nature mental health

Analysis

https://doi.org/10.1038/s44220-026-00590-z

Transcranial electrical stimulation for the treatment of obsessive–compulsive disorder: a triple meta-analysis

Received: 19 August 2024

Accepted: 15 January 2026

Published online: 16 March 2026

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Obsessive–compulsive disorder (OCD) is a condition with substantial disability and subclinical obsessive–compulsive behaviors affect up to 1 billion people globally. Transcranial electrical stimulation (tES) is emerging as a potential treatment for OCD, yet its effectiveness is uncertain due to the limited number of randomized controlled trials conducted so far. Here we applied 3 meta-analytic approaches to evaluate the pooled therapeutic effect size of included randomized controlled trials ($n_{tDCS} = 15$, $n_{tACS} = 1$) (pair-wise meta-analysis), compare the efficacy of various tES interventions (network meta-analysis), and explore how treatment effect size correlates with induced electrical field in the target brain regions (meta-modeling). With these 3 distinct meta-analytic approaches, we first show a significant moderate effect of tES interventions (standardized mean difference 0.61; 95% confidence interval [0.37 to 0.85]; $P < 0.001$) as a whole on reducing OCD severity, with larger therapeutic effects of twice-daily intervention, and with other stimulation parameters also moderating efficacy. Next, we identify specific tES interventions with superior indicated and estimated effects, including entraining alpha frequency alternating stimulation of the medial prefrontal cortex, excitability-diminishing cathodal stimulation over the supplementary motor area and orbitofrontal cortex, and excitability-enhancing anodal stimulation of the lateral prefrontal cortex. Finally, we show based on computational approaches that longer stimulation targeting the medial prefrontal and frontopolar cortices has greater therapeutic effects and suggest an optimized intervention accordingly. We finally discuss other potentially effective tES interventions according to the latest neurobiological theory of OCD. The results contribute to establishing the clinical efficacy of tES for OCD treatment while suggesting future studies to further evaluate current and future approaches to enhance the efficacy of interventions.

Obsessive–compulsive disorder (OCD) imposes a substantial burden on mental health and is associated with substantial disability[1,2]. With a lifetime prevalence of 2–3% (ref. 3), OCD often starts during childhood and follows a chronic course, is accompanied by functional impairment and higher risk of early mortality[4–6], and is often underdiagnosed and undertreated[2]. Individuals with OCD have unwanted and distressing thoughts (obsessions) and repetitive behaviors that the individual feels driven to perform (compulsions)[2]. While cognitive behavioral therapy and serotonin reuptake inhibitor medication are considered first-line treatments for OCD[7], less than 40% of patients respond fully to these treatments[8].

Non-invasive brain stimulation (NIBS) techniques, as applied across cognitive neuroscience and neurophysiology, offer a safe way to alter physiological parameters underlying human behavior and cognition (for example, cortical excitability, neuroplasticity, brain oscillations) in both healthy individuals and clinical populations[9–11]. NIBS,

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namely, deep repetitive transcranial magnetic stimulation (rTMS), was approved by the US Food and Drug Administration (FDA) for the treatment of OCD in 2018[12], suggesting that related interventions may also have therapeutic applications in OCD. Transcranial electrical stimulation (tES), another NIBS method, uses a weak electrical current to modulate brain activity[13,14] and its effectiveness for OCD treatment remains unclear despite several advantages over rTMS, such as fewer side effects, affordability and home-based applicability. The most common tES technique uses direct electrical current (known as transcranial direct current stimulation-tDCS) to change brain excitability[15], producing subthreshold neuronal membrane polarization[16], resulting in excitability-enhancing effects by anodal stimulation and excitability-reducing effects by cathodal stimulation at the macroscale level with typical protocols[17,18]. Transcranial alternating current stimulation (tACS), the next most common tES technique, uses weak oscillating electric currents hypothesized to entrain ongoing brain rhythms[19]. Transcranial random noise stimulation (tRNS) changes brain excitability via alternating currents at a mix of low or high frequencies[20,21].

The rationale behind the therapeutic use of NIBS includes restoring impaired plasticity or re-balancing abnormally altered brain functions including oscillatory activities (that is, up- or downregulation)[9,10,22,23]. In neuropsychiatric disorders including OCD, functional brain abnormalities (that is, hyper- or hypoactivity of specific brain regions and networks) are well documented. Functional imaging, lesion and deep brain stimulation studies have shown altered activations in several brain regions involved in OCD pathophysiology, including the pre-supplementary motor area (pre-SMA), insula, cingulate cortex, prefrontal cortex (PFC) and orbitofrontal cortex (OFC)[24–28], and altered cortical–subcortical connectivity (that is, hyper–hypoconnectivity)[29,30]. Furthermore, abnormal changes in neurotransmitter systems across frontostriatal pathways (for example, glutamatergic and dopaminergic hyperactivity) and frontolimbic systems (for example, serotonergic and γ-aminobutyric acid (GABA)-ergic hypoactivity) are observed in OCD[31–33]. Some of the observed brain alterations (for example, thinner precentral area, higher medial PFC–ventral striatal connectivity) are associated with treatment response to tDCS and rTMS in some studies[34,35]. These are common rationales behind applying rTMS or tES for OCD treatment. While the efficacy of rTMS for OCD treatment has been confirmed in previous studies[36,37], the efficacy of tDCS remains under investigation.

One reason is the insufficient number of randomized controlled trials (RCTs) that have applied tES for treatment of OCD. The recently published reviews and meta-analyses, and systematic reviews include 7 to 10 RCTs[38,39] with quasi-experimental studies included[40] or did not address the clinical efficacy of tES[41–43]. In the past 2 years, however, several RCTs have investigated the efficacy of tES, particularly tDCS, for OCD treatment[44–51]. These studies allow us to conduct multiple meta-analyses on the efficacy of tES intervention for OCD treatment with more included RCTs, as highlighted as a necessity in previous reports[40]. Consequently, we performed three meta-analyses and a systematic review to evaluate the effectiveness and safety of tES (including tDCS, tACS and tRNS) for patients with OCD.

To this end and to address the limitations of common meta-analytic approaches, we conducted three separate but related meta-analyses. (1) A classic (pairwise) meta-analysis to determine the pooled effect estimate, quantifying the overall impact of tES interventions on OCD treatment and (2) a network meta-analysis to compare the efficacy of various tES interventions against a sham condition[52]. The latter method provides a Bayesian summary of the rank distribution based on relative strength and estimated treatment effects[53], enabling a comprehensive assessment of the relative efficacy of different tES interventions in a single analysis[54]. This approach is essential for our research question, given the diverse intervention and stimulation protocols used in tES interventions for OCD symptoms. (3) Lastly, a computational meta-analysis focused on the correlations between tDCS-induced electrical field density in brain regions and treatment effect size, a recently introduced meta-analytic method for tES studies[55]. This three-level meta-analysis has been conducted to evaluate the efficacy of a NIBS intervention and is also an updated meta-analysis that solely contains tES RCTs published up to July 2025 (PROSPERO ID CRD42023485717). Our analyses, while revealing a statistically significant moderate therapeutic effect of tES for OCD treatment, highlight important stimulation parameters in this respect, with specific intervention shown to be more effective and model-suggested tES interventions.

Results

Literature search and study characteristics

The study selection process is shown in Fig. 1. The final search yielded 829 records. After removing duplicates and screening abstracts against the inclusion criteria, 39 records were left for full-text assessment and data extraction. Twenty-two studies were excluded for the following reasons: open-label trials ($n = 5$)[56–60], no control condition ($n = 2$)[61,62], proceedings report ($n = 2$)[63,64], lack of clinical measures or post-intervention Yale-Brown Obsessive Compulsive Scale (Y-BOCS) score ($n = 4$)[65–68] and case studies ($n = 9$)[69–77]. At the end, 17 studies with 25 experimental conditions remained for pairwise and network meta-analyses and the meta-modeling analysis[44–51,78–86]. However, owing to evidence of publication bias, the study by Shafiezadeh et al.[83] was identified as an outlier and excluded from the sensitivity analysis. In addition, five interventions from two studies[51,80] were excluded from the network meta-analysis due to non-sham control conditions. This exclusion ensured that the network analysis primarily compared treatment arms with sham conditions. The Shafiezadeh et al. study[83], however, was kept in the third meta-analysis as Spearman's rank correlation effectively handles non-normally distributed data and is less affected by outliers than the parametric Pearson coefficient. As a result of these exclusions, 16 RCTs (15 tDCS, 1 tACS, concluding 23 effect sizes) remained in the final pairwise meta-analysis, 14 RCTs (13 tDCS, 1 tACS, concluding 18 intervention and 23 effect sizes) remained in the network meta-analysis, and 16 tDCS studies (concluding 24 effect sizes), remained for meta-modeling analysis (Fig. 1; results with the outlier study[83] are in Supplementary Figs. 2 and 3). No tRNS RCT was among the included studies. In total, 551 patients with OCD were included ($n_{active} = 318$; $n_{sham} = 233$) and sample size per study ranged from 23 to 80 participants. The summary of studies, including study design, blinding, age, gender, stimulation parameters, primary and secondary outcome measures, and major findings about intervention efficacy and tolerability, are outlined in Table 1 and Supplementary Table 1.

Dropout and side-effects analysis

First, we systematically analyzed reported side effects, dropout rates and serious adverse events, if reported, among the included RCTs. Supplementary Table 1 summarizes the dropout rate, side effects (with percentage) and serious adverse events. In 14 tES studies that reported dropout rates, there was no significant difference between active (14/231, 6.06%) and sham/control (14/192, 7.29%) groups ($\chi^2 = 0.26$; $P = 0.61$; Fisher's exact test, $P = 0.69$). The total sample sizes were 231 for the active group and 192 for the sham/control group, excluding studies that did not report side effects or dropouts (Supplementary Fig. 4a). None of the RCTs that documented side effects reported any serious adverse events (Supplementary Table 1). Regarding side effects, only seven studies numerically reported them. These studies varied in the domains assessed and the methods of reporting (for example, occurrence in patients as numbers/percentages versus average intensity). A detailed summary of the reported side effects is available in Supplementary Table 1 and Supplementary Fig. 4b. The average occurrence of commonly reported side effects among patients in the active versus sham conditions was as follows: tingling (active, 44.01%; sham, 34.40%), sleepiness (including drowsiness) (active, 38.9%; sham,

https://doi.org/10.1038/s44220-026-00590-z

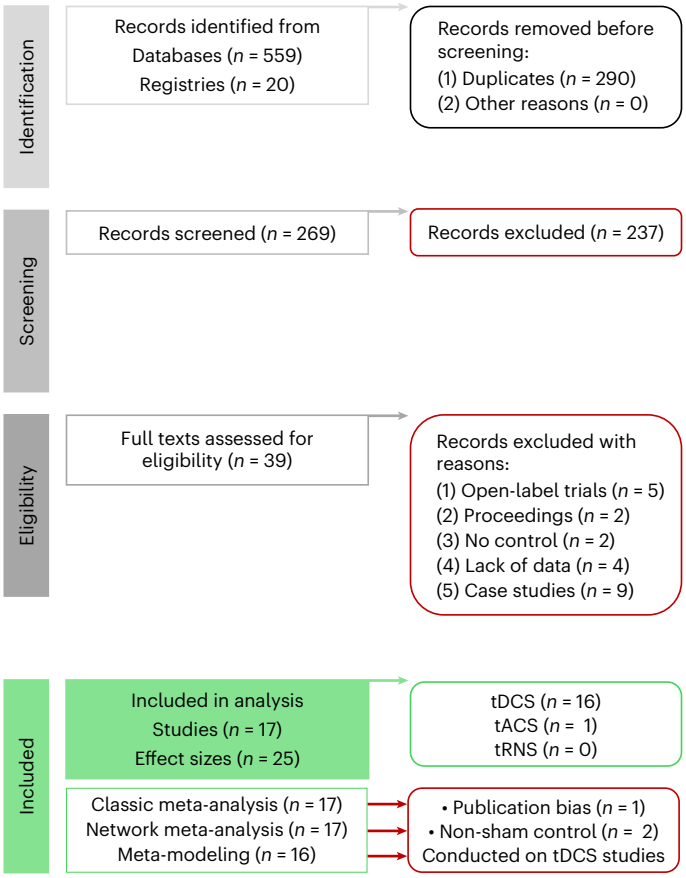


Fig. 1 | PRISMA flow diagram of included studies. Of studies investigating the effects of tES on reducing OCD symptom severity, 17 RCTs with sham or active control conditions were included in the final analysis, resulting in a total of 25 experimental conditions (effect sizes). The pairwise meta-analysis comprised 16 studies (15 tDCS and 1 tACS) with 25 effect sizes following excluding an RCT with publication bias ($n = 1$), while the network meta-analysis included 14 studies (13 tDCS and 1 tACS) with 23 effect sizes following excluding RCTs with non-sham control ($n = 2$) and publication bias ($n = 1$). The meta-modeling analysis encompassed all tDCS 16 studies, with 24 effect sizes.

37.17%), skin redness (active, 22.05%; sham, 9.77%), itching (active, 19.7%; sham, 15.3%) and pain (including headache and neck pain; active, 11.91%; sham, 11.33%). The only tACS study reported minor adverse events in 8 patients of 25, including headache (8%), phosphenes (20%), tingling (16%) and itching (8%).

Pairwise meta-analysis of overall tES efficacy and stimulation-parameter effects

The pooled effect size for the included studies (16 RCTs) with 23 experimental conditions was significant with a medium effect size (standardized mean difference (SMD) = 0.61; 95% confidence interval (CI), [0.37 to 0.85]; $P < 0.001$). The following tES studies had significant effect size (in descending order) for reducing OCD (indicating larger effect size) compared with the sham intervention or baseline scores: Chu et al.[51] with cathodal transcranial direct current stimulation (ctDCS) pre-SMA/left OFC (lOFC) + anodal transcranial direct current stimulation (atDCS) shoulder (SMD = 1.92; 95% CI, [0.57 to 3.26]); Perera et al.[47] applying peak alpha tACS over the medial PFC (SMD = 1.67; 95% CI, [0.62 to 2.72]); Kumar et al.[49] with ctDCS pre-SMA + atDCS left dorsolateral prefrontal cortex (lDLPFC; SMD = 1.30; 95% CI, [0.51 to 2.09]); Yekta et al.[85] combining atDCS right dorsolateral prefrontal cortex (rDLPFC) + ctDCS lDLPFC (SMD = 1.17; 95% CI, [0.04 to 2.31]); Fineberg et al.[44] with ctDCS-lOFC + atDCS shoulder (SMD = 1.12; 95% CI, [0.23 to 2.01]); and Alizadehgoradel et al.[45] with atDCS lDLPFC + ctDCS pre-SMA at 2 mA (SMD = 0.99; 95% CI, [0.11 to 1.86]) and 1 mA (SMD = 0.92; 95% CI, [0.04 to 1.80]) (Fig. 2a).

In addition, we did secondary analyses of effect sizes with respect to important stimulation parameters (cortical region, polarity, treatment frequency per day, treatment duration, number of sessions and stimulation intensity). For cortical regions, regardless of stimulation polarity, significant reductions in OCD symptoms were observed in the lOFC as well as single effects reported for the lOFC + pre-SMA, medial PFC, and rDLPFC (Supplementary Fig. 5). However, as effect sizes derived from each target region are misleading due to the common practice of positioning anode and cathode electrodes on separate regions, we calculated effect sizes for each cortical region based on the stimulation polarity. The results show that only cathodal stimulation of the SMA (SMD = 0.52; $k = 11$; 95% CI, [0.16 to 0.87]; medium), regardless of anodal electrode placement and anodal stimulation of lDLPFC (SMD = 0.81; $k = 4$, 95% CI, [0.04 to 1.59]; large), regardless of cathodal electrode placement led to a significant reduction in OCD symptoms (Fig. 2b,c).

Next, analysis of stimulation frequency per day shows that both twice-daily (SMD = 0.83; $k = 10$; 95% CI, [0.44 to 1.23]; large) and once-daily (SMD = 0.42; $k = 11$; 95% CI, [0.06 to 0.78]; small) stimulation had a significant impact on reducing OCD symptom severity, albeit with large and small effects, respectively (Fig. 2d). Analysis of treatment duration (range 2 days, 5 days, 2 weeks, 3 weeks, 4 weeks, 6 weeks and 8 weeks), irrespective of target region or stimulation type/polarity, shows significant effects for 2-week tDCS (SMD = 0.60; $k = 9$; 95% CI, [0.06 to 1.13]; medium) and 5-day tDCS (SMD = 0.69; $k = 7$; 95% CI, [0.39 to 0.98]; medium). In 5-day tDCS studies, only 2 tDCS protocols had significant effects (SMD = 0.92; 95% CI, [0.04 to 1.80] for 1 mA; SMD = 0.99; 95% CI, [0.11 to 1.86] for 2 mA) and these protocols applied 10 tDCS sessions twice daily (Fig. 2e). In relation to this, we also analyzed the effect size obtained for total sessions (range 4, 10, 15, 20 and 24 sessions) regardless of treatment duration. Only the effect size of studies with 10 sessions (SMD = 0.52; $k = 13$; 95% CI, [0.20 to 0.84]; medium) and 20 sessions (SMD = 0.73; $k = 5$; 95% CI, [0.14 to 0.1.31]; medium to large) were significant (Fig. 2f). Finally, analysis of stimulation intensity (1 mA, 1.5 mA and 2 mA) showed a moderate effect size for 2-mA tDCS in reducing OCD symptoms (SMD = 0.57; $k = 20$; 95% CI [0.31 to 0.82]) (Fig. 2g).

In summary, meta-analysis of 23 effect sizes suggests a moderate overall impact of tES interventions on reducing OCD symptoms, and secondary analyses show significant effects of ctDCS of the SMA, atDCS of the lDLPFC, twice- and once-daily stimulation sessions, stimulation duration of 5 days and 2 weeks, total tDCS sessions of 10 and 20, and stimulation intensity of 2 mA for reducing OCD symptoms. To overcome the limitations of pairwise meta-analyses on specific tES protocols—such as pooled effect sizes that overlook stimulation parameters, sole reliance on behavioral measures, and focus of secondary analyses on a single parameter with low number of studies—we examined active treatment arms versus sham condition for reducing OCD symptoms (network meta-analysis) and assessed the correlation between behavioral changes in Y-BOCS and protocol-induced electrical fields (meta-modeling).

Network meta-analysis to identify superior tES interventions against sham

Twenty-five interventions from 17 tES RCTs (16 tDCS, 1 tACS) were initially included in the analysis. In addition to 1 study, due to publication bias[83], 5 interventions from 2 studies[51,80] had a non-sham control condition (for example, healthy volunteers or active control) and were excluded, which resulted in 14 RCTs with 18 interventions and 23 effect sizes. As the network analysis focuses on comparing treatment arms with sham conditions, we excluded these 3 interventions, lowering statistical heterogeneity from high ($\tau^2 = 0.25$, $I^2 = 60.1\%$; $Q = 5.01$,

Table 1 | Summary of included studies that investigated the effects of tES for OCD treatment

Number	Author	Design	*n* active and control	Mean age±s.d.	Female percentage	Electrode position and size (cm^2)	Intensity and duration	Total session	On medication	OCD measure	Secondary measure	Major finding
1	Kumar et al.[49]	RCT Parallel Single-blind Sham control	Active = 21 Sham = 22 DO = 3	Active = 32.20±8.51 Sham = 30.70±8.22	Active = 65% Sham = 45%	Cathode: left pre-SMA (FC1)/7×5 Anode: left DLPFC (F3)/7×5	2 mA 20 min	10 in 2 weeks (weekday, daily sessions)	Yes (≥1 week stable)	Y-BOCS	HAM-D, HAM-A	The active tDCS significantly reduced Y-BOCS scores at 2, 4 and 6 weeks compared with the sham. Treatment was well tolerated with mild side effects.
2	Chu et al.[51]	RCT Parallel Single-blind Active control	Active 1=6 active 2=6 active 3=6 DO = 0	Active 1 = 37.67±11.84 Active 2 = 35.83±13.32 Active 3 = 30.67±9.20	Active 1=13.3% Active 2=16.7% Active 3=33.3%	Active 1: Cathode: left OFC (Fp1)/7×5 Anode: right cerebellum (O2)/7×5 Active 2: Cathode: pre-SMA[d]/5×5 Anode: right deltoid/7×5 active 3 (2×1 tDCS): Cathode 1: pre-SMA[d]/5×5 Cathode 1: left OFC (Fp1)/7×5 Anode: right deltoid/7×5	2 mA 20 min	20 in 2 weeks (twice daily sessions separated by 1 h)	Yes (≥1 month stable)	Y-BOCS	HAM-D, HAM-A, WHOQOL, cognitive functions, EEG	Post-intervention, between-group Y-BOCS changes were not significant. Within-group reductions were observed for cerebellum–OFC (active 1) and OFC–pre-SMA (active 3), with OFC–pre-SMA showing the largest symptom decrease and increased frontal network connectivity. Mild adverse effects reported.
3	Agrawal et al.[48]	RCT Parallel Single-blind Sham control	Active = 10 Sham = 8 DO = 3	Active = 14.4±2.4 Sham = 14.3±2.5	Active = 50% Sham = 25%	Cathode: left SMA (FC1)/5×5 Anode: right deltoid/5×5	2 mA 20 min	10 in 2 weeks (weekday, daily sessions)	Yes (≥1 month stable)	CY-BOCS	RCADS-H	CY-BOCS scores significantly decreased from baseline to week 2 (study endpoint) only in the active group with a greater mean change vs sham group. No serious adverse effects reported.
4	Wang et al.[50]	RCT Parallel Double-blind Sham control	Active = 23 Sham = 21 DO = 3	Active = 27.04±7.38 Sham = 29.33±7.21	Active = 60.09% Control = 23.08%	4×1 tDCS Cathode: right OFC (FP2)/NR Anodes: (AF8, AF4, AFZ, FPZ)/NR	1.5 mA 20 min	10 in 2 weeks (weekday, daily sessions)	Yes (≥8 weeks stable)	Y-BOCS	BDI-II BAI OCI-R	Both active and sham improved OCD, depression, and anxiety scores with similar response rates (26.1% vs 23.8%). No active–sham difference
5	Harika-Germaneau et al.[46]	RCT Parallel Double-blind Sham Control 1.5- and 3-month follow-ups	Active = 40 Sham = 40 DO = 0	Sham = 41.1±11.5 Active = 43.0±12.7	Sham = 50% Active = 73.91%	Cathode: SMA[d]/7×5 Anode: right orbitofrontal (FP2)/7×5	2 mA 30 min	10 in 2 weeks (weekday, daily sessions)	Yes (≥8 weeks stable)	Y-BOCS	CGI-S, CGI-I, MADRS, BABS, BAS, HADS, GAF, SDS	A significant decrease in Y-BOCS scores was found over time, regardless of treatment arm. Specific changes in Y-BOCS scores related to tDCS were observed not immediately, but 3 months after the intervention. tDCS was well tolerated with no adverse events.
6	Echevarria et al.[51]	RCT Parallel Triple-blind Sham control	Active = 13 Sham = 10 DO = NR	Active = 34.4±10.8 Sham = 38.9±12.7	Active = 46% Sham = 80%	Cathode: SMA[e]/5×5 Anode: left deltoid 5×5	2 mA 30 min	20 in 4 weeks (weekday, daily sessions)	Yes (≥6 weeks stable)	Y-BOCS	BDI-II, BAI fMRI	Active tDCS, unlike sham tDCS, significantly reduced OCD symptoms and enhanced connectivity between the DMN, temporal area and SMA, with symptom reduction linked to functional connectivity changes. Side effects NR.

https://doi.org/10.1038/s44220-026-00590-z

Table 1 (continued) | Summary of included studies that investigated the effects of tES for OCD treatment

Number	Author	Design	*n* active and control	Mean age±s.d.	Female percentage	Electrode position and size (cm^2)	Intensity and duration	Total session	On medication	OCD measure	Secondary measure	Major finding
7	Alizadehgoradel et al.[45]	RCT Parallel Double-blind Sham control 1-month follow-up	2 mA = 13 1 mA = 12 Sham = 12 DO = 2	Active 1=28.46±7.04 Active 2=33.91±9.52 Sham = 32.66±7.67	Active 1=76.92% Active 2=66.66% Sham = 66.66%	Cathode: right pre-SMA (FC2)/7×5 Anode: left DLPFC (F3)/7×5	2 mA 1 mA 20 min	10 in 1 week (weekday, two daily sessions with 30-min interval)	Yes (≥6 weeks stable)	Y-BOCS	BDI-II, BAI, WHOQUL, response inhibition, memory, EEG	The 2-mA intensified tDCS produced greater symptom reduction and broader improvements (cognition/functional connectivity) than 1 mA and sham up to 1 month follow-up. tDCS well-tolerated with no adverse events.
8	Perera et al.[47]	RCT Parallel Double-blind Sham control 3-month follow-up	Active = 13 Sham = 12 DO = 8	Active = 36.31±14.43 Sham = 36.17±12.04	Active = 46.15% Sham = 58.33%	tACS Electrode 1: mPFC (AFz)/7×6 Electrode 2: Inion (Iz)/7×6 Frequency: individualized peak alpha frequency (IAF)	1.5 mA 30 min	24 in 6 weeks (15 two daily sessions + 9 single sessions)	Yes (≥6 weeks stable)	Y-BOCS	BAI, QIDS-SR Sternberg working memory, EEG	Alpha tACS over the medial PFC significantly improved OCD severity compared with sham treatment, with a trend towards sustained improvement at the 3-month follow-up. Side effects NR.
9	Fineberg et al.[44]	RCT Crossover Double-blind Sham control 28-day follow-up	Active 1=6 Active 2=7 Sham = 6 DO = 2	45±16.6	48.4%	Anode: right deltoid/NR Cathode: SMA (Fz)/NR Cathode: left OFC (Fp1)/NR	2 mA 20 min	4 in 2 days (12 total sessions, two daily) 4-week washout	Yes (≥6 weeks stable) *n*=15	Y-BOCS	MADRS, SDS, CGI-S, BIS	All arms showed numerical Y-BOCS improvement. The left OFC arm yielded the largest effect and additional secondary-outcome gains. Adverse effects were transient/mild with no serious adverse events.
10	Akbari et al.[78]	RCT Parallel Double-blind Sham control 1-month follow-up	Active 1=10 Active 2=10 Active 3=10 Sham=10 DO=NR	NR (18–45 years)	NR	Active 1, 2 and 3: Anode: right cerebellum (O2)/7×5 Active 1, 2 and 3: Cathode 1: pre-SMA (C3/C4)/7×5 Cathode 2: left OFC (FP1)/7×5 Cathode 3: left cerebellum (O1)/7×5	2 mA 15 min	10 in 1 week (weekday, daily sessions)	NR	Y-BOCS	–	All three protocols significantly reduced OCD symptoms compared with the sham group. Anodal tDCS left, cathodal right cerebellum tDCS resulted in greater symptom reduction. Side effects NR.
11	Silva et al.[84a]	RCT Parallel Double-blind Sham control 8-week follow-up	Active = 22 Sham = 22 DO = 3	Active = 38.41±10.95 Sham = 36.9±12.23	Active = 59% Sham = 62%	Anode: left deltoid/5×5 Cathode: SMA[a]/5×5	2 mA 30 min	20 in 4 weeks (weekday, daily sessions)	Yes (≥6 weeks stable)	Y-BOCS	BDI, BAI, SAFTEE, CGI-I	Active tDCS significantly improved Y-BOCS versus sham, without added benefit for depression/anxiety. Adverse events were mostly mild tp moderate.
12	Shafiezadeh et al.[83]	RCT Parallel NR Sham control	Active 1=10 Active 2=8 Sham = 6 DO=NR	NR	Active 1=30% Active 2=37.5% Sham = 16.66%	Active 1: Anode: right DLPFC (F4)/7×5 Cathode: left supraorbital (FP1)/7×5 Active 2: Anode: left DLPFC (F3)/7×5 Cathode: right supraorbital (FP2)/7×5	2 mA 15 min	10 in 1 week (weekday, two daily sessions with 10-min interval)	NR	Y-BOCS	DASS-21	Y-BOCS score, but not DASS score, significantly reduced after the intervention in the group that received anodal left DLPFC cathodal right frontopolar tDCS. Side effects NR.

https://doi.org/10.1038/s44220-026-00590-z

Table 1 (continued) | Summary of included studies that investigated the effects of tES for OCD treatment

Number	Author	Design	*n* active and control	Mean age±s.d.	Female percentage	Electrode position and size (cm^2)	Intensity and duration	Total session	On medication	OCD measure	Secondary measure	Major finding
13	Yoosefee et al.[86]	RCT Parallel Double-blind Sham control 1-month follow-up	Active = 28 Sham = 30 DO = 2	Active = 38.6±12.6 Sham = 35.9±11.5	Active = 86.7% Sham = 76.7%	Anode: left DLPFC (F3)/7×5 Cathode: right OFC (F8)/7×5	2 mA 20 min	24 in 8 weeks (3 days per week)	Yes (≥8 weeks stable)	Y-BOCS	–	Active tDCS+fluoxetine showed no significant difference compared with sham tDCS+fluoxetine. Both groups experienced a significant reduction of OCD symptoms. tDCS was well tolerated with no adverse events.
14	Gowda et al.[82]	RCT Parallel Double-blind Sham control	Active = 12 Sham = 13 DO = 0	Active = 30.83±5.87 Sham = 25.92±5.15	Active = 33% Sham = 0%	Anode: pre-SMA (Fz)/7×5 Cathode: right supraorbital (Fp2)/7×5	2 mA 20 min	10 in 1 week (weekday, 2 daily sessions with 3-h interval)	Yes (≥3 months stable)	Y-BOCS	CGI-S, CGI-I, HDRS, HARS	Significant therapeutic effect of active pre-SMA tDCS versus sham tDCS in patients with SSRI-resistant OCD. Lack of serious adverse effects and dropouts due to intolerance.
15	Bation et al.[79]	RCT Parallel Double-blind Sham Control 1&3-mo follow-up	Active = 10 Sham = 11 DO = 0	Active = 44.8±19.9 Sham = 41.2±11.9	Active = 80% Sham =36.36%	Anode: left OFC (FP1)/7×5 Cathode: right cerebellum[f]/7×5	2 mA 20 min	10 in 1 week (weekday, 2 daily sessions with 3-h interval)	Yes (≥6 weeks stable)	Y-BOCS OCD-VAS	GAF, MADRS, STAI-YA, CGI-I	Active tDCS significantly reduced OCD symptoms immediately post-treatment versus sham, but not at 1- or 3-month follow-ups. Transient and mild adverse effects. tDCS well-tolerated with no serious adverse events.
16	D'Urso et al.[72b]	RCT Crossover Double-blind Active control	Active 1=6 Active 2=6 DO = 2	37.9±10.2	50%	Active 1: Anode: pre-SMA/5×5 Cathode: right deltoid/7×5 Active 2: Anode: right deltoid/7×5 Cathode: Pre-SMA[d]/5×5	2 mA 20 min	10 in 2 weeks (weekday, daily sessions)	Yes (≥1 month stable)	Y-BOCS	SDS, attention (TAP), response inhibition	Cathodal but not anodal tDCS over the pre-SMA significantly improved OCD symptoms. Only a few mild side effects were observed.
17	Yekta et al.[85c]	RCT Parallel NR Sham control	Active = 10 Sham = 10	Active =27.5±NR Sham = 26.5±NR	NR	Anode: right DLPFC (F4)/7×5 Cathode: left DLPFC (F3)/7×5	2 mA 20 min	15 in 3 weeks (weekday, daily sessions)	NR	Y-BOCS	BAI, decision-making	Active tDCS significantly reduced Y-BOCS symptoms and improved decision-making compared with the sham. Side effects NR.

DO, dropout; NR, not reported; Y-BOCS, Yale-Brown obsessive compulsive scale; CY-BOCS, children's Yale-Brown obsessive compulsive scale; DMN, default mode network; MADRS, Montgomery-Asberg Depression Rating Scale; SDS, Sheehan Disability Scale; CGI-S, Clinical Global Impression Severity; CGI-I, Clinical Global Impression Improvement; GAF, Global Assessment of Functioning; OCI-R, Obsessive Compulsive Inventory-Revised; BAS, Brief Anxiety Scale; BABS, Brown Assessment of Beliefs Scale; HADS, Hospital Anxiety and Depression Scale; BIS, Barratt Impulsiveness Scale; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; SAFTEE, Systematic Assessment for Treatment Emergent Effects; HAM-D/HDRS, Hamilton Depression Rating Scale; HAM-A/HARS, Hamilton Rating Scale for Anxiety; OCD-VAS, OCD visual analog scale; STAI-YA, State-Trait Anxiety Inventory; TAP, Test of Attentional Performance; DASS-21, Depression Anxiety and Stress Scale; RCADS-H, Revised Child Anxiety and Depression Scale-Hindi adaptation; WHOQOL, WHO Quality of Life Questionnaire; QIDS-SR, Quick Inventory of Depressive Symptoms-Self Report; SSRI, serotonin reuptake inhibitor. [a]Dropouts include two patients who withdrew from the study in the middle of the trial and one exclusion due to deviation from the intervention. [b]This study administered tDCS interventions in two phases, with phase 2 being contingent on the results of phase 1 after ten sessions. Consequently, the sample size differed between phases, and phase 1 scores were included in the analysis. [c]Post-intervention scores on Y-BOCS retrieved by contacting the corresponding author and from the respective thesis. [d]Sagittal midline at 15% of the distance between inion and nasion anterior to electrode position Cz. [e]1.5 cm anterior to electrode position Cz. [f]3 cm below the inion and 1 cm right of the midline.

https://doi.org/10.1038/s44220-026-00590-z

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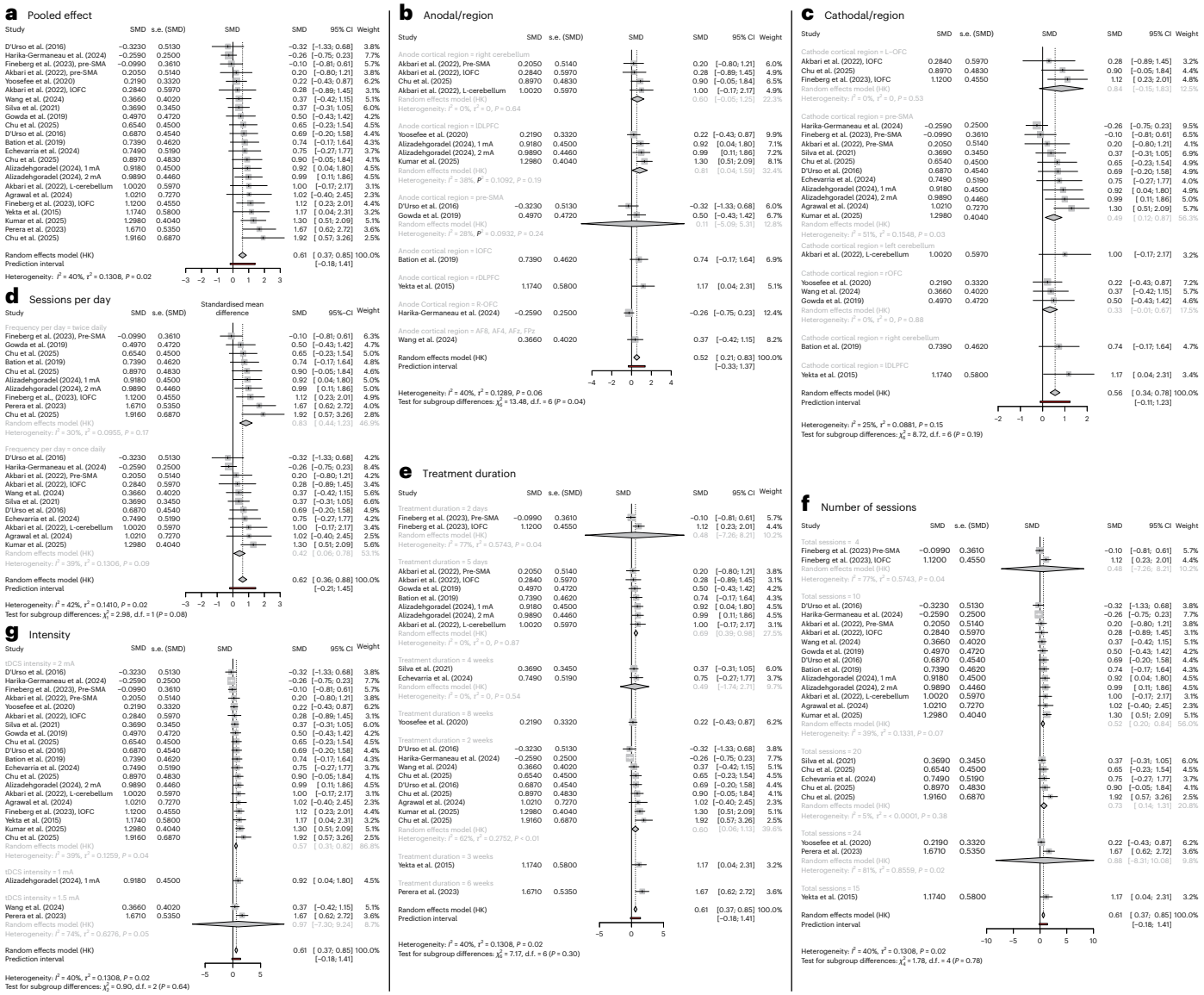


Fig. 2 | Pairwise meta-analysis of the tES interventions' effect sizes for reducing OCD symptoms. a, Forest plot showing pooled effect sizes of tES interventions[44–51,78–82,84–86] ($n = 16$, $k = 23$) with SMD, 95% CIs and measures of heterogeneity (SMD = 0.61; 95% CI, [0.37 to 0.85]; heterogeneity, $I^2 = 40\%$, $\tau^2 = 0.131$, $P = 0.02$). **b**, Forest plot of pooled and single effect size for anodal tDCS interventions over cortical regions ($k = 14$) including SMD and 95% CIs and measures of heterogeneity (SMD = 0.52; 95% CI, [0.21 to 0.83]; heterogeneity, $I^2 = 40\%$, $\tau^2 = 0.129$, $P = 0.06$). **c**, Forest plot of pooled and single effect size for cathodal tDCS interventions over cortical regions ($k = 20$), including SMD, 95% CIs and measures of heterogeneity (SMD = 0.56; 95% CI, [0.34 to 0.78]; heterogeneity: $I^2 = 25\%$, $\tau^2 = 0.088$, $P = 0.15$). **d**, Forest plot of pooled effect sizes for tES intervention at twice-daily ($k = 10$) versus once-daily ($k = 11$) frequency, including SMD, 95% CIs and measures of heterogeneity (SMD = 0.62; 95% CI, [0.36 to 0.88]; heterogeneity: $I^2 = 42\%$, $\tau^2 = 0.141$, $P = 0.02$). **e**, Forest plot of pooled and single effect size for treatment duration of 2 days ($k = 2$), 5 days or 1 week ($k = 7$), 2 weeks ($k = 9$), 4 weeks ($k = 2$) and 8 weeks ($k = 1$) of tES interventions (both tDCS and tACS), including SMD and 95% CIs and measures of heterogeneity (SMD = 0.61; 95% CI, [0.37 to 0.85]; heterogeneity: $I^2 = 40\%$, $\tau^2 = 0.131$, $P = 0.02$). **f**, Forest plot of pooled and single effect size for total sessions of 4 ($k = 2$), 10 ($k = 13$), 15 ($k = 1$), 20 ($k = 5$) and 24 ($k = 2$) of tES interventions (both tDCS and tACS), including SMD, and 95% CIs and measures of heterogeneity (SMD = 0.61; 95% CI, [0.37 to 0.85]; heterogeneity: $I^2 = 40\%$, $\tau^2 = 0.131$, $P = 0.02$). **g**, Forest plot of pooled and single effect size for stimulation intensity of 1 mA ($k = 1$), 1.5 mA ($k = 2$) and 2 mA ($k = 20$) in tES interventions, including SMD, 95% CIs and measures of heterogeneity (SMD = 0.61; 95% CI, [0.37 to 0.85]; heterogeneity, $I^2 = 40\%$, $\tau^2 = 0.131$, $P = 0.02$). SMD values were calculated using the Morris method. Larger SMD values indicate a larger reduction of OCD symptoms (measured by Y-BOCS). *n* represents the number of tES studies and *k* represents the number of effect sizes included in the main and secondary analyses. Squares represent individual study effect, diamonds represent pooled effect and lines represent CIs. SMD, standardized mean difference; CI, confidence interval; HK, Hartung-Knapp adjustment for random-effect meta-analysis.

$P = 0.08$) to low ($\tau^2 = 0.0$, $I^2 = 0$; $Q = 0.88$, $P = 0.35$). Figure 3a shows the network structure of the treatment arms for the primary outcomes (Y-BOCS). A total of 270 participants received the sham intervention and 264 were assigned to various tES interventions, including 1 alpha tACS and 15 tDCS interventions.

The following tES protocols significantly reduced OCD symptom severity compared with the sham control in descending order of effect size: peak alpha tACS over medial PFC (SMD = 1.67; 95% CI, [0.62 to 2.72]), ctDCS pre-SMA + atDCS lDLPFC (SMD = 1.30; 95% CI, [0.51 to 2.09]), ctDCS-lOFC + atDCS shoulder (SMD = 1.24; 95% CI, [0.39 to 2.10]), atDCS lDLPFC + ctDCS rDLPFC (SMD = 1.17; 95% CI, [0.04 to 2.31]), and atDCS lDLPFC + ctDCS pre-SMA at 2 mA (SMD = 0.99; 95% CI, [0.11 to 1.86]) and at 1 mA (SMD = 0.92; 95% CI, [0.04 to 1.80]) (Fig. 3b). We further analyzed the surface under the cumulative ranking (SUCRA)

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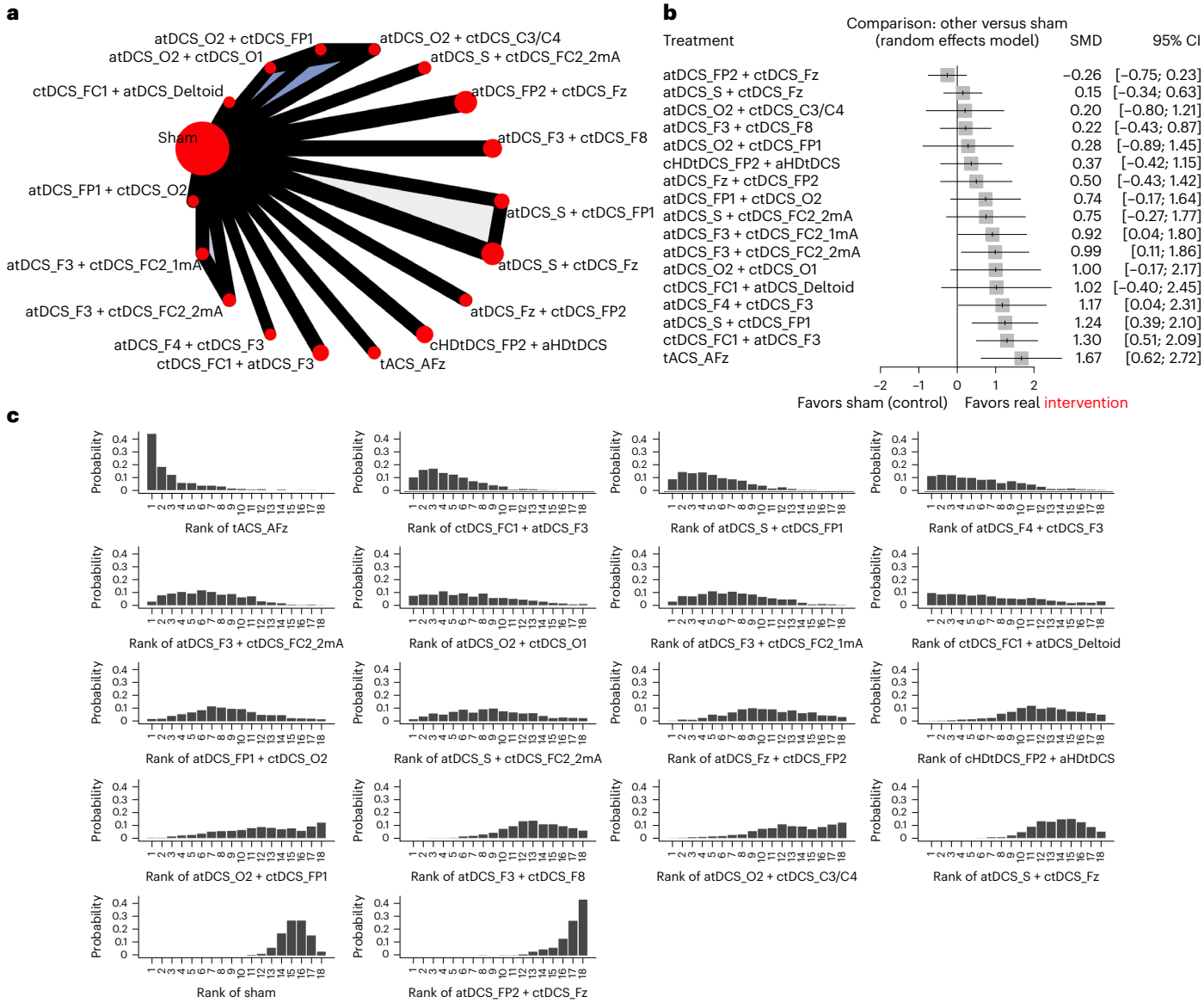


Fig. 3 | Network meta-analysis of tES interventions efficacy versus sham control on OCD symptoms reduction (*n* RCTs = 14). a, Network structure of the primary outcome. Each node represents a different tES intervention including sham ($n = 18$), with the size of the node proportional to the number of treatments. The edges between nodes represent direct comparisons between treatments ($n = 23$), with the thickness of the edges indicating the precision of the estimates (thicker lines represent smaller standard errors). The arrangement of nodes is optimized to enhance clarity. **b**, The network meta-analysis forest plot shows the SMD and 95% CIs for each treatment ($n = 17$) compared with the sham control ($n = 1$) in reducing OCD symptoms. Positive effect sizes indicate a greater reduction in OCD symptoms compared with sham. Squares represent individual study effect and lines represent CIs. **c**, Network ranking plots with each subplot representing the probability distribution of ranks for different treatments in the network meta-analysis. Higher probabilities at lower ranks indicate better treatment performance. The rankograms illustrate comparative effectiveness, with tACS_AFz showing the highest likelihood of being the most effective treatment, as reflected by its high SUCRA score, while the sham condition shows lower effectiveness as methodologically expected. We adopted the terminology from the papers for describing target regions which may not accurately explain the actual target region. Here is the clarification: Fz, FC1/FC2 and C3/C4 represent the supplementary and pre-SMAs; Fp1 denotes the lOFC and Fp2/F8 refers to the right OFC; F3 and F4 represent the lDLPFC and the rDLPFC, respectively. O1 and O2 represent the left and right cerebellum, respectively. AFz refers to the medial PFC. atDCS, anodal transcranial direct current stimulation; ctDCS, cathodal transcranial direct current stimulation; tACS, transcranial alternating current stimulation.

percentages representing the mean rank of interventions compared with an idealized hypothetical one based on 1,000 simulations. Among the top-7 interventions (>60% SUCRA) for reducing OCD severity, the above protocols ranked first (89.05%), second (78.56%), third (75.49%), fourth (72.72%), fifth (66.06%) and eighth (63.16%), respectively. In addition, interventions such as atDCS-O2 + ctDCS-O1 (SMD = 1; 64.55%), and ctDCS pre-SMA + atDCS shoulder (SMD = 1.02; 63.95%), ranked sixth and seventh for reducing OCD severity, showing promise for further study (Fig. 3c and Supplementary Tables 2 and 3).

Meta-modeling analysis of correlations between tDCS-induced electrical field and treatment response

The meta-modeling analysis was carried out on tDCS studies ($n = 16$) as this modeling approach is based on a consistent tDCS-induced polarity-dependent electrical field (while tACS electric fields have fluctuating polarities). The results show that tDCS is most effective in treating OCD symptoms if the electric fields target the medial prefrontal and frontopolar cortices (maximum performance–electric field correlation (PEC_E) = 0.351, $P = 0.046$, explained variance = 12.3%; Fig. 4a,

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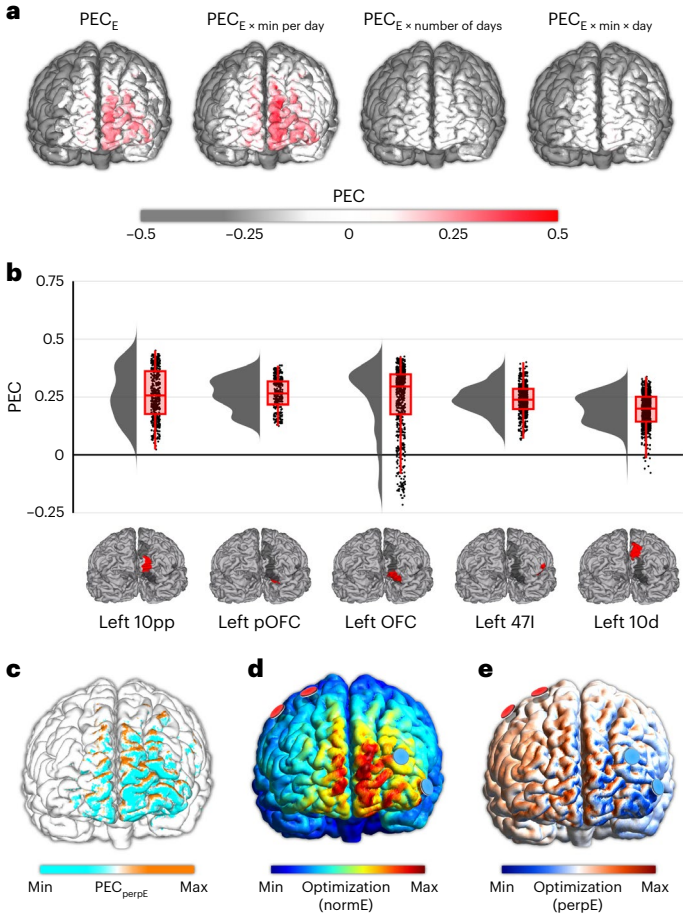


Fig. 4 | Meta-modeling analysis. a, PEC maps for correlations between effect size and electric-field strength (first map), cumulative charge in one session ($E \times$ min per day; second maps), cumulative charge across treatment days ($E \times$ number of days; third map), and total cumulative charge ($E \times$ min $\times$ day; fourth map). Color gradients indicate correlation strength: darker shades signify stronger positive correlations with symptom improvement, while lighter shades indicate negative correlations. **b**, The five functional brain regions (HCP-MMP atlas) with the largest average PEC$_{E \times min\ per\ day}$ values. Individual dots represent correlation values per brain model element within a region. Black dots represent individual correlation values per gray-matter element. The horizontal bar shows the median, the upper and lower boundaries show the 25th and 75th percentiles, respectively, and the whiskers show 5th–95th percentiles. **c**, Correlation between effect sizes and the perpendicular component of the electric field (PEC$_{perpE}$). The current direction follows an inward-to-outward (orange-to-blue) path. The most positive correlation between inward currents (perpE > 0) and effect sizes on the right flanks of gyri suggests a right-to-left current flow is associated with improvements in OCD symptoms. Gradient represents correlation with effect sizes; positive values (warmer shades per embedded color-bar key) indicate inward current flow associated with symptom improvement. **d**, An optimized montage showing the electric-field strength (normE) for improving OCD symptoms with tDCS. Anodes are shown in red and cathodes are shown in blue. Note that the largest normE values correspond to the largest PEC values as shown in **a**. **e**, The same as in **d**, but in this case, the perpendicular component of the electric field (perpE) is shown. Note that this distribution is similar to the one shown in **c**. 10pp, polar area 10; pOFC, posterior orbitofrontal cortex; OFC, orbitofrontal cortex; 47l, lateral area 47; 10d, dorsal area 10 according to the HCP-MMP atlas. PEC$_E$, performance–electric field correlation; normE, magnitude of the simulated electric field; perpE, perpendicular field component.

first map). This was most strongly observed in the left hemisphere. The positive relationship between electric-field strength and effect size was even more pronounced when considering stimulation duration per treatment session (maximum PEC$_{E \times min\ per\ day}$ = 0.369, P = 0.038, explained variance = 13.2%, Fig. 4a, second map). Conversely, when the number of treatment days was taken into account, the relationship between electric fields and effect sizes did not reach significance (maximum PEC$_{E \times number\ of\ days}$ = 0.209, maximum PEC$_{E \times min \times day}$ = 0.311, P > 0.05, Fig. 4a, third and fourth maps). Together, these results based on the included studies suggest that while longer stimulation durations at a given day benefit the therapeutic effect, longer total number of days of treatment may not.

Subsequently, we mapped the functional regions associated with the largest effects associated with the PEC$_{E \times min\ per\ day}$ results using the Human Connectome Project multimodal parcellation (HCP-MMP) atlas[87,88]. Better treatment response was mostly associated with stimulation of the left dorsomedial PFC and OFC, corresponding to Brodmann areas 10, 11 and 47 (Fig. 4b). Finally, we used the PEC maps to suggest an optimized montage for tDCS based on the computational modeling results. Crucially, the current direction determines the placement of anodal and cathodal electrodes. Therefore, the PEC value was calculated for the perpendicular component of the electric field, which indicates the direction of current flow (from the anode (inward currents) to the cathode (outward currents); Methods). We found that a current flow from the right to the left PFC was positively correlated (PEC$_{perpE}$) with effect sizes, while a current flow from the left to the right PFC was negatively correlated with effect sizes (Fig. 4c). As such, a positive treatment outcome would follow from right-atDCS targeting the DLPFC and left-ctDCS targeting the frontopolar cortex (including the OFC and the ventromedial PFC (vmPFC)). The exact montage was modeled and resulted in anodes over F4 and F2 (1 mA each) and cathodes over AF3 and AF7 (−1 mA each), as shown in Fig. 4d,e.

Risk of bias and publication bias

Supplementary Fig. 6 presents the overall and individual risk of bias assessment results for the studies. Most included studies showed low (n = 8) to moderate (n = 8) risk of bias, while one (n = 1) showed high risk due to the randomization process. We marked six studies with 'other bias' for not using or reporting side-effect surveys. Only one study examined blinding efficacy[47]. However, we did not label the others with 'other bias', as the updated CONSORT guidelines do not recommend evaluating blinding efficacy[89].

Publication bias was assessed using funnel plots (Supplementary Fig. 7a,b) and Egger's test of the intercept, which indicated significant asymmetry (intercept = 3.386; 95% CI, [1.74–5.03]; t = 4.023; P = 0.0006). We additionally used the P-curve method to evaluate evidential value and identify potential P-hacking. Of the included studies, 7 (30.43%) reported P < 0.05 and 4 (17.39%) reported P < 0.025. The full P-curve showed no significant right-skewness (zFull = −1.317; pFull = 0.094), whereas the lower half was significantly right-skewed (zHalf = −1.876; pHalf = 0.03), indicating evidential value. The flatness test confirmed evidential value, as there was no flat distribution. The P-curve's estimate of the true effect size (d = 0.508) was close to the meta-analytic estimate (SMD = 0.612), but the estimated statistical power was low (23%; 95% CI, 5–67.5%). These findings suggest that, despite small-study effects, the evidence base contains genuine effects, although the low power of individual studies warrants cautious interpretation.

Discussion

This study uses three distinct meta-analytic approaches to evaluate the efficacy of tES interventions for treating OCD symptoms. Different meta-analytic approaches were used to evaluate different aspects of treatment efficacy (for example, pooled effects, the effectiveness of interventions versus sham treatments, the ranking of promising interventions, the correlation between symptom reduction and induced electrical fields, and the prediction of optimized interventions) that cannot be obtained by one single analysis. Our analysis of 23 tES experimental conditions reveals a significant medium pooled effect size for reducing OCD symptoms (Fig. 5a). This effect is particularly strong

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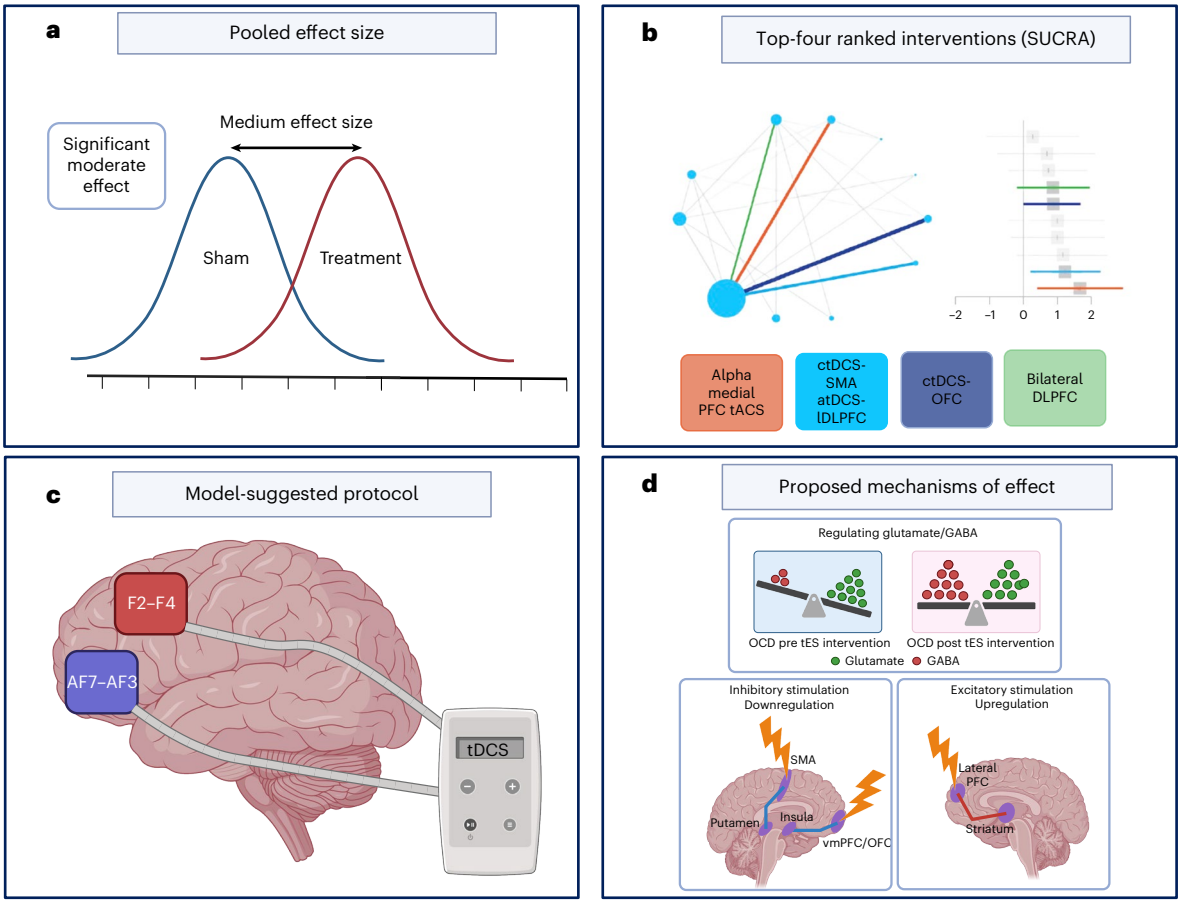


Fig. 5 | Efficacy of tES interventions for OCD treatment. a,**b**, Major findings of pairwise (**a**) and network (**b**) meta-analyses (for detailed results see Figs. 2 and 3). **c**, Model-estimated and suggested tES intervention based on computational modeling with atDCS over F2–F4 coupled with cathodal AF3–AF7. **d**, Proposed mechanisms of tES effects on reducing OCD severity by regulating glutamate/GABA levels, upregulating the prefrontal–striatum pathway, and downregulating the SMA–putamen and medial PFC–insula pathways. vmPFC, ventromedial prefrontal cortex; vlPFC, ventrolateral prefrontal cortex; DLPFC, dorsolateral prefrontal cortex; SMA, supplementary motor area; OFC, orbitofrontal cortex; tDCS, transcranial direct current stimulation; GABA, gamma-aminobutyric acid. Schematic diagrams and workflow illustrations were created with Microsoft Powerpoint and BioRender.com.

for interventions that primarily downregulate the SMA and the OFC and upregulate the lDLPFC with cathodal and anodal stimulation, respectively, with a large effect size for twice-daily stimulation per day, and moderate effect for 5-day, 2-week, 10-session and 20-session interventions, and stimulation intensity of 2 mA. The top tES interventions, compared with sham conditions, were alpha tACS over the medial PFC, cathodal SMA-anodal lDLPFC tDCS, ctDCS of the OFC, and bilateral anodal right DLPFC tDCS (Fig. 5b). Finally, our computational analyses of behavior–electrical-field correlations, in line with results of network meta-analysis, show that tDCS is more effective when targeting the medial PFC and frontopolar cortex, particularly when session durations are longer. This analysis further suggests anodal stimulation of the right lateral and medial PFC cortices (F2–F4), combined with cathodal stimulation of the left frontopolar cortex (AF3–AF7), may more effectively reduce OCD severity due to larger PEC values, indicative of gray-matter modulation (Fig. 5c). We discuss key findings regarding OCD pathophysiology and stimulation parameters, evaluate the therapeutic efficacy of tES for treating OCD, and conclude with a discussion of promising future tES interventions.

OCD pathophysiology and tES intervention

Although the pathophysiology of OCD is complex and not fully understood, functional and structural abnormalities in the cortico–striato–thalamo–cortical (CSTS) circuits are well documented[90–92]. At the cortical level, DLPFC, medial PFC, OFC, anterior cingulate cortex (ACC), SMA and pre-SMA are critical regions within CSTS circuits characterized by altered functional and structural connectivity[92–94]. Specifically, overactivity in the OFC, medial PFC and SMA coupled with hyperconnectivity with subcortical regions is prominent in OCD[92]. At chemical levels, excitatory and inhibitory neurotransmitter systems (for example, glutamate, GABA) show imbalanced activity in patients with OCD compared with healthy controls[33]. The effectiveness of tES interventions in alleviating OCD symptoms can be attributed to at least two explanations related to the functional, structural and chemical abnormalities within CSTS circuits (Fig. 5d).

First, restoring and/or rebalancing functional abnormalities is the primary mechanism of effect for tES interventions. According to the multifaceted neural circuit theory of compulsivity[92], three cortico–subcortical networks are involved in OCD-related pathophysiology (and behavior) that can be modulated by tES intervention. A hyperconnectivity and hyperactivity of medial OFC and vmPFC circuits that have projections to the ventral striatum and caudate is observed in patients with OCD, leading to compulsions and exaggerated habits against goal-directed behaviors. A similar hyperconnectivity is seen in the SMA–putamen network, which is also linked to compulsions. In contrast, hypoconnectivity in the lateral frontal–striatal network affects top-down executive control, and this loss contributes to the shift from goal-directed behavior to compulsive habits in OCD. Therapeutic effect of tES interventions that downregulate SMA and OFC activity (for example, ctDCS of the SMA and the OFC) can thus be due to modulating hyperactivity in these regions and their subcortical projections (for example, putamen, insula). A similar therapeutic effect is reported

for low-frequency rTMS of the SMA[95]. Another source of effect for tES interventions is related to upregulation of both lDLPFC and the rDLPFC with anodal stimulation, which is again in line with therapeutic effects of high-frequency rTMS over the bilateral DLPFC[95]. Accordingly, the top-four tES interventions identified in our network analysis aimed either to downregulate the SMA, OFC and medial PFC, or to upregulate the DLPFC. Nonetheless, this explanation is speculative owing to the lack of pre- and post-tES neuroimaging data, and altered connectivity may vary with brain state (for example, resting versus task functional MRI (fMRI)). For instance, in atDCS-fMRI study, anodal stimulation of the frontopolar region reduced negative connectivity between the medial PFC and the right insula/putamen and increased its connectivity with the medial and superior frontal gyri in OCD[96]. Although these changes were linked to improved safety learning, no anxiolytic effects of anodal frontopolar tDCS were observed.

The second explanation relates to the imbalanced levels of glutamate and GABA in key OCD regions, which are the major neurometabolites underlying the tES mechanism of effects. A recent study with 7 T proton magnetic resonance spectroscopy found that glutamate levels in the SMA correlated with the Y-BOCS compulsivity subscale and with measures of habitual responding in patients with OCD compared with healthy controls[33]. Excessive levels of glutamate and reduced levels of GABA in the ACC, and a correspondingly enhanced glutamate:GABA ratio (and hence altered excitatory:inhibitory balance), were also associated with enhanced habitual responding in these patients. Also, the excitatory/inhibitory effects of tES are linked to changes in glutamate and GABA concentrations. MRS studies showed a glutamate reduction after ctDCS and enhancement after atDCS while both atDCS and ctDCS reduce GABA[97–99]. Pharmacological studies using N-methyl-D-aspartate (NMDA) receptor blockers and GABA agonists have also shown that after effects of atDCS/ctDCS and tACS are dependent on NMDA-receptor activity[100,101]. Thus, the efficacy of cathodal SMA tDCS may be partly due to balanced glutamate levels following the intervention. The therapeutic effects of tES interventions targeting the medial PFC, a key area in our predicted montage from the third analysis, can also be partially attributed to the modulation of glutamate and GABA in the hyperactive ACC[92], which plays a role in conflict monitoring and inhibitory tasks in patients with OCD and receives projections from the medial PFC[94,102].

Stimulation parameters and therapeutic efficacy

Optimizing tES interventions is crucial for effectively changing cortical activity, restoring brain excitability and balancing imbalanced functions in OCD. Systematically investigating different parameters such as treatment duration, stimulation repetition and stimulation intensity is important for evaluating the efficacy of tES interventions. Although this is not sufficiently addressed in current tES RCTs (only five studies examined effects of different intensities[45], polarity[80] and target regions[44,51,78,83]), our results are still informative in some aspects. For cortical targeting, downregulation of the SMA and the OFC, upregulation of the DLPFC, and entrainment of brain oscillations in the medial PFC yielded promising results, which align with rTMS meta-analyses[37,103,104]. The predicted optimized configuration based on symptom reduction effect size and induced electrical fields more specifically suggests upregulation of the rDLPFC and the medial PFC with anodal and downregulation of left frontopolar cortex (including OFC) with cathodal stimulation. Regarding stimulation intensity, 2 mA was the most commonly utilized dosage. Although the only reported RCT using 3 mA tDCS over the inferior frontal cortex showed limited efficacy for OCD treatment[105], it remains unclear whether higher intensities (for example, ≥4 mA), delivered within established safety guidelines, improve outcomes, and this warrants further evaluation[14,106,107].

Another important stimulation parameter was the relevance of stimulation frequency per day for reducing OCD symptoms. Our pairwise analysis showed a large therapeutic effect for twice-daily tES sessions versus the small yet significant effects for once-daily sessions. In relation to this, our meta-modeling showed that longer stimulation durations on a given day, rather than an increased number of sessions, yield greater therapeutic effects. These findings align with recent meta-analyses of rTMS RCTs, which found that longer rTMS sessions, rather than more overall sessions, are associated with larger clinical improvement[37,103] and are further in line with the efficacy of accelerated rTMS (involving two or more sessions per day with short inter-session intervals) for OCD treatment[108]. Here it is noteworthy that twice-daily 3 mA tDCS over the inferior frontal cortex showed limited efficacy for OCD treatment[105], suggesting that intensifying tDCS beyond 2 mA may not improve outcomes, as shown in the human motor cortex[109]. Both 1-week and 2-week interventions showed significant therapeutic effects, unlike the 4-week intervention, a finding consistent with a recent rTMS meta-analysis[103] but requiring cautious interpretation due to the limited number of studies with 4-week intervention[103].

In sum, systematic investigations of tES parameters are crucial for optimizing interventions and enhancing therapeutic effects, which is currently insufficient. In addition to stimulation parameters, different OCD subtypes (for example, compulsive or obsessive) should be considered for protocol development (due to different pathophysiological profiles and circuitry[92]), which has not been investigated by current tES interventions. Finally, it is essential for future tES studies to standardize their designs and report intervention protocols in accordance with the recently published Report Approval for Transcranial Electrical Stimulation (RATES) checklist[110]. This approach enhances the interpretability and reproducibility of findings while enabling more effective comparisons between tES studies.

Therapeutic efficacy of tES interventions for OCD treatment

rTMS, the most used NIBS modality in clinical settings, is FDA-approved for treating OCD[12]. tES interventions follow a similar rationale for modulating OCD-related brain abnormalities, yet are more easily portable, more affordable, have fewer side effects and are home usable, suggesting them as a potentially first-line NIBS treatment[111] if proved effective. Our analysis showed that tES interventions show significant moderate therapeutic effects, comparable to the moderate efficacy reported for rTMS in recent meta-analyses (Hedges' $g = 0.50$ to 0.65)[37,95,103,112]. While this pooled medium effect shows promise, it is somewhat limited due to the heterogeneity of tES protocols and the small number of similar protocols used for OCD treatment, which is the reason we did a three-level analysis. Our network meta-analysis and specifically meta-modeling analysis suggest that tES interventions with specific stimulation configurations (downregulating OFC, medial PFC and SMA) may hold promise, as discussed above. The few available tACS RCTs have also shown promising effects of alpha and beta-gamma tACS over the medial PFC and OFC[47,113] and very promising results were also reported for gamma tACS for OCD treatment[114,115]. Future tES studies are required to assess the efficacy of promising interventions, and our model-suggested anodal F2–F4/cathodal AF3–AF7 protocol. With more tES studies emerging, analyzing clinical predictors of tES responses[116,117] and meta-regression analyses of tES predictors of response will help maximize its efficacy.

Potential tES interventions and approaches for OCD treatment

Despite variations in design and stimulation parameters, the tES interventions included in this analysis can be broadly classified as downregulatory (for example, SMA/OFC ctDCS) or upregulatory (for example, DLPFC atDCS). They still need to be evaluated in larger trials, yet other potential tES interventions can be inferred from the recent OCD pathophysiology framework[92]. The ventrolateral PFC (VLPFC) is a key region showing reduced connectivity with the caudate in OCD and is linked to impaired cognitive flexibility[118]. A recent study also confirmed its hypoconnectivity with the dorsal putamen[119]. In another

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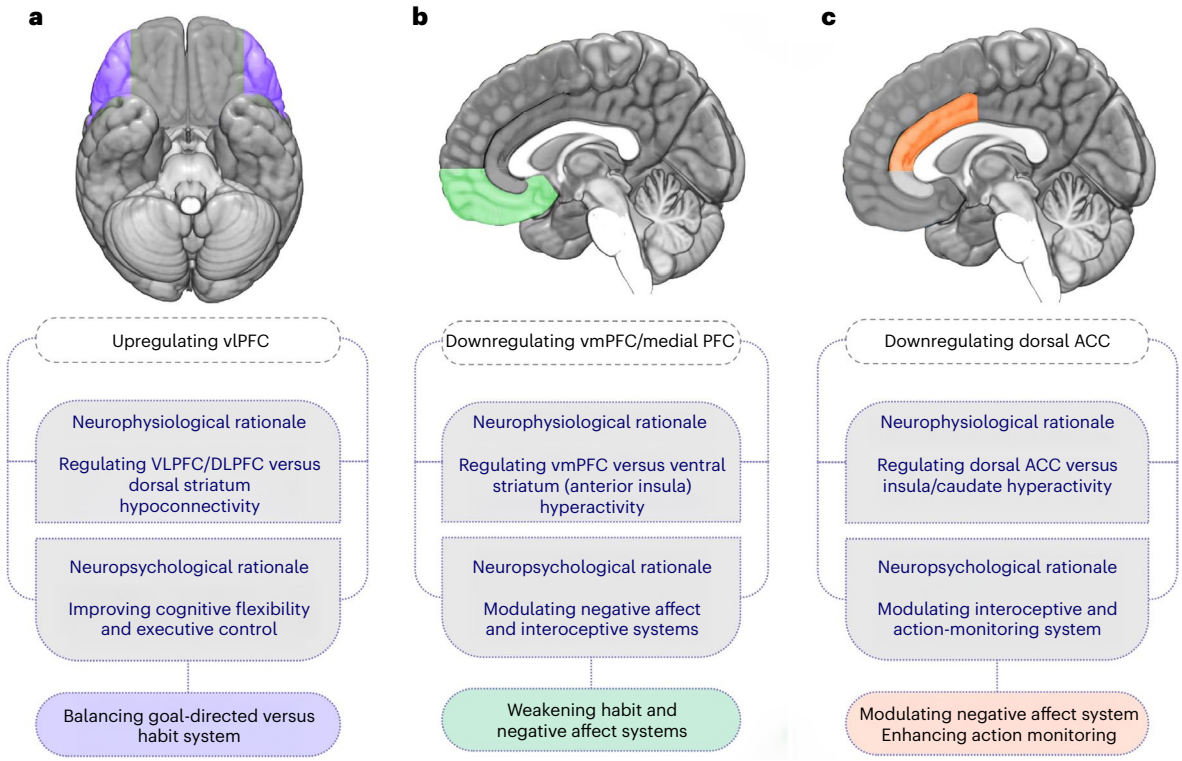


Fig. 6 | tES interventions with therapeutic potential. OCD features a complex pathophysiology involving various cortical and subcortical regions that influence disease severity. Neuropsychological and cognitive deficits are integral to OCD psychopathology and closely linked to its pathophysiology. According to the latest framework about OCD psychopathology and pathophysiology[92], several regions can be targeted by tES and other NIBS interventions. **a**, The VLPFC, an important region for the executive control system, is often hypoactive in OCD. This diminishes influence over the dorsal striatum and habit system, which can lead to compulsive behaviors. Enhancing VLPFC activity (for example, with atDCS) may benefit OCD by strengthening goal-directed behavior. **b**, The vmPFC is typically hyperactive in OCD. A downregulatory tES intervention targeting the medial PFC could alleviate negative feelings and urges to act by modulating the insula and caudate. **c**, The dorsal ACC, which is involved in action monitoring and interoceptive feelings through its connections to the insula, is also hyperactive in OCD. This hyperactivity can hinder action monitoring and amplify interoceptive urges, leading to compulsions. A downregulatory tES intervention on the dorsal ACC may help regulate these urges and improve action monitoring, potentially reducing compulsions. vmPFC, ventromedial prefrontal cortex; vlPFC, ventrolateral prefrontal cortex; ACC, anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex. Brain surface renderings are based on the MNI152 nonlinear 2009 (ICBM152) standard template.

recent study[120], reduced activity in the inferior frontal gyrus (including the VLPFC), alongside its hypoconnectivity with the putamen and the SMA, was linked to impaired prefrontal arbitration process and this was correlated with OCD severity. Accordingly, reduced activity and connectivity of the VLPFC with the dorsal striatum (caudate and putamen), associated with cognitive flexibility impairments, suggests that enhancing VLPFC activity via tES (for example, anodal tDCS) may help lower OCD severity by enhancing goal-directed behaviors over habitual ones (Fig. 6a). This was demonstrated in our recent study, where anodal tDCS over the dorsolateral PFC, combined with cathodal pre-SMA stimulation, improved inhibitory control and reduced attention bias toward OCD-related stimuli while reducing symptom severity in patients with OCD[45].

Two additional potential interventions relate to the downregulation of the medial PFC, vmPFC and the modulation of dorsal ACC activity (Fig. 6b,c). Symptom provocation fMRI studies typically showed enhanced activation of the vmPFC[121,122] and the ACC[123,124] in OCD. This activation correlates with hyperconnectivity to the ventral striatum and particularly the insula, which plays a role in negative interoceptive experiences and subjective urges to action in OCD[92,119,125]. Downregulating vmPFC and dorsal ACC may reduce negative interoceptive feelings that drive compulsive behaviors, consistent with a recent network meta-analysis showing that inhibitory rTMS of medial PFC and anterior ACC are more effective than sham interventions[104]. However, evidence supports the effectiveness of deep high-frequency rTMS over the medial PFC and ACC[36]. This is partly due to difficulty in precisely defining the vmPFC, which can contain elements of several Brodmann areas—14, 25, 32 and 24—and some controversy on whether this region is generally hyperactive or hypoactive in OCD[126,127]. Nevertheless, these proposed interventions are grounded in neuroimaging findings and merit exploration in future studies (For a detailed review of the empirical background supporting these interventions, see ref. 92).

Looking ahead, home-based tES[128], a unique advantage of tES versus rTMS, offers a promising avenue for ongoing treatment in natural settings, reducing anxiety-provoking clinic visits. Preliminary evidence from the only tACS study included in our analyses, which was delivered at home, suggests that tES can significantly alleviate OCD symptoms, with sustained effects observed at follow-up[47] in line with recent works on depression[129]. Similarly, closed-loop tES[130,131], adapting stimulation based on neural biomarkers, could further optimize efficacy by targeting dynamic symptom states such as obsessive ruminations. While primarily used in invasive neuromodulation[132], these adaptive systems can inspire non-invasive tES innovations for precise, on-demand interventions aligned with real-world symptom fluctuations. Future research should focus on large-scale trials to validate these modalities, assess long-term safety and integrate them with existing therapies for optimized and personalized tES[106,113,133] for OCD treatment.

Study strengths, limitations and conclusion

Our study comes with several strengths. It pioneers the use of a three-level meta-analysis in the NIBS field to assess the therapeutic efficacy of tES for OCD, offering a new perspective on evaluating NIBS

therapeutic efficacy. In addition, it incorporates the latest literature, includes more RCTs and excludes studies with bias, thereby improving statistical power. Sub-analyses of stimulation parameters, some of which are being explored for the first time (for example, stimulation frequency per day), are other innovative aspects of our work. Yet, several limitations exist. First, pairwise and network analyses are based on heterogeneous studies, and the findings across analyses require careful consideration due to potential overlap (for example, the model-optimized protocol excluded the SMA region). Next, the meta-modeling results on stimulation duration in tDCS efficacy rely on varying durations and frequencies. Lastly, we did not perform meta-regression to examine the influence of study-level characteristics on effect size because it was beyond our study's scope. Furthermore, the limited number of studies and inconsistent reporting of covariates made a robust meta-regression infeasible. This will remain an open research question for future systematic reviews and meta-analyses with larger, more consistent datasets. These limitations stem from the diversity of tES interventions, which could be addressed by more published RCTs; thus, current findings should be interpreted cautiously.

To conclude, this triple meta-analysis integrates three complementary meta-analytic approaches to provide a comprehensive analysis of eligible tES studies used to reduce OCD severity. Our results suggest that interventions that downregulate the OFC, medial PFC and SMA, or upregulate the lateral PFC show promise. Our analysis shows that tES is both safe and well tolerated in patients with OCD. However, many of the included studies implement strict inclusion criteria, often excluding individuals with multiple physical comorbidities, older adults or those at higher risk. Furthermore, in some studies conducted in low- and middle-income countries, patients unable to tolerate the intervention may be excluded. This underscores the importance of thoroughly examining the potential adverse effects of tES in patients with OCD. Future studies may build on findings from our pairwise, network and meta-modeling analyses, as well as the additional tES interventions with potential for OCD treatment (Fig. 6), to improve current tES protocols and investigate more effective modalities.

Methods

General study guidelines

This meta-analysis adhered to the latest update of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[134]. The study protocol was registered in PROSPERO (CRD42023485717).

Search strategy and eligibility criteria

Two authors (M.A.S. and A.H.-H.) systematically searched multiple electronic databases, including PubMed, Embase, Web of Science, Cochrane CENTRAL and Scopus, from the inception of each database until 31 July 2025. The search terms included: ['obsessive compulsive disorder' OR 'OCD' OR 'obsessive disorder' OR 'compulsive disorder'] AND ['transcranial electrical stimulation' OR 'transcranial direct current stimulation' OR 'transcranial alternating current stimulation' OR 'transcranial random noise stimulation' OR 'tES' OR 'tDCS' OR 'tACS' OR 'tRNS']. We also searched gray literature databases and examined the reference lists of relevant review articles and meta-analyses[41,135–137]. Peer-reviewed RCTs published in English were included in this meta-analysis and systematic review. The inclusion criteria were: (1) studies with human participants diagnosed with OCD; (2) administration of tDCS, tACS or tRNS to patients on a stable medication regimen (if applicable) without concurrent psychotherapy; (3) provision of both pre- and post-intervention OCD scores; (4) RCTs with sham control or active control groups; and (5) assessing OCD symptoms with Y-BOCS. Full texts of potentially eligible studies were assessed, with disagreements resolved through discussion or a third reviewer. Duplicates were identified and removed using EndNote, followed by manual verification to ensure accuracy. Each study's data were extracted independently by two reviewers using a standardized form, with discrepancies resolved via consensus.

Data extraction and outcome variables

Two authors (A.H.-H. and M.A.S.) independently extracted data from the included studies, including the first author's name, publication year, study design and blinding, sample size, mean age, percentage of female participants, target and return electrode site/size, stimulation intensity, duration, number of sessions, polarity, frequency (if applicable), OCD primary measure, secondary OCD measure (if applicable) and other clinical measures, and major findings. The corresponding authors were contacted for missing data. Efficacy was measured by the change in OCD symptom scores following tES interventions (pre versus post, active versus sham), using the Y-BOCS as a validated rating scale. If studies used multiple scales for core symptoms, we relied on Y-BOCS clinician ratings. We also noted any secondary outcome measures related to efficacy, including anxiety and cognitive performance rating scales.

Risk of bias and publication bias assessment

Two authors (M.A.S. and A.H.-H.) independently assessed the risk of bias in each included study using the revised Cochrane Collaboration's tool (v.2)[138]. It assesses biases from five domains arising due to: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. To identify and adjust for the impact of studies with potential unpublished negative results and small-study effects, we performed publication bias analyses using funnel plots, Egger's regression and *P*-curve methods.

Data synthesis and statistical analysis

Pairwise and network meta-analyses. Statistical analyses were conducted in R (v.4.1.2) using metafor, netmeta, meta and dmetar packages to compute the SMD[139], perform the network meta-analysis, generate forest plots, pooling effect sizes, and carry out sensitivity analyses and publication bias assessments[140,141]. We used the Morris method[142] for computing the SMDs of studies with a pre-test–post-test control group design (PPC). This method estimates a bias-corrected form of Hedge's *g* for PPCs (g_{PPC}). The primary outcome was the pre- to post-stimulation Y-BOCS total score change. SMD and variance for each study were computed with the escalc function of the metafor package and assuming an $r = 0.5$ pre-test–post-test correlation. Cross-over RCTs were included only if they reported pre- and post-intervention data separately for each treatment arm and implemented an adequate washout interval to minimize carry-over effects to qualify as an independent condition. When eligible, each treatment phase was treated as an independent comparison, with effect sizes calculated using the same methodology as parallel-group trials, while accounting for within-individual correlation ($r = 0.5$).

For the pairwise meta-analysis, we used Knapp–Hartung adjustments[143] to calculate the 95% CI of the pooled effect. Furthermore, heterogeneity was assessed by Cochran's *Q* (heterogeneity statistic), τ^2 (estimated between-study variance) and I^2 (proportion of total variability) in each condition. I^2 values above 50% were considered as evidence for high between-study heterogeneity. In addition to the primary analyses, we conducted pre-specified subgroup analyses by cortical target, treatment duration, tDCS intensity, total number of sessions, frequency-per-day subgroup and stimulation site by polarity. For the network meta-analysis, a network was created comparing treatments to a reference group ('sham'). Both fixed and random effect models were evaluated, with primary results derived from the random effect models. Network graphs and rankograms were used to visualize treatment connections, rankings and evidence consistency. SUCRA values were calculated to estimate the likelihood of each treatment being the most effective based on 1,000 simulated datasets of SUCRA

values, ranging from 0% to 100% for different scenarios of available interventions and outcomes[144]. Finally, sensitivity analyses were conducted by omitting specific studies with high heterogeneity to assess robustness. Publication bias was visually assessed with funnel plots and checked using Egger's test[145]. We also used the *P*-curve method[146] to investigate the evidential value of studies effect, determining whether our meta-analysis indicates a true effect and estimating its size. This method also explicitly addresses questionable research practices, such as *P*-hacking.

Meta-modeling. To explore which brain regions are associated with positive effects of tDCS on OCD symptoms, we performed the meta-modeling approach developed by Wischnewski et al.[55]. This computational approach correlates tDCS-related electric fields with behavioral effect sizes. First, the electric-field strengths (normE) of each intervention were calculated for every surface of a standard adult European male head model (~30 years of age). The electric-field simulations were performed in SimNIBS 3.2.[147,148] and standard realistic conductivities of head and brain tissues were used[149]. The gray matter was extracted for further analysis, which in this model consisted of 246,272 surface elements. As different montages were used in the included studies, this resulted in 19 electric-field distributions and a 246,272 × 19 matrix. Subsequently, each row of this matrix (19 values) was correlated with the 19 effect size values. This resulted in a column vector of 246,272 correlation values, with one correlation value for each gray-matter element (PEC_E). For the correlations, we used the non-parametric Spearman rank-order coefficient, as it can deal with non-normally distributed data and is less sensitive to outlying values compared with a parametric Pearson coefficient. Given the exploratory nature of this analysis, we report uncorrected one-sided *P* values.

We conducted additional analyses on factors affecting tDCS efficacy, specifically treatment duration (comprising daily stimulation duration (once or twice daily) and total session number). To account for this, we considered the 'cumulative charge' per day and over the entire treatment. For this, normE values were multiplied by (1) the total minutes of stimulation in one session ($PEC_{E\times min\,per\,day}$), (2) the total number of days of the treatment ($PEC_{E\times number\,of\,days}$), and (3) the total minutes of stimulation per treatment (minutes per session × number of days; $PEC_{E\times min\times day}$). After this, correlations were calculated in the same way as described above. To relate our findings to functional brain regions, the correlation values were averaged per brain region of the HCP-MMP atlas[87,88] which consists of 360 parcels. Subsequently, we displaced the five regions with the largest average PEC values. To ensure that our results were not biased due to peculiarities of our head model, all analyses described above were repeated in another head model (F, ~30 years of age), which was obtained from the Human Connectome Project (https://www.humanconnectome.org). Inter-map correlations were calculated for each analysis (PEC_E, $PEC_{E\times min\,per\,day}$, $PEC_{E\times number\,of\,days}$ and $PEC_{E\times min\times day}$), meaning that the values of each region of one head model were correlated to the values of the same region of the other head model.

Finally, we aimed to provide an optimized montage that targets the exact PEC map, which would result in the most beneficial results. To do so, we calculated the perpendicular direction of the electric field (perpE), which provides a measure of direction as it reflects locations of current influx and outflux[147]. As electrical current flows from the anodal to the cathodal electrode, an inward current (perpE > 0) occurs at a gyral bank facing the anode, while an outward current (perpE < 0) occurs at a gyral bank facing the cathode[150] (perpE < 0; Supplementary Fig. 1). Accordingly, a correlation between effect sizes and perpE provides information about optimal placement of anodes and cathodes for tDCS, which is necessary for optimization. This PEC_{perpE} was calculated in the same way as the other PEC values, described above. PEC_{perpE} was calculated only for brain regions where $PEC_E > 0$, as the goal was to provide an optimized montage for OCD symptom improvement.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The data that support the findings are available in the paper and are publicly available at https://osf.io/6taex/.

Code availability

The codes generated for data analyses are publicly available at https://osf.io/6taex/.

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Acknowledgements

We thank S. Karimi and A. Fathi Jouzdani for their technical assistance.

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M.A.S.: conceptualization, methodology, investigation, supervision, visualization, formal analysis, writing—original draft, writing—review and editing. A.H.-.H.: investigation, methodology, visualization, formal analysis. M.W.: formal analysis, visualization, writing—original draft (meta-modeling section), writing—review and editing. A.A., M.B., D.M.B., J.B., A.R.B., Z.J.D., S.N., F.P., A.T.S., M.S., O.A.v.d.H. and C.M.V.: methodology, writing—review and editing. Z.V.: investigation, writing—review and editing. T.W.R. and M.A.N.: supervision, writing—review and editing. All authors reviewed and approved the paper.

Funding

Open access funding provided by RWTH Aachen University.

Competing interests

M.A.N. is a member of the Scientific Advisory Boards of Neuroelectrics and Precisis. D.M.B. receives research support from CIHR, NIH, Brain Canada and the Temerty Family through the CAMH Foundation and the Campbell Family Research Institute. He received research support and in-kind equipment support for an investigator-initiated study from Brainsway Ltd. He was the site principal investigator for three sponsor-initiated studies for Brainsway Ltd. He also receives in-kind equipment support from Magventure for investigator-initiated research. He received medication supplies for an investigator-initiated trial from Indivior.

He is a scientific advisor for Sooma Oy Medical. F.P. is a member of the European Scientific Advisory Board of BrainsWay Inc. (Jerusalem, Israel), and the International Scientific Advisory Board of Sooma (Helsinki, Finland); he has received speaker honoraria from Mag&More GmbH, the neuroCare Group (Munich, Germany), and BrainsWay Inc.; his lab has received support with equipment from neuroConn GmbH (Ilmenau, Germany), Mag&More GmbH, and BrainsWay Inc. A.T.S. is scientific advisor for PlatoScience Medical and Alpha Brain Technologies, director of the Academy of Brain Stimulation (www.brainstimulation-academy.com) and the International Clinical TMS Certification Course (www.tmscourse.eu), receiving equipment support from MagVenture, Magstim, Deymed, Yingchi, and BrainsWay. T.W.R has consultancy for Cambridge Cognition, Supernus and Platea, and editorial honoraria for Springer Nature. These acknowledgments had no impact on the objectivity, integrity or value of the publication. The other authors declare no competing interests.

Additional information

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s44220-026-00590-z.

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Peer review information *Nature Mental Health* thanks Reza Moshfeghinia and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

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Last updated by author(s): Nov 27, 2025

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Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	Not applicable – this is a systematic review and meta-analysis of previously published studies, not an original clinical trial.
Study protocol	The full protocol is pre-registered in PROSPERO: CRD42023485717 (available at https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42023485717).
Data collection	No original clinical data were collected. All data were extracted from previously published studies identified through systematic literature search.
Outcomes	Primary outcome: standardized mean difference (Hedges' g) in Y-BOCS total score change (pre- vs. post-intervention) for active transcranial electrical stimulation versus sham/control in patients with obsessive-compulsive disorder.

Plants

Seed stocks	Not applicable
Novel plant genotypes	Not applicable
Authentication	Not applicable