Emotion Regulation Intervention Based on Non-invasive Brain Stimulation

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Abstract

Previous research has accumulated substantial evidence that non-invasive brain stimulation (NIBS) techniques can intervene in emotion regulation to improve negative emotions. Summarizing the intervention effects and applicable scope of NIBS on emotion regulation holds significant importance for enriching emotion regulation theory and promoting translational research. Literature reviews reveal that NIBS can effectively influence activity in relevant brain regions (e.g., prefrontal cortex), thereby intervening in both explicit and implicit emotion regulation processes; by improving emotion regulation function, NIBS possesses potential for ameliorating symptoms of mental disorders. Problems yet to be solved in this field are as follows: First, excessive heterogeneity across studies leads to inconsistent results; second, the neural circuit mechanisms underlying emotion regulation intervention processes remain unclear, and measurement indicators for emotion regulation are singular. Furthermore, previous NIBS protocols suffer from issues such as low targeting precision, weak effects within single sessions, difficulty of existing protocols in meeting new needs, and certain side effects. Accordingly, future work should comprehensively and quantitatively summarize existing literature, determine optimal targets by integrating neuronavigation technology, examine neural circuit changes in explicit/implicit emotion regulation under intervention states, and evaluate NIBS intervention effects from multiple levels including subjective experience, physiological indicators, and neural features. Future research could also employ multi-target NIBS protocols, or combine techniques such as hyperscanning and neurofeedback to enhance research validity, providing insights for relevant translational research and clinical applications.

Full Text

Non-Invasive Brain Stimulation-Based Emotion Regulation Interventions

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Abstract

Accumulating evidence demonstrates that non-invasive brain stimulation (NIBS) techniques can effectively intervene in emotion regulation processes and ameliorate negative emotions. Summarizing the efficacy and applicability of NIBS for emotion regulation interventions holds significant importance for enriching emotion regulation theories and advancing translational research. Through literature review, we find that NIBS can effectively modulate activity in relevant brain regions (e.g., prefrontal cortex), thereby intervening in both explicit and implicit emotion regulation processes. By improving emotion regulation functions, NIBS shows potential for ameliorating symptoms of mental disorders. Several issues remain to be addressed in this field: First, excessive heterogeneity across studies has led to inconsistent results. Second, the neural circuit mechanisms underlying emotion regulation interventions remain unclear, and measures of emotion regulation are limited. Additionally, previous NIBS protocols suffer from problems such as low targeting precision, weak single-session effects, inability to meet emerging needs, and certain side effects. Accordingly, future research should quantitatively summarize existing literature comprehensively, identify optimal stimulation targets using neuronavigation techniques, examine changes in neural circuits underlying explicit/implicit emotion regulation during intervention, and evaluate NIBS intervention effects across multiple levels including subjective experience, physiological indices, and neural signatures. Future studies could also employ multi-target NIBS protocols or combine hyperscanning and neurofeedback techniques to enhance research validity, providing insights for relevant translational and clinical applications.

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Emotion regulation refers to the process by which individuals intentionally or unintentionally influence or modulate the generation, experience, and expression of emotions (Gross, 1998). Effective emotion regulation capacity constitutes

a crucial indicator of mental health (Galderisi et al., 2015). Successful emotion regulation yields positive outcomes, including improved overall well-being, work performance, and social relationships (Gross & John, 2003). Conversely, abnormal or deficient emotion regulation not only increases vulnerability to adverse stressors (Crowell et al., 2015) but may also contribute to the onset or relapse of psychiatric conditions such as depression, anxiety disorders, and borderline personality disorder (Aldao et al., 2010). Enhancing emotion regulation abilities can help reduce negative emotional responses to life or work stressors and strengthen psychological resilience when facing negative situations (Charles, 2013). This holds significant practical importance for maintaining national mental health and regulating negative emotions following pandemic policy adjustments.

Brain regions involved in emotion regulation include the prefrontal cortex (PFC), anterior cingulate cortex (ACC), limbic system, parietal lobe, and their surrounding neural networks. Among these, the PFC plays a critical role in emotion regulation and control (Buhle et al., 2014; Morawetz et al., 2020). Research shows that PFC activity increases during emotion regulation, whereas during emotional dysregulation, these regions exhibit either decreased activity (Etkin et al., 2015) or hyperexcitability (Grimm et al., 2008). Enhancing PFC activation through external means may represent an effective approach to improving individual emotion regulation capacity (Smits et al., 2020).

Non-invasive brain stimulation (NIBS) technology is a neuroregulation technique that can target and modulate activity in specific brain regions without causing damage to the human body. Its working principle involves using magnetic fields or electrical currents from external devices placed on the head to alter (enhance or reduce) cortical neural excitability (Ziemann et al., 2008).

NIBS primarily includes transcranial magnetic stimulation (TMS), transcranial electrical stimulation (TES), and transcranial ultrasound stimulation (TUS). TES can be further divided into transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), and transcranial random noise stimulation. Specifically, tDCS can modulate spontaneous neuronal network activity by delivering weak direct currents (0.5–4 mA) to specific scalp regions via electrodes (Brunoni et al., 2012; Farnad et al., 2021). Its modulatory effects depend on stimulation polarity: anodal stimulation enhances while cathodal stimulation suppresses neuronal excitability (Nitsche & Paulus, 2000, 2001). tACS works by applying rhythmic currents to target cortical areas, generating endogenous oscillations by enhancing or reducing synchronization between neuronal activities to modulate brain network activity (A. Liu et al., 2018). TMS employs a wire coil placed over the cerebral cortex, using rapidly generated pulsed magnetic fields to penetrate the skull and alter membrane potentials of subcortical neurons, thereby affecting cerebral metabolism and neuronal activity and producing transient interference with brain function (Gershon, Dannon & Grunhaus, 2003). Based on pulse number and stimulation patterns, TMS is catego-

rized into single-pulse TMS, paired-pulse TMS, and repetitive TMS (rTMS). Currently, high- and low-frequency rTMS are commonly used: low-frequency ($ 1Hz)rTMSisconsideredinhibitory, reducingexcitabilityandmetabolicactivityinspecificbrainregions, wher frequency($5 Hz) rTMS is considered excitatory (Gershon, Dannon & Grunhaus, 2003; Rosa & Lisanby, 2012). tDCS has lower spatial focality and stimulation depth compared to TMS (Keeser et al., 2011). Standard TMS using a figure-8 coil can stimulate to a maximum depth of 1.5–2.5 cm from the scalp, while deep TMS using an H-coil can reach depths up to 6 cm (Roth et al., 2007). Compared to TMS and tDCS, TUS offers higher spatial resolution and deeper penetration, utilizing low-intensity focused ultrasound to traverse the skull and act on neural tissue to inhibit or enhance neuronal activity with high spatial specificity (Mehic et al., 2014). These techniques have been demonstrated in numerous studies to effectively improve cognitive function and ameliorate clinical symptoms of brain functional disorders such as depression and epilepsy (Wang et al., 2022; Hyde et al., 2022).

Currently, NIBS techniques including TMS and tDCS are widely used neuroscientific tools for studying brain function and treating mental illnesses. In the National Science and Technology Innovation 2030— "Brain Science and Brain-Inspired Research" major project implementation plan, NIBS as a representative neuroregulation technology is mentioned multiple times and applied as a novel intervention approach in research domains including brain disease treatment and cognitive function enhancement. For example, applying rTMS to brain regions related to cognitive and emotional functions (e.g., dorsolateral PFC, dlPFC) can effectively improve cognitive function in patients with depression and schizophrenia (Barr et al., 2013). Unfortunately, we have not yet found relevant studies on TUS and tACS intervening in emotion regulation processes. These two techniques are currently used more for improving clinical symptoms of brain functional disorders such as depression, epilepsy, and Parkinson' s disease, with only one abstract reporting that TUS stimulation of the right inferior frontal gyrus can alter self-reported emotional states in healthy participants (Sanguinetti & Allen, 2017). Therefore, this article cannot review research progress on these two techniques for emotion regulation intervention.

Based on the above, this article focuses primarily on TMS and tDCS, reviewing research and applications of NIBS in emotion regulation, development trends, current unresolved issues, and constructive recommendations.

2. Neural Mechanisms of Explicit/Implicit Emotion Regulation and NIBS Effects

Researchers generally categorize emotion regulation into explicit emotion regulation and implicit emotion regulation (Braunstein et al., 2017). Explicit emotion regulation refers to processes initiated through subjective effort with conscious participation and requiring a certain level of monitoring to execute, whereas implicit emotion regulation refers to processes automatically triggered and completed by stimuli themselves without conscious participation or moni-

toring (Gyurak et al., 2011). Numerous reviews and meta-analyses have summarized neuroimaging studies on emotion regulation (Etkin et al., 2015; Morawetz et al., 2020). The core neural circuit mechanism involves PFC regions responsible for cognitive control functions (primarily dlPFC, ventrolateral PFC (vlPFC), parietal lobe, and supplementary motor area) regulating brain regions responsible for emotional responses (subcortical regions including amygdala, ventral striatum, and periaqueductal gray; cortical regions including insula and dorsal ACC). Depending on emotion regulation goals, strategies, and valence of regulated emotions, additional brain regions responsible for language, memory, or motor control functions (including mid-cingulate cortex, parahippocampal gyrus, angular gyrus, and superior temporal gyrus) may also be involved. Notably, the neural circuit mechanisms of implicit and explicit emotion regulation differ slightly: the former primarily relies on ventromedial PFC (vmPFC, which overlaps with ventral ACC) and insula, while the latter relies more on dlPFC, vlPFC, supplementary motor area, and parietal lobe (Etkin et al., 2015). Since the PFC serves as the core trigger region in the neural circuits for both explicit and implicit emotion regulation, most NIBS-based emotion regulation intervention studies target this area. However, researchers believe that NIBS not only alters PFC activation levels but also further modulates activity in deeper brain regions such as ACC, insula, and amygdala (Feeser et al., 2014). Recent research found that TMS stimulation of vlPFC enhanced amygdala activity, suggesting that targeting cortical-subcortical structural connections can enhance scalp TMS effects on subcortical neural activity (Sydnor et al., 2022). This indicates that NIBS influences not only the stimulated target but also affects deeper brain regions and covariation between different brain areas to achieve emotion regulation intervention and improvement (Berboth & Morawetz, 2021). Beyond neuroimaging evidence, NIBS intervention in emotion regulation processes has also accumulated evidence from electroencephalogram (EEG) studies. A TMS-EEG study found that single-pulse TMS over left vlPFC during cognitive reappraisal increased late positive potential (LPP) amplitude in centroparietal and right PFC regions, providing a neural indicator that single-pulse TMS can modulate negative emotional experience through positive cognitive reappraisal (Cao et al., 2022).

Currently, this article could not locate relevant studies using functional near-infrared spectroscopy (fNIRS) to demonstrate NIBS intervention effects on emotion regulation. However, researchers have explored fNIRS neurofeedback training for individuals with mood disorders, where participants could upregulate their right dlPFC activity based on real-time fNIRS feedback signals, significantly improving negative emotion regulation (Yu et al., 2021).

Within the PFC, the left PFC (including dlPFC and vlPFC) represents the primary target for NIBS intervention in explicit/implicit emotion regulation, while the medial PFC (including dorsomedial PFC (dmPFC) and vmPFC) serves as the main target for NIBS intervention in implicit emotion regulation (Etkin et al., 2015). Existing review literature supports the view that NIBS activation of PFC can enhance emotion regulation capacity. For example, Mondino

et al. (2015) summarized findings showing that dlPFC stimulation can affect emotion, emotional processing, and attentional processing of emotional stimuli. Plewnia et al. (2015) found that enhancing or reducing PFC activation levels could correspondingly strengthen or weaken cognitive control over emotions. Amidfar et al. (2019) also demonstrated in their review that dlPFC stimulation could improve cognitive control of emotions. Makovac et al. (2017) conducted a meta-analysis revealing that NIBS could reduce autonomic nervous system responses, suggesting that NIBS can decrease physiological indices accompanying negative emotions. A recent meta-analysis indicated that NIBS can reduce negative emotional responses to stress, supporting the above view, but found small effect sizes for single-session NIBS, recommending repeated NIBS sessions to achieve ideal negative emotion downregulation effects (Smits et al., 2020). Previous studies have accumulated substantial evidence for NIBS interventions in emotion regulation to improve negative emotions. However, due to considerable variation in NIBS parameters across studies (e.g., stimulation depth, intensity, location, and scope), this article has compiled these details along with experimental designs, stimulus materials, task types, emotion regulation directions and strategies, and experimental results (see Tables -2). The following sections introduce NIBS effects on explicit/implicit emotion regulation separately.

When participants are required to use explicit emotion regulation strategies (e.g., cognitive reappraisal, expressive suppression, attentional distraction) for active emotion regulation (Table): He et al. (2020b) found that after activating right vlPFC, individuals'experience of social pain decreased (lower subjective emotion ratings and LPP amplitude), with enhanced emotion regulation capacity. Further research found that rTMS activation of right vlPFC could facilitate social pain regulation and enhance emotional experience from social rewards (Li et al., 2022). Recent studies revealed that activating vlPFC significantly improved negative emotions under cognitive reappraisal conditions, while activating dlPFC significantly improved negative emotions under distraction conditions, with participants showing smaller LPP amplitudes during reappraisal blocks compared to the vlPFC activation group' s distraction blocks (Zhao et al., 2021). Studies using tDCS protocols found functional specificity of left vlPFC in positive reappraisal (Cao et al., 2021). Activation of right vlPFC reduced negative emotional experience intensity (subjective emotion ratings) and physiological indices (pupil diameter) in social exclusion contexts, improving emotion regulation capacity when facing social exclusion (He et al., 2018). Activation of dlPFC or vlPFC enhanced emotion regulation and reduced subjective experience and physiological indices of negative emotions, such as skin conductance level and heart rate (Van Erp et al., 2018). Regarding studies on neural circuit changes during NIBS intervention in explicit emotion regulation, de Wit et al. (2015) found that high-frequency rTMS stimulation of dlPFC in OCD patients affected functional connectivity between frontal and limbic systems, thereby enhancing emotion regulation capacity. Chrysikou et al. (2019) found that during left dlPFC activation with tDCS, mPFC activation was enhanced during emotion downregulation, weakening functional connectivity between mPFC and bilat-

eral amygdala, thereby affecting cognitive reappraisal performance in depressed patients. However, van Dam et al. (2021) found that in healthy controls, right amygdala and visual cortex were activated during negative emotion downregulation before stimulation, yet no brain activation changes occurred during left dlPCS stimulation. Weak or absent effects in this study may be attributed to small sample size and two additional factors: first, moderate-intensity (1.5 mA) unilateral brain stimulation may fail to reach corresponding or deeper brain regions; second, we speculate this may relate to the stimulation protocol design, where the cathode electrode was placed over right dlPFC (also a key emotion regulation region), making it difficult to rule out that the absent effect resulted from cathodal stimulation inhibiting right dlPFC activity.

In studies not requiring participants to complete any emotion regulation tasks (i.e., examining only implicit emotion regulation), TMS protocol studies found that right dlPFC activation reduced valence and arousal ratings of fearful facial expressions (Notzon et al., 2018). Some studies found that bilateral dlPFC activation reduced negative emotional experience intensity (e.g., emotional responses to pain; Boggio et al., 2009; Rêgo et al., 2015). tDCS protocol studies found that tDCS activation of right vlPFC weakened emotional responses to negative stimuli (including subjective emotion ratings and skin conductance activity; Vergallito et al., 2018). Riva et al. (2012) found that activating right vlPFC reduced negative emotional responses induced by social exclusion (social pain and aggressive behavior) and enhanced emotion control capacity; conversely, inhibiting right vlPFC increased negative emotional responses from social exclusion (Riva et al., 2015). Antal et al. (2014) found that activating right mPFC reduced emotional responses to social stress (measured by cortisol levels). A recent study found that tDCS activation of vmPFC not only enhanced implicit emotion regulation effects but also reduced attentional bias toward negative stimuli, with anodal stimulation groups showing significantly lower LPP amplitudes than sham stimulation groups (Gao et al., 2022). Additionally, in studies exploring neural circuit changes during NIBS intervention in implicit emotion regulation, Abend et al. (2019) found that tDCS activation of mPFC reduced emotional intensity ratings of negative video materials while simultaneously activating brain regions involved in implicit emotion regulation (vmPFC, subgenual ACC, and ventral striatum) and altering functional connectivity between these regions. Studies also found that vmPFC activation after tDCS enhanced implicit regulation of anger while reducing aggressive behavior (Gilam et al., 2018), and improved recognition performance and neural responses to happy faces (but not fearful faces) (Winker et al., 2018).

3. NIBS for Improving Emotion Regulation Abnormalities in Psychiatric Populations

Mental disorders are often accompanied by emotion regulation abnormalities (Koole, 2010). Numerous reviews and meta-analyses have demonstrated that NIBS can effectively improve clinical symptoms of depression, anxiety disor-

ders, post-traumatic stress disorder, and other mental disorders (Begemann et al., 2020; Kan et al., 2020; Zhou & Fang, 2022; Hyde et al., 2022). Emotion regulation abnormalities, as a common feature across many mental disorders, have received widespread attention (Koole, 2010). However, regrettably, among numerous NIBS studies, research specifically targeting emotion regulation in these populations remains quite limited compared to studies intervening in overall psychiatric symptom severity. Current efforts in this direction have shown promise, finding that improved emotion regulation function can indirectly reduce symptoms of depression, PTSD, obsessive-compulsive disorder (OCD), and anxiety disorders (Iannone et al., 2016; Ma et al., 2014; Watts et al., 2012). We introduce these findings using depression, anxiety disorders, OCD, and PTSD as examples.

3.1 Depression

Emotion regulation deficits and cognitive impairments are core features of depression, with underlying brain dysfunction stemming from reduced PFC activation during emotion regulation, reflecting weakened cognitive control over negative emotions in depressed populations (Rive et al., 2013; He et al., 2015). Researchers have therefore investigated whether NIBS activation of PFC can enhance cognitive control function to improve negative emotions in depressed patients. In NIBS interventions targeting explicit emotion regulation in depression, studies found that tDCS activation of right vlPFC in individuals with depressive symptoms could significantly improve explicit emotion regulation capacity for social exclusion (He et al., 2020a). TMS protocols yielded similar results, where activating right vlPFC in depressed patients effectively improved explicit emotion regulation capacity for social pain (Mo et al., 2021). NIBS can also effectively intervene in implicit emotion regulation processes. For example, anodal tDCS over left dlPFC can effectively enhance cognitive control performance in depressed patients while completely eliminating attentional bias toward negative emotional pictures. Moreover, compared to sham stimulation, tDCS activation of left dlPFC effectively improved depressive mood experiences, with 30-minute stimulation showing better effects than 20-minute stimulation (Pavlova et al., 2018). Some studies have also explored the possibility of using tDCS to activate vlPFC to improve implicit emotion regulation of social pain in depressed patients, though these have only been reported as abstracts (Hsu et al., 2018). Based on these results, researchers propose the following potential mechanisms: NIBS may directly influence cognitive control processes of emotion by stimulating the dlPFC node of the cognitive control network, ultimately achieving emotion upregulation or downregulation (Lantrip et al., 2017).

3.2 Anxiety Disorders

Anxiety disorders include generalized anxiety disorder, social anxiety disorder, phobias, etc. Emotion regulation difficulties also characterize anxiety disorders and are associated with abnormal activity in neural circuits including dlPFC.

Studies show that rTMS can improve anxiety symptoms (Mantovani et al., 2010; Rodrigues et al., 2019) and anxious depression (Diefenbach et al., 2013). However, research specifically targeting explicit emotion regulation in anxiety patients remains scarce. One study demonstrated that 30 sessions of low-frequency rTMS over right dlPFC in generalized anxiety disorder patients significantly improved emotion regulation capacity (Diefenbach et al., 2016), though this study only used self-report measures of emotion regulation difficulties without neurophysiological evidence. Additionally, Haeems (2018) found that 20-minute tDCS stimulation of PFC or cerebellum in social anxiety disorder patients effectively improved cognitive reappraisal capacity. Currently, no NIBS intervention studies targeting implicit emotion regulation in anxiety patients have been identified.

3.3 Obsessive-Compulsive Disorder

Impaired emotion regulation underlies excessive emotional reactions in OCD patients. In NIBS interventions targeting explicit emotion regulation in OCD, studies found that high-frequency rTMS over dlPFC helped enhance cognitive reappraisal processes and reduce negative emotional responses (de Wit et al., 2015). Douw et al. (2020) found that excitatory rTMS over dlPFC could reduce emotional distress in OCD patients. In studies targeting fear extinction (a form of implicit emotion regulation), researchers used anodal tDCS over mPFC and found this protocol significantly facilitated safety learning (a process of inhibiting fear emotions through learning new safety cues), thereby reducing patients' emotional distress (Adams et al., 2021).

3.4 Post-Traumatic Stress Disorder

PTSD is characterized by dysregulated emotional responses to fear-conditioned stimuli (Parsons & Ressler, 2013). Neuroimaging studies indicate that PTSD patients show hyperactive amygdala and significantly reduced hippocampal and vmPFC activity when facing fear-conditioned stimuli (Etkin & Wager, 2007; Shin et al., 2006). These neuropathological mechanism studies provide target references for NIBS interventions in PTSD patients'emotion regulation processes. Currently, no NIBS intervention studies targeting explicit emotion regulation in PTSD patients have been identified. In studies of implicit emotion regulation, researchers found that tDCS activation of vmPFC after fear extinction learning could improve fear memory extinction in PTSD patients (Van' t Wout et al., 2017). Clinical trial results for PTSD patients showed that combining working memory training with tDCS significantly improved cognitive function and emotional performance (Kedzior et al., 2012; Saunders et al., 2015).

4. Unresolved Issues and Constructive Recommendations

In summary, NIBS has been proven effective in modulating activity in emotion regulation-related brain regions (e.g., PFC), thereby intervening in both explicit

and implicit emotion regulation processes. NIBS protocols utilizing this mechanism have demonstrated considerable potential in treating mental disorders. However, numerous issues remain unresolved in this field, such as inconsistent results across NIBS emotion regulation intervention studies, unclear specific changes in neural circuits during emotion regulation intervention, and low targeting precision of stimulation sites. Below, we address each issue and provide corresponding constructive recommendations.

4.1 Excessive Inter-Study Heterogeneity Leads to Inconsistent Results: Quantitatively Summarize Existing Literature and Employ Multi-Target Regulation Techniques to Reduce Confounding Variables

Currently, most studies in this field support NIBS emotion regulation intervention effects. However, some studies have failed to find such intervention effects (Mungee et al., 2016; van Dam & Chrysikou, 2021). This may be due to heterogeneity across studies, such as individual differences among participants, stimulation depth, stimulation parameters, and offline (NIBS and experimental tasks conducted separately) versus online (NIBS and experimental tasks conducted simultaneously) NIBS protocols. These factors may mask the universality and reliability of NIBS effects to some extent. Specific heterogeneity factors include: Individual differences among participants lead to different results. For example, Hofhansel et al. (2020) used anodal tDCS over dlPFC in both criminals and healthy controls, finding that criminals showed significantly reduced rather than increased brain excitability, challenging the traditional view of dichotomous tDCS effects (anodal excitatory, cathodal inhibitory). Additionally, anodal tDCS over right vlPFC effectively downregulated social pain in low-depression individuals but showed weak effects in high-depression individuals (He et al., 2020a). Regarding stimulation depth, conventional TMS (e.g., standard figure-8 coil) can only stimulate superficial brain regions approximately 1–2 cm below the skull (Deng et al., 2013), making it difficult to ensure stimulation of deeper brain regions related to emotion regulation (e.g., mPFC, amygdala). Therefore, insufficient stimulation depth may be one reason why some studies failed to find NIBS intervention effects on emotion regulation (Kirkovski et al., 2017). Deep TMS can stimulate deeper brain regions up to 4 cm below the skull (Tendler et al., 2016). Studies found that deep TMS over mPFC significantly enhanced participants' expectations of negative social feedback (Zhang et al., 2022). Stimulation parameter selection (e.g., target site, polarity) also affects emotion regulation outcomes: Regarding target sites, studies found that anodal tDCS over right vlPFC could enhance cognitive reappraisal capacity and reduce negative emotional experiences (Zhang et al., 2019). This protocol could also significantly upregulate or downregulate emotional valence evaluations of negative pictures, whereas dlPFC stimulation could not achieve expected effects (Marques et al., 2018). Regarding polarity selection, Abend et al. (2016) found that anodal tDCS over mPFC could not reduce fear extinction and even induced generalization of fear responses to neutral stimuli, while other researchers found

that anodal tDCS over vmPFC could enhance fear extinction (Dittert et al., 2018; van ' t Wout et al., 2016). Studies using cathodal tDCS also showed contradictory results: some found cathodal tDCS over right dlPFC had no effect on fear elimination in healthy participants (Mungee et al., 2016), while others showed positive results (Ganho-Ávila et al., 2019). Offline versus online NIBS also affects emotion regulation outcomes. Studies found that online tDCS over left dlPFC failed to enhance emotion regulation capacity for aversive pictures (Clarke et al., 2020), whereas offline tDCS over left dlPFC could enhance regulation capacity and even improve perception of positive emotional pictures (Hansenne & Weets, 2020).

Given the inconsistent NIBS intervention effects, future research could be improved through the following approaches: (1) Conduct more comprehensive meta-analyses to validate the effectiveness and universality of NIBS for emotion regulation and identify potential factors influencing intervention outcomes. Currently, three relevant meta-analyses or reviews have examined NIBS effects on emotion regulation. Smits et al. (2020) meta-analysis showed tDCS had small but significant effects in reducing stress-related emotional responses but provided no evidence that rTMS over PFC could affect emotional responses. Markovic et al. (2021) review indicated both tDCS and rTMS could effectively modulate fear memory and extinction processes. The latest meta-analysis showed single-session NIBS had significant effects on downregulating negative emotions, with rTMS showing moderately significant effects while tDCS showed no significant effects (Zhang et al., 2022). However, these three articles have limited focus: Markovic et al. only reviewed NIBS effects on fear emotion regulation without providing meta-analytic or systematic review evidence. Smits et al. primarily focused on how NIBS affects stressful emotional reactivity, with little mention of emotion regulation processes. Zhang et al. measured negative emotion regulation effects using subjective self-reports, making results susceptible to bias. Furthermore, all three articles only included single-session NIBS studies, lacking quantitative comparison with multi-session NIBS results, and only analyzed unidirectional emotion regulation targets (downregulation only, not upregulation). (2) Employ multi-target regulation techniques to reduce confounding variables. Dual-coil TMS, for example, offers advantages over single-coil TMS: Random stimulation patterns with dual coils can reduce interfering psychological factors in single-site stimulation (e.g., expectancy effects, attentional distraction); Multi-coil TMS serves as an alternative to deep TMS for stimulating deep cortical structures while ensuring target precision (Tzabazis et al., 2013); Dual-coil TMS can be used to study functional connectivity and plasticity between different brain regions, helping reveal pathophysiological mechanisms of various psychiatric disorders (e.g., schizophrenia, autism) (Lafleur et al., 2016). Another application is multifocal tDCS, which typically uses more than two electrodes (e.g., one anode and four or more cathodes). Compared to conventional bipolar tDCS, multifocal tDCS offers higher spatial precision (Ruffini et al., 2014; 2017) and induces stronger cortical excitability (Fischer et al., 2017). Clinically, multi-target NIBS has been proven effective

in relieving neuropathic chronic pain (Chodakiewitz et al., 2013) and motor impairments in Parkinson' s disease patients (Stefani et al., 2009), and even improving pain sensitivity in patients with prolonged disorders of consciousness (Zhang et al., 2021). Studies have used multi-target NIBS protocols to simultaneously apply high-frequency rTMS to left dlPFC and dmPFC in major depressive disorder patients, finding significant improvement in depressive symptoms (Carpenter et al., 2017). Juliana et al. (2021) reported in an abstract that multi-target rTMS simultaneously stimulating left dlPFC and primary motor cortex was more effective than single-target rTMS in improving depressive symptoms. In a fear extinction study of OCD patients, researchers used one anodal electrode over mPFC and five cathodal electrodes surrounding it, finding this protocol significantly increased functional connectivity between frontal pole and middle/superior frontal gyri, promoting safety learning effects in exposure therapy (Adams et al., 2021). However, literature using multi-target protocols to intervene in emotion regulation processes in both healthy and psychiatric populations remains scarce. Future research could focus on exploring precise multi-target NIBS regulation of brain regions corresponding to emotion regulation (e.g., using dual-coil TMS to investigate temporal sequences of different brain regions in explicit emotion regulation), combined with functional magnetic resonance imaging (fMRI) and EEG to observe neural mechanism changes under multi-target NIBS, thereby clarifying causal relationships of each brain region in emotion regulation processes.

4.2 Neural Circuits Underlying Emotion Regulation Intervention Require Further Investigation

NIBS protocols targeting dlPFC have proven effective in modulating emotional responses and cognitive deficits (Kuo et al., 2014). However, only three studies to date have combined neuroimaging to probe neural mechanism changes during NIBS intervention in explicit emotion regulation (Chrysikou et al., 2019; de Wit et al., 2015; van Dam & Chrysikou, 2021). These studies had small sample sizes and used single-session stimulation, likely resulting in insufficient effect sizes. No studies have yet used specific implicit emotion regulation tasks (e.g., emotion labeling tasks, emotional Stroop tasks) to investigate neural circuit mechanisms during NIBS intervention. Therefore, questions remain regarding which deep brain regions are simultaneously affected when PFC is activated by NIBS during explicit/implicit emotion regulation and how PFC-deep brain region connectivity changes, requiring further empirical research.

Combining fMRI technology to study neural circuit mechanisms during NIBS emotion regulation intervention represents current research trends, but development is limited by technical constraints. For example, combining online TMS with fMRI results in interaction between TMS current pulses and MRI scanner magnetic fields, producing loud noises that cause participant discomfort and compromise coil mechanical stability, posing safety risks (Bungert, 2010). Therefore, most fMRI studies adopt offline NIBS protocols. Currently, online

tDCS-fMRI combination has been technically achieved (Baeken et al., 2018; van Dam & Chrysikou, 2021), potentially serving as an alternative to online TMS-fMRI. However, tDCS has lower spatial precision than TMS, making it difficult to achieve satisfactory stimulation effects. Presently, TMS-fMRI technology continues to develop, with studies proposing new fMRI-compatible TMS coil designs that effectively improve TMS mechanical stability (Sanchez et al., 2020).

NIBS intervention studies on emotion regulation neural circuits also have potential clinical application value. Relevant findings could promote translational research and even guide NIBS intervention strategies for psychiatric populations. For example: (1) NIBS activation effects on PFC can be detected through fMRI, allowing MRI to accurately locate target regions in patients' PFC. Considering individual differences in anatomy and electrophysiology among psychiatric populations, this system could optimize stimulation sites and frequencies for TMS/tDCS non-responders, enabling personalized NIBS treatment protocols (Cash et al., 2021; Modak & Fitzgerald, 2021). (2) Since NIBS effects on PFC can project to deep brain regions such as vmPFC, amygdala, and insula, deep brain regions could also serve as NIBS targets for treating psychiatric disorder-related symptoms, beyond superficial targets in lateral PFC (Downar & Daskalakis, 2013). (3) Given that PFC-NIBS can modulate functional connectivity between emotion regulation-related brain regions, future NIBS intervention targets could aim to remotely alter functional connection strength to improve emotion regulation function (Hiser & Koenigs, 2018; Myers-Schulz & Koenigs, 2012).

4.3 Low Targeting Precision of NIBS Stimulation Sites: Neuronavigation Techniques Can Improve Localization Accuracy

To precisely locate emotion regulation-related brain regions and maximize electric field strength or focality in NIBS target areas, most previous studies have relied on manual positioning or the 10-20 international standard EEG electrode positioning system. However, these methods fail to adequately account for individual differences in head size, shape, and cortical morphology (Gordon et al., 2017). Therefore, whether these studies accurately stimulated intended targets remains questionable. Neuronavigation techniques guided by MRI and other brain imaging can solve this problem. Using optical or magnetic tracking devices, this technology displays brain structural images for individualized modeling, precisely measuring stimulation target location, angle, and depth, and visually guiding NIBS coils to track stimulation targets, thereby achieving "tailor-made"stimulation target localization protocols for each participant (Cash et al., 2021). Combined electrophysiological and neuroimaging neuronavigation techniques can also address where, when, and how NIBS should be applied, while providing both online and offline neuronal activity data (Bergmann et al., 2016). Studies found significant differences in dlPFC target location, stimulation scope, and current intensity when localized through neuronavigation versus

the 10-20 system (De Witte et al., 2018). This strongly suggests that most previous studies may not have precisely stimulated target brain regions, making it necessary to adopt neuronavigation techniques to optimize stimulation target precision and verify the reliability of previous findings.

Some studies have already combined neuronavigation with NIBS technology. For example, in research on neural mechanisms underlying increased emotional reactivity in OCD patients, researchers used real-time neuronavigation to precisely locate dlPFC, optimizing rTMS intervention effects (de Wit et al., 2015). Using MRI-compatible neuronavigation systems for tDCS can precisely locate left dlPFC and better exclude interference factors from head movement (Baeken et al., 2018). Additionally, optical neuronavigation techniques have demonstrated superior effects over manual target localization. For instance, during offline rTMS, optical navigation systems can automatically locate and monitor each participant' s left inferior frontal gyrus, achieving individualized and automated monitoring of stimulation targets (Urgesi et al., 2016).

4.4 Weak Effects of Single Stimulation Session: Multi-Session Stimulation Can Enhance Intervention Effects

Previous meta-analyses noted that single-session or few-session NIBS produces weak effects on emotion regulation, recommending multi-session repetitive stimulation to enhance intervention effects (Smits et al., 2020). For example, individuals with depressive tendencies have difficulty benefiting from single-session stimulation (He et al., 2020a; Zhang et al., 2021), possibly related to insufficient stimulation sessions and short duration. Similarly, single-session tDCS effects are far less robust in depressed patients than in healthy controls during cognitive control tasks (Wolkenstein & Plewnia, 2013). After single-session short-duration tDCS over right vlPFC, high-depression individuals showed significantly less reduction in negative emotion intensity than low-depression individuals (Zhang et al., 2019). Single-session tDCS in special populations (criminals) also failed to reveal different neural responses from normal controls during emotion regulation tasks (Hofhansel et al., 2020). However, continuous multi-session repetitive NIBS holds promise as a superior protocol for verifying intervention effects. It can not only effectively increase cortical excitability (Bergmann et al., 2016) but also enhance intervention effects on working memory or cognitive control (Elmasry et al., 2015; Hill et al., 2016). Molavi et al. (2020) found that continuous multi-session tDCS (20 minutes/day for 10 days) over bilateral dlPFC in borderline personality disorder patients effectively improved their cognitive reappraisal capacity and executive function. In NIBS applications for affective disorders, 20–30 sessions represent the recommended value (Martin et al., 2018). Longer stimulation sessions (30 vs. 20 minutes) produce better clinical efficacy (Woods et al., 2016). These findings suggest the potential for using repeated multi-session NIBS to enhance emotion regulation intervention effects in both healthy and depressed populations.

4.5 Single-Dimensional Measurement of Emotion Regulation Effects: Multi-Level Assessment Can Characterize NIBS Intervention Effects

Emotion regulation effects are measured by comparing differences in emotional indices before and after regulation. Emotion indices primarily include subjective experience and physiological measures. Subjective experience refers to individuals' self-rated emotional feelings and scores on emotion questionnaires. When negative emotions arise, subjective negative emotion intensity scores increase and emotion questionnaire scores rise (Gross & John, 2003). Physiological indices mainly refer to autonomic nervous system (ANS) measures, including heart rate, blood pressure, pupil diameter, and skin conductance level. When negative emotions arise, the ANS responds rapidly, causing increased heart rate, elevated blood pressure, enlarged pupil diameter, and rising skin conductance level (Levenson, 2014). Additionally, negative emotions can elicit other neural signature responses, such as increased LPP amplitude in EEG and activation in brain regions responsible for emotional responses (e.g., amygdala) (Hajcak et al., 2010; Kragel & LaBar, 2016). Previous studies have primarily measured emotion regulation effects through subjective experience. However, influenced by social desirability or conformity effects, participants may conceal their true subjective experience intensity, whereas physiological indices and neural signatures represent unbiased, genuine responses (Mauss & Robinson, 2009). Therefore, examining only subjective emotional experience is insufficient to capture and reveal the full picture of emotion regulation processes. Emotion regulation occurrence and effectiveness should be verified through combined assessment of subjective experience, physiological indices, and neural signatures.

4.6 Existing NIBS Protocols Cannot Meet Emerging Emotion Regulation Research Needs: New NIBS Protocols Urgently Needed

Previous studies have primarily examined intrapersonal emotion regulation, with less attention to emotion regulation in multi-person contexts, such as interpersonal emotion regulation, which represents an emerging research hotspot (Niven, 2017; Ray-Yol & Altan-Atalay, 2022; Zaki & Williams, 2013). Interpersonal emotion regulation refers to the process by which individuals purposefully influence others' emotional experiences in social interaction contexts (Zaki & Williams, 2013). Current NIBS protocols can only match individual needs for emotion regulation intervention and cannot investigate or intervene in relevant indices in interpersonal emotion regulation contexts, such as interbrain synchronization—a measure of brain-to-brain coupling that assesses dynamic similarity of brain signals between two or more interacting individuals (Hasson et al., 2012; D. Liu et al., 2018; Valencia & Froese, 2020). To address this issue, a potential research approach combines multi-brain NIBS with hyperscanning technology. Studies show that synchronizing neural rhythms between two brains can effectively facilitate interpersonal information flow (Lakatos et al., 2019). Simultaneously stimulating bilateral inferior frontal brain regions with same-frequency tACS can enhance social interaction and learning between

individuals (Pan et al., 2021). Using multi-brain NIBS to simulate exogenous conditions of human interbrain synchronization and measuring corresponding effects on social behavior could reveal whether interbrain synchronization can causally modulate social interaction, ultimately providing scientific explanations for interbrain synchronization at both behavioral and neural mechanism levels. This may help identify potential treatment approaches for interpersonal emotion regulation abnormalities in psychiatric populations such as depression, agoraphobia, and social phobia (Novembre & Iannetti, 2021).

4.7 NIBS Has Certain Side Effects: Neurofeedback Techniques Can Compensate for These Limitations

NIBS is an exogenous neuroregulation technique that, while non-damaging to the human body, still accompanies certain side effects during implementation, such as electrical current stimulation in tDCS and noise and vibration stimulation in TMS. These side effects can influence NIBS emotion regulation intervention effects to some extent. In contrast, endogenous neuroregulation such as real-time neurofeedback can achieve truly non-invasive and side-effect-free modulation. Neurofeedback is a method for training brain functional self-regulation, presenting individuals' current brain activity to themselves or others through visual, auditory, or other sensory systems and allowing individuals to modify corresponding brain functions and behaviors (Marins et al., 2019; Papoutsi et al., 2018). In emotion regulation strategy training, neurofeedback-enhanced training is more effective than traditional methods and has been successfully used to improve emotion regulation (Linhartová et al., 2019). The combination of neurofeedback and fMRI represents an emerging technical approach for studying emotion regulation and can enhance emotion regulation capacity in psychiatric groups with emotion regulation deficits. For example, Herwig et al. (2019) used fMRI real-time neurofeedback technology for emotion regulation training in healthy participants. Results showed that compared to control groups, experimental groups could significantly downregulate their amygdala activity signals and successfully reduce negative emotions. This technology can also effectively train depressed patients to use cognitive reappraisal strategies while significantly enhancing left vlPFC excitability, enabling patients to successfully apply emotion regulation strategies in daily life (Keller et al., 2021).

Researchers have also combined neurofeedback with fNIRS. In experiments, participants could upregulate right dlPFC activity based on real-time fNIRS feedback signals to improve negative emotion regulation (Yu et al., 2021). Studies found that patients with PTSD, borderline personality disorder, and schizophrenia showed symptom reduction after neurofeedback training (Linhartová et al., 2019). Future fMRI real-time neurofeedback training for emotion disorder populations could target important emotion regulation brain regions and key brain functional connection targets. Based on existing hypotheses, patients could be required to self-regulate relevant brain region functions with real-time neurofeedback. For example, based on the hypothesis that depressed patients' amygdala

shows excessive response to negative stimuli and reduced response to positive stimuli (Groenewold et al., 2013), corresponding neurofeedback targets might involve reducing amygdala activity when experiencing negative emotions or promoting amygdala activity when experiencing positive emotions to achieve emotion regulation. Currently, combined neurofeedback-NIBS is mainly used in exploratory research on neuropathic pain and insomnia (Kosari et al., 2019; Najafabadi et al., 2021), but remains unexplored in emotion regulation, warranting further investigation.

NIBS technology, due to its non-invasive, painless, safe, and flexible advantages, has been widely used across multiple disciplines and application fields, with numerous studies demonstrating its effectiveness in adjunctive treatment of mental disorders such as depression and PTSD. Recent evidence indicates that NIBS technology, as an intervention approach, can influence emotion regulation and reduce negative emotions, holding potential value for mental health improvement. Consequently, it has attracted widespread attention within and outside academia, with related research accumulating rapidly. However, brain mechanism research and clinical studies underlying this intervention process still contain substantial gaps, requiring more randomized double-blind controlled clinical trials to provide stronger evidence. We believe future research should comprehensively quantitatively summarize existing literature, combine neuronavigation techniques to determine universal and personalized precise treatment protocols for NIBS targets, examine changes in neural circuits underlying explicit/implicit emotion regulation during intervention, and evaluate NIBS intervention effects across multiple levels including subjective experience, physiological indices, and neural signatures. Additionally, we believe multi-target NIBS protocols and combinations of NIBS with neurofeedback and other techniques hold considerable promise for improving experimental validity in this field, awaiting exploration by relevant researchers.

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[The remaining references are English-language citations that were already in proper format in the original text and have been preserved as shown in the main

body of the translation.]

Note: Figure translations are in progress. See original paper for figures.