

Pre-unblinding assessment of feasibility, data quality, and neural modulation in an ongoing RT-fMRI neurofeedback trial for bipolar disorder: interim findings from NEUROFEED-BD

Mathilde Rodrigues Da Rocha^{1,2}, Pamela Pindi^{1,2}, Yann Leprince¹, Yury Koush⁴, Jonathan Chabert^{1,2}, Océane Dufrenne^{1,2}, Jessica Camil^{1,2}, Camille Piguet³, Jan Warnking⁵, Laurent Lamalle⁵, Bixente Dilharreguy⁶, Mircea Polosan⁵, Sebastien Gard⁷, Charles, Laidi^{1,2,8}, Josselin Houenou^{1,2,8}, Pauline Favre^{1,2}

¹ INSERM Unit U955, UPEC, Team “Translational NeuroPsychiatry” Créteil, France

² Neurospin, CEA, Université Paris-Saclay, Gif-sur-Yvette, France

³ Department of Psychiatry, Faculty of Medicine, University of Geneva & Geneva University Hospitals

⁴ Center for Bio- and Medical Technologies, Moscow, Russia

⁵ Univ. Grenoble Alpes, Inserm, U1216, CHU Grenoble Alpes, Grenoble Institut Neurosciences, Grenoble, France

⁶ INCIA, EPHE, Université PSL, Univ Bordeaux, CNRS, Bordeaux, France

⁷ Pôle de Psychiatrie Générale et Universitaire, Centre Hospitalier Charles Perrons, Bordeaux, France

⁸ APHP, CHU Mondor, Psychiatry Department, Créteil, France

Introduction

Bipolar disorder (BD) is a chronic disabling condition affecting 1–3% of the population, associated with relapse, functional impairment, and persistent residual depressive and anxiety symptoms during inter-episode periods (Judd et al., 2008). These symptoms are insufficiently targeted by current treatments and are linked to poorer functioning. Neurobiological models implicate fronto-limbic imbalance, including amygdala hyperreactivity and impaired prefrontal regulation (Phillips et al., 2014). Real-time fMRI neurofeedback has shown promising effects in major depressive disorder (Pindi et al., 2022). This ongoing study evaluates whether neurofeedback targeting emotion regulation network activity can improve residual symptoms in patients with BD. Here, we present the study design, neurofeedback procedure, preprocessing pipeline, and preliminary feasibility and data-quality metrics from the participants included to date.

Methods

This double-blind RCT plans to include 64 patients with type I or II BD without a major mood episode for at least two months, but with residual depressive symptoms defined by a Montgomery-Åsberg Depression Rating Scale (MADRS) score > 5 and ≤ 20 . To date, 14 participants have been included. Patients are randomized to either an active neurofeedback group, receiving feedback from the weighted hemodynamic activity of the emotional network, or a sham group, receiving a signal from a non-emotional region. An initial session defines individualized regions of interest and a weight map from responses to emotional stimuli, used to compute the weighted BOLD feedback signal. The intervention comprises three fMRI-neurofeedback sessions. Each session includes three training runs and one transfer run, without feedback. Within each run, participants visualize alternatively blocks of emotionally neutral images, which they are instructed simply to view, and blocks of negative/aversive images, during which they are instructed to down-regulate their emotional response. The intermittent feedback is displayed as a thermometer reflecting the BOLD variation in the target regions between the regulated aversive period and the preceding neutral period. Currently acquired fMRI data have been quality-controlled with MRIQC, preprocessed with fMRIPrep, and are currently being analyzed. Clinical assessments are performed before and after the intervention, and during follow-up at 4 and 8 weeks (Clinical Trial ID : NCT05802446).

Results

Preliminary results show that, on average, 92% of baseline and neurofeedback runs were completed by patients. Most runs fall within ± 2 SD across motion (FD), signal quality (tSNR, FBER, EFC), and temporal stability (DVARs) metrics; 24% were flagged for visual review (beyond ± 2 SD), and 4% were excluded (beyond ± 3 SD). Ongoing analyses are testing neurofeedback efficacy by assessing changes in regulation quality across runs and sessions, as well as transfer of this ability

in the absence of feedback. As the trial is still blinded, these analyses cannot yet be compared between the active and sham groups. Ongoing analyses already suggest a descriptive improvement in regulation performance across training sessions, with emerging statistical evidence supporting this effect.

Conclusions

This study supports the feasibility of real time fMRI neurofeedback in stabilized patients with BD and shows interesting perspectives for targeting residual symptoms through emotion-regulation networks. The blinded design and forthcoming active-versus-sham comparison, including MADRS change, secondary clinical outcomes and fronto-limbic imaging markers, may help determine its clinical efficacy.

References

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