Individual Differences in Cognitive Reappraisal Use and Emotion Regulatory Brain Function in Combat-Exposed Veterans with and without PTSD

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Key Words: Functional MRI; Brain imaging/Neuroimaging; Trauma; PTSD/Posttraumatic Stress Disorder; Biological markers

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Abstract

Background: Veterans with posttraumatic stress disorder (PTSD) exhibit marked deficits in emotion regulation. Past research has demonstrated under-engagement of the prefrontal cortex during regulation of negative affect in those with PTSD, but has been unable to find evidence of impaired down-regulation of the amygdala. One possibility is that there exists variability in amygdala reactivity that cuts across diagnostic status and which can be characterized using a continuous measure of individual differences. In healthy/non-traumatized volunteers, individual variability in amygdala engagement during emotion processing and regulation has been shown to relate to habitual use of regulation strategies. **Methods:** The current study examined whether self-reported use of cognitive reappraisal and expressive suppression regulation strategies correlated with brain activation during cognitive reappraisal in combat-exposed veterans with (n = 28) and without PTSD (combat-exposed controls, CEC; n = 20). **Results:** Results showed that greater self-reported use of cognitive reappraisal was associated with less activation in the right amygdala during volitional attempts to attenuate negative affect using reappraisal, irrespective of PTSD diagnosis. **Conclusions:** This finding is in line with prior work and extends evidence of an association between habitual use of regulation strategies and amygdala engagement during emotion regulation to a trauma-exposed sample of individuals both with and without PTSD. Furthermore, by providing evidence of individual differences in regulation-related amygdala response in a traumatized sample, this result may increase understanding of the neural mechanisms that support variability in symptom manifestation observed across individuals with PTSD.

1. Introduction

As many as 13% of veterans returning from Operations Enduring Freedom (OEF), Iraqi Freedom (OIF), and/or New Dawn (OND) have been diagnosed with PTSD[1], making it one of the most common injuries suffered as a result of military deployment.[2] Emotion dysregulation is considered a core deficit of PTSD,[3-6] which is also characterized by a heterogeneous array of other difficulties, including reoccurrence of traumatic memories, avoidance of trauma-related stimuli, negative changes in cognition and mood, and alterations in arousal and reactivity.[7] Work conducted in healthy individuals has shown that emotion regulation increases activation in the prefrontal cortex (PFC), and reduces activation in emotion-processing brain regions, such as the amygdala.[8,9] Relative to traumatized non-PTSD controls, individuals with PTSD engage PFC less during the regulation of negative affect.[10] Nonetheless, this work has failed to find evidence of group differences in reappraisal-related reductions in amygdala activity.[10,11] Given evidence that amygdala engagement during emotion regulation may be related to habitual (i.e., everyday) use of emotion regulation strategies[12-14], one possibility is that regulation-related change in amygdala activity in traumatized individuals can also be explained by a spectrum of individual differences in regulation use.

Cognitive reappraisal is an emotion regulation strategy in which individuals attempt to modulate the emotional salience of a stimulus by changing its meaning.[15] Increased use of cognitive reappraisal has been linked to physical and psychological well-being[16], and laboratory studies show that reappraisal reduces self-reported affective response to negative stimuli[17,18], as well as peripheral markers of emotional arousal.[18,19] Cognitive reappraisal also reduces amygdala activation[20-23] and increases PFC activation,[8,24] with decreases in amygdala responding inversely related to PFC engagement in some studies.[25] In contrast to cognitive reappraisal, expressive suppression is an emotion regulation strategy in which individuals attempt to inhibit outward displays of emotional response (e.g., facial expression).[15] Although suppression may have short-term benefits[26], it does not diminish

(and may even increase) physiological arousal[15,27], can have negative social

consequences[28] and is linked to poor physical and psychological health.[29] Further,

decreases in amygdala activation are not typically observed during expressive

suppression.[26,30]

Prior research that has investigated the neural correlates of reappraisal in individuals

with PTSD has yielded mixed results. For instance, New and colleagues[11] found that –

regardless of PTSD diagnosis – traumatized participants as a whole showed reduced lateral

PFC recruitment during reappraisal compared to non-traumatized controls.[11] On the other

hand, however, Rabinak and colleagues[10] found that, compared to combat-exposed controls

without PTSD, veterans with PTSD exhibited focal deficits in the dorsolateral prefrontal

cortex (dlPFC) during cognitive reappraisal.[10] Despite these differences in PFC engagement,

neither study found evidence of trauma or PTSD-related differences in modulation of

amygdala activity.[10,11]

This lack of group differences in amygdala activity during cognitive reappraisal is

consistent with findings from a broader body of research that has examined PTSD-related

aberrations in brain activation during emotion *processing* (e.g., using passive viewing

instead of emotion regulation tasks). For instance, some studies have found that individuals

with PTSD exhibit exaggerated amygdala response to negative images[3,31-33], negative

words[34], and emotional faces.[35,36] However, there is also evidence of hypo-engagement of

the amygdala during the viewing of negative imagery in traumatized individuals with and

without PTSD.[3,37,38] Finally, several studies have *failed* to find evidence of PTSD-related

differences in amygdala activation to negative stimuli.[3, 39-43]

An alternative approach towards conceptualizing amygdala response in those with

and without PTSD is to consider the existence of significant within-group variability in

amygdala reactivity that can be explained by individual difference measures. For instance,

greater use of cognitive reappraisal in daily life has been linked to diminished amygdala

responding during cognitive reappraisal (in individuals with remitted major depressive disorder MDD[14]), during the anticipation of negative stimuli (in MDD[12]) and during viewing of negative stimuli (in healthy individuals[13]). In addition, greater habitual use of cognitive reappraisal has been associated with increased PFC activation when inhibiting a behavioral response to sad faces (i.e., in the dlPFC[44]); during negative image processing (in the dlPFC, dorsomedial PFC (dmPFC) and orbitofrontal cortex (OFC)[13] and during fear extinction recall (in the ventromedial PFC (vmPFC)[45]). Greater habitual use of expressive suppression, on the other hand, has been associated with *reduced* OFC activation during anticipation of negative stimuli[46] and *increased* amygdala activation during response inhibition to sad faces.[44] Therefore, prior work suggests that greater use of cognitive reappraisal is related to neural functioning that sub-serves successful down-regulation of negative affect.[21] However, no study to date has examined whether such individual differences might also be evident in trauma-exposed individuals with and without PTSD, and whether a continuous measure of habitual emotion regulation might account for variability in amygdala responding that is not explained by diagnostic status alone.

To address this gap in the literature, the current study examined whether habitual use of cognitive reappraisal and expressive suppression were related to individual variability in amygdala response during reappraisal in combat-exposed veterans with and without PTSD. Based on prior work,[12-14] we hypothesized that greater habitual use of cognitive reappraisal would be associated with less amygdala activation during reappraisal in combat veterans with and without PTSD. Given prior reports that increased use of expressive suppression is positively associated with engagement of the amygdala during response inhibition to sad faces[44], we tested the relationship between brain activation during cognitive reappraisal and daily suppression use as well. However, owing to the fact that we did not utilize a suppression/inhibition task, we did not have specific predictions regarding this relationship. Main effects of task and group differences (PTSD, CEC) in subjective negative

affect ratings and BOLD activation during cognitive reappraisal can be found in prior published work.[10]

2. Materials and Methods

2.1. Participants

A total of 48 male OEF, OIF, and/or OND combat-exposed veterans with (n = 28) and without (Combat-exposed Controls, CEC; n = 20) PTSD were recruited at the Veterans Affairs (VA) Ann Arbor Healthcare System (Ann Arbor, MI). Inclusion criteria for all participants included discharge from active military service, aged 18-55 years, absence of head trauma that involved a loss of consciousness, free from psychoactive medication for at least four weeks prior to testing and negative urine drug screen at time of fMRI scanning, right-handedness, and ability to provide written consent. Exclusion criteria included the presence of a clinically-significant medical or neurologic illness, or life history of bipolar disorder, schizophrenia, or pervasive developmental disorder. Inclusion criteria for participants with PTSD were a primary diagnosis of PTSD, according to the Diagnostic and Statistical Manual of Mental disorders (DSM-IV) criteria and a score ≥ 40 on the Clinician-Administered PTSD Scale (CAPS[47]), reflecting moderate to severe PTSD symptoms[47]. Participants in the CEC group could not meet primary or subthreshold criteria for PTSD (i.e., they did not have any significant re-experiencing, avoidance, or hyperarousal symptoms) and could not have CAPS scores > 20. Exposure to combat was assessed using the Combat Exposure Scale (CES[48]), and all participants were required to meet a minimum level of combat-trauma related exposure (i.e., CES scores ≥ 17[48]) (see Table 1 for demographics and clinical composition of each group). All participants provided written informed consent for study participation and were monetarily compensated for their time as approved by the Institutional Review Boards of VA Ann Arbor and the University of Michigan Medical School.

2.2. Materials

Diagnostic criteria were assessed by one of two trained clinicians: (1) a board-certified research psychiatrist (KLP) or (2) a licensed social worker (AEK) using the Structured Clinical Interview for DSM Disorders (SCID[49]). In addition, all participants completed the Emotion Regulation Questionnaire (ERQ[50]) prior to scanning. The ERQ is a 10-item self-report measure developed by Gross and John,[50] which measures individual differences in the use of emotion regulation strategies - with a particular focus on use of cognitive reappraisal and expressive suppression (sample items include, "I control my emotions by changing the way I think about the situation I'm in" and "I keep my emotions to myself"). Responses are made on a 7-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree). The ERQ yields two orthogonal subscales: a six-item cognitive reappraisal factor (Cronbach's alpha = .79) and a four-item expressive suppression factor (Cronbach's alpha = .73).[50] Higher scores on a given subscale indicate a greater tendency to use that emotional regulation strategy.

2.3. fMRI acquisition and pre-processing

FMRI scanning was performed on a 3T GE Signa System (General Electric; Milwaukee, WI) using a standard radiofrequency coil at the University of Michigan Functional MRI Laboratory. Whole-brain functional images (i.e., blood oxygen level–dependent [BOLD]) were collected from 43 axial, 3-mm-thick slices using a T2*-sensitive gradient echo reverse spiral acquisition sequence (repetition time, 2,000 ms; echo time, 30 ms; 64 × 64 matrix; 220 mm field of view; flip angle, 90°), optimized to minimize susceptibility artifacts (signal loss) at the medial temporal lobe (including the amygdala).[51] The first 4 volumes from each run were discarded to allow magnetization to reach equilibrium.

Functional images were processed and analyzed using Statistical Parametric Mapping software (SPM8, Wellcome Trust Center for Neuroimaging, University College London, London, UK; www.fil.ion.ucl.ac.uk/spm). Images were temporally corrected to account for slice time acquisition differences and spatially realigned to the first image of the first run to correct for head movement; motion parameters were entered as regressors of no-interest to control for head movement during scanning. Images were normalized to a Montreal Neurological Institute (MNI) template using the echo-planar imaging (EPI) template, resampled to 2 mm^3 voxels and smoothed with an 8 mm isotropic Gaussian kernel.

2.4. ERT

Participants completed a block-design Emotion Regulation Task (ERT) during fMRI scanning. The ERT is a variant of a commonly used emotion regulation task[9,22] and has been used in prior studies of emotion regulation within our own laboratory.[10,25,52] In brief, participants were shown 64 negative and 32 neutral images from the International Affective Picture System (IAPS[53]) across three conditions (Look, Maintain, Reappraise). In the Look condition, participants were instructed to simply view neutral images. In the Maintain condition, participants were asked to view negative images without attempting to change their affective experience in any way (i.e., to experience the picture as they normally would). In the Reappraise condition, participants were instructed to view negative images and to attempt to decrease their affective response to these images by employing cognitive reappraisal. Prior to task execution, participants were trained in the technique of cognitive reappraisal. To reduce negative affect evoked by the pictures, participants were taught to either (1) conceptualize the depicted scenario in a less negative way (e.g., women crying outside of a church could be attending a wedding instead of a funeral); or (2) objectify the content of the pictures (e.g., a woman with facial bruises could be an actor in a movie). Following training, participants were shown five images not used in the actual task and

asked to practice using cognitive reappraisal while verbalizing their reappraisal strategies to a researcher, who provided feedback regarding use of these strategies. During task execution, participants were instructed to keep their eyes on the pictures at all times, which was confirmed by monitoring eye movement during scanning via an infrared camera mounted on the head-coil.

For each condition, there were two 20-s blocks per each of four runs (eight blocks in total), interspersed with 20-s blocks of a white fixation cross shown on a black background to enable the hemodynamic response to return to baseline. During baseline blocks, participants were instructed to "relax and clear your mind". Within each condition block, a total of four images were presented, each for 5-s without inter-stimulus interval. Block order was pseudo-randomized over the course of four separate runs, each lasting five minutes. Prior to each block, an instruction screen ("Look", "Maintain", or "Reappraise") was presented for 5-s. Following each block, participants viewed a screen that asked them to answer the question, "How negative to you feel?" Participants indicated their response on a 5-item Likert scale (1 = not at all; 5 = extremely) via a 5-button response using the dominant, right hand.

2.5. fMRI data analysis

At the first level, functional time series data were subjected to a general linear model, convolved with the canonical hemodynamic response function (HRF) and filtered with a 128 s high-pass filter. Box car regressors were used to model Look, Maintain, and Reappraise blocks with the main contrast of interest being Reappraise > Maintain representing regulated negative emotion processing. For completeness and to generate future hypotheses, we also examined and present results from the Maintain > Look contrast representing unregulated negative emotion processing. At the second level, one sample *t*-tests were used to regress ERQ Reappraisal and ERQ Suppression scores onto whole-brain activation for each contrast. Clusters of activation were identified using a whole-brain uncorrected voxel

threshold of $p < 0.001$ with at least 20 contiguous voxels per cluster, which allowed us to compare current findings to studies from others that have used similar significance thresholds[3,13] and which has been recommended as a balance between risk of Type I versus Type II error rates.[54] Moreover, for activation clusters falling within the amygdala, we corrected for multiple comparisons using Small Volume Correction (SVC) using a bilateral anatomically-defined mask derived from MAsks for Region of INterest Analysis (MARINA[55]). The focus of this analysis centered on results within bilateral amygdala as a region-of-interest (ROI); however, to obviate bias and in order to generate hypotheses for future research, complete whole-brain results at $p < 0.001$ with an 20 extant cluster threshold for both contrasts (e.g., Reappraise > Maintain and Maintain > Look) are reported in Tables 1 and 2, respectively. For significant effects, mean beta values from clusters were extracted using the MarsBaR Toolbox[56] to generate scatterplots for visual inspection, to clarify effects within each subgroup of our sample (i.e., PTSD, CEC) and generate Pearson product-moment correlations in Statistical Package for the Social Science (SPSS, Version 20.0).

Partial Pearson's product-moment correlations were run in SPSS to test the association between ERQ scores (Reappraisal, Suppression) and subjective ratings of negative affect collected during the ERT, controlling for age, years of education, and CES scores. Correlations were run using difference scores reflecting affect ratings for Maintain minus Reappraise trials (to mimic the contrast comparison used for fMRI data analysis).

3. Results

3.1. ERQ distribution

Scores from both ERQ Reappraisal and Suppression sub-scales were normally distributed (Shapiro-Wilk's test, p's > 0.44). The average ERQ Reappraisal score was 27.98 ± 7.11 and the average ERQ Suppression score was 17.50 ± 5.47. Between PTSD (27.04 ±

6.82) and CEC (29.30 ± 7.46) groups, there was no difference in the reporting of reappraisal use ($t(46) = 1.09$, $p > 0.28$). However, compared to controls (15.45 ± 5.69), those with PTSD (18.96 ± 4.90) reported using suppression to a greater extent ($t(46) = 2.29$, $p < .03$).

3.2. ERQ correlation with subjective ratings

No correlation was found between ERQ Reappraisal and Suppression scores and subjective negative affect during Reappraise > Maintain trials (all p's > 0.08).

3.3. Cognitive reappraisal and brain activation

ERQ reappraisal scores correlated negatively with Reappraise > Maintain activation in the right amygdala (peak MNI coordinate: 28, 2, -22; 432 mm^3; $Z = 3.98$; $p_{SVC} < 0.05$). This correlation remained when adding covariates age, years of education, and CES scores as regressors of no-interest (peak MNI coordinate: 28, 2, -22; 440 mm^3; $Z = 3.94$; $p_{SVC} < 0.05$). To determine if this relationship was driven by one or both sub-groups (PTSD, CEC), beta values were extracted and used in subsequent partial Pearson product-moment correlations. Significant correlations were evident for veterans with ($r(26) = - .44$, $p < 0.02$) and without ($r(18) = - .70$, $p < 0.01$) PTSD. In order to assess whether the strength of these correlations differed significantly between PTSD and CEC groups, correlation coefficients were first converted into z-scores using Fisher r-to-z transformation. Then, factoring in sample sizes for each group, z-scores were compared using formula 2.8.5 from Cohen and Cohen.[57,58] These correlations did not significantly differ between the groups ($p < 0.21$). Figure 1, Panel A depicts the spatial location of the negative correlation between ERQ Reappraisal scores and BOLD activation during Reappraise > Maintain. Figure 1, Panel B depicts the association between ERQ Reappraisal scores and activation in the right amygdala, such that high habitual use relates to negative beta values within the amygdala. Negative beta values

indicate amygdala activation is higher during Maintain trials than in Reappraise trials. Figure 1, Panel C depicts mean activation in the right amygdala during Reappraise > Maintain for individuals high versus low in ERQ Reappraisal scores (participants were categorized using a median split for visualization purposes only). Again, negative beta values for individuals with higher Reappraisal scores indicate that amygdala activation was greater during Maintain than Reappraise, suggesting reduced amygdala response during Reappraise (e.g., when task instruction was to decrease affective response).

To determine if this effect was driven by a correlation specific to the Reappraise or Maintain condition, given that the contrast reflected a comparison between Reappraise > Maintain trials, subsequent one sample t-tests were run in SPM regressing ERQ Reappraisal scores onto activation within Reappraise > Look and Maintain > Look contrasts. No significant correlations were observed in the amygdala for either contrast (p-value's > 0.001, uncorrected). Next, we used an analysis of covariance (ANCOVA) in SPM to determine whether a group difference would be evident in amygdala activation when controlling for ERQ Reappraisal scores. Reappraise > Maintain amygdala activation did not differ between the PTSD and CEC groups when controlling for ERQ Reappraisal scores (p-value > 0.001, uncorrected).

A complete list of regions that correlated with the ERQ are provided in Tables 1 and 2, listed separately for the Reappraise > Maintain and Maintain > Look contrasts, respectively. Correlations between ERQ Suppression scores and Reappraise > Maintain amygdala activation did not surpass our threshold for statistical significance.

4. Discussion

The current study examined the relationship between habitual use of emotion regulation strategies and amygdala response during cognitive reappraisal in trauma-exposed U.S. military veterans with and without PTSD. Results showed that habitual use of cognitive

reappraisal correlated negatively with differential activation in the right amygdala during cognitive reappraisal, irrespective of PTSD diagnosis and when controlling for age, years of education, and severity of combat exposure.

The results observed here are in line with prior work showing that, among individuals with remitted MDD, greater everyday use of reappraisal was associated with less amygdala activation during cognitive reappraisal.[14] More broadly, the results are also in line with findings showing that reappraisal use is related to amygdala responding during emotion processing (i.e., in healthy and depressed individuals viewing and anticipating negative imagery, respectively[12,13]). Here, findings suggest that individual differences in habitual use of cognitive reappraisal are predictive of amygdala activation during reappraisal in traumatized individuals, although controlling for variability in reappraisal use did not reveal group differences in amygdala engagement during reappraisal. Therefore, while we demonstrate that habitual use of reappraisal matters in predicting individual differences in neural response during regulation, more research is needed in order to isolate other factors that contribute to heterogeneity of amygdala response in this population. Additionally, it may be the case that traumatized individuals with versus without PTSD simply do not differ in amygdala engagement during cognitive reappraisal, even when controlling for individual differences that cut across diagnostic groups, although more research is needed in order to fully test this possibility. We note that while the correlation coefficients representing the strength of the relationship between daily reappraisal use and amygdala reduction during reappraisal appeared to differ between groups, we found that this difference was not significant. Nevertheless, this effect should be followed-up using larger samples sizes, which affords more power to detect group differences in this relationship should they exist.

From a broader perspective, the finding observed here is consistent with a growing body of work that has documented heterogeneity in amygdala response to negative stimuli in PTSD.[31-43] This heterogeneity may signal that not all individuals with PTSD are characterized

by hyper-responsivity to negative stimuli[59-67], in line with the notion that the disorder may consist of a number of distinct sub-types.[68]

Despite some evidence suggesting that individuals with PTSD show reduced PFC recruitment during reappraisal[10], they do not seem to exhibit deficits in the modulation of amygdala response when compared to traumatized controls.[10,11] Instead, greater experience with or an increased tendency to use reappraisal in everyday life may translate into improved ability to modulate amygdala responding, even for those exhibiting reduced recruitment of the PFC. Individual differences in reappraisal use may therefore signal alterations in the *effectiveness* of PFC engagement and/or the engagement of compensatory regions involved in the down-regulation of amygdala activity[8], though this hypothesis remains to be tested in future work.

Contrary to prior studies that found a relationship between reappraisal use and PFC engagement during tasks of emotion processing[13,44,45], we did not observe such a relationship during emotion regulation and within a traumatized sample. In previous work limited to a region-of-interest analysis focused on the dlPFC, Rabinak and colleagues[10] examined the relationship between reappraisal use and dlPFC activation and reported no evidence of a correlation between everyday use of reappraisal and engagement of this region across the sample[10], despite the fact that veterans with PTSD (as a group) under-engaged the dlPFC during cognitive reappraisal. Here, we extend these results to other regions of the PFC, finding that variability during cognitive reappraisal does not appear to map onto regulation use in traumatized individuals.

Additionally, we did not find evidence of a relationship between habitual use of expressive suppression and amygdala engagement in the present study, even though groups differed on daily use of expressive suppression. Prior work has found that expressive suppression use positively correlates with engagement of the amygdala during response inhibition to sad faces[44], although other studies have failed to find an effect when changes in

the amygdala were measured during cognitive reappraisal[13] and negative emotion anticipation.[12,46] Therefore, the relationship between suppression use and amygdala engagement may depend on task specificity, in that suppression use - which is an inhibitory emotion regulation strategy - may more closely relate to changes in amygdala responding when brain functioning is tested during suppression/inhibition. More research is needed on this topic as no study to-date has assessed whether suppression use is related to changes in amygdala engagement when individuals are asked to directly engage in this emotion regulation strategy.

We did not find evidence of a correlation between habitual reappraisal use and self-reported negative affect collected on-line during scanning. In line with these results, prior research also failed to find evidence of a correlation between reappraisal use and self-reported negative affect during fear conditioning[45] or self-reported success during response inhibition to sad faces.[44] Therefore, regular use of reappraisal seems to relate more to neural indices of affective processing during regulation (i.e., amygdala activity) than to an individual's subjective experience of negative affect. Future work may wish to explore whether subjective report of regulation *success* (i.e., rather than report of negative affect) aligns more closely with habitual reappraisal use.

Beyond findings within *a priori* ROIs (e.g., amygdala), the present study was also able to demonstrate a negative relationship between daily use of reappraisal and engagement within the medulla, culmen, precentral gyrus, and cuneus during cognitive reappraisal (Table 2). Prior work demonstrates that medullary neurons are involved in the initiation of a stress response to emotional triggers while lesions of this region suppress amygdala responding in rodents.[69] Therefore, the negative relationship to frequent reappraisal use and brain activation in the present study may be broadened to involve regions involved in stress responses that may, in turn, activate amygdala responding. Additionally, neuroimaging studies involving humans demonstrate increased engagement of the culmen[70,71] and cuneus[72] during the viewing of negative, compared to neutral, images.

Engagement of the culmen occurs during predictive motor responses (e.g., when participants anticipate a future event that requires visuo-motor coordination[73]) and while no behavioral response was required in the present study, the initiation of subtle motor responses may occur during the viewing of negative imagery with these responses dampened during reappraisal.[74] This line of thinking is supported by the fact that we also observed a negative correlation between reappraisal use and engagement of the left precentral gyrus[75,76], a region involved in voluntary movement.[77] Finally, while the cuneus is typically associated with visual processing[72], activation also occurs during the experience of pain.[78] Therefore, greater reappraisal use may also be associated with decreases in more than one aspect of a negative affect experience. Altogether, these results are in-line with the notion that frequent reappraisal use relates to diminished negative emotion responding, but demonstrate that this relationship is not specific to functioning of the amygdala.

Results of the current study should be viewed in light of several limitations. First, the sample was comprised of only male veterans and thus limits generalizability to civilians, non-combat traumas, and females, which may be relevant given prior evidence of sex differences in brain functioning during emotion processing[79] (but see[13]). Second, it is difficult to know whether the results observed here are specific to traumatized individuals, given the lack of a non-traumatized control group. Third, the ERQ was used as a single predictor of brain functioning during emotion regulation. While prior work documents the validity of the ERQ as a measure of habitual use of emotion regulation[50], future research might benefit from measuring additional dimensions of emotion regulation capacity apart from self-reported use. For instance, future work may wish to determine whether relationships between habitual use of cognitive reappraisal and brain activation change when more objective measures of regulation success are taken into account – perhaps via the inclusion of peripheral physiological markers of arousal response. Fourth, the current study did not utilize trauma-specific images; therefore, the relationship between regulation use and amygdala

modulation when negative imagery is more central to an individual's trauma remains to be tested.

5. Conclusion

Despite these limitations, the current study extends prior research documenting a relationship between habitual use of reappraisal and amygdala engagement to a traumatized sample. Moreover, the results provide added evidence of variability of amygdala response in traumatized samples that can be explained by regulation use. This study also offers unique perspective on the neurobiological underpinnings of emotion dysregulation in PTSD. That is, by demonstrating heterogeneity in amygdala response during emotion regulation, we show that not all individuals with PTSD exhibit deficiency in the *capacity* for emotion regulation, when measured at the neural level. In this regard, this study may ultimately help increase understanding of the neural mechanisms that support variability in symptom manifestation observed across individuals with PTSD.

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Table 1.

Sample Demographics

	CEC (*n* = 20)	PTSD (*n* = 28)		
	M (SD)	*M (SD)*	*test statistic*	*p*
Age	35.10 (9.70)	29.86 (7.02)	2.06	0.05
Years of Education	15.55 (1.73)	13.25 (1.48)	4.94	< 0.001
CES	20.95 (5.22)	25.32 (6.31)	2.54	0.02
ERQ				
Reappraisal	29.30 (7.46)	27.04 (6.82)	1.09	0.28
Suppression	15.45 (5.69)	18.96 (4.90)	2.29	0.03
CAPS	5.20 (5.54)	68.43 (12.98)	23.01	< 0.001
Intrusive	0.00 (0.00)	2.93 (1.15)	13.45	< 0.001
Avoidance	0.25 (0.55)	4.29 (1.01)	17.73	< 0.001
Hyperarousal	0.25 (0.44)	4.36 (0.68)	25.32	< 0.001
	n (%)	*n (%)*		
Race (Caucasian)	18 (90.00%)	27 (96.43%)	1.51	0.47

Note. CEC = combat exposed controls; PTSD = posttraumatic stress disorder; CES = Combat Exposure Scale; ERQ = Emotion Regulation Questionnaire; CAPS = Clinician Administered PTSD Scale. Group comparisons were performed using independent *t*-tests except for race, which was calculated using a Pearson chi-square.

Table 2.

Whole-brain ERQ correlations for Reappraise > Maintain Contrast

ERQ Sub-Scale	Brain region	Laterality	Volume (mm^3)	Z-score	peak MNI Coordinates x	y	z
Positive Correlation							
ERQ Reappraisal	*No significant clusters*						
ERQ Suppression	*No significant clusters*						
Negative Correlation							
ERQ Reappraisal	Medulla	Midline	368	4.24	0	-38	-46
	Amygdala	*R*	*824*	*3.94*	*28*	*2*	*-22*
	Culmen	L	288	3.77	-10	-42	-20
	Precentral gyrus	L	1,016	3.71	-46	-16	28
		L	536	3.68	-46	-14	60
	Cuneus	L	208	3.70	-6	-94	36
ERQ Suppression	*No significant clusters*						

Note. Display whole-brain threshold was *p* < 0.001, uncorrected with an extant threshold of 20 voxels. **Bold italics** reflect that the amygdala cluster finding was an *a priori* region-of-interest and significance reached p_{SVC} < 0.05. Results control for age, years of education, and CES scores. ERQ = Emotion Regulation Questionnaire; CES = Combat-Exposure Scale; R = right; L = left.

Table 3.

Whole-brain ERQ correlations for Maintain > Look Contrast

ERQ Sub-Scale	Brain region	Laterality	Volume (mm³)	Z-score	peak MNI Coordinates x	y	z
Positive Correlation							
ERQ Reappraisal	Middle frontal gyrus	R	328	3.87	24	22	50
	Parahippocampal gyrus	R	296	3.80	16	-10	-24
		R	304	3.55	20	-26	-12
	Angular gyrus	R	736	3.76	40	-68	38
	Insula	L	576	3.63	-30	-24	22
	Precuneus	R	504	3.46	20	-56	48
	Supramarginal gyrus	L	208	3.45	-42	-54	32
ERQ Suppression	Superior temporal gyrus	L	288	4.07	-30	12	-30
		L	208	3.40	-64	-38	6
	Uncus	R	768	3.96	16	4	-26
	Precuneus	R	232	3.52	14	-68	50
	Middle temporal gyrus	R	224	3.44	56	-40	-16
Negative Correlation							
ERQ Reappraisal	*No significant clusters*						
ERQ Suppression	vmPFC	L	960	3.79	-4	52	12

Note. Display whole-brain threshold threshold was p < .001, uncorrected with an extant threshold of 20 voxels. Results control for age, years of education, and CES scores. ERQ = Emotion Regulation Questionnaire; CES = combat-exposure scale; vmPFC = ventromedial prefrontal cortex; R = right; L = left.

Figure Legend

Figure 1. (A) Location of the negative correlation between ERQ Reappraisal scores and activation in right amygdala during Reappraise > Maintain cluster around peak Montreal Neurological Institute (MNI) coordinates (26, 0, -18), controlling for age, years of education, and CES scores. Display threshold is $p < 0.001$ (whole-brain uncorrected). (B) Scatterplot of ERQ Reappraisal scores and contrast values extracted from the right amygdala cluster, organized by group (PTSD, CEC). (C) Activation in right amygdala cluster during Reappraise>Maintain by median-split of ERQ Reappraisal scores, representing both Low and High Reappraisers (median-split for illustrative purposes only; error bars reflect ± 1 standard error). ERQ = Emotion Regulation Questionnaire; PTSD = posttraumatic stress disorder; CEC = combat-exposed controls; CES = Combat Exposure Scale.