

## Anterior capsulotomy for obsessive-compulsive disorder: a review of old and new literature

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Over the last two decades, deep brain stimulation (DBS) has gained popularity as a treatment of severe and medically refractory obsessive-compulsive disorder (OCD), often using brain targets informed by historical lesional neurosurgical procedures. Paradoxically, the use of DBS in OCD has led some multidisciplinary teams to revisit the use of lesional procedures, especially anterior capsulotomy (AC), although significant aversion still exists toward the use of lesional neurosurgery for psychiatric disorders. This paper aims to review all literature on the use of AC for OCD to examine its effectiveness and safety profile.

All publications on AC for OCD were searched. In total 512 patients were identified in 25 publications spanning 1961–2018. In papers where a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score was available, 73% of patients had a clinical response (i.e., > 35% improvement in Y-BOCS score) and 24% patients went into remission (Y-BOCS score < 8). In the older publications, published when the Y-BOCS was not yet available, 90% of patients were deemed to have had a significant clinical response and 39% of patients were considered symptom free. The rate of serious complications was low.

In summary, AC is a safe, well-tolerated, and efficacious therapy. Its underuse is likely a result of historical prejudice rather than lack of clinical effectiveness.

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**KEYWORDS** obsessive-compulsive disorder; psychosurgery; anterior capsulotomy; Gamma Knife; focused ultrasound; radiofrequency ablation; functional neurosurgery

**P**SYCHOSURGERY in all its guises often provokes a mélange of reactions. Recalling the era of unselective lobotomy from over half a century ago rouses fear and revulsion.<sup>19</sup> However, currently there is cautious optimism that psychosurgery or neurosurgery for mental disorders (NMD) has learned from its past. The field of NMD is undergoing a renaissance, buoyed by the popularity of deep brain stimulation (DBS) for movement disorders. Paradoxically, this surge in interest in DBS in psychiatry has reinvigorated the field of stereotactic lesional neurosurgery for mental illness.

Current stereotactic lesional procedures are vastly different from those of the 1950s through 1970s, having benefited immensely from new imaging, new technology, closer multidisciplinary work, and more robust follow-up.<sup>14</sup> However, there is consternation that their use represents a backward step in the evolution of functional neurosurgery. Nevertheless, many stereotactic lesional procedures of the

past showed promising and successful results.<sup>2,18</sup> Indeed, a small double-blind randomized controlled trial of capsulotomy for OCD has recently demonstrated significantly greater improvement in patients undergoing capsulotomy versus controls.<sup>22</sup> “Lesional surgery” is widely accepted in the field of epilepsy, and neurologists routinely refer patients for resection or ablation of significant volumes of brain tissue (for example, in temporal lobe epilepsy). However, psychiatrists are generally much more reticent to consider referral of patients for stereotactic ablation. History informs the selection of new DBS targets<sup>29</sup> and also helps develop and modernize the “old” lesional procedures that have been underused for a vast pool of severe, chronic, and refractory psychiatric diseases.

Obsessive-compulsive disorder (OCD) is a psychiatric condition that often runs a chronic and debilitating course. It affects 2% of the global population and in many patients continues to worsen or becomes refractory to medical and

**ABBREVIATIONS** AC = anterior capsulotomy; DBS = deep brain stimulation; GK = Gamma Knife; ICH = intracerebral hemorrhage; NMD = neurosurgery for mental disorders; OCD = obsessive-compulsive disorder; SSRI = selective serotonin reuptake inhibitor; Y-BOCS = Yale-Brown Obsessive Compulsive Scale.

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psychiatric management.<sup>9,40</sup> It is in these patients and within the context of a multidisciplinary team that neurosurgery should be considered. A number of brain targets have historically been selected in the treatment of severe OCD; procedures currently performed include anterior capsulotomy (AC),<sup>22</sup> cingulotomy,<sup>4</sup> and subcaudate tractotomy.<sup>42</sup> The anterior capsule has been one of the most widely used targets, with reported remission rates of 30% and clinical response rates of 75% in some publications.<sup>2,5,18,30</sup> Therefore, this data, no matter how historical, deserves analysis and evaluation. The accepted primary outcome measure in modern medical literature is the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), published in 1989.<sup>12</sup>

The aim of this paper is to assess both historical and modern outcomes of AC performed by any method (radiofrequency ablation, Gamma Knife [GK] radiosurgery, mechanical leukotomy, or MR-guided focused ultrasound) in the treatment of OCD in order to inform further treatment for patients with this highly refractory and difficult-to-treat condition.

## Methods

Publications on AC for OCD were obtained from the PubMed database, from proceedings of neurosurgical meetings, and from references from relevant papers published before September 2018. The search criteria used are in accordance with guidelines published in the Cochrane Library. PubMed was searched using a combination of optimal search strategies and the phrase(s): surg\* OR neurosurg\* OR psychosurg\* OR radiosurg\* OR capsuloto\* OR tractoto\* OR leucoto\* OR leukoto\* OR loboto\* OR radio-surg\* OR radiosurg\* OR stereota\* OR stereo-ta\* OR gamma kni\* OR gamma-ra\* OR deep brain stimulation OR DBS OR neurosurgical procedures/ AND obsessive compuls\* OR obsessive-compuls\* OR mood disorders OR anxiety disorders.

The included publications were all studies in which patients with obsessive-compulsive disorder/neurosis underwent AC by any surgical method. Where possible, details of baseline characteristics (diagnosis of OCD, neurosurgical procedure conducted, duration of OCD, age at surgery, Y-BOCS score, social functioning) and outcome (follow-up time, Y-BOCS or scoring system used at last follow-up, comment on social functioning) were collected. Whenever possible, duplicate cases were identified and removed.

Papers were also screened with respect to reported adverse events. Serious adverse events were defined as those that would contribute significantly to morbidity (infection, epilepsy, intracranial hemorrhage) or mortality, including suicide within the first 12 months after surgery. Persisting adverse events were defined as new-onset symptoms that persisted for more than 8 weeks after surgery. These could include headache, dizziness, nausea, sleep disturbance, apathy, disinhibition, other personality changes, and other symptoms. Whenever there was uncertainty about an adverse event (e.g., the length of time it lasted) it was still included in the results.

For papers reporting on patients without Y-BOCS scores, considered “old” publications, patients were grouped by outcome according to a combination of analy-

sis of social comments made about patients, the authors’ impression, and any scoring system described in the publication.

The outcome group criteria used for “old” publications were as follows: Group A—symptom free/return to normal life activities; Group B—symptoms much improved, independent, back to work with some help; Group C—symptoms and level of social functioning improved, back to work or conducting some normal activities with support; Group D—no or minimal improvement of symptoms that has no useful impact on social/work functioning; Group E—worse.

For papers reporting on patients with a Y-BOCS score, outcome was determined as follows. Remission requires that Y-BOCS scores drop below 8, considered equivalent to Group A above. Response is defined as 35% improvement or more in Y-BOCS, considered equivalent to Group C above. Nonresponder is when remission or response criteria are not met, considered equivalent to Group D above. Worse indicates a worsening of the Y-BOCS score from baseline, considered equivalent to Group E above.

When individual patient data was not available group averages were used.

## Statistical Analysis

Mean values were calculated. The Student t-test was used to compare continuous data. Fisher’s exact test, using a 2 × 2 contingency table, was used to compare the outcomes and complication rates in patients who had AC. A p value < 0.05 was considered statistically significant.

## Results

In total, 25 studies and 512 patients were identified in publications from 1961 through September 2018. In the “new” publication group, there were 16 studies<sup>3,5,6,8,13,16,17,20–23,30,34,37,38,43</sup> reporting outcome for 278 patients, and in the “old” publication group there were 9 studies<sup>1,2,10,15,18,25,27,28,36</sup> reporting outcome for 234 patients.

### Baseline Characteristics

Table 1 (“new” publications) and Table 2 (“old” publications) present baseline details of the number of patients in each study, age at surgery, length of follow-up, duration of OCD, and details of the surgical procedure. Table 3 summarizes the baseline characteristics of the patients in the 2 publication groups.

### Year of Publication

The number of published cases rapidly increased from the 1960s until the 1980s. There was a paucity of new publications from the 1980s and a clear resurgence from 2000 until the present (Fig. 1).

### Outcome

Over 7 in 10 (201 of 278) patients in the “new” group had a clinically significant response, with 24% (66 of 278) going into remission. In the “old” group, over 90% of patients (211 of 234) were considered to have a clinically significant response (outcome A, B, or C), with almost

**TABLE 1. Summary of clinical and demographic characteristics of patients in “new” AC publications**

Authors & Year	No. of Pts	Age in Yrs	Sex (M:F)	FU (mos)	Procedure	Mean/(individual) YBOCS Scores	
						Preop	Postop
Kim et al., 2018	11	Mean: 33	5:6	Mean: 24	FUS, 51–56°C >3 sec, 10-mm ellipse	34.4	21.3
Rasmussen et al., 2018	55	Mean: 34	35:20	Mean: 36	GKS, bilat, max 180 Gy	33.9	17.5
Liu et al., 2017	37	NR	26:11	Mean: 60	RF 70°C 60 sec & 80°C 70 sec	26.78	8.3
Lopes et al., 2014	12	Mean: 34	7:5	Mean: 55	GKS, bilat, max 180 Gy	33.1	17.3
Zhan et al., 2014	53	Mean: 29	32:21	Mean: 67.5	RF 80°C 60 sec	24.7	6.5
Sheehan et al., 2013	5	Mean: 37	3:2	Mean: 22	GKS, bilat, 140–160 Gy	32	16
D’Astous et al., 2013	19	Mean: 41	7:12	Mean: 84	BL, bilat, 20 × 5–6 mm	35	24
Kondziolka et al., 2011	3	37, 40, 55	1:2	Mean: 42	GKS, bilat, 140–150 Gy	(34, 39, 39)	(24, 7, 18)
Doshi, 2011	1	62	1:0	0.3	RF, bilat, 75°C	(38)	(9)
Gouvea et al., 2010	1	34	0:1	12	GKS, bilat, 180 Gy	(37)	(0)
Csigó et al., 2010	5	Mean: 32	3:2	Mean: 24	RF: bilat	38	18
Lopes et al., 2009	5	Mean: 35	2:3	Mean: 48	GKS, bilat, 180 Gy	32	21
Rück et al., 2008	24	Mean: 41	10:14	Mean: 124	GKS, bilat, 160–200 Gy & RF, unilat or bilat, 12–20 mm, 60°C	34	19
Liu et al., 2008	35	Mean: 30	22:13	Mean: 36	RF, bilat 70–80°C	21	4
Oliver et al., 2003	10	Mean: 34	9:6	Mean: 12	RF, bilat, 18 mm 75°C	30	17
Christensen et al., 2002	2	18, 64	2:0	Mean: 40	RF, bilat, 65–70°C	(30, 31)	(0, 8)

BL = Bertrand leucotomy; FU = follow-up; FUS = focused ultrasound; GKS = Gamma Knife surgery; NR = not reported; pts = patients; RF = radiofrequency ablation. The “new” publication group was defined as studies that included Y-BOCS scores.

40% considered symptom free (outcome A) at long-term follow-up. See Fig. 2 for more details. Supplemental Tables 1–7 summarize outcome and adverse events in each included publication.

### Outcome by Procedure

In total 90 patients described in the “new” publications underwent GK capsulotomy, and two-thirds of these patients (60 of 90) had a clinically significant response; 158 patients in the “new” publication group underwent radiofrequency ablation, and 79% (125 of 158) had a clinically significant response; 19 patients in the “new” publication group underwent mechanical leukotome capsulotomy, with 7 being considered responders; and 11 patients in the “new” group underwent MR-guided focused ultrasound,

with 6 being considered responders. Of the patients in the “old” publication group—that is, patients without a Y-BOCS score—93% (13 of 14) of those who underwent GK capsulotomy were considered responders; of the 208 patients who underwent radiofrequency ablation, 189 had a clinically significant response; and of the 12 patients who underwent mechanical leukotomy, 9 responded (see Tables 1 and 2 and Supplemental Tables 1–7 for more detailed information).

### Adverse Events

Figure 3 and Supplemental Tables 1–7 highlight reported adverse events in more detail. No surgical deaths were identified.

The rate of stroke was 2%, although the majority of

**TABLE 2. Summary of clinical and demographic characteristics of patients in “old” AC publications**

Authors & Year	No. of Pts (no. evaluated)	Age in Yrs (range)	Sex (M:F)	Duration of OCD, Yrs (range)	FU, Mos (range)	Procedure
Burzaco, 1981	85 (85)	Mean: 36.4	39:45	NR	(8–180)	RF, bilat, 65°C, 40–50 sec, 12–20 × 8 mm
Bingley et al., 1977	35 (35)	Mean: 40	14:21	Mean: 17	Mean: 35	RF, bilat 12–20 × 8 mm
Kullberg, 1977	8 (8)	NR	NR	NR	NR	RF, bilat, 25 × 10 × 6 mm
Mindus et al., 1995	24 (22)	NR	NR	NR	NR	RF, bilat
Rylander, 1979	45 (45)	Mean: 40	18:27	Mean: 17	Mean: 39	RF, bilat (38 pts); GKS, bilat (7 pts)
Herner, 1961	18 (18)	Mean: 37	3:15	Mean: 13	(24–84)	RF, bilat
Fodstad et al., 1982	2 (2)	42, 50	0:2	Mean: 25	Mean: 24	RF, bilat, height 8 mm
Mindus et al., 1987	8 (7)	Mean: 40	2:5	Mean: 16	Mean: 84	GKS, bilat, 100–60 Gy
Martinez et al., 1975	12 (12)	NR	NR	NR	NR	BL, bilat

The “old” publication group was defined as studies that did not include Y-BOCS scores.

**TABLE 3. Baseline characteristics of patients in “new” and “old” publication groups**

Characteristic	“New” Group	“Old” Group
No. of pts	278	234
No. of publications	16	9
Male (%)	58	40
Mean age at op (yrs)	35 ± 12	38
Mean duration of OCD (yrs)	17 ± 9	15
Mean duration of FU (mos)	61 ± 50	64
Mean preop Y-BOCS score	30 ± 7	NA

NA = not applicable.

Mean values are presented with standard deviations.

these either were asymptomatic or resulted in transient symptoms.

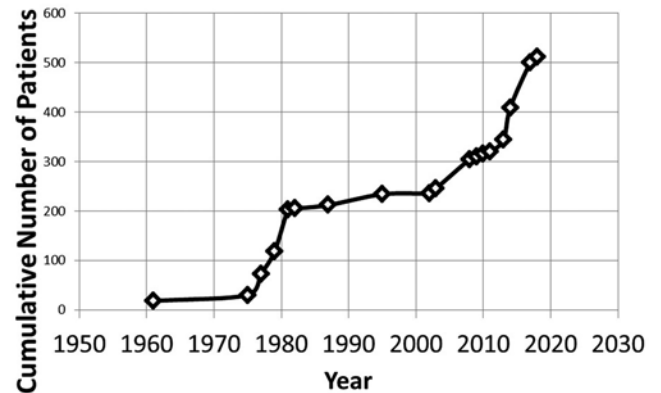
Nine (1.8%) of 512 patients had intracerebral hemorrhage (ICH); in most of these cases, the hemorrhages were asymptomatic, however, in 2 cases (0.4%), the patients required external ventricular drainage, and in 1 case (0.2%), ICH resulted in permanent hemiplegia. ICH was more common and severe when a leukotome was used and if patients treated with leukotome capsulotomy are excluded the ICH rate is 1% (5 of 493 patients), with no reported long-term sequelae.

In total, 4 of 512 patients showed focal neurological deficit postoperatively. Of the patients in the “new” publication group, one developed hemiplegia secondary to ICH (a leukotome was used)<sup>6</sup> and the other developed radiation necrosis<sup>37</sup> after GK capsulotomy with a dose of 200 Gy. In the “old” publication group, Bingley et al.<sup>1</sup> reported on 2 patients who suffered from transient hemiparesis after subcortical infarct postoperatively.

Seizures were noted in 2 of 512 patients.<sup>30,37</sup> One of these patients was considered to have developed epilepsy<sup>37</sup> after developing significant brain edema, again after GK capsulotomy with a dose of 200 Gy.

The most common side effect was weight gain, reported in 13% of all patients (69 of 512). Weight gain is a well-documented side effect of AC for OCD in both older<sup>1,2,15</sup> and newer publications.<sup>5,37</sup> In 1961, Herner<sup>15</sup> noted that the average weight gain was 11.6% of body weight. Other publications were not quite so explicit and merely noted that patients gained weight postoperatively and in some cases they returned to their preoperative weight.<sup>1,2</sup> Rück et al.<sup>37</sup> noted that the average weight gain was 11 kg regardless of whether OCD patients underwent thermo-capsulotomy or GK capsulotomy. In case series with a smaller number of patients 1 or 2 patients from each study were noted to have gained a significant amount of weight, although the actual values are often not reported.<sup>5,10,23</sup>

Almost 9% of patients (44 of 512) required a repeat procedure, often for nonresponse in the context of small lesion size. Rasmussen et al.<sup>34</sup> reported on 15 patients who underwent single-shot GK radiosurgery, which was repeated in 13 cases due to nonresponse. Of these the average Y-BOCS score reduction in this group (single shot repeated) was reported as 42%, with 7 of the original 15 patients considered responders. Rück et al.<sup>37</sup> reported 7 pa-

**FIG. 1.** Cumulative number of patients by publication year.

tients who required reoperation due to nonresponse with an average YBOCS reduction of 28% after reoperation, with 2 patients considered responders. Burzacco<sup>2</sup> reoperated on 17 patients because of relapse. Information regarding the specific reason for and outcome after reoperation is often not reported.

## Discussion

This paper summarizes the literature, both historical and contemporary, on the use of AC for OCD. Capsulotomy can be considered an effective and safe therapy for medically refractory OCD, with clinically meaningful results in over three-quarters of patients and remission in almost one-third of patients. Serious adverse events are rare and often associated with specific surgical techniques (use of a leukotome or excessively high radiation doses with GK capsulotomy).

Inconsistency in clinical outcome is likely a result of variability in the underlying pathology but may also be secondary to differences in lesion size and location. Unfortunately, many publications fail to include imaging or reports on exact lesion location and size. However, it has been suggested that smaller lesions placed in the most ventral aspect of the internal capsule are associated with better clinical outcomes.<sup>26</sup>

Anterior capsulotomy is by no means the first line or indeed the main treatment for OCD but should form a key component in selected patients who have not achieved sufficient symptom control after trying all other treatment options. Given its effectiveness and favorable side effect profile, AC is a viable tool in the surgical treatment of OCD and has almost certainly been underused since its inception seven decades ago.

## Old Literature

In this literature review, “old” publications had a propensity for more positive results. It seems anomalous that patients operated on in the earlier era had better outcomes than those operated on in modern times. Indeed, it is likely that these results are in large part due to bias at all levels. Part of this problem was summed up in 1979 by Dr. Price, a psychiatrist from Northwick Park Hospital, United Kingdom, who decried “bedside evidence” and bemoaned

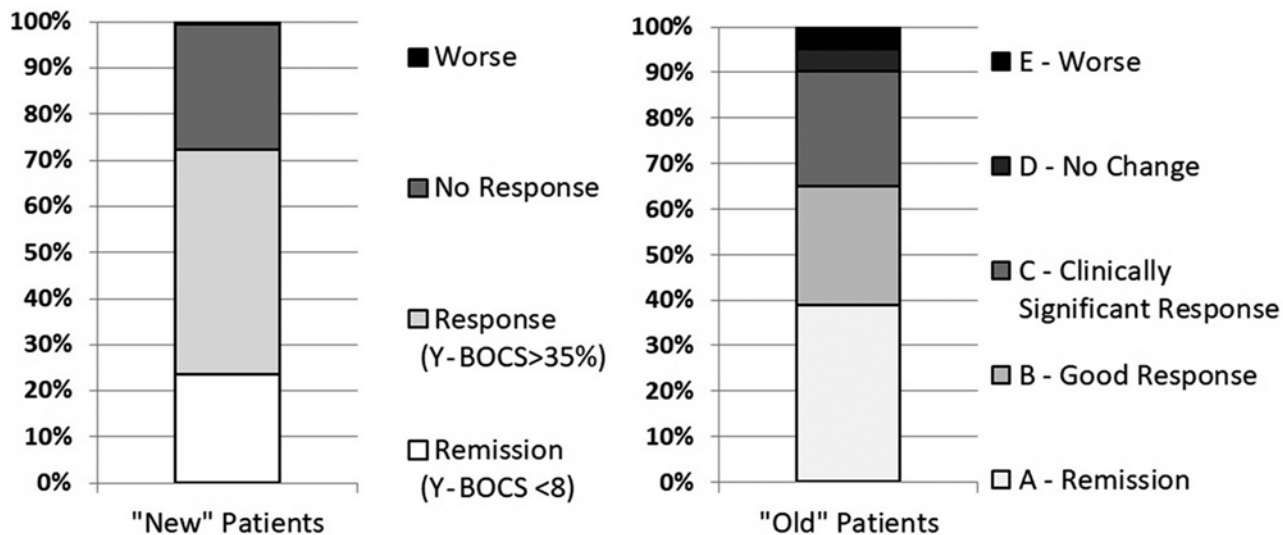


FIG. 2. Outcome by patient group. "New" and "old" refer to studies in which the Y-BOCS was used and studies in which it was not used, respectively.

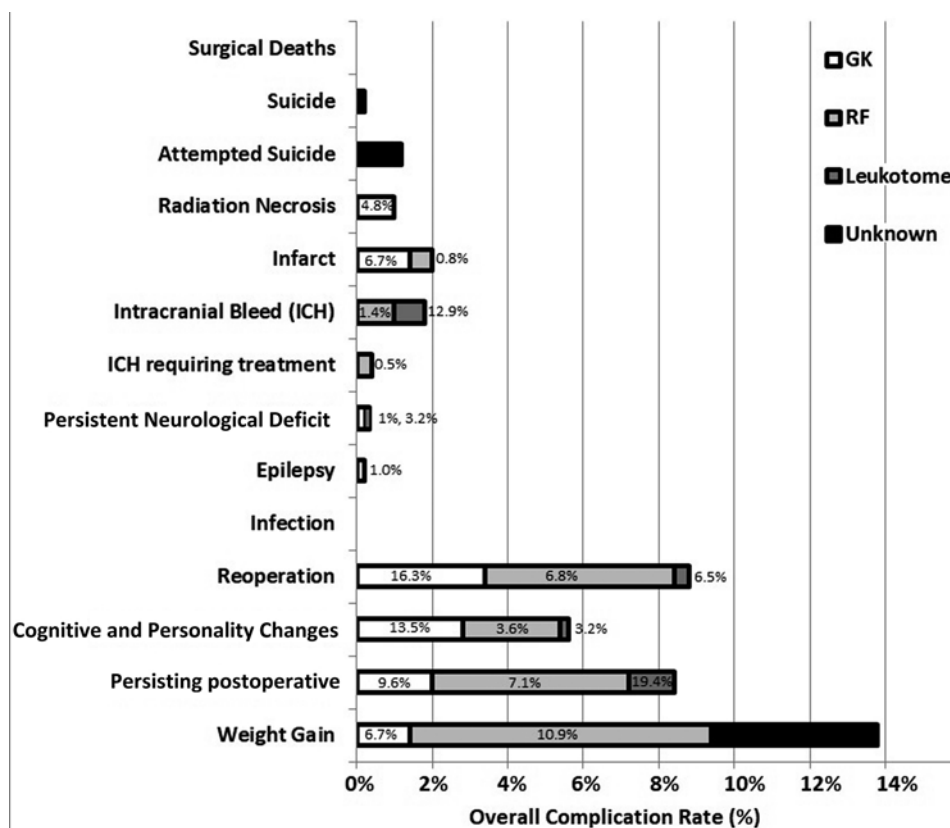


FIG. 3. Adverse events. "Persisting postoperative" refers to new-onset, often mild or nonspecific, symptoms that persisted for more than 8 weeks after surgery. These could include headache, dizziness, nausea, sleep disturbance, apathy, subtle personality changes, and other symptoms that do not fit into the other categories. The unknown group refers to patients in studies in which a mixture of surgical procedures took place and the study is not specific to which surgical group this complication occurred with.

the lack of randomization or control groups in psychosurgery.<sup>33</sup> This is a problem that still plagues psychosurgery in the modern era.

In “old” publications, whether by psychiatrists<sup>1,15,36</sup> or by neurosurgeons,<sup>2,25</sup> patient outcome is measured by seemingly “bedside” evidence. Burzaco<sup>2</sup> wrote an excellent paper that included robust selection criteria, meticulous recording of side effects, and prognosis. In evaluation of outcome, the psychiatrists’, patients’, and relatives’ opinions were analyzed together with the degree of activity and freedom, type of medical assistance required, and use of psychometric tests by the same clinical team. While this process of evaluation was ahead of its time, it is open to significant bias.

However, in many of the older publications, follow-up processes were robust with regular meetings by the neurosurgical team and the patient/relatives.<sup>2</sup> Often, outcome measures appear more pertinent than those used in the current era; indeed, many such publications provide useful clinical vignettes about patients<sup>10</sup> and note whether patients are achieving useful social milestones such as return to work.<sup>1,15,18</sup> In addition, many of the older publications use recognized outcome measures of the time such as the Pippard rating scale<sup>10,27</sup> and CPRS-OC scale (OC subscale of the Comprehensive Psychiatric Rating Scale).<sup>28</sup> This subjective information, although presented in older publications as a mere number in a group and again biased as a “bedside” evaluation, gives a far greater wealth of general information than a number in a scoring system, often the only available data published in “new” publications.

### “New” Literature

The “new” literature, classified as those papers where a Y-BOCS score is available, showed highly successful results when AC was performed on the most severely affected OCD patients. Three-quarters of patients had a clinical response and 1 in 4 were considered to be in remission (Y-BOCS score < 8).

The baseline characteristic data, while not allowing for statistical comparison, appears reasonably similar to the older literature in terms of age at surgery, duration of OCD, and length of follow-up. The rate of success may appear lower in the “new” literature since more “objective” evaluations take place, in the form of Y-BOCS, global assessment of function, and other standardized tests. In many of these studies, follow-up was conducted by a member of the team not involved in the initial patient selection or surgery<sup>37</sup> or by individuals entirely independent of the team,<sup>21</sup> reducing the chances of bias. However, in some modern publications this was not the case,<sup>17,23</sup> although standardized comparisons pre- and postsurgery were still used.

Selective serotonin reuptake inhibitors (SSRIs) are now considered “first-line” agents in the management of OCD. However, evidence of their efficacy only began to appear in the late 1980s; SSRIs may not have been available at the time of the publications in the “old” group, and even if one or more of these medications were available, the patients in these studies may not have received an appropriate trial of SSRI therapy prior to surgery.<sup>11</sup> Therefore, an additional possibility for the observed outcome discrepancy between “old” and “new” literature is that patients described in the

“new” publications represent a more refractory subpopulation.

The Y-BOCS rating scale is designed to be administered as a semi-structured interview to assess the severity and type of symptoms in OCD. Ten of the components of the Y-BOCS are scored from 0 (no symptoms) to 4 (incapacitating symptoms), giving a maximum score of 40. Each of the components is not necessarily equivalent, with a different impact on quality of life. An improvement in one component may be sufficient to improve quality of life to a significant degree. Therefore, the arbitrary cutoff of 35% symptom improvement for clinical response in some respects may under-represent those who do not improve and may explain some of the discrepancy in response rates between “new” and “old” publications.

Indeed, newer publications often suffer from over-reliance on scoring systems without evaluation of patients in their social context. Reduction of compulsions or obsessions should indeed be one aim of psychosurgery, but the chief aim should be improvement of quality of life as measured by reintegration into society, completing schooling, forming lasting relationships, etc. These more nuanced points are often lacking in newer publications.<sup>21,37</sup> Clinical studies reporting on fewer patients often provide detailed clinical vignettes<sup>3,17,38</sup> that are highly useful in assessing outcome by the clinician and patient. Even the meticulously detailed 2009 Sao Paulo/Brown University publication by Lopes et al.<sup>23</sup> flirts with this boundary, paying homage to the importance of recognizing educational attainment and work and relationship status, although it does not meaningfully elaborate on these issues with respect to patients’ postoperative condition, focusing instead on a multitude of scoring systems.

### Adverse Effects

There were no recorded deaths in direct relation to the surgical procedure in any publication. Based on this fact and the side effects reported in the literature spanning half a century, AC can be considered safe.

### Suicide and Attempted Suicide

One suicide was noted postoperatively in the study by Rück et al. from the Swedish Karolinska Institute.<sup>37</sup> This patient had extreme OCD and did not have any meaningful improvement despite multiple reoperations. It is unclear whether this suicide was related to the operation or underlying disease. Most authors other than the Karolinska group do not make note of postoperative suicide attempts. Rück et al. noted that many of their patients had attempted suicide preoperatively. It is probable that this pattern of behavior was not related to neurosurgery per se, although 4 of 7 patients who attempted suicide did so for the first time after surgery. Attempted suicide and suicidal ideation may occur in as many as 20% of patients with OCD<sup>7</sup> during the illness, and importantly, a number of authors specifically note that suicidal ideation was improved postoperatively.<sup>10,17</sup> Surgery may be viewed as a “last chance” by patients, leading them to contemplate or even attempt suicide if symptoms do not improve after AC. The importance of preoperative counseling and postoperative continuous psychiatric care (cognitive behavior therapy or other), em-

phasizing that symptoms may take many months to improve and may continue to improve over many months, cannot be overstated. Preoperative discussion should also include the possibility of repeat surgery in order to reduce the perception that AC is a “last-ditch” therapy.

#### Radiation Necrosis

Rasmussen et al.<sup>34</sup> delivered a maximum dose of 180 Gy and reported radiation necrosis in 1 patient who ultimately ended up in a minimally conscious state. Rück et al.<sup>37</sup> reported persistent symptomatic brain edema consistent with radiation necrosis in 2 patients after a dose of 200 Gy each, well above what is now considered safe.

A dose of 140–180 Gy (maximum dose) to the ventral aspect of the anterior limb of the internal capsule is normally used to perform a GK capsulotomy. However, modern GK units deliver oblate spheroidal isocenters associated with a higher rate of late radionecrosis than older machines that delivered prolate spheroidal isocenters. Recently, efforts to recreate a prolate shape with modern machines have been suggested.<sup>26</sup>

#### Reoperation

One of the most significant adverse effects in this review was the reoperation rate, with reoperation being required in roughly 1 of 12 patients. Reoperations were primarily done for failure of clinical improvement or relapse of symptoms, for the most part due to small lesion size or lesion absence.<sup>2,6,18,27,37</sup> Interestingly, lesions could not be found on postmortem examination or MRI in a set of GK capsulotomy patients from the old publication group who did not experience symptom improvement; one of these patients was exposed to only 80 Gy of radiation.<sup>27,36</sup> Minimizing the risk of reoperation by creating appropriately sized lesions is important to reduce the risk of morbidity associated with multiple capsulotomies.<sup>37</sup>

#### Cognitive and Personality Changes

The historical fear of frontal lobe syndrome or aberrant cognitive and personality changes following stereotactic capsulotomy does not appear to be well founded on review of the literature. While many of these studies do not publish the results of psychometric or personality tests,<sup>2,18,36</sup> most make note of personality and cognitive traits and generally report that these traits improve. If the traits worsen, the worsening either is temporary or does not have a meaningful effect on quality of life. Some report a more mixed picture, with some patients reporting marked fatigability years after surgery while others completed doctoral dissertations or staged public art exhibitions.<sup>1</sup>

In newer studies, where multiple psychometric, personality, and cognitive tests are performed, and adverse effects are thoroughly documented, the phenomenon of reduced initiative, apathy, and fatigability tends to be temporary.<sup>3,5,23</sup> However, Rück et al.<sup>37</sup> noted significant frontal lobe dysfunction in 10 (43%) of 23 patients using their own Execution, Apathy and Disinhibition Scale (EAD Scale) and compromised executive function in 6 of 7 patients tested using the Wisconsin Card Sorting Test at long-term follow-up. It must be noted that there was no presurgical evaluation of these patients and that 5 of 14 patients who

suffered cognitive/personality side effects had undergone GK radiosurgery with doses ranging from 180 to 200 Gy. It is therefore difficult to ascertain whether cognitive findings were present prior to surgery or only subsequent to excessive radiation doses. Gouvea et al.<sup>13</sup> also reported on a patient who performed worse on tests of frontal lobe function after AC, although this did not affect the patient's everyday life. In a study of 35 patients, Liu et al. reported that 9 patients suffered temporary cognitive defects and organic brain syndrome, noting permanent and marked personality changes in 2 (5.7%) of 35 patients.<sup>21</sup>

#### Weight Gain

Weight gain is a well-documented side effect of AC for OCD in both older<sup>1,2,15</sup> and newer publications.<sup>5,37</sup> It is extremely difficult to know whether or not weight gain and increased appetite is a specific by-product of capsulotomy. Perhaps patients who have been socially isolated with many of the comorbid diagnoses that often accompany OCD regain their appetite after relief of the vast symptom burden that previously dictated their daily routine. Weight gain is also a well-documented side effect in patients receiving medical treatment for a variety of psychiatric disorders.<sup>32,41</sup>

#### Adverse Effects by Lesion Method

The rate of serious and persistent complications is low and similar in different lesion methods, with a few notable exceptions. The rate of ICH is markedly higher in capsulotomy with a mechanical leukotome compared to other methods, resulting in persistent neurological deficit in 1 patient and a myriad of ongoing symptoms in a number of other patients. The rate of cerebral infarct was higher in patients who underwent GK capsulotomy compared to other methods, although the vast majority of these infarcts were asymptomatic and only evident on routine postoperative imaging.

The rate of reoperation was higher in patients who underwent GK capsulotomy, often due to clinical nonresponse. Rasmussen and colleagues<sup>34</sup> reported that a single GK shot located centrally in the capsule was ineffective. After a second more ventrally placed lesion a noticeable clinical improvement was observed, to produce similar response rates to patients who underwent a double shot.

In more modern studies, patients are proactively screened for all adverse effects. Indeed, this is done with varying degrees of effectiveness, vigor, and methodological quality among studies, making a direct head-to-head comparison between surgical methods challenging.

#### The Rise, Fall, and Reemergence of AC

As can be clearly seen from Fig. 1, there was clear interest in stereotactic AC for OCD from 1960 to 1980. Many of the studies were of high quality with rigorous patient selection criteria, given available scales at the time. Overall, the results were positive, so it may seem strange that AC should fall so completely and so quickly from the armamentarium for the treatment of severe, medication-refractory, and in many cases life-threatening OCD.

By the 1960s some 60,000 or so transorbital “ice-pick” lobotomies, popularized and aggressively promoted by

neurologist Walter Freeman, had been performed in the United States.<sup>35</sup> The backlash against all psychosurgery coincided with celebrities such as Rosemary Kennedy (President Kennedy's sister) and Warner Baxter (1950s' Hollywood actor) suffering complete cognitive destruction or death after lobotomy. At that time, many countries entirely banned psychosurgery. Additionally, the development and introduction of pharmacological agents, such as chlorpromazine and haloperidol in the 1950s, for the treatment of previously untreatable psychiatric conditions contributed to the demise of lobotomy and, with it, all forms of psychosurgery. The media also played an important role in establishing the antisurgical zeitgeist with respect to mental disorders, especially with Milos Forman's screen adaptation of Ken Kesey's book *One Flew Over the Cuckoo's Nest*, released in 1975.

The resurgent interest in stereotactic psychosurgery started following the popularization of DBS for movement disorders and its first applications in patients with OCD by Nuttin et al.,<sup>29</sup> who targeted with DBS the same "old" lesional target for OCD. Their publication helped to reinvigorate interest in stereotactic lesional surgery for OCD from early 2000 onward. Indeed, this same group has used AC as a "rescue procedure" after unsatisfactory DBS of the anterior capsule region, reporting treatment success in 2 of 3 patients.<sup>24</sup> In another publication, they reported better Y-BOCS outcomes in a cohort of capsulotomy patients than in a cohort of DBS patients.<sup>39</sup>

### Deep Brain Stimulation

When targeting the ventral capsule surgically, many groups tend to favor DBS over stereotactic ablation. Although there are no head-to-head comparisons, a recent review suggests that these techniques have similar safety profiles, but that stereotactic ablation may be associated with greater efficacy, without the high costs associated with implanted hardware and lifelong maintenance.<sup>31</sup>

### Limitations of This Review

#### Group Data

Group data rather than individual data was available for analysis in almost all the "old" publications<sup>1,2,18,25,28,36</sup> and a smaller number of more modern publications.<sup>5,6,20,21,30</sup> This poses a number of problems for analysis. The first is that any deductions are subject to the ecological fallacy. This fallacy means that the outcome of individuals is presupposed by the outcome of the group. Thus, large positive outliers in a few patients can vastly skew results positively even if a treatment has failed. The opposite is also true. In the publication by Liu et al.<sup>21</sup> the mean postoperative Y-BOCS score was 4.4 at 36 months after surgery, an overall average improvement of almost 80%. Thus all patients were noted to be in remission. However, there may have been a number who did not respond or were worse off and were not counted in the analysis. Of note, the standard deviation of the 36-month postoperative Y-BOCS score was 2.3, meaning that at least in this publication the majority of patients would have had a Y-BOCS score < 8 at long-term follow up. However, in the publication by Oliver et al.,<sup>30</sup> no standard deviation values are available. All patients were

considered to have been "responders," but large numbers of these patients may have gone into remission or have experienced worsening of symptoms.

#### Comparison Between "Old" and "New" Data

Direct comparison between "old" and "new" data could not be performed, due mostly to the use of different outcome and diagnostic criteria and the availability of key data for analysis.

#### Reoperation

Although every effort was made to remove duplicate patients, it is possible that some patients were reported twice (after the first and second operation).

#### Meta-Analysis

Equally, it was not possible to perform a formal meta-analysis, as the publications available were mostly small case reports or series without control groups.

## Conclusions

Anterior capsulotomy is a highly effective treatment for OCD with a favorable side-effect profile. Detailed clinical vignettes should be encouraged for each reported case. This could be included in publications as supplementary material. Tabulated information to include categories of education, sexual relationships, platonic relationships, and employment would also be useful. GK doses of more than 180 Gy and the use of a leukotome are both associated with more adverse effects and should be avoided. AC has been an underused treatment, which has contributed to a paucity of high-level evidence for its use. Psychiatrists should consider neurosurgery, including AC, when confronted with patients with severe refractory OCD. An increase in referrals to specialist neurosurgical centers will allow further good-quality research to improve understanding of the future role of stereotactic AC in managing severe refractory OCD.

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Conception and design: all authors. Acquisition of data: Pepper, Zrinzo. Analysis and interpretation of data: all authors. Drafting the article: all authors. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Pepper.

### Supplemental Information

#### Online-Only Content

Supplemental material is available with the online version of the article.

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