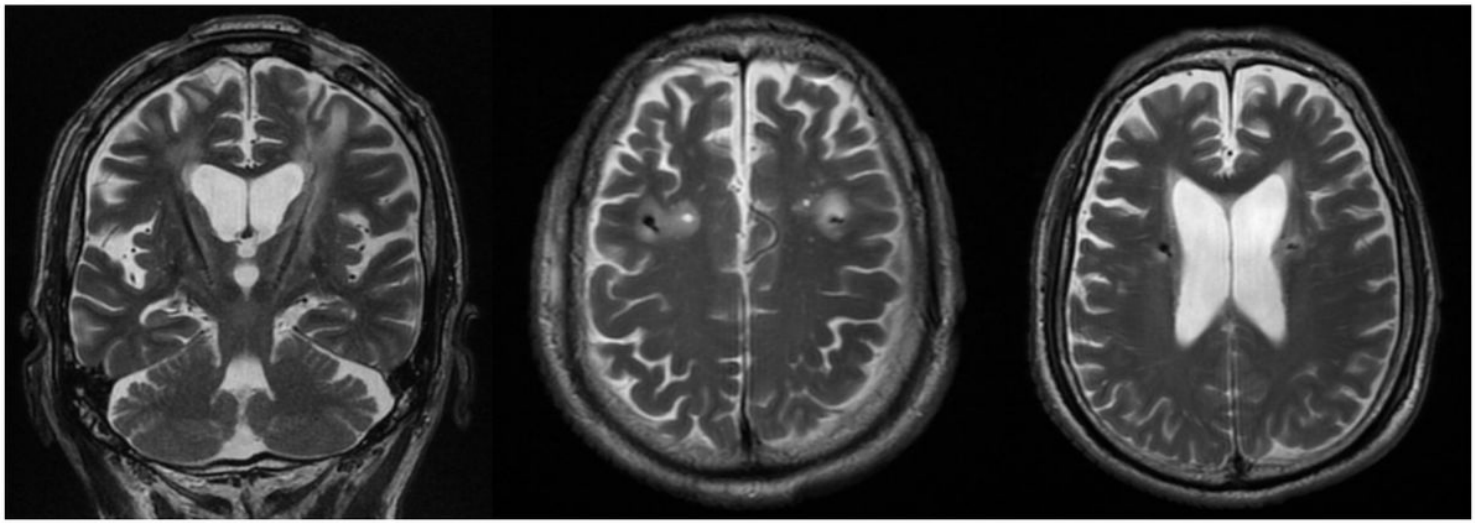

Figure 4

Postoperative MRI was routinely performed to verify the location of leads. Slight postoperative intracranial edema was identified by T2-weighted MRI On the forth postoperative day.

Supplementary Files

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- 4.doc