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What are the Implications of Using Deep Brain Stimulation to Treat and Improve Symptoms of Depression?

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ABSTRACT

Neuroscientific practice is constantly evolving, improving, and developing. Recent research has introduced novel methods to treat pressing conditions which have affected the human population for many decades. This paper delves into the potential of a stimulation technique- deep brain stimulation- to treat the symptoms of a mood disorder as complex and convoluted as depression. Overall, 5 domains were considered, including: an overview of the diagnostic factors of depression, the biological causative factors for depression, current treatment opportunities, the mechanism of DBS and its application to treating depression, and finally, the ethical and social implications of implementing DBS as a mainstream form of treatment for cases of extreme depression. Before its utilisation in mainstream practice, the ethical implications, as well as clinical trials assessing the true long-term impacts of such treatment, must be evaluated. How far should the brain be manipulated in order to treat depression, and how could this impact autonomy and patient safety? Across the literature reviewed, DBS serves as a viable and credible means for relieving symptoms of depression and poses a great potential to improve the lifestyle of treated patients, which is ultimately the desired outcome of a neuroscientific endeavour such as this one.

Keywords: Deep Brain Stimulation, Treatment-Resistant Depression, Neuromodulation, Mood Disorders, Nucleus Accumbens, Neuroethics, Psychiatric Treatment, Neural Circuitry.

INTRODUCTION

Depression is a systemic mood disorder, defined by the presence of multiple clinical features, and acknowledging the possibility of both psychological and biological etiology. According to the World Health Organization, an estimated 4% of the global population experience depression, which includes 5.7% of the adult population. 5.9% of adults aged 70 years old and above have depression, and the prevalence of this disorder is higher for women (6.9%) than it is for men (4.6%). Approximately 332 million people globally are diagnosed with depression and a cluster of symptoms and signs appear at the same time, which makes it an especially complex illness. For DSM-IV there are eight symptoms that qualify for major depression, and at least 5 of which should be present, together with a duration of 2 weeks or longer. Severity levels depend on the number of symptoms present, and these vary between individuals. Therefore, since depression is so specific to the individual, it is difficult to generalise exactly how it affects productivity; generally, patients with depression face low levels of motivation, feelings of guilt, and recurring feelings of worthlessness, which impact work functioning, social connectedness, decision making ability, and information retention in professional environments. In turn, not only is an individual's ability to perform day to day tasks impacted, they face a detrimental reduction in their quality of life and sense of self. Depression is multi-factorial; advancements in medicine, technology, and our general understanding of its potential causality have enabled researchers to formulate treatment plans tailored to the individual. Some types of depression can be treated using CBT, which aims to change negative, irrational thinking patterns to improve mood and behavior. A common form of treatment is using antidepressants which affect the biological processes in the brain which govern emotional processing. For cases of depression that do not respond to traditional treatments (TRD), a relatively new approach known as Deep Brain Stimulation (DBS) offers promise. This technique targets and stimulates malfunctioning neural circuits in the brain, relying heavily on precise regulation and monitoring. Hope is being offered to individuals who live under the shadow of their disorder, and these patients are being given a chance to regain control of their health and wellbeing. However, this exciting possibility must be weighed against ethical and social considerations regarding patient safety, autonomy, and long-term effectiveness. Some of the most pressing concerns regarding the ethics of DBS include questions around the possible effects on identity and personality changes post-surgery, dealing with issues surrounding patient expectations and how realistic treatment outcomes might be, a gray area when it comes to autonomy and informed consent for severely ill patients who use this treatment as a 'last resort' and do not fully understand how it works, and economic and affordability issues that arise with the utilization of advanced technology. This paper will holistically explore the clinical overview and general treatment of depression, and evaluate the use of a novel neuroscientific approach and the possible long - term and clinical implications it might present for patients, with the aim of examining how far the brain should be manipulated to treat depression.

OVERVIEW INTO DEPRESSION

Depression is a truly multifaceted mood disorder, and specialists have contributed to its holistic understanding over time. Medieval times recognized melancholia, and the occurrence of this was heavily linked to the humoral theory of causation, associated with black bile.

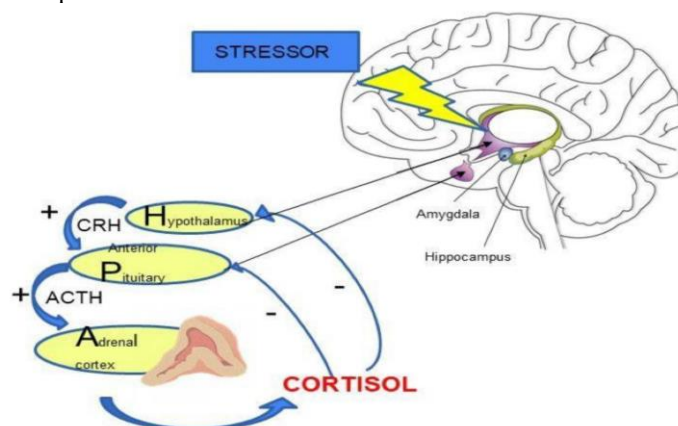
Over time, this broad nomenclature changed and included aspects of despair and mania; modern-day psychiatrists renamed the alteration between mania and melancholy as bipolar disorder (Paykel, “Basic Concepts of Depression”). Psychiatrists focused on medical models and biological causation, whereas psychoanalysts developed theories stating that depression was a result of extreme loss of the love of an object. As the understanding of depression grew, social, cognitive, and organic factors had to be considered, and the modern concept of depression is based on the foundational principle that it is defined by the presence of many clinical features, but psychological and biological causative factors underlie its development. It is important to realize that depression has existed for centuries, in all of its various forms and complexities.

The prevalence of depression over time has seen a steady increase. In 2019, the incidence of depressive disorders increased by 59.3% to 290 million cases globally (Wu et al.). An observable transition of incidences from young and middle-aged populations towards older populations was visible, which affirmed the presence of a correlation between the incidence of depression and age. The COVID-19 pandemic triggered an increase in the prevalence of depression and other mood disorders by 25% (World Health Organization: WHO). At this stage, it was mainly young people who were disproportionately affected by a high risk of suicide and self-harm; by the end of 2021, the severity of these cases had reduced and coping mechanisms made it easier to deal with mental health disorders, but the stressful situation has still left a strain on the world, which has prompted the world to implement mental health and psychosocial support to these patients. A survey conducted by WHO reported that 90% of countries are currently working to make rehabilitative resources more widely available to the general public. In 2025, an estimated 280 million people have depression, and it affects the majority of age groups across all demographics. Depression is also 50% more common in women than in men globally, and 10.3% of adult females have experienced a major depressive episode compared to 6.2% of adult males (Therapy Route, 2025). The gender disparity present with depression is a focus of research currently.

2 official classifications enshrine the concept of depression and all of its aspects, including symptoms, potential causes, diagnosis, and treatment. (Paykel, “Basic Concepts of Depression”) The DSM-IV states that 8 symptoms qualify for major depression: depressed mood, loss of pleasure, significant weight changes, sleep problems, psychomotor changes, persistent fatigue, poor concentration, and suicidal ideation. Moreover, one of the core symptoms must be present with a duration of 2 weeks or more for a patient to be diagnosed with depression (Wu et al.) . At least one core symptom out of the two listed in DSM-IV should be present; these two include depressed mood and loss of pleasure. For ICD-10, eligible symptoms are fairly similar to those for the DSM-IV, including the addition of one further symptom- loss of confidence. Identical to the DSM-IV, the presence of these symptoms should last for a duration of around 2 weeks or more (Theraplatform, 2024). Often, the number of symptoms a patient experiences depends on the severity of their depression; the more severe the case, the greater the number and/or intensity of the symptoms.

POTENTIAL CAUSATIVE FACTORS

There is no sole cause of depression; the development of this disorder can be affected by the interplay of various factors. The most credible causes are: the biological, cognitive, and sociocultural approaches. This paper will explore some of the main biological causes of depression: HPA axis dysregulation, 5-HT neurotransmitter dysfunction, and inflammatory responses. Individuals can have a genetic predisposition that makes them more likely to develop depression; they might have inherited specific genes from their parents, who might have been diagnosed with depression, and this may have correlated with their own diagnosis. Genetics cannot be isolated as the sole factor, however. The diathesis stress model suggests that whilst someone might have a genetic predisposition, the actual development of depression is influenced by an activating event in the environment, which triggers the predisposition. It has now become common knowledge that the brain is lateralised; specific areas carry out specific functions, such as decision making, impulse control, emotional regulation, movement, etc. Throughout decades of neuroscientific and psychological research, professionals have developed an understanding of the brain regions associated with mood and emotional processing, and the speculation is that damage to these areas can lead to impairment in such functions, resulting in psychiatric disorders like depression, hypomania, bipolar disorder, etc. From a biological point of view, depression is characterized by elevated stress levels and inflammatory factors. The Hypothalamic-pituitary-adrenal (HPA) axis is the brain’s stress response system, and it is dysregulated in depression. The axis is responsible for stimulating feedback loops involving the brain, the pituitary gland, and the adrenal gland, which regulate the production of cortisol. When someone experiences a high level of stress, the HPA axis becomes overactive, which results in an excess production of cortisol.



Stress as a factor activating the HPA axis; stress leads to a release of CRH from the hypothalamus. This stimulates the pituitary gland to release ACTH, which stimulates the adrenal cortex to release cortisol into the blood.

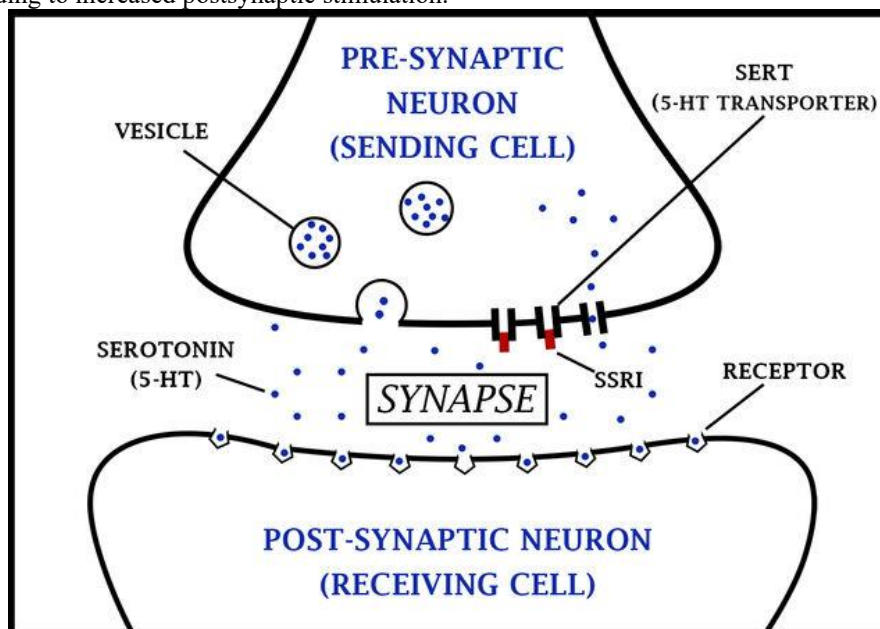
(Mikulska et al., Fig. 1)

TREATMENT

Treatment plans vary depending on the patient. Several factors determine the best course of action for treating a patient with depression, and some of these include: severity, cost-effectiveness, the presence of other underlying mental health disorders, medical history, personal preference, previous treatment efficacy, and therapist relationships.

This being said, the first line of treatment for depression has been antidepressants, since the advent of their origin in the 1950s. Antidepressants work directly on biological systems in the brain to regulate neurotransmitter levels. (López-Muñoz, 2009) Reuptake is a vital process carried out by neurons, and this occurs when neurotransmitters are reabsorbed into the presynaptic neuron from which they were released, before binding to the receptors on the postsynaptic neuron. This often involves transporter proteins in the plasma membrane of the neuron. Reuptake is significant because it regulates the concentration of neurotransmitters in the postsynaptic neuron, preventing excessive signaling. However, it also reduces the number of neurotransmitters in the synaptic cleft, leading to inefficiencies in signal transmission across neurons. This process occurs with serotonin, and lower levels of serotonin due to reuptake have been shown to contribute to mood disorders (López-Muñoz, 2009).

Antidepressants known as Selective serotonin reuptake inhibitors (SSRIs) block the reuptake of serotonin into the presynaptic neuron, so that more of the neurotransmitter is available to stimulate other neurons, which helps with improving mood and motivation in depressed patients (Moncrieff, 2023). This process involves the enhancement and prolongation of serotonergic neurotransmission, leading to increased postsynaptic stimulation.



SSRIs are blocking areas where serotonin can be reabsorbed back into the presynaptic neuron, therefore increasing the amount of serotonin available in the synapse.

(Cottone., fig. 2)

Another type of antidepressant is the monoamine-oxidase inhibitor (MAOI). Monoamine oxidase is a group of enzymes that catalyse the oxidative deamination of monoamine neurotransmitters such as serotonin, norepinephrine, and dopamine. MAOIs, therefore, limit the breakdown of these neurotransmitters by binding to the monoamine oxidase, allowing for a greater concentration of key neurotransmitters to diffuse across the synaptic cleft and into the postsynaptic neuron.

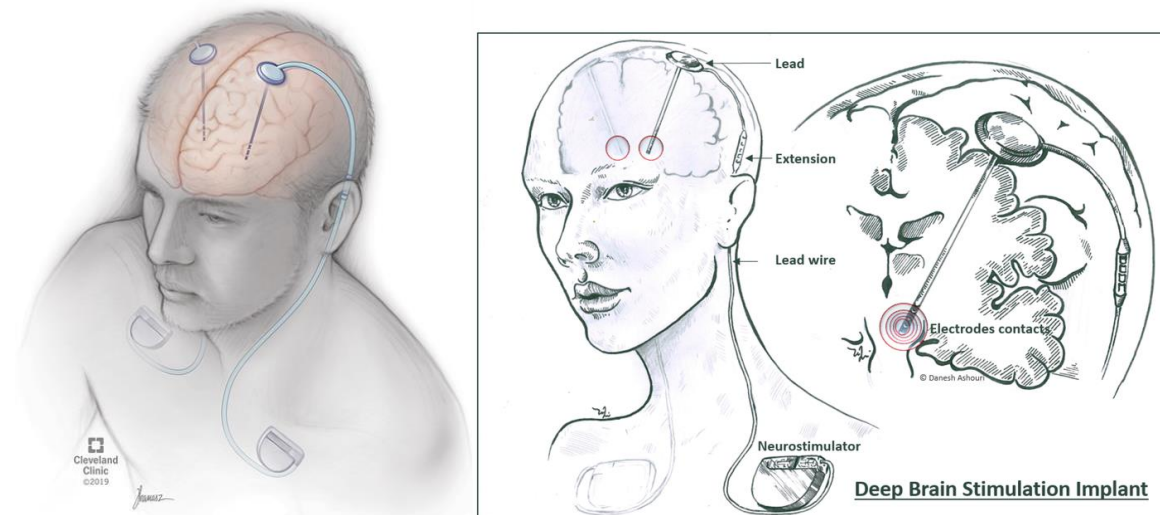
As with most drugs, antidepressants create adverse effects; for example, taking SSRIs has been known to lead to sexual dysfunction, headaches, and agitation. SNRIs can lead to excessive sweating (diaphoresis), nausea, insomnia, anxiety, etc. Serotonin modulators, which perform essentially a similar function to reuptake inhibitors, can result in heartburn and dizziness (Sheffler, 2023).

Another common form of treatment is Cognitive behavioral therapy (CBT), wherein a therapist works with a patient to identify irrational patterns in their thinking and reasoning, and then helps them create rational thinking processes to influence a change or improvement in their behavior. The basis of this treatment is challenging cognitive errors to help an individual control their own behaviour. This form of treatment is beneficial as it equips patients with coping strategies and teaches them lifelong skills that are applicable in various situations, rather than fostering dependency on a biological inhibitor. A problem arises, however, when symptoms persist despite trying standard treatments like medications or psychotherapy. Treatment-resistant depression is said to have developed when a patient is unresponsive to at least two different types of antidepressants, which had each been administered for a duration of six to eight weeks (Cleveland Clinic, 2025). This is an extreme form of depression wherein it is increasingly difficult to treat symptoms and this can occur due to various factors. Inadequate trial duration or non-adherence to treatment could affect the development of TRD (“Treatment-Resistant Depression: What It Is & Symptoms”).

DEEP BRAIN STIMULATION AND ITS APPLICATION TO THE TREATMENT OF DEPRESSION

Deep brain surgery is a relatively new neuroscientific surgical approach towards treating specific neurodegenerative disorders; it is most commonly used to treat motor inefficiencies such as Parkinson's disease, essential tremor, and dystonia, but is being increasingly applied to the treatment of mood disorders such as treatment-resistant depression (Volkman, 2024). The mechanism of deep brain surgery is relatively straightforward once we gain a comprehensive understanding of how lateralisation in the brain works. After decades of MRI scanning, fMRI research, and other imaging techniques, neuroscientists have understood that different regions of the brain undertake specific tasks, and this specialisation and division of labor allows the human brain to be a complexing efficient organ. When a patient has a neurodegenerative disorder like Parkinson's, their subthalamic nucleus (STN) and the internal segment of the globus pallidus (GPi) are affected (Volkman, 2024). These brain regions are responsible for movement modulation and coordination. When these areas are targeted, symptoms generally improve between 50%-70%; stimulation of the surrounding areas, however, can bring about negative side effects such as difficulty with speech or swallowing. The general idea is that by stimulating a specific brain region wherein neurons are misfiring, and exciting some pathways while inhibiting others, the compromised function can be restored.

It is imperative to point out however, that DBS is not offered to patients as a ‘cure’ for a disease, and it is not expected to completely inhibit the progression of the neurodegenerative process that underlies the disease; the purpose of DBS is to reduce symptoms by applying technical processes to the concept of brain lateralisation (Malek, 2019). Before a region is stimulated, MRI scanning is required to map out coordinates and possible probe trajectories. Once this is done, DBS leads are surgically implanted in the specific region that delivers a current to the target- the frequency, amplitude, pulse width, and electrode configurations are preset depending on the intensity of the current that needs to be delivered. ‘Contacts’ are the electrodes on the DBS lead that actually deliver the current. The electrode is connected to an implantable pulse generator (IPG) which is implanted on the anterior chest wall of the patient, and this acts as a power pack for the entire DBS system; the IPG sends the current to the electrode through insulated wires (Fariba, 2023).

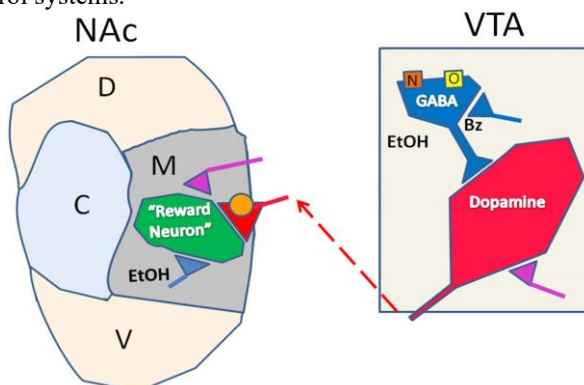


Positioning of DBS implant: the electrodes are placed in the brain, and the pulse generator under the collarbones.

(Deep Brain Stimulation (DBS), Fig. 3 and 4)

Illustration of a DBS implant; the implant consists of 4 main parts: electrode contacts, lead, lead wire, and implanted pulse generator (IPG). The IPG stimulates the contact by sending electrical impulses through the lead wire, and the contacts deliver current to the target tissue.

The mechanism behind DBS is relatively simple enough for the treatment to be applicable to Depression. In theory, using the same principle of targeting a specific brain region responsible for emotional regulation and production of mood, and delivering precise stimulation, could result in a promising treatment opportunity for those who don't benefit from any other treatments. Using DBS for depression could then revolutionize the medical perception of treatment resistant disorders; the scope is wide and it already looks promising. This paper will examine how one specific brain region could be targeted in DBS to alleviate symptoms of depression: the nucleus accumbens (NAc). the NAc is influenced by dopaminergic inputs and acts as a motivation gateway that connects emotional and motor control systems. Moreover, this area is a functional hub in reward system behaviour, which is altered in patients with depression, addiction, and OCD. Over 90% of the neurons in the NAc are GABAergic neurons- nerve cells that produce the neurotransmitter GABA which reduces neuronal excitability and controls impulses (Ruan, 2024). These neurons play a critical role in reinforcement of certain types of behavior, and the dysregulation of an area that heavily relies on the proper firing and functioning of these neurons results in detrimental consequences for those with depression. DBS has been used to stimulate the NAc previously, and results from human and animal studies have demonstrated the effectiveness of NAc regulation via DBS for disorders affecting reward efficiencies and emotion control systems.



This image shows the brain's reward system, focusing on the connection between the ventral tegmental area (VTA) and the nucleus accumbens (NAc). GABAergic neurons regulate dopamine signaling from the VTA to the NAc, and disruptions in this pathway are closely linked to reduced reward sensitivity, a key feature of depression.

(Olsen, Fig. 5)

Examining a case study of a patient who underwent DBS can allow us to acquire knowledge about the general after-effects of surgery, the immediate change post-surgery compared to pre-surgery, and the long-term efficacy of the treatment. An experimental research protocol at Emory University described the patient case of Brian, a 27-year-old caucasian male who presented with signs of a severe major depressive episode. Some of his symptoms included: depressed mood, decreased sleep, decreased appetite, fatigue, feelings of worthlessness, poor concentration, and frequent suicidal ideation. He did not meet any criteria for any other psychiatric illness, and was otherwise healthy.

Brian's first major episode occurred when he was 17, living a relatively 'normal' and 'happy' life; he went into full remission, and his symptoms reduced for two and a half years, until he turned 20. He received partial remission again, and was treated primarily using various drugs; his third major depressive episode occurred at the age of 21. He remained reasonably stable for about 3 years until this recent episode. Given the degree of his recurring depressive symptoms and frequent suicidal ideation, he sought participation in a clinical trial of DBS and underwent neurosurgical placement of DBS electrodes in the subcallosal cingulate white matter- a brain region located below the corpus callosum that is a key contributor in mood regulation. Brian began to notice a slight decrease in his level of suicidal ideation, and a subtle increase in his motivation. He reported no immediate adverse events relating to DBS, and over the next 8 weeks, he noted a decrease in negative mood, better concentration, and an increase in sleep quality. The improvement is slow, but consistent; no side effects are reported due to stimulation. After his 16-week visit, however, he noted feelings of guilt and continued to have occasional suicidal ideation, which demonstrates that recovery is not a linear process. He described feelings of loneliness and unhappiness.

After 2 years, Brian's depressive symptoms gradually resurfaced (although, not to the same intensity as they were pre-surgery), but on examination, it is discovered that his IPG was inactive, for which he receives a replacement. 4 weeks after the replacement is introduced, symptoms gradually decrease again. This demonstrates the long-term efficacy of DBS, and how it can genuinely improve a patient's quality of life. However, they must compensate for the reduction in their symptoms with reliance on the technical components of the actual implant, such as the IPG as shown in Brian's case (Holtzheimer & Mayberg, 2010).

Therefore, the utilisation of DBS as a mainstream medical treatment holds great promise for mood disorders like depression; large scale clinical trials have proven its efficacy. With correct, individualized treatment plans, the application of this could be beneficial to a multitude of patients facing treatment-resistant depression, who have not been positively influenced in the long term by other treatment variations (MK, 2013). What must now be considered are the implications of DBS beyond the psychiatric benefits; examining the overall implications on the patient and society as a whole is imperative.

ETHICAL IMPLICATIONS OF IMPLEMENTATION

Depression is a heterogenous syndrome, that includes the dysfunctioning of a broad range of pathological brain circuits, rather than just one diseased state (Unadkat, 2024). Therefore, treatment for depression cannot be generalized amongst all patients. DBS is a chance for TRD patients to gain the specific treatment they need, by focusing the procedure solely on their brain's interior architecture and the data received from MRI and fMRI scanning. Despite this specificity, DBS brings about ethical concerns regarding patient security, confidentiality, consent, and privacy; these concerns must be weighed against the benefits. Some of the core ethical considerations must be explored for neuroethical analysis: informed consent, beneficence and non-maleficence, privacy, and the management of treatment expectations (D'Imperio, 2024).

- i. There is a gray area when it comes to autonomy and informed patient consent in regards to neurodegenerative disorders; cognitive decline can lead to autonomy being compromised, which brings up ethical issues. For example, if a patient with amnesia undergoes a surgical operation, it becomes difficult to technically confirm whether they gave proper informed consent for their medical history to be accessed if they can't physically remember giving this consent pre-surgery.
- ii. There is a conflict between beneficence and non-maleficence in the practice of DBS. Acting in the patient's best interest can be challenged by the patient's worsening condition despite forms of treatment, and avoiding harm becomes difficult due to a patient's potential suicidal ideation and self-harm.
- iii. Respecting a patient's confidentiality, whether it be instances of recent suicidal thoughts, or details about previous depressive episodes, should be integral to the relationship between patient and professional. With DBS, balancing the patient's right to privacy with the need to share information to ensure their safety is extremely important; doctors may need to decide when it is best to communicate transparently with those who support the patient in their day to day lives.
- iv. While DBS offers promise to patients, it may fail to deliver the expected results. This can lead to further psychological stress and discomfort. It is imperative to honestly clarify to the patient the very real possibility of DBS being less effective than expected, and how the effects of surgery may not be immediate. Fostering hope while maintaining this honesty is a challenge, especially when patients with TRD choose to undergo this treatment as a 'last resort', without fully understanding the mechanism behind it. 100% alignment and realistic discussions around the treatment are essential.

DBS is currently a major focus in research and this is where methodology comes into question. Research and analysis are intertwined; any problems within research frameworks can clearly be reflected when data is analyzed. One of the major methodological issues that arise with DBS research include small sample sizes leading to a lack of population validity (Jiménez, 2025). Case reports make significant findings, but lack the statistical power needed to draw definitive conclusions. The specificity of DBS means that one treatment plan cannot be exactly generalized to a group of patients, and if DBS is to work, then an individualized approach has to be taken (Morishita, 2014). In research, this can lack practicality due to constraints on time, and may not be economical for both the patient and the provider. A well-designed randomized trial with sufficient statistical power would hence account for the variability in patient outcomes. Another issue that arises is the lack of standardized procedures in many studies; if a study is to be reliable and applicable to a variety of populations, then the methodology must be designed in an objective manner, so that results are fairly comparable. Again, the issue with DBS lies in its complexity. It is difficult to standardize procedures and maintain objectivity if participant variables muddle the process. It is unlikely that each patient will be experiencing the same symptoms of depression, or be on the same position of the severity spectrum.

DBS is still an experimental intervention for TRD. After a study is concluded and data is collected, participants with the psychiatric disorder may not continue to have access to the DBS electrodes (this is something that would have been formally disclosed by the researcher before the study took place). Despite formal disclosure, a significant ethical dilemma arises: patients who rely on the electrodes may lose the only form of treatment that helps them. The vulnerability of a patient undergoing a DBS trial is profound; the vulnerability from when the device is implanted continues until the treatment is over. Some might say that they are left more vulnerable after the procedure than before. This removal may also pose a physiological risk, which could worsen the patient's depressive symptoms (Sheth, 2022). Here, it is imperative to question whether DBS research, particularly, does more harm to the participant than it does good to the rest of the scientific community.

CONCLUSION

After studying and considering the literature surrounding the potential for DBS to become a mainstream form of treatment for Depression, I strongly believe in the scope and opportunity for DBS revolutionizing patient care and medical practice. The ethical and methodological concerns regarding current DBS research are indisputable, and they underscore the immediate need for transparent reporting practices, rigorous study designs, and sustained ethical reflection. To combat these concerns, clearer ethical guidelines and formal policies should be implemented to foster patient trust, honest patient-researcher relationships, and improve study quality. A clear method by which this could be achieved may be through the formation of an ethics committee including expert neurosurgeons, neuroscientists, government officials, psychiatrists, lawyers, and mental health activists, to review and approve study proposals for DBS trials on depressive patients. Post-trial obligations might be placed on researchers to ensure that long-term follow-up care is given, recruitment policies may aim to ensure representative and large samples within trials, and standardized reporting should become a requirement; researchers must publish detailed protocols to improve reproducibility and cross-study comparisons. It is important to note that the incidence of depression is proportionately increasing with time, and industrial living poses multiple risk factors, making people of all ages more prone to developing it; DBS is a call to action. Additionally, compared to general treatment in the form of antidepressants which promote dependency and tend to create adverse effects, DBS is a non-drug form of treatment that aims to genuinely improve depressive symptoms in the long run, rather than just providing immediate relief. Depression is a very personal condition in its nature, and generalized antidepressants may not be efficacious for every patient; DBS offers a treatment tailored to the individual. Moreover, we must acknowledge that DBS is a novel neuroscientific approach, and is still in the early stages of research. If the methodological issues can be overcome, it could certainly transform patient welfare, keeping scientific integrity at the core of its practice. Overall, DBS represents a profoundly humanitarian undertaking, aimed at relieving suffering and restoring the quality of life for those patients affected by depression, and the implementation of it would change countless lives globally, as well as reshaping our scientific understanding of the human brain and behaviour.

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