Neuroscience Letters 594 (2015) 12–16

Contents lists available at ScienceDirect

Neuroscience Letters

journal homepage: www.elsevier.com/locate/neulet

Research article

Hemispheric dorsolateral prefrontal cortex lateralization in the regulation of empathy for pain

Gabriel G. Rêgo[a], Olívia M. Lapenta[a], Lucas M. Marques[a], Thiago L. Costa[a], Jorge Leite[b,d], Sandra Carvalho[b,d], Óscar F. Gonçalves[b,d], André R. Brunoni[c], Felipe Fregni[e], Paulo S. Boggio[a,*]

[a] Social and Cognitive Neuroscience Laboratory and Developmental Disorders Program, Center for Health and Biological Sciences, Mackenzie Presbyterian University, 01241-001 Sao Paulo, Brazil
[b] Bouve College of Health Sciences, Department of Counseling and Applied Educational Psychology, Northeastern University, Boston, MA, USA
[c] Service of Interdisciplinary Neuromodulation (SIN), Department and Institute of Psychiatry and University Hospital, University of São Paulo, São Paulo, Brazil
[d] Neuropsychophysiology Lab – CIPsi School of Psychology, University of Minho, Braga, Portugal
[e] Spaulding Neuromodulation Center, Spaulding Rehabilitation Hospital and Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

HIGHLIGHTS

- Neuromodulation of DLPFC excitability changes empathic affective responses.
- It is proposed a common role for left and right PFC in personal distress modulation.
- It is proposed distinct roles for lateralized DLPFC activity in cognitive empathy.

ARTICLE INFO

Article history:
Received 22 January 2015
Received in revised form 2 March 2015
Accepted 20 March 2015
Available online 21 March 2015

Keywords:
Physical pain
Pain empathy
Emotion regulation
Dorsolateral prefrontal cortex
Transcranial direct current stimulation
Pupil dilation

ABSTRACT

The dorsolateral prefrontal cortex (DLPFC) is involved in the cognitive appraisal and modulation of the pain experience. In this sham-controlled study, with healthy volunteers, we used bi-hemispheric transcranial direct current stimulation (tDCS) over the DLPFC to assess emotional reactions elicited by pain observation. Left-cathodal/right-anodal tDCS decreased valence and arousal evaluations compared to other tDCS conditions. Compared to sham condition, both left-cathodal/right-anodal and left-anodal/right-cathodal tDCS decreased hostility, sadness and self-pain perception. These decreased sensations after both active tDCS suggest a common role for left and right DLPFC in personal distress modulation. However, the differences in arousal and valence evaluations point to distinct roles of lateralized DLPFC in cognitive empathy, probably through distinct emotion regulation mechanisms.

1. Introduction

Seeing other people experience pain, usually results in discomfort and distress. This affective response for pain has been investigated with neuroimaging studies [1]. These studies have shown the activation in brain areas such as the dorsolateral prefrontal cortex (DLPFC), the anterior cingulate cortex and the anterior insula [1,2].

Both left and right DLPFC activity have been related to decreased self-pain perception [3,4], and this modulating seems, appears to be associated with its main function on general emotional regulation processes, such as cognitive reappraisal and attention modulation of affective responses [5]. According to Ochsner, Silver and Buhle (2012) [5], different emotional regulation strategies are associated with a lateralized DLPFC activity: while the left side is often involved with the meaning reinterpretation of the affective response, the right side seems to play a role on psychological distancing from the emotional stimulus.

One useful tool to increase our understanding of the role of DLPFC in one's affective reaction when seeing other's pain is transcranial direct current stimulation (tDCS). This simple, but effective

* Corresponding author. Tel.: +55 11 2114 8001; fax: +55 11 2114 8001.
E-mail address: boggio@mackenzie.br (P.S. Boggio).

http://dx.doi.org/10.1016/j.neulet.2015.03.042
0304-3940/

method of neural modulation has been extensively used to assess cognitive processing [6,7]. The tDCS is characterized by the application of a low-intensity direct current through electrodes positioned on the scalp, where cortical activity under anodal electrode usually increases, whereas, it decreases under cathodal electrode [8].

Previous works with tDCS showed that, anodal stimulation over left DLPFC decreased self-reported responses of distress in volunteers seeing images of other people in pain [9]. However, the specific role of lateralized DLPFC in modulating the affective response to observing someone experiencing pain is still not clear. Given this, we aimed here to investigate the lateralized DLPFC role in affective pain empathy using a bifrontal TDCS montage, that would allow modifying left and right DLPFC areas in the opposite manner, during an emotional-laden movies visualization portraying people under painful situations. The motivation for this study was to understand further the specific contribution of DLPFC in the processing of several behavioral domains during affective pain empathy process. It has been shown that the affective areas of the pain matrix are the major neural areas involved when observing the experience of others in pain [2]. Nevertheless, the majority of studies investigating the lateralized aspects of DLPFC on emotion regulation and pain processing use of correlational techniques, leaving unexplained the causal role of such structures in these processes.

Given, the role of both left and right DLPFC on emotion regulation [5] and in decreased self-pain perception [3,4], we hypothesized that tDCS would diminish the impact of movies portraying people in pain, as expressed by self-reports of emotional valence and arousal of the videos, as well as self-reports of changes in mood and self-pain perception.

Finally, to provide physiological complementary information to the behavioral data, we include collected pupil dilation responses. Through its variations, it might be possible to clarify distinct cognitive engagement due to different lateralized DLPFC stimulation [10]. We expected shorter dilation after tDCS in comparison to sham condition.

2. Material and methods

2.1. Participants

Twenty-four healthy students of Mackenzie Presbyterian University volunteered (12 males, mean age 23 ± 2.57, range 18–28) for this study. Inclusion criteria were: (1) age between 18 and 35 years; (2) no history of neurological disorders; (3) no history of substance abuse or dependence; (4) no current use of central nervous system-effective medication; (5) no history of brain surgery, tumor, or intracranial metal implantation; (6) no implant of cardiac pacemaker. This study was conducted in accordance to the ethical standards of the Declaration of Helsinki and was approved by a local ethics committee (SISNEP, Brazil; CAAE no. 390,272,000-08).

2.2. Procedures

The study was a double-blinded, randomized, sham-controlled and single-center study, where the participants were randomly assigned to one of three different stimulation conditions (left-anodal/right-cathodal, left-cathodal/right-anodal or sham). Prior to the experiment, all participants responded to a demographic data survey.

Initially, they were assessed with a visual analog mood scale (VAMS). Immediately after, they underwent tDCS stimulation during 5 min while resting. The stimulation continued during videos presentation (pain stimuli task) while the participant's pupil diameter was measured. After each video the participants evaluated it's emotional valence and arousal. When finishing this task, the tDCS was turned off and the volunteers responded once more to the VAMS and also a self-pain perception scale. The instruments of evaluation and procedures are described in detail.

2.3. Emotional contagion for pain

The task comprised 8 highly arousing pain video clips from the Emotional Movie Database [11]. The selected movies were from the Pain movies categories (no. 1000, 1001, 1002, 1004, 1005, 1006, 1007, 1009), and the averaged validation rates for these stimuli were, in a 1 to 9-point scale: valence 2 ± 0.1 and arousal 7 ± 0.18. The videos were presented using the software Nyan 2.0 (Interactive Minds GmbH). Contrary to the majority of studies in pain empathy that used static images as stimuli, we used videos in order to make the pain scenes more real [12]. All videos consisted of painful situations and were 40 s long and had no audio. After the video, participants were shown two screens in which valence and arousal ratings were assessed. Participants were asked to rate the emotional impact of the experience of seeing the video clip on a 1 to 9-point Self-Assessment Manikin scale [13]. All the videos were presented during tDCS stimulation.

2.4. Visual analog mood scale (VAMS)

Before and after the study all participants were assessed using a visual analog mood scale (VAMS), which uses 5 different mood domains: alert/drowsy; confused/lucid; attentive/neglectful; happy/sad; hostile/friendly. Participants were asked to rate each domain from 0 to 9 (0 corresponding to 100% on one pole and 9 corresponding to 100% of the other pole [14,15].

2.5. Self-pain perception assessment – pain-related words

Immediately after watching all the clips and tDCS stimulation, participants were asked to respond to a subjective self-pain assessment. In this task, participants were requested to rate how much the following words described their feelings after the film clips: tortured, hurt and sore, using a 7-point scale (1 – nothing/7 – too much).

Finally, participants were asked to rate their discomfort with tDCS responding to a questionnaire, which screens for potential adverse effects.

2.6. Pupil dilation assessment and analysis

Pupil dilation data was registered 220 ms before video onset (i.e., baseline) and during film clips with EAS Binocular Series eye-tracking system (interactive minds GmbH) at 120 Hz (sampling rate) using the Nyan 2.0 software (interactive minds GmbH). In order to control for possible environmental interference and pupillary response to light, the study was conducted in a dark and silent room, where participants were seated comfortably at a distance of 1 m from a 19-inch monitor (Lenovo® L197) with their head stabilized by an ophthalmologic chinrest. For pupil dilation analysis, the average pupil dilation for the whole video was obtained and corrected by its baseline. The baseline used was the pupil dilation response in the 100 ms prior to video exposition, during a fixation cross screen.

2.7. Transcranial direct current stimulation

Participants were randomly assigned to one of the three different stimulation conditions in a between-subjects design: anode on the left DLPFC (F3 according to the 10–20 EEG system) and cathode on the right DLPFC (F4); cathode on the left DLPFC and anode on