Short Communication

Bilateral Transcranial Direct Current Stimulation Over Dorsolateral Prefrontal Cortex Changes the Drug-cued Reactivity in the Anterior Cingulate Cortex of Crack-cocaine Addicts

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ABSTRACT

Background: Patients addicted to crack-cocaine routinely have difficulty sustaining treatment, which could be related to dysfunctional cerebral activity that occurs in addiction.

Objective: To investigate the indirect electrophysiological effects of single transcranial direct current stimulation (tDCS) on cocaine-addicted brains.

Methods: The patients received either left cathodal/right anodal or sham stimulation over the DLPFC. The region of interest was the anterior cingulate cortex (ACC) during the N2 time window (200–350 ms). Event-related potentials in the ACC were measured during visual presentation of crack-related cues or neutral cues.

Results: Low-resolution brain electromagnetic tomography (LORETA) indicated that exposure to crack-related images led to increased activity in the ACC in the sham group, while the tDCS group showed decreased ACC activity after visualization of drug cues.

Conclusion: Prefrontal tDCS specifically modulated the ACC response during exposure to visual drug cues in crack-cocaine users.

Introduction

It has been suggested that prefrontal dysfunction, particularly dysfunction of cognitive control, may be related to the loss of control over drug use that can lead to addiction [1]. Thus, treatment aiming to improve cognitive control over drug intake is clinically useful. Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation technique that induces polarity-dependent alterations of cortical excitability [2–8]. It can modulate the function of deeper cortical areas, such as the anterior cingulate cortex (ACC) [9–12], which seems to be involved in drug-related attention bias [1]. Considering this evidence, we hypothesize that tDCS over the dorsolateral prefrontal cortex (DLPFC), a prefrontal area primarily involved in cognitive control, will extend its modulation of the ACC in the addicted brain, thereby changing drug-related cue processing. In this study, we examine the N2 component (200–350 ms) of ACC activity during visual presentation of drug-related cues after a single exposure of bilateral (left cathodal/right anodal) tDCS over the DLPFC.

Methods and materials

Subjects

Thirteen crack-cocaine addicted subjects, as defined by the DSM-IV, were recruited for this trial. The mean age of the participants was 30 ± 7 (SD) years, and the mean time of drug abstinence was 16 ± 23 (SD) days. Treatment and data collection were conducted according to the Declaration of Helsinki. This report is part of the results from the study registered in the ClinicalTrials.gov Protocol Registration System under identifier NCT01337297.

EEG recording

Electrophysiological recordings were obtained through a 32-channel system (QuickAmp40, BrainProducts Ltd, Munich, Germany) placed on the scalp according to the International 10-20...
EEG system. Data were recorded with a sampling rate of 1000 Hz and analog filtered between 0.016 and 1000 Hz with a common average reference.

Experimental design and task

The cue-reactivity paradigm was adapted [13] from standard cue-reactivity paradigms established for pictures [14]. To confirm that patients were aware of the picture presentations, the subjects were asked to press a button whenever a crack-related picture was presented (50%).

Data processing

All EEG data were processed using BrainVision Analyzer 2.0 Professional (BrainProducts Ltd, Munich, Germany). Low-resolution brain electromagnetic tomography (LORETA) was applied to estimate the three-dimensional intracerebral current density distribution (µA/mm²). The region of interest (ROI) included Brodmann areas 24, 32 and 33, corresponding to the ACC.

Brain stimulation

Neuromodulation was performed according to our previous study [15]. Briefly, the cathode (20 min; 2.0 mA) was placed over F3 and the anode over F4 according to the 10-20 international system for EEG electrode placement.

Statistical analyses

Data were presented as the mean and standard deviation (SD). The effect of tDCS on the N2 component recorded in the ACC was analyzed via a non-parametric paired test, the Wilcoxon signed rank test, as the activity (current density) did not fulfill the criteria for normality. A P-value of 0.0003 or less was considered statistically significant. GraphPad Prism 5.0 (GraphPad Software Inc, San Diego, CA, USA) was employed for statistical analyses and graphic presentations.

Results

The sham (n = 6) and tDCS (n = 7) groups were matched regarding socio-demographic characteristics and pattern of drug use (data not shown). Changes in the N2 component of the ACC activity (mean current density ± SD) were recorded during neutral or crack-related cue presentations (Fig. 1). The ACC activity during the N2 segment was similar for neutral images before and after brain stimulation or sham stimulation. However, the ACC activity was increased (P < 0.0001) during exposure to crack-related cues in the sham-tDCS group compared to baseline (pre-treatment) activity. In contrast, the ACC activity was decreased (P < 0.0001) during exposure to crack-related cues in the tDCS group compared to baseline.

Discussion

Here, we observe increased ACC activity in the sham group and decreased activity in the tDCS group during visualization of crack-related cues but not neutral cues. Our stimulation protocol involves left cathodal/right anodal stimulation. It is well-established that cathodal tDCS decreases cortical excitability [5–8]. This could suggest that the left cathode but not the right anode over the (left) DLPFC is related to the reduced activity in the ACC during crack-related image visualization after tDCS application. Patients addicted to crack-cocaine have great difficulty avoiding relapse, which could, in part, be due to dysfunctional PFC activity [16]. As a consequence of this dysfunction, PFC areas are hyper-activated when drug addicts are exposed to either the drug or drug cues [17–24]; the ACC is a key structure in these drug-related processes [25]. Although it is not clear if this increased activity is related to the drug craving or to the effort to control it, important evidence proposes that cognitive intervention should attenuate the cue-induced response in the PFC during drug abstinence [1]. In accordance with this view, we observe a significant decrease in the ACC activity during crack-related cues after bilateral tDCS, suggesting a modulatory effect of this noninvasive brain stimulation that may be of clinical importance.
Single prefrontal tDCS specifically modulates the ACC response during visual exposure to drug-related cues in crack-cocaine users. These findings may indicate tDCS as a promising adjunctive treatment for drug addiction.

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References


