Modulating Hippocampal Activity and Connectivity with HRV biofeedback: Interplay between Emotion Regulation and Memory Control

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Abstract:

This study investigated the effects of heart rate variability (HRV) biofeedback on emotional and memory functions in humans. HRV biofeedback, which involves adjusting respiratory rate and breathing patterns, has proven effective in regulating emotions by targeting the limbic system. The present study sought to investigate the impact of HRV interventions on memory functions instead. We collected functional magnetic resonance imaging (fMRI) data during an emotion regulation task from 51 young participants who underwent 5 weeks of HRV biofeedback training. When either up- or down-regulate emotions, we observed significant HRV-induced changes in the neural activity of amygdala, hippocampus (Hippo), anterior and posterior parahippocampal cortex (PHC). Notably, the anterior PHC was positively activated during up-regulation after HRV interventions. The change of task-evoked activity was associated with behavioral improvements in working memory. In contrast, the posterior PHC was negatively activated during down-regulation prior to the intervention but showed enhanced activity and psychophysiological interactions (PPI) connectivity with hippocamps and amygdala during down-regulation after the intervention, correlating with improved working memory performance post-HRV. The hippocampal connectivity of anterior PHC was negatively correlated with post-HRV working memory. These findings suggest that HRV biofeedback can effectively modify both emotion regulation process and working memory capacity through neural mechanisms involving the hippocampus and PHC and demonstrate critical but distinct roles of anterior of posterior PHC in emotion regulation. This highlights the therapeutic potential of HRV biofeedback to enhance emotional well-being and memory performance.

Keywords: Heart rate variability, fMRI, emotion regulation, working memory, hippocampus, parahippocampal cortex

Introduction

Memory control (MC) and emotion regulation (ER) are critical adaptive cognitive functions that are fundamental to maintaining mental health. MC entails the intentional efforts to forget undesirable memories by limiting encoding and suppressing retrieval. ER involves the capacity to monitor, assess, and modify emotional responses to external stimuli (Roelofs et al., 2023). Research has shown that the two processes are closely linked, sharing common neural pathways and transcriptional profiles (Liu et al., 2020). As one of the mostly used ER strategies, cognitive reappraisal conscious reinterprets the emotional impact of external stimuli by amplifying positive emotions and diminishing negative ones (Luo et al., 2024). It primarily engages brain areas involved in inhibitory control and emotional processing, for instance frontal and parietal regions (Engen et al., 2018; Mamat et al., 2023). However, whether and how ER impacts MC has been rarely examined.

In this study, we implemented a heart rate variability (HRV) biofeedback paradigm to regulate emotional and memory functions in humans. HRV biofeedback aims to adjust subjects' respiratory rate and breathing patterns, enhancing an individual's physical and emotional well-being. This technique has shown efficacy in alleviating emotional disorders such as hypertension and anxiety (Lehrer et al., 2020), and improving cognitive functions such as inhibitory control and working memory (Nashiro et al., 2023). Yet, the underlying neural mechanisms remain poorly understood. This study aims to explore investigate the interactions between ER and MC, examining the effects of HRV biofeedback on both processes. We hypothesized that, HRV biofeedback, primarily affecting limbic system and amygdala activity, has great potentials in regulating memory functions and hippocampal activity. We specifically investigated the changes in hippocampal activity and connectivity during emotion regulation task after 5-week HRV interventions and examined their association with behavioral performance in working memory and Stroop tasks.

Materials and Methods

Participants and task description We acquired behavioral and imaging data from 51 participants (age: 18-31, 25 female) enrolled in the HRV biofeedback project (https://openneuro.org/datasets/ds003823). Each participant completed a 5-week HRV biofeedback training program, underwent multimodal MRI imaging sessions and recorded behavioral performance before and after HRV intervention, including the List Sorting Working Memory Test (LSWM), Trait Anxiety Inventory (TAI), the Center for Epidemiological Studies Depression Scale (CES-D), Flanker and Stroop task. Additionally, during MRI scans, participants engaged in an emotion regulation task where they were instructed to either up-regulate or down-regulate their emotional responses to positive, negative, and neutral images. The control condition, termed "view," required participants to observe the images without altering their emotional responses. The majority of participants used the cognitive reappraisal strategy for emotion regulation. For detailed information on MRI data acquisition and experimental paradigms, please refer to (Min et al., 2023; Nashiro et al., 2023; Yoo et al., 2020).

Data analysis Multimodal MRI data were preprocessed using fMRIPrep (https://fmriprep.org/en/stable/) and spatially normalized to the MNI152_2mm template. We utilized the general linear model (GLM) to analyze brain activation for up-regulation (contrast: intensify>view) and down-regulation (contrast: diminish>view) during

the emotion regulation task. We specifically investigated the effects of HRV biofeedback on brain activity and PPI connectivity for both up- and down-regulation conditions, and correlating them with behavioral changes in working memory and inhibitory control.

Results

Behavioral data: After 5 weeks of HRV biofeedback, participants showed improved behavioral performance in LSWM (t=3.77, p=0.00004), response accuracy in Stroop (t=2.58, p= 0.0128), and diminished negative emotions (TAI: t=-4.83, p=0.003, CES-D: t=-4.58, p=0.029).

Emotion regulation task: We observed strong activation in the supplementary motor area (SMA), anterior insula and dorsal anterior cingulate cortex (ACC) before and after HRV (Figure 1), with significant changes of brain activity in hippocampus for down-regulating emotions. Similar enhanced neural activity in Hippo and PHC were observed for up-regulating emotions. Notably, we uncovered distinct roles of anterior and posterior PHC (aPHC and pPHC) during emotion regulation task, such that aPHC was positively activated for down-regulation after HRV intervention while pPHC was negatively activated for up-regulation before HRV. The changes of PHC activity were correlated with behavioral improvements in LSWM (r=0.36 and 0.28, respectively for aPHC and pPHC, p-values<0.05). Moreover, greater hippocampal activity and weaker aPHC activation were associated with improved accuracy in Stroop task (Hippo: r=0.29, p=0.04; aPHC: r=-0.33, p=0.019), as well as for weaker activity in pPHC associated with behavioral improvement in Flanker task (r=-0.32, p=0.021). Moreover, after HRV biofeedback, the activity in amygdala and hippocampus during emotion regulation was associated with the CSF abeta42/tau ratios (r=0.54 and 0.58, p-values<0.01). Our result revealed distinct functional roles of PHC subregions during emotion regulation, with the pPHC and aPHC responding differentially to emotional regulation and memory control.

PPI connectivity: We explored the PPI connectivity of the left Hippo, aPHC, and pPHC during emotion regulation task. We observed significant changes in their PPI connectivity during up- and down-regulating emotions after HRV intervention (Figure 2). Specifically, HRV regulation attenuated the Hippo/PHC connectivity with the insula for downregulation, whereas enhanced the pPHC connectivity with Hippo and Amg. Intriguingly, participants exhibiting stronger connectivity in these pathways demonstrated better performance on working memory tasks (Hippo: r=0.34, p=0.016; Amg: r=0.32, p=0.027). In contrast, during upregulation, we observed an increase in Hippo connectivity with PHC. Weaker connectivity was associated with better working memory performance (aPHC: r=-0.37, p=0.007, pPHC: r=-0.40, p=0.003).

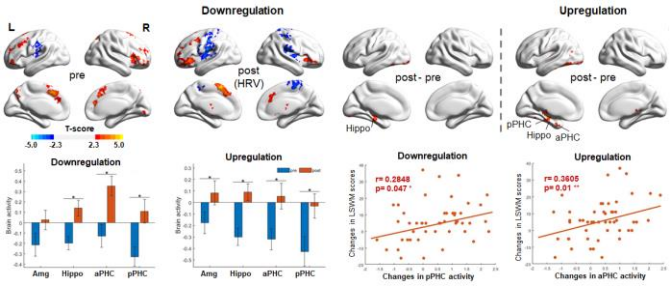

Figure 1: HRV biofeedback changes hippocampal and parahippocampal activity during emotion regulation.

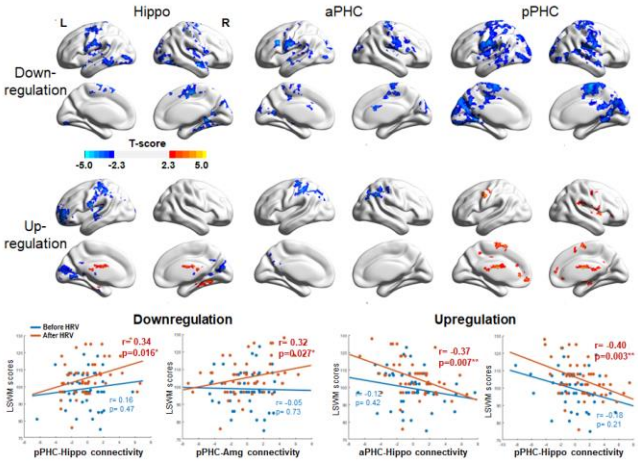

Figure 2: PPI connectivity of hippocampal and parahippocampal cortex after HRV biofeedback.

Conclusion

In this study, we investigated the effects of HRV-induced changes on behavioral scores and task-evoked brain activity during an emotion regulation task. Behaviorally, we observed significant improvements in working memory and inhibitory control following the HRV biofeedback intervention. These improvements coincided with increased brain activation and functional connectivity in the amygdala, hippocampus, and PHC. Notably, the anterior PHC was found to influence working memory levels and control ability during emotion upregulation, while the posterior PHC exhibited increased activation and connectivity that contributed to enhanced working memory during emotion downregulation. These findings highlight the complex interplay between emotional regulation and memory control. The current study yields substantial insights into the neural underpinnings of HRV biofeedback and its impact on ER and MC. The close interaction between ER and MC provides novel perspectives on potential avenues for future inventions on memory enhancement.

Acknowledgments

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