Modulation of negative emotions through anodal tDCS over the right ventrolateral prefrontal cortex

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Abstract

Increasing evidence suggests that the right ventrolateral prefrontal cortex (rVLPFC) plays a critical role in the emotion regulation, in particular concerning negative feelings regulation. In the present research, we applied anodal tDCS over the rVLPFC with a twofold purpose. First, we aimed at exploring the feasibility of modulating the subjective experience of emotions through tDCS in healthy participants. Second, we wanted to assess which specific emotion can be regulated (and which cannot) with this brain stimulation approach. We designed a double-blind, between-subjects, sham-controlled study in which 96 participants watched short video clips eliciting different emotions during anodal or sham tDCS over the rVLPFC. Emotional reactions to each video clip were assessed with self-report scales measuring eight basic emotions. Results showed that, in contrast to the sham condition, tDCS over the rVLPFC reduced the perceived extent of specific negative emotions, namely, fear, anxiety, and sadness, compared to other negative or positive feelings. Overall, these results support the role of rVLPFC in regulating negative emotions, mostly associated with the prevention of dangerous situations (i.e., fear, anxiety, and sadness).

Keywords

Emotion regulation, Emotional processing, Negative emotions, tDCS, rVLPFC

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Introduction

Emotions drive our existence, arousing our attention (e.g., Vuilleumier, 2005), shaping our memories (see Christianson, 2014, for a review), guiding our choices (Bechara et al., 1999) and influencing our social interactions (Keltner & Kring, 1998). Psychological theories of emotions agree about the claim that between a stimulus, either internal or external and the elicited physiological reactions, cognitive appraisal, i.e. individual's perception and judgement about the stimulus significance, takes place (Arnold, 1960; Gross, 1998, 2015; Lazarus, 1966; Schachter & Singer, 1962). Therefore, people might emotionally react to certain events in different ways according to their individual assessment of the situation, concurrent mindset and preferences (Lazarus, 1991).

Emotion perception process can be segregated in three different stages: (1) detection of the salience of a stimulus and the attribution of a certain emotional significance, dependent upon a cognitive evaluation; (2) the consequent production of an affective state and an emotional behavior; and (3) regulation of the affective state (Phillips, 2003). Focusing on the latter stage, scholars linked the genesis and maintenance of many psychiatric and psychopathological diseases with failures in emotion regulation and specifically with the chronic incapacity to suppress negative emotions, which is in turn associated to structural and functional brain abnormalities (Blair et al., 2012; Brockmeyer et al., 2012; Glenn & Klonsky, 2009; Gross, 2002; Keltner & Kring, 1998; Svaldi et al., 2012; Zapf, 2002). Patients with major depression for instance, in comparison to healthy controls, show decreased activity in prefrontal areas and increased activations in the amygdala and anterior cingulate cortex, as well as a structural reduction of the frontal lobe, hippocampus, and basal ganglia grey matter volumes (Brody et al., 2001). Crucially, symptom worsening is accompanied by greater abnormalities and studies examining mood amelioration from pre- to post-treatment showed an improvement of the altered brain activity (Taylor & Liberzon, 2007).

Neural correlates of emotion processing

A great amount of research has considered the neural correlates of emotional processing, employing a variety of techniques and specific experimental paradigms, involving both animals and human subjects. Recently, neuroimaging studies focused in particular on the neural correlates of emotion regulation processes (Beauregard et al., 2001; Domes et al., 2010; Ochsner et al., 2002, 2004; Schulze et al., 2011; Urry et al., 2006; van Reekum et al., 2007; Wager et al., 2008).

Broadly, results converge in suggesting that regulatory processes functionally depend upon cortical-subcortical connections involving bilateral prefrontal cortices (PFC)—including the VLPFC and the dorsolateral prefrontal cortex (DLPFC); the pre-supplementary motor areas (pre-SMA), encompassing regions belonging to the limbic system, such as the amygdala, the anterior cortex and middle cingulate cortex (ACC and MCC); and the insula (see Ochsner & Gross, 2007; Quirk & Beer, 2006, for qualitative reviews; see Kalisch, 2009, for meta-analysis).

An influential model (Phillips 2003, Phillips et al., 2008) has focused on the distinction between voluntary and automatic processes, suggesting the role of a wide cortico-subcortical network, roughly composed by two main neural systems: one predominantly ventral and one predominantly dorsal. The dorsal system, including the hippocampus and dorsal regions of the anterior cingulate gyrus and prefrontal cortex, including its dorsolateral portion, is recruited for executive functions such as selective attention, planning, and effortful regulation of affective states and consequent behavior. Conversely, the ventral system includes the amygdala, insula, ventral striatum, the ACC, the orbitofrontal cortex and the ventral portions of the prefrontal cortex, namely, the VLPFC. This system plays a crucial role in the detection of the emotional valence of a stimulus in the production of an affective state and in the automatic regulation of emotional responses. The VLPFC seems to play a key function in emotion processing. This area lies lateral to the orbitofrontal cortex on the ventral surface of the frontal lobes and includes the rostral and lateral regions of Brodmann area 47 and part of Brodmann area 45 (Öngür & Price, 2000). Overall, the VLPFC is involved in various forms of cognitive control (Ridderinkhof et al., 2004), such as motor control (Chikazoe et al., 2009), task switching (Braver et al., 2003) and response inhibition (Aron et al., 2004; Bunge et al., 2002; Cai et al., 2015; Konishi et al., 1999; Rubia et al., 2003). Regarding emotion perception, several neuroimaging studies provided evidence of a selective role of this area in handling material with emotional content (Fink et al., 1996; Johnston et al., 2010; Pardo et al., 1993; Reiman et al., 1997; Shin et al., 2000). Moreover, abnormal activation of the VLPFC has been found in emotional disorders (Drevets et al., 1992; Lawrence et al., 2004; Phillips, 2003). In particular, there is evidence on a specific role of the right VLPFC (rVLPFC) in the regulation of negative emotions (Berkman & Lieberman, 2009; Cohen et al., 2012; Kim & Hamann, 2007; Lieberman, 2007; Ochsner & Gross, 2007; Phillips et al., 2008; Wager et al., 2008) and previous work from our group further supported this claim showing an effect of tDCS over this region in modulating negative emotions associated with exposure to social exclusion and violent media (Riva et al., 2012, 2015, 2017).

Previous research, however, did not disentangle whether its activity might be triggered by specific types of emotion. Unveiling a link between a brain area and a specific emotion subjective experience paves the way to the chance of improving the regulation of that specific emotion in the diseases where it is dysfunctional by means on non-invasive brain stimulation.

Accordingly, in the past decades, neuromodulatory techniques such as Transcranial Magnetic Stimulation (TMS) and Transcranial Direct Current Stimulation (tDCS) have emerged as adjuvant treatment of psychiatric and mood disorders with promising, though sometimes controversial, results (George et al., 2009; Lisanby et al., 2002; Nitsche et al., 2009).

Aim of the study

In the present study, we sought to explore whether modulating the activity of rVLPFC through the application of anodal tDCS can influence the subjective experience of emotions elicited by affectively relevant video clips and, if this was the case, whether this effect is specific to a certain type of emotion (e.g., sadness, anger). On the basis of previous literature, we expected that, compared to sham stimulation, anodal tDCS over the rVLPFC would prominently reduce the perceived intensity of negative emotions induced by the video clips. However, given the lack of previous research on this topic, we had no a priori hypothesis regarding which specific negative emotion could have been modulated by tDCS.

Materials and methods

Participants

Ninety-six right-handed (Oldfield, 1971) volunteers (73 female; *M* age = 23.6, range 19–50), students at the University of Milano-Bicocca, Italy, participated in the study. All participants met the inclusion criteria required for undergoing tDCS (Antal et al., 2017), were native Italian speakers and were naïve to the experimental procedure. The study was approved by the local ethical committee of the University of Milano-Bicocca, and subjects were treated in accordance with the Declaration of Helsinki.

Material

We exposed our participants to five different video clips eliciting five primary emotional clusters: three negative (anger, fear and sadness), a positive one, (happiness) and a neutral video. The video clips were selected from a validated sample of seventy emotion-eliciting film excerpts (Schaefer et al., 2010). For the purposes of the present study, we selected from the database five video clips that elicited the five abovementioned specific emotions to the greatest extent. For eliciting fear we chose an excerpt of “The Blair Witch Project” (by Daniel Myrick and Eduardo

Sanchez, 1999; excerpt duration 2’05”); for anger, an excerpt from “Schindler’s List” (by Steven Spielberg, 1993; duration 1’59”); for sadness, a scene extrapolated from “Dangerous Minds” (by John N. Smith, 1995; duration 2’09”); for happiness, an extract from “A Fish Called Wanda” (by Charles Chichton, 1998; duration 2’56”). Finally, we showed a neutral scene from “Three Colors: Blue” (video 3 in the database, by Krzysztof Kieślowski, 1993; duration 42 s).

Procedure

Participants were tested individually. After giving informed consent, participants received instructions about the experimental procedure and completed the Positive and Negative Affect Scales (PANAS) questionnaire, a 60-item self-report measure monitoring the affective state of the subjects (Watson et al., 1988). The PANAS includes positive (PA) and negative affect (NA) factors, with subjects rating the extent to which they feel a particular emotion on a 5-point scale. The scale was used to assess the presence of baseline emotional distress, which might affect the results. All subjects enrolled in the experiment had a score on the NA scale of 23.2 (SD 6.2), which is within one SD above the mean value of a reference population (Crawford & Henry, 2004).

Next, participants were randomly assigned to two groups in which real anodal (49 subjects, 35 females, *M*age 23.5) or sham (47 subjects, 38 females, *M*age 23.8) tDCS was applied over the rVLPFC. TDCS is a non-invasive neuromodulatory technique which influences the spontaneous firing rate of neurons in a polarity-dependent way: anodal tDCS depolarizes membrane potential, while cathodal tDCS hyperpolarizes it (Bindman et al., 1964, Purpura and McMurtry, 1965). tDCS mechanisms and the way in which the current spreads are not fully understood, but studies with healthy participants (e.g. Romero Lauro et al., 2014, 2015; Varoli et al., 2018), psychiatric and neurological patients (see for critical reviews George et al., 2009; Bolognini et al., 2011), computational models (e.g. Bikson et al., 2012), animal in vivo studies (Fritsch et al., 2010; Vöröslakos et al. 2018) and human cadaver brains (Vöröslakos et al. 2018) are trying to understand which stimulation parameters are able to influence brain activity and behavior, with the aim to better comprehend its promising results.

TDCS was delivered using a constant current stimulator (DC-Stimulator, NeuroConn GmbH, Germany) through two electrodes. To stimulate the rVLPFC the anode was placed over F6 (Montreal Neurological Institute coordinates: 58, 30, 8; Onoda et al., 2010), consistent with the international 10-20 system for electroencephalography (EEG) electrode placement. The cathode was placed over the contralateral supraorbital area. The anode was 25 cm², whereas the cathode was 35 cm², to increase the focality of the stimulation (Nitsche et al., 2008). A three-dimensional (3D) numerical computation of electric fields generated by tDCS according to the used montage, based on an MR-derived finite element model, was computed using Comets Matlab toolbox (Jung et al., 2013; freely available at http://www.COMETStool.com). As shown in Figure 1, the strongest electric field occurred in the area underneath the anode, which was our target region.

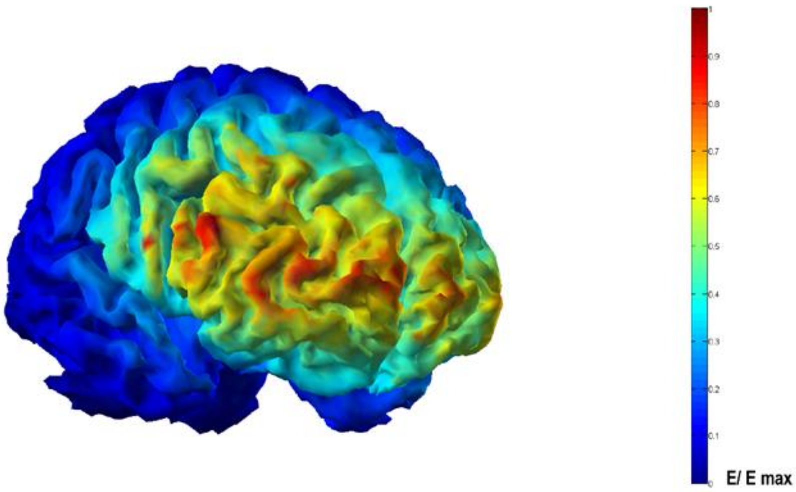

Figure 1. Computational model of tDCS-induced electric field. A simulation of the electrical field induced by the tDCS protocol used in the study was computed using Comets. The anode (25 cm2) was placed over the rVLPFC, corresponding to F6 electrode according to the 10-20 EEG system. The cathode (35 cm^2) was placed on the left sovraorbital area. Red colour indicates the strongest electrical field, occurring over the lateral and ventral portion of the right prefrontal cortex.

In the tDCS condition, a constant current of 1.5 mA intensity was applied for 20 minutes. In contrast, in the sham condition the stimulator turned off automatically after 30 s—a procedure that has been shown to be effective in blinding participants from their assigned condition (Ambrus et al., 2012; Gandiga et al., 2006; Woods et al., 2016). The tDCS device contained a study mode for double-blind trials (consisting of a preassigned numeric code, corresponding to either sham or anodal) that the experimenter entered to start the stimulation, thus being unaware of which stimulation condition followed.

Directly after the start of the tDCS protocol, participants sat comfortably in front of a computer screen and watched the five emotional videos. After each video clip participants completed a modified version of the Differential Emotional Scale (DES; Schaefer et al., 2010), to assess the emotions they felt while viewing the videos. The items of the DES consisted of emotional adjectives (e.g., happy, sad, surprised, angry) leading to nine emotional clusters: anger, happiness, anxiety, sadness, fear, disgust, interest, surprise, and warmth (see Figure 2 for the timeline of the experimental procedure). The cluster *interest*, however, was not included in the model as an emotional feeling since it is not an emotion but was scored separately as a manipulation check attesting that participants were paying attention to all the videos.

For each emotional cluster, participants were asked to rate three items on a Likert scale from 1 (“*Not at all*”) to 10 (“*Maximally intense*”) the extent to which they felt that emotional state while they were watching the video, leading to 27 items to rate for each video (see Supplemental Material for the item’s list). The order of the five videos was counterbalanced between subjects, and participants concluded the experimental procedure before the end of the stimulation.

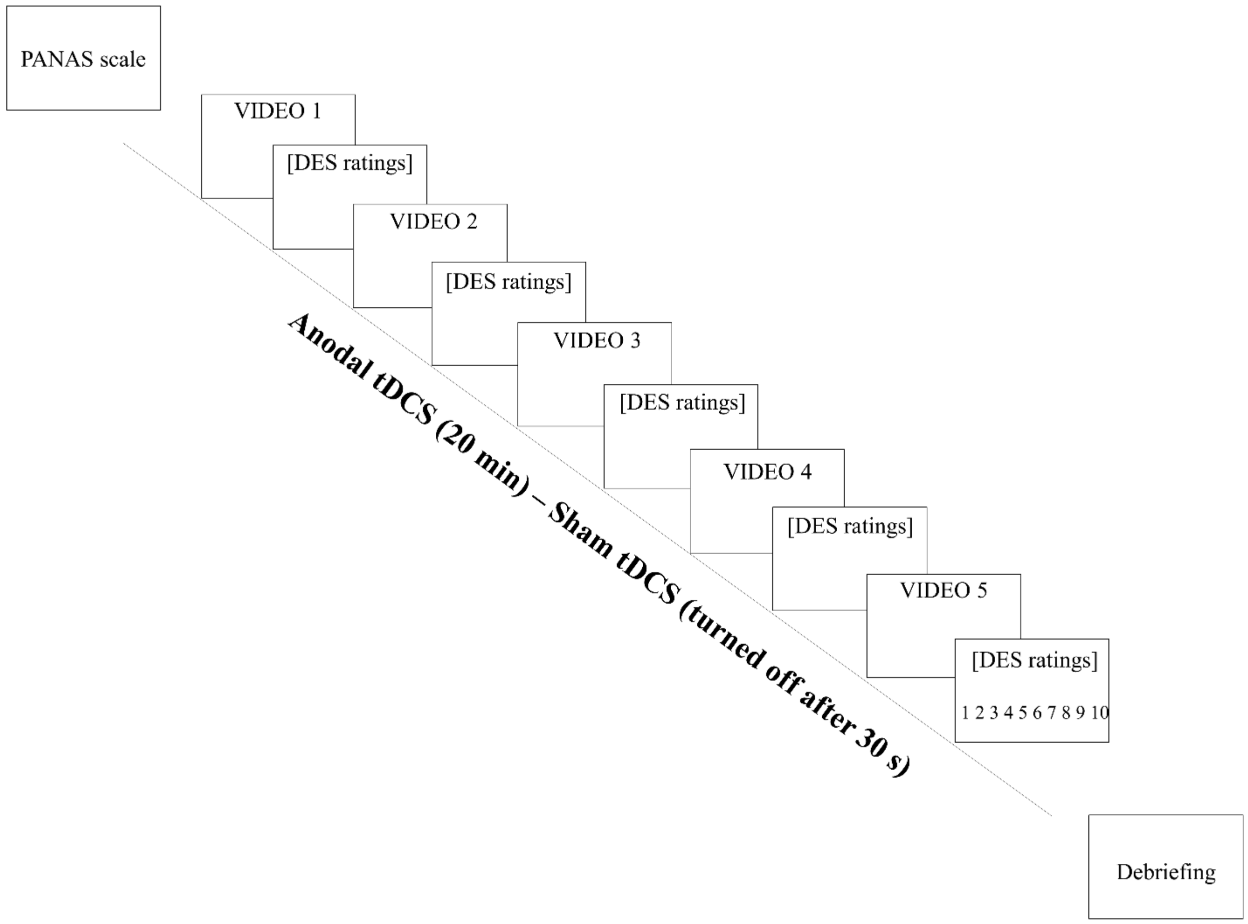

Figure 2. Timeline of the experimental procedure. First participants performed the PANAS questionnaire, followed by tDCS montage. Then tDCS was turned on at the same time participants started the experimental task. Participants saw 5 film excerpts (randomly presented), each one followed by a DES questionnaire, in which participants rated on a 10-point Likert scale to what extent they perceived a certain feeling while watching the video. A the end of the experiment, a debriefing on the experimental aims and procedures was delivered.

Design

The study employed a 2 (tDCS condition: sham vs. anodal) × 5 (video: Schindler's List, The Blair Witch Project, A Fish Called Wanda, Dangerous Minds and Three Colors: Blue) x 8 (emotional clusters: anger, happiness, anxiety, sadness, fear, disgust, surprise and warmth) mixed factorial design, with the first factor varying between-subjects and the other two factors varying within-subjects.

Data Analysis

Linear mixed models were performed as the main statistical procedure (Baayen et al., 2008) in R statistical environment (R core team, 2014) on emotional ratings, considered as a continuous dependent variable, using LMER procedure in “lme4” R package (version 1.1–5; Bates et al., 2014). The inclusion of fixed effects has been tested with a series of likelihood ratio tests, to evaluate whether their inclusion increased the model’s goodness of fit (Baayen et al., 2008; Gelman & Hill, 2006) using a forward stepwise inclusion method. With this procedure the tDCS condition (two levels: anodal vs sham), Video (five levels: Schindler’s List, The Blair Witch Project, A Fish Called Wanda, Dangerous Minds and Three Colors: Blue), and Emotional cluster (eight levels: anger, happiness, anxiety, sadness, fear, disgust, surprise and warmth), and their interactions were tested as fixed factors. The results of this procedure are summarized in Table 1.

Model Selection	**AIC**	**Chi2**	**p**
Emotional ratings ~ (1|Subject)	53931		
Emotional ratings ~ tDCS + (1|Subject)	53932	1.3	.25
Emotional ratings ~ tDCS + emotional cluster + (1|Subject)	53388	558.4	<.001
Emotional ratings ~ tDCS * emotional cluster + (1|Subject)	53393	8.4	.29
Emotional ratings ~ tDCS * emotional cluster + video + (1|Subject)	52001	1399.7	<.001
Emotional ratings ~ tDCS* emotional cluster + emotional cluster *video + tDCS*video+(1|Subject)	46953	5112	<.001
Emotional ratings ~ tDCS* emotional cluster *video+(1|Subject)	46984	25.1	.62

Table 1. **Model Selection.** Results of the LRT procedure used for model selection. Significant p values indicate main effects or interactions whose presence in the model significantly increases the goodness of fit.

Concerning the random effect structure, the by-subject intercept was included. We reported the parameters of the final best fitting model (Table 1), with significance levels based on Satterthwaite’s degrees of freedom approximation in the “lmerTest” R package (version 2.0–29, Kuznetsova et al., 2015). Post hoc comparisons were performed with the “phia” R package (Version

0.2-0; De Rosario-Martinez, 2015; freely available at http:\\CRAN.R-project.org/package=phia; Bonferroni-Holm correction applied).

Results

Preliminary Analysis

Intergroup variability

The two groups of participants were comparable for gender (X^2 = 1.17, *p* = .28) and age (*t*(94) = -.28, *p* = .21). PANAS scores were analyzed using a repeated measures ANOVA with PANAS scale (two levels: NA and PA) as within-subjects factor and tDCS group (two levels: anodal vs. sham) as between-subjects factors. Results showed a main effect of PANAS scale (*F*(1,94) = 87.9, *p* < .001, eta squared: .48) with greater scores in both groups for PA than NA. Importantly, the interaction tDCS group*PANAS scale was not significant (*F*(1,94) = .35, *p* = .85), indicating that the scores of the PANAS scales were not different in the two groups.

Stimulus sampling

As previously mentioned, the cluster Interest was considered separately as a manipulation check attesting whether participants were paying attention to all the videos. Mean values of this variable were high for all five videos (*M*Schindler's List = 7.44, *M*The Blair Witch Project = 7.06, *M*A A Fish Called Wanda = 6.38, *M*Three Colors: Blue = 5.64, *M*Dangerous Minds = 6.62). Post hoc analysis with Bonferroni correction showed that the interest score was significantly higher for Schindler's List (*p* < .001) compared to the other videos, except for The Blair Witch Project video (*p* = .245).

Physical sensation from electrodes

Similar to past research (Nitsche et al., 2008), we found that only a few participants (i.e., five of 96, or 5.2%) reported experiencing physical sensations from the electrodes. Importantly, a logistic regression showed that self-reported physical sensations did not vary across the two tDCS conditions (B = 1.41, SE = 1.14, Wald-Z = 1.53, p = .216)

Main Analyses

For full results of the final, best fitting, model see Table 1 (for results not reported in the main text see Supplementary materials). The final model included the main effects of tDCS, Emotional cluster and Video, as well as the tDCS by Emotional cluster, the tDCS by Video and the Video by Emotional cluster interactions. The main effect of tDCS was not significant ($\chi2(1) = 1.31$; p = .25). The main effects of Video ($\chi^2(4) = 2319.3$; $p < .001$) and Emotional cluster ($\chi^2(7) = 1008.3$; $p < .001$) were significant, as well as their interaction ($\chi^2(28) = 6401$; $p < .001$), suggesting that Emotional cluster were differently elicited by the various video clips. Post hoc comparisons on the Emotional cluster by Video interaction showed that more than a unique emotional dimension, each video rather induced a bunch of emotional clusters in a significantly more intense way, partially confirming their specific emotional valence (see Table 2).

Video

Emotional cluster	**Schindler's list**	**The Blair witch project**	**A fish called Wanda**	**Three colors: Blue**	**Dangerous Mind**
Anger	**6.04** (±2.87)	1.94 (±1.72)	1.4 (±1.02)	1.28 (±0.93)	1.99 (±1.69)
Happiness	1.28 (±0.75)	1.4 (±1.15)	**5.08** (±2.5)	1.95 (±1.53)	1.34 (±0.83)
Anxiety	4.79 (±2.81)	**6.53** (±2.82)	2.11 (±1.7)	**2.47** (±2.14)	**3.01** (±2.28)
Sadness	5.33 (±2.89)	2.26 (±1.89)	1.3 (±0.76)	1.48 (±1.16)	**4.67** (±2.8)
Fear	3.84 (±2.68)	**6.79** (±2.58)	1.27 (±0.64)	1.72 (±1.6)	1.8 (±1.41)
Disgust	**6.53** (±3.03)	2.83 (±2.47)	1.76 (±1.55)	1.18 (±0.74)	1.58 (±1.28)

Surprise	2.89 (±2.23)	3.05 (±2.26)	**4.89** (±2.72)	1.84 (±1.54)	2.12 (±1.7)
Warmth	1.68 (±1.54)	1.58 (±1.36)	3 (±2.19)	1.5 (±1.26)	1.74 (±1.51)

Table 2. **Emotional cluster *Video Interaction**. Average and SD emotional ratings for the five videos are reported. Within each video column, values in bold highlights the significantly highest scores.

In particular, the "Schindler's List" clip induced most of all anger (p<.001) and disgust (p<.001), but also elicited high values of anxiety and sadness, while "The Blair Witch Project" excerpt was associated with fear and anxiety more than other emotional clusters (p<.001). While looking at the video from "A Fish Called Wanda" participants felt instead positive emotions such as happiness (p<.001) and surprise (p<.001). For "Dangerous Minds," the top-rated emotional feelings were sadness (p<.001) and anxiety (p<.001), whereas in the video "Three colors: Blue" subjects reported overall less intense emotional ratings, mainly anxiety (p =.005; see Table s3 in supplementary material).

Importantly, the tDCS by Emotional cluster interaction was significant ($\chi^2(7) = 14.9$; p =.037; see Table 3).

tDCS condition

Emotional cluster	**Anodal**	**Sham**
Anger	2.51 (±2.54)	2.55 (±2.5)
Happiness	2.15 (±2.06)	2.27 (±2.11)
Anxiety	3.61 (±2.87)	3.96 (±2.93)
Sadness	2.86 (±2.65)	3.16 (±2.68)
Fear	2.92 (±2.77)	3.25 (±2.87)
Disgust	2.75 (±2.83)	2.8 (±2.75)
Surprise	2.94 (±2.5)	2.97 (±2.26)
Warmth	1.87 (±1.71)	1.93 (±1.67)

Table 3. Emotional cluster*tDCS interaction. Average and SD for emotional ratings are reported for the two different tDCS conditions.

The parameters of the interaction showed a differential effect of tDCS on the tested emotional clusters (see Figure 3). In particular, anodal tDCS compared to the sham condition reduced specific emotional clusters. In particular, anxiety ratings were significantly reduced as compared to anger (b = 3.12; t(11370) = 2.29; *p* = 0.02), surprise (b = 3.19; t(11370) = 2.34; *p* = 0.019), warmth (b = 2.87; t(11370) = 2.1; *p* = 0.035) and disgust (b = 3; t(11370) = 2.2; *p* = 0.027). Similarly, fear ratings were significantly reduced by anodal tDCS in comparison to anger (b = 2.9; t(11370) = 2.16; *p* = 0.03), surprise (b = 3.03; t(11370) = 2.2; *p* = 0.026), warmth (b = 2.7; t(11370) = 1.98; *p* = 0.047) and disgust (b = 2.84; t(11370) = 2.08; *p* = 0.037). Finally, sadness ratings tended to be lower after real tDCS in comparison to anger (b = 2.57; t(11370) = 1.89; *p* = 0.059), surprise (b = 2.65; t(11370) = 1.94; *p* = 0.052), disgust (b = 2.46; t(11370) = 1.8; *p* = 0.071) and warmth (b = 2.32; t(11370) = 1.7; *p* = 0.08).

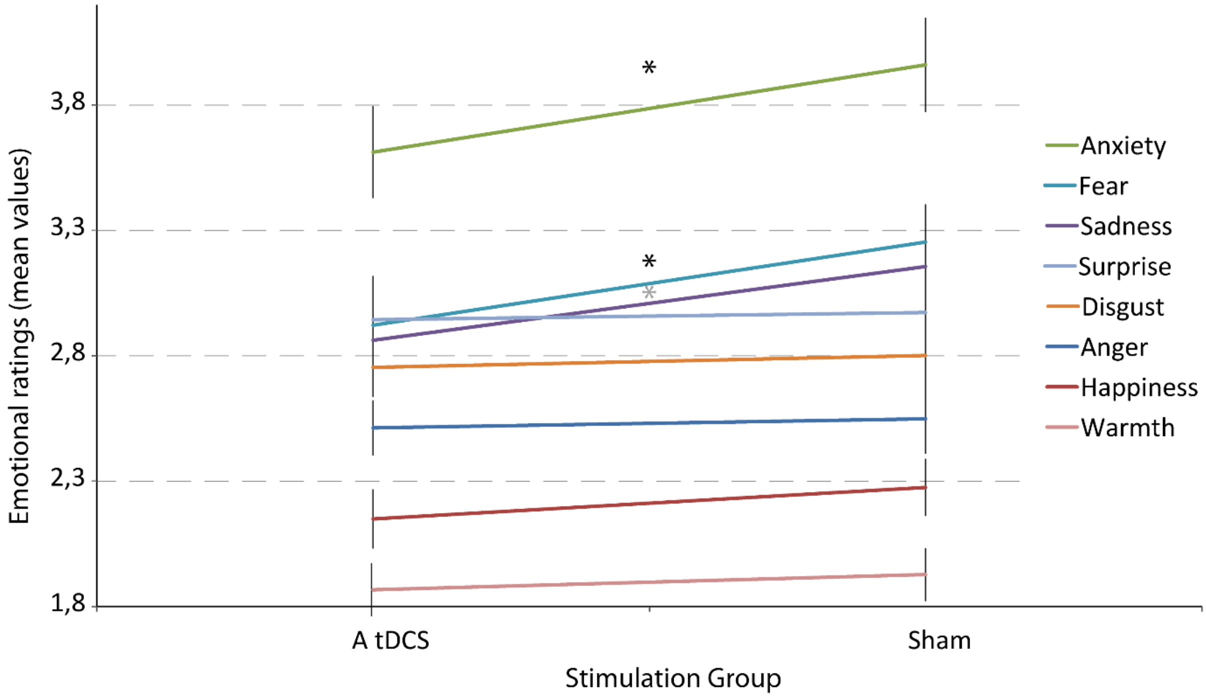

Figure 3. **TDCS* Emotional cluster Interaction.** Emotional rating mean values for anodal (A tDCS) and Sham groups are depicted. * indicates p<.05; * indicates a trend toward significance. The bars represent standard deviation.

Discussion

We performed a between-subject sham-controlled study to assess whether applying tDCS over the rVLPFC could modulate the subjective experience of specific emotions. Anodal tDCS successfully reduced the perceived extent of specific emotional dimensions, in particular, the ones with a negative valence. This suggests that rVLPFC is involved in emotion regulation and that this process can be externally modulated.

Our results are consistent with previous studies showing that the application of anodal or cathodal tDCS over rVLPFC affects hurt feelings and aggressive behavior elicited by social exclusion and violent video games (Riva et al., 2012, 2014, 2015, 2017). However, the present study suggests that tDCS effects over the rVLPFC are not limited to such contextual factors (e.g., social exclusion, violent media exposure) but broadly apply to a more general emotional experience domain. Considering together the results of the present study and those of past studies, there is evidence that tDCS can be effective in modulating negative emotions without an explicit request for doing so.

Effect of tDCS on specific emotions

The second aim of our study was to explore whether neuromodulation of rVLPFC generally influenced emotional processing or if the effect could be ascribed to specific types of emotion, going beyond the positive/negative valence segregation which is present in literature. Most of the research addressing brain stimulation's effects on emotion regulation, indeed, asked participants to rate the positive vs. negative emotional valence and/or the arousal elicited by picture presentation, without referring to specific emotions. To our knowledge, this is the first study in which the impact of non-invasive brain stimulation is assessed on more complex affective experiences, enabled by the use of evocative emotional video clips. Accordingly, several studies probed the effectiveness that videos can exert in eliciting strong, discrete physiological and emotional reactions (Baveye et al., 2013; Frazier et al., 2004; Gross & Levenson, 1995; Kolodyazhniy et al., 2011; Kreibig et al., 2007; Palomba et al., 2000). Our results indicate that across the five used video clips, anodal tDCS over the rVLPFC mainly affected only some of the negative valence emotions. Specifically, participants reported significantly lower levels of anxiety and fear and a trend toward significance for a reduction of sadness during anodal tDCS. These data are in line with a vast literature linking regions of the right hemisphere with negative emotions processing for both healthy subjects (Canli et al., 1998; Davidson, 1992) and neurological populations such as traumatic brain injury (Dal Monte et al., 2012), stroke (Salas et al., 2016), neurosurgical (Adolphs et al., 2001) and tumor patients (Mattavelli et al., 2017).

Concerning fear, studies on both animal (Baek et al., 2012; Quirk & Mueller, 2008) and human subjects (Guhn et al., 2012; Kalisch et al., 2006; Phelps et al., 2004) suggest that the right prefrontal cortex, in particular, the ventromedial portion, plays a crucial role in fear extinction learning. Accordingly, high-frequency rTMS over this region resulted in better extinction learning, as indicated by fear rating and skin conductance levels (SCL), in healthy subjects (Guhn et al., 2014) and patients with anxiety disorders (Herrmann et al., 2017). Moreover, in recent studies, anodal tDCS over the right prefrontal cortex successfully reduced sustained fear and SCL in a neutral-unpredictable threat paradigm (Herrmann et al., 2016) and improved reaction times on simple arithmetic decisions with decreasing cortisol concentrations (a biomarker of stress) in high mathematics-anxiety individuals (Sarkar et al., 2014).

As to anxiety, a growing body of evidence suggests promising though still preliminary results on the therapeutic effect of non-invasive brain stimulation over another hub of emotion regulation, namely the right DLPFC, on symptoms in patients with general anxiety disorder, such as PTSD panic disorder (Berlim & Van den Eynde, 2014; Bystritsky et al., 2008; Li et al., 2014; Shiozawa et al., 2014; Vennewald et al., 2013). However, it is noteworthy that in most studies the beneficial effects are induced by different stimulation paradigms, such as low-frequency rTMS and cathodal tDCS (known to decrease, rather than increase, cortical excitability).

Regarding sadness, Linden and coauthors (2012) tested the feasibility of a functional magnetic resonance imaging (fMRI) based neurofeedback approach to treat depressive patients resistant to standard pharmacological or psychotherapeutic approaches. The treatment entailed training the patients to regulate their brain activity through continuously updated signals on the activity level of a target area. Among target areas, the ability to upregulate the activity of bilateral VLPFC resulted in a greater symptom reduction. There is considerable evidence of tDCS effectiveness in treating patients with mild or moderate (Boggio et al., 2007, 2008; Fregni et al.,2006a, 2006b; Rigonatti et al., 2008) as well as severe, drug-resistant major depression (Ferrucci et al., 2009), but with the anode placed over the left DLPFC. Interestingly, in two of these studies (Boggio et al., 2007; Fregni et al., 2006b) tDCS over the left DLPFC led to an improvement in cognitive tasks execution, which did not correlate with mood amelioration. It is then plausible that the mechanisms underlying cognitive and mood improvement are independent. The rVLPFC could mediate mood regulation whereas the left DLPFC is involved in cognitive control, with both leading to a reduction in sadness or depressive symptoms.

Conversely, anger and disgust were not modulated by tDCS, despite being negative valenced emotions. In contrast to the valence theory of emotions classification, focusing on either positive or negative emotional valence, our results support a specific role of each emotion within the same valence type. Equally valenced emotions, such as sadness and anger, might indeed have different effects on decision-making (Lerner & Keltner, 2001; Nabi, 2003; Raghunathan & Pham, 1999), likelihood estimates (DeSteno et al., 2000; Keltner et al., 1993) and amount of processing (Bodenhausen et al., 1994; Nabi, 2002; Tiedens & Linton, 2001). Crucially, a distinction among negative emotions has been suggested according to the motivational system to which they belong (Carver & Harmon-Jones, 2009): anger pertains to an approach-related motivational system, whereas anxiety, fear and sadness pertain to an avoidance-related one. These two systems involve different neural substrates: specifically, the avoidance motivational system activates right anterior cerebral regions (Davidson, 1992, 1995; Nitschke et al., 2000), while the approach motivational system is lateralized to the left anterior cortex (Davidson & Fox, 1982; Fox & Davidson, 1986, 1988). Therefore, our results are in line with this distinction, suggesting that rVLPFC stimulation might have affected only the emotions belonging to the right-lateralized avoidance motivational system. Nevertheless, it must be noted that, for disgust, participants reported low scores for all videos, indicating that disgust was not strongly elicited by our experimental setting. Thus, it seems reasonable that tDCS could not further reduce the scores of this emotion. Only in Schindler's List (see Table 2 for mean scores) disgust received relatively higher scores.

Limitation of the study and future directions

A limitation of our experimental procedure concerns the low spatial resolution of tDCS. As shown in Figure 1, the tDCS-induced electrical field was stronger over the lateral and ventral surface of the PFC, but it was also approaching the DLPFC. This drawback prevents us from arguing for a *selective* role of rVLPFC in emotion regulation processes since it cannot be excluded that tDCS was also affecting the dorsolateral portion of PFC. However, this limit does not undermine the potentiality of our results, showing the feasibility of using tDCS over rVLPFC to modulate the subjective emotional experience and indicating the specific type of emotions that could be affected by such approach. In this sense, by proposing the rVLPFC as an effective target, our results could guide the refinement of non-invasive brain stimulation protocols as adjuvant approaches in the treatment of diseases characterized by an excessively intense experience of the emotions of fear, anxiety and sadness, such as Phobias, General Anxiety Disorder or Major Depression.

In conclusion, anodal tDCS over rVLPFC effectively reduced the perception of specific negative emotions, such as fear, anxiety and sadness regardless of their intensity and without instructing participants to carry out any emotion regulation strategy. Our results further confirm the involvement of the rVLPFC in emotion regulation and provide evidence of the possibility of using tDCS to modulate the subjective experience of these emotions.

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Supplemental Material

Italian version of the DES items used in the study

English	*Italian translation*
Interested, concentrated, alert*	interesse**, concentrato, attento
Fearful, scared, afraid	intimorito, spaventato, pauroso
Angry, irritated, mad	arrabbiato, irritato, infuriato
Warm hearted, gleeful, elated	caloroso, passionale, entusiasta
Joyful, amused, happy	gioioso, allegro, felice
Sad, downhearted, blue	triste, depresso, avvilito
Surprised, amazed, astonished	sorpreso, meraviglia**, stupore
Disgusted, turned off, repulsed	disgustato, nauseato, repulsione**

* The cluster interest was not included in analysis as an emotional cluster but was scored separately as a manipulation check attesting that participants were paying attention to the videos.

** In Italian these translations are nouns and not adjectives.

Table s1. **Video Main Effect**. Average and SD of the total emotional ratings are reported for each video

Table s1

		Average emotional ratings	SD emotional ratings
Video	Schindler's list	4.08	3.07
	The Blair witch project	3.3	2.91
	A fish called Wanda	2.6	2.32
	Three Colours: Blue	1.68	1.47
	Dangerous mind	2.28	2.05

Table s2. **Emotional cluster Main Effect**. Average and SD of the total emotional ratings for each Emotional cluster regardless of the Video

Table s2

		Average scores	SD scores
Emotional cluster	Anger	2.53	2.52
	Happiness	2.21	2.08
	Anxiety	3.78	2.9
	Sadness	3	2.67
	Fear	3.08	2.82
	Disgust	2.78	2.79
	Surprise	2.96	2.38
	Warmth	1.9	1.7

Table s3. **Post-hoc analysis of Video* Emotional cluster Interaction.** Results of post hoc comparisons with Holm correction among the emotional ratings for each emotional cluster, computed for each video, with the following order: A fish called Wanda, Schindler's list, The Blair witch project, Three Colours: Blue, Dangerous mind. * stands for $p \leq 0.5$;** stands for $p < .01$; *** stands for $p < .001$.

Table s3

		Anger	*Happiness*	*Anxiety*	*Sadness*	*Fear*	*Disgust*	*Surprise*	*Warmth*
A fish called Wanda	Anger	-							
	Happiness	***	-						
	Anxiety	***	***	-					
	Sadness	*ns*	***	***	-				
	Fear	*ns*	***	***	ns	-			
	Disgust	*ns*	***	*ns*	*ns*	*ns*	-		
	Surprise	***	*ns*	***	***	***	***	-	
	Warmth	***	***	***	***	***	***	***	-
Schindler's list	Anger	-							
	Happiness	***	-						
	Anxiety	***	***	-					
	Sadness	***	***	*	-				
	Fear	***	***	***	***	-			
	Disgust	*ns*	***	***	***	***	-		
	Surprise	***	***	***	***	***	***	-	
	Warmth	***	*ns*	***	***	***	***	***	-
The Blair witch project	Anger	-							
	Happiness	*	-						
	Anxiety	***	***	-					
	Sadness	*ns*	***	***	-				
	Fear	***	***	*ns*	***	-			
	Disgust	***	***	***	*	***	-		
	Surprise	***	***	***	***	***	*ns*	-	
	Warmth	*ns*	*ns*	***	**	***	***	***	-
Three Colours: Blue	Anger	-							
	Happiness	**	-						
	Anxiety	***	*ns*	-					
	Sadness	*ns*	*ns*	***	-				
	Fear	*ns*	*ns*	***	ns	-			
	Disgust	*ns*	***	***	*ns*	*	-		
	Surprise	*	*ns*	**	*ns*	*ns*	**	-	
	Warmth	*ns*	*ns*	***	*ns*	*ns*	*ns*	*ns*	-
Dangerous mind	Anger	-							
	Happiness	**	-						
	Anxiety	***	***	-					
	Sadness	***	***	***	-				
	Fear	*ns*	*ns*	***	***	-			
	Disgust	*ns*	*ns*	***	***	*ns*	-		
	Surprise	*ns*	***	***	***	*ns*	*ns*	-	
	Warmth	*ns*	*ns*	***	***	*ns*	*ns*	*ns*	-

tDCS*Video Interaction. The interaction between tDCS and movie showed that in *Schindler's list* video tDCS reduced the overall DES scores significantly more than in the other film excerpts: *The Blair witch project* (b=0.38; t(11370)=3.56; p<.001), *A fished called Wanda* (b=0.25; t(11370)=2.32; p=.02), *Three colours: blue* (b=0.39; t(11370)=3.65; p<.001) and *Dangerous mind* (b=0.33; t(11370)=3.05; p=.002).