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Research Letter: PTSD Symptom Severity and Multiple Traumatic Brain Injuries are Associated with Elevated Memory Complaints in Veterans with Histories of Mild TBI

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Abstract

Objective: The evaluation of memory complaints in mild traumatic brain injury (mTBI) remains an important clinical consideration especially in the context of comorbid psychiatric symptoms such as posttraumatic stress disorder (PTSD). We compared subjective memory complaints in Veterans with and without a history of mTBI, examined ratings between those with single versus multiple mTBIs, and investigated associations between memory complaints and PTSD symptom severity.

Methods: 117 outpatient Veterans (mTBI=79 [single-mTBI=22, multiple-mTBI=57], Military Controls (MCs)=38) completed a TBI history assessment, the Prospective-Retrospective Memory Questionnaire (PRMQ), and the PTSD Checklist-Military Version (PCL-M).

Results: Hierarchical multiple regression showed greater PCL-M scores significantly predicted elevated PRMQ-Total scores, accounting for 38% of the variance explained (p<.001). mTBI status predicted an additional 5% of variance in memory complaints (p<.01). The multiple-mTBI group endorsed more memory complaints than either MCs (p<.01) or the single-mTBI group (p<.05), who did not differ from MCs (p>.50).

Conclusions: Comorbid PTSD symptoms are an important factor when considering memory complaints in Veterans with a reported history of mTBI. However, independent of comorbid PTSD symptoms, mTBI status—particularly in the context of repetitive neurotrauma—uniquely contributes to memory complaints. Findings suggest Veterans with a history of multiple mTBIs may be a particularly vulnerable group in need of specialized interventions and/or psychoeducation.

INTRODUCTION

Although most individuals who sustain a mild traumatic brain injury (mTBI) experience a full recovery in the post-acute phase of injury, a subset of individuals report persisting cognitive, physical and emotional symptoms for months and even years following their injury[1]. In samples of US military Veterans with a history of mTBI, psychiatric symptoms such as posttraumatic stress disorder (PTSD) are consistently identified as key factors influencing persisting and heightened post-concussive symptoms[2–4]. Such findings are largely based on the use of the Neurobehavioral Symptom Inventory[5] (NSI), a 22-item measure of common post-concussive symptoms, which provides an aggregate measure of symptom severity across multiple neurological domains. However, with just four items related to cognition, the NSI provides only a screening of potential cognitive symptoms and includes only one item specifically related to memory (i.e., “forgetfulness”).

Considering that memory complaints are frequently reported by Veterans with mTBI[6], there remains a need to more thoroughly evaluate the extent to which memory complaints are elevated in Veterans with a history of mTBI and to evaluate the potential psychiatric influences on those associations. Moreover, there are conflicting reports regarding the effect of repetitive head trauma on symptom outcomes following mTBI[7,8], which have not previously been examined with respect to subjective memory complaints. Therefore, our understanding of the nature and etiology of subjective memory complaints in the post-acute phase of mTBI in Veterans remains limited, as does the possible relative contribution of TBI injury variables (e.g., number of mTBIs) and other key factors such as comorbid psychiatric distress.

In the present study, we examined whether a measure specifically designed to assess both retrospective and prospective memory complaints — the Prospective-Retrospective Memory Questionnaire[9] — may show group differences between Veterans with and without a history of mTBI after adjusting for current PTSD symptoms. We expected that greater memory complaints on the PRMQ would be related to higher PTSD symptom ratings, and the mTBI group would show greater PRMQ complaints compared to controls. Moreover, we investigated dose effects of single versus multiple mTBIs with respect to memory complaints, with the expectation that higher PRMQ ratings would be associated with multiple mTBIs.

METHODS

Participants and Procedures.

Participants included 117 Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn (OEF/OIF/OND) Veterans with and without a history of mTBI (mTBI: $n = 79$; mean age = 34.1 years, SD = 6.9; Military Control [MC]: $n = 39$; mean age = 31.8 years, SD = 6.9). Study data was collected from participants referred to a TBI specialty clinic within the VA San Diego Healthcare System (VASDHS, n = 34) and from Veterans enrolled in TBI-focused research programs at the VASDHS (n = 45). Information regarding TBI history was gathered from Veterans enrolled in the TBI specialty clinic via completion of a semi-structured clinical interview focused on their

TBI history conducted by clinical neuropsychologists or advanced doctoral trainees and by chart review. Participants whose TBI history data did not stem from assessments within the TBI specialty clinic were administered a modified version of the VA Semi-Structured Clinical Interview for TBI[10]. Across settings, information was gathered regarding the occurrence and duration of: (1) loss of consciousness (LOC); (2) post-traumatic amnesia (PTA); and/or (3) alteration of consciousness (AOC). All Veterans with mTBI were in at least the post-acute phase following mTBI (defined as being 7–12 weeks post-injury[11]). Detailed information regarding time since injury was not available for Veterans from the clinic-derived sample; however, such information was available for the 45 mTBI participants in the research-recruited sample (Mean time since injury = 6.9 years, SD = 4.8). All study procedures took place within the VASDHS campus. The present study was reviewed and approved by the local VA institutional review board and informed consent was obtained from all participants prior to study participation.

Mild TBI was defined by VA/DoD criteria[11] including: LOC ≤ 30 minutes, PTA ≤ 24 hours, and/or AOC ≤ 24 hours. TBI classification was based on self-reported duration of LOC, AOC, and PTA. TBI study criteria included a history of at least one head injury meeting the above diagnostic criteria for a mild TBI. Veterans with a history of a moderate or severe TBI were excluded. Control participants endorsed no history of TBI. Additional exclusion criteria were: (1) meeting DSM-IV-TR criteria for current substance/alcohol abuse or dependence, (2) having a primary psychotic disorder and (3) having a history of a serious medical illness or neurological disorder (e.g., epilepsy, stroke).

Measures.

Self-Report Questionnaires: The PRMQ is a well-validated measure designed to assess self-reported prospective and retrospective memory difficulties in everyday life. The 16-item scale contains eight prospective (e.g., forgetting to follow through with an intended task) and eight retrospective (e.g., forgetting information recently learned) memory complaints. A PRMQ total score was derived from the measure, as well as prospective and retrospective memory subscale scores[9].

PTSD symptoms were assessed using the PTSD Checklist–Military Version (PCL-M), a 17-item self-report measure scored on a scale from 17–85 with higher scores reflecting more severe symptoms of PTSD[12].

Statistical Analyses

Group differences in demographic and clinical variables were assessed using one-way ANOVA and chi-square analyses for continuous and categorical variables, respectively. This was done across all three groups as well as between the two mTBI subgroups. Hierarchical linear regression was performed in order to examine the relationship between mTBI status and PRMQ scores (i.e., total score, prospective and retrospective subscales) while adjusting for PTSD symptom severity (i.e., PCL-M total scores) and age. Three levels of mTBI status were identified: (1) no history of mTBI (i.e., MCs, n = 38), (2) single-mTBI (n = 22), and (3) multiple-mTBI (n = 57), and they were then dummy coded in the analysis. The MC group served as the comparison group for the two mTBI groups. A separate hierarchical

regression was run for each PRMQ score as the dependent variable including the total score and memory subscales. PCL-M scores and age were the only predictors included in the first level analysis and the two mTBI-coded dummy variables were added at the second level. Finally, an analysis of covariance (ANCOVA), adjusting for PTSD symptoms and age, was used to investigate the degree to which memory complaints differed between participants with single versus multiple mTBIs. All statistical analyses were conducted using SPSS version 26.

RESULTS

As shown in Table 1, the MC group and mTBI subgroupings did not significantly differ across demographic variables. However, as expected, PTSD symptomology significantly differed across groups with mTBI groups showing higher levels compared to the MC group ($p < .001$, $\eta_p^2 = .336$).

As shown in Table 2, across the entire sample, hierarchical regression confirmed that the PCL-M total score was a significant predictor of PRMQ-Total scores, accounting for 38% of the variance explained ($p < .001$, $\beta = .623$). When mTBI group was included in the model, PCL-M scores continued to account for the greatest portion (~18%) of unique variance in PRMQ-Total scores ($p < .001$, $\beta = .50$); however, an additional 5% of the variance in PRMQ-Total score was accounted for by mTBI status ($p = .01$, $\Delta R^2 = .05$), demonstrating that mTBI status confers additional unique information beyond what is accounted for by PCL-M scores alone. PRMQ scores of those reporting a single mTBI did not significantly differ from MCs ($p =. 59$, $\beta = .045$). However, those reporting multiple-mTBIs endorsed significantly higher PRMQ ratings than MCs, uniquely accounting for 4% ($p = .006$, $\beta = .271$) of the variance in PRMQ-Total scores (see Figure 1). Models using the prospective and retrospective subscales of the PRMQ as the outcome variable showed the same pattern of results with minimal variations in predictor effect sizes (see Table 2).

The multiple-mTBI subgroup endorsed significantly higher levels of PTSD symptoms on the PCL-M compared to the single-mTBI subgroup ($p = .03$, d =.53). As shown in Table 1, the two mTBI subgroups did not significantly differ on age, sex, ethnicity, mechanism of injury, time since injury, or proportion of AOC versus LOC (p's > .10). The multiple mTBI group reported a greater percentage of PTA compared to the single mTBI group ($p = .01$). Adjusting for PCL-M scores and age, a follow-up ANCOVA found that the multiple-mTBI subgroup endorsed significantly higher PRMQ-Total score ratings compared to the single-mTBI subgroup ($F_{1,75} = 5.448$, $p = .02$, $\eta_p^2 = .068$). Examination of PRMQ subscales revealed a significant difference by group such that the multiple-mTBI subgroup demonstrated higher scores than the single-mTBI subgroup on both the prospective memory ($F_{1,75} = 4.433$, $p = .04$, $\eta_p^2 = .056$) and retrospective memory ($F_{1,75} = 5.468$, $p = .02$, $\eta_p^2 = .068$) subscales.

DISCUSSION

Subjective memory complaints in the post-acute and chronic phases of mTBI are common in Veterans[6] and therefore, remain an important clinical consideration in the assessment

and care of this population. In this study, we show that PTSD *and* TBI history are both important factors to consider when evaluating memory complaints. TBI is highly comorbid with PTSD in Veteran populations, and there is significant overlap among the cognitive and emotional symptoms of PTSD and neurobehavioral sequelae of mTBI. As expected, we found that comorbid PTSD symptoms were a prominent factor associated with subjective memory complaints in Veterans with mTBI histories, which is consistent with other reports[2–4]. These findings further confirm the importance of considering mental health factors in the assessment and treatment of Veterans reporting chronic cognitive difficulties following mTBI. As such, PTSD represents a potentially modifiable factor that may contribute to persisting memory complaints as well as subjective distress and perceived functional ability[13]. Importantly, trauma-focused treatment has been shown to be associated with improvements in objective memory performance[14], and a promising treatment approach integrating compensatory cognitive training with trauma-focused therapy (called “SMART-CPT”) may improve objective memory performance as well as other cognitive functions[15]. With this in mind, an important avenue for future research will be to determine whether these treatments have similar benefits for Veterans with subjective prospective and retrospective memory complaints.

Increases in subjective post-concussive symptoms in Veterans have previously been reported in the context of cumulative blast exposure[7] and repetitive mTBI history[16]. Our results demonstrating that elevated *memory complaints* are associated with a history of multiple mTBIs, independent of PTSD symptoms, represent novel findings of the present study. Results further show the utility of using a dedicated memory measure rather than the limited scales available within a broad post-concussive symptom measure such as the NSI. One recent study using an NSI-derived cognitive subscale identified elevated cognitive symptoms in a group of Veterans with remote repetitive mTBIs compared to controls, but the NSI cognitive subscale failed to distinguish between those reporting repetitive mTBIs and those reporting only one or two mTBIs[16]. In contrast, the present study showed that the PRMQ is sensitive to memory complaints between multiple mTBI and controls as well as between Veterans with single and multiple mTBIs. These results add to the relatively limited findings showing unique effects of mTBI beyond comorbid psychiatric symptoms, especially in Veterans with *remote* mTBIs. Another unique aspect of the current work is our investigation of both prospective and retrospective memory complaints. Notably, as similar findings were observed between both PRMQ subscales, findings suggest a broad impact of repetitive mTBI on subjective reports of memory abilities across memory subtypes.

The findings further indicate that Veterans with a history of multiple mTBIs may be a particularly vulnerable group in need of specialized interventions and/or psychoeducation. Results suggest that the post-concussive symptoms, including complaints of memory difficulties, may be addressable via treatment of PTSD symptoms in those with single-event mTBI, whereas additional therapeutic targets (e.g., integrating cognitive rehabilitation[15]) may be warranted for Veterans with histories of multiple mTBIs. We note that subjective complaints may not align with objective performance[13] and that objective neuropsychological performance is also often tied to psychiatric factors rather than mTBI[17], though some recent findings have shown correspondence between subjective ratings and objective performances in Veterans with histories of mild to moderate TBI[18]. Our findings

do warrant further research aimed at disentangling the unique and shared effects of mTBI and PTSD symptoms in order to elucidate neurobiological underpinnings of each in the expression of persisting symptoms in Veterans with a reported history of multiple mTBIs.

There are some limitations associated with the current study that should be considered when interpreting the findings. While subjective measures are heavily relied upon in clinical practice, our use of self-report measures introduces potential sources of bias to the findings. Importantly, the present study only addresses the magnitude of symptoms associated with PTSD and does not include formal diagnostic information about PTSD status. The cross-sectional design of the study obscures our ability to investigate directionality and cause/effect relationships between reported mTBI history, PTSD symptoms, and memory complaints. Another limitation involves the recruitment of participants from within a research setting and those seeking treatment within a TBI specialty clinic. However, while pooling across settings may obscure some potential differences which may be present between these two samples, it does provide potentially more generalizable findings across the larger population of Veterans with histories of mTBI. Additionally, because the analysis focused on subjective memory complaints in Veterans with remote mTBI, we cannot rule out other factors beyond PTSD that may affect the presentation of post-concussive cognitive complaints. Thus, while multiple mTBIs do show a unique contribution to memory complaints in the present study, there are multiple other variables associated with mTBI in this population which may likewise impact one's subjective report of memory difficulties including combat exposure, number and length of deployments, depression, sleep disorders, pain, current life stressors and levels of social support. Nevertheless, these results offer evidence to suggest that Veterans with a history of multiple mTBIs may be a particularly vulnerable group in need of specialized interventions and/or psychoeducation. Future studies are needed to better understand the relationship between mTBI history and PTSD with respect to the presence of subjective memory difficulties reported by Veterans in the post-acute to chronic phases of injury, as well as the relative contributions of other important factors.

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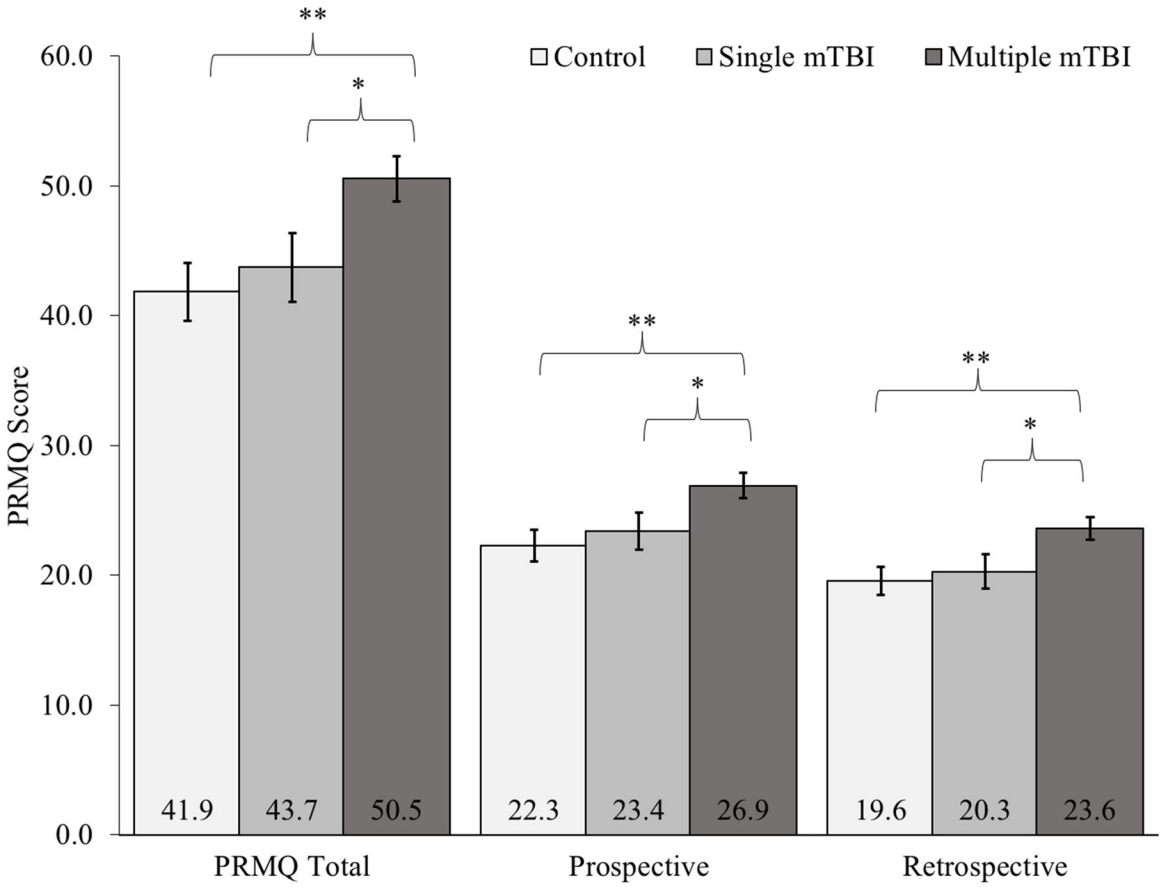

Figure 1.

PRMQ Total and Subscale Scores by mTBI Status.

Values indicate mean adjusted for PCL-M scores and age. Error bars represent one standard error. $^{**}p < .01$, $^{*}p < .05$. PCL-M = PTSD Check List-Military Version; mTBI = mild traumatic brain injury; PRMQ = Prospective Retrospective Memory Questionnaire.

Table 1.

Characteristics of Participants

	Military Control	Single mTBI	Multiple mTBI	*p* *All Groups*	*p* *mTBI Groups*
n	38	22	57		
Age	32.0 (6.9)	32.4 (6.5)	34.8 (7.0)	.12	.18
Education (Years)	14.8 (1.9)	13.9 (1.9)	14.3 (1.7)	.18	.35
% Male	81.60%	86.40%	84.20%	.88	.81
% White	50.00%	36.30%	54.40%	.36	.15
PCL-M Total Score	29.0 (17.2)	44.7 (18.9)	53.5 (15.6)	<.001	.04
PRMQ Total Score	36.0 (14.8)	43.9 (13.8)	54.4 (13.4)	<.001	.003
PRMQ Prospective Score	19.1 (7.7)	23.5 (7.8)	29.0 (7.6)	<.001	.005
PRMQ Retrospective Score	16.9 (7.5)	20.4 (6.4)	25.4 (6.4)	<.001	.003
No. of mTBIs Reported	-	1	3 (1.2)	-	<.001
% Blast mTBI		31.8%	52.6%	-	.097
Any LOC Reported	-	71.4%	63.6%	-	.522
Any PTA Reported	-	27.3%	58.2%	-	.014
Months Since Last mTBI*	-	90.0 (69.7) Range = 2–259 Median = 90.0	79.5 (53.0) Range = 12–267 Median = 68.5	-	.573

Values represent mean and (standard deviation), or percentage, as indicated. Displayed *p*-values represent omnibus comparison across all groups, and between mTBI subgroups. mTBI = mild traumatic brain injury; PCL-M = PTSD Checklist-Military Version; mTBI = mild Traumatic Brain Injury; PRMQ = Prospective Retrospective Memory Questionnaire; LOC = loss of consciousness; PTA = post-traumatic amnesia

*Months since last mTBI includes research participants only (n = 45 mTBI).

Table 2.

Hierarchical Regression Analyses of mTBI Status on PRMQ Total and Subscale Scores

	PRMQ Total			PRMQ Prospective			PRMQ Retrospective		
Variables	**B**	**Beta (β)**	**sp^2**	**B**	**Beta (β)**	**sp^2**	**B**	**Beta (β)**	**sp^2**
Step 1									
PCL-M	0.511***	0.623	.384	0.281***	0.627	.389	0.229***	0.585	.339
Age	0.095	0.041	.002	0.028	0.022	<.001	0.068	0.061	.004
	R^2 = .395			R^2 = .397			R^2 = .353		
	F = 37.181***			F = 37.477***			F = 31.046***		
Step 2									
PCL-M	0.409***	0.5	.178	0.227***	0.507	.183	0.182***	0.464	.154
Age	0.011	0.005	<.001	−0.017	−0.013	<.001	0.028	0.025	<.001
1 vs 0 mTBI	1.855	0.045	.001	1.125	0.05	.002	0.73	0.037	.001
2+ vs 0 mTBI	8.658**	0.271	.040	4.625**	0.264	.038	4.060**	0.265	.038
	ΔR^2 = .05			ΔR^2 = .043			ΔR^2 = .046		
	ΔF = 4.664*			ΔF = 4.312*			ΔF = 4.245*		

Note: Degrees of freedom from Step 1, F(2,114) and for Step 2 F(2,112)

*p<.05

**p<.01

***p<.001

B = unstandardized coefficients; Beta (β) = standardized coefficients ; sp^2 = semi-partial correlation squared; PCL-M = PTSD Checklist-Military Version; mTBI = mild traumatic brain injury; PRMQ = Prospective Retrospective Memory Questionnaire