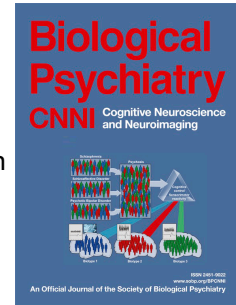


# Journal Pre-proof

Training in cognitive reappraisal normalizes whole-brain indices of emotion regulation in borderline personality disorder

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**Training in cognitive reappraisal normalizes whole-brain indices of emotion regulation in borderline personality disorder**

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### **Abstract**

**Background:** Borderline personality disorder is the prototypical disorder of emotion dysregulation. We have previously shown that borderline personality disorder patients are impaired in their capacity to engage cognitive reappraisal, a frequently-employed adaptive emotion regulation strategy. **Methods:** Here we report on the efficacy of longitudinal training in cognitive reappraisal to enhance emotion regulation in borderline patients. Specifically, the training targeted psychological distancing, a reappraisal tactic whereby negative stimuli are viewed dispassionately as though experienced by an objective, impartial observer. At each of 5 sessions over 2 weeks, 22 borderline (14 Female) and 22 healthy control (13 Female) participants received training in psychological distancing and then completed a widely-used picture-based reappraisal task. Self-reported negative affect ratings and functional magnetic resonance imaging (fMRI) data were acquired at the first and fifth sessions. In addition to behavioral analyses, we performed whole-brain pattern expression analyses using independently-defined patterns for negative affect and cognitive reappraisal implementation for each session. **Results:** Borderline patients showed a decrease in negative affect pattern expression following reappraisal training, reflecting a normalization in neural activity. They did not, however, show significant change in behavioral self-reports. **Conclusions:** To our knowledge, this study represents the first longitudinal fMRI examination of task-based cognitive reappraisal training. Using a brief, proof-of-concept design, the results suggest a potential role for reappraisal training in the treatment of borderline patients.

## Introduction

Emotion dysregulation or affective instability is a defining characteristic of borderline personality disorder (1). In addition to emotion dysregulation, borderline personality disorder is characterized by impaired interpersonal relationships, unstable identity, impulsivity and self-destructiveness (1-3), symptoms that are also related to emotional dysregulation. This impaired ability to regulate emotional responses is of great clinical relevance, negatively impacting social functioning, life satisfaction, and is associated with the self-destructiveness and identity disturbances in borderline patients (2, 3). Thus, the enhancement of emotion regulation represents a promising intervention target in borderline patients and in other affectively-disordered populations as well. (4-6).

Several cognitive-behavioral psychotherapies for borderline personality disorder, including dialectical behavior therapy (DBT; 7), employ non-specific emotion regulation skills training. While such treatments have shown efficacy, they are resource intensive and typically extend over many months. One study that documented reduced amygdala responsiveness to emotionally arousing cues incorporated 12 months of the combination of weekly individual DBT therapy, weekly skills training sessions, and telephone counseling (8). Little is known about the active ingredients of these treatments and their symptom and neural targets. Thus, the present study examined a specific, well-characterized and highly adaptive emotion regulation strategy, cognitive reappraisal, and exploits neuroimaging as a sensitive indicator of change. This approach has the potential to contribute to the development of more efficient, accessible and personalizable treatment methods.

We focus upon cognitive reappraisal, an emotion regulation strategy that involves changing the meaning of an emotional stimulus in a way that alters its emotional impact (9, 10). When employed to down-regulate negative emotion, reappraisal has been shown in healthy individuals to lead to reductions in self-reported negative affect (9 - 11) as well as attenuated activity in brain regions associated with negative emotion reactivity, including the amygdala, and increased activity in control regions such as the ventrolateral and dorsolateral prefrontal cortex (12 - 14). Increased prefrontal cortex activity, including in the ventrolateral and ventromedial prefrontal cortices, has been shown to predict attenuated amygdala activity (15, 16). We have shown previously that when reappraising vs. simply looking at negative pictures, borderline patients did not decrease amygdala activity or increase anterior cingulate activity as healthy volunteers did (18). This finding motivated our efforts to determine whether borderline patients could enhance their reappraisal capability with training.

Recent work in social cognitive neuroscience has begun to extend beyond examination of individual brain regions and toward examination of whole-brain functional networks (19 - 21). This approach has the advantage of vastly limiting the multiple comparison problem in neuroimaging data analysis (i.e., among disparate regions-of-interest; ROIs) as well as providing an independently-defined and multivariate basis against which to test hypotheses concerning the engagement of particular psychological states. One such method of interrogating whole-brain networks, employed in the present study, involves assessing the correspondence (i.e., whole-brain correlation) between independently-defined whole-brain patterns for particular psychological states (e.g., experiencing negative affect or implementing cognitive reappraisal) and fMRI

contrast maps for comparisons of interest for individual participants (19, 21). In the present work, we acquired and used whole-brain weighted pattern maps for both picture-induced negative affect (19) and reappraisal implementation (13).

Cognitive reappraisal can be operationalized via one or more regulatory tactics (22). Our examination of cognitive reappraisal focused on the reappraisal tactic, psychological distancing, which involves appraising an emotional stimulus by adopting the perspective of an objective, impartial observer (10,11) and/or increasing the perceived spatial or temporal distance between oneself and the emotional stimulus (24, 25), in line with construal level theory (26). Distancing stands in contrast to other reappraisal tactics, like reinterpretation, which involves generating a stimulus-specific narrative characterizing how a particular situation is not as bad as it first seemed, for example (9, 10). In healthy adults, we have previously shown that a four-session course of distancing training leads to longitudinal reductions in self-reported negative affect and uniquely leads to longitudinal attenuation of perceived stress in daily life in a pattern not observed in reinterpretation training (11). Thus, distancing represents a promising tactic for reappraisal training, particularly for populations of individuals who experience negative emotional stimuli as particularly arousing and overwhelming, as is the case in borderline personality disorder.

Prior neuroimaging evidence has suggested that borderline patients, relative to healthy adults, show anomalous neural activity in reacting to emotional cues and when implementing emotion regulation-via-reappraisal. Two neuroimaging meta-analyses have provided evidence of amygdala hyper-reactivity in borderline patients compared to healthy controls when reacting to negative emotional stimuli (27, 28). Further, two

studies found that, when invoking reappraisal-by-distancing, borderline patients could not decrease activity in regions of the salience network, the amygdala (18) and the insula (29), compared to healthy subjects.

In the present study, in line with prior work examining longitudinal reappraisal-by-distancing training behaviorally in healthy adults (5, 11), we examined a relatively-brief, five-session reappraisal-by-distancing training paradigm in borderline patients and healthy controls. Our primary aims were to compare post-training to pre-training behavioral effects and neural patterns related to emotion processing and regulation. We hypothesized that borderline patients would show behavioral and neural evidence of elevated negative emotion reactivity and impaired emotion regulation at baseline relative to healthy controls, and that longitudinal reappraisal training would attenuate these group differences and show evidence of a normalized pattern in borderline patients.

## **Methods and Materials**

### **Participants**

We recruited 31 borderline patients and 26 healthy control participants from outpatient clinics at the Mount Sinai Medical Center and the James J. Peters VA Medical Center in New York City, as well as from newspaper and online advertisements. All participants provided written informed consent after procedures were fully explained. Exclusions due to motion, signal quality, and related issues are detailed in Supplemental Material. In total, 9 borderline patients and 4 healthy controls were excluded, yielding an analyzable total of 22 borderline patients (mean age = 36.28 years; 14 female) and 22 healthy controls (mean age = 32.91 years; 13 female). Among these participants, behavioral data were not retrievable for a total of 4 non-scanned intermediate training

sessions from 4 participants. There were no significant age differences by group,  $t(42)=1.13, p=0.27, n.s.$ , and there were no significant differences in gender ratio,  $\chi^2(1,44)=0.10, p=0.76, n.s.$  See Table S1 for demographic and clinical features of the groups.

Borderline participants met DSM-IV criteria for borderline personality disorder, including the affective instability criterion. Borderline participants did not meet DSM-IV criteria for past or present bipolar I disorder, schizophrenia, schizoaffective disorder, avoidant personality disorder, posttraumatic stress disorder, substance dependence, or current major depression. All participants had to be psychotropic medication free for 2 weeks (6 weeks in the case of fluoxetine). Three borderline patients were in psychotherapy at time of participation. Healthy participants did not meet DSM-IV criteria for any axis I or axis II disorder. Diagnostic assessments were obtained using the Structured Clinical Interview for DSM-IV–Patient Edition and the Structured Clinical Interview for DSM-IV Axis II Personality Disorders. Our group has achieved an interrater reliability of 0.81 for diagnosing borderline personality disorder.

## **Materials**

300 negative and 150 neutral pictures were shown in the emotion regulation task. An additional comparable 60 negative and 30 neutral pictures were used for a third, follow-up scan session, the results of which are beyond the scope of the current analyses; these additional pictures were part of the counterbalanced stimulus bank (see Supplemental Material). All pictures (negative and neutral) were social, depicting two or more people interacting. Importantly, all negative pictures contained themes specifically relevant to borderline personality disorder, including interpersonal rejection, sadness,



frustration, anger, and violence. Pictures were drawn from the International Affective Picture System (IAPS; 31), Empathy Picture System (32), and online image repositories and rated using the Self-Assessment Manikin (33) for comparability (see Supplemental Material).

### **Task Design**

During each of five sessions, spaced approximately 1-2 days apart (average time between sessions = 1.97 days), participants received reappraisal-by-distancing training and then completed a widely-used picture-based reappraisal task (11, 14, 23).

#### *Reappraisal Training*

At the beginning of each session, participants received training in psychological distancing first via an approximately 15 minute one-on-one interaction with an experimenter in which a standardized set of instructions were given, in line with procedures used in prior work (11, 18); however, the instruction script was slightly modified from that used by Denny and Ochsner (11) in order to use language and examples that would be appropriate and well-suited to borderline patients. Demand characteristics were minimized by never mentioning the term *training* to participants at any time during the experiment; participants were simply told that they were taking part in a multi-session study involving fMRI scanning and the completion of a picture-based task.

During training, participants were told about the two types of instruction cues that they would see on a trial-by-trial basis: LOOK and DISTANCE. For pictures preceded by a LOOK cue, participants were instructed to simply look at and respond naturally to the picture. For pictures preceded by the DISTANCE cue, participants were instructed to

view the picture with a “detached, objective, impartial, and scientific mindset” (10, 23) “and/or imagine that the pictured events happened far away or a long time ago” (24-26).

Each day’s session began with three “walk-through” pictures that were presented for interactive training in the task, in parallel with procedures used previously (11). At each of the 5 sessions, one picture was used to illustrate the procedure for the LOOK negative picture condition, and two pictures were used to provide practice for the DISTANCE negative condition. In this process, the participant was encouraged to voice aloud his/her thinking in carrying out the tasks to allow the experimenter to model and shape the participant’s use of the distancing strategy. Walk-through pictures were unique for each of the 5 sessions and were counterbalanced across sessions. At Session 1 only, participants then completed 9 fixed-pace practice trials that demonstrated the timing of the actual picture-based task, described below. Afterward, at each of the 5 sessions, the participant completed the reappraisal task.

#### *Reappraisal Task*

The reappraisal task was very similar to one that has been described previously and used in numerous prior studies (11, 14, 18, 23, 34). The trial structure for the task is shown in Figure 1. For each trial, a cue (either LOOK or DISTANCE) was presented for 2 s, followed by presentation of a neutral or negative picture for 10 s, during which time participants were instructed to implement the LOOK or DISTANCE instruction, followed by a rating period in which participants rated their current strength of negative affect on a scale of 1 (least) to 5 (most) for 4 s, and finally an inter-trial fixation interval of either 3 or 5 s (average of 4 s).

Three different trial types were presented at each session: “Look Neutral” (i.e. LOOK instruction paired with a neutral picture), “Look Negative” (i.e. LOOK instruction paired with a negative picture), and “Reapp Negative” (i.e. DISTANCE instruction paired with a negative picture). 90 trials were presented per session with 30 trials each per trial type. These were presented across 3 task runs (with short breaks in between) comprised of 10 trials of each trial type per run. Unique stimuli were presented on each trial at all 5 sessions. Picture sets were counterbalanced across sessions and trial types. Within runs, trials were presented in a randomized order.

### **Data Acquisition and Analysis**

#### *Self-Reported Negative Affect*

At Session 1 and 5, self-reported negative affect ratings were acquired using a 5-button response glove during fMRI scanning and recorded using E-Prime software (Psychology Software Tools, Inc.). At Sessions 2, 3, and 4, self-reported negative affect ratings were acquired with participants seated at a computer running E-Prime software. Self-reported affect data were analyzed using a linear mixed model incorporating predictors for Group (borderline and healthy control), Session (1 through 5), and Trial Type (Look Neutral, Look Negative, Reapp Negative), and their interactions, as well as a random intercept for each participant.

#### *fMRI*

fMRI data were acquired at Sessions 1 and 5. Whole-brain fMRI data were acquired using the same scanner for each participant, either a 3.0T Philips Achieva scanner (11 borderline patients and 14 healthy controls) or a 3.0T Siemens MAGNETOM Skyra scanner (11 borderline patients and 8 healthy controls). There were no significant

differences in scanner allocation ratio by group,  $\chi^2(1,44)=.83, p=0.36, n.s.$  Acquisition and preprocessing information is provided in Supplemental Material.

At Sessions 1 and 5, for each participant, a random-effects general linear model (GLM) was computed with regressors for fMRI responses to the cue (differentiated by two cues: “LOOK” and “DISTANCE”), stimulus presentation (differentiated by the three Trial Types: Look Neutral, Look Negative, and Reappraise Negative), and rating period (undifferentiated by trial type). Further details are provided in Supplemental Material.

#### *Pattern Expression Analyses*

Task fMRI data were analyzed using the FMRIB Software Library (FSL) to generate participant-specific, whole-brain contrast maps reflecting activity, relative to fixation baseline, during the stimulus presentation period separately for Look Neutral, Look Negative, and Reappraise Negative trials.

We procured whole-brain patterns derived from whole-brain cross-validated machine learning analyses for picture-induced negative affect (PINES; 19) and a quantitative meta-analysis of reappraisal implementation (13) by contacting the authors of the respective studies. The PINES map included positive weights for regions including but not limited to amygdala, dorsomedial prefrontal cortex, and the posterior cingulate cortex (Figure 2A). The reappraisal implementation map from Buhle and colleagues (13) included the posterior dorsomedial prefrontal cortex, bilateral dorsolateral prefrontal cortex, ventrolateral prefrontal cortex, and posterior parietal lobe (Figure 2B).

For PCS calculation, we used the whole-brain unthresholded PINES pattern mask as shown in a representative sagittal view in Figure 2A. For RCS calculation, to reduce the influence of potentially noisy and spurious voxel data in each whole-brain pattern

map, we applied a lower bound threshold of  $Z = 2$  (see 21). We estimated each participant's correlation between each whole-brain pattern during the reappraisal task (i.e., individual contrast maps for Look Neutral, Look Negative, and Reappraise Negative, each versus fixation baseline) and the negative affect and reappraisal implementation pattern maps using AFNI's *3ddot* tool in order to assess the extent to which their brain activity during the reappraisal task engaged the reference whole-brain patterns (i.e., using "*3ddot -docor*" to compute the correlation coefficient for each participant). This resulted in one correlation coefficient per participant for each correspondence measure (i.e., PINES Correspondence Score [PCS] and Reappraisal Correspondence Score [RCS], respectively; for additional details, see 21). PCS and RCS values were analyzed using linear mixed models incorporating predictors for Group (borderline and healthy control), Session (1 and 5), and Trial Type (Look Neutral, Look Negative, Reapp Negative), and their interactions, as well as a random intercept for each participant. Exploratory models including age and gender as covariates are provided in Supplemental Material.

## Results

### Self-Reported Negative Affect

Figure 3 shows negative affect self-reports by trial type and session for each group. As expected, at baseline, borderline patients showed greater reactivity behaviorally to negative stimuli than healthy volunteers, ( $t(42)=2.04$ ,  $p < 0.05$ , two-tailed; Fig 3). When reappraising at baseline, however, the groups did not show a significant difference, ( $t(42)=1.04$ ,  $p=0.30$ , *n.s.*, two-tailed(Fig 3)).

A significant effect of Group was present,  $F(1,42)=4.15$ ,  $p<0.05$ , with borderline patients on average reporting greater negative affect during the task. A main effect of Session was also present,  $F(4,576)=6.03$ ,  $p<0.001$ , indicating a decreasing trend in self-reported negative affect over time overall. Further, a main effect of Trial Type was present,  $F(2,576)=618.71$ ,  $p<0.001$ . An omnibus Group-by-Trial Type by-Session interaction, including the Look Neutral trial type, was non-significant,  $F(8,576)=0.69$ ,  $p=0.70$ . A trend level Group-by-Trial Type interaction was present,  $F(2,576)=2.62$ ,  $p=.07$ . To examine comparisons of a priori interest, we conducted paired and independent sample t-tests assessing change over time (i.e., Session 5 versus Session 1) by Group and Trial Type. For Look Neutral trials, borderline patients showed a marginal decrease over time in self-reported negative affect,  $t(21)=1.85$ ,  $p < .08$ , two-tailed, as did healthy participants,  $t(21)= 2.07$ ,  $p < .06$ , two-tailed. For Look Negative trials, borderline patients showed a significant drop in self-reported negative affect over time,  $t(21)=3.30$ ,  $p = .003$ , two-tailed, while healthy controls showed a trend-level drop in negative affect over time,  $t(21) = 1.81$ ,  $p < .09$ , two-tailed. For Reappraise Negative trials, healthy control participants showed a significant drop in self-reported negative affect ( $t(21)=2.39$ ,  $p < .03$ , two-tailed) whereas borderline patients exhibited no significant drop in self-reported negative affect ( $t(21) = .79$ ,  $p = .44$ , *n.s.*, two-tailed).

### **Pattern Expression Analyses**

#### *PINES Correspondence Score*

Pattern expression analysis results using the independently-defined pattern map for picture-induced negative affect (PINES; 19) are shown in Figure 4. A main effect of

Session was present,  $F(1,210)=13.72, p<0.001$ , indicating some global attenuation in PCS across both groups across sessions. A main effect of Trial Type was also present,  $F(2,210)=79.95, p<0.001$ . When examining only negative picture trials across groups and sessions, there is also a main effect of Session,  $F(1,126)=8.54, p=0.004$ . We further examined these relationships via planned t-tests.

Following reappraisal training, borderline patients showed a significant decrease in PCS when reappraising negative pictures by distancing at Session 5 compared to Session 1 ( $t(21)=1.88, p<0.04$ , one-tailed); healthy controls showed a weaker effect in the same direction for this comparison,  $t(21)=1.36, p<0.10$ , one-tailed. At Session 1, healthy controls showed a descriptive decrease in PCS scores when distancing compared to looking at negative pictures that did not reach significance ( $t(21)=1.25, p=.11$ , one-tailed), whereas borderline patients did not show a decrease in PCS score at baseline when distancing compared to looking ( $t(21)=0.67, p=.51$ , two-tailed). However, by Session 5, after training, borderline patients showed a pattern suggestive of that of healthy controls in Session 1, with attenuation of PCS when reappraising compared to looking ( $t(21)=1.34, p<.10$ , one-tailed). In contrast, at Session 5, healthy controls did not show a significant decrease in ReappNeg vs LookNeg ( $t(21)=1.24, p=.23$ , two-tailed).

Notably for Look Negative trials, borderline patients showed no significant habituation in PCS,  $t(21)=0.60, p=.56$ , n.s., two-tailed, suggesting that PCS attenuation during reappraisal trials in borderline patients was not simply the effect of time or re-test exposure. Healthy controls also showed no significant attenuation in PCS for Look Negative trials over time,  $t(21)=1.57, p=0.13$ , two-tailed.

### *Reappraisal Implementation Network*

Reappraisal Correspondence Scores (RCS) derived from the pattern map for reappraisal implementation (13) are shown in Figure 5. A main effect of Trial Type was present,  $F(2,210)=46.90$ ,  $p<0.001$ , and a marginal effect of Session was present,  $F(1,210)=1.99$ ,  $p=.16$ . As expected, both borderline patients and healthy control subjects showed greater recruitment of the reappraisal implementation network during Reapp Neg trials relative to Look Neg trials at Session 1 (borderline patients:  $t(21) = 2.96$ ,  $p < .01$ , two-tailed; healthy controls:  $t(21) = 3.28$ ,  $p < .01$ , two-tailed) and Session 5 (borderline patients:  $t(21) = 2.70$ ,  $p = .01$ , two-tailed; healthy controls:  $t(21) = 2.96$ ,  $p < .01$ , two-tailed). There was no significant change over time in recruitment of the reappraisal network for Reapp Negative trials in healthy controls,  $t(21) = 1.28$ ,  $p = .21$ , n.s., two-tailed or borderline patients,  $t(21) = 0.59$ ,  $p = .56$ , n.s., two-tailed.

## **Discussion**

In this study, we examined whether longitudinal training in cognitive reappraisal-by-distancing would enhance emotion regulation in borderline personality disorder patients, who characteristically show significant emotion dysregulation. We examined the efficacy and neural correlates of a relatively brief, five-session training paradigm in borderline patients and healthy controls. To our knowledge, these results represent the first longitudinal fMRI examination of task-based cognitive reappraisal training in any population. We predicted that borderline patients would show behavioral and neural evidence of elevated negative emotion reactivity and impaired emotion regulation at



baseline relative to healthy controls, and that longitudinal reappraisal training would attenuate these group differences and show evidence of a normalizing neural pattern in borderline patients.

The neural findings were largely consistent with the hypothesized improvement in distancing-related downregulation of negative responses in borderline patients with training. As discussed below, borderline patients showed a reduction in a multivariate pattern of negative affect during reappraisal at Session 5, after training, compared to Session 1, as reflected in the whole brain neural signature of picture-induced negative affect.

For behavioral results, at baseline borderline patients showed elevated negative behavioral responses to negative images compared to healthy controls, as expected. They did not however show the expected reduced efficacy in distancing at baseline. This could be because self-reports are subject to demand effects or because of the small sample size.

Our primary analyses interrogated pattern correspondence of whole-brain functional networks rather than univariate brain activity (19, 20). This approach allowed us to assess in an unbiased manner the full neural ensembles engaged in negative affect response and in reappraisal implementation. It alleviated the multiple testing problem in brain imaging analysis and targeted our analyses to hypothesis-driven questions concerning engagement of and longitudinal change in multivariate neural patterns associated in prior work with picture-induced negative affective experience (PINES; 19) as well as reappraisal implementation (13). Further, using the pattern correspondence approach for PINES also permitted the contribution of negatively-weighted regions (i.e., those predictive of experiencing less negative affect) including the bilateral

parahippocampal gyrus, right superior temporal gyrus, left temporal parietal junction, right caudate, somatomotor cortex, and occipital cortex (19). The PINES pattern expression provides a more robust correspondence with a validated brain basis for negative affect than interrogation of discrete a priori or a posteriori-defined ROIs alone, and thus may have greater sensitivity than focus on individual ROIs.

*Implications for the neural mechanisms of reappraisal training via distancing in borderline patients*

Our findings suggest that it may be possible to train borderline patients to enhance their utilization of cognitive reappraisal-by-distancing with a relatively time-limited intervention, as reflected in an improved ability to downregulate the brain ensemble that reacts to negative stimuli and in a response pattern more like that of healthy individuals. Interestingly, the training did not result in increased pattern expression of the reappraisal implementation network, which includes the bilateral dlPFC, vlPFC, posterior dmPFC and posterior parietal cortex. This result suggests that, with training, BPD individuals may achieve downregulation of the PINES network through changes in bottom-up reactivity (30), or by engaging a different regulatory network than the one characteristically employed by healthy individuals for reappraisal.

Behaviorally, we did not observe significant attenuation of self-reported negative affect during reappraisal trials in borderline patients following reappraisal training. While contrary to our hypothesis, it is in line with recent work showing that, in short-duration cognitive control training interventions, behavioral effects may be limited or absent, whereas physiological effects may be more robust, less susceptible to demand effects, and potentially more reliable (35, 36). Further a number of studies have demonstrated a

disconnect between the reported experience of borderline patients and their physiological responses (37 – 39).

#### *Limitations and Future Directions*

Limitations of the current study include the relatively short duration of reappraisal training, not having an independent training success measure, an absence of an association between self-reported affect and neural change over time, not being pre-registered, and a modest sample size. The fMRI task used to measure the training effect was the task used in the training process, albeit with different images. While this permitted a focused neural assessment of the training, it limits the generalizability of the finding of successful reappraisal training to other reappraisal scenarios and to real-world situations. Future work should be done to examine the extent to which training inside the lab may translate to affective changes outside of the lab, including decreased symptomatology and improved function in daily life. Future work should also examine the durability of reappraisal training effects in borderline patients beyond the conclusion of active training.

In summary, the present work examined the efficacy and neural mechanisms of a novel, relatively-brief emotion regulation training paradigm in borderline patients to enhance an emotion regulation tactic that is highly adaptive and widely used by healthy individuals. While the findings must be interpreted with caution because of modest, though significant, statistical effects and the absence of some predicted behavioral findings, the significant decrease in the whole-brain pattern signature reflective of negative affect after reappraisal training calls for further investigation of distancing training as an approach to enhance emotion regulation in borderline patients.

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### **Disclosures**

The authors report no biomedical financial interests or potential conflicts of interest.

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### Figure Captions

Figure 1. Trial structure.

Figure 2. Generation of PINES and Reappraisal Implementation Correspondence Scores (PCS and RCS, respectively). Whole-brain patterns for (A) negative affect from Chang et al. (PINES; 19) and (B) cognitive reappraisal from the meta-analysis of Buhle et al. (13) are (C) correlated with each participant's contrast map (trial type vs. baseline) to (D) produce one PCS and one RCS value per trial type per session per participant.

Figure 3. Change over time in negative affect reports by group, session, and trial type. \*\* reflects a significant between-group difference,  $p < 0.05$ , two-tailed. \* reflects  $p < .05$ , one-tailed. + reflects  $p < .10$ , one-tailed.

Figure 4. PINES Correspondence Score (PCS) change with training. \*\*\*\* reflects  $p < 0.001$ , two-tailed. \* reflects  $p < 0.05$ , one-tailed. + reflects  $p < 0.10$ , one-tailed. Error bars reflect standard error of the mean.

Figure 5. Reappraisal Correspondence Score (RCS) change with training. \*\*\*\* reflects  $p < 0.001$ , two-tailed. \*\*\* reflects  $p < 0.01$ , two-tailed. \*\* reflects  $p < 0.05$ , two-tailed. \* reflects  $p < .05$ , one-tailed. Error bars reflect standard error of the mean.

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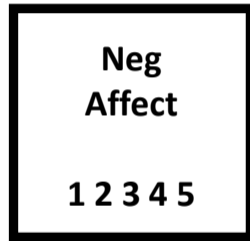
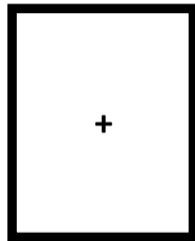
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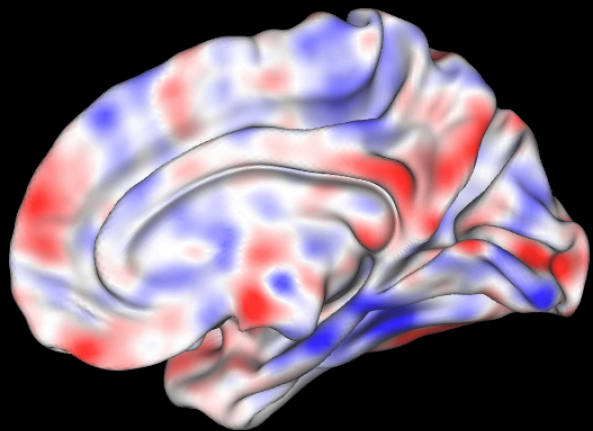
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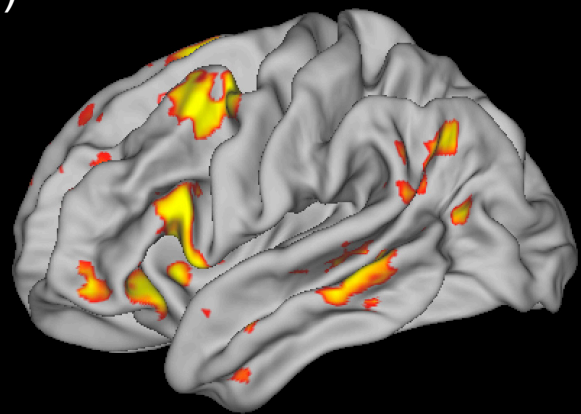
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**Cue****2 s****Neg or Neu Picture****10 s****Rating****4 s****ITI****3-5 s**

A)



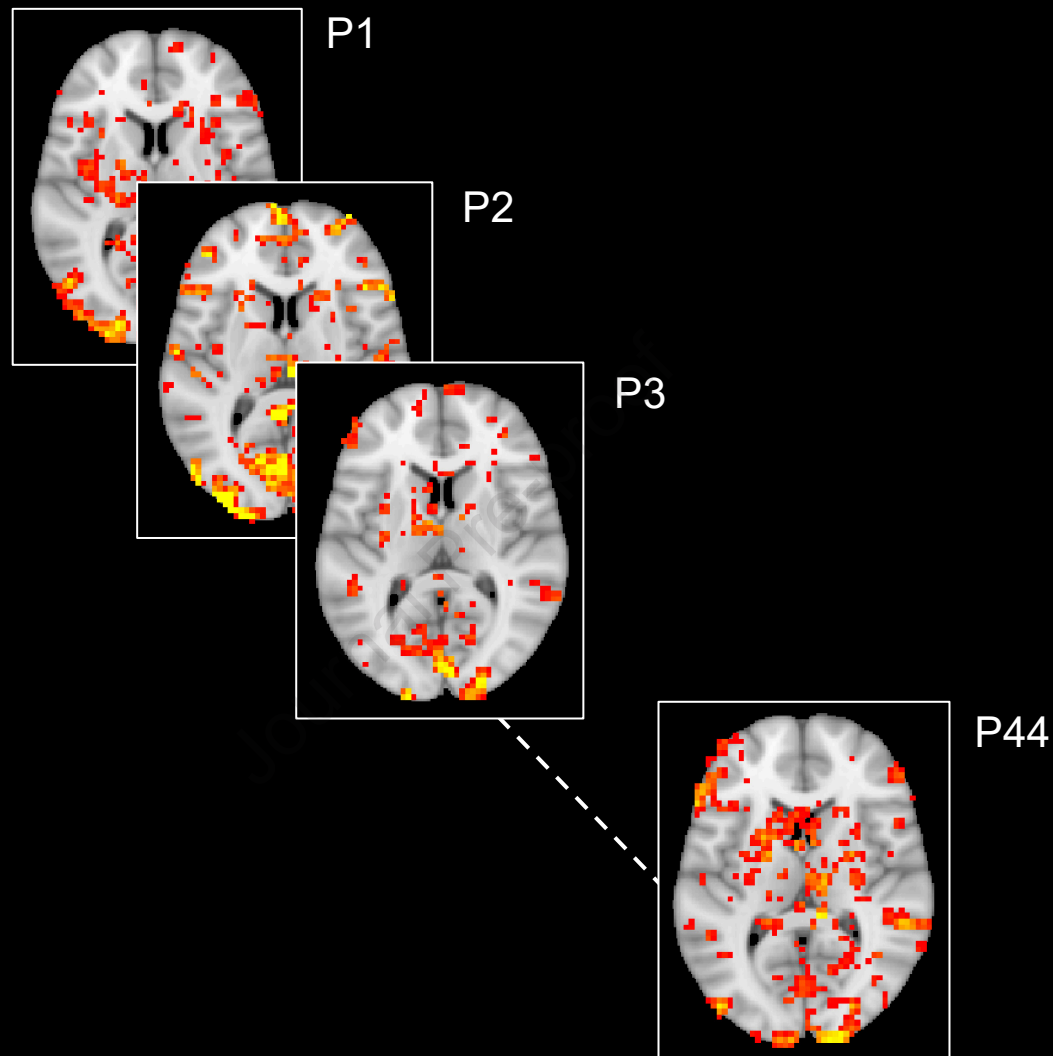
B)



Whole-brain patterns for negative affect (PINES; top) and cognitive reappraisal (bottom)

*Correlate with*

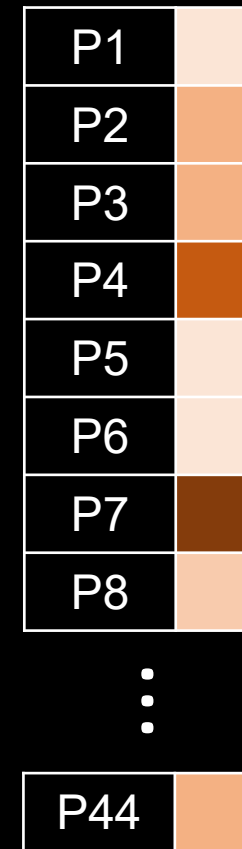
C)



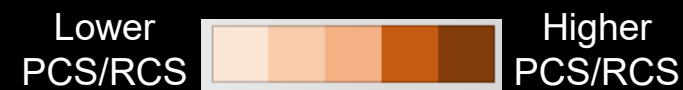
Each participant's contrast map (Trial Type vs. Baseline)

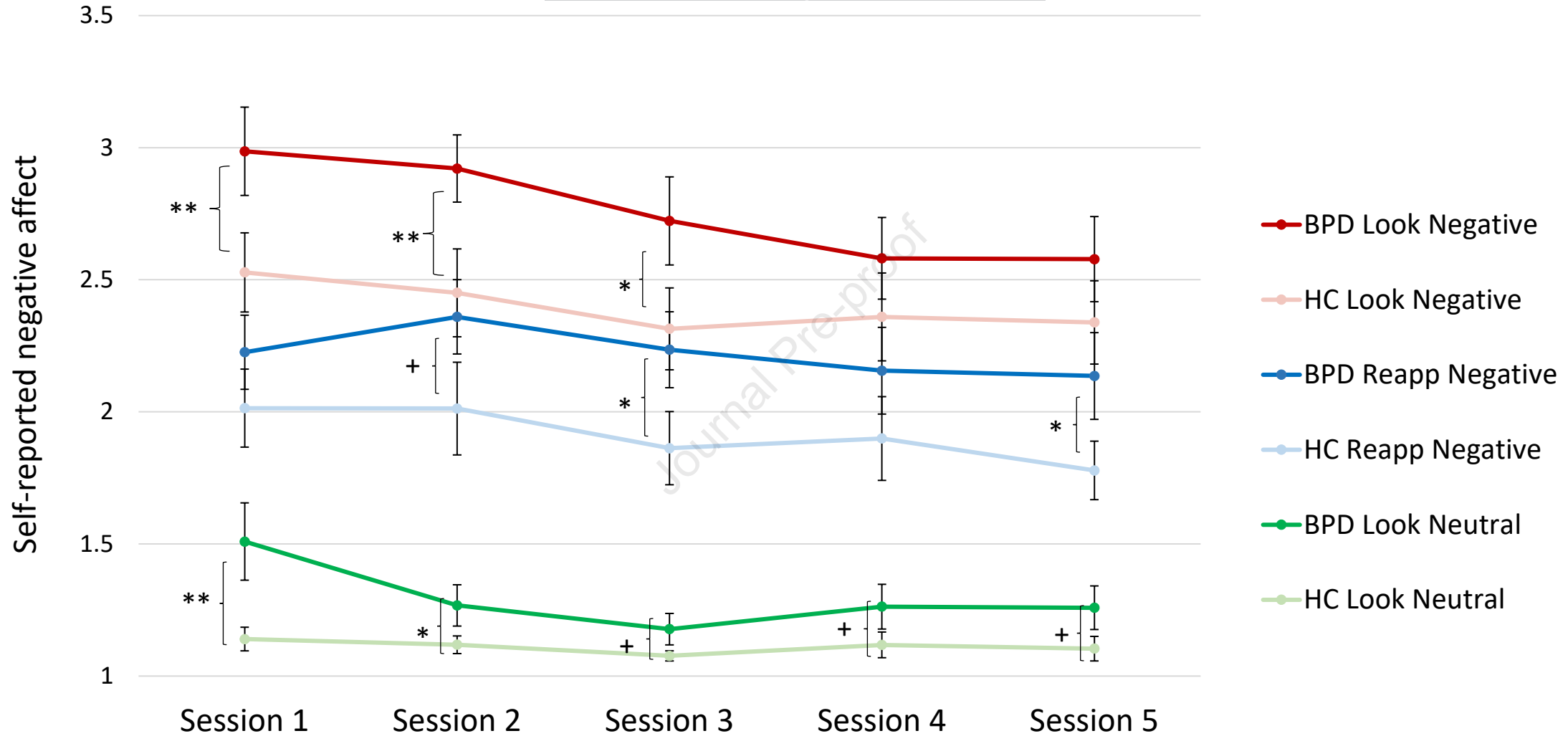
*Results in*

D)

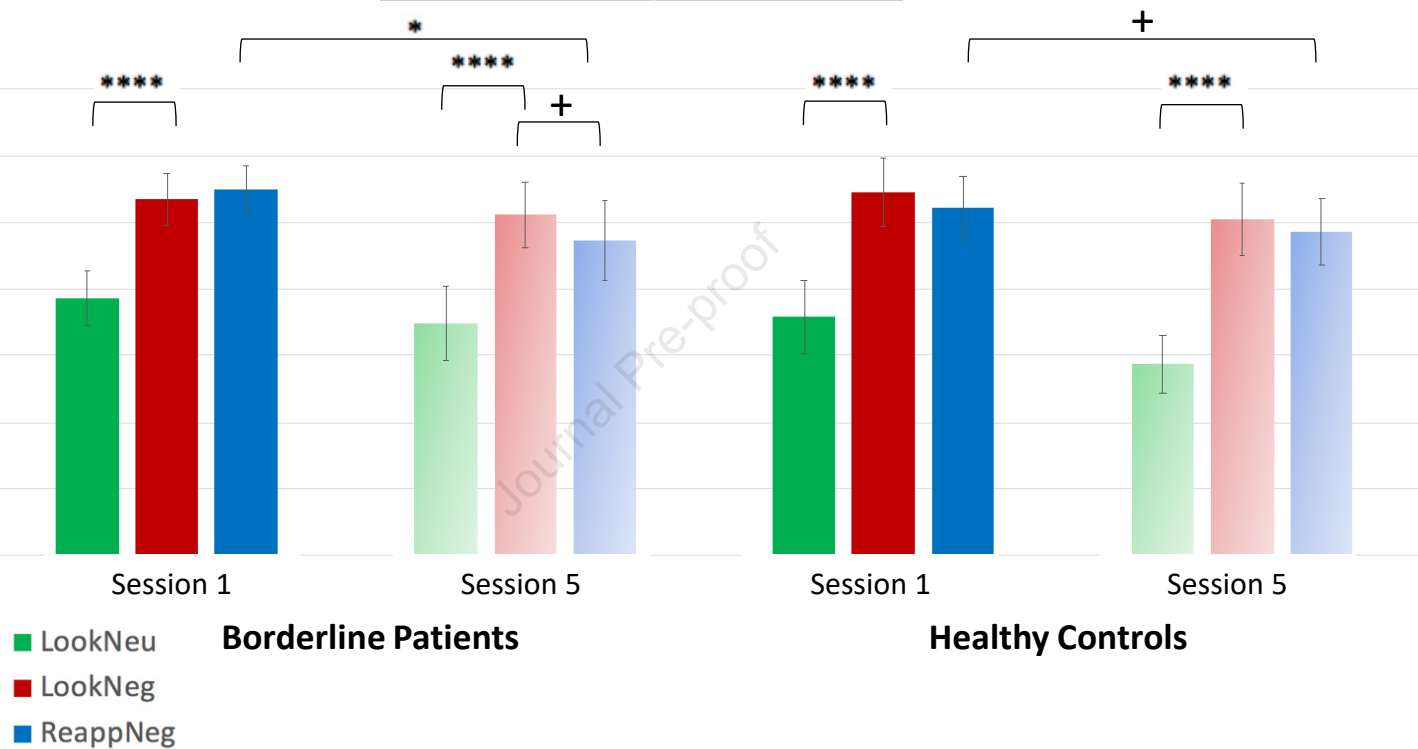


PINES and Reappraisal Correspondence Scores (PCS & RCS)



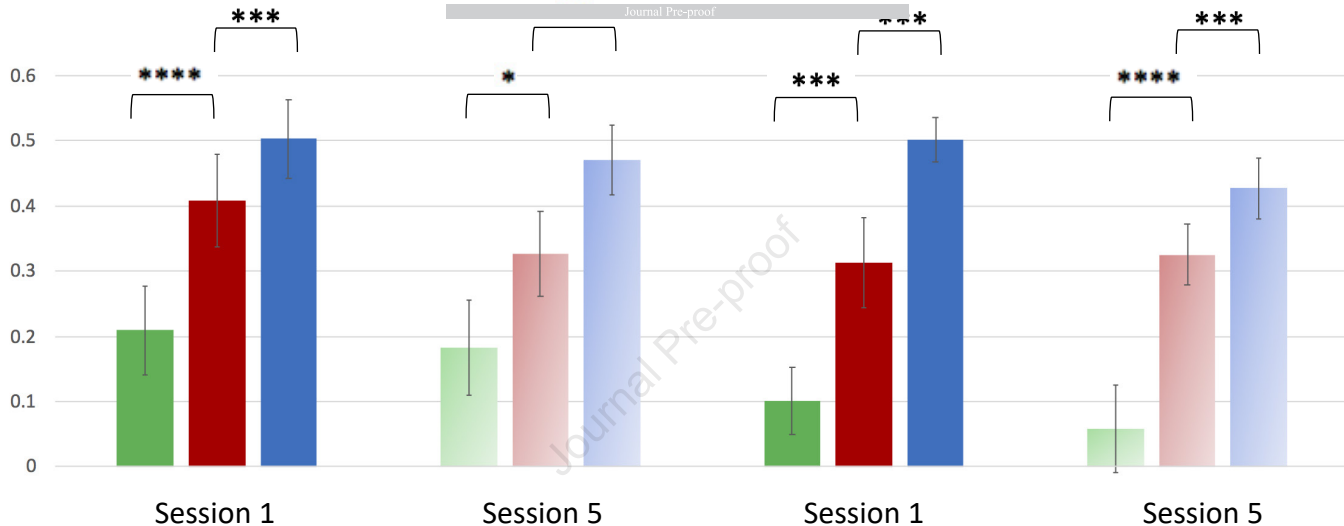


PINES Correspondence Score





Reappraisal Correspondence Score



Session 1

Session 5

Session 1

Session 5

**Borderline Patients**

**Healthy Controls**

- LookNeu
- LookNeg
- ReappNeg