

EEG-fMRI patterns of amygdala and ventral striatal activity as dynamic biomarkers of affective brain systems

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Introduction

A central challenge for brain-based interventions in psychiatry is to identify neural signals that are clinically meaningful, trainable, and measurable through scalable modalities. The EEG-fMRI Pattern (EFP) approach addresses this challenge by translating fMRI-defined therapeutic targets into EEG-guided interventions that can be delivered without patient-specific fMRI. Two clinically oriented models have been developed: the Amygdala-derived EFP (Amyg-EFP), an fMRI-informed EEG model of amygdala activity designed to target the emotion-regulation system^{1,2}, and the Reward-System EFP (RS-EFP), an analogous model of ventral striatal activity designed to target reward-processing circuits³. Clinical trials have shown that down-regulating Amyg-EFP or up-regulating RS-EFP during neurofeedback reduced symptoms of post-traumatic stress disorder⁴ or depression⁵, respectively. Beyond their demonstrated utility as neurofeedback targets, an open question is whether these EFPs can also serve as interpretable biomarkers of clinically relevant brain-system dynamics during naturalistic processing. To address this, we tested whether Amyg-EFP and RS-EFP fluctuations show separable whole-brain activation patterns, align with recurring large-scale brain states, and correspond to self-reported emotional valence during movie viewing.

Methods

A total of 115 healthy participants underwent concurrent EEG-fMRI during naturalistic stimulation with movie scenes and music excerpts and provided continuous emotional valence ratings of the movie stimuli outside the scanner. Existing Amyg-EFP and RS-EFP coefficients were applied to cleaned EEG data to generate two independent EFP time courses. To test whole-brain activation patterns associated with each EFP, we used voxel-wise GLM analyses to estimate coupling between each EFP and fMRI activity of each participant, interpreted in the context of large-scale functional networks. To test whether the EFPs track recurring whole-brain states, we used co-activation pattern (CAP) analysis: a data-driven clustering approach that groups momentary whole-brain fMRI activity patterns into recurring brain-state configurations. Finally, we examined whether affective processing is reflected in the joint dynamics of the two EFPs by clustering movie time points according to two dual-EFP features: dynamic Amyg-EFP/RS-EFP correlation and RS-EFP–Amyg-EFP amplitude difference. The resulting EFP-defined states were then compared across emotional valence ratings and corresponding fMRI activity patterns.

Results

Amyg-EFP and RS-EFP showed distinct coupling with fMRI-defined affective systems, with reproducible patterns observed across independent participant subgroups. In the GLM analyses, Amyg-EFP covaried with amygdala activity and with salience/sensory regions, including anterior insula and dorsal anterior cingulate cortex⁶, whereas RS-EFP covaried with ventral striatal activity and with default/control network regions. CAP analysis identified recurring whole-brain fMRI configurations, including a state that was positively associated with Amyg-EFP and negatively associated with RS-EFP, indicating that the two EFPs differentially tracked naturally recurring large-scale brain states. Dual-EFP clustering further showed that Amyg-EFP-dominant states corresponded to more negative emotional valence ratings, whereas RS-EFP-dominant states corresponded to more positive ratings; these EFP-defined states were also accompanied by distinct fMRI activation patterns. Together, the GLM, co-activation pattern, and EFP-cluster analyses converged in linking Amyg-EFP to salience/threat-related dynamics and RS-EFP to reward/positive-affect-related dynamics.

Conclusions

These findings support Amyg-EFP and RS-EFP as separable EEG-derived biomarkers of clinically relevant fMRI-defined affective systems, beyond their established utility as neurofeedback targets. Across complementary analyses, Amyg-EFP preferentially reflected salience/threat-related brain dynamics and negative emotional valence, whereas RS-EFP preferentially reflected reward/positive-affect-related dynamics. For neurofeedback, this suggests that EFPs may help characterize individual affective brain-system engagement, monitor target-relevant dynamics, and support more temporally precise intervention. More broadly, the results support the potential of EFPs as scalable EEG-based biomarkers for assessing dynamic emotion- and reward-system function beyond the neurofeedback setting.

Figures

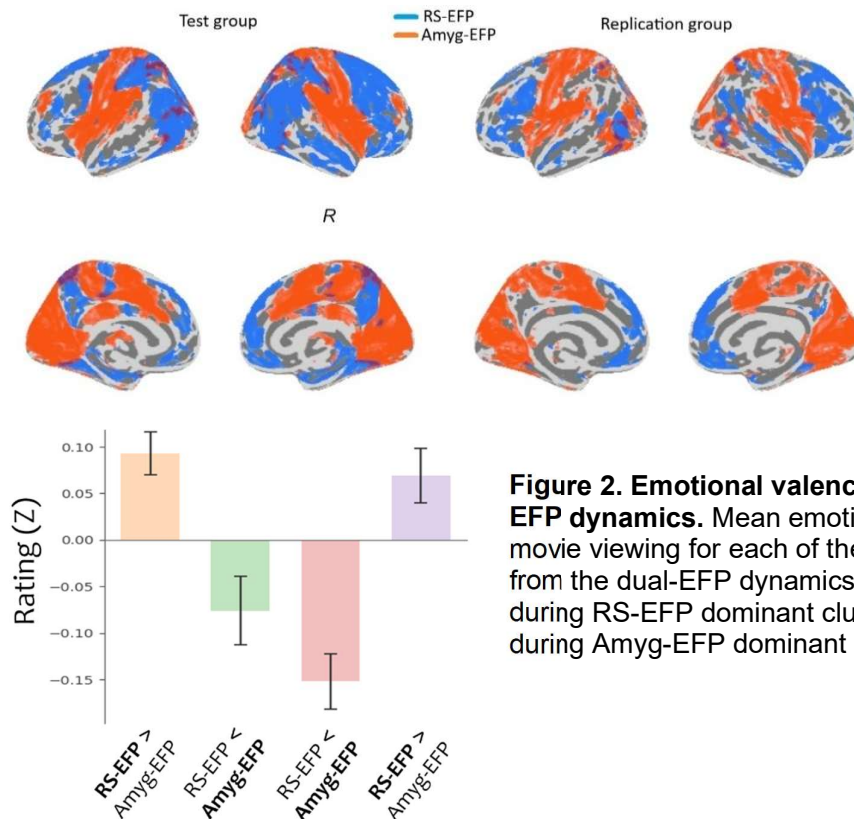


Figure 1. Whole-brain GLM analysis. Linear regression of fMRI activity with Amyg-EFP (orange) and RS-EFP (blue) signal fluctuations during movie viewing (threshold at FDR corrected $p < 0.05$), showing distinct EFP-associated whole-brain patterns.

Figure 2. Emotional valence corresponding to dual-EFP dynamics. Mean emotional valence ratings during movie viewing for each of the temporal clusters derived from the dual-EFP dynamics, showing positive valence during RS-EFP dominant clusters and negative valence during Amyg-EFP dominant clusters.

References

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