

Harnessing and understanding the psychedelic-induced enhanced neuroplasticity window for Neurofeedback augmentation

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Introduction

Neurofeedback (NF) has emerged as a promising approach for inducing targeted neuroplastic change. NF capacity appears to be limited by considerable individual differences, with poor NF literacy reaching up to 57% in EEG-NF studies (Alkoby et al., 2018). Psychedelic and psychedelic-like compounds, including ketamine, have been proposed to induce a transient window of enhanced neuroplasticity that may facilitate experience-dependent neural change. Yet, a direct demonstration of the proposed plasticity window in humans remains lacking. Here, we introduce a novel experimental framework designed to test whether ketamine-induced neuroplasticity can augment amygdala-targeted EEG-NF capacity by using fMRI informed electrical fingerprint of the Amygdala (Amyg-EFP). This combination may improve Amyg-EFP-NF capacity and thereby hold clinical booster for disorders involving amygdala dysregulation, such as PTSD and anxiety. In addition, this design leverage NF induced changes (neural and behavioral) as evidence for psychedelic-related plasticity processes in humans.

Methods

The study will use a randomized, placebo control, double-blind design. Healthy participants (N=90) will receive either IV ketamine or midazolam. Participants will undergo a baseline assessments with behavioral tasks, physiological, and neuroimaging measurements, followed by drug administration and then Amyg-EFP-NF training. To utilize ketamine's proposed plasticity window, 8 sessions of NF training will be conducted over consecutive days. The protocol will combine upregulation and downregulation of amygdala EFP signal. We hypothesize that ketamine will enhance NF learning, accelerate the acquisition of up or down regulation capacity, and increase regulation flexibility. More exploratory we presume that ketamine will enhance the contribution of emotion regulation, learning-related processes, interoception, and cognitive flexibility to the NF capacity.

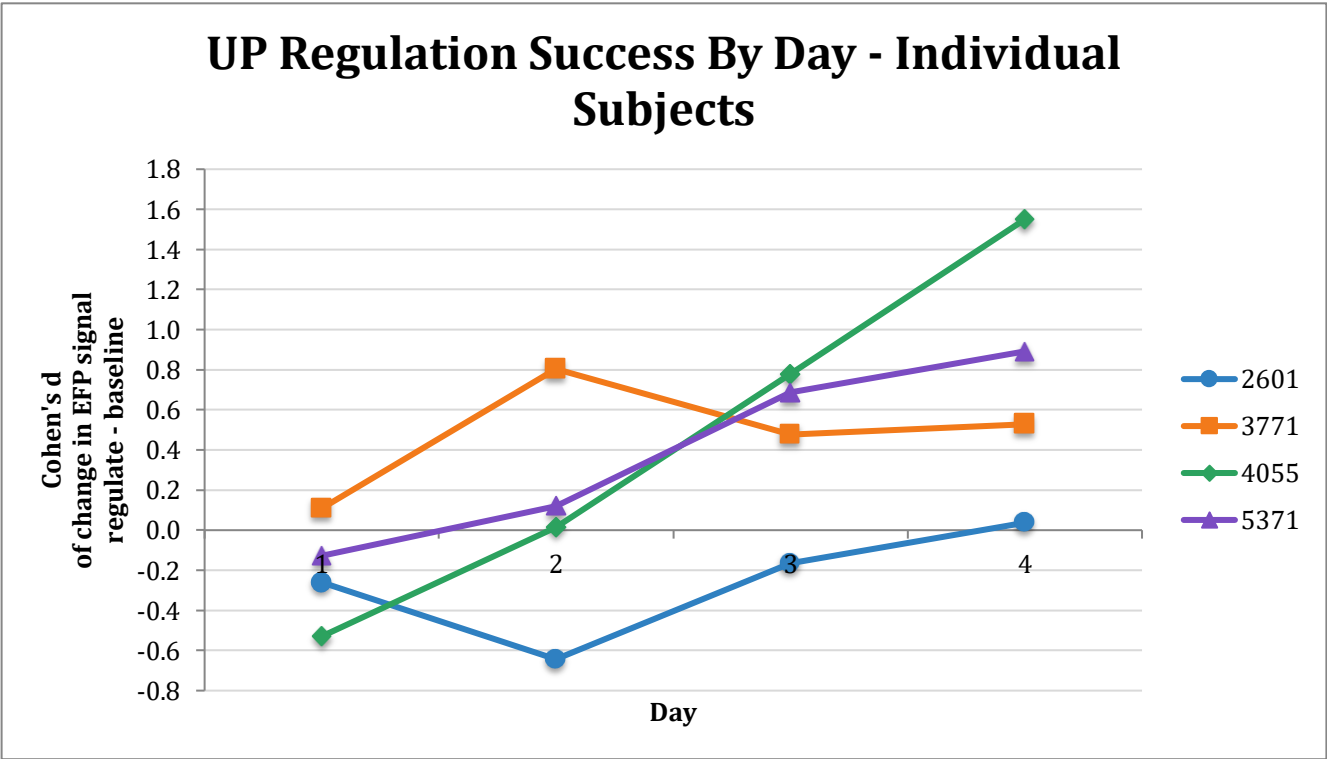
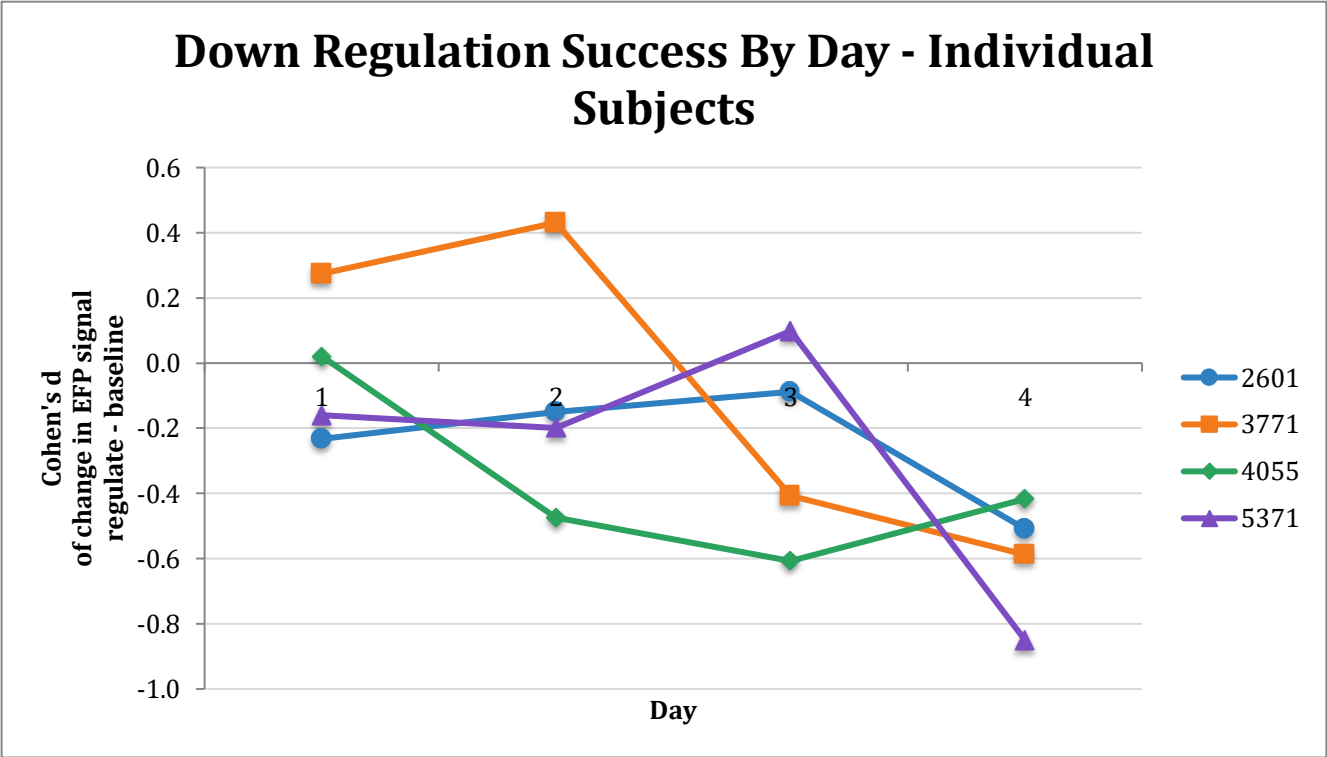
Results

A pilot was conducted to evaluate the feasibility and utility of the bidirectional Amyg-EFP NF protocol. Descriptive results across four training days indicated increasing separation between the two regulation conditions, with positive upregulation effects and negative downregulation effects by the final session. Participants differed in the magnitude and timing of regulation effects, the rate of change across sessions, and the shape of individual learning slopes. The observed variability across individuals and sessions (ES improvement from the first to the final session ranged from 0.276 to 0.862 for downregulation and 0.299 to 2.079 for upregulation) will enable us to examine ketamine-related differences in self-neuromodulation capacity and learning slopes across the study arms. More preliminary results, including data from the ketamine-NF arm, will be presented at the time of the conference.

Conclusions

This study introduces a novel framework for testing whether a pharmacologically induced plasticity can be harnessed to enhance NF capacity by affecting underlying processes of learning and regulation. This study may deepen mechanistic understanding of NF processes and provide support for the psychedelic-induced plasticity window hypothesis. In addition, it may inform the development of future novel clinical interventions in psychiatry.

Figures



References

Alkoby, O., Abu-Rmoleh, A., Shriki, O., & Todder, D. (2018). Can we predict who will respond to neurofeedback? A review of the inefficacy problem and existing predictors for successful EEG neurofeedback learning. *Neuroscience*, 378, 155-164.