Journal of Affective Disorders 190 (2016) 443–449

Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Research report

Emotional reactivity to valence-loaded stimuli are related to treatment response of neurocognitive therapy

Marie-Anne Vanderhasselt [a,b,*], Rudi De Raedt [c], Victoria Namur [d], Leandro C.L. Valiengo [e,f], Paulo A. Lotufo [e], Isabela M. Bensenor [e], Chris Baeken [a,g], Paulo S. Boggio [d], Andre R. Brunoni [e,f,**]

[a] Department of Psychiatry and Medical Psychology, Ghent University, Belgium
[b] Faculty of Medicine and Pharmacy, Free University Brussels, Brussels, Belgium
[c] Department of Experimental-Clinical and Health Psychology, Ghent University, Belgium
[d] Cognitive Neuroscience Laboratory and Developmental Disorders Program, Centre for Health and Biological Sciences, Mackenzie Presbyterian University, Sao Paulo, Brazil
[e] Interdisciplinary Center for Applied Neuromodulation & Clinical and Epidemiologic Research Center, University Hospital, University of São Paulo, São Paulo, Brazil
[f] Service of Interdisciplinary Neuromodulation & Laboratory of Neurosciences (LIM-27), Department and Institute of Psychiatry, University of São Paulo, São Paulo, Brazil
[g] University and Department of Psychiatry, University Hospital UZBrussel, Belgium

ARTICLE INFO

Article history:
Received 18 August 2015
Received in revised form
7 October 2015
Accepted 15 October 2015
Available online 28 October 2015

Keywords:
Emotional Context Insensitivity
Emotional reactivity
Positive and negative affect
Neurocognitive intervention
Depressive symptoms

ABSTRACT

Emotional Context Insensitivity (ECI) is a psychological feature observed in depressed patients characterized by a decreased emotional reactivity when presented to positive- and negative valence-loaded stimuli. Given that fronto-cingulate-limbic circuits are implicated in abnormal reactivity to valence-loaded stimuli, neurocognitive treatments engaging the prefrontal cortex may be able to modulate this emotional blunting observed in MDD. Therefore, our goal was to evaluate emotional reactivity in depressed patients before and after a combination of neurocognitive interventions that engage the prefrontal cortex (cognitive control training and/or transcranial direct current stimulation). In line with the premises of the ECI framework, before the start of the antidepressant intervention, patients showed blunted emotional reactivity after exposure to negative valence-loaded stimuli. This emotional reactivity pattern changed after 9 sessions of the intervention: positive affect decreased and negative affect increased after watching a series of negative valence-loaded stimuli (i.e. images). Interestingly, higher emotional reactivity (as indexed by a larger increase in negative affect after watching the valence-loaded stimuli) at baseline predicted reductions in depression symptoms after the intervention. On the other hand, higher emotional reactivity (as indexed by a decrease in positive affect) after the intervention was marginally associated with reductions in depression symptoms. To conclude, emotional reactivity increased after the neurocognitive antidepressant intervention and it was directly associated to the degree of depression improvement.

1. Introduction

Major Depressive Disorder (MDD) is worldwide one of the most common psychiatric conditions (Goodwin et al., 2006), affecting nearly 20% of the population (Kessler, 2002). Patients with MDD, despite presenting symptoms such as low mood and anhedonia, also display abnormal emotional responses immediately after being exposed to specific elicitors (operationalized as emotional reactivity). Compared to healthy individuals, MDD patients present a generalized blunting of emotional reactivity to positive and negative valence-loaded stimuli (for a meta-analysis, see Bylsma et al. (2008)), which is a well-studied phenomenon described as *Emotion Context Insensitivity* (ECI) (Rottenberg et al., 2005). The blunted response to positive information is a well-known and

* Corresponding author at: Department of Experimental Clinical and Health Psychology, Ghent University, Henri Dunantlaan 2, B-9000 Gent, Belgium. Fax: +32 1 9 264 64 87.
** Corresponding author at: Centro Interdisciplinar de Neuromodulação Aplicada, Hospital Universitário, Cidade Universitária, Av. Prof. Lineu Prestes 2565, CEP 05508-000 Butantã, Brazil. Fax: +55 11 3091-9246.
E-mail addresses: MarieAnne.Vanderhasselt@Ugent.be (M.-A. Vanderhasselt), Brunoni@usp.br (A.R. Brunoni).

http://dx.doi.org/10.1016/j.jad.2015.10.022
0165-0327/

frequently studied phenomenon (e.g., studies on anhedonia), whereas the blunted response to negative information is quite intriguing and is still a matter of debate.

Besides the vast amount of research studying this ECI phenomenon, limited research has considered individual differences in emotional reactivity longitudinally. In one of the few studies, increased emotional reactivity at the start of an antidepressant drug treatment was associated with less severe depressive symptom over the 18 months course this intervention (Peeters et al., 2010). These results are in line with the ECI view stating that blunted emotional reactivity predicts a more pernicious course of the depressive episode (for a systematic review, see Morris et al. (2009)). However, it remains unclear (1) whether emotional reactivity varies as a function of ameliorating depressive symptoms (e.g., after an antidepressant intervention), and (2) whether this potential change in emotional reactivity is associated with the improvement of depressive symptoms.

Abnormal processing of emotional information has been associated with a dysfunctional engagement of the prefrontal and the anterior cingulate cortex, neural correlates that are interacting with subcortical limbic areas (Davidson et al., 2002; Seminowicz et al., 2004; Johnstone et al., 2007; Ochsner and Gross, 2008). Prior research has reported blunted emotional reactivity to negative valence-loaded stimuli, and associated this blunted response with abnormal neural activity in areas that are part of the fronto-cingulated and limbic circuits (e.g., Baeken et al., 2010). For example, using event-related potentials, Foti and co-workers showed a blunted emotional reactivity to negative valence-loaded stimuli in MDD (Foti et al., 2010), specifically at late more elaborative processing stages (as compared to the early). Potentially, this blunted emotional reactivity results from an abnormal activation within the prefrontal cortex (Hajcak et al., 2010). Other studies showed blunted neural activity in the subgenual anterior cingulate to negative valence-loaded images in MDD (Baeken et al., 2010). Based on the results from neuroimaging studies, experimental research has demonstrated that modulating the prefrontal cortex results in a significant reduction of depressive symptoms and in adjusted emotional information processes (e.g., Vanderhasselt et al., 2009).

Amongst other, two neurocognitive interventions engaging the prefrontal cortex have been used in prior research in major depressed patients: Cognitive Control Training (CCT) and transcranial direct current stimulation (tDCS). CCT is performed using neurocognitive tasks that engage working memory (Siegle et al., 2007, 2014), thereby activating fronto-cingulate and limbic circuits (Siegle et al., 2007). tDCS, on the other hand, consists of the induction of a weak, direct electric current through electrodes placed over the scalp that can increase (anode) and decrease (cathode) cortical excitability, also beyond the period of stimulation (Nitsche et al., 2008). Both interventions aim to increase prefrontal activity, through either active task engagement (CCT) or passive electric stimulation (tDCS), and are found to ameliorate depressive symptoms (Siegle et al., 2014; Segrave et al., 2014; Brunoni et al., 2014). The CCT is administered *during* each neuromodulation session in order to have synergetic effects. This is because tDCS is known to induce global effects on neuroplasticity (Nitsche et al., 2008), and training (learning) may be a means to act synergistically with this effect, and thus making it more specific to cognitive functions that are disabled in MDD. All in all, given that the fronto-cingulate-limbic circuits are implicated in abnormal reactivity to valence-loaded stimuli, neurocognitive treatments specifically engaging the prefrontal cortex may be able to modulate the emotional blunting in patients with MDD.

Hence, in the current study, part of a larger clinical trial[1], we (1) investigated emotional reactivity before versus after the neurocognitive interventions, and (2) examined whether such emotional reactivity would be associated to beneficial changes in depressive symptoms. We specifically focused on reactivity to negative valence-loaded stimuli as these are most investigated and debated in the context of emotion sensitivity dysregulation (e.g. Baeken et al., 2010; Foti et al., 2010; Banks et al., 2007). Participants were presented a series of negative images, and were asked to report their affect right before and after the presentation of this series of images (self-reports of positive and negative affect; Watson and Tellegen, 1985). Based on the premises of the ECI, we hypothesized a blunted emotional reactivity (e.g., the change in affect before versus after watching these valence-loaded stimuli) at baseline. Given the lack of studies evaluating emotional reactivity following a neurocognitive antidepressant intervention engaging the prefrontal cortex, we explored emotional reactivity after the neurocognitive interventions. As alterations in emotional reactivity are functionally significant for the MDD course (e.g., for a review, see Morris et al., 2009), we expected the amount of emotional reactivity at baseline (before the neurocognitive intervention) to be associated with a larger reduction in depressive symptoms after the neurocognitive interventions. Finally, we also explored whether emotion reactivity at the end of the intervention would be associated with a reduction in depressive symptoms after the neurocognitive interventions. Given that our prior analyses revealed that tDCS did not show an additional effect above and beyond the antidepressant effects of cognitive training (Brunoni et al., 2014; Vanderhasselt et al., 2015), and that the sample size of the separate stimulation groups are rather small, we decided to collapse analyses across all participants.

2. Methods

The original study was approved by the Local and National Ethics Committee and is registered in clinicaltrials.gov (NCT01434836). All patients provided written informed consent. The trial was conducted in the University Hospital, University of São Paulo, Brazil and in the Mackenzie Presbyterian University, also situated in São Paulo, Brazil from September 2011 to May 2013. This present report focuses on the emotional reactivity patterns of this sample before and after treatment.[2]

2.1. Participants

Thirty-seven right-handed individuals (M/F, age range years; $M=44.03$, $SD=10.75$) meeting the DSM-IV criteria for MDD were included in this study. Patients were diagnosed with MDD by certified psychiatrists using the Portuguese-validated version of the Mini International Neuropsychiatric Inventory (MINI). Patients had to report a score of ≥ 21 on the 24-item Hamilton Rating Scale for Depression (HAM-D; (Hamilton, 1967)), report low suicide risk and be between 18 and 65 years old. They were in a stable drug regimen for at least 6 weeks before the start of the intervention and continued on steady pharmacotherapy during the trial. Antidepressant pharmacotherapy consisted basically of Selective Serotonin Reuptake Inhibitors (SSRI) or Selective Serotonin/ Noradrenalin Reuptake Inhibitors (SNRI). Benzodiazepine drugs were

[1] This clinical trial was set up to investigate the add-on effects of tDCS (one group receiving real, another group receiving sham) on the effects of the CCT. Given that these interventions and their clinical effects, as well the relationship with rumination were already reported, please refer to Brunoni et al. (2014) and Vanderhasselt et al. (2015) for further details.

[2] Indices of the sympathetic nervous system were also measured, such as cortisol and heart rate. Due to technical problems, data will not be reported.