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Mind the social feedback: effects of tDCS applied to the left DLPFC on psychophysiological responses during the anticipation and reception of social evaluations

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Abstract

The left dorsolateral prefrontal cortex (lDLPFC) is implicated in anticipatory (i.e., during anticipation of emotional stimuli) and online (i.e., during confrontation with emotional stimuli) emotion regulatory processes. However, research that investigates the causal role of the lDLPFC in these processes is lacking. In this study, 74 participants received active or sham transcranial direct current stimulation (tDCS) over the lDLPFC. Participants were told strangers evaluated them. These (rigged) social evaluations were presented, and in 50% of the trials, participants could anticipate the valence (positive or negative) of the upcoming social feedback. Pupil dilation (a marker of cognitive resource allocation), and skin conductance responses (a marker of arousal) were measured. The results indicate that active (compared to sham) tDCS reduced arousal during the confrontation with anticipated feedback, but only marginally during the confrontation with unanticipated feedback. When participants were given the opportunity to anticipate the social feedback, tDCS reduced arousal, irrespective of whether one was anticipating or being confronted with the anticipated feedback. Moreover, tDCS reduced cognitive resource allocation during anticipation, which was associated with resource allocation increases during the subsequent confrontation. Altogether, results suggest that the lDLPFC is causally implicated in the interplay between anticipatory and online emotion regulatory processes.

Keywords: Transcranial direct current stimulation, Dorsolateral prefrontal cortex, Anticipation, Emotional processing, Skin conductance response, Pupillary response

Introduction

The ability to regulate emotional responses to self-relevant events is of crucial importance in mental health (Gross & John, 2003). Building on the dual-mechanisms of control framework (Braver, 2012), there is a growing interest in anticipatory emotional processes (i.e., processes that occur in the anticipation of an emotional event). It has been proposed that these anticipatory processes may help or hinder individuals to cope when actually confronted with these events, and may be of crucial importance in emotion and stress regulation (De Raedt & Hooley, 2016). Specifically, as arousal increases over time in the emotion generative process, regulatory processes that act early on (e.g., during the anticipation of a public speech), require less effort to regulate the emotional response when actually confronted with the stressor, and may thus be more effective (Sheppes & Gross, 2011). In other words, engaging in anticipatory effortful adaptive emotion regulation contributes to more efficient online (i.e., during the actual stressor confrontation) regulation of emotional responses (Pulopulos, Vanderhasselt, & De Raedt, 2018; Vanderhasselt, Remue, Ng, & De Raedt, 2014b). It is therefore key to further investigate these anticipatory emotional processes in self-relevant emotional situations.

The dorsolateral prefrontal cortex (DLPFC), among other prefrontal brain regions, is an important corticolimbic hub to down- and upregulate limbic responses, resulting in decreased and increased emotional reactivity, respectively (Banks, Eddy, Angstadt, Nathan, & Phan, 2007; Ochsner et al., 2004; Ochsner, Silvers, & Buhle, 2012). Moreover, the DLPFC and associated prefrontal regions have been implicated in proactive control (i.e., preparatory processes that serve to enhance conflict resolution when it is presented; Braver; Braver, Paxton, Locke, & Barch, 2009; Irlbacher, Kraft, Kehrer, & Brandt, 2014), as well as anticipatory emotional processes (Herwig et al., 2007; Nitschke, Sarinopoulos, Mackiewicz, Schaefer, & Davidson,

2006; Wang, Lu, Hu, Zhang, & Yuan, 2018). For instance, when participants were anticipating an emotional stimulus with the instruction to prepare to down-regulate their emotional responses when the stimuli was presented, anticipatory left DLPFC activity was associated with decreased emotional reactivity during subsequent stimuli presentation (Seo et al., 2014). Given that the DLPFC is also implicated in online emotion regulation (Baeken et al., 2017; Brunoni et al., 2013; Peña-Gómez, Vidal-Piñeiro, Clemente, Pascual-Leone, & Bartrés-Faz, 2011), it can be concluded that these prefrontal regions are implicated in the modulation of both anticipatory and online emotional responses (ERs). However, research is lacking in which it is investigated a) whether the DLPFC is differentially implicated in the online modulation of ERs to anticipated versus unanticipated self-relevant emotional stimuli, b) whether, within anticipatory contexts (i.e., the stimuli anticipation and subsequent presentation), the DLPFC is differentially implicated in anticipatory versus online ERs modulation, and c) how, within anticipatory contexts, the DLPFC is implicated in the interplay between anticipatory and online ERs modulation.

Hence, the goal of the current study was to investigate these research questions using transcranial direct current stimulation (tDCS) in an ecologically valid experimental paradigm in which naturally occurring (i.e., absence of task instructions) psychophysiological ERs to self-relevant stimuli were measured. tDCS is a form of non-invasive brain stimulation (NIBS), which operates through the delivery of a constant low-intensity electrical current (e.g., 0.5 – 2.0 mA) to the scalp. This modulates the neuron membrane potential through depolarization (anodal tDCS; excitatory effect) or hyperpolarization (cathodal tDCS; inhibitory effect), resulting in a reduced or increased neuron firing threshold, respectively. It has been shown that tDCS can transiently modulate emotional and cognitive processes (Dedoncker, Brunoni, Baeken, & Vanderhasselt,

2016; Nitsche et al., 2008). In the paradigm, participants were presented a series of negative and positive self-relevant stimuli, in which half of the time the valence could be anticipated of an upcoming stimulus, prior to its presentation. The self-relevant stimuli consisted of social evaluations directed at the participant, as social belonging is a universal human need and the confrontation with social evaluations (e.g., praise, criticism) evokes strong ERs that naturally trigger self-regulatory processes (Baumeister & Leary, 1995; DeWall et al., 2011; Dickerson & Kemeny, 2004. Specifically, participants were led to believe that, based on their self-photographs, strangers had formed first impressions of them, and that they would be presented with this social feedback.

To objectively assess ERs, skin conductance responses (SCRs; Sabatinelli, Bradley, & Lang, 2001; Spinks, Blowers, & Shek, 1985) and pupillary responses (Moresi et al., 2008; Vanderhasselt et al., 2014b) were measured. SCRs reflect autonomic changes in skin conductivity, and are a reliable marker of emotional arousal and emotion regulatory success, with lower SCRs being associated with lower arousal and higher down-regulatory success, and vice versa (Eippert et al., 2007; Feeser, Prehn, Kazzer, Mungee, & Bajbouj, 2014; Urry, van Reekum, Johnstone, & Davidson, 2009). Moreover, decreased SCRs have been related with corticolimbic activity changes, showing increased prefrontal (e.g., DLPFC) activity and decreased limbic activity (Eippert et al., 2007; Wood, Ver Hoef, & Knight, 2014). Pupillary responses reflect changes in pupil diameter, where pupil constriction (i.e., a decrease in pupil size), caused by the iris sphincter muscle, is under control of the parasympathetic nervous system, and pupil dilation (PD; i.e., an increase in pupil size), caused by the iris dilator muscle, is under control of the sympathetic nervous system (Beatty & Lucero-Wagoner, 2000). Under constant luminance conditions, PD occurs as a function of increasing task difficulty, cognitive

load, conflict processing, mental effort (Iqbal, Zheng, & Bailey, 2004; Kahneman, 1973; Kahneman & Beatty, 1966; Van Steenbergen & Band, 2013), and emotion regulatory effort (Johnstone, van Reekum, Urry, Kalin, & Davidson, 2007; Kinner et al., 2017; Siegle, Steinhauer, Stenger, Konecky, & Carter, 2003; Urry et al., 2006; van Reekum et al., 2007). Moreover, PD is shown to correlate with DLPFC activity (Siegle et al., 2003). Summarizing, pupillary responses inform about (emotion) regulatory *processes*, reflecting the amount of cognitive resources that are allocated to process (emotional) stimuli, with larger PD reflecting increased resource allocation, and vice versa. (Einhäuser, 2017; Granholm & Steinhauer, 2004; Kinner et al., 2017; van der Wel & van Steenbergen, 2018). SCRs on the other hand, inform about (emotion) regulatory *success*, and reflect emotional arousal (Eippert et al., 2007; Feeser et al., 2014; Urry et al., 2009).

Based on research implicating the left DLPFC (lDLPFC) in both anticipatory (Lesh et al., 2013; Schmid, Kleiman, & Amodio, 2015; Seo et al., 2014) and online (emotion) regulatory processes (Baeken et al., 2017; Brunoni et al., 2013; Ochsner, Bunge, Gross, & Gabrieli, 2002), the lDLPFC was chosen as the stimulation target in the current study. For the first hypothesis (H1), we expected anodal tDCS over the lDLPFC (compared to sham tDCS) to influence ERs differentially during the confrontation with anticipated versus unanticipated social feedback. Specifically, we expected tDCS to reduce SCRs (i.e., decreased emotional arousal) during both anticipated and unanticipated feedback, but expected the SCRs reduction to be larger during anticipated feedback. For PD, based on studies showing excitatory NIBS applied over the lDLPFC increases a) cognitive control over emotional material (Dedoncker et al., 2016; Plewnia, Schroeder, Kunze, Faehling, & Wolkenstein, 2015), and b) increases PD to emotional stimuli (Allaert, Sanchez-Lopez, De Raedt, Baeken, & Vanderhasselt, 2019), we expected tDCS to

increase PD (i.e., increased resource allocation) during both anticipated and unanticipated social feedback, but again expected the PD increase to be larger during anticipated feedback. For the second and third hypothesis (H2 and H3), within anticipatory contexts (i.e., the anticipation of social feedback and the subsequent confrontation), we expected the tDCS effect on ERs to occur during the anticipation (H2), which then in turn would influence subsequent ERs during the confrontation (H3). Based on the notion that an enhancement of anticipatory effort mediated by the DLPFC contributes to a more efficient subsequent online regulation (De Raedt & Hooley, 2016; Vanderhasselt et al., 2014b), we expected active tDCS (versus sham) to be associated with larger PD during the anticipation, and this in turn would be associated with smaller PD during the subsequent confrontation. For SCRs, we expected active tDCS to be associated with lower SCRs during the anticipation, which in turn would be associated with lower SCRs during the subsequent anticipation.

Materials and Methods

Participants

Seventy-four[1] healthy female individuals (age M = 20.80, SD = 2.11) participated in the study. Given the consistent sex differences in emotional processing (Domes et al., 2010; Lithari et al., 2010; McRae, Ochsner, Mauss, Gabrieli, & Gross, 2008), to reduce the sample variability, only female participants were included. For an overview of the other selection criteria, see supplementary materials. Participants were recruited from the general community via internet postings on social media and posters in public places. The experiment was conducted with the

[1] A power analysis using G*Power suggested a total sample size of N = 70 to detect a small to medium effect (Cohen's f = .17) via an F-test for a within-between interaction, with a power of 80 % (Faul, Erdfelder, Lang, & Buchner, 2007). Based on past experiences from studies within our lab, to account for potential data loss due to technical problems, we increased this suggested sample size with 5 %, resulting in a final sample of N = 74.

approval of Ghent University's Medical Ethical Committee and in accordance with the Declaration of Helsinki. Participants provided informed consent at the start of the experiment and received € 15 for participating.

Materials

Social feedback paradigm. An adaption of a rigged social feedback paradigm was used (Vanderhasselt, De Raedt, Nasso, Puttevils, & Mueller, 2018; 2015). This adaptation was conceptually inspired by a previously employed paradigm in which participants passively viewed emotional images that were preceded by a cue indicating the emotional valence of the image (Allaert et al., 2019). Rather than employing images as stimuli, we chose to use social evaluations, in order to improve ecological validity. In our adapted paradigm, participants were provided explicit (positive and negative) social feedback based on the first impressions strangers would have about them. Unbeknownst to the participants, this feedback was experimentally rigged. The task comprised 80 trials, divided in 4 blocks (20 trials per block), with breaks in between. During block 1 to 3, the valence of the social feedback was equally distributed, whereas in the last block[2] negative feedback was more prevalent (80 %). In anticipatory contexts (40 trials), participants could anticipate the valence of the feedback, whereas in non-anticipatory contexts (40 trials), participants could not anticipate the feedback valence. Each trial started with an intertrial interval (ITI; 2500 ms) displaying a fixation cross. After the ITI, for an anticipatory context, a cue (8000 ms) indicated the valence (negative, positive), and afterwards a social feedback word was presented (anticipated target), next to an image of the evaluator and an image of the participant. For a non-anticipatory context, a social feedback word (unanticipated target;

[2] This was done to investigate emotional recovery from mainly negative social feedback, however these results fall outside the scope of the research questions of this manuscript.

8000 ms) and the self and evaluator images were directly presented after the ITI. At the end of every trial, regardless of its context-type, participants were displayed a visual analog scale (VAS) in which they had to indicate how they felt in response to the received social feedback. Figure 1 displays a visual representation of the experimental sequence for each trial type. All presented images were grey-scaled and matched on luminance values via the Matlab SHINE toolbox (Willenbockel et al., 2010), in order to prevent luminance-evoked pupillary responses (Bradley, Miccoli, Escrig, & Lang, 2008). To furthermore control luminance across the various phases of each trial sequence, a placeholder image of a cloud was presented on the location where the self and evaluator pictures are presented during the target phase, and placeholder symbols were presented during the ITI on the location where the cue and feedback words subsequently appeared. The social feedback word stimuli (see supplementary materials) were obtained from a validated normative database of Dutch words (Moors et al., 2013), and were matched on arousal between negative and positive valence trials. The stimuli of the so-called evaluators were obtained by taking photographs of volunteers outside of the participant pool, between the ages of 18 and 30. The order of the specific combinations of trial features (trial type, evaluator, gender of evaluator, social feedback word, location of the evaluator photograph) was counterbalanced over the four blocks, via a pseudo-randomization algorithm (see supplementary materials). The duration of the phases of interest (cue, target), was set to 8 s to ensure enough time for the SCRs to return to baseline, as the SCR rise and half-recovery time can take up to 4 s each (Dawson, Schell, & Filion, 2017). The paradigm was programmed in E-prime 2.0 Professional (Psychology Software Tools, Pittsburgh, PA).

Transcranial direct current stimulation (tDCS). TDCS was applied with a pair of rubber surface electrodes (5 × 7 cm = 35 cm^2) covered with electrode gel[3] and delivered with a battery-driven stimulator (DC-Stimulator Plus, neuroConn GmbH). The anodal electrode was vertically positioned over F3 (corresponding to the lDLPFC) according to the 10-20 international EEG system, whereas the cathode was placed over the contralateral supra-orbital area (Fp2). This electrode positioning is in accordance with previous tDCS studies on emotional processing and the level B recommendation for treating major depressive disorders (Dedoncker et al., 2016; Lefaucheur et al., 2017; Nitsche et al., 2008). A current of 2 mA (current density = .06), with 30 seconds of ramp up/down, was applied for 20 minutes. 50 % of the participants received active tDCS, whereas the others received sham tDCS (between-subject design). For sham tDCS (i.e., placebo) the current was directly ramped down after the initial ramp up phase (Nitsche et al., 2008). Figure 2 shows a visualization of the electric field simulation of the utilized tDCS montage, using Soterix HD-Explore software.

Skin conductance responses (SCR). Electrodermal activity was recorded at a sample rate of 1000 Hz with the Biopac EDA100c amplifier, in conjunction with the Biopac MP150 (Biopac Systems Inc., Santa Barbara, CA). For details on the recording parameters and the pre-processing of the SCR data, see supplementary materials.

Pupillary responses. Pupillary responses were recorded at a sampling rate of 300 Hz with a Tobii TX300 eye tracker (Tobii AB, Stockholm, Sweden), in conjunction with the E-Prime Extensions for Tobii (Psychology Software Tools, Pittsburgh, PA). Participants were comfortably seated approximately 60 cm from the eye tracker. Participants' gaze fixations were

[3] During piloting of the experiment, the usage of gel was favored over saline water, as the gel displayed more consistent optimal electrical conductivity.

calibrated using a standard 9-point calibration sequence. For details on the pre-processing of the pupil data, see supplementary materials.

Self-report measurements.

Online survey. To ensure comparable active and sham tDCS groups, an online survey assessing potential confounders (e.g., self-esteem, perceived criticism, symptoms of mood and anxiety disorders, habitual use of adaptive and maladaptive emotion regulation strategies), was carried out prior to the experiment. See supplementary materials for detailed information.

Mood. To evaluate mood changes during the experimental protocol, self-reported mood was measured at 3 time points (pre-stimulation [T1], post-stimulation [T2], and post-paradigm [T3]), by using 6 VASs (i.e., fatigue, vigorousness, angriness, tension, sadness, and happiness; McCormack, de L. Horne, & Sheather, 1988) presented on the computer screen and ranging from 'totally not' (0) to 'very much' (100).

Mood responses. At the end of every trial, mood responses to the social feedback were measured using a VAS, displaying "How do you feel in response to this evaluation?" and ranging from 'very bad' (0) to 'very good' (100).

Protocol

On a webpage, participants read the informed consent and completed the survey. Afterwards, participants were led to believe they would take part in a study in which the effects of tDCS on the processing of first impressions are investigated. It was stated that they had to form first impressions of strangers, based on their pictures. In return, these strangers would form impressions about them. On the webpage, participants were presented a series of 20 pictures of strangers along with 4 evaluative descriptive words (2 negative and 2 positive words, obtained

from a validated database of Dutch words [Moors et al., 2013]). For each picture, participants were asked to indicate which word corresponded the most with the first impression they had formed about the stranger. Afterwards, participants could upload a self-photograph. At the end, participants could schedule the experiment. Participants were pseudo-randomly assigned to one of the two groups, in order to have comparable groups based on the survey data. In the laboratory (see figure 3 for an overview), participants were seated in front of a computer screen and were connected to the physiological recording equipment. Participants underwent active or sham tDCS, and mood states were assessed before and after the stimulation session. Then, the social feedback paradigm started[4]. Finally, mood states were assessed and participants were debriefed and paid.

Data Analysis

All data was analyzed in R 3.5.0 (R Core Team, 2013) in conjunction with Rstudio 1.2.1335, using linear mixed-effects regression (LMER) models fitted via the *'lmerTest'* package (Kuznetsova, Brockhoff, & Christensen, 2017). *lmerTest* produces *p*-values for the fixed effects using the Satterthwaite approximations to degrees of freedom, and the statistical significance level was set to $p < .05$. Where applicable, to decompose interaction effects, pairwise comparisons were carried out using the *'emmeans'* package (Lenth, 2018). For a justification of the statistical approach, see supplementary materials.

First, to check whether tDCS influenced mood states over the course of the protocol, 6 LMER models (for each mood state; tiredness, vigorousness, angriness, tension, sadness, and

[4] During the social feedback paradigm, gaze behavior towards the various displays (i.e., self, evaluator, feedback) was also measured. However, these results will be reported elsewhere, as these fall outside of the scope of the current research questions.

happiness) were fitted with *group* (active tDCS, sham tDCS) and *time* (pre-stimulation [T1], post-stimulation [T2], post-paradigm [T3]) as fixed effects, and *subject* as random intercept. Furthermore, to investigate the potential tDCS on mood responses to anticipated (AT) versus unanticipated targets (UT), 1 LMER was fitted with *group* (active tDCS, sham tDCS), *type* (AT, UT) and *valence* (negative, positive) as fixed factors, *subject* as random intercept, and self-reported mood responses as dependent variable.

Second, to investigate the effects of tDCS on ERs to AT versus UT, 3 LMERs were fitted with *group* (active tDCS, sham tDCS), *type* (AT, UT), and *valence* (negative, positive) as fixed factors, *subject* as random intercept, and log(SCR), and PD as dependent variables, respectively (H1).

Third, to investigate the effects of tDCS on ERs during cue (C) versus AT, 2 LMERs were fitted with *group* (active tDCS, sham tDCS), *phase* (C, AT), and *valence* (negative, positive) as fixed factors, *subject* as random intercept, and log(SCR) and PD as dependent variables, respectively (H2).

Fourth, to investigate whether tDCS moderated the relationship between ERs during C and ERs during AT (H3), 2 LMERs were fitted with ERs (log(SCR) and PD) during C as continuous predictor, *group* as fixed factor, *subject* as random intercept, and log(SCR) and PD during AT as dependent variables, respectively (H3).

For brevity, the results that do not pertain to tDCS effects are reported in the supplementary materials.

Results

Participants were not able to correctly ascertain their stimulation group (active tDCS, sham tDCS), as the proportion of incorrect guesses (.80), was higher than chance level (.50), $p < .001$. Furthermore, to verify that no differences in potential inter-individual confounders were present between the active and sham tDCS group, independent t-tests showed non-significant comparisons on self-report measures (e.g., self-esteem, perceived criticism, symptoms of mood and anxiety disorders, habitual use of adaptive and maladaptive emotion regulation strategies; all *ts* < 1.55, all *p*s > .13), and a post-hoc analysis showed no significant difference in baseline emotional arousal (as indexed by tonic skin conductance level), $F(1,70) = .35$, $p = .56$. For detailed information, see supplementary materials.

Mood

The LMERs showed a non-significant *group* (all *Fs* < .66, all *p*s > .42), and *group* × *time* (all *Fs* < .88, all *p*s > .42) effect on tiredness, vigorousness, angriness, tension, sadness, and happiness, indicating tDCS did not affect reported mood states across the protocol.

Mood responses

The LMER showed non-significant *group*, *group* × *valence*, *group* × *type* and *group* × *valence* × *type* interaction effects (all *Fs* < .04, all *p*s > .83), indicating that tDCS did not affect self-reported mood responses to the social feedback.

Anticipated Social Feedback (AT) Versus Unanticipated Social Feedback (UT) (H1)

Skin conductance responses. The LMER showed a main effect of *group*, $F(1,68) = 4.61$, $p = .04$, with smaller SCRs in the active ($M = -5.86$) versus sham tDCS group ($M = -5.32$). However, the effect of *group* was accounted by a *group* × *type* interaction (see figure 4A), $F(1,1044) = 4.32$, $p = .04$. Pairwise comparisons showed that during AT, SCRs were lower in the

active (*M* = -6.02) versus sham (*M* = -5.41) group, *b* = -.62, *SE* = .25, *t* = -2.46, *p* = .02, whereas during UT, the difference in SCRs between active and sham was marginally significant, *b* = -.45, *SE* = .25, *t* = -1.78, *p* = .08. Furthermore, SCRs were lower during AT (active *M* = -6.02, sham *M* = -5.41) compared to UT (active *M* = -5.69, sham *M* = -5.24), both for the active, *b* = -.34, *SE* = .06, *t* = -5.88, *p* < .001, and sham tDCS group, *b* = -.17, *SE* = .06, *t* = -2.94, *p* = .003. All remaining tDCS effects (i.e., *group* × *valence*, and *group* × *valence* × *type*) were non-significant (all *Fs* < 1.74, all *p*s > .18).

Pupillary responses. The LMER showed a *group* × *type* interaction (see figure 4B), *F*(1,1082.06) = 9.89, *p* = .002. Pairwise comparisons showed no difference between the active and sham group during AT, *b* = .01, SE = .02, *t* = .56, *p* =.58, or UT, *b* = .02, SE = .02, *t* = 1.01 , *p* = .31. Conversely, in the sham group, PD was smaller during AT (*M* = .05) versus UT (*M* = .10), *b* = -.04, SE = .01, *t* = -5.04, *p* < .001, whereas in the active group, there was no difference between AT and UT, *b* = -.005, SE = .01, *t* = -.61, *p* = .54. All remaining tDCS effects (i.e., *group*, *group* × *valence*, and *group* × *valence* × *type*) were non-significant (all *Fs* < .67, all *p*s > .41).

Anticipation of Social Feedback (C) Versus Reception of Anticipated Social Feedback (AT) (H2)

Skin conductance responses. The LMER indicated a main effect of *group* (see figure 5A), *F*(1,68) = 4.55, *p* = .04, showing smaller SCRs in the active (*M* = -5.94) versus sham tDCS group (*M* = -5.40). All remaining tDCS effects (i.e., *group* × *valence*, *group* × *phase*, and *group* × *valence* × *type*) were non-significant (all *Fs* < 2.60, all *p*s > .11).

Pupillary responses. The LMER showed a *group* × *phase* interaction (see figure 5B), $F(1,1075.46) = 11$, $p < .001$. Pairwise comparisons showed that during C, PD was smaller in the active ($M = .004$) versus sham ($M = .04$) tDCS group, $b = -.03$, SE = .02, $t = -2.02$, $p = .04$, whereas during AT, there was no difference between active or sham tDCS, $b = .01$, SE = .02, $t = .79$, $p = .43$. Furthermore, in the active group, PD was larger during AT ($M = .07$) compared to C ($M = .004$), whereas this difference was only marginally significant in the sham group, $b = -.02$, SE = .01, $t = -1.91$, $p = .06$. All remaining tDCS effects (i.e., *group*, *group* × *valence*, and *group* × *valence* × *type*) were non-significant (all $Fs < 1.49$, all $ps > .22$).

Relationship Between the Anticipation of Social Feedback (C) and the Reception of Anticipated Social Feedback (AT) (H3)

Skin conductance responses. The LMER showed no significant *group* × SCR during C interaction, $b = .06$, $SE = .03$, $t = 1.89$, $p = .06$.

Pupillary responses. The LMER showed a significant *group* × PD during C interaction (see figure 5), $b = -.11$, $SE = .04$, $t = -2.48$, $p = .02$. LMERs for each group separately showed that PD during C predicted PD during TA only in the active group, $b = -.29$, $SE = .07$, $t = -4.11$, $p < .001$, but not in the sham group, $b = -.06$, $SE = .05$, $t = -1.14$, $p = .25$. Specifically, in the active group, as a function of decreasing PD during C, PD during TA increased. See figure 6 for an overview of these results.

Discussion

The aim of the present study was to investigate, using tDCS, the causal role of the lDLPFC (and its associated neural network) on a) emotional responses (ERs) to anticipated versus unanticipated positive and negative social evaluations (H1), b) ERs during the

anticipation versus subsequent confrontation (H2), and c) the relationship between anticipatory and subsequent online ERs (H3).

First, comparing ERs to anticipated versus unanticipated social feedback (H1), active tDCS over the lDLPFC (compared to sham tDCS) was associated with a decrease in emotional arousal (i.e., decreased SCRs) during the confrontation with anticipated positive and negative social feedback, whereas this decrease was only marginally significant during unanticipated social feedback. Moreover, the pupillary analysis seems to suggest that active tDCS applied to the lDLPFC contributes to an equal allocation of cognitive resource between the confrontation with anticipated versus unanticipated social feedback, whereas by default (i.e., sham tDCS) less resources are consumed during anticipated social feedback. In other words, these results suggest that - when being confronted with anticipated social feedback - the lDLPFC contributes to a relative increased allocation of cognitive resources (see also next paragraph for more information). Taken together, these results partially support our hypothesis, suggesting that the lDLPFC is specifically involved in the modulation of ERs in anticipatory as compared to non-anticipatory (i.e., where one cannot anticipate) contexts (Schmid et al., 2015). Even though previous NIBS research suggested that the lDLPFC is also causally involved in the modulation of ERs within non-anticipatory contexts (e.g., Brunoni et al., 2013; Peña-Gómez et al., 2011; Remue et al., 2016), these studies lack a direct comparison between ERs in anticipatory versus non-anticipatory contexts.

Second (H2 and H3), within anticipatory contexts (i.e., trials with the anticipation of feedback and the subsequent confrontation), the SCR analysis suggests that tDCS over the lDLPFC (as compared to sham) contributed to a general decrease in emotional arousal, independent of whether one was anticipating or actually being confronted with anticipated

feedback. Furthermore, the pupillary analysis seems to suggest that active tDCS over lDLPFC (as compared to sham) contributed to a decreased allocation of cognitive resources during the anticipation of feedback, which in turn was associated with a relative increase of cognitive resources consumption when subsequently being confronted with this feedback. In fact, during active tDCS over the lDLPFC, the fewer resources were used during the anticipation of social feedback, the more resources were consumed during the subsequent confrontation with this feedback, whereas this dynamic was not present in the sham group. This finding was counter to our expectations, as we had expected active tDCS over the lDLPFC to increase cognitive resource allocation during the anticipation of feedback, subsequently leading to decreased resource allocation during the confrontation (De Raedt & Hooley, 2016). One potential explanation for the observed inverse effect could be that participants refrain from cognitively elaborating on information presented during the anticipation phase, and thereby save valuable cognitive resources for the moment when they are confronted with the feedback. Perhaps, this may reflect a more efficient allocation of cognitive resources due to tDCS (as compared to sham) and suggests a shift towards the use of cognitive resource specifically when being confronted with the actual emotional stimuli. The fact that, within these anticipatory contexts, active tDCS was associated with a general decrease in SCRs (i.e., less emotional arousal), suggests that this resource allocation shift (observed in pupillary analyses) was adaptive. Another explanation for the inverse effect would be that the effects may be dependent on the paradigm characteristics (De Raedt & Hooley, 2016). Taken together, these results partially corroborate the second and third hypothesis, and suggest that, within anticipatory emotional contexts, the lDLPFC is a) causally involved in the general reduction of emotional reactivity (i.e., emotional arousal), and b)

implicated in the interplay between anticipatory and online emotion regulatory processes (Seo et al., 2014; Wager et al., 2004).

Of importance, tDCS did not modulate self-reported mood responses to the social feedback. This is consistent with research showing, that among healthy individuals, NIBS over the DLPFC does not subjectively affect mood, but is able to influence emotional processing (Mondino, Thiffault, & Fecteau, 2015). Furthermore, valence was not implicated in the tDCS effects, suggesting that the lDLPFC is not associated with valence specific emotional processing. Previous research has produced mixed results regarding valence-independent versus valence-dependent emotional processing in the DLPFC (Mondino et al., 2015; Wager, Phan, Liberzon, & Taylor, 2003).

As for clinical implications, how individuals cope with social evaluations plays an important role in the onset and maintenance of depressive disorders (Slavich, O'Donovan, Epel, & Kemeny, 2010; Slavich, Thornton, Torres, Monroe, & Gotlib, 2009). Specifically, negative evaluations can trigger negative self-referent cognitions (i.e., I'm undesirable) and emotions (i.e., shame), which can contribute to depressive symptoms, when not employing appropriate adaptive emotion regulatory processes. Furthermore, inefficient and counterproductive allocation of cognitive resources has been suggested to be a hallmark of depression, in which valuable cognitive resources are deployed to repetitively process negative self-relevant cognitions and emotions, instead of allocating these to task-relevant or more adaptive emotion regulatory processes (Connolly et al., 2014; Gotlib & Joormann, 2010; Johnstone et al., 2007; Levens, Muhtadie, & Gotlib, 2009). In addition, maladaptive anticipatory emotional processes have been observed within depressed individuals (Peira, Pourtois, & Fredrikson, 2013; Vanderhasselt et al., 2014a), which may play a crucial role in mood and anxiety disorders (De Raedt & Hooley, 2016;

Scherpiet et al., 2014; Schmid et al., 2015). Interestingly, within depressed individuals, increasing activity in the lDLPFC using NIBS has been shown to alleviate depressive mood (Baeken, Brunelin, Duprat, & Vanderhasselt, 2016; Baeken & De Raedt, 2011; De Raedt, Vanderhasselt, & Baeken, 2015; Dedoncker et al., 2016). One potential mechanism through which these anti-depressant effects are achieved may be by improving anticipatory emotional processes (by increasing lDLPFC activity; De Raedt & Hooley, 2016), contributing to more efficient cognitive resource allocation and reduced emotional reactivity. However, this notion is speculative and further research is required to investigate this proposed mechanism of action.

Besides several strengths, such as the inclusion of an ecological valid paradigm that allows individuals to naturally respond to self-relevant stimuli, it must be noted that the present study has some limitations. First, a between-subject design was employed and psychophysiological responses to the paradigm were not measured before receiving either active or sham tDCS, thereby lacking a within-subject control condition. The absence of this condition may hinder stringent interpretation of the observed results. Despite this implication, a between-subject design was utilized to prevent habituation and desensitization to the paradigm due to repeated exposure that would be present in a pre-post design. Furthermore, no separate control session was present prior to the stimulation session, as participants could potentially be emotionally affected by the rigged social evaluations between both sessions when no debriefing is giving after the control session. Moreover, prior to the experiment, groups were matched on a series of trait variables that could influence responding to the paradigm, and a post-hoc analysis on baseline skin conductance levels showed no difference between groups, suggesting that baseline emotional arousal does not differ between groups. Furthermore, the LMER models estimate baseline individual responses to the paradigm via the inclusion of a random subject

intercept and takes these into account for the computation of the main and interaction effects. Taken together, these arguments satisfy our confidence in the group comparability. Second, the sample only consisted of females, limiting the generalizability of the findings. Third, tDCS is known to produce diffuse effects, resulting in not only the neuro-modulation of the targeted brain region but also of its underlying neural network and neighboring brain regions (Keeser et al., 2011; Stagg et al., 2009). For instance, the ventromedial prefrontal cortex (vmPFC; Motzkin, Philippi, Wolf, Baskaya, & Koenigs, 2014), ventrolateral prefrontal cortex (VLPFC; Seifert et al., 2013) and medial prefrontal cortex (mPFC; Ueda et al., 2003) are located near the DLPFC and have been implicated in anticipatory emotional processes. Moreover, these brain regions have shown inter-correlations with the DLPFC during the anticipation of emotional stimuli (Seifert et al., 2013). Therefore, in the current study, tDCS applied to the lDLPFC likely affected not only the DLPFC, but its associated neural network (e.g., VLPFC, vmPFC, mPFC). Future NIBS studies would benefit by including neuro-imaging methods, allowing to investigate how the neural network is specifically affected. Fourth, only mood was measured during the task as a self-report measure. As previous studies have shown that mood is typically unaffected by tDCS over the lDLPFC (Mondino et al., 2015), other self-report measures, such as perceived valence and arousal could have been measured instead (Feeser et al., 2014; Peña-Gómez et al., 2011). However, we wanted to retain the natural flow of the paradigm as much as possible, and refrain participants from being to pre-occupied with taxing self-report measures (e.g., perceived arousal) that could potentially disrupt the results. Therefore, we focused on unobtrusive psychophysiological measures, as these also prevent potential social desirability biases that may be present in self-report measures (Van de Mortel, 2008).

In conclusion, the results from the current study suggest that the lDLPFC (and its underlying neural network) is causally implicated in the modulation of emotional responses within anticipatory contexts featuring the anticipation of and confrontation with self-relevant emotional stimuli (e.g., social evaluations). Moreover, within these contexts, the results suggest that the lDLPFC is causally implicated in the interplay between anticipatory and online emotion regulatory processes.

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Figure 1. Social feedback paradigm

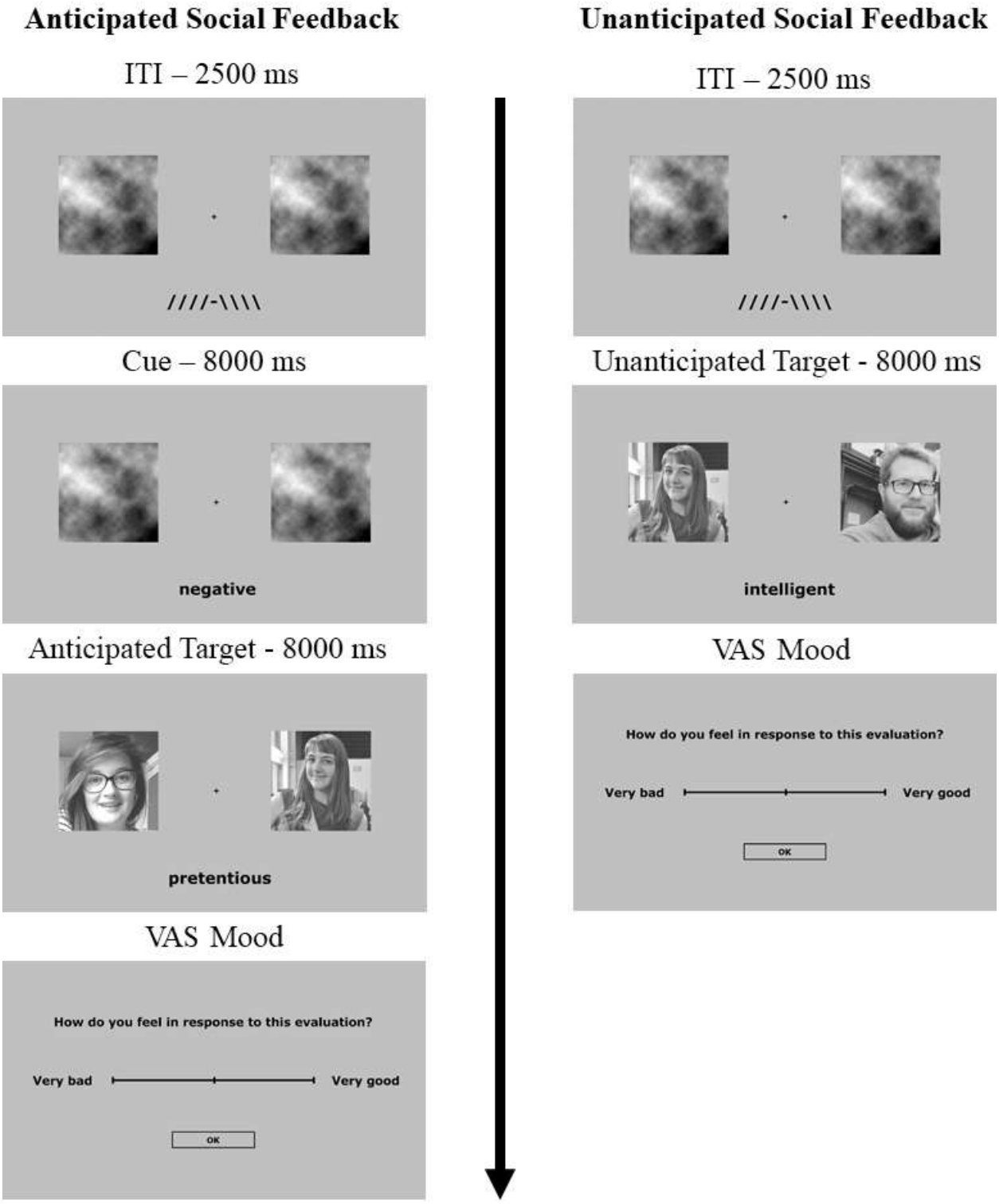


Figure 2. Electric field simulations of the tDCS montage.

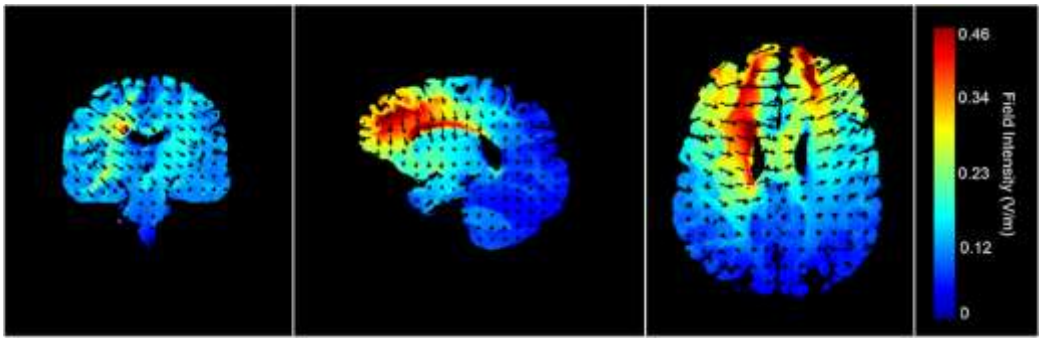


Figure 3. Experimental procedure

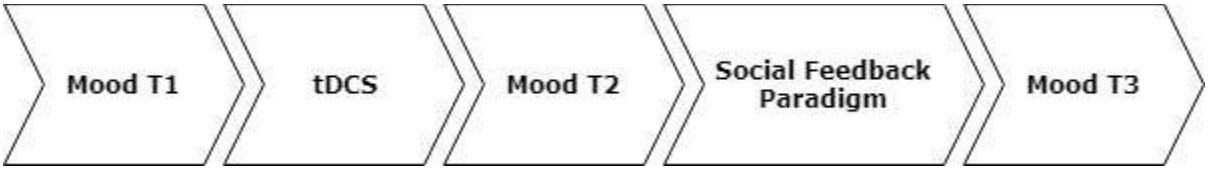
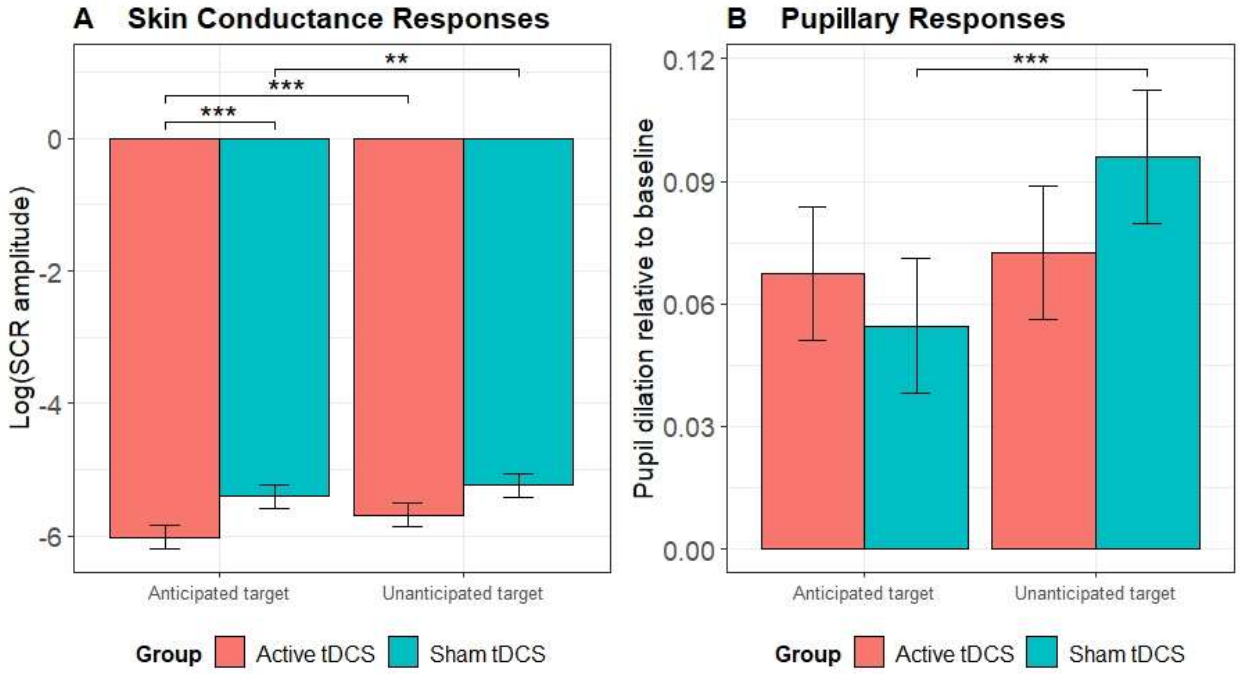
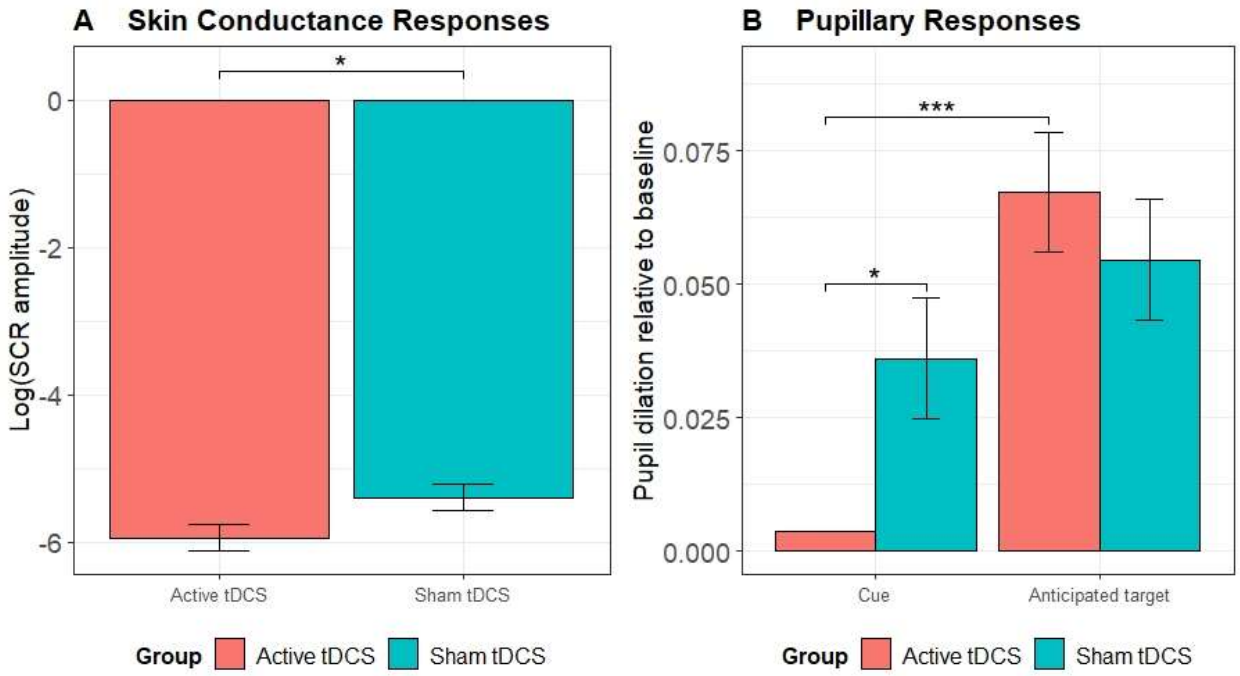


Figure 4. Anticipated target versus unanticipated target



Notes. Error bars reflect the standard error; *p < .05; ** p < .01; *** p < .001. Figure 4A shows that active tDCS over the left DLPFC (compared to sham tDCS) was associated with decreased SCRs during the confrontation with anticipated social feedback, whereas this effect was only marginally significant during the confrontation with unanticipated feedback. Figure 4B shows that active tDCS was associated with similar PD to the confrontation with anticipated and unanticipated feedback, whereas sham tDCS was associated with larger PD during the confrontation with unanticipated versus anticipated feedback.

Figure 5. Cue versus anticipated target



Notes. Error bars reflect the standard error; *p < .05; *** p < .001. Figure 5A shows that active tDCS over the left DLPFC (compared to sham tDCS) was associated with a general SCRs decrease, irrespective of whether one was anticipating or being confronted with anticipated social feedback. Figure 5B shows that active tDCS (compared to sham tDCS) was associated with smaller PD during the anticipation of feedback, but during the anticipated confrontation. Moreover, active tDCS was associated with larger PD during the anticipated confrontation versus anticipation, whereas during sham tDCS, this was not the case (marginally significant).

Figure 6. Relationship between pupillary responses during cue and anticipated target