Temporary Interruption of Deep Brain Stimulation for Parkinson's Disease During Outpatient Electroconvulsive Therapy for Major Depression: A Novel Treatment Strategy

Simon Ducharme, M.D.
Alice W. Flaherty, M.D., Ph.D.
Stephen J. Seiner, M.D.
Darin D. Dougherty, M.D., M.Sc.
Oscar G. Morales, M.D.

The safety of electroconvulsive therapy (ECT) in patients with deep brain stimulation (DBS) has not been established. Cases reported had no adverse events, but DBS was withheld throughout the weeks of the ECT course. The authors report the first case of temporary interruption of DBS only during the minutes of each outpatient ECT.

(The Journal of Neuropsychiatry and Clinical Neurosciences 2011; 23:194–197)

Deep brain stimulation (DBS) is a novel neuromodulation treatment for refractory neurological and psychiatric disorders. Current neurological indications include Parkinson's disease (PD), tremor, and dystonia.[1,2] More recently, subgenual cingulate cortex and ventral capsule/ventral striatum DBS have shown promising results for treatment-refractory depression and obsessive-compulsive disorder.[3–5] Larger, pivotal studies are currently under way. Among neurological indications, PD has an extremely high rate of comorbid depression, reaching as high as 40% in some studies.[6] Given this high comorbidity and the extension of DBS to psychiatric illnesses, clinicians are likely to see an increasing number of cases of severe major depression in patients with DBS devices already in place.

Despite the advances in psychopharmacology, electroconvulsive therapy (ECT) remains the most efficacious treatment for major depression.[7] However, no controlled study has looked at the efficacy and safety of ECT in patients with DBS stimulators. Safety concerns include potential neurological damage from the heat generated by the electricity of the ECT transmitted to the intracranial electrodes[8,9] and a shift in the position of the DBS electrodes due to seizure-induced motor activity, although neither adverse event has been reported with ECT in patients with DBS. However, both permanent and reversible neurological damage has been reported secondary to head and neck diathermy treatments in patients with DBS.[9,10]

Five cases of ECT for major depressive episodes in patients with DBS have been published. One patient had a left unilateral ventral-thalamic nucleus DBS for essential tremor, and three patients had subthalamic nucleus (STN) DBS for Parkinson's disease.[11–14] One of these patients had two courses of bitemporal ECT.[13] The fifth case report was a woman with a depressive relapse 6 months after partially successful treatment with subcallosal cingulate gyrus DBS for treatment-refractory depression.[15]

In all cases, ECT treatments were bilateral, and patients had good clinical responses with only the usual side effects. No significant adverse events related to DBS were reported. Importantly for this case report, all patients were hospitalized, and the DBS device was turned off throughout the ECT courses.

We report the case of a patient with bilateral STN DBS for Parkinson's disease who had two successful outpatient treatment courses with modified bifrontal ECT for major depression. It is the first patient in whom the DBS device was turned off only temporarily for the acute ECT delivery and turned on quickly afterwards in the recovery room, as opposed to being turned off throughout the ECT course. This prevented an increase in his PD symptoms during the ECT treatment.

Received June 1, 2010; revised August 1, 2010; accepted August 3, 2010. From McGill University, Montreal, QC, Canada, and Division of Neurotherapeutics, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA; Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA; McLean Hospital, Harvard Medical School, Belmont, MA. Send correspondence to Oscar G. Morales, M.D., McLean Hospital, 115 Mill St., Belmont, MA 02478; ogmorales@partners.org (e-mail).

CASE REPORT

This 71-year-old married man was referred by his treating psychiatrist for ECT evaluation in August 2008. The patient, a retired university professor, had been diagnosed with idiopathic PD in 1989. He initially had a good response to *L*-dopa, but gradually developed a disabling, predominantly right-sided hand tremor. Therefore, a bilateral subthalamic DBS device was installed in 2003. The procedure was well-tolerated, and the clinical response was such that he was able to stop *L*-dopa medication and return to work. Batteries had to be replaced frequently because of the high voltage parameters (left: 7.0V, PW 90, 185 Hz, 3+1–0-; right: 2.3V, PW 60, 185Hz, 3+2–1-). The rest of his medical history was unremarkable.

The patient had a first major depressive episode in 1972. He was then on and off medication for many years, with limited clinical response. Although his father suffered from bipolar type I disorder and was successfully treated with ECT, the patient himself never experienced a manic episode. He had been treated with right-unilateral ECT in 1996 for a recurrent depression, with good clinical response and minimal side effects. He then had two other successful courses of bilateral ECT in 2000 and 2002, before the DBS surgery. In February 2008, he relapsed into a major depressive episode with anxious ruminations about the future. Over the next few months, he lost about 50 pounds, but never expressed any suicidal ideation. He did not respond to escitalopram, bupropion, and a 1-month course of pramipexole. He was also exhibiting mild executive-function problems that antedated the depressive relapse, probably secondary to his PD. The main DSM-IV diagnosis was major depressive disorder, recurrent and severe. Given the poor response to medication, the patient himself requested another ECT course. After neurological and medical evaluations, it was decided that ECT was indeed the treatment of choice.

With the DBS turned off, the patient's severe disabling tremor would recur within seconds. In that context, it was deemed that stopping the DBS for the complete duration of the ECT course was unacceptable. Therefore, we decided to turn off the DBS generator just before the ECT stimulus, and restart it in the recovery area before the patient regained full consciousness (about 2 minutes of DBS interruption). A modified bifrontal lead placement was chosen to avoid bitemporal placement, which is closer to the electrodes, while maximizing efficacy.[16] He was initially treated as an outpatient at the McLean Hospital in October 2008 with 8 bilateral ECT treatments, 3 times per week. The stimulus was given with a MECTA machine at 0.8mA, PW 1ms, frequency 40Hz, and durations from 1.25 sec to 3.5 sec. The clinical response was adequate, and the patient was maintained on antidepressants.

In March 2010, a depressive relapse required another course of ECT. After discussion with the device manufacturer (Medtronic, Inc.), we decided to set the voltage to 0V just before the ECT stimulus, and adjust it back to the regular settings in the recovery area. This was different from the first ECT course, during which the DBS was simply turned off. Changing the voltage to 0V, as opposed to setting the device at Off, prevents the small theoretical risk that the electrical stimulus could inadvertently turn on the DBS generator during the treatment. With similar bilateral modified bifrontal placement (0.8mA, PW 1ms, frequency 40Hz, and duration up to 4.5 sec), he received 7 treatments, 3 times per week, with almost a complete remission of symptoms. The treatments were then gradually tapered down in frequency, and it was decided to continue maintenance ECT every 4 to 6 weeks. At this point, the patient has received a total of 17 treatments, which is the most reported in conjunction with DBS. There were no complications related to the DBS. The brief interruption of voltage proved to be safe, and the control of his tremor was sustained. The patient elected not to have post-ECT brain imaging; however, the lead position is almost certainly adequate, given that DBS remained effective for the tremor. The mild cognitive impairment that was present before the treatment remained stable.

DISCUSSION

The need for ECT in patients with DBS devices is likely to go up in the next few years, increasing the need for safety data. Although the safety of this procedure has not been formally established, six cases of ECT in patients with DBS for various pathologies have been reported, and all patients had good clinical outcomes, without any unexpected adverse events. Of note, the impact that potential ECT complications, such as prolonged seizures or repeated stimulations within one session because of inadequate seizures, might have on DBS electrodes has not been documented.[17] On follow-up, involved physicians need to regularly verify stimulation parameters and impedance to

ensure the absence of damage creating a short or an open circuit, as described in current consensus statements.[18] Also, it is crucial before proceeding to ECT to make sure that depressive or other neuropsychiatric symptoms are not uniquely secondary to DBS, either in the postoperative period or due to voluntary or accidental changes in stimulation parameters.[18]

This patient is the first in whom the DBS system was turned off or put to 0V only for the brief moment of the acute ECT stimulus and restarted immediately after the convulsion. Although all previous cases reported that DBS was stopped for the complete ECT course, there is no clear theoretical rationale for this decision. In PD, the temporary improvement of neurological symptoms with ECT might alleviate the need for continuous DBS, but, clearly, not in all patients, as our case illustrates.[19] In our opinion, there is no additional risk to a short-term interruption of DBS treatment, and there were no complications for this patient despite his high DBS voltage. The strategy of setting the generator at 0V instead of turning it off is theoretically safer, as it prevents undesired activation of the generator. However, this requires a programming device, as opposed to simply turning the DBS off with the patient's own access device. Importantly, the clinical response to both ECT for major depression and bilateral STN DBS for his PD were robust and sustained. Finally, this case provides evidence supporting the potential of safely administering outpatient ECT in a patient with DBS for PD.

In summary, although the safety of ECT in patients with DBS remains to be formally studied, all 6 patients reported on thus far have had good outcomes. The temporary interruption of the DBS device only during the ECT procedure itself might be a safe strategy that minimizes negative impacts on the underlying condition requiring DBS. This strategy could also be more potent in patients with DBS for major depression who might benefit from augmentation with ECT because of incomplete response or breakthrough episodes of depression. This treatment strategy will need further investigation, but it underscores the growing interest in the potential of combining different neurotherapeutic techniques in a single patient. In that context, there is a need to eventually develop guidelines on the use ECT in patients with DBS devices.

Dr. Ducharme, Dr. Flaherty, and Dr. Seiner have no disclosure or conflict of interest related to this topic. Dr. Dougherty's research has been funded by NIMH, NARSAD, TSA, and OCF. He has received honoraria, consultation fees, and/or royalties from Wyeth, Jazz Pharmaceuticals, Bristol-Myers Squibb, Medtronic, Eli Lilly, Northstar, McNeil, Brand Ideas, and Reed Elsevier. He has also participated in research funded by Medtronic, Cyberonics, Eli Lilly, McNeil and Northstar.

Dr. Morales is the inventor on a patent application owned by McLean Hospital that is related to the subject matter of this manuscript, but this application is still pending and is not licensed to any for-profit entity, and Dr. Morales receives no income or revenues attributable to that patent application. Dr. Morales is the PI on a clinical trial agreement that is not yet executed, but is under negotiation with Brainsway, Inc., and McLean Hospital.

References

1. Higgins E, George M: Brain stimulation therapies for clinicians. Washington, DC, American Psychiatric Publishing, Inc., 2009
2. Hardesty D, Sackeim H: Deep brain stimulation in movement and psychiatric disorders. Biol Psychiatry 2007; 61:831–835
3. Mayberg H, Lozano A, Voon V, et al: Deep brain stimulation for treatment-resistant depression. Neuron 2005; 45:651–660
4. Malone D Jr, Dougherty D, Rezai A, et al: Deep brain stimulation of the ventral capsule/ventral striatum for treatment-resistant depression. Biol Psychiatry 2009; 65:267–275
5. Greenberg B, Malone D Jr, Friehs G, et al: Three-year outcomes in deep brain stimulation for highly-resistant obsessive-compulsive disorder. Neuropsychopharmacology 2006; 31:2384–2393
6. Cummins J, Masterman D: Depression in patients with Parkinson's disease. Int J Geriatr Psychiatry 1999; 14:711–718
7. Pagnin D, de Queiroz V, Stefano P: Efficacy of ECT in depression: a meta-analytic review. J ECT 2004; 20:13–20
8. Yamamoto T, Katayama Y, Fukaya C, et al: Thalamotomy caused by cardioversion in a patient treated with deep brain stimulation. Stereotact Funct Neurosurg 2000; 74:73–82
9. Nutt J, Anderson V, Peacock J, et al: DBS and diathermy interaction induces severe CNS damage. Neurology 2001; 56: 1384–1386
10. Roark C, Whicher S, Aviva A: Reversible neurological symptoms caused by diathermy in a patient with deep brain stimulators: case report. Neurosurgery 2008; 62:E256
11. Chou KL, Hurtig HI, Jaggi JL, et al: Electroconvulsive therapy for depression in a Parkinson's disease patient with bilateral subthalamic nucleus deep brain stimulators. Parkinsonism Relat Disord 2005; 11:403–406
12. Bailine S, Kremen N, Kohen I, et al: Bitemporal electroconvul-

sive therapy for depression in a Parkinson disease patient with a deep-brain stimulator. J ECT 2008; 24:171–172
13. Nasr S, Murillo A, Katariwala N, et al: Case report of electroconvulsive therapy in a patient with Parkinson disease concomitant with deep brain stimulation. J ECT 2011; 27:89–90
14. Moscarillo F, Annunziata C: ECT in a patient with a deep-brain stimulating electrode in place. J ECT 2000; 16:287–290
15. Puigdemont D, Poriella M, Pérez-Egea R, et al: Depressive relapse after initial response to subcallosal cingulate-gyrus deep brain stimulation in a patient with a treatment-resistant depression: electroconvulsive therapy as a feasible strategy. Biol Psychiatry 2009; 66:e11–e2
16. Bakewell C, Russo J, Tanner C, et al: Comparison of clinical efficacy and side effects for bitemporal and bifrontal electrode placement in electroconvulsive therapy. J ECT 2004; 20:145–153
17. Meldrum B: Physiological changes during prolonged seizures and epileptic brain damage. Neuropadiatrie 1978; 9:203–212
18. Deuschl G, Herzog J, Kleiner-Fisman G, et al: Deep brain stimulation: postoperative issues. Mov Disord 2006; 21:S219–S237
19. Douyon R, Serby M, Klutchko B, et al: ECT and Parkinson's disease revisited: a "naturalistic" study. Am J Psychiatry 1989; 146:1451–1455