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# Resting Heart Rate Variability Is Associated with Neural Adaptation When Repeatedly Exposed to Emotional Stimuli

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## Abstract

Higher heart rate variability (HRV) at rest is associated with better emotion regulation ability. While the neurovisceral integration model explains this by postulating that HRV can index how the brain adaptively modulates responses to emotional stimuli, neuroimaging studies directly supporting this idea are scarce. We examined the neural correlates of regulating negative and positive emotion in relation to resting HRV based on the functional neuroimaging and heart rate data of one hundred young adults. The results showed that those with higher HRV better recruit the medial prefrontal cortex while intensifying positive compared to negative emotion. We also examined how individual differences in resting HRV are associated with adjusting brain activity to repeated emotional stimuli. During repeated viewing of emotional images, subjects with higher resting HRV better reduced activity in the medial prefrontal cortex, posterior cingulate gyrus, and angular gyrus, most of which overlapped with the default mode network. This HRV-DMN association was observed during passively viewing emotional images rather than during actively regulating emotion. While the regulating trials can better detect task-induced changes, the viewing trials might approximate resting state, better revealing individual differences. These findings suggest two possibilities: people with higher resting HRV might have a tendency to spontaneously engage with emotion regulation or possess a trait helping emotional arousal fade away.

### Keywords

heart rate variability; emotion regulation; default mode network; neural adaptation; neurovisceral integration model; functional neuroimaging

## Introduction

Everyday life exposes us to events that require regulating emotions. Emotion regulation (ER) typically involves moderating feelings in the moment. However, amplifying emotion is often necessary or even desirable in some social contexts (e.g., emphasizing positive aspects of

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an event to motivate oneself or exaggerating anger to appeal an unfair decision in sports) (Gross, 2015). This effort of calming down or amping up emotional arousal might be easier for some people than others and could often be automatically performed (Mauss et al., 2007). Whether effortful or automatic, ER ability is consequential for social relationships as well as psychological and somatic health (Lopes et al., 2005; Verkuil et al., 2010). On the other hand, compromised ER capacity is one of the major characteristics of patients with anxiety and depressive disorders (Joormann & Gotlib, 2009; Mennin et al., 2005). Individuals with lower ER ability also show a stronger relationship between stress and cardiovascular risk factors than those with higher ER ability (Roy et al., 2018).

Functional magnetic resonance imaging (fMRI) studies suggest an inverse relationship between activities of the prefrontal cortex (PFC) and amygdala (e.g., greater PFC activity associated with lower amygdala activity) during active emotion down-regulation (Goldin et al., 2008; Kim & Hamann, 2007; Ochsner et al., 2004; Phan et al., 2005). In contrast, the PFC-amygdala relationship during up-regulation seems synchronized as both PFC and amygdala activities are increased (Eippert et al., 2007; Kim & Hamann, 2007). ER ability is represented not only by the PFC-amygdala relationship but is also associated with physiological regulation, which is reflected in cardiac activity (Mather & Thayer, 2018).

Heart rate variability (HRV) measures fluctuations in time intervals between adjacent heart beats. Research suggests that higher HRV at rest is associated with better ER ability (Thayer & Lane, 2009). People with higher resting HRV show better emotional health (Thayer et al., 2012) and self-control (Zahn et al., 2016). In contrast, reduced HRV was observed in those experiencing anxiety and depression (Chalmers et al., 2014; Koch et al., 2019; Koenig et al., 2016). To explain this relationship, the neurovisceral integration model (Thayer & Lane, 2009) posits that HRV reflects the quality of ongoing interactions between the cortical and subcortical regions (e.g., medial PFC and amygdala) responsible for autonomic balance. The model views ER as an adapting process to situational demands which relies on the same inhibitory cortico-subcortical neural circuits as HRV; thus individual differences in resting HRV relate to individual differences in ER (Thayer & Lane, 2009).

While numerous behavioral studies reported associations between resting HRV and ER ability (Chalmers et al., 2014; Koch et al., 2019; Koenig et al., 2016; Mather & Thayer, 2018; Thayer et al., 2012), neuroimaging findings that directly support those associations are scarce (Sakaki et al., 2016; Steinfurth et al., 2018; Wei et al., 2018). Resting HRV, measured as the root mean square of successive differences (RMSSD), was correlated with the functional connectivity between the medial PFC (mPFC) and amygdala (Sakaki et al., 2016). People with higher RMSSD showed a greater covarying relationship between the gray matter volume of the amygdala and that of the dorsomedial PFC (Wei et al., 2018). Finally, individuals with higher RMSSD better recruited the PFC to modulate amygdala activity while regulating negative emotion via cognitive reappraisal (Steinfurth et al., 2018). Together, these studies suggest that people with greater resting HRV can better regulate emotion due to enhanced functional and structural connectivity between their PFC and amygdala.

While these three studies support the neurovisceral integration model, they largely focused on the amygdala and mPFC. Even though these regions are core HRV-related structures (Thayer & Lane, 2009), relying on the region of interest (ROI) analysis might neglect other regions that also participate in ER and heart rate control. Furthermore, the task-based fMRI study investigating the relationship between ER and resting HRV (Steinfurth et al., 2018) was based on a small sample size (N=27) and focused on negative emotions. However, modulating positive emotions is also necessary to achieve social goals (e.g., resisting laughter during an interview or maximizing the excitement of a victory), and studies showed associations between resting HRV and positive emotion (Duarte & Pinto-Gouveia, 2017; Weiss et al., 2021). In addition, standard event-related techniques employing randomly intermixed trials and contrasting different conditions of trials might not capture how brain activity adjusts as participants repeat trials. This makes it hard to corroborate the idea (Thayer & Lane, 2009) that enhanced HRV promotes better adaptation to environmental demands. To address these limitations, we used a mixed block/event-related design (Petersen & Dubis, 2012) where three same-condition trials repeat within each block of regulating emotion or passively viewing emotional pictures.

Benefitting from a large sample of young adults (N=100), we aimed to investigate how resting HRV is associated with neural activity during regulating emotions. The study samples were pooled from the baseline pre-intervention data of a clinical trial study (Nashiro et al., 2023; Yoo et al., 2023). The first goal was to replicate prior findings (Steinfurth et al., 2018) while adding a positive emotion condition and focusing on the whole brain activity. The second goal was to examine how individual differences in resting HRV relates to transient BOLD activity as participants are repeatedly exposed to emotional stimuli during ER. To measure adjustment in brain activity, we employed a mixed block/event-related design where three same-condition events are repeated in each block. While we mainly relied on whole-brain analyses in the current study, we also examined how the amygdala changes its response in repeated trials as the amygdala is sensitive to novel stimuli and quick to adapt to repeated stimuli (Plichta et al., 2014).

## Methods

### Participants

The current study is based on data collected during the ER task during the pre-intervention phase of a HRV biofeedback intervention study (ClinicalTrials.gov Identifier: NCT03458910), approved by University of Southern California's Institutional Review Board (Nashiro et al., 2023; Yoo et al, 2023). We recruited participants without serious medical or psychiatric illness via USC's subject pool, USC's online bulletin board, Facebook, and flyers. Participants signed informed consent forms before starting and were paid $15 per hour for their participation upon completion. The basic findings from the pre-intervention ER task have been published (Min et al., 2022), and the current study was initially based on the same pool of participants (N=105). Among the participants, we excluded three participants who did not have RMSSD measures at pre-intervention and two participants who had extreme RMSSD values (RMSSD > 200 ms) when considering their relatively small mean heartbeat intervals. Thus, we analyzed the data of 100 participants,

consisting of 51 males and 49 females and aged from 18 to 31 years ($M_{age}$ = 22.81, $SD_{age}$ = 2.75).

## Task and Procedure

The task was based on a previously published ER task design where participants used cognitive reappraisal strategies to up- or down-regulate emotion for positive and negative emotions (Kim & Hamann, 2007). The task lasted for 10 minutes with 42 trials. Each trial consisted of three phases: instruction, regulation, and rating (Min et al., 2022). During the 1-second instruction, participants were presented with “intensify,” “diminish,” or “view” on a black screen. During the 6-second regulation phase, they regulated or passively experienced emotions elicited by the presented images, which were negative, positive, or neutral. During the 4-second rating, they rated the strength of their feeling in the moment (levels of emotional intensity) with an ascending order of 1 to 4.

These event trials were organized in a block-wise manner such that three events of the same condition were contained in each block and separated by a fixation cross lasting for a varying interval (Figure 1). The two intervals separating three events within each block summed to 4 seconds. This design enabled us to test whether participants with higher resting HRV showed greater adaptiveness in neural correlates of ER when they experienced the three same-condition trials consecutively. The blocks were separated by a 5-second fixation cross and presented in a pseudorandom order such that participants did not experience two blocks with the same instruction and image valence in a row. The task’s 42 trials were grouped into seven conditions: view-negative, view-positive, view-neutral, diminish-negative, diminish-positive, intensify-negative, and intensify-positive (six trials per condition). We selected six sets of images with the same average valence ($M_{negative}$ = 2.3, $M_{positive}$ = 7.2, $M_{neutral}$ = 5.0) and same arousal scores ($M_{negative}$ = 5.4, $M_{positive}$ = 5.4, $M_{neutral}$ = 2.8) from the International Affective Picture System. Each set consisted of 18 negative, 18 positive, and 6 neutral pictures, and the images were shuffled within each valence category. The identifiers of the images presented during the task were recorded and publicly shared at OpenNeuro (Yoo et al, 2023).

Before their MRI scans, participants were encouraged to employ their own reappraisal strategies while they practiced all seven types of trials. They were given examples of cognitive reappraisal strategies such as reinterpreting the situation or adjusting their distance from the scene. They were also advised to avoid generating an opposite emotion to diminish the negative or positive emotion. After the scan, we asked participants to describe their regulation strategies and how successful they felt for each regulation condition (1: not successful at all; 3: moderately successful; 5: very successful) for the four emotion-regulating conditions (diminish-negative, diminish-positive, intensity-negative, and intensity-positive). For the four conditions, 90%-100% of participants reported the use of cognitive reappraisal strategies, and 91-98% of participants expressed medium to high levels (3 to 5) of confidence.

### MRI data acquisition

We collected MRI data at USC's Dana and David Dornsife Cognitive Neuroimaging Center using a 3T Siemens MAGNETOM Prisma MRI scanner with a 32-channel head coil (Min et al., 2022). We obtained a T1-weighted MPRAGE anatomical image (TR = 2,300 ms, TE = 2.26 ms, slice thickness = 1.0 mm, flip angle = 9°, field of view = 256 mm, voxel size = 1.0 mm isotropic). We acquired 250 whole brain volumes of T2*-weighted functional images using multi-echo planar imaging sequence (TR= 2,400 mm, TE 18/35/53 ms, slice thickness = 3.0 mm, flip angle = 75°, field of view = 240 mm, voxel size = 1.0 mm isotropic).

### HRV data acquisition and processing

On the same day as the MRI scan, we obtained heartbeat data from participants sitting in a chair spontaneously breathing for five minutes during daytime at the research lab. Using HeartMath emWave Pro software and its infrared pulse plethysmograph (PPG) ear sensor, the heartbeat data were sampled at 370 Hz and its inter-beat interval data were recorded after emWave's built-in artifact removal process (HeartMath, 2016). The inter-beat interval data were entered into Kubios HRV Premium 3.1 software with the automatic beat correction option which computed both heart rate and RMSSD for each participant (Tarvainen et al, 2014).

### Behavioral and HRV data analysis

To obtain the measures of emotion regulation outcome, we averaged self-reported emotional intensity separately for the seven conditions. We first tested how the conditions (valence and regulation) in the ER task affected ratings in emotional intensity by running a 2-by-3 analysis of variance (ANOVA) when controlling for RMSSD. We then ran correlations between RMSSD and changes in the ratings during ER. We used SPSS (SPSS IBM Statistics 28) for the ANOVA and correlations.

### MRI data and statistical analyses

We performed multi-echo independent component analysis to remove artifact components from time series data based on the linear echo-time dependence of BOLD signal fluctuations (Kundu et al., 2012). After denoising the data, we used FMRIB Software Library (FSL) version 6.0 for the individual- and group-level analysis (Jenkinson et al., 2012; Woolrich et al., 2001, 2004). During the individual-level analysis, each functional image was registered to the MNI152 T1 2mm template via its T1-weighted anatomical image using affine linear transformation with 12 degrees of freedom. Individual-level analysis also included a preprocessing of motion correction, spatial smoothing with 5 mm FWHM, and high-pass filtering with a 600-second cutoff.

For the first analysis examining which brain regions' activity correlated with individual differences in resting HRV during ER, we modeled individual whole-brain BOLD time-series by setting seven ER regressors during the 6-second regulation period (diminish-negative, diminish-positive, view-negative, view-positive, intensify-negative, intensify-positive, view-neutral) along with their temporal derivatives, each of which were convolved with a double-gamma hemodynamic response function. For the group-level analysis, we added demeaned RMSSD as a regressor to FSL's mixed-effects model (FLAME 1) to

examine the neural correlates of RMSSD during emotion regulation. The results were corrected for family-wise error at $p < .05$ with the cluster-wise threshold at $Z > 2.3$. We conducted correlation analyses by treating RMSSD as a continuous regressor rather than comparing two median-split groups. This approach preserves information regarding individual variability whereas median splits might decrease power and increase risk of Type II error (lacobucci et al., 2015).

In the second analysis, we investigated brain regions whose BOLD activity changed from the first to last trials within each same-condition block as a function of resting HRV. For this, we needed to separately model trials based on their relative positions (first, second, or third) within same-condition blocks. We modeled each participant's whole-brain BOLD time-series with 12 regressors. Each regressor was set to represent the order of trials within each condition. For example, to see how brain regions responded only to the first trials of the diminish-emotion condition, one regressor would be the timing of all the first trials within the diminish-emotion blocks. Regressors for the second and third trials were set in the similar manner. Since this analysis classified trials into three groups for each condition, the number of trials per condition decreased. The first analysis did not show clear differences in valence during up- and down-regulating emotion (Figure 2). To compensate for the reduced number of trials per condition, we combined positive and negative valence into emotional conditions. This resulted in four regressors: diminish-emotion, intensify-emotion, view-emotion and view-neutral. As we had the four types of blocks and three trials within each block, we had 12 total regressors for the individual-level analysis. We then contrasted the regressors representing different orders within the same condition. For example, we contrasted the first events against the third ones within diminish-emotion blocks to find brain regions that decreased activity as trials proceeded from the first to last event while diminishing emotion. For the group-level analysis, we added demeaned RMSSD as a covariate regressor of interest to FSL's mixed-effects model and tested the correlations between RMSSD and BOLD activity change from the first to last trials for each condition.

In addition to the whole-brain analysis, we performed an amygdala ROI analysis, as the amygdala's activity is involved in HRV as well as ER (Thayer & Lane, 2009). To assess its BOLD activity changes, we individually segmented the amygdala region from each participant's T1-weighted image using FreeSurfer version 6 (Fischl et al., 2002, 2004) and created the left and right amygdala masks in the native space. We then applied FSL FLIRT (Jenkinson et al., 2002; Jenkinson & Smith, 2001) to transform the masks to the standard MNI space and input them to *Featquery*. Using *Featquery*, we extracted each participant's percent signal change values in the amygdala activity separately from the first and last trial periods for each condition (diminish-emotion, view-emotion, intensify-emotion). We then correlated RMSSD with changes in amygdala activity from the first to last trials while controlling for amygdala activity during the first trials for each condition because the magnitude of possible change depends on the magnitude of the initial response.

## Results

The analysis was based on 100 participants, consisting of 51 males and 49 females and aged from 18 to 31 years ($M_{age} = 22.81$, $SD_{age} = 2.75$). Their mean heart rate (HR) ranged from

48.35 to 100.07 beats per minute ($M_{HR}$ = 72.66, $SD_{HR}$ = 9.67); mean heart period (HP) ranged from 559.56 to 1240.89 milliseconds (ms) ($M_{HP}$ = 840.91, $SD_{HP}$ = 116.78); and mean RMSSD ranged from 22.62 to 187.17 ms ($M_{RMSSD}$ = 61.06, $SD_{RMSSD}$ = 29.81).

### Self-rated emotional intensity and HRV

A 2 by 3 repeated-measure ANOVA when adjusted for RMSSD revealed main effects for both valence and regulation. Self-rated emotional intensity differed across the three ER conditions (diminish, view, and intensify), $F(2, 196) = 27.86$, $\eta_p^2 = 0.22$, $p < 0.001$. The emotional intensity was lowest (M = 1.88, SE = 0.06) for diminishing, middle (M = 2.45, SE = 0.06) for viewing and highest (M = 3.24, SE = 0.05) for intensifying ($p < 0.001$ for all three pairwise contrasts). There was also a main effect of valence, $F(1, 98) = 5.54$, $\eta_p^2 = 0.05$, $p = 0.02$, with self-rated intensity higher on negative (M = 2.50, SE = 0.04) than on positive (M = 2.41, SE = 0.05) emotional trials. There was not a significant interaction of valence and regulation conditions, $F(2,196) = 2.17$, $p = 0.11$, $\eta_p^2 = 0.02$.

We next tested whether RMSSD correlated with between-condition differences in self-rated emotional intensity levels. While RMSSD was not correlated with ratings during view-negative minus diminish-negative, view-positive minus diminish-positive, and intensify-positive minus view-positive (all $p > 0.4$), there was a non-zero but only marginally significant correlation between RMSSD and ratings during intensify-negative minus view-negative, $t(98) = 0.18$, $p = 0.07$.

To explore adaptiveness in self-rated emotional intensity in relation to RMSSD, we tested whether HRV correlated with changes in emotional intensity from the first to last trials during each condition when controlling for the emotional intensity in the first trials. One participant was removed because he did not respond to all the third trials during the view condition, which left 99 participants. During the diminish-negative condition, RMSSD was correlated with emotional intensity change from the first to last trials when we controlled for the intensity in the first trials, $t(96) = 0.266$, $p = 0.008$. During the intensify-positive condition, RMSSD was negatively correlated with emotional intensity change from the first to last trials when we controlled for the intensity in the first trial, $r = -0.199$, $p = 0.049$. All other correlations were non-significant (all $p$s > 0.4). We also tested the correlations between RMSSD and emotional intensity during the first trials of each condition. All correlations were non-significant (all $p$s ranged from 0.13 to 0.98).

### Brain regions associated with emotion regulation

For negative and positive emotional trials, contrasting diminish against view revealed similar clusters in the insular cortex, inferior frontal gyrus, anterior cingulate gyrus, and supplementary motor area (Figure 2A & 2B). The two contrasts differed only in the angular gyrus for positive compared to negative emotion during diminish > view (Figure 2B). For negative and positive emotional trials, contrasting intensifying against viewing showed broad clusters including the insular cortex, inferior frontal gyrus, anterior cingulate gyrus, frontal pole, thalamus, caudate, amygdala, and cerebellum including vermis VI, crus I and crus II (Figure 2C & 2D). Except for in the occipital and cerebellar areas (Figure 2C), significant differences were not found in the intensify-negative > view-negative and intensify-positive

> view-positive contrasts. We note that no brain regions show correlations between their BOLD activity and RMSSD for the four regulation contrasts (diminish > view and intensify > view for negative and positive emotions).

## Brain regions associated with RMSSD in relation to valence

Contrasting positive with negative emotion for each regulation condition showed brain regions whose BOLD activity differed between negative and positive emotion. During diminishing positive emotion compared to negative emotion, increased BOLD activity was found in the angular gyrus, superior lateral occipital cortex, and PFC regions including the middle frontal gyrus and frontal pole (Figure 3A, red). Contrasting diminish-negative against diminish-positive revealed the inferior frontal gyrus, precentral gyrus, inferior lateral occipital cortex, and frontal orbital cortex (Figure 3A, blue). During diminishing positive compared to negative emotion, BOLD signal in the cerebellum (the left crus I) was negatively correlated with RMSSD (Figure 3A, yellow).

During viewing positive compared to negative emotion, we found increased BOLD activity in the posterior cingulate gyrus, precuneus, occipital pole, lingual gyrus, cerebellum (left and right crus I), and mPFC regions including the frontal medial cortex, frontal pole, anterior cingulate gyrus, and paracingulate gyrus (Figure 3B, red). Contrasting view-negative against diminish-positive revealed the inferior lateral occipital cortex (Figure 3B, blue), which overlapped with the clusters of diminish-negative > diminish-positive (Figure 3A, blue). During viewing positive compared to negative emotion, RMSSD was positively correlated with activity in clusters involving the precuneus, thalamus, parahippocampal gyrus, cerebellum (right and left I-IV), and brainstem areas surrounding periaqueductal gray (Figure 3B, yellow).

During intensifying positive compared to negative emotion, we found increased BOLD activity in the posterior cingulate gyrus, angular gyrus, middle frontal gyrus and mPFC regions including the frontal medial cortex, frontal pole, anterior cingulate gyrus, and paracingulate gyrus (Figure 3C, red). Contrasting intensify-negative against intensify-positive revealed clusters covering the inferior lateral occipital cortex, temporal occipital fusiform cortex, cerebellum (left and right VI), inferior frontal gyrus, and precentral gyrus (Figure 3C, blue). During intensifying positive compared with negative emotion, RMSSD was correlated with BOLD activity in the paracingulate gyrus and frontal medial cortex (Figure 3C, yellow).

## Brain regions whose activity changed in response to repeated stimuli in relation to RMSSD

In the second analysis, we tested how resting RMSSD is associated with changes in brain activity over repeated same-condition trials while regulating emotion or viewing emotional images. Change in BOLD activity was obtained by contrasting the first trials against the last ones during each condition. Testing correlations between BOLD activity change and resting RMSSD during viewing emotional images showed that higher resting RMSSD was associated with reduced activity in the frontal pole, paracingulate gyrus, anterior cingulate gyrus, posterior cingulate gyrus, and angular gyrus (Figure 4A). These areas overlap with the primary nodes of the default mode network (DMN; Laird at al., 2011). The correlation

between BOLD activity in these regions and RMSSD was positive during the first view-emotion trials, but negative during the last view-emotion trials (Figure 4B). We did not find a significant relationship in the intensify condition. However, during the diminish condition, we found that those with higher resting RMSSD increased BOLD activity in the occipital pole, occipital fusiform gyrus, and inferior and superior lateral occipital cortex from the first to third trials during diminishing emotion (Figure 4C).

### Amygdala ROI analysis for the repeated view-emotion trials

As we were interested in how resting RMSSD is associated with the adjustment of amygdala activity over repeated trials during viewing emotional images, we tested the correlation between RMSSD and amygdala activity change from the first to third trials in the same-condition blocks while controlling for its first-trial activity. During viewing emotion, resting RMSSD correlated with decrease in the left amygdala's activity from the first to last trials while controlling for first-trial activity, $r(97) = 0.25$, $p = 0.01$ (Figure 5). This relationship was attenuated for the right amygdala, $r(97) = 0.16$, $p = 0.13$. During diminishing and intensifying emotion, RMSSD was not correlated with activity changes in the left and right amygdala when controlling for its first-trial activity (all $p$s > 0.5).

As we found significant clusters in the view-emotion condition (Figure 4A), we examined the effect of passively experiencing emotion by contrasting view-emotion against view-neutral. This revealed a set of clusters (Figure 6) including the occipital pole, inferior lateral occipital cortex, lingual gyrus, hippocampus, amygdala, thalamus, periaqueductal gray, middle frontal gyrus, paracingulate gyrus, frontal pole, inferior frontal gyrus, superior frontal gyrus, and anterior cingulate cortex. Among them, the medial PFC regions involving the frontal pole, posterior cingulate gyrus, and angular gyrus resembled the DMN and overlapped with the brain regions which decreased activity over the repeated viewing trials for individuals with greater RMSSD (Figure 4A).

## Discussion

The neurovisceral integration model postulates that resting HRV carries information on how successfully an organism adapts to its environment (Thayer & Lane, 2009). According to the model, ER behavior can be seen as a process of adjusting responses to emotional challenges, and the quality of ER can be predicted by resting HRV. We tested this idea by employing two separate analyses: a standard trial-based analysis and an analysis by separating trials based on their sequential order within same-condition blocks. In the first analysis, we could not directly replicate Steinfurth et al.'s findings (2018) but found that HRV was associated with mPFC activity and positive emotion. During viewing positive images compared to negative images, individuals with higher HRV showed stronger BOLD activity in the periaqueductal gray area typically associated with emotional arousal (Figure 3B, yellow), suggesting that those with higher HRV might experience more emotional arousal with positive emotion than negative emotion. We next observed that HRV was correlated with BOLD activity in the mPFC area (Figure 3C, yellow) during intensifying positive emotion compared to negative emotion. The mPFC area also overlapped with the clusters revealed by intensify-positive > intensify-negative (Figure 3C, red). This suggests that the mPFC

is associated with amplifying positive compared to negative emotion and individuals with higher HRV can better recruit the mPFC areas during up-regulating positive emotion. These observations are in line with previous findings that higher HRV is associated with positive mood (Geisler et al., 2010) and mPFC activity is correlated with increased positive ratings while processing safety signals (Harrison et al., 2017). Whereas the mPFC areas covering the frontal medial cortex, frontal pole, anterior cingulate gyrus, and paracingulate gyrus were involved with positive compared to negative emotion (Figure 3B & 3C, red), the inferior lateral occipital cortex areas were associated with negative compared to positive emotion across the diminish, view, and intensify conditions (Figure 3A, 3B, and 3C, blue).

In the second analysis, we examined how brain BOLD activity changed in relation to resting HRV as the same-condition trials proceeded from the first to the last. The whole-brain analysis showed that those with higher HRV better decreased BOLD activity during the repeated trials of viewing emotional images in the frontal pole, paracingulate gyrus, anterior cingulate gyrus, posterior cingulate gyrus, and angular gyrus (Figure 4A). During the first trials of viewing emotional images, activity in the regions were positively correlated with resting HRV, but during the third trials, activity in the regions were negatively correlated with HRV (Figure 4B). The significant clusters (Figure 4A) showed a clear overlap with the DMN such that 85.3% of 2,300 significant voxels in the clusters overlapped with the DMN mask (Laird et al., 2011). Activity decrease in the DMN over three consecutive trials was not observed in the active regulatory conditions (intensify-emotion or diminish-emotion).

The DMN informs emotional states by representing discrete emotions through the abstraction of emotional instances (Satpute & Lindquist, 2019). Patients with major depressive disorders accompanying rumination, a maladaptive ER strategy, show increased BOLD activity in the DMN relative to the other task-related network (Hamilton et al., 2011). Depressed individuals also show reduced functional connectivity within the DMN compared to healthy controls (Yan et al., 2019) and fail to reduce DMN activity when both passively viewing and appraising negative images (Sheline et al., 2009). Furthermore, more successful ER is associated with decreased functional connectivity between the right amygdala and the major nodes of the DMN such as the mPFC and PCC (Andrews-Hanna, 2012). To test whether the DMN's activity was associated with appraisal of emotional state in our study, we examined the contrast of viewing emotional images against neutral ones. The contrast of view-emotion > view-neutral revealed significant BOLD activity in the mPFC, PCC, and angular gyrus (Figure 6, red). These clusters overlapped with the DMN regions (Figure 4A) as well as the clusters which decreased activity in response to repeated emotional stimuli for individuals with higher HRV (Figure 6, yellow).

The correlations between resting HRV and DMN activity during viewing emotional images suggest that individuals with greater resting HRV might spontaneously engage in implicit ER more than those with lower resting HRV. In one study which did not instruct participants to regulate emotion while viewing negative film clips, people with higher resting HRV more frequently used cognitive reappraisal than those with lower HRV (Volokhov & Demaree, 2010). In contrast, individuals with dysphoria, a typical symptom of depression, were more often spontaneously engaged with suppression and rumination, maladaptive ER strategies (Quigley & Dobson, 2014). By automatically engaging with adaptive ER strategies when

facing emotional challenges, individuals with greater HRV might be able to reduce DMN activity more efficiently. However, since we did not assess whether participants were automatically engaged with ER during the viewing trials, we can only speculate on this possibility.

It is also possible that individuals with higher resting HRV might also possess an intrinsic capacity to be either less disturbed by or more resilient to external stressors (An et al., 2020; Perna et al., 2020). In other words, higher HRV might serve as a trait with which participants are either 1) less reactive to emotional stimuli in the first place or 2) their emotional arousal fades away faster. To investigate less reactiveness with higher HRV, we tested whether HRV correlated with self-reported emotional intensity from the first trials of each condition and found no significant relationships. We also tested whether emotional arousal wanes more for higher HRV. As trials proceeded from the first to the third positions, those with higher HRV reported reduced emotional intensity during down-regulating negative emotion and increased emotional intensity during up-regulating positive emotion when we controlled for emotional intensity from the first trials. The results support the second possibility that higher HRV can help flexibly attenuate negative emotion and amplify positive emotion.

How does DMN activity decrease over the repeated trials of viewing emotional images indicate better adaptation? Although our study did not present identical images, its design where same-condition trials were repeated is based on the concept of habituation. Habituation is a learning process where an organism reduces its response to a repeated or prolonged stimulus in the absence of a significant reward or threat (Rankin et al., 2009). Because filtering out familiar and unnecessary signals saves neural resources and helps redirect attention to other consequential information, rapid habituation at the neural and behavioral level is associated with a greater adaptability to surroundings. Since the first report (Breiter et al., 1996), habituation has been mostly studied on amygdala signal changes to repeated emotional faces (Plichta et al., 2014). Slower habituation is linked to socially maladaptive conditions such as social anxiety disorder and autism spectrum disorder (Avery & Blackford, 2016; Kleinhans et al., 2009). People with these conditions could not successfully decrease their amygdala activity across repeated stimuli compared to their counterparts without the conditions. A similar pattern was observed with our data. BOLD signal decreases in the left amygdala between the first and third trials of viewing emotional images were correlated with HRV (Figure 5), suggesting that higher HRV was associated with greater habituation. Besides the amygdala, the whole-brain results showing decreased DMN activity for higher HRV suggests that people with higher HRV show greater habituation in the DMN. Studies indicated that individuals with higher HRV exhibit context-appropriate emotional responses whereas those with lower HRV show perseverative responses or threat responses to neutral stimuli (Ruiz-Padial et al., 2003; Ruiz-Padial & Thayer, 2014; Yang et al., 2021). The present study is the first to demonstrate this relationship between resting HRV and BOLD signal adjustment in the whole brain when exposed to emotional stimuli.

We also note that individuals with higher resting HRV increased BOLD activity in the occipital cortex during repeated trials of diminishing emotion (Figure 4C). Viewing emotional images compared to neutral images increased BOLD activity in the primary visual

areas (Figure 6), which are also observed in prior fMRI studies on emotional arousal (Lang et al, 1998; Mather et al., 2006; Mitchell et al., 2006; Ochsner et al, 2009; Sabatinelli et al, 2005). Studies employing multivariate pattern analyses of BOLD responses to emotional stimuli further demonstrated that the primary visual areas might represent emotional states and discriminate various emotional categories (Kragel et al, 2019; Bo et al, 2021) and that activity patterns in a cluster involving the visual cortex and adjacent precuneus cortex could distinguish different emotion regulation strategies in younger adults (Martins et al., 2015). At glance, our results might seem to suggest reduced ER ability for individuals with higher HRV, contrary to the neurovisceral integration model, because the visual area has increased activity when they were supposed to down-regulate emotion. However, the role of occipital activity during ER does not seem clear. Both down-regulating and up-regulating emotion enhanced activity in the lateral occipital cortex and lingual gyrus (Min et al, 2022; Table 2, 3). Activity in the occipital cortex during viewing emotional pictures was attenuated for individuals with major depression disorders (Li et al, 2013) who tend to show decreased HRV and ER ability (Kock et al, 2019; Joormann & Gotlib, 2009). Occipital activity also increased during directed attention (Kastner et al, 1999), emotional arousal enhanced attention to relevant stimuli (Mather & Sutherland, 2011), and attention maintenance was associated with higher HRV (Siennicka et al, 2019). Thus, the increased occipital activity for higher-HRV individuals during emotion down-regulation (Figure 4C) might be due to better sustained attention over the repeated task trials rather than diminished ER ability. Future research is needed to evaluate the role of the occipital cortex during emotion regulation in relation to HRV, arousal, and attention.

Although the cerebellum has received little attention in the field of emotion regulation, its subregions have been reported to increase BOLD activity during emotional arousal (Min et al., 2022; Kanske et al., 2011; Kim & Hamann, 2007; Ochsner et al., 2004). In our study, the cerebellum also increased activity during emotional arousal. The crus I and vermis crus II were activated during viewing emotional images against neutral images (Figure 6, red), and the vermis VI, crus I, and crus II were activated during intensifying negative and positive emotion against viewing (Figure 2 C & D). These are in line with prior studies showing that the vermis is associated with arousal and the VI and crus areas were related with negative emotions (Baumann & Mattingley, 2012; Colibazzi et al., 2010). We also note that greater HRV was associated with reduced BOLD activity in the cerebellum (left crus I) during diminishing positive emotion compared to negative emotion (Figure 3A, yellow) and increased BOLD activity in the cerebellum (left V) during viewing positive emotion compared to negative emotion (Figure 3B, yellow). A review study reported that the cerebellum's activity was associated with HRV during stress-inducing tasks (de Morree et al., 2013), suggesting the role of the cerebellum during our emotionally stressful tasks in relation to HRV.

Our study is limited in that we measured HRV once at the lab while participants were sitting in a chair for five minutes. This might not be ideal because resting HRV in the scanner would be more proximal to the emotion regulation task. In addition, the current study did not address how phasic HRV during ER interacts with brain activity, which could reveal different relationships (e.g., Tupitsa et al., 2023). Another limitation is that the task consisted of forty-two trials, relatively small considering seven conditions, which might increase

within-subjects errors and impact statistical power (Baker et al, 2021; Phillips & Jiang, 2016). However, this type of error can be mitigated through the large number of participants (N = 100), which provides 80% power to detect small-to-medium within-subjects effect (Faul et al. 2007).

In conclusion, our study adds evidence to the neurovisceral integration model which views emotion regulation as an adaptive process to challenging environments. We demonstrated that higher resting HRV was associated with better adaptation of BOLD activity in the DMN-overlapped regions during the consecutive viewing of emotional images. It is noteworthy that the HRV-DMN association was seen during passively viewing emotional images rather than during actively regulating emotion. While emotion-regulating trials (e.g., intensifying or diminishing) might better detect task-induced changes, trials of passively viewing images might approximate resting state, thus better reflecting individual differences. Although our study could not identify underlying mechanisms, it suggests two possibilities. First, during viewing emotional pictures, the HRV-DMN association might be driven by the tendency of high-HRV individuals to automatically engage with the higher-level control of emotion. Second, resting HRV might serve as a trait that involves lower-level processing of emotional arousal and helps induced arousal fade away. Future research is needed to further explore these possibilities.

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## References

An E, Nolty AAT, Amano SS, Rizzo AA, Buckwalter JG, & Rensberger J (2020). Heart Rate Variability as an Index of Resilience. Military Medicine, 185(3–4), 363–369. 10.1093/MILMED/USZ325 [PubMed: 31642481]

Andrews-Hanna JR (2012). The brain's default network and its adaptive role in internal mentation. Neuroscientist, 18(3), 251–270. 10.1177/1073858411403316 [PubMed: 21677128]

Avery SN, & Blackford JU (2016). Slow to warm up: the role of habituation in social fear. Social Cognitive and Affective Neuroscience, 11(11), 1832–1840. 10.1093/SCAN/NSW095 [PubMed: 27445209]

Baker DH, Vilidaite G, Lygo FA, Smith AK, Flack TR, Gouws AD, & Andrews TJ (2021). Power contours: Optimising sample size and precision in experimental psychology and human neuroscience. Psychological methods, 26(3), 295–314. 10.1037/met0000337 [PubMed: 32673043]

Baumann O, & Mattingley JB (2012). Functional topography of primary emotion processing in the human cerebellum. NeuroImage, 61(4), 805–811. 10.1016/j.neuroimage.2012.03.044 [PubMed: 22465459]

Bo K, Yin S, Liu Y, Hu Z, Meyyappan S, Kim S, Keil A, & Ding M (2021). Decoding Neural Representations of Affective Scenes in Retinotopic Visual Cortex. Cerebral cortex, 31(6), 3047–3063. 10.1093/cercor/bhaa411 [PubMed: 33594428]

Breiter HC, Etcoff NL, Whalen PJ, Kennedy WA, Rauch SL, Buckner RL, Strauss MM, Hyman SE, & Rosen BR (1996). Response and Habituation of the Human Amygdala during Visual Processing of Facial Expression. Neuron, 17(5), 875–887. 10.1016/S0896-6273(00)80219-6 [PubMed: 8938120]

Chalmers JA, Quintana DS, Abbott MJ-A, & Kemp AH (2014). Anxiety Disorders are Associated with Reduced Heart Rate Variability: A Meta-Analysis. Frontiers in Psychiatry, 5, 80. 10.3389/fpsyt.2014.00080 [PubMed: 25071612]

Colibazzi T, Posner J, Wang Z, Gorman D, Gerber A, Yu S, Zhu H, Kangarlu A, Duan Y, Russell JA, & Peterson BS (2010). Neural Systems Subserving Valence and Arousal During the Experience of Induced Emotions. Emotion, 10(3), 377–389. 10.1037/a0018484 [PubMed: 20515226]

Côté S, Gyurak A, & Levenson RW (2010). The ability to regulate emotion is associated with greater well-being, income, and socioeconomic status. Emotion (Washington, D.C.), 10(6), 923–933. 10.1037/a0021156 [PubMed: 21171762]

de Morree HM, Szabó BM, Rutten GJ, & Kop WJ (2013). Central nervous system involvement in the autonomic responses to psychological distress. Netherlands Heart Journal, 21(2), 64–69. 10.1007/s12471-012-0351-1 [PubMed: 23184602]

Duarte J, & Pinto-Gouveia J (2017). Positive affect and parasympathetic activity: Evidence for a quadratic relationship between feeling safe and content and heart rate variability. Psychiatry Research, 257, 284–289. 10.1016/J.PSYCHRES.2017.07.077 [PubMed: 28783577]

Eippert F, Veit R, Weiskopf N, Erb M, Birbaumer N, & Anders S (2007). Regulation of emotional responses elicited by threat-related stimuli. Human Brain Mapping, 28(5), 409–423. 10.1002/hbm.20291 [PubMed: 17133391]

Faul F, Erdfelder E, Lang AG. et al. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior Research Methods 39, 175–191 10.3758/BF03193146 [PubMed: 17695343]

Fischl B, Salat DH, Busa E, Albert M, Dieterich M, Haselgrove C, van der Kouwe A, Killiany R, Kennedy D, Klaveness S, Montillo A, Makris N, Rosen B, & Dale AM (2002). Whole Brain Segmentation: Automated Labeling of Neuroanatomical Structures in the Human Brain. Neuron, 33(3), 341–355. 10.1016/S0896-6273(02)00569-X [PubMed: 11832223]

Fischl B, van der Kouwe A, Destrieux C, Halgren E, Ségonne F, Salat DH, Busa E, Seidman LJ, Goldstein J, Kennedy D, Caviness V, Makris N, Rosen B, & Dale AM (2004). Automatically Parcellating the Human Cerebral Cortex. Cerebral Cortex, 14(1), 11–22. 10.1093/CERCOR/BHG087 [PubMed: 14654453]

Geisler FCM, Vennewald N, Kubiak T, & Weber H (2010). The impact of heart rate variability on subjective well-being is mediated by emotion regulation. Personality and Individual Differences, 49(7), 723–728. 10.1016/J.PAID.2010.06.015

Goldin PR, McRae K, Ramel W, & Gross JJ (2008). The Neural Bases of Emotion Regulation: Reappraisal and Suppression of Negative Emotion. Biological Psychiatry, 63(6), 577–586. 10.1016/j.biopsych.2007.05.031 [PubMed: 17888411]

Gross JJ (2015). Emotion Regulation: Current Status and Future Prospects. Psychological Inquiry, 26(1), 1–26. 10.1080/1047840X.2014.940781

Hamilton JP, Furman DJ, Chang C, Thomason ME, Dennis E, & Gotlib IH (2011). Default-Mode and Task-Positive Network Activity in Major Depressive Disorder: Implications for Adaptive and Maladaptive Rumination. Biological Psychiatry, 70(4), 327–333. 10.1016/J.BIOPSYCH.2011.02.003 [PubMed: 21459364]

Harrison BJ, Fullana MA, Via E, Soriano-Mas C, Vervliet B, Martínez-Zalacaín I, Pujol J, Davey CG, Kircher T, Straube B, & Cardoner N (2017). Human ventromedial prefrontal cortex and the positive affective processing of safety signals. NeuroImage, 152, 12–18. 10.1016/j.neuroimage.2017.02.080 [PubMed: 28254509]

Heartmath. (2016). EmWave Pro Plus. In https://store.heartmath.com/emwave-pro-plus/

Iacobucci D, Posavac SS, Kardes FR, Schneider MJ, & Popovich DL (2015). Toward a more nuanced understanding of the statistical properties of a median split. Journal of Consumer Psychology, 25(4), 652–665. 10.1016/j.jcps.2014.12.002

Jenkinson M, Bannister P, Brady M, & Smith S (2002). Improved optimization for the robust and accurate linear registration and motion correction of brain images. NeuroImage, 17(2), 825–841. 10.1016/S1053-8119(02)91132-8 [PubMed: 12377157]

Jenkinson M, Beckmann CF, Behrens TEJ, Woolrich MW, & Smith SM (2012). FSL. NeuroImage, 62(2), 782–790. 10.1016/J.NEUROIMAGE.2011.09.015 [PubMed: 21979382]

Jenkinson M, & Smith S (2001). A global optimisation method for robust affine registration of brain images. Medical Image Analysis, 5(2), 143–156. 10.1016/S1361-8415(01)00036-6 [PubMed: 11516708]

Joormann J, & Gotlib IH (2009). Emotion regulation in depression: Relation to cognitive inhibition. 10.1080/02699930903407948, 24(2), 281–298. 10.1080/02699930903407948

Kanske P, Heissler J, Schönfelder S, Bongers A, & Wessa M (2011). How to regulate emotion? Neural networks for reappraisal and distraction. Cerebral Cortex, 21(6), 1379–1388. 10.1093/cercor/bhq216 [PubMed: 21041200]

Kastner S, Pinsk MA, De Weerd P, Desimone R, & Ungerleider LG (1999). Increased activity in human visual cortex during directed attention in the absence of visual stimulation. Neuron, 22(4), 751–761. 10.1016/s0896-6273(00)80734-5 [PubMed: 10230795]

Kim SH, & Hamann S (2007). Neural Correlates of Positive and Negative Emotion Regulation. Journal of Cognitive Neuroscience, 19(5), 776–798. 10.1162/jocn.2007.19.5.776 [PubMed: 17488204]

Kleinhans NM, Johnson LC, Richards T, Mahurin R, Greenson J, Dawson G, & Aylward E (2009). Reduced neural habituation in the amygdala and social impairments in autism spectrum disorders. American Journal of Psychiatry, 166(4), 467–475. 10.1176/APPI.AJP.2008.07101681/ASSET/IMAGES/LARGE/U315F3.JPEG [PubMed: 19223437]

Koch C, Wilhelm M, Salzmann S, Rief W, & Euteneuer F (2019). A meta-analysis of heart rate variability in major depression. Psychological Medicine, 49(12), 1948–1957. 10.1017/S0033291719001351 [PubMed: 31239003]

Koenig J, Kemp AH, Beauchaine TP, Thayer JF, & Kaess M (2016). Depression and resting state heart rate variability in children and adolescents — A systematic review and meta-analysis. In Clinical Psychology Review (Vol.46, pp. 136–150). Elsevier Inc. 10.1016/j.cpr.2016.04.013 [PubMed: 27185312]

Kragel PA, Reddan MC, LaBar KS, & Wager TD (2019). Emotion schemas are embedded in the human visual system. Science advances, 5(7), eaaw4358. 10.1126/sciadv.aaw4358 [PubMed: 31355334]

Kundu P, Inati SJ, Evans JW, Luh WM, & Bandettini PA (2012). Differentiating BOLD and non-BOLD signals in fMRI time series using multi-echo EPI. NeuroImage, 60(3), 1759–1770. 10.1016/j.neuroimage.2011.12.028 [PubMed: 22209809]

Laird AR, Fox PM, Eickhoff SB, Turner JA, Ray KL, McKay DR, Glahn DC, Beckmann CF, Smith SM, & Fox PT (2011). Behavioral interpretations of intrinsic connectivity networks 6. J Cogn Neurosci., 23(12), 4022–4037. 10.1162/jocn_a_00077 [PubMed: 21671731]

Lang PJ, Bradley MM, Fitzsimmons JR, Cuthbert BN, Scott JD, Moulder B, & Nangia V (1998). Emotional arousal and activation of the visual cortex: an fMRI analysis. Psychophysiology, 35(2), 199–210. [PubMed: 9529946]

Li J, Xu C, Cao X, Gao Q, Wang Y, Wang Y, Peng J, & Zhang K (2013). Abnormal activation of the occipital lobes during emotion picture processing in major depressive disorder patients. Neural regeneration research, 8(18), 1693–1701. 10.3969/j.issn.1673-5374.2013.18.007 [PubMed: 25206466]

Lopes PN, Salovey P, Côté S, & Beers M (2005). Emotion regulation abilities and the quality of social interaction. Emotion, 5(1), 113–118. 10.1037/1528-3542.5.1.113 [PubMed: 15755224]

Martins B, Ponzio A, Velasco R, Kaplan J, & Mather M (2015). Dedifferentiation of emotion regulation strategies in the aging brain. Social Cognitive and Affective Neuroscience, 10(6), 840–847. 10.1093/scan/nsul29 [PubMed: 25380765]

Mather M, Mitchell KJ, Raye CL, Novak DL, Greene EJ, & Johnson MK (2006). Emotional Arousal Can Impair Feature Binding in Working Memory. Journal of Cognitive Neuroscience, 18(4), 614–625. 10.1162/jocn.2006.18.4.614 [PubMed: 16768364]

Mather M, & Sutherland MR (2011). Arousal-Biased Competition in Perception and Memory. Perspectives on psychological science : a journal of the Association for Psychological Science, 6(2), 114–133. 10.1177/1745691611400234 [PubMed: 21660127]

Mather M, & Thayer JF (2018). How heart rate variability affects emotion regulation brain networks. In Current Opinion in Behavioral Sciences (Vol. 19, pp. 98–104). NIH Public Access. 10.1016/j.cobeha.2017.12.017 [PubMed: 29333483]

Mauss IB, Bunge SA, & Gross JJ (2007). Automatic Emotion Regulation. Social and Personality Psychology Compass, 1(1), 146–167. 10.1111/J.1751-9004.2007.00005.X

Mennin DS, Heimberg RG, Turk CL, & Fresco DM (2005). Preliminary evidence for an emotion dysregulation model of generalized anxiety disorder. Behaviour Research and Therapy, 43(10), 1281–1310. 10.1016/J.BRAT.2004.08.008 [PubMed: 16086981]

Min J, Nashiro K, Yoo HJ, Cho C, Nasseri P, Bachman SL, Porat S, Thayer JF, Chang C, Lee TH, & Mather M (2022). Emotion Down-Regulation Targets Interoceptive Brain Regions While Emotion Up-Regulation Targets Other Affective Brain Regions. Journal of Neuroscience, 42(14), 2973–2985. 10.1523/JNEUROSCI.1865-21.2022 [PubMed: 35193926]

Mitchell KJ, Mather M, Johnson MK, Raye CL & Greene EJ (2006). A functional magnetic resonance imaging investigation of short-term source and item memory for negative pictures. NeuroReport, 17 (14), 1543–1547. doi:10.1097/01.wnr.0000234743.50442.e5. [PubMed: 16957605]

Nashiro K, Min J, Yoo HJ et al. Increasing coordination and responsivity of emotion-related brain regions with a heart rate variability biofeedback randomized trial. Cogn Affect Behav Neurosci 23, 66–83 (2023). 10.3758/s13415-022-01032-w [PubMed: 36109422]

Ochsner KN, Ray RD, Cooper JC, Robertson ER, Chopra S, Gabrieli JDE, & Gross JJ (2004). For better or for worse: Neural systems supporting the cognitive down- and up-regulation of negative emotion. NeuroImage, 23(2), 483–499. 10.1016/j.neuroimage.2004.06.030 [PubMed: 15488398]

Ochsner KN, Ray RR, Hughes B, Mcrae K, Cooper JC, Weber J, … Gross JJ (2009). Bottom-up and top-down processes in emotion generation: Common and distinct neural mechanisms. Psychological Science, 20(11), 1322–1331. 10.1111/j.1467-9280.2009.02459.x [PubMed: 19883494]

Perna G, Riva A, Defillo A, Sangiorgio E, Nobile M, & Caldirola D (2020). Heart rate variability: Can it serve as a marker of mental health resilience?: Special Section on “Translational and Neuroscience Studies in Affective Disorders” Section Editor, Maria Nobile MD, PhD. Journal of Affective Disorders, 263, 754–761. 10.1016/J.JAD.2019.10.017 [PubMed: 31630828]

Petersen SE, & Dubis JW (2012). The mixed block/event-related design. NeuroImage, 62(2), 1177–1184. 10.1016/j.neuroimage.2011.09.084 [PubMed: 22008373]

Phan KL, Fitzgerald DA, Nathan PJ, Moore GJ, Uhde TW, & Tancer ME (2005). Neural substrates for voluntary suppression of negative affect: A functional magnetic resonance imaging study. Biological Psychiatry, 57(3), 210–219. 10.1016/j.biopsych.2004.10.030 [PubMed: 15691521]

Phillips GW & Jiang T (2019). Measurement Error and Equating Error in Power Analysis, Practical Assessment, Research, and Evaluation, 21, Article 9. 10.7275/0snn-zm67

Plichta MM, Grimm O, Morgen K, Mier D, Sauer C, Haddad L, Tost H, Esslinger C, Kirsch P, Schwarz AJ, & Meyer-Lindenberg A (2014). Amygdala habituation: A reliable fMRI phenotype. NeuroImage, 103, 383–390. 10.1016/J.NEUROIMAGE.2014.09.059 [PubMed: 25284303]

Quigley L, & Dobson KS (2014). An examination of trait, spontaneous and instructed emotion regulation in dysphoria. 10.1080/02699931.2013.848786, 28(4), 622–635. 10.1080/02699931.2013.848786

Rankin CH, Abrams T, Barry RJ, Bhatnagar S, Clayton DF, Colombo J, Coppola G, Geyer MA, Glanzman DL, Marsland S, McSweeney FK, Wilson DA, Wu CF, & Thompson RF (2009). Habituation revisited: An updated and revised description of the behavioral characteristics of habituation. Neurobiology of Learning and Memory, 92(2), 135–138. 10.1016/J.NLM.2008.09.012 [PubMed: 18854219]

Roy B, Riley C, & Sinha R (2018). Emotion regulation moderates the association between chronic stress and cardiovascular disease risk in humans: a cross-sectional study. 10.1080/10253890.2018.1490724, 21(6), 548–555. 10.1080/10253890.2018.1490724

Ruiz-Padial E, Sollers JJ, Vila J, & Thayer JF (2003). The rhythm of the heart in the blink of an eye: Emotion-modulated startle magnitude covaries with heart rate variability.

Ruiz-Padial E, & Thayer JF (2014). Resting heart rate variability and the startle reflex to briefly presented affective pictures. International Journal of Psychophysiology, 94(3), 329–335. 10.1016/j.ijpsycho.2014.10.005 [PubMed: 25449955]

Sakaki M, Yoo HJ, Nga L, Lee TH, Thayer JF, & Mather M (2016). Heart rate variability is associated with amygdala functional connectivity with MPFC across younger and older adults. NeuroImage, 139, 44–52. 10.1016/j.neuroimage.2016.05.076 [PubMed: 27261160]

Sabatinelli D, Bradley MM, Fitzsimmons JR, & Lang PJ (2005). Parallel amygdala and inferotemporal activation reflect emotional intensity and fear relevance. NeuroImage., 24(4), 1265–1270. 10.1016/j.neuroimage.2004.12.015 [PubMed: 15670706]

Satpute AB, & Lindquist KA (2019). The Default Mode Network's Role in Discrete Emotion. Trends in Cognitive Sciences, 23(10), 851–864. 10.1016/j.tics.2019.07.003 [PubMed: 31427147]

Sheline YI, Barch DM, Price JL, Rundle MM, Vaishnavi SN, Snyder AZ, Mintun MA, Wang S, Coalson RS, & Raichle ME (2009). The default mode network and self-referential processes in depression. Proceedings of the National Academy of Sciences, 106(6), 1942–1947. 10.1073/PNAS.0812686106

Siennicka A, Quintana DS, Fedurek P, Wijata A, Paleczny B, Ponikowska B, & Danel DP (2019). Resting heart rate variability, attention and attention maintenance in young adults. International journal of psychophysiology, 143, 126–131. 10.1016/j.ijpsycho.2019.06.017 [PubMed: 31255739]

Steinfurth ECK, Wendt J, Geisler F, Hamm AO, Thayer JF, & Koenig J (2018). Resting state vagally-mediated heart rate variability is associated with neural activity during explicit emotion regulation. Frontiers in Neuroscience, 12(NOV), 794. 10.3389/fnins.2018.00794 [PubMed: 30455624]

Thayer JF, Åhs F, Fredrikson M, Sollers JJ, & Wager TD (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. Neuroscience and Biobehavioral Reviews, 36(2), 747–756. 10.1016/j.neubiorev.2011.ll.009 [PubMed: 22178086]

Thayer JF, & Lane RD (2009). Claude Bernard and the heart-brain connection: Further elaboration of a model of neurovisceral integration. In Neuroscience and Biobehavioral Reviews (Vol. 33, Issue 2, pp. 81–88). Pergamon. 10.1016/j.neubiorev.2008.08.004 [PubMed: 18771686]

Tarvainen MP, Niskanen J-P, Lipponen JA, Ranta-Aho PO, & Karjalainen PA (2014). Kubios HRV–heart rate variability analysis software. Computer Methods and Programs in Biomedicine, 113(1), 210–220. [PubMed: 24054542]

Tupitsa E, Egbuniwe I, Lloyd WK, Puertollano M, Macdonald B, Joanknecht K, Sakaki M, & van Reekum CM (2023). Heart rate variability covaries with amygdala functional connectivity during voluntary emotion regulation. NeuroImage, 274, 120136. 10.1016/j.neuroimage.2023.120136 [PubMed: 37116768]

Verkuil B, Brosschot JF, Gebhardt WA, & Thayer JF (2010). When Worries Make You Sick: A Review of Perseverative Cognition, the Default Stress Response and Somatic Health. Journal of Experimental Psychopathology JEP, 1, 87–118. 10.5127/jep.009110

Volokhov RN, & Demaree HA (2010). Spontaneous emotion regulation to positive and negative stimuli. Brain and Cognition, 73(1), 1–6. 10.1016/J.BANDC.2009.10.015 [PubMed: 20347515]

Wei L, Chen H, & Wu GR (2018). Structural covariance of the prefrontal-amygdala pathways associated with heart rate variability. Frontiers in Human Neuroscience, 12. 10.3389/FNHUM.2018.00002/FULL

Weiss NH, Schick MR, Waite EE, Haliczer LA, & Dixon-Gordon KL (2021). Association of Positive Emotion Dysregulation to Resting Heart Rate Variability: The Influence of Positive Affect Intensity. Personality and Individual Differences, 173. 10.1016/J.PAID.2020.110607

Woolrich MW, Behrens TEJ, Beckmann CF, Jenkinson M, & Smith SM (2004). Multilevel linear modelling for FMRI group analysis using Bayesian inference. NeuroImage, 21(4), 1732–1747. 10.1016/J.NEUROIMAGE.2003.12.023 [PubMed: 15050594]

Woolrich MW, Ripley BD, Brady M, & Smith SM (2001). Temporal Autocorrelation in Univariate Linear Modeling of FMRI Data. NeuroImage, 14(6), 1370–1386. 10.1006/NIMG.2001.0931 [PubMed: 11707093]

Yan CG, Chen X, Li L, Castellanos FX, Bai TJ, Bo QJ, Cao J, Chen GM, Chen NX, Chen W, Cheng C, Cheng YQ, Cui XL, Duan J, Fang YR, Gong QY, Guo W. bin, Hou ZH, Hu L, … Zang YF (2019). Reduced default mode network functional connectivity in patients with recurrent major depressive disorder. Proceedings of the National Academy of Sciences of the United States

of America, 116(18), 9078–9083. 10.1073/PNAS.1900390116/-/DCSUPPLEMENTAL [PubMed: 30979801]

Yang X, Spangler DP, Thayer JF, & Friedman BH (2021). Resting heart rate variability modulates the effects of concurrent working memory load on affective startle modification. Psychophysiology, 58(8), e13833. 10.1111/PSYP.13833 [PubMed: 33913180]

Yoo HJ, Nashiro K, Min J et al. Multimodal neuroimaging data from a 5-week heart rate variability biofeedback randomized clinical trial. Sci Data 10, 503 (2023). 10.1038/s41597-023-02396-5 [PubMed: 37516756]

Zahn D, Adams J, Krohn J, Wenzel M, Mann CG, Gomille LK, Jacobi-Scherbening V, & Kubiak T (2016). Heart rate variability and self-control—A meta-analysis. Biological Psychology, 115, 9–26. 10.1016/J.BIOPSYCHO.2015.12.007 [PubMed: 26747415]

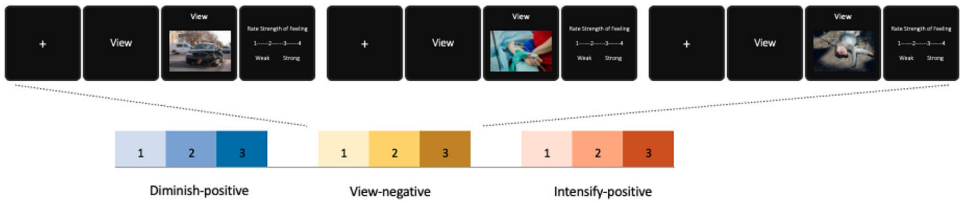


**Figure 1. Example of mixed block/event-related design**

*Note*. The current study employed a mixed block/event-related design. This example shows how three same-condition trials were presented consecutively within a block of the view-negative condition.

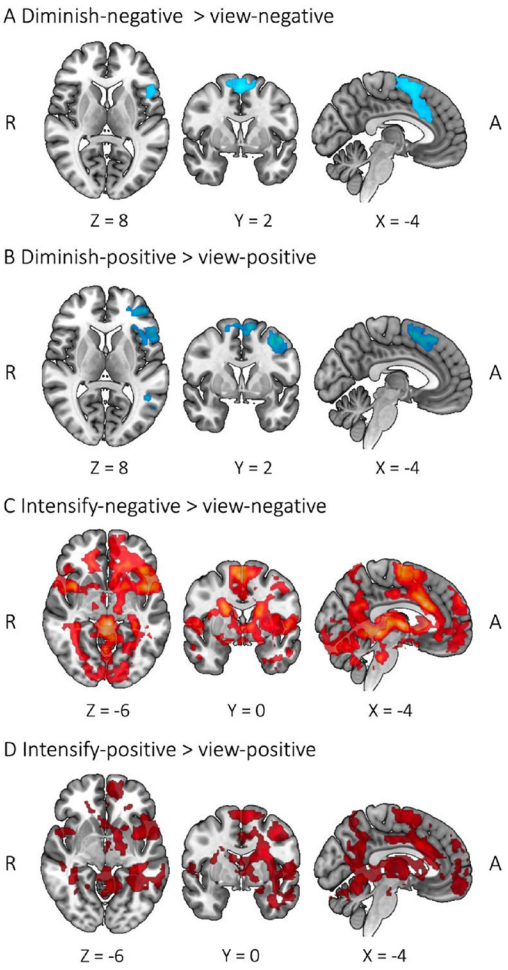


**Figure 2. Brain regions associated with emotion regulation**

*Note*. A shows the clusters (light blue) from the contrast of diminish-negative > view-negative. B shows clusters (dark blue) from the contrast of diminish-positive > view-negative. C shows the clusters (light red) from the contrast of intensify-negative > view-negative. D shows the clusters (dark red) from the contrast of intensify-positive > view-positive. No correlations were found between brain activity and RMSSD for the four contrasts.

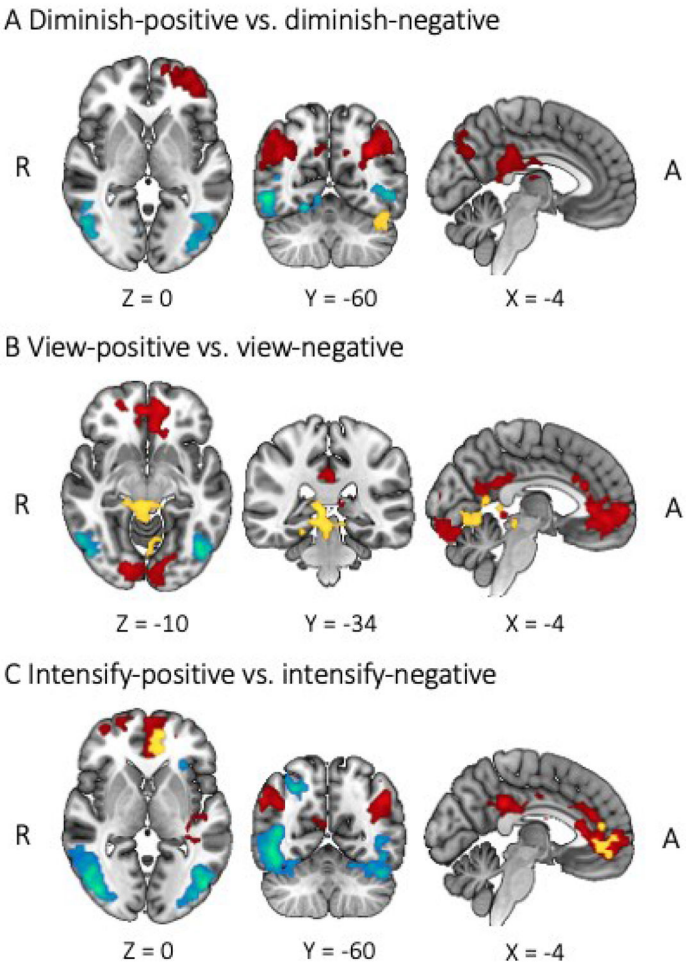


**Figure 3. Brain regions associated with RMSSD during emotion regulation**

*Note*. A shows clusters (red) from the contrast of diminish-positive > diminish-negative, clusters (blue) from diminish-negative > diminish-positive, and clusters (yellow) whose BOLD activity negatively correlated with RMSSD during diminish-positive > diminish-negative. B shows clusters (red) from the contrast of view-positive > view-negative, clusters (blue) from view-negative > view-positive, and clusters (yellow) whose BOLD activity positively correlated with RMSSD during view-positive > view-negative. C shows clusters (red) from the contrast of intensify-positive > intensify-negative, clusters (blue) from intensify-negative > intensify-positive, and the clusters (yellow) whose BOLD activity positively correlated with RMSSD during view-positive > view-negative.

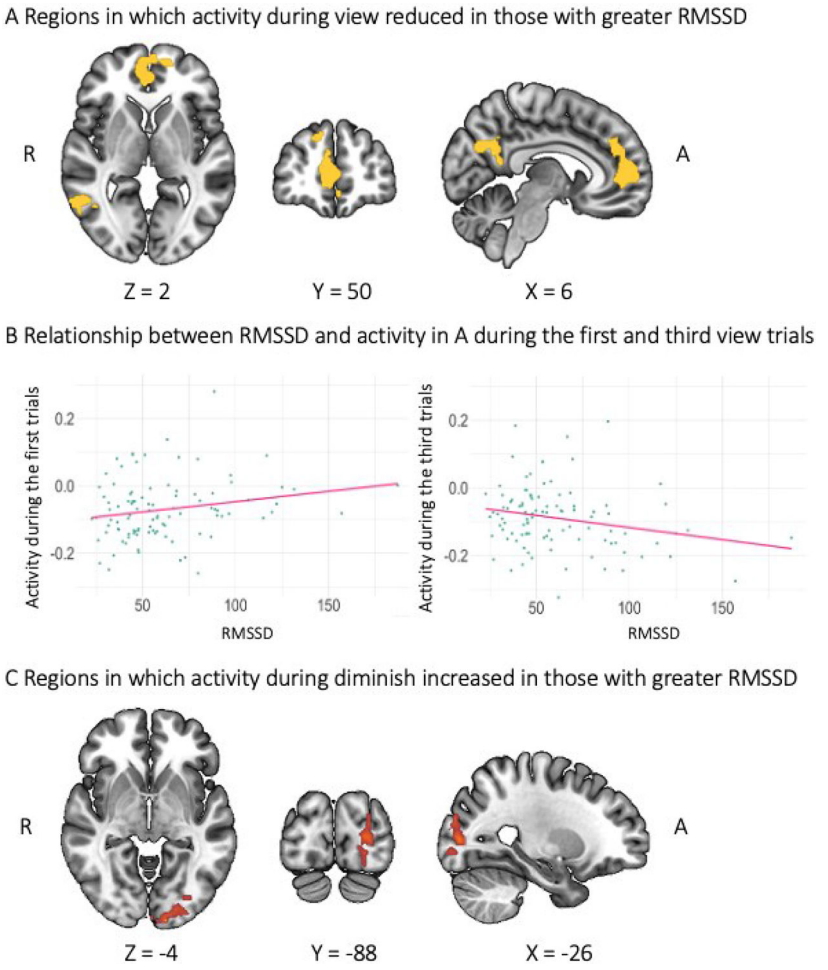


**Figure 4. Regions where individuals with higher resting RMSSD showed a greater decrease in BOLD activity as trials proceeded from the first to last during viewing and diminishing emotions.**

*Note*. A shows clusters (yellow) whose decrease in BOLD activity correlated with RMSSD while passively viewing emotional images over three trials. B shows the relationship between RMSSD and BOLD activity in the clusters of A (yellow) during the first and third trials. C shows clusters (brown) whose increase in BOLD activity correlated with RMSSD while actively diminishing emotion over three trials.

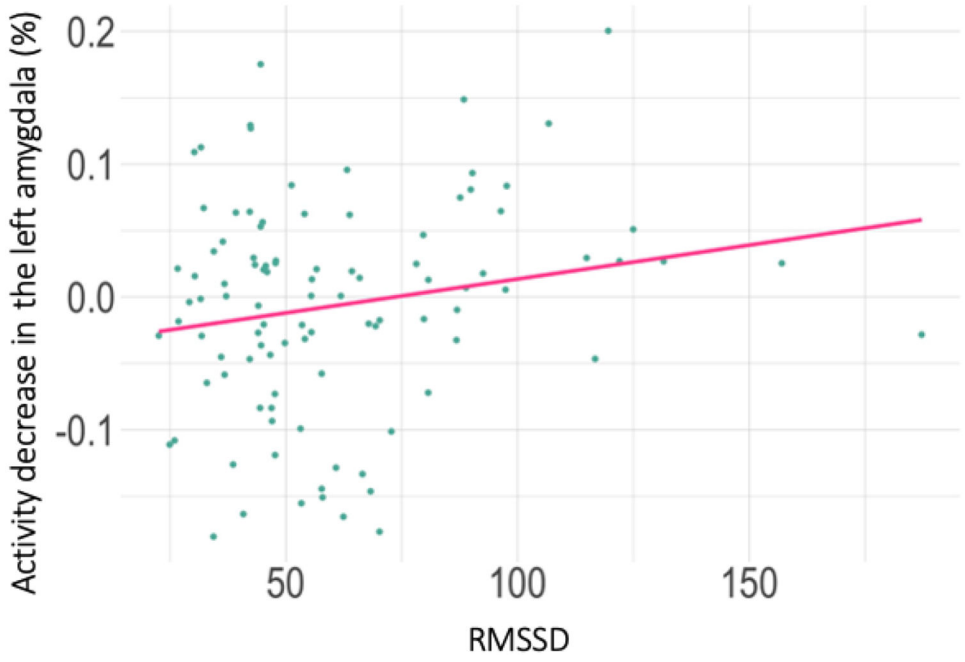


**Figure 5. Relationship between resting RMSSD and decrease in left-amygdala's BOLD activity from the first to the last trials while viewing emotional images**

*Note*. The figure shows a correlation between RMSSD and decrease in amygdala activity from the first to last trials while the text reports a partial correlation after controlling for the first-trial activity in the left amygdala.

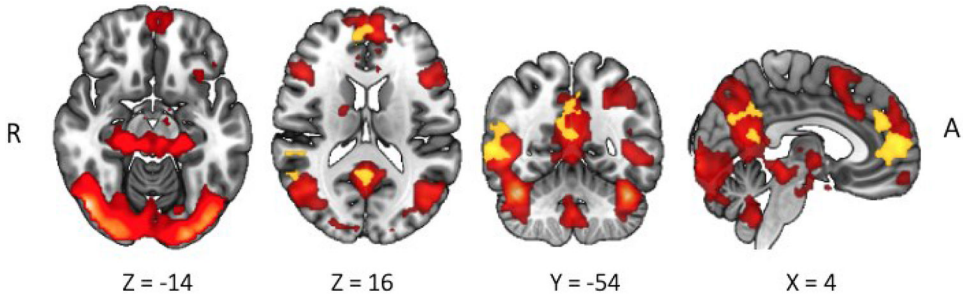


**Figure 6. Regions activated during viewing emotional images versus neutral images**

*Note*. Activity decrease in the regions (yellow) was correlated with RMSSD while repeatedly viewing emotional images (Figure 4A). The regions (yellow) overlapped with the regions (red) which increased activity while viewing emotional images compared to viewing neutral images.