Neurosurgical forum
Letters to the editor

Deep brain stimulation interruption and suicidality

To the Editor: In this issue of the Journal, Lozano et al. (Lozano AM, Giacobbe P, Hamani C, et al: A multicenter pilot study of subcallosal cingulate area deep brain stimulation for treatment-resistant depression. Clinical article. J Neurosurg 116:315–322, February 2012) illustrate the efficacy of deep brain stimulation (DBS) of the subcallosal gyrus in 21 patients with treatment-resistant major depression. Of these 21, 13 patients had at least a 40% improvement in scores on the 17-item Hamilton Depression Rating Scale–17 (HDRS-17) at 1 year. On two occasions, one patient unknowingly experienced deactivation of the implanted pulse generator. The first time deactivation occurred the individual attempted suicide. The second time, which occurred following submission of Lozano and colleagues’ article, provoked a depressive relapse with active suicidal thoughts. This is the first report of suicidality prompted by discontinuation of therapeutic DBS of which we are aware.

The patient is a woman in her late 40s who experienced the first onset of depressive symptoms in her mid-30s. She originally presented with low mood with diurnal variation (morning worsening), poor concentration, anhedonia, low energy, loss of appetite, increased need for sleep, and intermittent suicidal ideation. She described prominent comorbid generalized anxiety. She reported a positive family history of both generalized anxiety and obsessive-compulsive disorder (OCD). Medical comorbidities included hypothyroidism, gastroesophageal reflux disease, chronic temporomandibular joint pain, and a history of deep vein thrombosis and pulmonary embolism. Therapeutic interventions over a period of 12 years included pharmacotherapy with multiple agents including selective serotonin reuptake inhibitors, tricyclic antidepressants, lithium, monoamine oxidase inhibitors, and atypical antipsychotics. The patient also underwent several courses of electroconvulsive therapy limited by relapses and memory impairment. Group and individual cognitive-behavioral therapy, in addition to long-term supportive therapy, did not provide a sustained antidepressant response. There were multiple suicide attempts by overdose, usually in response to psychosocial stressors, at a frequency of approximately 2 per year.

The patient gave written informed consent to participate in a pilot study of DBS, approved by the Clinical Research Ethics Board of the University of British Columbia. During implantation of the device and intraoperative testing, she reported a lightening of her mood with the electrode contacts in the target region. Over the initial months following initiation of stimulation of the white matter adjacent to the subcallosal gyrus, she exhibited a gradual response, with symptomatic improvement in her depressive symptoms. At a follow-up appointment 6 months after onset of stimulation, her HDRS-17 score had decreased to 40% of her pre-DBS baseline score. In addition, her cognitive-intellectual function appeared to be gradually improving. Eighteen months following the initiation of stimulation, her HDRS-17 score was 13, putting her in the mildly depressed range, which was an improvement of 63% over a baseline score of 35.

Despite her overall improved mood, she still noted suicidal ideation but only in the context of severe psychosocial stressors. For example, on one occasion in the 1st year of stimulation, when overwhelmed by a number of deadlines and in the context of a family conflict, she took an overdose of acetaminophen, ibuprofen, diphenhydramine, dimenhydrinate, and aspirin. Following the resolution of the stressors, she returned to her overall improved mood state within a number of weeks. However, 26 months following the initiation of stimulation, in the absence of any evident psychosocial stressors, she was taken to the emergency department following an overdose of 250 tablets of clonazepam. One week prior she had seen her regular psychiatrist who noted continual progress with regard to her mood, coping mechanisms, and overall functioning. Five days after the overdose, when the patient’s implantable pulse generator for the DBS was assessed, battery depletion was registered and the device was off. Her depressive symptoms improved within 2 weeks of an expedited battery replacement.

Fifty-six months following the initiation of stimulation, the patient was shopping at a store with a magnetic theft detection device. She experienced a rapid mood deterioration characterized by a loss of motivation, social isolation and avoidance, and increased abdominal discomfort, with no significant change in her neurovegetative functioning or any notable increase in anxiety. She became actively suicidal for the first time in many months. She interrogated her device and found it to be deactivated. Her mood stabilized within 24 hours of her reactorivating the device.

The first study demonstrating the efficacy of DBS in treating refractory depression reported that 4 of 6 patients experienced clinical benefit at 6 months following initiation of DBS of the subcallosal gyrus. The investigators attempted, with consent, a blinded discontinuation of stimulation in one patient who then had a subsequent relapse in depressive symptomatology, including a loss of energy and initiative and impaired concentration, which was reversed within 48 hours of reactivation. Similarly, 6 patients receiving DBS of the anterior limb of the internal capsule for refractory OCD disclosed rapid moderate clinical worsening in depressive symptoms while unaware of stimulator battery depletion. Symptom reversal coincided with resumption of stimulation. Finally, in
a patient in whom benefit was reported with DBS of the ventral caudate nucleus for OCD and depression, worsening of his obsessive-compulsive symptomatology and functionality occurred after his pulse generator battery unknowingly failed. Somatic preoccupations and checking compulsions were reported to stabilize 3 months after replacement of the battery.1

Controlled studies will be necessary to rigorously demonstrate the efficacy of DBS of the white matter adjacent to the subcallosal gyrus in the treatment of refractory depressive illness. Although we cannot rule out spontaneous worsening of depression, this case offers indirect supportive evidence of the therapeutic effects of subcallosal stimulation reported in the multicenter pilot study in this issue. This patient’s unique experiences remind us that, in a population highly susceptible to suicide, it is prudent to regularly and carefully monitor stimulation status. For most cases of DBS used in the treatment of psychiatric conditions, the available data suggest that loss of benefit from pulse generator failure is rapid. Because these individuals are vulnerable to suicidal ideation and self-injurious behavior, a deactivation of the pulse generator, similar to that seen in movement disorders,3 should be considered a medical emergency.

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Low-grade gliomas

To The Editor: The interesting retrospective study of Chang and colleagues2 (Chang EF, Clark A, Smith JS, et al: Functional mapping–guided resection of low-grade gliomas in eloquent areas of the brain: improvement of long-term survival. Clinical article. J Neurosurg 114:566–573, March 2011) indicates that functional intraoperative mapping methods may help to identify low-grade gliomas potentially accessible via gross-total resection. In some cases the authors assumed a not-completely-resectable tumor preoperatively and then realized intraoperatively via a functional mapping technique that the tumor was resectable. The variable resectability, as defined by preoperative imaging and/or intraoperative mapping, turned out to be of favorable prognostic influence; that is, patients with resectable tumors fared better in terms of progression-free survival and duration of survival. A finding like this may help to improve classification, prognostic evaluation, and management strategies of a highly heterogeneous disease and therefore be considered in prognostic models beside other clinical and molecular-genetic covariates. It might be tempting to assume—as suggested in the accompanying editorial by Sampson— that the described prognostic impact of resectability promotes a concept of aggressive resection for all low-grade gliomas. An attempt in this direction, however, is based on a misinterpretation of the data of Chang and colleagues.2 Resectable tumors are more likely to be anatomically circumscribed, of small size, and located in less eloquent regions, and they might behave in a different manner biologically. They should not be confused with their counterparts, for example, tumors growing diffusely along U-fibers, infiltrating several regions of a hemisphere including eloquent ones. Notably, only 153 of 281 gliomas surgically treated in the series turned out to be resectable gliomas.2 Given the fact that the median relative extent of resection was only in the range of 30%–60% in the poor prognosis group (as compared with > 90% in the resectable group), one might question the concept of microsurgical volume reduction in terms of the efficacy and risk of the applied procedure. Indeed, histological and molecular-genetic classification could be determined in these patients by partial open tumor resection—although small anaplastic foci might be missed even then unless detected and localized beforehand by sophisticated imaging procedures. However, a similar or even better classification and characterization of these lesions with their complex locations and compositions might be achieved using a minimally invasive molecular stereotactic biopsy technique (as demonstrated previously).3,5 Thus, inspired by the data of Chang and colleagues,2 we consider any scientific attempt extremely