Frontal tDCS and emotional reactivity to negative content: Examining the roles of biased interpretation and emotion regulation

Clarke, P.J.F.; Haridas, S.M.P.; Van Bockstaele, B.; Chen, N.T.M.; Salemink, E.; Notebaert, L.

Citation for published version (APA):
Clarke, P. J. F., Haridas, S. M. P., Van Bockstaele, B., Chen, N. T. M., Salemink, E., & Notebaert, L. (2021). Frontal tDCS and emotional reactivity to negative content: Examining the roles of biased interpretation and emotion regulation. *Cognitive Therapy and Research*, *45*(1), 19-30. https://doi.org/10.1007/s10608-020-10162-9

ORIGINAL ARTICLE

Frontal tDCS and Emotional Reactivity to Negative Content: Examining the Roles of Biased Interpretation and Emotion Regulation

Patrick J. F. Clarke[1] · Sumitra M. P. Haridas[1] · Bram Van Bockstaele[2,4] · Nigel T. M. Chen[1] · Elske Salemink[2,3] · Lies Notebaert[4]

Abstract

Background Given findings showing that emotion regulation may be enhanced through prefrontal neurostimulation, the present study examined whether the effect of transcranial direct current stimulation on emotional reactivity is mediated via biased interpretation, and whether emotion regulation goals further moderate this relationship.

Methods Healthy participants (n = 79) were allocated to one of four conditions to receive either active or sham tDCS concurrently with an emotion regulation task during which they were instructed to maintain or down-regulate their emotional reactions (between groups). A homograph priming task assessed biased interpretation, and emotional reactivity was assessed in response to a negative video viewing task.

Results Those receiving active tDCS showed smaller elevations in negative mood in response to viewing negative videos compared to sham stimulation. Neither tDCS condition nor emotion regulation condition had an impact on interpretive bias, and there was no evidence for tDCS-enhancement of emotion regulation. As such, interpretive bias did not significantly mediate the relationship between tDCS and emotional reactivity, and no moderating role of emotion regulation was observed.

Conclusions The present results are consistent with neural models implicating increased frontal activity with reduction in emotional reactivity, but provides no support for the role of interpretive bias in this relationship, and no evidence that tDCS enhanced the effects of emotion regulation.

Keywords Emotion reactivity · Emotion regulation · Interpretation bias · Neurostimulation · tDCS

✉ Patrick J. F. Clarke
Patrick.Clarke@curtin.edu.au

1 School of Psychology, Curtin University, Kent St, Bentley, WA 6102, Australia

2 Department of Psychology, University of Amsterdam, Amsterdam, The Netherlands

3 Department of Clinical Psychology, Utrecht University, Utrecht, The Netherlands

4 School of Psychology, University of Western Australia, Crawley, Australia

Introduction

A considerable body of literature has sought to describe the neural architecture that underpins the cognitive and emotional regulatory processes operating in anxiety and depression. In particular, neural models of emotional disorders have highlighted that anxious and depressed populations tend to show hypoactive neural activity in lateral prefrontal areas (Etkin and Wager 2007; Siegle et al. 2007) which are commonly associated with the top-down regulation of emotion and the selective processing of emotional information (Bishop 2007; Siegle et al. 2007). The identification of such regions implicated in the regulation of emotion has given rise to interventions employing non-invasive neurostimulation techniques designed to modulate neural activity in these areas (Brunoni et al. 2016; Vicario et al. 2019). One such emerging intervention approach is transcranial direct current stimulation (tDCS).

tDCS is a non-invasive neurostimulation technique in which a weak electrical current is passed through the scalp via a conductive silicone electrode to alter cortical excitability of underlying neural tissue. Specifically, anodal stimulation is thought to raise the membrane resting potential of neurons to increase cortical excitability while cathodal stimulation lowers resting potential, decreasing cortical excitability (Nitsche et al. 2008). Findings have shown that tDCS stimulation can contribute to neuromodulatory effects which last up to 90 min following administration (Bindman et al. 1964; Nitsche and Paulus 2001). The modulation of neural activity via tDCS has been increasingly examined as a potential therapeutic intervention (Brunoni et al. 2016; Vicario et al. 2019). Findings have also demonstrated that frontal tDCS can attenuate negative emotional reactivity in healthy samples (Smits et al. 2020). As such, tDCS also provides a tool to experimentally investigate emotional psychopathology, and to understand the ways in which cognitive and neural processes together modulate emotional experience (e.g. Brunoni et al. 2014; Clarke et al. 2020; Heeren et al. 2017).

In seeking to understand the interaction between neural, cognitive, and emotional processes, research has suggested that tDCS may exert positive effects on emotion by changing patterns of cognitive bias. Cognitive theories propose that emotional pathology is underpinned by patterns of biased cognition that skew emotional experience to more negative and threatening aspects of the environment (Williams et al. 1997). These include patterns of biased attention that favour the selective processing of threatening information, and patterns of biased interpretation that favour more negative/threatening resolutions of emotionally ambiguous material (Bar-Haim et al. 2007; Hirsch et al. 2016). Findings have shown that tDCS may exert positive effects on emotion by changing patterns of cognitive bias (e.g. Heeren et al. 2017; Ironside et al. 2016).

A number of studies have now confirmed that excitatory tDCS stimulation (anodal) targeting the left DLPFC can reduce patterns of attention bias to negative information. Brunoni et al. (2014) found that a single session of tDCS reduced interference of emotional information (negative and positive) in an emotional Stroop task for individuals with major depressive disorder. Similarly, Ironside et al. (2016) also showed that tDCS eliminated attention bias to fearful face stimuli that was otherwise present under sham stimulation (subsequently replicated by Heeren et al. 2017), with other studies also confirming reductions in attention bias for emotional content in response to left DLPFC tDCS (Sanchez-Lopez et al. 2018). In the study of Sanchez-Lopez et al. left DLPFC tDCS increased the ability to top-down disengage attention away from emotional face stimuli (independent of valence). Furthermore, there is also evidence that such reductions in biased attention may mediate the effects of tDCS on emotional reactivity. Using an eye-tracked video

stress task Chen et al. (2017) showed that not only did tDCS attenuate biased attention to negative information, but that the tDCS-induced pattern of attention mediated emotional reactivity to the stress task. Thus, increased lateral prefrontal activity reduces biased attention for threat, and such reductions may partially carry the effects of tDCS on emotional reactivity to negative emotional content. However, we are aware of no research that has investigated the potential involvement of other thoroughly described cognitive biases, such as biased interpretation, in the effects of tDCS on emotional reactivity. Biased interpretation is a consistent feature of anxiety and depressive disorders that is thought to play a causal role in their maintenance (Hirsch et al. 2016). To the extent that frontal tDCS could potentially contribute to increased emotional resilience by enhancing the inhibition of more negative meanings associated with ambiguity, biased interpretation could also serve as a mediator of the relationship between tDCS and emotional reactivity. Therefore, the first aim of the current study was to examine whether biased interpretation potentially mediates the effect of tDCS on reactivity to negative emotional content.

Another process that is strongly implicated in mood and anxiety dysfunction is emotion regulation. Emotion regulation refers to the process via which individuals influence their emotional experience including which emotions they have, when they occur, and the way in which they express them (Gross 1998). Emotion regulation includes the ability to alter emotional states in line with an individual's current active intent which can be influenced by changing situational demands. Dysfunctional emotion regulation is a recognised as a vulnerability and maintaining factor for emotional disorders (Berking et al. 2014; Cisler and Olatunji 2012; Joormann and Gotlib 2010).

Of potential relevance to the enhancement of adaptive emotion regulation, research has shown that altering cortical activity via tDCS can potentially enhance the effects of emotion regulation in line with an individual's current goals. Feeser et al. (2014) found that, relative to sham stimulation, the delivery of tDCS to the right DLPFC concurrently with an emotion regulation task led to greater or less emotional reactivity to viewing negative emotional content when the individual's goal was to respectively up or down-regulate their emotional reactions. Thus there is evidence that increased frontal activation via tDCS may enhance the effects of emotion regulation (Feeser et al. 2014).

Indeed, in addition to evidence that emotion regulation intent may interact with tDCS to influence emotion, there is also some evidence for potential interactions between emotion regulation and biased interpretation. Specifically Everaert et al. (2017) demonstrated that the tendency to impose more benign resolutions on emotional ambiguity was associated with the use of positive reappraisal. This finding was taken to suggest that those with a stronger tendency to
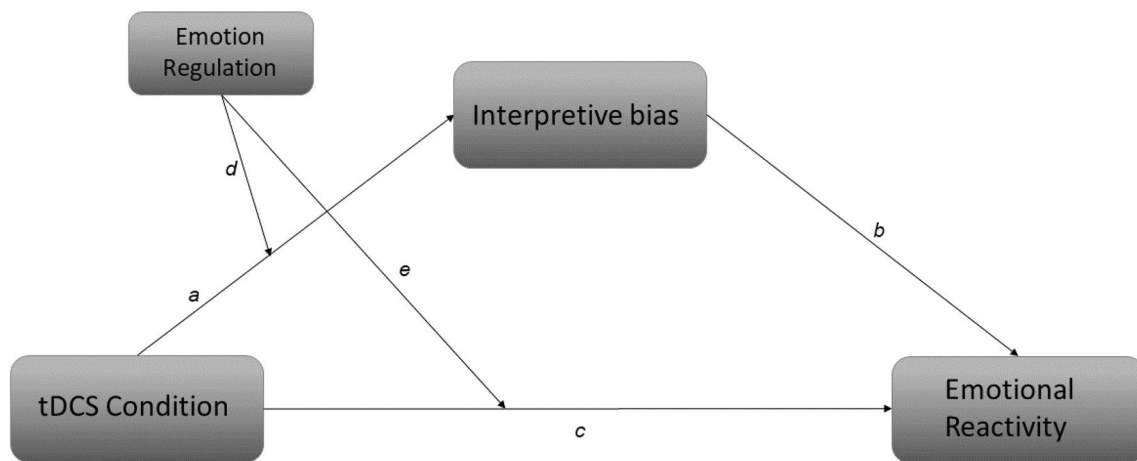
Fig. 1 Depiction of effects under examination in the current study. The first hypothesis seeks to examine whether the effects of tDCS condition on emotional reactivation are mediated by interpretive bias via the *a-b* pathway. If emotion regulation intent significantly enhances the effect of tDCS on interpretive bias and emotional reactivity, then we would anticipate a significant interaction via moderated mediation of emotion regulation through paths *d* and *e*

impose more positive resolutions on ambiguity were also more likely to employ positive reappraisals in emotion regulation. Therefore, given the observation that tDCS can potentially enhance the effects of emotion regulation (Feeser et al. 2014; Peña-Gómez et al. 2011), combined with the relationship between biased interpretation and emotion regulation (Everaert et al. 2017; Joormann and D'Avanzato 2010), the second aim of the current study was to examine the extent to which emotion regulation intent moderates any observed mediating effect of biased interpretation in the relationship between tDCS and emotional reactivity.

To achieve these aims, the current study compared the effects of alternative emotion regulation goals delivered in combination with either active or sham tDCS. tDCS targeted the left DLPFC, a region consistently targeted due to its proposed role in affect regulation (Bishop 2007). Active and sham tDCS stimulation was delivered concurrently with the completion of an emotion regulation task involving the viewing of negative images. To examine the legacy of tDCS delivered concurrently with the repeated practice of a specific emotion regulation goal, emotion regulation instructions were delivered between groups, with one group instructed to maintain their emotional reactions to negative emotional stimuli (maintain condition) while the other group was instructed to use reappraisal to consistently down-regulate their emotional reactions to these stimuli (down-regulate condition). Given past findings showing that tDCS effects may be observed more frequently in response-time measures (Hill et al. 2016) we sought to include a measure of interpretive bias likely to register effects associated with response time that incorporated simple stimuli with rapid processing time. As such, interpretive bias was assessed offline (following the cessation of stimulation) after the emotion regulation task using a homograph priming task. The

homograph priming task measure also has the benefit of being more immune to response bias as compared to some other interpretive bias measures (e.g. scrambled sentences, fragment completion). Finally, to assess the impact of each condition on emotional reactivity, participants completed a video viewing task involving the assessment of mood before and after the presentation of emotionally negative movie clips.

Figure 1 provides a summary of the over-arching model under examination. We first separately examined the individual and interactive effects of frontal tDCS and emotion regulation conditions on: (i) emotional reactions during intentional emotion regulation, (ii) interpretive bias, and (iii) reactivity to negative emotional content. Second, these component effects were then combined in a moderated mediation analysis. If tDCS exerts an impact on emotional reactivity via interpretive bias, this would be demonstrated by a significant indirect *a-b* pathway depicted in the Fig. 1. Furthermore, if emotion regulation intent influences this moderation relationship, we would anticipate a significant effect of the emotion regulation interaction factor (paths *d* and *e*). Specifically, we would anticipate that practicing down-regulation of negative emotional reactions (down-regulation condition) while receiving active tDCS would lead to lower interpretive bias and less emotional reactivity compared to the delivery of tDCS in combination with no emotion regulation intent (maintain condition).

Method

Participants

Participants were recruited through the Curtin University Undergraduate participant pool. Participants were required

to be eighteen years or over, and self-identify as not meeting medical exclusion criteria for tDCS. This included experiencing migraines, current psychoactive medication, active skin conditions, unstable medical conditions, neurological disorders, or metal implants. Participants were made aware of exclusion criteria prior to registering for the study, and again upon arrival. A total of 79 participants aged between 18 and 50 years ($M = 23.17$, $SD = 6.77$) were recruited to the study (54 female, 25 male). While the current sample is similar in size (per condition) to the prior study of Feeser et al. (2014) which showed effects of tDCS on emotion regulation, this prior study did not report effect sizes. While no prior studies to our knowledge have examined the effects of tDCS on interpretive bias, effect sizes from studies examining the impact of tDCS on other cognitive biases (e.g. attention) have tended to report medium effect sizes ($\eta_p^2 = 0.09$–0.14; Chen et al. 2017; Heeren et al. 2015). With a medium effect size ($f = 0.25$), and $\alpha = 0.05$, the current sample would provide approximately 90% chance of detecting an effect.

Baseline Questionnaires

Measures of general emotional vulnerability were assessed with the 21 item version of the Depression Anxiety and Stress Scale (DASS-21; Lovibond and Lovibond 1995) and the Positive and Negative Affect Schedule (PANAS; Watson et al. 1988). Both are commonly used emotional assessment measures and show good internal consistency, with Cronbach's alpha in our study varying between 0.74–0.91.

Transcranial Direct Current Stimulation

tDCS was administered using a battery-powered, current-controlled device (Chattanooga Group, United States). Current was transferred via two 4×6 cm silicone electrodes covered in a saline-soaked sponge. Anodal stimulation targeted the left DLPFC with the electrode placed at F3 according to the 10–20 international system. The cathode was placed on the left superior trapezius (lower neck). This extracephalic reference location was used to avoid potential confounding effects of inhibitory stimulation of other cortical sites (Chen et al. 2017; Clarke et al. 2014; Martin et al. 2013). The dose was set to 2.0 mA/min (current density $= 0.07$/cm^2) with a 30 s ramp up/down time. For those in the active stimulation condition, current was delivered for 20 min. For those in the sham condition, stimulation was delivered for one minute before the current was ramped down and switched off without their knowledge. Participants were not alerted to the alternative tDCS conditions.

Emotion Regulation Task

The emotion regulation task was delivered in one of two conditions: down-regulate emotional reaction, or maintain emotional reactions. The instructions for these were adapted from similar conditions employed in past studies (Feeser et al. 2014; Ochsner et al. 2004; Van Bockstaele et al. 2019). Those in the down-regulate condition were told that while viewing the images they should attempt to feel less negative about the picture by trying to change the meaning of it. Participants were provided examples of reappraisal strategies that they could employ to down-regulate their emotional reactions, such as imagining a more positive outcome, or viewing the situation in an impartial way (similar to a doctor). Those in the maintain condition were instructed to try and maintain their emotional reactions to what they see in the picture without attempting to change it, to allow themselves to experience their natural emotional reaction to the picture without suppressing how they feel about it.

The stimuli employed in the task were 48 negative IAPS images, 24 of which were high arousal images (e.g. depicting imminent danger or violence, normative arousal ratings between 5.63 and 7.35), and 24 were low arousal images (e.g. depicting sadness and loss, normative arousal ratings between 3.85 and 5.35). These images were selected on the basis of IAPS ratings of valence and arousal (Lang et al. 1997). All 48 images had low mean and standard deviation scores for valence ($M \leq 3.94$, $SD \leq 1.70$), indicating they had been consistently rated as unpleasant.[1] Images depicted a wide range of content and people (different cultures and ethnicities), ensuring that specific demographics or groups were not over/under-represented.

The emotion regulation task itself consisted of 48 trials. On each trial, a central fixation cross was initially presented for 2000 ms. A negative stimulus image was then presented for 8000 ms. Following the presentation of this image, participants were presented with the question "How did you feel viewing that image?", accompanied by a 12 cm line with the anchors "Not at all negative" to "Extremely negative". Participants indicated their response by clicking a point along the length of the line with the mouse, yielding a score from 0 to 12, with higher scores indicating more negative affect. The participant's response cleared the screen and the next trial commenced.

---

[1] High arousal image numbers: 1304; 2703; 3103; 3120; 3350; 6230; 6312; 6520; 6560; 8485; 9050; 9163; 9250; 9254; 9410; 9412; 9413; 9414; 9423; 9429; 9424; 9600; 9911; 9921.

Low arousal image numbers: 2141; 2276; 2301; 2456; 2692; 2718; 2799; 3181; 3300; 4621; 7520; 9000; 9010; 9186; 9295; 9331; 9419; 9426; 9430; 9584; 9435; 9610; 9922; 9927.

Interpretive Bias Assessment Task

To assess interpretive bias we employed a homograph priming task and stimuli previously used by Clifton et al. (2016). This task has been shown to be sensitive to induced changes in interpretive bias. Stimuli on this task consisted of 52 homographs (e.g. 'ARMS') each of which had 4 associate words: a related threatening word (e.g. 'WEAPONS'), a related benign word (e.g., 'LEGS'), an unrelated threatening word (e.g., 'GREEDY'), and an unrelated benign word (e.g., 'TROUSERS'). On each trial of the task, a central fixation cross was presented for 500 ms. The homograph prime was then presented for 250 ms, followed by a blank screen for 500 ms, and then one of the four associate words. Participants were required to determine whether this target word was related or unrelated to the prime by pressing the corresponding "R" or "U" button respectively. Response latencies for negative-related compared to benign-related targets provided the critical dependent measure, with disproportionate speeding to identify negative as compared to benign-related associates taken to indicate a greater interpretive bias favouring negative interpretations of ambiguous content. The task involved a total of 104 trials consisting of two repetitions of each homograph, presented with a different associate word on the second presentation. The type of associate presented with each word was counter-balanced across participants in one of two rotations. In each rotation, half of the homographs were presented once with a negative-related associate and once with a benign-unrelated associate, while the other half were presented once with a benign-related associate and negative-unrelated associate.

Emotional Reactivity Assessment Task

The impact of experimental conditions on emotional reactivity was assessed via exposure to emotionally negative video clips. Participants viewed four negative video clips sourced from popular movies, each lasting around 2 min. The clips were presented consecutively, without a break, lasting a total duration of 8 min 26 s. These videos depicted negative emotional content that was both high arousal (e.g. fleeing armed militia—Blood Diamond) and low arousal (e.g. death of Mufasa – Lion King). Immediately prior to and following viewing of the video clips, participants completed ratings of their current mood on two scales. This was done on two 12 cm visual analogue scales, one with "Happy" and "Sad" as anchors, and the other with "Relaxed" and "Anxious" as anchors. Participants marked the relevant point between these two anchors on each scale, which were combined to yield a single measure of negative mood between 0 and 12, with higher scores representing more negative emotional state.

tDCS Manipulation Check Question

At the conclusion of the experiment, participants were informed that that there were two tDCS conditions, "Active" and "Non-active", and asked to indicate which condition they believed they had been in.

Procedure

The study was approved by the University Human Research Ethics Committee. Upon arrival participants first read and indicated their informed consent to participate in the study. Participants then completed the baseline questionnaire measures. Next, they were fitted with tDCS equipment and stimulation was initiated (according to experimental condition). Six minutes following initiation of tDCS, participants received instructions on the completion of the emotion regulation task, along with instructions associated with the respective emotion regulation conditions. They then initiated the emotion regulation task (around 8 min post tDCS-initiation) which lasted approximately 12 min. On the completion of this task (approx. 20 min post-tDCS initiation), tDCS stimulation was terminated (for those in the active condition still receiving stimulation) and the equipment removed (for all participants). Participants then completed the homograph priming task. They were encouraged to respond as fast as possible without compromising accuracy. Participants completed 20 practice trials consisting of non-negative, non-homograph stimuli, before commencing the priming task. Following the priming task, participants completed a brief (seven-minute) target discrimination response-time task associated with an alternative project. This task involved registering simple reaction time responses to the detection of a neutral stimulus with no time pressure or restrictions, and no error feedback making it unlikely that this task would have exerted effects on subsequent emotional reactivity. Finally, participants completed the emotional reactivity assessment task, including emotional ratings and video viewing. Participants were offered the opportunity to view two positive videos prior to the end of the study to ensure no perseveration of negative mood. Participants then completed the tDCS manipulation check question before being fully debriefed.

Results

Data Preparation

In preparing data from the homograph priming task, individual response times over 2000 ms, and under 100 ms were initially excluded (7.85% of trials), along with trials containing incorrect responses (15.53% of trials). For each participant,

Table 1 Descriptive baseline data for emotional assessment measures and gender across experimental conditions. Standard error given parentheses

	Active tDCS		Sham tDCS	
	Down-regulate	Maintain	Down-regulate	Maintain
Participants/condition	18	19	18	18
Gender ratio F/M	12/6	13/6	13/5	12/6
DASS				
Depression	10.31 (0.83)	12.53 (1.28)	12.78 (1.01)	11.39 (1.22)
Anxiety	11.28 (0.59)	12.63 (0.93)	11.83 (0.83)	11 (0.70)
Stress	13.42 (0.71)	15.42 (0.85)	15.17 (1.00)	14 (0.83)
PANAS				
Positive	31.78 (1.57)	31.68 (1.46)	30.11 (1.44)	30.5 (1.53)
Negative	17.44 (1.00)	20.79 (1.67)	21.5 (1.93)	18.72 (1.39)

Table 2 Dependent measures from the emotion regulation task (E-R task; arousal ratings), homograph priming task (related-negative and related-benign trials), and assessment of emotional reactivity (video task). Standard error given in parentheses

	Active tDCS		Sham tDCS	
	Down-regulate	Maintain	Down-regulate	Maintain
E-R task stimulus ratings				
High arousal stim	5.57 (.50)	7.19 (.49)	4.87 (.50)	7.15 (.49)
Low arousal stim	3.82 (.50)	5.25 (.49)	3.37 (.50)	5.33 (.50)
Homograph priming RTs				
Related-negative	972.21 (50.33)	1002.32 (47.51)	979 (50.13)	917.17 (47.65)
Related-benign	949.68 (52.14)	1008.81 (49.61)	955.82 (52.04)	899.97 (48.34)
Negative affect				
Pre-video	3.53 (.57)	5.24 (.55)	3.36 (.57)	3.82 (.57)
Post-video	5.69 (.57)	6.97 (.55)	6.39 (0.57)	7.21 (.57)

reaction times beyond 3*SD* from their mean reaction time for each individual trial type were then excluded (7.28% of correct trials). D-prime (d') values were calculated for responses to related-negative and related-benign trials. The d' measure provides an index of sensitivity where the proportion correct is a function of hits relative to false alarms. As per Clifton et al. (2016) participants with d' below 1.00 were excluded (3 participants). Three participants were observed to have extreme outlying response times for either the related-negative or related-benign trials (*SD* = 3.63—4.82) and were also excluded from analyses. All data reported in the following analyses (excluding individual participant details) are available at https://osf.io/zvkft/.

Baseline Measures

Group characteristics across the four experimental conditions revealed no significant differences in baseline mood measures across any DASS subscales or the PANAS scales, (all $F < 1.45$, all $p > 0.235$, nor significant differences in gender ratio, χ^2 (3, 73) = 0.17, $p = 0.982$. Final participant numbers per condition and baseline characteristics across groups are given in Table 1.

The following analyses first individually consider the effects of experimental condition on each dependent measure

(emotion regulation stimulus ratings, interpretive bias, and emotional reactivity) before examining these in the overall moderated mediation model.

The Effect of tDCS and Emotion Regulation on Stimulus Ratings

Average stimulus ratings across conditions are shown in Table 2. To examine the effects of tDCS and emotion regulation conditions on emotional responses to stimuli in the emotion regulation task, we conducted a Linear Mixed Model (LMM) with the fixed factors of tDCS Condition (between-groups: active vs. sham) and Emotion Regulation Condition (between-groups: down-regulate vs. maintain), and Stimulus Arousal Level (within-groups: high vs. low-arousal images). Participant was entered a random factor and the model terms were tested with the Satterthwaite method (all LMM and GLMM analyses were conducted in JASP; JASP Team 2020). In line with the expected impact of emotion regulation on stimulus ratings, a significant main effect of Emotion Regulation Condition was observed, $F(1, 69) = 14.14$, $p < 0.001$. As anticipated, participants in the maintain condition consistently rated stimuli as more negative ($M = 6.23$, $SE = 0.34$) compared to those in the down-regulate condition ($M = 4.41$, $SE = 0.34$). A significant main effect of Stimulus

Arousal Level was also found, $F(1, 69) = 301.42$, $p < 0.001$, with high-arousal images ($M = 6.19$, $SE = 2.48$) rated significantly more negative than low-arousal images ($M = 4.44$, $SE = 2.48$). Inconsistent with the predicted impact of tDCS on emotion regulation, no other main effects or interactions were observed (all $F < 1.53$, all $p > 0.219$).

The Effect of tDCS and Emotion Regulation on Interpretive Bias

Reaction time data from the homograph priming task were subject to a Generalised Linear Mixed Model with tDCS Condition (between-groups), Emotion Regulation Condition (between-groups), and target valence (negative vs. benign target word; within-groups) as fixed factors. Participant was entered as a random factor, and the model was tested with likelihood ratio tests method, with inverse Gaussian family, and identity link function. No significant main effects or interactions were observed (all $\chi^2 < 0.93$, all $p > 0.336$), indicating that groups did not systematically differ according to interpretive bias, nor was there any general tendency to interpret homographs in favour of either more negative or benign meanings.

The Effect of tDCS and Emotion Regulation on Emotional Reactivity

A LMM was conducted to assess the impact of both emotion regulation and tDCS on emotional reactivity to an acute stressor. This involved the fixed factors of tDCS Condition (between-group) and Emotion Regulation Condition (between-group) and Time (within-group: pre vs post-video viewing). Participant was entered as a random factor and the model terms were tested with the Satterthwaite method. A significant main effect of Time was observed, $F(1,70) = 80.32$, $p < 0.001$, consistent with an increase in negative affect from pre-video ($M = 3.99$, $SE = 0.28$) to post-video ($M = 6.56$, $SE = 0.28$). There was also a significant main effect of Emotion Regulation Condition, $F(1,70) = 4.79$, $p = 0.032$. This showed that participants in the down-regulate condition on average reported lower levels of negative affect ($M = 4.74$, $SE = 0.34$) compared to those in the maintain condition ($M = 5.81$, $SE = 0.34$). This suggests that the instruction to down-regulate emotion had a general effect on reducing negative mood but showed no evidence of attenuating emotional reactivity (i.e. did not interact with mood assessment time).

A significant interaction was also observed between tDCS Condition and Time, $F(1, 69) = 4.81$, $p = 0.032$. As depicted in Fig. 2, the nature of this interaction was such that those in the sham tDCS condition recorded a larger increase in negative affect $t(36) = 6.90$, $p < 0.001$, $d = 1.15$

from pre to post-video exposure compared to those in the active tDCS condition who recorded a smaller elevation $t(36) = 5.85$, $p < 0.001$, $d = 0.96$. This finding is consistent with tDCS attenuating emotional reactivity to negative emotional content. Interestingly, the groups did not differ on level of emotional vulnerability at either pre or post video (all $t < 1.45$, $p > 0.15$), indicating that the effect was carried by the magnitude of the change in mood in response to the video viewing task. There were no other significant main effects or interactions (all $F < 0.77$ all $p > 0.384$).

The Mediating Role of Interpretive Bias and Moderating Role of Emotion Regulation in the Relationship Between tDCS and Emotional Reactivity

To examine the influence of tDCS on emotional reactivity via interpretive bias, we first computed a single index measure of interpretive bias by subtracting response times for trials with related-negative targets from response times for trials with related-benign targets, resulting in an index where higher values represent greater levels of threat-related interpretive bias. The indirect effect of tDCS on emotional reactivity through interpretive bias, and the moderating role of emotion regulation was then assessed using the bias-corrected bootstrapping procedure outlined by Preacher and Hayes (2004) using the Process macro in SPSS (Hayes 2017). Post-video mood was entered as the dependent (Y) variable with pre-video mood as a covariate. Results are summarised in Fig. 3.

The direct effect of tDCS condition on emotional reactivity was not significant nor was the effect of tDCS condition on interpretive bias. A significant effect of interpretive bias on emotional reactivity was observed, reflecting a small negative correlation between interpretive bias and post-video mood (controlling for pre-video mood), $r(70) = -0.25$, $p = 0.032$. This indicated that those with higher interpretive biases tended to show lower levels of negative emotion following the video than those with lower interpretive bias. The interactive effects between tDCS condition and emotion regulation condition on both interpretive bias, and emotional reactivity were not significant. When examining the stand-alone mediation, the confidence interval for the indirect effect of tDCS condition on emotional reactivity via interpretive bias, path ab = 0.04, did overlap zero, CI = [−0.2062, 0.4807], indicating that biased interpretation did not significantly mediate this effect. The over-arching index of moderated mediation (-0.04) also overlapped zero, CI = [−0.7161, 0.5670], indicating that there was no evidence of moderated mediation.

Fig. 2 Interaction between mood assessment point and tDCS condition. Error bars = standard error
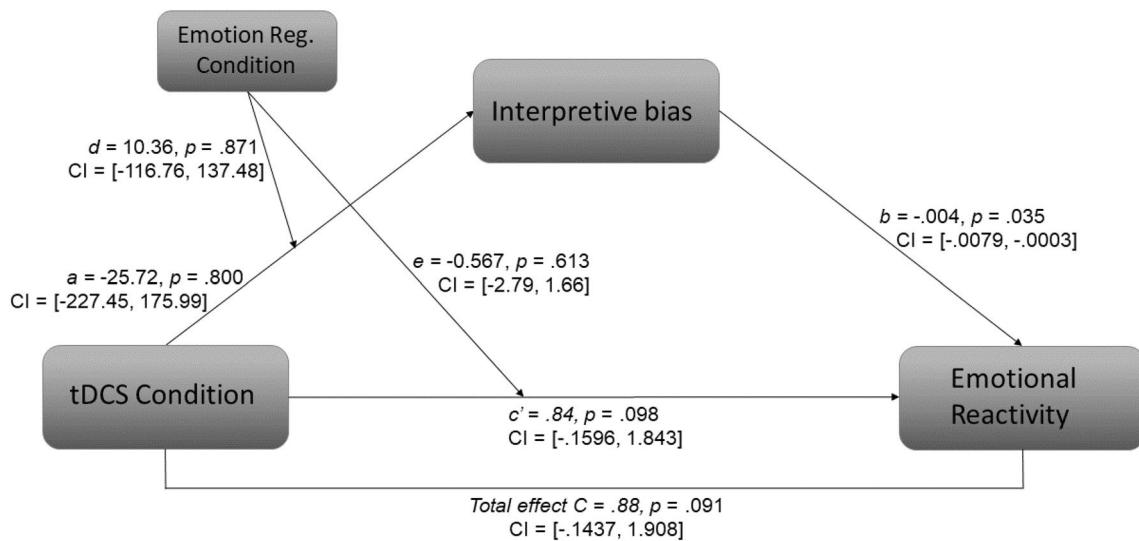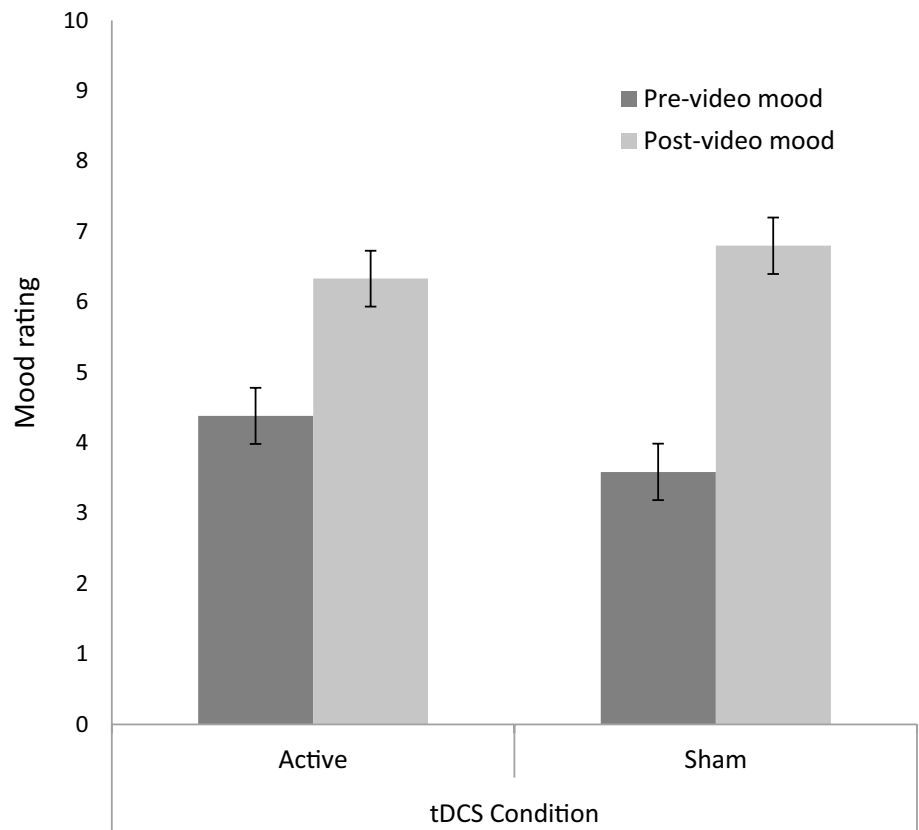

Fig. 3 Results from the mediation analysis showing path coefficient, significance levels, and 95% confidence intervals (CI). *a*-path = effect of tDCS condition on interpretive bias (non-significant); b-path = effect of interpretive bias on emotional reactivity (significant); *c*'- path = direct effect of tDCS condition on emotional reactivity (non-significant), *d*-path = interactive effect of tDCS condition and emotion regulation condition on interpretive bias (non-significant); *d*-path = interactive effect of tDCS condition and emotion regulation condition on emotional reactivity (non-significant). The index of moderated mediation = -.04, CI = [− .7161, .5670] was not significant

Manipulation Check Question

A chi-square test of contingencies ($\alpha = 0.05$) showed that participants in Active- versus Sham-tDCS conditions did not differ significantly in levels of awareness about which experimental condition they were assigned to, $\chi^2 (3, 73) = 2.72$, $p = 0.099$.

Discussion

The current study examined the effects of tDCS and emotion regulation on interpretive bias, and emotional reactivity to negative content. In doing so we also sought to assess the potential mediating role of interpretive bias in the relationship between tDCS and emotional reactivity, and the role of emotion regulation in moderating this relationship. In line with expectations, we observed a small, significant relationship between tDCS and emotional reactivity. Specifically, those receiving active tDCS showed smaller increases in negative mood in response to the emotional reactivity assessment task as compared to those receiving sham tDCS. This finding is consistent with past research showing that increased activation of the DLPFC contributes to less emotional reactivity in response to negative emotional content (Peña-Gómez et al. 2011). It is also consistent with recent meta-analytic findings showing a small effect of tDCS attenuating emotional reactivity in healthy samples (Smits et al. 2020). However, when the pre-video mood was added as a covariate with post-video mood as the dependent measure in the mediation this relationship was no longer significant. As noted in the LMM analysis of emotional reactivity, it is possible that this reflects the fact that that the interaction between tDCS and the pre-post video mood ratings was not due to a significant difference between active and sham tDCS groups at either the pre or post video mood ratings, but reflected the smaller increase in negative mood in the active tDCS condition and a larger increase in the sham condition.

Emotion regulation condition had the anticipated effect on mood ratings of negative stimulus images during the emotion regulation task, with those in the down-regulate condition reporting less negative responses to these images than those in the maintain condition. There was no observed interaction between emotion regulation condition and tDCS condition on these stimulus ratings, nor any interaction between these on negative mood in response to that emotional reactivity assessment task. There was however a main effect of emotion regulation condition on mood during the emotional reactivity assessment task, with those in the down-regulate condition showing less negative mood on average at both the pre and post-video assessment points. This effect did not interact with the assessment time (pre-post video) however, suggesting a general lowering of negative mood but no evidence of influencing the degree of emotional reactivity.

Of particular note, we did not observe the anticipated interaction between tDCS condition and emotion regulation condition. Specifically, there was no evidence that active tDCS enhanced the ability to down-regulate emotional reactivity to negative content compared to sham stimulation. This is inconsistent with the findings of Feeser et al. (2014) who found that frontal tDCS can enhance the effects of deliberate emotion regulation. A number of differences between these designs could potentially have contributed to the absence of this effect in the current study. The first possibility concerns the location targeted for stimulation. In their study Feeser et al. (2014) targeted the right DLPFC for anodal stimulation finding evidence for the enhancement of both up and down-regulation of emotional responses to negative images. In contrast, Marques et al. (2018) found no evidence that any tDCS (left or right DLPFC or VLPFC) enhanced emotion regulation. This study found only that left VLPFC stimulation led to reductions in the negative appraisal of aversive stimuli that was not further modified by emotion regulation intent. As such, evidence that tDCS can enhance emotion regulation intent appears restricted to Feeser et al. (2014), while others (Marques et al. 2018; Peña-Gómez et al. 2011) have shown only that tDCS can attenuate negative appraisals of stimuli, and not that it can enhance the effects of intentional emotion regulation.

Another distinction between the Feeser et al. (2014) and Marques et al. (2018) studies, and the present design, is that both previous studies included contralateral cathodal stimulation, whereas the present study employed an extracephalic reference electrode. As such, while findings from these previous studies have been attributed to enhanced cortical activity via anodal stimulation locations, it is also possible that the additional effects of the contralateral cathode could have contributed to the pattern of results. Given that cathodal stimulation is not reliably associated with a reversal of anodal effects (e.g. Baumert et al. 2019), it is possible that a contralateral array may further enhance the likelihood of observing tDCS-induced effects of emotion regulation and/or stimulus appraisal.

Somewhat unexpectedly, we observed a small negative relationship between interpretive bias and the degree of increase in negative mood in response to the emotional reactivity task, suggesting that a more negative interpretive bias was associated with less elevation of negative mood. One possible account for this is that those with a more negative bias accurately predicted negative outcomes depicted in the video segments, and as such experienced less elevation in negative mood. It is possible therefore that this type of unambiguous video content may not capture individual differences in emotional vulnerability associated with the possession of a negative interpretive bias.

To capture the negative emotional effects of interpretive bias it may therefore be important for future studies to incorporate an emotional reactivity assessment task that involves greater ambiguity; for example, films where the degree of negative outcome is indeterminate (e.g. Wilson et al. 2006).

It is important to acknowledge limitations associated with the present design. One of these concerns the alternative emotion regulation conditions employed. The decision to include down-regulate and maintain emotion regulation conditions was principally due to interest in comparing conditions involving the intent to reduce emotional reactivity, with a 'baseline' in which there was no requirement to alter emotional reactions. However, many studies examining the effects of emotion regulation and their interactions with tDCS (including; Feeser et al. 2014; Marques et al. 2018) include an 'upregulate' condition where participants were instructed to increase their emotional reactions to stimuli. While the between-subjects design adopted in the current study meant that the inclusion of a further two groups to incorporate such an additional upregulation condition was not practical with available time and resources, it is possible that such a condition may have increased the likelihood of detecting effects. That is, rather than providing comparison against a 'baseline' of no emotional change, the inclusion of the upregulate condition could have provided a condition producing higher emotional responsivity as a contrast to the down-regulate condition. While the absence of a 'maintain' condition would remove a condition capable of capturing baseline effects, future between-subject designs may nevertheless wish to contrast up and down-regulate conditions in order to maximise the likelihood of detecting between-group differences.

The emotion regulation task employed in the current study involves participants responding to the explicit instruction to execute a specific pattern of control over emotional reactions (i.e. down-regulate and maintain). It is possible that the use of explicit instruction in such tasks could contribute to demand effects which, in turn potentially mask smaller tDCS effects. One possible means of addressing this is via the use of electrophysiological measures of arousal (e.g. skin conductance, heart rate variability) which can serve to corroborate and/or contrast patterns of effects observed on self-report measures. Given that research has shown that tDCS can contribute to changes in such physiological indicators of arousal (Allaert et al. 2020; Marques et al. 2018) the absence of such measures in the current study could be considered a limitation and future research would benefit from their inclusion. It may also be worthy to consider alternative and more ecologically valid methods of assessing emotion regulation. For example it may be possible to contrive lab-based situations that initially elevate arousal (e.g. stress task), followed by a task in which it is highly adaptive to rapidly down-regulate arousal to perform optimally.

It is important to also note that the sample size employed in the current study was under-powered for detecting small effects. While medium-large effects have been reported in some prior studies for measures relevant to the current study (e.g. Heeren et al. 2017), others have reported small or no effects (Marques et al. 2018; Smits et al. 2020). Indeed, a recent meta-analytic findings showing that tDCS induced effects of emotional reactivity in healthy samples tend to be relatively weak (Smits et al. 2020). As such the sample size in the current study must be acknowledged as a limitation given the small effects often associated with cognitive biases (Pergamin-Hight et al. 2015) and tDCS (Smits et al. 2020). This speaks to the need to employ larger sample sizes in future research, particularly those involving between-subject designs that necessarily involve greater variance than other within-subject comparisons involving tDCS (e.g. Ironside et al. 2019).

The absence of baseline measures relating to biased interpretation and emotion regulation should also be acknowledged as a limitation of the present design. The current study did include baseline measures of general emotional vulnerability, and positive and negative affect with the absence of group differences in these providing some general reassurance that the experimental groups were unlikely to systematically differ. Nevertheless, it would be optimal for future research to include baseline measures of direct relevance to the dependent measures examined in the study, in particular biased interpretation and emotion regulation, to ensure similarity between groups on these measures prior to the implementation of experimental manipulations.

In summary, we examined the potential mediating role of biased interpretation in the relationship between prefrontal tDCS and emotional reactivity to negative content, and further determined the potential moderating role of emotion regulation intent. We found evidence that active tDCS attenuated emotional reactions to negative content but no evidence that tDCS reduced biased interpretation, or that biased interpretation mediated the relationship between tDCS and emotional reactivity. No evidence for tDCS enhancement of emotion regulation was observed. An unexpected negative relationship between interpretive bias and emotional reactivity suggested that those with a more negative interpretive bias showed the least increase in negative mood in response to the emotional reactivity task. The present findings provide additional support for the capacity of left frontal tDCS to attenuate negative emotional reactions, but did not support past findings suggesting such stimulation can enhance the effects of intentional emotion regulation.

Compliance with Ethical Standards

Conflict of Interests The authors report no financial interests or potential conflicts of interest.

References

Allaert, J., De Raedt, R., Sanchez-Lopez, A., Baeken, C., & Vanderhasselt, M.-A. (2020). Mind the social feedback: effects of tDCS applied to the left DLPFC on psychophysiological responses during the anticipation and reception of social evaluations. *Social Cognitive and Affective Neuroscience*. https://doi.org/10.1093/scan/nsaa066.

Bar-Haim, Y., Lamy, D., Pergamin, L., Bakermans-Kranenburg, M. J., & van Ijzendoorn, M. H. (2007). Threat-related attentional bias in anxious and nonanxious individuals: A meta-analytic study. *Psychological Bulletin, 133*(1), 1–24. https://doi.org/10.1037/0033-2909.133.1.1.

Baumert, A., Buchholz, N., Zinkernagel, A., Clarke, P., MacLeod, C., Osinsky, R., et al. (2019). Causal underpinnings of working memory and Stroop interference control: Testing the effects of anodal and cathodal tDCS over the left DLPFC. *Cognitive, Affective, & Behavioral Neuroscience.*. https://doi.org/10.3758/s13415-019-00726-y.

Berking, M., Wirtz, C. M., Svaldi, J., & Hofmann, S. G. (2014). Emotion regulation predicts symptoms of depression over five years. *Behaviour Research and Therapy, 57*, 13–20. https://doi.org/10.1016/j.brat.2014.03.003.

Bindman, L. J., Lippold, O. C. J., & Redfearn, J. W. T. (1964). The action of brief polarizing currents on the cerebral cortex of the rat (1) during current flow and (2) in the production of long-lasting after-effects. *The Journal of Physiology, 172*(3), 369–382. https://doi.org/10.1113/jphysiol.1964.sp007425.

Bishop, S. J. (2007). Neurocognitive mechanisms of anxiety: an integrative account. *Trends in Cognitive Sciences, 11*(7), 307–316. https://doi.org/10.1016/j.tics.2007.05.008.

Brunoni, A. R., Moffa, A. H., Fregni, F., Palm, U., Padberg, F., Blumberger, D. M., et al. (2016). Transcranial direct current stimulation for acute major depressive episodes: meta-analysis of individual patient data. *The British Journal of Psychiatry, 208*(6), 522–531.

Brunoni, A. R., Zanao, T. A., Vanderhasselt, M. A., Valiengo, L., Oliveira, J. F., Boggio, P. S., et al. (2014). Enhancement of affective processing induced by bifrontal transcranial direct current stimulation in patients with major depression. *Neuromodulation Technology at the Neural Interface, 17*(2), 138–142. https://doi.org/10.1111/ner.12080.

Chattanooga Group, H. (United States). Chattanooga Dual Channel Iontophoresis System. Hixon, TN, USA: Encore Medical.

Chen, N. T. M., Basanovic, J., Notebaert, L., MacLeod, C., & Clarke, P. J. F. (2017). Attentional bias mediates the effect of neurostimulation on emotional vulnerability. *Journal of Psychiatric Research, 93*, 12–19. https://doi.org/10.1016/j.jpsychires.2017.05.008.

Cisler, J. M., & Olatunji, B. O. (2012). Emotion Regulation and Anxiety Disorders. *Current Psychiatry Reports, 14*(3), 182–187. https://doi.org/10.1007/s11920-012-0262-2.

Clarke, P. J. F., Browning, M., Hammond, G., Notebaert, L., & MacLeod, C. (2014). The Causal Role of the Dorsolateral Prefrontal Cortex in the Modification of Attentional Bias: Evidence from Transcranial Direct Current Stimulation. *Biological Psychiatry, 76*(12), 946–952. https://doi.org/10.1016/j.biopsych.2014.03.003.

Clarke, P. J. F., Sprlyan, B. F., Hirsch, C. R., Meeten, F., & Notebaert, L. (2020). tDCS increases anxiety reactivity to intentional worry. *Journal of Psychiatric Research, 120*, 34–39. https://doi.org/10.1016/j.jpsychires.2019.10.013.

Clifton, J. L., Hedley, S., Mountier, E., Tiszai, B., & Grimshaw, G. M. (2016). Practice makes perfect: Training the interpretation of emotional ambiguity. *Cognition & Emotion, 30*(4), 654–668. https://doi.org/10.1080/02699931.2015.1020768.

Etkin, A., & Wager, T. D. (2007). Functional Neuroimaging of Anxiety: A Meta-Analysis of Emotional Processing in PTSD, Social Anxiety Disorder, and Specific Phobia. *American Journal of Psychiatry, 164*(10), 1476–1488. https://doi.org/10.1176/appi.ajp.2007.07030504.

Everaert, J., Grahek, I., Duyck, W., Buelens, J., Van den Bergh, N., & Koster, E. H. W. (2017). Mapping the interplay among cognitive biases, emotion regulation, and depressive symptoms. *Cognition and Emotion, 31*(4), 726–735. https://doi.org/10.1080/02699931.2016.1144561.

Feeser, M., Prehn, K., Kazzer, P., Mungee, A., & Bajbouj, M. (2014). Transcranial Direct Current Stimulation Enhances Cognitive Control During Emotion Regulation. *Brain stimulation, 7*(1), 105–112.

Gross, J. J. (1998). The emerging field of emotion regulation: An integrative review. *Review of General Psychology, 2*(3), 271–299. https://doi.org/10.1037/1089-2680.2.3.271.

Hayes, A. F. (2017). *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach* (2nd ed.). New York, United States: Guilford Press.

Heeren, A., Baeken, C., Vanderhasselt, M.-A., Philippot, P., & de Raedt, R. (2015). Impact of anodal and cathodal transcranial direct current stimulation over the left dorsolateral prefrontal cortex during attention bias modification: An eye-tracking study. *PLoS ONE, 10*(4), e0124182. https://doi.org/10.1371/journal.pone.0124182.

Heeren, A., Billieux, J., Philippot, P., De Raedt, R., Baeken, C., de Timary, P., et al. (2017). Impact of transcranial direct current stimulation on attentional bias for threat: a proof-of-concept study among individuals with social anxiety disorder. *Social Cognitive and Affective Neuroscience, 12*(2), 251–260. https://doi.org/10.1093/scan/nsw119.

Hill, A. T., Fitzgerald, P. B., & Hoy, K. E. (2016). Effects of Anodal Transcranial Direct Current Stimulation on Working Memory: A Systematic Review and Meta-Analysis of Findings From Healthy and Neuropsychiatric Populations. *Brain stimulation, 9*(2), 197–208. https://doi.org/10.1016/j.brs.2015.10.006.

Hirsch, C. R., Meeten, F., Krahé, C., & Reeder, C. (2016). Resolving Ambiguity in Emotional Disorders. *The Nature and Role of Interpretation Biases, 12*(1), 281–305. https://doi.org/10.1146/annurev-clinpsy-021815-093436.

Ironside, M., Browning, M., Ansari, T. L., Harvey, C. J., Sekyi-Djan, M. N., Bishop, S. J., et al. (2019). Effect of Prefrontal Cortex Stimulation on Regulation of Amygdala Response to Threat in Individuals With Trait Anxiety: A Randomized Clinical Trial. *Jama Psychiatry, 76*(1), 71–78. https://doi.org/10.1001/jamapsychiatry.2018.2172.

Ironside, M., O'Shea, J., Cowen, P. J., & Harmer, C. J. (2016). Frontal Cortex Stimulation Reduces Vigilance to Threat: Implications for the Treatment of Depression and Anxiety. *Biological Psychiatry, 79*(10), 823–830. https://doi.org/10.1016/j.biopsych.2015.06.012.

JASP Team. (2020). JASP (Version 0.13.1). Retrieved from https://jasp-stats.org/

Joormann, J., & D'Avanzato, C. (2010). Emotion regulation in depression: Examining the role of cognitive processes. *Cognition and Emotion, 24*(6), 913–939. https://doi.org/10.1080/02699931003784939.

Joormann, J., & Gotlib, I. H. (2010). Emotion regulation in depression: Relation to cognitive inhibition. *Cognition and Emotion, 24*(2), 281–298. https://doi.org/10.1080/02699930903407948.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1997) International affective picture system (IAPS) Technical manual and affective ratings. NIMH Center for the Study of Emotion and Attention, 39–58.

Lovibond, P., & Lovibond, S. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy, 33*(3), 335–343.

Marques, L. M., Morello, L. Y. N., & Boggio, P. S. (2018). Ventrolateral but not Dorsolateral Prefrontal Cortex tDCS effectively impact emotion reappraisal—effects on Emotional Experience and Interbeat Interval. *Scientific Reports, 8*(1), 15295. https://doi.org/10.1038/s41598-018-33711-5.

Martin, D. M., Liu, R., Alonzo, A., Green, M., Player, M. J., Sachdev, P., et al. (2013). Can transcranial direct current stimulation enhance outcomes from cognitive training? A randomized controlled trial in healthy participants. *International Journal of Neuropsychopharmacology, 16*(9), 1927–1936. https://doi.org/10.1017/s1461145713000539.

Nitsche, M. A., Cohen, L. G., Wassermann, E. M., Priori, A., Lang, N., Antal, A., et al. (2008). Transcranial direct current stimulation: State of the art 2008. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation, 1*(3), 206–223. https://doi.org/10.1016/j.brs.2008.06.004.

Nitsche, M. A., & Paulus, W. (2001). Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. *Neurology, 57*(10), 1899–1901. https://doi.org/10.1212/wnl.57.10.1899.

Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D. E., et al. (2004). For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *NeuroImage, 23*(2), 483–499. https://doi.org/10.1016/j.neuroimage.2004.06.030.

Peña-Gómez, C., Vidal-Piñeiro, D., Clemente, I. C., Pascual-Leone, Á., & Bartrés-Faz, D. (2011). Down-regulation of negative emotional processing by transcranial direct current stimulation: effects of personality characteristics. *PLoS ONE, 6*(7), e22812.

Pergamin-Hight, L., Naim, R., Bakermans-Kranenburg, M. J., van Ijzendoorn, M. H., & Bar-Haim, Y. (2015). Content specificity of attention bias to threat in anxiety disorders: A meta-analysis. *Clinical Psychology Review, 35*, 10–18. https://doi.org/10.1016/j.cpr.2014.10.005.

Preacher, K. J., & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods Instruments & Computers, 36*(4), 717–731. https://doi.org/10.3758/bf03206553.

Sanchez-Lopez, A., Vanderhasselt, M.-A., Allaert, J., Baeken, C., & De Raedt, R. (2018). Neurocognitive mechanisms behind emotional attention: Inverse effects of anodal tDCS over the left and right DLPFC on gaze disengagement from emotional faces. *Cognitive, Affective, and Behavioral Neuroscience, 18*(3), 485–494. https://doi.org/10.3758/s13415-018-0582-8.

Siegle, G. J., Thompson, W., Carter, C. S., Steinhauer, S. R., & Thase, M. E. (2007). Increased Amygdala and Decreased Dorsolateral Prefrontal BOLD Responses in Unipolar Depression: Related and Independent Features. *Biological Psychiatry, 61*(2), 198–209. https://doi.org/10.1016/j.biopsych.2006.05.048.

Smits, F. M., Schutter, D. J. L. G., van Honk, J., & Geuze, E. (2020). Does non-invasive brain stimulation modulate emotional stress reactivity? *Social Cognitive and Affective Neuroscience, 15*(1), 23–51. https://doi.org/10.1093/scan/nsaa011.

Van Bockstaele, B., Notebaert, L., Salemink, E., Clarke, P. J. F., MacLeod, C., Wiers, R. W., et al. (2019). Effects of interpretation bias modification on unregulated and regulated emotional reactivity. *Journal of Behavior Therapy and Experimental Psychiatry, 64*, 123–132. https://doi.org/10.1016/j.jbtep.2019.03.009.

Vicario, C. M., Salehinejad, M. A., Felmingham, K., Martino, G., & Nitsche, M. A. (2019). A systematic review on the therapeutic effectiveness of non-invasive brain stimulation for the treatment of anxiety disorders. *Neuroscience & Biobehavioral Reviews, 96*, 219–231. https://doi.org/10.1016/j.neubiorev.2018.12.012.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063–1070. https://doi.org/10.1037/0022-3514.54.6.1063.

Williams, J. M. G., Watts, F. N., MacLeod, C., & Mathews, A. (1997). *Cognitive psychology and emotional disorders* (2nd ed.). Oxford, England: John Wiley & Sons.

Wilson, E. J., MacLeod, C., Mathews, A., & Rutherford, E. M. (2006). The causal role of interpretive bias in anxiety reactivity. *Journal of Abnormal Psychology, 115*(1), 103–111. https://doi.org/10.1037/0021-843X.115.1.103.