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Transcranial direct current stimulation of the prefrontal cortex modulates the desire for specific foods

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Abstract

We aimed to assess whether modulation of the dorsolateral prefrontal cortex (DLFPC) with noninvasive brain stimulation, namely transcranial direct current stimulation (tDCS), modifies food craving in healthy subjects. We performed a randomized sham-controlled cross-over study in which 23 subjects received sham and active tDCS (anode left/cathode right and anode right/cathode left) of the DLPFC. Subjects were exposed to food and also watched a movie of food associated with strong craving. Desire for food consumption was evaluated by visual analogue scales (VAS) and food consumption before and after treatment. In addition we measured visual attention to food using an eye tracking system. Craving for viewed foods as indexed by VAS was reduced by anode right/cathode left tDCS. After sham stimulation, exposure to real food or food-related movie increased craving; whereas after anode left/cathode right tDCS, the food-related stimuli did not increase craving levels, as revealed by the VAS scale. Moreover, compared with sham stimulation, subjects fixated food-related pictures less frequently after anode right/cathode left tDCS and consumed less food after both active stimulation conditions. These changes were not related to mood changes after any type of tDCS treatment. The effects of tDCS on food craving might be related to a modulation of neural circuits associated with reward and decision-making.

Keywords: Food craving; Smoking; Substance addiction; Brain stimulation; Transcranial direct current stimulation; Brain polarization

Introduction

Increasing evidence suggests that the control of eating origins in neural networks associated with decision-making (Pignatti et al., 2006). Although several factors influence the decision of food consumption, such as levels of blood sugar, hormonal changes, food availability, emotional state (including anxiety and depression), physical activity, memory, this information is finally processed in the neural networks associated with decision-making such as the prefrontal cortex, resulting in a final action. Therefore one possible approach to regulate food craving might be to interfere with this decision-making process by changing the activity of the dorsolateral prefrontal cortex (DLPFC).

Several studies from our and other groups have already shown that the prefrontal cortex modulates drug craving and decision-making. For instance, noninvasive brain stimulation, namely repetitive transcranial magnetic stimulation (rTMS), of the DLPFC significantly reduces smoking (Eichhammer et al., 2003; Fregni et al., in press), cocaine (Camprodon, Martinez-Raga, Alonso-Alonso, Shih, & Pascual-Leone, 2007) and alcohol (Boggio et al., 2008) craving. Indeed, one of the most important areas participating in the cue-associated anticipation and planning of drug use involves DLPFC, an area involved in planning and memory (Wilson, Sayette, & Fiez, 2004). For food craving, it was shown that high-frequency (10 Hz) rTMS

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of the left dorsolateral prefrontal cortex decreases food craving in women with frequent cravings for food. Specifically, the results of this study demonstrated that food craving during exposure to foods remained constant in the active treatment group but increased in the sham treatment group (Uher et al., 2005) after exposure to real food. Finally, we showed that stimulation of the dorsolateral prefrontal cortex is associated with decreased risk-taking in the BART task (Fecteau et al., 2007a). Indeed it has been shown that craving (particularly for cocaine) is associated with specific sensations similar to those of individuals engaged in risky behavior (Goeders, 2002).

In the present study, we tested whether modulation of prefrontal cortex with another technique of noninvasive brain stimulation, transcranial direct current stimulation (tDCS), modulates food craving-related behavior. We chose this technique because it modulates brain activity significantly in a safe, powerful and painless way and its effects can last for more than an hour (Nitsche & Paulus, 2000, 2001). It is a technically simple tool in which a continuous weak electric current is applied to the brain via large electrodes that are placed on the scalp of the subject. The effects of tDCS depend on the direction of the electric current, anodal stimulation increases brain activity and excitability and cathodal stimulation reduces it (Nitsche et al., 2003; Antal et al., 2001). Several well-conducted studies in animals and humans confirmed the behavioral and neurophysiological effects of tDCS (Bindman, Lippold, & Redfearn, 1964; Purpura & McMurtry, 1965). In fact, in humans, it has been shown that: anodal stimulation increases cortical excitability in the motor and visual cortex and cathodal stimulation decreases it (Nitsche & Paulus, 2000, 2001). Furthermore the effects of 13 min of tDCS on cortical excitability can last up to 90 min after the end of the stimulation (Nitsche & Paulus, 2001), most probably due to changes of NMDA receptor-efficacy (Nitsche et al., 2003). TDCS, as used in current protocols, is safe in humans as shown by neuropsychological testing (Fregni, Boggio, Lima et al., 2006; Iyer et al., 2005), EEG assessment (Iyer et al., 2005), a neuroimaging study (Nitsche et al., 2004) and brain metabolites evaluation (Nitsche & Paulus, 2001). Finally, recent modeling studies have shown that the amount of electric current going to the brain is large enough to induce a modulation of brain activity (Miranda, Lomarev, & Hallett, 2006; Wagner et al., 2007).

In this study, we tested the hypothesis that bilateral stimulation of prefrontal cortex with tDCS is suited to reduce food craving. Therefore a placebo-tDCS-controlled, randomized, double-blind, crossover study was performed.

Methods

Study subjects

Subjects were recruited by local advertising in websites, flyers and notices distributed throughout local universities. We used the same inclusion criteria as the study of Uher et al. (2005): subjects had frequent ($\geq$3 times/day) and strong urges to eat one of the foods we chose for our experiment (see the list). We included healthy subjects aged between 18 and 55 years. Subjects were excluded if they had any neuropsychiatric disorder, current or past history of alcohol or other drugs abuse, were taking any psychiatric medication or were pregnant. Finally, we excluded subjects with eating disorder as clinically assessed and according to the DSM-IV criteria for eating disorders.

Twenty-three subjects (mean age of 23.7 $\pm$ 7.2, 21 females) were enrolled in this study and 21 completed the entire study (3 different sessions of treatment); 2 subjects did not complete the study – performing only the first session (sham tDCS) in one case and two sessions (sham tDCS and anode right/cathode left) in the other case – the main reason in both cases was that school work precluded them to return to the other stimulation sessions.

This study was performed at Universidade Presbiteriana Mackenzie (Sao Paulo, Brazil). The subjects gave written informed consent for the study, and approval was obtained from the local and also national research ethics committee (SISNEP number CAAE-0004.0.272.000-07). The study was carried out in conform to the principles of the Declaration of Helsinki.

Study protocol

This study was a crossover study in which subjects received three different types of bilateral stimulation of DLPFC with tDCS: (1) active anode left/cathode right tDCS, (2) active anode right/cathode left tDCS and (3) sham tDCS. A 48-h inter-session-interval was used to avoid the potential of any carry-over effects due to stimulation. The order of stimulation was randomized and counterbalanced across subjects using a Latin square design. Participants and the evaluating investigators (except the investigators that applied tDCS) were blinded to the treatment arm.

All stimulation sessions were carried out by the same researchers and at the same time of the day. In addition, subjects were instructed to come 3 h after breakfast or lunch. Demographic and food habits profile data were collected at baseline. The following instruments of evaluation were used:

(1) *Baseline evaluation*: subjects were instructed to complete a visual analogue scale (VAS) with 16 items evaluating mood and a visual analogue scale to measure food craving that consists of four items (similarly to the study of Uher et al., 2005):
   i. Urge to eat (0–10 with 0 corresponding to no urge to eat and 10 corresponding to extremely strong urge to eat)
   ii. Appearance (0–10 with 0 corresponding to very poor appearance and 10 corresponding to the best food appearance)
   iii. Smell (0–10 with 0 corresponding to very unpleasant smell and 10 corresponding to very pleasant smell).
   iv. Taste (0–10 with 0 corresponding to an extremely awful taste and 10 corresponding to the best taste) – note that this item was only evaluated after treatment when subjects were allowed to eat *ad-libitum* (i.e., subjects were invited to eat as much as they wanted of the foods we offered to them).