

Restoring emotional stability through Neurofeedback and AI for transformative Empowerment

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Abstract.

Emotion regulation is a core transdiagnostic mechanism underlying affective disorders, such as major depressive disorders (MDD), generalized anxiety disorders (GAD), and post-traumatic stress disorder (PTSD). Converging evidence implicates dysfunction within prefrontal–limbic networks supporting emotion regulation as a key mechanism underlying symptom onset and persistence in MDD [1]. Despite established pharmacological and psychotherapeutic interventions, approximately 40–60% of MDD patients do not achieve remission, highlighting the need for scalable, mechanism-driven treatments targeting neural circuitry. Neurofeedback (NF) based on functional magnetic resonance imaging has shown promise in enhancing voluntary modulation of emotion-related brain networks [2,3]; however, its cost and limited accessibility constrain clinical use. The present study evaluates an electroencephalography (EEG)-based neurofeedback intervention targeting emotion regulation circuitry as an adjunctive treatment for MDD, with or without anxiety symptoms. The approach uses standardized weighted low-resolution brain electromagnetic tomography (swLORETA) for source-level EEG reconstruction, enabling circuit-guided feedback targeting prefrontal–limbic systems. Prior work supports the feasibility of this approach for modulating emotion regulation networks with clinically relevant outcomes [4]. In this ongoing randomized controlled study, 72 patients with MDD are assigned to NF, yoked-sham NF, or control conditions. The NF group receives 10 sessions over five weeks (two per week), targeting emotion regulation circuitry. In the yoked-sham condition, participants undergo identical procedures, but feedback is derived from another participant's neural activity, controlling for non-specific effects. The control group receives treatment as usual. Clinical and cognitive outcomes are assessed at baseline and post-intervention. The study aims to evaluate clinical efficacy and characterize neurophysiological changes associated with the modulation of emotion regulation circuits. In parallel, exploratory analyses apply deep learning methods to EEG time-series data to identify neural signatures of training response and predictors of individual responsiveness. At submission, data collection is ongoing, and analyses are based on an interim sample (n=43). Linear mixed-effects models are applied with fixed effects of group, time, sex, and their interaction, and random intercepts for participants. Preliminary results indicated significant group-by-time interactions across outcomes. Compared with controls and yoked-sham groups, the NF group showed greater reductions in depressive symptoms on the Montgomery–Åsberg Depression Rating Scale ($\beta=-14.79$,

$p < .001$) and Hamilton Depression Rating Scale ($\beta = -12.7$, $p < .001$). Similar effects were observed in Beck Depression Inventory total score ($\beta = -21.31$, $p < .001$) and its cognitive subscale ($\beta = -4.44$, $p = .01$), and in rumination (RRS: $\beta = -10.07$, $p = .041$). The sham condition showed smaller effects, with a significant reduction only in Beck Depression Inventory score ($\beta = -13$, $p = .007$), and no significant changes in clinician-rated symptoms, rumination, or cognition-related metrics. Interestingly, NF improved cognitive flexibility (AAQ-II: $\beta = -15.26$, $p = .001$), whereas no effect was observed in the yoked-sham group ($p = .96$). Across outcomes, effect sizes were larger in the NF group. Taken together, these findings provide preliminary evidence that circuit-targeted electroencephalography neurofeedback may induce clinically meaningful improvements across both affective and cognitive domains in MDD. The observed divergence between neurofeedback and yoked-sham conditions supports the specificity of the intervention. However, given the ongoing nature of the trial, these findings should be considered preliminary. Full cohort completion is required to confirm efficacy, robustness, and generalizability.

References

- [1] Fitzgerald, P. B., Laird, A. R., Maller, J., & Daskalakis, Z. J. (2008). A meta-analytic study of changes in brain activation in depression. *Human brain mapping*, 29(6), 683-695.
- [2] Linhartová, P., Látalová, A., Kóša, B., Kašpárek, T., Schmahl, C., & Paret, C. (2019). fMRI neurofeedback in emotion regulation: A literature review. *NeuroImage*, 193, 75-92.
- [3] Trambaiolli, L. R., Kohl, S. H., Linden, D. E., & Mehler, D. M. (2021). Neurofeedback training in major depressive disorder: a systematic review of clinical efficacy, study quality and reporting practices. *Neuroscience & Biobehavioral Reviews*, 125, 33-56.
- [4] Wu, Y. C., Yu, H. E., Yen, C. F., Yeh, Y. C., Jian, C. R., Lin, C. W., & Lin, I. M. (2024). The effects of swLORETA Z-score neurofeedback for patients comorbid with major depressive disorder and anxiety symptoms. *Journal of affective disorders*, 350, 340-349.