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RESEARCH ARTICLE

Dissociating the role of dACC and dlPFC for emotion appraisal and mood regulation using cathodal tDCS

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Abstract

Several neuroimaging studies have shown that a distributed network of brain regions is involved in our ability to appraise the emotions we experience in daily life. In particular, scholars suggested that the dorsal anterior cingulate cortex (dACC) may play a role in the appraisal of emotional stimuli together with subcortical regions, especially when stimuli are negatively valenced, and the dorsolateral prefrontal cortex (dlPFC) may play a role in regulating emotions. However, proofs of the causal role of these regions are lacking. In the present study, we aim at testing this model by stimulating both the dACC and the left dlPFC via cathodal tDCS. Twenty-four participants were asked to attend and rate the arousal and valence of negative and neutral emotional stimuli (pictures and words) in three different experimental sessions: cathodal stimulation of dACC, left dlPFC, or sham. In addition to the experimental task, the baseline affective state was measured before and after the stimulation to further assess the effect of stimulation over the baseline affective state after the experimental session. Results showed that cathodal stimulation of dACC, but not the left dlPFC, was associated with reduced arousal ratings of emotional stimuli, both compared with the sham condition. Moreover, cathodal stimulation of left dlPFC decreased participant's positive affective state after the session. These findings suggest for the first time, a dissociation between the dACC and dlPFC, with the former more involved in emotion appraisal, and the latter more involved in mood modulation.

Keywords Emotion · Emotion Regulation · Mood · tDCS · Neurostimulation

Introduction

Individuals tend to react differently to harmful or stressful situations. The way that they react has important consequences on both their mental and physical health (Berking & Wupperman, 2012; Dadomo et al., 2018; Frederickson et al., 2018; Grecucci et al., 2017, 2019, 2020; Gross & Muñoz, 1995; Kok et al., 2013; Pappaianni et al., 2020). Hence, emotional appraisal—the evaluations of events and situations—and emotion regulation, which is the ability to implement strategies to modulate the appraisal of an emotion (Frederickson et al., 2018; Grecucci et al., 2020; Gross, 2015), might play a crucial role in human well-being (Dadomo et al., 2016; DeSteno et al., 2013; Messina et al., 2021: Sulpizio et al., 2021). The neural correlate of stimulus appraisal is thought to recruit a ventromedial and a dorsal system including prefrontal areas, such as the dorsomedial prefrontal cortex (dmPFC) and the dorsal anterior cingulate cortex (dACC)(Ochsner & Gross, 2005; Phillips et al., 2008), that make sense of the affective response generated by subcortical regions, such as the amygdala, the ventral striatum, and the insula (Grecucci et al., 2013a, b, 2020; Ochsner & Gross, 2005; Phillips et al., 2008).

The dACC has indeed been associated with the appraisal of emotions, especially when negatively valenced (Etkin et al., 2011). When individuals are exposed to fear inducing stimuli, the dACC activation positively correlates with physiological measures of arousal, such as skin-conductance(Milad et al., 2007) and heart rate (Wager et al., 2009). Neuropsychological

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studies on individuals undergoing cingulotomy (i.e., surgical lesion of dACC to treat chronic pain or psychiatric conditions) showed that these patients, together with a reduction of pain symptoms, reported a reduction of anxiety and rumination (Cohen et al., 2001). In addition, transcranial direct current stimulation (tDCS) applied to the dACC (Sençο et al., 2015) to treat obsessive-compulsivedisorder—a condition characterized by high level of anxiety and impaired emotion regulation abilities (Berking & Wupperman, 2012; Taylor & Liberzon, 2007)—showed a 30% reduction of patient's symptom severity when the stimulation was cathodal (inhibitory) and a worsening of symptom severity when it was anodal (inducing activation) (D'Urso et al., 2016b). Besides its role in tracking fear and anxiety, the dACC activation also was found in association with other negative emotions, such as disgust (Benuzzi et al., 2008; Mataix-Cols et al., 2008), anger (Dougherty et al., 1999), rejection (Eisenberger et al., 2003), and pain perception (Lamm et al., 2011).

However, it is worth noting that the role of dACC in emotional processing also might include emotion regulation (Bush et al., 2000; Shenhav et al., 2013). Indeed, meta-analyses on studies of functional neuroimaging studies investigating neural substrates of emotion regulation showed a consistent activation of dACC, together with other dorso- and ventrolateral prefrontal areas (dlPFC and vlPFC), presupplementary motor area (pre-SMA), inferior frontal gyrus/anterior insula and superior parietal lobule (Buhle et al., 2014; Kohn et al., 2014). In addition, dACC volume positively correlates with the ability to regulate emotions (Giuliani et al., 2011). The activation of dACC during the implementation of emotion regulation strategies might index its role in controlling emotions through inhibition of the ventral system (Delgado et al., 2008; Phillips et al., 2008). Indeed, the damage of dACC leads to patients' impaired inhibition abilities (Cohen et al., 1999; Floden & Stuss, 2006; Ochsner et al., 2001). A plethora of studies tested for the abilities of participants to regulate emotions through a specific strategy, such as reappraisal, and found increased activity of the dACC (Buhle et al., 2014). Hence, the activation of dACC may play a role in both appraisal and reappraisal, by integrating emotional information necessary for updating the meaning of a stimulus.

In addition to the dACC, the dlPFC was found to be involved in emotion appraisal (Boggio et al., 2009; Nejati et al., 2021). Indeed, two neurostimulation studies reported that the anodal tDCS on the left dlPFC induced the modulation of valence ratings of emotional stimuli (Boggio et al., 2009; Nejati et al., 2021). Specifically, Boggio and collaborators (2009) found that the anodal tDCS on the left dlPFC was associated with increased valence ratings of negatively valenced pictures compared with a sham condition. Another study showed that the same stimulation protocol was associated with a significant reduction of participants' valence ratings of positively valenced stimuli than a sham condition. These findings suggest that left dlPFC might also have a role in emotional appraisal, not being only involved in emotion regulation, as reported by several studies (Buhle et al., 2014; Diekhof et al., 2011; Grecucci et al., 2013a, b; Kalisch, 2009; Kohn et al., 2014). However, it also should be taken into account that the role of dlPFC in affective processing is much more complex, involving mood regulation (Palmiero & Piccardi, 2017). It is a well-established finding that the hypoactivation of left dlPFC is a marker of depression (Palmiero & Piccardi, 2017). In addition, anodal stimulation of the same area was found effective in treating major depression disorder than sham stimulation (Moffa et al., 2020; Razza et al. 2020). Hence, the effect of dlPFC stimulation on mood could influence participants' valence ratings.

In the present study, we tried to disambiguate the role of dACC and dlPFC during the appraisal of emotional stimuli. Notably, because the type of emotional stimuli might recruit different brain areas behind the sensory modality involved (Flaisch et al., 2015; Grecucci et al., 2020; Kensinger & Schacter, 2006; Sulpizio et al., 2021), we also decided to manipulate the format of stimuli, by including emotional and neutral words, beside emotional and neutral pictures. We tested a sample of healthy individuals using cathodal transcranial direct current stimulation (tDCS) on either dACC, left dlPFC, or a sham condition, during the execution of an emotional rating task. Specifically, participants were asked to rate arousal and valence of pictures and words while stimulation was applied. Hence, we are able to discriminate whether dACC might influence stimuli appraisal that are limited to a specific format or not. Several reasons motivated our decision of adopting only the cathodal polarity of stimulation. First, cathodal stimulation studies are less represented in the literature than those using anodal stimulation (Friehs & Frings, 2019), possibly because cathodal stimulation was associated to a lower probability of finding inhibitory effects on cognitive functions (i.e., 48%) than that of anodal stimulation of generating excitatory effects on cognitive functions (i.e., 81%) (Jacobson et al., 2012). Second, previous tDCS studies on emotional appraisal only used anodal stimulation (Boggio et al., 2009; Nejati et al., 2021), and not the cathodal one. Third, the effects of cathodal stimulation, which is usually inhibitory, might be more easily comparable with findings from lesion studies in patients.

Based on previous findings, we predict that if dACC is involved in appraisal of negative emotions (Buhle et al., 2014; Diekhof et al., 2011; Kalisch, 2009; Kohn et al., 2014) we should observe a reduction of emotional ratings associated with the negative stimuli presented during cathodal stimulation. Conversely, if the dACC is not involved in processing emotional appraisal, its stimulation should not induce any variation of participants' ratings compared with sham stimulation. In addition, we predict dlPFC stimulation to not affect the emotional ratings of participants, because this region is mainly involved in emotion regulation (Braunstein et al., 2017), a process not directly considered in our study, and not in emotional appraisal. Alternatively, if the dlPFC plays a role also for emotion appraisal, we may find a reduction of valence ratings for negatively valenced stimuli compared to the sham condition. Moreover, if it is true that dlPFC might exert a role in mood processing, and its left-lateralized hypoactivation is associated with depression (Mondino et al., 2015), we predict that its inhibition (through cathodal stimulation) might decrease positive mood. Additionally, in case both dACC and left dlPFC but not sham, will induce modulation of participants' emotional rating with the same direction, the effect could be attributable to a general stimulation effect. Hence, the active stimulation of two brain areas was important to provide evidence to rule out such a generalized stimulation effect and to find possible dissociations between the two areas considered.

Material and methods

Participants

To obtain a fully counterbalanced design and based on previous tDCS studies using similar paradigms to the present study (Pena-Gomez et al., 2011; Pripfl & Lamm, 2015; Schroeder et al. 2015), we set the sample size to 24 individuals. A total number of 24 right-handed participants (14 females) aged between 19 and 30 (mean age = 23.11, SD = 3.78) took part in the study. However, the analyses were performed only on the data of 22 participants, because 2 participants (i.e., participant #6 and participant #19) were not blind to the stimulation protocol. Exclusion criteria were the presence of neurological (e.g., migraine, epilepsy), psychiatric or cardiological disease, pregnancy or metallic implants on the head. Before starting the experiment, participants signed the informed consent. The study protocol complied the Declaration of Helsinki and was approved by the ethical committee of the SISSA (International School for Advanced Studies) (Trieste, Italy).

Stimulation procedure

For the stimulation procedure we used a battery-driven direct current stimulator (Magstim neuro Conn DC stimulator, https://www.neurocaregroup.com/dc_stimulator.html, neuroCare GroupGmbH, Munich, Germany) connected to two electrodes (anodal electrode surface = 6.5 x 9.5 cm^2; cathodal electrode surface = 5.0 x 4.5 cm^2) inserted in two sponges dipped in saline solution. To enhance conductivity, an electro-conductive gel was placed between the electrodes/sponges and the skin, as done in previous studies (Fertonani et al., 2015; Grasso et al., 2020; Vecchio et al., 2016). This allowed to avoid interposition of air between electrode and skin, improving scalp contact and reducing the impedance (Fertonani et al., 2015). Participants were stimulated in three different sessions during the execution of an experimental task, with an interval of more than 24 hours between each session (mean interval between session 1 and 2 = 4.13 days ± 2.63; mean interval between session 2 and 3 = 3.46 days ± 3.51). No difference in the interval (in days) between sessions 1 and 2 and sessions 2 and 3 emerged ($t(21) = 0.71$, $p > 0.05$). The three sessions included the cathodal stimulation of the dACC, the left DLPFC and sham, as a control condition. The electrode on the dACC was located at a distance of 15% of the nasion-inion length, anteriorly from the vertex on the midline (D'Urso et al., 2016). The electrode stimulating left DLPFC was placed over F3 following the International EEG 10-20 system (at 20% of the nasion-inion distance, anteriorly to the vertex, and 20% of the distance between the two tragi, on the left from midlineThe anode was placed over the upper part of the right arm, in any of the three stimulation conditions. During the stimulation a current of 1.5 mA was delivered for a maximum time of 20 minutes. A previous study simulating the electric field on our montage over the dACC showed that it is effective in targeting the dACC (Sençο et al., 2015). However, it must be acknowledged that the functioning of other areas might be influenced by this stimulation montage, as anterior basal ganglia. The other montage adopted in this study (i.e., cathode positioned over left dlPFC and anode on the right arm) was found to be effective in a study simulating electric field distribution (Im et al., 2012).

The sham condition was characterized by an initial period of active stimulation lasting 30 seconds after which the engine turned off as in previous studies (Mengotti et al., 2018; Osimo et al., 2019). In the sham sessions, the cathode electrode was placed over the left dlPFC in 50% of the sample, and on dACC on the remaining 50% of the sample. The anode was always placed on the right arm. The different site of application of the electrodes did not give rise to any difference in the arousal and valence ratings (all *ps* > 0.05) (see supplementary materials 1). The order of the stimulation condition was counterbalanced across participants. While the experimenters were not blind to the stimulation session, participants were not informed about whether the stimulation was real or a sham stimulation. At the beginning of each session, participants were asked to wait for 2 minutes to get used to the stimulation.

Stimuli

Stimuli included emotional words and pictures. Words were selected from the Italian version of the Affective Norms for English Words (ANEW) database (Montefinese et al., 2014) and included three sets of neutral and three sets of negative words (Table 1), which were used in the three experimental sessions. All sets, which included 13 stimuli each, were matched for letter length, written frequency, familiarity,

Table 1 Note: This data is mandatory. Please provide

Session		Valence				Arousal			
		Negative		Neutral		Negative		Neutral	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
1	Pictures	2.17	0.40	4.97	0.20	6.44	0.41	3.03	0.53
	Words	2.48	0.66	5.27	0.68	6.10	0.84	5.07	0.55
2	Pictures	2.12	0.45	4.97	0.21	6.41	0.48	3.34	0.41
	Words	2.59	0.59	4.95	0.55	6.34	0.67	5.17	0.61
3	Pictures	2.23	0.38	4.98	0.21	6.42	0.55	3.18	0.53
	Words	2.40	0.48	4.92	0.57	6.08	0.75	5.06	0.52

Note. Average valence and arousal ratings of the normative sample for each stimulus set.

imageability, and the number of orthographic neighbours (all *p*s > 0.05). Neutral and negative sets differed significantly in valence and arousal, with negative sets being more negative and arousing than the neutrals (all *p*s < 0.05). In addition, the negative sets, as well as the neutral ones, were matched on both arousal and valence (all *p*s > 0.05). Pictorial stimuli were selected from the International Affective Picture System (IAPS) database (Lang, 2005) and also included three sets of neutral (N = 13 for each set) and three sets of negative stimuli (N = 13 for each set) (Table 1). Neutral and negative pictorial sets differed for valence and arousal, with negative stimuli showing lower valence and higher arousal than neutrals (all *p*s < 0.05). The three neutral sets did not differ on these two variables, nor did the negative sets (all *p*s > 0.05). The comparisons of valence and arousal among pictorial and word stimuli sets showed that, even among different formats of stimuli (e.g., neutral picture set vs. negative word set), neutral sets were associated with higher valence and lower arousal than the negatives (all *p*s < 0.05). However, it is worth noting that neutral word sets were always associated with higher arousal ratings than neutral pictures (all *p*s < 0.05); no difference was present in the valence scores among neutral and negative sets (all *p*s > 0.05) in the two formats. In addition, the negative word set used in session 2 was associated with higher valence scores than the negative picture set used in the same session ($p = 0.03$) and in session 1 ($p = 0.05$).

Experimental task

The experimental task was presented using the software "E-prime 2.0" (version 2.0.10.261, https://pstnet.com/) on a computer placed approximately 50 cm from the subject. The beginning of each trial consisted in the presentation of a fixation cross for 2,000 ms (Figure 1). Then, the stimulus was presented for 1,000 ms. After the stimulus offset, participants had to rate 1) the valence (1 to 9 Likert scale: 1 "unpleasant" and 9 "pleasant"), and 2) the arousal of the stimuli (1 to 9 Likert scale: 1 "not intense" and 9 "extremely intense"). Hence, the valence rating scale ranged from 1, indicating negative valence (i.e., high levels of negativity), to 9, indicating positive valence (i.e., low levels of negativity). Five indicated neutral valence, whereas arousal rating scale ranged from 1—low arousal to 9—high arousal.

Participants were allowed to respond without any time limit. Stimuli were presented in two blocks: one for pictures and one for words, whose order was randomised across participants. In each block, a total amount of 26 items were displayed and stimuli presentation was in random order. Before starting the first stimulation session, participants performed a short practice block to become familiar with the experimental task.

Cognitive tests

The effect of stimulation on the experimental task might reflect the effect on cognitive functions. Indeed, it might be plausible that the disruption of inhibitory or attentional processes has an effect on both valence and arousal ratings. To take into consideration the effect of cognitive functions on emotional ratings, participants were tested on two cognitive tests after performing the experimental task. Specifically, we tested inhibition (Stroop test, Comalli Jr et al., 1962), attention (Trail Making Test part A - TMT-A), and switching abilities (Trail Making Test part B (TMT-B, Corrigan & Hinkeldey, 1987). The Stroop test is characterized by three steps: the first consists of asking participants to read colour names (printed with black ink); the second part consists of naming colours; and the third part involves naming the ink colour of words that are incongruent with respect to their meanings (e.g., "red" is printed with green ink) (interference). The Stroop score was calculated subtracting the average time of the reading and colour naming tasks to the interference task. The TMT consists in connecting printed items in consecutive order, as fast as possible, without detaching the pen from the paper. In TMT–A, participants had to joint progressively only numbers. In TMT–B, they were asked to alternate numbers and alphabet letters. Two scores were used: TMT–A (i.e., time to perform the test) and TMT-AB (i.e., difference between TMT–B and TMT–A execution time).

Questionnaires

Because participants' performance might be influenced by their own affective state and because stimulation might affect participants' affective state, we decided to include in the protocol the positive and negative affect scale (PANAS, Crawford & Henry, 2004). This questionnaire, which provides one index of positive and one index of negative affective state, was administered before and after each stimulation session. In addition, after each experimental session, participants

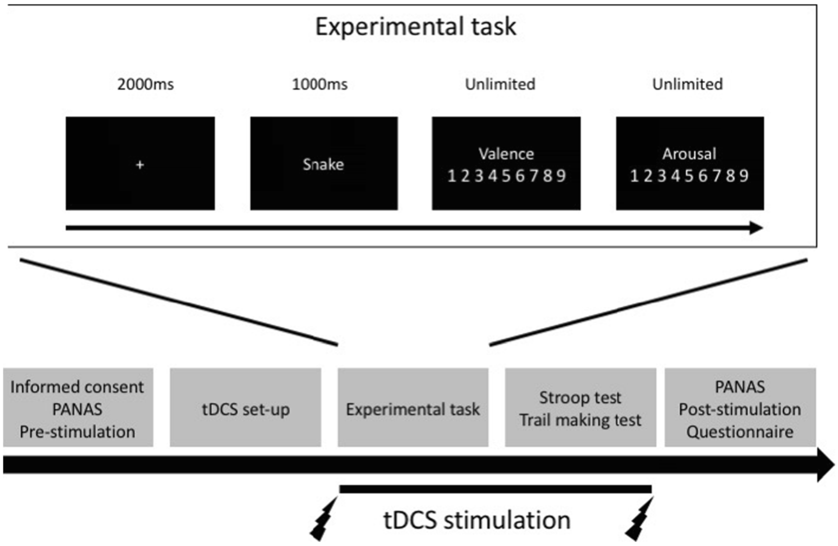

Fig. 1 Timeline of the experiment

were asked to complete a questionnaire, concerning side effects related to the stimulation, rating the intensity of six common side effect (burning sensation, heat, irritating itching (in Italian: pizzicore), itching, metallic taste, pain, weariness) on a scale from 0 to 3 (0 = not at all, 1 = mild, 2 = moderate, 3 = severe) and a question to check their blindness to the stimulation procedure (i.e., question: "Do you think that the stimulation was real?"; response options: 0 = yes, 1 = not sure, 2 = no).

Statistical analysis

We performed our analyses (see Table S1 in the supplementary materials) using a linear mixed-effect models implemented in the software "R" (version: 3.5.1, https://www.r-project.org/) through the function *lmer* implemented in the package lme4 (https://cran.r-project.org/web/packages/lme4/).

To account for subject- and item-specific variability, each subject and each stimuli item were set as random factors, except for the analyses on cognitive tasks, in which we could only include the subjects as random factors. Analyses on arousal and valence ratings were performed through two different models including the stimulation condition (dACC, left dlPFC, sham), the stimuli format (pictures, words), the stimuli valence (neutral, negative) as fixed factors, and their interactions and the session (1, 2, 3) as covariate. The analyses of the different cognitive functions scores included only the stimulation conditions and the session as fixed factors. The analyses on participants' affective state (PANAS) were conducted by including in the model the stimulation condition, the valence of the stimuli (positive, negative), and the moment of administration of the questionnaire (prestimulation, poststimulation), and their interactions as fixed-effects terms. In addition, the session was included as covariate and subjects and stimuli as random factors. Post-hoc tests were obtained using the function "emmeans" (https://cran.r-project.org/web/packages/emmeans/) and were corrected using the Bonferroni correction for multiple comparisons. Because data from the post-tDCS questionnaire were not normally distributed, we used the software Jamovi (version 0.9.5.12, https://www.jamovi.org/) to perform Friedman test to compare ratings across the three stimulation conditions and the Durbin-Conover test (Pohlert, 2018) to perform multiple comparisons. Effect size was calculated by using the R package *effectsize* (https://cran.r-project.org/web/packages/effectsize/index.html) through the function *F_to_Eta2*.

Results

Rating task

The analysis on arousal ratings (Table 2; Figure 2a) revealed a significant main effect of stimulation condition ($F(2, 3256.4.0) = 8.79$, $p < 0.001$, $\eta^2 = 0.005$, CI 0.00–0.01), with dACC stimulation producing significantly lower arousal ratings than both left dlPFC (dACC vs. left dlPFC: $p < 0.001$) and sham conditions (dACC vs. sham: $p = 0.03$). No difference in arousal ratings was evident between sham and left dlPFC stimulation conditions ($p > 0.05$). Moreover, the analysis showed significant main effects of valence ($F(1, 155.1) = 442.96$, $p < 0.001$, $\eta^2 = 0.74$, CI 0.69–0.78), and format ($F(1, 155.1) = 17.67$, $p < 0.001$, $\eta^2 = 0.10$, CI 0.04–0.18) and a significant interaction of valence and format ($F(1, 155.1) = 73.49$, $p < 0.001$, $\eta^2 = 0.32$, CI 0.23–0.41). While negative pictorial stimuli were associated with higher arousal ratings than negative word stimuli ($p < 0.001$), neutral pictures were rated as less arousing than neutral words ($p = 0.01$). In

Table 2 Note: This data is mandatory. Please provide

Fixed effects	β	SE	t	*p* value
Intercept	3.322	0.354	9.38	<0.001
Stimulation condition (left dlPFC)	0.361	0.136	2.65	<0.01
Stimulation condition (dACC)	−0.065	0.136	−0.48	0.632
Format (word)	0.692	0.206	3.36	<0.001
Valence (negative)	3.812	0.206	18.53	<0.001
Session	−0.441	0.075	−5.88	<0.001
Stimulation condition (left dlPFC) * Format (word)	−0.386	0.193	−2.01	<0.05
Stimulation condition (dACC) * Format (word)	−0.086	0.193	−0.44	0.656
Stimulation condition (left dlPFC) * Valence (negative)	−0.376	0.193	−1.95	0.051
Stimulation condition (dACC) *Valence (negative)	−0.191	0.193	−0.991	0.322
Format (word) * Valence (negative)	−2.312	0.193	−7.94	<0.001
Stimulation condition (left dlPFC) * Format (word) * Valence (negative)	0.517	0.272	1.90	0.057
Stimulation condition (dACC) * Format (word)* Valence (negative)	0.122	0.272	0.45	0.654

Note. Summary of the mixed effects model on arousal ratings.

addition, negative stimuli gave rise to higher arousal ratings than the neutral ones (negative pictures vs. neutral pictures: $p < 0.001$; negative words vs. neutral words: $p < 0.001$). A significant main effect of session ($F(1, 155.5) = 34.61$, $p < 0.001$, $\eta^2 = 0.18$, CI 0.10–0.28) also was evident, with a decrease in arousal intensity over session ($\beta = -0.441$).

Error bars indicate standard errors of the mean. While arousal ratings when stimulating dACC were lower than Sham ($p < 0.05$) and dlPFC ($p < 0.001$), no effect was evident for the valence ratings.

The analysis of valence ratings (Table 3; Figure 2b) showed no significant main effect of the site of stimulation ($F(2, 3255) = 0.61, p > 0.05$). However, it revealed significant main effects of valence ($F(1, 155.5) = 723.70, p < 0.001, \eta^2 = 0.82$, CI: 0.79–0.85), format ($F(1, 155.5) = 7.89, p = 0.006, \eta^2 = 0.05$, CI: 0.01–0.11), and session ($F(1, 155.8) = 5.03$, $p = 0.03, \eta^2 = 0.03$, CI 0.00–0.09), and a significant interaction of valence and format ($F(1, 155.5) = 34.60, p < 0.001, \eta^2 = 0.18$, CI 0.10–0.27). Valence ratings were significantly lower for negative stimuli than neutral stimuli (negative pictures vs. neutral pictures: $p < 0.001$; negative words vs. neutral words: $p < 0.001$). In addition, negative pictures were associated with lower valence ratings than negative words ($p < 0.001$), but no difference was evident between neutral pictures and neutral words ($p > 0.05$).

Cognitive tasks

In the analyses of the Stroop task (Figure 3c), stimulation condition was not significant (all *p*s > 0.05) but session was ($F(1,44) = 36.49, p < 0.001, \eta^2 = 0.45$, CI 0.27–0.59), as the execution time decreased over session ($\beta = -1.77$). In contrast, for the trail making task (Figures 3a and b), the analyses revealed a significant effect of the stimulation condition for the TMT-AB score ($F(2, 44) = 5.32, p < 0.01, \eta^2 = 0.19$, CI

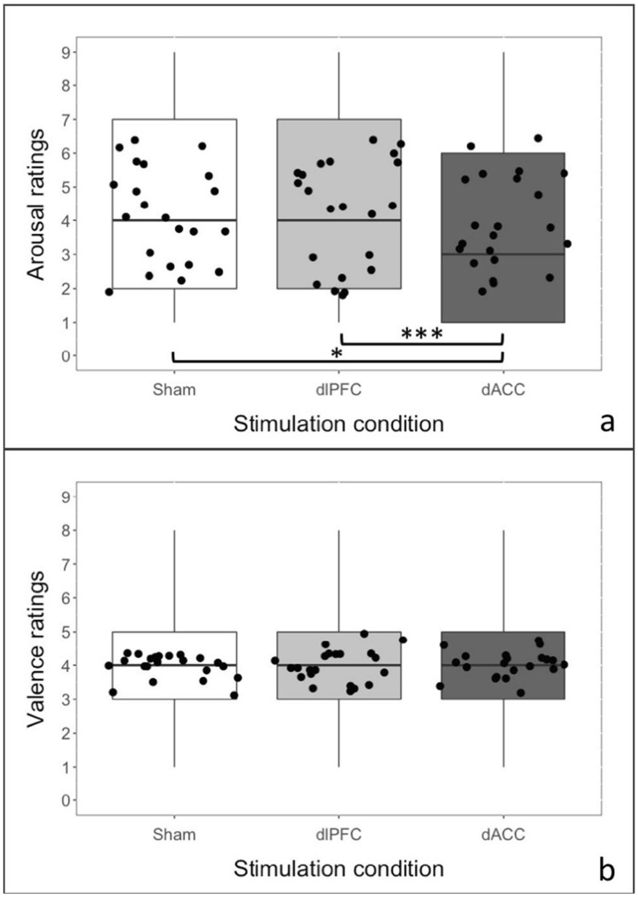

Fig. 2 Participants' arousal (**a**) and valence (**b**) ratings in the three stimulation conditions. $^*p < 0.05$; $^{**}p \leq 0.01$; $^{***}p < 0.001$

Table 3 Note: This data is mandatory. Please provide

Fixed effects	beta	SE	t	*p* value
Intercept	5.122	0.178	29.81	<0.001
Stimulation condition (left dlPFC)	−0.014	0.086	−0.16	0.873
Stimulation condition (dACC)	−0.005	0.086	−0.51	0.609
Format (word)	−0.295	0.150	−1.97	0.050
Valence (negative)	−3.080	0.150	−20.52	<0.001
Session	0.128	0.057	2.42	0.026
Stimulation condition (left dlPFC) * Format (word)	0.007	0.013	−0.05	0.956
Stimulation condition (dACC) * Format (word)	0.035	0.125	0.28	0.779
Stimulation condition (left dlPFC) * Valence (negative)	0.076	0.125	0.62	0.53
Stimulation condition (dACC) *Valence (negative)	0.022	0.125	0.17	0.863
Format (word) * Valence (negative)	1.170	0.212	5.52	<0.001
Stimulation condition (left dlPFC) * Format (word) * Valence (negative)	−0.098	0.177	−0.55	0.579
Stimulation condition (dACC) * Format (word)* Valence (negative)	−0.133	0.177	−0.75	0.452

Note. Summary of mixed effects model on valence ratings.

0.03–0.35), but not for the TMT-A score ($F(2, 44) = 0.45$, $p > 0.05$). Specifically, the stimulation of the left dlPFC was associated with longer execution times than both the sham ($p = 0.01$) and dACC ($p = 0.01$) conditions. In addition, both the analyses on TMT-A and AB scores showed significant main effect of sessions (TMT-A: $F(1, 44) = 12.34$, $p = 0.001$, $\beta = -1.71$, $\eta^2 = 0.22$, CI: 0.06–0.39; TMT-AB: $F(1, 48) = 11.87$, $p = 0.001$, $\beta = -4.64$, $\eta^2 = 0.21$, CI 0.06–0.38).

Questionnaires

The analysis of the responses on the PANAS (Figure 4) questionnaire revealed significant main effects of stimulation condition ($F(2, 2597.97) = 4.69$, $p < 0.01$, $\eta^2 = 0.004$, CI 0.00–0.1), with left dlPFC associated with a significant decrease in the affective score than dACC ($p = 0.01$), of valence ($F(1, 19.8) = 45.45$, $p < 0.001$, $\eta^2 = 0.70$, CI: 0.48–0.81), with higher affective positive than negative scores ($p < 0.001$) and of session ($F(1, 2597.96) = 22.66$, $p < 0.001$, $\eta^2 = 0.009$, CI 0.00–0.02),6 with affective score decreasing over sessions ($\beta = -0.088$). Moreover, a significant stimulation condition x valence interaction ($F(2, 2597.97) = 5.92$, $p < 0.01$, $\eta^2 = 0.002$, CI 0.00–0.01), and a significant interaction of stimulation condition, valence. and block ($F(2, 2597.97) = 3.49$, $p < 0.05$, $\eta^2 = 0.003$, CI 0.00–0.01) also were evident. To explore the three-way interaction, we performed contrasts between pre- and poststimulation affective scores in each condition, because we were specifically interested in exploring the contribution of tDCS on affective state. After the stimulation of left dlPFC, positive affective scores were reduced with respect to those registered before stimulation ($p = 0.01$). No difference emerged between pre- and postaffective scores in the other stimulation conditions (all p values > 0.05).

The analysis of the tDCS-related symptoms (see Table 4) showed no differences across stimulation conditions in the intensity of itching ($\chi^2(2) = 2.65$, $p > 0.05$, all ps > 0.05), pain ($\chi^2(2) = 1.00$, $p > 0.05$, all ps > 0.05), heat ($\chi^2(2) = 0.93$, $p > 0.05$, all ps > 0.05), irritating itching (in Italian: *pizzicore*) ($\chi^2(2) = 1.85$, $p > 0.05$, all ps > 0.05), whereas metallic taste and burning sensation were more intense for both dACC and dlPFC condition than the sham condition (burning sensation: $\chi^2(2) = 8.39$, $p = 0.02$, sham vs. dACC: $p = 0.003$ e sham vs. dlPFC: $p = 0.06$, dACC vs. dlPFC: $p > 0.05$; metallic taste ($\chi^2(2) = 5.33$, $p = 0.07$, sham vs. dACC: $p > 0.05$, sham vs. dlPFC: $p < 0.05$, dACC vs. dlPFC: $p < 0.05$). In addition, the stimulation of dlPFC was associated with increased weariness ($\chi^2(2) = 10.30$, $p < 0.01$) with respect to both sham ($p < 0.05$) and the dACC ($p < 0.05$) conditions.

The analysis of participants' answers to the question about their blindness to the stimulation procedure showed no significant effect ($\chi^2(2) = 3.16$, $p > 0.05$; left dlPFC: mean rating = 1.72, SD = 0.55; dACC: mean rating = 1.73, SD = 0.46; sham

Table 4 Note: This data is mandatory. Please provide

Symptom	dACC	Left dlPFC	Sham
Burning sensation	0.86 ± 0.89	0.64 ± 0.66	0.36 ± 0.49
Heat	0.36 ± 0.66	0.45 ± 0.60	0.45 ± 0.67
Irritating itching	1.18 ± 0.59	1.18 ± 0.66	0.95 ± 0.57
Itching	0.81 ± 0.73	0.68 ± 0.65	0.54 ± 0.60
Metallic taste	0.23 ± 0.53	0.23 ± 0.53	0.00 ± 0.00
Pain	0.32 ± 0.65	0.23 ± 0.53	0.14 ± 0.47
Weariness	0.09 ± 0.29	0.36 ± 0.49	0.09 ± 0.29

Note. Means and standard deviations of the intensity ratings of each tDCS-associated symptom.

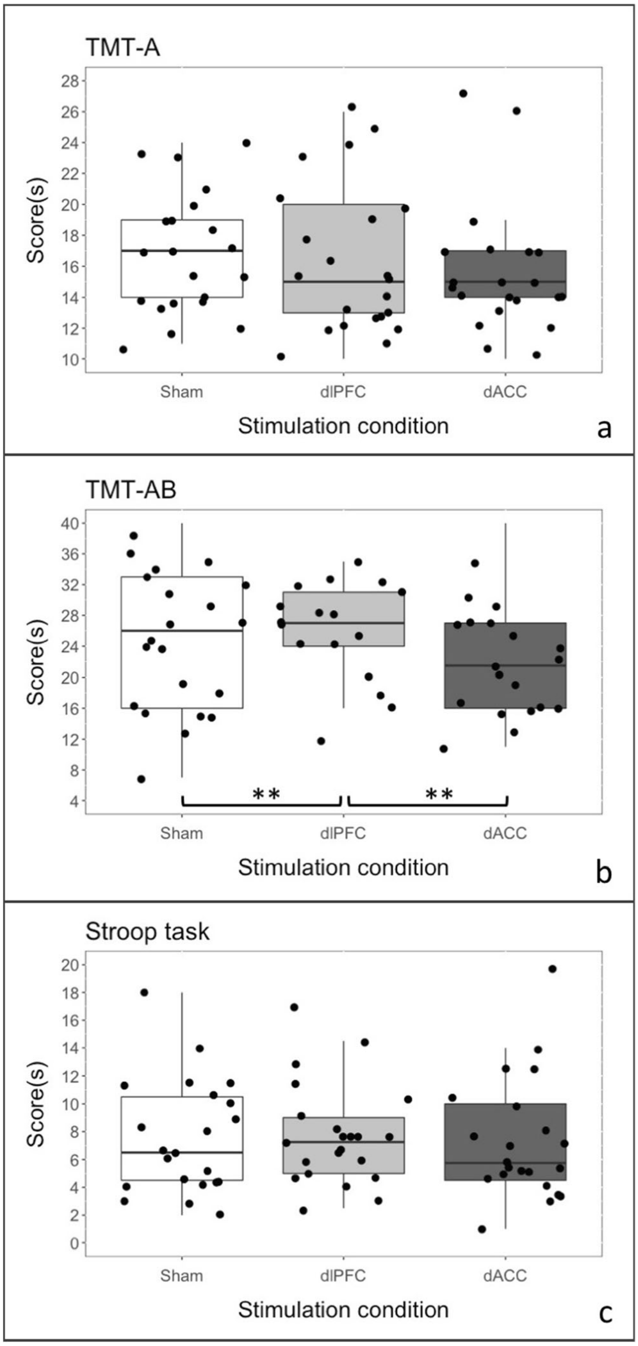

Fig. 3 Participants' scores on the TMT–A (**a**), TMT-AB (**b**), and Stroop test (**c**) in the three stimulation conditions. $*p < 0.05$; $**p \leq 0.01$; $***p < 0.001$

condition: mean = 1.55, SD = 0.51), indicating that our participants were blind to the stimulation condition.

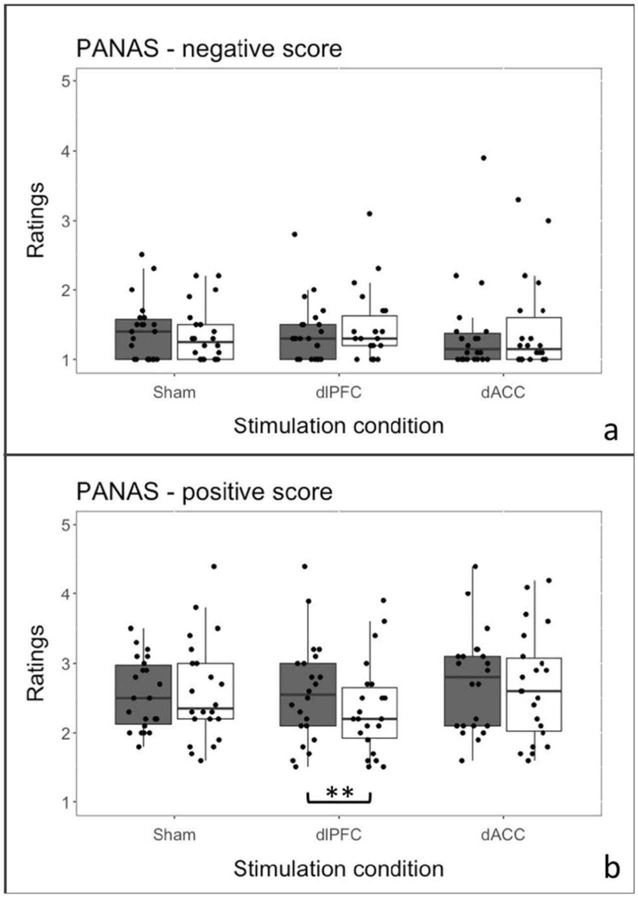

Fig. 4 Participants' ratings pre- (dark grey) and post- (light grey) stimulation in the negative (**a**) and positive (**b**) scores of the PANAS. $*p < 0.05$; $**p \leq 0.01$; $***p < 0.001$

Discussion

Previous research highlighted the key role of dACC and left dlPFC in tasks involving emotional processing, but the specific contribution of the two areas to specific processes still needs to be clarified. Functional neuroimaging studies suggest that the dACC play some role in both appraising and controlling emotional aspects of stimuli (Buhle et al., 2014; Grecucci et al., 2013a, b, 2019; Kohn et al., 2014; Messina et al., 2021). In addition, dlPFC is associated with cognitive control and attentional processing that might be involved in the selection of a regulation strategy in emotion regulation tasks but also might influence emotional appraisal. To establish the exact role of these regions, we compared participants' performances on word and picture rating tasks while they underwent cathodal dACC, left dlPFC, and sham stimulation. To assess eventual changes in baseline mood, we also assessed positive and negative affective state before and after the stimulation session.

Our key result is that the cathodal stimulation of dACC, but not the left dlPFC, led to reduced arousal ratings of both neutral and negative stimuli than sham. In contrast, no effect of the stimulation on participants' valence ratings, their baseline affective state and visuospatial attention and executive functions was found. These findings are consistent with previous neuropsychological studies on patients who underwent cingulotomy, which showed reductions of the intensity of anxiety, and depressive symptoms in patients (Cohen et al., 2001; Kim et al., 2003). Our results suggest that this region might be involved in stimuli appraisal as suggested by Etkin and collaborators (2011). Indeed, disrupting the integration of external and internal information that are necessary to appraise an emotional stimulus (Etkin et al., 2011) might lead to experience stimuli with reduced intensity and less negative valence. The consistent dACC activations in neuroimaging studies investigating emotion regulation might be due to high prevalence of studies focusing on *reappraisal*(Buhle et al., 2014; Kohn et al., 2014), a strategy consisting in the reinterpretation of stimuli meaning in order to down- or up-regulate the emotional experience. Hence, the involvement of the dACC in those studies is more likely to have been triggered by the process of integrating information necessary for updating the meaning of a stimulus.

The effect of dACC on emotional experience seems to be limited to contingent stimuli/situations. Indeed, while dACC stimulation was shown to interfere with stimuli appraisal, participant's baseline affective state was not affected. This might seem in contrast with previous neuro-stimulation studies on patients with obsessive-compulsive disorder who experience anxiety and depression reduction, as well as obsession intensity reduction, after dACC inhibitive neurostimulation (D'Urso et al., 2016a; b). However, it is worth noting that in patient studies, the effects measured were the product of prolonged inhibition of dACC (i.e., tDCS daily stimulation) and that the baseline affective state of obsessive-compulsive patients is highly dependent on the occurrence of obsessions. Hence, the modification of the baseline affective state of patients with obsessive-compulsive disorder might be secondary to the reduction of obsession-related anxiety that is associated with tDCS and surgical treatment targeting dACC. This might explain why we did not observe any modification of the participants' baseline affective state.

In previous studies the dACC functioning was especially associated with negative emotions (Colibazzi et al., 2010; Cunningham et al., 2004; Lewis et al., 2007). Conversely, our results seem to indicate that the observed effect is not valence specific, because the arousal reduction associated with dACC cathodal stimulation was not limited to negatively valenced stimuli but also included the neutral ones. However, since participants' emotional experience of positively valenced stimuli was not tested, it is not possible to establish whether the effect is specific to negative stimuli, as previous studies linking dACC and negatively valenced emotions could suggest (Etkin et al., 2011), or whether it also involves the positive ones.

In contrast with previous tDCS studies reporting an association between anodal tDCS on the left dlPFC and valence modulation (Boggio et al., 2009; Nejati et al., 2021), in the current study the cathodal stimulation of the left dlPFC did not induce any modification in participants' emotional experience (subjective ratings) of the stimuli presented. The polarity of stimulation might have played a role in this inconsistency; as reported in other fields (Jacobson et al., 2012), the cathodal tDCS tend to be associated with a lower probability of inducing inhibitory effects than excitatory effects of the anodal. However, it is worth noting that cathodal tDCS over the left dlPFC showed significant effects on other measures we collected (i.e., PANAS, Trail-Making test), suggesting that the functional inhibition on this brain area was effective. Indeed, left dlPFC cathodal stimulation was associated with the reduction of positive mood, as manifested by a decrease in the positive affective subscale of PANAS, and with longer execution times of the TMT-AB, which measures switching abilities. This pattern of findings is consistent with the view of dlPFC as contributing to both top-down control of emotions (Buhle et al., 2014; Grecucci et al., 2013a, b, 2020; Kohn et al., 2014; Messina et al., 2021) and cognitive functions (Elliott, 2003). These findings suggest that this area might play a crucial role in modulating the baseline affective states. Conversely, they confirm previous evidence on the role of the left dlPFC in processing executive functions (Elliott, 2003) and, specifically, switching abilities (Müller et al., 2014). Although the reduction of PANAS positive score associated with left dlPFC cathodal stimulation also might be related to the higher incidence of side effects, as weariness, in participants after the stimulation procedure, it also is convergent with studies on patients with depression showing more reduced activation of dlPFC than controls (Baxter et al., 1989; Biver et al., 1994; Galynker et al., 1998) and reduced intensity of depressive symptoms after anodal tDCS on dlPFC (Nitsche et al., 2009). In contrast, left dlPFC cathodal stimulation did not induce any modulation of the subjective emotional experience towards upcoming stimuli. This might be due to the fact that participants were not implementing any cognitive strategy to regulate their emotions during the execution of the task. Indeed, it has been proposed that dlPFC might be involved in the initiation of the implementation of a strategy (e.g., reappraisal) to regulate their emotional experience (Kohn et al., 2014). Hence, the disruption of left dlPFC might induce an effect on emotion regulation towards upcoming stimuli only when a conscious strategy is implemented. In sum, we provided new evidence for a dissociable role of dACC and dlPFC for emotion appraisal and mood modulation.

Beside the findings, some limitations must be taken into account. First, in the present study we used only cathodal stimulation. This was done to avoid excessive number of the experimental sessions, and, consequently, the probability of participants' drop-out. Second, cigarette smoking habits, which was found to alter cortical excitability (Grundey et al., 2013), was not included in the participants' exclusion criteria and might have affected the efficacy of stimulation in a subgroup of participants. Third, the experimenters were not blind to the stimulation protocol (i.e., verum or sham), and this might have influenced participants' behaviour, although the specificity of the effects found cannot be explained by the knowledge of participants. Fourth, the limited number of trials used in the experiment might have influenced the participants' performance stability. Fifth, the use of neutral and only negative stimuli limits the generalizability of our findings. Using positive stimuli could help to better separate eventual valence and arousal specificity due to the stimulation. Also, eventual lateralization effects could be explored. Future studies may want to test also for anodal stimulation over the same areas targeted in the present experiment, and over contralateral areas.

To conclude, the subjective emotional experience of both negative and neutral stimuli was modulated by dACC, but not left dlPFC, cathodal stimulation suggesting that dACC has a role in the appraisal of upcoming stimuli. In addition, participants' baseline affective state was modulated by the cathodal stimulation of left dlPFC, but not dACC, highlighting a possible role for dlPFC in mood processing. Hence, these areas might be involved in two different aspects emotional processing, with dACC involved in appraising emotional stimuli and left dlPFC in mood modulation. Further studies need to be performed to test the relevant contribution of dACC and dlPFC in emotion appraisal.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.3758/s13415-021-00952-3.

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