

# Enhancing Reappraisal of Negative Emotional Memories With Transcranial Direct Current Stimulation

**Nadja Doerig**

University of Zurich

**Rosa Bohlender**

University of Giessen

**Marius Moisa**

University of Zurich

**Erich Seifritz**

University of Zurich

**Christian Ruff**

University of Zurich

**Birgit Kleim** (✉ [birgit.kleim@uzh.ch](mailto:birgit.kleim@uzh.ch))

Department of Psychiatry, Psychotherapy and Psychosomatics, Psychiatric University Hospital Zurich,  
Lenggstrasse 31, 8032 Zurich, Switzerland

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## Research Article

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Enhancing reappraisal of negative emotional memories with transcranial direct current  
stimulation

Nadja Doerig<sup>\*1,2</sup>, Rosa Bohlender<sup>\*1,2,3</sup>, Marius Moisa<sup>4,5</sup>, Erich Seifritz<sup>1,5</sup>, Christian C. Ruff<sup>4,5</sup>  
& Birgit Kleim<sup>1,2,5#</sup>

<sup>1</sup> Department of Psychiatry, Psychotherapy and Psychosomatics, Psychiatric University Hospital Zurich, Lenggstrasse 31, 8032 Zurich, Switzerland

<sup>2</sup> Department of Psychology, University of Zurich, Binzmühlesatrsse 14, Box 8, 8050 Zurich, Switzerland

<sup>3</sup> Department of Psychology, University of Giessen, Giessen, Germany

<sup>4</sup> Zurich Center for Neuroeconomics (ZNE), Department of Economics, University of Zurich, Zurich, Switzerland

<sup>5</sup> Zurich Neuroscience Center (ZNZ), University of Zurich, Zurich, Switzerland

\* shared first authorship

# corresponding author: Prof Birgit Kleim, PhD, Department of Psychiatry, Psychotherapy and Psychosomatics, Lenggstrasse 31, 8032 Zurich, Switzerland, Email: [birgit.kleim@uzh.ch](mailto:birgit.kleim@uzh.ch), Phone: +41 44 384 2351

**Abstract**

Reappraisal of negative memories and experiences is central for mental health and well-being. Deficiency of reappraisal lies at the core of many psychiatric disorders and is a key target for treatment. Here we apply transcranial direct current stimulation (tDCS) to enhance reappraisal of negative emotional memories. In a randomized, sham-controlled, 2x2 between-subject and double-blinded study, we applied single sessions of anodal and sham tDCS over the right dorsolateral prefrontal cortex (DLPFC) of 101 healthy participants while reappraising a personal negative memory or engaging in a control task. We hypothesized that (i) reappraisal decreases negative valence, arousal and evaluations of the memory and leads to improved decision making, and (ii) tDCS leads to additional changes in these reappraisal outcomes. In line with these hypotheses, participants' personal memories were rated as less negative and less arousing following reappraisal. Anodal tDCS stimulation during reappraisal was associated with significant additional reductions in negative valence compared to sham stimulation. Our results indicate that tDCS may enhance some of the effects of reappraisal. If replicated, our findings suggest potential benefits elicited by tDCS stimulation that may help to optimize current treatment approaches for psychiatric disorders.

*Key words:* Reappraisal, tDCS, emotional memory, cognitive control

## **Introduction**

Negative memories of personal experiences are often associated with emotional reactions that individuals wish to regulate e.g. by reinterpreting and reframing the meaning of the affective situation to change its emotional impact (Gross & John, 2003; Braunstein, Gross, & Ochsner, 2017). Such successful regulation is a key success factor for mental health. Difficulties in the capacity to reappraise, on the other hand, have been associated with affective disorders (Gotlib & Joormann, 2010). Not surprisingly then, reappraisal is a key element of current psychotherapy treatment, such as cognitive-behavior therapy (CBT), an evidence-based first-line therapy for emotional disorders. Reappraisal may help provide alternative explanations, which, in turn, foster adaptive emotional response to distressing memories or situations.

Successful regulation of emotions also influences cognitive processes and may have positive effects on various outcomes of emotion and action control, including decision making (e.g. Bjälkebring, Västfjäll, Svenson, & Slovic, 2016; Miu, Heilman, & Houser, 2008; Szasz, Hofmann, Heilman, & Curtiss, 2016). That is, changes in cognitions and emotions following reappraisal may influence subjective judgements on probability and utility of future outcomes and may lead to changes in decision making and risk taking (Panno, Lauriola, & Figner, 2013; Braunstein, Herrera, & Delgado, 2014). Effective reappraisal may thus lead to better self-regulation and changes in experience of positive and negative emotions (Gross & John, 2003), as well as cognitive and behavioral consequences, such as more effective decision making (van't Wout, Chang, & Sanfey, 2010; Sokol-Hessner, Hsu, Curley, Delgado, Camerer, & Phelps, 2009).

## **Modulating Reappraisal using transcranial direct current stimulation**

A number of studies have investigated ways of enhancing reappraisal processes by, for instance, longitudinal training in specific reappraisal processes, such as psychological distancing (Denny & Ochsner, 2014), mindfulness (Garland, Fredrickson, Kring, Johnson,

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Meyer, & Penn, 2010) or self-compassion (Diedrich, Hofmann, Cuijpers, & Berking, 2016).

Most recently, reappraisal has been modulated using non-invasive transcranial direct current stimulation (tDCS) (e.g. Feeser, Prehn, Kazzer, Mungee, & Bajbouj, 2014). TDCS is a contemporary, portable, non-invasive neuromodulatory technique that delivers a low (1-2 mA) electric current to the scalp, leading to an unfocal neuromodulatory effect that is thought to influence subthreshold neuronal excitability in a polarity-dependent manner. While the precise neurophysiological effects and mechanisms-of-action of tDCS are debated and hard to predict for any given setup (Bestman et al., 2015), there are numerous reports that the stimulation can have replicable and polarity-dependent effects on behavior and neural activity (Polania et al., 2018). Anodal stimulation is thought to result in increased neuronal excitability and cathodal tDCS in decreased neuronal excitability (Nitsche & Paulus, 2001). Such dichotomous rules-of-thumb need to be treated carefully, however, especially for complex cognitive tasks (Boehringer, Macher, Dukart, Villringer, & Pleger, 2013; Macher, Boehringer, Villringer, & Pleger, 2014;).

Even a single session of tDCS can modulate cognitive functioning in healthy adults (Jacobson, Koslowsky & Lavidor, 2012; Nitsche et al., 2008). Anodal tDCS over the dlPFC, for instance, modulated various neural networks implicated in a range of complex cognitive functions (e.g. Hoy, Emonson, Arnold, Thomson, Daskalakis, & Fitzgerald, 2013). Recent work showed a potential impact of anodal left tDCS on cognitive control for emotional information in healthy and depressed individuals (Wolkenstein & Plewnia, 2013) as well as on reducing negative affect of emotion appraisal in healthy smokers (Pripfl & Lamm, 2015). Feeser and colleagues (Feeser et al., 2014) studied tDCS over the right dlPFC to investigate the effects of increased dlPFC excitability on cognitive reappraisal and reported that tDCS facilitated cognitive reappraisal in both directions, by either increasing or decreasing emotional responsiveness as indexed by subjective emotional arousal ratings and skin conductance responses. Further, Peña-Gómez and colleagues (Peña-Gómez, Vidal-Piñeiro,

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Clemente, Pascual-Leone, & Bartrés-Faz, 2011) reported that tDCS over the left dlPFC reduced perceived negative valence of picture cues, by boosting cognitive control over the experience of emotion when processing the pictures. Also in line with these results, two studies reported effects of left prefrontal cortex tDCS on reappraisal (Boggio, Zaghi, & Fregni, 2009; Marques, Morello, & Boggio, 2018), indexed by decreased discomfort ratings during the presentation of images depicting human pain, and ratings, as well as physiological response to emotional pictures, respectively.

Most studies examined the effect of reappraising emotional responses to standardized stimuli, such as IAPS pictures, rather than to personal material, such as autobiographical memories. Investigation into reappraisal modulation in the context of personal material, such as emotional autobiographical memories, appears crucial for translating findings to clinical settings.

In terms of cortical areas and targets for enhanced reappraisal, numerous studies accord that cognitive reappraisal recruits frontal and parietal cortical control regions in particular (e.g. Buhle et al., 2014). The dorsolateral prefrontal cortex (dlPFC) has been suggested as relevant region, due to the proposed inhibitory top-down control function on affective and impulsive influences (Kanske, Heissler, Schönfelder, Bongers, & Wessa, 2011; Ochsner et al., 2004; Urry, van Reekum, Johnstone, & Davidson, 2009). Both recall and reappraisal of autobiographical memories rely on dlPFC activity associated with manipulating the products of retrieval in working memory during recall (Cabeza & St Jacques, 2007) and with maintaining and manipulating emotional information in working memory during subsequent reappraisal (Ochsner & Gross, 2008). These studies have also suggested that the right, in comparison to the left dlPFC, is more involved in decreasing rather than increasing emotions (Ochsner, Silvers & Buhle, 2012, but see Marques, Morello & Boggio, 2018). In accord with theoretical accounts of hemisphere specialization, the right dlPFC has been associated with

processing negative emotions and the left dlPFC for positive emotions (Allaert, Sanchez-Lopez, De Raedt, Baeken & Vanderhasselt, 2019). Based on all these previous findings and theoretical proposals, we therefore selected the right dlPFC as a target region for our investigation.

### The current study

We investigated the effect of anodal tDCS applied over the right dlPFC on reappraising a negative emotional autobiographical memory. We first hypothesized that reappraisal reduces negative memory characteristics, i.e. self-reported negative valence, and arousal, increases positive evaluations, and changes behavioral decision making as a consequence of these affective influences. Secondly, we hypothesized that tDCS may enhance these effects and leads to reductions in negative memory characteristics and evaluations. Whilst we therefore expected reappraisal under sham-tDCS to lead to positive effects, compared to the control group, we expected additional outcome changes on top of these general effects for the tDCS group, in line with the hypothesis that tDCS modulates neural processes involved in reappraisal. Moreover, based on the general association between affect and decision making (Bjälkebring, Västfjäll, Svenson, & Slovic, 2016), we also investigated whether tDCS (by means of its effects on reappraisal) leads to more optimal decision making, using a standard clinical decision-making task. We compared reappraisal outcomes for a group receiving active versus sham tDCS, as well as a group that completed a reappraisal versus a control task. Our study expands on previous studies by investigating reappraisal of personal negative autobiographical memories rather than standardized stimulus material. We employ high methodological rigor by testing a large sample of 101 healthy participants, the largest participant number in studies employing tDCS in the context of reappraisal, and we employ identification of neuroanatomical target sites by using neuronavigation in a significant subgroup of participants.

## Methods

### **Participants**

The study comprised a sample of 101 healthy adults ( $n= 60$  women, 59.4%) with a mean age of 24.10 years,  $SD= 3.74$  [95% CI 23.36-24.84], all native German speakers with an overall high level of education ( $n= 98$ , 97% with high school or university degree). Individuals had no history of neurological or psychiatric conditions, indexed with the Structured Clinical Interview screening of DSM-IV (Wittchen, Zaudig, & Fydrich, 1997) and no other contraindication to tDCS.

Participants were recruited from a participant database at the University of Zürich, as well as local advertisements. They were randomly assigned to experimental groups, i.e., stimulation condition (anodal vs sham) and task condition (reappraisal vs control). Table 1 summarizes demographic and personality variables as well as general memory characteristics for the four different groups. There were no differences in key demographic characteristics between the experimental groups, all  $p$  values  $> .661$ .

– Please insert Table 1 approximately here –

### **Study Design and Procedure**

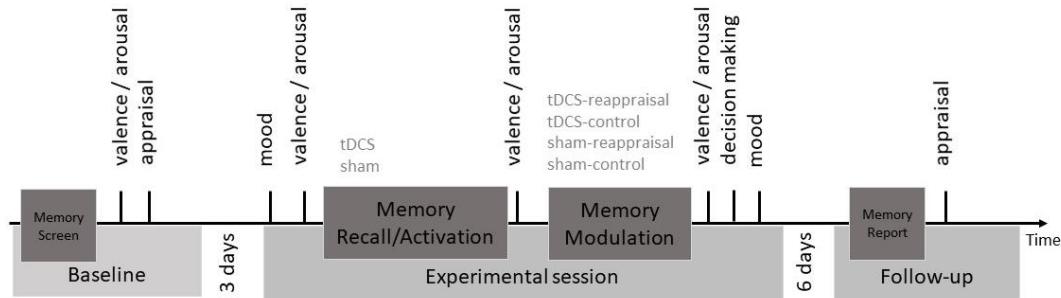
The study was designed as a 2 (tDCS, sham) x2 (reappraisal, control task) double-blind, between-subjects, sham-controlled trial that consisted of three individual sessions per participant. It was approved by the local ethics committee (Cantonal Ethics Committee, Zurich), and all participants provided written informed consent. All methods were performed in accordance with these guidelines and the research was performed in accordance with the Declaration of Helsinki. Participants were reimbursed according to local standards (30 CHF per hour participation or total amount of approximately 100 CHF). Three graduate students trained in tDCS application conducted sessions under expert supervision for tDCS (MM,

CCR). The overall study consisted of a baseline, an experimental, as well as a follow-up session.

Based on our three-factorial study design, we calculated minimal effect sizes that we could detect at 80% power given our factors stimulation (active vs SHAM), task type (reappraisal vs control) and time (pre vs post- audio). According to the PANGEA shiny app (Westfall, 2016), we would be able to detect an effect size of .45 for the three-way interaction (stimulation x audio type x time). There are only limited previous studies to derive effect sizes from, as none of the existing tDCS study reported results for such a three-way interaction. However, based on Feeser et al., 2014, we can expect a large effect of tDCS on reappraisal outcomes (that study reported effects of  $d= 1.61, 1.69$ , respectively, for tDCS vs SHAM effects on arousal during down- or upregulation, respectively). However, not all of their tDCS effects were significant, thus leaving some inconsistencies. Our study design and sample size was also guided by sample sizes of previous tDCS studies, to which our study compares favourably. In the baseline session, participants completed questionnaires including sociodemographic, personality and clinical variables and a working memory assessment. They were asked to select a negative emotional memory, describe the memory to the experimenter to screen and select suitable emotional memory content (negative valence >50 on a scale to 100, stressful, but non-traumatic). Memory content was thus idiosyncratic, e.g., death of a grandparent, death of a pet, relationship breakup, arguments with best friend. The experimenter checked whether memories fulfilled these criteria and were thus suitable for our study. Participants also rated memory characteristics, i.e., valence, arousal (both indexed using self-rating mannequins), as well as positive and negative evaluations, e.g., negative emotions and cognitions associates with the memory, all indexed by self-report. This procedure is in line with standard methods in experimental psychopathology to standardize and control for the emotional valence of memories, rather than using one set of stimuli that would elicit very

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different emotional responses in different participants. See Figure 1 for a timeline of the experiment.



**Figure 1.** Timeline of the experiment. At baseline, participants' negative emotional memory was screened and participants rated valence, arousal of the memory and evaluations (memory screen). During the experimental session, participants completed a mood state questionnaire and again rated valence and arousal (memory recall/activation). Anodal or sham tDCS was applied over participants' right dlPFC. The tDCS stimulation began 3 minutes prior to the beginning of the testing, to allow neuroplastic effects to stabilize. In these three minutes, participants engaged in a standardized breathing protocol (see above). To minimize the cutaneous sensation of current onset and offset, tDCS was ramped up in the beginning to maximum intensity over a period of 5 seconds and ramped down over 5 seconds in the end. Stimulation was applied for 20 consecutive minutes throughout the experiment, starting from the beginning of the experimental session and continued throughout the experiment. Participants then rated valence and arousal of the memory. They then listened to the reappraisal or the control audio tape for memory modulation and completed valence and arousal ratings (memory modulation). Decision making and mood were assessed. During follow-up, positive and negative evaluations were assessed.

In the experimental session, approximately 3 days after baseline, tDCS/sham was applied (see below for details) and participants reappraised their personal negative memory according to an audio-guided reappraisal task (see below). Prior to tDCS/sham setup and stimulation point localization, participants completed a mood state questionnaire and rated valence and arousal. Two experimenters were present during this session and the one interacting with the participants was blind to all conditions. The experiment then started in a separate room. Either tDCS or sham stimulation were started directly before the start of testing and continued for 20

minutes throughout the experiment, i.e. during reappraisal vs control task. Participants followed instructions from either reappraisal or control audio tape (see below for more detailed description). Specifically, participants first engaged in a brief standardized breathing exercise (~3min), then vividly imagined again their memory (activation; ~3min), completed valence and arousal ratings (~1min) as well as memory-related evaluations (~1 min). In the following 2 minutes, participants were asked to write down their most important insights (reappraisal condition) or their most accurate memory (control condition), and again rated valence and arousal (~1min). Finally, they completed the Iowa gambling task and provided mood ratings.

A *follow-up session* took place approximately six days following the experimental session. Participants returned to the lab where they were asked to remember vividly their memory and filled in questionnaires indexing evaluations.

#### *Reappraisal and control task*

We used a standardized 20 minute audio-guided reappraisal task with ten open questions facilitating personal reappraisal of the experience described in the personal memory by taking other perspectives. Participants were asked to think about and take on these perspectives to the best of their abilities, engaging in those perspectives that they could endorse best, e.g. “in every situation is also something good”, “good events happen much more often than bad events”, “I learned a lot out of that experience”, all of which were adapted from previous studies (Gross & John, 2003; Schartau, Dalgleish, & Dunn, 2009; Webb, Miles, & Sheeran, 2012). After each question, participants were asked to think about and engage in the question for 60 seconds. The control task consisted of the same structure and timing, including the same number of questions, but these referred instead to external information without focus on cognitions or emotional aspects of the memory, such as external facts (e.g., time, season, participants clothes).

*Transcranial direct current stimulation*

TDCS was applied through a pair of saline-soaked surface sponge tDCS electrodes (DC-stimulator Plus, NeuroConn). The large cathodal electrode ( $10 * 10 \text{ cm}^2$ ) was over the vertex, defined for each subject as the point of confluence between the left and right central sulci. In the interhemispheric fissure. A smaller anodal tDCS electrode ( $5*7 \text{ cm}^2$ ) was placed over our target, the right dlPFC. The localization of the right dlPFC was conducted by means of T1-weighted MR scans for 36 participants for whom such data were available from prior studies (T1-weighted 3D turbo field echo, 181 sagital slices, matrix size 256X256, voxel size = 1x1x1 mm). The standardized coordinates were applied to the individual native headspace using the software Brainsight 2.2 Frameless Stereotaxy (Rogue Research; <https://www.rogue-research.com/>). The points were marked on the participants' scalp and used as the electrodes' center points. For all other participant without existing MR scans, the stimulation site was localized by averaging the 36 individual points and fixing the center of the electrode over this center-of-mass (see Maréchal, Cohn, Ugazio & Ruff, 2017, 2017 for development of this procedure, which ensures that the electrode is localized over the neuroanatomical target). Importantly, there was no significant difference in distribution of participants with and without MRI scan across the two groups ( $\chi^2=.708$ , df=3, p=.871) and the presence of an MRI scans had no effect on changes in valence due to both task and stimulation condition ( $\chi^2=9.710$ , df=9, p=.374). Thus, differences in the precision of target localization cannot have affected our results.

The tDCS stimulation began 3 minutes prior to the beginning of the testing, to allow neuroplastic effects to stabilize. In these three minutes, participants engaged in a standardized breathing protocol (see above). To minimize the cutaneous sensation of current onset and offset, tDCS was ramped up in the beginning to maximum intensity over a period of 5 seconds and ramped down over 5 seconds in the end. There was a waiting period of 3 minutes prior to starting the experimental task. Perceived stimulation was indexed after stimulation

and thus referred to the whole experiment, not the peak of sham stimulation. No differences were detected between groups.

## Measures

Main outcome measures comprised ratings of emotional memory characteristics, namely (i) valence and arousal, (ii) negative and positive evaluations and (iii) decision making as a behavioral measure. See Figure 1.

We assessed *valence and arousal* using subjective ratings of negative valence indexed on a scale from 1-10 (not at all - very much) using self-report mannequins (Bradley & Lang, 1994).

We assessed memory-related *evaluations* using self-report questionnaires, comprising scales with two items each indexing positive and negative evaluations, i.e., for negative evaluations (“I feel negative emotions associated with the event”, “I have negative cognitions associated with the event”) and for positive evaluations (“I feel positive emotions associated with the event, too”, “I have positive cognitions associated with the event”) on a scale from 1-7 (not at all – very much).

We assessed *mood* using the Multidimensional Mood Questionnaire (MDBF, Steyer, Schwenkmezger, Notz & Eid, 1994), indexing three mood dimensions in German language, with good psychometric properties ( $\alpha = .86-.94$ ).

Internal consistency for the ADS-K ( $\alpha = .88-.95$ ), the NEO-FFI ( $\alpha = .72-.87$ ) and both subscales of the ERQ (cognitive reappraisal  $\alpha = .89-.90$ ; expressive suppression  $\alpha = .76-.80$ ) have reported to be acceptable to very good (Hautzinger et al., 1993; Borkenau & Ostdorf, 2007; Abler & Kessler, 2011).

We assessed *decision making* using the Iowa Gambling Task (IGT) (Bechara, Damasio, Damasio, & Anderson, 1994). The IGT is a standardized, clinically-used laboratory measure of real-life decision-making that factors uncertainty of premises and outcomes as well as variable rewards and punishments. For IGT performance scores, a total net score and separate

net scores were calculated. The total net score results from subtracting the disadvantageous deck choices from the advantageous choices during the entire test. The same procedure can be calculated for each block to derive separate net scores. Total score, quartiles and quintiles were computed, indexing the ratio of advantageous to disadvantageous choices during the course of the task.

Additional questionnaires were completed at *baseline session*, including demographics, psychopathology (German version of the short form of the Center for Epidemiologic Studies-Depression Scale (ADS-K: Hautzinger, Bailer, Hofmeister, & Keller, 1993), personality traits (NEO Five-Factor Inventory (NEO-FFI, German version: Borkenau & Ostendorf, 2007) and emotion regulation styles (Emotion Regulation Questionnaire, ERQ, German version: Abler & Kessler, 2011).

### **Statistical Analyses**

Group differences in sociodemographic and other measures for the four groups were computed using independent t-tests or  $\chi^2$ -statistics. We computed intraclass correlations of baseline levels of our dependent variables to test for random subject effects. Participants did not differ significantly in the baseline measurement of these variables (all  $F > 3.08$ ,  $p > .081$ ). We used ANCOVAs for testing our main hypotheses, controlling for the small interindividual variability by adding baseline levels of dependent variables, as well as age and sex as covariates based on recent recommendations (Polania, Nitsche & Ruff, 2018). Models were run with the between-subject factors task (reappraisal vs control) and stimulation (anodal vs sham). We measured effects over time (within-subject) for valence, arousal, mood and evaluations (see Figure 1), and simple group effects for decision making outcome, as this was indexed at follow-up, i.e. only at one timepoint.

We were specifically interested in the interaction between task x stimulation x time, hypothesizing that tDCS may lead to enhancements on reappraisal outcomes over time that are greater than effect on other tasks. In line with this directed hypothesis, we tested the three-

way interactions using a one-tailed significance level of  $p < 0.05$ , all other undirected analyses were tested at two-tailed  $p < 0.05$ . All statistical analyses were performed in PASW Statistics version 24.0 (IBM, Switzerland) and R (R Core Team, 2017).

## Results

There were no group differences in key demographic, personality and clinical variables between the four groups (tDCS reappraisal, tDCS control, sham reappraisal, sham control), see Table 1.

### **Reappraisal effects on memory characteristics, evaluations and decision making**

Groups did not differ in memory characteristics at baseline. They rated their memory as equally negative, according to the memory valence rating:  $F(3, 93) = 0.98, p = .406, \eta^2 = .031$ . There were also no group differences in arousal ( $F(3, 91) = 0.58, p = .631, \eta^2 = .019$ ) or memory-related evaluations ( $p > .897$ ) at baseline. Following reappraisal, repeated measures for memory valence revealed significant interactions of task x time ( $F(1, 93) = 8.79, p = .004, \eta^2 = .086$ ), indicating that individuals in the reappraisal condition reported greater decrease in negative valence over time compared to individuals in the control condition (independently of stimulation condition). For arousal, there was a significant interaction of task x time ( $F(1, 91) = 5.32, p = .023, \eta^2 = .055$ ). Participants in the reappraisal condition reported less arousal over time compared to those in the control condition. For evaluations, repeated measures ANCOVA results showed no significant task x time interaction for negative evaluations ( $F(1, 94) = 0.27, p = .603, \eta^2 = .003$ ) or positive evaluations ( $F(1, 94) = .001, p = .957, \eta^2 < .001$ ) (Figure 3). Participants in the reappraisal condition did not differ from those in the control condition in decision making, as indexed by the gambling

task, i.e., no significant effect of task on total score, all four quartiles and all five quintiles (all:  $F(1, 90) > 0.97$ ,  $p > .326$ ,  $\eta p^2 > .011$ )

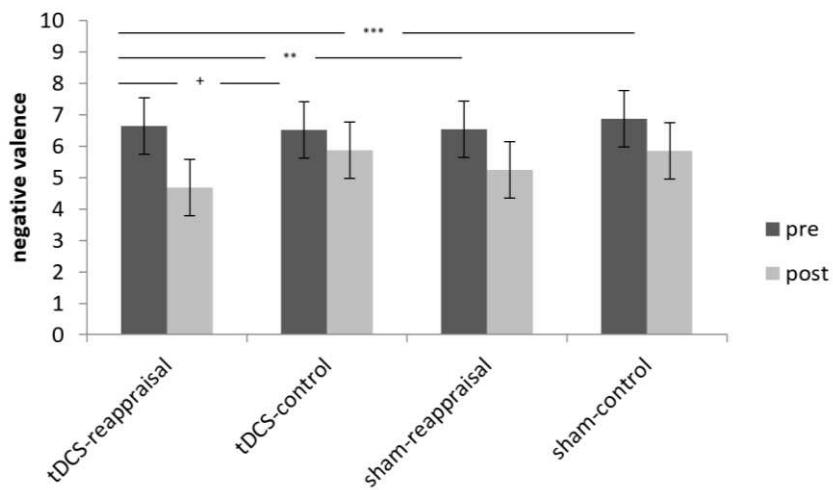
### **TDCS effects on reappraisal outcomes**

There were no group differences in participants' perceived stimulation group membership (active tDCS vs sham stimulation), confirming participants' blindness to stimulation condition ( $\chi^2 (1, N= 101) = 1.67$ ,  $p = .196$ ).

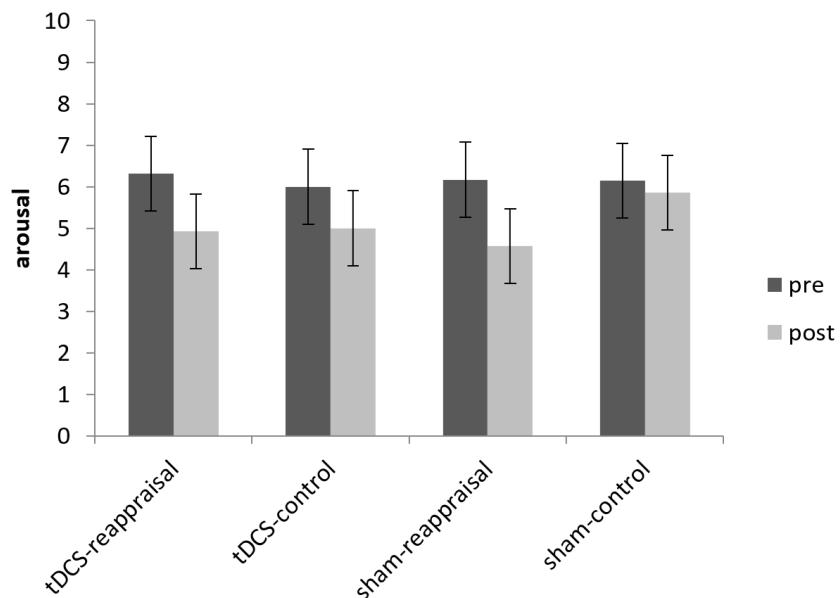
Repeated measures ANCOVA results for valence revealed no significant interaction for stimulation x time ( $F(1, 93) = 0.09$ ,  $p = .764$ ,  $\eta p^2 = .001$ ), but for the hypothesized three-way-interaction task x stimulation x time ( $F(1, 93) = 4.68$ ,  $p = .033$ ,  $\eta p^2 = .048$ ), see Figure 2. LSD post-hoc t-tests showed that participants who had reappraised under active tDCS described their emotional memories as less negative compared to those in the control condition under sham stimulation (-1.01, 95%-CI[-1.78, -0.24],  $p = .011$ ), or under tDCS (-1.26, 95%-CI[-2.03, -.48],  $p = .002$ ), as well as to those who reappraised under sham stimulation (-.695, 95%-CI[-1.47, -.082],  $p = .079$ ). Follow-up simple effects revealed a significant task x time interaction in the tDCS ( $F=12.37$ ,  $p=.001$ ), but not in the SHAM group ( $F=.822$ ,  $p=.294$ ). There were significant time effects for both the reappraisal and control condition in both the tDCS and the SHAM group (tDCS: reappraisal:  $T=5.21$ ,  $p<.001$ ; control condition:  $T=2.70$ ,  $p=.013$ ; SHAM: reappraisal:  $T=4.36$ ,  $p<.001$ ; control condition:  $T=4.612$ ,  $p>.001$ ).

The groups did not differ in the amount of arousal they experienced in association with their memory. There was no significant interaction of stimulation x time ( $F(1, 91) = 0.73$ ,  $p = .4$ ,  $\eta p^2 = .008$ ) or the three-way-interaction task x stimulation x time ( $F(1, 91) = 1.68$ ,  $p = .198$ ,  $\eta p^2 = .018$ ).

A



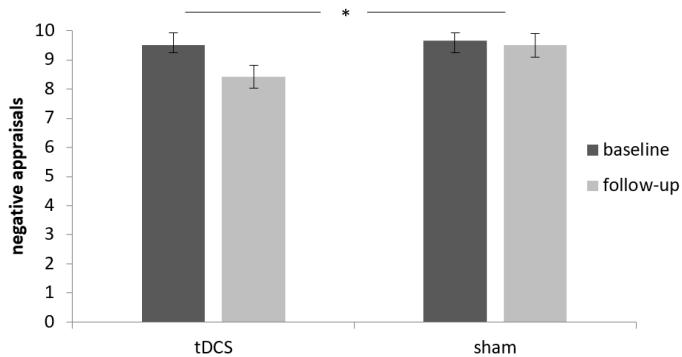
B



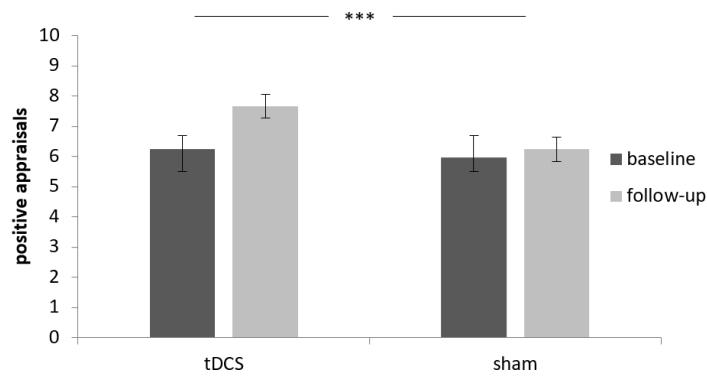
**Figure 2.** Results from repeated-measure ANCOVA for memory-related arousal and valence ratings during the experimental session. Depicted are differences in negative valence (A) and arousal (B) pre- and post- reappraisal for the four groups (tDCS-reappraisal, tDCS-control, sham-reappraisal, sham-control). Differences between groups in arousal were nonsignificant. Error bars represent standard errors (95% CI), \*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$ .

For negative evaluations, repeated measures ANCOVA revealed a significant interaction for stimulation x time ( $F(1, 94) = 4.5, p = .037, \eta^2 = .046$ ). Participants in the active tDCS group reported less negative appraisals as compared to individuals with sham stimulation and this effect was independent of whether participants were in the reappraisal or control condition. There was no significant three-way-interaction task x stimulation x time ( $F(1, 94) = 2.33, p = .13, \eta^2 = .024$ ). Further, ANCOVA for positive appraisal showed a significant interaction for stimulation x time ( $F(1, 94) = 7.93, p = .006, \eta^2 = .078$ ) with participants in the active tDCS group reporting more positive appraisal over time compared to sham stimulation and this effect was again independent of reappraisal condition. There was no significant three-way-interaction task x stimulation x time ( $F(1, 94) = .001, p = .957, \eta^2 < .001$ ) (Figure 3).

A



B



**Figure 3.** Results from repeated-measure ANCOVA for negative and positive appraisals. Depicted are differences in negative appraisals (A) and positive appraisals (B) at baseline versus follow-up sessions for the two stimulation groups, tDCS versus sham stimulation. Error bars represent standard errors (95% CI). Covariates sex and age. Error bars represent standard errors (95% CI), \*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$ .

We observed no significant stimulation x time interaction (all  $F(1, 94) > 0.85$ ,  $p > .36$ ,  $\eta^2 > .009$ ) or task x time (all  $F(1, 94) > 0.82$ ,  $p > .366$ ,  $\eta^2 > .009$ ) on mood. There were also no significant effects of stimulation on decision making (all  $F(1, 90) > 1.36$ ,  $p > .246$ ,  $\eta^2 > .015$ ), and no significant interactions between task and stimulation (all  $F(1, 90) > 1.37$ ,  $p > .246$ ,  $\eta^2 > .015$ ).

### Discussion

Reappraisal is an emotion regulation strategy that enables individuals to change an emotional response by reinterpreting the meaning of the emotional stimulus (Ochsner & Gross, 2005). The current study investigated whether noninvasive brain stimulation using tDCS over the right dlPFC modulates reappraisal. Whereas previous tDCS studies mostly investigated reappraisal of standardized material, such as standardized emotional pictures, we investigated individuals' capacity to reappraise personal emotional memories. Our results thus provide a more nuanced and clinically relevant view on modulating reappraisal. We first corroborated previous findings that reappraising personal emotional memories leads to more positive outcomes compared to a control condition. Emotional memories were rated as less negative and associated with less arousal in the reappraisal compared to the control condition where individuals engaged in factual memory-related thoughts. Noninvasive tDCS over the dlPFC significantly modulated some, but not all of these reappraisal effects and we found an effect on the negativity which the emotional memory was perceived after compared to before

reappraisal under tDCS. As hypothesized, participants who received tDCS stimulation while reappraising their emotional memory experienced the memory as less negative compared to those who reappraised under sham stimulation. These results mostly applied to the immediate effects, as participants showed comparable effects on positive and negative self-reported evaluation independent of reappraisal or control condition at 1-week follow-up. Interestingly, tDCS alone had an effect on negative appraisals, which were reported as less negative following tDCS compared to sham, independent of whether participants reappraised their memory or not, i.e. the control condition.

We found that participants who reappraised a negative emotional memory perceived this memory as less negative following the reappraisal and this effect was stronger than in the control group which engaged in factual memory-related thoughts rather than reappraising. We were specifically interested in whether this effect could be modulated by tDCS. As hypothesized, individuals who reappraised under active tDCS reported most favorable reappraisal outcomes, and showed significant additional reductions in negative valence of their memory that exceeded reductions reported by the other groups. These results mostly applied to the immediate effects, as all groups showed comparable effects on positive and negative self-reported appraisal at 1-week follow-up. This may not be surprising, as we studied reappraisal in healthy participants, where such effects may be less pronounced. Indeed, our participants already entered the study with rather high levels of reappraisal capacity at baseline. Most previous studies have indexed immediate effects of reappraisal, although one study did show reduced levels of self-reported negative responses to distressing autobiographical memories one week after a reappraisal training (Schartau et al., 2009). It is also of note that participants in all groups activated their memory several times throughout the experiment, which presumably also led to decreases in memory-related negative valence and arousal.

We assessed multivariate reappraisal outcomes, including a behavioral decision-making task. There were, however, no effects of reappraisal or tDCS-boosted reappraisal on decision making. This may partly due to the facts that participants in our study generally scored high in this task and future studies should investigate further behavioral effects, for instance by using other, potentially more sensitive tasks or diary-based daily decision assessments in everyday life (e.g. Bjälkebring et al., 2016).

Whilst there were no interaction effects on follow-up measures, there was a main effect of tDCS on some of these outcomes. Interestingly, tDCS stimulation enhanced affective processing independently of the reappraisal condition, leading to more positive and less negative appraisal at 1-week follow-up in participants with active tDCS. Such results are in accord with previous findings that tDCS over the ventromedial PFC modulates emotional face processing (Winkler et al., 2019) and that anodal tDCS over the right dlPFC reduces negative affect in healthy smokers (Pripfl & Lamm, 2015). A recent review suggested that tDCS application, independent of additional psychosocial intervention, might be equally effective in decreasing negative affect as antidepressant medication (Brunoni et al., 2016). Future studies are warranted into these effects and the active mechanisms of tDCS, including the neural mechanisms involved in mediating these effects. This is particularly important since tDCS is rather unfocal spatially, and since its precise neural effects are debated (Bestmann et al 2015). Our current results, and those of previous studies, therefore only show that the stimulation is effective, but not by what mechanisms and how it could be optimized. One way to approach this question in future studies would thus be to combine the existing protocols with neuroimaging and/or some more mechanistic models of the specific neuro-cognitive processes potentially targeted by the tDCS (Polania et al, 2018).

Our study is not without limitations. We investigated healthy participants who reappraised a negative personal autobiographical memory. To what extend our results can be generalized to other, clinical populations remains to be investigated. Reappraisal training was delivered via

an audio-guide, which maximises standardization, but might, in some cases, not have paid attention to individual negative distorted thoughts. Thus, reappraisal in a face-to-face therapeutic setting might be more effective by targeting individual cognitions and emotions. We chose to compare reappraisal to an active control condition for which individuals had to recall external facts and information, without an explicit focus on cognitive or emotional aspects. While both interventions led to significant changes, the significant interaction effect of task x time on perceived negative valence indicates that reappraisal had stronger effects on this outcome compared to the control condition. However, since tDCS is not temporally specific to only the reappraisal phase of our protocol, our results do not imply that the stimulation only exerted its effect by selectively modulating this cognitive process, rather than also retrieval of the memory. With respect to stimulation, we focused on one stimulation site suggested by recent research (right dlPFC). However, other studies have shown that the ventromedial, rather than the dlPFC effectively impacts on reappraisal using tDCS (Marques, Morello & Boggio, 2018). Further studies are thus needed to investigate both regions concurrently using personal emotional material, such as the negative emotional autobiographical memories studied here. Besides, several studies stimulated the left dlPFC, rather than the right dlPFC, as we did here, and these found significant effects (e.g., Peña-Gómez et al., 2011). It would thus be relevant to directly study whether or not there are hemispheric differences in the effectiveness of dlPFC tDCS effects on reappraisal. Finally, we investigated reappraisal of idiosyncratic personal memories and these varied between participants in valence and content. Although we randomized participants into experimental groups and the groups did not differ on key memory characteristics, we cannot fully exclude that there were nevertheless differences between our groups. These limitations of our study are met by a number of key strengths, including a rather large sample size, precise localization of stimulation sites using neuronavigation in a significant subgroup of our participants, high

external validity of our task and relevance to modulation of negative memories using reappraisal in psychotherapy.

Together, our results indicate that tDCS may enhance reappraisal, at least in the short-term. If replicated, such effects could in turn be exploited in promising ways in multiple settings. The non-invasiveness of tDCS and its effectiveness at small current strengths may offer ample opportunities for use in clinical settings, and future studies should focus on trying to optimize the relevant protocols by providing a more mechanistic understanding of how exactly tDCS may enhance the effectiveness of reappraisal. Future studies should also expand this investigation to reappraisal of ongoing personal experiences, rather than emotional memories from the past, which might be more challenging to implement and to modulate (see Holland & Kensinger, 2013; Kross et al. 2009). In any case, reappraisal constitutes a core ingredient of many clinical applications, such as CBT, and tDCS could be used to optimize them (Abend et al., 2016). Such evidence-based psychotherapeutic approaches belong to the first-line treatments of most psychiatric disorders, but they are still in dire need for improvement (Holmes, Craske, & Graybiel, 2014). Noninvasive methods of boosting key processes of such treatments would be much warranted and our results suggest a potential way to optimize CBT.

### **Open science statement and data availability**

All anonymized data and analyses scripts based on R are available from the corresponding author and will also be made available on OSF. We also share upon request from the corresponding author our audioscripts used in reappraisal and control conditions.

### **Author contributions**

ND, CR and BK developed the study concept. ND and RB performed the study setup and data collection, with general support from MM, CR and BK. ND and RB performed the data analysis and interpretation under the supervision of BK and CR. ND drafted the paper, and

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RB, MM, CR, ES and BK provided critical revisions. All authors approved the final version of the manuscript for submission.

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**Tables****Table 1: Demographic, Personality and clinical variables and tests for group differences**

Variable	Healthy Participants (N=101)				Statistic <sup>1</sup>	p-value
	Reappraisal-tDCS (N = 25)	Reappraisal-sham (N=25)	Control-tDCS (N = 25)	Control-sham (N = 26)		
Female sex (%)	16 (64)	14 (56)	15 (60)	16 (61.53)	.35	.950
Age [95% CI]	24.36 [22.89- 25.83]	23.21 [21.98- 24.43]	24.96 [23.26- 26.66]	23.85[22.15- 25.54]	.29	.834
Memory age (months past) [95% CI]	74.28 [47.23- 101.33]	56.44 [36.21- 76.67]	74.60 [45.32- 103.88]	75.77 [49.09- 102.45]	.29	.834
Subjective distress at retrieval [95% CI]	4.00 [3.31-4.69]	4.04 [3.43-4.65]	3.56 [2.85-4.27]	3.77 [3.17-4.37]	.49	.689
Suppression (ERQ) [95% CI]	14.12 [12.41- 15.83]	13.80 [11.47- 16.13]	13.44 [11.66- 15.22]	14.19 [12.40- 15.98]	.14	.938
Reappraisal (ERQ) [95% CI]	30.28 [27.63- 32.93]	27.60 [25.49- 29.71]	29.12 [27.55- 30.69]	27.88 [25.06- 30.71]	1.15	.330
Extraversion (Neo-FFI) [95% CI]	43.16 [41.02- 45.30]	41.92 [40.17- 43.67]	42.56 [40.05- 45.07]	41.38 [39.53- 43.24]	.59	.624
Neuroticism (Neo-FFI) [95% CI]	31.12 [28.98- 33.26]	32.80 [31.26- 34.34]	32.68 [30.75- 34.61]	33.00 [31.20- 34.80]	.91	.438
Openness (Neo-FFI) [95% CI]	35.16 [33.74- 36.58]	34.64 [33.46- 35.82]	33.40 [32.17- 34.63]	34.85 [33.49- 36.20]	1.48	.224
Agreeableness (Neo-FFI) [95% CI]	35.28 [34.24- 36.32]	35.00 [33.34- 36.66]	35.64 [34.16- 37.12]	35.81 [34.37- 37.24]	.28	.841
Conscientiousness (Neo-FFI) [95% CI]	42.24 [39.97- 44.51]	43.44 [41.15- 45.73]	42.40 [40.48- 44.32]	41.50 [39.39- 43.61]	.59	.623
Depressive symptoms (CES-D) [95% CI]	5.44 [3.82-7.06]	7.72 [5.84-9.60]	5.28 [4.027-6.53]	6.54 [4.84-8.24]	2.03	.114

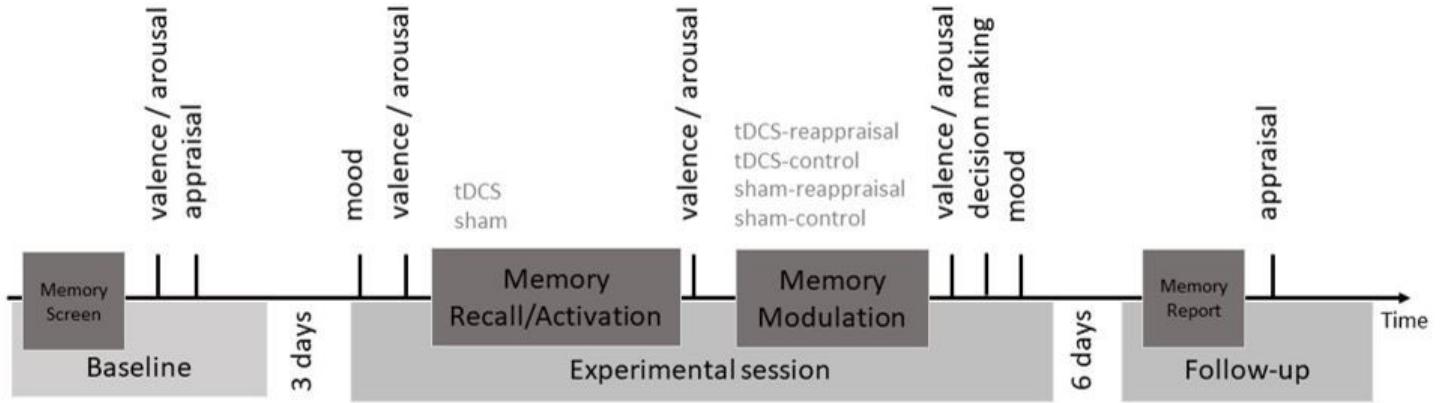
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Mood (MDBF-A) [95% CI]	18.40 [17.73- 19.07]	17.32 [16.42- 18.22]	18.20 [17.59- 18.81]	17.27 [16.27- 18.27]	2.20	.092
Tiredness (MDBF-A) [95% CI]	15.36 [14.28- 16.44]	14.92 [13.83- 16.01]	14.88 [13.91- 15.85]	15.04 [13.79- 16.29]	.16	.921
Calmness (MDBF-A) [95% CI]	16.36 [15.52- 17.20]	15.24 [13.98- 16.50]	16.60 [15.52- 17.68]	15.69 [14.53- 16.85]	1.35	.262

*ERQ*, Emotion Regulation Questionnaire; *NEO-FFI*, NEO-Five Factor Inventory; *ADS-K*, German version of the short form of the Center for Epidemiologic Studies-Depression Scale, *MDBF-A*, Multidimensional State Questionnaire Version A

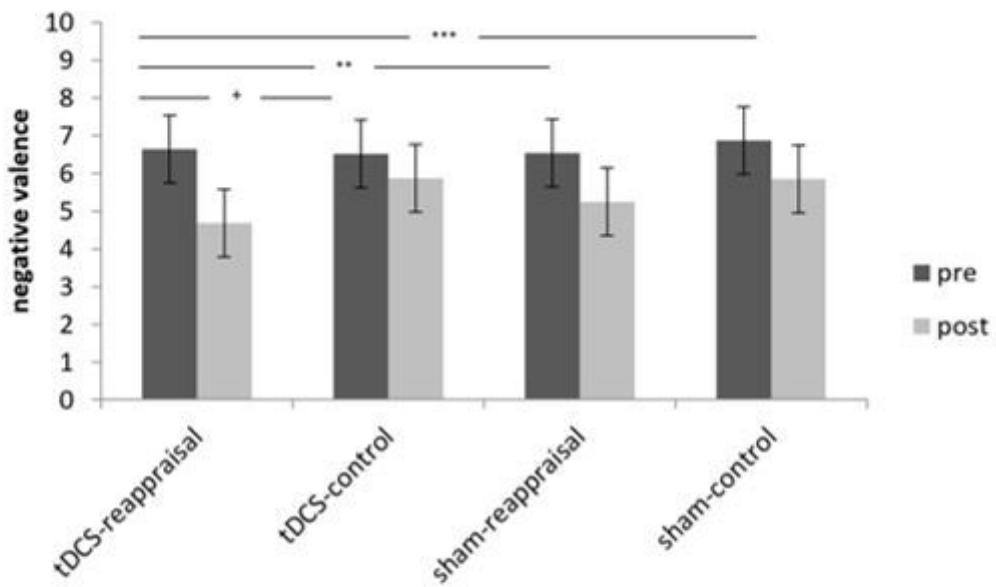
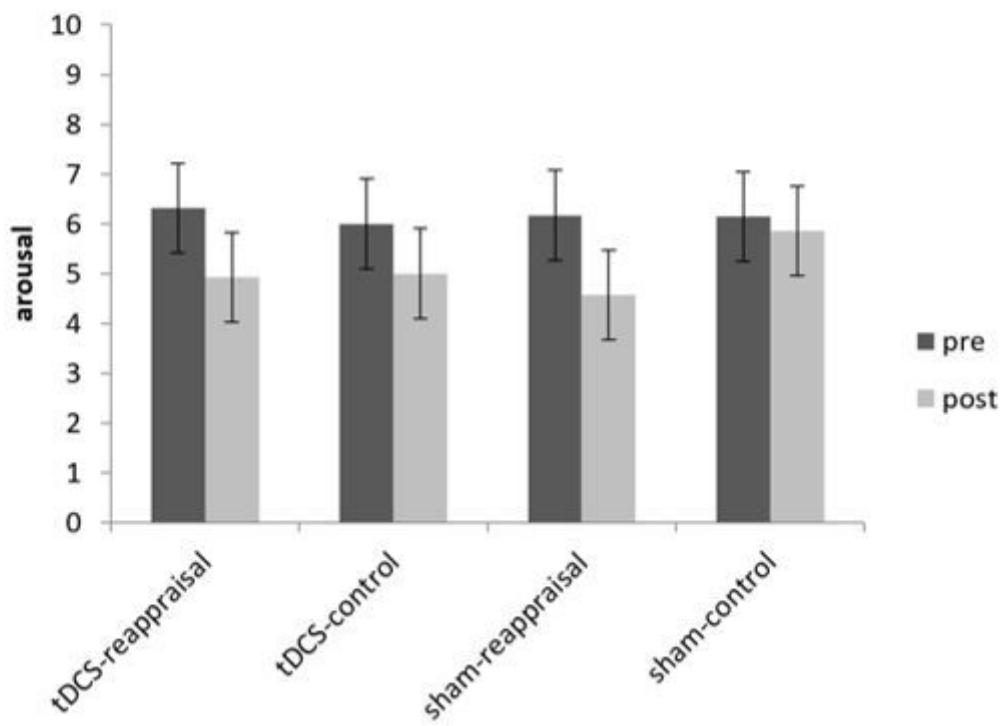
<sup>1</sup>  $\chi^2$ -tests for categorical data, ANOVA *F*-test for continuous data

# Figures

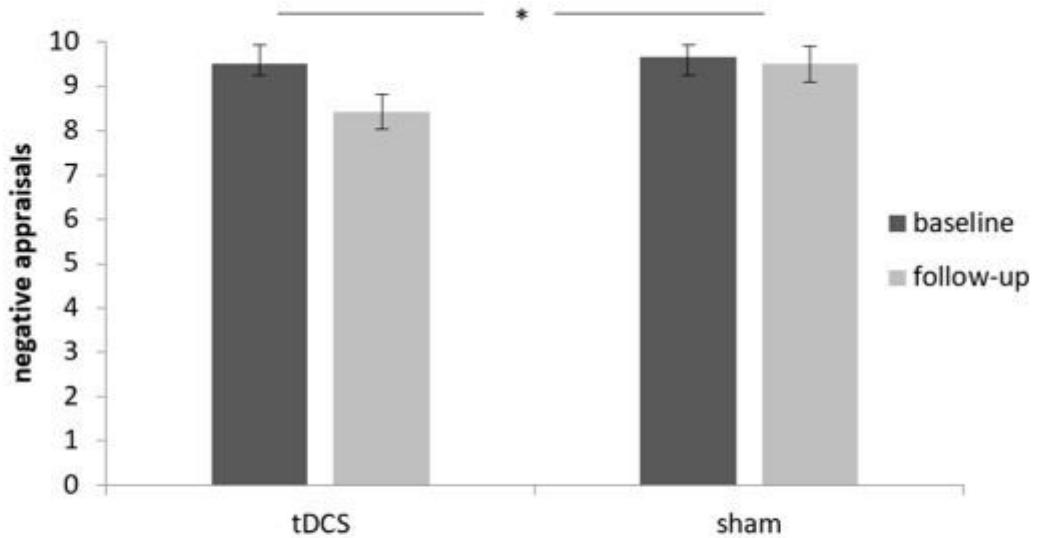
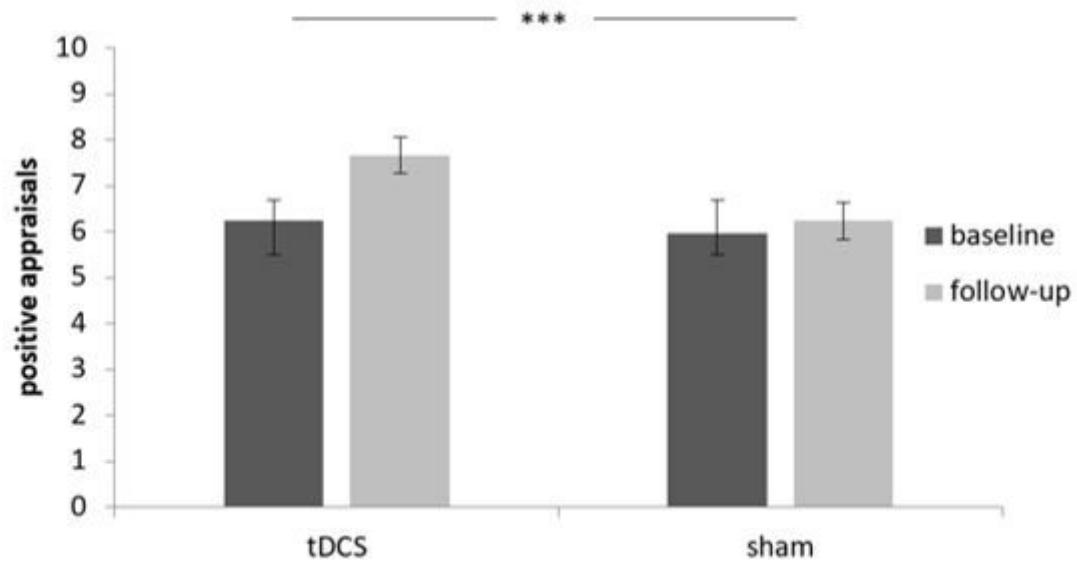


**Figure 1**

Timeline of the experiment. At baseline, participants' negative emotional memory was screened and participants rated valence, arousal of the memory and evaluations (memory screen). During the experimental session, participants completed a mood state questionnaire and again rated valence and arousal (memory recall/activation). Anodal or sham tDCS was applied over participants' right dlPFC. The tDCS stimulation began 3 minutes prior to the beginning of the testing, to allow neuroplastic effects to stabilize. In these three minutes, participants engaged in a standardized breathing protocol (see above). To minimize the cutaneous sensation of current onset and offset, tDCS was ramped up in the beginning to maximum intensity over a period of 5 seconds and ramped down over 5 seconds in the end. Stimulation was applied for 20 consecutive minutes throughout the experiment, starting from the beginning of the experimental session and continued throughout the experiment. Participants then rated valence and arousal of the memory. They then listened to the reappraisal or the control audio tape for memory modulation and completed valence and arousal ratings (memory modulation). Decision making and mood were assessed. During follow-up, positive and negative evaluations were assessed.

**A****B****Figure 2**

Results from repeated-measure ANCOVA for memory-related arousal and valence ratings during the experimental session. Depicted are differences in negative valence (A) and arousal (B) pre- and post-reappraisal for the four groups (tDCS-reappraisal, tDCS-control, sham-reappraisal, sham-control). Differences between groups in arousal were nonsignificant. Error bars represent standard errors (95% CI), \*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$ .

**A****B****Figure 3**

Results from repeated-measure ANCOVA for negative and positive appraisals. Depicted are differences in negative appraisals (A) and positive appraisals (B) at baseline versus follow-up sessions for the two stimulation groups, tDCS versus sham stimulation. Error bars represent standard errors (95% CI). Covariates sex and age. Error bars represent standard errors (95% CI), \* p< .05, \*\* p< .01, \*\*\* p< .001.