

Real-Time fMRI Neurofeedback Targeting Hippocampal–Cortical Connectivity to Enhance Memory Consolidation

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Introduction

Memory consolidation depends on post-experience neural activity and interactions between the hippocampus and distributed cortical regions. Functional magnetic resonance imaging (fMRI) studies have shown that hippocampal–cortical connectivity following encoding predicts subsequent memory performance (Tambini et al., 2010, 2019). Functional connectivity (FC) can also be regulated by reward and novelty, both of which enhance memory (Murty et al., 2019), and successful memory retrieval is associated with stronger hippocampal–cortical coupling (Vilberg et al., 2013). However, these findings remain correlational. Here, we present preliminary findings from an ongoing randomized, double-blind real-time fMRI neurofeedback (rtfMRI-NF) study designed to test whether hippocampal–lateral occipital complex (LOC) connectivity causally contributes to associative memory consolidation.

Methods

This ongoing pilot study aims to recruit 20 healthy adults aged 18 years or older. Participants are randomly assigned to one of two groups: an increase group trained to enhance hippocampal–lateral occipital complex (LOC) functional connectivity (FC) and a decrease group trained to reduce this connectivity. The overall study design and neurofeedback procedures are adapted from previous rtfMRI-NF studies (He et al., 2023; Kobayashi et al., 2025). The protocol consists of three study days. On Day 1, participants undergo anatomical imaging (T1), resting-state fMRI scans before and after NF training, and rtfMRI-NF training. On Day 2, participants complete object–face associative encoding and memory assessments, followed by resting-state fMRI scans acquired before and after a second rtfMRI-NF training session. On Day 3, participants complete a delayed follow-up memory test. MRI data are acquired on a 3T Siemens Prisma scanner at Columbia University. Whole-brain fMRI images are collected using a multi-band EPI sequence (multi-band factor = 2, TR = 1 s, TE = 24 ms, 3 × 3 × 3.5 mm voxel size). High-resolution T1-weighted anatomical images (0.8 mm isotropic resolution) are acquired to map hippocampal and LOC regions of interest (ROIs) defined in MNI space to each participant's local EPI space. Both real-time and offline fMRI preprocessing and analyses are performed in SPM12 using procedures similar to those described by He et al. 2023 and Kobayashi et al. 2025. Resting-state fMRI scans acquired before and after NF training are used to quantify changes in hippocampal–LOC connectivity. Each NF trial consists of an 8-second rest period, a 20-second induction period followed by a 2-second calculation window, and a 6-second feedback period. During the induction period, participants are instructed to explore their own mental strategies to maximize the size of a green circle presented on the screen, which reflects their neurofeedback signal. Preliminary analyses focused on the relationship between NF learning, resting-state FC changes, and associative memory performance in those participants who completed the protocol.

Results

At the time of submission, three participants (NF01, NF02, and NF03, respectively) had completed the three-day study protocol. NF performance differed across participants, with NF03 showing the clearest increase in average NF score from the first to the second NF session, suggesting individual variability in NF learning. Resting-state analyses indicated that NF training modulated hippocampal–LOC connectivity, although the effects were highly individual and session-dependent. During the first NF session, NF scores showed a weak, non-significant positive association with resting-state FC changes. In contrast, during the second session, higher NF scores were associated with larger decreases in resting-state FC. Although this latter association reached

significance, it should be interpreted cautiously given the very small sample size (Figure 1). Behavioral analyses did not reveal statistically significant improvements in associative memory performance across memory assessments. However, exploratory analyses suggested that higher NF performance during the second training session was associated with reduced forgetting in some memory comparisons, particularly between Memory Test 2 and the delayed follow-up Memory Test 3.

Conclusions

Overall, these preliminary findings demonstrate the feasibility of using rtfMRI-NF to modulate hippocampal-LOC resting-state connectivity and suggest that the magnitude and direction of neurofeedback-related neural changes may depend on individual learning trajectories, baseline network states, and other session-specific factors. Although evidence for behavioral enhancement of memory consolidation remains limited at this stage, the observed associations between NF performance and resting-state connectivity provide initial support for the neural modulation effects of NF. Ongoing data collection in the full sample will be critical for determining whether these neural changes translate into reliable improvements in memory consolidation.

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References

He, X., et al. (2023). Connectivity based real-time fMRI neurofeedback training in youth with a history of major depressive disorder. arXiv. <https://arxiv.org/abs/2301.11846>

Kobayashi, Y., et al. (2025). Enhancement of the left frontoparietal network through real-time functional magnetic resonance imaging functional connectivity-informed neurofeedback and its impact on working memory in schizophrenia: A pilot study. *Psychiatry and Clinical Neurosciences*, 79(9). <https://doi.org/10.1111/pcn.13849>

Murty, V. P., DuBrow, S., Davachi, L. (2019). Decision-making increases episodic memory via postencoding consolidation. *Journal of Cognitive Neuroscience*, 31(9), 1308–1317. https://doi.org/10.1162/jocn_a_01321

Tambini, A., Davachi, L. (2019). Awake reactivation of prior experiences consolidates memories and biases cognition. *Trends in Cognitive Sciences*, 23(10), 876–890. <https://doi.org/10.1016/j.tics.2019.07.008>

Tambini, A., Ketz, N., Davachi, L. (2010). Enhanced brain correlations during rest are related to memory for recent experiences. *Neuron*, 65(2), 280–290. <https://doi.org/10.1016/j.neuron.2010.01.001>

Vilberg, K. L., Davachi, L. (2013). Perirhinal–hippocampal connectivity during reactivation is a marker for object-based memory consolidation. *Neuron*, 79(6), 1232–1242. <https://doi.org/10.1016/j.neuron.2013.07.013>

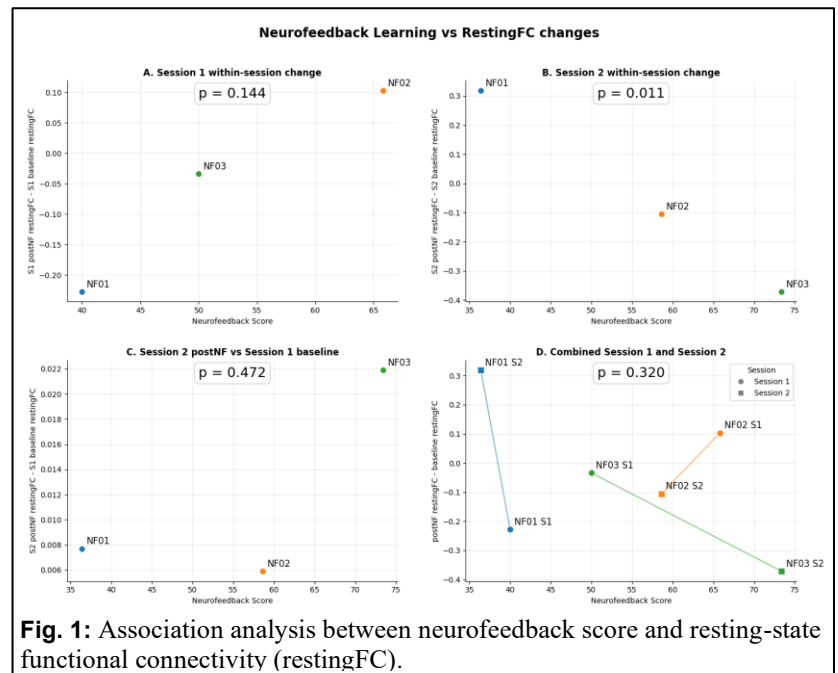


Fig. 1: Association analysis between neurofeedback score and resting-state functional connectivity (restingFC).