Ablative neurosurgery for mental disorders: is there still a role in the 21st century? A personal perspective

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Object. The author presents his personal perspective on ablative neurosurgical techniques used to perform bilateral anterior cingulotomy (BACI) and bilateral anterior capsulotomy (BACA) for ameliorating the symptoms of refractory obsessive-compulsive disorder (OCD) and treatment refractory depression (TRD). With depression predicted to be the second most common cause of disability in the world by the year 2020 and the birth of electric neurostimulation representing an attractive alternative treatment option for TRD and OCD, it is desirable to revisit the pros and cons of these treatment options.

Methods. The author reviewed the surgical methods and outcome (including neuroimaging findings) in all cases in which ablative neurosurgery was performed at Ninewells Hospital and Medical School over the last 2 decades.

Results. The advantages of ablative procedures (BACI and BACA) from patients' and psychiatrists' perspectives are that the ablative procedures are one-off procedures that do not require lifelong commitment to program the stimulation devices, fix hardware failures, or change exhausted batteries. From the perspective of healthcare funding bodies, the relatively low cost of these treatments is an advantage. The main disadvantages of BACI and BACA are the perceived higher complication rates, the irreversibility of the surgical lesions, and the stigma associated with brain destruction in psychiatric patients that are still unpalatable in the community at large. However, some patients still choose a one-off procedure in preference to any other options presented to them.

Conclusions. There is still place for BACI and BACA in modern neurosurgery for mental disorders, at least in the short term for those who do not want to commit to lifelong device programming and maintenance. (DOI: 10.3171/FOC/2008/25/7/E4)

KEY WORDS • ablation • capsulotomy • cingulotomy • depression • obsessive-compulsive disorder

**Abbreviations used in this paper:** BACA = bilateral anterior capsulotomy; BACI = bilateral anterior cingulotomy; DBS = deep brain stimulation; ECT = electroconvulsive therapy; HRSD = Hamilton Rating Scale for Depression; HRSD-17 = 17-item HRSD; OCD = obsessive-compulsive disorder; TRD = treatment refractory depression; VNS = vagus nerve stimulation.
TABLE 1

Inclusion and exclusion criteria for neurosurgery for mental disorders in Ninewells Hospital and Medical School*

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td>patient age (yrs)</td>
<td>&gt;20</td>
<td>≤20</td>
</tr>
<tr>
<td>Dx</td>
<td>ICD-10 criteria for: Severe Depressive Episode w/ or w/o psychotic Sx;</td>
<td>ICD-10 criteria for F32.2, F32.3, F33.1–F33.3,</td>
</tr>
<tr>
<td></td>
<td>Recurrent Depressive Disorder, current episode moderate to severe; or</td>
<td>F31.4–F31.5 not fulfilled; current Dx of substance</td>
</tr>
<tr>
<td></td>
<td>Bipolar Affective Disorder, current episode severe depression w/ or w/o</td>
<td>misuse, fulfilling criteria for ICD-10 F10–19;†</td>
</tr>
<tr>
<td></td>
<td>psychotic Sx</td>
<td>a Dx of organic brain syndrome fulfilling criteria</td>
</tr>
<tr>
<td>duration</td>
<td>absolute minimum of 3 yrs, w/ ≥2 years of unremitting Sx despite Tx</td>
<td>for ICD-10 F00-09, including Alzheimer disease</td>
</tr>
<tr>
<td>consent</td>
<td>valid informed consent as assessed by the Mental Health Commission for</td>
<td>&amp; vascular &amp; other dementias</td>
</tr>
<tr>
<td></td>
<td>Scotland (psychiatrist &amp; 2 lay officers)</td>
<td>insufficient</td>
</tr>
<tr>
<td>previous Tx</td>
<td>adequate</td>
<td>inadequate</td>
</tr>
</tbody>
</table>

* ICD-10 = International Statistical Classification of Diseases and Related Health Problems, 10th revision.
† Mental and Behavioral Disorders Due to Psychoactive Substance Use.
‡ Adequate therapy is defined as any of the following: at least 2 “adequate” courses of treatment with a tricyclic antidepressant drug; at least 1 “adequate” course of treatment with a selective serotonin reuptake inhibitor; at least 1 “adequate” course of treatment with a monoamine oxidase inhibitor (not moclobemide); at least 1 of the above plus lithium augmentation for a period of 4–6 weeks with a 12-hour postmedication plasma lithium level of 0.4–0.8 mmol/L; at least 1 “adequate” course of treatment with an antidepressant drug as defined above, plus the prescription of a typical or atypical antipsychotic drug for a period of 6 weeks at a dose within the British National Formulary recommended range (Where psychotic symptoms are prominent in the clinical presentation, trials of both typical and atypical drugs should be performed;); at least 2 “adequate” trials of ECT, spaced 6 months apart (minimum of 8 bilateral applications of ECT with recorded evidence of seizure duration exceeding 15 seconds per treatment).

Methods

This is a retrospective review of ablative procedures for mental disorders performed in Dundee with emphasis on the surgical technique. The sources of information included operative notes, operating room logbooks, feedback from psychiatrists about the 12-month outcome, intraoperative data collection, and postoperative neuroimaging studies performed within 1 week of surgery and 12 months after surgery.

Bilateral Anterior Cingulotomy

Patient Selection. Patients were selected for the procedure according to the inclusion and exclusion criteria summarized in Table 1. At the beginning of the series BACI was the preferred second choice, but as experience was gained and results accumulated, BACI became the first choice for TRD.

Preparation and Planning. General anesthesia was induced using intravenous anesthetic agents. The Zamorano-Dujovny stereotactic frame reference ring was applied in a plane parallel to the glabella-inion line symmetrically to avoid tilt, yaw, and rotation of the head in relation to the stereotactic frame localizer. Surface fiducial markers were placed on the forehead and 1.5 cm on either side of the midline in front of the coronal suture to mark the entry points (Fig. 1).

The patient’s head was fixed to the CT table so that the frame angles were 0°. This was achieved by making sure that the stereotactic frame localizer was at the center of the gantry using the scanner’s laser light alignment system and a water level. A volumetric contiguous axial CT scan was obtained parallel to the stereotactic frame reference ring, and DICOM images were transferred to the workstation where the frame-link software (Medtronic Sofamor Danek) was available to plan the procedure. The patient was then transferred to a 1.5-T MR imaging unit, and volumetric MP-RAGE (magnetization-prepared rapid gradient echo), T2-weighted, T1-weighted, and diffusion tensor image sequences were obtained at 0° (relative to the anterior commissure-posterior commissure line). The images were again transferred into the frame-link software workstation.

The frame-link software was used to merge the CT and MR images automatically and calculate the stereotactic cube. The merged images were then reviewed very carefully for any inaccuracies; particular attention was paid to the anatomical fit of the ventricles and the surface skin fiducials.

The stereotactic frame localizer was automatically recognized and identified by the frame-link software and an average transformation error was displayed. I accepted a transformation error < 0.6 mm. The middle point of the anterior commissure and the posterior commissure was identified manually and stored digitally. An additional 3 midline points were then manually identified and stored to correct for any residual tilt, yaw, or rotation of the brain.

The target was then manually identified by measuring 20 mm posterior to the tip of the ipsilateral frontal horn in the sagittal images, 7 mm from the midline in the coronal images, and 1 mm above the roof of the lateral ventricle using both sagittal and coronal images. The x, y, and z stereotactic coordinates of these 2 targets were obtained.

Operation. The stereotactic frame reference ring was fixed to the operating table in the operating room, using a modified connection to the Mayfield head fixation system.

Fig. 1. Photograph showing the external skin markers used in BACI and BACA.
The patient’s head was slightly flexed forward and elevated to 30°. The scalp was prepared by shaving a very small area where the scalp incisions were to be made, 1.5 cm on either side of the midline and just in front of the coronal suture. The scalp was cleansed with antiseptic iodine solution. Before the scalp preparation the anesthetist gave 1.5 g of cefuroxime intravenously. The stereotactic coordinates of the right-side target were translated into the stereotactic frame-aiming bow, which was fixed to the stereotactic frame reference ring. Surgical draping of the operative field was completed, making sure that access to the aiming bow mechanism to translate the stereotactic coordinates of the left-side target was not obscured by the drapes.

Two small (2-cm) scalp incisions were made and a small bur hole was made on either side. A radiofrequency probe with a 6-mm-long, 3-mm-wide exposed tip (Integra Radionics) was connected to a radiofrequency lesion generator (Integra Radionics) and positioned in the right-side target. The probe tip was heated to 70°C for 90 seconds; this procedure was repeated twice to produce a lesion of 8 × 8 mm.

The stereotactic coordinates of the left-side target were then translated onto the stereotactic frame-aiming bow and the same procedure repeated to produce a lesion on the left side.

The aponeurosis and skin layers of the scalp were sutured by 3-0 Vicryl suture (Ethicon, Inc.), and the incisions were glued using Dermabond (Ethicon, Inc.).

Postoperative Care. Patients were cared for in the recovery room until they were fully awake from anesthesia, then observed in the high-dependency unit overnight before being transferred to the ward. The average length of stay in the neurosurgical unit was 3 days. The average stay in the psychiatric unit varied from patient to patient depending on the number of postoperative tests required and the distance the patient had to travel from his or her town of residence to the unit.

Magnetic resonance imaging was performed to confirm positions and sizes of the lesions during the 1st week following surgery (Figs. 2 and 3). Patients underwent psychiatric testing similar to that administered preoperatively. They were followed up by members of the psychiatric staff and received therapy as needed. Follow-up MR imaging was performed at 12 months after surgery (Fig. 4).

Bilateral Anterior Capsulotomy

Bilateral anterior capsulotomy refers to stereotactic ablation of the most anterior portion of the anterior limb of the internal capsule lateral to the head of the caudate nucleus, the white matter bundle connecting the frontal and the anterior cingulate cortex with the thalamus, the hippocampus, and the amygdala. The procedure was first described by Talairach et al. in 1949 and was later modified by Lars Leksell for the treatment of chronic pain.

Preparation and Planning. The steps involved in preparation of the patient and planning of the procedure were exactly the same for BACA as those described under BACI except that the targets were different. The targets were the anterior third of the anterior limb of the internal capsule lateral to the head of the caudate nucleus, the white matter bundle connecting the frontal and the anterior cingulate cortex with the thalamus, the hippocampus, and the amygdala.
eral to the head of the caudate nucleus on either side of the brain. They were contoured using the frame-link software starting as caudally as possible and extending to the rostral level of the head of the caudate. The trajectories were chosen by drawing a line from the center of the most inferior part of the contoured target to the center of the top of the target on either side, and the 2 lines were extended toward the skull surface. The intersection of the 2 lines with the outer surface of the skull marked the site of the entry point on either side. The x, y, and z stereotactic coordinates and the 2 trajectory angles of these 2 targets were obtained.

Operation. Transfer of the patient to the operating table, head fixation, scalp preparation, antibiotic prophylaxis, and bur-hole formation followed steps similar to those described above under BACI. A radiofrequency probe with a 6-mm-long, 3-mm-wide exposed tip was connected to the radiofrequency lesion generator (both from Integra Radionics) and positioned so that its tip lay in the most caudal part of the contoured right target. The probe tip was heated to 70°C for 90 seconds. The probe was then withdrawn 6 mm and another lesion was made in the same fashion to produce a lesion 8 mm wide and 12 mm long along the contoured right target. The stereotactic coordinates and trajectory angles for the left target were then translated onto the stereotactic frame reference ring and the same procedure was repeated to produce the lesion on the contoured left target.

The aponeurosis and skin layers of the scalp were closed as in BACI.

Postoperative Care. Patients were cared for similarly to those who underwent BACI. As in the cases in which patients were treated with BACI, follow-up MR imaging was performed 12 months postoperatively (Fig. 5).

Outcome Assessment

Depression was considered in remission in patients who scored 7 on the HRSD-17 or 10 on the Montgomery-Åsberg Depression Rating Scale (MADRS). Treatment response was defined by reduction in baseline HRSD-17 or MADRS score of 50% or a CGI-I (Clinical Global Impression) score of 1 or 2. Neurocognitive performance was assessed using a standard battery of clinical tests focusing on executive function and the Cambridge Neuropsychological Test Automated Battery (CANTAB, www.cantabellcipse.com).

Results

Twelve-month follow-up data were available for 25 of 30 patients with TRD. The mean age (standard deviation) was 43 ± 9.8 years; 22 of these 25 patients were women, and 43.3% were inpatients at the time of surgery. The mean duration of illness was 10.5 years with a mean total duration of hospitalization of 2.5 years. The mean number of adequate treatment trials was 9.1 ± 3.2. The 12-month response rates for BACA and BACI were 25 and 60%, respectively. The remission rate was 10% (2 of 20 patients) for BACA and 20% (1 of 5 patients) for BACI. Longer-term remission rates were similar following both procedures at 40%, but the numbers of patients for whom longer-term follow-up data were available are too small to allow for generalization.

Minor transient adverse events were recorded as follows: headache in 15 patients (4 who underwent BACI and 11 who underwent BACA), nausea in 5 (4, BACI; 1, BACA), dizziness in 2 (1 in each treatment category), incontinence in 4 (1, BACI; 3, BACA), confusion in 6 (all BACA), and facial swelling in 5 (3, BACI; 2, BACA). Serious adverse events included epilepsy in patient following BACI and 1 intracerebral hemorrhage leading to permanent hemiparesis following BACA.

More detailed results of the service are beyond the scope of this paper and were published extensively elsewhere.

Discussion

Ablative procedures for mental disorders continue to be provided on a small scale worldwide to help those who have not responded to nonsurgical therapies. In recent years a group of researchers from Boston reported the 12-month outcomes for 13 patients with severe TRD who were treated by means of BACI,8,28 Functional brain imaging was performed pre- and postoperatively to look for changes predictive of a positive response to BACI. At 12 months after the procedure, 38.5% of the patients demonstrated a 50% or greater reduction in depression symptom scores. The results of functional imaging suggested that elevated preoperative metabolism in the left subgenual prefrontal cortex (Area 25) and left thalamus was associated with superior outcome following BACI. Another group reported the outcomes from a prospective audit of BACA for 15 patients with OCD.27 The authors concluded that outcomes were generally favorable, but not all data were available for every patient. The response rate after BACA in Dundee was 25% and the remission rate was 10%, compared with a 60% response rate and a 20% remission rate after BACI in TRD. Due to the perceived better response rate of TRD patients after BACI and the perceived lower complication rate of BACI compared with BACA, after consulting with my psychiatric colleagues I have shifted the procedure of preference in TRD to BACI and have not performed BACA for the treatment of TRD since 2000.

Nonablative procedures such as VNS represent a very attractive option. Vagus nerve stimulation entails no risk of permanent neurological or intracranial complications and does not damage brain tissue. The clinical results of VNS in 205 patients with TRD were reported after 9 and 12 months of unblinded, active treatment.30 For the total group, the response rate (defined as a 50% drop in HRSD score) after 12 months of VNS was 27.2%, with a remission rate (sustained 24-item HRSD score > 10) of 15.8%. Of note, the severity of TRD in these patients was much less than that reported in patients undergoing BACI and BACA at our center as well as that reported by other researchers.8 The response and remission rates following VNS were significantly lower than the Dundee experience with BACI despite the fact that the illness was more protracted in our patients. Nevertheless, the attraction of VNS is the absence of permanent neurological deficit arising from intracranial complications of permanent neural tissue ablation. Severe adverse effects from VNS were very low in comparison to BACI or BACA. However, 14.6% of patients treated by means of VNS experienced worsening of their depression severe enough to require hospitalization.
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during the year. The most common adverse effects directly related to stimulation included voice alteration (54%), which was expected. However, breathlessness occurred in 16%, neck pain in 13%, and cough in 5%. There were 3 deaths in this case series, one of which was by suicide after 5 weeks of VNS. The results of chronic VNS in TRD are favorable when compared to continuing TRD treatment as usual, where only 13% met the criteria for response and only 3% went into remission in 12 months.16

More recently, several groups published their experience with DBS in TRD and OCD.1,3,4,12,15,18,23,26 The reported outcome of DBS therapy compares favorably to that reported following BACI and BACA. Mayberg et al.23 reported on a series of 6 patients with TRD who were treated with Area 25 DBS. The criteria for response were fulfilled in 4 (66%) of the 6 cases and the criteria for remission in 2 (33%). These results compared very well with the 60% response and 20% remission rates we experienced with BACI. However, TRD and OCD in patients treated with DBS were not as protracted as they were in patients treated with BACI and BACA in Dundee. It is also important to point out that DBS therapy in OCD and TRD is more expensive than treatment with BACI or BACA, due to the continuing costs of programming, hardware failure, and battery changes.27 Although the complication rates of DBS therapy are likely to be less than those attributed to BACI and BACA, the reported complications are not insignificant,35 and include an infection rate of 6%, a short-term (24-month) hardware failure rate of 1.4%,2 and a long-term failure rate of 26.2%. Furthermore, DBS implantation precludes any future treatment with ECT. However, DBS therapy for OCD and TRD is here to stay and is likely to replace ablative procedures as the targets become more defined and the outcome of DBS improves. There are compelling reasons for embracing VNS and DBS therapy: lack of intended brain destruction, as well as reversibility and flexibility of stimulation.

Conclusions

In appropriately selected patients, BACI, BACA, VNS, and DBS therapies provide significant improvement. Both BACI and BACA are relatively safe and when performed by a multidisciplinary team can offer good outcome for many patients who otherwise would be denied the chance of enjoying a better life. However, if the choice were based on the perceived risk of irreversible brain damage or the risk of permanent neurological deficit, VNS would come first, DBS second, BACI third, and finally BACA.

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References


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