Inefficient Attentional Control Explains Verbal Memory Deficits Among Military Veterans with Posttraumatic Reexperiencing Symptoms

Supplemental Material

Participant Recruitment and Criteria

"Study 1" and "Study 2" represent two separate studies funded by the US Department of Veterans Affairs (I01RX000622) and the US Department of Defense (PT074550), respectively. The studies had similar research goals, mainly to recruit veterans with posttraumatic stress symptomatology and mild traumatic brain injury, and contrast the neurobiological and cognitive characteristics of these conditions through the use of experimental and clinical measures. Study 1 was executed from 2008 – 2012 while Study 2 was executed from 2012 – 2016. Study designs were similar and recruitment was undertaken using similar sources. Given the availability of the California Verbal Learning Test Second Edition (CVLT-II; Delis, 2000; Donders, 2008) and Wide Range Achievement Test (WRAT; Wechsler, 2001) in both studies, we opted to include participants from both samples in analyses of these measures to increase statistical power and generalizability of findings.

Exclusion criteria for Study 1. 1) a neurological condition or major DSM-IV-TR Axis I mental disorder prior to deployment [First, Spitzer, Gibbon, & Williams, 2002], 2) current DSM-IV-TR-defined psychotic disorder, 3) current or past *DSM-IV-TR*-defined substance dependence other than alcohol, caffeine, or nicotine, 4) current *DSM-IV-TR*-defined substance abuse other than alcohol, caffeine, or nicotine, 5) testing positive for elevated blood alcohol content the day of the study, 6) current or past formal diagnosis of attention-deficit/hyperactivity disorder, 7) significant risk of suicidal or homicidal behavior, 8) current or past unstable medical condition likely affecting brain functioning (e.g., clear anoxic episode, cardiac arrest, current uncontrolled diabetes), 9) head injury from a source other than blast resulting in loss of consciousness greater than 10 minutes, post-traumatic amnesia greater than one hour, skull fracture, positive neuroradiological findings, or hospitalization for more than 24 hours, or, 10) has been a frequent boxer or kickboxer. If currently receiving mental health services, veterans were not asked to alter any potential ongoing care as a prerequisite to study participation. We opted to include one individual with multiple blast-related mild TBI events who may have sustained one "moderate" blast-related TBI (rated based on reported 30 - 120 minute possible loss of consciousness). Excluding this individual did not substantively alter effect sizes for key findings within this report.

Exclusion criteria for Study 2. Participants were excluded if they shared evidence of current or past unstable medical conditions that would likely alter brain functioning (e.g., clear anoxic episode, current uncontrolled diabetes), neurological conditions, current *DSM-IV-TR* psychotic disorders, current or past *DSM-IV-TR* substance dependence other than alcohol, caffeine, or nicotine, current *DSM-IV-TR* substance abuse other than alcohol, caffeine, or nicotine, or current or past formal diagnosis of attention-deficit/hyperactivity disorder (ADHD). Exclusion also occurred when participants reported head injury with loss of consciousness greater than 30 minutes, post-traumatic amnesia for more than 24 hours, skull fracture, positive neuroradiological findings, or hospitalization for more than 24 hours due to head injury (i.e., TBI that was moderate in severity or greater). Frequent boxers and kickboxers were excluded. Participants who tested positive for elevated blood alcohol content on the day of the study were

excluded. In keeping with the cross-sectional design evaluating the range of typical post-deployment functioning among veterans, individuals currently receiving mental health treatment were not asked to alter ongoing care. Participants in Study 2 were allowed to have a history of a major DSM-IV-TR Axis I mental disorder prior to deployment (e.g., major depression) excepting the conditions listed above (e.g., psychosis, ADHD).

Demographics and Clinical Characteristics for Study 1 Laboratory Participants Only

For the Study 1 sample participating in the laboratory task of verbal memory, groups did not differ by gender or age, $ps \geq .068$ (Table S1). Although there were no differences in ethnic minority status between PTSD groups, $p = .435$, participants with histories of blast-related mTBI less frequently identified as ethnic minority, $\chi^2 = 4.02$, $p = .045$, *Cramer's V* = .165. There was a PTSD effect for years of education, $F(1,135) = 4.83$, $p = .030$, $\eta_p^2 = .035$. On average, individuals meeting study criteria for PTSD reported approximately 0.7 less years of education. There were no main or interaction effects with mTBI for education, ps $\geq$ .593. Among veterans with blast mTBI, there were group differences between individuals with and without PTSD based on months since experiencing their blast mTBI event, $F(1,63) = 10.01$, $p = .002$, $\eta_p^2 = .137$. On average, veterans with mTBI and PTSD were 1.5 years more distal from their blast events than individuals with mTBI and without PTSD. However, yes-mTBI/no-PTSD individuals were still assessed approximately three years away from their mTBI events, on average. Individuals with PTSD were more likely to meet criteria for comorbid depressive disorder, $\chi^2 = 20.60$, $p < .001$, *Cramer's V* = .374, and comorbid alcohol dependence $\chi^2 = 10.37$, $p < .001$, *Cramer's V* = .266. Individuals with blast-related mTBI histories were also more likely to meet criteria for a depressive disorder, $\chi^2 = 6.61$, $p = .010$, *Cramer's V* = .212, but there were no group differences in rates of comorbid alcohol dependence, $p = .115$.

Statistical Isolation of the Delayed Memory Effect for Study Neuropsychological Measures

In order to further test the specificity of the observed assocation with Delayed Recall on the California Verbal Learning Test Second Edition, we conducted additonal follow-up analyses. We computed linear regressions predicting Delayed Recall from the reexperiencing symptom severity score and from each of the other CVLT-II domain or WRAT neuropsychological scores. In this way, we utilized covariates to isolate statistical variance specific to the Delayed Recall domain of functioning. Across all four models (Table S2), reexperiencing symptom severity remained a significant predictor of memory performance. Thus, we confirmed the specificity of the relationships between intrusive reexperiencing symptomatology and explicit verbal memory. This relationship could not be explained by general word processing performance.

Validation for for the Combined Full and Subthreshold PTSD Criterion

To better describe the study sample and contextualize the findings with respect to the categorical criteria for PTSD, we performed one-way between-subjects ANOVAs predicting CAPS Total Score (frequency + intensity; Weathers, Keane, & Davidson, 2001) as well as global assessment of functioning (GAF) ratings from the Structured Clinical Interview for DSM-IV-TR (Aas, 2010; First, Spitzer, Gibbon, & Williams, 2002). We included PTSD Status as a categorical predictor with three levels: comparison control, subthreshold PTSD, and full-threshold PTSD. As described in the main body of the manuscript, subthreshold PTSD was defined as at least one symptom within each of the Criterion B-D domains while full-threshold PTSD required one Criterion B, three Criterion C, and two Criterion D symptoms (American Psychiatric

Association, 2000). Data from both Study 1 and Study 2 were combined together (subthreshold PTSD $n = 51$, full-threshold PTSD $n = 61$).

There was a main effect of PTSD Status on CAPS total score, $F(2,195) = 165.59$, $p < .001$. On average, individuals with subthreshold PTSD presented with an intermediate severity of overall symptoms (mean = 35.9, SD = 14.1) between comparison controls (mean = 18.5, SD = 12.0) and individuals with full-threshold PTSD (mean = 64.2, SD = 19.1; all post-hoc comparisons ps < .001). A similar main effect was observed for PTSD Status on GAF scores, $F(2,237) = 100.1$, $p < .001$. On average, comparison controls were rated as experiencing transient and expectable reactions to psychosocial stressors (i.e., mean = 71.5, SD = 9.0). Individuals with subthreshold PTSD reported mild-moderate symptoms or psychosocial difficulties (i.e., mean = 61.6, SD = 6.6). Individuals with full-threshold PTSD reported moderate symptoms or psychosocial difficulties (i.e., mean = 55.7, SD = 6.6). The combined results are consistent with clinically meaningful presentations of posttraumatic stress symptomatology among the individuals meeting study criteria for subthreshold PTSD.

Associations with Signal Detection Response Bias During Laboratory Task

For the Recognition portion of the laboratory verbal memory task, the signal detection metric of C was calculated in addition to D' to assess response bias. We performed a PTSD (2) - by- mTBI (2) ANOVA predicting C. However, there were no main or interaction effects for PTSD or mTBI, $p \geq .394$. Furthermore, partial correlations between PTSD symptom groupings and C while controlling for blast-related mTBI severity were not significant, $p \geq .201$. Thus, neither categorical nor dimensional clinical variables were not significantly associated with yea-saying or nay-saying with regards to target detection on the cued-recognition portion of the task.

Statistical Isolation of Lexical Implicit Priming Effect

As a stronger test of the implicit priming effect on response time (RT) during the lexical decision-making task, we performed additional ANCOVA analyses. Old word RT was predicted using PTSD (2) -by- mTBI (2) between-subjects factors, but new word RT was used as a covariate. In this way, the RT enhancement effect for old relative to new words could be modeled statistically and predicted using the same categorical predictors. Unsurprisingly, new word RT was a significant predictor of old word RT, $F(1,142) = 1098.90$, $p < .001$, $\eta_p^2 = .886$. However, there were no main or interaction effects for PTSD or mTBI, $p \geq .072$. Additionally, we computed partial correlations between posttraumatic stress symptom grouping severity scores (reexperiencing, avoidance, dysphoria, hyperarousal; Yufik & Simms, 2010), and old word RT. New word RT and total blast mTBI severity were included as covariates. None of the partial correlations reached significance, ps $\geq .230$. Therefore, this more targeted assessment of the lexical priming effects revealed no associations between implicit memory functioning and the primary clinical variables of interest.

Tables

Table S1

Demographics and Clinical Characteristics for Study 1 Laboratory Participants Only.

	Participant Status											
	No PTSD						PTSD					
	No mTBI			TBI			No mTBI			TBI		
Variable	*n*	*Mean*	*SD*	*n*	*Mean*	*SD*	*n*	*Mean*	*SD*	*n*	*Mean*	*SD*
Total	41			17			41			48		
Female	6			0			3			2		
Minority	6			0			4			2		
Age, years[a]		33.4	8.7		35.1	8.8		32.6	8.7		30.7	6.2
Education, years[a]		15.0	1.6		15.1	2.0		14.5	1.8		14.2	1.6
Time Since Blast mTBI, months[a]												
Depressive disorder[b]	2			4			17			24		
Alcohol dependence[c]	2			4			14			16		
CAPS All Sections Completed	4			6			41			48		

Note. PTSD = posttraumatic stress disorder, mTBI = mild traumatic brain injury, CAPS = Clinician-Administered PTSD scale for *DSM-IV*.

[a] Presented as group mean values using all available data.
[b] Current DSM-IV-TR major depressive disorder or dysthymia.
[c] Current DSM-IV-TR alcohol dependence.

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Table S2

Predicting CVLT-II Delayed Recall with CVLT-II and WTAR Covariates.

Predictors	*b*	β	*SE*	*t*	*p*
Model A					
CAPS Reexperiencing	-.057	-.103	.028	-2.009	.046
CVLT-II Attention Span	1.281	.594	.111	11.549	< .001
Model B					
CAPS Reexperiencing	-.056	-.102	.024	-2.304	.022
CVLT-II Learning					
Efficiency	1.243	.720	.076	16.353	< .001
Model C					
CAPS Reexperiencing	-.056	-.102	.024	-2.893	.004
CVLT-II Inaccurate					
Recall	1.243	.720	.076	-4.678	< .001
Model D					
CAPS Reexperiencing	-.100	-.177	.035	-2.827	.005
WTAR	.094	.172	.034	2.758	.006

Note. Linear regression predictors of Delayed Memory performance during the neuropsychological assessment performed with this study. CVLT-II = California Verbal Learning Test Second Edition, WTAR = Wide Range Achievement Test, CAPS = Clinician-Administered PTSD Scale for DSM-IV, SE = standard error.

Table S3
Mediation Models Testing Indirect Effects of Cognitive Processes to Explain Verbal Memory Performance.

| | | | | Bootstrap Results | | |
| | | | | | 95% CI | |
Predictor (*a*)	**Outcome (*Y*)**	**Mediator (*b*)**	**Indirect Effect (*ab*)**	*SE*	*LL*	*UL*
Encoding Inefficiency Hypothesis:						
Model A						
Reexperiencing	Free Recall	Encoding Accuracy	-.0263	.0364	-.1013	.0431
Reexperiencing	**Free Recall**	**Encoding RT**	**-.0464**	**.0259**	**-.1069**	**-.0029**
Model B						
Reexperiencing	Recognition	Encoding Accuracy	-.0021	.0028	-.0078	.0034
Reexperiencing	**Recognition**	**Encoding RT**	**-.0030**	**.0015**	**-.0063**	**-.0003**
Non-specific Inefficiency Hypothesis:						
Model C						
Reexperiencing	Free Recall	Lexical Overall Accuracy	-.0045	.0231	-.0616	.0357
Reexperiencing	Free Recall	Lexical Overall RT	-.0387	.0244	-.0903	.0033
Model D						
Reexperiencing	Recognition	Lexical Overall Accuracy	-.0005	.0025	-.0060	.0043
Reexperiencing	Recognition	Lexical Overall RT	-.0017	.0018	-.0053	.0019
Implicit Memory Hypothesis:						
Model E						
Reexperiencing	Free Recall	Lexical Old Word RT	.0011	.0107	-.0243	.0229
Model F						
Reexperiencing	Recognition	Lexical Old Word RT	.0001	.0010	-.0020	.0022

Note. Summary of the indirect effect estimates for the mediation models employed in the main body of the manuscript. The same effects are depicted in graphical form within Figure 2. Models E and F included a covariate term for the new word RT condition. CI = confidence interval, SE = standard error, LL = lower limit, UL = upper limit, RT = response time.

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Table S4
Delayed Recall.

	F	p	η_p^2
Model A			
PTSD (Full)	**4.63**	**.032**	**.019**
mTBI	1.38	.241	.006
PTSD (Full) * mTBI	.86	.355	.004
Model B			
PTSD (Full+Sub)	**5.23**	**.023**	**.021**
mTBI	1.18	.279	.005
PTSD (Full+Sub) * mTBI	.05	.827	.000

Note. Comparison of ANOVA model effects predicting Delayed Recall performance using either the full or full plus subthreshold PTSD criteria. PTSD = posttraumatic stress disorder, mTBI = mild traumatic brain injury.

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Table S5.
Encoding RT.

	F	*p*	η_p^2
Model A			
PTSD (Full)	2.40	.123	.017
mTBI	1.81	.180	.013
PTSD (Full) * mTBI	2.13	.147	.015
Model B			
PTSD (Full+Sub)	3.50	.063	.024
mTBI	2.23	.138	.015
PTSD (Full+Sub) * mTBI	1.22	.272	.008

Note. Comparison of ANOVA model effects predicting Encoding response time (RT) using either the full or full plus subthreshold diagnostic criteria. PTSD = posttraumatic stress disorder, mTBI = mild traumatic brain injury.

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Table S6.
Free Recall.

	F	p	η_p^2
Model A			
PTSD (Full)	2.89	.091	.020
mTBI	3.36	.069	.023
PTSD (Full) * mTBI	.07	.787	.001
Model B			
PTSD (Full+Sub)	**4.80**	**.030**	**.032**
mTBI	3.53	.062	.024
PTSD (Full+Sub) * mTBI	1.22	.271	.008

Note. Comparison of ANOVA model effects predicting laboratory task free recall performance using either the full or full plus subthreshold diagnostic criteria. PTSD = posttraumatic stress disorder, mTBI = mild traumatic brain injury.

Table S7.
Lexical RT.

	F	p	η_p^2
Model A			
PTSD (Full)	**5.55**	**.020**	**.037**
mTBI	1.04	.310	.007
PTSD (Full) * mTBI	.68	.412	.005
Condition	**149.17**	**<.001**	**.678**
Condition * PTSD (Full)	1.84	.162	.025
Condition * mTBI	.61	.545	.009
Condition * PTSD (Full) * mTBI	2.30	.104	.031
Model B			
PTSD (Full+Sub)	**4.81**	**.030**	**.033**
mTBI	1.06	.306	.007
PTSD (Full+Sub) * mTBI	.07	.799	<.001
Condition	**127.95**	**<.001**	**.643**
Condition * PTSD (Full+Sub)	.49	.616	.007
Condition * mTBI	.35	.707	.005
Condition * PTSD (Full+Sub) * mTBI	2.00	.140	.027

Note. Comparison of MANOVA model effects predicting lexical decision making response time (RT) using either the full or full plus subthreshold diagnostic criteria. Condition (3) effects were modeling using levels of old word, new word, and nonword. PTSD = posttraumatic stress disorder, mTBI = mild traumatic brain injury.

Table S8.

Recognition D'

	F	*p*	η_p^2
Model A			
PTSD (Full)	**6.61**	**.011**	**.044**
mTBI	2.01	.159	.014
PTSD (Full) * mTBI	1.27	.262	.009
Model B			
PTSD (Full+Sub)	**7.14**	**.008**	**.048**
mTBI	.95	.331	.007
PTSD (Full+Sub) * mTBI	.81	.370	.006

Note. Comparison of ANOVA model effects predicting laboratory task recognition performance using either the full or full plus subthreshold diagnostic criteria. PTSD = posttraumatic stress disorder, mTBI = mild traumatic brain injury.

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