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ORIGINAL ARTICLE

Reducing negative affect with anodal transcranial direct current stimulation increases memory performance in young—but not in elderly—individuals

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Abstract

Affect can directly influence memory storage and retrieval, which offers the opportunity to improve memory performance by changing affective responses. A promising target is the left dorsolateral prefrontal cortex (dlPFC), as it is functionally involved in both affect and memory. This study explores whether anodal transcranial direct current stimulation (tDCS) to the left dlPFC improves memory retrieval through the reduction of negative affect and if this interacts with age. We randomly assigned 94 healthy individuals ($n = 43$ young, $n = 51$ elderly) to either sham or active tDCS during encoding of a verbal episodic memory task. Participants completed two questionnaires assessing affective states pre- and post-stimulation. They had to recall items unexpectedly 20 min after encoding and to name which feelings were associated with this free recall. We applied mediation models to explore the relation between tDCS, change in affect, and memory retrieval. In young participants, the reduction of negative affect via anodal tDCS fully mediated the increase in memory retrieval ($R^2 = 57\%$; $p < 0.001$); that is, a stronger reduction of negative affect via tDCS led to better memory performance. We did not observe these effects in the elderly. Our study provides a further link between affect and memory: as increased activity in the dlPFC is crucial for successfully coping with affective interference, anodal tDCS seems to help preventing irrelevant negative thoughts, thus foster attention allocation. Studies applying anodal tDCS to the left dlPFC in healthy young participants should consider changes in affect when interpreting the effect of stimulation on memory performance.

Keywords dlPFC · tDCS · Negative affect · Episodic memory · Non-invasive brain stimulation · Mediation

Introduction

For a stimulus or an event to be remembered, at least three memory stages must be passed successfully (Kensinger 2009). First, we need to encode the stimulus. Second, we have to consolidate it into a stable and lasting representation and finally, we need to retrieve the stimulus. It is now widely accepted that emotions, mood, or affective states, in general, can have a direct impact on all of these three stages of memory processing (Phelps 2004): when a stimulus or an event elicits an arousal response, affect-specific processes enhance the likelihood that a stimulus is encoded, consolidated, and retrieved (Kensinger 2009). Theoretically, this offers the opportunity to increase memory performance by shaping affective responses.

On the neuronal level, the left dorsolateral prefrontal cortex (dlPFC) holds a functionally necessary role in affect as well as memory processing (Fletcher 1998a, b; Ochsner et al. 2012). Higher activity of the left dlPFC is associated with positive affect, while higher activity of the right dlPFC is linked to negative affect (Lee et al. 2004; Grimm et al. 2008; but see Wager et al. 2003 for a different view). For learning and memory, enhanced activity of the left dlPFC during encoding leads to better performance during

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subsequent retrieval (Paller and Wagner 2002). This might explain why non-invasive brain stimulation techniques, which modulate region-specific brain activity, have been put forward as an effective tool to modulate either affect or memory. Yet, no study so far tried to elucidate the interplay between both. Likewise, it remains untested if manipulating affective responses would lead to an enhanced memory performance. For other cognitive functions (i.e. processing speed), a reduction of negative affect via anodal tDCS improved performance (Plewnia et al. 2015). In that study, healthy young individuals received anodal tDCS during a (typically) frustrating processing speed task. By stimulating the left dlPFC for 20 min, less task-related negative affect appeared (possibly due to enhanced cognitive control over affective interference) and the reduction of negative affect was correlated with performance gains (Plewnia et al. 2015).

The current study strives to identify whether these effects similarly apply to learning and memory. Comparable to Plewnia and colleagues, we used anodal tDCS to the left dlPFC to find out whether active stimulation reduces task-related negative affect compared to sham stimulation. On top of that, we explored if this change would be associated with memory performance gains in a verbal episodic memory task. Episodic memory is the recollection of previously encountered personal experiences (Tulving 2002); verbal learning tasks are a common way to assess episodic memory as they include a free recall of a list of previously learned words after a short delay. We included both healthy young and elderly individuals as there is evidence for diverging effects of non-invasive brain stimulation in these populations (Heise et al. 2014). More precisely, physiological effects as well as the behavioural outcome after tDCS seem to depend on age with regard to direction, extent, and timing (Heise et al. 2014; Leach et al. 2018). For verbal episodic memory, we focused on free delayed recall as we expected to find task-related negative affect particularly in this (typically surprising) task. A surprising retrieval task demands more effortful retrieval than an immediate retrieval task and affective states tend to change most with demanding tasks (Ellis et al. 1995). These tasks increase the production of irrelevant, intruding thoughts that prevent the allocation of attentional resources to the criterion task—thus limiting performance. We hypothesise that active tDCS suppresses (or reduces) irrelevant thoughts and thus, lead to less task-related negative affect, thereby improving performance at recall.

Methods

Participants

We included 94 healthy, right-handed individuals in the study (Table 1). We recruited participants via flyers circulated in Freiburg, Germany. The Ethics Commission approved the study and we conducted all experiments according to the Declaration of Helsinki. All participants gave written informed consent prior to testing and received financial compensation.

Table 1 Sociodemographic characteristics of the sample

	Healthy elderly ($n=51$)				Healthy young ($n=43$)				p value (interaction)[a]
	Sham ($n=26$)		Active ($n=25$)		Sham ($n=21$)		Active ($n=22$)		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Female/male (n)	17/9		15/10		11/10		11/11		0.59
Age (years)	69.2	6.4	68.3	5.2	25.1	3.3	24.6	2.6	0.87
Verbal delayed recall (words)	16.3	5.8	16.1	5.5	25.6	6.8	29.7	5.4	0.05
BDI-II	6.0	6.1	7.9	4.9	3.4	3.4	4.6	3.8	0.71
GDS	1.2	1.2	1.8	1.6	1.1	1.4	1.1	1.6	0.26
Hours of sleep	7.2	0.8	6.7	1.3	7.6	1.1	7.4	0.9	0.53
Quality of sleep (0–10)	7.1	1.7	5.9	2.4	7.6	1.4	7.0	2.1	0.46
Ability to concentrate (0–10)	7.5	1.6	6.1	1.5	7.4	1.4	7.7	1.2	0.01

SD standard deviation, *BDI-II* Beck's Depression Inventory II, *GDS* Geriatric Depression Scale (short version). For the subjective ratings of sleep quality and the current ability to concentrate, a score of 0 denotes 'very bad', while a score of 10 indicates 'very good'

[a]Sociodemographic variables were analysed using multivariate analysis of variance with group (young/elderly) and stimulation mode (sham/real) as between-subject variables. Please note that the p value represents the interaction between group and stimulation mode and not the difference between young and elderly individuals

Inclusion and exclusion criteria

Prior to enrolment, we screened all participants on the telephone and only invited them to the study if deemed eligible. The participants had to be 20–30 years of age to be included in the healthy young group and 60–80 years of age for the healthy elderly group. They all had to be native German speakers, non-smokers, with normal or corrected-to-normal vision, and no history of psychiatric or neurological disorders. Further exclusion criteria were any history of seizures, current psychotropic medication, dermatosis, current or lifetime alcohol abuse, brain damage, or current/possible pregnancy. We assessed depressive symptoms with the Beck Depression Inventory II (BDI-II; Beck et al. 1996) as well as the Geriatric Depression Scale (GDS; Yesavage and Sheikh 1986). We included participants if they scored ≤ 13 in the BDI-II and ≤ 6 in the GDS. We assessed cognitive functioning in the healthy elderly using the Montreal Cognitive Assessment (MoCA; Nasreddine et al. 2005); elderly participants were included with a MoCA score ≥ 26.

Study procedure and experimental schedule

In this double-blind, sham-controlled, parallel-group study, we randomly assigned the participants to one of two groups (sham and active stimulation). We computerized and programmed the experiments with Presentation® (Version 18.1, Neurobehavioral Systems, Inc., Berkeley, CA). The participants performed the task while sitting in front of a 14-inch computer screen in a well-lit, quiet room. Prior to stimulation, the participants were asked to report the hours of sleep during the last night and to rate the quality of sleep as well as their current concentration (on a scale ranging from 0 to 10). Following mounting of the electrodes, we started the stimulation simultaneously with the first block of an attention task (duration: 5 min; Fig. 1) in which the participants were required to respond to the appearance of a single white cross on a black screen, either preceded by an auditory cue or not (i.e. phasic and intrinsic alertness). During this time span, the participants could accustom themselves to the tingling sensation associated with the ramp-up phase of tDCS (sham and active condition). Moreover, previous research suggested that anodal tDCS effects on cortical excitability arise after 5 min of stimulation (Nitsche and Paulus 2000). Sham stimulation lasted only for a few seconds and was terminated before the start of the verbal episodic memory task (see below).

Verbal episodic memory task

We selected eighty nouns from parallel versions of the revised California Verbal Learning Test (Woods et al. 2006) and a set of emotionally connoted words (Herold 2008). We chose two to three times more words than previous studies (Elmer et al. 2009; Nikolin et al. 2015) to lower the risk of ceiling effects (i.e. when participants' scores cluster towards the best possible score of the instrument). In pilot studies with ten participants (or seven participants in case of healthy elderly individuals), we affirmed that the chosen number of words was sufficient to avoid ceiling effects. The verbal memory task comprised three encoding and three immediate retrieval phases as well as one delayed recall after approximately 20 min.

During encoding, we presented 40 words on the computer screen in randomized order (one at a time), in a white against black background. Please note that for the group of older adults, we reduced the list of words to 32 because of the results of the pilot study. After a fixation cross, presented for 200 ms, each word remained on display for 1000 ms and was followed by an interstimulus interval (ISI) of 500–2500 ms. After each block, we asked participants to orally retrieve as many words as possible within 2 min. We recorded answers

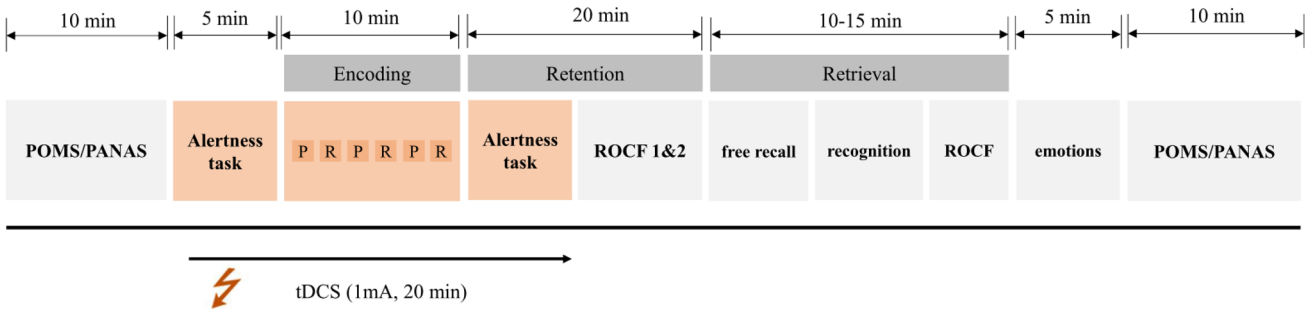

Fig. 1 Study procedure. Following the evaluation of affective states (POMS, PANAS), the participants performed an alertness task and encoding of an episodic memory task. Encoding consisted of the presentation (P) and immediate recall (R) of 40 words in three successive rounds. During the retention interval, we repeated the attention task and participants copied as well as retrieved the Rey–Osterrieth complex figure task (ROCF 1&2). In the retrieval phase of the experiment, participants performed a delayed free recall and recognition of words as well as another retrieval of the ROCF directly followed by the evaluation of their feelings towards the unexpected free recall as well as another evaluation of their affective states

in separate audio files. During the retention interval, the participants copied and immediately retrieved the Rey–Osterrieth complex figure (Rey 1941) as well as completed the attention task a second time (Fig. 1). During delayed recall, the participants' first performed a free recall of the memorized words and then completed a recognition task. Therein, we asked participants to indicate, by pressing a button, whether each of the eighty presented nouns belonged to the list of initially memorized words or was deemed a new word (i.e. distractor). After having completed the recognition task, we asked the participants to draw the Rey–Osterrieth complex figure once again from memory.

We focused on the verbal delayed recall as a primary outcome measure (Voss et al. 2012), results of the other tasks might be reported elsewhere.

Mood or affective state ratings

Positive and negative affect schedule (PANAS)

The PANAS is a self-report measure and comprises two 10-item, self-rated mood scales—positive affect (PA) and negative affect (NA). High PA scores indicate a state of high energy as well as more positive emotions, while low PA scores are indicative of sadness and low energy. High NA scores indicate higher distress and negative mood states, whereas low NA scores indicate a state of calmness. The items are rated on a five-point Likert scale ranging from 'not at all' to 'very much'. Psychometrics indicate adequate reliability, validity and sensitivity for the PANAS (Crawford and Henry 2004). For the current study, the participants had to indicate to what extent they experienced each of the 20 affective states at the precise moment both pre- and post-stimulation. When administered with short-term instructions (i.e. 'right now, at this moment'), the PANAS is sensitive to momentary mood fluctuations (Watson et al. 1988).

Due to previous research indicating a change only in negative affect after tDCS (Plewnia et al. 2015), we focused on the NA scores in all analyses. We implemented the raw change in NA scores (i.e. change in prior to post tDCS) in statistical analyses.

Profile of mood states (POMS)

The POMS is a self-rating questionnaire, which assesses six mood subscales: tension–anxiety, depression, anger–hostility, vigor, fatigue, and confusion. High vigor scores and low scores in the other subscales reflect a good mood or emotion. Besides the six subscales, a total mood disturbance score can be calculated by adding the five negative subscale scores (tension–anxiety, depression, anger–hostility, vigor, fatigue, and confusion), subtracting the vigor score, and adding 100 (to not receive a negative value). Higher scores for the total mood disturbance score indicate a greater degree of mood disturbance.

We used the raw change in total mood disturbance for later analyses (again, prior to post tDCS).

Evaluation of feelings elicited by the free delayed recall

To assess directly which feelings are linked to the (typically unexpected) delayed recall, we asked participants to name 'which feelings were elicited in the moment they had to (again) retrieve as many words as possible'.

We used the number of negative feelings for statistical analyses by summing up feelings declared as negative by the participants.

Transcranial direct current stimulation (tDCS)

The anodal electrode was placed over the left dlPFC at position F3 according to the 10–20 system (Herwig et al. 2003) and the cathodal electrode was placed on the contralateral supraorbital region. We used two rubber electrodes coated with saline solution-soaked sponges (5×7 cm) with the device to deliver the current over the scalp. TDCS was applied with a DC-plus stimulator (Neuroconn GmbH, Ilmenau, Germany) that delivered direct current with an intensity of 1 mA. We chose 1 mA because prior studies evinced reliable malleability of memory functions (Ruf et al. 2017) and to prevent inversion of the effects due to higher intensities (Mosayebi et al. 2018). Total current density did not exceed 0.03 mA/cm^2 at any point in time and thus remained below safety limits (Poreisz et al. 2007). The stimulator was operated in 'study mode', such that neither the participant nor the examiner was aware of the experimental condition (i.e. double-blind study). A person not involved in the data collection (JP) allotted the codes for sham or active anodal tDCS, thus providing an effective blinding for both participant and experimenter. We started the stimulation 5 min before the episodic memory task began (see experimental schedule).

Active anodal tDCS consisted of a 15-s ramp-up phase after which the current remained constant at 1 mA for 20 min and was ramped down for another 15 s afterwards (Fig. 1). For sham stimulation, the current was immediately ramped down after similarly ramping up the current to 1 mA, (i.e. for a few seconds). This sham procedure was previously shown to produce the same sensations as active stimulation but without exerting any stimulation effects (Gandiga et al. 2006). During the subsequent tasks, the electrodes and equipment remained in place but no stimulation was given. At the end of the experiments, the participants and the experimenter had to guess which stimulation condition they completed and we assessed possible side effects.

In agreement with the questionnaire proposed by Brunoni et al. (2011), we enquired about perceived side effects of the stimulation and controlled the consistent blinding of the participants with respect to the stimulus condition.

Statistical analyses

We used SPSS (version 21.0; IBM Inc., USA) for statistical analyses and applied parametric tests whenever Kolmogorov–Smirnoff tests indicated no violation of the normality assumption. We applied a critical $p < 0.05$ for statistical significance. Towards our primary research question (i.e. does tDCS improve memory retrieval through the reduction of negative affect and is this modulated by age) we performed mediation analyses. As a plausibility check, we further tested simple effects (i.e. does tDCS significantly modulate affect and/or verbal retrieval). This also allowed a more direct comparison to previous studies, which focused on simple effects rather than mediation analyses. Finally, we tested if tDCS significantly modulates negative feelings associated with an unexpected free recall. In all these models, we tested for an interaction with age; that is, we wanted to find out whether the effects were different for younger and older adults. We did not apply post hoc tests and, therefore, did not control for multiple comparisons.

Mediation between change in negative affect and verbal delayed recall

We analysed if the modulation of negative affect via tDCS influenced verbal delayed recall by computing mediation analysis with the SPSS PROCESS macro [version 2.10; (Hayes 2013)]. Mediation analysis tests the assumption that the bivariate relationship between a predictor variable *X* and an outcome variable *Y* is mediated by a third variable *M*, with *M* assumed to be affected by *X* and in turn to predict *Y*, thereby contributing to the effect of *X* on *Y*. To specify our model, we included group as a moderating variable since the relation between our variables of interest must not be identical for young and older participants (Fig. 2). Therefore, we computed a moderated mediation (Model 8 of the PROCESS macro), using stimulation as a focal predictor *X*, verbal delayed recall as outcome variable *Y* and change in negative affect as the mediator *M* as well as group (young vs. old participants) as a weight factor *W* (Fig. 2).

To ensure that change in task-related negative affect via tDCS influences memory retrieval and not vice versa, we also tested the reverse model (i.e. change in negative affect as outcome and verbal delayed recall as mediator). We preferred Bootstrapping (10.000 iterations) over the Sobel test because it provides greater statistical power in testing the significance of the indirect effect (Hayes 2013).

Modulating negative affect with anodal tDCS

We analysed the effect of tDCS on negative affect, total mood disturbance, and negative feelings associated with the free delayed recall in healthy young and elderly individuals with multivariate ANOVA using group (young vs. elderly) and stimulation (sham vs. active) as between-subject factors and change in negative affect as within-subject factor.

Modulating verbal delayed recall with anodal tDCS

We calculated the effect of tDCS on verbal delayed recall with univariate ANOVA using group and stimulation as between-subject factors as well as time (pre- to post-stimulation) as within-subject factor.

Results

We found a significant interaction between group and stimulation mode only for the ability to concentrate: Healthy elderly participants in the active tDCS group were less able to concentrate (prior to the stimulation) than younger participants of the active tDCS group ($F_{(1,90)} = 10.98$, $p = 0.01$; Table 1). We found no other significant differences for sociodemographic variables but healthy young participants slept longer compared to healthy elderly participants

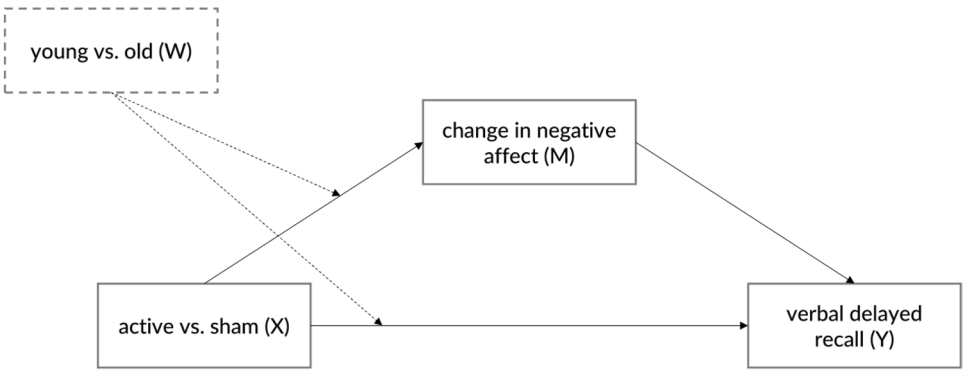

Fig. 2 Schematic of a moderated mediation. The predictor *X* has both direct and indirect effects on *Y* (through *M*), but the effect of *X* on *Y* is moderated by *W*—that is, the effects of *X* on *Y* are conditional, depending on the value of *W*

($F_{(1,90)}=5.91$, $p=0.02$). Therefore, we included age, hours of sleep, and the ability to concentrate as covariates in all statistical analyses. Please note that we did not assess years of education in the group of younger participants as these were all students (and thus, obtained at least 13 or 14 years of education). In the group of older adults, the mean level of education was 16.0 ± 3.7 for the sham tDCS group and 15.3 ± 3.9 for the active tDCS group. This difference was not statistically significant.

The participants tolerated the stimulation well. Tingling (67.0%), erythema (29.7%), burning sensation (27.7%), and itching (26.7%) were the most commonly reported sensations, manifesting with mild to medium intensities. Sham and anodal stimulation did not significantly differ in any of the perceived side effects. Forced guessing as to stimulation group assignment subsequent to the stimulation was at chance level for both participants (Pearson's $\chi^2_{(1)}=0.05$, $p=0.82$) and examiner (Pearson's $\chi^2_{(1)}=1.31$, $p=0.25$) in healthy young participants. However, in the healthy elderly, we found that both participants (Pearson's $\chi^2_{(1)}=7.15$, $p=0.012$) and examiners (Pearson's $\chi^2_{(1)}=8.63$, $p=0.005$) were more accurate in identifying active tDCS.

Mediation between change in negative affect and episodic memory

Change in negative affect (PANAS) significantly mediated the effect of tDCS on verbal delayed recall ($F_{(7,86)}=16.24$, $R^2=0.57$, $p<0.001$; bootstrapped 95% CI of indirect effect [0.26 3.05], $B=1.31$, SE= 0.70). We found a significant effect only in young individuals (bootstrapped 95% CI of indirect effect [0.06, 1.87], $B=0.66$, SE= 0.43) but not in older adults (bootstrapped 95% CI of indirect effect [− 1.89, 0.01], $B=-0.65$, SE= 0.47).

Likewise, change in total mood disturbance (POMS) mediated the effect of tDCS on verbal delayed recall ($F_{(7,86)}=16.33$, $R^2=0.58$, $p<0.001$; bootstrapped 95% CI of indirect effect [0.16 3.57], $B=1.28$, SE= 0.82). Again, the effect was only significant in younger participants (bootstrapped 95% CI of indirect effect [0.05, 2.10], $B=0.78$, SE= 0.49) but not in older adults (bootstrapped 95% CI of indirect effect [− 1.95, 0.19], $B=-0.50$, SE= 0.52).

None of the reverse models yielded in significant results. That is, verbal delayed recall did not mediate the effect of tDCS on negative affect ($F_{(7,86)}=2.79$, $R^2=0.18$, $p=0.01$; bootstrapped 95% CI of indirect effect [− 0.01 0.09], $B=0.03$, SE= 0.02]. Likewise, verbal delayed recall did also not mediate the effect of tDCS on total mood disturbance ($F_{(7,86)}=2.74$, $R^2=0.19$, $p=0.01$; bootstrapped 95% CI of indirect effect [− 0.14 7.44], $B=2.52$, SE= 1.79].

In sum, these results indicate that greater reduction in negative affect via active tDCS significantly increased memory retrieval in healthy young individuals. This was not the case in healthy elderly adults.

Modulating negative affect with anodal tDCS

We found a significant three-way interaction ($F_{(3,87)}=3.64$, $p=0.02$) indicating that stimulation acted differently on negative affect in young and elderly individuals (Fig. 3). This was the case for both measures of change in negative affect between begin and end of the experiments (i.e. PANAS [($F_{(1,87)}=4.99$, $p=0.03$)] and POMS [($F_{(1,87)}=4.37$, $p=0.04$)] and for negative feelings towards the unexpected free recall [($F_{(1,87)}=7.19$, $p=0.01$; Fig. 4)].

Modulating verbal delayed recall with anodal tDCS

For verbal delayed recall, a trend towards a significant interaction was found indicating that stimulation effects on verbal delayed recall were different for young and elderly individuals ($F_{(1,87)}=3.7$, $p=0.057$; Fig. 4).

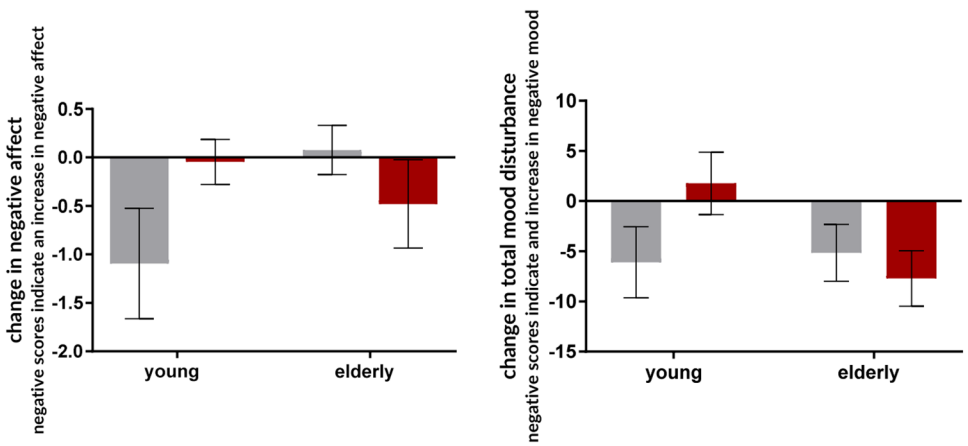

Fig. 3 Change in negative affect and total mood disturbance as assessed with the positive and negative affect schedule (PANAS) as well as the profile of mood states (POMS) in healthy young and elderly individuals receiving active or sham transcranial direct current stimulation over their left dorsolateral prefrontal cortex. Please note that bars represent the change scores pre- to post-stimulation. Stars indicate significant differences

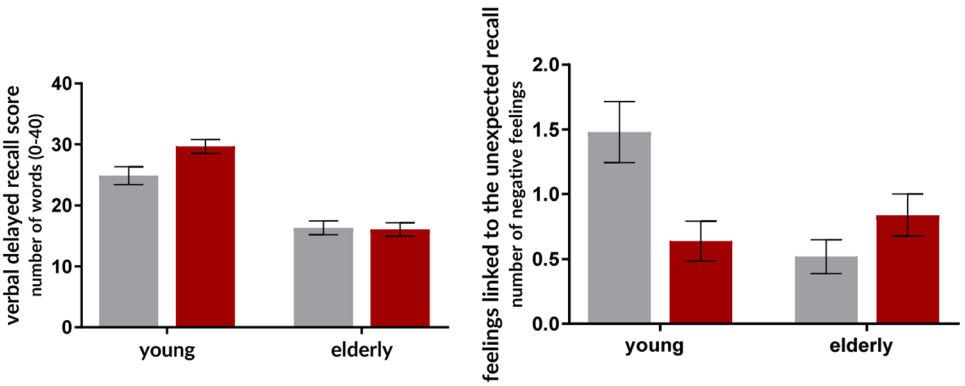

Fig. 4 Verbal delayed recall scores as well as feelings associated with this unexpected retrieval in healthy young and elderly individuals receiving either sham or active transcranial direct current stimulation over their left dorsolateral prefrontal cortex. Stars indicate significant differences

Discussion

This is the first study to investigate whether a causal link exists between manipulating affective responses via anodal tDCS and episodic memory retrieval. In addition, this study tested if this relationship is depending on age. The main result of our study is that a stronger reduction of task-related negative affect via anodal tDCS to the left dlPFC significantly enhanced episodic memory retrieval. Thus, modulating affective responses directly improves memory performance—which has never been reported with non-invasive brain stimulation so far [but see a similar effect for processing speed in Plewnia et al. (2015)]. Intriguingly, this causal relation only applies to healthy young but not to healthy elderly participants (but the lack of an effect in the healthy elderly might be due to imperfect blinding).

Unlike to classic philosophers and psychologists, it is now widely accepted that affect and memory are fundamentally intertwined such that affective responses modulate memory processing and vice versa (Brosch et al. 2013). Therefore, it is surprising that so far tDCS studies targeted either episodic memory or affect but never tried to elucidate the interplay between both. For memory processes alone, anodal tDCS applied over the left and right dlPFC during retrieval of concrete and abstract words, enhanced recognition performance in healthy young individuals (Manenti et al. 2013). Another study, applying anodal tDCS over the left dlPFC during encoding of a list of words in young participants found a significantly improved short-term learning, but no effects on retrieval (Nikolin et al. 2015). However, the individuals markedly showed ceiling effects that might have prevented an enhancing effect of tDCS. When applied during encoding of pictures, anodal tDCS increased, while cathodal stimulation reduced the number of false alarms during recognition memory testing (Zwissler et al. 2014). Other studies only rarely applied cathodal tDCS to modulate episodic memory. Two studies found impaired free recall or recognition performance in younger adults after cathodal tDCS over the left dlPFC (Elmer et al. 2009; Javadi and Walsh 2012), while stimulating the right dlPFC enhanced recognition performance for nonverbal material (Smirni et al. 2015). In healthy aging, anodal tDCS over the left dlPFC during recognition reduced forgetting of learnt words (Sandrini et al. 2014) and enhanced retrieval of concrete and abstract words (Manenti et al. 2013) when applied during retrieval. No study so far examined cathodal tDCS to modulate episodic memory in healthy aging. In our study, we found diverging effects of tDCS on verbal delayed recall modulation in healthy young and elderly individuals, when stimulating the left dlPFC with 1 mA during encoding.

For the role of the dlPFC in affect, a hemispherical specialization has been proposed: activity of the left dlPFC has been associated with positive affect, whereas activity of the right dlPFC has been linked to negative affect (Canli et al. 1998; Lee et al. 2004; but see Wager et al. 2003 for a more complicated picture). Thus, anodal stimulation of the left dlPFC should—theoretically—lead to a more active left dlPFC and thus, more positive affect. Yet, the literature on affect enhancement by non-invasive brain stimulation techniques is somewhat controversial. While some studies found a modulation of affect via transcranial magnetic stimulation (TMS) or tDCS, others did not (see Mondino et al. 2015 for a critical review). Comparable to the results of our study, Plewnia and colleagues found a reduction of task-related negative affect when stimulating the left dlPFC with anodal tDCS (Plewnia et al. 2015). They concluded that anodal tDCS supports focused cognitive processing, that is, a shift in processing resources towards task-oriented performance away from concern with task-related negative affect (e.g. irrelevant thoughts or rumination). Others failed to find similar effects but they applied shorter stimulation intervals (i.e. 12 min; Morgan et al. 2014) or different stimulation protocols (i.e. bifrontal stimulation; Plazier et al. 2012). In our study, the significant modulation of negative affect was found in two self-report measures (i.e. POMS and PANAS) as well as in the number of self-reported negative feelings (i.e. when participants were asked to name feelings associated with the unexpected verbal delayed recall). In all three measures, active tDCS significantly modulated negative

affect, lending further support for the possibility to shape affective responses with non-invasive brain stimulation. The results support the view that tDCS is able to allocate attention towards task-oriented behaviour instead of task-irrelevant negative affect—at least in young participants.

The diverging effect of tDCS between healthy young and elderly individuals has rarely been addressed so far as studies including both age groups are limited (see Perceval et al. 2016 for a review). Up to now, only one study included young and elderly adults and investigated the effect of tDCS on memory functions: Manenti and colleagues stimulated the left and right dlPFC with anodal tDCS during retrieval of verbal episodic memory and found a facilitating effect on retrieval performance (Manenti et al. 2013). In particular, they found that tDCS over both the left and the right dlPFC induced better recognition performance in young participants while only tDCS applied over the left dlPFC was beneficial for older adults. Yet, recognition is different from free recall in a way that it includes cues, while free recall does not (during recognition, you compare an item to information stored in your memory, and if you find a match, you 'recognize' it, while free recall designates the retrieval of details from memory). For free recall, several studies have shown that aging is associated with decline in performance (e.g. Nyberg 2017). This decline is usually accompanied with a decrease in neuronal activity of the temporal cortex, coupled with an increase in frontal cortex activity as stated in the PASA model (Davis et al. 2008). At younger age, a hemispheric asymmetry in encoding and retrieval of verbal episodic memories has been suggested, with the left dlPFC being critical for encoding and the right dlPFC being crucial for retrieval (Tulving et al. 1994; Habib et al. 2003). In the healthy elderly, this hemispheric asymmetry is reduced according to the HAROLD model, with both left and right dlPFC being active during encoding and retrieval (Cabeza 2002). Thus, future studies might try bilateral stimulation to test our mediation model in the healthy elderly. Another study has investigated the effect of tDCS on language functions in both age groups: The study by Martin et al. (2017) applied uni- and bi-hemispheric motor cortex tDCS on word generation in younger as well as older individuals. They found that anodal tDCS significantly improved semantic word generation in both groups. Differences between young and elderly participants were only found on the network level, where a shift toward enhanced left laterality was identified in the older age cohort. On the contrary, a study by Heise et al. (2014) investigated effects of anodal tDCS on motor performance nd found beneficial effects of tDCS mainly in the older sample as well as in tasks requiring higher dexterity. Our results support the diverging effects of tDCS in both cohorts and favour individually tailored application of tDCS with respect to specific target groups.

Limitations

The results in the healthy elderly group might be limited by the inadequate blinding. However, we found significant mediation effects of active tDCS only in younger participants where blinding was successful. Typically, blinding failures appear in tDCS studies using 2 mA rather than 1 mA (O'Connell et al. 2012; Wallace et al. 2016) but when using the latter, insufficient blinding has also been reported (Vaseghi et al. 2014). One reason for inadequate blinding in the group of elderly participants might be that they were very sensitive to the short ramp-up phase. It has been suggested that longer ramp-up phases are more suitable and result in more adequate blinding (Brunoni et al. 2014). Future studies might, therefore, consider longer ramp-up phases in elderly participants.

Another limitation might be that younger participants showed better memory retrieval compared to the elderly and at the same time, their BDI-II scores were lower. We cannot exclude the possibility that these differences in baseline characteristics influenced the results. Of note, however, none of the participants had more than minimal depressive symptoms and including BDI-II scores in our statistical model did not change results substantially. Moreover, we applied both the GDS and the BDI-II in our study and the GDS scores were highly comparable between younger and older participants (see Table 1).

Conclusion

Taken together, we provide evidence that tDCS over the left dlPFC is able to modulate task-induced negative affect in healthy young individuals and by that increase episodic memory performance. We support the view that tDCS alters memory processing by allocating attention towards task-oriented behaviour instead of task-irrelevant negative affect. In the healthy elderly, bilateral stimulation might be more suitable but future studies should address this in detail.

Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest

Ethical approval The Ethics Commission (University of Freiburg, Germany) approved the study and all experiments were conducted according to the Declaration of Helsinki.

Informed consent All participants gave written informed consent prior to testing and received financial compensation.

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