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ORIGINAL ARTICLE

Does Transcranial Direct Current Stimulation Affect Post-stressor Intrusive Memories and Rumination? An Experimental Analogue Study

Maria Voss[1] · Thomas Ehring[1] · Larissa Wolkenstein[1]

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Abstract

Deficits in cognitive control have been linked to intrusive memories after traumatic life events as well as rumination. However, causal relations are still unclear. Causality can be investigated by directly influencing a brain region associated with cognitive control via transcranial direct current stimulation (tDCS). In this study, we investigated the effects of tDCS over the left dorsolateral prefrontal cortex (dlPFC) on one aspect of cognitive control—resistance to proactive interference (PI)—as well as on intrusive memories and rumination. Using a between-subject design, we expected active tDCS to affect intrusive memories and rumination by influencing resistance to PI. $N = 118$ healthy individuals completed the modified California Verbal Learning Test twice, once without stimulation and once during 20-min tDCS (anodal, cathodal, or sham). Following tDCS, participants watched a trauma film; afterwards, intrusive memories and rumination were assessed. TDCS neither affected resistance to PI nor film-related intrusive memories or rumination. Furthermore, individuals with low resistance to PI did not experience more intrusive memories or rumination. These results question the role of the left dlPFC as well as the well-established link between resistance to PI and intrusive memories. Future studies are needed to replicate these findings and to address possible methodological shortcomings of this study.

Keywords tDCS · dlPFC · Cognitive control · Proactive interference · Intrusive memories · Rumination

Natural disasters, armed conflicts, accidents, or interpersonal violence: many individuals experience a life-threatening event at least once in their life. However, only a minority develops persistent symptoms of post-traumatic stress disorder (PTSD), including trauma-related intrusive memories and rumination (Kilpatrick et al. 2013). Intrusive memories are unwanted recurring memories of the traumatic event that often take the form of sensory fragments of the experience (APA 2013). In contrast, rumination is a maladaptive processing style that is experienced as uncontrollable repetitive verbal thinking about the trauma, its causes, and consequences (Ehlers and Clark 2000; Ehring et al. 2008). Both phenomena include difficulties in controlling unwanted memories and/or thoughts that grab an individual's attention and affect current behavior. There is growing evidence that these difficulties are linked to individual differences in cognitive control as a basic cognitive mechanism (Aupperle et al. 2012; Joormann et al. 2010; Polak et al. 2012; Whitmer and Gotlib 2013).

Cognitive control comprises meta-level functions that are associated with working memory and keep thoughts or actions focused on goals despite goal-irrelevant interferences (e.g., Miyake et al. 2000). Since traumatic representations in long-term memory are easily activated by internal or external cues, cognitive control is needed to prevent them from intruding into consciousness and from interfering with goal-directed behavior (Wessel et al. 2008). Thus, individuals with limited cognitive control might be unable to ignore those cues and therefore experience persistent intrusive memories. Furthermore, persistent rumination might be maintained by a limited capacity to update cued negative representations in working memory and to inhibit currently irrelevant information (e.g., Brinker et al. 2013; De Lissnyder et al. 2012; Vanderhasselt et al. 2013; Zetsche et al. 2012). Indeed, associations of intrusive memories and rumination with deficits in cognitive control have been empirically demonstrated across clinical and healthy samples (e.g., Beckwé et al. 2014; Brewin and Beaton 2002; Brewin and Smart 2005; Klein and Boals 2001; Joormann

✉ Larissa Wolkenstein
Larissa.Wolkenstein@psy.lmu.de

[1] LMU Munich, Leopoldstrasse 13, 80802 Munich, Germany

and Gotlib 2008; Polak et al. 2012). However, causality remains unclear: pre-trauma deficits in cognitive control might be a risk factor for intrusive memories and rumination, but intrusive memories and rumination might also induce stress levels that in turn reduce performance in cognitive control tasks.

Establishing causality in the context of post-trauma symptomatology is difficult. It requires the manipulation of relevant processes either pre- or shortly post-trauma, a procedure that posits serious practical and ethical challenges. Therefore, the trauma film paradigm if often used as a laboratory analogue, whereby healthy individuals are confronted with a film depicting traumatic situations. In doing so, stressor-related intrusive memories and rumination can be assessed, and their modulation by experimental manipulations of key processes can be tested (Holmes and Bourne 2008). Earlier studies have used the trauma film paradigm to investigate the relationship between cognitive control and the development of intrusive memories (e.g., Verwoerd et al. 2011; Wessel et al. 2008). These studies have focused on resistance to proactive interference (PI), a specific aspect of cognitive control that describes the inhibition of information that is no-longer relevant in working memory (Friedman and Miyake 2004). For example, Verwoerd et al. (2011) showed that a poor ability to resist PI, as measured by a modified California Verbal Learning Test (CVLT), is linked to more intrusive memories 1 week after watching a trauma film in a healthy sample. Thus, first evidence suggests that low ability to overcome PI might be a vulnerability factor for intrusive memories after a stressful event. Nevertheless, due to the design of previous studies, it cannot be ruled out that both, PI and intrusive memories, are affected by a third variable and thus do not causally influence each other.

Therefore, the present study aimed at modulating activation in a brain region that is associated with cognitive control and, in particular, resistance to PI to investigate causal effects on intrusive memories and rumination. A well-established method to induce such a modulation is transcranial direct current stimulation (tDCS). This safe, non-invasive, and effective method manipulates cortical excitability in a specific brain area by hyper- or depolarization of resting membrane potentials (Nitsche and Paulus 2001; Priori 2003; Wassermann and Grafman 2005). Whereas cathodal stimulation decreases cortical excitability, anodal stimulation increases cortical excitability. When applied for several minutes, these tDCS-induced changes persist for at least 1 h (Nitsche et al. 2008). We proposed the left dorsolateral prefrontal cortex (dlPFC) to be a promising target brain area for such a modulation, for a number of reasons.

Firstly, cognitive control in general but also interference resolution in particular are linked to frontal cortices, with the dlPFC being an important component of this network (e.g., Blasi et al. 2006; Bunge et al. 2001; Curtis and D'Esposito 2003; Dulas and Duarte 2016; Nee et al. 2007b; Postle et al. 2001, 2004; Wolf et al. 2010). For example, Wolf et al. (2010) used a PI task with varying contextual demands and investigated corresponding activity in different brain regions. They proposed that increased cognitive control exerted by the left dlPFC is relevant for decreasing susceptibility to PI. Secondly, the dlPFC has been associated with controlling unwanted memories and thoughts as well as with symptoms of PTSD (e.g., Anderson et al. 2004; Arnsten et al. 2015; Clark et al. 2003). For instance, in a suppressing versus recalling task of memory contents, healthy individuals showed greatest dlPFC activation when intrusive memories needed to be controlled and individuals with negative coupling between dlPFC and hippocampus during early suppression attempts experienced fewer intrusive memories later on (Benoit et al. 2014). Thirdly, beneficial effects of anodal tDCS and detrimental effects of cathodal tDCS over the left dlPFC on cognitive control have been documented in previous research (Andrews et al. 2011; Fregni et al. 2005; Wolkenstein and Plewnia 2013; Wolkenstein et al. 2014; Zaehle et al. 2011). Moreover, it has been shown that the effect of anodal tDCS over the left dlPFC on state rumination, as measured several minutes after stimulation termination, is mediated by an enhancement of cognitive control in healthy individuals (Vanderhasselt et al. 2013). In sum, in the current study we focus on the left dlPFC as there is consistent evidence that it plays a major role in cognitive control, including resistance to PI. However, it should of course be noted that resistance to PI and the control of intrusive memories and rumination can be expected to be supported by a complex inhibitory network, involving different brain regions that might also be promising targets for tDCS in future research (e.g., Anderson et al. 2015; Badre and Wagner 2005; Blasi et al. 2006; Caplan et al. 2007; D'Esposito et al. 1999; Feredoes et al. 2006; Johnson et al. 2001; Kühn et al. 2012; Nee et al. 2007a).

Overall, the major goal of this randomized, sham-controlled, double-blind analogue study was to identify causal relations between cognitive control and intrusive memories/rumination in a healthy sample. To achieve this goal, we manipulated the activity of the left dlPFC via anodal and cathodal tDCS and explored the impact of this manipulation on resistance to PI as an indicator of cognitive control. We hypothesized cathodal tDCS to decrease and anodal tDCS to increase resistance to PI, compared to sham stimulation (H1). Furthermore, we examined offline effects of tDCS on intrusive memories and rumination after a trauma film to further clarify the role of pre-stressor differences in cognitive control for re-experiencing. As mentioned above, tDCS effects last for at least 1 h (e.g., Nitsche et al. 2008) and offline designs have been used successfully in former studies (e.g., Dedoncker et al. 2016a; Hill et al. 2016; Vanderhasselt et al. 2013; Wolkenstein et al. 2014). We predicted cathodal tDCS to increase and anodal tDCS to decrease intrusive memories (H2) and rumination (H3) after a trauma film, compared to sham stimulation. Finally, we assumed that higher resistance to PI is associated with less intrusive memories (H4) and less rumination (H5) after the trauma film.

Methods

Design, Randomization, and Blinding

This randomized, double-blind, sham-controlled analogue study followed a between-subject design with the between-factor stimulation condition (anodal vs. cathodal vs. sham). For resistance to PI, time point was an additional within-subject factor (pre vs. post tDCS). Allocation to stimulation condition was randomized via automated randomization software (randomizer.org). For blinding, all participants were informed that they would be randomly assigned to one of three stimulation conditions. These conditions would include 20 min of stimulation but vary in electrode placement and stimulation intensity. The application of predefined codes to start the stimulator further allowed for a computerized double-blind assignment to the sham or verum condition.

Sample

$N = 120$ healthy women between 18 and 40 years were recruited via advertisements at LMU Munich. Two participants were excluded due to violations to the study protocol. The final sample consisted of 118 women with a mean age of 23.32 ($SD = 4.46$). Exclusion criteria were diseases of the central nervous system; cardiovascular, respiratory and neuroendocrine diseases; seizures; first-degree relatives suffering from epilepsy; a history of traumatic brain injury; metallic particles around the head; a cardiac and cerebral pacemaker, cochlea implants and hearing aid devices; strong allergic reactions to sensing electrodes; current pregnancy; left-handedness as assessed by a version of the Edinburgh Handedness Inventory (EHI; Oldfield 1971); psychotropic medication; a substance use disorder with less than 2 years of abstinence; a history of psychiatric disorders as assessed by the M.I.N.I. International Neuropsychiatric Interview for DSM-IV (Ackenheil et al. 1999) and the PTSD Checklist for DSM-5 (PCL-5; Krüger-Gottschalk et al. 2017); and a history of psychological treatment. Inclusion criteria were an educational qualification of university entrance diploma or higher and sufficient knowledge of the German language. We solely included females to preclude effects of gender. The administered stressful film fragment depicted the rape of a woman and thus might be differently processed by male compared to female participants.

tDCS

A direct current of 1 mA was delivered via a battery-driven stimulator (NeuroConn GmbH, Ilmenau, Germany) and a pair of 0.9% NaCL-soaked sponge electrodes (35 cm^2 surface). One electrode was placed on the scalp over F3 according to the international 10–20 system of electrode placement. The reference electrode was placed on the right deltoid muscle. The current was applied for 20 min plus a 5 s fade-in and fade-out phase. The sham stimulation also lasted 20 min with the current being applied only for the first 30 s and then ramped down. Thus, a temporary tingling experience comparable to that induced by verum stimulation was elicited. Active tDCS was only applied during the assessment of resistance to PI and not during the film or the assessment of intrusive memories and rumination.

Stressful Film Fragment

Participants watched a 14 min fragment from “Irréversible” by Gaspar Noé depicting an extreme sexual and physical abuse of a woman. This fragment has been frequently used in trauma film research (Arnaudova and Hagenaars 2017, for an overview). All participants were explicitly informed in the study advertisement and in the informed consent that they would be exposed to a film with violent content. The film was presented on an 18-inch screen in a darkened room.

Outcome Measures

Resistance to PI

We used a modified version of the CVLT (Delis et al. 1987) as used by Verwoerd et al. (2011) to assess resistance to PI. This task was applied with identical parameters on both time points. The test contained two word lists. List 1 consisted of ten names of vegetables, ten names of animals and ten names of flowers. List 2 consisted of ten new names of vegetables, ten new names of animals and ten names of musical instruments. Hence, the two lists shared the categories vegetables and animals. Both lists were matched on word frequency. The order of the two lists was counterbalanced between participants. First, participants were presented the words of List 1 in a randomized order on the computer screen for 1000 ms each, with a 1000 ms inter-stimulus interval. They were instructed to learn the words to the best of their ability. This phase was followed by a 4 min free-recall phase in which participants had to speak out loud all words they could remember. The examiner documented the responses. Second, learning and free recall of List 1 were repeated, with participants being instructed to learn and recall more words than during the first trial. Third, participants again completed the procedure of the first trial but with List 2.

Following Verwoerd et al. (2011), we computed a PI index as a measure of resistance to PI. We multiplied the total number of words recalled on Trial 1 with the total number of shared category words that were recalled on Trials 1 and 2. Next we divided this outcome by the total number of words recalled on Trials 1 and 2 and finally subtracted the number of shared words recalled from List 2 (PI = ((total recall Trial 1 × (recall shared words Trial 1 + Trial 2))/(total recall Trial 1 + total recall Trial 2)) − recall shared words List 2). Higher values on this index indicate poorer resistance to PI.

Post-film Intrusive Memories

We assessed the occurrence of intrusive memories after the film by a 6-item questionnaire based on Weidmann and Papsdorf (2010). The questionnaire began with a short definition of intrusive memories. Subsequently, participants were asked to indicate how often they had experienced intrusive memories during the resting period. They also indicated the percentage of time (from 0 to 100) they had experienced intrusive memories and the predominant quality of them ("thought", "image", "short film scene", "feeling", "sound", "something else", "I do not know", "I did not have intrusive memories"). Additionally, level of distress caused by the intrusive memories, level of vividness of the intrusive memories and level of control were rated on a six-point Likert-scale (1 = "not at all" to 6 = "very").

Post-film Rumination

Rumination after the film was assessed by a modified version of the Perseverative Thinking Questionnaire (PTQ; Ehring et al. 2011). Six items from the original version of the PTQ were excluded because they referred to thoughts unlikely to occur after watching films. The remaining nine items captured the core characteristics of rumination (repetitiveness, intrusiveness, difficulties to disengage), were adapted for measuring film-related rumination (e.g., "I could not stop thinking about the film")[1] and rated on a five-point scale (1 = "never" to 5 = "almost always"). Internal consistency of the questionnaire was excellent (Cronbach's α = 0.946).

Control Measures

Trait Rumination

The habitual use of rumination was measured by the German version of the 10-Item Response Styles Questionnaire (RSQ-10D; Huffziger and Kühner 2012). Participants indicated their thoughts and actions in response to sad or depressed feelings (e.g., "I think 'Why do I always react this way?'") on a four-point scale, ranging from 1 = "almost never" to 4 = "almost always".

Trait Film-Related Intrusive Memories and Rumination

The trait tendency to experience intrusive memories and rumination in response to stressful films was measured by modified versions of the questionnaires for post-film intrusive memories and post-film rumination. This time the participants had to rate their typical responses to films that trigger negative emotions in general. For the frequency of intrusive memories, answers were given on a five-point-scale (1 = "never" to 5 = "always").

Neuropsychological Control Measures

We assessed visual-motor conceptual screening and cognitive flexibility by use of the Trail Making Test (TMT A/B; Reitan 1992) and short-term and working memory capacity by use of a digit span test forward and backward (a version similar to the Wechsler Adult Intelligence Scale; Petermann 2012). These measures were only used to rule out group differences in cognitive functioning prior to tDCS. They were not used as covariates.

Mood and Arousal

To assess possible effects of tDCS and the film scene on participants' mood and arousal, we administered two Self-Assessment-Manikins (SAM; Bradley and Lang 1994) at several time points (see "Procedure"). In the SAMs, participants had to indicate how they felt (1 = "very negative" to 9 = "very positive") and how aroused they were (1 = "very calm" to 9 = "very high arousal").

Film-Related Emotion Regulation

To check whether groups differed in their emotional processing and responding to the film, we assessed participants' spontaneous use of reappraisal and suppression to regulate emotions during film presentation and resting period. Specifically, reappraisal and suppression during the presentation of stressful stimuli have been found to influence emotional distress and post-traumatic symptoms afterwards (e.g., Cavanagh et al. 2014; Dunn et al. 2009). For reappraisal, we used four adapted and slightly rephrased items (e.g., "I changed my thoughts about the film in a way that made me experience less negative emotions") from Ehring et al. (2010) as well as from the Emotion Regulation Questionnaire (ERQ; Gross and John 2003). For suppression, we used four adapted items (e.g., "Whenever possible, I avoided realizing my feelings") from the Heidelberg Form for Emotion

[1] All items used in this study can be obtained upon request.

Regulation Strategies (HFERST; Izadpanah et al. 2017). Participants rated the extent to which the statements applied to them in the period during and after film presentation on a five-point scale (1 = "does not apply" to 5 = "does apply").

Film Exposure and Distress

Participants estimated the amount of time they had looked away from the screen during the film on a five-point scale (1 = "never" to 5 = "almost always"). For measuring subjective distress during the film, participants also indicated their mood (1 = "very negative" to 9 = "very positive") and arousal (1 = "very calm" to 9 = "very high arousal") during film presentation retrospectively on two SAMs. To assess how attentively participants had followed the film, they completed 22 self-generated single choice, multiple choice and open-ended questions about the film (e.g., "What was the color of the victim's handbag?"). We calculated a sum score for correct answers. Moreover, we assessed whether participants had seen the film before and whether they watched similar films frequently.

Procedure

Each participant performed two sessions at the lab with an average inter-session-interval of 7.22 days ($SD = 0.85$). First, sociodemographic and health data were assessed and M.I.N.I. and PCL-5 were administered to check exclusion criteria. Furthermore, participants completed TMT A/B and digit span test, a baseline measurement of the modified CVLT via E-prime, and a set of questionnaires (EHI, RSQ-10D, trait film-related intrusive memories/rumination) via Unipark (EFS Survey, Questback GmbH). At session 2, participants were screened for changes in exclusion criteria and tDCS was applied for 20 min. The modified CVLT started 5 min after the onset of stimulation to reach maximum effects and took 15 min. After that, the room was darkened and the experimenter left the room while the participants watched the film scene. After the film scene, participants were asked to lean back for a moment and do nothing until the experiment would continue after 10 min. Thus, there were no environmental demands that could trigger intrusive memories or rumination (see also Vanderhasselt et al. 2013). Finally, participants completed questionnaires for post-film intrusive memories, post-film rumination, emotion regulation and film exposure and distress via Unipark (EFS Survey, Questback GmbH). SAMs were administered at baseline, after 5 min of tDCS and after resting period. Heart rate and respiration rate were recorded via a respiration belt and three electrodes on the upper body and additional emotional measures were assessed during session 2. However, the obtained data was not subject to this paper.

Data Analyses

Data were analyzed by use of SPSS® Version 24.0. First, we examined whether tDCS groups significantly differed in any of the baseline control measures assessed on t1 to check comparability of groups. Furthermore, we examined group differences for control variables assessed after film presentation, i.e. film-related emotion regulation, film-elicited distress, time looked away and film-related attentiveness. All analyses were performed by use of Analyses of Variance (ANOVAs) and Kruskal–Wallis tests. Additionally, changes in SAM mood and arousal ratings over the course of the experiment were analyzed by use of two separate mixed ANOVAs with the between-subject factor stimulation condition (sham vs. anodal vs. cathodal) and the within-subject factor time point (baseline vs. after tDCS start vs. after resting period). For main analyses, a mixed ANOVA with the between-subject factor stimulation condition (sham vs. anodal vs. cathodal) and the within-subject factor time point (session 1 vs. session 2) was performed on the index of resistance to PI (H1). Effects of tDCS on intrusive memories (H2) and rumination (H3) were analyzed by use of a Multivariate Analysis of Variance (MANOVA) with the number of post-film intrusive memories, the percent of time they have been experienced and post-film rumination as dependent variables. For all subjects who reported intrusive memories, an exploratory MANOVA was conducted to investigate effects of tDCS on level of distress, vividness and control. Next, correlational analyses were performed to test associations between resistance to PI and the intrusive memories measures (H4) as well as rumination (H5). Lastly, in exploratory post-hoc analyses, we examined whether resistance to PI, rumination and number of intrusive memories significantly correlated with any of the control measures and we analyzed the result patterns for CVLT performance in shared and non-shared trials by use of mixed ANOVAs. Moreover, we calculated Bayes factors to quantitate the relative strength of evidence for our main findings. For all correlation analyses, the p values were Bonferroni–Holm-corrected and Greenhouse–Geisser corrected tests are reported when the assumption of sphericity was violated in mixed ANOVAs.

We determined sample size by use of G*power (version 3.1, University of Duesseldorf, Germany; Faul et al. 2007), assuming a statistical power of 0.80 and an alpha level of 0.05. For resistance to PI, we calculated a total sample of 42 participants for the interaction between tDCS condition and time point ($f = 0.25$). For the global effect of tDCS on number of post-film intrusive memories, the percent of time they have been experienced and post-film rumination, we calculated a total sample of 114 participants ($f^2(V) = 0.0625$). Lastly, for correlational analyses, a total sample of 84 ($r = .3$) participants was determined.

Table 1 Descriptive statistics and group differences of the control variables

	Min–max	Sham ($n=40$) *M* (*SD*)	Anodal ($n=40$) *M* (*SD*)	Cathodal ($n=38$) *M* (*SD*)	*p*
Age	18.00–40.00	22.58 (4.50)	24.30 (5.13)	23.08 (3.51)	ns
Inter-session interval	6.00–10.00	7.10 (0.90)	7.40 (0.93)	7.16 (0.68)	ns
TMT-A t1	10.50–50.00	26.73 (9.54)	22.81 (6.31)	23.31 (7.60)	ns
TMT-B t1	21.70–120.00	54.04 (19.00)	49.45 (15.63)	52.78 (15.17)	ns
Digit span forward t1	5.00–12.00	9.00 (1.93)	9.53 (1.28)	9.11 (1.45)	ns
Digit span backward t1	4.00–12.00	7.85 (2.07)	7.83 (2.18)	7.87 (2.11)	ns
Trait rumination t1	10.00–33.00	19.95 (4.55)	20.25 (4.60)	21.47 (5.10)	ns
Trait film-related rumination t1	9.00–36.00	16.70 (5.44)	17.10 (6.08)	17.92 (5.95)	ns
Trait film-related IM t1	1.00–5.00	1.95 (0.71)	2.05 (0.90)	2.21 (1.02)	ns
Trait distress of IM t1	1.00–5.00	2.03 (0.85)	2.24 (1.00)	2.50 (1.07)	ns
Trait vividness of IM t1	1.00–6.00	2.67 (1.06)	2.59 (1.05)	2.82 (1.31)	ns
Trait control of IM t1	1.00–6.00	4.60 (1.35)	4.14 (1.27)	3.93 (1.61)	ns
Film-related suppression t2	4.00–20.00	9.75 (3.83)	10.35 (3.82)	9.87 (3.74)	ns
Film-related reappraisal t2	4.00–20.00	11.58 (3.86)	11.50 (4.62)	11.00 (4.10)	ns
Time looked away t2	1.00–5.00	1.48 (0.88)	1.68 (0.86)	1.74 (0.98)	ns
SAM valence during film t2	1.00–5.00	2.05 (0.88)	2.03 (1.07)	2.29 (1.25)	ns
SAM arousal during film t2	1.00–9.00	7.03 (1.48)	7.60 (1.39)	6.66 (1.92)	.03
Film-related attentiveness t2	9.00–20.00	13.58 (2.71)	14.69 (2.82)	13.53 (2.77)	ns

Analyses for distress, control and vividness of intrusive memories were performed only for individuals who reported to experience intrusive memories at least seldom (sham $n=30$, anodal $n=29$, cathodal $n=28$); anodal $n=39$ for film-related attentiveness

TMT Trail Making Test, *IM* intrusive memories, *SAM* Self-Assessment Manikin, *ns* nonsignificant

Results

The data reported in this study is openly accessible in the associated OSF repository (https://osf.io/bcq6y/).

Descriptive Statistics and Group Differences in Control Measures

Descriptive statistics and group comparisons for control variables are presented in Table 1. 6.8% of participants already knew the film fragment and 32.2% of participants reported having watched similar films before. The amount of time participants had looked away during film presentation was low. Regarding film-related distress, participants reported to have experienced negative mood and to have felt aroused during film presentation. The stimulation groups did not differ in any of the control measures except for their arousal during film presentation, $H(2)=6.88$, $p<.05$, with a mean rank of 55.92 for the sham group, 70.47 for the anodal group and 51.71 for the cathodal group. However, we also compared valence and arousal ratings over time (baseline vs. after tDCS start vs. after resting period). For valence there was a significant main effect of time, $F(1.88, 216.26)=227.67$, $p<.001$, $\eta^2=0.66$, with mood worsening from baseline ($M=6.84$, $SD=1.25$) to tDCS start ($M=6.14$, $SD=1.60$) and from tDCS start to resting period ($M=3.67$, $SD=1.62$). For arousal there was also a significant main effect of time, $F(1.75, 200.99)=107.24$, $p<.001$, $\eta^2=0.48$, with all participants feeling less aroused from baseline ($M=3.78$, $SD=1.98$) to tDCS start ($M=3.11$, $SD=1.87$) and more aroused from tDCS start to resting period ($M=5.97$, $SD=1.84$). However, there was neither a main effect of group nor a group × time interaction (all $ps>.10$).

Resistance to PI

Descriptive statistics for the dependent variables are presented in Table 2. In contrast to H1, the tDCS conditions did not differentially affect resistance to PI as indicated by a non-significant time × group interaction, $F(2, 115)=0.41$, $p=.66$, $\eta^2=0.01$. Unexpectedly, all individuals showed more PI at t2 ($M=2.74$, $SD=2.65$) compared to t1 ($M=0.05$, $SD=2.58$), $F(1, 115)=94.92$, $p<.001$, $\eta^2=0.45$.

Post-film Intrusive Memories and Post-film Rumination

Overall, 22.9% of participants reported intrusive memories during resting period in form of thoughts, 12.7% in form of images, 30.5% in form of a short film scene, 8.5% in form of feelings and 1.7% in form of sounds. 19.5% of participants did not experience any intrusive memories. 1.7% experienced a mix of different modalities and the remaining 2.5% included one participant who did not specify the modality of

Table 2 Descriptive statistics of the dependent variables

	Min–max	Sham ($n=40$) *M* (*SD*)	Anodal ($n=40$) *M* (*SD*)	Cathodal ($n=38$) *M* (*SD*)
CVLT PI t1	−7.53 to 7.36	−0.18 (2.53)	−0.09 (2.56)	0.45 (2.69)
CVLT PI t2	−2.59 to 8.90	2.86 (2.41)	2.42 (2.73)	2.97 (2.83)
Post-film rumination	9.00–45.00	25.05 (8.84)	25.88 (8.94)	23.26 (9.67)
Post-film number of IM	0.00–20.00	4.78 (5.75)	3.93 (3.93)	3.45 (3.17)
Post-film % of time IM	0.00–100.00	31.35 (26.12)	32.33 (30.05)	27.45 (27.60)
Post-film distress of IM	1.00–6.00	3.15 (1.33)	3.77 (1.28)	3.38 (1.35)
Post-film control of IM	1.00–6.00	4.06 (1.39)	3.29 (1.58)	3.66 (1.57)
Post-film vividness of IM	1.00–6.00	3.12 (1.41)	3.81 (1.28)	3.45 (1.24)

Analyses for distress, control and vividness of intrusive memories were performed only for individuals who reported at least one intrusive memory (sham $n=34$, anodal $n=31$, cathodal $n=29$)

CVLT California Verbal Learning Test, *PI* proactive interference, *IM* intrusive memories

Table 3 Spearman-rho-correlation coefficients for the dependent variables

	2.	3.	4.	5.	6.	7.	8.
1. CVLT PI t1	.36**	−.19	−.11	−.15	−.27	.08	−.31*
2. CVLT PI t2	–	−.23	−.22	−.20	−.24	−.06	−.22
3. Post-film rumination		–	.59***	.71***	.65***	−.60***	.40**
4. Post-film number of IM (square-root)			–	.81***	.51***	−.45***	.33*
5. Post-film % of time IM (square-root)				–	.73***	−.57***	.42***
6. Post-film distress of IM					–	−.58***	.60***
7. Post-film control of IM						–	−.45***
8. Post-film vividness of IM							–

Analyses for distress, control and vividness of intrusive memories were performed only for individuals who reported at least one intrusive memory, $n=94$

CVLT California Verbal Learning Test, *PI* proactive interference, *IM* intrusive memories

*$p<.05$; **$p<.01$; ***$p<.001$, two-tailed, Bonferroni–Holm-corrected *p* values are reported

the intrusive memories, one participant who indicated "some kind of paranoia" and one participant who reflected about the quality of the movie. Removing these individuals from analyses did not change the main results. We applied square-root transformations for both intrusive memories measures to improve normality of the data distribution and reduce the impact of one extreme value. Using Pillai's trace, the three tDCS groups neither differed in post-film rumination nor in the two intrusive memories measures, $V=0.02$, $F(6, 228)=0.45$, $p=.84$, $\eta^2=0.01$. These results are in contrast to H2 and H3. Exploratory analyses of effects of tDCS on intrusion-related level of distress, level of vividness and level of control for those individuals who had experienced intrusive memories did also not reveal significant group differences, all $ps>.10$.

Link Between Resistance to PI, Post-film Intrusive Memories and Post-film Rumination

Since tDCS did not differentially affect resistance to PI on t2, post-film rumination or intrusive memories, we explored links between these variables across stimulation groups. Correlations are depicted in Table 3. The more individuals had ruminated during the resting period, the more intrusive memories they had experienced. Furthermore, the more intrusive memories occurred, the more distressing, uncontrollable and vivid they were rated. Surprisingly, there were no significant positive correlations between experience of PI on t2 and number of intrusive memories (H4) or rumination (H5). Since there was a significant change in resistance to PI from t1 to t2, we also calculated correlation coefficients between resistance to PI on t1, rumination and intrusive memories to assess possible associations before any manipulation. However, these correlations patterns were generally in line with the ones found for resistance to PI on t2 (see Table 3) except that a negative correlation between the experience of PI and vividness of post-film intrusive memories still reached significance after Bonferroni–Holm correction.

Post-hoc Analyses

Exploratory Correlation Analyses

Recent research reported that decrements in cognitive performance in the face of stress are relevant for psychopathology (e.g., Quinn and Joorman 2015). Thus, we exploratory analyzed associations between change in PI, as calculated by subtracting PI on t2 from PI on t1, and post-film number of intrusive memories and post-film rumination. However, these analyses did not show substantial correlations, all $ps > .10$. Additionally, we explored correlations between PI on t2, post-film rumination, post-film number of intrusive memories and control measures. After Bonferroni–Holm correction, post-film rumination was still significantly correlated with trait film-related rumination, $r = .47$, $p < .001$, mood during the film, $r = -.54$, $p < .001$, and arousal during the film, $r = .49$, $p < .001$. Similarly, post-film intrusive memories showed significant correlations with a trait tendency for film-related intrusive memories, $r = .33$, $p < .05$, mood during the film, $r = -.35$, $p < .01$, and arousal during the film, $r = .38$, $p < .01$.[2]

Evaluation of the Modified CVLT

Previous research also administering the CVLT reported a between-lists performance decrease for shared trials and a between-lists performance increase for non-shared trials (Verwoerd et al. 2011). For the CVLT on t1, there was no between-lists performance decrease for shared trials ($M = 10.09$, $SD = 2.71$ for List 1; $M = 10.09$, $SD = 2.69$ for List 2), $F(1, 115) = 0.00$, $p = .98$, $\eta^2 = 0.00$, but a significant increase in recall performance for non-shared trials from List 1 ($M = 5.05$, $SD = 1.63$) to List 2 ($M = 5.79$, $SD = 1.60$), $F(1, 115) = 18.78$, $p < .001$, $\eta^2 = 0.14$. In contrast, for the CVLT on t2, all individuals showed a decreased recall performance for shared trials on List 2 ($M = 10.72$, $SD = 3.18$) compared to List 1 ($M = 13.42$, $SD = 3.07$), $F(1, 115) = 108.76$, $p < .001$, $\eta^2 = 0.49$. However, increase in recall performance for non-shared items on List 2 ($M = 6.72$, $SD = 1.72$) compared to List 1 ($M = 6.61$, $SD = 1.65$) did not reach significance, $F(1, 115) = 0.43$, $p = .51$, $\eta^2 = 0.00$. The three tDCS groups did not significantly differ in these results, all $ps > .10$.

[2] Control variables that showed significant correlations with dependent variables were inserted as covariates in the main analyses. However, they did not significantly change the main findings.

Bayesian Analyses

To quantitate the relative strength of evidence for the non-significant findings, Bayesian hypothesis testing was additionally performed. A Bayes factor (BF_{01}) is a statistical index that quantifies how well a hypothesis predicts observed data over an alternative hypothesis (Dienes 2014). We calculated BF_{01} using JASP statistical software version 0.9.0.1 for our main hypotheses (JASP Team 2018). Whereas a $BF_{01} < 1$ implies that a result is more likely to occur under an alternative hypothesis (H_1) than under a null hypothesis (H_0), a $BF_{01} > 1$ indicates that a result is more likely to occur under a H_0 than under a H_1 (Wagenmakers et al. 2011). For the first hypothesis, we expected a significant tDCS × time interaction on PI. A Bayesian mixed ANOVA was performed with default prior scales. The results showed a BF_{01} of 8.387, with the interaction model (assuming the main effects of tDCS and time and their interaction) as the H_1 versus the main-effect model (assuming the main effects only) as the H_0. Thus, there was substantial evidence in favor of the H_0 (Wagenmakers et al. 2011), indicating no interaction between tDCS condition and time. For testing the second and third hypotheses on the effects of tDCS on post-film intrusive memories and post-film rumination, we ran three separate Bayesian ANOVAs with the number of post-film intrusive memories, the percentage of time they have been experienced (both measures square-root transformed), and post-film rumination as dependent variables. The H_1 stated that the three tDCS groups differed in these variables whereas the H_0 stated no group differences. We found a BF_{01} of 8.551 for the number of intrusive memories, a result indicating that the observed data is 8.551 times more likely to occur under the H_0 than under the H_1 and thus providing substantial evidence for no effect of tDCS condition (Wagenmakers et al. 2011). Furthermore, there was $BF_{01} = 9.730$ for percentage of time of intrusive memories and $BF_{01} = 6.321$ for post-film rumination. These analyses also provided substantial evidence in favor of the H_0 (Wagenmakers et al. 2011). Lastly, we calculated Bayesian Pearson correlations for the associations between PI and both post-film intrusive memories measures as well as post-film rumination. In line with our hypotheses, we tested whether the data were more likely to occur under the H_0 (no association between PI and intrusive memories or rumination) or under the H_1 (a positive association between PI and intrusive memories or rumination). Results are depicted in Table 4. Similar to previous analyses, sample correlations were weak and negative. Bayesian analyses implied strong evidence in favor of the H_0, indicating no positive associations between PI and intrusive memories or rumination (Wagenmakers et al. 2011).

Table 4 Bayesian Pearson correlation coefficients

		CVLT PI t2	Post-film rumination	Post-film number of IM (square-root)	Post-film % of time IM (square-root)
CVLT PI t1	*r*	.35	−.21	−.12	−.17
	BF_{0+}	0.003	27.84	18.61	23.72
CVLT PI t2	*r*	–	−.21	−.19	−.19
	BF_{0+}		28.47	26.20	25.63

For all tests, the H_1 specifies that the correlation is positive

CVLT California Verbal Learning Test, *PI* proactive interference, *IM* intrusive memories

Discussion

The present study tested causal relations between cognitive control and intrusive memories as well as rumination in a healthy sample. A brain area associated with cognitive control, the left dlPFC, was stimulated via tDCS. We hypothesized cathodal tDCS to decrease and anodal tDCS to increase resistance to PI, an indicator of cognitive control, as well as cathodal tDCS to increase and anodal tDCS to decrease intrusive memories and rumination after a trauma film. We found neither an effect of tDCS on resistance to PI nor on intrusive memories or rumination. Furthermore, we expected individuals with higher resistance to PI to show less intrusive memories and less rumination after the trauma film. However, there was no significant positive association between experience of PI in the CVLT and intrusive memories or rumination. In contrast, the trait tendency for film-related rumination and intrusive memories as well as valence and arousal during the film were linked to post-film intrusive memories and rumination.

The absence of a significant positive association between susceptibility to PI and intrusive memories is surprising as a link between these variables has been found in earlier research (Verwoerd et al. 2009, 2011; Wessel et al. 2008). However, the present study slightly differed from previous research in the assessment of intrusive memories and resistance to PI. Whereas previous studies recorded the occurrence of post-film intrusive memories after a period of 24 h (Wessel et al. 2008) or during a 1-week diary assessment (Verwoerd et al. 2011), we measured intrusive memories after a short post-film resting period. This procedure had been used before in studies testing the short-term tDCS effects on rumination (e.g., Vanderhasselt et al. 2013), and therefore seemed appropriate to be used in our study, too. Interestingly, participants in the current study reported an even greater number of intrusive memories in this short period compared to the 1-week assessment by Verwoerd et al. (2011). Thus, the film fragment we used appears to be suitable for inducing intrusive memories. Furthermore, to enhance comparability, we administered the modified CVLT also used by Verwoerd et al. (2011) for measuring resistance to PI. Using this modified version also carried the advantage of a high number of items, which was expected to be useful to preclude ceiling effects in a healthy sample. However, all participants showed a performance decrease in the modified CVLT from session 1 to session 2, although positive practice effects on the regular CVLT have been reported (Duff et al. 2001; Woods et al. 2006). It cannot be ruled out that this decrease was caused by somewhat higher stress levels in session 2, which may have been triggered by the tDCS electrode placement, reduced motivation by participants, or increased task difficulty caused by word interferences from session 1. Furthermore, in contrast to Verwoerd et al. (2011), there was no significant between-lists performance decrease for shared trials on session 1 and no between-lists performance increase for non-shared trials on session 2 in the present study. These changes were to be expected and—according to Verwoerd et al. (2011)—would have underlined the sensitivity of the modified CVLT for interference effects. It should be noted that we examined an exclusively female sample and Verwoerd et al. (2011) reported interference effects to be stronger for men compared to women. Nevertheless, the modified CVLT has only rarely been used in earlier research and information regarding convergence with other established measures or on sensitivity to tDCS are largely lacking. Our results indicate that the modified CVLT index should be used with caution in future research. Apart from restrictions of the modified CVLT, in a recent study by Swick et al. (2017), the ability to overcome PI (as assessed by a probes working memory task with non-affective verbal and visual stimuli) was also unrelated to the severity of re-experiencing symptoms in combat veterans diagnosed with PTSD. Therefore, our results support recent research that questions the link between resistance to PI and intrusive memories in general.

Concerning rumination, previous research posited that deficits in resolving interference from no-longer relevant information in working memory are related to recurring ruminative thoughts (De Lissnyder et al. 2012; Pe et al. 2012; Vanderhasselt et al. 2013; Zetsche et al. 2012; Zetsche and Joormann 2011). However, most of these studies applied interference tasks with affective stimuli or focused on naturally occurring rumination. In contrast, we examined the link between resistance to PI and experimentally induced rumination by use of non-affective stimuli. Thus, persistent rumination might be exclusively linked to deficits in controlling no-longer relevant emotional information. Interestingly, a recent meta-analysis by Zetsche et al. (2018) analyzed a large body of published and unpublished research on the link between cognitive control and self-reported trait repetitive negative thinking. Results from this meta-analysis also showed that ruminators do rather experience specific deficits in removing no longer relevant information from working memory than general deficits in cognitive control, although effects were small in magnitude after controlling for depressive symptoms. Importantly, stimulus valence was not a significant moderator of this association. Nevertheless, the authors pointed out that, due to task heterogeneity, analyses only contrasted emotionally neutral versus emotionally mixed stimuli and thus did not differ between positive and negative affective material. Future research should further clarify whether deficits in resolving PI are selectively linked to negative information as well as investigate the role of varying induction and assessment methods of rumination.

Furthermore, we did not find the expected tDCS effect on resistance to PI. As already mentioned in the introduction, the ability to resist PI is supported by a complex network including various brain areas (e.g., Blasi et al. 2006; D'Esposito et al. 1999; Johnson et al. 2001). We focused on the left dlPFC as one part of this network as neuromodulation of this region has been associated with cognitive control shifts in former studies (Andrews et al. 2011; Fregni et al. 2005; Frings et al. 2018; Wolkenstein and Plewnia 2013; Zaehle et al. 2011). However, these studies used different tasks to assess cognitive control. Thus, it is possible that there are other brain areas supporting the requirements of the modified CVLT more than the left dlPFC; these brain areas may then be more suitable stimulation sites when aiming to modify the resistance to PI. Therefore, we encourage future studies to further clarify causal relations by stimulating different brain areas or by using varying assessment methods of cognitive control. We recommend the use of tasks other than the modified CVLT due to the constraints mentioned above. In particular, tasks that rely on reaction times instead of accuracy rates might be more adequate, given that a recent meta-analysis reported that, at least for healthy individuals, effects of tDCS over the dlPFC on cognitive control become manifest predominantly in altered reaction times (Dedoncker et al. 2016a).

Despite the non-significant results concerning resistance to PI, general deficits in cognitive control have been empirically linked to intrusive memories and rumination in different samples (Aupperle et al. 2012; Brewin and Beaton 2002; Brewin and Smart 2005; Klein and Boals 2001; Polak et al. 2012; Whitmer and Gotlib 2013) and tDCS over the left dlPFC has been reported to influence cognitive control processes (e.g., Andrews et al. 2011; Fregni et al. 2005; Wolkenstein and Plewnia 2013). Moreover, the activation of the left dlPFC has not only been associated with cognitive control but also with intrusive memories and rumination (e.g., Anderson et al. 2004; Benoit et al. 2014; Vanderhasselt et al. 2013). Therefore, even with no tDCS effect on resistance to PI and no significant correlation between resistance to PI and intrusive memories or rumination, we would have expected tDCS-induced changes in intrusive memories and rumination following stimulation of the dlPFC. However, similar to resistance to PI, the control of unwanted memories and thoughts relies on a complex network, also including other brain structures such as the right dlPFC or the anterior cingulate cortex (Anderson et al. 2004, 2015; Kühn et al. 2012; Mandell et al. 2014). At least for rumination, two studies that combined working memory training with bilateral or left stimulation of the dlPFC also found no effects of tDCS on rumination (De Putter et al. 2015; Vanderhasselt et al. 2015). Compared with the present study, both studies relied on smaller sample sizes, used different stimulation parameters, or focused on naturally occurring rumination. Nevertheless, since our results also indicate no effects of tDCS over the left dlPFC on the occurrence of unwanted thoughts, it might be worthwhile to examine other brain areas in future research. Furthermore, we found that individuals with a trait tendency for post-film rumination and intrusive memories experienced more rumination and intrusive memories after film presentation. Therefore, future research could benefit from selecting participants based on these trait tendencies to strengthen the effects of neuromodulation. This assumption is also supported by a recent study indicating that base-level performance in cognitive control moderates tDCS effects—that is, participants whose cognitive control is impaired the most, profit the most from anodal tDCS (Wolkenstein et al., in prep.).

In general, there is an ongoing debate about the effectiveness of neuromodulation. This study fits into this debate and some general limitations regarding tDCS should be considered. First, the stimulation period of 20 min only comprised the CVLT administration and not the trauma film. Nitsche et al. (2008) claimed even shorter periods to produce stable effects that last for at least 1 h. However, the stability of effects varies as a function of stimulation period, current intensity, and target brain area (Nitsche et al. 2008). Thus, it cannot be ruled out that the manipulation of the dlPFC rapidly declined after tDCS. Second, we used an extracephalic position of the reference electrode to avoid effects on other brain areas. Although this procedure has been successfully administered in other studies (e.g., Wolkenstein and Plewnia 2013), it may reduce stimulation intensity (Moliadze et al. 2010). Third, we had a young, highly-educated, healthy sample. Previous research has pointed towards possible ceiling effects for anodal tDCS in healthy samples (e.g., Furuya et al. 2014). Although we used a modified CVLT with 30 instead of 12 words per list to prevent those effects, we cannot rule them out. Furthermore, even though there are experimental studies reporting significant deteriorating effects of cathodal tDCS on cognitive control (e.g., Wolkenstein et al. 2014), a recent meta-analysis found no reliable effects of cathodal tDCS of the dlPFC on cognitive functioning in within-subject studies (Dedoncker et al. 2016b). This result questions the suitability of cathodal tDCS over the dlPFC to inhibit cognitive control. Interestingly, Nieratschker et al. (2015) showed that effects of cathodal tDCS can be moderated by specific genetic factors, suggesting that future studies in the area of neuromodulation should also consider genetic variability to reduce inconsistencies of results. Lastly, it should be noted that working mechanisms of tDCS are divisive. In a recent study examining the effects of direct transcranial electric stimulation on brain activity, Vöröslakos et al. (2018) showed that electric stimulation does influence brain networks in healthy subjects as long as induced electric fields are sufficiently strong (> 1 mV/mm at least). According to the authors, results from human cadaver brains suggest that scalp-applied current intensity is attenuated by skin, soft tissue, or skull thickness. Thus, scalp-applied currents of 4–6 mA or higher are needed to achieve a high voltage gradient. However, due to safety reasons, conventional stimulation protocols do not recommend currents larger than 2 mA. Our stimulation protocol was in line with this convention. Moreover, tDCS-associated changes in cognitive control by use of 1 mA have been reported (e.g., Wolkenstein and Plewnia 2013; Wolkenstein et al. 2014). Nevertheless, future studies should further investigate how to maximize direct effects on brain activity by use of alternative stimulation protocols (e.g., Chhatbar et al. 2017) or new stimulation methods (e.g., Vöröslakos et al. 2018). Furthermore, we had to keep the post-stimulation period as short as possible in this study. Therefore, we did not include a second cognitive control task to test whether cortical excitability had been achieved. Future investigations should also include additional cognitive measures to verify manipulation. Apart from these restrictions concerning tDCS, we measured the occurrence of intrusive memories retrospectively, a procedure that notoriously includes the risk of cognitive biases. The ability to remember and report the amount of film-related intrusive memories might be related to individual differences in cognitive functioning, e.g., short-term and working memory capacity. Compared to previous investigations that covered much longer assessment intervals, our measurement directly followed a relatively short resting period. Nevertheless, an alternative assessment method could be instructing individuals to directly indicate an intrusive memory once it occurred. However, addressing the assessment of intrusive memories prior to resting period might focus participant's attention on film-related thoughts and therefore trigger rumination or further intrusive memories, an effect that would reduce validity of the assessment. Furthermore, as already noted in previous research using diary assessments for intrusive memories (e.g., Wessel et al. 2008), monitoring contents of working memory and maintaining a task goal (i.e., tapping intrusive memories) is also a core characteristic of cognitive control and in turn subject to individual differences in cognitive functioning.

Despite these limitations, this study contributed to the challenging task of establishing causality in post-trauma symptomatology. Even though the hypotheses were not confirmed, the results extend existing research. To investigate causal relations, an indicator of cognitive control as well as a corresponding brain area had to be determined that are both associated with intrusive memories/rumination and susceptible to tDCS. Based on existing findings, we chose resistance to PI as measured by the modified CVLT as well as the left dlPFC. However, we found no associations with intrusive memories or rumination as expected and no effects of tDCS. At the same time, our results highlight the potential role of boundary conditions that should be further differentiated in future research, e.g., administering cognitive control tasks that include reaction times, using affective stimuli, or focusing on other brain areas for neuromodulation. Furthermore, selecting participants based on trait-measures of cognitive control or rumination/intrusive memories could be an important step to enhance effects of neuromodulation in the future. In sum, until now we are not able to conclude whether differences in cognitive control are a risk factor for the occurrence of intrusive memories or rumination. And clearly, more research is needed to consider chances and limits of tDCS in the domain of PTSD-related symptomatology. Nevertheless, the current study offers starting points for future investigations to finally answer the question of what determines individual vulnerability for intrusive memories and rumination after life-threatening events.

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Compliance with Ethical Standards

Conflict of Interest Maria Voss, Thomas Ehring and Larissa Wolkenstein declare that they have no conflict of interest.

Informed Consent All participants signed informed consent and were reimbursed with 30 Euros or course credit. The study was approved by the local ethics committee and was conducted in accordance with the provisions of the World Medical Association Declaration of Helsinki.

Animal Rights This article does not contain any studies with animals performed by any of the authors.

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