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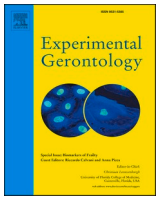

Review article

A systematic review and meta-analysis for the efficacy of transcranial direct current stimulation (tDCS) in OCD treatment: A non-pharmacological approach to clinical interventions

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ABSTRACT

Obsessive-compulsive disorder (OCD) is a prevalent mental condition characterized by recurrent, unwanted thoughts (obsessions) and repetitive behaviors (compulsions), significantly disrupting daily functioning and social interactions. Transcranial direct current stimulation (tDCS) presents a promising non-invasive treatment modality aimed at alleviating symptoms. However, the evidence regarding its effectiveness remains inconclusive. This study seeks to address this gap by conducting a systematic review and meta-analysis of clinical trials, offering improved guidance for clinical intervention. A comprehensive search strategy was implemented across multiple databases, including PubMed, Cochrane CENTRAL, Embase, Scopus, and Web of Science. This search focused strictly on randomized controlled trials (RCTs) involving 147 patients. These trials evaluated the efficacy of tDCS in OCD patients. Subsequent data extraction, risk of bias assessment, and statistical analysis using Review Manager software revealed the potential efficacy of tDCS in reducing OCD symptoms. The meta-analysis not only fails to demonstrate significant superiority of active tDCS over sham tDCS but also suggests that sham tDCS may be more effective than active tDCS in reducing OCD symptoms. This finding diminishes the promise of tDCS as an effective treatment for OCD. Larger trials are warranted to further elucidate these findings.

1. Introduction

Obsessive-compulsive disorder (OCD) is the fourth most common mental disorder worldwide, with a lifetime prevalence rate of 2–3 % (Brem et al., 2014) (Bendriss et al., 2023), where a person has recurring, unwanted thoughts, ideas, or sensations (obsessions) and to get rid of these thoughts, they feel driven to do something repetitively (compulsions) such as hand washing, checking on things, and mental acts like counting or other activities (Singh et al., 2023). These activities can significantly interfere with a person's daily activities and social interactions. OCD affects men, women, and children and occurs in childhood almost identically to that seen in adults unlike other mental disorders (Mathes et al., 2019). There isn't confirmed cause for this disorder, but some studies have shown a relationship with dysfunction in the following areas: cortico-striatal-thalamo-cortical circuits (CSTC), anterior cingulate cortex, dorsolateral prefrontal cortex (DLPFC), orbitofrontal cortex (OFC), medial frontal cortex (MFC), supplementary motor area (SMA) and basal ganglia (Del Casale et al., 2011; Jalal et al.,2023). One possible etiological cause is also a hormonal imbalance such as serotonin (Del Casale et al., 2019). OCD medications include

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SSRIs, cognitive-behavioral therapy (CBT), and deep brain stimulation (DBS) (POTS team 2004; Rozenman et al., 2019). These medications act by inhibiting the reuptake of serotonin. DBS is a surgical procedure that involves implanting electrodes in the brain to regulate abnormal brain activity associated with OCD (Aum and Tierney, 2018), generating stimulant waves like repetitive trans direct current stimulation (rtDCS). TDCs is a non-invasive procedure brain stimulation works on the reduction of OCD symptoms by the application of a low-intensity electrical current to specific areas of the brain through electrodes (Lavezzi et al., 2022), so it affects the neuronal membrane which is found in dysfunctional neural circuits implicated in the disorder (Woods et al., 2016). Some studies show that tDCS may help normalize irregular neural activity associated with OCD symptoms, such as intrusive thoughts and repetitive behaviors (Pinto et al., 2022). However, these studies were limited to prove the role of tDCS on OCD patients, so there was a need to conduct new studies in this field. In this study, we aimed to solve this gap in the literature in this item by conducting a systematic review and meta-analysis of clinical trials that examined the efficacy of tDCS in OCD treatment by alleviating symptoms of this disease.

2. Methods

We conducted a systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. The protocol for this review was registered in PROSPERO (CRD42024499084).

2.1. Search strategy

A comprehensive review of medical literature was conducted across databases, including PubMed, Cochrane, Scopus, Web of Science, and Embase till January 2024. Our search strategy involved using specific keywords and relevant Medical Subject Headings (Mesh) terms related to “Obsessive-compulsive disorder”, “Transcranial direct current stimulation”, and other relevant terms. We used the MESH database and the following search strategy ((“obsessive compulsive disorder”[MeSH] OR “OCD”)) AND (“Transcranial direct current stimulation”[MeSH] OR “tDCS”)) AND (“randomized clinical trial” OR”RCT”) Furthermore, we applied filters to include only english and human studies. Additionally, we identified further studies through manual searches of reference lists from relevant studies and review articles.

2.2. Studies selection and eligibility criteria

Four independent authors screened titles and abstracts for eligibility criteria, followed by a full-text review of the eligible abstracts. Any discrepancies were resolved through consultation with a fifth author. Inclusion criteria included the following: 1) Study design: randomized controlled trials examining the efficacy of tDCS in patients with OCD compared to placebo or sham, 2) Population: studies involving OCD patients meeting DSM criteria. 3) Comparator: studies with a control group receiving either placebo or sham and 4) Outcome: studies assessing the effect of tDCS on OCD symptoms using standardized measurements such as Yale-Brown Obsessive compulsive Scale (Y-BCOS). Exclusion criteria included the following: 1) non-RCTs, observational studies, case reports or series and reviews 0.2) studies using other transcranial electrical stimulation intervention than tDCS. 3) non english studies.

2.3. Data extraction

Data extraction was performed independently by four authors using an online sheet. This included study characteristics (author, year of publication, country), demographics of the study population (age, disease), intervention details, and study outcome (mean and standard deviation in effect Y-BOCS scores for both intervention and control groups).

2.4. Risk of bias assessment

We assessed the risk of bias using Cochrane Collaboration's tool, which evaluates the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other potential sources of bias. Each study was assessed independently by four authors as having low, high, or unclear risk.

2.5. Data synthesis

Statistical analysis was performed using Review Manager software (version 5.4). The mean difference (MD) was chosen as the effect estimate. The inverse variance method was employed to analyze the continuous outcomes of Y-BOCS scores, with the difference between the pre- and post-mean and standard deviation for both intervention and control groups. A fixed-effect model was chosen assuming homogeneity across studies. The heterogeneity between studies was assessed using I-square and Chi-Square tests. Sensitivity analysis was conducted in case of significant heterogeneity (Chi-Square $P < 0.1$). Publication bias was deemed inapplicable for evaluation considering the limited number of included studies, which was fewer than ten studies.

3. Results

3.1. Literature search results

We found 547 unique studies. After title and abstract screening, 33 full-text articles were screened for eligibility. Finally, 6 randomized controlled trials with a total number of 147 patients (81 in the active group and 66 in the sham group) were included for analysis as shown in the study flow diagram Fig. 1. A summary of the main results of the included studies is shown in Table 1 and Baseline characteristics of the included studies are shown in Table 2.

3.2. Risk of bias assessment results

Summary of quality assessment domains of the included studies was from moderate to high quality based on the Cochrane risk of bias assessment tool as shown in the risk of bias graph Fig. 2.

3.3. Meta-analysis

3.3.1. Comparison between baseline and endpoint

The overall mean difference between the baseline and endpoint favored the endpoint (MD = 7.89, 95 % CI [4.40, 11.38], $P < 0.00001$). Pooled studies were not homogenous ($i^2 = 98$ %, $P < 0.00001$).

3.3.1.1. Subgroup analysis. To resolve the heterogeneity, we applied a subgroup analysis that showed that there is no heterogeneity between (Bation et al., 2019) study and (Gowda et al., 2019) ($i^2 = 0$ %, $P = 0.77$). Also, in (Fineberg et al., 2023) study and (Perera et al., 2023) study ($i^2 = 0$ % $P = 0.58$) as shown in forest plot A Fig. 3.

3.3.2. Comparison between endpoints of active and sham tDCS

The overall mean difference between active and sham tDCS at the endpoint favored active tDCS (MD = −1.13, 95 % CI [−5.35, 3.10], P = 0,60). Pooled studies weren't homogenous ($i^2 = 70$ %, $P = 0.005$) as shown in forest plot B1 Fig. 4.

Sensitivity analysis:

To resolve this heterogeneity, we conducted a sensitivity analysis in multiple scenarios excluding one study in each scenario. Heterogeneity was best resolved by excluding (Fineberg et al., 2023) study ($i^2 = 0$ %, P

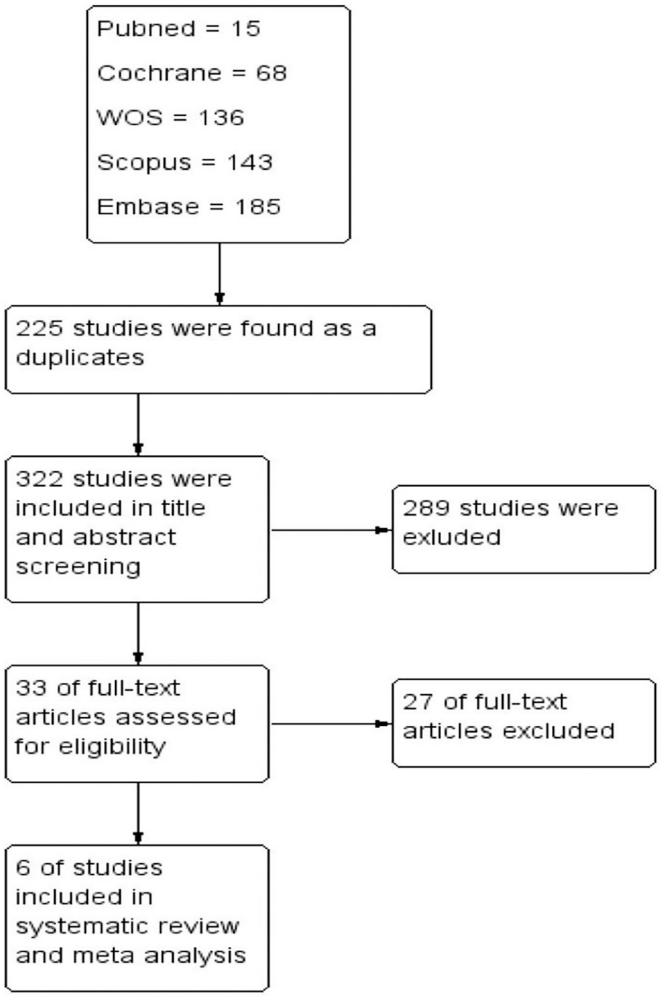

Fig. 1. PRISMA flow diagram.

= 0.79). After removing Fineberg et al., 2023 study the overall mean difference is still in favor of active tDCS as shown in forest plot B2 Fig. 5.

4. Discussion

This meta-analysis is the first comprehensive investigation to explore the efficacy of tDCS for OCD and identify potential moderators of treatment response. Our analysis includes 6 RCTs, encompassing 147 participants. Overall, the studies included did not indicate any significant biases that could affect the results. Additionally, no evidence of publication bias was detected.

The primary finding of this meta-analysis demonstrates a substantial improvement in OCD symptoms following tDCS treatment from baseline to endpoint (MD = 7.89, 95 % CI [4.40, 11.38], $P < 0.00001$).This aligns with previous studies suggesting tDCS as a promising therapeutic approach for OCD (D'Urso et al., 2018; Rachid, 2019).

While these results are encouraging, the considerable heterogeneity among studies (I^2 = 98 %, P < 0.00001) underscores the need for caution in generalizing findings. This heterogeneity likely stems from variations in montage configuration, treatment duration, and OCD symptom severity. Subgroup analysis, though limited, supports this heterogeneity, revealing differences in efficacy across montage configurations (I^2 = 94.1 %, P < 0.00001). This emphasizes the importance of optimizing montage parameters for specific OCD subtypes as proposed by (Pinto et al., 2022). Notably, two pairs of studies exhibited no heterogeneity: Bation et al., 2019 and Gowda et al., 2019; and Fineberg et al., 2023 and Perera et al., 2023. This suggests that specific study characteristics, potentially related to patient populations, intervention protocols, or outcome measures, may influence the observed effect. Further research is warranted to elucidate these potential moderators. In clinical practice, individual patient factors must be considered when recommending tDCS, as treatment response may vary accordingly.

Although the overall effect size is statistically significant, its clinical significance requires further elucidation. Determining the magnitude of the effect relative to the minimal clinically important difference (MCID) for OCD symptoms is crucial for assessing the practical implications of these findings.

Direct comparison of active and sham tDCS yielded a statistically significant benefit for active treatment (mean difference 18.10, 95 % CI [7.58, 28.62]), which remained robust after sensitivity analysis (mean difference − 3.03, 95 % CI [−5.26, −0.81]). This consistency, coupled with high homogeneity following sensitivity analysis (I^2 = 0 %), strengthens the evidence for tDCS' efficacy in reducing OCD symptoms in the short term. However, the clinical significance of these findings necessitates further investigation, as statistical significance does not inherently equate to meaningful symptom improvement.

The results of this meta-analysis, after sensitivity analysis, provide evidence supporting the efficacy of tDCS in reducing OCD symptoms in the short term. The observed improvement in OCD symptoms translates to a substantial reduction in OCD-related distress and impairment, suggesting clinical meaningfulness. While larger studies are needed, these findings position tDCS as a valuable treatment option for patients with OCD, particularly when integrated with other therapeutic approaches.

5. Limitations and future directions

While this meta-analysis suggests the potential of tDCS as a promising intervention for reducing symptoms of OCD, caution is advised when interpreting the findings due to the lack of a significant effect when comparing active tDCS to sham stimulation. Several factors may contribute to this absence of positive results.

Firstly, the meta-analysis included only six randomized controlled trials, and these studies had relatively small sample sizes overall. Such limitations in sample size can affect the statistical power and generalizability of the findings, making it challenging to draw definitive conclusions.

Secondly, there was a high heterogeneity of tDCS protocols across these studies, especially in terms of electrode montage. Consequently, both the limited sample sizes and the high heterogeneity in tDCS protocols pose significant limitations that constrain our ability to firmly establish the effects of tDCS as a treatment for OCD. Therefore, it is important to interpret the results cautiously and recognize the need for further research with larger samples and standardized protocols to gain a clearer understanding of tDCS efficacy in treating OCD.

Furthermore, the underlying neural mechanisms of tDCS's action in OCD require further elucidation. Combining tDCS with neuroimaging techniques like functional magnetic resonance imaging (fMRI) could shed light on a more detailed understanding of the neural mechanisms underlying behavioral effects, potentially benefiting research and clinical settings, and the specific brain circuits modulated by tDCS and their association with symptom improvement (Meinzer et al., 2014).

6. Conclusion

While the meta-analysis provides evidence for the potential of tDCS in treating OCD, the heterogeneity of results emphasizes the need for more rigorous research to identify optimal treatment parameters. Future studies should focus on larger sample sizes, standardized methodologies, and long-term outcomes to establish the clinical efficacy and durability of tDCS for OCD.

It is crucial to interpret these findings with caution due to the limitations of the meta-analysis. The potential for publication bias, where

Table 1
Summary of the included studies.

Study ID	Study Design	Velocity	Area of stimulation	Follow up period (Days)	Results
Fineberg et al., 2023	double-blind randomized, sham-controlled, multi- centre cross-over trial	2 mA active tDCS	Cathode: over L-OFC or SMA, anode: over right deltoid	28	Clinicians showed willingness to recruit participants and recruitment to target was achieved. Adherence to treatment and study interventions was generally good, Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scores were numerically improved from baseline to 24 h after the final stimulation across all intervention groups but tended to worsen thereafter. The greatest effect size was seen in the L-OFC arm, suggesting this stimulation site should be pursued in further studies.
Bation et al., 2019	randomized sham controlled study	2 mA active tDCS	Cathode: over FP1 to target left OFC Anode: over right cerebellum 3 cm below inion and 1 cm from midline	84	Compared with the sham tDCS, active tDCS significantly decreased OCD symptoms immediately after the 10th tDCS session However, no significant differences were observed between the active and sham groups in terms of changes in YBOCS score or the number of responders one and 3 months after tDCS.
Gowda et al., 2019	randomized, double blinded, sham controlled trial	2 mA active tDCS	Cathode: over right supra-orbital area Anode: over Pre-SMA	NR	The results of this RCT suggest that tDCS may be effective in treating SSRI-resistant OCD. Future studies should examine the efficacy in larger samples of OCD and explore other potential target regions using randomized sham-controlled designs, in addition to examining the sustainability of the beneficial effects.
Perera et al., 2023	randomized, double blinded, sham controlled trial	1.5 mA active tDCS	Two rectangular rubber elec-trodes encased in 7 cm × 6 cm sponges (contact area 42 cm2 were positioned at the 10–20 EEG system locations of AFz and Iz.)	90	A six-week, home-based treatment course of individualized alpha-tACS targeting the mPFC is capable of improving OCD symptoms. Further large-scale clinical trials are required to definitively establish tACS as a therapy for OCD.
Shafiezadeh et al., 2021	randomized sham controlled trial	2 mA active tDCS	right and left dorsolateral prefrontal cortex (DLPFC)	5	The scores of the Yale-Brown scale in the Left DLPFC group showed significant changes after treatment with tDCS. Hereupon, this study demonstrated that transcranial direct current stimulation may cause improvements in symptoms of OCD.
De Melo Felipe Da Silva et al., 2021	double-blind, randomized, and sham-controlled	2 mA active tDCS	Cathode: over the supplementary motor area (SMA) Anode: over the left deltoid	84	Cathodal tDCS over the SMA is an effective add-on strategy in treatment resistant OCD.

Table 2
Baseline characteristics for population of the included studies.

	Baseline criteria			
Study ID	Sample Size	Age Mean (SD)	Gender Male(%)	Y-BOCS Mean(SD)
Fineberg et al., 2023	19	45 (16.6)	10(52.6 %)	47.8 (10.6)
Bation et al., 2019	21	Active:44.8(19.9 %) Sham:41.2(11.9 %)	9(42.8 %)	29 (4.55)
Gowda et al., 2019	25	Active:30.83(5.87 %) Sham:25.92 (5.15 %)	21(84 %)	25.83 (4.88)
Perera et al., 2023	25	Active:36.31(14.43 %) Sham:36.17(12.04 %)	12(48 %)	28.62 (4.57)
Shafiezadeh et al., 2021	43	NR	17(70.8 %)	44.12 (9.469)
De Melo Felipe Da Silva et al., 2021	24	Active:38.41(10.95 %) Sham:36.9 (12.23 %)	17(39.5 %)	30.64 (5.47)

Notes: L-OFC: left orbitofrontal cortex, SMA: supplementary motor area, Y-BCOS: Yale-Brown Obsessive Compulsive Scale, tACS: transcranial alternating current stimulation, mPFC: medial prefrontal cortex, DLPFC: Dorsolateral Prefrontal Cortex.

unpublished or negative studies are not included, may have affected the results. Additionally, the limited number of studies available for inclusion might have limited the statistical power to detect more subtle effects and fully explore the sources of heterogeneity.

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Consent for publication

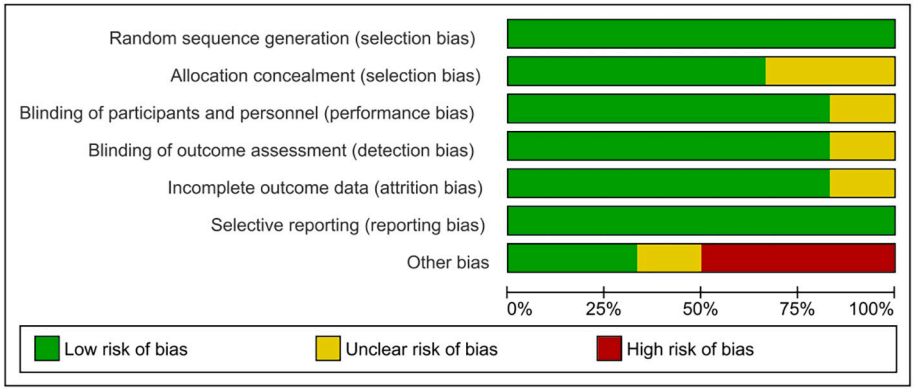
Not applicable.

Ethical approval

Not applicable.

CRediT authorship contribution statement

Ismail A. Ibrahim: Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Ahmed Hosney Nada:** Methodology, Formal analysis. **Rand Ibrahim:** Writing – original draft, Methodology, Data curation. **Rawan Ahmed Farouk:** Writing – original draft, Methodology, Formal analysis. **Almonzer Al-Qiami:** Writing – original draft, Software, Methodology. **Sarah A. Nada:** Writing – original draft, Formal



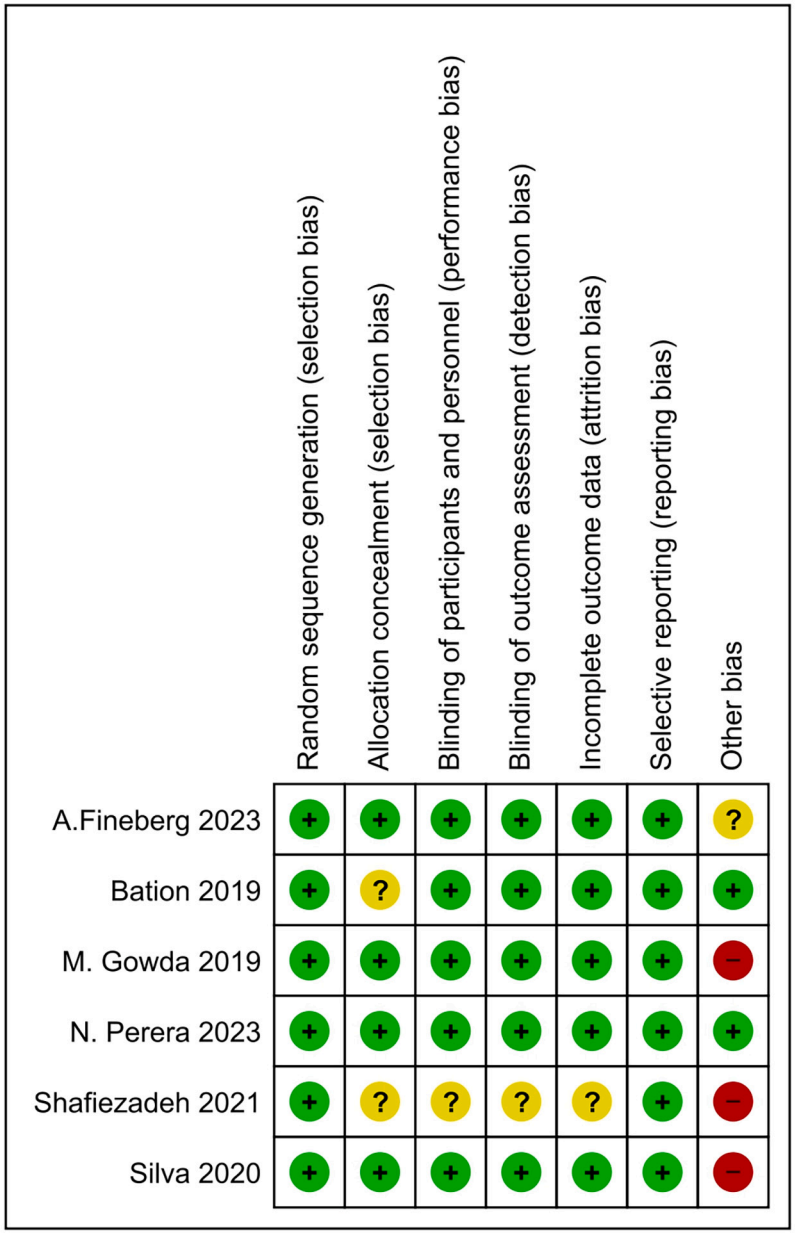


Fig. 2. Risk of bias assessment summary.

analysis. **Parisa Alizadeh Oghyanous:** Writing – original draft, Formal analysis. **Seyed Ali Noorbakhsh:** Writing – review & editing, Supervision, Methodology, Formal analysis.

Declaration of competing interest

The authors of this work declare that they have no conflicts of interest.

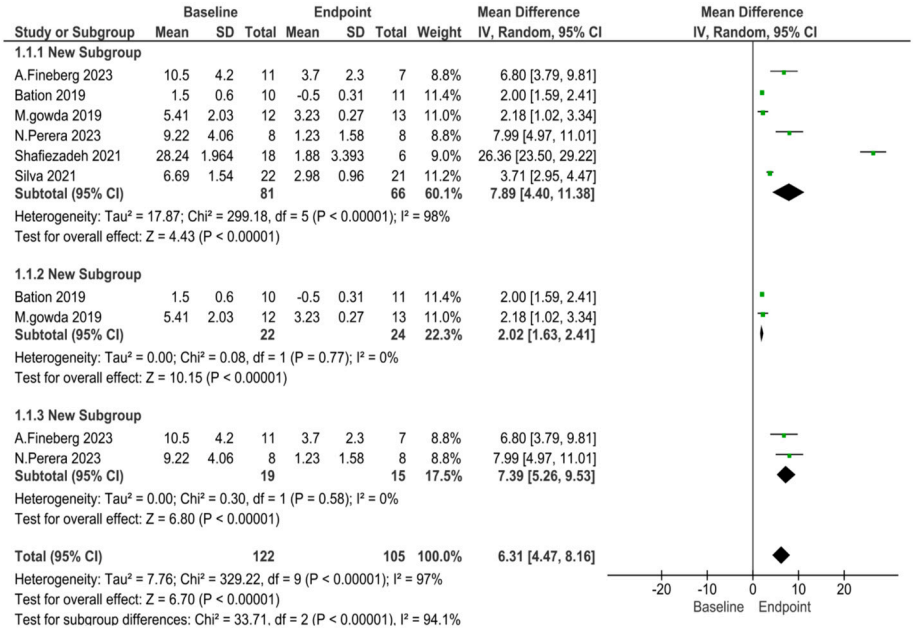


Fig. 3. Forest plot A: mean difference (MD) between pre- treatment (baseline) and post-treatment(endpoint) with 95 % confidence interval.

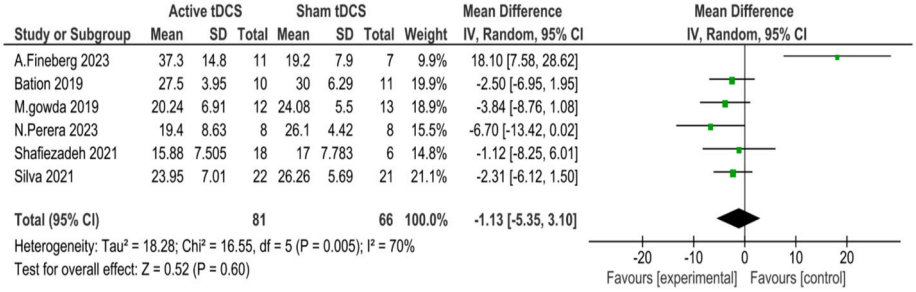


Fig. 4. Forest plot B1: mean difference between active and sham tDCS with significant heterogeneity.

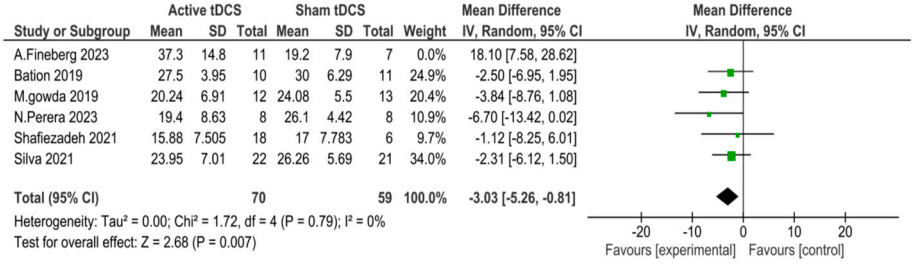


Fig. 5. Forest plot B2: results after excluding A. Fineberg's et al., 2023 study to resolve heterogeneity.

Data availability

Data will be made available on request.

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