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Research report

Induction of a depression-like negativity bias by cathodal transcranial direct current stimulation

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ABSTRACT

Cognitive control (CC) over emotional distraction is of particular importance for adaptive human behaviour and is associated with activity in the left dorsolateral prefrontal cortex (dlPFC). Deficient CC, e.g., presenting as negativity bias, has been suggested to underlie many of the core symptoms of major depression (MD) and is associated with impairments of dlPFC function. Correspondingly, enhancement of dlPFC activity with anodal transcranial direct current stimulation (tDCS) can ameliorate these impairments in patients with MD. Here, we tested the hypothesis that a reduction of dlPFC activity by cathodal tDCS induces CC deficits, thus triggering a depression-like negativity bias in healthy subjects. Twenty-eight individuals participated in a double-blinded, balanced randomized crossover trial of cathodal (1 mA, 20 min) and sham tDCS applied to the left dlPFC. To assess CC we conducted a delayed response working memory (DWM) task and an arithmetic inhibition task (AIT) with pictures of varying valent content (negative, neutral, positive) during and immediately after stimulation. Cathodal tDCS led to impaired CC specifically over negative material as assessed by reduced response accuracy in the DWM and prolonged response latency in the AIT. Hence, the current study supports the notion that left dlPFC is critically involved in CC over negative material. Together with previously reported beneficial anodal effects, it indicates that the hypoactivation of left dlPFC causes deficits in CC over negative material, which is a possible aetiological mechanism of depression.

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1. Introduction

Cognitive control (CC) is necessary to maintain goal-directed behaviour in the presence of competing, goal-irrelevant information and requires, for example, inhibition of the processing of previously relevant or goal-irrelevant information. A topographically distributed system with subcomponents in frontal and parietal cortices is involved in CC processes (D'Esposito, Postle, Jonides, & Smith, 1999; Nee, Wager, & John, 2007). An association between dorsolateral prefrontal cortex (dlPFC) activity and enhanced CC over emotional processing (Beer, Knight, & D'Espositio, 2006; Herrington et al., 2005) and reciprocal interconnection between dlPFC and the affective circuitry (Dolcos & McCarthy, 2006; Sheline, Price, Yan, & Mintun, 2010) suggest that reduced frontal activity causes amygdala hyperactivation and thus deficient CC over emotional material (Ochsner & Gross, 2005). Especially the left dlPFC participates in CC in the processing of emotional material (De Raedt et al., 2010; Herrington et al., 2005). An increased recruitment of dlPFC in cognitive tasks including emotional distraction is assumed to reflect its role in counteracting the distraction by increasing task-specific activity (Cromheeke & Mueller, 2014; Wessa, Heissler, Schönfelder, & Kanske, 2013).

Individuals with major depression (MD) have difficulties in disengaging from processing negative material (Goeleven, de Raedt, Baert, & Koster, 2006; Gotlib, Krasnoperova, Yue, & Joormann, 2004; Kanske, Heissler, Schönfelder, & Wessa, 2012). In addition, depressed individuals do not activate dlPFC as efficiently as healthy controls when confronted with distracting negative material (Berman et al., 2011). Various studies using different methods (e.g., PET, fMRI, SPECT, rTMS) provide evidence for a hypoactivity of especially the left dlPFC (Fitzgerald, Laird, Maller, & Daskalakis, 2008; Grimm et al., 2008) and decreased connectivity between dlPFC and amygdala in patients with MD (Siegle, Thompson, Carter, Steinhauer, & Thase, 2007). Thus, it has been proposed that a hypoactivation of the dlPFC contributes to the onset and maintenance of MD (De Raedt & Koster, 2010; Mayberg, 1997). The hypothesis is that impaired CC over emotional interference, which is associated with decreased dlPFC activity, is one source of the negativity bias characteristic for MD (Fales et al., 2008).

Research that has investigated the neural substrates of impaired CC processes and negative biases in depression has been mainly correlational. What remains unclear is as to whether a hypoactivation of the dlPFC causes deficits in CC and thereby negativity bias or whether both hypoactivation of the dlPFC as well as CC deficits are epiphenomena of depression. Direct experimental modulation of spontaneous brain activity in healthy individuals could provide crucial evidence regarding this question. Such modulation can be induced by transcranial direct current stimulation (tDCS), which – using specific stimulation configurations (most commonly applied at 1 mA for up to 20 min) – has been shown to facilitate (anodal) or inhibit (cathodal) cortical excitability (Nitsche & Paulus, 2000; Priori, 2003; Wolkenstein & Plewnia, 2013). While it has been shown that tDCS of the left dlPFC modulates functional connectivity in the CC network (Keeser et al., 2011), and that anodal tDCS applied to left dlPFC improves CC over emotional material in MD (Wolkenstein & Plewnia, 2013), no study thus far has investigated whether cathodal tDCS of the left dlPFC impairs CC in healthy individuals. We therefore examined the effects of cathodal tDCS on CC in healthy subjects. We hypothesized that cathodal tDCS of the left dlPFC impairs CC and thereby evokes a negativity bias in healthy individuals.

2. Material and methods

2.1. Participants

Twenty-eight participants were recruited through advertisements posted on the internet. Potential participants first completed a phone screening, after which they were invited for an interview if deemed eligible. A trained interviewer administered the Structured Clinical Interview for DSM-IV Axis I and II (SCID; First, Spitzer, Gibbon, & Williams, 1996). Participants were excluded if they had a current or lifetime psychiatric disorder, were taking psychotropic medication, were left-handers or ambidexters (LQ < 70) as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971), showed clinically relevant depressive symptoms (BDI-II > 13) as assessed by Becks Depression Inventory (Hautzinger, Keller, & Kühner, 2009), or had a verbal IQ of less than 80 as assessed by the Multiple Choice Word Fluency Test (MWT-B; Lehrl, 1992). We further administered the Verbal Learning and Memory Test (VLMT; Helmstaedter, Lendt, & Lux, 2001) to account for verbal memory and the Trail Making Test (TMT; Reitan, 1992) to account for complex attention, motor speed, visual-motor conceptual screening, and executive functions. All participants provided written informed consent. The study was approved by the local ethics committee and was conducted in compliance with the Declaration of Helsinki.

2.2. Delayed response working memory task (DWM)

The first task we used to assess CC over emotional material was a DWM task (see Fig. 1). The pictures included in this task were taken from the Emo-Pics (Wessa et al., 2010) and were of either negative, neutral, or positive valence. Picture selection was based on normative values (Wessa et al., 2010) and negative and positive pictures were counterbalanced regarding their valence and arousal scores (i.e., arousal: (positive = negative) > neutral; valence: positive > neutral > negative). In each trial, participants first saw a 1000 msec fixation display presented on a computer monitor. This was followed by a set of six letters that was simultaneously presented for 2000 msec. During the following distraction phase, participants saw interfering pictures of either negative, neutral, or positive valence, or a blank slide (control condition), respectively. After the distraction phase, a probe letter was presented for 4000 msec and participants were instructed to indicate as quickly and as accurately as possible whether the probe letter was one of the original six letters presented before. The next trial began after 4000 msec had elapsed in which the probe letter was displayed independently of when the participants responded. Each condition (negative, neutral, positive, control) consisted of 15 trials resulting in 60 trials overall, which were presented in a randomized order. Responses and response latencies were