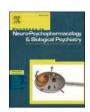


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Transcranial direct current stimulation (tDCS) for cognitive impairment in schizophrenia: A systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Background: Cognitive deficits represent a core symptom domain in schizophrenia, with limited responsiveness to pharmacological interventions. Transcranial direct current stimulation (tDCS) has emerged as a promising non-invasive neuromodulatory technique targeting cognitive enhancement. This systematic review and meta-analysis synthesized randomized controlled trials (RCTs) assessing the efficacy of tDCS on cognitive outcomes in schizophrenia.

Methods: A comprehensive literature search identified 33 RCTs (n=1372) evaluating cognitive effects of tDCS in patients with schizophrenia or schizoaffective disorder. Studies varied in montage, intensity, duration, and session count. Risk of bias was assessed using the Jadad scale and Cochrane RoB 2 tool. Quantitative meta-analyses were conducted across eight cognitive domains using multilevel random-effects models.

Results: Working memory and verbal learning were the most frequently improved domains. Meta-analytic results revealed a statistically significant effect in verbal learning (Hedges' $g=0.26,\,p=.034$), with negligible heterogeneity. Other domains (e.g., working memory, processing speed, problem solving) showed small, non-significant trends toward improvement, while attention and social cognition demonstrated inconsistent or null effects. Outcomes were influenced by stimulation parameters, with $\geq \! 10$ sessions and DLPFC-targeted montages associated with better efficacy. Methodological heterogeneity and moderate risk of bias were prevalent.

Conclusions: tDCS shows domain-specific potential for cognitive enhancement in schizophrenia, particularly in verbal learning. However, the small effect sizes, high heterogeneity, and limited methodological rigor of included trials warrant cautious interpretation. Future research should emphasize standardized protocols, robust trial designs, and integration with cognitive remediation strategies.

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1. Introduction

Schizophrenia is a disabling neuropsychiatric syndrome with multifactorial etiology that disrupts critical key networks underlying everyday functioning (Carpenter and Buchanan, 1994). It remains one of the most prevalent and severe mental disorders, affecting nearly 1 % of the global population (Tandon et al., 2013). The clinical phenotype encompasses positive, negative and cognitive symptoms (Carpenter and Buchanan, 1994). Among these, cognitive symptoms are traditionally regarded as the core features of the disorder, often emerging before the onset of psychosis (Carbon and Correll, 2014). These symptoms remain relatively stable across the different phases of the disease and are strongly predictive of functional outcomes (Jauhar et al., 2022).

Cognitive impairment in schizophrenia is primarily characterized by deficits in neurocognitive processes and social cognition, defined as the mental operations required for acquiring, processing, and utilizing information (Nuechterlein et al., 2008). These include domains such as speed of processing, attention/vigilance, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition (Nuechterlein et al., 2008). A substantial proportion of patients with schizophrenia exhibit impairments across multiple cognitive domains, with cognitive performance typically ranging from one and two standard deviations below that of demographically matched healthy controls (Gebreegziabhere et al., 2022).

Despite extensive pharmacological research targeting glutamatergic, cholinergic, nicotinic neurotransmission and other neurobiological targets, cognitive deficits have proven largely resistant to conventional treatments (Harris, 2023). This therapeutic gap has driven interest in non-pharmacological strategies aimed at enhancing cognitive function. Among these, neurocognitive remediation, cognitive behavioral therapy along with non-invasive brain stimulation (NIBS) modalities have shown preliminary efficacy (Jauhar et al., 2022).

Of particular interest is transcranial direct current stimulation (tDCS), a low-cost and well-tolerated neuromodulation technique that modulates cortical excitability and neuroplasticity (Lefaucheur et al., 2017). Recent studies suggest that tDCS, especially when applied over frontoparietal networks implicated in working memory and executive control, may yield clinically meaningful improvements in cognition (García-Fernández et al., 2025). However, variability in protocols and patient characteristics has led to mixed results, underscoring the need for a systematic evaluation of the efficacy, optimal parameters, and long-term effects of tDCS in patients with schizophrenia (Fregni et al., 2021; Safwi et al., 2025).

tDCS exerts its effects primarily through modulation of cortical excitability, involving calcium influx and NMDA receptor activity, which promote neuroplastic changes (Pelletier and Cicchetti, 2015). It also influences GABAergic and glutamatergic transmission, pathways implicated in the neurobiology of schizophrenia (Nitsche et al., 2003; Stagg and Nitsche, 2011), and closely linked to cognitive processes such as learning, memory, and executive function. Given these mechanisms, tDCS has emerged as a promising tool to target the neural substrates underlying cognitive dysfunction. While initially explored for treatment-resistant symptoms such as hallucinations and negative symptoms, its potential role in enhancing cognitive performance has gained growing attention due to its safety profile and neuromodulatory capacity (Bulubas et al., 2021).

Specifically, concerning cognition, early investigations into the cognitive effects of tDCS in schizophrenia have yielded promising but heterogeneous results. Clinical trials have reported modest to moderate improvements in global cognition, with working memory consistently emerging as one of the most responsive domains(García-Fernández et al., 2025; Kostova et al., 2020; Orlov et al., 2017a; Smith et al., 2020; Yu et al., 2020). Improvements have also been observed in attention, processing speed, verbal and visual learning, and problem-solving, although these effects are often small and variable in magnitude (Grover et al., 2023).

Furthermore, emerging evidence suggests that stimulation parameters may play a critical role in modulating treatment efficacy. For instance, higher current intensity, increased session frequency, and extended stimulation duration have been associated with enhanced cognitive gains (Cheng et al., 2021; Kim et al., 2018). In addition, protocols involving twice-daily stimulation or individualized electrode montages targeting frontoparietal or dorsolateral prefrontal circuits have demonstrated particularly encouraging results in small-scale studies (Bhattacharya et al., 2022; Hyde et al., 2022).

Despite this preliminary support, the field remains limited by several methodological challenges. These inconsistencies stem from variability in study designs, small sample sizes, differing stimulation protocols, and limited methodological rigor. Importantly, while recent reviews have addressed the potential of tDCS in psychiatric populations more broadly (Lefaucheur et al., 2017), few have focused exclusively on its cognitive effects in individuals with schizophrenia using a meta-analytic approach restricted to randomized controlled trials (RCTs) (Cheng et al., 2020).

Given the central role of cognitive impairment in schizophrenia and its profound implications for functional recovery, a comprehensive synthesis of the existing RCT evidence is critically needed. Therefore, the present study aims to conduct a systematic review of RCTs and meta-analysis examining the efficacy of tDCS on cognitive functioning in schizophrenia. By evaluating the magnitude of cognitive improvement across domains and identifying potential moderators, this review seeks to clarify the therapeutic potential of tDCS and inform the design of future interventions targeting cognitive deficits in this population.

2. Methods

2.1. Selection criteria and search strategy

A systematic review was conducted to evaluate the efficacy of tDCS in enhancing cognitive function among patients with schizophrenia or schizoaffective disorder. The review was conducted in accordance with the 2020 PRISMA guidelines (Page et al., 2021), and the protocol was prospectively registered in PROSPERO (Registration No.: CRD42024508989). Eligible participants met diagnostic criteria for schizophrenia or schizoaffective disorder according to the DSM-5-TR classifications (American Psychiatric Association, 2022), had received at least one session of tDCS, and were assessed for cognitive outcomes attributable to the intervention.

Studies were eligible if they included participants of any gender, age, or disease stage. Only peer-reviewed studies published in English up to June 30, 2025, were considered. The search was limited to human studies and included only randomized controlled trials (RCTs). Narrative reviews, case reports, letters or editorials were excluded.

To comprehensively explore the relationship between tDCS and cognitive enhancement, studies with any electrode montage (anode/cathode placement), stimulation intensity, session duration, and number of sessions were eligible. Additionally, studies combining tDCS with cognitive training were also included, as were those with any duration of follow up.

Studies presenting duplicate data from the same patient samples were excluded to maintain data integrity.

A systematic literature search was performed in multiple databases, including PubMed (MEDLINE), Embase, Web of Science, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL). For PubMed, the following precise search strategy was utilized: ((transcranial direct current stimulation [Title/Abstract] OR tDCS[Title/Abstract] AND cognit*[Title/Abstract] AND (schizo*[Title/Abstract] OR psychos* [Title/Abstract])). Filters were applied to limit results to human studies. This syntax was then adapted for the other databases to align with their respective search operators and subject headings. To ensure comprehensive coverage, the reference lists of all included articles and relevant review papers were also manually screened for additional eligible studies.

Eligibility criteria were defined using the PICO framework: Participants (patients with schizophrenia and schizoaffective disorder), Intervention (tDCS), Comparator (sham or placebo tDCS), and Outcome (cognitive improvement).

2.2. Study selection

Two reviewers (LGF, APMG) independently screened the titles and abstracts of potentially relevant studies. Full texts of articles deemed eligible were then assessed for inclusion based on predefined criteria. Discrepancies between reviewers were resolved through discussion, and a senior reviewer (RRJ) was consulted when consensus could not be reached.

2.3. Methodological quality assessment

The methodological quality of included RCTs was initially assessed using the Jadad scale (Jadad et al., 1996), a widely adopted tool recognized for its simplicity and utility in systematic reviews. The scale evaluates five domains: randomization and its methodology, blinding and its methodology, and reporting of withdrawals and dropouts, yielding a score ranging from 0 (high risk of bias) to 5 (low risk of bias). This assessment enabled a structured and time-efficient screening of studies during the full-text review phase.

To ensure a baseline threshold of methodological rigor, RCTs scoring below 3 on the Jadad scale were excluded from the final synthesis. These excluded trials commonly exhibited substantial methodological shortcomings, including lack of double-blinding (often employing single-blind or open-label designs), insufficient details regarding the randomization process, and inadequate reporting of participant attrition. The implementation of this quality threshold aimed to enhance the internal validity and robustness of the review's conclusions.

Given the recognized limitations of the Jadad scale, namely, its inability to evaluate critical aspects such as allocation concealment and selective outcome reporting, all included RCTs were further assessed using the revised Cochrane Risk of Bias tool (RoB 2) (Sterne et al., 2019). This tool provides a comprehensive, domain-based evaluation of bias across five dimensions: the randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of the reported results. Two independent reviewers applied the RoB 2 tool, and risk-of-bias judgments were categorized as "low risk," "some concerns," or "high risk" for each domain and overall.

To preserve clarity in the main manuscript, detailed Jadad scores and full RoB 2 assessments for each study are provided in the supplementary materials. This dual-assessment strategy ensured both efficient preliminary screening and rigorous evaluation of internal validity, informing the evidence base for the design of future RCTs investigating the cognitive effects of tDCS in schizophrenia.

2.4. Data synthesis

Given the methodological heterogeneity among the included studies, in terms of cognitive domains assessed, stimulation parameters applied, and outcome profiles, a narrative synthesis approach was employed. Results were organized according to cognitive domains tDCS parameters (intensity, number of sessions), and overall study findings (positive, null, or mixed). This structured synthesis allowed for the identification of emergent patterns and key sources of variability across trials, facilitating a nuanced interpretation of the current evidence base.

All studies included in the systematic review were re-screened for eligibility in the meta-analysis. Studies lacking sufficient or complete quantitative data were excluded from the meta-analysis. Details of excluded studies and reasons for exclusion are provided in the supplemental material, Table 1.

Cognitive outcomes were grouped into separate domains. Each outcome was treated as a separate effect size, as they represented

distinct measures within the same cognitive construct. Meta-analyses were then conducted separately for each cognitive domain using a multilevel random-effects model to account for statistical dependence when studies contributed multiple outcomes. Pooled effect sizes were calculated using Hedges' g, and both 95 % confidence intervals (CIs) and prediction intervals (PIs) were reported. Pooled effect sizes were calculated using Hedges' g, and both 95 % confidence intervals (CIs) and prediction intervals (PIs) were reported. Heterogeneity was assessed using the Q statistic and the I² index. Potential publication bias was evaluated through funnel plot asymmetry using meta-regression, weighted regression, and rank correlation methods. All meta-analyses were conducted using JASP software (JASP Team, 2025).

To synthesize the findings, the statistical comparisons reported in each reviewed study regarding cognitive outcomes were extracted and analyzed.

3. Results

3.1. Study selection and characteristics

The systematic search yielded a total of 1712 records. After removing duplicates, 983 unique articles were screened, of which 928 were excluded based on title and abstract. Fifty-five full-text articles were assessed for eligibility, and 22 were excluded for reasons including low methodological quality, data duplication, irrelevant interventions, or incomplete data. Ultimately, 33 RCTs met the inclusion criteria and were included in the final synthesis. A PRISMA flowchart summarizing the study selection process is provided in Fig. 1.

All included studies employed randomized, double-blind, sham-controlled designs, encompassing a total sample of 1372 participants diagnosed with schizophrenia or schizoaffective disorder. The stimulation protocols varied in terms of intensity (1–2 mA), duration (20–30 min), and total number of sessions (range: 1–40). The most common montage involved anodal stimulation over the left dorsolateral prefrontal cortex (DLPFC; F3), with the cathode positioned over the right supraorbital area (Fp2).

A complete summary of study characteristics, stimulation parameters, outcomes, and bias assessments is presented in Table 1.

3.2. Risk of bias assessment

The methodological quality of the included trials was evaluated using both the Jadad scale and the Cochrane RoB 2 tool. Of the 33 studies, 31 were rated as "some concerns" or "high risk" in at least one RoB 2 domain. Only two trials were judged to be at low overall risk of bias. The most frequent sources of bias were related to inadequate reporting of the randomization process (81.8 %) and potential selective outcome reporting (42.4 %). Conversely, outcome measurement was consistently robust, with 97 % of studies receiving a low risk of bias in this domain (supplemental material, Table 2).

Figure 2 displays the distribution of risk of bias assessments across the five RoB2 domains. Most studies were judged to present some concerns in at least one domain, with D1-randomization and D2-intervention showing the highest proportion of non-low ratings. The overall risk was driven primarily by issues in missing data handling and selective reporting.

3.3. Summary of cognitive outcomes

To systematically categorize the findings, study outcomes were classified as "positive," "no significant effects," or "mixed/partial." A study was deemed positive if it reported a statistically significant improvement in favor of active tDCS on at least one primary cognitive outcome or a global cognitive composite score. A study was classified as no significant effects if it found no significant differences between the active tDCS and sham groups on any of the reported cognitive measures.

 Table 1

 Summary of included randomized controlled trials evaluating the effects of transcranial direct current stimulation (tDCS) on cognitive function in schizophrenia.

N	First Author, date	Study Design	Population, N (% female)	Stimulation intensity (mA), session duration (min), total number of sessions	Comparison (N)	Outcome	Quality*	Overall Risk of Bias+
1	Hoy et al. (2014)	Randomized, sham- controlled, double-blind	Patients with schizophrenia, $N=18$ (33.3 % female)	1 mA tDCS, 2 mA tDCS, and sham, 20 min, single session for each condition. Assessed at 0-, 20-, and 40-mins post- stimulation. No FU.	Anodal tDCS over left DLPFC (F3), cathode over right supraorbital ridge (Fp2) (withinsubjects comparison of 1 mA, 2 mA, and Sham conditions, $N = 18$).	2 mA tDCS (but not 1 mA or sham) led to a significant improvement in working memory performance over time, with the effect emerging between 0- and 20-min post-stimulation.	4	Some Concerns
2	Smith et al. (2015)	Randomized, sham- controlled, double-blind	Outpatients with schizophrenia or schizoaffective disorder who were smokers, $N = 37$ randomized (27.3 % female in analyzed sample).	2 mA tDCS or sham, 20 min/session, 5 daily sessions. No FU (FU description only for PANSS).	Anodal tDCS over left DLPFC (F3), cathode over right supraorbital ridge (Fp2) ($N = 14$ analyzed) vs. Sham tDCS ($N = 15$ analyzed).	Active tDCS significantly improved overall cognitive performance (MCCB Composite score), as well as Working Memory and Attention-Vigilance domains, compared to sham.	5	Some Concerns
3	Shiozawa et al. (2016)	Randomized, sham- controlled, double-blind	Patients with schizophrenia, $N=9$ (66.7 % female).	2 mA tDCS or sham, 20 min/session, twice daily for 5 days (10 sessions total). FU at 4 weeks.	Anodal tDCS over left DLPFC (F3), cathode over right DLPFC (F4) vs. Sham tDCS ($N=10$ randomized, 9 analyzed).	The study failed to demonstrate improvement in cognitive performance, though no quantitative cognitive data was presented.	3	Some Concerns
4	Impey et al. (2017)	Randomized, sham- controlled, double-blind	Patients with schizophrenia, $N = 12$ (16.7 % female).	2 mA tDCS or sham, 20 min, single session for each of three conditions (anodal temporal, anodal frontal, sham). No FU.	Within-subjects comparison (<i>N</i> = 12) of anodal tDCS over left temporal cortex (T7) or left DLPFC (F3), cathode over contralateral orbit vs. sham.	Anodal frontal tDCS significantly improved working memory performance (accuracy and reaction time on a 2-back task) compared to temporal or sham stimulation. Active tDCS did not	4	Some Concerns
5	Gögler et al. (2017)	Randomized, sham- controlled, double-blind	Patients with schizophrenia, $N = 20$ (35 % female).	2 mA anodal tDCS or sham, 20 min, single session. FU at 24 h.	Anodal tDCS over left DLPFC (F3), cathode over right supraorbital area (FP2) (N = 10) vs. Sham tDCS (N = 10).	improve visual attentional parameters; instead, it appeared to interfere with practice- related improvements seen in the sham group. Active tDCS significantly	5	Some Concerns
6	Orlov et al. (2017a)	Randomized, sham- controlled, double-blind	Schizophrenia or schizoaffective disorder, N = 40 for working memory analysis (17.5 % female).	2 mA, 30 min/session, 2 sessions (on day 1 and day 14). No FU.	Anodal tDCS left DLPFC (F3) / cathodal right supraorbital (Fp2) (<i>N</i> = 19) vs. Sham tDCS (<i>N</i> = 21).	improved working memory performance compared to sham, with effects seen at next-day (day 2) and long-term (day 56) follow-ups, suggesting an effect on the consolidation of learning. The tDCS group showed	5	Some Concerns
7	Orlov et al., 2017b	Randomized, sham- controlled, double-blind	Schizophrenia or schizoaffective disorder, $N=24$ for working memory analysis (20.8 % female).	2 mA, 30 min, 1 session (during fMRI). 2 mA, 30 min/session, 2 per day over 4 days (Day 1, 2, 14, 56). During day 14: 28 patients accepted fMRI	Anodal tDCS left frontal cortex (F3) / cathodal right supraorbital area (Fp2) ($N = 13$) vs. Sham tDCS ($N = 11$) for working memory analysis.	a significant improvement in working memory performance 24 h post-stimulation, but not during the online task. Improved executive function performance was associated with reduced activity in the anterior cingulate cortex.	5	Some Concerns
8	Schwippel et al. (2018)	Randomized, sham- controlled, double-blind, cross-over	Patients with schizophrenia, $N = 32$ (28.1 % female), split into two experiments of $N = 16$ each	Two experiments: EXP I (1 mA tDCS or sham) and EXP II (2 mA tDCS or sham), 21 min/session, one active and one sham session per participant. No FU.	Anodal tDCS over right DLPFC (F4), cathode on contralateral deltoid muscle vs. Sham tDCS (within-subjects comparison, EXP I: N = 16, EXP II: N = 16) vs. Sham tDCS (N = 32).	1 mA tDCS had no effect. 2 mA tDCS increased spatial working memory accuracy on the most difficult task (3-back), especially in patients with lower baseline cognition, but also slowed response time.	4	Some Concerns

Table 1 (continued)

N	First Author, date	Study Design	Population, N (% female)	Stimulation intensity (mA), session duration (min), total number of sessions	Comparison (N)	Outcome	Quality*	Overall Risk of Bias+
9	Jeon et al. (2018)	Randomized, sham- controlled, double-blind	Patients with schizophrenia, N = 56 randomized (51.9 % female at baseline)	2 mA tDCS or sham, 30 min, once daily for 10 weekdays (10 sessions). FU at 12 weeks.	Anodal tDCS over left DLPFC (F3), cathode over right DLPFC (F4) (N = 28) vs. Sham tDCS (N = 28).	Active tDCS group showed significant improvement over time in working memory and overall composite scores on the MCCB compared to the sham group at 12- week follow-up.	5	High Risk
10	Gomes et al. (2018)	Randomized, sham- controlled, double-blind	Patients with schizophrenia, $N = 24$ (29.2 % female).	2 mA tDCS or sham, 20 min/session, 10 daily sessions over 2 weeks. FU at 3 months.	Anodal tDCS over left DLPFC (F3), cathode over right DLPFC (F4) (N = 12) vs. Sham tDCS (N = 12).	No significant improvement in working memory or any other cognitive domain was found for the active tDCS group compared to sham.	4	Some Concerns
11	Papazova et al. (2018)	Randomized, sham- controlled, double-blind, cross-over	Patients with schizophrenia, $N = 40$ (22.5 % female).	Two experiments: EXP I (1 mA tDCS or sham) and EXP II (2 mA tDCS or sham), 21 min/session, one active and one sham session per participant. No FU.	Within-subjects comparison of anodal tDCS over left DLPFC (F3) with cathode on the right deltoid muscle vs. Sham tDCS. (EXP I: 1 mA, $N = 20$; EXP II: 2 mA, $N = 20$).	1 mA active tDCS significantly improved working memory accuracy compared to sham. 2 mA tDCS did not produce a statistically significant improvement. No significant effects on reaction time were found for either intensity. No statistically	4	Some Concerns
12	Mellin et al. (2018)	Randomized, sham- controlled, double-blind	Schizophrenia or schizoaffective disorder, $N = 22$ (31.8 % female).	2 mA, 20 min/session, 10 sessions (twice daily for 5 days). FU at 1 month	10 Hz, 2 mA tACS ($N=8$) vs. 2 mA Anodal tDCS left dl-PFC (F3/Fp1) / cathodal left TPJ (T3/P3) ($N=7$) vs. Sham ($N=7$).	significant group differences were found on the Brief Assessment of Cognition in Schizophrenia (BACS). However, effect size calculations showed the largest cognitive effect for the tDCS group.	5	Some Concerns
13	Koops et al. (2018)	Randomized, sham- controlled, double-blind	Psychotic disorders (primarily schizophrenia), <i>N</i> = 54 (53.7 % female).	2 mA, 20 min/session, 10 sessions (twice daily for 5 days). FU at 1 and 3 months.	Anodal tDCS left DLPFC (F3)/ cathodal left TPJ (TP7) (N = 28) vs. Sham tDCS (N = 26).	No evidence was found that tDCS is more effective than placebo for medication-resistant auditory hallucinations. No significant improvements in cognition (Stroop, TMT) were observed.	5	Some Concerns
14	Weickert et al. (2019)	Randomized, sham- controlled, double-blind	Schizophrenia or schizoaffective disorder, $N=12$ (50 % female).	2 mA, 20 min/day, 20 sessions over 4 weeks. No FU.	Anodal tDCS right DLPFC (F4) / cathodal left TPJ (midway T3-P3) ($N = 6$) vs. Sham tDCS ($N = 6$).	Anodal tDCS improved language-based working memory after 2 weeks and verbal fluency after 2 and 4 weeks, showing that benefits can transfer to other cognitive domains.	3	High risk
15	Chang et al. (2019)	Randomized, sham- controlled, double-blind	Patients with schizophrenia, $N = 60$ (55 % female).	2 mA tDCS or sham, 20 min/session, twice daily for 5 days (10 sessions total). FU to 3 months.	Anodal tDCS over left DLPFC (F3), cathode over left temporoparietal junction (TP7) ($N = 30$) vs. Sham tDCS ($N = 30$).	The study found a trend- level improvement in planning ability (Tower of London accuracy) that did not survive correction for multiple comparisons. No significant effects were observed for other neurocognitive domains.	4	Some Concerns
16	Lindenmayer et al. (2019)	Randomized, sham- controlled, double-blind	Ultra-treatment-resistant schizophrenia, $N=28$ (14.3 % female).	2 mA, 20 min/session, 40 sessions (twice daily for 4 weeks). No FU.	Anodal tDCS left prefrontal cortex (midway F3/FP1) / cathodal left temporoparietal junction (midway T3/P3) (N = 15) vs. Sham tDCS (N = 13).	Working Memory was the only cognitive domain that showed improvement for the active tDCS group.	4	High Risk

Table 1 (continued)

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N	First Author, date	Study Design	Population, N (% female)	Stimulation intensity (mA), session duration (min), total number of sessions	Comparison (N)	Outcome	Quality*	Overall Risk of Bias+
17	Boudewyn et al. (2020)	Randomized, sham- controlled, double-blind	Schizophrenia or schizophrenia spectrum disorder, <i>N</i> = 27 (29.6 % female).	2 mA, 20 min, 1 session (crossover design). No FU.	Crossover design (N = 27): Anodal tDCS left DLPFC (F3) / cathodal right supraorbital (FP2) vs. Sham tDCS.	Active stimulation enhanced proactive cognitive control, evidenced by a significant change in the pattern of error rates on the DPX task and increases in delay-period EEG gamma power. The reaction time on a 2-	4	High Risk
18	Sreeraj et al. (2020)	Randomized, sham- controlled, double-blind	Schizophrenia, $N = 23$ (39.1 % female).	2 mA, 20 min, 1 session (partial crossover design). No FU.	Partial crossover design comparing online-tDCS ($N=11$) vs. offline-tDCS ($N=12$), where each patient received both active and sham stimulation. Montage: anodal left DLPFC (F3)/cathodal left TPJ (TP7).	back task improved after performing a different working memory task during sham stimulation (online-sham), but not during active stimulation. This suggests the cognitive task itself improved performance, but combining it with active tDCS did not add benefit. No significant cognitive	5	Some Concerns
19	Smith et al. (2020)	Randomized, sham- controlled, double-blind	Chinese patients with schizophrenia, $N = 45$ (60 % female).	2 mA tDCS or sham, 20 min/session, 10 daily sessions over ~2 weeks. FU at 2 and 4 weeks.	Anodal tDCS over left DLPFC (F3), cathode over right supraorbital ridge (Fp2) ($N=24$) vs. Sham tDCS ($N=21$).	improvements were found immediately after the intervention. At 2-week follow-up, the active tDCS group showed significantly greater improvement in Speed of Processing	3	High risk
20	Schilling et al. (2021)	Randomized, sham- controlled, double-blind	Patients with schizophrenia, schizoaffective disorder, or acute transient psychotic disorder, <i>N</i> = 48 (18.8 % female)	2 mA tDCS or sham, 20 min, 1 session. No FU.	Anodal tDCS over left DLPFC (F3), cathode over right supraorbital ridge (FP2) (N = 24) vs. Sham tDCS (N = 24).	compared to sham. No acute enhancement of executive functions. Exploratory analysis suggested active tDCS impaired performance on a response inhibition task post-stimulation.	5	Low risk
21	Bulubas et al. (2021)	Randomized, sham- controlled, double-blind	Patients with schizophrenia with prominent negative symptoms, $N = 90$ (20 % female).	2 mA tDCS or sham, 20 min/session, twice daily for 5 days (10 sessions total). Follow-up at 6 for Penn-CNB. Additional FU at week 2, 4, 6 and 12 for PANSS-based cognitive-disorganized factor.	Anodal tDCS over left prefrontal cortex (F3), cathode over left temporoparietal junction (TP7) ($N = 48$) vs. Sham tDCS ($N = 42$).	Active-tDCS showed no beneficial effects. Improvements in executive functions and delayed memory were observed in favor of the sham group.	4	Some Concerns
22	Meiron et al. (2021)	Randomized, sham- controlled, double-blind, cross-over	Chronic medicated schizophrenia patients, <i>N</i> = 19 (15.8 % female).	2 mA tDCS or sham, 20 min/session, twice daily for 5 days (10 sessions total). FU up to 12 weeks (every 4 weeks).	Anodal tDCS over left DLPFC (F3), cathode over vertex (Cz) ($N=11$) vs. Sham tDCS ($N=8$).	The active tDCS group showed significant working memory accuracy improvement from baseline to immediately post-intervention, reaching a level comparable to healthy controls.	4	High Risk
23	Fathi Azar et al. (2021)	Randomized, sham- controlled, double-blind	Patients with schizophrenia, $N=24$ (0 % female).	2 mA tDCS or sham, 20 min/session, twice daily for 6 nonconsecutive days (12 sessions total). No FU.	Anodal tDCS over left DLPFC (F3), cathode over right supraorbital area (Fp2) (N = 12) vs. Sham tDCS (N = 12), with both groups receiving psychosocial occupational therapy.	The combination of tDCS and occupational therapy significantly improved spatial memory, visual learning, and attention compared to sham tDCS with occupational therapy. No changes were observed in higher-level	4	Some Concerns
24	Chang et al. (2021)	Randomized, sham- controlled, double-blind	Schizophrenia or schizoaffective disorder, $N = 60$ (50 % female).	2 mA, 20 min/session, 10 sessions (twice daily for 5 days). FU at 1 month	Bi-anodal tDCS over bilateral PFC (midway F3/Fp1 and F4/Fp2) with bilateral forearm reference electrodes (N	cognitive functions. Active stimulation significantly enhanced clinical insight into the disease and symptoms, as well as beliefs about	4	Some Concerns

Table 1 (continued)

N	First Author, date	Study Design	Population, N (% female)	Stimulation intensity (mA), session duration (min), total number of sessions	Comparison (N)	Outcome	Quality*	Overall Risk of Bias+
					= 30) vs. Sham tDCS (N = 30).	medication adherence. No effects were observed on cognitive insight. A single session of		
25	Klein et al. (2021)	Randomized, sham- controlled, double-blind	Schizophrenia spectrum disorders, <i>N</i> = 69 (44.9 % female).	2 mA, 20 min, 1 session of active and 1 session of sham (crossover design). No FU.	Crossover design comparing active vs. sham stimulation at two different sites: 1) rTPJ stimulation (<i>N</i> = 36) and 2) dmPFC stimulation (<i>N</i> = 33).	stimulation had a limited effect. It failed to impact visual attention or emotion recognition accuracy. However, mentalizing accuracy significantly improved after stimulation to the dmPFC.	4	Some Concerns
26	Lisoni et al. (2022)	Randomized, sham- controlled, double-blind	Clinically stabilized outpatients with schizophrenia, $N=50$ (22 % female).	2 mA tDCS or sham, 20 min/session, once daily for 15 sessions (3 weeks_ Monday to Friday). No FU.	Anodal tDCS over left DLPFC (F3), cathodal over right orbitofrontal (Fp2)) ($N = 25$) vs. Sham tDCS ($N = 25$).	Active tDCS produced significant improvements in working memory (digit sequencing task). No significant improvements were found for other cognitive	5	Some Concerns
27	Orlov et al. (2022)	Randomized, sham- controlled, double-blind	Schizophrenia or schizoaffective disorder, $N = 39$ for behavioral analysis (17.9 % female).	2 mA, 30 min/session, 2 sessions (on day 1 and day 14). No FU.	Anodal tDCS left mPFC (F3) / cathodal right supraorbital (Fp2) (N = 21) vs. Sham tDCS (N = 18).	domains. Active tDCS significantly improved performance on a stochastic sequence-learning task (SSLT) compared to sham. The improvements were evident at the next-day and long-term (day 56) follow-ups, indicating a sustained effect on learning after a consolidation period.	5	High Risk
28	Xu et al. (2023)	Randomized, sham- controlled, double-blind	Individuals with chronic schizophrenia, $N = 56$ (39.3 % female).	2 mA HD-tDCS or sham, 20 min/day for 10 consecutive days (10 sessions total). No FU.	Anodal HD-tDCS over left DLPFC (F3) with 4 returned cathodal electrodes (4 × 1 ring: AF3, F5, F1, and FC3) (N = 28) vs. Sham HD-tDCS (N = 28).	Active HD-tDCS group showed a significant increase in the RBANS attention score compared to the sham group. No significant effects were observed in other cognitive domains.	5	High Risk
29	Zhou et al. (2023)	Randomized, sham- controlled, double-blind	Long-term hospitalized patients with chronic schizophrenia and tardive dyskinesia, <i>N</i> = 38 (28.9 % female).	2 mA tDCS or sham, 30 min/session, 15 sessions over 5 weeks. No FU.	Anodal tDCS over left DLPFC (F3), cathode over right supraorbital area (Fp2) (N = 21) vs. Sham tDCS ($N = 17$).	No significant improvements were found in cognitive function (visual recognition memory and executive function) in the active tDCS group compared to sham.	4	High Risk
30	Shafiee- Kandjani et al. (2025)	Randomized, sham- controlled, double-blind	Patients with schizophrenia, $N=40$ (50 % female)	2 mA tDCS or sham, 20 min/session, twice daily for 5 days (10 sessions). No FU.	Anodal tDCS over left DLPFC (F3), cathode over left temporoparietal junction (TP7) ($N=20$) vs. Sham tDCS ($N=20$).	Active tDCS significantly improved working memory (Forward Digit Span and Letter-Number Span tasks) after day 4 compared to sham. Active PPC stimulation	5	Low risk
31	Hou et al. (2024)	Randomized, sham- controlled, double-blind	Clinically stable patients with schizophrenia and below-average working memory, N = 60 (56.7 % female).	2 mA HD-tDCS or sham, 20 min/session, twice daily for 5 days (10 sessions total) with concurrent cognitive task. FU at 1 and 2 weeks.	Anodal HD-tDCS over left DLPFC (F3) (N = 20) vs. anodal HD-tDCS over left PPC(P3) (N = 20) vs. Sham tDCS (N = 20).	was superior to active DLPFC stimulation for improving working memory. Compared to sham, active PPC stimulation did not significantly improve the primary outcome (spatial span) but did improve a secondary working memory measure.	5	Some Concerns
32	García- Fernández et al. (2025)	Randomized, sham- controlled, double-blind	Schizophrenia, $N = 139$ (33.1 % female).	2 mA, 20 min/session, 10 sessions (once daily). No FU	Anodal tDCS left DLPFC (F3) / cathodal right DLPFC (F4) (<i>N</i> = 62) vs. Sham tDCS (<i>N</i> = 58).	Active tDCS significantly improved performance in Working Memory and the overall	5	Some Concerns

Table 1 (continued)

N	First Author, date	Study Design	Population, N (% female)	Stimulation intensity (mA), session duration (min), total number of sessions	Comparison (N)	Outcome	Quality*	Overall Risk of Bias+
33	Fan et al. (2025)	Randomized, sham- controlled, double-blind	Schizophrenia spectrum disorders, <i>N</i> = 50 (52 % female).	2 mA, 20 min/session, 2 sessions per condition (active/sham). No FU	Crossover design (N = 50) comparing active stimulation (anode over right VLPFC/F6, cathode over left VLPFC/F5) vs. Sham tDCS.	Neurocognition composite score compared to sham. Active stimulation led to greater reductions in state paranoia and improvements in paranoia-related social cognitive biases (e.g., lower hostile attributions). Ecological Momentary Assessment (EMA) data showed higher social interaction motivation.	4	High Risk

The table presents key study characteristics including authorship, sample size, diagnosis, stimulation parameters (intensity, duration, number of sessions), electrode montage, cognitive outcomes, methodological quality (Jadad score), and overall risk of bias (RoB 2 classification).

DLPFC: Dorsolateral Prefrontal Cortex; dmPFC: Dorsomedial Prefrontal Cortex; DPX: Dot Pattern Expectancy task; EEG: Electroencephalogram; EXP: Experiment; fMRI: Functional Magnetic Resonance Imaging; FU: Follow-Up; HD-tDCS: High-Definition Transcranial Direct Current Stimulation; MCCB: MATRICS (Measurement and Treatment Research to Improve) Consensus Cognitive Battery; PANSS: Positive and Negative Syndrome Scale; Penn-CNB: Penn (Pennsylvania) Computerized Neurocognitive Battery; PFC: Prefrontal Cortex; PPC: Posterior Parietal Cortex; RBANS: Repeatable Battery for the Assessment of Neuropsychological Status; tDCS: Transcranial Direct Current Stimulation; TMT: Trail Making Test; TPJ (TP7, left TPJ): Temporo-Parietal Junction; VLPFC: Ventrolateral Prefrontal Cortex.

+ Risk of Bias assessed by RoB 2 Cochrane classificatio.

^{*} Quality of clinical trial according to Jadad scale.

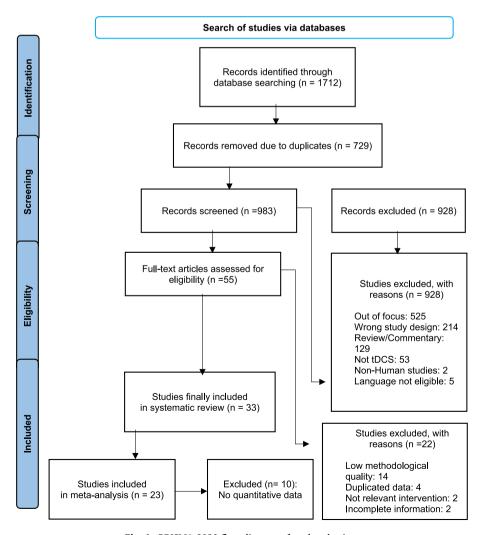


Fig. 1. PRISMA 2020 flow diagram of study selection.

Table 2Summary of meta-analytic results across cognitive domains.

Cognitive Domain	Hedges' g	SE	95 % CI	<i>p</i> -value	I ² (%)
Speed of processing	0.19	0.087	[-0.00, 0.38]	0.054	23.9
Attention	-0.14	0.341	[-0.86, 0.58]	0.697	79.6
Working memory	0.17	0.094	[-0.02, 0.37]	0.075	58.0
Verbal learning	0.26	0.112	[0.02, 0.50]	0.034	0.0
Visual learning	0.11	0.207	[-0.33, 0.55]	0.597	44.3
Problem solving	0.19	0.093	[-0.02, 0.39]	0.074	27.6
Social cognition	0.06	0.064	[-0.08, 0.20]	0.373	5.3
Executive functions	0.15	0.137	[-0.15, 0.44]	0.303	63.4
Overall cognition	0.24	0.123	[-0.03, 0.52]	0.079	40.8

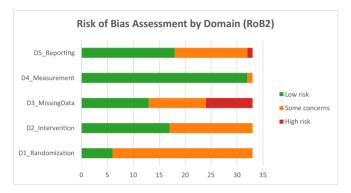


Fig. 2. Risk of bias assessment by domain according to the RoB 2 Tool. Distribution of risk of bias across the included randomized controlled trials (n=33), as evaluated using the Cochrane Risk of Bias 2 (RoB 2) tool. A total of 31 studies were rated as having "some concerns" or "high risk" in at least one domain.

Finally, an outcome was categorized as mixed/partial if the findings were nuanced: for example, when benefits were limited to secondary cognitive outcomes but not primary ones; when improvements were observed only under specific stimulation parameters; or when active stimulation led to performance decrements in certain tasks while improving others. Across the 33 included studies, 23 (69.7 %) reported statistically significant improvements in cognitive outcomes following active tDCS compared to sham stimulation. Eight studies (24.2 %) reported no significant cognitive effects, and two studies (6.1 %) demonstrated mixed or domain-specific results.

The most frequently improved domain was working memory, followed by attention. In addition, several studies reported improvements in overall cognitive performance as assessed by standardized batteries: the MATRICS Consensus Cognitive Battery (MCCB) (Nuechterlein et al., 2008), the Brief Assessment of Cognition in Schizophrenia (BACS) (Keefe et al., 2004), and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) (Randolph et al., 1998). Improvements were also reported in executive functions, language, speed of processing, and social cognition in a subset of trials.

3.4. Domain-specific effects

Improvements in attention-related tasks were observed in studies using daily stimulation protocols over 1–2 weeks (Smith et al., 2015; Xu et al., 2023).

Processing speed enhancements were less consistent and typically emerged at follow-up rather than immediately post-intervention.

Nineteen studies evaluated working memory, with thirteen reporting significant improvements post-tDCS. Protocols showing positive effects commonly involved $\geq \! 10$ sessions of 2 mA anodal stimulation over the left DLPFC (García-Fernández et al., 2025; Jeon et al., 2018; Shafiee-Kandjani et al., 2025).

Language improvements following extended stimulation protocols targeting frontal areas were reported in two studies (Meiron et al., 2021;

Weickert et al., 2019).

Six trials reported enhancements in executive functions. Improvements in proactive control mechanisms, as indexed by DPX task performance and frontal gamma power, were observed in one study (Boudewyn et al., 2020).

Improvements in social cognitive biases and mentalizing accuracy were found in two trials (Fan et al., 2025; Klein et al., 2021), suggesting a potential role for tDCS in modulating higher-order social processes.

3.5. Heterogeneity and moderators

Substantial methodological heterogeneity was observed across studies in terms of stimulation parameters, participant characteristics, and outcome measures. Multi-session protocols (≥ 10 sessions) were more frequently associated with positive outcomes compared to single-session interventions. Furthermore, studies combining tDCS with concurrent cognitive training or occupational therapy (Fathi Azar et al., 2021) tended to report greater cognitive gains, highlighting the potential for synergistic effects.

Interestingly, stimulation intensity did not display a linear relationship with efficacy; one study found that 1 mA improved working memory, whereas 2 mA did not (Papazova et al., 2018).

3.6. Meta-analysis procedures and statistical synthesis

To further contextualize these findings, we conducted a domain-level meta-analysis to quantitatively assess the overall efficacy of tDCS across the different cognitive domains.

Of the 33 studies included in the systematic review, each was carefully examined to extract the necessary data (means, standard deviations [SDs], or pooled SDs) for calculating Cohen's d, Hedges's g, standard error (SE), variance, and 95 % confidence intervals. However, 10 studies lacked sufficient data to compute these values and, although methodologically relevant, were excluded from the quantitative analysis due to missing information (supplemental material, Table 1).

Ultimately, 23 studies provided usable data, yielding a total of 146 individual cognitive outcomes. Given the heterogeneity of cognitive measures, outcomes were categorized into one of the following cognitive domains: speed of processing (n=12), attention (n=18), working memory (n=36), verbal learning (n=15), visual learning (n=16), problem solving (n=11), social cognition (n=13), executive functions (n=15) and overall cognition (n=10).

Meta-analyses were conducted separately for each cognitive domain to evaluate the effects of tDCS on cognitive performance in patients with schizophrenia or schizoaffective disorder. For each domain, pooled effect sizes along with their corresponding confidence and prediction intervals were calculated. The analyses revealed varying degrees of heterogeneity, with some domains showing substantial between-study variability. In several domains, outcomes differed notably depending on the specific cognitive task or assessment used. Funnel plot inspections and statistical tests for asymmetry were performed for each domain, revealing no consistent evidence of publication bias, although these analyses are limited in domains with a small number of studies and should be interpreted with caution. No formal correction for multiple comparisons was applied due to the exploratory nature of the domainlevel analyses. Overall, the results suggested domain-specific patterns, with some domains exhibiting greater variability and uncertainty in the estimated effects than others (Table 2 and Fig. 3).

Speed of processing showed a small effect size (g = 0.19, SE = 0.09, p = .054) that narrowly missed statistical significance. The 95 % CI [–0.00, 0.38] and prediction interval [–0.00, 0.38] suggest consistent though weak benefits. Heterogeneity was low (I $^2\approx$ 24 %), and variance estimates were negligible.

Attention yielded a non-significant and near-zero pooled effect (g = -0.14, SE = 0.36, p = .697). The 95 % CI [-0.86, 0.58] and high heterogeneity (I $^2 \approx 80$ %) indicate large inconsistencies between studies.

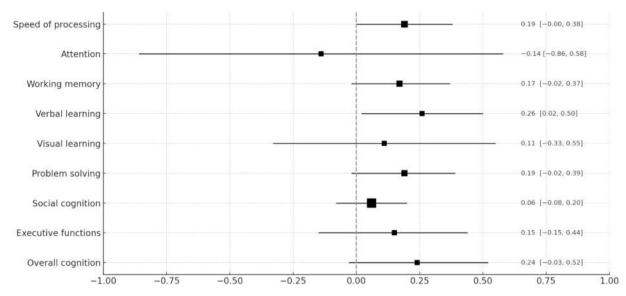


Fig. 3. Domain-level forest plot. Forest plot displaying the pooled effect sizes and 95 % confidence intervals for the impact of transcranial direct current stimulation (tDCS) across nine cognitive domains in individuals with schizophrenia.

Working memory yielded a small pooled effect size (g = 0.17, SE = 0.09, p = .075) that approached but did not reach statistical significance. The 95 % CI [-0.02, 0.37] and prediction interval [-0.55, 0.90] reflect substantial between-study variability. Heterogeneity was high (I² \approx 58 %), and variance was primarily due to differences at the outcome level.

Verbal learning showed a small-to-moderate and statistically significant effect of tDCS on verbal cognition (g = 0.26, SE = 0.11, p = .034), with a narrow 95 % confidence interval [0.02, 0.50] and zero heterogeneity (I^2 = 0 %). The prediction interval [-0.09, 0.61] suggests that while future studies are likely to show positive effects, the true effect size could range from a small negative effect to a moderate positive effect.

Visual learning showed a small, non-significant effect (g = 0.11, SE = 0.21, p = .597) with a wide 95 % CI [-0.33, 0.55] and very high prediction interval [-0.88, 1.11]. Moderate heterogeneity (I² \approx 44 %) and considerable variance suggest study-level differences influence outcomes.

Problem solving revealed a small pooled effect (g = 0.19, SE = 0.09, p = .074), with a 95 % CI of [-0.02, 0.39] and an identical prediction interval. Heterogeneity was low to moderate ($I^2 \approx 28$ %), and variability across studies was minimal.

Social Cognition revealed a small, statistically non-significant effect (g = 0.06, SE = 0.06, p = .373), with a 95 % CI of [-0.08, 0.20] and virtually no heterogeneity ($I^2 \approx 5$ %).

Executive functions analysis showed a small, non-significant effect (g = 0.15, SE = 0.14, p = .303), with a wide confidence interval [-0.15, 0.44]. Moderate heterogeneity was present (I 2 \approx 63 %), pointing to inconsistency across studies.

A borderline significant pooled effect was found for overall cognition (g = 0.24, SE = 0.12, p = .079), with a 95 % CI of [-0.03, 0.52]. The prediction interval [-0.12, 0.61] suggests moderate consistency with some variation. Heterogeneity was moderate (I² \approx 40.8 %), though outcome-level variance remained low.

To complement the quantitative synthesis, a GRADE-based appraisal was conducted to assess the certainty of evidence across cognitive domains (supplemental material, table 3). The overall quality ranged from moderate to low.

4. Discussion

This systematic review and meta-analysis aimed to clarify the cognitive effects of tDCS in patients with schizophrenia by integrating data from 33 RCTs. The overall pattern of findings reveals that, while a

significant proportion of trials (\approx 70 %) reported at least one cognitive benefit following active tDCS, the quantitative synthesis highlights a more selective impact, with verbal learning emerging as the only cognitive domain showing a statistically significant pooled effect (Hedges' g = 0.26, p = .034), and no observed heterogeneity ($I^2 = 0$ %). This lack of heterogeneity likely reflects the methodological convergence across trials, particularly in stimulation site and task measures.

This result is of particular interest given that **working memory** was the most frequently reported domain with positive findings in the systematic review, echoing previous reviews that emphasized its responsiveness to frontally targeted neuromodulation (García-Fernández et al., 2025; Kostova et al., 2020; Yu et al., 2020). However, in the meta-analysis, the effect on working memory was only borderline significant (g=0.17, p=.075) and associated with substantial heterogeneity ($I^2\approx58$ %). This discrepancy likely reflects methodological variability across trials, such as stimulation intensity, session frequency, task type, and participant characteristics. For instance, several studies demonstrating working memory improvement employed ≥10 sessions of 2 mA anodal stimulation over the left DLPFC (García-Fernández et al., 2025; Jeon et al., 2018; Shafiee-Kandjani et al., 2025), whereas single-session studies typically yielded null results (Gögler et al., 2017; Schilling et al., 2021).

Conversely, the consistent benefit observed in verbal learning, despite its relatively lower frequency in the systematic review, may indicate that this domain is more robustly and reliably modulated by tDCS. The low heterogeneity and narrow confidence intervals support its replicability, and the effect size, though modest, aligns with clinically meaningful improvement. Neuroanatomically, this could be related to modulation of left frontotemporal circuitry, particularly when stimulation targets the left DLPFC, a region implicated in verbal encoding and retrieval processes (Orlov et al., 2017a; Weickert et al., 2019). This configuration is known to enhance excitability and neuroplasticity via NMDA receptor-dependent mechanisms and calcium influx (Fritsch et al., 2010; Stagg and Nitsche, 2011), consistent with the observed improvements.

The absence of significant effects in attention, visual learning, social cognition, and executive functions, despite their theoretical relevance in schizophrenia, highlights the specificity of tDCS efficacy. In attention, for instance, the meta-analysis revealed no overall benefit (g=-0.14, p=.697), and substantial heterogeneity ($I^2\approx 80$ %) suggests context-dependent or task-specific effects. These results contrast with earlier individual trials reporting benefits in attention and speed of processing

(Smith et al., 2015; Xu et al., 2023), and may reflect variability in outcome measures or differences in baseline attentional deficits.

Similarly, effects on executive function (g = 0.15, p = .303) and social cognition (g = 0.06, p = .373) were non-significant, though some individual trials noted localized improvements in proactive control (Boudewyn et al., 2020) or mentalizing ability (Fan et al., 2025). These findings underscore the importance of interpreting individual study results within the broader context of domain-level analyses, where statistical power and replication are critical. Furthermore, high between-study variability and wide prediction intervals in these domains suggest that uniform effects are unlikely and that more targeted approaches are warranted.

One consistent moderator across studies appears to be protocol intensity and behavioral engagement. Trials using extended protocols (≥10 sessions) (García-Fernández et al., 2025) or concurrent cognitive or occupational tasks (Fathi Azar et al., 2021; Shiozawa et al., 2016) reported more robust improvements. This aligns with the hypothesis that tDCS primarily facilitates activity-dependent neuroplasticity, and its effects are enhanced when coupled with cognitive engagement (Monte-Silva et al., 2009). In contrast, studies using brief or single-session stimulation often reported null effects, suggesting that dosing threshold and task-state are critical determinants of efficacy.

Importantly, stimulation intensity did not show a linear doseresponse relationship. Although 2 mA was the most commonly used setting, at least one study found greater cognitive benefits at 1 mA (Papazova et al., 2018), supporting a possible inverted U-shaped response curve, consistent with findings in both motor and cognitive domains (Monte-Silva et al., 2009). An additional consideration is the non-linear, U-shaped dose-response effect of tDCS, which has been described in both motor and cognitive research. Excessive current intensity may disrupt rather than enhance neuroplasticity, whereas moderate stimulation can optimize excitatory-page 13, paragraph 1). inhibitory balance. This phenomenon may partly explain the variability observed across cognitive domains in our meta-analysis, as protocols employing higher intensities or fewer sessions did not consistently yield significant effects. In contrast, studies applying moderate intensities in repeated sessions more reliably demonstrated cognitive benefits, particularly in verbal learning. These findings underscore the importance of dose optimization and suggest that heterogeneity in stimulation intensity could have contributed to domain-specific differences in pooled outcomes. Similarly, the efficacy of different electrode montages varied: studies using unilateral DLPFC-supraorbital montages generally outperformed bilateral or extracephalic configurations (Hoy et al., 2014; Gomes et al., 2018), likely due to more focused modulation of taskrelevant networks. Given the small number of studies per subgroup, no formal moderator or stratified analyses could be performed, so protocol and diagnosis related effects should be interpreted cautiously.

Methodological limitations in the current literature also merit consideration. Only two studies were rated as low risk across all Cochrane RoB 2 domains, and many exhibited unclear or high risk in randomization and selective reporting. Most included trials allowed stable antipsychotic treatment, and concurrent medication use was generally balanced across active and sham groups; therefore, while potential confounding by antipsychotic dose cannot be entirely excluded, its impact on the observed effects is likely limited. The variability in cognitive batteries, ranging from MCCB and BACS to isolated task measures, compromises comparability and generalizability. As these domain-level analyses were exploratory, no correction for multiple testing was applied. Long-term effects remain largely unexplored, although several trials suggest that improvements may persist for weeks post-stimulation (Jeon et al., 2018; Smith et al., 2020; Meiron et al., 2021). Thus, the domain-level findings should be regarded as exploratory and interpreted with caution.

Overall, these findings support the view that tDCS exerts its effects through a targeted, domain-specific mechanism rather than producing a broad, global pro-cognitive enhancement. This is consistent with the

notion that each cognitive domain relies on distinct neurophysiological substrates, and while some overlap may exist, cognitive functions are fundamentally heterogeneous. These insights further align with the principles of precision medicine, emphasizing that cognition is not a unitary construct. In addition, verbal learning appears to be a particularly promising target, while other domains may require more tailored protocols or multimodal strategies to elicit consistent effects.

To advance the clinical application of tDCS, future research should adopt rigorous, hypothesis-driven protocols with clearly defined cognitive targets, standardized stimulation parameters, and validated cognitive outcome measures, such as the MCCB or BACS. Moreover, combining tDCS with concurrent behavioral or cognitive training may help harness activity-dependent neuroplasticity and maximize therapeutic outcomes. Longitudinal designs with follow-up assessments are essential to determine the durability and functional relevance of cognitive gains. In summary, while the overall cognitive efficacy of tDCS remains modest, its selective and replicable effects in verbal learning support further investigation within precision-targeted neuro-modulation strategies for schizophrenia.

Declaration of generative AI in scientific writing

No generative AI or AI-assisted technologies were used in any of the processes involved in the creation of this study.

CRediT authorship contribution statement

Lorena García-Fernández: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Alberth Patricio Muñoz-Gualan: Writing – review & editing, Writing – original draft, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Verónica Romero-Ferreiro: Writing – review & editing, Formal analysis. Sergio Padilla: Writing – review & editing, Methodology, Formal analysis, Data curation. Daniel de los Santos: Writing – review & editing. Sergio Cardona-Bejarano: Writing – review & editing. Manuela Martín-Bejarano García: Writing – review & editing. Rolf Wynn: Writing – review & editing, Supervision, Conceptualization.

Submission declaration

The authors affirm that the work described in this manuscript has not been previously published nor is under consideration for publication elsewhere. Its submission and publication have been approved by all authors, as well as by the relevant authorities at the institutions where the work was conducted. If accepted, this article will not be published elsewhere.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pnpbp.2025.111526.

Data availability

The data supporting the findings of this study are derived from published randomized controlled trials and are publicly available through the original sources cited in the manuscript. No new primary data were generated by the authors. Extracted datasets used in the meta-analysis are available from the corresponding author upon reasonable request.

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Glossary

DLPFC (Dorsolateral Prefrontal Cortex) A brain region frequently targeted by tDCS due to its role in working memory and executive control.:

Effect Size (Hedges' g) A standardized measure used in meta-analyses to indicate the magnitude of the difference between groups.:

MATRICS Consensus Cognitive Battery (MCCB) A standardized test battery developed to assess cognitive functioning in schizophrenia.:

PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses; a set of guidelines to improve the transparency and quality of systematic reviews.:

RCT (Randomized Controlled Trial) An experimental study design in which participants are randomly assigned to treatment or control conditions.:

RoB 2 Tool The revised Cochrane Risk of Bias tool used for assessing methodological quality in randomized trials.:

tDCS (Transcranial Direct Current Stimulation) A non-invasive brain stimulation technique that delivers a constant, low electrical current to specific brain areas via scalp electrodes.: