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Bilateral Anterior Capsulotomy for Treatment-Resistant Obsessive-Compulsive Disorder

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Abstract
Introduction: Ablative surgery is an intervention of last resort for treatment-resistant obsessive-compulsive disorder (TROCD). Our center has been using bilateral anterior capsulotomy (BAC) for the past 20 years for patients eligible for limbic surgery. This report details our experience with BAC for TROCD. ***Method:*** Five patients with OCD met eligibility criteria for BAC. Entry protocols were complex and took around 6 months to complete. Stereotactic radiofrequency was used to produce the capsulotomies. Lesion length varied between 5.7 and 16.9 mm in the coronal plane. Patients were followed between 4 and 20 years. ***Results:*** All 5 patients (100%) were responders as defined by the widely accepted criteria of a reduction of ≥35% in Yale-Brown Obsessive Compulsive Scale (YBOCS) score at 18-month follow-up. Four patients remained responders at the 48 months. One patient was lost to follow-up. Responder status when viewed from the perspective of the YBOCS was sustained over the 4- to 20-year follow-up with one relapse 19 years postsurgery when medications were discontinued. Real-world psychiatric outcomes were different as other vulnerabilities surfaced illustrating the multifactorial determinants of mental health. No patient had any significant long-term neurocognitive or physical side effects. ***Conclusion:*** BAC should remain an option of last resort for patients with severe OCD who remain unresponsive to all other interventions.

Introduction

Treatment-resistant obsessive-compulsive disorder (TROCD) is usually defined as OCD that fails to respond to 3 adequate trials of selective serotonin reuptake inhibitors (SSRIs), including the tricyclic antidepressant clomipramine, in addition to cognitive behavioral therapy (CBT) [1]. Up to 40–60% of OCD patients will have an unsatisfactory response to these interventions. Other strategies that can be considered are second-generation antipsychotics such as oral aripiprazole and risperidone or intravenous clomipramine [1, 2]. Electroconvulsive therapy, while a standard practice in refractory depression, has an uncertain place in TROCD [3–5].

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When all else fails, neurosurgical interventions are then considered. Surgical strategies include deep brain stimulation and limbic surgery. In deep brain stimulation, there is no preference between the multiple studied targets [6]. Limbic surgery has settled on 3 targets used alone or in combination: bilateral anterior capsulotomy (BAC), bilateral anterior cingulotomy (BCING), and bilateral subcaudate tractotomy (BSCT). The combination of BAC and BSCT is known as limbic leukotomy [6].

In this report, we describe our 20-year experience with BAC in TROCD. The major advantage of our data is that the same surgeon performed all procedures and that all patients were followed from their original assessments until the present by the chief author. This offers a unique perspective on the effectiveness and the long-term outcomes of BAC for TROCD.

Methods

The Vancouver Limbic Surgery Group (VLSG) was formed in 1998 to offer ablative surgical treatment for refractory depression and obsessive-compulsive disorder. A review of available literature on surgical targets for TROCD and treatment-resistant major depression resulted in the selection of the BAC technique for both.

The use of BAC for TROCD was approved by the Department of Psychiatry and Division of Neurosurgery at the University of British Columbia. Approval was also granted by the Vancouver Hospital and Health Sciences Centre's Medical Advisory Board and Ethics Committees. From 2016 onward, this study was conducted under ethical approval from the UBC Clinical Research Ethics Board (H16-01722 and H21-02230).

Eligibility

To be eligible for BAC, the patient had to be 18 years or older and have had a disease duration of 5 years or more, a Yale-Brown Obsessive-Compulsive Scale score of ≥16, which equated to moderate to severe OCD, and a Global Assessment of Functioning (GAF) Scale of 50 or less, which indicated serious symptoms or serious impairment in functioning (DSM-IV) [7–9]. They must have failed at least 2 trials with 2 different SSRIs and 1 trial of clomipramine given in adequate doses and of adequate duration (at least 8 weeks each) and failed a trial of CBT.

Each patient had to be competent to make a decision about surgery and had to give written informed consent to undergo the procedure. The patient had to agree to participate in the preoperative evaluation program and the postoperative rehabilitation program with the expectation that they would be followed for at least 10 years. Each patient also had to have a community treating psychiatrist who accepted responsibility for the patient's postoperative long-term management.

The entry protocols were complex and took 6 months to complete. Eligibility for surgery was assessed by 2 psychiatrists, one of whom was the primary author, while competency to consent was assessed by 2 separate additional independent psychiatrists. The patient was then interviewed by the neurosurgeon, who explained the procedure and its potential side effects. Finally, after these 5 assessments, the patient was interviewed by an independent legal counsel who had in their possession the 5 prior consultations to ensure that the entry protocol had been followed and the patient adequately informed. After all these assessments, a meeting of the limbic surgery committee, consisting of the legal counsel, neurosurgeon, and the 2 assessing psychiatrists, was convened to review eligibility, consent capacity, and protocol compliance. If all conditions were met, permission to proceed was granted by the committee.

Preoperative Assessments

Preoperatively, all patients underwent formal neurological examination, and completed or were administered the Beck Depression Inventory (BDI-1), the Global Assessment of Functioning (GAF), and the Yale-Brown Obsessive Compulsive Scale (YBOCS). All had extensive neuropsychological testing. Domains evaluated include attention, mental speed, verbal memory, visual memory, phonemic fluency, semantic fluency, abstraction/executive function, visuomotor construction, and motor abilities as well as frontal behavior (Table 1). Baseline brain magnetic resonance imaging (MRI) and single-photon emission computed tomography (SPECT) scan completed the preoperative investigations.

Exclusion Criteria

Patients were excluded if they were younger than 18 years of age or had another comorbid Axis I diagnosis such, psychotic disorder, or substance abuse disorder. They were also excluded if they had a cluster B personality disorder or brain pathologies such as dementia or tumor.

Follow-Up and Response Criteria

The patients were maintainded on their preoperative medications postoperatively for at least 6 months. After this interval, medications were tapered or adjusted as tolerated per the judgement of the patient's community psychiatrist. Follow-up occurred at 2 months, 6 months, 18 months, and 2 years thereafter. Where possible, further follow-up was conducted with the intention to follow patients up for at least 10 years. MRI and SPECT scan were repeated at 2 months and at 12 months postoperatively. Neuropsychological testing was repeated at 2 months, 1 year, and 2 years postoperatively if impairments were found at the 1-year assessment.

Treatment response in OCD was defined as a ≥35% reduction in the Y-BOCS score in line with the previous literature [1]. For patients with comorbid depression, treatment response was defined as a ≥50% reduction in the BDI-1 score when comparing preoperative with postoperative metrics [10]. For neuropsychological testing, a change in a given neuropsychological domain was identified if there was a difference of 2 or more scaled-score points between presurgical and postsurgical test performance. A change in behavioral domains was defined as a difference of 10 or more T-score points between presurgical and postsurgical ratings by self or others.

Procedure

Bilateral capsulotomies were performed under local anesthesia using frame-based stereotactic techniques. The location of the most inferior lesion was selected from a thin-cut T1-weighted axial MRI through the lowest portion of the anterior limb of the internal capsule (ALIC). The target was the midpoint of the anterior limb of the ALIC in its anterior-posterior and medial-lateral extent. Radiofrequency lesions were made with a 2.1-mm diameter, 5-mm exposed length electrode (Radionics, Burlington, MA, USA)

Table 1. Domains assessed by neuropsychological testing

Domain	Neuropsychological tests
Attention	WAIS Digit Span, Mental Arithmetic, Corsi Blocks
Mental speed	Trails A, Stroop Words/Colors, WAIS Digit Symbol
Verbal memory	Rey Auditory Verbal Learning Test
Visual memory	Rey-Osterrieth Complex Figure
Phonemic fluency	Controlled Oral Word-Association Test
Semantic fluency	Animal Category Fluency Test
Abstraction	WAIS Similarities
Executive functioning	Wisconsin Card-Sorting Test, Trails B; Stroop Interference; Tinkertoy Test
Visuomotor construction	Rey-Osterrieth Complex-Copy, WAIS Block Design
Motor	Finger-Tapping Test, Grooved Pegboard Test
Behavioral ratings: self and family	Frontal System Behavior Scale

heated to 80°C for 60 s. Four lesions, each overlapping 1 mm, were completed in a sequentially more rostral column following the superior-lateral deviation of the ALIC in the coronal plane [10].

In 2018, we decided to tailor the Vancouver capsulotomy using presurgical high-definition tractography to target the ventral part of the ALIC. This strategy was applied to our two most recent individuals who had this procedure in late 2017 and early 2018. The ventral pathway was generated using the "prefrontal thalamus" (anterior, mediodorsal, and ventral anterior nuclei) and substantia nigra and ventral tegmental area as seed regions of interest and the ALIC and the ventromedial prefrontal cortex (PFC) as waypoints [11]. In our OCD cohort, the ventrally targeted capsulotomy was done in only 1 patient (patient #1). All the others were treated with our older and longer lesion [11, 12].

Results

In the 22 years since the limbic surgery program's inception, only 5 patients met the eligibility and consent requirements. Several additional patients were screened but were rejected as they had not had the benefit of adequate pharmacological trials or CBT. The limbic surgery program in Vancouver is the only such program in the province and is well known. This low number in a provincial population of 5 million people indicates the infrequency of truly treatment-refractory, severe, and functionally disabling OCD. Alternatively the low number could reflect a low rate of referral. The patent demographics are outlined in Table 2. The details and outcome of 1 patient of our OCD cohort described in this report (patient #1) have been included in prior publications about the Vancouver capsulotomy [11, 12].

All capsulotomies were performed between 2002 and 2018. In this report, we present tabulated comparative follow-up data for up to 48 months for 4 patients. This follow-up interval was selected to align with our most recently treated patient, who had been followed for this period at the time of analysis. One patient was lost to follow-up at 18 months. Narrative accounts of the last interview with the patients are described below. The follow-up interval varied depending on the patients' availabilities for assessment.

Preoperative and postoperative psychometrics are given in Table 3. The graphed trajectories are given in Figure 1.

The capsulotomy size was calculated from the mature capsulotomy lesion measured on an MRI done between 6 and 54 months postoperatively. Data were only available for 4 patients. The capsulotomy lesions were roughly cylindrical in shape. The largest visualized dimensions in the axial, coronal, and sagittal planes were measured. The volume of the cylinder was then calculated from the largest diameter in the axial plane and the height in the coronal plane using the formula $\pi r^2 h$.

Capsulotomy length ranged from 9.8 to 16.9 mm on the right (average length = 14.5 mm) and 5.7 to 15.4 mm on the left (average length = 12.3 mm). The volume of the ellipsoid ranged from 22 mm^3 to 2,243 mm^3 (Table 4).

Narrative Account

Four patients were followed for 4–20 years postoperatively. Their trajectories are described in narrative accounts detailed below.

Patient 1

Patient 1 was last seen 4 years postoperatively. At 4 years postoperatively, the patient reported a return of more intrusive perfectionism but not obsessions nor compulsions. The patient's perfectionism dated from childhood. Everything had to be done perfectly and everything had to be kept completely tidy. Task completion

Table 2. Patient demographics

Patient	1	2	3	4	5
Age at surgery	56	52	22	38	40
Sex	F	M	M	F	M
Duration of illness at the first consult, years	30	43	7	32	33
Preoperative hospitalizations, *n*	2	2	1	5	4
Postoperative hospitalizations, *n*	0	0	0	11	0

Table 3. Pre- and postoperative psychometrics

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Preoperative					
BDI	44	32	13*	35	22
GAF	41–50	31–40	31–40**	21–30	41–50
YBOCS	30	35	18**	30	30
2 months					
BDI	9 (80%)	19 (41%)	2 (85%)		
GAF	–	41–50	–		
YBOCS	20 (33%)	26 (26%)	l4 (22%)		
6 months					
BDI	8 (82%)	14 (56%)		10 (71%)	7 (68%)
GAF	–	–		41–50	61–70
YBOCS	10 (67%)	22 (37%)		17 (43%)	5 (83%)
18 months					
BDI		13 (59%)			
GAF		51–60			
YBOCS		14 (60%)			
48 months					
BDI	7 (84%)		0 (100%)	29 (17%)	5 (77%)
GAF	51–60		71–80	61–70	51–60
YBOCS	8 (73%)		8 (56%)	13 (57%)	18 (40%)

BDI, Beck Depression Inventory; GAF, Global Assessment of Functioning; YBOCS, Yale-Brown Obsessive Compulsive Scale. Percent reduction compared to preoperative scores is indicated in parentheses: *2 days preoperatively; **1 year prior to surgery.

was slow and deliberate to ensure that a standard was met at each step. There were no behavioral/task repetitions and orderliness was egosyntonic. Preoperatively, the time taken to do some activities resulted in procrastination or task avoidance because the tasks seemed too overwhelming to tackle. Postsurgically at 4 years, task avoidance and slowness to task completion were still present but were 60% reduced compared to prior to surgery. Moreover, quality of life was rated as reasonable with satisfaction from the capsulotomy given its benefit. The YBOCS score was 8, indicating mild OCD and a 73% reduction in the YBOCS score compared to preoperative measurements. Additionally, a 4-year postoperative BDI score was 7, indicating no depression. This was a reduction of depression by 84% compared to the preoperative score of 44.

Patient 2

Patient 2's last psychometrics were done 18 months postoperatively. On the YBOCS, the patient scored 14, indicating mild OCD and a 60% reduction in the YBOCS score compared to preoperative measurements. At 18-month follow-up the BDI was 13 indicating minimal depression. This score contrasted with the preoperative score of 32 and represented a 59% reduction in depression. Hereafter, the patient was lost to follow-up.

Patient 3

The last psychometrics for patient 3 were completed 8 years postoperatively. On the YBOCS, the patient scored 8, indicating mild OCD, with a 56% reduction in

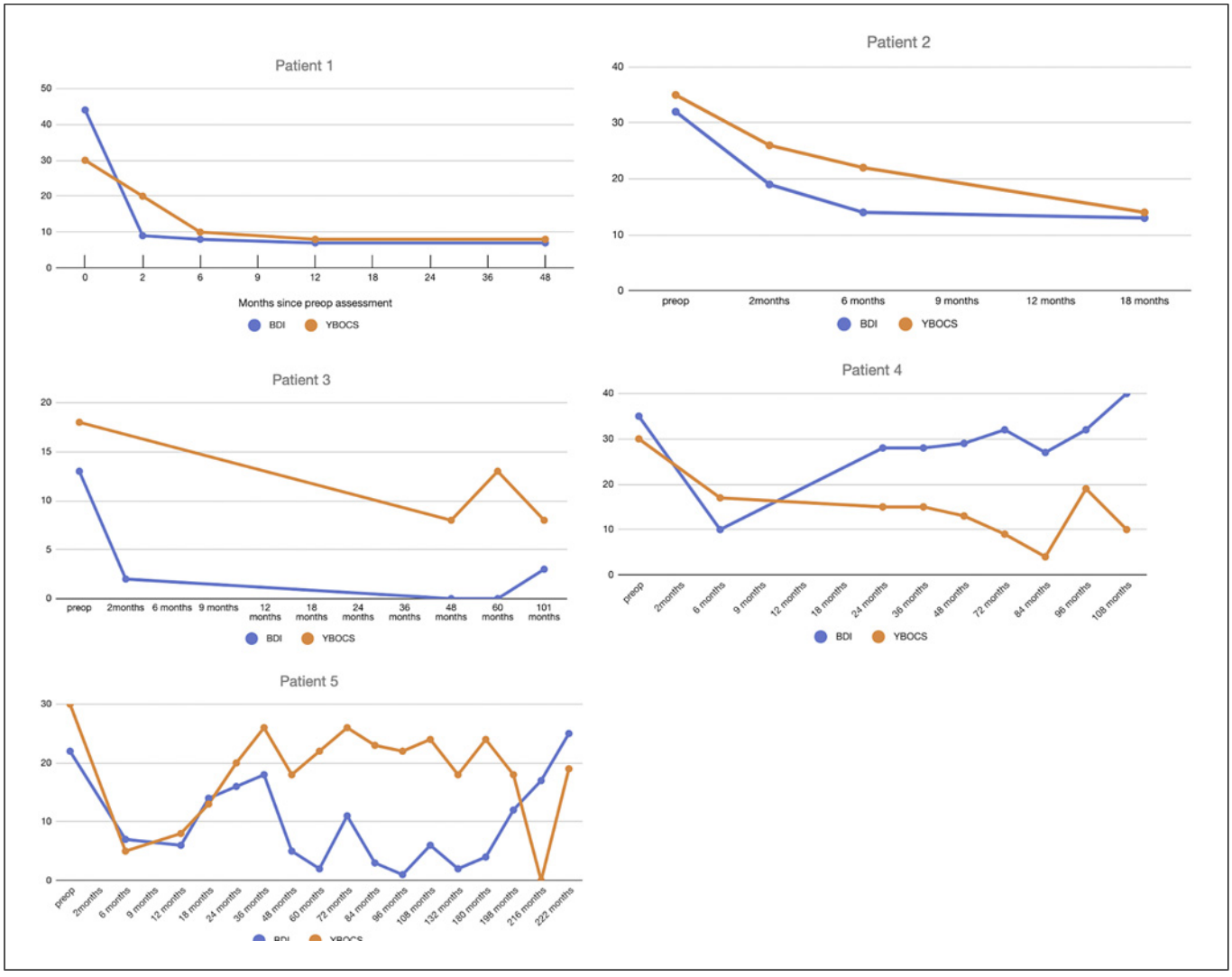

Fig. 1. Graphed postoperative trajectories. BDI, Beck Depression Inventory; YBOCS, Yale-Brown Obsessive-Compulsive Scale.

Table 4. Postoperative capsulotomy dimensions

	Planar measurements (R, mm)			Volume (mm^3)	Planar measurements (L, mm)			Volume (mm^3)
	length	diameter coronal	diameter axial		length	diameter coronal	diameter axial	
OCD101	9.8	3.6	5.9	268	5.7	1.8	2.2	22
OCD103	15.8	4.4	6.3	503	13.5	4.7	6.2	408
OCD104	15.2	2.5	8.9	952	14.6	2.1	7.5	642
OCD105	16.9	4.9	13	2243	15.4	5.5	10.4	1,307

the YBOCS score compared to preoperative measurements. Obsessions and compulsions appeared minor, with compulsions appearing to have a tic component secondary to sensory buildup. The BDI score was 3, indicating no depression. This score demonstrated a 77% reduction from a preoperative score of 13, indicating minimal depression. Clinically, the patient was doing well but was still living at home and needed prompts to live up

to the family's standards of tidiness. The patient had completed a diploma at a community college and was working with an occupational therapist to identify a career.

Patient 4

Patient 4's last psychometric assessment of OCD and depression was done 13 years postcapsulotomy. The YBOCS score was 0, indicating a total resolution of OCD (100% reduction). The BDI was 31, compared with 35 preoperatively. The lack of any meaningful response on assessments of mood correlated with the clinical presentation of ongoing severe demoralization in addition to medication noncompliance and new-onset hypothyroidism.

Patient 4 was repeatedly hospitalized post-BAC for suicidal ideation and failure to cope. The patient had been ill since childhood and had never been able to acquire adaptive coping skills that emerge during critical developmental periods [13].

When obsessions, compulsions, and depression were meaningfully attenuated by surgery, the patient, now freed from this burden, was unprepared to manage the day-to-day demands of life. The patient failed to benefit from 2 years of living in a group home specifically designed for psychosocial rehabilitation. Everyday challenges created intolerable anxiety, which in turn provoked suicidal ideation and visits to hospital emergency rooms. The patient could only adapt by retreating into the virtual world of electronics and fantasies about idolized heroes dating from childhood and adolescence. Further, the patient slept during the day and woke at night. This sleep cycle inversion was conducted primarily to avoid facing the challenges of normal daily living. During 4 hospitalizations, each several weeks in duration, there was no evidence of resurfaced OCD or MDD.

At the last contact 13 years postoperatively, gender dysphoria had surfaced. There were ongoing social avoidance and reliance on family for support. There was evidence of severe demoralization from a life characterized by a marginal existence, feelings of hopelessness, and feelings of being a failure. This demoralization significantly contributed to the elevated BDI score of 31 (severe depression). There were no obsessions or compulsions, but there were persistent idiosyncratic behavioral rules. These rules had been established in adolescence and governed specific life situations. When asked, the patient could not recall the initial motivation for these rules but felt no reason to deviate from them.

Patient 5

Patient 5's last psychometrics were completed 20 years postsurgically. The YBOCS was 20, indicating moderate OCD and representing a 33% reduction in OCD compared to the presurgical score of 30. Obsessions and compulsions, although significantly better compared with the preoperative condition, had worsened because of stopping fluvoxamine 9 months previously. While still on fluvoxamine, the YBOCS was 19 representing a 37% reduction in OCD compared to the preoperative YBOCS score of 30 and making the patient a treatment responder. The BDI score was 8, which indicated no depression and a 64% reduction in score from the preoperative score of 22.

Patient 5 was also known to have bipolar disorder with maladaptive social psychosexual and social behavior which were overshadowed and obscured by severe treatment-refractory OCD and depression. When OCD and depression were successfully treated by capsulotomy, these precapsulotomy social deficits came to the forefront creating problems in daily living.

Despite intensive community psychiatric support over a period of 20 years postsurgery, preexisting personality traits remained and led to problematic psychosocial dysfunction with poor judgment motivated by entitlement and the pursuit of desired goals with no consideration of the consequences. The patient had high expectations of compensation because of psychiatric disability and felt exempted from normal social rules.

The patient began contravening rules and making unsound financial decisions postsurgically. The patient was smoking marijuana at a self-reported cost of up to $600 a month with the need to pawn off possessions to cover this expense. The patient smoked indoors despite building regulations and took in undesirable and illegal roommates. Repeated rule contraventions such as these caused conflict with landlords and resulted in eviction. These dysfunctional behaviors only settled in the 2 years prior to last contact when given subsidized community housing where rules were strictly enforced.

At the last contact, the patient was alert and neatly groomed with euthymic mood and minimal overfamiliarity. There was no expansiveness or grandiosity. Nine months prior to the last contact, under the guidance of his community psychiatrist, fluvoxamine was stopped. The patient had felt that this medication was no longer needed. However, some obsessions and compulsions had returned. These included repeatedly checking that there was no fecal contamination of

Table 5. Postoperative complications

Patient	Postop – 6 months	6 months to 1 year	1 year to long term
1	Psychobehavioral disinhibition resembling disinhibited frontal lobe syndrome. Childlike regressive behavior with no insight. Complete resolution by postoperative day 21	Nil	Nil
2	Right hemifacial edema and bifrontal headache in the first week postoperatively	Nil	Nil
3	Postoperative delirium and a grand mal seizure at 3 months postoperatively due to abrupt clonazepam discontinuation. Notably, there had been a seizure 2 years prior to surgery, also in the setting of medication adjustment	Motivational failure for mundane ADLs	Motivational failure for mundane ADLs
4	Frontal apathy, flat effect, and fatigue in the first month postoperatively. Symptoms resolved by the end of the first month postoperatively	Decreased motivation	Burden of normality
5	Dulled emotions, decreased attention to personal grooming, poor judgment, increased appetite with weight gain, and mild memory impairment	Nil	Nil

clothes or checking every 10 min for the presence of wallet, cell phone, and spectacles. The YBOCS score was 20, indicating moderate OCD, but the patient was managing and did not want to restart another anti-obsessive agent because of concern that medications would numb feelings.

Neuropsychological Performance

Neuropsychological data were missing for 2 patients. In the remaining 3 patients, there was worsening of verbal memory at 2 months, which returned to baseline at 12 months. In 1 individual, phonemic fluency and motor speed were impaired at 2 months and 12 months. In this same individual, motor dexterity deteriorated at 2 months but returned to baseline at 12 months.

No patients demonstrated changes in psychobehavioral regulation, frontal lobe deficits, or executive abilities. In summary, there were no systematic losses of neurocognitive capacity, while only 1 patient showed neurocognitive and neuromotor slowing that persisted at 12 months postoperatively. These neuropsychological data are consistent with our previous analysis of 10 patients who received the identical procedure for treatment-resistant depression [10].

All data considered; the Vancouver capsulotomy does not appear to cause any neurocognitive deficits. Our capsulotomy also does not cause deficits in psychobehavioral regulation, frontal lobe functioning, or executive abilities. The protection of these abilities is likely because the Vancouver capsulotomy limits the dorsal extent of the lesion, thereby avoiding the fibers that connect to the dorsolateral PFC [10].

Side Effects

Side effects are described in Table 5. The only notable side effect was the emergence in 1 patient, patient #4, of an intractable psychobehavioral syndrome known as the "burden of normality." This syndrome was first described by an Australian group in 2001 and captures the clinical course of individuals with intractable temporal lobe epilepsy who were successfully treated by temporal lobectomy [14]. Instead of the anticipated psychosocial recovery from being "cured" by surgery, some patients became avoidant. They failed to acquire adaptive coping skills and resisted any attempts to change their psychosocial circumstances. Our patient's psychosocial regression and avoidant behaviors are described in her narrative account.

One other patient in our case series had selective motivational failure for mundane activities of daily living such as living up to family standards of tidiness. By contrast, there were no problems with motivation for desired activities such as studying or recreational activities.

Discussion

This study involved a rigorous analysis and a follow-up of 5 patients by one clinician after anterior capsulotomy for TROCD conducted by one neurosurgeon. Overall, this study reveals BAC to be highly successful in the treatment of TROCD as well as in the treatment of MDD. By predefined and widely accepted criteria between 18 and 48 months, 5/5 (100%) patients were responders with respect to OCD and

Table 6. Rounded responder rates at 1 year and in the long-term scale of months

Study	*n*	Studied procedure	Mean height of lesion, mm	1-Year responder rate	Long-term follow-up (months) rounded means	Long-term responder rate
Sheth et al. [19], 2013	34	Single BCING (single pair)	–	50%	59	38%
Sheth et al. [19], 2013	27	Multiple BCING or BCING + BSCT	–	19%	65	59%
Jung et al. [20], 2006	17	Single BCING (double pair)	18	41%	24	47%
Oliver et al. [15], 2003	15	TBAC	18	53%	24	–
Liu et al. [16], 2008	35	TBAC	–	91%	36	–
Rück et al. [21], 2008	9	TBAC	18	56%	131	56%
Zhan et al. [22], 2014	53	TBAC	–	–	68	77%
Liu et al. [23], 2017	37	TBAC	–	–	60	73%
Rück et al. [21], 2008	6	GBAC	–	50%	131	67%
Sheehan et al. [24], 2013	5	GBAC	–	–	22	80%
Kondziolka et al. [25], 2011	3	GBAC	–	–	42	67%
Lopes et al. [26], 2009	5	GBAC	–	40%	48	60%
Lopes et al. [27], 2014	12	GBAC	–	25%	55	50%
Rasmussen S et al. [28], 2018	40	GBAC	–	55%	36	75%
Peker S et al. [29], 2020	20	GBAC	–	45%	36	75%
Gupta A et al. [30], 2019	40	GBAC	–	–	36 (median)	45%
Spatola G et al. [31], 2019	10	GBAC	–	–	41	70%
D'Astous et al. [17], 2013	19	MBAC	20	–	84	37%

% responders at 1 year; % responders at long-term follow-up.

4/5 (80%) were responders with respect to comorbid depression. In 1 patient, depression was minimal prior to surgery but absent postsurgery. Improvement of depression was not unexpected, as we have previously shown the benefit of BAC in the treatment of depression [10].

Our results with capsulotomy show better outcomes over an extended observational period when compared to other centers that use BAC for TROCD, with the caveat that our sample size is small. Below, we tabulated the results of reports that have used the same criterion of a ≥35% decrease in YBOCS to define a responder and in which the YBOCS score was specified per individual presurgery and at the follow-up intervals. Reports that expressed outcome as a group mean were excluded. Moreover, the analysis was restricted to only patients who had a single bilateral procedure.

Some capsulotomy reports do not indicate individual YBOCS scores but provide the % of responders who meet the responder criterion. These summarized responder outcomes may include patients who had repeat procedures. These data are included in the table as it was not possible to identify and exclude the few patients in each case series who had more than one surgery [15–17].

For BAC, we have separated the outcomes by the method of ablation. There are 3 established methods – thermal via radiofrequency lesioning (TBAC), radiation necrosis via gamma radiation (GBAC), and mechanical via leukotome (MBAC). Thermal and gamma radiation methods of ablation are not equivalent as the extent and discreteness of the lesion may vary, while in GBAC, there may be delayed radionecrosis, which may potentially impact benefit [18]. Mechanical ablation is an outmoded technology and is no longer in use.

We also compare the outcome from BCING. For BCING, single cingulotomies are often ineffective and the procedure is often repeated up to two times before being combined with BSCT if no benefit is observed with the first treatment [19]. As data on BCING are limited, our analysis includes patients who had more than one surgery (Table 6).

The long-term responder rates for BAC varied between 37% and 80% with a mean of 64%. This rate in the BCING population varied between 38% and 59% with a mean of 48%. Altogether, these data suggest that BAC is a more effective procedure for treating TROCD than BCING.

More recently, ablation has been performed using Magnetic Resonance-Guided Focused Ultrasound Surgery (MRgFUS). MRgFUS is an incision-less surgery that uses high-intensity acoustic energy to produce discrete lesions in the brain. This is a novel technology and still in its infancy; there are no long-term outcome data associated with this procedure. There are significant, unsolved technical challenges in safety and reliability associated with this technique [32].

The preliminary results appear promising. The Toronto group treated 6 patients with TROCD [33]. Four out of six (66.7%) were responders, with a demonstrated improvement in the YBOCS score of ≥35% at 6- to 12-month follow-up. The Seoul group treated 11 patients with TROCD [34]. At 12 months, they had a responder rate of 54% (6/11). At 24 months, the responder rate remained 54% (6/11), but 1 responder at 12 months became a nonresponder at 24 months, while 1 nonresponder at 12 months became a responder at 24 months.

Although sample sizes from each report were mostly small, the evidence from the worldwide experience indicates that ablative surgery and BAC in particular should remain an option in patients with TROCD, as there is an expected response rate of 45–100% (mean 67%) after the procedure if our data are included. This is better than the response rates to antidepressants, where the expected response rate, as indicated by a reduction of ≥50% in the score of a standard depression assessment scale, lies between 42% and 53% [35, 36].

However, cross-sectional and longitudinal observations for up to 4 years after BAC do not provide the full clinical picture of real-world outcomes, no matter how successful BAC is in treating the core circumscribed syndromes as measured by psychometric scales. The longer-term narratives demonstrate the complexity of the psychopathology of the individuals who were screened and found eligible for BAC; these narratives are stark examples of the multifactorial determinants of mental health. Mental illness with psychological dysfunction cannot be addressed by treating the brain alone separate from the individual's personality, coping styles and circumstances [37].

After surgery, preexisting vulnerabilities or maladaptive behavioral patterns acquired during patients' lengthy presurgical illnesses dominate, and a different set of regressive, poorly adaptive behaviors may emerge. These behaviors are coupled with reactive dysphoria as BAC does not blunt emotional capacity. BAC severs axons of passage. The terminus emotional neuroanatomical loci themselves are left intact and remain available to valence internal and external events as they arise [38].

These cautionary narrative accounts illustrate the need for comprehensive assessment of individuals prior to undertaking ablative surgery, as the prediction of long-term outcomes will be dependent on factors other than the primary psychiatric disorder targeted by surgery. Patients need to be carefully screened for premorbid vulnerabilities and resilience. This is especially important in those patients who have been ill since early adolescence. Their illness interferes with critical developmental phases and the acquisition of adaptive coping responses that occur during this time. When patients' OCD is successfully treated, they may then find themselves unprepared to deal with the demands of everyday life and as such remain marginally functional, support-dependent, and overwhelmed by the "burden of normality." A much milder version of the burden of normality in our study was the delayed acquisition of the expected age-appropriate standards of personal and social conduct and responsibility in patient #3.

The "burden of normality" is not a side effect in the standard sense, but rather the impact of "curing" an illness and exposing the patient's vulnerabilities. These problems surface over the years postoperatively and are only identified if the patients are followed over decades. This highlights the need for a careful review of the

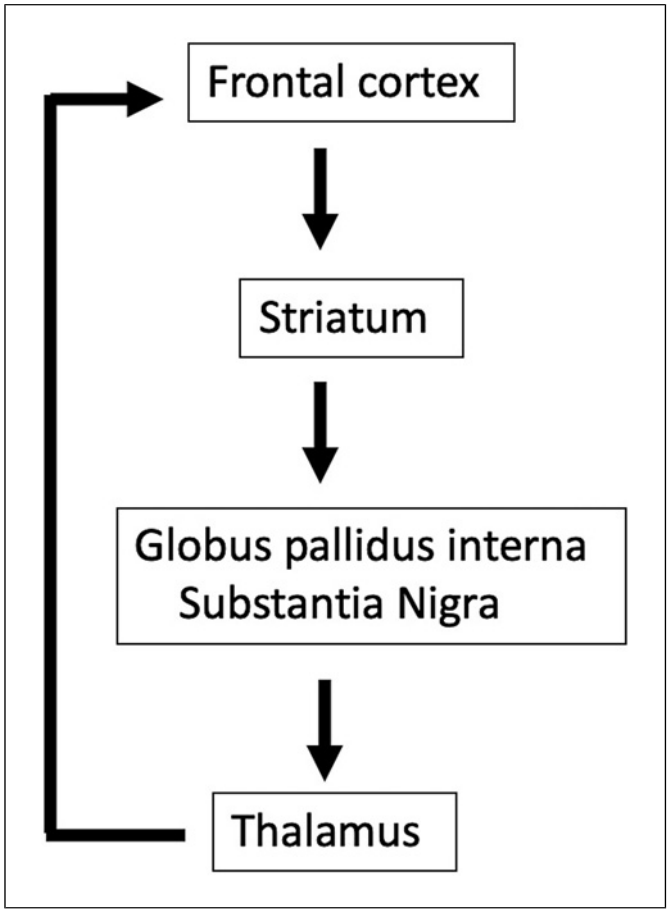

Fig. 2. Cortico-striato-thalamo-cortical circuit.

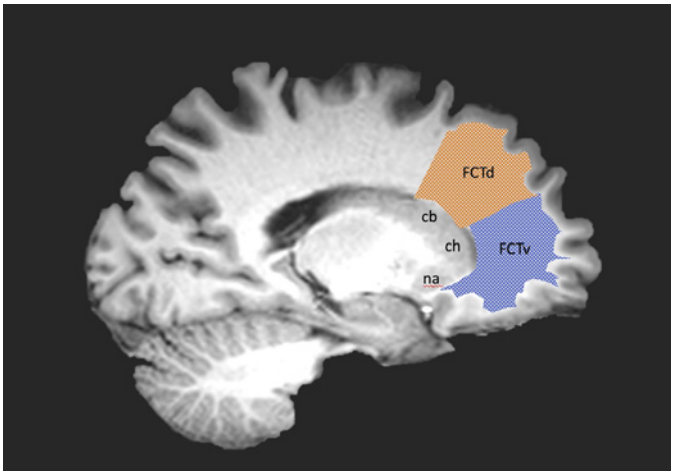

Fig. 3. An illustration of the frontocaudate tracts. The dorsal frontocaudate tract (FCTd) and ventral frontocaudate tract (FCTv) fibers connect to the body (cb) and caudate head (ch) of the caudate nucleus. The caudate head and the nucleus accumbens (na) form the major part of the ventral striatum.

patient's presurgical longitudinal coping behavior. Coping vulnerabilities should not exclude a patient from surgery if the suffering from OCD is relentless and intolerable despite all other treatments. However, outcome expectations need to be appropriately adjusted. Experience has shown that self and family acceptance of postsurgical performance/functioning is easier said than done and is always a work in progress.

Aside from the above, capsulotomy appears to be a safe procedure. There are no predictable long-term physical adverse events from BAC based on the ablation location [39]. Moreover, there is good evidence that capsulotomy does not compromise neurocognitive performance in any systematic way, nor does it produce frontal lobe or executive deficits provided that the capsulotomy size does not exceed 15 mm in length and is targeted to its ventromedial portion [10, 39].

All of our patients remained on medications such as SSRIs, second-generation antipsychotics, mood stabilizers, and benzodiazepines. When 1 patient (patient #5) stopped fluvoxamine 19 years postcapsulotomy, OCD relapsed over a period of 9 months but was not as severe as it was preoperatively. When patient #1 stopped clomipramine 1-year postsurgery, long-standing obsessionality intensified but neither residual obsessions nor compulsions intensified. The lesson here is that patients may still require lifelong medication and that capsulotomy attenuates but does not eliminate the underlying disturbed neurobiology.

The mechanism of action of BAC in treating TROCD remains unresolved, but accumulating biological data now point strongly to aberrant signaling in cortico-striato-thalamo-cortical (CSTC) circuits that are remodeled by any effective treatment for OCD including BAC [40].

The CSTC circuit consists of neuronal nodes with connecting projection axons linking nodes sequentially. The CSTC circuit has a basic structure. It originates in a cortical node of origin (CNO), leads to the striatum, courses through the globus pallidus interna/substantia nigra, runs through the thalamus, and terminates back in the CNO (Fig. 2). This basic structure is known as the direct pathway and is excitatory. Variations in this loop give rise to the indirect and hyper-direct pathways both of which are inhibitory [41].

Research has most consistently found hyperactivity in the orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) during active OCD [42]. After any effective treatment of OCD, including BAC, both the OFC and ACC show decreased activity [40]. Effective treatment of

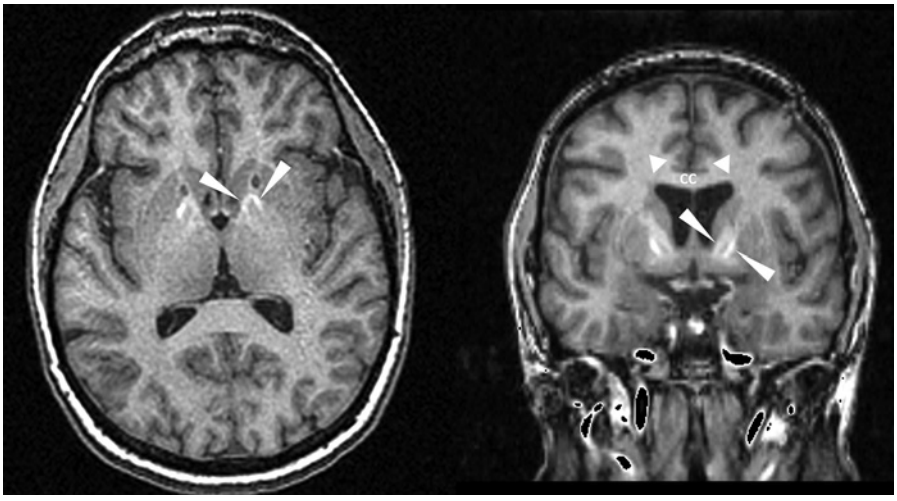

Fig. 4. T1-weighted spoiled gradient echo MRI at 2 months postoperatively. Planar aligned axial and coronal T1-weighted spoiled gradient echo (SPGR) MRI at 2 months postoperatively. Long arrowheads show medial and lateral axonal bundles caudal to capsulotomy, while short arrowheads show the cingulate gyrus. Here, the CC denotes the corpus callosum.

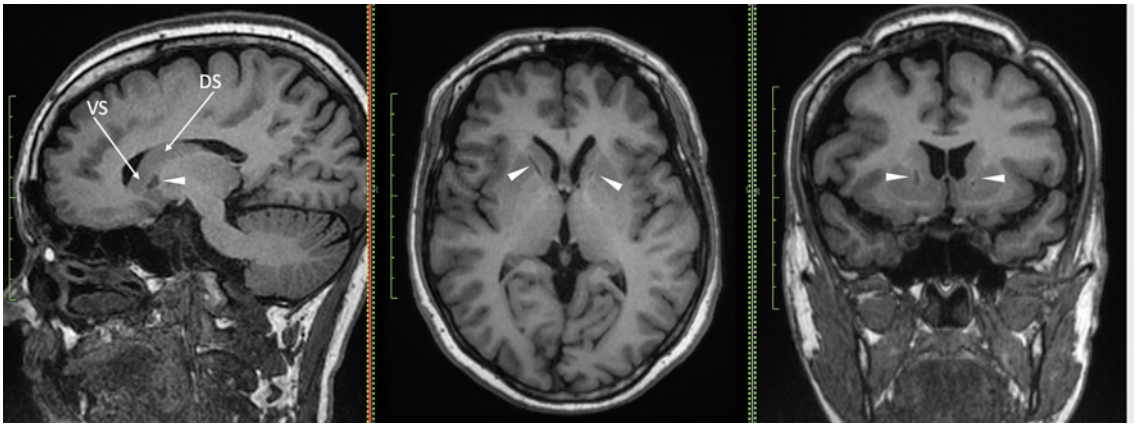

Fig. 5. Sagittal, axial, and coronal MRI 1-year post-BAC. The capsulotomy, indicated by the arrowheads, is small and located in the most ventral aspect of the ALIC. VS, ventral striatum; DS, dorsal striatum.

OCD also produces decreased activity in the thalamus, caudate, and the PFC [40].

The OFC and ACC are spaced-apart CNOs and the point of termination of 2 of 5 classical CSTC loops [43]. In the original formulation, CSTC loops were felt to be parallel but segregated and nonoverlapping [44]. More recent data have shown that these circuits converge and overlap in hubs. Hubs cross-link information across diverse systems to achieve functional integration. Within the CSTC circuits, both the ventral striatum (rostral caudate in particular for projections from the PFC) and thalamus are exchange hubs. The hub effect may account for the positive correlation between the OFC and ACC CSTC circuits before and after treatment in patients with OCD [45–47].

It is furthermore likely that within the striatal hub, the OFC CSTC circuit is dominant. PFC connects to the striatum via the Muratoff fronto-caudate tract (FCT) [48]. The FCT is divided into a ventral (FCTv) and dorsal segment (FCTd). FCTv contains projection fibers from OFC, while FCTd contains projection axons from the dACC. FCTv connects to the head of the caudate nucleus, while FCTd connects to the body of the caudate nucleus. FCTv is thicker and bulkier than FCTd, suggesting the dominance of FCTv over FCTd [48] (Fig. 3).

While the mechanism of action of most treatments of OCD is open to debate and speculation, the mechanism of action of white matter ablative lesions is straightforward and unequivocal. White matter ablation severs axons of passage disconnecting neurons of origin from neurons of termination.

BAC appears to sever 2 corticopetal pathways. In a prior publication, these pathways were visualized in the

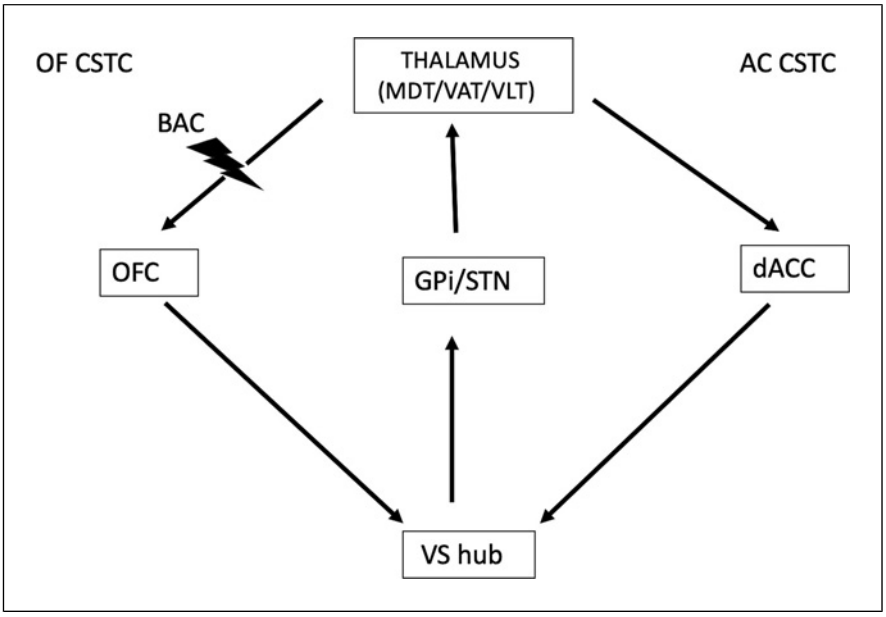

Fig. 6. A thalamocentric model of OCD based on the observed clinical benefit of BAC on OCD and early imaging studies. AC, anterior cingulate; dACC, dorsal anterior cingulate cortex; BAC, bilateral anterior capsulotomy; CSTC, cortico-striato-thalamo-cortical; GPi, globus pallidus interna; MDT, mediodorsal nucleus of the thalamus; OF, orbitofrontal; OFC, orbitofrontal cortex; STN, substantia nigra; VAT, ventral anterior nucleus of thalamus; VLT, ventrolateral nucleus of thalamus; VS, ventral striatum.

2-month post-BAC MRI. Two bundles, medial and lateral, are apparent because of accumulating lipoproteins in the proximal axons of the surviving perikarya as they attempt to repair themselves (Fig. 4). The accumulated lipoprotein is responsible for the hyperintense signal on the T1-weighted MRIs. By contrast, the axons distal to the capsulotomy undergo Wallerian (anterograde) degeneration and are not seen on the T1 images. At about 1 year postcapsulotomy, the hyperintense signal in these proximal segments starts to fade and eventually disappear as retrograde degeneration supervenes and the perikaryon dies [49].

The medial bundle, a thalamocorticolimbic pathway, appears to arise from the thalamus. The specific thalamic nuclei of origin remain uncertain but, based upon the pattern of atrophy visualized in the 1-year post-BAC MRIs, include the dorsomedial and anterior nuclei [49]. The full course of this thalamocorticolimbic pathway in humans has now been mapped by postmortem dissection [50].

The lateral bundle, a mesocorticolimbic pathway, appears to arise in the ventral tegmental area [49]. Both bundles appear to be unidirectional as there are no returning axonal bundles that have revealed themselves rostral to the capsulotomy. For an OFC CSTC travelling in the ALIC, this is not unexpected as the OFC joins the CSTC loop by connecting to the VS via the vFCT terminating directly on the VS and not passing through the ALIC [48].

Within the ALIC, the location of the OFC connecting axons predictably lies in its most ventral aspect [51, 52]. The last two capsulotomies conducted by our group specifically targeted the ventral aspect of the ALIC [11]. The ventral-dorsal dimensions of our older capsulotomies were 14.2–14.8 mm in length [38]. More recently, our ventrally targeted BAC was reduced by up to half this length (6.3–11.2 mm) while retaining all the clinical benefits [12]. As can be seen in the 1-year postsurgical MRI, the ventrally targeted BAC lies in the most ventral aspect of the ALIC and lies caudal to VS and ventral to dACC and distant from vFCT and dFCT (Fig. 5).

After BAC, VS to dACC connectivity is strikingly reduced [53]. Ventral striatum to OFC connectivity is also reduced, but only in cases that showed a clinical response [53]. These investigators did not, however, show any connectivity pattern changes related to the mediodorsal nucleus of the thalamus, which is one of the source thalamic nuclei that innervate OFC and dACC. The other thalamic nuclei that innervate the OFC are the ventral anterior and ventrolateral [54, 55]. The mediodorsal nucleus of the thalamus is large and has widespread connectivity that includes the entire PFC, frontal eye fields, amygdala, temporal lobe, and the brainstem. The preservation of these connectivities together with other OFC innervating thalamic nuclei could obscure any connectivity pattern changes to OFC after BAC [56].

Integrating all these data into a model of OCD where BAC is an effective treatment yields a thalamocentric CSTC model of OCD in which the primary disturbance lies in an overactive thalamus driving OFC. After BAC and via the hub effect, a less-driven OFC influences dACC to downregulate (Fig. 6). In support of the thalamocentric

model is a monkey model of compulsive-like behaviors that were elicited by overactivating the ventral anterior nucleus of thalamus but not DMT [57]. DMT overactivation led to motor hypoactivity with autonomic changes such as heart rate variation [57].

How OFC-CSTC overactivity correlates with OCD phenomenology remains uncertain. A compelling model suggests that overactivity in the OFC-CSTC circuits generates intrusive aversive thoughts and images that override other sensorimotor input [58, 59]. Subsequently, the resultant anxiety provokes anxiety-relieving rituals (compulsions) [60].

Conclusion

In 5 patients with TROCD, BAC achieved a responder rate of 100% when followed over an interval of 18 months. Four patients remained responders at the 48-month postsurgical mark. One patient was lost to follow-up. Four patients were followed for 4–20 years. All 4 patients remained responders except 1, who relapsed 19 years postcapsulotomy when he stopped taking his SSRI. In our sample, BAC had no significant long-term neurocognitive or physical side effects.

Our results in treating TROCD with BAC compare favorably to those published by other centers, but the reasons for our good results are uncertain. The major limitation of our results is our small sample size and the lack of generalizability of our results. Small samples are characteristics of most reports of ablative surgery for psychiatric illness, as the procedure is an intervention of last resort and is as such used infrequently. However, our results are consistent with the worldwide experience of the benefit of BAC for TROCD. The strength of our sample lies in the fact that the same team has been involved with these patents for over 20 years and provides a unique perspective on the longitudinal trajectories of patients with OCD who are treated with targeted ablations.

BAC eliminated the neurobiological etiology of our patients' suffering and remained effective over the long term, provided that they remained on medications to continue managing their OCD postoperatively. Real-world outcomes were, however, different, as other vulnerabilities surfaced postsurgically. This illustrated the multifactorial determinants of mental health and the need for careful screening so that expectations can be appropriately adjusted.

Based on our results and other reports worldwide, BAC should remain an option of last resort for patients with severe OCD who remain unresponsive to all other interventions. Its use may increase as the availability of MRgFUS increases. While this technology is still in its infancy and technical challenges still need to be solved, it may provide the same benefit as other ablative techniques.

Statement of Ethics

Ethics approval was obtained from the Vancouver Hospital and Health Sciences Centre's Medical Advisory Board and Ethics Committees. From 2016 onward, this study was conducted under ethical approval from the UBC Clinical Research Ethics Board (H16-01722 and H21-02230). All patients gave written informed consent to undergo capsulotomy. Four of the 5 patients gave written consent for anonymized medical details from their records to be included in this report. These details are contained in their narrative accounts. One patient (patient 2) was lost to follow-up after 18 months and was unreachable. There is no narrative account for this patient.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Dr. Trevor Hurwitz is the lead for the limbic surgery program in Vancouver and is the principal author. He was responsible for the conception, design, analysis, and drafting/revising of the paper. Dr. Christopher Honey was the neurosurgeon who performed the procedure and was responsible for the conception, design, and revision of the paper. Dr. Nicolas Bogod is the neuropsychologist who administered the neuropsychological test battery and was responsible for analyzing the data as well as the revision of the paper. Dr. Geoffrey Ching is a physician, who worked as a research assistant on this project. He was responsible for researching and summarizing recent literature on OCD, and its neurosurgical treatments. He was also responsible for revising the paper.

Data Availability Statement

All data generated or analyzed during this study are included in this article. For ethical reasons, patient charts that contain unrelated personal information are not publicly available. Further inquiries can be directed to the corresponding author.

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