See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/318050515

# Associations Among Posttraumatic Stress Disorder Symptoms, Substance Use, and Affective Attentional...

# Article in The Journal of nervous and mental disease · June 2017

DOI: 10.1097/NMD.000000000000002

CITATION: 0	S	reads <b>21</b>	
8 autho	<b>rs</b> , including:		
T	Melissa M Amick U.S. Department of Veterans Affairs 51 PUBLICATIONS 1,056 CITATIONS SEE PROFILE		Blair Wisco University of North Carolina at Greensboro <b>31</b> PUBLICATIONS <b>1,808</b> CITATIONS SEE PROFILE
	Brian P Marx U.S. Department of Veterans Affairs 172 PUBLICATIONS 4,272 CITATIONS SEE PROFILE		Regina E Mcglinchey Harvard Medical School 145 PUBLICATIONS 2,865 CITATIONS SEE PROFILE

# Some of the authors of this publication are also working on these related projects:



Project

Metabolic Regulation, Cortical Organization and Aging View project

Translational Research Center for Traumatic Brain Injury and Stress Disorders (TRACTS) View project

All content following this page was uploaded by Brian P Marx on 14 July 2017.

# Associations Among Posttraumatic Stress Disorder Symptoms, Substance Use, and Affective Attentional Processing in OEF/OIF/OND Veterans

Gabrielle I. Liverant, PhD,\* Melissa M. Amick, PhD,†‡ Shimrit K. Black, PhD,‡§ Michael Esterman, PhD,†‡ Blair E. Wisco, PhD,// Molly C. Gibian, BA,† Brian P. Marx, PhD,‡¶ and Regina E. McGlinchey, PhD†#

**Abstract:** The majority of research examining affective attentional bias in posttraumatic stress disorder (PTSD) has not examined the influence of co-occurring psychiatric disorders. This study examined the individual and interactive effects of PTSD symptoms and substance use disorders (SUDs) on affective attentional processing among 323 veterans deployed to Iraq or Afghanistan. Participants were divided into those with SUD (SUD+, n = 46) and those without (SUD-, n = 277). Substance use disorder was determined using the Structured Clinical Interview for *DSM-IV*. Posttraumatic stress disorder was measured using the Clinician Administered PTSD Scale. A computerized go/no-go task (Robbins et al., 1994, Robbins et al., 1998) assessed affective attentional processing. Relative to those without SUD, those with SUD showed a significant association between PTSD symptoms and increased omission and commission accuracy rates and decreased d prime. No effects of valence were found. Findings suggest the need to consider co-occurring SUD when investigating the effects of PTSD on attentional control.

Key Words: PTSD, substance use disorder, attention, affect, inhibition, veterans

(J Nerv Ment Dis 2017;00: 00-00)

**P** osttraumatic stress disorder (PTSD) and substance use disorders (SUDs) are relatively common military-related psychiatric illnesses, which are both marked by disrupted attentional control (Drobes et al., 2006; Harvey et al., 1996). Individuals with PTSD are hypothesized to display both an attentional bias toward and difficulty disengaging from information with a threatening or general negative valence (Naim et al., 2014; Pineles et al., 2007). Despite research showing the effects of SUD on attentional bias/inhibitory control (Field and Cox, 2008; Field et al., 2009; Lambe et al., 2014), it is currently unknown if PTSD-related affective attentional bias might be exacerbated when the commonly co-occurring condition of SUD is present (Seal et al., 2011). In this study, we examine the relative and combined contributions of these disorders in the critical domain of affective attentional bias/inhibitory control.

Attentional bias toward threat-related information has been implicated in both the onset and maintenance of PTSD (Armstrong et al., 2013; Kimble et al., 2010). This threat-related bias may have an impact on both information processing and subsequent behavior, as it functions as a gating mechanism that directs attention based on stimulus valence

ISSN: 0022-3018/17/0000–0000

DOI: 10.1097/NMD.000000000000002

(Constans, 2005). For example, studies using the Stroop paradigm have demonstrated that, compared with individuals without PTSD, those with PTSD demonstrate slower reaction times when asked to name the color of the ink for trauma- and threat-related, relative to neutral, words (Cisler et al., 2011; Constans et al., 2004). It is possible that the additional effort involved in inhibiting prepotent response tendencies in the context of information with a threat-related valence accounts for these slowed response times (for review see Buckley et al., 2000). In contrast, research using visual attention tasks has shown that affective attentional bias can facilitate performance. Specifically, relative to those without PTSD, those with PTSD more quickly identify visual targets when the stimuli consist of negatively valenced words (Bryant and Harvey, 1997) or threatening faces (Fani et al., 2012). Overall, the literature examining affective attentional bias in PTSD remains inconsistent, with several studies failing to find an association between PTSD and attentional bias for negatively valenced stimuli (Ashley et al., 2013; Elsesser et al., 2005). Subsequent research has highlighted that these inconsistent findings may be due to variability in task methods and/or stimulus type (Cisler et al., 2011; Olatunji et al., 2015). Moreover, it remains unclear whether alterations in affective attentional processing in PTSD result from enhanced threat detection, difficulty disengaging from threat-related stimuli, and/or deficits in inhibitory control (Aupperle et al., 2012; Esterman et al., 2013; DeGutis et al., 2015).

The majority of research examining affective attentional bias among those with PTSD has neither controlled for nor examined the influence of co-occurring psychiatric disorders (Bryant and Harvey, 1997; Constans et al., 2004), although there are several exceptions. For example, two recent studies have explored the impact of co-occurring depression on attentional bias in PTSD (Wittekind et al., 2015; Hauschildt et al., 2013). This research, using tasks with visual affective cues, supports the effects of depression as opposed to PTSD, on affective attentional bias after trauma exposure. In addition, Amick et al. (2013) found a moderating effect of mild traumatic brain injury (mTBI) on the association between PTSD and affective-related attentional control. Specifically, among individuals with mTBI, increasing PTSD symptom severity was associated with a more liberal response pattern to positively versus negatively valenced stimuli. However, this association was not evident among individuals without TBI. Cumulatively, these preliminary findings underscore the need to investigate the influence of co-occurring deployment-related conditions to more precisely characterize the association between PTSD symptoms and affective attentional processing, and clarify inconsistencies in this literature.

Similar to those with PTSD, individuals with SUDs demonstrate alterations in attentional control. Findings show differential attentional bias toward substance-related cues (Field and Cox, 2008; Weinstein and Cox, 2006), which has been proposed as a key predictor of addictive behaviors (Cox et al., 2002; Marissen et al., 2006). Experimental studies using modified Stroop tasks have demonstrated support for this drug-related attentional bias in a variety of SUDs, including nicotine, alcohol, cocaine, and heroin use (Cox et al., 2002; Hester et al., 2006). Notably, one study found that drug-related attentional bias was

The Journal of Nervous and Mental Disease • Volume 00, Number 00, Month 2017

<sup>\*</sup>Psychology Department, Suffolk University; †New England Geriatric Research, Education, and Clinical Center and the Translational Research Center for Traumatic Brain Injury and Stress Disorders, VA Boston Healthcare System; ‡Department of Psychiatry, Boston University School of Medicine; §Mental Health Service, VA Boston Healthcare System, Boston, Massachusetts; ||University of North Carolina at Greensboro, Greensboro, North Carolina; ¶National Center for PTSD, Behavioral Science Division, VA Boston Healthcare System; and #Department of Psychiatry, Harvard Medical School, Boston, Massachusetts.

Send reprint requests to Gabrielle I. Liverant, PhD, Psychology Department, Suffolk University, 73 Tremont St, Boston, MA 02114. E-mail: gliverant@suffolk.edu. Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.

exacerbated after trauma cue exposure among cocaine-dependent inpatients with PTSD, suggesting interactive effects of PTSD and SUD on attention (Tull et al., 2011).

Although the majority of findings have highlighted an attentional bias for substance-related cues among those with SUDs, recent research has extended this to examine the presence of affective attentional bias related to positively and negatively valenced cues more broadly. Although studies are limited, preliminary findings support the influence of affective stimuli (*i.e.*, both positive and negative valence versus neutral) on attentional/inhibitory control performance among individuals with alcohol (Lambe et al., 2014), as well as opiate use disorders (Dunning et al., 2011; Lubman et al., 2008).

Given the high rates of comorbidity between PTSD and SUD (Seal et al., 2011) and the independent effects of each disorder on attentional bias (e.g., Cisler et al., 2011; Hester et al., 2006), it is important to investigate the relative and interactive influence of each disorder on attentional bias, as this information is critical to a more thorough understanding of the mechanisms that contribute to impaired attentional control in this population. Thus, this study examined the effects of PTSD and co-occurring SUD on performance using a validated affective go/no-go task (Robbins et al., 1998; Robbins et al., 1994) that has been shown to be sensitive to alterations in affective attentional bias in other related clinical samples (Amick et al., 2013; Kaplan et al., 2006; Seymour et al., 2015; Steiner et al., 2013). Task performance was examined among a sample of Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn (OEF/OIF/OND) Veterans recruited from a large metropolitan area in the Northeastern United States. This study investigated the effects of PTSD and SUD, as well as their interaction, on several different indices of attentional performance, including commission and omission accuracy, reaction time, and signal detection indices of discriminability and response bias. We predicted that errors of omission and commission would be significantly greater in response to negative versus positive stimuli. Consistent with existing literature, we predicted that, relative to those without PTSD, individuals with PTSD would show significantly more errors of commission. In addition, we hypothesized that there would be a significant PTSD × SUD interaction, such that PTSD symptom severity would be more strongly associated with decrements in omission and commission accuracy in response to negative affective stimuli among those with SUD than among those without this comorbidity.

# METHODS

# Recruitment

An initial sample of 359 consecutively enrolled veterans was recruited from the longitudinal cohort study of the VA Rehabilitation Research and Development–supported Traumatic Brain Injury National Network Research Center: The Translational Research Center for TBI and Stress-Related Disorders (TRACTS; McGlinchey et al., 2017). Inclusion criteria for this larger study were OEF/OIF/OND deployment and the age of 18 to 65 years. Exclusion criteria included the following: a) history of neurological illness or seizures unrelated to head injury, b) current diagnosis of psychotic disorder, c) current diagnosis of bipolar disorder, d) cognitive disorder due a medical condition other than TBI, and e) psychiatrically instability (*i.e.*, homicidal/suicidal ideation that required immediate crisis intervention or current, unstable psychological diagnosis that would interfere with accurate data collection).

#### **Participants**

From this initial sample of 359 individuals, 25 participants were excluded for poor performance on effort measures and 11 were excluded for history of moderate or severe TBI. The final sample was composed of 323 participants: 46 (42 men) individuals with a current substance abuse/dependence diagnosis (SUD+ group) and 277

2 www.jonmd.com

(248 men) participants without current substance abuse/dependence (SUD- group). Before completing any of the experimental procedures, all participants provided written informed consent. The local institutional review board approved all study procedures. Participants were recruited from the Boston Metropolitan and surrounding areas by a fulltime recruitment specialist via events involving Army and Air National Guard, Marine and Marine Reserves, and Army and Army Reserve Units.

# Materials and Procedure

For the majority of participants, study measures were collected in one-day sessions with a standardized order of test administration. Data in the analyses described in this article are a subset of the larger TRACTS database. After obtaining informed consent, a doctoral-level psychologist assessed TBI, PTSD, SUD, and other *DSM-IV*Axis I diagnoses using structured interviews. A consensus diagnosis for TBI, PTSD, SUD, and other Axis I disorders was determined via case review by at least three psychologists and/or psychiatrists. Diagnostic assessment was followed by administration of neuropsychological tests including the go/no-go task and self-report measures.

#### Assessments

#### Substance Abuse/Dependence

The Structured Clinical Interview for *DSM-IV* Axis I Disorders (SCID-I/NP; First et al., 2002) is a semistructured interview that includes modules designed to assess either the lifetime or current (past-month) experience of *DSM-IV* Axis I psychiatric disorders (http:// www.scid4.org/psychometric/). All participants received the SCID-I/NP to determine eligibility and to characterize the individual's psychological history. The SCID-I/NP was used to diagnose participants with current alcohol/substance abuse or dependence. Participants meeting criteria for current alcohol or substance abuse or dependence were included in the SUD+ group; those who did not meet current criteria were included in the SUD- group.

#### **Posttraumatic Stress Disorder**

The Clinician-Administered PTSD Scale (CAPS-IV; Blake et al., 1995) was used to assess the presence and severity of PTSD symptoms as well as PTSD diagnostic status. The CAPS is a wellvalidated and reliable structured clinical interview used to evaluate the DSM-IV-TR re-experiencing (criterion B), avoidance/numbing (criterion C), and hyperarousal (criterion D) symptoms of PTSD (Blake et al., 1993; Blake et al., 1995). Participants are queried about the intensity (0-4) and frequency (0-4) of each of the 17 DSM-IV-TR PTSD symptoms, from which a total score is derived (minimum score = 0, maximum = 136), reflecting overall symptom severity. The CAPS total score was used for primary analyses to examine the dynamic interaction of PTSD symptom severity and SUD status upon behavioral measures of inhibitory control. The CAPS also was used to determine what percentage of participants met full DSM-IV-TR diagnostic criteria for PTSD; participants considered to have PTSD if they endorsed at least one B, three C, and two D symptoms (frequency rating  $\geq 1$  and intensity rating  $\geq 2$  were required to be counted as a symptom).

#### Effort

To ensure that all participants included in the analyses were adequately motivated to perform the tasks of interest, we administered the Green's Medical Symptom Validity Test. Adequate effort was determined using established cutoffs (Green, 2003).

#### **TBI Diagnosis**

The Boston Assessment of TBI-Lifetime (BAT-L; Fortier et al., 2013) was used to assess potential brain injury during three

© 2017 Wolters Kluwer Health, Inc. All rights reserved.

lifetime periods: premilitary, military, and postmilitary. Preliminary validation in a subsample of participants (n = 131) demonstrated excellent correspondence between the BAT-L and the Ohio State TBI Assessment Method (Kendall's tau b = 0.95), a validated method for TBI identification (Fortier et al., 2013). Traumatic brain injury criteria including altered mental state, posttraumatic amnesia, and loss of consciousness were evaluated through open-ended questioning. Participants were excluded from analyses if they had any history of a moderate or severe TBI, as these injuries can have lasting impairments on cognitive performance.

#### Affective Go/No-Go

Participants performed the affective Go/No-Go task (Robbins et al., 1998; Robbins et al., 1994) after the clinical interviews. The affective go/no-go task is a continuous performance task. A series of stimulus words with either positive or negative valence was presented on the center of a monitor for 300 milliseconds with a 900-millisecond interstimulus interval. Participants completed 10 blocks. Each block contained 18 words (9 positive and 9 negative valence). For each block, target word valence (positive or negative) was constant and switched every two blocks. Valence of the target and distractor words was nonspecific (e.g., unrelated to deployment trauma). Order of presentation was counterbalanced across participants. The first two blocks of the task served as practice trials. The critical data set consisted of the remaining eight blocks. Within each block, there were nine words that were consistent with the target valence ("go" target words) and nine words that were inconsistent with the target valence ("no-go" distractor words).

At the start of each block, the participant was informed of the targeted valence for that block (either positive or negative). The participant's task was to determine if the valence of the presented word matched (go condition) or did not match (no-go condition) the targeted valence. The participant was instructed to press the spacebar when the valence of the stimulus word matched the targeted valence and to withhold pressing the spacebar when the valence of the stimulus word did not match the targeted valence. Participants were asked to press the button as quickly and accurately as possible. Reaction times and errors of omission and commission were recorded for each trial.

#### Affective Go/No-Go Task Outcome Measures

Dependent measures included indices of omission errors (*i.e.*, failure to press the space bar for a word that matched the targeted valence), commission errors (*i.e.*, pressing the space bar for a nonmatched word for a targeted valence), and reaction time (RT; in milliseconds). Omission accuracy is an index of the percent of correct responses on potential omission trials and was calculated as  $[1 - (\text{omission accuracy} \text{ was calculated as } [1 - (\text{commission accuracy} \text{ was calculated as } [1 - (\text{commission accuracy} \text{ was calculated as } [1 - (\text{commission errors})] \times 100$ .

In addition, d prime (d') and criterion were examined as measures of discrimination accuracy and response bias during the task. d' is an index of overall stimulus discriminability, or sensitivity, and was calculated separately for the positive and negative blocks. d' was calculated according to the following formula: d' = Z(hit rate) - Z(false alarm rate). Criterion is a measure of response bias (to respond or withhold), which is calculated according to the following formula: criterion = [-Z] (false alarm rate) + Z(hit rate)]/2. Negative criterion values indicate a liberal response bias (resulting in more hits and also more false alarms). A positive criterion value indicates a more conservative response bias, with fewer hits and fewer false alarms. If criterion equals zero, then the subject's criterion is neutral, showing no decision bias toward either response type (*i.e.*, go or no-go). For analysis, univariate outliers (*i.e.*, participant

task outcomes that were greater or less than 3 standard deviations from the sample mean) were identified and removed.

#### **Statistical Analyses**

Statistical analyses were performed using SPSS 19.0 software. Participant characteristics were compared using  $\chi^2$  analyses for categorical variables and *t* tests and analyses of variance for continuous variables.

Analysis of go/no-go task data was performed using a general linear model (GLM) with repeated measures. General linear model was performed for each of the dependent measures with substance abuse/dependence group (SUD group) as the between subjects factor and block valence (positive and negative) as the repeated within subjects factor. Each GLM model included total CAPS scores, and a CAPS score  $\times$  SUD group interaction as covariate terms. SPSS examines the effects of constant covariates and covariate interactions as betweensubjects factors, allowing us to examine our primary question of interest, namely, whether the association between PTSD symptom severity and behavioral performance differed as a function of substance abuse/ dependence status. The total CAPS score, rather than PTSD presence or absence, was examined because the critical question to be examined was if the association between PTSD symptom severity and performance on the go/no-go task varied in the SUD+ compared with the SUD- group. To control for any potential effects of age, education, current depressive disorder, and lifetime mTBI (y/n), these variables also were included as covariates in these models as all of these variables are known to influence performance on tasks of executive functioning. Our previous work did not find a main effect of mTBI upon go/no-go performance (Amick et al., 2013). However, as our prior work found an interaction between mTBI and PTSD, and research shows effects of mTBI in related areas of cognitive performance (e.g., Karr et al., 2014), we included mTBI as a covariate in all analyses. To clarify the nature of significant PTSD  $\times$  SUD interactions, Pearson correlations were conducted to examine the relationship between PTSD symptom severity and performance on the go/no-go task separately for each SUD group.

# RESULTS

#### **Participant Characteristics**

The SUD+ and SUD- groups did not differ with respect to age, education, sex, number of lifetime mTBIs, or the presence of anxiety or mood disorders. As expected, the groups did differ with respect to PTSD symptom severity and number of individuals with a PTSD diagnosis. That is, among those in the SUD+ group, PTSD symptom severity was significantly higher and significantly more individuals were diagnosed with PTSD, relative to those in the SUD- group (see Table 1).

# Affective Go/No-Go

# **Reaction Times**

For the repeated measures GLM involving RTs, there was no effect of block valence, SUD group, CAPS score, or their interaction (block valence × SUD group or CAPS × SUD group). None of the covariate terms were significant (P > 0.05).

#### **Commission Accuracy**

The main effect of valence and all of the interactions involving valence were not significant (all p's > 0.32). The main effect of SUD group [F(1,315) = 1.22, p = 0.27; partial eta square = 0.004] was not significant. The main effect of CAPS score [F(1,315) = 5.10, p = 0.025; partial eta square = 0.016] and the interaction between SUD group and CAPS score [F(1,315) = 4.34, p = 0.038, partial eta square = 0.014] were significant. As shown in Figure 1A, within the SUD+ group, commission accuracy decreased with increasing PTSD

© 2017 Wolters Kluwer Health, Inc. All rights reserved.

www.jonmd.com 3

	SUD+ Group	SUD- Group		
	(n = 46)	(n = 277)	t Value	р
Age, yr	30.76 (7.73)	32.06 (8.59)	-0.96	0.34
Sex (male:female)	42:4	248:29	0.14	0.71
Education, yrs	13.54 (1.74)	13.98 (1.96)	-1.42	0.16
No. lifetime mTBI	1.85 (2.97)	1.52 (2.07)	0.94	0.35
Current anxiety disorder DX (Y:N)	12:34	54:223	1.05	0.30
Current mood disorder DX (Y:N)	15:31	69:208	1.22	0.27
Current PTSD DX	37:9	160:117	8.52	0.004
CAPS total score	60.02 (28.96)	48.31 (28.95)	2.54	0.012

TABLE 1. Demographic and Psychiatric Characteristics of the Sample as a Function of Substance Use Disorder Diagnosis

SUD+, participants who met criteria for a diagnosis of a substance use disorder; SUD-, participants who did not meet criteria for a substance use disorder diagnosis; No. Lifetime mTBI, number of lifetime mild traumatic brain injuries; Current anxiety disorder DX (Y:N), current anxiety disorder diagnosis; Current mood disorder DX (Y:N), current mood disorder diagnosis; current PTSD DX, current posttraumatic stress disorder diagnosis; CAPS total score, total score on the clinician-administered PTSD scale; yr, year.

symptom severity (CAPS score, r = -0.33, p = 0.026), but the SUD– group showed no association between commission accuracy and CAPS scores (r = -0.09, p = 0.12). There was a main effect of education [F(1,315) = 7.15, p = 0.008, partial eta square = 0.022], but not age, current major depressive disorder, or lifetime history of mTBI (all p's > 0.4).

#### **Omission Accuracy**

Like the commission errors, there was no main effect of valence, and all of the interactions involving valence were also not significant (all *p*'s > 0.23). The main effects of SUD group [*F*(1, 315) = 4.80, p = 0.03; partial eta square = 0.02] and CAPS scores [*F*(1,315) = 5.11, p = 0.02; partial eta square = 0.016] and the interaction between SUD group and CAPS scores [*F*(1, 315) = 7.560, p = 0.006, partial eta square = 0.023] were significant. As shown in Figure 1B, within the SUD+ group, omission accuracy decreased with increasing PTSD symptom severity (CAPS score, r = -0.39, p = 0.007), whereas in the SUD– group, there was no association between omission errors and CAPS scores (r = 0.01, p = 0.81). There was a main effect of education [*F*(1,316) = 9.57, p = 0.002, partial eta square = 0.029], but not age, current depressive disorder, or history of lifetime mTBI (all *p*'s > 0.25).

#### d Prime

There was no main effect of valence, and all of the interactions involving valence were not significant (all *p*'s > 0.28). The main effect of SUD Group [*F*(1,315) = 2.47, *p* = 0.12, partial eta square = 0.008] was not significant. CAPS scores [*F*(1,315 = 5.7, *p* < 0.02, partial eta square = 0.02] and the interaction of SUD group and CAPS scores [*F*(1,315) = 6.00; *p* = 0.015; partial eta square = 0.019] were significant. Within the SUD+ group, d' (an index of overall discriminability) decreased with increasing PTSD symptom severity (CAPS scores, *r* = -0.38, *p* = 0.009), whereas in the SUD– group, there was no association between overall stimulus discriminability and CAPS scores (*r* < -0.05, *p* > 0.32). There was a main effect of education [*F*(1,315) = 12.45, *p* < 0.001, partial eta square = 0.038], but not age, current depressive disorder, or lifetime number of mTBI (*p*'s > 0.5).

# Criterion

There was no main effect of valence or any of the interactions involving valence (all p's > 0.25). The main effect of SUD group [F(1,315) = 2.17, p = 0.14, partial eta square < 0.01] or CAPS scores [F(1,315 = 0.12, p = 0.73, partial eta square < 0.0001] and the interaction of SUD group and CAPS scores [F(1,315) = 1.77, p = 0.19; partial]

eta square = 0.006] were not significant. None of the covariate terms were significant (all p's > 0.18).

# DISCUSSION

This study investigated the independent and interactive effects of PTSD symptom severity and SUD on affective attentional processing. Veterans with and without SUD who were deployed to Iraq or Afghanistan demonstrated differential associations between PTSD symptoms and responding using an affective go/no-go task (Robbins et al., 1994; Robbins et al., 1998). Among SUD+ individuals, commission and omission accuracy on the go/no-go task decreased as PTSD symptom severity increased. Similarly, among SUD+ participants, go/no-go task discriminability (as indexed by d' score) decreased with more severe PTSD symptoms. Conversely, there was no significant association between PTSD symptom severity and commission accuracy, or discriminability in the SUD– group.

Indices of attentional/inhibitory control were negatively associated with PTSD severity. Consistent with prior research demonstrating cognitive dysfunction in PTSD (e.g., Gillie and Thayer, 2014; DeGutis et al., 2015; Esterman et al., 2013; Falconer et al., 2008; Leskin and White, 2007; Vasterling et al., 1998), there was a main effect of PTSD symptom severity on errors of commission and omission. Furthermore, for both types of attentional errors, accuracy declined with increasing PTSD symptom severity among the SUD+ group. In terms of omission accuracy, this could indicate lapses in attention or vigilance with increasing PTSD severity, which may then lead to lack of responding among individuals with SUD (e.g., Wright et al., 2014). In terms of commission accuracy, there was a significant negative association between PTSD symptom severity and commission accuracy in the SUD+, but not the SUD- group. Taken together, these findings do suggest an enhanced relation between PTSD symptoms and attentional/ inhibitory control deficits when SUD, a disorder marked by impaired inhibitory control (Smith et al., 2014), co-occurs.

Within the SUD+ group, discriminability declined with increasing PTSD severity suggesting that, regardless of stimulus valence, the PTSD × SUD interaction resulted in disrupted attentional control or greater difficulty with identification/discrimination of emotional stimuli. This latter interpretation is supported by findings showing deficits in emotion recognition among individuals with SUD (*e.g.*, Castellano et al., 2015) and may suggest that deficits in this domain contribute to observed PTSD × SUD interactions in both omission and commission accuracy.

Contrary to hypotheses, stimulus valence did not alter performance on any index of the affective go/no-go task, suggesting that

4 www.jonmd.com

© 2017 Wolters Kluwer Health, Inc. All rights reserved.

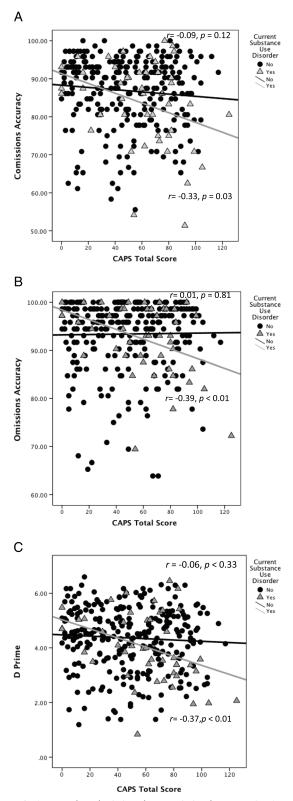


FIGURE 1. Scatter plots depicting the association between CAPS total symptom severity scores (total scores on the Clinician-Administered PTSD Scale) and commission accuracy (A) omission accuracy (B) and d' (C) collapsed across valence.

© 2017 Wolters Kluwer Health, Inc. All rights reserved.

effects may be due to general deficits in cognitive control and inhibitory function, rather than affective attentional bias among individuals with PTSD and SUD (Aupperle et al., 2012; Conrod and Nikolaou, 2016). The lack of an association between PTSD symptom severity and response to negatively valenced targets in this study adds to inconsistent findings in this literature, offering further support for studies that have failed to find evidence of affective attentional bias in PTSD (Bryant and Harvey, 1997; Cisler et al., 2011; Elsesser et al., 2005; Wittekind et al., 2015). Of note, using the identical task, we previously did not observe an association between affective attentional control and PTSD symptom severity, when mTBI was not comorbid (Amick et al., 2013).

Overall, study results extend previous literature showing individual effects of PTSD and SUD symptoms on disrupted behavioral responding using tasks requiring attentional control (*e.g.*, Field and Cox, 2008; Lambe et al., 2014; Esterman et al., 2013; DeGutis et al., 2015). It is possible that the affective go/no-go task, with its specific demands upon inhibitory processes in addition to affective information processing may be more sensitive to the subtle effects of co-occurring SUD on attention and inhibitory control. Thus, findings may point to clinically relevant alterations in inhibitory control and attention function in response to emotionally valenced stimuli that may be unique to individuals with both disorders.

Despite the novel and significant contributions of the current investigation, several limitations should be noted. This study did not include biochemical verification of substance abstinence and instead relied on self-report and clinician assessment of substance free status before testing. In addition, in this preliminary research, all SUDs were collapsed into a single category (SUD+ versus SUD-) rather than examining the individual or dimensional contributions of each type of SUD. Future studies with larger sample sizes should investigate the effects of different SUDs on the relation between PTSD and attentional processing. This may be particularly important given results suggesting variable effects of SUD on attentional processing among individuals with alcohol, nicotine, heroin, and cocaine use disorders (e.g., Rzetelny et al., 2008; Lambe et al., 2014). In addition, future research should explore more complex, three-way interactions among PTSD and co-occurring conditions with established effects on attentional bias (e.g., mTBI; Amick et al., 2013), such as depression, anxiety, and sleep disorders. The study sample was primarily composed of male veterans. Thus, caution should be used when generalizing findings to nonveteran or female populations. Lastly, future investigations should incorporate different attentional bias/inhibitory control tasks to better elucidate the influence of PTSD and SUD on affective attentional bias specifically as opposed to attention and inhibitory control more broadly. These investigations should include investigation of varied stimulus type (verbal versus visual affective stimuli) and task design/methods to more comprehensively characterize the nature of interactive effects of this comorbidity on affective attentional bias.

In conclusion, existing research supports individual effects of SUD and PTSD on affective attentional processing and inhibitory function (*e.g.*, Aupperle et al., 2012; Buckley et al., 2000; Conrod and Nikolaou, 2016; Drobes et al., 2006; Pineles et al., 2009). Results from this initial investigation highlight the need to consider the impact of SUD and other commonly co-occurring disorders when examining relationships between PTSD and affective and nonaffective attentional processing, cognitive control, and behavioral responding to more accurately identify the nature of each disorders' unique and interactive effects on these processes (Amick et al., 2013; Samuelson et al., 2006).

# ACKNOWLEDGMENTS

We thank all of the individuals who participated in this study. We are grateful to all the members of the Human Characterization Core of TRACTS for their expert assessment skills. We would also like to thank Walter Musto CMS (ret), RING for his extraordinary recruitment efforts.

# DISCLOSURE

This work was supported by the VA Rehabilitation Research and Development Traumatic Brain Injury National Network Research Center at VA Boston Healthcare System, The Translational Research Center for TBI and Stress Disorders (B9254-C), a VA CSR&D Merit Review to R.E.M., and by Veterans Affairs Career Development Award-II to M.E. (11K2CX000706). The study sponsors had no role in study design or implementation or in manuscript preparation.

All authors assert that there are no conflicts of interest related to this research.

#### REFERENCES

- Amick MM, Clark A, Fortier CB, Esterman M, Rasmusson AM, Kenna A, Milberg WP, McGlinchey R (2013) PTSD modifies performance on a task of affective executive control among deployed OEF/OIF veterans with mild traumatic brain injury. *J Int Neuropsychol Soc.* 19:792–801.
- Armstrong T, Bilsky SA, Zhao M, Olatunji BO (2013) Dwelling on potential threat cues: An eye movement marker for combat-related PTSD. *Depress Anxiety*. 30: 497–502.
- Ashley V, Honzel N, Larsen J, Justus T, Swick D (2013) Attentional bias for traumarelated words: Exaggerated emotional Stroop effect in Afghanistan and Iraq war veterans with PTSD. *BMC Psychiatry*. 13:86. 1–11.
- Aupperle RL, Melrose AJ, Stein MB, Paulus MP (2012) Executive function and PTSD: Disengaging from trauma. *Neuropharmacology*. 62:686–694.
- Blake DD, Weathers FW, Nagy LM (1993) A clinician rating scale for assessing current and lifetime PTSD: The CAPS-I. *Behav Ther.* 18:187–188.
- Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Gusman FD, Charney DS, Keane TM (1995) The development of a clinician-administered PTSD scale. *J Trauma Stress.* 8:75–90.
- Bryant RA, Harvey AG (1997) Attentional bias in posttraumatic stress disorder. J Trauma Stress. 10:635–644.
- Buckley TC, Blanchard EB, Neill W (2000) Information processing and PTSD: A review of the empirical literature. *Clin Psychol Rev.* 20:1041–1065.
- Castellano F, Bartoli F, Crocamo C, Gamba G, Tremolada M, Santambrogio J, Clerici M, Carrà G (2015) Facial emotion recognition in alcohol and substance use disorders: A meta-analysis. *Neurosci Biobehav Rev.* 59:147–154.
- Cisler JM, Wolitzky-Taylor KB, Adams TG Jr, Babson KA, Badour CL, Willems JL (2011) The emotional Stroop task and posttraumatic stress disorder: A metaanalysis. *Clin Psychol Rev.* 31:817–828.
- Conrod PJ, Nikolaou K (2016) Annual research review: On the developmental neuropsychology of substance use disorders. J Child Psychol Psychiatry, 57:371–394.
- Constans JI (2005) Information-Processing Biases in PTSD. In Vasterling JJ, Brewin CR (Eds), *Neuropsychology of PTSD: Biological, cognitive, and clinical perspectives* (pp. 105–130). New York, NY: Guilford Press.
- Constans JI, McCloskey MS, Vasterling JJ, Brailey K, Mathews A (2004) Suppression of attentional bias in PTSD. J Abnorm Psychol. 113:315–323.
- Cox WM, Hogan LM, Kristian MR, Race JH (2002) Alcohol attentional bias as a predictor of alcohol abusers' treatment outcome. Drug Alcohol Depend. 68:237–243.
- 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. *J Int Neuropsychol Soc.* 21: 342–352.
- Drobes DJ, Elibero A, Evans DE (2006) Attentional bias for smoking and affective stimuli: A Stroop task study. *Psychol Addict Behav.* 20:490–495.
- Dunning JP, Parvaz MA, Hajcak G, Maloney T, Alia-Klein N, Woicik PA, Telang F, Wang GJ, Volkow ND, Goldstein RZ (2011) Motivated attention to cocaine and emotional cues in abstinent and current cocaine users–an ERP study. *Eur J Neurosci.* 33:1716–1723.
- Elsesser K, Sartory G, Tackenberg A (2005) Initial symptoms and reactions to traumarelated stimuli and the development of posttraumatic stress disorder. *Depress Anxiety*. 21:61–70.

6 www.jonmd.com

- Esterman M, DeGutis J, Mercado R, Rosenblatt A, Vasterling JJ, Milberg W, McGlinchey R (2013) Stress-Related Psychological Symptoms Are Associated with Increased Attentional Capture by Visually Salient Distractors. J Int Neuropsychol Soc. 19:835–840.
- Falconer E, Bryant R, Felmingham KL, Kemp AH, Gordon E, Peduto A, Olivieri G, Williams LM (2008) The neural networks of inhibitory control in posttraumatic stress disorder. J Psychiatry Neurosci. 33:413–422.
- Fani N, Tone EB, Phifer J, Norrholm SD, Bradley B, Ressler KJ, Kamkwalala A, Jovanovic T (2012) Attention bias toward threat is associated with exaggerated fear expression and impaired extinction in PTSD. *Psychol Med.* 42:533–543.
- Field M, Cox WM (2008) Attentional bias in addictive behaviors: A review of its development, causes, and consequences. Drug Alcohol Depend. 97:1–20.
- Field M, Munafö MR, Franken IH (2009) A meta-analytic investigation of the relationship between attentional bias and subjective craving in substance abuse. *Psychol Bull*. 135:589–607.
- First MB, Spitzer RL, Gibbon M, Williams JB (2002) Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-Patient Edition (SCID-I/NP). New York, NY: Biometrics Research, New York State Psychiatric Institute.
- Fortier CB, Amick MM, Grande L, McGlynn S, Kenna A, Morra L, Clark A, Milberg WP, McGlinchey RE (2013) The Boston Assessment of Traumatic Brain Injury-Lifetime (BAT-L) semistructured interview: Evidence of research utility and validity. J Head Trauma Rehabil. 29:89–98.
- Gillie BL, Thayer JF (2014) Individual differences in resting heart rate variability and cognitive control in posttraumatic stress disorder. *Front Psychol.* 5:758.
- Green P (2003) Green's Medical Symptom Validity Test (MSVT) for Windows: User's manual. Edmonton, Canada: Green's Publishing.
- Harvey AG, Bryant RA, Rapee RM (1996) Preconscious processing of threat in posttraumatic stress disorder. Cogn Ther Res. 20:613–623.
- Hauschildt M, Wittekind C, Moritz S, Kellner M, Jelinek L (2013) Attentional bias for affective visual stimuli in posttraumatic stress disorder and the role of depression. *Psychiatry Res.* 207:73–79.
- Hester R, Dixon V, Garavan H (2006) A consistent attentional bias for drug-related material in active cocaine users across word and picture versions of the emotional Stroop task. *Drug Alcohol Depend.* 81:251–257.
- Kaplan JS, Erickson K, Luckenbaugh DA, Weiland-Fiedler P, Geraci M, Sahakian BJ, Charney D, Drevets WC, Neumeister A (2006) Differential performance on tasks of affective processing and decision-making in patients with panic disorder and panic disorder with comorbid major depressive disorder. J Affect Disord. 95: 165–171.
- Karr JE, Areshenkoff CN, Duggan EC, Garcia-Barrera MA (2014) Blast-related mild traumatic brain injury: A Bayesian random-effects meta-analysis on the cognitive outcomes of concussion among military personnel. *Neuropsychol Rev.* 24: 428–444.
- Kimble MO, Fleming K, Bandy C, Kim J, Zambetti A (2010) Eye tracking and visual attention to threating stimuli in veterans of the Iraq War. J Anxiety Disord. 24: 293–299.
- Lambe L, Hudson A, Stewart SH (2014) Drinking motives and attentional bias to affective stimuli in problem and non-problem drinkers. *Psychol Addict Behav.* 29: 312–316. Advance online publication.
- Leskin LP, White PM (2007) Attentional networks reveal executive function deficits in posttraumatic stress disorder. *Neuropsychology*. 21:275–284.
- Lubman DI, Allen NB, Peters LA, Deakin JF (2008) Electrophysiological evidence that drug cues have greater salience than other affective stimuli in opiate addiction. *J Psychopharmacol.* 22:836–842.
- Marissen MA, Franken IH, Waters AJ, Blanken P, van den Brink W, Hendriks VM (2006) Attentional bias predicts heroin relapse following treatment. *Addiction*. 101:1306–1312.
- McGlinchey RE, Milberg WP, Fonda JR, Fortier CB (2017) A methodology for assessing deployment trauma and its consequences in OEF/OIF/OND veterans: The TRACTS longitudinal prospective cohort study. *Int J Methods Psychiatr Res.* 2017;e1556. doi: 10.1002/mpr.1556. [Epub ahead of print].

© 2017 Wolters Kluwer Health, Inc. All rights reserved.

- Naim R, Wald I, Lior A, Pine DS, Fox NA, Sheppes G, Halpern P, Bar-Haim Y (2014) Perturbed threat monitoring following a traumatic event predicts risk for posttraumatic stress disorder. *Psychol Med.* 44:2077–2084.
- Olatunji BO, Armstrong T, Bilsky SA, Zhao M (2015) Threat modulation of visual search efficiency in PTSD: A comparison of distinct stimulus categories. *Psychi*atry Res. 229:975–982.
- Pineles SL, Shipherd JC, Mostoufi SM, Abramovitz SM, Yovel I (2009) Attentional biases in PTSD: More evidence for interference. *Behav Res Ther*. 47:1050–1057.
- Pineles SL, Shipherd JC, Welch LP, Yovel I (2007) The role of attentional biases in PTSD: Is it interference or facilitation? *Behav Res Ther.* 45:1903–1913.
- Robbins TW, James M, Owen AM, Sahakian BJ, Lawrence AD, McInnes L, Rabbitt PM (1998) A study of performance on tests from the CANTAB battery sensitive to frontal lobe dysfunction in a large sample of normal volunteers: Implications for theories of executive functioning and cognitive aging. Cambridge Neuropsychological Test Automated Battery. J Int Neuropsychol Soc. 4:474–490.
- Robbins TW, James M, Owen AM, Sahakian BJ, McInnes L, Rabbitt P (1994) Cambridge Neuropsychological Test Automated Battery (CANTAB): A factor analytic study of a large sample of normal elderly volunteers. *Dementia*. 5:266–281.
- Rzetelny A, Gilbert DG, Hammersley J, Radtke R, Rabinovich NE, Small SL (2008) Nicotine decreases attentional bias to negative-affect-related Stroop words among smokers. *Nicotine Tob Res.* 10:1029–1036.
- Samuelson KW, Neylan TC, Metzler TJ, Lenoci M, Rothlind J, Henn-Haase C, Choucroun G, Weiner MW, Marmar CR (2006) Neuropsychological functioning in posttraumatic stress disorder and alcohol abuse. *Neuropsychology*. 20:716–726.
- Seal KH, Cohen G, Waldrop A, Cohen BE, Maguen S, Ren L (2011) Substance use disorders in Iraq and Afghanistan veterans in VA healthcare, 2001–2010:

Implications for screening, diagnosis and treatment. *Drug Alcohol Depend*. 116: 93–101.

- Seymour KE, Kim KL, Cushman GK, Puzia ME, Weissman AB, Galvan T, Dickstein DP (2015) Affective processing bias in youth with primary bipolar disorder or primary attention-deficit/hyperactivity disorder. *Eur Child Adolesc Psychiatry*. 24: 1349–1359.
- Smith JL, Mattick RP, Jamadar SD, Iredale JM (2014) Deficits in behavioural inhibition in substance abuse and addiction: A meta-analysis. *Drug Alcohol Depend*. 145:1–33.
- Steiner AR, Petkus AJ, Nguyen H, Wetherell JL (2013) Information processing bias and pharmacotherapy outcome in older adults with generalized anxiety disorder. *J Anxiety Disord.* 27:592–597.
- Tull MT, McDermott MJ, Gratz KL, Coffey SF, Lejuez CW (2011) Cocaine-related attentional bias following trauma cue exposure among cocaine dependent in-patients with and without post-traumatic stress disorder. *Addiction*. 106: 1810–1818.
- Vasterling JJ, Brailey K, Constans JI, Sutker PB (1998) Attention and memory dysfunction in posttraumatic stress disorder. *Neuropsychology*. 12:125–133.
- Weinstein A, Cox WM (2006) Cognitive processing of drug-related stimuli: The role of memory and attention. J Psychopharmacol. 20:850–859.
- Wittekind CE, Muhtz C, Jelinek L, Moritz S (2015) Depression, not PTSD, is associated with attentional biases for emotional visual cues in early traumatized individuals with PTSD. *Front Psychol.* 5:1474.
- Wright L, Lipszyc J, Dupuis A, Thayapararajah SW, Schachar R (2014) Response inhibition and psychopathology: A meta-analysis of go/no-go task performance. *J Abnorm Psychol.* 123:429–439.