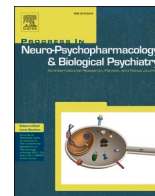




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On the possibility to modulate psychopathic traits via non-invasive brain stimulation: A systematic review and meta-analysis

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ABSTRACT

The affective and interpersonal features of psychopathy describe impairments in socio-affective processes such as affective empathy, prosocial motivation and guilt. Research in neuroscience shows that these processes are associated with distinct neural circuits and cortical excitability patterns that appear to be dysregulated in individuals with psychopathy, with emerging research suggesting the potential of non-invasive brain stimulation (NIBS) to address such disruptions. To investigate this possibility, we conducted a meta-analysis of 64 sham- or active-controlled studies (122 effects) across three modalities: repeated transcranial magnetic stimulation (rTMS), theta-burst stimulation (TBS), and transcranial direct current stimulation (tDCS). Protocols were classified as excitatory (high-frequency rTMS, anodal tDCS) or inhibitory (low-frequency rTMS, continuous TBS, cathodal tDCS) depending on the expected polarity and directionality of their effects. Excitatory protocols yielded small-to-moderate improvements in socio-affective outcomes (Hedges' $g \approx 0.33-0.33$), whereas only cathodal tDCS produced modest reductions among inhibitory protocols ($g = -0.43$). However, over 90 % of the included studies were conducted in healthy adult samples, limiting direct generalizability to psychopathy. In fact, the only available study in psychopathic individuals reported null effects. Together, these findings provide preliminary proof-of-concept for the potential of NIBS to modulate socio-affective processes relevant to psychopathy but also point to substantial methodological variability and the absence of direct evidence for psychopathy treatment in current research. Addressing these gaps is essential to evaluate the feasibility of implementing NIBS methods as a viable intervention for psychopathy.

1. Introduction

Psychopathy describes a complex socio-affective disorder mainly characterized by persistent antisocial behaviors and marked emotional deficits (Hare, 2003; Hare and Neumann, 2008) – most frequently observed in forensic populations with high psychiatric comorbidity (Hare, 2006). Conceptually, psychopathy is most commonly defined under Hare's Psychopathy Checklist-Revised (PCL-R) (Hare, 2003; Hare, 2006), which delineates two broad dimensions with distinct

predictive and clinical significance. Antisocial and lifestyle features such as impulsivity, irresponsibility, and chronic rule-breaking (Factor 2) tend to be stronger predictors of overt outcomes such as violence and recidivism, reflecting their close ties to behavioral deviance (Kennealy et al., 2010). However, affective-interpersonal traits such as callousness, shallow affect, lack of remorse, and manipulateness (Factor 1) are often regarded as more central to the construct of psychopathy (Hare, 2016), as they represent more stable features that distinguish it from related disorders such as antisocial personality disorder (Venables et al.,

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2014; Hare, 1996; Hare et al., 1991; Anderson and Kelley, 2022), and uniquely predict serious forms of aggression like instrumental or predatory violence (Kennealy et al., 2010; Declercq et al., 2012; Glenn and Raine, 2009) – even when expressed at subclinical levels (Camara et al., 2025). In fact, recent evidence shows that while offenders with elevated Factor 2 traits show higher recidivism than general offenders, those with pronounced Factor 1 traits – often described as prototypical psychopathic offenders – are at the greatest risk of both violent and general recidivism (Lehmann et al., 2019), underscoring the potential role of affective-interpersonal features in sustaining persistent and severe offending.

Current interventions in forensic and correctional contexts most commonly rely on traditional psychotherapies like cognitive-behavioral therapy, anger management, or social skills training (Polaschek, 2014; Harris and Rice, 2006). The success of these interventions, however, typically depends on patients' capacity for guilt, sensitivity to punishment, or empathic concern – qualities that individuals with Factor 1 traits demonstrably lack (Felthous, 2011; Felthous, 2015). In fact, while these individuals present a marked incapacity to resonate with others' emotions (i.e., affective empathy), their ability to recognize such emotions (i.e., cognitive empathy) remains relatively intact (De Ridder et al., 2016). This poses significant challenges for interventions that aim to foster emotional understanding for behavioral improvement, as such approaches may inadvertently foster manipulative skills in these cohorts by giving them insight into others' vulnerabilities without addressing their lack of emotional engagement (Kiehl and Hoffman, 2011). This problem is compounded by the fact that treatment progress is often judged by observable behavior, which can create a misleading impression of compliance and contribute to premature release or underestimation of risk (Chialant et al., 2016). In fact, data show that offenders with psychopathy are 3–4 times more likely to reoffend within a year compared to other offenders, with over 70 % of them relapsing into violent crimes over longer periods (Kiehl and Hoffman, 2011; Anderson and Kiehl, 2014). Such outcomes highlight the limited success of existing interventions in achieving lasting behavioral change, underscoring the potential utility of targeting affective-interpersonal deficits to improve treatment prognosis (Felthous, 2015; Weaver et al., 2022).

Advances in neuroscience suggest that these deficits could be partially attributed to dysregulations in cortical excitability (Kiehl and Hoffman, 2011; Anderson and Kiehl, 2012; Blair, 2003; Blair, 2013; Blair et al., 2006). Meta-analytic evidence reveals abnormalities in limbic and paralimbic emotion circuits like the amygdala, the insula and the anterior cingulate cortex (ACC), as well as within prefrontal regions like the ventromedial prefrontal cortex (VMPFC) and the orbitofrontal cortex (OFC) (Deming and Koenigs, 2020). For instance, individuals with psychopathy often show reduced amygdala responses to fear or distress cues, which has been linked to impaired threat detection and blunted empathic responding (Ermer et al., 2012; Ermer et al., 2013; Finger et al., 2012; Jones et al., 2009; Marsh et al., 2013; Yang et al., 2009; Yang et al., 2010; Blair, 2010). Research using functional magnetic resonance imaging (fMRI) further reveals a link between PCL-R interpersonal-affective traits and reduced ACC/insula activation during exposure to others' pain, alongside increased activation in the ventral striatum (a reward-processing area) (Decety et al., 2013). By contrast, in non-psychopathic populations, ACC/insula activation correlates with greater compassion and altruism, suggesting that diminished responses in these regions may contribute to the callous-unemotional style characteristic of psychopathy. These functional patterns are reinforced by structural evidence showing reduced gray matter in the amygdala-hippocampal complex, the VMPFC and the OFC, along with disrupted connectivity between limbic and prefrontal circuits contributing to affective regulation (Anderson and Kiehl, 2012; Deming and Koenigs, 2020). Similarly, electrophysiological (EEG) research indicates that deficits in emotion regulation and sensitivity to punishment may also be attributed to atypical oscillatory dynamics and dysregulated cortical excitability (Van Dongen et al., 2018). Collectively, these findings

indicate that psychopathy's affective-interpersonal core is not merely behavioral but rooted in atypical neural functioning, supporting the case to move beyond purely behavioral interventions to explore the possibility of neuromodulation as a complementary treatment avenue (Canavero, 2014; Van Dongen, 2020; Sergiou et al., 2020).

One conventional approach to neuromodulation involves pharmacological treatments that target neurotransmitter or endocrine imbalances (Demirtas-Tatlidede et al., 2013). However, these treatments have only been proven effective in alleviating psychiatric comorbidities in psychopathic cohorts, having minimal direct effects on the core symptoms of psychopathy itself (Kiehl and Hoffman, 2011; Chialant et al., 2016; Reidy et al., 2013). Moreover, the use of psychiatric medication often comes with adverse side effects that deter long-term adherence (Romero-Martínez et al., 2020). This has led researchers to explore alternative neuromodulatory strategies for psychiatric treatment, among which non-invasive brain stimulation (NIBS) has gained increased popularity within the past decades. Techniques like transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) offer a non-invasive means to modulate cortical neuronal excitability and underlying psychological processes by applying changing magnetic fields or weak electrical currents to the scalp (Polanía et al., 2018; Stagg et al., 2018). High-frequency repetitive TMS (HF-rTMS; 5–20 Hz), for example, increases cortical excitability and enhances facilitatory neuroplasticity via mechanisms akin to long-term potentiation (Bliss and Cooke, 2011; Monte-Silva et al., 2013; Nitsche et al., 2003), while low-frequency rTMS (LF-rTMS; <5 Hz) is typically associated with excitatory-diminishing effects (Finger et al., 2012). Additionally, rTMS can be delivered in bursts of three at 50 Hz with an inter-burst interval of 5 Hz, mirroring theta brain oscillations. When applied intermittently, theta-burst stimulation (TBS) increases cortical excitability (iTBS), while continuous TBS (cTBS) tends to have more inhibitory effects (Huang et al., 2005). Similarly, tDCS applies low-intensity electrical currents either via anodal (A-tDCS) or cathodal (C-tDCS) stimulation, which respectively enhance and reduce neural excitability (Nitsche et al., 2008; Nitsche and Paulus, 2000). Additionally, electrical stimulation can be applied via transcranial alternating current stimulation (tACS), which modulates excitability by entraining oscillatory activity at functionally relevant frequencies (Antal and Paulus, 2013).

While cortical excitability effects have been most consistently demonstrated in motor regions (Polanía et al., 2018; Stagg et al., 2018), growing evidence indicates that similar neuromodulatory principles extend to brain networks involved in emotion and social cognition (Polanía et al., 2018; Bliss and Cooke, 2011; Monte-Silva et al., 2013; Nitsche et al., 2003). For example, HF-rTMS applied to the right dorsolateral prefrontal cortex (DLPFC) has been shown to increase willingness to help others in simulated contexts (Balconi and Canavesio, 2013), and A-tDCS over the left DLPFC reduced self-reported aggression while increasing the perceived moral wrongness of aggressive acts (Choy et al., 2018). Extending these findings to forensic contexts, Molero-Chamizo and colleagues (Molero-Chamizo et al., 2019) reported that anodal stimulation of the DLPFC reduced aggression in violent offenders, highlighting its potential relevance for psychopathy. Comparable findings have been reported in other relevant areas. For example, A-tDCS over the temporoparietal junction (TPJ), a region implicated in perspective-taking and empathy, enhanced empathic responses in healthy adults with lower baseline empathy (Peled-Avron et al., 2019), suggesting its potential utility for counteracting the empathy deficits characteristic of psychopathy. Conversely, cathodal stimulation of the TPJ has been linked to reduced emotional arousal to others' pain (Coll et al., 2017). Similarly, cathodal tDCS over the OFC and VMPFC has been associated with diminished feelings of guilt (Karim et al., 2010), as well as increased willingness to harm and reduced willingness to help others (Chen et al., 2021a). These findings converge with meta-analytic evidence showing that excitatory protocols – A-tDCS (Bahji et al., 2021; Darby and Pascual-Leone, 2017; Smits et al., 2020; Yuan et al., 2021),

HF-rTMS (Darby and Pascual-Leone, 2017; Smits et al., 2020; Christian and Soutschek, 2022) and iTBS (Yang et al., 2018) – reliably improve empathy, perspective-taking, and prosocial decision-making, whereas paradigms like C-tDCS have been associated with reduced prosociality (Yuan et al., 2021).

Collectively, evidence supports the view that different NIBS methods can exert predictable, bidirectional influences on socio-affective behavior, suggesting their potential to modulate the neural dysfunctions underlying psychopathy. Yet findings from existing meta-analyses remain limited in their relevance to socio-affective features specific to psychopathy. For instance, while previous reviews have investigated the effects of NIBS on empathy, they typically conflate cognitive and affective components of empathy, rather than focusing exclusively on affective empathy. Moreover, to our knowledge, no previous review has systematically investigated the effects of NIBS on guilt-related behaviors, which are central to understanding treatment resistance in psychopathy. Furthermore, prior reviews often restrict their scope to a single stimulation modality (either TMS or tDCS), with only two meta-analyses attempting cross-modal comparisons, and even then restricted to broad moral judgments (Darby and Pascual-Leone, 2017) or general emotional responses including aggression (Smits et al., 2020). These gaps leave open critical questions regarding the capacity of NIBS to address the core socio-affective deficits of psychopathy. The present meta-analysis seeks to address this question by evaluating the effects of both magnetic and electrical NIBS protocols on behavioral outcomes directly relevant to the affective–interpersonal dimension of psychopathy, including affective empathy, prosociality, and guilt. For simplicity, we labelled all studies using electrical stimulation as ‘tDCS’, given that tACS involves constantly changing the direction of the current (Antal and Paulus, 2013). We conducted separate analyses for high- and low-frequency rTMS as well as anodal and cathodal tDCS, enabling direct comparisons across excitatory and inhibitory protocols. Guided by established neurophysiological principles, we hypothesized that protocols typically associated with excitatory effects (HF-rTMS, iTBS, A-tDCS) would lead to significant improvements in the targeted outcomes, whereas those typically associated with inhibition (LF-rTMS, cTBS, C-tDCS) were expected to attenuate socio-affective responses.

2. Methods

This research followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009; Page et al., 2021). All study materials, including data extraction spreadsheets, quality assessments, and the R script used for analyses, are openly available at https://osf.io/v9y7w/?view_only=23ea2970387640f48f06b93204a5ba75.

2.1. Eligibility criteria

Eligibility criteria were described following the population-intervention-comparison-outcome (PICO) framework and included: a) Population: adults aged 18 to 64 with or without a psychiatric disorder. The inclusion of non-psychopathic clinical samples is justified by the fact that deficits in the targeted socio-affective processes are present across multiple clinical populations. Studies testing clinical samples were only included provided they controlled for the use of psychotropic drugs; b) Intervention: TMS protocols, including single pulse TMS, rTMS, cTBS and iTBS, and tDCS protocols, including tACS and respective high-definition variants (HD-tDCS and HD-tACS). Studies that included multiple stimulation methods were only considered eligible if they tested the effects of these different methods separately; c) Comparison: studies included a control condition involving either sham stimulation or a control stimulation site for comparison, with a within-subjects or between-groups design and a randomized assignment procedure; d) Outcome: behavioral data collected during or after stimulation, including assessments of psychopathy, affective empathy, prosociality,

and/or guilt.

2.2. Search strategy and study selection

We conducted an electronic search through November 2024 using Scopus, PubMed, and Web of Science, using the following keywords for title and abstract screening: (“transcranial brain stimulation” OR “transcranial magnetic stimulation” OR “theta burst stimulation” OR “transcranial direct current stimulation” OR “transcranial electrical stimulation” OR “transcranial alternating current stimulation”) AND (“callous” OR “psychopathy” OR “empathy” OR “emotional reactivity” OR “guilt” OR “prosocial” OR “altruism” OR “cooperation” OR “helping behavior”). Additional studies were identified through reference lists and forward citations. Study selection was limited to articles written in English and testing adult human participants, using specific filters in each database (see Supplementary section 1). Exclusions included systematic reviews, case studies, and editorials, with additional reasons outlined in Supplementary section 2.

Titles and abstracts were independently screened by three study authors, reaching an interrater agreement of 95 %. Other two study authors subsequently reviewed the full texts of the selected articles, reaching an interrater agreement of 92.5 %. Out of 256 records (including gray literature), 66 studies met the criteria for quantitative analysis (see PRISMA flowchart in Fig. 1). Any disagreements were resolved through consensus among the reviewers.

2.3. Data extraction

Extracted information included: a) study details (study ID, first author and year of publication, country where experiment was conducted); b) participant details (sample type, sample size, gender distribution, age); c) intervention details (experimental design, number of participants per condition, targeted region, stimulation paradigm, intensity, duration, number of sessions, control method); and d) outcome details (target outcome and behavioral measure, mean scores with corresponding standard deviations on behavioral outcomes in each condition).

If studies assessed identical outcomes using different stimulation protocols or various stimulation sites we treated each site trial as a separate unit of analysis. To mitigate the risk of bias and prevent double counting of outcomes, we averaged the effects for studies reporting multiple outcomes of the same measure. Additionally, when studies incorporated various control conditions, we prioritized data extraction from sham control conditions, as these provide a reliable baseline for evaluating the true effects of stimulation. When numerical data were presented graphically, we used Plot Digitizer software ([plotdigitizer.sourceforge.net](https://sourceforge.net)) to extract numerical values and corresponding standard deviations. Most studies included behavioral scales in which higher scores denoted improvements in socio-affective responses (see Supplementary section 3 for a descriptive summary). For scales with inverse trends, we adjusted mean scores by subtracting the group mean values from the maximum scale score, ensuring consistency across study observations (Smits et al., 2020). For studies assessing stimulus-evoked emotional responses, we extracted data consistent with the stimulus valence, on the basis that affective resonance requires alignment between the individual’s response and the emotion conveyed (Vachon and Lynam, 2016). When final scores were not provided, we used change-from-baseline scores as a proxy, which are theoretically comparable to final scores in randomized controlled studies (Higgins and Green, 2011). Refer to Supplementary section 3 for additional details. Any discrepancies or missing information were addressed by contacting the study authors.

2.4. Quality and risk of bias assessment

Two reviewers independently evaluated the methodological quality

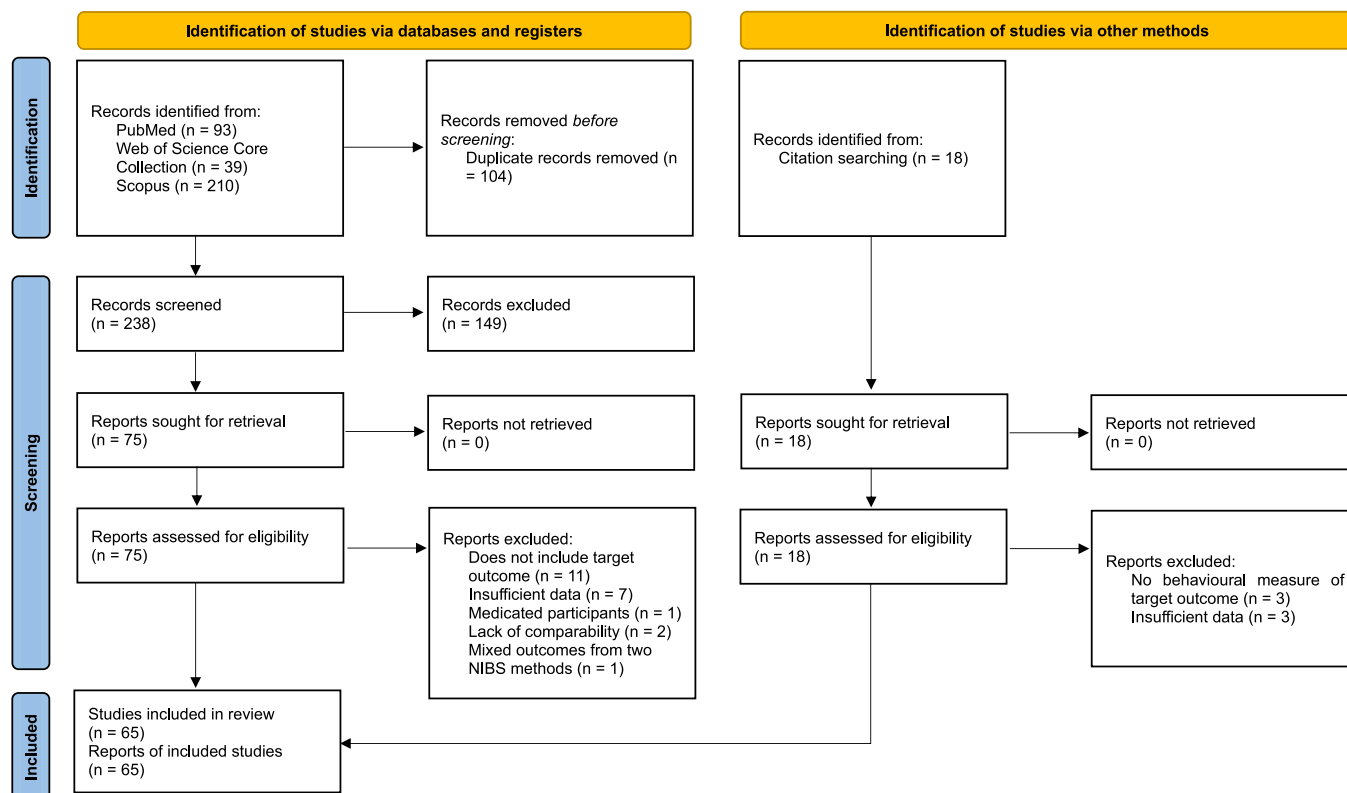


Fig. 1. PRISMA flow chart.

of the included studies. Quality assessment was conducted using the Cochrane Collaboration's Risk of Bias tool (Higgins et al., 2011), which assesses potential bias across six domains: (1) Selection bias, which considers the adequacy of random sequence generation and allocation concealment; (2) Performance bias, relating to the blinding of participants and study personnel; (3) Detection bias, which addresses whether outcome assessors were blinded to group allocation; (4) Attrition bias, concerning the completeness of outcome data and the handling of participant drop-outs or exclusions; (5) Reporting bias, which evaluates the possibility of selective outcome reporting; and (6) Other bias, which includes additional sources of bias such as sample size, baseline imbalances, or other methodological concerns. For each domain, the risk of bias was rated as "low," "high," or "unclear." Discrepancies between reviewers were resolved through discussion to reach consensus. Additionally, we assessed publication bias through funnel plots and Kendall's tau (τ) rank-order correlations (Begg and Mazumdar, 1994).

2.5. Meta-analysis strategy

We conducted a series of multilevel random-effects meta-analyses to evaluate the effects of NIBS on behavioral outcomes, categorized by stimulation modality (magnetic vs. electrical) and expected polarity of effects (excitatory vs. inhibitory). Studies using HD-tDCS or bilateral bipolar montages over the region of interest (ROI) were categorized separately for exploratory analyses, given that the directionality of effects in these protocols is less well established (Garnett et al., 2015) (see Supplementary section 4).

All analyses were conducted in R using the metafor package (Viechtbauer, 2010). Intervention effects on behavioral targets were evaluated by calculating weighted standardized mean difference (Hedge's g) (Durlak, 2009), derived from reported group means and standard deviations (SD). When SDs were not reported, they were computed from standard errors (SE) using the formula: $SD = SE \times \sqrt{n}$, where n is the sample size. To ensure comparability across study designs, within-

subject effect sizes were adjusted for the correlation between pre- and post-intervention scores (assumed $r = 0.5$). Statistical significance was evaluated using 95 % confidence intervals (95 % CI) and p values for statistical significance (setting the significance threshold at $p < 0.05$). Significant effects were visualized using forest plots and further examined via sensitivity analyses, including leave-one-out methods (Willis and Riley, 2017), influence diagnostics and Baujat plots to detect potential outliers (Wang, 2023) (data reported in Supplementary sections 5–7). Between-study heterogeneity was tested via prediction intervals (PI), tau-squared (τ^2), and I^2 statistics (Borenstein, 2023; Higgins and Thompson, 2002), with interpretations made before and after outlier exclusion. Prediction intervals were computed manually using the following formula: $g \pm 1.96 \sqrt{\tau^2}$ (Borenstein et al., 2017), where g represents the pooled effect size. We additionally tested the potential moderating effects of factors related to stimulation parameters, outcome measures, participant characteristics, and experimental settings via subgroup meta-regressions. In accordance with methodological guidance, moderator analyses were restricted to situations where at least 10 studies contributed data to the meta-analysis, to avoid unreliable estimates (Schwarzer et al., 2015). Main effects interpretation and subgroup analyses excluded identified outliers for more reliable conclusions.

3. Results

3.1. Study characteristics

This review covers research published between 2009 and 2024, including 21 studies using rTMS and 44 using tDCS. Additionally, we identified 9 tDCS studies applying bipolar montages over ROIs (Brunoni et al., 2013; Wang et al., 2014; Lisoni et al., 2024; Rêgo et al., 2015; Chen et al., 2019; Snowdon and Cathcart, 2018; Vanderhasselt et al., 2016; Fecteau et al., 2013; Wang et al., 2016), and 6 HD-tDCS studies (Sergiou et al., 2022; Li et al., 2020; Hu et al., 2017; Wu et al., 2018; Long et al., 2023; Zhang et al., 2023). Interestingly, studies using rTMS

were predominantly conducted in Europe (16 studies), whereas nearly half of the studies involving tDCS (23 studies) were specifically conducted in China. Most studies recruited adult participants (ranging 18–45 years old) with no reported psychiatric diagnoses or criminal records. Only three rTMS studies (de Wit et al., 2015; Jansen et al., 2019; Light et al., 2019) and four tDCS studies (Lisoni et al., 2024; Sergiou et al., 2022) tested clinical samples – one of which examined forensic inpatients using HD-tDCS (Sergiou et al., 2022). Additional study details are provided in Tables 1 and 2 and further described in the sections below.

3.2. Effects of rTMS

3.2.1. HF-rTMS

A total of 9 studies ($k = 21$) employed HF-rTMS, with stimulation intensities ranging from 90 % to 120 % of participants' resting motor threshold (rMT). Target outcomes included aspects of affective empathy – particularly emotional responses reflecting affective resonance – and prosocial behavior. Regarding affective resonance, findings were heterogeneous and appeared to depend on both the stimulation site and treatment duration. For example, a single session of 10 Hz rTMS to the right ventrolateral prefrontal cortex (VLPFC) reduced affective resonance to negative stimuli relative to the sham condition (Yu et al., 2023), while another study including two sessions reported no significant changes (He et al., 2023). Similar short-term 10 Hz stimulation protocols (1–2 sessions) targeting the DLPFC also yielded no significant changes in affective resonance – whether applied to the left (de Wit et al., 2015; Möbius et al., 2016) or right (Berger et al., 2017) hemisphere. Interestingly, empathy improvements were observed only in clinical samples receiving extended stimulation over the prefrontal cortex – specifically, 20 sessions to the left DLPFC at 10 Hz (Light et al., 2019) or 10 sessions to the bilateral dorsomedial prefrontal cortex (DMPFC) at 5 Hz (Enticott et al., 2014). In contrast, enhancements in prosocial behavior were more consistently reported following HF-rTMS, particularly at 10 Hz. For example, increased charitable giving was observed after a single session of right VLPFC stimulation (Yu et al., 2023), and three sessions of online bilateral DLPFC stimulation led to improvements in helping behavior (Balconi and Canavesio, 2014). Additionally, one study reported improved social relatedness in adults with autism spectrum disorder (ASD) following 10 offline sessions of 5 Hz bilateral DMPFC stimulation (Enticott et al., 2014). Only one study failed to find significant changes in prosocial behavior (Gallo et al., 2018); this study targeted the left primary somatosensory cortex (S1) at 6 Hz using a two-session online protocol. None of the included studies explicitly examined guilt-related emotions.

Despite the mixed literature, the pooled estimate suggested that HF-rTMS enhances socio-affective responses overall, with a moderate effect size of $g = 0.54$, $p = 0.022$. Nevertheless, the heterogeneity assessment revealed substantial between-study heterogeneity, with a wide prediction interval (95 % PI -1.50 to 2.58) suggesting that a substantial amount of future similar studies would find negative effect sizes, albeit the majority would find positive effect sizes. Sensitivity analyses indicated that the overall effect was especially influenced by one study (Balconi and Canavesio, 2014), whose removal reduced the pooled effect size to $g = 0.39$, $p = 0.043$. However, as shown in Table 3, heterogeneity values remained significant. These results indicate that, regardless of outlier exclusion, HF-rTMS effect on the target outcomes highly varies across studies and may not generalize to all settings or populations.

3.2.2. LF-rTMS and cTBS

We identified 9 studies ($k = 21$) using LF-rTMS at 1 Hz and 6 studies ($k = 13$) using cTBS, all reporting offline paradigms. LF-rTMS intensities ranged from 90 % to 120 % of participants' rMT, whereas cTBS protocols were typically applied at 80 % of the active motor threshold (aMT). Despite differences in stimulation parameters and underlying

mechanisms, we grouped these protocols together to examine their hypothesized inhibitory effects. Most interventions targeted the PFC, yet findings were highly heterogeneous.

On one hand, some studies reported reductions in prosocial behavior following LF-rTMS over the right or left DLPFC – regardless of whether participants received one (Soutschek et al., 2015; Müller-Leinß et al., 2018) or three (Strang et al., 2015) stimulation sessions. Additionally, decreases in affective resonance were reported after a single cTBS session over the right DLPFC (Keuper et al., 2018), and similar findings were observed in LF-rTMS studies targeting the right TPJ (Miller et al., 2020) or the right supplementary motor area (SMA) (Balconi and Bor-tolotti, 2012). Nevertheless, other studies found no significant changes in socio-affective behavior following LF-rTMS over the DLPFC (de Wit et al., 2015; Berger et al., 2017) or VLPFC (Yu et al., 2023), indicating inconsistent results across similar stimulation parameters. Furthermore, most cTBS studies seemed to produce effects opposite to the anticipated inhibitory outcomes. Notably, while one study reported no behavioral changes after cTBS to the right TPJ relative to sham (Tei et al., 2021), studies using active stimulation controls generally found enhancements in socio-affective behavior. For example, single-session cTBS to the right TPJ (Obeso et al., 2018), right DLPFC (Zinchenko et al., 2021) and medial PFC (Christov-Moore et al., 2017) increased prosocial decisions, and stimulation of the medial PFC also led to greater empathic concern for others' distress (Holbrook et al., 2020).

Heterogeneous observations across individual studies were mirrored in the meta-analytic results (Table 3), although effect estimates for both LF-rTMS ($g = -0.83$, $p = 0.112$) and cTBS ($g = 0.06$, $p = 0.678$) were non-significant. Further illustrating the variability and inconsistency of these effects, both meta-analyses exhibited substantial heterogeneity (values reported in Table 3). Due to the non-significant pooled effects, we did not perform further sensitivity analyses for these categories.

3.3. Effects of tDCS

3.3.1. A-tDCS

A total of 28 studies ($k = 44$) applied unilateral anodal stimulation, all using sham-controlled designs. Stimulation intensities ranged from 1 to 2 mA, typically delivered in single sessions of 15–20 min. Affective empathy outcomes were assessed in the majority of studies, but findings were inconsistent. In line with the original hypothesis, several studies reported increases in affective empathy – including heightened arousal to negative stimuli and greater empathic concern – after a single session of A-tDCS over the left insula (Ottaviani et al., 2018; Salvo et al., 2022), medial PFC (Yuan et al., 2017), right medial frontal gyrus (MFG) (Gao et al., 2023), or left DLPFC (Szeremeta et al., 2023). Additionally, one study reported improved empathic concern in adults with ASD across 30 sessions of right TPJ stimulation (Wilson et al., 2021). However, these positive effects were not substantiated by many other studies targeting the left (Boggio et al., 2009; Clarke et al., 2020a; Clarke et al., 2020b; Di Bello et al., 2023; Maeoka et al., 2012) or right DLPFC (Feeser et al., 2014), which reported diminished affective resonance after stimulation. Intervention effects on prosocial behaviors were also mixed. For example, while some studies reported increased charitable giving after stimulation to the right TPJ (Hao et al., 2021; Wu et al., 2023; Yang et al., 2021) or VMPFC (Zheng et al., 2016), other studies using comparable protocols over these same sites showed no significant effects (Zhang et al., 2022; Yu et al., 2022). Similarly, A-tDCS improved cooperative behavior in some studies targeting the right lateral (Liu et al., 2020) and medial PFC (Liao et al., 2018), while other studies targeting these areas reported no change (Chen et al., 2019) or even reduced cooperation (Chen et al., 2021a). Three studies additionally examined guilt-related emotions, targeting the right OFC (Karim et al., 2010), left insula (Salvo et al., 2022), or right DLPFC (Nihonsugi et al., 2015), but only the latter reported higher levels of guilt in the A-tDCS condition relative to sham.

The pooled effect size of these outcomes revealed a moderate

Table 1
Characteristics of rTMS studies.

Reference	Design	Sample	ROI	Montage	Stimulation	Outcome	Intervention effect
Normative and healthy sample							
Balconi and Bortolotti, 2012	Between, Sham and active control	18 (8 men, 10 women), 23.4 ± 2.60	SMA	LF-rTMS	Offline, 1 Hz, 120 %rMT, 400pulses, 3 sessions	Emotional faces task	Reduced the affective response to emotional faces
Balconi and Canavesio, 2014	Between, Sham and active control	25 (14 men, 11 women), 23.78 ± 1.16	middle DLPFC	HF-rTMS	Online, 10 Hz, 120 %rMT, 2400pulses, 3 sessions	Helping behavior	Increased prosocial intervention in conflictual scenarios
Berger et al., 2017	Between, Sham, Single-blind	20 (all women), 23.55 ± 2.58	right DLPFC	HF-rTMS LF-rTMS	Offline, 10 Hz/1 Hz, 110 % rMT, 900pulses, 2 sessions	Emotional reactivity	Not significant
de Wit et al., 2015	Within, Active control, Single-blind	38 (18 men, 20 women), 39.60 ± 11.40	left DLPFC	LF-rTMS	Offline, 1 Hz, 110 %rMT, 3000pulses, 1 session	Emotional reactivity	Not significant
Gaesser et al., 2019	Between, Active control	17 (7 men, 10 women)	right TPJ	LF-rTMS	Offline, 1 Hz, 60 %MSO, 1020pulses, 2 sessions	Helping intentions	Not significant
Gallo et al., 2018	Between, Sham	18 (12 men, 6 women), 25 ± 7	left S1	HF-rTMS	Online, 6 Hz, 90 %rMT, 1440pulses, 1 session	Charitable giving	Reduced participants' decision to give away reward money
He et al., 2023	Within, Sham	117 (57 men, 60 women), 20.38 ± 0.23	right VLPFC	HF-rTMS	Offline, 10 Hz, 90 %rMT, 438pulses, 2 sessions	Emotional reactivity	Reduced negative feelings to social exclusion scenarios
Jansen et al., 2019	Within, Sham, Single-blind	36 (20 men, 16 women), 43.75 ± 10.90	right DLPFC	HF-rTMS	Offline, 10 Hz, 110 %rMT, 1 session	Emotional reactivity	Intensified experienced emotions in response to positive and neutral images
Knoch et al., 2009	Within, Sham, Single-blind	87 (all men), 22.6 ± 0.31	right DLPFC left DLPFC	LF-rTMS	Offline, 1 Hz, 900pulses, 1 session	Reciprocity	Right DLPFC:reduced willingness to reciprocate; left DLPFC: not significant
Miller et al., 2020	Within, Active control	34 (9 men, 25 women), 20.86 ± 2.75	right TPJ	LF-rTMS	Offline, 1 Hz, 100 %rMT, 1200pulses, 1 session	Emotional reactivity	Reduced compassion and increased irritation/annoyance to sad video
Möbius et al., 2016	Between, Sham	23, 21.5 ± 3.0	left DLPFC	HF-rTMS	Offline, 10 Hz, 110 %rMT, 1500pulses, 2 sessions	Emotional reactivity	Not significant
Müller-Leinß et al., 2018	Between, Sham	47 (21 men, 26 women), 24.59 ± 3.47	right DLPFC left DLPFC	LF-rTMS	Offline, 1 Hz, 110 %rMT, 1200pulses, 1 session	Charitable giving	Right DLPFC:decreased fairness; left DLPFC: not significant
Notzon et al., 2018	Within, Sham, Single-blind	40 (17 men, 23 women), 26.525 ± 4.75	right DLPFC	LF-rTMS	Offline, 1 Hz, 120 %rMT, 1800pulses, 1 session	Emotional reactivity	Not significant
Soutschek et al., 2015	Within, Active control	56 (29 men, 27 women), 26.67 ± 4.53	left DLPFC right DLPFC	LF-rTMS	Offline, 1 Hz, 110 %rMT, 480pulses, 1 session	Cooperative behavior	Reduced cooperation rates
Strang et al., 2015	Between, Sham, Double-blind	17 (all men), 23.5 ± 1.23	right DLPFC left DLPFC	LF-rTMS	Offline, 1 Hz, 110 %rMT, 900pulses, 3 sessions	Charitable giving	Right DLPFC:reduced transfers; left DLPFC: not significant
Yu et al., 2023	Within, Active control	108 (54 men, 54 women), 20.43 ± 0.32	right VLPFC	HF-rTMS LF-rTMS	Offline, 10 Hz/1 Hz, 90 % rMT/110 %rMT, 1170pulses/900pulses, 1 session	Charitable giving Emotional reactivity	LF-rTMS: reduced charitable giving; HF-rTMS: increased charitable giving and positive emotions
Christov-Moore et al., 2017	Within, Active control	58 (28 men, 30 women), 21.31 ± 0.29	right DLPFC DMPFC	cTBS	Offline, 5 Hz/50bursts, 80 % aMT, 600pulses, 1 session	Charitable giving	Increased offers
Holbrook et al., 2020	Within, Active control	95 (35 men, 60 women), 20 ± 1.41	MPFC (right DLPFC & pre-SMA)	cTBS	Offline, 5 Hz/50bursts, 80 % aMT, 600pulses, 1 session	Sympathy	Increased reported sympathy for both adversarial and affiliative students
Keuper et al., 2018	Within, Active control	48 (23 men, 25 women), 21.46 ± 4.25	right DLPFC	cTBS	Offline, 5 Hz/50bursts, 50 % MSO, 600pulses, 1 session	Emotional reactivity	Reduced negative resonance
Obeso et al., 2018	Within, Active control	32 (15 men, 17 women), 23 ± 0.34	right TPJ	cTBS	Offline, 5 Hz/50bursts, 80 % aMT, 600pulses, 2 sessions	Charitable giving	Reduced monetary self-interest and increased offers
Soutschek et al., 2016	Within, Active control	exp1: 43 (24 men, 19 women), 23.10 ± 2.30 exp2: 38 (8 men, 30 women), 24.10 ± 2.90	right TPJ	cTBS	Offline, 5 Hz/50bursts, 80 % aMT, 600pulses, 1 session	Charitable giving	Increased prosocial reward
Tei et al., 2021	Between, Sham	25 (all men), 26.50 ± 3.90	right TPJ	cTBS	Offline, 5 Hz/50bursts, 80 % aMT, 600pulses, 2 sessions	Cooperative behavior	Not significant
Zinchenko et al., 2021	Within, Active control	46 (23 men, 23 women), 21.70 ± 2.10	right DLPFC	cTBS	Offline, 5 Hz/50bursts, 80 % rMT, 600pulses, 1 session	Charitable giving	Increased charitable giving

Clinical sample

(continued on next page)

Table 1 (continued)

Reference	Design	Sample	ROI	Montage	Stimulation	Outcome	Intervention effect
de Wit et al., 2015 (OCD)	Within, Active control, Single-blind	43 (21 men, 22 women), 38.4 ± 10	left DLPFC	HF-rTMS	Offline, 10 Hz, 110 %rMT, 3000pulses, 1 session	Emotional reactivity	Not significant
Jansen et al., 2019 (Alcoholism)	Within, Sham, Single-blind	39 (26 men, 13 women), 41.64 ± 8.63	right DLPFC	HF-rTMS	Offline, 10 Hz, 110 %rMT, 1 session	Emotional reactivity	Reduced emotional reactivity
Light et al., 2019 (Depression)	Within, Sham, Double-blind	19 (7 men, 12 women), 45.21 ± 11.21	left DLPFC	HF-rTMS	Offline, 10 Hz, 120 %rMT, 3000pulses, 20 sessions	Emotional reactivity	Increased empathic happiness
Enticott et al., 2014 (Autism)	Within, Sham, Double-blind	28 (23 men, 5 women), 32.20 ± 10.25	Bilateral DMPFC	HF-rTMS	Offline, 5 Hz, 110 %rMT, 1500pulses, 10 sessions	Social relatedness Empathic concern	Reduced social relatedness

Note. active motor threshold (aMT), continuous theta burst stimulation (ctBS), dorsolateral prefrontal cortex (DLPFC), dorsomedial prefrontal cortex (DMPFC), Hertz (Hz), high-frequency repetitive transcranial magnetic stimulation (HF-rTMS), low-frequency repetitive transcranial magnetic stimulation (LF-rTMS), maximum stimulator output (MSO), primary somatosensory cortex (S1), region of interest (ROI), resting motor threshold (rMT), supplementary motor area (SMA), temporoparietal junction (TPJ), ventrolateral prefrontal cortex (VLPFC).

positive effect of A-tDCS ($g = 0.56$, $p = 0.036$), though with a large prediction interval (95 % PI -2.86 to 3.98). Sensitivity analyses showed that this pooled effect might be inflated by a single influential study (Yuan et al., 2017); removing this study reduced the effect estimate to $g = 0.33$, $p = 0.017$. However, the analysis still showed high levels of heterogeneity (Table 3) and a wide prediction interval (95 % -1.38 to 2.04), suggesting again that some future studies are likely to find negative effect sizes.

3.3.2. C-tDCS

A total of 15 studies ($k = 23$) applied unilateral cathodal stimulation, all using sham-controlled designs. Stimulation was delivered almost exclusively at 1.5–2 mA in single sessions of 13–20 min, with two studies applying stimulation at 1 mA (Karim et al., 2010; Li et al., 2018) and one study using 3 sessions (Salvo et al., 2022). Across studies, some results were consistent with the hypothesized inhibitory effect of C-tDCS. For example, stimulation to the anterior PFC reduced self-reported feelings of guilt (Karim et al., 2010), whereas lateral PFC stimulation was associated with reduced cooperation (Li et al., 2018) and norm compliance (Liu et al., 2020). Decreases in affective resonance were also observed following stimulation of the left ventral premotor cortex (PMv) (Colombo et al., 2021), right MFG (Gao et al., 2023), and multi-session stimulation of the left insula (Salvo et al., 2022). Only one study contradicted these effects, reporting increases in charitable giving following left TPJ stimulation (Hao et al., 2022).

Nonetheless, the majority of effects indicated no measurable impact of C-tDCS on the target outcomes (Chen et al., 2021a; Chen et al., 2019; Salvo et al., 2022; Hao et al., 2021; Zheng et al., 2016; Liao et al., 2018; Chen et al., 2021b; Repetti et al., 2022). Despite this, the meta-analysis suggested an overall small-to-moderate inhibitory effect across C-tDCS studies, with a pooled effect of $g = -0.43$, 95 % CI -0.79 to -0.68 , $p = 0.020$. Sensitivity analyses further showed that this effect was largely robust to the exclusion of individual studies. However, the analysis also identified substantial between-study heterogeneity ($\tau^2 = 0.73$, $I^2 = 91.77\%$) and a wide prediction interval (95 % PI -2.10 to 1.25), indicating considerable variability in true effects across studies.

3.4. Moderator analyses

Subgroup/meta-regression analyses were restricted to tDCS protocols given the limited number of rTMS studies, although all subgroup models exhibited significant heterogeneity (see values reported in Table 4). For A-tDCS, study design significantly moderated effects ($Q(2) = 6.35$, $p = 0.042$), with between-subjects studies showing stronger effects ($g = 0.43$, 95 % CI 0.07 to 0.78 , $p = 0.018$, $k = 26$) than within-subjects studies ($g = 0.19$, 95 % CI -0.25 to 0.62 , $p = 0.397$, $k = 17$).

Interestingly, studies applying single-session stimulation reported larger effects ($g = 0.43$, 95 % CI 0.09 to 0.78 , $p = 0.014$, $k = 27$) than studies delivering A-tDCS over multiple sessions ($g = 0.16$, 95 % CI -0.28 to 0.61 , $p = 0.468$, $k = 16$; $Q(2) = 6.52$, $p = 0.038$). Effects were strongest for medial PFC stimulation ($g = 0.97$, 95 % CI 0.35 to 1.59 , $p = 0.002$, $k = 8$; $Q(5) = 12.15$, $p = 0.033$) and for outcomes assessing prosocial behavior ($g = 0.60$, 95 % CI 0.19 to 1.00 , $p = 0.004$, $k = 19$; $Q(3) = 9.33$, $p = 0.025$). Furthermore, studies using moderate sample sizes (30–60 participants) ($g = 0.39$, 95 % CI 0.03 to 0.76 , $p = 0.033$, $k = 25$; $Q(3) = 6.00$, $p = 0.111$) and conducted in East Asian countries – specifically China and Japan – ($g = 0.58$, 95 % CI 0.21 to 0.95 , $p = 0.002$, $k = 24$; $Q(2) = 9.79$, $p = 0.007$) were also associated with larger effect sizes. By contrast, only sample size emerged as a significant moderator of C-tDCS effects ($Q(2) = 5.68$, $p = 0.058$), with studies testing moderate sample sizes showing stronger negative effects on behavioral outcomes ($g = -0.50$, 95 % CI -0.94 to -0.07 , $p = 0.023$, $k = 17$) compared to studies with larger samples (≥ 60 participants; $g = -0.25$, 95 % CI -0.92 to 0.42 , $p = 0.465$, $k = 7$). No other study, stimulation, or design characteristics significantly explained the variance in effects across these modalities.

3.5. Study quality and risk of bias

Fig. 2 presents an overview of methodological quality and risk of bias across studies using rTMS and tDCS. Overall, the majority of studies demonstrated low risk for detection, attrition, and reporting bias, with both significant and non-significant findings being consistently reported and dropout rates either negligible or unrelated to stimulation. The most frequent methodological weaknesses were in selection and performance bias. While many studies reported random allocation of participants to conditions, only one specified the method of random sequence generation (Lisoni et al., 2024) and none indicated allocation concealment. Additionally, blinding procedures were often either absent, vaguely described, or not checked for effectiveness. A small subset of studies demonstrated high risk of bias in specific domains, primarily due to inadequate randomization and reporting or analytical practices that could distort results. For rTMS, two studies did not describe allocation methods (Balconi and Bortolotti, 2012; Zinchenko et al., 2021) and one study did not specify the allocation method (Gallo et al., 2018). Attrition bias was also flagged in one study where dropout details were incomplete (Light et al., 2019). In tDCS studies, high risks were largely linked to reporting and attrition issues, including collapsing data from originally randomized groups (Vanderhasselt et al., 2016; Long et al., 2023), not specifying final sample sizes after exclusions (Repetti et al., 2022), and inconsistencies in sample reporting coupled with potential subjectivity in outcome assessment (Nihonsugi et al., 2015).

Table 2
Characteristics of tDCS studies.

Reference	Design	Sample	ROI	Montage	Stimulation	Outcome	Intervention effect
Normative and healthy sample							
Boggio et al., 2009	Between, Sham/active, Double-blind	23 (11 men, 12 women), 21.3 ± 5.6	left M1 left DLPFC	Anodal	Offline, 2 mA, 5 min, 4 sessions	Emotional reactivity	Left DLPFC: reduced emotional responses; left M1: not significant
Clarke et al., 2020a	Within, Sham, Double-blind	37, (12 men, 25 women), 23.17 ± 6.77	left DLPFC	Anodal	Online, 2 mA, 20 min, 1 session	Emotional reactivity	Reduced emotional reactivity
Clarke et al., 2020b	Within, Sham, Single-blind	116 (36 men, 80 women), 23.03 ± 7.43	left DLPFC	Anodal	Online, 2 mA, 20 min, 1 session	Emotional reactivity	Attenuated reactions to negative emotional content
Colombo et al., 2021	Within, Sham, Single-blind	40, 19.80 ± 1.56	left PMv	Cathodal	Online, 1.5 mA, 20 min, 1 session	Emotional reactivity Dispositional empathy	Reduced arousal and increased self-reported empathy levels
Di Bello et al., 2023	Within, Sham, Single-blind	93 (17 men, 76 women), 23.98 ± 8.13	right FTL	Anodal	Online, 2 mA, 14 min, 1 session	Altruistic behavior	Not significant
Feeser et al., 2014	Within, Sham, Double-blind	42 (20 men, 22 women), 28.45 ± 6.65	right DLPFC	Anodal	Online, 1.5 mA, 20 min, 1 session	Emotional reactivity	Not significant
Gao et al., 2023 exp2	Within, Sham	91 (17 men, 74 women), 21.22 ± 2.28	right MFG	Anodal Cathodal	Online, 1.5 mA, 20 min, 1 session	Emotional reactivity	Anodal: increased negativity; Cathodal: decreased negativity
Hao et al., 2021	Within, Sham, Single-blind	90 (40 men, 50 women), 20.1 ± 0.07	right TPJ	Anodal Cathodal	Offline, 1.5 mA, 20 min, 1 session	Charitable giving	Anodal: increased offer; Cathodal: not significant
Hao et al., 2022	Within, Sham, Single-blind	90 (37 men, 53 women), 21.46 ± 0.10	left TPJ	Anodal Cathodal	Online, 1.5 mA, 20 min, 1 session	Charitable giving	Cathodal: increased investment; Anodal: not significant
Zhang et al., 2022	Within, Sham, Single-blind	107 (39 men, 68 women), 20.07 ± 1.55	DMPFC right TPJ	Anodal	Offline, 1.5 mA, 20 min, 1 session	Altruistic behavior	DMPFC: increased altruism; right TPJ: not significant
Zhang et al., 2023	Within, Active, Single-blind	71 (33 men, 38 women), 20.77 ± 1.88	right DLPFC	Anodal	Offline, 1.5 mA, 20 min, 1 session	Altruistic behavior	Not significant
Zheng et al., 2016	Within, Sham, Single-blind	60 (29 men, 31 women), 21.5 ± 0.23	VMPPFC	Anodal Cathodal	Online, 2 mA, 20 min, 1 session	Altruistic behavior Reciprocity	Anodal: increased altruistic behavior; Cathodal: not significant
Zheng et al., 2016	Within, Sham, Single-blind	60 (28 men, 32 women), 21.55 ± 0.23	right DLPFC	Anodal Cathodal	Online, 2 mA, 20 min, 1 session	Altruistic behavior Reciprocity	Not significant
Li et al., 2018	Within, Sham	83 (42 men, 41 women), 24.04 ± 2.75	right DLPFC	Anodal Cathodal	Offline, 1 mA, 15 min, 1 session	Charitable giving	Anodal: increased compliance; Cathodal: decreased compliance
Yu et al., 2022	Within, Sham	90 (38 men, 52 women), 20.66 ± 0.06	VMPPFC	Anodal Cathodal	Online, 1.5 mA, 20 min, 1 session	Altruistic behavior	Not significant
Karim et al., 2010	Between, Sham, Double-blind	22 (13 men, 9 women), 25.6 ± 4.9	anterior PFC	Cathodal	Online, 1 mA, 13 min, 1 session	Guilt	Reduced feelings of guilt
Karim et al., 2010	Between, Sham, Double-blind	22 (9 men, 13 women), 24.8 ± 3.9	anterior PFC	Anodal	Online, 1 mA, 13 min, 1 session	Guilt	Not significant
Liao et al., 2018	Within, Sham, Single-blind	60 (30 men, 30 women), 20.80 ± 2.56	MPFC	Anodal Cathodal	Online, 2 mA, 20 min, 1 session	Helping behavior	Anodal: increased helping behavior; Cathodal: not significant
Maeoka et al., 2012	Between, Sham, Single-blind	15 (10 men, 5 women), 22.2 ± 1.4	left DLPFC	Anodal	Offline, 1 mA, 20 min, 2 sessions	Emotional reactivity	Reduced reported unpleasantness in response to negative stimuli
Nihonsugi et al., 2015	Between, Sham	22 (13 men, 9 women), 20.5 ± 1.5	right DLPFC	Anodal	Online, 2 mA, 15 min, 2 sessions	Reciprocity	Increased cooperation and guilt aversion
Chen et al., 2017	Within, Sham, Single-blind	48 (15 men, 33 women), 19.58 ± 3.23	left DLPFC	Anodal	Online, 2 mA, 20 min, 1 session	Emotional reactivity	Not significant
Ottaviani et al., 2018	Between, Sham, Single-blind	37 (12 men, 25 women), 26.78 ± 5.04	left Ins	Anodal	Online, 2 mA, 15 min, 2 sessions	Emotional reactivity Guilt	Increased reported disgust and pity, but not guilt
Repetti et al., 2022	Within, Sham, Single-blind	102, 19.81 ± 2.36	right TPJ	Cathodal	Online, 2 mA, 20 min, 1 session	Pain empathy	Not significant
Salvo et al., 2022	Between, Sham	36 (18 men, 18 women), 22.44 ± 3.3	left Ins	Anodal Cathodal	Online, 2 mA, 15 min, 3 sessions	Emotional reactivity Guilt	Anodal: increased disgust ratings; Cathodal: decreased disgust ratings

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Table 2 (continued)

Reference	Design	Sample	ROI	Montage	Stimulation	Outcome	Intervention effect
Chen et al., 2019	Within, Sham, Single-blind	162 (54 men, 108 women), 20.78 ± 0.04	right DLPFC	Anodal Cathodal	Online, 1.5 mA, 20 min, 1 session	Cooperative behavior	Not significant
Szeremeta et al., 2023	Within, Sham, Single-blind	101 (34 men, 67 women), 22.57 ± 5.6	left DLPFC	Anodal	Offline, 1.5 mA, 20 min, 1 session	Emotional reactivity	Increased arousal for positive content and reduced it for negative content
Wu et al., 2023	Within, Sham/active, Single-blind	106 (40 men, 66 women), 20.92 ± 1.65	right TPJ	Anodal	Offline, 1.5 mA, 20 min, 1 session	Altruistic behavior	Increased altruistic propensity
Xu et al., 2021	Within, Sham, Single-blind	80 (40 men, 40 women), 19.7 ± 1.68	left DLPFC	Anodal	Online, 1.5 mA, 20 min, 1 session	Emotional reactivity	Increased empathic responses
Yang et al., 2021	Within, Sham	96 (24 men, 72 women), 21.23 ± 0.10	right TPJ	Anodal Cathodal	Online, 1.5 mA, 20 min, 1 session	Charitable giving	Anodal: increased donation; Cathodal: decreased donation
Chen et al., 2021a	Within, Sham, Single-blind	180 (78 men, 102 women), 20.3 ± 0.04	VMPPFC	Anodal Cathodal	Offline, 1.5 mA, 20 min, 1 session	Cooperative behavior	Anodal: decreased cooperation; Cathodal: not significant
Chen et al., 2021b	Within, Sham, Single-blind	189 (92 men, 97 women), 20.2 ± 0.07	VMPPFC	Anodal Cathodal	Online, 1.5 mA, 20 min, 1 session	Helping behavior	Not significant
Liu et al., 2020	Within, Sham, Double-blind	55 (30 men, 25 women)	Right LPFC	Anodal Cathodal	Offline, 1 mA, 15 min, 1 session	Normative behavior	Anodal: improved normative judgement; Cathodal: reduced normative judgement
Yuan et al., 2017	Within, Sham	64 (38 men, 26 women), 23.57 ± 2.1	MPFC	Anodal	Offline, 1.5 mA, 30 min, 1 session	Emotional reactivity	Increased emotional arousal
Brunoni et al., 2013	Between, Sham	20 (3 men, 17 women), 24.9 ± 3.8	bilateral DLPFC	left and right anodal/ cathodal	Online, 1.5 mA, 33 min, 3 sessions	Emotional reactivity	Not significant
Fecteau et al., 2013	Within, Sham, Double-blind	36 (11 men, 25 women), 21.6 ± 3.8	bilateral DLPFC	left and right anodal/ cathodal	Online, 2 mA, 20 min, 1 session	Psychopathy	Not significant
Wang et al., 2016	Within, Sham	60 (25 men, 35 women), 22.37 ± 0.08	right OFC, right DLPFC	anodal OFC, cathodal DLPFC	Offline, 2 mA, 15 min, 1 session	Reciprocity	Increased money transfer
Wang et al., 2014	Within, Sham, Single-blind	27 (9 men, 18 women), 23.6 ± 2.9	right OFC, left DLPFC	left and right anodal/ cathodal	Online, 2 mA, 5 min, 1 session	Pain empathy	Not significant
Rêgo et al., 2015	Within, Sham, Double-blind	24 (12 men, 12 women), 23 ± 2.57	bilateral DLPFC	left and right anodal/ cathodal	Online, 2 mA, 15 min, 1 session	Pain empathy	Left anodal/right cathodal: decreased negative feelings and arousal; left cathodal/right anodal: not significant
Chen et al., 2019	Within, Sham, Single-blind	162 (54 men, 108 women), 20.78 ± 0.04	bilateral DLPFC	left and right anodal/ cathodal	Online, 1.5 mA, 20 min, 1 session	Cooperative behavior	Left anodal/right cathodal: increased cooperation rates; left cathodal/right anodal: not significant
Snowdon and Cathcart, 2018	Within, Sham, Single-blind	103, 23.07 ± 5.36	bilateral DLPFC	left and right anodal/ cathodal	Online, 1.5 mA, 20 min, 1 session	Charitable giving	Not significant
Brunoni et al., 2013	Between, Sham	20 (3 men, 17 women), 24.9 ± 3.8	bilateral DLPFC	left and right anodal/ cathodal	Online, 1.5 mA, 33 min, 3 sessions	Emotional reactivity	Not significant
Li et al., 2020	Within, Sham, Double-blind	102 (55 men, 47 women), 22.64 ± 7.19	right TPJ	Anodal HD-tDCS Cathodal HD-tDCS	Online, 2 mA, 11.79 min, 1 session	Charitable giving	Anodal: increased donations; Cathodal: not significant
Hu et al., 2017	Between, Sham, Double-blind	114 (39 men, 75 women), 20.77 ± 2.11	right DLPFC	Cathodal HD-tDCS	Online, 2 mA, 18 min, 3 sessions	Helping behavior	Decreased helping behavior
Long et al., 2023	Between, Sham/active	30 (all women), 21.38 ± 2.40	right IPL right ATL	Anodal HD-tDCS	Offline, 1 mA, 20 min, 3 sessions	Dispositional empathy	Reduced reported emotional empathy
Wu et al., 2018	Between, Sham, Single-blind	23 (6 men, 17 women), 24.39 ± 3.47	right IFG	Anodal HD-tDCS Cathodal HD-tDCS	Online, 1.5 mA, 20 min, 3 sessions	Affective sharing	Not significant
Zhang et al., 2023	Within, Sham, Double-blind	63 (32 men, 31 women), 19.83 ± 1.16	right DLPFC right VLPFC	Anodal HD-tDCS	Online, 2 mA, 20 min, 10 sessions	Emotional reactivity	Right DLPFC: reduced responses to social exclusion; right VLPFC: not significant

Clinical sample

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Table 2 (continued)

Reference	Design	Sample	ROI	Montage	Stimulation	Outcome	Intervention effect
Wilson et al., 2021 (Autism)	Between, Sham, Double-blind	7 (5 men, 2 women), 26.1 ± 5.71	right TPJ	Anodal	Online, 2 mA, 30 min, 2 sessions	Empathy	Increased self-reported levels of empathy
Zheng et al., 2021	Within, Sham, Single-blind	90 (36 men, 54 women), 20.46 ± 0.09	bilateral DLPFC	left and right anodal/cathodal	Online, 1.5 mA, 20 min, 1 session	Altruistic behavior	Not significant
Lisoni et al., 2024 (Schizophrenia)	Within, Sham, Double-blind	50 (39 men, 11 women), 42.7 ± 12.17	left DLPFC, right OFC	left anodal/right cathodal	Offline, 2 mA, 20 min, 15 sessions	Guilt	Reduced reported guilt
Vanderhasselt et al., 2016 (Depression)	Within, Sham	37 (26 men, 11 women), 44.03 ± 10.75	bilateral DLPFC	left anodal/right cathodal	Offline, 2 mA, 30 min, 10 sessions	Emotional reactivity	Increased positive affect and decrease negative affect
Sergiou et al., 2022 (Forensic patients with addiction)	Within, Sham, Double-blind	50 (all men), 37.4 ± 9.19	VMPPFC	Anodal HD-tDCS	Offline, 2 mA, 20 min, 10 sessions	Emotional reactivity Dispositional empathy Psychopathy	Not significant

Note. Anterior temporal lobe (ATL), dorsolateral prefrontal cortex (DLPFC), frontal temporal lobe (FTL), high-definition transcranial direct current stimulation (HD-tDCS), inferior frontal gyrus (IFG), inferior parietal lobule (IPL), insula (Ins), medial frontal gyrus (MFG), medial prefrontal cortex (MPFC), milliampere (mA), orbitofrontal cortex (OFC), Prefrontal cortex (PFC), primary motor cortex (M1), region of interest (ROI), supplementary motor area (SMA), temporo-parietal junction (TPJ), transcranial direct current stimulation (tDCS), ventral premotor cortex (PMv), ventrolateral prefrontal cortex (VLPFC), ventromedial prefrontal cortex (VMPPFC).

Table 3

Summary of effect estimates and heterogeneity across rTMS and tDCS protocols.

Variables	k	g	95 % CI based on g		τ^2	I ²	95 % PI based on τ	
			LL	UL			LL	UL
rTMS protocols								
HF-rTMS	21	0.54*	0.08	1.01	1.08	93.86	-1.50	2.58
HF-rTMS ^a	20	0.39*	0.01	0.76	0.65	90.48	-1.19	1.97
LF-rTMS	21	-0.83	-1.86	0.19	5.56	98.11	-5.45	3.79
cTBS	13	0.06	-0.22	0.34	0.19	70.71	-0.79	0.91
tDCS protocols								
A-tDCS	44	0.56*	0.04	1.09	3.04	98.17	-2.86	3.98
A-tDCS ^a	43	0.33*	0.06	0.60	0.76	93.21	-1.38	2.04
C-tDCS	23	-0.43	-0.79	-0.68	0.73	91.77	-2.10	1.25

Note. Anodal transcranial direct current stimulation (A-tDCS), cathodal transcranial direct current stimulation (C-tDCS), confidence interval (CI), continuous theta burst stimulation (cTBS), effect size (g), high-frequency repetitive transcranial magnetic stimulation (HF-rTMS), proportion of variation between studies within a group (I²), number of effects (k), low-frequency repetitive transcranial magnetic stimulation (LF-rTMS), lower limit (LL), prediction interval (PI), upper limit (UL), variation of true effects (τ^2).

* Significant at $p < 0.05$.

^a Analysis after outlier exclusion.

Follow-up assessments additionally indicated potential publication bias across stimulation categories. Specifically, the analyses revealed funnel plot asymmetry in HF-rTMS ($r\tau = 0.36$; $p = 0.022$), LF-rTMS ($r\tau = -0.42$; $p = 0.007$), A-tDCS ($r\tau = 0.26$; $p = 0.011$), and C-tDCS ($r\tau = -0.38$; $p = 0.008$), but not for cTBS ($r\tau = 0.12$; $p = 0.559$). Outlier exclusion removed funnel plot asymmetry in HF-rTMS studies ($r\tau = 0.08$; $p = 0.690$), while the potential for publication bias in A-tDCS remained significant despite excluding the identified outlier ($r\tau = 0.24$; $p = 0.023$). Funnel plots illustrating these patterns are reported in Supplementary section 8.

4. Discussion

The present study aimed to evaluate the potential of NIBS to modulate socio-affective processes that are typically disrupted in psychopathy, focusing on affective empathy, prosociality, and guilt. These constructs were selected based on their established relevance to the affective-interpersonal features of psychopathy, which are believed to present greater difficulties for treatment prognosis (Hare and Neumann, 2008; Hare, 2006; Waller et al., 2020). We limited our analysis to TMS and tDCS due to their widespread use and comparability with prior meta-analytic work. Based on previous findings, we hypothesized that excitatory stimulation would lead to improvements in socio-affective responses and that inhibitory stimulation would attenuate them. The

findings partly supported these predictions but also revealed considerable variability across stimulation protocols and outcome domains.

4.1. Main findings

For rTMS, HF-rTMS was the only protocol to yield a significant pooled effect, with moderate improvements observed in empathy and prosocial behavior. However, these effects were highly heterogeneous and particularly dependent on stimulation site, treatment duration, and population characteristics. Improvements in empathy emerged only in clinical samples following multiple stimulation sessions, while prosociality was more consistently enhanced across both healthy and clinical groups. By contrast, LF-rTMS and cTBS did not produce the expected inhibitory effects. Instead, results across these protocols were inconsistent, with some studies reporting decreases in socio-affective outcomes while others paradoxically found enhancements, leading to overall null meta-analytic effects. For tDCS, the results of both anodal and cathodal meta-analyses were consistent with mechanistic predictions, though qualitative assessment of individual studies revealed that many C-tDCS studies individually reported no effect. In contrast, studies employing anodal stimulation more consistently reported significant intervention effects, although some studies reported that the stimulation diminished expressions of affective empathy and prosocial behavior, further emphasizing the high variability in study outcomes.

Table 4
Subgroup analyses for tDCS protocols.

Variables	Anodal tDCS								Cathodal tDCS							
	k	g	95 % CI based on g		τ^2	I ²	95 % PI based on τ		k	g	95 % CI based on g		τ^2	I ²	95 % PI based on τ	
			LL	UL			LL	UL			LL	UL			LL	UL
Region																
East Asia ^a	24	0.58	0.21	0.94	1.11	93.37	-1.49	2.64	17	-0.37	-0.81	0.07	0.84	91.48	-2.17	1.43
Other ^b	20	0.06	-0.33	0.44	0.27	86.71	-0.96	1.08	7	-0.56	-1.24	0.11	0.56	92.20	-2.03	0.91
Sample																
Moderate	25	0.39	0.03	0.76	0.62	92.25	-1.15	1.93	17	-0.50	-0.94	-0.07	0.78	91.87	-2.23	1.23
Large	16	0.19	-0.27	0.66	1.16	95.26	-1.92	2.30	7	-0.25	-0.92	0.42	0.69	92.06	-1.88	1.38
Design																
Within	17	0.19	-0.24	0.62	0.27	86.61	-0.83	1.21	-	-	-	-	-	-	-	-
Between	26	0.43	0.07	0.78	1.10	93.92	-1.63	2.49	21	-0.47	-0.86	-0.08	0.85	91.54	-2.28	1.34
Paradigm																
Online	24	0.32	-0.05	0.69	0.40	89.20	-0.92	1.56	16	-0.42	-1.07	0.20	1.07	94.52	-2.45	1.61
Offline	19	0.35	-0.07	0.76	1.26	94.97	-1.85	2.55	8	-0.43	-0.88	0.03	0.22	75.16	-1.35	0.49
Sessions																
Single	27	0.43	0.09	0.78	1.05	93.74	-1.58	2.44	21	-0.47	-0.86	-0.08	0.85	91.54	-2.28	1.34
Multiple ^c	16	0.16	-0.28	0.61	0.28	87.37	-0.88	1.20	-	-	-	-	-	-	-	-
Duration																
5-30 min	43	0.02	0.00	0.03	0.76	93.21	-1.69	1.73	24	-0.02	-0.04	-0.00	0.72	91.76	-1.68	1.64
Intensity																
1-2 mA	39	0.12	-0.34	0.28	0.71	92.98	-1.53	1.77	24	-0.18	-0.44	0.08	0.88	93.21	-2.01	1.66
Outcome																
Empathy	20	0.06	-0.33	0.45	0.30	86.76	-1.01	1.13	-	-	-	-	-	-	-	-
Prosocial	19	0.60	0.19	1.00	1.35	94.31	-1.68	2.88	17	-0.36	-0.81	0.09	0.84	91.83	-2.16	1.44
Target																
IPFC	18	0.30	-0.11	0.72	0.77	91.72	-1.42	2.02	9	-0.49	-1.11	0.13	1.20	92.98	-2.64	1.66
mPFC	8	0.97	0.35	1.59	1.07	93.38	-1.06	3.00	6	-0.70	-1.46	0.06	0.98	92.71	-2.64	1.24
Ins	9	0.15	-0.42	0.72	0.13	80.58	-0.56	0.86	-	-	-	-	-	-	-	-
TPJ	6	-0.16	-0.89	0.56	1.36	94.46	-2.45	2.13	-	-	-	-	-	-	-	-

Note. Confidence interval (CI), effect size (g), insula (Ins), lateral prefrontal cortex (IPFC), lower limit (LL), medial prefrontal cortex (mPFC), number of effects (k) (we do not report categories with fewer than 5 effect sizes), prediction interval (PI), proportion of variation between studies within a group (I²), temporoparietal junction (TPJ), transcranial direct current stimulation (tDCS), upper limit (UL), variation of true effects (τ^2).

^a East Asian countries included China and Japan.

^b Other regions included Germany, The Netherlands, Italy, United States, Brazil and Australia.

^c Multiple-session studies ranged from 2 to 4 stimulation sessions.

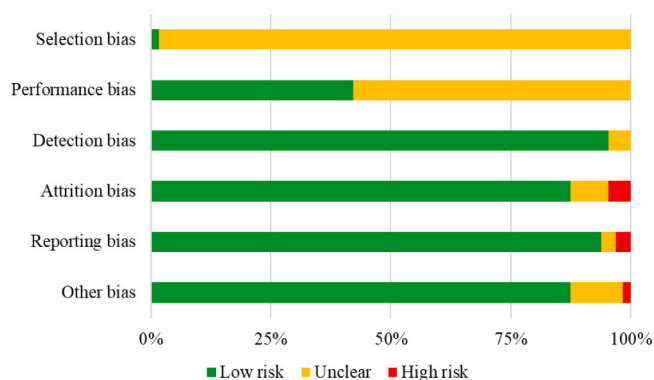


Fig. 2. Summary of quality assessment.

Furthermore, sensitivity analyses suggested that the magnitude of effects of both HF-rTMS and A-tDCS was partly driven by individual influential studies. Interestingly, the identified outliers either assessed participants' emotional responses to witnessing aggression (Yuan et al., 2017) or their predispositions to intervene in such scenarios (Balconi and Canavesio, 2014). This could suggest that excitatory effects on the socio-affective response in normative (non-psychopathic) cohorts may be relative to the emotional saliency of the presented stimuli, which is exacerbated in tasks depicting interpersonal conflict (Yuan et al., 2019). Moderator analyses removing these outliers indicated that A-tDCS effects were stronger in between-subjects designs, single-session interventions and studies testing East Asian samples. Moreover, A-tDCS studies targeting medial PFC regions and prosocial outcomes more

consistently produced behavioral improvements. These patterns suggest that such protocols may hold particular promise for applications in psychopathy, given that disruptions in the medial PFC have been linked to impairments in prosocial and affective functioning frequently observed in psychopathic cohorts (Kiehl and Hoffman, 2011). However, the variability in stimulation sites, together with mixed findings across individual studies, indicates that these apparent subgroup effects should be interpreted as tentative rather than definitive.

4.2. Study limitations

One of the main challenges of interpreting the results from this meta-analysis lies in the inconsistency of the observed outcomes, mainly highlighted through considerably large prediction intervals across all analyses. While previous research indicates that over 70 % of meta-analyses report prediction intervals that include zero (Int'Hout et al., 2016), our qualitative review still highlighted significant variability among the studies included in our meta-analyses. In particular, studies differed widely in stimulation parameters (frequency, intensity, session duration, and online vs. offline protocols), as well as in ROIs, ranging from medial and lateral PFC regions to TPJ, insula, and motor-related areas. Moreover, outcome measures were operationalized inconsistently, with affective empathy, prosocial behavior, and guilt each indexed through diverse and sometimes non-comparable tasks. Few studies employed multi-session designs that might support more durable neural adaptations, although follow-up assessments of long-term effects were almost entirely absent. These issues are further compounded by differences in the neurophysiological impact of the stimulation techniques themselves. For example, subtle changes in coil placement can produce inconsistent outcomes in TMS studies, particularly when

applied online (Walsh and Cowey, 2000). On the other hand, some findings suggest that A-tDCS can potentially cause inhibitory effects when applied at higher intensities (Goldsworthy and Hordacre, 2017). Such technique-specific inconsistencies, combined with the broader methodological variability described above, complicate interpretation of study outcomes and make it challenging to determine optimal stimulation parameters with confidence.

Furthermore, the generalizability of our findings is limited by insufficient research on psychopathy-relevant samples. Responses to NIBS in individuals with psychopathy may differ from those of non-psychopathic populations, as evidence indicates that individuals with psychopathy exhibit distinct neurobiological profiles compared with non-psychopathic cohorts (Blair, 2013). In fact, the only available study we identified in which excitatory NIBS (specifically A-tDCS) was applied to individuals meeting the criteria for psychopathy reported no significant effects (Sergiou et al., 2022). Additionally, although our findings speak to processes relevant to the affective-interpersonal features of psychopathy, only two studies in this review directly assessed psychopathic traits. This reflects the limited availability of NIBS research explicitly targeting psychopathy, presenting a broader shortcoming in the field. Indeed, socio-affective processes such as empathy, prosociality and guilt are relevant in the expression of psychopathy and contribute to treatment resistance, but they do not encompass the full range of affective-interpersonal deficits that characterise the disorder. As such, while the present synthesis offers insight into how NIBS may modulate socio-affective processes commonly impaired in psychopathy, it does not provide direct evidence of its efficacy in psychopathic cohorts or of its capacity to address psychopathy more broadly, highlighting a key gap in the current literature.

4.3. Practical implications and future directions

Despite its limitations, this research provides preliminary proof-of-concept useful for informing future research. For example, while most data were retrieved from healthy samples, the inclusion of studies testing clinical samples with conditions like ASD or depression – while not directly translatable to psychopathy – provides a tentative foundation for exploring NIBS in populations where socio-affective dysfunction is clinically significant. At the same time, however, the heterogeneity and scarcity of this work prevent strong conclusions, underscoring the need for standardization of methods and systematic replication in clinically relevant samples to advance this line of work. Direct comparisons of stimulation parameters (e.g., frequency, montage, session duration, online vs. offline application) are critical for determining the conditions under which NIBS reliably modulates socio-affective behavior. Such efforts would reduce heterogeneity, clarify the role of dose-response relationships, and help distinguish site-specific from network-level effects. Multi-site collaborations and pre-registered protocols could also play an important role in increasing reproducibility and reducing selective reporting, both of which currently contribute to the uncertainty in effect estimates. Additionally, studies should also address the short-term focus of existing work which leaves unresolved whether NIBS can produce enduring changes in socio-affective function. Implementing follow-up assessments over days or weeks, alongside longitudinal designs that track cumulative effects across repeated sessions, would be critical for establishing the durability of stimulation-induced changes.

Furthermore, future work would benefit from integrating neurophysiological measures to determine whether observed behavioral changes correspond to alterations in cortical excitability or connectivity. Incorporating techniques like EEG or fMRI can provide converging evidence on how stimulation modulates neural activity at both regional and network levels. For example, fMRI can clarify whether behavioral improvements correspond to enhanced recruitment of medial prefrontal circuits, while EEG connectivity analyses can detect alterations in oscillatory dynamics that underlie targeted behaviors. Such multimodal approaches would not only strengthen mechanistic interpretations but

also help refine the selection of stimulation targets (Polanía et al., 2018). This is especially relevant for conditions like psychopathy, where functional impairments extend across distributed networks rather than being confined to isolated cortical regions (Kiehl and Hoffman, 2011; Blair, 2013; Carré et al., 2013; Marsh et al., 2011). As such, techniques like cortico-cortical paired associative stimulation – ccPAS for short – represent a particularly promising avenue for future research, as they can induce temporally coordinated plasticity between interconnected cortical sites (Zhang, 2024), potentially allowing more effective targeting of the network-level functional abnormalities commonly observed in individuals with psychopathy.

5. Conclusion

Psychopathy remains one of the most treatment-resistant conditions in psychiatry, with research suggesting that socio-affective processes such as empathy, prosociality, and guilt may be key targets for intervention. In this review, we provide preliminary support for the potential of NIBS to influence these processes, although generalizability to psychopathy is limited by the predominance of research in non-clinical populations and methodological inconsistencies across studies. As such, the discussions in this review should be viewed as proof-of-concept rather than a basis for clinical insight. Moving forward, systematic and standardized investigations in clinically relevant cohorts are needed, ideally incorporating longitudinal designs and neurophysiological measures to optimize stimulation targets. Alongside methodological rigor, it is necessary to also consider ethical safeguards around consent and risk-benefit balance, particularly in forensic contexts. Overcoming these challenges is essential both to determine whether NIBS can be an effective treatment for individuals with psychopathy and support its application in high-risk settings.

CRediT authorship contribution statement

Célia F. Camara: Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Carmen S. Sergiou:** Writing – review & editing, Validation, Methodology, Investigation, Data curation, Conceptualization. **Andrés Molero Chamizo:** Writing – review & editing, Validation, Methodology, Investigation, Data curation, Conceptualization. **Alejandra Sel:** Writing – review & editing, Validation. **Nathzidy G. Rivera Urbina:** Writing – original draft, Validation, Methodology, Investigation, Data curation, Conceptualization. **Michael A. Nitsche:** Writing – review & editing, Validation, Project administration, Methodology, Investigation, Conceptualization. **Paul H.P. Hanel:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pnpbp.2025.111582>.

Data availability

I have shared the link to my data

On the possibility to modulate psychopathy traits via non-invasive brain stimulation: A systematic review and meta-analysis (Original data) (Open Science Framework)

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