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Strategies for the return of behavioral surgery

Sam Eljamel

Centre of Neurosciences, Department of Neurosurgery, Consultant Neurological Surgeon, Ninewells Hospital and Medical School, Scotland, UK

E-mail: *Sam Eljamel - m.s.eljamel@dundee.ac.uk

*Corresponding author

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Abstract

Background: Behavioral surgery (BS) is resurging because of unmet clinical need, advances in basic sciences, neuroimaging, neurostimulation, and stereotaxy. However, there is a danger that BS will fall unless acceptable strategies are adopted by BS providers.

Methods: A critical review of conditions leading to rise of psychosurgery (PS) and concerns resulting in its fall was conducted to learn lessons and safeguard BS of the future.

Results: PS rose and spread in 1960 like wildfire without adequate preclinical and clinical studies. Hundreds of patients had PS without adequate preoperative diagnosis or assessment, proper consent, and non-objective reporting of outcome. Furthermore, there was public opposition against PS because of its potential abuse to control violent behavior and dissidents. Advances in neurostimulation, neuroimaging, and stereotaxy, and emergence of treatment-resistant mental disorders led to increased interest in BS. Several recent studies have shown BS to be safe and effective. However, concerns related to strength of evidence, safety, efficacy, consent, and objectivity of studies have been raised. Unless clinical and regulatory governance structures are adopted in each jurisdiction, BS will face the same fate as that of PS in the past.

Conclusion: The future of BS as a safe and effective therapy is dependent upon adopting clear moral ethical and governance standards on the following lines: Patients must have failed adequate therapies; must be assessed by psychiatrist-led multidisciplinary teams; patients' abilities to give consent and diagnosis must be verified by independent authorities designated for this purpose by the state; and the independent authority must also decide whether the teams were adequately trained to perform BS.

Key Words: Capsulotomy, cingulotomy, neurostimulation, psychosurgery, stereotaxy, vagus nerve stimulation

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INTRODUCTION

Behavioral disorders such as major depressive disorders (MDDs), anxiety disorders, obsessive compulsive disorders (OCD), and schizophrenias are associated with huge direct and indirect costs to sufferers, their families and communities, and countries as a whole. It is estimated that 20–40% of sufferers become either resistant or refractory

to standard therapeutic options, leading to increased demands on finite healthcare resources and significant unmet need for alternative therapeutic options.[1,6,29] Behavioral surgery (BS) is one such promising emerging therapy. However, BS is still shrouded by uncertainties, skepticism, and barefaced resistance due to its appalling past record. The rise of psychosurgery (PS) in the sixties was a result of lack of alternative effective treatments and the huge unmet need of patients incarcerated in mental asylums.[3,26] The fall of PS in the seventies was due to the discovery of more effective and safer alternative to PS (chlorpromazine) and unprecedented public fear of PS and its potential abuse to pacify violent behavior, political unrest, or political opposition. BS is on the verge of becoming a realistic, safe, effective treatment option for many resistant and refractory patients with mental disorders. In order to prevent replication of the rise and fall of PS, new strategies need to be adopted by all healthcare professionals involved in the referral, selection of patients, and provision of this ground-breaking, safe, and effective therapy.

MATERIALS AND METHODS

This study is a critical review of the issues and concerns that led to the rise and fall of PS in 1960–1970 and a review of the advances and potential ethical issues that affect the emergence of BS in the 21st century.

RESULTS

Concerns that shrouded PS in the past

The most important central concern that surrounded PS in the past was the lack of scientific evidence to justify its use. The data upon which PS was introduced were at most inconclusive or contradictory.[3] Furthermore, psychosurgeons of the past were accused of vague unverifiable preoperative diagnosis, vague selection criteria, vague invalid assessment methods, and lack of objectivity of postoperative outcome reporting. The procedures performed were crude, imprecise, and inaccurate. Most of the procedures were carried out as part of practice without proper research protocol, without independent assessments of outcome, and without precise categorization of the mental illness being treated.[26] The practice of PS in the past was applied to humans after very few animal experiments were conducted, which gave unreliable and unpredictable results.[27]

The second concern surrounding PS was informed consent and how informed consent was obtained, e.g. Can an appropriate candidate for PS give valid consent for PS or can a third party, family, or society who might benefit from PS give consent on behalf of a patient. Some argued that PS may produce irreversible change in behavior, self, or mind of the consenting individual on the same bar as mutilation.[4]

Finally, opponents of PS voiced their concern that PS had been, may be, or will be used or abused as a social or political tool to control and subdue those who are considered abnormal to justify controlling dissidents, minorities, or bothersome individuals.[1]

Recent changes that made behavioral surgery a safe, effective therapeutic reality

Unmet need

It is clear that current standard therapeutic options cannot help a significant number of mentally ill patients. For example, the prevalence of OCD is 2.5% with 30–40% of sufferers becoming treatment resistant (TRes).[1,6] On the other hand, MDD is the leading cause of disability in North American adults under the age of 50 years,[29] of whom 20% become TRes or treatment-refractory (TRef).[11] Therefore, there is a need for new treatment options. Nevertheless, the mere fact that large number of mentally ill patients could not be helped with standard therapy and availability of BS is not a good reason for the patients to jump onto the bandwagon of BS and for surgeons to provide it without applying rigorous scientific studies to establish the effectiveness and safety of BS. The introduction of PS in 1935 by Ego Moniz after listening to a single case report by Fulton describing a single agitated chimpanzee calming down after destruction of the prefrontal brain areas, by Jacobsen, was too far and daring step. Moniz ignored all the potential side effects observed on humans after damage of their frontal lobes, such as those observed following motor vehicle accidents.[24] Moniz went ahead and experimented on humans without confirming Jacobsen's animal experiments and before confirming the exact location of Jacobsen's surgery. This was a daring step that should not have been taken and should never be allowed to be taken in the future ever again.

Scientific basis

Contrary to the common belief of PS opponents, BS of today is based on scientific evidence. Positron emission tomography (PET) demonstrated reduced cerebral blood flow (CBF) in the prefrontal, premotor, dorsal anterior cingulate gyrus, and anterior insula of the cerebrum, and elevated CBF in the subgenu cingulate gyrus in patients with MDD.[18] Chronic deep brain simulation (DBS) of the subgenu cingulate gyrus normalized CBF changes observed in patients with MDD. Brain imaging was also supportive of the hypothesis that OCD is a result of underlying pathology in the striatum.[23] Structural brain imaging revealed significantly reduced volume, increased gray matter density of corticostriatal-thalamic circuits, and increased baseline activity in the orbitofrontal cortex, cingulate gyrus, and striatum in patients with OCD.[14,24]

Preoperative diagnosis and selection of patients

In recent years, patients referred for BS are considered for surgery after thorough critical review of their

diagnosis and adequacy of previous treatments. In my institution, prospective patients for BS are evaluated by a multidisciplinary team in the Advanced Interventions Service (AIS) led by experienced psychiatrists and psychotherapists in this field.[5,7] On average, the AIS screens 40–50 patients annually and only a handful of patients move on to have BS. The definitions of TRes- and TRef-MDD or -OCD have also been established. TRes-OCD was defined as failure of at least three adequate trials of serotonin-release inhibitors (SRIs) including clomipramine, failure of standard augmentation therapy, and failure of behavioral therapy including exposure to feared stimuli and the prevention of subsequent responses.[13] In the latter, the therapist prompts OCD patients to list their obsessions and associated compulsions in a hierarchal order. The patient is then exposed to the least feared stimulus from the list while the therapist discourages the associated compulsive response till the patient no longer finds the stimulus fearful. Exposure therapy continues to the next feared stimulus on the list in turn till all the stimuli are no longer feared and the compulsions become no longer bothersome. TRes-MDD has also been defined along stringent criteria: failure to respond to at least four different adequate antidepressant therapies including medications, psychotherapy, and electro-convulsive therapy (ECT) administered at adequate doses and for adequate duration.[8] In practice, most patients I treated were much more resistant than what is considered the minimum criteria for TRes-MDD, so our patients are considered TRef-MDD [Table 1].

Pre- and postoperative assessments

Recently, BS has been conducted with the most stringent ethical, moral, and regulatory approvals, and its outcome is assessed with validated objective scales, performed by those who do not perform the actual BS. In my institution and other centers, OCD patients are assessed by the Yale–Brown Obsessive-Compulsive scale (YBOCS)[12] and MDD patients are assessed by the Hamilton Depression Rating Scale (HDRS), Montgomery–Asberg Depression Rating Scale (MADRS), and the Clinical Global Impression (CGI) scale.[5,7] Therefore, the outcomes reported after BS in the 21st century are objective, reliable, and real. BS of today consistently achieved objective and independently verified good outcome. In TRes-OCD and -MDD patients, 40–60% responded, and in TRes–MDD patients, remission occurred in 40%. When everything else had failed, BS achieved remarkable and unprecedented outcomes with significant gains in the quality of life and huge cost savings.[5,7,18-20]

Table 1: Characteristics of TRef–major depressive disorder treated with behavioral surgery at Ninewells Hospital and Medical School

Features	Average	Range (SD)
Age at first episode (years)	27.8	13.6–48.4
Age of onset of last MDD before BS (years)	34.8	16.9–55.6
Duration of current episode before BS (weeks)	393.5	137.5–1296.3
Number of episodes	1.9	1–6
Total duration of illness (all episodes, weeks)	545.6	184.6–1311.6
Number of hospital admissions	6.5	1–15
Total duration of hospital admissions (weeks)	130.6	5.6–468.9
Number of adequate treatment trials	9.1	(3.2)
Number of adequate ECTs	2.6	(1.3)

SD: Standard deviation, MDD: Major depressive disorder, BS: Behavioral surgery

Accuracy and precision of BS

In contrast to PS where prefrontal lobotomy is performed by a leucotome or an ice-pick with no imaging guidance or postoperative imaging confirmation, current BS procedures are guided by stereotactic image guidance systems including stereotactic frames and robotic systems, with submillimetric accuracies and precision.[8,9] With the advent of computerized tomography (CT) and magnetic resonance imaging (MRI), it is possible to determine the exact position of lesions, and their size and DBS-contact placement [Figure 1]. Furthermore, prospective correlation of lesion location and outcome was analyzed in bilateral anterior cingulotomy (BACI) where the more anterior the lesion was, the better the results were in TRef-MDD.[25] In OCD, DBS-contact location of bilateral anterior capsular stimulation, the closer the active contact was to the anterior commissure, the better the results were.[20]

Lesion versus deep brain simulation

One of the most controversial issues concerning PS is the fact that psychosurgeons make large irreversible permanent destructive brain lesions. If the lesion is made

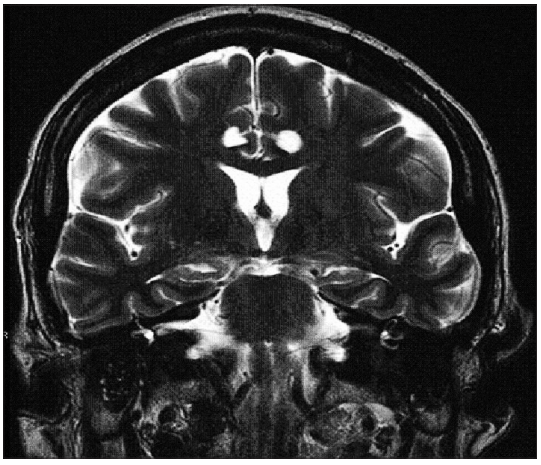

Figure 1: Coronal postoperative T2-weighted MRI image demonstrating modern bilateral anterior cingulotomy

too small to be effective, repeat surgery is required, and if the lesion is made too large, it cannot be reduced in size. Furthermore, lesions made in non-responders cannot be reversed with the knowledge that surgery has not worked. With DBS and vagus nerve stimulation (VNS), the effects of stimulation can be reversed by switching off the implanted pulse generator (IPG) at the flick of a button, so in a way, the patient can decide before surgery to proceed or not and after surgery to continue with DBS/VNS or not. DBS/VNS provides a way of testing whether or not TRes-OCD or TRes- and TRef-MDD patients will respond. It gives them a chance of experiencing firsthand the effects of stimulation and how much function will they gain by this treatment.[7]

The issue of consent

BS today is performed in academic centers following specific treatment and research protocols with stringent and rigorous consenting processes. In my own institution, patients deemed to be candidates for BS by experienced dedicated psychiatrists at the academic center are referred to an independent mental healthcare commission (MHCC) consisting of independent psychiatrists and lay individuals. The MHCC reviews the diagnosis, the proposed BS, and whether the sufferer is able to give informed consent. The consenting process takes several consultations with the sufferer and his/her carer, and BS is carried out only after the referring psychiatrist and MHCC are satisfied that the sufferer understood the ins and outs of the proposed BS and the aftercare required thereafter. It is also of note that BS is only offered to patients who can give informed consent. When the patients in our institution were given the choice of ablative procedures, DBS, or VNS, they had a very clear idea about the procedure they preferred and it was not always DBS or VNS.[7]

DISCUSSION

The cry for PS was expressed by a schizophrenic adolescent in 1976: "Please give me an inhuman operation to take away the sacredness" – A schizophrenic adolescent, Philadelphia, USA, 1976. This was a cry of suffering, expecting relief from an impersonal inhuman procedure, recognizing there is something wrong with the operation.[26] By reviewing what had happened in 1960s, I hope that neurosurgeons and psychiatrists stop and think carefully before repeating that. It is true that BS using DBS and VNS are reversible, can be performed precisely and safely, and are effective in TRes-OCD and TRes- or TRef-MDD patients. There is, however, a great danger of implementing this therapy without appropriate governance structures in place. Trying this technology in other mental disorders may lead to similar justifiable reactions from the public, politicians, and law makers in this century. There is a real and justifiable fear that BS can be abused to control dissidents and political opponents or used to subdue those with violent behavior or rioters. Not long ago (1970), in a book entitled "Violence and the brain," the authors called for the development of an early warning test to detect those with low threshold for impulsive violence. The authors had also called for better and more effective methods of treating such people once they were identified.[10] Another psychosurgeon was quoted saying, "A person convicted of a violent crime should have the chance for a corrective operation." He went on to say, "Each violent young criminal incarcerated from 20 years to life costs the taxpayers about $100,000. For roughly $6000, society can provide medical treatment which will transform him into a responsible, well-adjusted citizen."[4] It is these extreme views that almost killed PS in the past. In reality, PS is a very expensive and difficult way to be used to subdue violent behavior, dissidents, or political opponents. There are much easier, cheaper, and effective ways of mass control, including the use of media, television, medicines, and education systems. Historically, PS was not based on proper scientific studies; it started by a self-centered failed politician who turned to PS as a means to be in the limelight and for fame to obtain a Nobel Prize. Ego Moniz used lobotomy on patients after hearing of Fulton's case report of a single chimpanzee lobotomized by Jacobsen where the agitated chimp became calm. There has been no verification of the exact location of the lesion or report of its potential serious side effects.[4] Almost everyone at the time ignored these important ethical issues because they felt they were morally obliged to help thousands of incarcerated mentally ill patients. They were blinded by the huge unmet need and the greed for wealth and power. After the introduction of Moniz's lobotomy in the USA, it spread like wildfire and was practiced in smaller and less-equipped hospitals.[26] It was the actions of Walter Freeman, who was neither a neurosurgeon nor a psychiatrist, which brought PS to disrepute. Recognizing PS was a "Catch 22" situation; while PS relieved symptoms of psychosis, it was very costly in terms of loss of affect and creativity. Despite this fact, Walter Freeman continued the procedure and introduced the transorbital lobotomy instead of reflecting and auditing his results.[26]

BS and the way it is practiced today is very different from that of PS of the past ; BS is accurate and precise, and it can allay most of the concerns encountered in the past in this field of neurosurgery. However, a review of the literature on DBS for mental disorders uncovers a plethora of articles on BS; a total of 90 publications during 2009–2011 compared to only 17 articles between 2002 and 2005 [Table 2]. The vast majority of these publications reported the outcome of small selected study patients, and some of the publications fired the first shot of warning against the widespread use of BS.

Table 2: Number of publications on Deep brain simulation-Behavioral surgery between 2002 and 2011

Year of publication	DBS for MDD	DBS for OCD	Total
2009–2011	68	22	90
2006–2008	32	9	41
2002–2005	8	9	19

DBS: Deep brain simulation, MDD: Major depressive disorder, OCD: Obsessive compulsive disorders

My own concern is that many mental disorder patients are being treated in small groups outside multicenter, controlled, prospective trials and without robust clinical and regulatory governance frameworks. In a survey of North American Functional Neurosurgeons published in 2011, 50% of the responders were engaged in some sort of BS, mainly DBS for OCD or MDD, and saw BS as a growing field of business.[16] DBS and VNS are neither destructive nor irreversible and give sufferers the option to discontinue the stimulation if they wished to do so. But these are not reasons good enough to use them outside properly constituted clinical and regulatory governance frameworks. Although DBS had Food and Drug Administration (FDA) approval for OCD under Humanitarian Device Exemption (HDE) rules and VNS had FDA approval for MDD, some concerns had been raised regarding their use. These concerns are based on lack of strong scientific evidence on their safety and efficacy in the long run, the numerous conflicts of interests held by investigators such as holding patents for certain procedures, and the ambiguity and lack of transparency of research sponsored by commercial partners.[10] However, studies on ablative, VNS-, and DBS-BS of the 2 1st century were performed within stringent protocols that stood the heat of scientific rigor and scrutiny of peer reviewers.[5,7,18-20,25] The outcomes reported in these studies were objective and based on objective assessments. Reduction of YBOCS score of 35% is considered a clinical response in OCD, while a reduction of 50% on MADRS or HDRS is considered a worthwhile response in MDD. However, careful observation and further studies of BS procedures are required to establish their long-term efficacy, longevity, and side effects. Increased impulsivity was reported in two cases recently by increasing the stimulation.[17] Nevertheless, there remain ethical and social challenges facing BS in the 21st century; consensus guidelines, workshops, and public engagement are just a few things that need to be done to overcome these challenges.[2] BS must be approached with caution and commitment for long-term care. The data so far on BS demonstrated that BS can be implemented most successfully by dedicated interdisciplinary teams in the context of multimodal treatment plan. BS is complicated by issues involving patient categorization and selection criteria, the long-term management of these patients, and the different patterns of potential benefits and burdens.[22] The Canadian Network for Mood and Anxiety Treatments (CANMAT) reviewed the role of neurostimulation including ECT, repetitive transcranial magnetic stimulation (rTMS), VNS, and DBS in MDD, and concluded that while there was good evidence for ECT as first-line treatment, some evidence for rTMS as second-line treatment, the evidence for VNS was less robust, and DBS remained experimental therapy.[15] Therefore, there is a need for stringent ethical, governance, and regulatory frameworks to be put in place in each legal jurisdiction in the world to prevent potential misuse of BS. In Scotland, the service was centralized at Ninewells Hospital and Medical School. It is regulated by six-monthly review visits from the National Services Division of the Scottish Department of Health. Each patient's diagnosis, suitability for BS, and his/her ability to give informed consent are determined by independent MHCC. In the state of Victoria, Australia, each request for BS must be approved at a hearing of an independent Psychosurgery Review Board.[21] The aforementioned are just a few examples of how some jurisdictions around the world ensure the continuation of provision of BS under stringent regulatory and clinical governance frameworks. Unless similar stringent rules are adopted by other jurisdictions, BS will face the same fate as its predecessor.

CONCLUSIONS

The main concerns surrounding BS are the same as those that surrounded PS in the past. If we do not develop and agree strategies, BS will face the same destiny as PS. These new strategies should include the following points to allay these concerns:

1. Patients considered for BS must have failed adequate therapies:
   a. In OCD failure of at least three adequate trials of SRIs including clomipramine and augmentation and behavioral therapies.
   b. In MDD failure of at least four adequate antidepressive therapies including medicines, psychotherapy, and ECT.
2. Patients should be assessed by psychiatrist-led multidisciplinary team of experienced healthcare professionals, who must validate the diagnosis, adequacy of previous treatments, and the ability of patients to give consent.
3. Ability of patients to give informed consent and the diagnosis must be verified by an independent authority designated for this purpose under jurisdiction of the state where BS will be carried out, e.g. MHCC or Behavioural Surgery Review Board.
4. The independent body or authority must also decide whether the treating team is adequately trained to perform the procedure and provide aftercare.

5. These procedures should only be performed within adequately resourced centers subject to annual inspections and robust clinical and regulatory governance frameworks.

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