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Effectiveness of deep brain stimulation in alleviating treatment-resistant schizophrenia: a systematic review

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Abstract

The complexity of schizophrenia, particularly in cases resistant to traditional pharmacological treatments, poses significant challenges for clinicians and researchers. This systematic review synthesizes existing evidence on the effectiveness of deep brain stimulation in treating treatment-resistant schizophrenia. Utilizing the PRISMA 2020 guidelines, a comprehensive literature search was conducted in March 2025 using the "Connected Papers" tool and other sources such as Web of Science, PubMed, PsycINFO, Embase, and Scopus, focusing on studies related to "deep brain stimulation," "treatment-resistant schizophrenia," and "refractory schizophrenia." Four studies met the eligibility criteria, revealing that deep brain stimulation targeting specific brain regions, particularly the nucleus accumbens, can lead to significant symptomatic improvements in approximately 30% of patients unresponsive to conventional antipsychotics. Despite ten adverse events recorded across thirteen procedures, deep brain stimulation offers potential benefits for select individuals. While not universally superior to existing treatments, deep brain stimulation could inform clinical practice and decision-making, highlighting its role in multidisciplinary treatment frameworks. The findings underscore the importance of innovative therapeutic approaches in psychiatry and suggest broader implications for neuromodulation techniques across various psychiatric and neurological disorders, promoting personalized and effective treatment paradigms in mental healthcare.

Key Words: deep brain stimulation, electrical stimulation of the brain, treatment-resistant schizophrenia, refractory schizophrenia, schizophrenia.

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The complexity of schizophrenia presents a formidable challenge for clinicians and researchers alike, especially when addressing cases that resist traditional pharmacological interventions.[1,2] Schizophrenia, affecting roughly 1% of the population, frequently manifests with debilitating symptoms such as delusions and hallucinations, which in many cases remain unresponsive to conventional treatments like antipsychotics.[3] Approximately 30% of patients with schizophrenia do not achieve adequate symptom relief from standard treatments, which involve failing two or more antipsychotic trials.[1,4] Such patients are often prescribed clozapine, the most effective antipsychotic medication available. However, clozapine is reserved for cases of treatment-resistant schizophrenia because it carries the risk of agranulocytosis, a potentially life-threatening condition characterized by dangerously low levels of white blood cells.[5,6] Even with clozapine treatment, only about 30% to 60% of patients experience improvement.[5] For individuals who don't respond to or cannot tolerate clozapine, alternative treatments are limited and often ineffective.[7] Since schizophrenia imposes a substantial societal burden due to management costs and psychosocial impacts, there is an urgent need for improved methods of symptom control.[8-12]

Deep brain stimulation is emerging as a promising non-pharmacological option, particularly for cases resistant to conventional therapies.[13] Its success in neuropsychiatric conditions such as Parkinson's disease,[14] treatment-resis-

tant depression,[15] obsessive-compulsive disorder,[16] substance use disorders,[17] and Tourette syndrome[18] suggests that deep brain stimulation could effectively modulate dysfunctional brain circuits in schizophrenia, offering hope for improved management of the disorder.[13] Pioneering studies have notably highlighted the possibility of using deep brain stimulation to target specific brain regions, such as the nucleus accumbens (likely the strongest candidate for deep brain stimulation electrode placement in schizophrenia), the subgenual anterior cingulate cortex, the ventral tegmental area, the substantia nigra pars reticulata, and the habenula.[13] These regions have been connected to the modulation of dopaminergic, glutamatergic, and GABAergic pathways, which may provide insights into the neurochemical underpinnings of schizophrenia.[19] However, deep brain stimulation has been minimally explored as a treatment for treatment-resistant schizophrenia. An early study from the 1950s reported intense rage and fear during amygdala stimulation in a patient with schizophrenia, but subsequent research on this application of deep brain stimulation was lacking until recent years.[20] Accordingly, this systematic review aims to synthesize existing evidence regarding the effectiveness of deep brain stimulation in treating treatment-resistant schizophrenia, addressing both the observed clinical benefits and the challenges to the widespread implementation of this therapeutic approach. By examining the nuances of stimulation techniques, patient selection criteria, and the neurobiological mechanisms involved, this review will illuminate promising avenues for future research while acknowledging the ongoing ethical discussions regarding informed consent and the management of adverse effects associated with surgical interventions. Furthermore, as our understanding of the underlying pathophysiology of schizophrenia continues to evolve, there is a pressing need for innovative approaches that encompass multidisciplinary perspectives and integrate findings from neuroimaging, clinical evaluations, and patient-reported outcomes. Therefore, this review not only highlights the necessity for rigorous methodological designs in deep brain stimulation trials but also calls for a collaborative effort to unravel the patient-specific factors that might enhance the precision and effectiveness of deep brain stimulation as a viable treatment for those suffering from this complex and often debilitating disorder.

Materials and Methods

Search strategy

The study adhered to the PRISMA 2020 checklist and conducted a systematic review of the literature in March 2025 using "Connected Papers" (www.connectedpapers.com)—a visual exploration tool that accesses data from the Semantic Scholar Paper Corpus, which is licensed under ODC-BY, as well as other sources such as Web of Science, PubMed, PsycINFO, Embase, and Scopus.[21] The search focused on studies related to "deep brain stimulation," "treatment-resistant schizophrenia," and "refractory schizophrenia," employing specific Boolean modifiers to refine the results. Two independent researchers evaluated the titles and abstracts of potential articles, selecting those that met the eligibility criteria for further analysis. When primary evaluators disagreed about including a study, a third evaluator was consulted to make the final decision.

Eligibility criteria

The study focused on original research articles related to treatment-resistant schizophrenia and deep brain stimulation treatment, excluding other disorders, non- deep brain stimulation treatments, non-human studies, and review articles. The selected articles were peer-reviewed and included case reports, case series, or randomized trials in English. There was no exclusion based on the publication date.

Data extraction

Two authors created a citation list by screening titles and abstracts, and then independently evaluated full-text articles based on agreed-upon eligibility criteria. They extracted data on the country, study design, number of patients, participant characteristics, minimum duration of illness, target location(s), primary outcome measure(s), length of follow-up, mean score improvement, responders (*i.e.*, those with a Positive and Negative Syndrome Scale (PANSS) or Brief Psychiatric Rating Scale (BPRS) reduction of ≥25%), and the number and time to resolution of transient/serious adverse events for comparison. Due to the small number of patients in eligible studies, they couldn't quantitatively assess the strength of the evidence. Three primary scales were used: the PANSS, the BPRS, and the Scale for the Assessment of Negative Symptoms (SANS). PANSS is a 30-item scale that assesses positive symptoms, negative symptoms, and general psychopathology, with each item rated from one to seven to indicate symptom severity.[22] BPRS examines up to 24 psychotic symptoms, also using a one-to-seven rating system for severity.[23] SANS evaluates negative symptoms with a 25-item scale scored from zero to five per item.[24]

Quality assessment

Two authors independently evaluated the risk of bias for each study's outcome, following AHRQ guidelines.[25]

Results

Study selection

A comprehensive search of "Connected Papers" yielded 90 titles. No additional articles were identified from other sources such as Web of Science, PubMed, PsycINFO, Embase, and Scopus. A bibliometric co-authorship analysis using VOSviewer (version 1.6.20) revealed that 195 authors met the minimum threshold of one document per author, as presented in Figure 1. After removing duplicates, 77 unique titles remained. Following a screening process based on titles and abstracts, ten articles were shortlisted. However, further evaluation led to the exclusion of two review articles, one study protocol, a repetitive longitudinal study, a

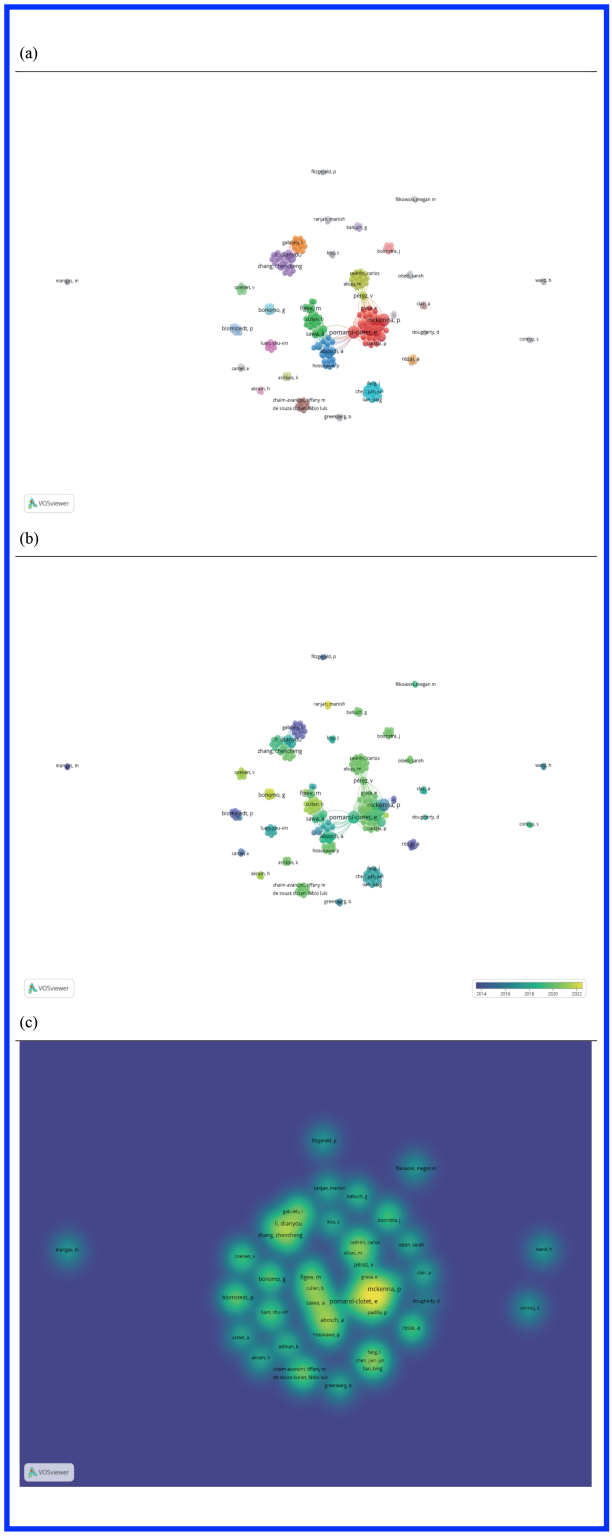

Figure 1. *The bibliometric analysis of co-authorship using VOSviewer: (a) network visualization based on document weights; (b) overlay visualization based on document weights and average publishing year, with a minimum score of 2014 and a maximum of 2022; (c) density visualization of 30 clusters, 933 links, and a total link strength of 1056.*

case report, and a case series due to data similarity with a randomized trial. Ultimately, four articles met the eligibility criteria and were included in the final selection, as depicted in Figure 2.

Study design

In a review of four selected studies, one was a pilot randomized crossover clinical trial, two were case series, and one was a case report focusing on deep brain stimulation for treatment-resistant schizophrenia. A total of 13 patients (6 females and 7 males) were involved across these studies, although one patient was excluded due to complications but was later replaced by another patient. The studies aimed to treat both positive and negative symptoms using deep brain stimulation and assessed the effects over varying follow-up periods. Wang *et al.*[26] intended a 12-month stimulation period but faced deviations, with one patient receiving only 10 months of stimulation. The other studies reported stimulation durations of 12 months.[27,28] The randomized trial allowed continued stimulation until clinical stability was achieved, followed by a double-blind crossover phase for patients with significant improvement (≥ 25% PANSS reduction).[29] Subsequently, these eight patients, including the replacement case, successfully completed a three-year follow-up.[30]

The study examined four different brain regions in 13 patients: the subgenual anterior cingulate cortex (n = 4), nucleus accumbens (n = 6), habenula (n = 2), and substantia nigra pars reticulata (n = 1), all linked to the pathophysiology of schizophrenia. The subgenual anterior cingulate cortex is part of the default mode network, which controls the brain's resting state. Some studies suggest that patients with schizophrenia exhibit decreased deactivation of this network during tasks, although this remains debated.[31-33] There is more consensus regarding dopamine dysregulation in schizophrenia. A proposed model indicates that abnormal excitatory input from the hippocampus to the nucleus accumbens causes the ventral tegmental area to be released from ventral pallidal inhibition, leading to excessive dopamine release back into the nucleus accumbens.[34-37] The dopamine system can also be directly targeted through the substantia nigra, a key brain structure involved in dopamine regulation. In schizophrenia, reduced cortical function decreases striatal inhibition of the substantia nigra, resulting in increased dopamine release to the striatum and inhibited thalamic activity, amplifying cortical dysfunction.[38,39] Additionally, the habenula's inhibitory inputs to the substantia nigra and ventral tegmental area are questioned for their role in schizophrenia, as habenular dysfunction can cause excessive dopamine release from these areas.[40,41]

Outcomes

The study involved 13 patients undergoing stimulation for an average of 26.61 ± 12.36 months (see Table 1). Twelve patients showed improvement in their outcome measures, whereas one patient's condition deteriorated.[26-30] Despite initial improvements in their PANSS score by 10.8% at six months and 20.3% at seven months, this patient was even-

tually withdrawn due to a psychotic episode after ten months. At this point, their PANSS score had decreased by 9.5% from the baseline, with significant increases in both positive (69.2%) and negative (4.3%) symptoms, leading to their hospitalization.[26]

Out of the twelve patients with lower outcomes at follow-up, only four (one person from each brain stimulation region) showed significant improvement, achieving a reduction of 25% or more in PANSS or BPRS scores. The other patients exhibited varied levels of symptom improvement.

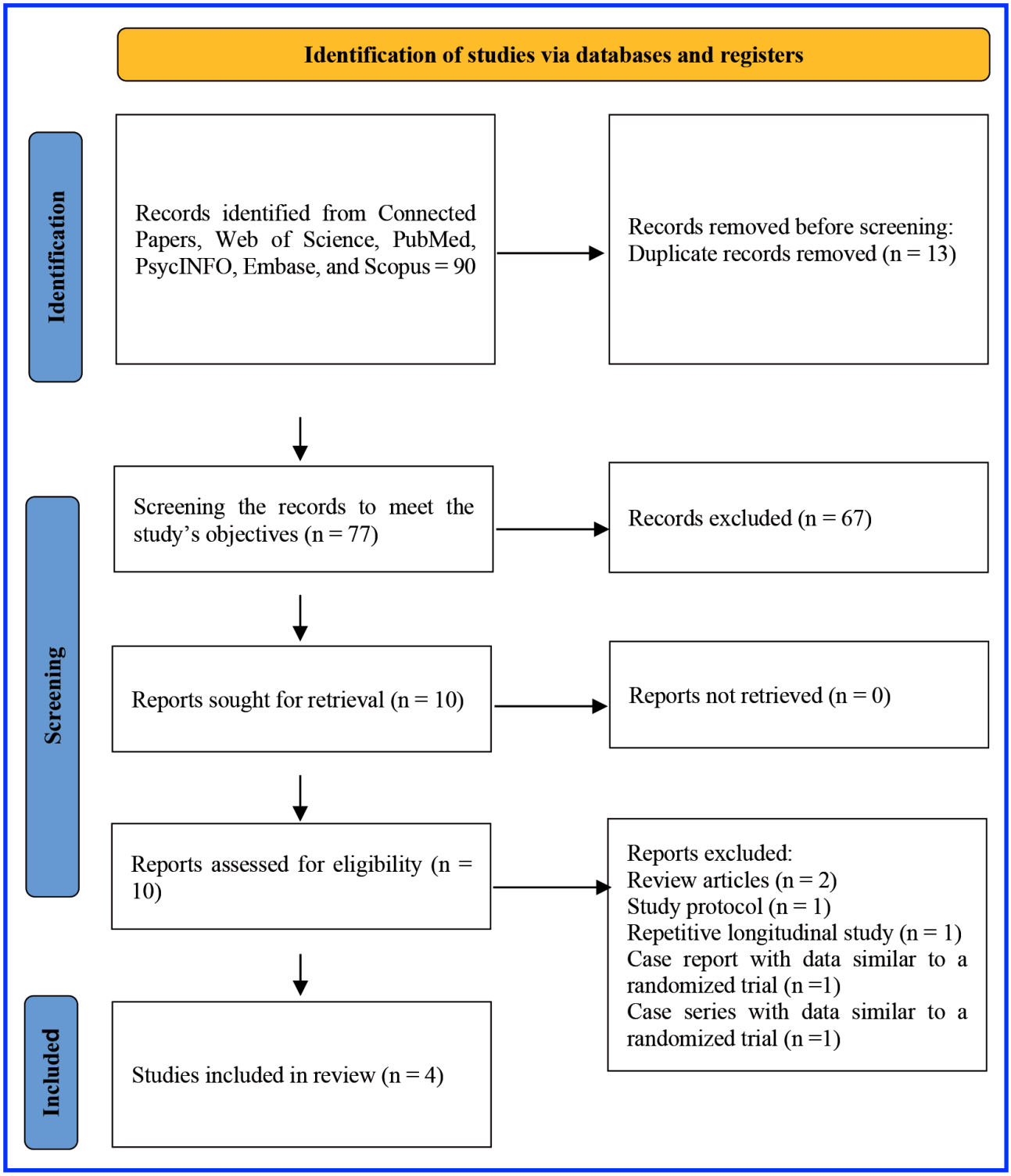

Figure 2. *PRISMA flow diagram.*

Table 1. *Characteristics of the articles included.*

	Authors (year)			
	Corripio *et al.*, 2020[29]/Aibar-Durán *et al.*, 2023[30]*	**Wang *et al.*, 2020[26]**	**Cascella *et al.*, 2021[28]**	**Bioque *et al.*, 2023[27]**
Country	Spain	China	United States	Spain
Study design	Randomized clinical trial	Case series	Case report	Case series
Number of patients	8	2	1	2
Median age (year) / Female (%)	43 / 62.5%	23.5 / 0%	35 / 100%	49 / 0%
Minimum duration of illness (year)	5	4	16	19
Electrode placement	Bilateral NAc (n=4) Bilateral sgACC (n=4)	Bilateral Hb	Bilateral SNr	Bilateral NAc
Length of follow-up (months)	36	10 to 12	12	12
Primary outcome measure(s)	PANSS	PANSS	BPRS, SANS	PANSS
Mean score improvement (%)	Bilateral NAc T-PANSS: 17% P-PANSS: 19.75% N-PANSS: 10% G-PANSS: 19.75% Bilateral sgACC T-PANSS: 15.5% P-PANSS: 17.75% N-PANSS: 9.75% G-PANSS: 16.5%	T-PANSS: 11.1% P-PANSS: -7.7% N-PANSS: 13.7% G-PANSS: 14.35%	BPRS: 52.38% SANS: Not specified	T-PANSS: 21.76% P-PANSS: Not specified N-PANSS: Not specified G-PANSS: Not specified
Responders (*i.e.*, those with a PANSS or BPRS reduction of ≥25%)	Bilateral NAc T-PANSS: 0 P-PANSS: 3 N-PANSS: 0 G-PANSS: 2 Bilateral sgACC T-PANSS: 1 P-PANSS: 2 N-PANSS: 1 G-PANSS: 1	T-PANSS: 1 P-PANSS: 1 N-PANSS: 1 G-PANSS: 0	BPRS: 1 SANS: Not specified	T-PANSS: 1 P-PANSS: Not specified N-PANSS: Not specified G-PANSS: Not specified

**Durán* et al.'s *study summarizes the outcomes of the participants in Corripio* et al.'s *study after a three-year follow-up. Although in Corripio* et al.'s *study one patient was withdrawn due to serious complications (n=7), in Durán* et al.'s *study this vacancy was filled by another patient (n=8).*
BPRS, brief psychiatricrating scale; Hb, habenula; NAc, nucleus accumbens; PANSS, positive and negative syndrome scale; T-PANSS, PANSS total score; P-PANSS, PANSS positive subscale; N-PANSS, PANSS negative subscale; G-PANSS, PANSS general psychopathology subscale; SANS, scale for the assessment of negative symptoms; sgACC, subgenual anterior cingulate cortex; SNr, substantia nigra pars reticulata.

One patient with a subgenual anterior cingulate cortex implant and another with a nucleus accumbens implant showed increased negative PANSS scores.[29] Meanwhile, a patient implanted in the substantia nigra pars reticulata experienced a substantial reduction in positive symptoms but only slight reductions in some negative symptoms. This same patient also had mixed results in cognitive testing, with decreased performance in verbal and visuospatial learning/memory but improved performance in verbal fluency.[28]

In a crossover phase trial involving deep brain stimulation for schizophrenia, only three of the original seven patients participated. One patient with a nucleus accumbens implant began with active stimulation, while two others with a subgenual anterior cingulate cortex implant started without it. Both patients in the no-stimulation group experienced worsened symptoms and were withdrawn before completing the crossover. The patient who commenced with stimulation also reported worsening negative symptoms when the stimulation was turned off but completed the trial. However, these symptoms persisted even after resuming stimulation. A fourth patient with a nucleus accumbens implant qualified for the crossover phase but declined to participate; this patient's symptoms had previously worsened during an accidental lapse in stimulation. Overall, when stimulation was turned off, all four participating patients exhibited worsened symptoms compared to their condition during active stimulation.[29] This pattern, along with the overall improvement observed in 12 out of 13 patients across various studies, indicates that deep brain stimulation could be a promising treatment for refractory schizophrenia.[26-30]

Quality assessment

The risk of bias for each study is comprehensively evaluated and detailed in Table 2.

Table 2. *Assessment of risk of bias in each study.*

	Authors (year)			
	Corripio *et al.*, 2020[29]/Aibar-Durán *et al.*, 2023[30]	Wang *et al.*, 2020[26]	Cascella *et al.*, 2021[28]	Bioque *et al.*, 2023[27]
Selection bias				
Randomization	Yes	Not applicable	Not applicable	Not applicable
Accounted for confounding	No	No	No	No
Performance bias				
Accounted for concurrent intervention/ unintended exposure	Yes	No	No	No
Fidelity to intervention protocol	Yes	Yes	Yes	Yes
Attrition bias				
Missing data handled appropriately	Yes	No	Not applicable	Not applicable
Detection bias				
Interventions defined using reliable measures	Yes	Yes	Yes	Yes
Outcomes defined using reliable measures	Yes	Yes	Yes	Yes
Outcome assessors blinded	No	No	No	No
Reporting bias				
Outcomes prespecified	Yes	No	No	No

Adverse events

In the four studies, ten adverse events were recorded across thirteen procedures. Eleven adverse events occurred, with six classifieds as serious.[26-30] Most of the serious adverse events were observed in a single randomized trial, primarily affecting one patient.[29] This patient was scheduled to receive nucleus accumbens deep brain stimulation, but due to postoperative complications, including a right internal capsule hemorrhage and subsequent device infection, they did not undergo stimulation. This necessitated complete hardware removal three months after surgery. Although the patient did not suffer permanent neurological deficits, they experienced seizures that were manageable with antiepileptic drugs. Another significant serious adverse event involved mood instability with occasional suicidal thoughts, which correlated with the patient's discontinuation of their antipsychotic regimen (see Table 3). Previously, a combination of antipsychotics and deep brain stimulation had shown symptom reduction for this patient.[29]

Five transient adverse events were experienced by individuals during the deep-brain stimulation procedure.[28,29] Initially, akathisia occurred when the stimulation was shifted from unilateral to bilateral but was effectively resolved by reverting to unilateral stimulation. Secondly, one individual experienced occasional electrical sensation in the trunk and head following specific body movements, which were mitigated by switching the stimulation from unipolar to bipolar mode. Thirdly, confusion arose after a right-sided perioperative hemorrhage but subsided naturally after four days without intervention.[29] Another case involved increased appetite over three months, resulting in a significant weight gain of 33 pounds (15 kg), which also resolved itself over time. Lastly, one patient showed decreased performance in verbal and visuospatial learning and memory tests; however, the details surrounding this final event were not specified.[28]

Discussion

Striking a balance between innovative therapeutic strategies and established treatment protocols is crucial in addressing the complexities of treatment-resistant schizophrenia. Within this context, the systematic review elucidates the efficacy of deep-brain stimulation as a potential intervention. Findings indicate that deep brain stimulation effectively alleviates symptoms in a significant proportion of individuals with treatment-resistant schizophrenia, with approximately 30% of patients reporting symptomatic relief, particularly in positive symptoms such as hallucinations and delusions.[26-30] The outcomes align with previous studies that demonstrate similar efficacy rates for deep brain stimulation in treating refractory neuropsychiatric conditions.[14-18] Despite reports that higher amplitudes of nucleus accumbens stimulation can exacerbate psychotic symptoms when treating severe depression,[42] a randomized trial in treatment-resistant schizophrenia found that four patients did not experience worsening symptoms with higher stimulation parameters.[29,30] This finding is supported by earlier evidence where an individual with obsessive-compulsive disorder and a history of psychosis also showed no symptom worsening with increased stimulation amplitude.[27] These observations suggest that higher nucleus accumbens stimulation may not universally exacerbate psychotic symptoms in depression or obsessive-compulsive disorder patients. One of the key mechanisms by which deep brain stimulation may be effective in treating treatment-resistant schizophrenia is its ability to modulate the activity of specific brain regions associated with the disorder. Studies have shown that electrical stimulation can influence the flow of impulses through neural pathways, potentially restoring the balance and proper functioning of the affected brain circuits.[43,44] In addition to its direct impact on brain activity, deep brain stimulation may also have indirect effects on the underlying pathophysiology of schizophrenia. Some research suggests that the technique may have neuroprotective properties, potentially slowing or even reversing the progressive neurodegeneration observed in schizophrenia.[44,45] Furthermore, deep brain stimulation has been associated with improvements in cognitive function and overall quality of life in some patients with schizophrenia.[47,48] The improvements in scores on other scales, such as the Calgary Depression Scale for Schizophrenia, the Hamilton Depression Rating Scale, the Quality-of-Life Scale, and the WHO-5 Well-Being Index, further underscore the potential multidimensional benefits of deep brain stimulation. These benefits extend beyond mere symptom management to enhance overall functional outcomes. Nevertheless, despite its potential benefits, the precise mechanism by which deep brain stimulation exerts its therapeutic effects in treatment-resistant schizophrenia remains largely unknown, necessitating further investigation to fully understand and optimize this treatment modality.[29,30]

Given the heterogeneity of treatment-resistant schizophrenia, different structures may be the ideal targets for deep-brain stimulation, depending on the specific symptoms. The findings from this review reiterate and support data presented in earlier investigations, where heterogeneous responses to different targets—such as the nucleus accumbens versus the subgenual anterior cingulate cortex—highlight critical implications for personalized medicine.[29,49] In particular, results showing that the nucleus accumbens plays a predominant role in symptom improvement for treatment-resistant schizophrenia[29,30] align with existing literature that emphasizes the need for careful patient selection and optimization of stimulation parameters to maximize therapeutic benefits.[50,53] This finding serves as a seal of approval for current theories on the disease's pathophysiology, which propose that overactivity of the hippocampus increases inhibitory signals from the nucleus accumbens to the ventral pallidum. This reduces inhibition on the ventral tegmental area, leading to increased dopamine release back onto the nucleus accumbens and producing the disease's positive symptoms.[34,37] Nonetheless, significant variability in response rates across studies necessitates further exploration into the underlying neurobiological mechanisms driving these differences, particularly as previous research identifies dopamine-glutamate-GABA interactions as pivotal in the pathology of schizophrenia.[26-20,54,57]

Table 3. *Adverse events reported in each study.*

	Authors (year)			
	Corripio *et al.*, 2020[29]/Aibar-Durán *et al.*, 2023[30]	**Wang *et al.*, 2020[26]**	**Cascella *et al.*, 2021[28]**	**Bioque *et al.*, 2023[27]**
Number of procedures	8	2	1	2
Transient adverse events		No transient adverse events were reported related to the surgery, implanted hardware, or neurostimulation		No transient adverse events were reported related to the surgery, implanted hardware, or neurostimulation
Electrode placement	(i) NAc (ii) NAc (iii) NAc		(i) SNr (ii) SNr	
Adverse events	(i) Akathisia occurred after changing the stimulation from unilateral to bilateral (ii) An occasional electrical sensation in the trunk and head triggered by specific body movements (iii) Confusion following a right-sided peri-operative hemorrhage		(i) An increased appetite for three months, resulting in a weight gain of 33 pounds over this period, reaching a total weight of 314 pounds (142 kg) and a body mass index of 54 kg/m² (ii) Decreased performance on tests of verbaland visuospatial learning/ memory	
Number of adverse events	(i) 1 (ii) 1 (iii) 1		(i) 1 (ii) 1***	
Time to resolution	(i) Eventually, this adverse event was resolved when the stimulation was changed back to unilateral (ii) Switching the stimulation from unipolar to bipolar mode led to a resolution of the symptoms (iii) It recovered after four days and without any intervention		(i) It resolved after 3 months and without any intervention (ii) Not specified	
Serious adverse events			No serious adverse events were reported related to the surgery, implanted hardware, or neurostimulation	No serious adverse events were reported related to the surgery, implanted hardware, or neurostimulation

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Table 3. *Continued from previous page.*

	Authors (year)			
	Corripio *et al.*, 2020[29]/Aibar-Durán *et al.*, 2023[30]	**Wang *et al.*, 2020[26]**	**Cascella *et al.*, 2021[28]**	**Bioque *et al.*, 2023[27]**
Electrode placement	(i) NAc (ii) NAc (iii) NAc (iv) NAc (v) NAc	(i) Hb		
Adverse events	(i) Daily mood fluctuations, impulsive behavior, and occasional suicidal thoughts (ii) Perioperative internal capsule hemorrhage (iii) Device infection (iv) Seizures occurred six months after being withdrawn from the trial (v) Behavioral changes consistent with hypomania and psychotic symptoms occurred after a total of 11 months of stimulation	(i) Aggravated psychotic symptoms requiring hospitalization		
Number of adverse events	(i) 1* (ii) 1 (iii) 1 (iv) 1 (v) 1**	(i) 1		
Time to resolution	(i) Mood fluctuations were hard to manage with mood stabilizers and changes in deep brain stimulation parameters, but they improved after the reinstatement of the antipsychotic medication aripiprazole (ii) It was resolved after the removal of the generator and electrodes (iii) It was resolved after the removal of the generator and electrodes (iv) Seizure attacks were controlled with anticonvulsant medication (v) Responded to treatment with antipsychotics in the inpatient setting	(i) It was resolved after the removal of the generator and electrodes		

**The number of recurrences of suicidal thoughts was not specified. **The patient stopped their antipsychotic medication before exhibiting hypomanic and psychotic symptoms, along with an initial reduction in stimulation parameters due to some improvement. ***The patient showed decreased performance during follow-up, but it remains uncertain if this trend will persist.*
Hb, habenula; NAc, nucleus accumbens; SNr, substantia nigra pars reticulata.

Limitations

The study underscores significant limitations, primarily due to the scarcity of evidence, which makes a meta-analysis unfeasible. Of the thirteen patients included, eight were from the same trial, which could potentially introduce bias. The review highlights the potential of deep brain stimulation for treating treatment-resistant schizophrenia, while emphasizing the need for larger, randomized trials to facilitate target-specific analyses. In addition, all patients studied were on antipsychotic medication during deep brain stimulation treatment, with no known cases of deep brain stimulation being used alone for treatment-resistant schizophrenia.

Clinical implications and future directions

As the clinical landscape evolves, the implications of these findings emphasize the importance of personalized treatment approaches that consider individual symptom profiles and the specific mechanisms underlying each patient's condition. Moreover, the concurrent observation of serious adverse events in around 15% of patients highlights the need for careful monitoring and individualized adjustment of stimulation parameters to mitigate risks. Additionally, the analysis underscores the necessity for multidisciplinary collaboration among psychiatrists, neurosurgeons, and neurologists to ensure optimal patient selection and treatment planning, thereby maximizing therapeutic benefits while minimizing potential complications.[58] Future research should focus on larger, multi-center trials to substantiate these findings and explore the underlying mechanisms of deep brain stimulation more thoroughly. This includes investigating the neural pathways involved in symptom relief and the relationship between specific stimulation sites and clinical outcomes to refine targeting strategies. Furthermore, incorporating advanced imaging techniques may enhance our understanding of how deep brain stimulation interacts with brain circuits associated with schizophrenia symptoms.

Conclusions

The systematic review on the efficacy of deep brain stimulation for treatment-resistant schizophrenia has highlighted several key findings regarding this intervention. Primarily, evidence indicates that deep brain stimulation, when targeting certain brain regions, particularly the nucleus accumbens, can lead to significant symptomatic improvements in patients who have not responded to conventional antipsychotic treatments. Specifically, a response rate of approximately 30% was reported, with 4 out of 13 patients showing marked improvement in positive symptoms such as hallucinations and delusions, as indicated by a reduction of 25% or more in PANSS or BPRS scores. It seems that the potential of deep brain stimulation as a treatment modality for treatment-resistant schizophrenia heralds a paradigm shift in mental health care, emphasizing the need for a more nuanced approach to treatment. As we continue to unravel the complexities of the disorder, integrating evidence from emerging research can lead to the development of standardized guidelines for implementing deep brain stimulation in clinical practice, paving the way for improved outcomes for individuals grappling with the debilitating effects of treatment-resistant schizophrenia. By addressing both clinical efficacy and methodological integrity, the future of treatment-resistant schizophrenia treatment can offer renewed hope and a pathway toward recovery for those in need.

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Conflict of interest

The author declares that he has no conflict of interest.

Ethics approval and consent to participate

Not applicable.

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