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Transcranial direct current stimulation enhances soothing positive affect and vagal tone

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ABSTRACT

Transcranial Direct Current Stimulation (tDCS) is a promising tool for the treatment of depression and the dorsolateral prefrontal cortex (dlPFC) is often targeted when exploring tDCS effects on mood. However, the basic effects of tDCS on momentary emotions are inconsistent. We tested whether a single-session of anodal tDCS over the left temporal lobe (T3), topographically closer to the insular cortex than dlPFC, had effects on both vagally-mediated heart rate variability (HRV) and momentary affect in healthy participants. Thirty-four subjects underwent both sham and active tDCS in a counterbalanced random order. ECG was continuously recorded to derive both time and frequency domain HRV indexes. Before and after the tDCS protocol, participants completed momentary affect assessments. Results showed that HRV and soothing positive affectivity were both enhanced after a single-session of tDCS over T3, while negative and activating positive affect were not modulated by the stimulation. After controlling for sex, age, and levels of anxiety and depression a significant association emerged between increases in soothing positive affect and concomitant increases in vagally-mediated HRV. Deficits in soothing positive emotions have consistently been associated with psychopathology and psychotherapeutic approaches aimed to develop this type of emotionality have shown to improve psychological well-being. Thus, present exploratory results may impact future research investigating potential moderators (site of stimulation) and mediators (specificity for a determined type of momentary affect) of the effects of tDCS on psychopathological conditions such as depression.

1. Introduction

Transcranial Direct Current Stimulation (tDCS) is a novel and promising tool for the treatment of depression (Brunoni et al., 2016 for a meta-analysis). At the neuronal level, the primary mechanism of action is the induction of polarity-dependent changes in cortical excitability (Priori et al., 1998). Because of its role in mood (Davidson and Irwin, 1999), the dorsolateral prefrontal cortex (dlPFC) is often targeted when exploring tDCS effects on emotionality. Studies suggest that anodal tDCS over the dlPFC exerts beneficial effects on clinical symptoms of major depression, with significant mood improvement after active compared to sham tDCS (e.g., Fregni et al., 2006; Boggio et al., 2007; Ferrucci et al., 2009).

Despite such clinically relevant results, however, the basic effects of tDCS on momentary emotions seem to be inconsistent. Existing studies seem to indicate that stimulation of dlPFC by tDCS could possibly enhance positive affect (Palm et al., 2012) but report contradictory or no effects on negative affect (Brunoni et al., 2013; Maeoka et al., 2012; Morgan et al., 2014; Motohashi et al., 2013, Nitsche et al., 2012; Peña-Gómez et al., 2011; Plazier et al., 2012; Plewnia et al., 2015; Vanderhasselt et al., 2013). In light of these results, a recent review on the topic reaches the conclusion that tDCS selectively modulates processing of emotional information without significantly influencing mood (Mondino et al., 2015).

In interpreting such contradictory results, it has to be noted that stimulation of dlPFC by the use of tDCS has also effects on the

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autonomic nervous system (see Makovac et al. (in press) for a recent meta-analysis). For example, Gonçalves (2012) found that tDCS over the left dlPFC increases parasympathetic activity and decreases sympathetic activity. Brunoni et al. (2013) consistently found higher vagal activity during emotional negative stimuli viewing and left anodal tDCS as compared to neutral images viewing and sham stimulation. Particularly relevant to our aim, the authors also observed a significant correlation between higher vagal activation and higher mood scores for anodal stimulation.

Existing literature suggests that if the effects of dlPFC on affectivity were partly due to its influence on the parasympathetic modulation of heart rate (HR), this would be particularly true for the so-called “soothing” positive affect. In fact, two different but interactive positive affect regulation systems have been described: “activating” (high approach) positive affect, encompassing excitement, joy, and vitality, and “soothing” (low approach) positive affect associated with peacefulness, contentment, and well-being, and linked to the experience of affiliation and social safety (Depue and Morrone- Strupinsky, 2005; Gable, and Harmon-Jones, 2010; Gilbert et al., 2008). Indeed, high levels of soothing and ‘safety-based’ positive emotions are physiologically indexed by increased HR variability (HRV), which reflects the parasympathetic regulation of the heart via the vagus nerve (Kreibig, 2010; Petrocchi et al., in press; Porges, 2003; Thayer et al., 2012). In line with studies showing that physiology can shape emotional experience (e.g., Gray et al., 2007), it has been suggested that this relationship might be bi-directional, with increases in HRV eliciting increases in soothing positive affect (Stellar et al., 2015).

The first aim of the present exploratory study is to study if a single-session of anodal tDCS has effects on both vagally-mediated HRV and momentary affect in healthy participants compared to sham tDCS. For the reasons reviewed above, we hypothesize to find no impact of the stimulation on negative affect. However, we hypothesize that by enhancing the parasympathetic modulation of HR, tDCS stimulation would specifically trigger soothing (low approach) positive emotions. As such, we also expect changes in vagally-mediated HRV, induced by anodal tDCS, to be correlated with changes in positive soothing affect.

In light of recent accounts linking the left insular cortex with positive, parasympathetically dominated emotional responses (*safety based social emotions*; Lamm and Singer, 2010), the best target area to stimulate for the current aim would be the insular cortex instead of the dlPFC. The insula integrates information about the salience of environmental stimuli with the effects that these stimuli have on the body state, and is involved in the regulation of autonomic responses (Craig, 2011; Critchley et al., 2002; Makovac et al., 2015; Terasawa et al., 2013), consistent with a functional organization that integrates cardiovascular response patterns in the service of emotional behaviours.

A few studies have now been conducted in favor of the notion that electrical stimulation applied over the temporal lobe (T3) can reach surrounding deep cerebral areas like the insula (Lang et al., 2005), with significant effects on parasympathetic and sympathetic modulation of HR (Montenegro et al., 2011; Okano et al., 2015). In light of these promising results, the present study compared anodal and sham tDCS applied on the left temporal lobe.

2. Methods and materials

2.1. Participants

After excluding 10 subjects because of missing data or excessive artifacts and 16 subjects who were taking medications that affect the autonomic nervous system (3 angiotensin receptor blockers, 4 ACE inhibitors, 1 diuretic, 2 calcium antagonists, 2 statins, 3 alphalitics, and 1 steroid), the final sample was composed of 34 subjects (20 women), mean age =43.74 (SD =17.99) years. Healthy participants were recruited from public advertisement and from staff and students of Policlinico Umberto I. Only 1 participant was non-Caucasian. Exclusionary criteria were: age younger than 18 years and self-reported prior history of head injury, major medical neurological or psychiatric disorder, cognitive impairment, history of substance or alcohol abuse or dependence, diagnosis of heart disease, obesity (body mass index (BMI)≥30 kg/m^2), and pregnancy. All participants provided written informed consent. The study has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The study was approved by the Bioethical Committee of S. Lucia Foundation, Rome, Italy. Participants were compensated for their time.

2.2. Procedure

Participants first read and signed the consent form, then completed a series of questionnaires, and lastly underwent the anodal or sham tDCS session while practicing paced breathing. Before and after the tDCS protocol, participants completed the momentary affect assessment. A randomized, sham-controlled, within-subjects design was used. Subjects were randomized in a counterbalanced order to receive both anodal and sham tDCS stimulation with a 1-week interval between sessions. All sessions occurred between 12 p.m. and 4 p.m. Subjects were asked to avoid drinking coffee and smoking cigarettes for at least 24 h prior to the sessions.

2.3. Questionnaires

Participants completed a set of questionnaires accessing socio-demographic (age, BMI, level of education) and lifestyle (nicotine, alcohol, caffeine consumption, medication, and physical activity) information as well as levels of trait anxiety (STAI-Trait; Spielberger et al., 1970) and depressive symptoms (CES-D; Radloff, 1977).

The trait version of the STAI is a 20-item scale that evaluates relatively stable aspects of “anxiety proneness”, including general states of calmness, confidence, and security (e.g., I am a steady person). High validity and reliability (Cronbach's alpha from .86 to .95) have been documented (Spielberger, 1989).

The CES-D is a 20-item self-report scale that assesses the frequency of occurrence of symptoms of depression during the previous week (e.g., I felt that everything I did was an effort). Total score ranges from 0 to 60. Standard cut-offs are 16 for mild depression and 23 for clinical depression. Cronbach's alphas are above .85 in the general population and .90 in depressed patients confirming high reliability (Radloff, 1977).

2.4. tDCS

An anodal or sham tDCS was applied in a counterbalanced random order over T3 (2 mA during 15 min), using the BrainSTIM device (EMS s.r.l., Italy). A cathodal tDCS condition was not included for the reason that, whereas it is well established that anodal tDCS increases cortical excitability, the effects of cathodal tDCS are still a matter of debate (Monte-Silva et al., 2010).

The electric current was applied using a pair of sponges soaked in saline solution (140 mM of NaCl dissolved in Milli-Q water. The anodal and cathodal electrodes (35 cm^2) were connected to a constant current stimulation device with three power batteries (9 V) presenting a maximal output of 10 mA.

For the anodic stimulation targeting left insular cortex, the anode was placed over T3 area according to the international EEG 10–20 system. The cathode was placed over the supraorbital contralateral area (Fp2) and fixed by elastic bands. The electrodes were placed in the same position of the anodal stimulation to perform the sham condition; however, the stimulator was turned off after 30 s. Thus, the subjects reported to feel a tingling or itching sensation coming from the initial electrical stimulation, but they did not receive any further current. This procedure allowed the subjects to remain “blind” in respect to the type