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TRANSCRANIAL DIRECT CURRENT STIMULATION OF THE DORSOLATERAL PREFRONTAL CORTEX INCREASED PAIN EMPATHY ☆

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Abstract—Empathy for pain, a widely studied sub-form of empathy, is an ability to recognize and share the pain of others. It involves brain regions associated with the emotional component of pain. Recent studies found that emotional pain could be modulated by stimulating the dorsolateral prefrontal cortex (DLPFC) with transcranial direct current stimulation (tDCS). We hypothesized that tDCS of the DLPFC could modulate empathy for pain as well. In the present study, healthy subjects were asked to watch pictures depicting somebody under painful or non-painful conditions and to evaluate the pain intensity of others as well as their own pain-related unpleasantness before and after tDCS of the DLPFC. It was found that ratings for others' pain increased in subjects with an anodal tDCS of the DLPFC in comparison to those with sham tDCS, indicating enhanced pain empathy with the anodal tDCS. Furthermore, the changes of ratings for others' pain were positively correlated with the changes of pain-related self-unpleasantness. These findings indicate that tDCS could modulate pain empathy and be used as a potential tool for modulating diseases accompanied with empathy deficits.

Key words: transcranial direct current stimulation (tDCS), dorsolateral prefrontal cortex (DLPFC), pain empathy, pain-related emotion.

INTRODUCTION

Empathy for pain is the ability to recognize the pain perception of another person by imaging or observing other individuals in pain (Singer et al., 2004). It is measured by evaluating the severity of others' pain by observers (Singer et al., 2004; Jackson et al., 2005). Empathy for pain is the most studied sub-form of empathy, which plays a key role in the prosocial behaviors of human beings and is involved in many psychopathological disorders characterized by empathy deficits (Decety and Moriguchi, 2007). Investigating the modulation of empathy for pain will help treat these disorders.

There is evidence that empathic pain involves brain regions responsible for emotional pain processing. Neuroimaging studies found that when one was watching somebody receiving painful stimuli (Singer et al., 2004; Lamm et al., 2011), the brain regions associated with the emotional component of pain were activated, including the anterior cingulate cortex (ACC), insular cortex and prefrontal cortex (Treede et al., 1999; Tracey, 2005). The ACC and insular cortex are positively related with empathic pain behaviors (Jackson et al., 2005). In contrast, lesions on these brain regions, for example, lesions of the anterior insular cortex, lead to pain empathy deficits (Gu et al., 2012). These findings support the 'emotional-sharing' theory of pain empathy (Singer et al., 2004; Jackson et al., 2005; Gu et al., 2012).

Evidence shows that emotional pain could be modulated by transcranial direct current stimulation (tDCS), a non-invasive brain stimulation technique that increases or decreases the excitability of brain regions (Nitsche and Paulus, 2000; Utz et al., 2010). A previous study reported that tDCS of the left dorsal lateral prefrontal cortex (DLPFC) with 2 mA for 5 min altered the emotional discomfort evoked by pictures depicting painful events in healthy subjects (Boggio et al., 2009). It is known that the DLPFC has extensive connections with the ACC and anterior insular (Singer et al., 2009). In addition, an functional magnetic resonance imaging (fMRI) neuroimaging study confirmed that tDCS of the DLPFC could activate the ACC and DLPFC (Keeser et al., 2011; Weber and Messing, 2014; Nelson et al., 2014). Thus, we hypothesized that tDCS of the DLPFC could modulate empathy for pain.

To test this hypothesis, the present study investigated the observer's rating for other's pain and the relationship with the observer's pain-related emotion when viewing pictures of someone under painful and unpainful

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Abbreviations: ACC, anterior cingulate cortex; ANOVA, analysis of variance; DLPFC, dorsolateral prefrontal cortex; IRI, Interpersonal Reactivity Index; SAM, self-assessment manikin; tDCS, transcranial direct current stimulation.

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conditions after an anodal, cathodal or sham tDCS modality.

EXPERIMENTAL PROCEDURES

Subjects

Twenty-seven healthy right-handed subjects (mean age of 23.6 ± 2.9 years, 18 females) participated in the study. All the subjects had no history of epilepsy, psychiatric disease and were medication-free during the experiments. There were no metal implantations in their bodies as well. All the participants gave their written informed consent in accordance with the principles of the Declaration of the Helsinki. Subjects were blind to the purpose of the research. This experiment was approved by the Ethics Committee of the Beijing Normal University, China.

Experimental procedure

After measuring trait empathy, the subjects were randomly assigned into three experimental groups: the anodal stimulation group (eight subjects), the cathodal stimulation group (nine subjects) and the sham stimulation group (10 subjects). The subjects were blind to the grouping. The other-pain rating and pain-related self-unpleasantness rating tests were performed before and after the tDCS (Fig. 1).

Trait empathy. The Interpersonal Reactivity Index (IRI) was applied to estimate trait empathy (Davis, 1996). The Chinese version of the IRI has been evaluated by Siu and Shek (2005). This survey consists of 28 items, including empathic concern (EC), personal distress (PD), perspective taking (PT) and fantasy scale (FS) subscales. Each item was rated by a five-point Likert scale, ranging from 0 (does not describe me well) to 4 (describes me well). The subjects gave their scores for each item (Table. 1).

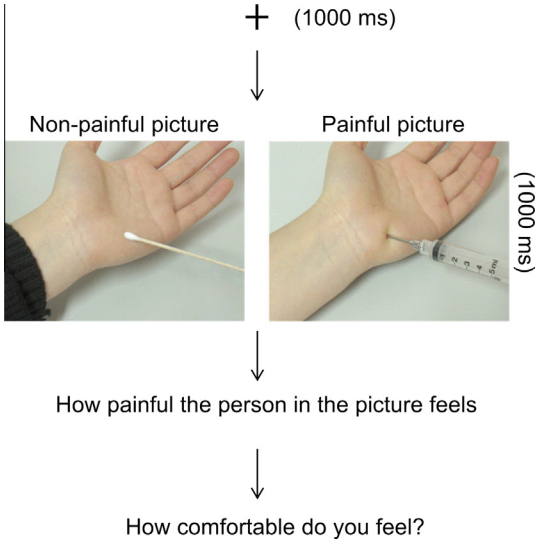

Fig. 1. Diagram of the experimental procedure. After a cross line shown on the screen, a picture depicting painful or non-painful conditions was presented for 1 s. The subjects were then asked to rate the pain intensity of the person in the picture by a 0–9 scale. When subjects finished the rating by pressing a number in the keyboard, subjects then responded to a question on how comfortable they felt when watching the picture by a scale of 0–5.

Other-pain rating. The subjects sat in front of a screen at a distance of one meter. Pictures depicting right hands being injured and matched pictures showing intact hands (20 of each) were presented on the computer screen with the E-prime software version 2 (Psychology Software Tools, Inc., Pittsburgh, Pennsylvania, USA). Each picture lasted for 1 s and was followed by a question assessing how painful the person in this picture felt. The subjects were instructed to evaluate the pain intensity of the person in the picture on a scale of 0–9 (0: no pain at all, 9: extreme pain). These pictures appeared randomly.

Pain-related self-unpleasantness rating. After evaluating pain in others, the subjects were asked to estimate their own comfortableness when shown a scale showing six self-assessment manikin (SAMs), from smiling (0: pleasant) to crying (5: most unpleasant).

tDCS. Direct current was delivered by a battery-driven, constant current stimulator (DC-STIMULATOR, NeuroConn GmbH, Ilmenau, Germany) and applied to the scalp through a saline-soaked pair of surface sponge electrodes (35 cm^2). During the stimulation, a constant current of 2 mA was applied for 5 min (including 15 s ramped up and 15 s ramped down). For the anodal stimulation, an anode electrode (positive current input) was placed over the left DLPFC, the F3 according to the international 10–20 system for Electroencephalography (EEG) electrode placement, which was validated by a previous neuronavigational study (Herwig et al., 2003) and a cathodal electrode was placed on the FP2. For the cathodal stimulation, the cathodal electrode was placed on the F3, while the anodal on the FP2. The placement of sham stimulation was equal to anodal stimulation but with a 2-mA current for 30 s.

Statistical analysis

One-way analysis of variance (one-way ANOVA), with group as the independent variable, was used for the comparison of the differences among the three groups. Bonferroni Post hoc analysis was used if the ANOVA findings were significant. The eta squared (η^2) was calculated for estimating the effect sizes. The significance level was set at $p < 0.05$.

RESULTS

Anodal tDCS increased pain empathy

The effect of tDCS on pain empathy was evaluated by the difference of ratings for others' pain before and after tDCS. The tDCS modulated the rating for others' pain when subjects were viewing others under painful conditions ($F_{(2,26)} = 3.824$, $p = 0.036$, $\eta^2_{(group)} = 0.242$). After the anodal stimulation of the left DLPFC, the rating