The Role of Right Ventrolateral Prefrontal Cortex in Socio-Emotional Regulation in Adults with High Depression Levels: A tDCS Study Postprint

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Abstract

Existing transcranial direct current stimulation (tDCS) research has demonstrated that the right ventrolateral prefrontal cortex (RVLPFC) is a crucial brain region for social emotion regulation, and activating the RVLPFC can significantly reduce the intensity of individuals' experiences of social negative emotions. Impaired social functioning is one of the important characteristics of patients with depression or individuals with depressive tendencies. This population exhibits high sensitivity to social rejection and reduced capacity for regulating negative social emotional experiences. In the present study, we employed an explicit emotion regulation task to investigate changes in emotion regulation capacity in two groups of adult participants with high and low depression levels after receiving anodal tDCS over the RVLPFC. The results indicated that although tDCS activation of the RVLPFC could help participants reduce negative emotional experiences through emotion regulation (cognitive reappraisal), the decrease in negative emotion intensity was significantly smaller in the high-depression-level participants compared to the low-depression-level participants. Additionally, this study also found that the tDCS effect was stronger for negative emotions of social origin (i.e., social rejection) compared to negative emotions of personal origin. This study represents the first attempt to use electrical or magnetic stimulation to enhance social emotion regulation capacity in depressed populations. The experimental results demonstrated that the emotion regulation capacity of high-depression-level adults was not significantly improved by single, short-duration (34 min) tDCS activation of the RVLPFC. This suggests that interventions or treatments for individuals with depressive tendencies or patients with depression require multiple tDCS sessions.

Full Text

The Role of Right Ventrolateral Prefrontal Cortex in Social Emotion Regulation Among Adults with High Depression Levels: A tDCS Study

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Abstract

Previous transcranial direct current stimulation (tDCS) studies have demonstrated that the right ventrolateral prefrontal cortex (RVLPFC) is a crucial brain region for social emotion regulation, and that activating the RVLPFC can significantly reduce the intensity of negative social emotional experiences. Impaired social functioning represents a key characteristic of individuals with depression or depressive tendencies. This population exhibits heightened sensitivity to social rejection and diminished capacity for regulating negative social emotional experiences. In the present study, we employed an explicit emotion regulation task to examine changes in emotion regulation capacity among two groups of adult participants with high versus low depression levels following anodal tDCS over the RVLPFC. Results indicated that while tDCS activation of the RVLPFC helped participants reduce negative emotional experiences through emotion regulation (cognitive reappraisal), the decrease in negative emotion intensity was significantly smaller for the high-depression group compared to the low-depression group. Additionally, we found that the tDCS effect was stronger for socially derived negative emotions (i.e., social exclusion) than for personally derived negative emotions. This study represents the first attempt to use electrical or magnetic stimulation to enhance social emotion regulation capacity in depressed populations. Our findings suggest that a single, brief (34-minute) tDCS session targeting the RVLPFC does not significantly improve emotion regulation capacity in adults with high depression levels, implying that intervention or treatment for depressive tendencies or clinical depression may require multiple tDCS sessions.

Keywords: depression tendency; transcranial direct current stimulation; right ventrolateral prefrontal cortex; social exclusion; negative emotion
Classification Codes: B845; R395

Depression constitutes a major global public health concern. Impaired interpersonal functioning and social dysfunction represent important features of depression (Henriques & Davidson, 2000; Kupferberg, Bicks, & Hasler, 2016). Compared with healthy controls, individuals with depression experience lower levels of pleasure in social interactions (social anhedonia) and demonstrate reduced motivation and frequency in social activities (Hammen, 2005). Strengthening research on the neural mechanisms underlying social dysfunction in depression and depressive populations, and applying these findings to guide prevention and treatment strategies, holds significant importance for improving public mental health.

Social exclusion (also termed social pain) refers to the systematic deprivation of rights, opportunities, and resources that enable individuals or groups to integrate into society. Social exclusion frequently occurs in daily life and has become a focus of media attention, manifesting in phenomena such as employment discrimination, housing difficulties, and school bullying. As a typical negative social experience, social exclusion leads to diminished self-esteem (Onoda et al., 2010) and poses a strong threat to fundamental human needs, including the need for belonging and control (Baumeister & Leary, 1995; Williams, 2007). Individuals who experience social exclusion develop negative emotional experiences and feelings of hurt (Eisenberger, Lieberman, & Williams, 2003), and this social pain elicits psychological responses similar to physical pain (Riva, Wirth, & Williams, 2011). Research indicates that the degree of social pain experienced by individuals correlates with their mental health status. Depressed individuals exhibit lower thresholds for social pain and consequently show greater sensitivity to social rejection (MacDonald, Kingsury, & Shaw, 2005). Emotion regulation serves as an effective coping strategy for managing negative emotions triggered by social exclusion. However, emotion dysregulation represents a core feature of both major depressive disorder and autism spectrum disorder (Mazefsky et al., 2013; Rive et al., 2013; Samson et al., 2014). We propose that enhancing the emotion regulation capacity of individuals with depression or depressive tendencies when facing negative social situations such as social exclusion may represent an effective approach for improving their social functioning deficits. This study employs transcranial direct current stimulation (tDCS) to investigate whether electrical activation of brain regions involved in social emotion regulation can enhance emotion regulation capacity in college students with high depressive tendencies.

Numerous meta-analyses and neuroimaging studies have demonstrated that both the dorsolateral prefrontal cortex (DLPFC) and ventrolateral prefrontal cortex (VLPFC) constitute core regions for emotion regulation (Buhle et al., 2014; Kohn et al., 2014), particularly in the down-regulation of negative emotions (Zilverstand, Parvaz, & Goldstein, 2017). During general emotion regulation tasks (where emotions originate from personal subjective or objective factors), individuals with depression show abnormal activation in the DLPFC, ventral striatum (primarily the nucleus accumbens), and anterior cingulate cortex (Donofry, Roecklein, Wildes, Miller, & Erickson, 2016). When down-regulating negative emotional experiences, patients with depression exhibit weaker lateral prefrontal activation compared to healthy controls (Rive et al., 2013). In regulating negative emotions elicited by social exclusion, the ventral anterior cingulate cortex (VACC) and VLPFC represent the two most critical brain regions (Riva

& Eck, 2016). Current experimental research has not yielded consistent results regarding the neural response of the VACC during social exclusion emotion regulation: some studies have found that regulating negative social emotions is accompanied by enhanced VACC activation (Cristofori et al., 2013), while others have reported decreased or unchanged VACC activation during social emotion regulation (Somerville, Heatherton, & Kelley, 2006). In contrast to these inconsistent findings regarding the VACC, neuroimaging evidence consistently indicates that the VLPFC (particularly the right VLPFC, i.e., RVLPFC) shows significantly enhanced activation when individuals experience social exclusion (Eisenberger et al., 2003; Onoda, et al., 2010). The degree of RVLPFC activation during social exclusion correlates negatively with self-reported pain intensity, suggesting that this brain region plays a key role in reducing social pain (Eisenberger et al., 2003; Masten et al., 2009). Additionally, individual difference studies on responses to social exclusion have found that individuals with higher levels of trust in others or greater self-confidence report less social pain during social exclusion tasks, and this negative correlation is mediated by RVLPFC activation levels (Yanagisawa et al., 2011). Furthermore, individuals with higher rejection sensitivity show lower RVLPFC activation during social exclusion compared to those with lower rejection sensitivity (Kross, Egner, Ochsner, Hirsch, & Downey, 2007).

In summary, the RVLPFC serves as a core brain region for social emotion regulation. Based on this evidence, Riva and colleagues (2012, 2015a, 2015b) employed tDCS to demonstrate that the RVLPFC plays a causal role in reducing negative emotional responses (such as social pain and social aggression) elicited by social exclusion. However, Riva and colleagues' series of studies did not require participants to complete any explicit emotion regulation tasks, meaning they only examined the role of the RVLPFC in implicit emotion regulation. As a follow-up to Riva et al. (2012, 2015a, 2015b), our research group' s previous experiment (He et al., 2018) employed explicit emotion regulation tasks to further clarify the role of the RVLPFC in emotion regulation, demonstrating that activating this brain region can enhance social emotion regulation capacity and reduce negative emotional experience intensity. Due to its non-invasive nature, safety, and high comfort level (compared to transcranial magnetic stimulation), tDCS has been increasingly applied in the treatment of clinical depression patients (Sellar, Nitsche, & Colzato, 2016). As a follow-up to He et al. (2018), the primary objective of the current study was to explore whether tDCS activation of the RVLPFC could improve emotion regulation capacity in individuals with depressive tendencies, specifically examining whether this tDCS effect differs between high- and low-depression groups. Additionally, building upon social emotion regulation, this study included a "personal emotion regulation" condition, requiring participants to regulate both socially derived negative emotions and personally derived negative emotions across different blocks. By comparing tDCS effects across these two conditions, this experiment could reveal the specificity of the RVLPFC for social emotion regulation—that is, whether social emotion regulation relies more heavily on this region than "personal emotion regulation."

2.1 Participants

Participants in this study were recruited from undergraduate and graduate students at Shenzhen University. We screened participants using the Beck Depression Inventory (Beck, Steer, & Brown, 1996), which includes 21 items assessing depressive symptoms over the past two weeks, with scores ranging from 0 to 63 (higher scores indicate greater depressive tendency). Only volunteers with scores ≤ 2 (low depressive tendency group) and scores ≥ 18 (high depressive tendency group) were invited to participate.

The formal experiment was conducted within one week following the Beck Depression Inventory screening. Prior to the experiment, all participants completed the Self-Rating Depression Scale (SDS; Zung, Richards, & Short, 1965) and the Trait form of Spielberger' s State-Trait Anxiety Inventory (STAI-T; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). Given that emotion regulation capacity can also be influenced by anxiety (Amstadter, 2008; Cisler & Olatunji, 2012), this study only selected participants with moderate trait anxiety levels to exclude the influence of anxiety on the results. Based on the SDS norms proposed by Zung et al. (1965), where scores below 0.5 indicate no depression and scores above 0.5 indicate mild, moderate, or severe depression, we divided participants into two groups according to their SDS scores: SDS $<$ 0.5 as the low depressive tendency group (n = 51) and SDS $\geq$ 0.5 as the high depressive tendency group (n = 47). The four groups of participants showed no significant differences in age, gender, or STAI-T scores (Table 1). ANOVA (with 2\$$\times 2 between - subject variables) revealed a main effect of "group" on SDS scores, F(1, 94) = 74.13, p < 0.001, \eta$^{2}\$p = 0.441, with the high depressive tendency group showing significantly higher SDS scores (0.56 ± 0.09) than the low depressive tendency group (0.44 ± 0.05). No significant age differences were found among the four groups, F(1, 94) = 0.02 ~ 2.01, p = 0.162 ~ 0.916, ^{2}p = 0.006 ~ 0.015. We controlled STAI-T scores to ensure no significant differences across the four groups, F(1, 94) = 0.63 ~ 1.47, p = 0.241 ~ 0.454, ^{2}p = 0.021 ~ 0.000. All participants had no history of epilepsy or brain injury, and had normal or corrected-to-normal vision. All participants were right-handed. High- and low-depressive tendency participants were randomly assigned to either the real tDCS group or the sham stimulation group, with 50 participants (25 in the high depressive tendency group and 25 in the low depressive tendency group) receiving anodal tDCS. The experimental protocol was approved by the Medical Ethics Committee of Shenzhen University. Participants provided informed consent prior to the experiment.

Table 1 Demographic characteristics of the four groups of participants (mean ± SD)

Group	Low Depressive Tendency + tDCS	High Depressive Tendency + tDCS	Low Depressive Tendency + Sham	High Depressive Tendency + Sham
n	25	25	26	22
Age	20.73 ± 2.47	21.73 ± 3.65	21.55 ± 3.22	20.89 ± 2.21
Gender (M/F)	13/13	13/11	13/12	12/11
SDS	0.45 ± 0.04	0.57 ± 0.08	0.43 ± 0.05	0.54 ± 0.09
STAI-T	41.82 ± 6.67	41.81 ± 4.62	40.88 ± 6.09	42.23 ± 3.65

2.2 Experimental Design and Materials

Following Elliott et al. (2012), this experiment included four variables. The within-subject variables were "picture type" (individual negative pictures/social exclusion pictures) and "task" (passive viewing/cognitive reappraisal), while the between-subject variables were "group"(high depressive tendency/low depressive tendency) and "tDCS type" (anodal stimulation/sham stimulation).

Sixty social exclusion pictures and sixty individual negative pictures were used (Figure 1 [Figure 1: see original paper]A). Each social exclusion picture depicted one excluded individual and a group of excluders (at least three people). Each individual negative picture contained only one person. The social exclusion pictures were identical to those used in our previous study (He et al., 2018), while the individual negative pictures were selected from the International Affective Picture System (Lang, Bradley, & Cuthbert, 1995) and the Chinese Affective Picture System (Bai, Ma, Huang, & Luo, 2005), primarily reflecting individual sadness. All 120 pictures in this study were rated by 20 healthy adults (on a 1-9 scale) recruited from Shenzhen University undergraduates and graduates who did not participate in the formal experiment. The rating results showed no significant differences between individual negative pictures and social exclusion pictures in terms of "emotional valence" (t(19) = -1.33, p = 0.215; individual = 2.76 ± 0.81, social = 2.53 ± 0.72) or "arousal" (t(19) = 1.43, p = 0.187; individual = 3.42 ± 1.67, social = 3.79 ± 2.01). Picture brightness and contrast were matched, and pictures were presented at the center of an LCD monitor with a viewing angle of 3.0° × 3.5°.

tDCS Parameters

The tDCS parameters (Brainstim; EMS, Bologna, Italy) were consistent with our previous study (He et al., 2018). The electrode size was 5 × 5 cm^2, with the anode placed at F6 (Cai et al., 2016; He et al., 2018; Riva et al., 2015b) and the cathode placed at Fp1 (Feeser, Prehn, Kazzer, Mungee, & Bajbouj, 2014; He et al., 2018; Miranda, Lomarev, & Hallett, 2006; Riva et al., 2015b). The current intensity was set at 2.5 mA (i.e., 0.1 mA/cm^2), which has been demonstrated to be safe for healthy adults (Cogiamanian et al., 2011; He et al., 2018; Koenigs, Ukueberuwa, Campion, Grafman, & Wassermann, 2009). tDCS activation began 4 minutes before the formal experimental task, with the "real stimulation group" receiving continuous tDCS throughout the experiment (totaling 34 minutes), while the "sham stimulation group" received current for only 30 seconds. This 30-second stimulation produces scalp itching sensations similar to those in the real stimulation group but does not affect neural activity during the formal task (Feeser et al., 2014; Riva et al., 2015b). All 98 participants reported scalp itching at the onset of stimulation but no other adverse reactions, and all believed they had received electrical stimulation throughout the entire task.

Figure 1 Schematic diagram of experimental procedure. (A) Examples of experimental materials. (B) Stimulus presentation in a single trial (using individual negative pictures as an example).

The experiment consisted of four blocks corresponding to the four within-subject conditions, with each block containing 30 trials. To avoid the influence of emotion regulation tasks on passive viewing tasks, participants first completed the passive viewing task followed by the cognitive reappraisal task (He et al., 2018). Both tasks included a "social pictures" block and an "individual pictures" block, with the order of "social" and "individual" blocks counterbalanced across participants.

The instructions for the four blocks were as follows. Passive viewing of individual negative pictures: "In this part of the experiment, imagine you are the protagonist in the picture. After viewing the picture, please rate your level of negative emotion." Passive viewing of social exclusion pictures: "In this part of the experiment, imagine you are the isolated individual in the picture. After viewing the picture, please rate your level of negative emotion." Viewing individual negative pictures with emotion regulation: "In this part of the experiment, continue to imagine you are the protagonist in the picture. Please try to make your emotions less negative. For example, you could imagine that the sad things are not actually that bad and could be significantly improved through your efforts. Then rate your level of negative emotion." Viewing social exclusion pictures with emotion regulation: "In this part of the experiment, continue to imagine you are the isolated individual in the picture. Please try to make your emotions less negative. For example, you could imagine that the group of people in the picture are not criticizing you, but perhaps discussing your strengths or topics you are not interested in. Then rate your level of negative emotion."

Each trial lasted 15 seconds. As shown in Figure 1B, each trial began with a 2-second central fixation point, followed by 8-second picture presentation during which participants were required to either passively view the picture or regulate their emotions using cognitive reappraisal strategies as instructed. Finally, participants rated their negative emotion intensity on a 1-9 scale (maximum response time of 5 seconds), with higher scores indicating greater negative emotion intensity. Ratings were completed by clicking a box above the number using a mouse.

2.5 Statistical Analysis

Statistical analyses were conducted using SPSS Statistics 20.0 (IBM, Somers, USA). Unless otherwise specified, descriptive statistics are presented as "mean ± standard deviation." Multi-factor repeated measures ANOVA was performed with picture type and task as within-subject factors, and group and tDCS type as between-subject factors. The significance level was set at $p < 0.05$.

The four-way repeated measures ANOVA revealed three significant main effects. First, the main effect of task was significant, $F(1, 94) = 35.94$, $p < 0.001$, $^{2}p = 0.276$, with negative emotion intensity in the emotion regulation (cognitive reappraisal) task (5.17 ± 1.24) significantly lower than in the passive viewing task (5.70 ± 0.98), demonstrating the effectiveness of the explicit emotion regulation instructions in this experiment.

Second, the main effect of group was significant, $F(1, 94) = 7.75$, $p = 0.006$, $^{2}p = 0.076$, with the low depressive tendency group showing significantly lower negative emotion intensity (5.24 ± 1.25) than the high depressive tendency group (5.63 ± 0.99). Third, the main effect of stimulation was significant, $F(1, 94) = 14.74$, $p < 0.001$, $^{2}p = 0.135$, with the anodal stimulation group exhibiting significantly lower negative emotion intensity (5.17 ± 1.24) than the sham stimulation group (5.70 ± 0.97).

More importantly, the ANOVA revealed two significant three-way interactions. First, a significant three-way interaction emerged among group, stimulation type, and task, $F(1, 94) = 4.43$, $p = 0.038$, $^{2}p = 0.045$ (Figure 2 [Figure 2: see original paper]A). Simple simple effects analysis indicated that the task effect was most pronounced in the low depressive tendency group under anodal tDCS, with participants reporting significantly lower negative emotion intensity in the emotion regulation task (3.93 ± 1.10) compared to the passive viewing task (5.52 ± 0.92; $F(1, 94) = 81.07$, $p < 0.001$, $^{2}p = 0.463$). However, this task effect was not significant in the high depressive tendency group (anodal tDCS: $F(1, 94) = 2.20$, $p = 0.140$, $^{2}p = 0.023$; sham tDCS: $F < 1$), and was less significant in the low depressive tendency group under sham tDCS ($F(1, 94) = 6.20$, $p = 0.015$, $^{2}p = 0.062$).

Second, a significant three-way interaction was found among picture type, stimulation type, and task, $F(1, 94) = 5.03$, $p = 0.027$, $^{2}p = 0.051$ (Figure 2B). Simple simple effects analysis revealed that the task effect was most pronounced when participants viewed social exclusion pictures under anodal tDCS, with negative emotion intensity in the emotion regulation task (4.39 ± 1.34) significantly lower than in the passive viewing task (5.88 ± 1.02; $F(1, 96) = 77.8$, $p < 0.001$, $^{2}p = 0.501$). This task effect was not significant in the sham tDCS group viewing individual pictures ($F < 1$), less significant in the sham tDCS group viewing social exclusion pictures ($F(1, 96) = 8.24$, $p = 0.005$, $^{2}p = 0.084$), and less significant in the anodal tDCS group viewing individual pictures ($F(1, 96) = 5.43$, $p = 0.022$, $^{2}p = 0.068$).

Additionally, the ANOVA revealed four significant two-way interactions. First, the interaction between group and task was significant ($F(1, 94) = 28.37$, $p < 0.001$, $^{2}p = 0.231$), with the low depressive tendency group showing significantly lower negative emotion intensity in the cognitive reappraisal task (4.74 ± 1.30) than in the passive viewing task (5.75 ± 0.97; $F(1, 96) = 52.9$, $p < 0.001$, $^{2}p = 0.076$). This task effect was not significant in the high depressive tendency group ($F < 1$; reappraisal = 5.60 ± 1.00, viewing = 5.66 ± 0.99).

Second, the interaction between stimulation and task was significant ($F(1, 94) = 19.24$, $p < 0.001$, $^{2}p = 0.169$), with participants in the anodal tDCS group showing significantly lower negative emotion intensity in the cognitive reappraisal task (4.71 ± 1.28) than in the passive viewing task (5.64 ± 1.01; $F(1, 96) = 41.59$, $p < 0.001$). This difference was not significant in the sham tDCS group ($F(1, 96) = 1.31$, $p = 0.255$; reappraisal = 5.63 ± 1.00, viewing = 5.77 ± 0.94).

Third, the interaction between picture type and task was significant ($F(1, 94) = 65.05$, $p < 0.001$, $^{2}p = 0.409$), with the task effect being significant when participants viewed social exclusion pictures ($F(1, 94) = 78.92$, $p < 0.001$; reappraisal = 4.96 ± 1.29; passive viewing = 5.94 ± 0.96) but not when viewing individual pictures ($F < 1$; reappraisal = 5.38 ± 1.14; passive viewing = 5.47 ± 0.95).

Finally, the interaction between group and stimulation was significant ($F(1, 94) = 13.87$, $p < 0.001$, $^{2}p = 0.128$), with the tDCS effect existing only in the low depressive tendency group ($F(1, 95) = 14.10$, $p < 0.001$; anodal stimulation = 4.72 ± 1.28; sham = 5.76 ± 0.98) and not in the high depressive tendency group ($F < 1$; anodal stimulation = 5.62 ± 1.02; sham = 5.64 ± 0.96).

Figure 2 Results of negative emotion intensity ratings. (A) Three-way interaction among task, group, and tDCS type. (B) Three-way interaction among task, picture type, and tDCS type. Error bars represent standard error. *p < 0.05,* ***p < 0.01,*** p < 0.001.

tDCS serves not only as a powerful tool for investigating brain function (Filmer, Dux, & Mattingley, 2014) but has also been increasingly applied in the treatment of depression patients in recent years (Sellar et al., 2016). This study utilized this technique to investigate the causal relationship between the RVLPFC brain region and negative emotion regulation function in adults with high versus low depression levels during explicit emotion regulation tasks. The experiment yielded two main findings. First, when low-depression-level participants received anodal tDCS while simultaneously engaging in emotion regulation, their experienced negative emotion intensity decreased significantly, whereas this was not the case for high-depression-level participants. This indicates that the emotion regulation capacity of low-depression individuals improved significantly after RVLPFC activation via tDCS. This result confirms the conclusion from our previous study (He et al., 2018) that the RVLPFC is a core brain region for emotion regulation. Compared with low-depression individuals, high-depression individuals exhibit lower thresholds for both physical and psychological pain (MacDonald & Leary, 2005). In the same negative situations (whether personal or social in origin), a single, brief tDCS intervention may not produce obvious effects in reducing negative emotional experiences. Previous research using eye-tracking technology has found that healthy adult participants can reduce their experienced negative emotion intensity through emotion regulation (cognitive reappraisal strategies), with successful down-regulation of negative emotions accompanied by enhanced self-focus, manifested as longer gaze duration on the protagonist region (the isolated individual) of the pictures (He et al., 2018). According to Beck' s cognitive model of depression (Beck & Bredemeier, 2016), depression is accompanied by the formation of negative self-cognitive schemas. Individuals with high depression levels exhibit reduced self-evaluation and increased negative expectations, always anticipating the worst outcomes and believing that current negative situations will persist indefinitely. In this experiment, negative events (viewing two types of negative pictures and imagining oneself in the situation) elicited excessive self-blame and self-criticism in high-depression-tendency individuals with negative self-cognitive schemas, and the 34-minute tDCS intervention did not significantly improve emotion regulation capacity in this group. Previous reviews have noted that tDCS effects are quite weak, with cognitive function changes following single-session (Horvath, Forte, & Carter, 2015) or even five-session tDCS treatments being difficult to achieve significance (Aparício et al., 2016). Our results based on high-depression-level participants suggest that tDCS treatment targeting the RVLPFC must employ multiple repeated sessions to potentially improve emotion regulation capacity in depression patients.

Second, when tDCS was used to activate the RVLPFC, participants could significantly reduce negative emotional experiences elicited by social exclusion through emotion regulation (cognitive reappraisal strategies), though this emotion regulation effect was somewhat weaker for negative emotions triggered by individual negative situations. This result suggests that the VLPFC is not only an important brain region for general emotion regulation (Buhle et al., 2014; Kohn et al., 2014) but also shows specificity for emotion regulation in socially negative situations such as social exclusion. Previous neuroimaging experiments have found that participants' RVLPFC and dorsal anterior cingulate cortex (dACC) both show significant activation during social exclusion situations (Eisenberger et al., 2003). We speculate that the VLPFC may reduce individuals' social pain experience by regulating dACC activity levels. This study enhanced the regulatory effect of this brain region on the dACC through tDCS activation of the RVLPFC, resulting in participants reporting lower negative emotion intensity compared to the sham stimulation group. We recommend that future studies consider both VLPFC and dACC as tDCS targets or combine tDCS with neuroimaging techniques to further investigate the neural mechanisms of social exclusion emotion regulation (Riva et al., 2015a). Some researchers have previously used tDCS to activate the RVLPFC to treat emotion dysregulation in autism spectrum disorder and improve patients' prefrontal emotion control functions (Scarpa & Reyes, 2011; Pitskel, Bolling, Kaiser, Pelphrey, & Crowley, 2014). The contribution of this experiment lies in our addition of the individual negative picture condition and direct comparison between individual and social negative pictures, which provides evidence for the specificity of the RVLPFC in social emotion regulation beyond previous studies (Eisenberger et al., 2003; Masten et al., 2009; Onoda et al., 2010; Riva et al., 2012; 2015a; 2015b; Yanagisawa et al., 2011). This result suggests that the RVLPFC may be the most direct target for treating emotion regulation deficits related to social exclusion, and that activating this brain region via tDCS could potentially significantly improve emotion regulation capacity and social functioning in patients with social dysfunction (such as depression, social anxiety disorder, and autism spectrum disorder) (Rive et al., 2013; Kupferberg et al., 2016).

A slight limitation is that this study did not find a four-way interaction among group, task, tDCS stimulation type, and picture type (the four-way interaction effect in this study: $F(1, 94) = 2.23$, $p = 0.139$, $^2p = 0.023$). Our expectation for a four-way interaction was based on the reasoning that, compared with low-depression participants, high-depression participants exhibit higher rejection sensitivity and lower social pain thresholds (MacDonald & Leary, 2005), tending to interpret others' remarks as insults, ridicule, and contempt (Beck & Alford, 2009). Therefore, the tDCS effect might be weaker for high-depression participants in social exclusion conditions than in individual negative emotion conditions. The failure to obtain a four-way interaction may be due to insufficient sample size (98 participants across four groups), as a recent meta-analysis on tDCS effects suggested that to achieve stable tDCS treatment effects in depression populations, each group should include no fewer than 49 participants (Meron, Hedger, Garner, & Baldwin, 2015). We therefore recommend that future related studies increase the sample size per group. Additionally, this study only examined participants with depressive tendencies, and there exist qualitative and quantitative differences between "high depressive tendency"and "clinical depression." Therefore, caution is needed when generalizing our findings to clinical depression patients, and further research in confirmed patients is urgently needed.

This study demonstrates that activating the RVLPFC via tDCS can improve emotion regulation capacity (using cognitive reappraisal strategies) and reduce negative emotional experience intensity. However, this tDCS effect was only observed in low-depression-level participants, with no significant improvement in emotion regulation capacity among high-depression-level participants. Furthermore, tDCS activation of the RVLPFC brain region shows some specificity for improving social emotion regulation capacity, with more pronounced emotional improvement in social exclusion situations compared to individual negative situations. We hope these conclusions will provide valuable theoretical and clinical guidance for further research on the emotion regulation function of the RVLPFC and its application in depression treatment.

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The Role of Right Ventrolateral Prefrontal Cortex on Social Emotional Regulation in Subclinical Depression: An tDCS Study

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Abstract

So far as we know, three studies demonstrated that that the right ventrolateral prefrontal cortex (RVLPFC) plays an important role in down-regulating the emotional response to social exclusion. In a previous study, we explored the causal relationship between transcranial direct current stimulation (tDCS) and dominant emotional regulation in the context of social exclusion. Depression is an disorder that shows deficits of social functions. Compared with healthy controls, depressive individuals enjoy less in social interaction and the activation of the lateral prefrontal lobe of depressive subjects usually reduces. The current study aimed to explore whether the anodal tDCS targeting at RVLPFC could also improve the emotional regulation of social exclusion in subjects with high depressive levels. Furthermore, this study added individual negative images as a baseline to test the specificity of the RVLPFC on emotional regulation of social exclusion.

Before the experiment, we classified the participants with a Beck Depression Inventory score of < 3 as low depressive tendency group and those with a score of ≥ 18 as high depression tendency group. Participants also completed a Self-Rating Depression Scale (SDS) on the day of the tDCS experiment. Finally, a total of ninety-eight participants were included. They were randomly divided into anodal tDCS group (including 25 high depressive and 25 low depressive subjects) and sham tDCS group. All participants viewed social exclusion images and individual negative images separately in two blocks. In the no-reappraisal condition, participants were instructed to passively view images; in the reappraisal condition, they reappraised images so to down-regulate the negative emotional responses. Ratings of negative emotion experience were provided at the end of each trial.

There was a significant three-way interaction of group, tDCS type, and task. Simple simple effect analysis showed that in the reappraisal condition, anodal tDCS over the RVLPFC resulted in a decreased negative emotion rating in subjects with low-depressive levels, while this task effect (i.e., emotional regulation) was not significant in subjects with high-depressive levels.

Another three-way interaction was found among image type, tDCS type, and task: when participants were presented with social exclusion images, in the reappraisal condition, anodal tDCS over the RVLPFC resulted in a decreased negative emotion rating in the emotional regulation condition; however this task effect was less significant when participants were presented with individual negative images. Besides the two three-way interactions, this study also observed significant main effects of task, group, and tDCS type, as well as two-way interactions of group and task, tDCS type and task, image type and task, and group and tDCS type.

The current findings indicate that the improvement of emotion regulation via tDCS targeting at RVLPFC may be invalid for depressive patients if only one session of tDCS is performed; thus multiple sessions are highly suggested for clinical practice. Furthermore, this is the first tDCS study that compared the RVLFPC role of emotional regulation of social versus individual based negative experiences. The result provides evidence of direct causal relationship between RVLPFC and emotional regulation in the context of social exclusion, highlighting the functional specificity of this brain region on emotional regulation.

Key words: depression tendency; transcranial direct current stimulation; right ventrolateral prefrontal cortex; social exclusion; negative emotion

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