Modern Neurosurgery for Psychiatric Disorders

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OBJECTIVE: The evolution, rationale, and results of modern functional neurosurgery to treat psychiatric disorders are documented. The potential benefits of neurosurgical treatment for selected, critically ill, psychiatric patients are considered.

METHODS: The history, anatomic features, and evolution of and contemporary indications for the four currently used procedures (cingulotomy, subcaudate tractotomy, limbic leukotomy, and capsulotomy) are reviewed. Available outcome, neuropsychological assessment, and functional imaging data are presented.

RESULTS: Recently, there has been a renaissance of interest in the surgical treatment of psychiatric disease. Modern psychiatric neurosurgical procedures are quite safe, with extremely low surgical mortality rates and transient postoperative morbidity. In selected cases, patients with conditions that had previously been completely refractory to comprehensive medical and behavioral intervention demonstrated significant improvement. This improvement was usually observed in the absence of long-term adverse neuropsychological consequences.

CONCLUSION: Recent outcome studies, together with advances in neurobiology, psychiatry, functional imaging, and stereotaxy, support the further investigation of modern functional neurosurgical procedures to treat psychiatric disorders and their application for a subset of psychiatric patients with conditions refractory to all other therapies. (Neurosurgery 47:9–23, 2000)

Key words: Capsulotomy, Cingulotomy, Limbic leukotomy, Psychosurgery, Subcaudate tractotomy

Psychiatric neurosurgery (“psychosurgery”), i.e., functional neurosurgery to treat psychiatric disorders, occupied a central but controversial position in psychiatric treatment for several decades beginning in the 1940s and early 1950s, especially in the United States. Gottlieb Burckhardt, a Swiss psychiatrist who first reported the results of cortical excisions for psychiatric patients in 1891 (19), is considered the founder of psychosurgery. Later, inspired by the effects of frontal cortical ablation on primate behavior reported in 1935 by Fulton and Jacobsen (36), the Portuguese neurologist Egas Moniz, together with his neurosurgeon colleague Almeida Lima, performed the first prefrontal leukotomies (severing of white matter tracts) for psychiatric patients (84). The operations performed by Moniz, in addition to earning him a retrospectively controversial Nobel Prize in 1949, served as a stimulus for similar operations in the United States, which were initiated and popularized by the neurologist Walter Freeman and the neurosurgeon James Watts. The Freeman-Watts frontal lobotomy or leukotomy was a closed operation in which leu kotomes were inserted bilaterally through 1-cm burr holes on both sides of the frontal area and were swept back and forth to sever white matter tracts (35). The main indications for this operation were intractable mental illnesses such as schizophrenia, depression, anxiety, or obsessive-compulsive disorder (OCD). However, with such blind leukotomies marked side effects often occurred, including hemorrhage, epilepsy and the “frontal lobe syndrome,” which was characterized by apathy, impulsivity, and labile affect. Both the often-unacceptable side effects of this treatment and the advent of psychotropic drugs, beginning with the introduction of chlorpromazine in 1954, led to waning enthusiasm for psychosurgery; however, it was increasingly realized that severe side effects accompanied chemotherapeutic approaches as well (in particular, the tardive dyskinesia observed with neuroleptic agents). Therefore, in the 1960s there was a revival of interest in psychosurgery, in the context of the greater precision afforded by the continuing evolution of stereotactic principles. In particular, during the 1960s, stereotactic limbic operations were developed and refined in the attempt to treat refractory affective disorders. Despite the refinement of these procedures and the accompanying reduction in side effects compared with those observed for the
original frontal lobotomies, public outcry against psychosurgery in the 1970s led to such political and social pressures that psychiatrists and neurosurgeons were effectively proscribed from recommending and performing these procedures. This “rise and fall” of psychosurgery has been extensively chronicled (5, 30, 62, 73, 97, 116, 117). In response to public concern, a national commission on psychosurgery was convened in the late 1970s. This commission issued a remarkably favorable report on psychosurgery, while recommending that it be a treatment of last resort not to be performed for minors, prisoners, or patients incapable of giving informed consent (28, 86). Despite this favorable report, in the 1980s and 1990s psychiatric surgery fell out of public view and largely also out of general medical and psychiatric practice. However, psychiatric surgery survives (14, 21, 89, 93, 102), and it is the purpose of this review to document the nature and efficacy of procedures currently in use.

MODERN OPERATIONS, INDICATIONS, AND OUTCOMES

In the 1980s and 1990s, only a few centers around the world consistently performed neurosurgical operations for psychiatric disorders. These included centers in Boston (6), London (16), Sydney (41), Stockholm (75), Madrid (20), and Belgium and the Netherlands (27). Each center tended to perform and study one type of psychosurgical procedure for specific psychiatric indications. Below is a summary of the most common currently performed procedures, together with indications and outcome study findings regarding efficacy.

Selection of lesion sites

The selection of lesion sites in psychiatric disorders was greatly influenced by the proposal of an anatomic basis of emotions in 1937 by Papez (91). Papez hypothesized that emotional stimuli passed, via the cingulum bundle (in the cingulate gyrus), from the septum to the hippocampus and then, via the fornix, to the hypothalamus (mammillary bodies), from the hypothalamus to anterior thalamic nuclei, and from thalamic radiations back to the cingulate gyrus (the “Papez circuit”) (Fig. 1). Later, MacLean (69, 70) designated the structures comprising the phylogenetically older rim of the cortex around the brainstem and their connections the limbic system and emphasized the association of this system with emotion and visceral functions. These general hypotheses regarding the anatomic features of emotion subsequently gained broad experimental support from a multitude of anatomic, lesion, and stimulation studies in animals and human patients. Each of the currently performed surgical procedures (Table 1) targets the Papez circuit directly (anterior cingulotomy), connections between the frontal cortex and the limbic system (subcaudate tractotomy and capsulotomy), or both (limbic leukotomy).

Anterior cingulotomy

The anterior cingulum was first suggested as a psychosurgical target by Fulton in 1947, on the basis of evidence that stimulation of the anterior cingulum in monkeys produced autonomic responses of a type associated with emotion and that lesions in this region resulted in less fearful and aggressive animals (107, 120). The following year (1948), Sir Hugh Cairns at Oxford introduced the bilateral open cingulotomy (122). This operation involved a craniotomy, followed by observation and resection of a portion of the cingulum. Cingulotomy was noted to be effective in reducing affective and obsessional symptoms and demonstrated fewer side effects on personality and behavior than did the earlier frontal lobotomies (122). Later, Foltz and White (34) and Ballantine et al. (7) used air ventriculography to observe the cingulum, allowing stereotactic ablation of that structure via small bilateral burr holes and eliminating the need for open craniotomies. Ventriculography has more recently been replaced with magnetic resonance imaging (MRI)-guided stereotactic techniques (26). In the procedure developed by Ballantine and colleagues (25, 72), thermistor electrodes are placed in the cingulum bilaterally and heated to 85°C for 90 seconds, producing lesions that are 1 cm in diameter and 2 cm in height and span the cingulum bundle (thermocoagulation) (Fig. 2).

In the past 20 years, the primary site of psychiatric surgery in the United States has been the Massachusetts General Hospital in Boston, where an interdisciplinary team (the Massachusetts General Hospital Cingulotomy Unit) under the direction of the late H. Thomas Ballantine (now under the direction of Dr. G. Rees Cosgrove) has studied stereotactic bilateral anterior cingulotomy (25). The primary indication for this procedure has been medically intractable OCD, but some patients with treatment-refractory chronic anxiety and major affective disorders have also been considered. Cingulotomy, which seems to reduce the affective component of the experience of pain, has also been used effectively by other investigators for the treatment of chronic pain states (123). All patients accepted for treatment are required to pass stringent preoperative assessments. The referring psychiatrist must complete a questionnaire and a written statement to document that the patient has experienced failure of intensive nonsurgical treatment, including behavioral and pharmacological therapies. This material is assessed at the Massачus-
TABLE 1. Summary of Procedures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Target</th>
<th>Rationale</th>
<th>Current Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior cingulotomy</td>
<td>Anterior cingulum</td>
<td>Disconnect Papez circuit</td>
<td>Affective disorders, OCD, anxiety disorders</td>
</tr>
<tr>
<td>Subcaudate tractotomy</td>
<td>Frontobasal white matter</td>
<td>Disconnect frontolimbic connections</td>
<td>Affective disorders, OCD, anxiety disorders, OCD, affective disorders</td>
</tr>
<tr>
<td>Limbic leukotomy</td>
<td>Anterior cingulum and frontobasal white matter</td>
<td>Cingulotomy + subcaudate tractotomy</td>
<td>OCD, anxiety disorders, panic disorder</td>
</tr>
<tr>
<td>Capsulotomy</td>
<td>Anterior limb of internal capsule</td>
<td>Disconnect frontolimbic and caudate-putaminal connections</td>
<td>OCD, anxiety disorders, panic disorder</td>
</tr>
</tbody>
</table>

*OCD, obsessive-compulsive disorder.

FIGURE 2. Postoperative sagittal (A) and coronal (B) T1-weighted MRI scans obtained after cingulotomy (reprinted with permission from, Spangler WJ, Cosgrove GR, Ballantine HT, Cassem EH, Rauch SL, Nierenberg A, Price BH: Magnetic resonance image-guided stereotactic cingulotomy for intractable psychiatric disease. Neurosurgery 38:1071–1076, 1996 [109]).

In 1987, Ballantine et al. (6) reported the results from a 24-year retrospective study of 198 patients who underwent anterior cingulotomy, with a mean follow-up period of 8.6 years (Table 2). For these patients, extensive trials of psychotherapy, pharmacotherapy, and electroconvulsive therapy had failed. Most of these patients had a major affective disorder (unipolar, bipolar, or schizoaffective) or OCD, but a few patients had anxiety disorders, schizophrenia, or personality disorders. Clinical evaluations were conducted preoperatively and during long postoperative follow-up periods, using a categorical functional/symptomatic rating scale. Using this scale, 123 of 198 patients (62%) demonstrated long-term improvements after cingulotomies. The degree of improvement was related to the diagnosis; efficacy was greatest for affective and anxiety disorders, intermediate for OCD, and least for schizophrenia and personality disorders.

An important result from the study reported by Ballantine et al. (6) was that this procedure was demonstrated to be extremely safe. There were no surgery-related deaths, and postoperative complications were limited to medication-responsive seizures (1%), hemiplegia (0.3%), and suicide (9%). It is notable that all 18 patients lost to suicide had reported preoperative suicidal ideation and 13 had made preoperative suicide attempts. This suicide rate of 1%/yr is similar to the rate observed by Pokorny (92) for high-risk patients with affective disorders. Notably, nearly one-half of the patients required more than one operation.

Importantly, a detailed prospective neuropsychological study of a cohort of these patients was performed for the United States government by an independent group at the Massachusetts Institute of Technology, directed by Suzanne Corkin, in 1977 (114) (Table 3). That group observed that, in contrast to early frontal lobotomies, there was no evidence of diminution of intellectual function or emotional tone for these patients. Indeed, the study noted no evidence of neurological or behavioral deficits (except a decline in Taylor Complex Figure task performance for patients more than 40 yr of age) and actually demonstrated postoperative gains in Wechsler intelligence quotient scores (24). However, a more recent study of 12 patients who underwent cingulotomies for control of chronic pain demonstrated mild impairment of sustained attention after cingulotomy (22).

The subset of cingulotomy-treated patients with OCD has been studied more carefully. In a long-term retrospective follow-up study of 33 patients with OCD who had undergone cingulotomies at Massachusetts General Hospital between 1965 and 1986, Jenike et al. (48) estimated, using conservative criteria, that 25 to 30% of patients benefited substantially from cingulotomy. However, only 18% of those patients had undergone trials of clomipramine hydrochloride and only 9% had undergone trials of behavioral therapy before surgery. Therefore, the authors began a prospective study limited to patients who had undergone appropriate but unsuccessful trials of both medical and behavioral therapy. They recently reported the results of a prospective study of 18 patients in this category who had undergone cingulotomies at Massachusetts General Hospital since 1989, using a variety of symptom-rating scales and global assessment of function (3). Outcomes were assessed with clinical global improvement ratings, as well as psychometric scales (Yale-Brown Obsessive-Compulsive Scale [38] and Beck Depression Inventory [10]), both before cingulotomy and a mean of 7 months and 26.8 months after cingulotomy. In that study, the authors noted that 28% of patients met conservative criteria for clinical im-
### TABLE 2. Summary of Results from Selected Psychiatric Surgery Studies

<table>
<thead>
<tr>
<th>Series (Ref. No.)</th>
<th>No. of Patients</th>
<th>Diagnoses</th>
<th>Procedure</th>
<th>Complications</th>
<th>Outcome Method</th>
<th>Follow-up Period</th>
<th>Patients with Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herner, 1961 (43)</td>
<td>116</td>
<td>OCD, other diagnoses</td>
<td>Capsulotomy</td>
<td>Epilepsy (3.4%), incontinence, weight gain</td>
<td>Categorical rating scale, psychometric test battery</td>
<td>2–7 yr</td>
<td>50% (OCD), 53% (depression), 27% (schizophrenia), 20% (anxiety)</td>
</tr>
<tr>
<td>Kelly et al., 1977 (52)</td>
<td>66</td>
<td>OCD, anxiety, depression, schizophrenia</td>
<td>Limbic leukotomy</td>
<td>Postoperative confusion and lethargy, transient incontinence</td>
<td>Categorical rating scale, psychiatric rating scales</td>
<td>6 wk</td>
<td>67% (best for OCD and depression)</td>
</tr>
<tr>
<td>Kelly and Mitchell-Heggs, 1973 (50)</td>
<td>30</td>
<td>OCD, anxiety, depression, schizophrenia</td>
<td>Limbic leukotomy</td>
<td>Postoperative confusion and incontinence, increased wakefulness</td>
<td>Categorical rating scale, psychiatric rating scales</td>
<td>Mean, 17 mo</td>
<td>80% (best for OCD and depression)</td>
</tr>
<tr>
<td>Goktepe et al., 1975 (37)</td>
<td>159</td>
<td>Affective disorders, OCD, anxiety</td>
<td>Subcaudate tractotomy</td>
<td>Personality changes (7%), epilepsy (2.2%)</td>
<td>Categorical functional scale, psychiatric rating scales</td>
<td>Mean, 2.3 yr</td>
<td>68% (affective disorders), 62.5% (anxiety), 50% (OCD)</td>
</tr>
<tr>
<td>Mitchell-Heggs et al., 1976 (62)</td>
<td>35</td>
<td>OCD</td>
<td>Capsulotomy</td>
<td>Categorical rating scale</td>
<td>Mean, 3 yr</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>Bingley et al., 1977 (11)</td>
<td>24</td>
<td>OCD, anxiety</td>
<td>Capsulotomy</td>
<td>Categorical rating scale</td>
<td>Mean, 7 yr</td>
<td>73%</td>
<td></td>
</tr>
<tr>
<td>Kullberg, 1977 (59)</td>
<td>85</td>
<td>OCD</td>
<td>Capsulotomy</td>
<td>Categorical rating scale</td>
<td>Mean, 7 yr</td>
<td>73%</td>
<td></td>
</tr>
<tr>
<td>Burzaco, 1981 (20)</td>
<td>26</td>
<td>OCD, anxiety, depression, schizophrenia</td>
<td>Capsulotomy</td>
<td>Postoperative confusion and affective dysfunction with capsulotomy</td>
<td>Categorical rating scale</td>
<td>Mean, 7 yr</td>
<td>73%</td>
</tr>
<tr>
<td>Fodstad et al., 1982 (33)</td>
<td>4</td>
<td>OCD</td>
<td>Capsulotomy</td>
<td>Categorical rating scale</td>
<td>Mean, 7 yr</td>
<td>73%</td>
<td></td>
</tr>
<tr>
<td>Ballantine et al., 1987 (6)</td>
<td>198</td>
<td>Affective disorders, OCD, anxiety, schizophrenia, personality disorders</td>
<td>Cingulotomy</td>
<td>Seizures (1%), hemiplegia (0.3%), suicide (9%)</td>
<td>Categorical functional scale, global psychiatric/social status</td>
<td>Mean, 8.6 yr</td>
<td>123/198 (62%) (better for affective disorders, medium for OCD, worse for schizophrenia and personality disorders)</td>
</tr>
<tr>
<td>Puynton et al., 1988 (95)</td>
<td>9</td>
<td>Bipolar disorder</td>
<td>Stereotactic subcaudate tractotomy</td>
<td>Categorical rating scale</td>
<td>Mean, 13.1 yr</td>
<td>25–30%</td>
<td></td>
</tr>
<tr>
<td>Jenike et al., 1991 (48)</td>
<td>33</td>
<td>OCD</td>
<td>Cingulotomy</td>
<td>Categorical rating scale</td>
<td>Mean, 13.1 yr</td>
<td>25–30%</td>
<td></td>
</tr>
<tr>
<td>Hay et al., 1993 (42)</td>
<td>26</td>
<td>OCD</td>
<td>Limbic leukotomy</td>
<td>Categorical rating scale</td>
<td>Mean, 10 yr</td>
<td>38%</td>
<td></td>
</tr>
<tr>
<td>Bridges et al., 1994 (16); Hodgkinson et al., 1995 (44)</td>
<td>249</td>
<td>Major affective disorder, OCD, anxiety</td>
<td>Stereotactic subcaudate tractotomy</td>
<td>Postoperative disorientation (10%) that resolved by 1 mo, seizures, (1.6%), suicide (1%)</td>
<td>Global functional scale, symptom-rating scales</td>
<td>1 yr</td>
<td>34% (similar for all diagnoses)</td>
</tr>
<tr>
<td>Baer et al., 1995 (3)</td>
<td>18</td>
<td>OCD</td>
<td>Cingulotomy</td>
<td>Categorical rating scale</td>
<td>Mean, 7 and 26.8 mo</td>
<td>28%</td>
<td></td>
</tr>
<tr>
<td>Spangler et al., 1996 (109)</td>
<td>34</td>
<td>Affective disorders, OCD</td>
<td>Cingulotomy</td>
<td>Seizures (6%)</td>
<td>Categorical rating scale</td>
<td>Mean, 17 mo</td>
<td>38%</td>
</tr>
</tbody>
</table>

* OCD, obsessive-compulsive disorder.

...improvement, consistent with the results of their previous retrospective study (48).

The most recent report from the Massachusetts General Hospital group describes its experience since 1991 with MRI-guided stereotactic cingulotomies performed for 34 patients with OCD or major affective disorders (109). With categorical ratings, results for the MRI-guided procedures were similar to those of previous studies (38% responders, 23% possible responders, and 38% nonresponders). From that study and the aforementioned studies, those authors concluded that more than one-quarter of patients with OCD that is intractable to all other treatment methods might be helped by cingulotomy.
TABLE 3. Neuropsychological Outcome Studiesa

<table>
<thead>
<tr>
<th>Series (Ref. No.)</th>
<th>No. of Patients</th>
<th>Diagnoses</th>
<th>Procedure</th>
<th>Assessment Periods</th>
<th>Neuropsychological Tests Performed</th>
<th>Positive Results</th>
<th>Negative Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teuber et al., 1977 (114);</td>
<td>57</td>
<td>Depression, anxiety, schizophrenia, OCD, OCD, anxiety, schizophrenia, OCD, OCD, chronic pain</td>
<td>Capsulotomy vs cingulotomy</td>
<td>Preoperatively and several weeks to months postoperatively</td>
<td>Comprehensive battery of cognitive, sensory, and motor tests</td>
<td>Postoperative gain in Wechsler IQ score</td>
<td>Decline in Taylor Complex Figure task for patients older than 30 years</td>
</tr>
<tr>
<td>Corkin et al., 1979 (24)</td>
<td></td>
<td>Variety of diagnoses</td>
<td>Capsulotomy</td>
<td>Preoperatively and 1–2 yr postoperatively</td>
<td>Cognitive tests (IQ, spatial memory, verbal memory)</td>
<td>No change in general intelligence</td>
<td>Capsulotomy interfered with verbal memory, cingulotomy with spatial memory in some patients</td>
</tr>
<tr>
<td>Vasko and Kulberg, 1979</td>
<td>37</td>
<td>Anxiety</td>
<td>Capsulotomy</td>
<td>Preoperatively and 1 yr postoperatively</td>
<td>Personality inventories, Rorschach test, Karolinska Scales of Personality</td>
<td>Decreases in anxiety, no adverse personality changes</td>
<td>Transient deterioration in recognition memory tasks in 2 wk assessment (correlated with edema in MRI scans)</td>
</tr>
<tr>
<td>Diedrichsen et al., 1991</td>
<td>23</td>
<td>Unipolar depression and bipolar disorder</td>
<td>Stereotactic subcaudate tractotomy</td>
<td>6–9 d preoperatively and 2 wk and 6 mo postoperatively</td>
<td>Comprehensive battery of tests including intelligence, memory, frontal and nonfrontal cognitive, speed, and attention tests</td>
<td>No long-term cognitive deficits</td>
<td></td>
</tr>
<tr>
<td>Mindus et al., 1988 (81)</td>
<td>9</td>
<td>Anxiety</td>
<td>Capsulotomy</td>
<td>Preoperatively and 1 yr postoperatively</td>
<td>Anxiety and OCD scales</td>
<td>Improvements on anxiety scales</td>
<td></td>
</tr>
<tr>
<td>Cumming et al., 1995 (29)</td>
<td>17</td>
<td>OCD</td>
<td>Limbic leukotomy</td>
<td>Preoperatively and mean 10 yr postoperatively</td>
<td>Cognitive battery including intelligence, memory, and cognitive association tests</td>
<td>No impairment of intellectual or memory function</td>
<td>Reduced scores on Wisconsin Card Sort Test</td>
</tr>
<tr>
<td>Poynton et al., 1995 (96)</td>
<td>23</td>
<td>Unipolar depression and bipolar disorder</td>
<td>Stereotactic subcaudate tractotomy</td>
<td>Preoperatively and 2 wk and 6 mo postoperatively</td>
<td>Hamilton and Beck depression scales, Taylor Manifest Anxiety Scale, Present State Examination</td>
<td>Decreases in depression rating scale scores, no change in anxiety scale scores</td>
<td></td>
</tr>
<tr>
<td>Cohen et al., 1999 (22)</td>
<td>12</td>
<td>Chronic pain</td>
<td>Cingulotomy</td>
<td>Preoperatively and 3 and 12 mo postoperatively</td>
<td>Attention, executive function, and response production tests</td>
<td>No long-term global deficits of attention or executive function</td>
<td>Impairment of response production and sustained attention</td>
</tr>
<tr>
<td>Mindus et al., 1999 (80)</td>
<td>19</td>
<td>Anxiety, OCD</td>
<td>Capsulotomy</td>
<td>Preoperatively and 1 and 8 yr postoperatively</td>
<td>Karolinska Scales of Personality</td>
<td>Improvements on anxiety scales at 8 yr postoperatively</td>
<td>1 patient with deviant score for psychopathic traits postoperatively</td>
</tr>
</tbody>
</table>

a OCD, obsessive-compulsive disorder; IQ, intelligence quotient; MRI, magnetic resonance imaging.

Subcaudate tractotomy

Stereotactic subcaudate tractotomy (SST) was introduced in 1964 by Geoffrey Knight (54, 55). This procedure was developed from his previous experience with restricted orbital undercutting, in which the goal was to interrupt white matter tracts between the orbitofrontal cortex and subcortical limbic structures (53). The original SST involved implantation of a row of radioactive yttrium (90Y) seeds to destroy tissue in the region of the substantia innominata, below the head of the caudate nucleus, in the ventromedial frontal lobes (Fig. 3). This destruction would presumably lesion relays to and from the posterior orbital cortex and subcortical structures such as the cingulate gyrus, amygdala, thalamus, and hypothalamus (56, 57). The seeds were implanted via a cannula attached to a stereotactic frame and produced lesions, by β-irradiation, to tissue up to 2 mm from the rod surface. Improvements after this procedure were initially observed for two-thirds of patients with depression or OCD (56, 57). In an early outcome review in 1975, Goktepe et al. (37) reported results for 208 patients, with a mean follow-up period of 2.5 years. Using a categorical outcome scale, those authors observed significant improvement in 68% of cases with depression, 62.5% with anxiety, and 50% with OCD.

In Britain, 20 to 30 psychosurgical procedures have been performed annually in the past decade (93, 94). The vast majority of these have been performed at the Geoffrey Knight National Unit for Affective Disorders (founded in 1970) at the Brook General Hospital in London, where approximately
1300 SSTs have been performed since 1961 (15). The surgical indications have included treatment-resistant major affective disorders (unipolar or bipolar), OCD, and chronic anxiety states. An interdisciplinary team pursues all nonsurgical options before patients are accepted for psychosurgical intervention. Their approach for treatment-resistant major depression, for example, includes a trial of first-line pharmacotherapy (e.g., selective serotonin reuptake inhibitors or tricyclic antidepressants), followed by second-line pharmacotherapy (e.g., lithium, clonazepam, carbamazepine, or monoamine oxidase inhibitors) and/or electroconvulsive therapy, followed by additional courses of antidepressant combinations, before surgery is considered (17).

Recently, Bridges and colleagues (16, 44) summarized their long experience with SST. Because responses to the procedure were generally delayed for 3 to 6 months, outcome analyses included both global clinical categorical and symptom-rating scale assessments performed 1 year after surgery. According to these criteria, SST allowed 40 to 60% of patients to lead “normal or near-normal lives” after surgery. Like cingulotomy, the greatest efficacy was observed for affective disorders (unipolar or bipolar depression) and the least for psychosis.

Like cingulotomy, SST has been largely free of major complications. The most troublesome short-term complication is transient postoperative disorientation, which is observed for approximately 10% of patients. This complication is thought to be related to postoperative edema (visible on MRI scans), which may last as long as 1 month. The most common long-term complications are seizures, which are observed for 1.6% of patients. In the experience of Knight and colleagues with approximately 1300 cases, there was only one death, which was the result of malpositioning of an yttrium seed in the striatum (57). The authors stated that they have not observed significant adverse effects on personality characteristics attributable to the operation, although early reports by Goktepe et al. (37) reported nondisabling personality changes for 7% of patients. The suicide rate among 303 SST patients who were monitored for 3 to 13 years after surgery was 1%, compared with the rate of 9% after stereotactic cingulotomy reported by Ballantine et al. (6) and rates as high as 15 to 30% for major affective disorders (39, 92).

Longer follow-up data and more detailed neuropsychological studies have been reported for subsets of these patients. Of nine female patients with bipolar disorder who were studied 2 to 4 years after SST, five demonstrated marked improvement and four demonstrated mild improvement, as assessed using categorical outcome scales (95). The first prospective study of the neuropsychological effects of this operation was reported in 1991. In that study (49), 23 patients who underwent SST were subjected to a battery of psychometric tests 6 to 9 days before surgery (preoperative assessment), 2 weeks after surgery (postoperative assessment), and 6 months after surgery (follow-up assessment). The main finding was that SST did not produce any significant long-term cognitive deficits. However, in the postoperative assessment, patients demonstrated transient deterioration in recognition memory tests and in card-sorting tests thought to be sensitive to frontal lobe dysfunction (74, 87). Both of these deficits were well correlated with the widespread postoperative frontal edema visible on MRI scans and, with the edema, were completely resolved by the 6-month follow-up examinations. In 1995, Poynton et al. (96) reported psychiatric outcome data for this same group of 23 patients, using a variety of rating scales for mental state assessments. Of these patients, 70% had unipolar depression and 30% had bipolar disorder. By the 6-month follow-up assessments, the group as a whole demonstrated significant decreases in scores on Hamilton (40) and Beck (10) depression-rating scales but no changes in scores on the Taylor Manifest Anxiety Scale (113). Prospective studies such as these are necessary to establish the efficacy of any form of psychiatric neurosurgery, and longer detailed follow-up studies are needed.

**Limbic leukotomy**

Limbic leukotomy, which was introduced by Kelly et al. (52) in 1973 and has since been used by Kelly’s group at Atkinson Morley’s Hospital in south London, combines bilateral cingulotomy with subcaudate tractotomy. The idea was that this dual-lesion technique would produce better functional results than either method alone. The ventromedial frontal lesion was targeted to interrupt frontolimbic connections (as with subcaudate tractotomy), whereas the cingulum lesion was targeted to interrupt the Papez circuit (51). Both lesions were created using either a cryoprobe or thermocoagulation (100). Original surgical indications included OCD, anxiety states, and depression, as well as some other psychiatric diagnoses (50, 52). In 1976, Kelly’s group assessed 66 patients a mean of 16 months after surgery, using a five-point global rating scale; according to their criteria, those authors noted improvement for 89% of patients with OCD, 66% of patients with chronic anxiety, and 78% of patients with depression (82). Isolated case studies reporting the efficacy of stereotactic limbic leukotomy in the treatment of Tourette’s syndrome are also interesting (98, 101), especially in relation to case reports of cingulotomies for patients with OCD complicated by Tourette’s syndrome (4, 61) and the notable similarities between Tourette’s syndrome and OCD (23).

Limbic leukotomy is much less commonly performed in Great Britain than subcaudate tractotomy. For example, 14 subcaudate tractotomies were performed in Britain in 1993, compared with only 1 limbic leukotomy (93). In Australia, a...
The initial results of capsulotomies for the treatment of schizophrenia (27% response) and chronic anxiety (20% response) were disappointing (43). However, the efficacy of capsulotomies for the treatment of OCD seems to be much better. A variety of outcome studies have reached the general conclusion that significant improvements are observed for approximately 70% of patients with intractable OCD who undergo capsulotomies (11, 20, 43, 75). Bingley et al. (11) demonstrated that capsulotomies allowed many previously intractable OCD patients to undergo a new psychiatric intervention for which sham control procedures are possible. Current inclusion criteria for capsulotomy include intractable obsessive-compulsive disorder (OCD), panic disorder of more than 5-year duration (75). Patients are accepted for capsulotomy if they give informed consent and agree to participate in pre- and postoperative evaluation and rehabilitation programs and if the referring psychiatrist is willing to accept responsibility for long-term postoperative care.

FIGURE 4. Postoperative axial (A) and coronal (B) T1-weighted MRI scans after radiosurgical (gamma knife) capsulotomy. Arrows, bilateral radiosurgical lesions in the anterior limb of the internal capsule (reprinted with permission from, Mindus P, Bergstrom K, Levander SE, Noren G, Hindmarsh T, Thuomas KA: Magnetic resonance images related to clinical outcome after psychosurgical intervention in severe anxiety disorder. J Neurol Neurosurg Psychiatry 50:1288–1293, 1987 [78]).
incapacitated patients to return to partial or full working capacity after surgery. The potential adverse effects of capsulotomy are of concern, however. Some patients seem to exhibit transient postoperative cognitive and affective dysfunction, manifested as decreases in cognitive and affective domains. Mindus and Jenike (76) claimed that, as for limbic leukotomy, this dysfunction was correlated with postoperative lesions visible on MRI scans and disappeared with resolution of the edema. Consistent with this hypothesis, a prospective study of personality changes after capsulotomy for nine patients, as assessed using personality inventories, Rorschach tests, and Karolinska Scales of Personality before and 1 year after capsulotomy, did not note significant adverse personality changes (81). In a larger study of 24 patients who underwent capsulotomy for treatment of anxiety disorders, Mindus and Nyman (77) did not observe adverse personality changes but instead noted marked improvements on anxiety scales. Longer-term follow-up data for 19 capsulotomy patients confirmed the stability of the psychiatric improvements and demonstrated no apparent increases in adverse personality changes with time (80). Taken together, the available studies suggest that capsulotomy seems to benefit more than one-half of patients with OCD that is intractable to all other treatments, with a low likelihood of adverse long-term consequences.

Comparison of procedures

A few studies have attempted to directly compare different procedures, in particular the efficacy of cingulotomy versus capsulotomy. One report of four patients with OCD claimed better efficacy for capsulotomy than for cingulotomy (33). Another study examined the efficacy of capsulotomy versus cingulotomy for 24 patients who were surgically treated between 1966 and 1974, with a minimal follow-up period of 1 year (59). For this small number of patients with OCD or anxiety, capsulotomy seemed to be more efficacious than cingulotomy but was accompanied by transient disturbances in cognitive and affective functioning in a significant proportion of the patients. In a subsequent study in which patients were assessed using specific cognitive tests, Vasko and Kullberg (119) observed no postoperative changes in general intelligence but concluded that capsulotomy tended to interfere with verbal memory, whereas cingulotomy tended to interfere with spatial tasks for some patients. In a review of 12 studies of surgical intervention in 253 cases of OCD, Waziri (121) estimated that, overall, 67% of patients exhibited significant improvement after surgery.

IMAGING STUDIES

Modern imaging has the potential to contribute substantially to defining the pathoanatomic basis of mental disorders. Moreover, imaging studies may be quite useful in determining the effects of various psychosurgical interventions. First, MRI may be used to document the specificity of surgical lesions, as well as delayed secondary effects (32, 79). Second, anatomic features of MRI scans obtained at various times after surgery can be correlated with clinical outcome. For example, Mindus et al. (78) demonstrated that the extent of lesion on MRI scans correlated with clinical improvement following capsulotomy in patients with severe anxiety disorder. In addition, a recent study of lesion topography after thermal or gamma knife capsulotomy successfully correlated anatomic lesion location within the anterior limb of the right internal capsule with efficacy independent of the treatment modality (67). Third, functional imaging studies may demonstrate the ability of various procedures to reverse metabolic brain abnormalities. This type of approach was pioneered in 1978 by Kullberg and Risberg (60), who used a 133Xe-inhalation method to demonstrate regional changes in cerebral blood flow after various psychosurgical operations. In a more recent example, Biver et al. (12) used positron emission tomography (PET) to pre- and postoperatively examine brain glucose metabolism in a 37-year-old woman who underwent SST for treatment of refractory OCD. Glucose metabolism has been shown to be abnormally high in the orbitofrontal cortex and caudate nucleus of patients with OCD (68, 99) and normalizes in these areas with pharmacotherapeutic interventions that are clinically effective (8, 111, 115). Similarly, in the report by Biver et al. (12), surgical treatment reduced glucose metabolism, as assessed with PET, maximally in the orbitofrontal cortex. In another study, the beneficial effects of SST for a patient with Tourette’s syndrome correlated with postoperative reduction of metabolism in the caudate nucleus, cingulate gyrus, and medial frontal lobe in PET scans (104). Studies such as these need to be expanded upon to validate PET or other imaging methods (such as functional MRI) as measures of efficacy of neurosurgical intervention in normalizing metabolism in specific brain areas. Of course, more detailed knowledge of specific metabolic abnormalities in psychiatric syndromes localized to specific brain areas by imaging will help refine operations and develop tools to measure the efficacy of surgical intervention.

DISCUSSION

Functional neurosurgery for psychiatric disorders once occupied an important, if controversial, place in the clinical treatment armamentarium. However, public outcry and political pressures led to its near-demise, despite the generally favorable report issued by the National Commission in 1977 (28). Despite remarkable advances in pharmacotherapy, the side effects of many drugs can be debilitating, and a substantial number of patients treated with drugs and behavioral therapy either do not improve or relapse (31, 45, 47). Unfortunately, the prognoses of treatment-resistant affective disorders and OCD are quite poor, so these patients and their families are burdened with extreme emotional and psychic costs, as well as marked suicide risk (46).

Therefore, there has recently been a renaissance of interest in surgical approaches to psychiatric disease (21, 66, 102, 108). First, the modern procedures described above are quite safe. Extremely low surgical mortality rates and usually transient postoperative morbidity have been reported. Second, although efficacy may be limited to 30 to 70% of patients, depending on diagnosis, type of procedure, and assessment conservatism, it is clear from analysis of outcome reports and
individual cases that many patients previously completely refractory to medical and behavioral intervention are significantly improved. This improvement is nearly always observed in the absence of long-term adverse neuropsychological consequences. It is clear that these modern procedures are not just making patients “benign” and less combative, as previously thought. Individual case results are quite impressive, such as a patient who celebrates the anniversary of her cingulotomy as her “re-birthday” (6, p 812) and a patient who states that “the operation was the turning point in my life” (50, p 879). Third, another beneficial effect of surgery may be to restore favorable responses to treatment modalities that were previously ineffective (76).

Methods for outcome studies

The difficulty of evaluating the efficacy of these procedures cannot be overemphasized (76). Several factors make the analysis of efficacy difficult. First, until recently all psychosurgical outcome reports described long-term retrospective studies, and diagnostic criteria, patient populations, and outcome assessments were not necessarily constant for the course of each study. Most recent outcome reports describe shorter-term prospective studies of more well-defined patient populations. Second, the clinicians or center responsible for selecting the patients and performing the surgical procedures also performed the clinical outcome assessment, introducing potential rating bias. Only a few critical evaluations by independent investigators have been published (e.g., Reference 24). Third, estimates of outcome (even using categorical rating scales) are difficult to compare between studies. Fourth and most difficult is the issue of appropriate control groups. A randomized, double-blind, prospective study of surgical versus nonsurgical treatments is definitely needed. Factors that undermine the ability to perform such a study include the ethics of withholding treatment in the patient population selected for surgery, the practical difficulty of identifying control patients with severe disease who are not surgical candidates, and the ethics of sham open neurosurgical procedures, with the attendant risks. The lack of sham operations in a control group creates two problems. First, a placebo effect of the operation cannot be ruled out; second, outcome assessment cannot be completely double-blind. In this regard, the development of the gamma knife technique may more easily allow for control “sham” procedures. In the absence of double-blind prospective studies, the best current evidence of efficacy is derived from pre- and postoperative evaluation in individual patients.

There also remains the logistics of action for physicians contemplating surgical intervention for their patients. Referring psychiatrists must be familiar with (76): 1) selection criteria, 2) indications (surgery is indicated for treatment-resistant affective disorders, OCD, and anxiety, whereas personality disorders and psychotic disorders are relative contraindications), 3) procedures available and their rationale, relative efficacy, and potential side effects, and 4) preoperative workup and logistics of postoperative evaluation and rehabilitation. In addition, it is important that widely distributed clinical practice guidelines reflect the availability of surgical therapy for patients refractory to other treatments (71).

The future

Given that there is enough general promise for further investment of effort to study surgical interventions for psychiatric disease, what are some areas of potential future progress? First, more precise delineation of the anatomic bases of normal emotions is critical. This goal is increasingly being realized with the application of modern functional imaging techniques. It is not sufficient, in the new millennium, to state that emotions are transmitted in the Papez circuit or limbic system; rather, specific anatomic areas or networks are being linked to specific emotional states. For example, the amygdala has been implicated in the functional recognition of human fear (1, 2, 85, 105).

Second, imaging techniques will more precisely reveal the pathological anatomy of disease states. Comparison of brain activation during resting states versus during symptom provocation have been performed for OCD (115), psychosis (106), and recently bipolar disorder (13). Therefore, the functional neuroanatomic study of psychiatric disorders is entering an entirely new realm of discovery, which should facilitate interventions more precisely tailored anatomically to specific deficits.

Third, such interventions may not be limited to destruction of brain tissue. Psychiatric conditions may not all involve local brain hyperactivity (as in OCD); some may involve hypoactivity (cf. hypofrontality in schizophrenia). Conceivably, other surgical interventions may be developed not only to decrease activity within an area (by lesioning) but also to increase activity. Implantation of minipumps or drug-secreting capsules, transplantation of cells, local electrical stimulation, and implantation of genetically modified vectors for gene delivery may all be relevant methods (124, 125). Preliminary experience in these areas has already been provided by transplantation therapies for Parkinson’s disease (90) and deep brain stimulation for the treatment of movement disorders (110). Indeed, two recent studies demonstrated the application of deep brain stimulation for the treatment of Tourette’s syndrome (118) and OCD (88). In the future, psychiatric surgery could be viewed as constructive, not solely destructive.

Fourth, the continuing technical evolution of stereotactic and functional techniques should facilitate more precise anatomic localization of therapies, with minimal perturbation of surrounding normal brain tissue (18). One could even envision interactive image-guided neurosurgery tailored specifically to metabolic abnormalities seen on preoperative functional scans obtained during symptom provocation in individual patients.

Fifth, more specific psychometric testing methods could be used to better define positive and negative cognitive and psychological outcomes. For example, it is becoming increasingly clear that dorsolateral and ventromedial areas of prefrontal cortex subserve different functions; although card-sorting tests (such as the Wisconsin Card Sort Test) may be sensitive to primarily dorsolateral frontal lobe dysfunction, Damasio and colleagues (9) have created a gambling test that...
is sensitive to ventromedial prefrontal cortex lesions. Analysis of such tests and any functional deficits should lead to more precise understanding of the cognitive risks and consequences of various procedures.

While it is clear that neurosurgical approaches to psychiatric disease are still in their infancy, are we to abort the opportunity, the potential to alleviate the suffering of at least a proportion of patients completely refractory to all other forms of therapy? Whether psychiatric surgery is in a “terminal coma or a hibernation from which it will emerge with new vigor” (103, p 426) will depend on our collective ingenuity in analyzing, developing, and refining novel treatments for these devastating disorders. As Ballantine has emphasized, “an exciting collaborative effort among psychiatrists, neurosurgeons and basic neuroscientists awaits the appearance of imaginative leaders in these areas” (5, p 127). If we think, like Hippocrates, that “from the brain and from the brain only arise our pleasures, joys, laughter, and jests as well as our sorrows, pains, griefs, and tears” (58, p 8), then we must consider that judicious neurosurgical intervention may alleviate the suffering of some patients in desperate need.

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REFERENCES


COMMENTS

This article provides an excellent review of the history of psychosurgery and its current status. I agree with the authors that the procedures need a new name. “Functional neurosurgery for the treatment of psychiatric disorders” is better than psychosurgery. Psychosurgery conjures up 1950s-vintage images of psychiatrists poking ice picks through the orbital roof and neurosurgeons performing frontal lobotomies that turn likeable people into vegetables, as in the movie One Flew Over the Cuckoo’s Nest.

The hysteria concerning psychiatric surgery reached its peak in the 1970s, when it was charged that psychosurgery was being used to control activists and minorities. This led to the formation of the national commission, which in 1977 issued its report based on the testimony of surgeons, psychiatrists, patients and families, clergy, and representatives of some of the activist groups and scientific contract groups (1–3). The results were surprising to some, i.e., that psycho-
surgery was not being used for social control and that psychosurgery had helped many patients. The commission recommended that a board be established to monitor studies of the efficacy of psychosurgery. To date, the board has not been established and the state of psychosurgery remains medicolegally uncertain.

Because of these developments and the efficacy of psycholegic medications, psychosurgery became almost extinct except at a handful of American centers, such as the Massachusetts General Hospital and the University of Texas Medical Branch at Galveston. Desperate American patients not infrequently needed to travel to Europe, where centers did not fear medical malpractice lawsuits.

Desperate psychiatric diseases are as tragic as any neurological condition. Patients unable to leave a room or a hospital because of obsessive-compulsive behavior, suicidal thoughts, or overwhelming anxiety are just as disabled (and in some cases more disabled) than hemiplegic patients with brain tumors. Patients who kill themselves are just as dead as the victims of head injuries. Neurosurgeons compete with each other for 31,000 brain tumor procedures each year and attend courses and meetings regarding cranial base tumors, which exhibit an annual incidence of approximately 2500 in the United States, but we forget the many patients with psychiatric diseases we could help. For example, there are probably more than 500,000 patients in the United States with severe obsessive-compulsive disorder, and one-half of these conditions are medically intractable. Many of these patients could be helped by cingulotomy, anterior capsulotomy, or limbic leukotomy.

The disadvantage of performing psychiatric surgery is the risk of being sued and, of course, not being paid. Psychosurgery is still controversial among “nonorganic” psychiatrists. Some have encouraged patients to sue their neurosurgeons, despite the fact that many of the patients underwent psychosurgery to treat debilitating psychiatric illnesses from which they recovered to the point of being able to initiate a lawsuit. In addition, few insurance companies pay for psychosurgery, because a 1986 Office of Health Technology Assessment report concluded that psychosurgery had never been studied in a scientific manner (i.e., in prospective, randomized, double-blind studies) and should be considered experimental.

In the new millennium, it is hoped that barriers created by the legal and insurance industries will decrease in the presence of the enormous public health problem of medically intractable psychiatric diseases. New minimally invasive or noninvasive procedures based on functional imaging and an improved knowledge of psychiatric diseases may use neuroaugmentative or transplantation methods. These new methods may change the attitudes of governments, psychiatrists, third-party payers, and society, which now equate psychosurgery with the destructive procedures of the past 50 years. Additionally, we must establish a new name for these procedures (perhaps “restorative psychiatry” or “augmentative psychomodulation”).

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There is doubtless a great need to promote awareness of the possibilities offered by modern surgical approaches for the treatment of the most severe and incapacitating cases of certain therapy-resistant mental disorders. Therefore, the topic review by Binder and Iskandar, which describes the current state of the field, is well timed. Although psychosurgery seems to have been in a state of hibernation for the past two decades, it is still practiced in a few centers. With attitudes in the psychiatric community shifting to a more biological orientation, there are signs of renewed interest in psychosurgery. In a well-balanced critical editorial written by Ovsiew and Frim (4) in 1997, it was concluded that “any time for daring in psychosurgery has passed” . . . and it is “. . . a rarely used but irreplaceable procedure to relieve distress and save lives.” However, it seems that the few of us who practice that form of surgery share the opinion that the treatment outcomes tend to be somewhat less favorable than those observed in the 1970s and 1980s. This situation is reflected in a few recent studies referred to in this review (2, 5), which reported relatively moderate rates of successful results after cingulotomy. A possible reason for this observation is that modern pharmacological and behavioral therapies are becoming more efficacious; consequently, patients referred for surgery are even more seriously ill and resistant to treatment. Nevertheless, considering the severity and chronicity of the incapacitating diseases of these patients, “success” probabilities as low as 30 to 40% justify surgery. Moreover, as stated in the editorial referred to above, “Possibly even an intervention that risks subtle neuropsychological impairment or mild adverse personality change could be judged acceptable under such circumstances” (4). Slightly impaired frontal lobe function can be tolerated as long as it has no practical implications for the general level of functioning. In fact, this sequela is generally of more academic than practical interest, because it is often demonstrable only with the use of dedicated tests such as Wisconsin Card Sort Test.

As indicated by Binder and Iskandar, there are many reasons why we might anticipate a renaissance of psychosurgery. I think that the most important reason for such a possible development involves the new findings regarding the biological, anatomic, and biochemical bases of many psychiatric disorders. In particular, the development of functional imaging has played a pivotal role in providing a rational basis for surgical interventions. Therefore, psychosurgery may progressively shift from being predominantly empirically based.

Psychosurgery has been much criticized because it has been documented mainly by anecdotal and retrospective reports with biased evaluations. Certainly, there is a lack of well-controlled, prospective, randomized studies. As is true for most surgical treatment methods, it is difficult to foresee psychosurgery ever fulfilling the strict criteria of evidence-based medicine, which is becoming required for treatments to be recognized as useful and acceptable therapies. Given the severity and rarity of the very advanced forms of mental disorders considered for surgery, prospective randomized studies are virtually impossible to pursue. Therefore, well-designed studies with patients serving as their own controls, with evaluation by disinterested third parties, must remain the only realistic goal. The possibility of performing sham surgery has been discussed by the authors, and for obvious reasons such studies raise serious ethical concerns. Sham surgery has been debated in conjunction with fetal tissue grafting for the treatment of Parkinson’s disease, and several prominent scientists have argued that it is not ethically justifiable to expose patients to the risk of surgery without any benefit. With the use, however, of radiosurgical procedures (implying surgical intervention without opening of the cranium), it would be possible to perform sham procedures, provided that the patients could be completely shielded from the radiation. However, it might be argued that requiring informed consent for sham interventions from seriously ill patients who expect to undergo “last resort” treatment is ethically doubtful.

In view of the impressive advances in the treatment of Parkinson’s disease with the introduction of deep brain stimulation, it is natural to consider this approach in psychosurgery as an option for producing lesions. This possibility was discussed in a commentary by Cosgrove et al. (1), who rightly emphasized the difficulties involved. Perhaps the most critical issue in the development of electrical intracerebral “stimulation” as a treatment method in psychosurgery is that we do not understand what the application of relatively high-frequency electrical pulses to various brain structures actually implies. In a sense, it is deceptive to use the term “stimulation” when the generally desired end result is a blocking effect or postsynaptic inhibition. The application of a stimulating current is indeed unpredictable; stimulation of the sensory thalamus produces persisting paresthesia, i.e., activation, whereas in the Vim nucleus evoked tingling sensations are transitory and associated with the suppression of tremor. The situation is no less complicated when current is applied to white matter (internal capsules or cingulum). From an ongoing multicenter study (Leuven and Stockholm; two American centers will be included), it was recently reported that, in a case of obsessive-compulsive disorder, “stimulation” of the internal capsules could produce almost instantaneous relief of anxiety and oppression (3). Considering that the beneficial effects of both capsulotomy and cingulotomy on obsessive-compulsive disorder symptoms generally do not appear until several months after surgery, the long-term positive effects of stimulation remain to be demonstrated. Of course, for psychosurgery, the reversible and nondestructive nature of deep...
brain stimulation is particularly attractive. These characteristics would make this treatment more acceptable to the general public, as well as to the psychiatric community, and would circumvent possible ethical issues. The practical and theoretical problems associated with the application of deep brain stimulation in psychosurgery should not be underestimated, but it is indeed a challenge for the further development of the surgical treatment of mental disorders.

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It is appropriate that the role of neurosurgery in the treatment of psychiatric disorders be reviewed at this time, and Binder and Iskandar have provided a comprehensive overview of this topic. Given a responsible multidisciplinary approach to decision-making for patient selection, choice of procedure, follow-up monitoring, and assessments, neurosurgical treatments may well benefit a larger number of patients than are currently being treated. Further advances in both neuroimaging and surgical procedures should produce great improvements in efficacy and safety. The identification of psychological substrates for diseases (e.g., using positron emission tomography) and the use of nonablative techniques, such as reversible deep brain stimulation, should lead to a significant resurgence of interest in this area.

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13th century fresco from Duomo, Anagni, Italy. Galen (left) and Hippocrates are engaged in consultation, even though Hippocrates lived almost 500 years before Galen.