CORTEX 145 (2021) 295–314

Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Research Report

Punishment and reward normalize error-related cognitive control in PTSD by modulating salience network activation and connectivity

Travis C. Evans [a,b,*], Joseph DeGutis [a,c,d], David Rothlein [a], Audreyana Jagger-Rickels [a,b,e], Ayumu Yamashita [a], Catherine B. Fortier [c,d,f], Jennifer R. Fonda [b,c,d], William Milberg [c,d,f], Regina McGlinchey [c,d,f] and Michael Esterman [a,b,e,g]

[a] Boston Attention and Learning Lab, VA Boston Healthcare System, USA
[b] Department of Psychiatry, Boston University School of Medicine, USA
[c] Translational Research Center for TBI and Stress Disorders (TRACTS), VA Boston Healthcare System, USA
[d] Department of Psychiatry, Harvard Medical School, USA
[e] National Center for PTSD, VA Boston Healthcare System, USA
[f] Geriatric Research, Education, and Clinical Center (GRECC), VA Boston Healthcare System, USA
[g] Neuroimaging Research for Veterans (NeRVe) Center, VA Boston Healthcare System, USA

ARTICLE INFO

Article history:
Received 24 February 2021
Reviewed 6 May 2021
Revised 3 August 2021
Accepted 15 September 2021
Action editor Jordan Grafman
Published online 2 October 2021

Keywords:
PTSD
Reward
Punishment
Post-error slowing
Cognitive control
Motivation

ABSTRACT

Posttraumatic Stress Disorder (PTSD) symptomatology disrupts inhibitory control during sustained attention. However, PTSD-related inhibitory control deficits are partially ameliorated when punishments and rewards are administered based on task performance, which suggests motivational processes contribute to these deficits. Additionally, PTSD may also impair error-related cognitive control following inhibitory control failures as measured by post-error slowing (PES). However, it remains unclear if motivational processes also contribute to impaired error-related cognitive control in PTSD. Using an incentivized sustained attention paradigm in two independent samples of post-9/11 veterans, we characterized PTSD-related differences in PES during both non-motivated conditions (no task-based incentives) and motivated conditions (task-based rewards and punishments). In Study 1 ($n = 139$), PTSD symptom severity was modestly associated with smaller PES in the non-motivated condition, whereas no PTSD-related association was observed in the motivated condition. In Study 2 ($n = 35$), we replicated and extended these results by using fMRI to characterize modulation of the triple network system comprised of the Salience Network (SN), Frontoparietal Control Network (FPCN), and Default Mode Network (DMN). In the non-motivated condition, PTSD symptom severity was associated with non-specific SN and FPCN hyperactivation during both failed and successful inhibitory control. In the motivated condition, PTSD symptom severity was associated with greater focal activation of both the SN and Superior Parietal Lobule cluster (an FPCN node) during punished inhibitory control failures and weaker SN-FPCN connectivity during

* *Corresponding author*. VA Boston Healthcare System, 150 S. Huntington Avenue, Boston, MA, 02130, USA.
E-mail address: travis.evans@va.gov (T.C. Evans).
https://doi.org/10.1016/j.cortex.2021.09.004
0010-9452/Published by Elsevier Ltd.

rewarded inhibitory control successes. Together, these results suggest that dysregulated motivational processes in PTSD may contribute to impaired error-related cognitive control.
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1. General introduction

Posttraumatic stress disorder (PTSD) is a chronic and impairing psychiatric condition, which develops in approximately 14% of post-9/11 veterans (Tanielian, Tanielian, & Jaycox, 2008). In addition to hallmark symptoms of emotional dysregulation, intrusive memories, and avoidance, research suggests that PTSD is also characterized by deficits in cognitive processes (for reviews, see Aupperle, Melrose, Stein, & Paulus, 2012; Polak, Witteveen, Reitsma, & Olff, 2012). In particular, PTSD may be characterized by deficits in inhibitory control as well as recruitment of error-related cognitive control following failures of inhibitory control (Clemans, El-Baz, Hollifield, & Sokhadze, 2012; Esterman et al., 2019; Swick, Honzel, Larsen, Ashley, & Justus, 2012; but see also,; Swick, Honzel, & Turken, 2015). To date, inhibitory control deficits in PTSD have been predominantly attributed to concomitant deficits in more global executive function. However, recent research suggests that PTSD symptomatology disrupts inhibitory control above and beyond disruptions to executive function (DeGutis et al., 2015; Vasterling et al., 2002). Moreover, deficient inhibitory control in PTSD is partially ameliorated when reward and punishment are administered based on task performance (Dutra, Marx, McGlinchey, DeGutis, & Esterman, 2018). Together, these findings suggest that inhibitory control deficits in PTSD may be at least partially attributable to dysregulated motivational processes. However, it remains unclear if motivational processes also contribute to error-related cognitive control, which is also modulated by motivational processes and may be similarly disrupted in PTSD (Clemans et al., 2012). To address these issues, we conducted a behavioral experiment (Study 1) and fMRI experiment (Study 2) in independent samples of post-9/11 veterans.

PTSD is characterized by deficits in several cognitive processes such as inhibitory control (Aupperle et al., 2012). Broadly defined, inhibitory control involves stopping and/or adjusting an automatic response as well as suppressing distracting information that may impede goal-directed behavior (Lustig, Hasher, & Tonev, 2001). In sustained attention paradigms, for example, individuals with PTSD exhibit more failures to withhold automatic responses to infrequent "no-go" trials (i.e., comission errors; for a review, see Fortenbaugh, DeGutis, & Esterman, 2017). Additionally, individuals with PTSD exhibit more failures to initiate responses to more frequent "go" trials (i.e., omission errors), either as a means to reduce potential commission errors or due to task-related disengagement (for a review, see Aupperle et al., 2012). Importantly, deficits in inhibitory control are not simply attributable to trauma exposure, but are exclusively present in individuals who develop PTSD following trauma exposure (Polak et al., 2012). Thus, inhibitory control deficits may reflect either a consequence of PTSD or a premorbid risk factor for the development of PTSD (Samuelson et al., 2020). Although the distinction between sequela and risk factor remains an important empirical question, a growing body of research nevertheless suggests that PTSD is characterized by inhibitory control deficits.

Although PTSD-related deficits in inhibitory control were initially proposed to be attributable to global deficits in executive function and/or intellectual ability, recent findings challenge this conceptualization. First, PTSD-related differences in inhibitory control continue to be observed after statistically controlling for executive function or intellectual ability, which suggests PTSD symptomatology disrupts inhibitory control beyond deficits in global executive function (DeGutis et al., 2015; Vasterling et al., 2002). Second, PTSD-related differences in inhibitory control are partially ameliorated when reward and punishment are administered based on task performance (Dutra et al., 2018). In this study, PTSD symptom severity was associated with poorer inhibitory control when no incentives were provided for task performance. However, PTSD symptoms exerted a weaker influence on inhibitory control when successful inhibitory control was rewarded (money gain) and failed inhibitory control was punished (money loss). Put another way, PTSD was characterized by deficits of inhibitory control during non-motivated states, but these PTSD-related deficits were smaller in magnitude during motivated states. Thus, it seems unlikely that PTSD-related inhibitory control deficits are entirely attributable to globally impaired executive function. Instead, these recent studies suggest that PTSD-related differences in inhibitory control may be at least partly attributable to dysregulated motivational processes (Dutra et al., 2018; Stein & Paulus, 2009).

Similarly, dysregulation of motivational processes may also impair recruitment of error-related cognitive control following inhibitory control failures. Typically, error-related cognitive control is measured as the degree to which behavioral responses and/or neural systems are adaptively adjusted in response to errors (Kerns et al., 2004). Following an error, individuals typically exhibit an increase in reaction time commonly known as post-error slowing (PES), which serves to adaptively adjust behavioral performance (for a review, see Danielmeier & Ullsperger, 2011). Specifically, PES putatively reflects a recruitment of cognitive control following an error, which reduces the probability of subsequent errors (Danielmeier & Ullsperger, 2011; Hajcak, McDonald, & Simons, 2003). For example, PES is *decreased* when cognitive control is weakened, which occurs independent of error frequency (Regev & Meiran, 2014). Conversely, error-related cognitive control is *increased* when errors are rewarded and/or punished, which suggests that motivational processes contribute to error-related cognitive control (Maruo, Schacht, Sommer, &

Masaki, 2016; Stürmer, 2011). Therefore, it is possible that dysregulated motivational processes in PTSD may also impair error-related cognitive control following failures of inhibitory control.

Although less well-studied, some research suggests that PTSD is also characterized by impaired error-related cognitive control following errors (e.g., inhibitory control failures). For example, one EEG study demonstrated that individuals with PTSD exhibit blunted neural responses following errors compared to individuals without PTSD (Clemans et al., 2012). However, a separate study demonstrated that PTSD was not characterized by significantly smaller neural responses or PES compared to a control group (Swick et al., 2015). Mixed findings across these two studies may be attributable to task-related differences (e.g., different numbers of trials), differential diagnostic co-morbidities (e.g., mild traumatic brain injuries), or the relatively small PTSD samples ($n = 10$ and $n = 14$, respectively). Given these equivocal findings, it remains unclear if PTSD is characterized by impaired error-related cognitive control following failed inhibitory control and if motivational processes contribute to these putative impairments.

In summary, it is necessary to characterize and replicate the relationships between PTSD, motivational processes, and error-related cognitive control. Recent research suggests that motivational processes play a role in PTSD-related deficits of inhibitory control, which are partly ameliorated when exogeneous rewards and punishments are administered based on task performance (Dutra et al., 2018). Given that motivational processes also contribute to error-related cognitive control, motivational processes may similarly contribute to PTSD-related deficits in error-related cognitive control (Esterman, Reagan, Liu, Turner, & DeGutis, 2014). Therefore, it is important to characterize PTSD-related differences in error-related cognitive control during both non-motivated and motivated states.

2. Objectives of the current studies

To address these issues, the current studies aimed to characterize how motivational processes moderate PTSD-related differences in error-related cognitive control following failures of inhibitory control. To this end, we recruited two independent samples of post-9/11 veterans to complete the incentivized gradual onset continuous performance task (gradCPT) as part of a behavioral study (Study 1) or fMRI study (Study 2). The incentivized gradCPT paradigm measures post-error slowing while inhibitory control is alternatively not incentivized (non-motivated) or incentivized via exogenous reward and punishment (motivated). We report how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.

3. Study 1

To determine the extent to which motivational processes contribute to error-related cognitive control deficits in PTSD, we first administered the incentivized gradCPT paradigm to a large sample of deployed veterans who varied in PTSD symptom severity and PTSD diagnosis. Based on previous research (Dutra et al., 2018), we hypothesized that PTSD would be characterized by weaker error-related cognitive control (i.e., smaller PES) during non-motivational states, which would be normalized during motivational states (i.e., no PTSD-related differences in PES).

4. Method

4.1. Participants

In Study 1, 171 Veterans (see Table 1 for sample characteristics) were sequentially recruited within the Translational Research Center for Traumatic Brain Injury and Stress Disorders (TRACTS; McGlinchey, Milberg, Fonda, & Fortier, 2017). Notably, some veterans ($n = 81$) overlapped with those reported in a previous study by our group (Dutra et al., 2018). Given that study sample (previously reported *vs* unreported) did not moderate any of the primary results (all $ps > .35$), we conducted all analyses on the larger combined sample.

Within the larger TRACTS cohort, Veterans were excluded if they reported (a) a bipolar or psychotic disorder; (b) current suicidal or homicidal plans; (c) neurological illness; or (d) seizures unrelated to TBI. Veterans were also excluded if they reported a history of moderate/severe TBI ($n = 3$), exhibited significant neurological impairment ($n = 2$), or failed the verbal component of the Medical Symptom Validity Test (MSVT; $n = 8$; Green, Lees-Haley, & Allen III, 2003).

4.2. Task-based participant exclusions

First, response data was not collected for several participants ($n = 4$) due to technical failure. Second, some participants ($n = 8$) exhibited extended periods of inactivity as evidenced by either a failure to respond to >50% of gradCPT trials or as a lack of response on 37 or more consecutive trials (Fortenbaugh, Rothlein, McGlinchey, DeGutis, & Esterman, 2018). Third, several participants ($n = 7$) did not make any commission errors in one or both task conditions, which precluded measurement of PES. All analyses were conducted on a final sample of 139 participants for PES analyses and 146 participants for d-prime analyses.

4.3. Procedure

As part of the larger, longitudinal TRACTS program, all veterans completed an extensive, structured battery of psychiatric and neuropsychological assessments across multiple time points. All veterans completed the incentivized gradCPT at either the baseline visit or first follow-up visit. To approximate a cross-sectional design, we modelled current psychiatric/neurological symptoms from the same time point that the incentivized gradCPT was completed. Sample size was determined based on previous research that demonstrated PTSD-related differences in gradCPT performance with a sample of 80 veterans.

Table 1 – Final sample characteristics.

Measure	Study 1 ($n = 146$)	Study 2 ($n = 35$)	Difference
Age	36.72 (± 9.18) [Range: 24 – 64]	36.46 (± 9.34) [Range: 21 – 59]	$p = 0.88$
Sex (% Male)	95.90%	80.00%	$p = 0.001$
Education (Years)	14.42 (± 2.43) [Range: 8 – 20]	15.26 (± 2.44) [Range: 11 – 20]	$p = 0.07$
Racial Identity			
% Caucasian	76.00%	82.90%	$p = 0.39$
% Asian	4.10%	2.90%	$p = 0.73$
% Black	8.20%	8.60%	$p = 0.95$
% Native American	0.70%	0.00%	$p = 0.62$
% Declined/Unknown	11.00%	11.40%	$p = 0.85$
Psychiatric Diagnosis			
%PTSD Dx	54.10%	25.70%	$p = 0.003$
%Mood Dx	29.50%	14.30%	$p = 0.07$
%Anxiety Dx	13.00%	11.40%	$p = 0.80$
%Substance Dx	19.20%	22.90%	$p = 0.62$
CAPS Total	48.11 (± 28.45) [Range: 0 – 116]	30.86 (± 33.25) [Range: 0 – 108]	$p = 0.002$
DRRI-2 Combat Experience	18.74 (± 11.94) [Range: 0 – 64]	18.26 (± 14.12) [Range: 0 – 58]	$p = 0.53$
# Military TBI	1.19 (± 1.84) [Range: 0 – 16]	0.77 (± 1.50) [Range: 0 – 6]	$p = 0.23$

Note: Data are presented for final study samples following all exclusions. Dx = Diagnosis; CAPS = Clinician Administered PTSD Scale (4th Edition); DRRI-2 = Deployment Risk and Resilience Inventory (2nd Edition); TBI = Traumatic Brain Injury.
To statistically compare sample characteristics of Study 1 and Study 2, we utilized independent samples t-tests for continuous variables (Age, Education, CAPS, combat exposure, and # military TBIs) and Pearson Chi-Square tests for dichotomous variables (Sex, Racial Identities, and Psychiatric Diagnoses).

All research procedures were conducted in accordance with the Institutional Review Board of Human Studies Research at the VA Boston Healthcare System. Veterans provided written consent and were equally compensated for their participation regardless of gradCPT performance. Study procedures and analyses were not pre-registered prior to the research being conducted.

4.4. *Clinical measures*

4.4.1. *Clinician-Administered PTSD Scale (CAPS-IV)*

The CAPS-IV is a structured clinical interview that assesses the intensity and frequency of PTSD symptoms to establish a diagnosis of PTSD (Blake et al., 1995). In both Study 1 and Study 2, the CAPS-IV was administered by doctoral-level psychologists. Clinicians rate both the intensity and frequency for each of the 17 PTSD symptoms derived from the *DSM-IV*. CAPS total scores range from 0 to 136, which provides a measure of overall PTSD symptom severity. Additionally, the CAPS was also used to provide a *DSM-IV* diagnosis of PTSD based on the presence of one Cluster B symptom, three Cluster C symptoms, and two Cluster D symptoms (frequency ≥1 and intensity ≥2). All CAPS-IV diagnoses were reviewed and validated at weekly diagnostic consensus meetings that consisted of at least three doctoral-level psychologists and a psychiatrist.

4.4.2. *Structured Clinical Interview for Axis I Disorders (SCID)*

The SCID is a semi-structured interview that assesses both lifetime and current presence of *DSM-IV* psychiatric disorders (First, Spitzer, Gibbon, & Williams, 2002). The SCID was administered by doctoral-level psychologists and used to diagnose comorbid anxiety disorders, mood disorders, and substance use disorders (SUDs). Current *DSM-IV* diagnoses were utilized to assess if co-morbidities modulated task performance and/or moderated PTSD-related effects. All SCID diagnoses were reviewed and validated at the aforementioned weekly diagnostic consensus meetings.

4.4.3. *The Boston Assessment of TBI-Lifetime (BAT-L)*

The BAT-L is a semi-structured interview that assesses an individual's history of TBI experienced before, during, and after military deployment with a focus on military blast exposure (Fortier et al., 2014). The BAT-L was administered by doctoral-level psychologists. TBI diagnoses made using the BAT-L exhibit strong interrater reliability (Cohen's k's > .80) and excellent convergence with other TBI diagnostic

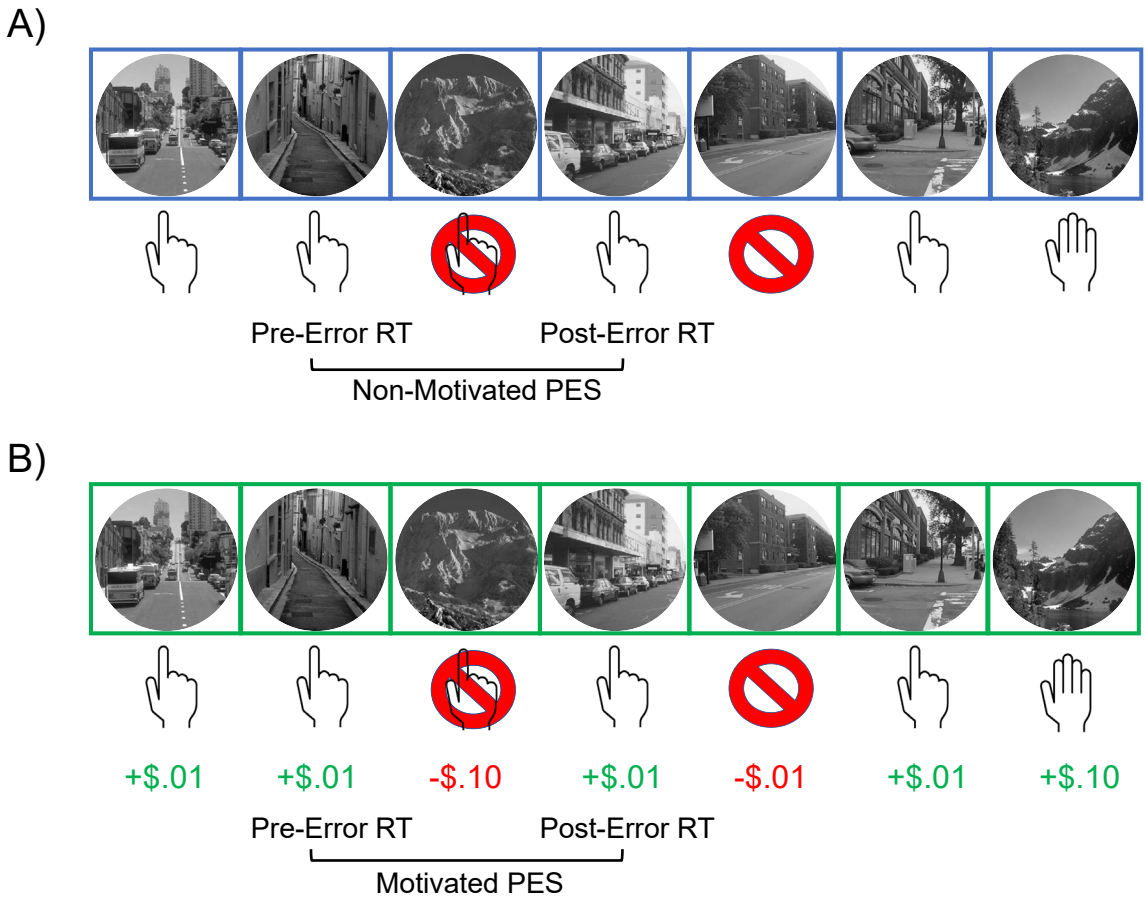

Fig. 1 – Incentivized Gradual Onset Continuous Performance Task (gradCPT). *Legend:* Participants were instructed to press a button in response to city images, but withhold responses to mountain images. Images gradually transitioned every 800 ms with no intertrial interval. During Non-Motivated blocks (A; blue frames), participants received no incentives. During Motivated blocks (B; green frames), participants gained $.10 for correctly withholding responses to mountain images or lost $.10 for incorrectly pressing to mountain images. Additionally, participants gained or lost $.01 for responding or failing to respond to city images, respectively. All participants completed 4 Non-Motivated blocks and 4 Motivated blocks.

measures (Fortier et al., 2014). All BAT-L diagnoses were reviewed and validated at the aforementioned weekly diagnostic consensus meetings.

4.4.4. *The Deployment Risk and Resilience Inventory-2 (DRRI-2)*

To characterize the degree of combat exposure in the current sample, we utilized the Combat Experiences Scale of the DRRI-2 (Vogt et al., 2013). Veterans reported the frequency to which they were exposed to 17 combat experiences (e.g., "I fired my weapon at enemy combatants") during their deployment (0 = *Never*; 4 = *Daily or Almost Daily*). Control analyses using this measure differ in degrees of freedom as not all veterans completed the DRRI-2 as part of the larger TRACTS research program.

4.5. *Incentivized gradCPT paradigm*

The gradCPT paradigm is designed to capture dynamic fluctuations in sustained attention (Esterman, Noonan, Rosenberg, & DeGutis, 2012). In the gradCPT, gray-scale images are continuously presented to participants (see Fig. 1). Images consist of city scenes (90% frequency) and mountain scenes (10% frequency). Participants are instructed to respond to city images and withhold responses to mountain images. In the gradCPT, images are linearly interpolated from one stimulus to the next at a rate of approximately 800 ms to ensure gradual transitions between images.

In the incentivized gradCPT, all participants completed the task during alternating blocks in which task performance is either incentivized or not incentivized. In motivated blocks, participants were informed that they could gain money (reward) or lose money (punishment) based on task performance (see Fig. 1).[1] In non-motivated blocks, participants were instructed that task performance will not result in

[1] Similar to previous motivation research (e.g., Stürmer, 2011), we refer to money gain as "reward" and money loss as "punishment". From a behavioral perspective, however, money gain is classically considered a positive reinforcer, whereas money loss is classically considered a negative reinforcer. We use the terms reward and punishment to maintain consistency with previous PES studies.

money gain or money loss. For all participants, task performance was alternatively incentivized (4 Motivated blocks) or not incentivized (4 Non-Motivated blocks).

To display the current block throughout the task, images were presented alternatively within either a green border (Motivated) or blue border (Non-Motivated). During Motivated blocks, correct and incorrect responses to mountain images produced a gain or loss of $.10, respectively. Additionally, correct and incorrect responses to city images produced a gain or loss of $.01, respectively. During Non-Motivated blocks, no money gain or loss occurred regardless of task performance. All participants completed 4 Motivated blocks and 4 Non-Motivated blocks of the incentivized gradCPT.

Prior to starting the incentivized gradCPT paradigm, veterans were provided with instructions regarding these protocols and completed a 30-second practice task to ensure comprehension of instructions. Following task completion, all veterans were ultimately provided with an $8.00 payout regardless of task performance.

4.5.1. *gradCPT data processing*

Based on the gradual transitions between city and mountain images, a previously validated algorithm was used to assign button responses for each trial (Esterman et al., 2012). Specifically, reaction times (RTs) were computed based on the point at which each image began to transition. For example, an RT of 800 ms indicates that the response was made when the current trial image reached 100% opacity and the previous trial image reached 0% opacity. In contrast, shorter RTs such as 600 ms indicate that the response was made when the current trial image reached 75% opacity and the previous trial reached 25% opacity. For RTs longer than 800 ms, responses were assigned to the next trial if longer than 1,366 ms.

4.5.2. *Error-related cognitive control (post-error slowing)*

To compute PES, we used a robust computation approach (Dutilh et al., 2012). Specifically, PES is computed by indexing RT on correct city trials immediately following an error against RT on correct city trials immediately preceding an error (i.e., $RT_{PostError} - RT_{PreError;}$ see Fig. 1).

4.5.3. *Sustained inhibitory control (d-prime)*

Given that PTSD is characterized by deficits in both commission errors and omission errors, we measured sustained inhibitory control using d-prime (Dutra et al., 2018). D-prime is calculated as the standardized ratio of correct omissions to mountain trials (i.e., "hits") to incorrect omissions to city trials (i.e., "false alarms"). If participants exhibited 100% or 0% accuracy rates, one-half error was respectively added or deducted per standard procedures.

4.6. *Data analytic approach*

All statistical analyses were conducted using SPSS software ver. 24.0 (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM). For all analyses, we considered PTSD-related differences to be significant at a threshold of $p \leq .05$ (two-tailed).

4.6.1. *Primary analyses*

Our primary behavioral analyses aimed to determine if PTSD (CAPS scores or PTSD Diagnosis) was differentially associated with post-error slowing (PES) within the Non-Motivated condition and Motivated condition. Given the relationship between PES and inhibitory control, our secondary analyses aimed to determine if PTSD was also differentially associated with sustained inhibitory control (d-prime) within the Non-Motivated condition and Motivated condition.

To test our primary hypothesis, we used a Repeated Measures Analyses of Covariance (RM-ANCOVA) analytic approach with PES measures entered as dependent variables. In these RM-ANCOVA models, motivation condition (Non-Motivated *vs* Motivated) was entered as a within-subjects factor. Additionally, PTSD was entered as a between-group factor using either a continuous (CAPS) or dichotomous (PTSD diagnosis) covariate of interest. Using this approach, RM-ANCOVA models tested for a significant 2 (Motivation: Non-Motivated *vs* Motivated) × PTSD (CAPS/PTSD Dx) interaction effect.

Following significant continuous Motivation × CAPS interactions, we conducted follow-up Pearson correlations to examine the relationships between CAPS scores and PES measures within each motivation condition. Following significant dichotomous Motivation × PTSD Dx interactions, we conducted independent-samples *t*-tests to compare PES in each motivation condition between the PTSD group and Deployed Control (DC) group. An identical analytic approach was employed for our secondary hypotheses regarding sustained inhibitory control (d-prime).

Based on visual inspection (see Supplemental Information), PES measures were approximately normally distributed in the Non-Motivated condition (Skewness = .90; Kurtosis = 1.12), Motivated condition (Skewness = .58; Kurtosis = 1.29), and the difference in PES between the Non-Motivated and Motivated conditions (Skewness = .04; Kurtosis = 1.72). However, Kolmogorov–Smirnov tests provided more mixed evidence of normality across PES measures. Specifically, these tests indicated that PES measures exhibited some deviations from normality in the Non-Motivated condition ($D(139) = .09$, $p = .01$) and Motivated condition ($D(139) = .09$, $p = .01$), but no deviations from normality for motivation-related differences in PES (i.e., Motivated PES − Non-Motivated PES; $D(139) = .07$, $p = .10$). Overall, PES measures generally met parametric assumptions for RM-ANCOVA models given that the Motivation × PTSD interaction effectively tests the relationship between PTSD and motivation-related differences in PES. Nevertheless, we also conducted secondary RM-ANCOVA models on log-transformed PES measures that exhibited more consistent evidence of normality based on Kolmogorov–Smirnov tests (all $Ds < .07$, all $ps > .12$).

4.6.2. *Control analyses*

4.6.2.1. Independence of PTSD-related differences in PES and d-prime. Some research suggests that PES is influenced by inhibitory control (Steinborn, Flehmig, Bratzke, & Schröter, 2012). Previous research also suggests that PTSD symptoms are associated with inhibitory control deficits (Dutra et al., 2018). To address these issues, we conducted control

analyses to determine if PTSD-related differences in PES were independent of sustained inhibitory control. First, we used Pearson correlations to test if motivation-related changes in PES (i.e., Non-Motivated PES − Motivated PES) were associated with motivation-related changes in d-prime (i.e., Non-Motivated dprime − Motivated dprime). Second, we regressed Non-Motivated and Motivated d-prime measures on Non-motivated and Motivated PES measures, which produced PES measures that were orthogonal to d-prime. Third, we repeated our RM-ANCOVA analyses using these residualized PES scores. Finally, we conducted partial correlations between CAPS scores and PES measures while controlling for d-prime measures within each motivation condition.

4.6.2.2. Independence of PTSD-related differences, combat exposure, and psychiatric comorbidities. In a second set of control analyses, we tested if the Motivation × PTSD interaction effects remained significant while controlling for several deployment-related and psychiatric variables. Specifically, we tested the effects of controlling for degree of combat exposure (DRRI-II), comorbid psychiatric conditions including current mood, anxiety, or substance use disorder (SCID), or the number of TBIs experienced during military deployment (BAT-L).

To this end, we repeated our primary Motivation × PTSD RM-ANCOVA models while separately including each of these variables as a covariate of non-interest. Like the primary RM-ANCOVA model, PES measures were entered as dependent variables with motivation condition (Non-Motivated *vs* Motivated) entered as a within-subjects factor. Similarly, PTSD was entered as a between-group factor using either a continuous (CAPS) or dichotomous (PTSD diagnosis) covariate of interest. For control RM-ANCOVA models, however, we also entered covariates of non-interest in the first step of the model. Specifically, combat exposure and number of military TBIs were each entered as a continuous covariate of non-interest, whereas current comorbid diagnoses (Mood disorders,

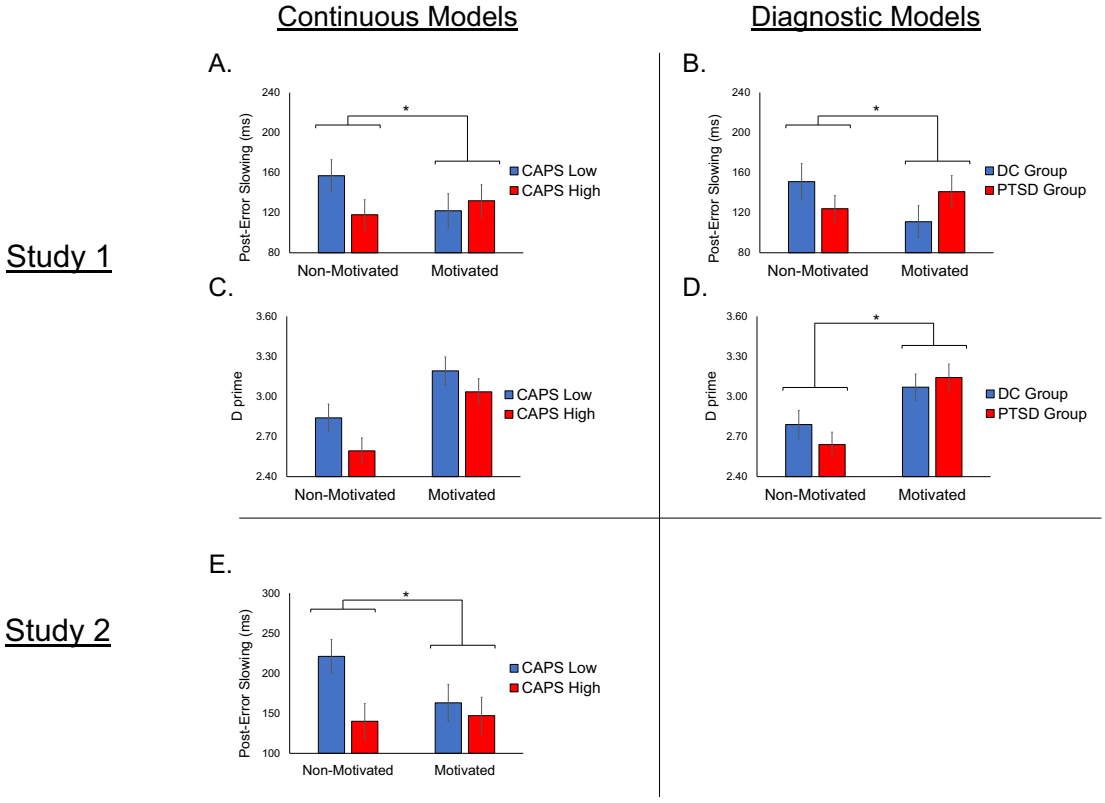

Fig. 2 − Motivation Normalizes PTSD-Related Differences in Post-Error Slowing. ***Legend*****: (A) In Study 1, PTSD symptom severity was linearly associated with smaller PES during the Non-Motivated condition, but not the Motivated condition. (B) In Study 1, the PTSD group (red bars) exhibited smaller PES in the Non-Motivated condition, but larger PES in the Motivated condition, compared to the Deployed-Control (DC) group (blue bars). (C) In Study 1, PTSD symptom severity was not linearly associated with motivation-related changes in d-prime. (D) In Study 1, the PTSD group (red bars) exhibited larger motivation-related increases in d-prime between the Non-Motivated and Motivated conditions compared to the DC group (blue bars). (E) Study 2 replicated the continuous model results of Study 1. In Study 2, PTSD symptom severity was again linearly associated with smaller PES during the Non-Motivated condition, but not the Motivated condition. *$p \leq .05$. Note: For display purposes only, continuous model results (A, C, & E) are depicted using simple slope intercepts estimated at high levels of PTSD symptoms (+1SD; Red) and low levels of PTSD symptoms (-1SD; Blue). However, we note that all continuous analyses were conducted using CAPS-IV scores as a continuous covariate. Continuous model results (A, C, & E) are also presented as scatterplots in the Supplemental Information.**

Anxiety disorders, or Substance use disorders) were each entered as a dichotomous covariate of non-interest.

5. Results

5.1. Error-related cognitive control (PES)

Within the *continuous* RM-ANCOVA model, we observed a significant Motivation × PTSD (CAPS-IV) interaction ($F_{(1,137)} = 3.92$, $p = .050$; $\eta_p^2 = .03$; see Fig. 2A). Using log-transformed PES measures, we observed a similar, but marginally significant, Motivation × PTSD interaction ($F_{(1,137)} = 3.51$, $p = .06$; $\eta_p^2 = .03$). Within the Non-Motivated condition, higher PTSD symptom severity was modestly associated with *smaller* PES ($r(137) = -.15$, $p = .08$; 95% CI [−.31, .02]). Within the Motivated condition, however, PTSD symptom severity was not associated with PES ($r(137) = .04$, $p = .64$; 95% CI [−.12, .21]).

Within the *diagnostic* RM-ANCOVA model, we also observed a significant Motivation × PTSD (Diagnosis) interaction ($F_{(1,137)} = 5.42$, $p = .02$, $\eta_p^2 = .04$; see Fig. 2B). Using log-transformed PES measures, we observed a similar Motivation × PTSD interaction ($F_{(1,137)} = 5.06$, $p = .03$; $\eta_p^2 = .04$). The Motivation × PTSD (Diagnosis) interaction was driven by opposite pattern of PTSD-related differences across the motivation conditions. In the Non-Motivated condition, the PTSD group ($M = 123.70$ ms, $SD = 113.69$) exhibited smaller PES compared to the DC group ($M = 150.60$ ms, $SD = 140.99$, $t(137) = 1.09$, $p = .28$, 95% CI [−.02, .07]). In the Motivated condition, however, the PTSD group ($M = 141.50$ ms, $SD = 137.95$) exhibited larger PES compared to the DC group ($M = 110.90$ ms, $SD = 131.75$; $t(137) = -1.33$, $p = .19$, 95% CI [−.08, .01]). In summary, the PTSD group exhibited non-significantly *smaller* PES in the Non-Motivated condition ($t(137) = 1.09$, $p = .28$), but non-significantly *larger* PES in the Motivated condition ($t(137) = -1.33$, $p = .19$), which produced a significant Motivation × PTSD interaction ($F_{(1,137)} = 5.42$, $p = .02$).

5.2. Sustained inhibitory control (d-prime)

Within the *continuous* RM-ANCOVA model, we did not observe a significant Motivation × PTSD (CAPS-IV) interaction ($F_{(1,144)} = .92$, $p = .38$; $\eta_p^2 = .01$; see Fig. 2C).

Within the *diagnostic* RM-ANCOVA model, however, we observed a significant Motivation × PTSD (Diagnosis) interaction ($F_{(1,144)} = 4.94$, $p = .03$; $\eta_p^2 = .03$; see Fig. 2D), which was driven by opposite pattern of PTSD-related differences across the motivation conditions. In the Non-Motivated condition, the PTSD group ($M = 2.63$, $SD = .83$) exhibited smaller d-prime compared to the DC group ($M = 2.79$, $SD = .87$; $t(144) = -1.09$, $p = .28$, 95% CI [−.12, .43]). In the Motivated condition, the PTSD group ($M = 3.14$, $SD = .89$) exhibited larger d-prime compared to the DC group ($M = 3.07$, $SD = .81$; $t(144) = .51$, $p = .61$, 95% CI [−.35, .21]). In summary, the PTSD group exhibited non-significantly *smaller* d-prime in the Non-Motivated condition ($t(144) = -1.09$, $p = .28$), but non-significantly *larger* PES in the Motivated condition ($t(144) = .51$, $p = .61$), which produced a significant Motivation × PTSD interaction ($F_{(1,144)} = 4.94$, $p = .03$).

5.3. Control analyses

5.3.1. Independence of PTSD-related differences in PES and d-prime

First, Pearson correlations demonstrated that motivation-related changes in PES were not associated with motivation-related changes in d-prime ($p = .31$). Second, using residualized PES values, the Motivation × PTSD interaction remained essentially unchanged for both the continuous model ($p = .056$) and diagnostic model ($p = .01$), but became marginally significant in the continuous control model. Third, partial correlations controlling for d-prime continued to demonstrate an association between CAPS scores and smaller PES in the Non-Motivated condition ($r(136) = -.18$, $p = .04$), which was not observed in the Motivated condition ($r(136) = .02$, $p = .84$).

5.3.2. Independence of PTSD-related differences, combat exposure, and psychiatric comorbidities

When controlling for individual differences in combat exposure, we continued to observe a significant Motivation × PTSD interaction for both the continuous RM-ANCOVA PES model ($p = .03$) and dichotomous RM-ANCOVA model ($p = .02$). When controlling for psychiatric comorbidities (i.e., Current Mood Disorder, Current Anxiety Disorder, Current Substance Use Disorder, or number of military TBIs), the Motivation × PTSD (CAPS-IV) interaction remained significant or marginally significant across the continuous control models ($ps = .04$–$.08$) and remained significant across all diagnostic control models ($ps = .02$–$.03$).

6. Discussion

Consistent with our hypotheses, PTSD was associated with smaller PES in the Non-Motivated condition, but not when task performance was incentivized in the Motivated condition. Although we originally hypothesized that incentivizing task performance would normalize error-related cognitive control in PTSD by *increasing* PES, we observed a more complex pattern of motivation-related changes. Specifically, PTSD symptomatology was characterized by relatively *smaller* PES in the Non-Motivated condition, but relatively *larger* PES in the Motivated condition. Contrary to our original hypotheses, however, lower PTSD symptom severity was unexpectedly characterized by relatively *smaller* PES in the Motivated condition.

When considered in isolation, motivation-related differences in the relationship between PTSD and PES could be interpreted in two, mutually exclusive manners. First, the Motivated condition may *adaptively* normalize error-related cognitive control processes in PTSD. This adaptive interpretation is consistent with the reduced association between PTSD symptom severity and PES observed in the motivated condition (see Fig. 2). Alternatively, it could be argued that PTSD is characterized by a *maladaptive* failure to reduce PES in the Motivated condition unlike individuals with lower PTSD symptom severity. Based on motivation-related changes in d-prime, however, we believe the PES results are more consistent with the *adaptive* normalization hypothesis. Specifically,

incentivization robustly increased d-prime in both the PTSD and DC groups, which reduced PTSD-related differences in sustained inhibitory control (see Fig. 2). Given that PTSD was associated with motivation-based improvements in sustained inhibitory control, we believe that these PES results are more consistent with an adaptive normalization of error-related cognitive control deficits in PTSD.

Nevertheless, it is notable that low PTSD symptom severity was unexpectedly associated with a *decrease* in PES in the motivated condition, rather than an *increase* in PES as originally hypothesized. This pattern of PES results may be explained by the contribution of two distinct control processes to error-related cognitive control. Dual-Mechanism frameworks propose that control processes may be *reactively* recruited to adjust behavior *after* attentional lapse or *proactively* recruited to adjust behavior *before* an attentional lapse (Braver, 2012). Specifically, utilizing reactive control processes *after* an error produces larger behavioral adjustments (e.g., *larger* PES), whereas utilizing proactive control processes *before* an error reduces the need for behavioral adjustments (e.g., *smaller* PES). In the Non-Motivated condition, lower PTSD symptom severity was characterized by comparatively larger PES and larger d-prime, which may reflect adaptive use of reactive control processes. In the Motivated condition, however, individuals with less severe PTSD symptoms may increasingly utilize *proactive* control processes. Consistent with this interpretation, low PTSD symptom severity was associated with *decreased* PES and *increased* d-prime in the Motivated condition. This pattern of results mirrors healthy control samples who demonstrate a shift toward utilizing proactive control processes when task performance is incentivized (Esterman, Poole, Liu, & DeGutis, 2017; Savine & Braver, 2010). In contrast, individuals with higher PTSD symptom severity in the Motivated condition demonstrated an increase in both PES and d-prime, which may suggest better utilization of *reactive* control processes and/or less utilization of proactive control processes.

Prior to further discussion, however, PTSD-related differences in PES were relatively modest and became marginally significant in several control analyses, which necessitates replication in an independent sample (see Study 2). Additionally, exogeneous reward and punishment may normalize error-related cognitive control in PTSD via several distinct mechanisms, which cannot be disentangled using RT measures. In order to replicate and disentangle the mechanisms that contribute to normalization of error-related cognitive control in PTSD, Study 2 utilized functional magnetic response imaging (fMRI) in conjunction with the incentivized gradCPT paradigm in an independent sample of post-9/11 veterans.

7. Study 2

Based on a triple network framework of psychopathology (Menon, 2011), recent research suggests that PTSD symptomatology may disrupt activation and connectivity of the salience network (SN), frontoparietal control network (FPCN), and default mode network (DMN; for a review, see Akiki, Averill, & Abdallah, 2017). Specifically, PTSD is putatively characterized by hyperactivity of the SN, which lowers the threshold for orienting attention to stimuli as evidenced by hypervigilant patterns of attention (Yoon & Weierich, 2016). Moreover, the SN is directly involved in error-related processing, which recruits the FPCN to facilitate behavioral adjustments (Ham, Leff, de Boissezon, Joffe, & Sharp, 2013; Velanova, Wheeler, & Luna, 2008). Relatedly, individuals with PTSD putatively exhibit impaired FPCN activation, which disrupts top-down modulation of attention such as post-error behavioral adjustments (Hamilton & Grafton, 2007; Swick, Honzel, Larsen, & Ashley, 2013). Finally, PTSD is also characterized by weaker DMN *de*activation, which disrupts inhibition of intrusive, internal experiences (Tursich et al., 2015). Moreover, weaker DMN *de*activation is also associated with impaired error-related cognitive control as evidenced by more errors and mind-wandering (Fortenbaugh et al., 2018; Kucyi, Hove, Esterman, Hutchison, & Valera, 2017). Thus, PTSD is associated with dysregulation within a triple network system that also plays a key role in facilitating error-related cognitive control.

Although PTSD is putatively characterized by disrupted connectivity across this triple network system, the SN likely plays the most critical role in error-related cognitive control (Ham et al., 2012). Hyperactivation of the SN may non-selectively assign salience value to external stimuli, which impairs selective allocation of attention (Yoon & Weierich, 2016). In PTSD, non-specific SN activation to both errors and correct responses may produce SN-FPCN hyperconnectivity, which subsequently impairs error-related cognitive control (Rabellino et al., 2015). Similarly, SN hyperactivation may non-selectively assign high salience value to internal stimuli (e.g., intrusive thoughts), which disrupts attention towards external stimuli. In PTSD, hyperconnectivity between the SN and DMN may augment processing of interoceptive information or intrusive thoughts at the expense of recruiting error-related cognitive control (Sripada et al., 2012). In summary, PTSD has been characterized by hyperactivation of the SN as well as exaggerated SN-FPCN and SN-DMN connectivity (Akiki et al., 2017), which may contribute to dysregulated error-related cognitive control in PTSD. Guided by the central role of the SN in supporting error-related cognitive control, Study 2 aimed to test three alternative hypotheses regarding the mechanisms by which incentivization normalizes error-related cognitive control in PTSD.

First, the SN amelioration hypothesis predicts that maladaptive PTSD-related differences in SN activation/connectivity will be observed in the Non-Motivated condition, but these maladaptive differences are *ameliorated* in the Motivated condition. In the Non-Motivated condition, PTSD symptom severity will be associated with greater SN activation/connectivity to both errors and correct responses (i.e., *maladaptive* PTSD-related differences), which impairs recruitment of error-related cognitive control. In the Motivated condition, however, PTSD symptom severity will be characterized by *similar* error-specific SN activation/connectivity (i.e., no PTSD-related differences), which serves to *ameliorate* deficits in error-related cognitive control. In summary, the SN amelioration hypothesis posits that PTSD symptoms disrupt SN activation/connectivity during non-motivated states, which is normalized during motivated states via exogeneous reward and punishment.

Second, the SN augmentation hypothesis predicts that PTSD-related differences in SN activation/connectivity will not be observed in the Non-Motivated condition, but that *compensatory* PTSD-related differences will be observed in the Motivated condition. In the Non-Motivated condition, PTSD symptom severity will not be associated with SN activation/connectivity (i.e., no PTSD-related differences). In the Motivated condition, however, PTSD symptom severity will be associated with *greater* error-specific SN activation/connectivity (i.e., *compensatory* PTSD-related differences), which serves to *augment* error-related cognitive control. In summary, the SN augmentation hypothesis posits that PTSD symptoms do not disrupt SN function during non-motivated states, but intact SN function is not sufficient to produce error-related cognitive control in PTSD. In motivated states, however, exogeneous reward and punishment augments SN function in PTSD above normative levels, which normalizes error-related cognitive control in a compensatory fashion.

Third, the SN reinforcement hypothesis predicts that PTSD symptom severity will be not be associated with SN activation/connectivity in either the Non-Motivated or Motivated condition. Instead, PTSD symptom severity will be associated with activation/connectivity of distinct neural mechanisms outside the triple network system (e.g., striatal reward system), which serves to *reinforce* error-related cognitive control. In summary, the SN reinforcement hypothesis posits that error-related cognitive control deficits in PTSD are not directly attributable to SN dysfunction in isolation. Instead, PTSD symptoms disrupt the functioning of neural circuits that reinforce the triple network system, which are re-established by exogeneous rewards and punishment.

To summarize, the SN amelioration hypothesis predicts that PTSD symptoms will be associated with greater, *non-focal* SN activation/connectivity to both errors and correct responses during the Non-Motivated condition (High PTSD: CE = CO; Low PTSD: CE > CO), which is *normalized* in the Motivated condition (High PTSD: CE > CO; Low PTSD: CE > CO). In contrast, the SN augmentation hypothesis predicts that PTSD symptoms will not be associated with error-related SN function during the Non-Motivated condition (High PTSD: CE > CO; Low PTSD: CE > CO), but will instead be associated with *augmentation* of error-related SN activation/connectivity during the Motivated condition (High PTSD: CE >>> CO; Low PTSD: CE > CO). Finally, the SN reinforcement hypothesis predicts that PTSD symptoms will not be associated with SN activation/connectivity in either the Non-Motivated condition or Motivated condition (High PTSD: CE > CO; Low PTSD: CE > CO). Instead, the SN reinforcement hypothesis predicts that PTSD symptoms will be associated with greater error-related activation of circuits *outside* the triple network system during the Motivated condition, which does not occur at lower levels of PTSD symptoms (High PTSD: CE > CO; Low PTSD: CE = CO).

To arbitrate among these hypotheses, Study 2 administered the incentivized gradCPT during fMRI scanning to examine PTSD-related differences in error-related neural activation and neural connectivity. To address the amelioration and augmentation hypotheses, we separately examined PTSD-related associations with error-related SN activation and SN-FPCN/SN-DMN connectivity in the Non-Motivated and Motivated conditions. To address the reinforcement hypothesis, we conducted exploratory whole-brain analyses to identify PTSD-related differences in error-related activation outside the triple network system.

8. Method

8.1. Participants

In Study 2, an *independent* sample of 45 Veterans (see Table 1 for sample characteristics) were recruited from the larger TRACTS cohort. Like Study 1, Veterans were excluded if they reported a history of moderate/severe TBI ($n = 2$), exhibited significant neurological impairment ($n = 0$), or failed the MSVT ($n = 3$).

8.2. Task-based participant exclusions

First, response data was not collected for one participant due to technical failure. Second, some participants ($n = 3$) exhibited a failure to respond to >50% of gradCPT trials or to respond on 37 or more consecutive trials (Fortenbaugh et al., 2018). Finally, one subject was removed due to excessive motion during the fMRI scan (>30% TRs censored). Following these exclusions, all behavioral and neural analyses were conducted in a final sample of 35 veterans (see Table 1).

8.3. Procedure

All measures and procedures for Study 2 were identical to Study 1. Research procedures were conducted in accordance with the Institutional Review Board of Human Studies Research at the VA Boston Healthcare System. Veterans provided written consent and were equally compensated for their participation regardless of gradCPT task performance. Sample size was not determined *a priori*, but was instead limited to the number of veterans who agreed to complete task fMRI scanning as part of the larger TRACTS program. Study procedures and analyses were not pre-registered prior to the research being conducted.

8.4. fMRI data acquisition

fMRI data were collected using a 3T Siemens MAGNETON Prisma system scanner (Erlangen, Germany) with a 20-channel head coil. For functional imaging, multi-band acceleration was employed (TR = 750 ms, TE = 37 ms, flip angle = 52°, FOV = 208 mm × 208 mm, 72 interleaved axial slices, acceleration factor = 8, 2 mm^3). Additionally, two anatomical magnetization-prepared rapid gradient-echo (MPRAGE) structural scans were collected for co-registration and aggregated using FreeSurfer (TR = 2530 ms, TE = 3.32 ms, flip angle = 7°,1 mm^3). Preprocessing was carried out in two stages using fMRIPrep software and Analysis of Functional NeuroImages (AFNI) software (Cox, 1996; Esteban et al., 2019; for preprocessing details, see Supplemental Information). Network templates for the SN, FPCN, and DMN were defined using a standardized 7-network parcellation (Yeo et al., 2011).

8.5. Data processing

8.5.1. Neural activation

To compute a network-based composite measure of neural *activation*, we averaged activation estimates across all voxels within a given network based on a 7-network standardized network parcellation (Yeo et al., 2011). For example, Salience Network activation for each participant was estimated by averaging task-related activation for all voxels within a standardized Salience Network (SN) template. Using this network-based approach, we quantified composite metrics of event-related activation for the SN, FPCN, and DMN (see network templates in Fig. 3).

To compute neural activation measures, first-level GLMs modeled both stimulus events (correct omissions, commission errors, and omission errors) as well as block events (Non-Motivated and Motivated). Correct commission trials were modeled as part of the baseline model. Stimulus events and block events were respectively modeled using an impulse function or box car function, which was subsequently convolved with a gamma variate function. Nuisance regressors included 24 motion parameters (6 rigid body regressors, temporal derivatives, and quadratic terms), the mean timeseries extracted from WM and CSF masks, and a linear trend to model slow drift throughout the scan session.

For whole-brain exploratory analyses, we used AFNI's 3dLME program (Chen, Saad, Britton, Pine, & Cox, 2013). To control family-wise error (FWE), we used a combined voxel-wise and cluster threshold estimated with a more stringent non-parametric model (Cox, Chen, Glen, Reynolds, & Taylor, 2017). Based on a voxel-wise threshold of $p \leq .001$ and the observed smoothness of estimated residuals (ACF parameters: .82, 5.25, 16.78), a 102-voxel (816 mm^3) cluster level threshold corrected for multiple comparisons at $p \leq .05$.

8.5.2. Neural connectivity

Similar to neural activation analyses, we computed a network-based composite measure of task-related SN-FPCN and SN-DMN connectivity for statistical analyses. Specifically, we averaged all voxel timeseries within the standardized SN template to create a composite SN "seed" timeseries. Next, we modelled gPPI task-related connectivity from the composite SN "seed" timeseries to a composite FPCN or DMN "target" timeseries. Using this network-based approach, we quantified composite measures of task-related network-to-network connectivity.

To compute network-to-network connectivity, we used a generalized form of context-dependent psychophysiological interaction analyses (gPPI; McLaren, Ries, Xu, & Johnson, 2012). For first-level connectivity models, we computed interaction terms between the time series of each neural network and task regressors. As stimulus onset times were slightly desynchronized with TR acquisition (800 ms *vs* 750 ms), we upsampled the neuronal time series and task regressors. Next, we convolved the upsampled neuronal time series with the upsampled stimulus (impulse) or block (box car) regressors. After computing gPPI regressors, gPPI interaction terms were downsampled back to the original TR resolution of the fMRI data (750 ms).

To ensure that differences in gPPI connectivity were orthogonal to stimulus-evoked activation and intrinsic connectivity, first-level gPPI models included event-related regressors that modeled event-related activation as well as the mean time series of the seed network. First-level gPPI models employed identical nuisance regressors (24 motion parameters, CSF signal, WM signal, and linear drift parameter) and motion censoring procedures used for activation analyses.

8.6. Data analytic approach

All statistical analyses were conducted using SPSS software ver. 24.0 (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM). For all analyses, we considered PTSD-related differences to be significant at a threshold of $p \leq .05$ (two-tailed).

8.6.1. Behavioral analyses

In Study 2, we exclusively used a continuous analysis approach given the small sample size. Identical to the RM-ANCOVA model in Study 1, PES measures were entered as the dependent variables and motivation condition (Non-Motivated *vs* Motivated) was entered as a within-subjects factor. Additionally, PTSD symptoms (CAPS) were entered as a between-group factor, which were modeled as a continuous covariate of interest. Using this approach, we again tested for a significant Motivation × CAPS interaction effect. To decompose a significant Motivation × CAPS interaction, we again used Pearson correlations to test the relationship between CAPS scores and PES within the Non-Motivated and Motivated conditions separately.

Based on visual inspection (see Supplemental Information), PES scores were approximately normally distributed in both the Non-Motivated condition (Skewness = .90; Kurtosis = 1.12) and Motivated condition conditions (Skewness = .19; Kurtosis = −.59). Similarly, Kolmogorov–Smirnov tests demonstrated consistent evidence of normality for Non-Motivated PES ($D(35) = .07$, $p = .92$), Motivated PES ($D(139) = .08$, $p = .78$), and the difference in PES between the Non-Motivated and Motivated conditions ($D(139) = .12$, $p = .21$). Nevertheless, we also conducted secondary RM-ANCOVA analyses using log-transformed PES measures to replicate Study 1.

8.6.2. Neural analyses

Given our *a priori* hypotheses and relatively small sample, we did not conduct more complex 3-way interaction models for neural analyses. Instead, we examined PTSD-related associations with error-related contrasts in the Non-Motivated and Motivated condition separately (i.e., 2-way interaction effects). To isolate error-related neural signatures in each motivation condition, we contrasted neural activation and neural connectivity during commission error trials (CE) and correct omission trials (CO). Specifically, we tested for PTSD-related interactions in neural activity and neural connectivity measures using RM-ANCOVA models. In

these models, neural activity or neural connectivity measures were entered as dependent variables and Trial (CE *vs* CO) was entered as a within-subjects factor. Additionally, PTSD symptoms (CAPS) were entered as a between-group factor, which was modeled as a continuous covariate of interest. Using this approach, we tested for a significant Trial × CAPS interaction effect within each motivation condition separately. To decompose significant Trial × CAPS interactions, we separately examined associations between CAPS scores and neural activation/connectivity on CE trials and CO trials.

In addition to being aligned with our hypotheses, this analysis approach ensures that PTSD-related differences were specific to error-related cognitive control (i.e., CE − CO), rather than general reactivity to infrequent mountain trials (e.g., an oddball effect). Additionally, we repeated all neural analyses while controlling for individual differences in head motion using the Euclidean norm of the 6 linear motion temporal derivatives (i.e., AFNI ENORM), which was computed for all non-censored TRs. All PTSD-related effects remained significant after controlling for head motion with the exception of one effect (FPCN activation), which we describe in the respective results section.

8.6.3. *Brain–behavior relationships*

To limit multiple comparisons, we exclusively conducted brain-behavior analyses using activation/connectivity derived from neural networks that exhibited significant PTSD-related interactions. Within each motivation condition, we correlated PES with the corresponding error-related contrast (i.e., CE–CO).

9. Results

9.1. *Behavioral analyses*

Replicating Study 1, we observed a significant Motivation × CAPS interaction ($F_{(1,33)} = 4.34$, $p = .045$, $\eta_p^2 = .12$; see Fig. 2E). Using log-transformed PES measures, we also observed a significant Motivation × PTSD interaction ($F_{(1,33)} = 4.73$, $p = .04$; $\eta_p^2 = .12$). Within the Non-Motivated condition, PTSD symptom severity was associated with *smaller* PES ($r(34) = -.43$, $p = .01$, 95% CI [−.67, −.11]; see Fig. 2E). Within the Motivated condition, however, PTSD symptom severity was not associated with PES ($r(34) = -.09$, $p = .62$, 95% CI [−.41, .25]; see Fig. 2E).

9.2. *Control analyses*

9.2.1. *Independence of PTSD-related differences in PES and d-prime*

First, we observed that motivation-related changes in PES were not associated with motivation-related changes in d-prime ($p = .22$). Second, using residualized PES values, the Motivation × CAPS interaction remained significant ($p = .03$). Third, partial correlations controlling for d-prime continued to demonstrate an association between CAPS scores and smaller PES in the Non-Motivated condition ($r(32) = -.43$, $p = .01$), which was not observed in the Motivated condition ($r(32) = -.07$, $p = .70$).

9.3. *Neural activation analyses*

9.3.1. *Salience network (SN)*

In the Non-Motivated condition, we did not observe a significant CAPS × Trial interaction ($F_{(1,33)} = .24$, $p = .63$, $\eta_p^2 = .01$). However, we did observe a significant main effect of CAPS ($F_{(1,33)} = 8.11$, $p = .008$, $\eta_p^2 = .20$). Specifically, higher PTSD symptom severity was associated with greater SN activation to both CE and CO trials (see Fig. 3A).

In the Motivated condition, however, we did observe a significant CAPS × Trial interaction ($F_{(1,33)} = 5.13$, $p = .03$, $\eta_p^2 = .13$; see Fig. 3B). Follow-up analyses demonstrated that higher CAPS scores were associated with greater SN activation to punished CEs ($r(34) = .38$, $p = .03$, 95% CI [.05, .63]), but not to rewarded COs ($r(34) = .01$, $p = .96$, 95% CI [−.32, .34]).

9.3.2. *Frontoparietal control network (FPCN)*

In the Non-Motivated condition, we did not observe a significant CAPS × Trial interaction ($F_{(1,33)} = .38$, $p = .85$, $\eta_p^2 = .001$). However, we did observe a significant main effect of PTSD symptom severity ($F_{(1,33)} = 4.19$, $p = .049$, $\eta_p^2 = .11$). In response to both CE and CO trials, PTSD symptom severity was associated with greater FPCN activation (see Fig. 3C). However, we note that the main effect of CAPS on FPCN activation became marginally significant after controlling for head motion ($p = .049$ *vs* $p = .08$). Although head motion did not exert a main effect or interactive effect on FPCN activation (both *p*s > .20), this nevertheless suggests that PTSD-related differences in FPCN activation should be interpreted more cautiously.

In the Motivated condition, we did not observe a significant CAPS × Trial interaction ($F_{(1,33)} = 1.33$, $p = .26$, $\eta_p^2 = .04$) or main effect of CAPS ($F_{(1,33)} = .04$, $p = .84$, $\eta_p^2 = .001$; see Fig. 3D).

9.3.3. *Default mode network (DMN)*

In the Non-Motivated condition, we did not observe a significant CAPS × Trial interaction ($F_{(1,33)} = .17$, $p = .68$, $\eta_p^2 = .001$) or main effect of CAPS ($F_{(1,33)} = 3.24$, $p = .08$, $\eta_p^2 = .09$; see Fig. 3E).

In the Motivated condition, we did not observe a significant CAPS × Trial interaction ($F_{(1,33)} = .74$, $p = .68$, $\eta_p^2 = .02$) or main effect of CAPS ($F_{(1,33)} = .74$, $p = .40$, $\eta_p^2 = .02$; see Fig. 3F).

9.3.4. *Whole brain exploratory analysis*

In the Non-Motivated condition, no clusters survived FWE correction for the CAPS × Trial interaction.

In the Motivated condition, however, whole-brain analyses revealed a cluster bordering the left Superior Parietal Lobule and extending into the dorsal aspect of the left Precuneus (SPL/PCu; [0, −68, 48], 186 voxels, 1488, mm^3) that survived the FWE threshold for the CAPS × Trial interaction (uncorrected: $F_{(1,33)} = 11.37$, $p < .001$; see Fig. 3H). Follow-up Pearson correlations demonstrated that PTSD symptom severity was associated with greater SPL/PCu activation to

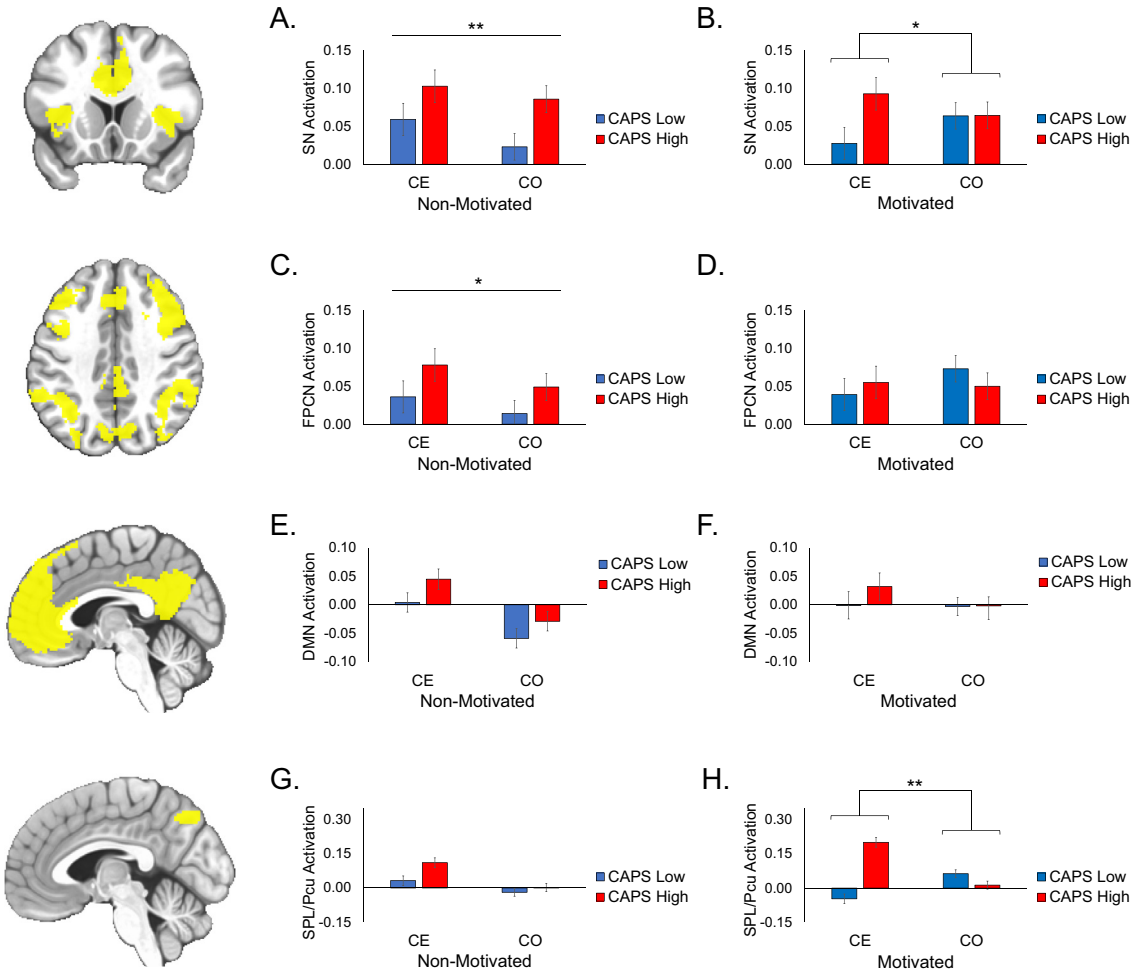

Fig. 3 – PTSD Associations with Task-Related Neural Network Activation. *Legend*: PTSD-related differences in event-related activation for commission errors (CE) and correct omissions (CO) during Non-Motivated (A, C, E, H) and Motivated (B, D, F, G) conditions within the incentivized gradCPT paradigm. For panels A–F (yellow overlay), *a priori* network-based masks were derived using the Yeo 7-network parcellation for the Salience Network (SN; A & B), Frontoparietal Control Network (FPCN; B), and Default Mode Network (DMN; C). For panels H & G (yellow overlay), a Superior Parietal Lobule/Precuneus (SPL/PCu) cluster survived multiple-comparison correction for whole-brain voxel-wise exploratory analyses. (A) In the Non-Motivated condition, PTSD symptoms were linearly associated with greater SN activation in response to both CE and CO trials. (B) In the Motivated condition, PTSD symptoms were linearly associated with greater SN activation to CE trials, but not CO trials. (C) In the Non-Motivated condition, PTSD symptoms were linearly associated with greater FPCN activation in response to both CE and CO trials. (D) In the Motivated condition, PTSD symptoms were not associated with FPCN activation to CE or CO trials. (E & F) PTSD symptoms were not associated with DMN activation to CE or CO trials in the Non-Motivated or Motivated conditions. (G) In the Non-Motivated condition, PTSD symptoms were not associated with SPL/PCu activation to CE or CO trials. (H) In the Motivated condition, PTSD symptoms were linearly associated with greater SPL/PCu activation to CE trials, but not CO trials. *$p \leq .05$; **$p \leq .01$, ***$p \leq .001$. Note: For display purposes, neural activation measures are depicted using simple slope intercepts estimated at high levels of PTSD symptoms (+1SD; Red) and low levels of PTSD symptoms (-1SD; Blue). However, we note that all statistical analyses were conducted using CAPS-IV scores as a continuous covariate. All neural activation results are also presented as scatterplots in the Supplemental Information.

punished CEs ($r(34) = .48$, $p = .004$, 95% CI [.17, .70]), but not associated with SPL/PCu activation to rewarded COs ($r(34) = -.22$, $p = .20$, 95% CI [−.51, .12]). Consistent with FWE-corrected results, we did not observe a CAPS × Trial interaction for this SPL/PCu cluster at an uncorrected threshold within the Non-Motivated condition (uncorrected: $F_{(1,33)} = .94$, $p = .34$; see Fig. 3G).

9.4. *Neural connectivity analyses*

9.4.1. *SN-FPCN connectivity*

In the Non-Motivated condition, we did not observe a significant CAPS × Trial interaction ($F_{(1,33)} = .003$, $p = .90$, $\eta_p^2 < .001$) or main effect of PTSD ($F_{(1,33)} = .03$, $p = .99$, $\eta_p^2 < .001$; see Figs. 4A and 5E).

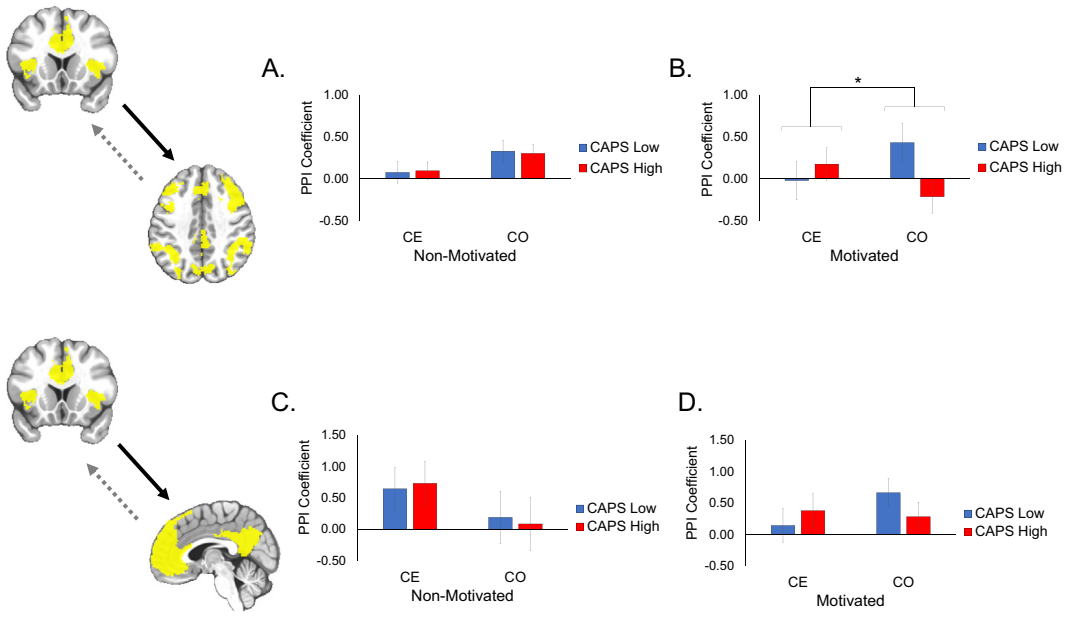

Fig. 4 – PTSD Associations with Salience Network Task-Related Connectivity. *Legend:* PTSD-related differences in task-related connectivity for commission errors (CE) and correct omissions (CO) during Non-Motivated (A & C) and Motivated (B & D) conditions within the incentivized gradCPT paradigm. For panels A & B (yellow overlay), the Yeo 7-network parcellation was used to generate a composite Salience Network (SN) seed timeseries as well as a composite Frontoparietal Control Network (FPCN) target timeseries and Default Mode Network (DMN) target timeseries. To estimate task-related connectivity, we used these network-based composite timeseries in conjunction with generalized psychophysiological interaction (gPPI) analyses. (A) In the Non-Motivated condition, PTSD symptoms were not associated with SN-FPCN connectivity. (B) In the Motivated condition, PTSD symptoms were linearly associated with weaker SN-FPCN connectivity to CO trials, but not CE trials. (C & D) PTSD symptoms were not associated with SN-DMN connectivity in the Non-Motivated or Motivated conditions. *$p \leq .05$; **$p \leq .01$, ***$p \leq .001$. Note: For display purposes, neural connectivity measures are depicted using simple slope intercepts estimates at high levels of PTSD symptoms (+1SD; Red) and low levels of PTSD symptoms (-1SD; Blue). However, we note that all statistical analyses in Study 2 were conducted using CAPS-IV scores as a continuous covariate. All neural connectivity results are also presented as scatterplots in the Supplemental Information.

In the Motivated condition, however, we observed a significant CAPS × Trial interaction ($F_{(1,33)} = 6.92$, $p = .01$, $\eta_p^2 = .17$; see Figs. 4B and 5F). Follow-up analyses demonstrated that PTSD symptoms severity was not associated with SN-FPCN connectivity to punished CEs ($r(34) = .13$, $p = .48$, 95% CI [−.21, .44]), but was associated with *weaker* SN-FPCN connectivity to rewarded COs ($r(34) = -.45$, $p = .006$, 95% CI [−.68, −.14]). Notably, this pattern of results was not observed when neural connectivity was modeled in the reverse direction (i.e., FPCN–SN; see Supplemental Information).

9.4.2. *SN-DMN connectivity*

In the Non-Motivated condition, we did not observe a significant CAPS × Trial interaction ($F_{(1,33)} = .70$, $p = .79$, $\eta_p^2 = .002$; see Fig. 4C) or main effect of PTSD ($F_{(1,33)} < .01$, $p = .98$, $\eta_p^2 < .001$).

In the Motivated condition, we similarly did not observe a significant CAPS × Trial interaction ($F_{(1,33)} = 2.24$, $p = .14$, $\eta_p^2 = .06$) or main effect of PTSD ($F_{(1,33)} = .79$, $p = .79$, $\eta_p^2 = .002$; see Fig. 4D).

9.5. *Brain–behavior analyses*

9.5.1. *SN activation*

In the Non-Motivated condition, we did not observe a significant correlation between error-related SN activation and PES ($r(34) = -.09$, $p = .59$, 95% CI [−.41, .25]). In the Motivated condition, we similarly did not observe a correlation between error-related SN activation and PES ($r(34) = .06$, $p = .76$, 95% CI [−.27, .39]).

9.5.2. *SN-FPCN connectivity*

In the Non-Motivated condition, we observed a significant correlation between error-related SN-FPCN connectivity and PES ($r(34) = .39$, $p = .02$, 95% CI [.06, .64]; see Fig. 5A). Follow-up analyses demonstrated that larger PES was associated with *stronger* SN-FPCN connectivity to CEs ($r(34) = .50$, $p = .002$, 95% CI [.20, .71]), but was not associated with SN-FPCN connectivity to COs ($r(34) = -.05$, $p = .77$, 95% CI [−.38, .29]).

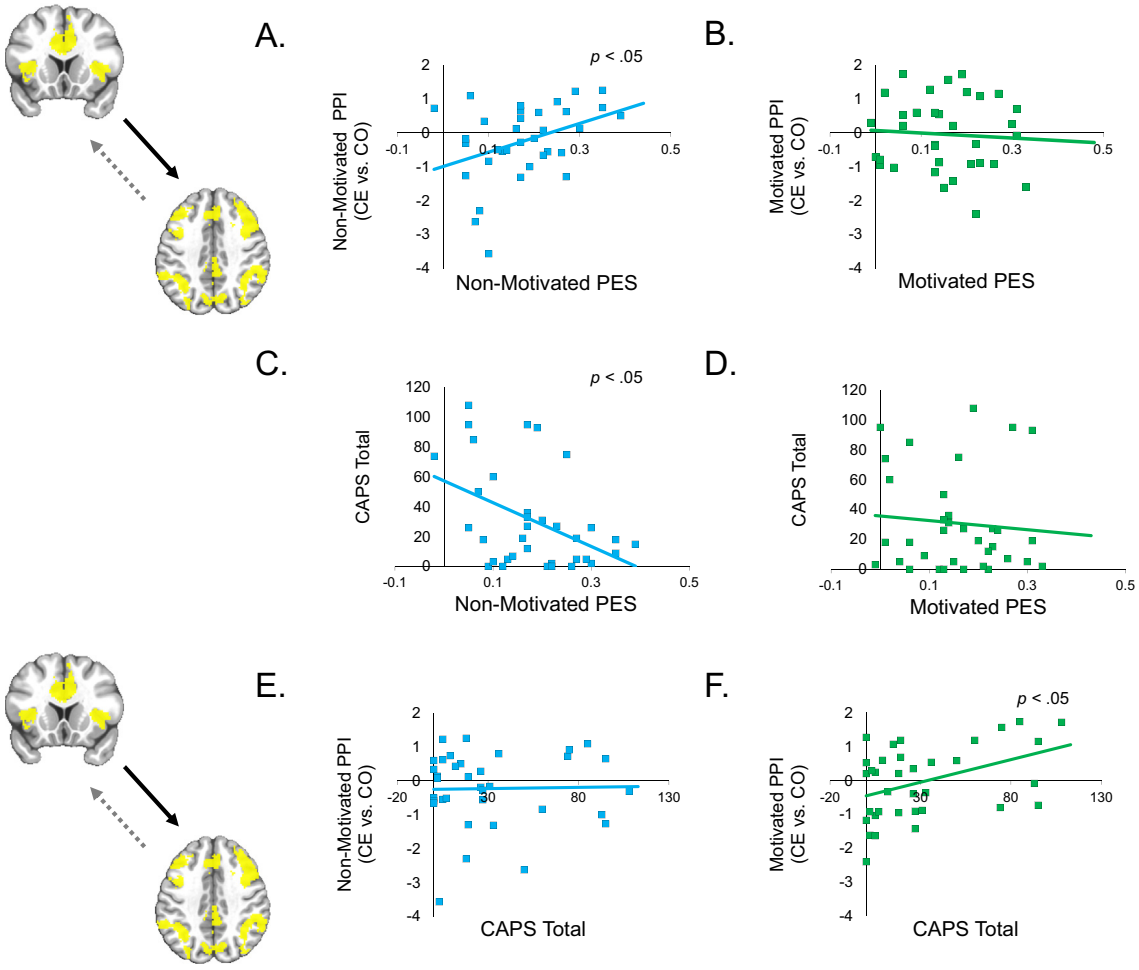

Fig. 5 – Error-Related Connectivity between the Salience Network and Frontoparietal Control Network is Differentially Associated with Post-Error Slowing and PTSD Symptoms. ***Legend:*** **Task-related connectivity was estimated between the Salience Network (SN; yellow overlay) and Frontoparietal Control Network (FPCN; yellow overlay) using generalized psychophysiological interaction (gPPI) analyses. Error-related connectivity was computed by contrasting gPPI estimates for commission errors and correct omissions (CE *vs* CO). Error-related SN-FPCN connectivity exhibited differential associations with PES and PTSD symptoms in the Non-Motivated (blue scatter) and Motivated (green scatter) task conditions. (A) SN-FPCN error-related connectivity was linearly associated with larger PES in the Non-Motivated condition. (B) SN-FPCN error-related connectivity was not associated with PES in the Motivated condition. (C) PTSD symptoms were associated with PES in the Non-Motivated condition. (D) PTSD symptoms were not associated with PES in the Motivated condition. (E) SN-FPCN error-related connectivity was not associated with PTSD symptoms in the Non-Motivated condition. (F) Greater SN-FPCN error-related connectivity was linearly associated with higher PTSD symptoms in the Motivated condition. *$p \leq .05$; **$p \leq .01$, ***$p \leq .001$.**

In the Motivated condition, however, we did not observe a correlation between error-related SN-FPCN connectivity and PES ($r(34) = -.05$, $p = .77$, 95% CI [−.38, .29]), (see Fig. 5B).

10. Discussion

In Study 2, we replicated the behavioral results observed in Study 1. To summarize, PTSD symptoms were again associated with weaker error-related cognitive control in the Non-Motivated condition, but not when task performance is incentivized in the Motivated condition. In addition to replicating the behavioral results of Study 1, we also extended these behavioral results by demonstrating a similar motivation-based dissociation in the relationship between PTSD symptomatology, SN activation, and SN-FPCN connectivity. Within the Non-Motivated condition, PTSD symptom severity was associated with greater SN and FPCN activation on both CE and CO trials. In the Motivated condition, however, PTSD symptom severity was associated with greater error-related activation of the SN and an SPL/PCu cluster within the FPCN (see Fig. 3B and H). Similarly, PTSD symptom severity was not associated with error-related SN-FPCN connectivity in the Non-Motivated condition, but PTSD symptom severity was associated with greater error-related SN-FPCN connectivity in the Motivated condition (see Fig. 4B). Together,

these results were most consistent with the SN augmentation hypothesis. Specifically, PTSD symptom severity was associated with more error-specific SN activation and connectivity in the Motivated condition, which may serve a compensatory function to normalize PES.

Notably, brain–behavior relationships mirrored brain–symptom relationships. Specifically, error-related SN-FPCN connectivity was associated with PES in the Non-Motivated condition, but not in the Motivated condition (see Fig. 5A and B). Similarly, PTSD symptom severity was associated with PES in the Non-Motivated condition, but not in the Motivated condition (see Fig. 5C and D). In contrast, PTSD symptom severity was associated with error-related SN-FPCN connectivity in the Motivated condition, but not in the Non-Motivated condition (see Fig. 5E and F). In summary, correlations between SN-FPCN connectivity and PES (i.e., brain-behavior) as well as correlations between PTSD and PES (i.e., symptom-behavior) were observed exclusively in the Non-Motivated condition, whereas correlations between PTSD and SN-FPCN connectivity (i.e., symptom-brain) were observed exclusively in the Motivated condition.

11. General discussion

Across two independent samples, PTSD symptom severity was associated with weaker error-related cognitive control in non-motivated states, which was normalized when reward and punishment were used to instantiate motivated states. In Study 2, we demonstrated distinct patterns of PTSD-related associations within and across the SN and FPCN as a function of motivational state. During non-motivated states, PTSD symptom severity was associated with indiscriminate hyperactivation of the SN and FPCN to both errors and correct responses, but more error-specific hyperactivation of the SN and SPL/PCu (an FPCN node) during motivated states. Mirroring neural activation results, PTSD symptom severity was associated with greater error-related connectivity between the SN and FPCN exclusively during motivated states. Together, these findings demonstrate that error-related cognitive control deficits in PTSD may be partly attributable to motivational processes, which are supported by neural dynamics within and between the SN and FPCN.

Overall, PTSD-related deficits in PES were diminished when task performance was motivated via monetary reward and punishments, which suggests that motivational systems may contribute to cognitive dysfunction in PTSD. In Study 1, motivation-based normalization of PES was observed whether PTSD was measured continuously or diagnostically, which was independent of comorbid psychiatric conditions. In Study 2, we replicated motivation-based normalization of PES in an independent sample with lower levels of PTSD symptom severity. Together, these results suggest that motivation-based normalization of error-related cognitive control is replicable and generalizes across a range of PTSD symptomatology. Overall, these results are consistent with previous research, which demonstrated that monetary rewards and punishments also reduced PTSD-related deficits in sustained inhibitory control (Dutra et al., 2018). Importantly, however, normalization of error-related cognitive control was orthogonal to normalization of sustained inhibitory control in the current study. Together, these results suggest that motivational systems play an important role in PTSD-related dysfunction across several facets of sustained attention.

In Study 2, we aimed to disentangle whether normalization of error-related cognitive control in PTSD was attributable to *amelioration*, *augmentation*, or *reinforcement* of SN functionality within the larger triple network system (Akiki et al., 2017). These hypotheses predicted normalization of error-related cognitive control in PTSD via *amelioration* of impaired SN functionality in non-motivated states, *augmentation* of SN functionality in motivated states, or *reinforcement* of SN functionality via a neural mechanism outside the triple network system. Although we observed some evidence for the SN amelioration hypothesis, PTSD-related associations were generally most consistent with the SN augmentation hypothesis. Consistent with the SN amelioration hypothesis, PTSD symptom severity was associated with indiscriminate SN and FPCN activation to both errors and correct responses within the Non-Motivated condition, which was not observed in the Motivated condition. Inconsistent with the SN amelioration hypothesis, however, non-specific SN activation was not associated with deficits in error-related cognitive control within the Non-Motivated condition. Instead, PTSD symptom severity was associated with more error-specific activation of the SN, as well as an SPL/PCu cluster within the FPCN, within the Motivated condition, which is most consistent with the SN augmentation hypothesis. Further supporting the SN augmentation hypothesis, PTSD symptom severity was also associated with stronger error-related SN-FPCN connectivity within the Motivated condition. Although these results were most consistent with the augmentation hypothesis, PTSD-related associations with SN and FPCN dynamics were unexpectedly complex.

Specifically, augmentation of SN/Precuneus activation and SN-FPCN connectivity were driven by distinct motivational processes. In the Motivated condition, PTSD-related differences in error-related SN and SPL/PCu *activation* were driven by greater activation to punished inhibitory control failures. In contrast, PTSD-related differences in error-related SN-FPCN *connectivity* were driven by weaker connectivity to rewarded inhibitory control successes. From a functional perspective, punishment increases the salience of errors, which is consistent with stronger PTSD-related SN activation (Maruo et al., 2016). Increased SN signaling in response to punished errors subsequently recruits a greater degree of top-down control via the FPCN (Cai et al., 2015). Given that PTSD is putatively characterized by limited top-down control, however, it may not be possible to directly facilitate behavioral adjustments by further strengthening SN-FPCN coupling to punished commission errors (Akiki et al., 2017). Instead, this process may be facilitated indirectly by *weakening* SN-FPCN coupling to inhibitory control successes, which allows greater cognitive resource allocation towards behavioral adjustments following inhibitory control failures. Thus, error-related cognitive control normalization in PTSD may be achieved at the cost of diminished reward processing, which is consistent with the prioritization of avoiding threats over obtaining rewards in PTSD (Weaver et al., 2020).

Consistent with this conceptualization, our brain-behavior results suggested that exogenous motivation normalized error-related cognitive control in PTSD via a more indirect route. In non-motivated states, we observed associations between error-related SN-FPCN connectivity and PES (brain–behavior) as well as between PTSD symptoms and PES (symptom–behavior). In motivated states, however, we exclusively observed an association between PTSD symptom severity and error-related SN-FPCN connectivity (symptom–brain). Put another way, brain–behavior and symptom–behavior associations were exclusively observed in the Non-Motivated condition, whereas symptom–brain associations were exclusively observed in the Motivated condition (see Fig. 5). This complex pattern of correlations suggests that PTSD-related differences in SN-FPCN connectivity do not directly influence error-related cognitive control in motivated states. Instead, augmentation of SN-FPCN connectivity during *motivated* states may indirectly reduce the deleterious influence of PTSD symptom severity on error-related cognitive control typically observed during *non-motivated* states. Thus, PTSD-related augmentation of SN-FPCN connectivity during motivational states may indirectly normalize error-related cognitive control by reducing the influence of PTSD symptoms, rather than by directly augmenting error-related cognitive control.

Alternatively, it is possible that this complex pattern of brain–behavior relationships reflects PTSD-related differences in the recruitment of proactive versus reactive control processes in motivated states. In Study 1 and Study 2, low PTSD symptom severity was unexpectedly characterized by relatively *smaller* PES, rather than relatively larger PES, in the Motivated condition. One potential explanation for this unexpected pattern of PES results is that error-related cognitive control may supported by both reactive and proactive control processes (Braver, 2012). In motivated states, individuals with lower PTSD symptoms may exhibit a greater utilization of *proactive* control processes, which reduces the need for behavioral adjustments following an attentional lapse (i.e., smaller PES). In contrast, individuals with higher PTSD symptoms may be less able to utilize proactive control processes in motivated states. Instead, individuals with higher PTSD symptoms may more efficiently utilize *reactive* control processes, which increases behavioral adjustments after an attentional lapse (i.e., larger PES). Thus, it is possible that the lack of overall brain–behavior relationships in the Motivated condition is attributable to PTSD-related differences in the utilization of proactive and reactive control processes, which exert competing influences on PES. In sum, motivation-induced enhancements of error-related cognitive control may be driven by different control processes as a function of PTSD severity. Although the current study cannot dissociate between reactive and proactive control processes, these results nevertheless suggest that motivational processes contribute to error-related cognitive control in PTSD.

Additionally, our results may implicate a more complex role of the triple network system in PTSD. In short, triple network frameworks propose that PTSD is characterized by SN *hyper*activation, FPCN *hypo*activation, and DMN *hyper*-activation (Akiki et al., 2017). In the current study, however, PTSD symptom severity was associated with both SN and FPCN *hyper*activation in the Non-Motivated condition. Moreover, we observed no PTSD-related associations with DMN activation or SN-DMN connectivity in either motivational state. Such discrepancies could be resolved within dual-mechanism frameworks of attention (Braver, 2012). In the current study, we examined neural activation and neural connectivity in response to inhibitory control failures (i.e., *after* commission errors). However, PTSD symptomatology may differentially influence triple network functionality during *proactive* recruitment of inhibitory control (i.e., *before* targets), which may influence *reactive* error-related cognitive control. Thus, we do not believe our results contradict triple network models of PTSD, but instead support further refinement of these models.

Although these findings provide interesting insights, several limitations should be noted. First, a primary limitation in the current study is the lack of a healthy control comparison group of veterans that were not deployed and/or exposed to trauma. Namely, the findings observed in the DC Group and at lower levels of PTSD symptoms may indicate a resilience to the deleterious effects of trauma exposure, rather than normative functioning per se. For example, individuals without a history of trauma exposure may exhibit patterns of PES and SN function that are distinct relative to both deployed veterans with PTSD and deployed veterans without PTSD. As such, it will be necessary for future work to directly compare PES and error-related SN function across individuals with PTSD, trauma-exposed individuals without PTSD (i.e., trauma controls), and individuals with no history of trauma exposure (i.e., healthy controls). Second, the TRACTS cohort is representative of veterans who seek services through the larger VA system (Lippa et al., 2015), but is not representative of the larger population of adults with PTSD. Specifically, the current studies were predominantly comprised of male Veterans who self-identified as Caucasian, which limits the generalization of results to more nationally representative populations. Thus, it will be important for future research to replicate these findings in more diverse samples of adults with PTSD. Finally, we did not employ a stringent Bonferroni correction to account for conducting network-based analyses using the SN, FPCN, and DMN given our *a priori* hypotheses regarding the triple network system. As such, our less robust statistical results should be interpreted cautiously in absence of strict multiple comparison correction and/or replication in an independent sample.

Despite these limitations, the current study also offers several methodological strengths and important implications for understanding cognitive control deficits in PTSD. From a methodological perspective, we utilized a validated sustained attention paradigm to replicate our behavioral results in two independent samples of post-9/11 veterans that were well-characterized in terms of neuropsychiatric and cognitive function. Overall, our findings suggest that motivational processes play an important role in PTSD-related impairments of error-related cognitive control, which may be attributable to dysfunction within and between the SN and FPCN. From a clinical perspective, these results offer important implications by demonstrating that dysregulated motivational processes contribute to cognitive control deficits in PTSD. More broadly, these collective results suggest that cognitive (dys)function in PTSD may be better understood as an interaction between motivational systems and attentional systems.

Statement regarding accessibility of raw data

Raw data presented in the current studies are owned by the United States Department of Veterans Affairs and are available only upon request from the United States Department of Veterans Affairs. The Department of Veterans Affairs will make this data publicly available and requests for the data can be made by interested individuals by filing a Freedom of Information Act request to the Privacy Officer at VA Boston Healthcare System (vhabhsFOIAofficers@va.gov) or the FOIA Intake Center (https://www.va.gov/foia/Requests.asp).

Funding information and sources

This research was supported by the U.S. Department of Veterans Affairs through the Translational Research Center for TBI and Stress Disorders (B9254-CAQ18 and B3001-C) to G.M., a VA Rehabilitation Research and Development Traumatic Brain Injury National Research Center, a Merit Review Award from the VA Clinical Sciences Research and Development Service (I01CX001653) to M.E, and an Office of Academic Affairs fellowship to T.E.

Credit statement

Travis C. Evans: Conceptualization, Methodology, Formal analysis, Writing - original draft, Visualization. **Joseph DeGutis:** Conceptualization, Visualization, Writing - review & editing. **David Rothlein:** Investigation, Data processing, Writing - review & editing. **Audreyana Jagger-Rickels:** Data processing, Writing - review & editing. **Ayumu Yamashita:** Data processing, Writing - review & editing. **Catherine B. Fortier:** Investigation, Project administration, Data curation, Writing - review & editing. **Jennifer Fonda:** Project administration, Data curation, Writing - review & editing. **William Milberg:** Investigation, Project administration, Resources, Writing - review & editing. **Regina McGlinchey:** Investigation, Project administration, Resources, Writing - review & editing. **Michael Esterman:** Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data curation, Visualization, Supervision, Project administration, Writing - review & editing.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cortex.2021.09.004.

REFERENCES

Akiki, T. J., Averill, C. L., & Abdallah, C. G. (2017). A network-based neurobiological model of ptsd: Evidence from structural and functional neuroimaging studies. *Current psychiatry reports, 19*(11), 81. https://doi.org/10.1007/s11920-017-0840-4, 81.

Aupperle, R. L., Melrose, A. J., Stein, M. B., & Paulus, M. P. (2012). Executive function and ptsd: Disengaging from trauma. *Neuropharmacology, 62*(2), 686–694. https://doi.org/10.1016/j.neuropharm.2011.02.008

Blake, D. D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Gusman, F. D., Charney, D. S., et al. (1995). The development of a clinician-administered ptsd scale. *Journal of Traumatic Stress, 8*(1), 75–90.

Braver, T. S. (2012). The variable nature of cognitive control: A dual mechanisms framework. *Trends in Cognitive Sciences, 16*(2), 106–113. https://doi.org/10.1016/j.tics.2011.12.010

Cai, W., Chen, T., Ryali, S., Kochalka, J., Li, C.-S. R., & Menon, V. (2015). Causal interactions within a frontal-cingulate-parietal network during cognitive control: Convergent evidence from a multisite–multitask investigation. *Cerebral Cortex, 26*(5), 2140–2153. https://doi.org/10.1093/cercor/bhv046

Chen, G., Saad, Z. S., Britton, J. C., Pine, D. S., & Cox, R. W. (2013). Linear mixed-effects modeling approach to fmri group analysis. *NeuroImage, 73*, 176–190. https://doi.org/10.1016/j.neuroimage.2013.01.047

Clemans, Z. A., El-Baz, A. S., Hollifield, M., & Sokhadze, E. M. (2012). Single trial time–frequency domain analysis of error processing in post-traumatic stress disorder. *Neuroscience Letters, 525*(2), 105–110. https://doi.org/10.1016/j.neulet.2012.07.051

Cox, R. W. (1996). Afni: Software for analysis and visualization of functional magnetic resonance neuroimages. *Cancer Biotherapy & Radiopharmaceuticals, 29*(3), 162–173. https://doi.org/10.1006/cbmr.1996.0014

Cox, R. W., Chen, G., Glen, D. R., Reynolds, R. C., & Taylor, P. A. (2017). Fmri clustering and false-positive rates. *Proceedings of the National Academy of Sciences, 114*(17), E3370–E3371. https://doi.org/10.1073/pnas.1614961114

Danielmeier, C., & Ullsperger, M. (2011). Post-error adjustments. *Frontiers in Psychology, 2*, 233.

DeGutis, J., Esterman, M., McCulloch, B., Rosenblatt, A., Milberg, W., & McGlinchey, R. (2015). Posttraumatic psychological symptoms are associated with reduced inhibitory control, not general executive dysfunction. *Journal of the International Neuropsychological Society: JINS, 21*(5), 342–352. https://doi.org/10.1017/s1355617715000235

Dutilh, G., Vandekerckhove, J., Forstmann, B. U., Keuleers, E., Brysbaert, M., & Wagenmakers, E.-J. (2012). Testing theories of post-error slowing. *Attention, Perception, & Psychophysics, 74*(2), 454–465. https://doi.org/10.3758/s13414-011-0243-2

Dutra, S. J., Marx, B. P., McGlinchey, R., DeGutis, J., & Esterman, M. (2018). Reward ameliorates posttraumatic stress disorder-related impairment in sustained attention. *Chronic Stress (Thousand Oaks)*, 2. https://doi.org/10.1177/2470547018812400

Esteban, O., Markiewicz, C. J., Blair, R. W., Moodie, C. A., Isik, A. I., Erramuzpe, A., et al. (2019). Fmriprep: A robust preprocessing pipeline for functional mri. *Nature Methods, 16*(1), 111–116. https://doi.org/10.1038/s41592-018-0235-4

Esterman, M., Fortenbaugh, F. C., Pierce, M. E., Fonda, J. R., DeGutis, J., Milberg, W., et al. (2019). Trauma-related psychiatric and behavioral conditions are uniquely associated with sustained attention dysfunction. *Neuropsychology, 33*(5), 711–724. https://doi.org/10.1037/neu0000525

Esterman, M., Noonan, S. K., Rosenberg, M., & DeGutis, J. (2012). In the zone or zoning out? Tracking behavioral and neural fluctuations during sustained attention. *Cerebral Cortex, 23*(11), 2712–2723. https://doi.org/10.1093/cercor/bhs261

Esterman, M., Poole, V., Liu, G., & DeGutis, J. (2017). Modulating reward induces differential neurocognitive approaches to sustained attention. *Cerebral cortex (New York, N.Y. : 1991), 27*(8), 4022–4032. https://doi.org/10.1093/cercor/bhw214

Esterman, M., Reagan, A., Liu, G., Turner, C., & DeGutis, J. (2014). Reward reveals dissociable aspects of sustained attention.

Journal of Experimental Psychology. General, 143(6), 2287–2295. https://doi.org/10.1037/xge0000019

First, M., Spitzer, R. L., Gibbon, M. L., & Williams, J. (2002). *Structured clinical interview for dsm-iv-tr axis i disorders, research version* (non-patient edition).

Fortenbaugh, F. C., DeGutis, J., & Esterman, M. (2017). Recent theoretical, neural, and clinical advances in sustained attention research. *Annals of the New York Academy of Sciences, 1396*(1), 70–91. https://doi.org/10.1111/nyas.13318

Fortenbaugh, F. C., Rothlein, D., McGlinchey, R., DeGutis, J., & Esterman, M. (2018). Tracking behavioral and neural fluctuations during sustained attention: A robust replication and extension. *NeuroImage, 171*, 148–164. https://doi.org/10.1016/j.neuroimage.2018.01.002

Fortier, C. B., Amick, M. M., Grande, L., McGlynn, S., Kenna, A., Morra, L., et al. (2014). The boston assessment of traumatic brain injury-lifetime (bat-l) semistructured interview: Evidence of research utility and validity. *The Journal of Head Trauma Rehabilitation, 29*(1), 89–98. https://doi.org/10.1097/HTR.0b013e3182865859

Green, P., Lees-Haley, P. R., & Allen, L. M., III (2003). The word memory test and the validity of neuropsychological test scores. *Journal of Forensic Neuropsychology, 2*(3–4), 97–124.

Hajcak, G., McDonald, N., & Simons, R. F. (2003). To err is autonomic: Error-related brain potentials, ans activity, and post-error compensatory behavior. *Psychophysiology, 40*(6), 895–903. https://doi.org/10.1111/1469-8986.00107

Ham, T. E., de Boissezon, X., Leff, A., Beckmann, C., Hughes, E., Kinnunen, K. M., et al. (2012). Distinct frontal networks are involved in adapting to internally and externally signaled errors. *Cerebral Cortex, 23*(3), 703–713. https://doi.org/10.1093/cercor/bhs056

Hamilton, A. F., & Grafton, S. T. (2007). Action outcomes are represented in human inferior frontoparietal cortex. *Cerebral Cortex, 18*(5), 1160–1168. https://doi.org/10.1093/cercor/bhm150

Ham, T., Leff, A., de Boissezon, X., Joffe, A., & Sharp, D. J. (2013). Cognitive control and the salience network: An investigation of error processing and effective connectivity. *Journal of Neuroscience, 33*(16), 7091–7098.

Kerns, J. G., Cohen, J. D., MacDonald, A. W., Cho, R. Y., Stenger, V. A., & Carter, C. S. (2004). Anterior cingulate conflict monitoring and adjustments in control. *Science, 303*(5660), 1023. https://doi.org/10.1126/science.1089910

Kucyi, A., Hove, M. J., Esterman, M., Hutchison, R. M., & Valera, E. M. (2017). Dynamic brain network correlates of spontaneous fluctuations in attention. *Cerebral cortex (New York, N.Y. : 1991), 27*(3), 1831–1840. https://doi.org/10.1093/cercor/bhw029

Lippa, S. M., Fonda, J. R., Fortier, C. B., Amick, M. A., Kenna, A., Milberg, W. P., et al. (2015). Deployment-related psychiatric and behavioral conditions and their association with functional disability in oef/oif/ond veterans. *Journal of Traumatic Stress, 28*(1), 25–33. https://doi.org/10.1002/jts.21979

Lustig, C., Hasher, L., & Tonev, S. T. (2001). Inhibitory control over the present and the past. *European Journal of Cognitive Psychology, 13*(1–2), 107–122. https://doi.org/10.1080/09541440126215

Maruo, Y., Schacht, A., Sommer, W., & Masaki, H. (2016). Impacts of motivational valence on the error-related negativity elicited by full and partial errors. *Biological Psychology, 114*, 108–116. https://doi.org/10.1016/j.biopsycho.2015.12.004

McGlinchey, R. E., Milberg, W. P., Fonda, J. R., & Fortier, C. B. (2017). A methodology for assessing deployment trauma and its consequences in oef/oif/ond veterans: The tracts longitudinal prospective cohort study. *International Journal of Methods in Psychiatric Research, 26*(3), e1556. https://doi.org/10.1002/mpr.1556

McLaren, D. G., Ries, M. L., Xu, G., & Johnson, S. C. (2012). A generalized form of context-dependent psychophysiological interactions (gppi): A comparison to standard approaches. *NeuroImage, 61*(4), 1277–1286. https://doi.org/10.1016/j.neuroimage.2012.03.068

Menon, V. (2011). Large-scale brain networks and psychopathology: A unifying triple network model. *Trends in Cognitive Sciences, 15*(10), 483–506.

Polak, A. R., Witteveen, A. B., Reitsma, J. B., & Olff, M. (2012). The role of executive function in posttraumatic stress disorder: A systematic review. *Journal of Affective Disorders, 141*(1), 11–21. https://doi.org/10.1016/j.jad.2012.01.001

Rabellino, D., Tursich, M., Frewen, P. A., Daniels, J. K., Densmore, M., Théberge, J., et al. (2015). Intrinsic connectivity networks in post-traumatic stress disorder during sub- and supraliminal processing of threat-related stimuli. *Acta Psychiatrica Scandinavica, 132*(5), 365–378. https://doi.org/10.1111/acps.12418

Regev, S., & Meiran, N. (2014). Post-error slowing is influenced by cognitive control demand. *Acta Psychologica, 152*, 10–18. https://doi.org/10.1016/j.actpsy.2014.07.006

Samuelson, K. W., Newman, J., Abu Amara, D., Qian, M., Li, M., Schultebraucks, K., et al. (2020). Predeployment neurocognitive functioning predicts postdeployment posttraumatic stress in army personnel. *Neuropsychology, 34*(3), 276–287. https://doi.org/10.1037/neu0000603

Savine, A. C., & Braver, T. S. (2010). Motivated cognitive control: Reward incentives modulate preparatory neural activity during task-switching. *The Journal of Neuroscience, 30*(31), 10294. https://doi.org/10.1523/JNEUROSCI.2052-10.2010

Sripada, R. K., King, A. P., Welsh, R. C., Garfinkel, S. N., Wang, X., Sripada, C. S., et al. (2012). Neural dysregulation in posttraumatic stress disorder: Evidence for disrupted equilibrium between salience and default mode brain networks. *Psychosomatic Medicine, 74*(9), 904–911. https://doi.org/10.1097/PSY.0b013e318273bf33

Steinborn, M. B., Flehmig, H. C., Bratzke, D., & Schröter, H. (2012). Error reactivity in self-paced performance: Highly-accurate individuals exhibit largest post-error slowing. *The Quarterly Journal of Experimental Psychology: QJEP, 65*(4), 624–631. https://doi.org/10.1080/17470218.2012.660962

Stein, M. B., & Paulus, M. P. (2009). Imbalance of approach and avoidance: The yin and yang of anxiety disorders. *Biological psychiatry, 66*(12), 1072–1074. https://doi.org/10.1016/j.biopsych.2009.09.023

Stürmer, B. (2011). Reward and punishment effects on error processing and conflict control. *Frontiers in Psychology, 2*(335). https://doi.org/10.3389/fpsyg.2011.00335

Swick, D., Honzel, N., Larsen, J., & Ashley, V. (2013). Increased response variability as a marker of executive dysfunction in veterans with post-traumatic stress disorder. *Neuropsychologia, 51*(14), 3033–3040. https://doi.org/10.1016/j.neuropsychologia.2013.10.008

Swick, D., Honzel, N., Larsen, J., Ashley, V., & Justus, T. (2012). Impaired response inhibition in veterans with post-traumatic stress disorder and mild traumatic brain injury. *Journal of the International Neuropsychological Society: JINS, 18*(5), 917–926. https://doi.org/10.1017/s1355617712000458

Swick, D., Honzel, N., & Turken, U. (2015). Intact error monitoring in combat veterans with post-traumatic stress disorder. *Psychiatry research, 234*(2), 227–238. https://doi.org/10.1016/j.pscychresns.2015.09.016

Tanielian, T. L., Tanielian, T., & Jaycox, L. (2008). *Invisible wounds of war: Psychological and cognitive injuries, their consequences, and services to assist recovery* (Vol. 1). Rand Corporation.

Tursich, M., Ros, T., Frewen, P. A., Kluetsch, R. C., Calhoun, V. D., & Lanius, R. A. (2015). Distinct intrinsic network connectivity patterns of post-traumatic stress disorder symptom clusters.

Acta Psychiatrica Scandinavica, 132(1), 29–38. https://doi.org/10.1111/acps.12387

Vasterling, J. J., Duke, L. M., Brailey, K., Constans, J. I., Allain, A. N., Jr., & Sutker, P. B. (2002). Attention, learning, and memory performances and intellectual resources in vietnam veterans: Ptsd and no disorder comparisons. *Neuropsychology, 16*(1), 5–14. https://doi.org/10.1037//0894-4105.16.1.5

Velanova, K., Wheeler, M. E., & Luna, B. (2008). Maturational changes in anterior cingulate and frontoparietal recruitment support the development of error processing and inhibitory control. *Cerebral Cortex, 18*(11), 2505–2522. https://doi.org/10.1093/cercor/bhn012

Vogt, D., Smith, B. N., King, L. A., King, D. W., Knight, J., & Vasterling, J. J. (2013). Deployment risk and resilience inventory-2 (drri-2): An updated tool for assessing psychosocial risk and resilience factors among service members and veterans. *Journal of Traumatic Stress, 26*(6), 710–717.

Weaver, S. S., Kroska, E. B., Ross, M. C., Sartin-Tarm, A., Sellnow, K. A., Schaumberg, K., et al. (2020). Sacrificing reward to avoid threat: Characterizing ptsd in the context of a trauma-related approach–avoidance conflict task. *Journal of Abnormal Psychology, 129*(5), 457–468. https://doi.org/10.1037/abn0000528

Yeo, B. T., Krienen, F. M., Sepulcre, J., Sabuncu, M. R., Lashkari, D., Hollinshead, M., et al. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology, 106*(3), 1125–1165. https://doi.org/10.1152/jn.00338.2011

Yoon, S. A., & Weierich, M. R. (2016). Salivary biomarkers of neural hypervigilance in trauma-exposed women. *Psychoneuroendocrinology, 63*, 17–25. https://doi.org/10.1016/j.psyneuen.2015.09.007