JOURNAL OF NEUROSURGERY:
Case Lessons

J Neurosurg Case Lessons 1(1):CASE2031, 2021
DOI: 10.3171/CASE2031

Diplopia associated with loop routing in deep brain stimulation: illustrative case

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BACKGROUND Deep brain stimulation (DBS) is a powerful surgical option for drug-resistant movement disorders; however, electromagnetic interference (EMI) from external sources poses a potential risk for implanted electronics.

OBSERVATIONS A 61-year-old woman with Parkinson's disease originally had two implantable pulse generators (IPGs) for bilateral subthalamic DBS, which were then replaced with one dual-channel IPG routed in a loop. After the replacement surgery, with the same DBS programming as before the IPG replacement (bipolar setting for right, unipolar setting for left), the patient began to complain of transient paroxysmal diplopia. After multiple attempts to adjust the stimulation parameters, the diplopia was resolved by changing the left unipolar setting to a bipolar setting. At the authors' institution, before the present case, four other patients had undergone IPG replacement with loop routing. None of these previous patients complained of diplopia; however, two of the four presented with diplopia in an experimental unipolar setting.

LESSONS Clinicians should be aware that loop-routed circuits may generate distortion of the stimulus field in DBS, even in the absence of external EMI sources.

https://thejns.org/doi/abs/10.3171/CASE2031

KEYWORDS deep brain stimulation; adverse effect; diplopia; convergence insufficiency; electromagnetic interference; loop circuit

Deep brain stimulation (DBS) is widely accepted to be a powerful therapeutic option for movement disorders such as Parkinson's disease, dystonia, and some tremors of central origin. Before the advent of dual-channel implantable pulse generators (IPGs), two single-channel DBS systems were implanted bilaterally to treat bilateral symptoms. Dual-channel IPGs with primary cells were at first only available in a limited number of countries, and these IPGs were later replaced by another lineup of dual-channel IPGs with rechargeable or non-rechargeable batteries. One manufacturer (Medtronic) describes the potential risk of electromagnetic interference (EMI) in their implantation manual as follows: 1) "When multiple leads are implanted, route the lead-extensions so the area between them is minimized. If the lead-extensions are routed in a loop, the loop will increase the potential for EMI," and 2) "Do not replace two Soletra Model 7426 Neurostimulators with one bilateral neurostimulator unless re-tunneling is performed so both lead-extensions are on the same side of the body. Otherwise, the 'looped' configuration formed by the lead/extensions increases the potential for EMI effects."

However, such extra maneuvers (i.e., retunneling) in replacement surgery require general anesthesia and carry the potential risk of fracturing the old and fragile leads. In our hospital, we comply with the manufacturer's manual for patients with newly implanted DBS devices. Over the previous two decades, we experienced about 50 cases of replacement surgery per year with single-channel devices. More recently, we experienced a limited number of cases (n = 5) of battery replacement in which we combined two systems into one dual-channel system by using a loop-routed circuit. In these cases, we had used one pocket adapter crossing in front of the sternum to connect two bilateral extensions to one dual-channel IPG (loop routing). The case in the present report was the first in which we encountered any adverse effects after the loop routing procedure. The presentation of the current case was approved by the institutional review board of Fukuoka Mirai Hospital.

Illustrative Case

A 61-year-old woman developed Parkinson's disease at the age of 43 years and underwent implantation of a DBS lead to the subthalamic nucleus (STN) at the age of 52 years, using single-channel IPGs (Activa SC Model 37602, Medtronic). Her axial symptoms (e.g., camptocormia, gait disturbance, and speech problems) had

ABBREVIATIONS DBS = deep brain stimulation; EMI = electromagnetic interference; IPG = implantable pulse generator; STN = subthalamic nucleus.

INCLUDE WHEN CITING Published January 4, 2021; DOI: 10.3171/CASE2031.
SUBMITTED October 9, 2020. **ACCEPTED** October 14, 2020.

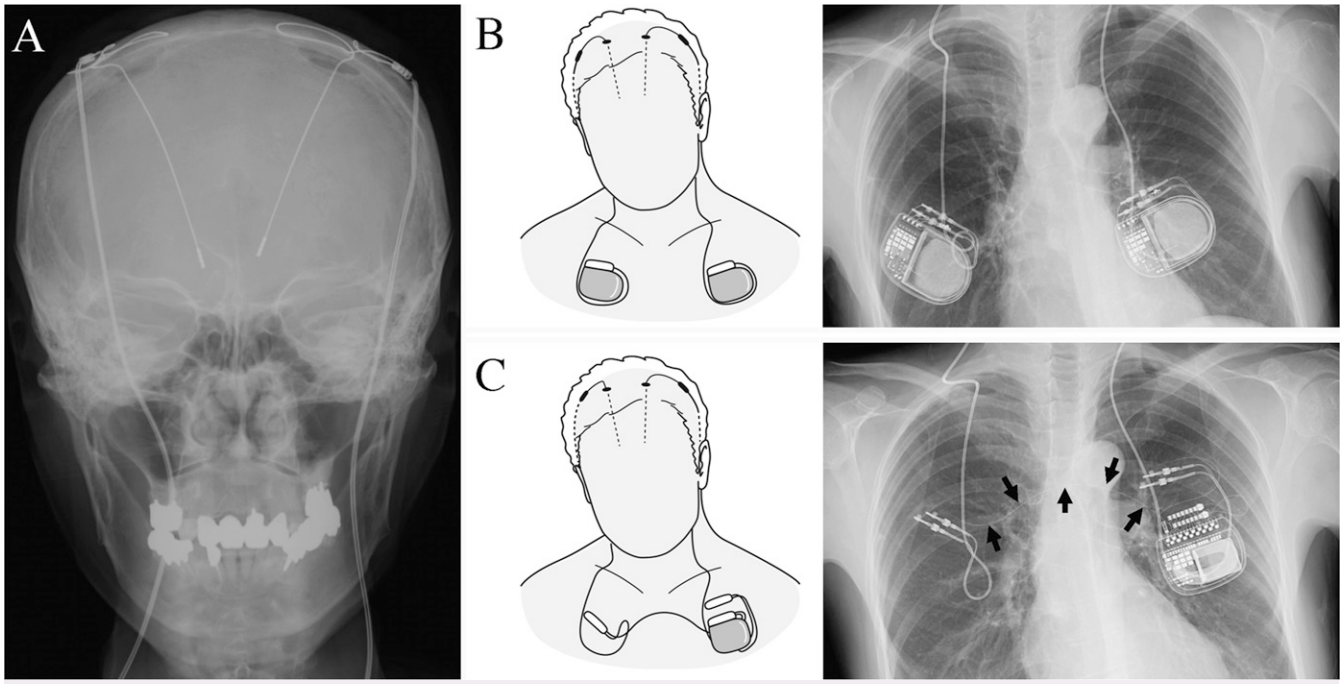

FIG. 1. Radiography showing the DBS system. **A:** Bilateral leads in the skull and extensions descending along the neck on each side. **B:** Before replacement, each of two extensions was connected to a single-channel IPG on each side as two independent circuits. **C:** After replacement, two extensions were connected to two pocket adapters. The right adapter was routed subcutaneously, crossing in front of the sternum to the left (*arrows*). Two pocket adapters from both sides were connected to one dual-channel rechargeable IPG (loop routing).

progressed, but she had never experienced diplopia. At the age of 58 years, when the IPGs' batteries displayed the elective replacement indicator, she asked for the devices to be changed to a rechargeable IPG because the lack of subcutaneous fat on her chest made the devices uncomfortable and conspicuous. She gave informed consent, knowing that her DBS system would contraindicate magnetic resonance imaging of the entire body, and the replacement surgery was performed under mild sedation with intravenous midazolam and local anesthesia. After the extension cables from the old IPGs in her chest were disconnected, the cables were connected to the pocket adapters (Model 64001). The right adapter was routed subcutaneously to the left, crossing the midline, and was connected along with the left adapter to one dual-channel IPG (Activa RC, Model 37612) with loop routing (Fig. 1). Stimulation was resumed with the same settings as in the preoperative program: (right) 3.65 V, contacts 1–2– 0+, 210 μsec/130 Hz; (left) 3.1 V, contacts 10–11–case+, 210 μsec/130 Hz. The patient did not notice any immediate stimulus-related differences from the previous IPGs that had been used. However, when the effects of midazolam wore off, she began to complain of frequent paroxysmal diplopia, which lasted for a few seconds and was associated with convergence insufficiency (Fig. 2). The diplopia occurred transiently when the patient raised her head or turned sideways, regardless of her posture or environment. Computed tomography imaging did not detect any abnormalities in the brain or any changes in lead positions. The most ventral active contacts were located at (right) 12.1 mm lateral, 1.7 mm posterior, and 0.8 mm inferior; and (left) 11.4 mm lateral, 1.1 mm posterior, and 0.3 mm inferior to the midcommissural point. When the DBS system was turned off, the diplopia immediately ceased; however, akinesia and tremor quickly returned in this condition. Repetitive measurements of system impedances revealed no abnormalities, regardless of the occurrence of convergence insufficiency. Because the patient had no history of diplopia with the previous bilateral programs, the IPG replacement was determined as a

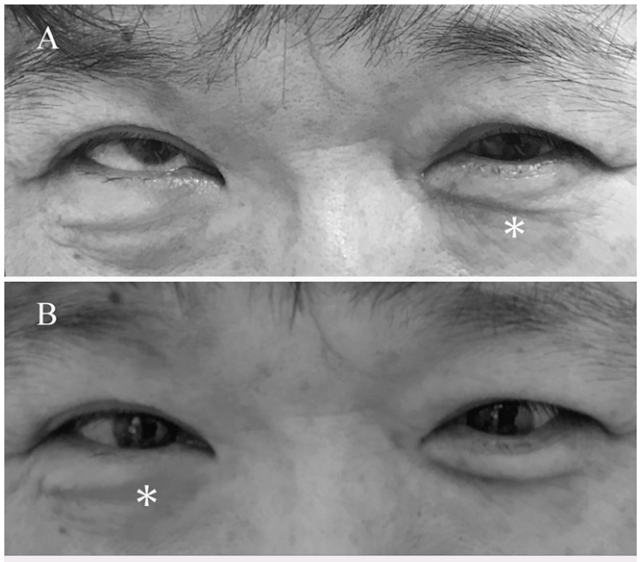

FIG. 2. Photographs of convergence insufficiency during a complaint of diplopia. The position of the patient's eyes shows a cross-eyed appearance. The *asterisks* indicate the eye looking at the camera (**A**, *left*; **B**, *right*).

TABLE 1. Summary of five cases of bilateral replacement with a single dual-channel IPG routed in a loop (June 2016 to October 2017)

Case No.	Age (yrs)	Gender	H-Y Stage	Disease Duration (yrs)	DBS Duration (yrs)	No. of Previous Replacements	IPG Model		Use of Pocket Adaptor	Stimulation Setting*			Coordinates of Active Contact (mm)†			Diplopia? (w/unipolar)
							Before	After			Before	After	x	y	z	
1	65	F	4	28	12	3	Activa SC 37602	Activa RC 37612	Yes	Rt	4.2 V, 2–3– 1+, 330 μsec/130 Hz	4.3 V	10.6	1.5	3.6	No (yes)
										Lt	4.5 V, 2–3– 1+, 330 μsec/130 Hz	4.6 V	12.2	1.0	3.9	
2	72	F	3	32	7	7	Soletra 7426	Activa PC 37601	Yes	Rt	2.5 V, 2– case+, 60 μsec/130 Hz	2.5 V	11.1	0.1	0.1	No
										Lt	2.5 V, 2– case+, 60 μsec/130 Hz	2.5 V	13.0	1.4	1.4	
3	78	M	4	14	7	2	Activa SC 37602	Activa PC 37601	Yes	Rt	3.8 V, 0–1– 3+, 210 μsec/130 Hz	NC	12.1	3.2	2.6	No (yes)
										Lt	3.8 V, 0–1– 3+, 210 μsec/130 Hz	NC	12.3	3.2	5.0	
4	68	M	3	10	5	0	Activa SC 37603	Activa PC 37601	No	Rt	3.2 V, 1– case+, 60 μsec/130 Hz	NC	11.2	1.9	1.3	No
										Lt	3.2 V, 1– case+, 60 μsec/130 Hz	NC	11.4	2.5	2.0	
5 (present case)	61	F	4	15	6	0	Activa SC 37602	Activa RC 37612	Yes	Rt	3.65 V, 1–2– 0+, 210 μsec/130 Hz	NC	12.1	1.7	0.8	No (yes)
										Lt	3.1 V, 1–2– case+, 120 μsec/130 Hz	4.0 V, 10–8+, 240 μsec/130 Hz	11.4	1.1	0.3	

H-Y = Hoehn & Yahr; NC = no change.

* Values refer to intensity (V), active contacts (cathode or anode), pulse width (μsec), and frequency (Hz).

† Values refer to lateral (x), posterior (y), and inferior (z) from the midcommissural point.

possible cause of her paroxysmal diplopia. She underwent multiple reprogramming attempts to modify the program, including reducing the voltage, changing the contact configuration, and using the constant-current mode. It was finally found that changing the left contact configuration from a unipolar to a bipolar setting produced stable relief from diplopia without causing deteriorations in the patient's parkinsonism symptoms. The settings used were 4.0 V, contacts 10–8+, 240 μsec/130 Hz.

The patient in this case was the first in our hospital to complain of diplopia after IPG replacement. After this experience, we investigated the occurrence of diplopia in patients who had undergone IPG replacement with loop routing. In our medical records, there were 60 cases of IPG replacement surgery from June 2016 to October 2017; of these, five cases had undergone replacement of bilateral single-channel IPGs with one dual-channel IPG routed in a loop, including the present case (Table 1). Of the previous four cases, two (cases 1 and 3) had bipolar settings on both sides, and two (cases 2 and 4) had unipolar settings on both sides. None of the four had ever experienced diplopia; however, when the settings of cases 1 and 3 were experimentally changed to unipolar, they both complained of diplopia associated with convergence insufficiency (internal strabismus) before the stimulation intensity reached a level that alleviated their parkinsonism. Therefore, including the present case, three (60%) of five cases with loop-routed DBS developed diplopia under unipolar settings. The diplopia ceased when the settings were changed to bipolar (Table 1). Of the three patients who experienced diplopia under unipolar settings, the laterality of the active contacts was within 10.6–12.3 mm from the midline.

Discussion

Observations

Diplopia is a frequent symptom of Parkinson's disease[1] and is also a well-documented adverse effect of STN-DBS, as well as eye deviation.[2,3] There are two types of eye deviation related to STN-DBS: conjugate deviation and ipsilateral eye deviation. Intraoperative stimulation at the laterality of the STN leads to conjugate deviation to the opposite side, which is seldom associated with diplopia and is usually not seen postoperatively. In contrast, stimulation medial to the STN leads to ipsilateral ocular deviation, which does not habituate.[4,5] Because the lead locations were neither very lateral nor very medial in our cases with diplopia under unipolar settings, and because all cases presented with internal strabismus but not conjugate deviation, it may be that the oculomotor fibers running medial to the STN were improperly stimulated. In DBS, a short circuit (with extremely low impedances) between multiple contacts may result in unexpected current diffusion to neighboring structures[6]; however, there were no abnormalities in system impedances in our case series. In the present case, the only difference between the conditions before and after the replacement was the loop-routed circuit for DBS (Fig. 1B and C). The manufacturer's manual contained a warning that routing the lead extensions in a loop could potentially increase the potential for EMI, but it only mentioned EMI generated by external sources, such as medical equipment or devices found in everyday environments. In the unipolar setting, in which the IPG acts as the anode, the stimulus current spreads without directionality in a spherical shape, whereas the bipolar setting restricts current spreading around the cathodes. We hypothesize that current spreading in the unipolar setting may be distorted in the medial direction because of self-generated EMI in the loop. However, EMI generation in the DBS circuit itself caused by loop routing is highly speculative, and simulation studies are required to understand the potential risk of in-circuit EMI in loop-routed DBS. We have never encountered any patients with symptomatic EMI generated by external environments, and to the best of our knowledge, no case has previously been reported in which an adverse event was considered to be generated by the loop routing itself.

Lessons

Battery replacement by loop routing can be easily accomplished under local anesthesia without the risk of lead fracture, but this procedure may result in the DBS circuit becoming susceptible to external EMI sources, and the manufacturer's manual recommends against this. In cases of DBS system replacement performed with loop routing, the potential risk of extra current diffusion generated around the active contact by the DBS itself, even in the absence of external EMI sources, is worthy of clinicians' consideration and caution.

Acknowledgments

We thank Hiroko Eguchi (Movement Disorder Unit Nurse) and Yasutaka Ezaki (Medical Engineer) for their special involvement in the clinical management of the patients. We also thank Bronwen Gardner, PhD, from Edanz Group for editing a draft of this manuscript.

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Disclosures

Dr. Miyagi receives personal fees from Kyowa Kirin Co., Otsuka Pharmaceutical Co., Sumitomo Dainippon Pharma Co., AbbVie GK, Novartis Pharmaceuticals Co., FP Pharmaceutical Co., Eisai Co., Takeda Pharmaceutical Co., Ono Pharmaceutical Co., Boston Scientific Japan, and Medtronic Japan.

Author Contributions

Conception and design: both authors. Acquisition of data: both authors. Analysis and interpretation of data: both authors. Drafting the article: both authors. Critically revising the article: both authors. Reviewed submitted version of manuscript: both authors. Approved the final version of the manuscript on behalf of both authors: Miyagi. Statistical analysis: Miyagi. Administrative/technical/material support: both authors. Study supervision: Urasaki.

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