

A psychophysiological investigation of emotion regulation in chronic severe posttraumatic stress disorder

STEVEN H. WOODWARD,^a ASHLEY A. SHURICK,^b JENNIFER ALVAREZ,^c JANICE KUO,^d
 YULIANA NONYIEVA,^e JENS BLECHERT,^f KATERI McRAE,^g AND JAMES J. GROSS^b

^aNational Center for PTSD, Dissemination and Training Division, VA Palo Alto Health Care System, Palo Alto, California, USA

^bDepartment of Psychology, Stanford University, Stanford, California, USA

^cTrauma Recovery Programs, VA Palo Alto Health Care System, Palo Alto, California, USA

^dPsychology Department, Ryerson University, Toronto, Ontario, Canada

^ePalo Alto University, Palo Alto, California, USA

^fDivision of Clinical Psychology, Psychotherapy, and Health Psychology, Department of Psychology, University of Salzburg, Salzburg, Austria

^gDepartment of Psychology, University of Denver, Denver, Colorado, USA

Abstract

There have been few direct examinations of the volitional control of emotional responses to provocative stimuli in PTSD. To address this gap, an emotion regulation task was administered to 27 Operation Enduring Freedom/Operation Iraqi Freedom combat veterans and 23 healthy controls. Neutral and aversive photographs were presented to participants who did or did not employ emotion regulation strategies. Objective indices included corrugator electromyogram, the late positive potential, and the electrocardiogram. On uninstructed trials, participants with PTSD exhibited blunted cardiac reactivity rather than the exaggerated cardioacceleratory responses seen in trauma cue reactivity studies. On interleaved regulation trials, no measure evidenced group differences in voluntary emotion regulation. Persons with PTSD may not differ from normals in their capacity to voluntarily regulate normative emotional responses to provocative stimuli in the laboratory, though they may nevertheless respond differentially on uninstructed trials and endorse symptoms of dyscontrol pathognomonic of the disorder outside of the laboratory.

Descriptors: Stress, Traumatic, Emotion, Heart rate, Electromyogram, Late positive potential

Posttraumatic stress disorder (PTSD) is a prevalent psychiatric illness often associated with significant functional impairments (Keane, Marshall, & Taft, 2006). Exaggerated reactivity to trauma reminders has been extensively documented in PTSD (Blanchard, 1990; Orr, Pitman, Lasko, & Herz, 1993; Pitman, Orr, Foa, de Jong, & Claiborn, 1987; Pole, 2007), and the extinction of such responses has been the primary target of established treatments informed by learning theory (Foa, 2006; Rothbaum & Davis, 2003). Recently, a broadened approach to the disorder has emerged driven in part by neuroimaging studies demonstrating compromise of forebrain regions such as anterior cingulate cortex, which are thought to subserve a more general construct, emotion regulation, not limited to regulation of the amygdala (Bremner, 2002; Bryant et al., 2005; Etkin & Wager, 2007; Hayes, Hayes, & Mikedis, 2012; Liberzon & Martis, 2006; Pitman, Shin, & Rauch, 2001;

Woodward et al., 2006). There is also now ample evidence that persons diagnosed with PTSD exhibit exaggerated amygdala responses not only to trauma reminders but also to generic aversive stimuli such as fearful faces (Bryant et al., 2007, 2008; Felmingham et al., 2010; Rauch et al., 2000; Shin et al., 2005; Williams et al., 2006). Clinicians have responded by designing interventions intended to enhance emotion regulation in PTSD, advancing them as adjuncts or even alternatives to existing treatments (Bryant et al., 2013; Cloitre et al., 2011).

A comprehensive “process model” of emotion regulation has been offered which distinguishes five subcomponents: situation selection, situation modification, attentional deployment, cognitive change, and response modulation (Gross, 1998; Gross & Thompson, 2007). A subset of these components can be executed during or immediately following the presentation of a provocative stimulus and so are especially amenable to laboratory study. The proposition that, in healthy persons, executing strategies to acutely modulate emotional responses to provocative stimuli enlists frontal cortex to regulate the amygdala, first reported by Ochsner et al. (2002), is now supported by a large number of studies using fMRI (reviewed in Ochsner & Gross, 2005; Ochsner, Silvers, & Buhle, 2012) and multiple meta-analyses (Buhle et al., 2014; Diekhof, Geier, Falkai, & Gruber, 2011; Kalisch, 2009).

Despite the vigor of this research area, and its transdiagnostic applicability to multiple psychiatric disorders (Gross & Munoz,

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Address correspondence to: Steven H. Woodward, Ph.D., NCPTSD, VA Palo Alto HCS, 3801 Miranda Ave., Palo Alto, CA 94304, USA. E-mail: Steve.woodward@va.gov

1995), the fMRI/emotion modulation paradigm has been employed only rarely in clinical samples. To date, the strongest support for its translatability is found in social phobia (Goldin & Gross, 2010; Goldin, Manber et al., 2009; Goldin, Manber-Ball et al., 2009; Jazaieri, Goldin, Werner, Ziv, & Gross, 2012), and secondarily in major depression (Greening, Osuch, Williamson, & Mitchell, 2014; Heller et al., 2013). Only one study has included persons with panic disorder (Ball, Ramsawh, Campbell-Sills, Paulus, & Stein, 2013), even though acute dysregulatory episodes are the lead criterion of that diagnosis. PTSD would appear to be a natural focus of this work insofar as it is characterized by (a) compromise of many of the same frontal cortical regions as those implicated in emotion regulation, (b) exaggerated amygdala responses to aversive stimuli, and (c) maladaptive dysregulation of emotion and mood.

Two refereed studies have assessed voluntary emotion regulation in PTSD using functional neuroimaging. New et al. (2009) used an event-related design to assess blood oxygen level-dependent (BOLD) responses to generic aversive and neutral photographic stimuli in female sexual assault survivors and controls. They reported that participants were instructed to “imagine a less negative outcome.” Assault survivors with PTSD were found to be less able than nontraumatized controls to reduce subjective negative affect by following this instruction, and to exhibit less activation of cortical regions thought to be involved in emotion regulation (i.e., dorsolateral prefrontal cortex, dlPFC); however, a similar pattern of results characterized assault survivors without PTSD. As well, though the instructions reduced amygdala activation, they did so comparably across all three groups. Rabinak et al. (2014) used a blocked design to elicit BOLD responses to generic aversive photographs in U.S. military veterans of Operation Iraqi Freedom and Operation Enduring Freedom (OIF/OEF) with and without PTSD that were closely matched on combat exposure. Participants without PTSD again exhibited more activation of (left hemisphere) dlPFC during “diminish” blocks when instructed to reduce responses to aversive stimuli than those with PTSD; however, neither group demonstrated reduced subjective negative affect or reduced amygdala activation during diminish blocks. In sum, these first studies of emotion regulation in PTSD using fMRI/emotion modulation paradigms have shown little agreement with studies in healthy samples. Though the PTSD samples in both of the above studies exhibited reduced dlPFC activation relative to controls during emotion regulation, this reduction did not consistently distinguish patients from controls, or correlate with decreases in negative emotion or amygdala activation.

This paper reports the first psychophysiological study of voluntary emotion regulation in PTSD using a paradigm similar to those used in many fMRI studies. Studies employing psychophysiological methods have played a major role in developing our understanding of PTSD (Orr & Roth, 2000; Pitman, Orr, & Steketee, 1989; Pitman et al., 2012; Pole, 2007), and can complement fMRI studies in domains of temporal resolution, cost, sample bias, and disseminability. This study compared U.S. military OEF/OIF veterans diagnosed with PTSD and engaged in inpatient treatment for PTSD to healthy nontraumatized controls. Aversive photographs, including some with trauma-related content, and neutral photographs were shown to participants in an unblocked pseudorandom order. Following cues presented at picture onset, participants executed one of two emotion regulation strategies or “responded freely.” The two strategies were a cognitive reappraisal or rationalize strategy, or a notice strategy derived from the acceptance-based psychotherapies (cf. Hayes, Follette, & Linehan, 2011; Kabat-Zinn, 1990).

The consequences of emotion regulation were indexed via subjective negative affect, corrugator electromyogram (EMG), and the late positive potential (LPP) of the scalp EEG. The corrugator is a “frown” muscle whose activity increases concurrently with negative affect and decreases with positive affect (Cacioppo, Petty, Losch, & Kim, 1986; Larsen, Norris, & Cacioppo, 2003). It responds analogously to photographs varying in valence (Lang, Greenwald, Bradley, & Hamm, 1993). A recent combined fMRI/psychophysiological study by Heller, Lapate, Mayer, and Davidson (2014) found that, in normals, corrugator EMG covaried on a trial-by-trial basis with amygdala activation. A number of studies have now observed reduced corrugator EMG activity when healthy participants voluntarily decreased negative affect induced by neutral and negative pictures (Bernat, Cadwallader, Seo, Vizueta, & Patrick, 2011; Lee, Shackman, Jackson, & Davidson, 2009; Ray, McRae, Ochsner, & Gross, 2010). Wolgast, Lundh, and Viborg (2011) observed reduced corrugator EMG activity in both reappraise and accept conditions in a study presenting provocative film clips to healthy controls. In the first study to examine effects of emotion regulation on corrugator EMG in a psychiatric (schizophrenic) sample, Perry, Henry, Nangle, and Grisham (2012) found no overall effect of regulation and no differences among reappraisal, suppression, and acceptance strategies.

The LPP is an ERP characterized by a relatively late (~ 500 ms) positive deflection of the time-locked EEG average maximal over central and posterior vertex scalp sites. It overlaps but is later than the P300, is modulated by the arousal levels of visual stimuli, and is especially large following aversive visual stimuli (Hajcak, MacNamara, & Olvet, 2010; Schupp, Flaisch, Stockburger, & Junghofer, 2006). Combined fMRI/electrophysiological studies have associated the LPP with activation of a network including occipital, inferotemporal, and prefrontal cortices and amygdala (Liu, Huang, McGinnis-Deweese, Keil, & Ding, 2012; Sabatinelli, Lang, Keil, & Bradley, 2007). Reappraisal-related LPP amplitude reduction has been demonstrated in healthy samples (Hajcak & Nieuwenhuis, 2006; Moser, Hajcak, Bukay, & Simons, 2006; Moser, Krompinger, Dietz, & Simons, 2009). To our knowledge, this is the first test of modulation of the LPP by emotion regulation in an adult psychiatric sample. Using magnetoencephalography, Pietrek, Popov, Steffen, Miller, & Rockstroh (2012) elicited a neuromagnetic event overlapping the time course of the LPP which exhibited, in controls, lateralized modulation by valence/arousal during passive viewing of International Affective Picture System (IAPS) photographs (Lang, Bradley, & Cuthbert, 1999) and by cognitive reappraisal to diminish negative affect. The first effect emerged 300–600 ms poststimulus, and the second, 600–1,000 ms poststimulus. Modulation by stimulus aversiveness was normal in participants diagnosed with major depression, borderline personality disorder, or both; but modulation by cognitive reappraisal was absent, especially when these diagnoses were compounded by early life stress. Depressive and borderline participants did not differ.

Inter-beat interval (IBI) has not exhibited responsivity to nonsuppressive emotion regulation strategies (Bernat et al., 2011; Gross, 1998); however, IBI has distinguished persons with PTSD from controls in numerous studies assessing passive responses to trauma reminders (Pole, 2007); hence, its inclusion is expected to provide a useful psychophysiological context in which to interpret effects of regulation.

Based upon evidence available when the study was designed, PTSD participants were predicted to demonstrate less attenuation of negative affect, EMG, and LPP than controls when instructed to

regulate their emotional responses to aversive slides. It was also predicted that the notice strategy would exhibit enhanced efficacy in PTSD because it does not rely on the rapid generation of an interpretive narrative (cf. Matsuo et al., 2003; Wild & Gur, 2008). On uninstructed trials, participants meeting criteria for PTSD were expected to exhibit relative increases in negative affect, corrugator EMG activity, LPP amplitude, and heart rate in response to aversive stimuli relative to controls.

Method

Participants

Participants provided written informed consent to undergo the following experimental procedures approved by the Stanford/VA Palo Alto HCS Institutional Review Board. Screening exclusion criteria were current medical illness, history of head injury inducing loss of consciousness longer than 30 min, current substance abuse/dependence, psychotic disorder, mania, current medication on benzodiazepines, beta blockers, antipsychotics, blood thinners, thyroid hormone influencing agents, diabetic medications, or anticonvulsants. Inclusion criteria were male gender, age between 19 and 46 years, and right-handedness. Participants underwent structured interviews using the Structured Clinical Interview for the DSM-IV (SCID) and the Clinician-Administered PTSD Scale (CAPS). The original sample included 29 OEF/OIF combat veterans recruited from among inpatients of the Men's Trauma Recovery Program at the VA Palo Alto Health Care System and 25 age-matched healthy controls recruited via advertisements on craigslist (an online advertising service). PTSD-positive participants met criteria for current PTSD related to traumas sustained during their military deployments in Iraq and/or Afghanistan. Seventy-one percent of the PTSD participants also met DSM-IV criteria for major depressive disorder (MDD) or mood disorder NOS (not otherwise specified); 71% met criteria for alcohol dependence; 64% met criteria for dependence on at least one nonalcohol substance. Fifty-seven percent of the PTSD participants were prescribed a sedative/hypnotic, 50% an antidepressant, 11% a mood stabilizer, 11% an opiate receptor blocker, and 4% an atypical antipsychotic. Healthy controls were free of PTSD, lifetime, and endorsed few or no PTSD Category A qualifying events. Healthy controls were also free of current or recurrent major depression, panic disorder, agoraphobia, social phobia, simple phobia, or obsessive-compulsive disorder. A single past episode of MDD without recurrence was admissible. No healthy controls were taking psychotropic medication.

Two participants (one PTSD, one healthy control) were identified as cardiac response outliers and one (PTSD) as a movement outlier and excluded. (Outlier status was triggered when more than 30% of change scores across all conditions and time intervals were outside the envelope defined by two sample standard deviations above and below the sample mean of corresponding values. Movement response outliers were excluded from this sample to create equivalent samples across this report and a companion paper.) One additional control was lost due to a recording failure. The final sample included 27 PTSD participants and 23 healthy controls. Additional sample characteristics are presented in Table 1.

Procedure

Participants underwent the application of electrodes for recording of corrugator EMG, EEG (Cz and Pz referenced to linked mas-

Table 1. Psychometrics

	Healthy controls		PTSD		<i>t</i>	<i>p</i>
	Mean	<i>SD</i>	Mean	<i>SD</i>		
Age	27.5	6.6	29.5	5.8	1.15	.26
BDI	2.3	3.0	29.4	15.0	7.1	< .001
BAI	1.8	2.1	21.0	12.5	6.1	< .001
CES			30.8	6.9		
CAPS total			81.0	13.0		

Note. Psychometrics characterizing the PTSD and healthy control participants. BDI = Beck Depression Inventory-II; BAI = Beck Anxiety Inventory; CES = Combat Exposure Scale; CAPS total = CAPS Total Severity Score.

toids), and electrocardiogram (ECG). Participants were seated approximately 36 inches (91.4 cm) from the 19-inch (48.4 cm) computer monitor upon which images were displayed. A small table was located so that the participant's right hand rested on a keyboard that they used to respond to posttrial queries. Approximate durations of session components were sensor application, 60 min; instructions, 25 min; stimulus presentation, 35 min; sensor removal, 15 min; postsession web-based questionnaires, 40 min. Participants were continuously video recorded.

Stimuli, Trials, and Blocks

The experimental design is summarized in Figure 1. Photographs containing aversive or neutral content were presented for 10 s each. Aversive stimuli included 48 photographs containing Iraq and Afghanistan conflict-related content. In light of the recency of combat trauma and the severity of current PTSD in the veteran subsample, the OEF/OIF-related images were only moderately explicit in their military content, with one half containing only tangential content (e.g., American flag burnings, anti-American protests). An additional 24 negative and 24 neutral photographs were chosen from the IAPS.¹ Each photograph was preceded by a 2-s fixation cross followed by the appearance of a colored frame at the borders of the screen. The color of the frame cued the participant to regulate their emotional response to the subsequent photograph using the rationalize strategy (blue), the notice strategy (purple), or instead to respond freely (green). On rationalize trials, participants were instructed to "think of something to tell yourself that helps you feel less negative about the photo." On notice trials, participants were instructed to "... notice your beating heart and your angry or fearful thoughts, and do not resist these reactions in any way ... let the emotion flow over you like a wave." After the colored frame was presented for 2 s, the stimulus photograph appeared within it, the frame remaining in place for the duration of the photograph. Each trial was followed by a response-terminated period during which participants answered the question, "How negative do you feel?" using a scale of 1 to 9 with text anchors at 1 (*not at all*), 5 (*somewhat*), and 9 (*very much*).

1. IAPS aversive: 1300, 2053, 3030, 3051, 3100, 3102, 3110, 3120, 3140, 3170, 3180, 3350, 6360, 6550, 8230, 9240, 9250, 9140, 9300, 9410, 9571, 9800, 9810, 9921; mean valence: 2.07; *SD*: 0.50; mean arousal: 6.29; *SD*: 0.56. IAPS neutral: 2560, 5250, 5533, 5700, 5731, 5800, 5992, 6150, 7080, 7092, 7100, 7140, 7170, 7207, 7233, 7284, 7286, 7500, 7550, 7820, 7830, 8250, 8280, 8300; mean valence: 5.78; *SD*: 0.70; mean arousal: 3.72; *SD*: 1.02.

Design Summary

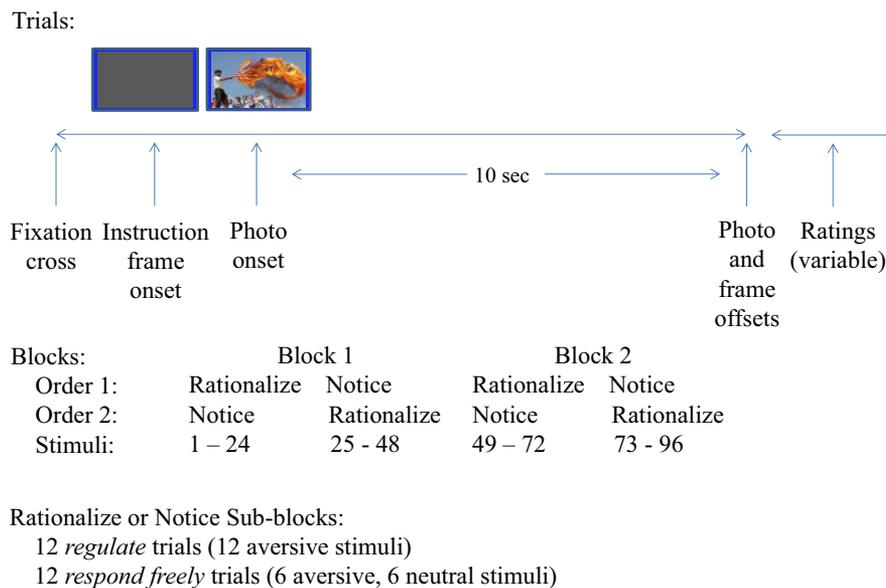


Figure 1. Design summary presenting trial structure, block/strategy counterbalancing across replicate blocks, and subblock trial composition.

Verbal instructions were followed by two self-paced, eight-trial, practice series, one for each emotion regulation strategy. The first four trials of each series were experimenter guided; the second four were performed with the experimenter out of the room. Participants were then presented with the 96 photographs in two fully replicated blocks of 48 trials. Within each block, rationalize and notice trials were segregated to separate subblocks of 24 trials. Each of these subblocks contained 12 regulate trials and 12 respond freely trials, pseudorandomly ordered. All regulate trials presented aversive content. Respond freely trials were divided equally between aversive and neutral content. The regulation strategy exercised first was counterbalanced across participants (order factor).

The stimulus series contained predominantly aversive content. To facilitate adaptation to and from the experimental context, the stimulus series was preceded and followed by two amusing 2-min videos. No participants withdrew from the experiment due to unmanageable distress, and no clinical interventions were required for participants upon return to the Trauma Recovery Program.

Data Reductions and Analyses

Prior to digitization, data were analog filtered as follows: EMG, 10–300 Hz; EEG, 0.1–100 Hz; and ECG, 1–100 Hz. All data were digitized at 600 Hz with 16-bit amplitude resolution. One data channel was used to record square-wave pulses synchronized with image onsets enabling offline extraction of 22-s epochs of trialwise data.

Corrugator EMG. Per-trial filtered EMG was rectified and integrated over a 2,000-ms time constant. EMG responses were averaged over trials per block and condition after baseline correction by reference to the mean of the last second prior to stimulus onset. Ten per second postonset means were then computed from these averages.

LPP. EEG was digitally filtered to 0.1–30 Hz. Vertical electrooculogram artifacts were then removed using the Gratton procedure² (Gratton, Coles, & Donchin, 1983) applied to 22-s stimulus-locked epochs. EEG epochs were smoothed to an approximate 0.1–3 Hz bandwidth using a polynomial Savitsky-Golay filter (order = 3, frames = 61), which provided a narrow passband without imposing edge transients. Three-second segments of EEG (1-s prestimulus baseline and 2-s poststimulus) were averaged to yield ERPs per block and condition. Median voltages, peak voltages, and peak latencies at Pz and Cz were determined in a 500-ms search window centered at 500 ms poststimulus, the expected latency of the LPP maximum. Preliminary comparisons of LPP at Cz and Pz indicated substantial differences in amplitude, with LPP being much smaller at Cz (2.17 vs. 5.56 μ V, median levels in the aversiveness contrast). LPP was therefore estimated at Pz only. Preliminary analyses found no group difference in the peak latency of the LPP (PTSD: 485 ± 127 ms; controls: 512 ± 117 ms), which could be expected to bias amplitude estimates. Preliminary analyses indicated that the effects of diagnosis, regulation, and aversiveness were essentially equivalent for median and peak voltages, so only the former are reported.

IBI. R waves were first detected in the ECG signal. IBIs were then calculated and resampled to real time. Mean IBI responses were averaged over trials within blocks and condition after baseline correction by reference to the mean of the last second prior to stimulus onset. Ten per second postonset means were then computed from these averages. Statistical analysis of cardiac responses employed IBI rather than heart rate following the recommendations of Graham (1978) and Jennings et al. (1981).

2. As implemented in the ECMP plug-in available at https://github.com/widmann/erptools/blob/experimental/eeeg_emcp.m

Statistical analyses employed linear mixed modeling (SAS v9.2) to accommodate moderate imbalance in the order factor (29 vs. 21). The random effect of participant was nested in diagnosis and order. All variables were centered (Kraemer & Blasey, 2004). Temporal variations in IBI and corrugator EMG activity were modeled as first-order autoregressive processes. Denominator degrees of freedom were adjusted according to the recommendations of Pinheiro and Bates (2000). Preliminary analyses included diagnosis and order (of regulation strategy) as between-subjects factors, and block (1/2), regulation (yes/no), strategy (rationalize/notice), and time as within-subjects factors. In preliminary analyses it was determined that the strategy factor was associated with no main effects and no interactions with diagnosis or regulation.³ Accordingly, strategy was collapsed and responses averaged across rationalize and notice trials to enable more reliable tests of the remaining effects.

The aversiveness contrast compared responses to aversive versus neutral photographs on uninstructed trials and so included an aversiveness factor. The regulation contrast compared rationalize/notice trials with respond freely trials and so included a regulation factor. (Responses to aversive photographs on respond freely trials contributed to both regulation and aversiveness contrasts.) The time factor is discussed below only when it informs a higher-order result, as when a nonsignificant main effect could be better interpreted as an artifact of a truncated response window. The order factor is modeled to avoid misallocation of variance to diagnosis, but will not be further discussed as participants were assigned to order groups at random and the strategy factor was collapsed.

Subanalyses of the aversiveness factor were also performed. The aversive stimuli were divisible into three categories: generic aversive (from the IAPS), indirectly trauma-related but without military content (e.g., flag burnings in Middle East/South Asian contexts), and directly trauma-related with military content. As the *n*-of-average per aversiveness category following the respond freely instruction was only four per block, the block factor was collapsed for these analyses. As well, to promote convergence in models crossing regulation with three levels of aversiveness, the time factor was downsampled into 2-s bins.

Results

There were no effects of diagnosis, aversiveness, or regulation on prestimulus values of corrugator EMG. Raw IBI calculated across all the time-locked cardiac responses exhibited an expected trend towards elevated heart rates in PTSD participants relative to controls (828 ± 115 vs. 884 ± 125 ms; $F(1,46) = 2.66$, $p = .11$; corresponding to 74.0 ± 9.5 vs. 69.6 ± 10.3 bpm).

Uninstructed Responses to Aversive Versus Neutral Photographs

Negative affect. As is evident in Table 2a, aversive photographs induced higher levels of negative affect than neutral photographs on uninstructed trials (5.0 vs. 1.4; $F(1,92) = 682.0$, $p < .001$). There was a Block \times Aversiveness interaction, $F(1,92) = 9.0$, $p = .003$, in which negative affect ratings of aversive but not neutral photographs increased significantly from block 1 to block 2 (aversive: 4.7 to 5.4; $F(1,92) = 12.6$, $p < .001$; neutral: 1.5 to 1.4;

Table 2. Negative Affect Ratings

		Block 1		Block 2	
		Mean	SE	Mean	SE
(a) Aversiveness contrast					
CONT	Neutral	1.3	0.28	1.2	0.28
CONT	Aversive	3.8	0.28	4.6	0.28
PTSD	Neutral	1.7	0.24	1.5	0.24
PTSD	Aversive	5.5	0.24	6.1	0.24
(b) Regulation contrast					
CONT	Respond freely	3.8	0.37	4.6	0.37
CONT	Regulate	3.9	0.37	4.1	0.37
PTSD	Respond freely	5.5	0.31	6.1	0.31
PTSD	Regulate	5.5	0.31	5.8	0.31

Note. Photograph-induced negative affect ratings by contrast: regulation vs. no regulation following aversive photographs, and uninstructed responses to aversive vs. neutral photographs. Values are estimated marginal population means and standard errors assuming a balanced population. CONT = control.

$F(1,92) = 0.48$, $p = .49$). Negative affect ratings were higher overall in block 2 (3.1 vs. 3.4; $F(1,46) = 4.11$, $p = .05$). PTSD participants reported more photograph-induced negative affect than controls (3.7 vs. 2.7; $F(1,46) = 13.0$, $p < .001$); however, this held only for aversive photographs (5.8 vs. 4.2; $F(1,92) = 27.7$, $p < .001$) and not neutral ones (1.6 vs. 1.2; $F(1,92) = 1.43$, $p = .24$; Diagnosis \times Aversiveness interaction, $F(1,46) = 26.7$, $p < .001$).

Corrugator EMG. Corrugator EMG activity is plotted in Figure 2. Corrugator EMG responses exhibited a main effect of aversiveness, being larger during aversive slides (neutral vs. aversive: -0.084 vs. 0.081 $\mu\text{V}/\text{ms}$; $F(1,92) = 6.29$; $p = .014$). There was also a Block \times Aversiveness interaction, $F(1,92) = 4.85$, $p = .030$, as the effect of aversiveness was significant in block 2, $F(1,92) = 11.09$, $p = 0.001$, but not in block 1, $F(1,92) = 0.05$, $p = .83$ (see Figure 3a). The effect of aversiveness on corrugator EMG did not interact with diagnosis (Diagnosis \times Aversiveness: $F(1,92) = 0.58$, $p = .45$; Diagnosis \times Aversiveness \times Time: $F(9,1638) = 1.00$, $p = .44$). The main effect of time was significant, $F(9,1638) = 2.33$, $p = .01$, as EMG activity attenuated after second = 7.

LPP. As shown in Figure 4a, the LPP exhibited a large effect of aversiveness, with aversive photographs eliciting larger potentials than neutral (5.56 vs. 3.62 μV , $F(1,92) = 12.91$, $p < .001$). The main effect of block was significant, with LPPs being larger in block 2 (5.31 vs. 3.87 μV , $F(1,46) = 7.21$, $p = .01$). The Diagnosis \times Aversiveness interaction did not approach significance, $F(1,92) = 0.01$, $p = .95$.

IBI. Across groups, aversive photographs elicited larger cardiac decelerations than neutral photographs, $F(1,92) = 11.50$, $p < .001$; Aversiveness \times Time interaction: $F(4,1638) = 6.21$, $p < .001$ (see Figure 5a). Also significant were the Diagnosis \times Aversiveness interaction, $F(1,92) = 5.85$, $p = .012$; and the Diagnosis \times Aversiveness \times Time interaction, $F(4,1638) = 2.19$, $p = .02$. Decomposing the latter, the Diagnosis \times Time interaction was significant at time points after poststimulus second = 2. Controls exhibited a significant effect of aversiveness (negative vs. neutral: 24.47 vs. 8.78 ms; $F(1,92) = 14.53$, $p < .001$) while PTSD participants did not (13.36 vs. 10.73 ms; $F(1,92) = 0.56$, $p = .45$).

3. This null finding is in line with Wolgast et al. (2011).

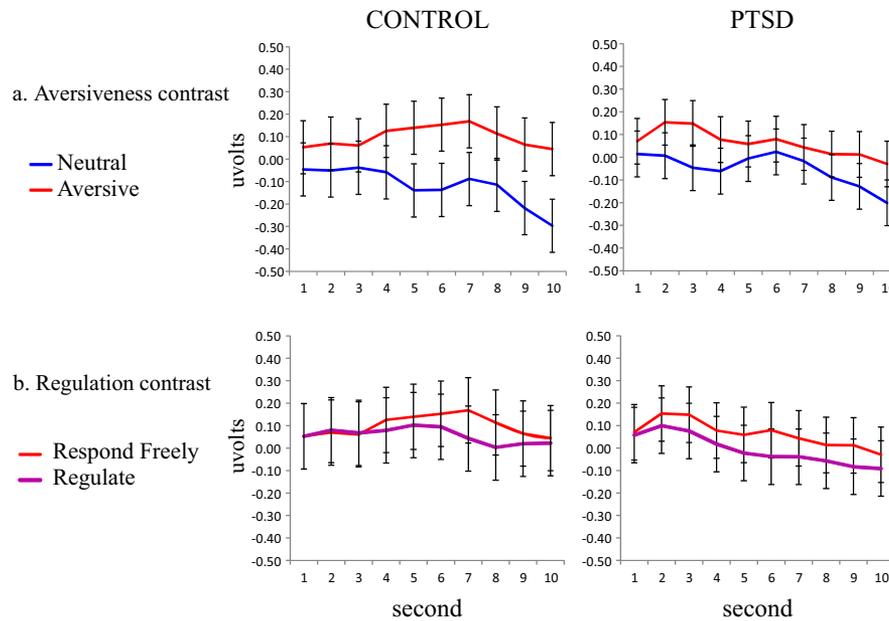


Figure 2. Poststimulus corrugator EMG by diagnosis and contrast. a: Uninstructed responses to aversive (red) versus neutral (blue) photographs. b: Responses to aversive photographs under respond freely (red) versus regulate (violet) instructions. Left: controls; right: PTSD.

Regulation Versus No Regulation Following Aversive Photographs

Negative affect. Presented in Table 2b, negative affect ratings following aversive photographs exhibited a Block \times Regulation interaction, $F(1,92) = 5.8$, $p = .018$, in which regulation moderated negative affect only in block 2 (block 2: 4.9 vs. 5.4; $F(1,92) = 10.04$, $p < .002$; block 1: 4.7 vs. 4.7; $F(1,92) = 0.03$, $p = .87$). The main effect was also significant (least squares means: 5.0 vs. 4.8; $F(1,92) = 4.68$, $p = .033$). Negative affect ratings were

also higher overall in block 2 (5.2 vs. 4.7; $F(1,46) = 25.59$, $p < .001$). PTSD participants endorsed more poststimulus negative affect overall than healthy controls (5.7 vs. 4.1; $F(1,46) = 12.44$, $p = .001$); but the Diagnosis \times Regulation interaction did not approach significance, $F(1,92) = 0.02$, $p = .88$.

Corrugator EMG. There was an interaction of Block \times Regulation, $F(1,92) = 4.35$, $p = .039$, such that the effect of regulation was significant in block 2 only, $F(1,92) = 4.45$, $p = .038$ (see Figure 3a); however, this interaction appeared to be significant due to accentuation of corrugator EMG responses on uninstructed trials from block 1 to block 2. The main effect of block was also significant, $F(1,47) = 4.17$, $p = .047$, as EMG activity was higher in block 2 (-0.005 vs. $0.12 \mu\text{V}$). In any case, this effect did not interact with diagnosis (Diagnosis \times Block \times Regulation: $F(1,92) = 0.27$, $p = .61$). The main effect of regulation on corrugator EMG did not approach significance, $F(1,92) = 0.94$, $p = .37$; Regulation \times Time: $F(9,1638) = 0.22$, $p = .99$.

LPP. Group mean LPPs for regulate versus respond freely trials are plotted in Figure 4b. In the regulation contrast, median voltage of the LPP exhibited no effect of diagnosis (PTSD: $4.78 \mu\text{V}$, controls: $5.72 \mu\text{V}$; $F(1,46) = 0.84$, $p = .36$), no effect of regulation (respond freely: 5.53 vs. regulate: $4.97 \mu\text{V}$; $F(1,92) = 1.41$, $p = .23$), and no Diagnosis \times Regulation interaction, $F(1,92) = 0.33$, $p = .57$.

IBI. As shown in Figure 5b, cardiac responses to aversive photographs were monotonically deceleratory (effect of time: $F(4,1638) = 34.61$, $p < .001$). As expected, IBI did not exhibit a main effect of regulation, $F(1,92) = 0.32$, $p = .57$; Regulation \times Time: $F(4,1638) = 0.45$, $p = .91$. In addition, there was no Diagnosis \times Regulation interaction, $F(1,92) = 0.06$, $p = .81$; Regulation \times Time interaction: $F(4,1638) = 0.56$, $p = .83$. Controls exhibited larger cardiac decelerations to aversive stimuli than did PTSD participants (25.45 vs. 13.76 ms; $F(1,46) = 10.41$, $p = .002$; Diagnosis \times Time interaction: $F(9,1638) = 5.32$, $p < .001$).

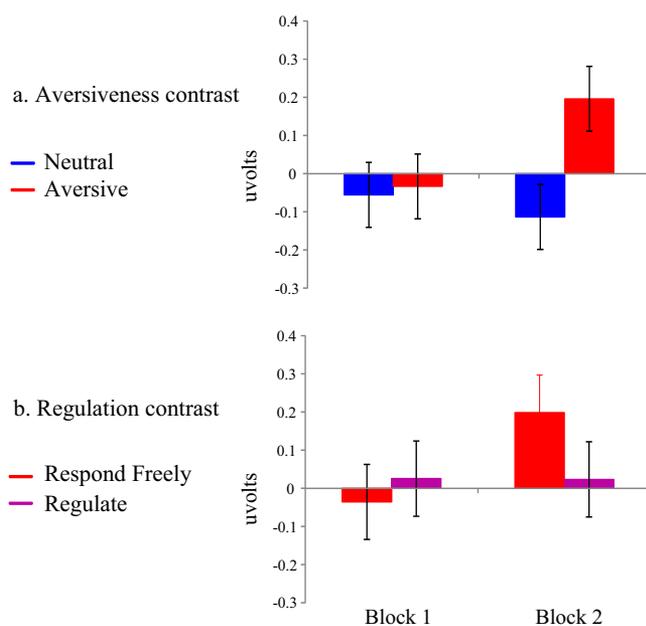


Figure 3. Interactions of (a) block and aversiveness, and (b) block and regulation on corrugator EMG.

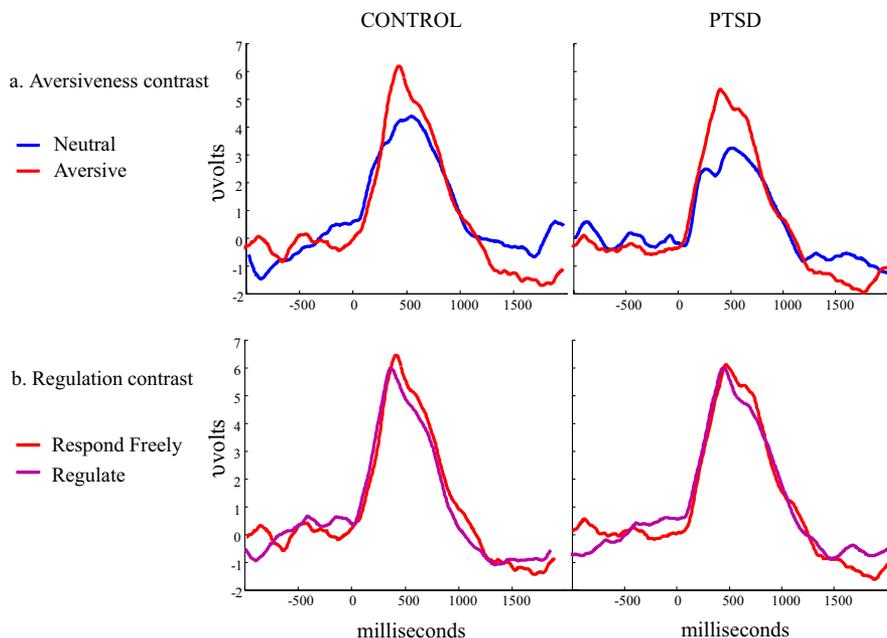


Figure 4. LPPs by diagnosis and contrast. a: Uninstructed responses to aversive (red) versus neutral (blue) photographs. b: Responses to aversive photographs under respond freely (red) versus regulate (violet) instructions. Left: controls; right: PTSD.

Aversive Stimulus Category

IBI exhibited no effect of aversiveness category, $F(2,168) = 1.88, p = .15$, no Diagnosis \times Aversiveness Category interaction, $F(2,168) = 1.17, p = .31$, and no Diagnosis \times Aversiveness Category \times Time interaction, $F(8,1072) = 0.68, p = .71$. Corrugator EMG exhibited no main effect of aversiveness category,

$F(2,168) = 2.21, p = .011$, but did exhibit an interaction of Diagnosis \times Aversiveness Category, $F(2,168) = 4.85, p = .009$, in which controls exhibited maximum EMG activity in response to aversive IAPS stimuli, while PTSD participants exhibited maximum EMG activity in response to military content (see Figure 6a). LPP amplitude exhibited a main effect of aversiveness category, $F(2,168) = 5.97, p = .003$, being larger in response to aversive

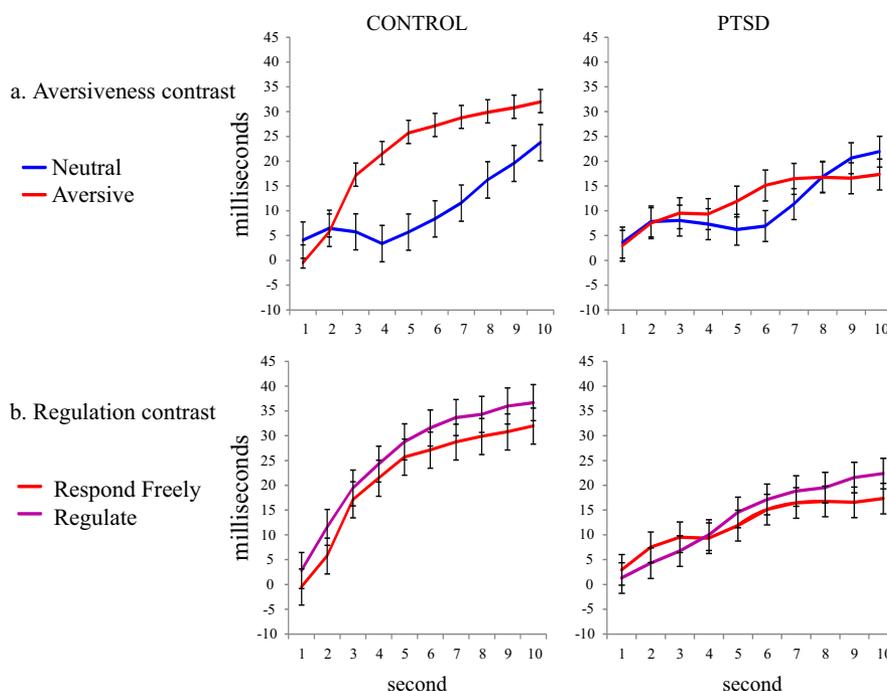
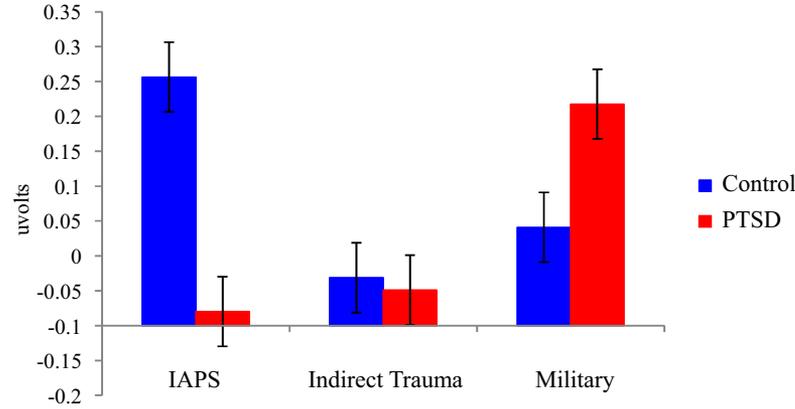


Figure 5. Poststimulus IBI by diagnosis and contrast. a: Uninstructed responses to aversive (red) versus neutral (blue) photographs. b: Responses to aversive photographs under respond freely (red) versus regulate (violet) instructions. Left: controls; right: PTSD.

a. Corrugator EMG activity



b. Late Positive Potential

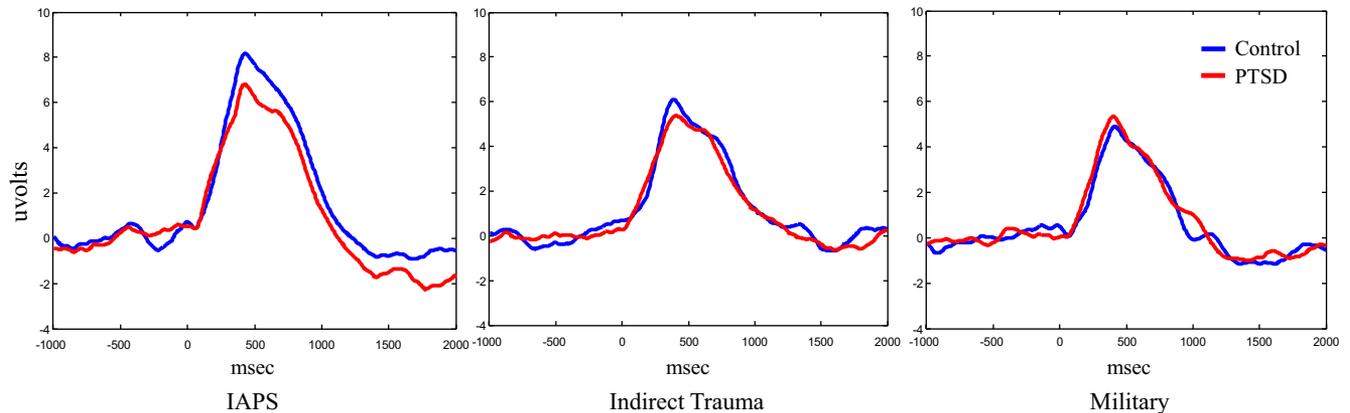


Figure 6. a: Plot of the interaction of diagnosis and aversiveness category on corrugator EMG in which controls responded most strongly to generic aversive IAPS photographs, while combat veterans with PTSD responded most strongly to photographs containing military content. b: Plot of the main effect of aversiveness category on LPP in which, across groups, generic aversive IAPS photographs induced the largest LPPs and those containing military content induced the smallest.

IAPS photographs than to photographs indirect or directly relevant to trauma (see Figure 6b). The interaction of diagnosis and aversiveness category on LPP amplitude exhibited a near-significant trend, $F(2,168) = 2.49$, $p = .086$, as the LPP elicited by military content was larger in PTSD participants than in controls, whereas controls' LPPs were larger in response to the other categories. Aversiveness category did not interact with regulation to influence IBI, corrugator EMG, or LPP amplitude.

Discussion

The aim of this study was to administer a well-tested laboratory emotion regulation paradigm to U.S. military veterans diagnosed with PTSD in whom emotion regulation deficits are a source of functional impairment and a focus of treatment. Despite the broad consensus that PTSD involves emotion regulation difficulties, the literature is inconclusive as to whether persons diagnosed with PTSD respond differentially to instructions to regulate their emotions. While both New et al. (2009) and Rabinak et al. (2014) observed less activation of dlPFC in PTSD samples instructed to regulate their responses to aversive photographs, neither study observed PTSD samples to reduce amygdala activation less than

controls, and only New et al. (2009) observed differential reduction of negative affect. The present psychophysiological study also did not observe expected differences in emotion regulation between persons with PTSD and a healthy control group. Though effects of regulation were detectable for negative affect and for corrugator EMG in block 2, participants diagnosed with PTSD did not exhibit less emotion regulation as indexed by either measure or by the LPP. Furthermore, aversiveness category effects did not interact with regulation, suggesting that the absence of differences between PTSD participants and controls in objective indices of emotion regulation were general and not tied to specific content or measure.

In contrast to the absence of predicted regulation effects, main effects of aversiveness were demonstrated by all indices. As well, negative affect and IBI demonstrated $\text{Diagnosis} \times \text{Aversiveness}$ interactions. More specific associations were also seen in analyses of aversiveness category (within the regulation contrast) as PTSD participants exhibited exaggerated corrugator responses to military content and a similar trend in the LPP. In the first test of aversiveness effects on LPP in an adult psychiatric sample, Foti, Olvet, Klein, and Hajcak (2010) found normal enhancement of LPPs by fearful and angry faces, but no enhancement in response to threatening faces in persons with MDD. Interestingly, when

analyzing a frontocentral magnetolectric event exhibiting strong correspondences to the LPP, Pietrek et al. (2012) found a different pattern—impaired emotion regulation in participants with early life stress but no Mood Disorder \times Aversiveness interactions.

Aversive and neutral photographs induced differential cardiac responses, both main effects and Diagnosis \times Aversiveness interactions. Surprisingly, however, across both groups, the cardiac responses to both aversive and neutral photographs were deceleratory. This was the case across aversiveness categories. The results in controls were consistent with those that Bradley, Codispoti, Cuthbert, and Lang (2001) obtained in a large, healthy undergraduate sample assessed under passive viewing conditions. At first glance, the observation of a similar, if attenuated, slowing of heart rate in a chronic severe PTSD sample appears inconsistent with the large literature documenting cardiac accelerations in response to standardized and ideographic trauma reminders (reviewed in Pole, 2007). An important difference between the current design and virtually all prior trauma cue reactivity studies is the presentation of aversive and neutral stimuli in an unblocked, pseudorandomized sequence. Typical of trauma cue reactivity designs is the large, multisite study of Keane et al. (1998), which included two exposure components: one involved six consecutive, 1-min, audiovisual, trauma-related stimuli alternating with blocked neutral stimuli, and the other, four consecutive 1-min ideographic imagery procedures alternating with rest periods. Blocked stimulation enables the continuous recruitment of sympathetic activation, which may here have been interrupted by the interposition of neutral trials and/or by regulation task demands. To our knowledge, only three other studies have presented unblocked aversive and neutral photographs to PTSD samples. Ehlers et al. (2010) observed generally deceleratory heart rate responses to both generic aversive and trauma-relevant photographs in persons with PTSD, though patient and control groups were discriminated by small differences in mean cardiac responses to trauma-relevant photographs. When Elssesser, Sartory, and Tackenberg (2005) assessed civilian trauma victims at 1 month posttrauma, they observed heart rate accelerations in response to unblocked trauma-related photographs; however, when they presented the same stimuli 2 months later, they observed decelerations, attributing the change to improved clinical status. In a design concomitantly measuring heart rate and startle responses to unblocked neutral, aversive, and trauma-related stimuli, Elssesser, Sartory, and Tackenberg (2004) found that only recent trauma victims with acute stress disorder exhibited unambiguous heart rate accelerations in response to trauma-related stimuli when interleaved with generically aversive and neutral stimuli. In sum, the unblocked stimulation format typical of emotion regulation studies probably elicits a cardiac response pattern distinct from that seen in the PTSD trauma cue reactivity literature. The present data do not leave us in a strong position to speculate as to the source(s) of the attenuated cardiac deceleratory response seen in our PTSD sample. Candidate mechanisms include reduced attentional deployment to the aversive photographs consistent with avoidance symptomology, or countervailing sympathetic activation (though the short duration of the response period would limit sympathetic influence). It is worth noting that the veterans tested in this study exhibited a near-significant trend toward elevated experiment-wide heart rate reminiscent of the preexperiment heart rates commonly observed in trauma cue reactivity studies (Pole, 2007) and so were typical in that regard.

In interpreting the current results, it may be useful to consider the pervasive and consistent effects associated with the factor of block.

In all cases, experimental effects were stronger in block 2. Block interacted with the effects of regulation and aversiveness on negative affect and corrugator EMG. Because effects of aversiveness strengthened in block 2, it was only in that block that effects of regulation were detectable. There were also main effects of block on negative affect and LPP amplitude. The most likely source of block effects is continuing task acquisition after the nominal instruction/practice period. Combining practice and testing in a single session was intended to minimize interference with participants' treatments; nevertheless, the instruction periods typically required 20 to 30 min and were terminated only when the experimenter judged the participant to have comprehended the task. The reporting of instructional procedures is variable in this literature, so it is difficult to compare them across studies. Neither the New nor the Rabinak studies reported on instructional procedures or practice. Ochsner, Bunge, Gross, and Gabrieli (2002) reported providing their participants (undergraduates at a major research university) "extensive instruction in reappraisal," "one to three days before scanning" (p. 1225). (See also Ochsner et al., 2004). The difficulty of the foreground task employed to elicit emotion regulation, the effectiveness of training procedures, and differential learning rates could be important mediators of emotion regulation effects in functionally compromised samples. Future studies assessing emotion regulation in psychiatric samples may need to employ direct tests to insure that their estimates of emotion regulation derive from a posttask-acquisition phase of measurement.

It is important to note several limitations of the present study. The clinical participants were relatively homogeneous in that they were all men drawn from a veteran's hospital inpatient treatment service. The results of McRae, Ochsner, Mauss, Gabrieli, and Gross (2008) suggest that males, relative to females, have access to relatively automated emotion regulatory mechanisms. In their fMRI study, males exhibited more downregulation of amygdala activity during reappraisal than females, while simultaneously exhibiting less activation of brain regions implicated in the support of reappraisal (dorsal anterior cingulate, superior frontal and inferior frontal gyri). We can then ask whether more automated regulatory processes associated with less dorsolateral cortical activation are less likely to manifest both central (LPP) and peripheral (EMG) effects. The studies of Moser et al. (2006, 2009) and Hajcak and Nieuwenhuis (2006) employed predominantly female samples (63%–79%). Ray et al. (2010) employed only females in their study. Future studies of emotion regulation in PTSD should endeavor to study males and females, especially as the prevalence of this disorder is two to three times as high among the latter (Kessler et al., 1994). It is possible that the PTSD participants in this study, though highly symptomatic, benefited from treatment in a manner that reduced group differences in emotion regulation. In future research, it will be important to consider a broader range of patients. Though we sought to collect a diverse array of psychophysiological measures of affective responding (see also companion paper), it may be important in future work to expand this set to obtain adequate assessments of the effects of emotional reactivity and emotion regulation. The absence of effects of reappraisal on the LPP in the healthy controls, as observed by Moser et al. (2009), may reflect the relatively low *n*-of-average employed here. While this study met the eight-trial criterion determined by Moran, Jendrusina, and Moser (2013) for the base LPP, in their study of emotion regulation effects on the LPP, Moser et al. (2009) averaged 30 trials per instruction category. The pairing of cue color and instruction was invariant across participants. Ideally, these would be counterbalanced to preclude unassessed but func-

tional color-instruction associations being confounded with effects of interest. Finally, in studies in normal samples, emotion regulation strategies are applied and evaluated with respect to normative emotion responses to provocative stimuli. In psychopathological conditions, it is *abnormal* emotional responses to stimuli, events, and conditions that are the focus of intervention. While persons with PTSD may exhibit normative responses to provocative stimuli, and exhibit uncompromised volitional regulation of those responses, making inferences from such phenomena to their regulation of abnormal emotional responses entails a conceptual leap that may not be warranted.

The applicability of the theoretical framework of emotion regulation to psychiatric disorders was recognized almost 2 decades ago (Gross & Munoz, 1995). This promise has been supported by the replicability of fMRI-based emotion regulation effects, particular those of reappraisal, in healthy samples (Buhle et al., 2014; Ochsner & Gross, 2005). Further insights into the functioning of the neural systems underlying emotion regulation in PTSD and other psychiatric disorders are clearly desirable; and the parsing of neurocognitive mechanisms underlying emotion regulation success and failure in psychopathology presents the prospect of organizing treatment effects, matching patients to treatments, and suggesting

new avenues of intervention. The use of psychophysiological variables as objective outcomes can extend the reach of clinical research to samples inaccessible to neuroimaging for reasons of cost, geography, or a need to limit sample bias. The current data suggest that, with regard to PTSD, future studies should consider reducing task complexity and employing a stimulation protocol that induces psychophysiological response patterns that are unambiguously pathognomonic of the disorder under study.

Finally, future studies in this area may seek guidance from recent work supporting a dissociative subtype of PTSD (Lanius, Brand, Vermetten, Frewen, & Spiegel, 2012), which has now been codified in DSM-5 (APA, 2013). At the core of this conceptualization is divergence in emotion regulation between “overmodulatory” and “undermodulatory” modes, which may differ over individuals and groups and alternate within individuals over time. A challenge and opportunity presented by this framework is that psychophysiological studies of dissociation in PTSD have yet to converge on a coherent model of how state or trait dissociative propensity manifests in autonomic responses to trauma reminders in the laboratory (cf. Griffin, Resick, & Mechanic, 1997; Kaufman et al., 2002; Orr et al., 1990; Sledjeski & Delahanty, 2012).

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