Surgery for intractable neuropsychiatric illness has generated considerable controversy for a variety of scientific, social, and philosophical reasons. Much of the controversy relates to the widespread and indiscriminate use of psychosurgery in the 1940s and 1950s when no effective psychotropic agents were available. With the introduction of chlorpromazine in 1954, effective medical management led to a rapid decline in surgery for mental illness. Despite the vast array of new, selective psychotropic medications available today, however, many neuropsychiatric illnesses remain refractory and, consequently, some patients remain severely disabled. These patients might be considered appropriate candidates for surgery if the overall result and level of functioning could be improved.

Ablative neurosurgical procedures continue to be performed at a handful of centers in a very limited number of patients with obsessive–compulsive disorder (OCD) and major depression that have proved completely refractory. Although data from modern prospective surgical series have demonstrated that a substantial percentage of patients experience improvement following anterior cingulotomy, anterior capsulotomy, or limbic leukotomy, there remains considerable resistance to surgery because it is ablative and irreversible.

On the other hand, deep brain stimulation (DBS), which has been widely used in surgery for Parkinson disease, is both reversible and adjustable. In fact, the reversibility of DBS has allowed neurosurgeons to explore targets in many different locations in the brain with enhanced safety, and therefore it seems appropriate to consider DBS in the treatment of patients with neuropsychiatric illness. The case report presented by Aouizerate, et al., is a good example of these early efforts.

The authors should also be congratulated on their thoughtful evaluation, meticulous implementation, and rigorous assessment of this single case study. The unfortunate man clearly suffers from chronic, severe, and disabling OCD together with major depression. The case study was approved and overseen by the local Institutional Review Board and a committee of multidisciplinary physicians including two psychiatrists, a neurologist, and a neurosurgeon. Published criteria for intractable OCD were met by ensuring that the patient had been treated at maximally tolerated doses of at least five of the selective serotonergic reuptake inhibitors for a minimal duration of 10 weeks as well as augmented doses of buspirone hydrochloride and lithium carbonate. The preoperative psychiatric assessment included a structured clinical interview and baseline measurements on clinically validated rating scales: Yale–Brown Obsessive Compulsive Scale (Y-BOCS), Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale (HARS), and Global Assessment of Functioning. Independent assessment by unbiased observers at 3-month intervals was performed using appropriate criteria for outcome, namely a 50% improvement on the HDRS and the HARS and a greater than 35% improvement on the Y-BOCS.

Although the authors report on only one case, the results are encouraging: a clinically significant remission of depressive symptoms after 6 months of DBS followed by a clinically significant response in the symptoms of OCD after 12 months of DBS. The latency period to improvement was quite similar to what we have observed in patients who have undergone cingulotomy for OCD. What is especially impressive in this case report is that no pharmacological treatments were administered during DBS, whereas they are always continued in patients undergoing ablative surgery. In general, surgery is considered only as an adjunct to appropriate care, and ongoing pharmacological and behavioral therapies are often essential for continued remission.

The authors should also be commended on the detailed neuropsychological testing that was performed at baseline, at the 1-month follow up, and the 6-month follow up, the results of which convincingly demonstrate a cognitive performance unimpaired by DBS. In fact, if anything, there appears to be an improvement in certain cognitive abilities during DBS, which raises many scientific and even philosophical issues.

Deep brain stimulation has substantially changed the face of stereotactic and functional neurosurgery by allowing us to explore discrete subcortical gray and white matter targets
Editorial

that had previously been thought too dangerous to manipulate. It is a technology and methodology that is now reliable, dependable, and familiar to both physicians and the patient. Most importantly, the concept of “stimulation” compared with “ablation” has clearly reduced the psychological barrier in the patient and in the referring neurologists and psychiatrists.

Data from this case report adds to the initial favorable findings reported by Nuttin, et al.,1 in four patients with severe OCD who had undergone bilateral DBS of the anterior capsule. Three of the four patients experienced a favorable response. This promising but limited experience has prompted a Phase I clinical trial of DBS in 15 patients with severe refractory OCD. Enrollment in this study has been completed, but the results are not yet available. Nevertheless, several important observations have already been made, including the fact that in most cases both the patients and the evaluators know when DBS is on and thus it is impossible to perform a truly blinded study. Many patients undergoing DBS appear more alert, spontaneous, less anxious, and less depressed. It is clear that the earliest improvement occurs in the affective component of the patient’s disease rather than the obsessive-compulsive symptoms. If improvement in OCD occurs (as indicated by an improved score on Y-BOCS), it will be sustained if DBS is continued. If there is any failure in delivery of the stimulation or if the battery fails, however, the improvement will be lost and often the patient experiences a psychiatric emergency characterized by a sudden, profound depression of mood and reactivation of the OCD. Note that the optimal effect of stimulation appears to be contact-dependent.

Deep brain stimulation is currently accepted in the treatment of tremor, Parkinson disease, dystonia, and pain, but moral, ethical, social, scientific, and philosophical concerns have been raised about using DBS for psychiatric indications. Most practitioners realize that many of the disorders for which we use DBS have a variety of neuropsychiatric manifestations, and therefore the difference between purely neurological and psychiatric indications seems artificial and unwarranted. This fact does imply that an honest and rigorous assessment of the risks of intervention balanced against the potential benefits of treatment must be discussed with any patient and that the patient must be able to give his or her informed consent. The latter remains the critical issue in the decision-making process. Fortunately, most of the patients with severe refractory OCD and major depression are completely aware of their circumstances and able to render informed consent.

A multitude of significant issues remains regarding the use of DBS for neuropsychiatric illness. The optimal targets, stimulation parameters, and long-term effects remain unknown. The exact mechanisms of DBS and how it alters cerebral function also remain a mystery. The procedure is expensive and requires an enormous amount of time on the part of the practitioners, both preoperatively and postoperatively for programming and case management. Another important consideration is that DBS is device based, and currently there is only one supplier of the technology. We must therefore be ever mindful of potential conflicts of interest and maintain the highest professional, moral, and ethical standards throughout the coming years.

In conclusion, it appears that the preliminary experience with DBS for neuropsychiatric illness is encouraging; however, it remains experimental and investigational at this time. Although more than 25,000 DBS procedures have been performed worldwide, only approximately 25 have been intended for neuropsychiatric indications. Because the early results seem so promising, we can proceed thoughtfully and cautiously, but we must guard against repeating the mistakes that characterized the lobotomy era. In this regard, DBS for psychiatric illness should only be performed by experienced and expert multidisciplinary teams of psychiatrists, neurologists, and neurosurgeons. It is the responsibility of these teams to select appropriate patients and to ensure the accuracy of the psychiatric diagnosis and the completeness of pharmacological and behavioral therapies. All of these activities should be performed only with Institutional Review Board approval and only in patients who are able to give informed consent. The procedure should be conducted only to relieve a patient’s suffering and to restore more normal function—not for political or social purposes or for the enhancement of function. Outcomes must be assessed using clinically validated rating scales so that comparisons can be made across centers and with respect to different targets, stimulation parameters, contacts, and so forth.

Deep brain stimulation may provide a unique opportunity to help patients who suffer horribly from the consequences of severe depression and OCD. It may also provide an opportunity to explore mechanisms of brain function and unravel certain mysteries of the human mind. These early efforts must go forward only with the highest ethical, moral, and scientific standards to ensure that this historic opportunity is not wasted. Much is at stake.

Reference


RESPONSE: We sincerely thank Dr. Cosgrove for his editorial focusing on the novel indications of DBS in chronic severely incapacitating refractory forms of OCD and major depression. Despite noticeable advances in psychopharmacology, a significant percentage of these disease entities fail to respond favorably to pharmacotherapy alone or in combination with psychological treatments. In this context, different lesion-producing techniques for the management of intractable forms of OCD and major depression have been shown to have significant benefit in patients, with relatively few serious or undesirable effects. Note, however, that DBS is becoming especially interesting because this surgical procedure is reversible, adjustable, and offers new opportunities in terms of targeting brain regions that cannot be reached using the ablative techniques (for example, the nucleus accumbens and subthalamic nucleus).

A surprising result in the case we report on is the differential effects of DBS over time, with improvement in depressive symptoms occurring within the first 3 months, remission at 6 months, and the delayed antidepressive response at 12 months. These effects indicate the involvement of distinct neuronal networks within the frontal-subcortical loops in either OCD or major depression. Interestingly, perhaps the functional reorganization within the neuronal networks more specifically involved in OCD.