

## ABSTRACT

**Background:** Considerable number of patients suffering from depression (unipolar or bipolar) does not reach a relief undergoing pharmacological or psychotherapeutic treatments available. There is a need for a new treatment approach or a clinically relevant predictor of antidepressant response to improve the treatment results. Non-invasive neurostimulation methods (NIBS) like repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS) are the subject on clinical and research field on the treatment of depression in past decades. There is paucity of data comparing these two NIBS techniques. Early change of prefrontal theta cordance seems to be a promising EEG predictor of antidepressant response. The aim of this thesis is to explore and compare the efficacy of rTMS and tDCS in the treatment of depression and add more information on the predictive value of prefrontal cordance change on antidepressant treatment.

**Methods:** In Study 1 (n = 57), we compared the antidepressant effect of 4-week course of tDCS vs. pharmacological treatment by venlafaxine (VNF) in patients suffering from major depressive disorder. In Study 2 (n = 117), we made an indirect comparison of efficacy and acceptability of three different approaches (left anodal tDCS, low-frequency (LF) rTMS applied on right dorsolateral prefrontal cortex (DLPFK) and VNF) in treatment course of major depressive disorder. In Study 3 (n = 60), we compared three different rTMS protocols (10Hz rTMS over the right ventrolateral prefrontal cortex (VLPFK), the left 10Hz DLPFK rTMS, and sham stimulation) as an add-on treatment in patients with bipolar depression (BDE). In Study 4 (n = 103), we evaluated EEG changes (frontal and occipital alpha 1, alpha 2, asymmetry (FAA1/2, OAA1/2), theta power along with prefrontal theta cordance (PFC)) during antidepressant treatment and its effectiveness in prediction of treatment response.

**Results:** The findings of Study 1 suggest that tDCS and VNF are similarly effective in the acute treatment of unipolar depression and early relapse prevention. In study 2, our analysis found comparable efficacy and acceptability of LF-rTMS, tDCS, and VNF, indicating the potential clinical relevance of these interventions in the acute treatment of major depressive disorder. In study 3, we did not detect superiority of the two selected active rTMS protocols over placebo rTMS administered as adjunctive treatment to BDE. In study 4, we found that only a decrease in PFC in responders and an increase in OAA1/2 at week 1 in non-responders were related to antidepressant treatment outcomes.

**Conclusions:** Our studies highlight the clinical potential of tDCS and rTMS in the acute treatment of unipolar depression. We have not demonstrated the efficacy of 10Hz rTMS in BDE treatment. Finally, we confirmed the clinical potential of early PFC change as a predictor of response to antidepressant treatment.

**Keywords:** Depressive disorder, Bipolar affective disorder, Treatment, Response prediction, Noninvasive Brain Stimulation – NIBS; Repetitive transcranial magnetic stimulation – rTMS, Transcranial direct current stimulation – tDCS