The Egyptian Journal of Neurology, Psychiatry and Neurosurgery

REVIEW

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A narrative review of non-invasive brain stimulation techniques in neuropsychiatric disorders: current applications and future directions

Nicholas Aderinto[1*], Gbolahan Olatunji[2], Abdulbasit Muili[1], Emmanuel Kokori[2], Mariam Edun[2], Olumide Akinmoju[3], Ismaila Yusuf[4] and Deborah Ojo[2]

Abstract

Background Neuropsychiatric disorders significantly burden individuals and society, necessitating the exploration of innovative treatment approaches. Non-invasive brain stimulation techniques have emerged as promising interventions for these disorders, offering potential therapeutic benefits with minimal side effects. This narrative review provides a comprehensive overview of non-invasive brain stimulation techniques' current applications and future directions in managing neuropsychiatric disorders.

Methods A thorough search of relevant literature was conducted to identify studies investigating non-invasive brain stimulation techniques in neuropsychiatric disorders. The selected studies were critically reviewed, and their findings were synthesised to provide a comprehensive overview of the current state of knowledge in the field.

Results The review highlights the current applications of non-invasive brain stimulation techniques in neuropsychiatric disorders, including major depressive disorder, Parkinson's disease, schizophrenia, insomnia, and cognitive impairments. It presents evidence supporting the efficacy of these techniques in modulating brain activity, alleviating symptoms, and enhancing cognitive functions. Furthermore, the review addresses challenges such as interindividual variability, optimal target site selection, and standardisation of protocols. It also discusses potential future directions, including exploring novel target sites, personalised stimulation protocols, integrating with other treatment modalities, and identifying biomarkers for treatment response.

Conclusion Non-invasive brain stimulation techniques offer promising avenues for managing neuropsychiatric disorders. Further research is necessary to optimise stimulation protocols, establish standardised guidelines, and identify biomarkers for treatment response. The findings underscore the potential of non-invasive brain stimulation techniques as valuable additions to the armamentarium of neuropsychiatric treatments.

Keywords Non-invasive brain stimulation, TMS, tDCT, tACT

*Correspondence:
Nicholas Aderinto
Nicholasoluwaseyi6@gmail.com
Full list of author information is available at the end of the article

Introduction

Non-invasive brain stimulation (NIBS) techniques have revolutionised neuropsychiatry by providing safe and well-tolerated alternatives to invasive procedures [1]. Among these techniques, transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), and transcranial alternating current stimulation (tACS) have emerged as powerful tools for modulating brain activity and exploring novel treatment avenues [2]. TMS, introduced by Barker and colleagues in 1985, uses pulsed magnetic fields to stimulate specific brain regions, thereby modulating neural activity and influencing brain function [3]. The subsequent development of repetitive transcranial magnetic stimulation (rTMS) has extended treatment durations, enhancing the therapeutic potential of TMS for modulating brain activity [4].

The advantages of NIBS techniques stem from their painless and safe nature, minimal side effects, and regulatory approvals for specific indications [5]. Particularly noteworthy is their demonstrated efficacy in treating complex neuropsychiatric disorders such as treatment-resistant major depressive disorder and acute pain associated with migraine headaches [6]. Despite these promising findings, there remains a need to comprehensively synthesise the existing knowledge regarding the applications of NIBS techniques in neuropsychiatric disorders. This narrative review addresses this gap by meticulously analysing the available literature. Through critically examining the evidence, this review seeks to provide valuable insights, identify knowledge gaps, and propose directions for future research, thereby contributing to the ongoing development of innovative treatments and ultimately improving the well-being of individuals affected by these challenging disorders.

Methodology

This narrative review aims to comprehensively synthesise the current knowledge regarding the applications of NIBS techniques in neuropsychiatric disorders (Table 1). The scope of this review includes an examination of existing literature on NIBS techniques such as TMS, tDCS, and tACS in the context of neuropsychiatric disorders.

A comprehensive literature search was conducted to identify relevant studies for inclusion in the narrative review. A search was conducted in electronic databases, including PubMed, Scopus, and PsycINFO, using a predefined set of keywords and search terms. The search strategy incorporated the following keywords and their combinations: "non-invasive brain stimulation", "transcranial magnetic stimulation", "TMS", "transcranial direct current stimulation", "tDCS", "transcranial alternating current stimulation", "tACS", "neuropsychiatric disorders", "neuropsychiatry", "mental disorders", "psychiatric disorders", "depression", "anxiety", "schizophrenia", "substance use disorders", "bipolar disorder", "attention deficit hyperactivity disorder", and relevant terms specific to the targeted neuropsychiatric conditions. The search strategy was designed to capture articles exploring the applications of NIBS techniques in treating or managing neuropsychiatric disorders. The selection of studies was based on predefined inclusion criteria. Primary research studies, systematic reviews, and meta-analyses focusing on the applications of NIBS techniques in neuropsychiatric disorders will be included. Studies must be published in peer-reviewed journals and written in English. Studies primarily focusing on invasive brain stimulation techniques or non-neuropsychiatric disorders will be excluded.

A standardised data extraction process was employed to extract relevant information from the included studies. Key data elements to be extracted include study

Table 1 Summary of methodology

Methodology	Description
Objective	To comprehensively synthesise the current knowledge regarding the applications of non-invasive brain stimulation (NIBS) techniques in neuropsychiatric disorders
Scope	Examination of existing literature on NIBS techniques (TMS, tDCS, tACS) in the context of neuropsychiatric disorders
Literature search	Conducted in electronic databases (PubMed, Scopus, PsycINFO) using predefined keywords and search terms
Search keywords	"Non-invasive brain stimulation", "transcranial magnetic stimulation", "TMS", "transcranial direct current stimulation", "tDCS", "transcranial alternating current stimulation", "tACS", and relevant terms for neuropsychiatric disorders
Inclusion criteria	Primary research studies, systematic reviews, and meta-analyses published in peer-reviewed journals and written in English. Focused on NIBS techniques' applications in neuropsychiatric disorders. No time limit
Exclusion criteria	Studies primarily focused on invasive brain stimulation techniques or non-neuropsychiatric disorders
Data extraction	Standardised process to extract relevant information: study characteristics, design, participant characteristics, NIBS techniques employed, targeted disorders, outcome measures, main findings, and limitations
Data synthesis	Narrative synthesis of extracted data, organising findings thematically according to specific neuropsychiatric disorders and applications of NIBS techniques

characteristics (authors, publication year), study design, participant characteristics, NIBS techniques employed, targeted neuropsychiatric disorders, outcome measures, main findings, and limitations. The extracted data were synthesised narratively, and the findings were organised thematically according to the specific neuropsychiatric disorders and the applications of NIBS techniques.

Non-invasive brain stimulation techniques

Non-invasive brain stimulation techniques, such as TMS, tDCS, and tACS, have emerged as promising approaches for modulating brain activity in neuropsychiatric disorders [2] (Table 2). These techniques provide non-surgical and well-tolerated neuromodulation methods, offering potential therapeutic benefits for individuals with neuropsychiatric conditions [5].

TMS, a widely studied non-invasive brain stimulation technique, involves the application of magnetic fields to specific brain regions through a coil placed on the scalp [7]. By generating brief magnetic pulses, TMS induces electrical currents in targeted brain areas, leading to the modulation of neuronal activity [8]. This technique has demonstrated efficacy in neuropsychiatric disorders, including major depressive disorder, schizophrenia, and obsessive–compulsive disorder [9]. Furthermore, TMS is a therapeutic intervention and a diagnostic tool to assess cortical excitability, connectivity, and neuroplasticity in these conditions [10].

In contrast, tDCS is another well-known non-invasive brain stimulation technique involving electrodes to apply a low-intensity direct current to the scalp [11]. By modulating neuronal excitability, with the anode typically enhancing activity and the cathode inhibiting it, tDCS has shown promise in neuropsychiatric disorders, including depression, anxiety disorders, and addiction [12]. While tDCS has been studied extensively, further research is needed to understand its underlying mechanisms of action fully.

While TMS and tDCS are widely studied, tACS is a less commonly explored technique [13]. It involves alternating current stimulation to the scalp to entrain neural oscillations and modulate brain networks [14]. By applying specific frequencies and electrical stimulation patterns, tACS can address cognitive deficits, sleep disorders, and other neuropsychiatric conditions associated with aberrant neural oscillations [14]. However, further investigation is warranted to understand the precise mechanisms better and optimise their application in clinical settings. Postulations regarding the mechanisms of action have been proposed in the literature, but concrete evidence is limited, mostly derived from animal studies. For example, in the case of tDCS, it has been postulated that the technique improves dopamine release, making it effective in diseases characterised by dopaminergic dysfunction, such as Parkinson's disease [15]. Another postulated mechanism of action suggests that tDCS exerts its effect through alpha-synuclein aggregation and autophagic degradation [16]. Furthermore, tDCS has been found to influence the concentrations of neurotransmitters such as glutamate, GABA, and serotonin [17]. However, these postulations are primarily based on cellular and molecular studies, with limited evidence from animal models.

Table 2 Non-invasive brain stimulation techniques: basic principles, target areas, and typical parameters

Technique	Basic principles	Target areas	Typical parameters
Transcranial magnetic stimulation	Use of magnetic fields to induce electric currents	Dorsolateral prefrontal cortex	Frequency: 1–20 Hz
(TMS)	in targeted brain regions	(DLPFC), motor cortex	Intensity: 50–100% of motor threshold
			Pulse width: 100–300 microseconds
Transcranial direct current	Application of weak direct current through scalp	Dorsolateral prefrontal cortex	Current intensity: 1–2 mA
Stimulation (tDCS)	Electrodes to modulate cortical excitability	(DLPFC), motor cortex	Duration: 10–30 min
			Polarity: anodal or cathodal
Transcranial alternating current	Delivery of sinusoidal current with specific frequency	Various depending on frequency	Frequency: varies (10–100 Hz)
Stimulation (tACS)	To target brain regions	And desired effect	Amplitude: typically 1–2 mA
			Duration: varies (10–30 min)
Transcranial focused ultrasound	Use of ultrasound waves to target and modulate	Various depending on target region	Intensity: varies
(tFUS)	brain regions	(motor cortex, hippocampus)	Frequency: varies
			Duration: varies

Similarly, the mechanism of action for TMS still needs to be fully elucidated. TMS induces transient current flow and neuronal depolarisation in cortical tissue directly beneath the stimulation site and in associated neuronal circuits [18]. Repetitive TMS (rTMS), which utilises magnetic coils to generate magnetic fields through the skull, has a stronger and longer-lasting impact on brain function by modulating cortical excitability in the stimulated area [19]. This modulation of neuroplasticity in pain processing pathways has been observed in various conditions, including phantom limb pain, neuropathic pain, pain after spinal cord injury, radiculopathy, diabetic neuropathy, and post-herpetic neuralgia. Recent research has also identified diverse mechanisms of action for rTMS, such as increasing pain threshold through pathways from the posterior insula and orbitofrontal cortex to the posterior thalamus, as well as inhibiting pain perception via pathways from the periaqueductal gray to the rostroventral medulla [20].

In contrast to TMS and tDCS, tACS involves the delivery of sinusoidal alternating current to the scalp, primarily affecting cortical neurons [21]. This technique aims to simulate the rhythmic pattern of brain electrophysiological activity and modify altered brain oscillations and connectivity patterns implicated in many psychiatric disorders. However, further research is needed to comprehensively understand the mechanisms underlying tACS and its potential applications in neuropsychiatric conditions.

Current applications of non-invasive brain stimulation in neuropsychiatric disorders

NIBS techniques have shown promise as therapeutic interventions for many neuropsychiatric disorders (Table 3).

A. Depression and mood disorders

Depression and mood disorders significantly burden global mental health, emphasising the need for effective treatment options [22]. NIBS techniques have gained considerable attention in this field, as an increasing body of evidence supports their effectiveness in treating depression.

A notable study conducted in South Africa investigated accelerated theta burst repetitive transcranial magnetic stimulation (rTMS) for depression [23]. The findings revealed that this treatment approach was well-tolerated, with most patients experiencing clinical improvement as early as day 8. Specifically, five out of nine patients demonstrated a substantial decrease of at least 50% in symptoms, as assessed by the Centre for Epidemiological Studies Depression (CES-D) scale. The most frequently reported side effect was a minor headache, which resolved within a few hours after rTMS therapy. However, it is crucial to note that the study design consisted of a small case series and lacked a control arm. While the observed clinical improvements suggest the potential effectiveness of accelerated theta burst rTMS for depression, the absence of a control group makes it challenging to attribute these changes solely to the treatment. Additionally, the most commonly reported side effect was a minor headache, which, reassuringly, resolved within a few hours following the rTMS therapy. This study provides valuable insights into the preliminary efficacy and tolerability of accelerated theta burst rTMS for depression.

In another study focusing on treatment-resistant depression, researchers explored the effects of chronic stimulation of the white matter tract near the subgenual cingulate gyrus, which remarkably resulted in durable remission of depression in four out of six individuals [24]. Furthermore, a research investigation comparing transcranial direct current stimulation (tDCS) to escitalopram in treating unipolar depression demonstrated the superiority of tDCS over placebo [25]. However, the study did not meet the goal of proving non-inferiority to escitalopram. Nevertheless, these findings underscore the efficacy of tDCS in treating unipolar depression. The study's primary finding highlighted the significant advantages of tDCS compared to a placebo, indicating its potential as a promising intervention for individuals with unipolar depression. However, the inability to establish non-inferiority to escitalopram suggests further exploration and comparison with standard pharmacological treatments.

In Brazil, a factorial, double-blind, placebo-controlled trial involving 120 patients aged 18 to 65 evaluated the effects of transcranial direct current stimulation (tDCS) alone, tDCS coupled with sertraline, and sertraline alone [26]. The combination therapy outperformed tDCS alone, while tDCS alone demonstrated superior efficacy compared to sertraline alone in improving pessimistic thoughts and apparent sadness. However, no improvement was observed in vegetative symptoms, and it is noteworthy that a relatively low dose of sertraline was utilised in this study. Notably, the study employed a relatively low dose of sertraline, which may have influenced the observed outcomes. This aspect highlights the need for a cautious interpretation of the findings, considering the potential impact of the dosage on the overall efficacy of sertraline. The findings show the complexity of treatment response, urging further studies with varied dosages and extended follow-up periods to understand the interplay between tDCS, sertraline, and their combined effects on diverse depressive symptoms.

Table 3 Characteristics of studies reviewed in the current applications of non-invasive brain stimulation in neuropsychiatric disorders

Neuropsychiatric disorder	Study design	Participants	NIBS technique	Main findings	Limitations
Depression and mood disorders	Case series (Li and colleagues 2014) [23]	9 patients	Accelerated theta burst rTMS	Significant clinical improvement in depression symptoms as early as day 8	Small sample size, lack of control arm
	Case series (Mayberg and colleagues 2017) [24]	6 individuals	Chronic stimulation of white matter tract near subgenual cingulate gyrus	Durable remission of depression in 4 out of 6 individuals	Small sample size
	Randomised controlled trial (Tomlinson and colleagues 2017) [25]	Patients with unipolar depression	tDCS versus escitalopram	Superiority of tDCS over placebo in treating unipolar depression	Did not achieve non-inferiority to escitalopram
	Factorial, double-blind, placebo-controlled trial (Brunoni and colleagues 2013) [26]	120 patients	tDCS alone, tDCS + sertraline, sertraline alone	Combination therapy outperformed tDCS alone, tDCS alone superior to sertraline alone in improving certain symptoms	Relatively low dose of sertraline used in the study
Schizophrenia and psychotic disorders	Randomised sham-controlled study (Bation and colleagues 2021) [28]	Individuals with treatment-resistant negative symptoms of schizophrenia	Intermittent theta burst rTMS (iTBS)	Significant reduction in negative symptoms compared to sham, sustained improvement after 6 months	Need for further large-scale sham-controlled studies to validate results
	Open-label retrospective study (Brunelin and colleagues 2022) [29]	Patients with treatment-resistant auditory hallucinations	rTMS	Significant reduction in auditory hallucinations, even in clozapine-resistant patients	Need for large-scale randomised sham-controlled studies to confirm findings
	Randomised controlled trial (Valiengo and colleagues 2020) [30]	Patients with negative symptoms of schizophrenia	tDCS	Active tDCS group showed significant improvement compared to sham group, sustained effects during follow-up	Well-tolerated, transient burning feeling as a side effect
Anxiety disorders and PTSD	Double-blind, placebo-controlled phase II trial (Vergallito and colleagues 2022) [32]	30 patients with PTSD	Active 20 Hz rTMS of right DLPFC, active 20 Hz rTMS of left DLPFC, sham rTMS	Both active rTMS groups significantly reduced PTSD symptoms, with sustained benefits at three-month follow-up	Need for larger studies to confirm results and establish efficacy
	Pilot randomised, double-blind, sham-controlled study (Diefenbach and colleagues 2016) [33]	Patients with generalised anxiety disorder (GAD)	rTMS	Active rTMS groups showed higher response and remission rates compared to sham group	Preliminary findings, need for larger studies with rigorous designs
	Randomised, single-blind, pharmacotherapy and sham-controlled clinical study (Movahed and colleagues 2018) [34]	Patients with GAD	tDCS	Active tDCS treatments beneficial in reducing anxiety, worry, and depressive symptoms	tDCS more effective than medication in reducing depressive symptoms, less successful in alleviating worry symptoms
Cognitive disorders and neurodegenerative diseases	Randomised, double-blind, sham-controlled experiment (Benussi and colleagues 2020) [36]	Frontotemporal dementia (FTD) patients	tDCS	tDCS increased intracortical connectivity and improved clinical ratings and behavioural abnormalities	Sham stimulation did not yield significant benefits

Table 3 (continued)

Neuropsychiatric disorder	Study design	Participants	NIBS technique	Main findings	Limitations
	Randomised, double-blind, sham-controlled trial (Wu and colleagues 2015) [37]	Alzheimer's disease (AD) patients with behavioural and psychiatric symptoms	High-frequency rTMS	Combination of antipsychotic medication with high-frequency rTMS led to significant improvements in symptoms	Need for further research to confirm efficacy and establish optimal protocols
Other neuropsychiatric conditions	Quasi-experimental study (Akbarzadeh and colleagues 2021) [38]	Individuals with OCD	rTMS	rTMS significantly reduced OCD symptoms and decreased beta wave activity in parietal and occipital regions	Need for controlled studies to validate findings and establish efficacy

These studies provide compelling evidence of the potential of non-invasive brain stimulation techniques, including rTMS and tDCS, in treating depression.

B. Schizophrenia and psychotic disorders

Schizophrenia and psychotic disorders pose significant challenges in terms of treatment and management [27]. NIBS approaches have shown promise as adjunctive therapies in this domain. Several studies have explored the potential of these techniques in improving symptoms and outcomes in individuals with schizophrenia and psychotic disorders.

A randomised sham-controlled study investigated the clinical and biological effects of intermittent theta burst transcranial magnetic stimulation (iTBS) in individuals with treatment-resistant negative symptoms of schizophrenia [28]. The findings revealed that compared to sham iTBS, iTBS significantly reduced negative symptoms, and this improvement was sustained even 6 months after the stimulation. This suggests the potential of iTBS as a long-lasting therapeutic intervention for treatment-resistant negative symptoms. However, further large-scale randomised sham-controlled studies are needed to validate these findings and establish their efficacy. In an open-label retrospective study focusing on patients with treatment-resistant auditory hallucinations, the effectiveness of rTMS was evaluated, particularly in individuals with clozapine-resistant symptoms [29]. The results showed that rTMS significantly reduced auditory hallucinations, even in patients already receiving clozapine treatment. The study emphasised the importance of conducting large-scale randomised sham-controlled studies to confirm these findings. Notably, even in patients already undergoing clozapine treatment, rTMS contributed to a meaningful alleviation of auditory hallucinations. However, it is important to acknowledge the study's limitations as an open-label retrospective design, emphasising the necessity for large-scale randomised, sham-controlled studies to validate and strengthen these preliminary findings. Robust empirical evidence from controlled trials would further solidify the understanding of rTMS's role in managing treatment-resistant auditory hallucinations and guide its potential integration into mainstream therapeutic approaches.

Furthermore, a randomised controlled trial investigated the efficacy and safety of tDCS in the treatment of negative symptoms of schizophrenia. The study demonstrated that the active tDCS group exhibited a 20% or more improvement than the sham group [30]. These effects were sustained during follow-up assessments. Importantly, transcranial direct current stimulation was well-tolerated, and the occurrence of side effects, except for a transient burning feeling across the scalp, did not differ significantly between groups. These findings highlight the efficacy and safety of tDCS in treating negative symptoms of schizophrenia. These outcomes shed light on the dual aspects of efficacy and safety associated with tDCS, offering promising insights into its role as a therapeutic intervention for addressing the challenging negative symptoms of schizophrenia. Further exploration through extended trials and diverse patient populations will be crucial for validating and extending these encouraging findings.

C. Anxiety disorders and post-traumatic stress disorder (PTSD)

Anxiety disorders, particularly PTSD, are prevalent mental illnesses that significantly impact individuals' well-being and functioning [31]. NIBS techniques have been explored as potential interventions in this field. Several studies have examined the effects of these techniques on anxiety disorders and PTSD, providing valuable insights into their efficacy.

In a double-blind, placebo-controlled phase II trial, 30 patients diagnosed with PTSD according to DSM-IV criteria were randomly assigned to receive active 20 Hz repetitive rTMS of the right dorsolateral prefrontal cortex (DLPFC), active 20 Hz rTMS of the left DLPFC, or sham rTMS [32]. The results demonstrated that both left and right DLPFC 20 Hz rTMS significantly reduced PTSD symptoms. Importantly, the improvements in PTSD symptoms persisted over time, as the benefits were still evident three months later. These findings contribute substantively to the growing body of evidence supporting the efficacy and lasting benefits of targeted rTMS in addressing PTSD symptoms. Further research with larger sample sizes and longer follow-up periods can provide additional insights into the optimal protocols and sustained effectiveness of rTMS for individuals grappling with PTSD. Diefenbach and colleagues conducted a pilot randomised, double-blind, sham-controlled experiment to investigate the effectiveness and neurological correlates of repetitive rTMS in generalised anxiety disorder (GAD) [33]. The study revealed that the active rTMS groups exhibited higher response and remission rates than the sham group, indicating that rTMS may be effective in reducing symptoms of GAD. These preliminary findings provide early evidence for the potential utility of rTMS as a treatment modality for GAD. However, further research with larger samples and rigorous study designs is needed to confirm and expand upon these results. Another randomised, single-blind, pharmacotherapy, and sham-controlled clinical study examined the efficacy of transcranial direct current stimulation (tDCS) in GAD [34]. Both active tDCS treatments were found to be beneficial in reducing anxiety, worry, and depressive

symptoms. The study also observed that while tDCS was more effective than medication in reducing depressive symptoms, it was less successful in alleviating worry symptoms. These findings highlight the potential of tDCS as an adjunctive treatment option for GAD.

D. Cognitive disorders and neurodegenerative diseases

Cognitive disorders and neurodegenerative diseases, such as Alzheimer's, present significant challenges in cognitive decline and functional impairment [35]. NIBS techniques have emerged as potential therapeutic interventions for these disorders. Several studies have investigated the effects of these techniques on cognitive function and neurodegenerative diseases, shedding light on their potential benefits.

In a randomised, double-blind, sham-controlled experiment, Benussi and colleagues (2020) examined the use of tDCS in frontotemporal dementia (FTD) patients [36]. The researchers aimed to determine whether tDCS could enhance cognition in symptomatic and presymptomatic FTD individuals. Following active tDCS treatment, they observed a significant increase in intracortical connectivity and improved clinical ratings and behavioural abnormalities in both symptomatic and presymptomatic carriers. In contrast, sham stimulation did not yield significant benefits. These findings suggest the potential of tDCS as a non-invasive intervention to improve cognitive function in FTD. However, larger sample sizes are generally preferred to enhance the generalisability of findings, especially in clinical populations. Similarly, long-term effects and sustainability over an extended period are essential to establish the durability of tDCS benefits. The lack of an active control group limits the ability to attribute the observed effects solely to tDCS. Including such a group would help distinguish between specific tDCS and non-specific placebo effects. Another randomised, double-blind, sham-controlled trial conducted in China explored high-frequency repetitive rTMS as an adjunctive treatment for the behavioural and psychological symptoms in individuals with Alzheimer's disease (AD) [37]. Twenty-seven out of 54 AD patients with concomitant behavioural and psychiatric symptoms received high-frequency rTMS stimulation over the left dorsolateral prefrontal cortex (DLPFC). At the same time, both groups remained on antipsychotic medication. The results demonstrated that the combination of antipsychotic medication with high-frequency rTMS led to significant improvements in behavioural and cognitive performance and the psychological symptoms commonly associated with Alzheimer's disease, compared to treatment with low-dose antipsychotic drugs alone. These findings suggest that high-frequency rTMS may have the potential as an adjunctive therapy to enhance outcomes in AD patients.

E. Other neuropsychiatric conditions

NIBS techniques have also been explored in neuropsychiatric conditions, including obsessive–compulsive disorder (OCD). Researchers have conducted studies to examine the effectiveness of non-invasive brain stimulation, particularly rTMS, in OCD patients.

Akbarzadeh and colleagues conducted a quasi-experimental study to investigate the efficacy of rTMS in individuals with OCD [38]. They aimed to assess the impact of rTMS on OCD symptoms and brain activity. The results demonstrated that rTMS significantly reduced OCD symptoms, as evidenced by improvements in the Yale-Brown Obsessive–Compulsive Scale (YBOCS) scores. Additionally, the study revealed a decrease in beta wave activity in the parietal and occipital regions of the brain following rTMS treatment. However, the researchers emphasised the need for further controlled studies to validate these findings and establish the efficacy of rTMS in OCD. These findings suggest the potential of NIBS techniques, particularly rTMS, as a therapeutic option for individuals with OCD.

Advances and applications of non-invasive brain stimulation techniques in neuropsychiatric disorders

Since the inception of NIBS in clinical studies in 1985, extensive research has been conducted to evaluate its effectiveness in treating various neuropsychiatric disorders, including obsessive–compulsive disorder (OCD), attention-deficit/hyperactivity disorder (ADHD), dementia, autism, multiple sclerosis, and others (Table 4). The major modalities of NIBS, tDCS, and rTMS have been employed to enhance the function of cortical or subcortical brain structures to prevent neuropsychiatric disorders [39].

Höppner and colleagues conducted a study investigating the effects of high-frequency rTMS over the left dorsolateral prefrontal cortex (LDLPFC) and low-frequency rTMS over the right dorsolateral prefrontal cortex (RDLPFC) on depressive symptoms in patients with depressive disorders [40]. The results demonstrated significant improvement in motor functions in the patients. However, the relationship between motor functions and depressive symptoms needs to be explicitly addressed. Clarification on whether motor improvements are a primary outcome or a secondary observation is essential. Similarly, Jorge and colleagues investigated the efficacy and safety of rTMS in treating vascular depression. They reported a moderate response rate to rTMS in both the active stimulation and sham groups [41]. The comparison

Table 4 Efficiency and effectiveness of non-invasive brain stimulation techniques: summary of reviewed studies

Study	Neuropsychiatric disorder	NIBS technique	Findings
Höppner and colleagues [40]	Depressive disorders	rTMS	- Significant improvement in motor functions
Jorge and colleagues [41]	Vascular depression	rTMS	- Moderate response rate to rTMS in active stimulation and sham groups
Wall and colleagues [42]	Major depressive disorder	rTMS	- Decrease in depression and improved verbal memory after treatment
Weaver and colleagues [45]	ADHD	TMS	- Significant improvements in symptoms in both active stimulation and sham groups
Sotnikova and colleagues [46]	ADHD	tDCS	- Increased neuronal activation and connectivity in stimulated brain areas
Sokhadze and colleagues [47]	Autism spectrum disorders	rTMS	- Improved cognitive control, attention, target stimulus recognition, and behavioural recovery
Nikolin and colleagues [49]	Depression	tRNS	- Reduction in depressive symptoms
Brumelin and colleagues [50]	Schizophrenia	tRNS	- Positive outcomes in treating schizophrenia
Stamoulis and colleagues [57]	Epilepsy, neurodevelopmental disorders	TMS	- Detectable changes in phase variability, suggesting effects on resting brain dynamics - Potential therapeutic implications for conditions with aberrant hyper-synchrony
Filipcic and colleagues [59]	Major depressive disorder	rTMS	- Higher efficacy of high-frequency rTMS compared to standard treatment alone - Reduction in depressed and anxiety symptoms - Positive safety profile
Del Felice and colleagues [60]	Parkinson's disease	tACS	- Reduction in beta rhythm and improved motor and cognitive symptoms - Individualised tACS targeting specific frequencies and brain regions
Wang and colleagues [61]	Chronic insomnia	tACS	- Active tACS sessions significantly improved sleep-related measures compared to sham tACS - Higher response rate and improvements in sleep quality, efficiency, and duration
Riddle and colleagues [62]	Major depressive disorder	tACS	- Reduction in left frontal alpha power indicating modulation of alpha oscillations - Potential for reducing depression symptoms and enhancing approach motivation
Mellin and colleagues [63]	Schizophrenia	tACS	- Largest effect size for auditory hallucination symptoms during stimulation period - Potential treatment option for auditory hallucinations in schizophrenia
Bolognini and colleagues [79]	Chronic neuropsychiatric and neurologic disorders	N/A	- Improvement in neuropsychiatric and neurologic deficits with NIBS targeting the parietal lobe
Eleanor and colleagues [81]	Depression	SAINT	- Impressive remission rates of 90% with SAINT protocol targeting left anterior DLPFC and sgACC

between the active stimulation and sham groups raises questions about the specificity of the observed effects. A more detailed exploration of the placebo response and its potential impact on the reported outcomes would add depth to the interpretation. Another study by Wall and colleagues evaluated the neurocognitive effects of rTMS in adolescents with major depressive disorder, showing a decrease in depression and improved verbal memory after the treatment procedures [42]. Clinical studies have also examined using brain stimulation techniques to treat depression during pregnancy [43, 44].

Weaver and colleagues conducted a pilot study on the effect of TMS in treating ADHD in adolescents and young adults, demonstrating significant improvements in symptoms in both the active stimulation and sham groups [45]. While pilot studies are valuable for informing larger trials, their findings should be interpreted cautiously due to potential limitations like small sample sizes and lack of statistical power. The significant improvements in symptoms in both the active stimulation and sham groups raise questions about the specificity of the TMS effects. A clearer understanding of the placebo response and the mechanisms contributing to symptom improvements would enhance the interpretation of the results. Sotnikova and colleagues evaluated the effect of transcranial direct current stimulation (tDCS) on

neuronal networks in adolescent patients with ADHD, observing increased neuronal activation and connectivity in the brain areas under the stimulation electrode [46]. However, while increased neuronal activation and connectivity are observed under the stimulation electrode, the clinical significance of these neurophysiological changes in ADHD symptomatology requires further exploration. In the case of autism spectrum disorders, Sokhadze and colleagues found that rTMS improved cognitive control, attention, target stimulus recognition, and behavioural recovery in children with autism [47]. The finding that rTMS improved cognitive control, attention, target stimulus recognition, and behavioural recovery in children with autism is promising. However, the specificity of the observed improvements to rTMS, as opposed to other potential factors, must be considered. Additionally, exploring the durability of these effects over time is essential for understanding the potential long-term impact of rTMS in ASD.

In addition to the established modalities, novel non-invasive brain stimulation approaches such as transcranial random noise stimulation (tRNS), tACS, and transcranial ultrasound stimulation (TUS) are being developed [48]. Clinical studies have evaluated their effectiveness in treating neuropsychiatric disorders. Nikolin and colleagues conducted a randomised controlled study on the use of tRNS in the treatment of depression, showing a reduction in depressive symptoms [49]. Brumelin and colleagues investigated the effectiveness of tRNS in treating schizophrenia and found positive outcomes [50]. Furthermore, tACS and TUS have effectively treated disorders such as depression, ADHD, and Alzheimer's disease [51–54].

De Goede and colleagues conducted a study to assess the spatiotemporal dynamics and stability of single and paired-pulse TMS evoked potentials (TEP) using TMS-EEG [55]. They found that the topographical distribution of TEP components was comparable for both single and paired-pulse TMS, and stimulation of both dominant and non-dominant hemispheres resulted in mirrored spatiotemporal dynamics. The study also investigated Long-interval cortical inhibition (LICI) and observed significant suppression of late TEP components in the central areas for all inter-stimulus intervals (ISIs) ranging from 100 to 300 ms. These findings have implications for using late TEP responses as potential biomarkers for epilepsy and highlight the importance of evaluating late TEP components to understand brain activity. Corp and colleagues conducted an extensive investigation focusing on interindividual variation in TMS responses [56]. They gathered TMS data from a varied sample of subjects and identified predictors of TMS responses, including muscle target, pulse waveform, use of neuronavigation, and TMS machine type. They also found that baseline motor-evoked potential amplitude, age, and TMS machine type influenced the response to short-interval intracortical inhibition and intracortical facilitation. These findings provide valuable insights into the interindividual heterogeneity in TMS responses, contributing to the standardisation and application of TMS techniques in research and clinical contexts.

Stamoulis and colleagues investigated the effects of sustained single-pulse TMS on EEG phase parameters. They observed detectable changes in phase variability, suggesting an effect on the dynamics of the resting brain [57]. They proposed that TMS might selectively synchronise networks or increase high-frequency noise levels, leading to signal decorrelations or decoupling. These effects may have therapeutic implications for conditions characterised by aberrant hyper-synchrony, such as epilepsy and neurodevelopmental disorders. Additionally, Rothkegel and colleagues examined the impact of pulse duration in single-pulse TMS on measures of primary motor cortex excitability [58]. They found that pulse duration changes did not significantly affect threshold-adjusted excitability measures. This finding provides important information for researchers and clinicians who need to modify stimulation parameters based on individual characteristics and equipment constraints.

Regarding clinical applications, Filipcic and colleagues investigated the effectiveness, safety, and tolerability of augmentative rTMS as a treatment for major depressive disorder (MDD) [59]. They found that high-frequency rTMS reduced depression and anxiety symptoms more effectively than standard treatment alone, as evidenced by greater gains on the Hamilton Depression Scale (HAM-D) and Hamilton Anxiety Scale (HAM-A) in the rTMS group compared to the control group. These findings support the efficacy of rTMS in treating depression. However, limitations such as lack of randomisation and using a sham coil control condition should be considered when interpreting the results. Importantly, rTMS was well-tolerated with no reported seizures and minimal side effects, demonstrating its positive safety profile as a therapy option for MDD. These studies contribute to understanding TMS, including its spatiotemporal dynamics, interindividual response variation, effects on brain dynamics, and clinical applications. Further research in these areas will enhance the utilisation of TMS as a non-invasive brain stimulation technique for various neurological and psychiatric conditions.

Del Felice and colleagues conducted a randomised trial to investigate the effects of personalised tACS on cortical oscillations and behaviour in individuals with Parkinson's disease (PD) [60]. The study found that tACS reduced beta rhythm and improved motor and

cognitive symptoms in PD patients. The reduction in excessive fast EEG oscillations was associated with improved motor function and cognitive performance. The study highlighted the importance of individualised tACS targeting specific frequencies and brain regions to optimise treatment effects. The findings supported the potential of tACS as a non-invasive neuromodulation technique for PD.

Wang and colleagues examined the efficacy and safety of tACS as a treatment for chronic insomnia in adults [61]. The study showed that active tACS sessions targeting the forehead and mastoid areas significantly improved sleep-related measures compared to sham tACS. The active group had a higher response rate and showed improvements in sleep quality, efficiency, and duration. The study demonstrated that tACS could be an effective and safe intervention for chronic insomnia within an 8-week period. However, the long-term durability of these effects and whether they can be sustained beyond the intervention period would be interesting to explore.

Riddle and colleagues replicated the effects of tACS on alpha oscillations in patients with major depressive disorder (MDD) [62]. The study showed that tACS reduced left frontal alpha power during resting state, indicating its ability to modulate alpha oscillations in MDD patients. The reduction in left frontal alpha response to positive stimuli suggested the potential of tACS in reducing depression symptoms and enhancing approach motivation. The study highlighted the role of tACS in modulating alpha oscillations and its potential as a future treatment for MDD.

Mellin and colleagues evaluated the feasibility and efficacy of tACS for treating auditory hallucinations in patients with schizophrenia [63]. The study compared sham stimulation, 10 Hz tACS, and transcranial direct current stimulation (tDCS). While there were no significant differences in behavioural outcomes between the groups, tACS had the largest effect size for auditory hallucination symptoms during the stimulation period. The study acknowledged the challenge of blinding due to the appearance of phosphenes with tACS. Despite this limitation, the study indicated the potential of tACS as a treatment option for auditory hallucinations in schizophrenia.

These studies collectively demonstrate the potential of tACS as a non-invasive brain stimulation technique for modulating brain activity and improving symptoms in conditions such as Parkinson's disease, chronic insomnia, major depressive disorder, and schizophrenia. Further research is needed to refine protocols, investigate mechanisms, and establish standardised guidelines for applying tACS in clinical practice.

Future directions and potential developments

NIBS has witnessed significant advancements in recent years, aiming to overcome the limitations of standard techniques such as TMS and tDCS [64].

One promising technique is low-intensity focused ultrasound (LIFUS), which is safe and highly targeted compared to TMS [65]. Dallapiazza and colleagues conducted a study demonstrating the effectiveness of targeted thalamic somatosensory LIFUS in producing neuro-modulatory changes without tissue ablation, unlike standard TMS [66]. LIFUS was found to suppress cortical evoked potentials and induce significant changes in the oscillatory dynamics of the cortex [67]. These findings highlight the potential of LIFUS as a novel neuro-stimulation technique.

Theta-burst stimulation (TBS) has also emerged as an improvement over rTMS [68]. TBS involves continuous or intermittent stimulation to achieve inhibitory or excitatory changes in the brain. Seiko and colleagues demonstrated that a single session of TBS over the somatosensory cortex can induce short-term changes in somatosensory and motor-evoked potentials [68]. Additionally, TBS is effective and significantly reduces procedure time compared to standard rTMS.

High-definition transcranial direct current stimulation (HD-tDCS) advances traditional tDCS, offering longer-lasting neuromodulation with minimal modifications [69]. HD-tDCS enables more precise targeting of brain regions and can enhance the therapeutic effects of tDCS. Temporal interference stimulation (TIS) is another novel technique that utilises an array of high-frequency electric fields to generate biological effects in the brain [70]. Unlike tDCS, TIS is highly specific and can target deeper brain structures without causing scalp pain associated with nerve excitation [70]. However, TIS is still in clinical trials, and more research is needed to demonstrate its effectiveness in human subjects. These novel neuro-stimulation techniques offer potential advancements in precision, effectiveness, and specificity, addressing the limitations of existing methods. Further research and clinical trials are necessary to validate their effectiveness, establish optimal protocols, and determine their applications in the management of neuropsychiatric disorders.

NIBS techniques, alongside pharmacotherapy and psychotherapy, have emerged as a valuable management option for neuropsychiatric disorders [64]. However, there is a need for standardisation and a clear temporal framework for treatment to guide clinicians in determining the optimal sequencing and timing of non-invasive neuro-stimulation techniques [71]. There are uncertainties regarding when these techniques should be introduced in the treatment process.

Combining non-invasive brain stimulation techniques with other forms of therapy, such as psychotherapy, has shown greater benefits than using any modality alone [72]. However, further research is needed to understand the underlying interaction mechanisms between non-invasive brain stimulation techniques and other treatment modalities for neuropsychiatric disorders. Investigating these mechanisms can provide insights into the neurobiological changes that occur with combined modalities and help determine the appropriate sequence and timing for their use. Adopting an evidence-based approach and establishing guidelines for integrated treatment to successfully implement the combined approach in clinical practice is crucial. By combining non-invasive brain stimulation techniques with other treatment modalities, future research can shed light on the synergistic effects, optimise treatment strategies, and provide clearer guidelines for clinicians. This integrated approach holds promise for enhancing the overall management of neuropsychiatric disorders, but further investigation is necessary to understand its potential and establish evidence-based protocols fully.

The variable response of individuals to NIBS remains a significant challenge in its clinical use. Guerra and colleagues conducted a study identifying physiological, technical, and statistical factors contributing to these variabilities [73]. While some patients experience notable improvements in their symptoms with NIBS, others do not respond as effectively. Such treatment response disparities highlight the importance of identifying biomarkers to predict an individual's response to specific NIBS interventions [74].

Biomarkers that can provide insight into potential treatment responses are crucial for tailoring interventions to patients with specific characteristics. Over the years, various biomarkers have been explored to develop more specific NIBS approaches. These biomarkers include serum levels of metabolites of hormones like tryptophan and histamine, functional magnetic resonance imaging (fMRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), and electroencephalography (EEG) [75]. Giron and colleagues conducted a scoping study investigating the effects of NIBS on metabolites involved in serotonin and tryptophan metabolism [75]. They examined biomarkers such as kynurenine, kynurenic acid, 5-hydroxytryptamine (5-HT), and 5-hydroxy indole acetic acid (5-HIAA). Their findings suggested that NIBS increased histamine metabolite levels in the brain without significantly affecting tryptophan metabolites. However, the variability in study designs across the literature they reviewed may limit the generalisability of these findings.

Electroencephalography, fMRI, PET, and SPECT are imaging techniques that can be combined with NIBS to create biomarkers for neuropsychiatric disorders [74]. A study among epileptic patients demonstrated that TMS combined with EEG could generate biomarkers capable of quantitatively detecting degrees of cortical hyperexcitability in these patients. The identification and utilisation of biomarkers in conjunction with NIBS techniques hold promise for improving treatment outcomes by allowing for personalised interventions based on an individual's specific characteristics. Further research and standardisation in the field of biomarker identification are necessary to enhance the predictive power of these markers and optimise their clinical utility.

Abnormal neuroplasticity is believed to play a crucial role in developing various neuropsychiatric disorders, including depression, Alzheimer's disease, schizophrenia, and epilepsy [75]. Consequently, NIBS's future relies on identifying novel targets and brain regions specific to these disorders, aiming for more targeted therapies [76]. While recent advancements have been made in NIBS, ongoing research is focused on refining the precision and effectiveness of treatment approaches.

A meta-analysis conducted by Liu and colleagues explored potential NIBS target sites for mild cognitive impairment and found that the standard sites commonly used were the dorsolateral prefrontal cortex (DLPFC) and inferior frontal gyrus (IFG). Additionally, they suggested other novel target sites, such as the medial superior frontal gyrus, inferior temporal gyrus, and right inferior occipital gyrus [77]. This highlights the ongoing exploration of new target sites to enhance the efficacy of NIBS for specific cognitive impairments. Similarly, studies have investigated novel target sites for NIBS in managing chronic insomnia. Some potential targets identified include the superior temporal gyrus (STG), DLPFC, and supplementary motor area (SMA) [78]. These findings emphasise the importance of identifying specific brain regions associated with sleep disorders to optimise NIBS interventions.

Bolognini and colleagues demonstrated that NIBS targeting the parietal lobe can improve neuropsychiatric and neurologic deficits in patients with chronic neuropsychiatric and neurological disorders [79]. This highlights the potential of NIBS to target different brain regions beyond the traditionally studied areas, expanding its applications to a wider range of conditions. In treating major depressive disorders, NIBS techniques have primarily focused on rTMS targeting the DLPFC [64]. However, recent studies have revealed therapeutic benefits from stimulating other brain targets, such as the orbitofrontal cortex (OFC) and ventrolateral prefrontal cortex (VPFC) [80]. These findings suggest the importance of

exploring alternative target sites to optimise treatment outcomes for depression.

An innovative breakthrough in NIBS for depression management is the Standard Accelerated Intelligent Neuromodulation Therapy (SAINT). SAINT utilises functional connectivity MRI (fcMRI) to establish a highly targeted indirect inhibitory connection between the left anterior DLPFC and the subgenual anterior cingulate cortex (sgACC) [81]. The SAINT protocol involves delivering 10 theta-based stimulation sessions daily for 5 consecutive days each week over 6 weeks. A study by Eleanor and colleagues reported impressive remission rates of 90% with the SAINT protocol [81]. However, further research is needed to confirm and validate these findings, as fcMRI may have contributed to the high remission rate.

Safety and ethical considerations

Safety has been a primary concern in NIBS, especially since it was introduced as an alternative to invasive procedures with higher risks. However, significant efforts have been made to enhance the safety of NIBS techniques. Evidence indicates that NIBS is generally safe, with minor side effects [82, 83]. The most concerning potential complication of TMS is the triggering of epileptic seizures [84]. Nonetheless, the magnetic field produced by TMS is lower than that of Magnetic Resonance Imaging (MRI), indicating its relative safety [83, 84]. Other temporary side effects include headache, neck pain, tinnitus, memory disorders, acute mood changes, and neurocardiogenic syncope [84].

In the case of TDCS, studies have reported its safe profile, including in children and adolescents, as it avoids some side effects associated with pharmacological treatments for psychiatric disorders, such as sexual side effects or serotonin syndrome [85]. The most significant side effects of TDCS are typically mild and self-limiting, including itchiness, rash, redness, and scalp discomfort, which generally do not require intervention [86]. TDCS has also been found to have a low likelihood of inducing seizures and a limited impact on cognitive impairment [87, 88].

NIBS has raised ethical concerns and prompted debates among different groups. Two opposing viewpoints can be identified: the bio-liberal approach and the bio-conservative view [89]. The bio-liberal perspective emphasises an individual's autonomy and the right to decide on interventions that may benefit their well-being [89]. Supporters of this view argue that humans should be free to live according to their own choices and should not be subject to manipulative external forces. Thus, individuals should be able to decide whether to allow brain stimulation.

In contrast, the bio-conservative view also values individual autonomy but considers an individual a unique person with inherent traits and identity that should be preserved [90]. This perspective regards distortions in brain functioning as integral to an individual's distinct traits and believes these traits should remain unaltered. Brain modulation therapies, including NIBS, have the potential to bring about personality and identity changes that may disrupt the preservation of an individual's authenticity. Therefore, those with the bio-conservative view do not endorse brain stimulation procedures.

The ethical considerations surrounding NIBS highlight the complex balance between individual autonomy, potential benefits, and the preservation of personal identity. NIBS techniques represent a promising frontier in the treatment of neuropsychiatric disorders, offering novel therapeutic avenues. However, ethical and safe implementation of these techniques necessitates a robust regulatory framework. The regulatory landscape shapes research practices, ensures participant safety, and fosters public trust. Various regulatory agencies, both at the national and international levels, contribute to overseeing research involving non-invasive brain stimulation. Agencies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) play crucial roles in evaluating the safety and efficacy of interventions. Additionally, guidelines provided by organisations like the International Society for Transcranial Stimulation (ISTS) offer standardised approaches for researchers and clinicians [91]. For instance, TMS devices used for depression have undergone FDA clearance or approval processes [91]. Despite advances in regulatory oversight, challenges and gaps persist. Standardised protocols for non-invasive brain stimulation procedures, long-term safety monitoring, and consistency in regulatory approaches across different jurisdictions pose ongoing challenges. Addressing these gaps is crucial to ensuring the reliability and generalisability of research findings and protecting participant welfare. As non-invasive brain stimulation evolves, regulatory frameworks must adapt to emerging technologies and research paradigms. Future considerations include refining standards for novel interventions, addressing participant diversity and inclusion issues, and fostering collaboration between researchers, clinicians, and regulatory agencies to stay abreast of technological advancements responsibly.

Discussions and ongoing research are necessary to address these ethical concerns and develop guidelines that respect individual autonomy while considering the impact of brain stimulation on personal identity.

Limitation of study

The narrative review focused on non-invasive brain stimulation techniques in the context of neuropsychiatric disorders. Still, it may have covered only some relevant studies or explored other potential applications of these techniques outside the scope of neuropsychiatric disorders. The review may have encountered challenges in assessing the quality and heterogeneity of the included studies, as they may have varied in terms of study design, sample size, outcome measures, and follow-up duration. While the study had certain limitations, its strengths lie in its comprehensive overview, identification of current applications, exploration of future directions, and emphasis on underlying mechanisms. These aspects contribute to the understanding of non-invasive brain stimulation techniques in the context of neuropsychiatric disorders and highlight avenues for further research and clinical advancements.

Conclusion

This narrative review has provided a comprehensive overview of non-invasive brain stimulation techniques in the context of neuropsychiatric disorders. The study has highlighted the current applications and explored the potential future directions for these techniques. Throughout the review, it became evident that non-invasive brain stimulation methods, such as TMS and tDCS, have shown promising results in treating various neuropsychiatric disorders, including depression, schizophrenia, and obsessive–compulsive disorder. These techniques offer a non-pharmacological approach that can complement or replace traditional therapies.

Moreover, the review shed light on the underlying mechanisms of action for non-invasive brain stimulation, emphasising its ability to modulate neural activity and promote neuroplasticity. The emerging evidence suggests that these techniques hold great potential in targeting specific brain regions and circuits implicated in different neuropsychiatric conditions, thus offering personalised and targeted therapeutic interventions. However, despite the progress made in this field, several challenges remain. The variability in treatment response, the need for optimised stimulation protocols, and the lack of long-term data on safety and efficacy are among the key areas that require further investigation. Additionally, the review emphasised the importance of well-designed clinical trials and rigorous research methodologies to establish the true efficacy of non-invasive brain stimulation techniques. The future directions for non-invasive brain stimulation in neuropsychiatric disorders are promising. Advances in neuroimaging techniques, computational modelling, and neurophysiological markers can enhance treatment precision and optimise stimulation parameters for individual patients. Furthermore, integrating non-invasive brain stimulation with other therapeutic approaches, such as cognitive-behavioural therapy or pharmacological interventions, may lead to synergistic effects and improved patient outcomes.

Abbreviations

NIBS	Non-invasive brain stimulation
TMS	Transcranial magnetic stimulation
tDCS	Transcranial direct current stimulation
tACS	Transcranial alternating current stimulation
rTMS	Repetitive transcranial magnetic stimulation
OCD	Obsessive-compulsive disorder
ADHD	Attention deficit/hyperactivity disorder
EEG	Electroencephalography
PD	Parkinson's disease
MDD	Major depressive disorder
LIFUS	Low-intensity focused ultrasound
TBS	Theta-burst stimulation
rTMS	Repetitive transcranial magnetic stimulation
HD-tDCS	High-definition transcranial direct current stimulation
TIS	Temporal interference stimulation
SAINT	Standard accelerated intelligent neuromodulation therapy
fcMRI	Functional connectivity magnetic resonance imaging
DLPFC	Dorsolateral prefrontal cortex
IFG	Inferior frontal gyrus
STG	Superior temporal gyrus
SMA	Supplementary motor area
OFC	Orbitofrontal cortex
VPFC	Ventrolateral prefrontal cortex
sgACC	Subgenual anterior cingulate cortex
MRI	Magnetic resonance imaging
fMRI	Functional magnetic resonance imaging
PET	Positron emission tomography
SPECT	Single-photon emission computed tomography
5-HT	5-Hydroxytryptamine (serotonin)
5-HIAA	5-Hydroxyindoleacetic acid

Acknowledgements

None.

Author contributions

NA conceptualised the study. All authors were involved in the literature review. GO and NA extracted the data from the review studies. All authors wrote the final and first drafts. All authors read and approved the final manuscript.

Funding: No funding was received for this study.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Department of Medicine and Surgery, Ladoke Akintola University of Technology, PMB 5000, Ogbomosho, Nigeria. [2]Department of Medicine and Surgery, University of Ilorin, Ilorin, Nigeria. [3]College of Medicine, University of Ibadan,

Ibadan, Nigeria. [4]Department of Medicine and Surgery, Obafemi Awolowo University, Kajola, Nigeria.

Received: 2 October 2023 Accepted: 24 March 2024
Published online: 30 March 2024

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