Deep Brain Stimulation for obsessive-compulsive disorder

In severe cases, medication and therapy may not be enough to relieve symptoms, and in these instances, surgical interventions such as deep brain stimulation (DBS) may be considered. DBS involves the placement of electrodes in specific areas of the brain, which deliver electrical impulses to regulate brain activity and reduce symptoms of OCD. However, this is considered a last resort and only after a thorough evaluation and consultation with a specialist. It's important to note that the safety and effectiveness of DBS for OCD is still being studied and it's not yet a widely accepted treatment.

Targets

DBS targets explored for obsessive-compulsive disorder include the anterior limb of the internal capsule (ALIC), nucleus accumbens (NAc), ventral capsule / ventral striatum (VC/VS), subthalamic nucleus (STN), and inferior thalamic peduncle (ITP).

The FDA granted a humanitarian device exemption approving the use of VC/VS DBS for medically intractable OCD.

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.

Pepper et al. aimed 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 [1)].

Deep brain stimulation (DBS) for neuropsychiatric disorders needs to be investigated in proper research trials. However, there are rare circumstances in which DBS could be offered to psychiatric patients as a form of surgical innovation, therefore potentially blurring the lines between these research trials and health care.

Bell et al discuss the conditions under which surgical innovation may be accepted as a practice falling

at the frontiers of standard clinical care and research per se. However, recognizing this distinction does not settle all ethical issues.

The article offers ethical guideposts to allow clinicians, surgical teams, institutions, and institutional review boards to deliberate about some of the fundamental issues that should be considered before surgical innovation with psychiatric DBS is undertaken. They provide key guiding questions to sustain this deliberation. Then the review the normative and empirical literature that exists to guide reflection about the ethics of surgical innovation and psychiatric DBS with respect to general ethical questions pertinent to psychiatric DBS, multidisciplinary team perspectives in psychiatric DBS, mechanisms for oversight in psychiatric DBS, and capacity and consent in psychiatric DBS. The considerations presented here are to recognize the very specific nature of surgical innovation and to ensure that surgical innovation in the context of psychiatric DBS remains a limited, special category of activity that does not replace appropriate surgical research or become the standard of care based on limited evidence [2)].

Deep brain stimulation (DBS) has been proposed as an alternative to ablative surgery for severe treatment-resistant Obsessive Compulsive Disorder (OCD), although with partially discrepant results probably related to differences in anatomical targetting and stimulation conditions.

Alonso et al. searched the literature on DBS for OCD from 1999 through January 2014 using PubMed/MEDLINE and PsycINFO. They performed fixed and random-effect meta-analysis with score changes (pre-post DBS) on the Yale Brown Obsessive Compulsive Scale (Y-BOCS) as the primary-outcome measure, and the number of responders to treatment, quality of life and acceptability as secondary measures.

Thirty-one studies involving 116 subjects were identified. Eighty-three subjects were implanted in striatum areas-anterior limb of the internal capsule, ventral capsule and ventral striatum, nucleus accumbens and ventral caudate-27 in the subthalamic nucleus and six in the inferior thalamic peduncle. Global percentage of Y-BOCS reduction was estimated at 45.1% and global percentage of responders at 60.0%. Better response was associated with older age at OCD onset and presence of sexual/religious obsessions and compulsions. No significant differences were detected in efficacy between targets. Five patients dropped out, but adverse effects were generally reported as mild, transient and reversible.

The analysis confirms that DBS constitutes a valid alternative to lesional surgery for severe, therapy-refractory OCD patients. Well-controlled, randomized studies with larger samples are needed to establish the optimal targeting and stimulation conditions and to extend the analysis of clinical predictors of outcome [3)].

Recommendations

Based on the data published in the literature, the following recommendations can be made:

(1) There is Level of evidence 1, based on a single class 1 study, for the use of bilateral subthalamic deep brain stimulation for the treatment of medically refractory OCD.

(2) There is Level of evidence 2, based on a single class 2 study, for the use of bilateral nucleus

accumbens DBS for the treatment of medically refractory OCD.

(3) There is insufficient evidence to make a recommendation for the use of unilateral DBS for the treatment of medically refractory OCD [4].

DBS of the anterior limb of the internal capsule/ventral striatum received Conformité Européene (CE) mark and Food and Drug Administration (FDA) approvals for the treatment of intractable OCD. Remarkably, this is the first such approval for neurosurgical intervention in a strictly psychiatric indication in modern times.

Further directions in the surgical treatment of OCD will require better preoperative predictors of postoperative responses, optimal selection of individualized targets, and rigorous reporting of adverse events and standardized outcomes. To meet these challenges, centers must be equipped with a multidisciplinary team and patient-centered approach to ensure adequate screening and follow up of patients with this difficult-to-treat condition [5].

Ventral capsule/ventral striatum (VC/VS) is one of the promising targets; however, whether or not acute stimulation test can provide substantial information for chronic stimulation is not yet known.

Four adult patients with refractory OCD were implanted with Model 3387 leads bilaterally in an area of VC/VS. Postoperative test stimulation was performed at least 2 weeks after surgery.

Patients presented smile, laughter, euphoria, increased heart rate, increased blood pressure, smell, chest vibration, dizziness, nausea, heat, or increased sexual drive during acute stimulation. The higher the percentage of smile/laughter (34.3%, 31.3%, 56.3%, and 12.5% for four cases), the greater the reduction in the Yale-Brown Obsessive Compulsive Scale (30.6%, 38.9%, 58.8%, and 7.7% respectively at 15-month DBS).

This study showed that acute DBS of the VC/VS might cause mood change, cardiovascular, sensory, or motor effects. These effects were transient or habituated over six months, suggesting stimulation-induced smile/laughter may be a possible predictor for long-term DBS outcome. Larger studies, genetic studies, and imaging studies are needed to evaluate the effects of different parameters and possible predictors in the treatment of OCD

Stimulation-induced smile/laughter may be a possible predictor for long-term DBS outcome. Larger studies, genetic studies, and imaging studies are needed to evaluate the effects of different parameters and possible predictors in the treatment of OCD [6].

DBS remains an experimental treatment for medication refractory OCD. Target selection and programming paradigms are not yet standardized, though an improved understanding of the relationship between the DBS lead and the surrounding neuroanatomic structures will aid in the selection of targets and the approach to programming [7].

Deep brain stimulation (DBS) has emerged as a treatment for severe cases of therapy-refractory obsessive-compulsive disorder (OCD), and promising results have been reported. The literature might, however, be somewhat unclear, considering the different targets used, and due to repeated inclusion of individual patients in multiple publications.

Deep-brain stimulation (DBS) for treating refractory obsessive-compulsive disorder (OCD) has shown positive results in small clinical trials. Ventral capsule/ventral striatum (VC/VS) might cause mood change, cardiovascular, sensory, or motor effects. These effects were transient or habituated over six months.

Stimulation-induced smile/laughter may be a possible predictor for long-term DBS outcome. Larger studies, genetic studies, and imaging studies are needed to evaluate the effects of different parameters and possible predictors in the treatment of OCD [8].

Outcome

A study aimed to understand perceptions of deep brain stimulation (DBS) for severe obsessive-compulsive disorder (OCD) in adolescents among two groups: parents of children with a history of OCD and adults with a history of OCD. Methods: Two hundred sixty participants completed a questionnaire exploring their treatment history, relevant symptom severity, DBS knowledge, and DBS attitudes using an acceptability scale and a series of statements indicating levels of willingness or reluctance to consider DBS for adolescents with severe OCD or severe epilepsy. Results: Overall, participants found DBS to be fairly acceptable for adolescents with severe OCD, with 63% reporting at least 7/10 on a 0-10 acceptability Likert scale. Respondents were more willing to consider DBS for epilepsy than for OCD. Several factors were associated with a greater willingness to consider DBS for OCD, including familiarity with DBS, the presence of suicidal thoughts, assurances of daily functioning improvements, and assurances of substantial symptom reduction. Concerns about safety, personality changes, and long-term effects on the body were associated with the greatest reluctance to consider DBS for OCD. Conclusions: Our findings support the importance of increasing parents' familiarity with DBS, monitoring factors participants identified as most important to their DBS perceptions in future DBS research, and communicating benefits and risks clearly. We also highlight the need for further research on perceptions of DBS for severe and refractory OCD in adolescents [9].

Case series

Fifty patients with severe treatment-refractory OCD received DBS of the ventral part of the anterior limb of the internal capsule and were followed for at least 3 years following implantation (mean 6.8 ± 3 years). Primary effectiveness was assessed by change in Yale-Brown Obsessive Compulsive Scale scores. Secondary effectiveness measures included Hamilton Anxiety Rating Scale, Hamilton Depression Rating Scale, World Health Organization Quality of Life Scale-Brief Version, Global Assessment of Functioning, and a scale assessing functioning in work, family, and social life. Adverse effects of DBS were examined with a structured interview (n = 38).

Results: At long-term follow-up, OCD symptoms decreased by 39% ($p < .001$), and half of the patients were responders (≥35% decrease of Yale-Brown Obsessive Compulsive Scale score). Anxiety and depressive symptoms decreased significantly, with reductions of 48% and 50%, respectively. The World Health Organization Quality of Life Scale-Brief Version general score improved significantly, as did 3 of 4 subdomains. Both clinician- and patient-rated functioning improved substantially ($p < .001$). The unemployment rate decreased from 78% at baseline to 58% at last follow-up ($z = -1.90$, $p = .058$), and 21 patients stopped or decreased psychotropic medication ($z = -2.887$, $p = .004$). Long-term adverse effects included cognitive complaints and fatigue. Serious adverse events included 1 suicide attempt, related to comorbid depression.

Conclusions: Our results provide evidence that DBS of the ventral part of the anterior limb of the internal capsule is effective and tolerable for treatment-refractory OCD in the long term and improves functioning and overall well-being [10].

2016

Deep brain stimulation (DBS) of the ventral capsule/ventral striatum (VC/VS) region has shown promise as a neurosurgical intervention for adults with severe treatment-refractory obsessive-compulsive disorder (OCD). Pilot studies have revealed improvement in obsessive-compulsive symptoms and secondary outcomes following DBS. Fayad et al sought to establish the long-term safety and effectiveness of DBS of the VC/VS for adults with OCD.

A long term follow-up study (73-112 months) was conducted on the six patients who were enrolled in the original National Institute of Mental Health pilot study of DBS for OCD. Qualitative and quantitative data were collected.

Reduction in OCD symptoms mirrored the one-year follow-up data. The same four participants who were treatment responders after one year of treatment showed a consistent OCD response (greater than 35% reduction in Yale Brown Obsessive Compulsive Scale (YBOCS)). Another subject, classified as a non-responder, achieved a 26% reduction in YBOCS score at long term follow-up. The only patient who did not achieve a 25% or greater reduction in YBOCS was no longer receiving active DBS treatment. Secondary outcomes generally matched the one-year follow-up with the exception of depressive symptoms, which significantly increased over the follow-up period. Qualitative feedback indicated that DBS was well tolerated by the subjects.

These data indicate that DBS was safe and conferred a long-term benefit in reduction of obsessive-compulsive symptoms. DBS of the VC/VS region did not reveal a sustained response for comorbid depressive symptoms in patients with a primary diagnosis of OCD [11].

Six patients receiving ventral capsule/ventral striatum (VC/VS) DBS for OCD underwent oxygen-15 positron emission tomography (15O-PET) scanning. Monopolar DBS was delivered at each of the 4 different electrodes on the stimulating lead in the VC/VS. The data were analyzed using SPM5. Paired t-tests were run in SPSS to identify significant changes in regional cerebral blood flow (rCBF) between stimulation conditions. Pearson's r correlations were run between these significant changes in rCBF and changes in OCD and depressive symptom severity. RESULTS Perfusion in the dorsal anterior cingulate cortex (dACC) significantly increased when monopolar DBS was turned on at the most ventral DBS contact, and this increase in dACC activity was correlated with reductions in depressive symptom severity ($r(5) = -0.994$, $p = 0.001$). Perfusion in the thalamus, striatum, and globus pallidus significantly increased when DBS was turned on at the most dorsal contact.

DBS of the VC/VS appears to modulate activity in the regions implicated in the pathophysiology of OCD. Different regions in the cortico-striatal-thalamic-cortical circuit showed increased perfusion based on whether the stimulation was more ventral or dorsal along the lead axis in the VC/VS. Evidence was found that DBS at the most ventral site was associated with clinical changes in depressive symptom severity, but not OCD symptom severity [12].

Case reports

Barcia et al report 2 patients diagnosed with OCD, one having symmetry obsessions and the other one with sexual-religious obsessive thoughts. They were implanted bilaterally with deep electrodes located at both STN and nucleus accumbens. The effectiveness of the stimulation was tested for every possible paired combination of electrodes guided by the Yale-Brown Obsessive Compulsive Scale (Y-

BOCS) score reduction.

In both cases, the combination of electrodes which best relieved the OCD symptoms was both the left STN and left accumbens. In case 1, the preoperative Y-BOCS score was 33, and 1 month after stimulation it was 16. In case 2, the Y-BOCS scores were 33 and 3, respectively, with the patient being free of obsessions.

Some reports suggest that lesion stimulation or stimulation of only the right side relieves OCD symptoms. However, anatomical and functional studies are not conclusive as to which side is most affected in OCD. Possibly, each OCD patient has an individualized optimal side to stimulate [13].

Animal studies

Luyck et al., recently showed that deep brain stimulation (DBS) in the bed nucleus of the stria terminalis (BST) reduces obsessions, compulsions and associated anxiety in patients suffering from severe, treatment-refractory obsessive-compulsive disorder. They investigated the anxiolytic effects of electrical BST stimulation in a rat model of conditioned anxiety, unrelated to obsessions or compulsions. Two sets of stimulation parameters were evaluated. Using fixed settings at 100 Hz, 40 µs and 300 µA (Set A), they observed elevated freezing and startle levels, whereas stimulation at 130 Hz, 220 µs and individually tailored amplitudes (Set B) appeared to reduce freezing. In a follow-up experiment, they evaluated the anxiolytic potential of Set B more extensively, by adding a lesion group and an additional day of stimulation. They found that Electrostimulation significantly reduced freezing, but not to the same extent as lesions. Neither lesions nor stimulation of the BST affected motor behavior or unconditioned anxiety in an open-field test. In summary, Electrostimulation of the BST was successful in reducing contextual anxiety in a rat model, without eliciting unwanted motor effects. The findings underline the therapeutic potential of DBS in the BST for disorders that are hallmarked by pathological anxiety. Further research will be necessary to assess the translatability of these findings to the clinic [14].

Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines

Based on the data published in the literature, the following recommendations can be made: (1) It is recommended that clinicians utilize bilateral subthalamic nucleus DBS over best medical management for the treatment of patients with medically refractory OCD (level I). (2) Clinicians may use bilateral nucleus accumbens or bed nucleus of stria terminalis DBS for the treatment of patients with medically refractory OCD (level II). There is insufficient evidence to make a recommendation for the identification of the most effective target. The full guidelines can be accessed at https://www.cns.org/guidelines/browse-guidelines-detail/deep-brain-stimulation-obsessive-compulsive-disord [15]

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