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Association between spatial working memory and Re-experiencing symptoms in PTSD

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ABSTRACT

Background and objectives: Few studies have evaluated the link between working memory (WM) and post-traumatic stress disorder (PTSD). Further, it is unknown whether this relationship is accounted for by other relevant variables including negative affect, emotional dysregulation, or general non-WM-related cognitive control deficits, which are associated with PTSD. The purpose of this study was to determine the extent to which a computerized WM task could predict PTSD symptomology incrementally beyond the contribution of other relevant variables associated with PTSD.

Methods: Thirty veterans were eligible to complete emotional symptom questionnaires, a heart-rate variability measure, and computerized tasks (i.e., emotional Stroop and automated complex span tasks). A three-stage hierarchical regression was conducted with the PCL-5 total score and symptom clusters (i.e., re-experiencing, avoidance, hyperarousal, and negative cognition/mood) as the dependent variable.

Results: Results revealed that only the re-experiencing symptom cluster was significantly predicted by executive, verbal, and visuospatial WM tasks, which explained an additional 29.7% of the variance over and above other relevant variables. Most notably, the visuospatial task was the only WM task that significantly explained PCL-5 re-experiencing symptoms.

Limitations: This study was based on a small sample of veterans with PTSD and causality cannot be determined with this cross-sectional study.

Conclusions: Overall, the results suggest that deficits in visuospatial WM are significantly associated with PTSD re-experiencing symptoms after controlling for other relevant variables. Further research should evaluate whether an intervention to improve visuospatial WM capacity can be implemented to reduce re-experiencing symptoms.

1. Introduction

Post-traumatic stress disorder (PTSD) includes re-experiencing, avoidance, hyperarousal, and negative cognition/mood following exposure to trauma (American Psychiatric Association, 2013). Researchers suggest that PTSD may be maintained by the encoding and retrieval of traumatic memories (Brewin et al., 1996), and have found an association between PTSD and working memory (WM) deficits (Saunders et al., 2015; Schweizer & Dalgleish, 2011). WM is a limited capacity workspace that temporarily holds and manipulates information for complex tasks (Baddeley & Hitch, 1974). Individuals with elevated trait-anxiety display WM deficits, which may impede relevant task processes (Eysenck & Calvo, 1992; Stout et al., 2015; Bishop, 2007). Given that PTSD is often comorbid with other anxiety disorders (Zoellner et al., 2011; Conwayet al., 2005) and high trait anxiety is a vulnerability factor for the disorder (Schweizer, Samimi, et al., 2017), it is expected that similar WM deficits would be observed in PTSD. Evidence suggests that WM deficits lead to recurrent intrusions in those with PTSD due to inefficient filtering of threatening material, which may result in re-experiencing symptoms (i.e., images, flashbacks, and

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nightmares; Bishop, 2007; Schweizer & Dalgleish, 2011).

Re-experiencing symptoms are central to PTSD and may cause extreme distress, functional impairment, or dissociation from present surroundings (Ashley, Honzel, Larsen, Justus, & Swick, 2013; Michael, Ehlers, Halligan, & Clark, 2005). Additionally, intrusive memories are experienced as visual stimuli more than other sensory types (Ehlers et al., 2002; Hackmann et al., 2004). Re-experiencing symptoms are associated with deficits in visuospatial performance (Gurvits et al., 2002), increased heart rate (Chou et al., 2014), sensory components (Ehlers et al., 2002), and a poor ability to exercise cognitive control and disengage from salient cues (Verwoerd et al., 2009), for which adaptive WM functioning is crucial (Angelidis et al., 2019; Berggren, 2020; Stout et al., 2015; Ye et al., 2018). These intrusive experiences are considered a hallmark feature of PTSD and are more frequently endorsed in these individuals (Durham et al., 1985; Genest et al., 1990; Matthijssen et al., 2017). Therefore, some investigators suggest that other PTSD symptoms clusters like hyperarousal, avoidance, and mood/cognition are secondary to intrusions (Laposa & Rector, 2012).

Despite the association between WM and PTSD, there is little research on the relationship between PTSD symptom clusters and WM domains (e.g., operational, verbal, spatial). Therefore, examining the pattern of WM deficits associated with PTSD symptom clusters is important to understand the specificity of cognitive deficits in PTSD. Research has shown that lower operational and visuospatial WM performance is associated with greater intrusive symptoms (Brewin & Smart, 2005) and that impaired visual WM is a risk factor for re-experiencing symptoms (Mirabolfathi et al., 2016). Further, repeated trauma exposure is associated with poorer visuospatial memory function (Smith et al., 2015; Tempesta et al., 2012). Brain regions associated with visuospatial attention and WM processes (Shackman et al., 2006), are activated during periods of intense stress and anxiety (Keller et al., 2000). Tapping or eye-movements during visuospatial tasks reduced intrusions, suggesting that individuals were able to distract themselves from fully encoding triggering memories (Holmes et al., 2004; Lilley et al., 2009). Indeed, studies in eye-movement desensitization and reprocessing (EMDR) therapy, a treatment that focuses on re-experiencing PTSD symptoms (Matthijssen et al., 2017), has shown a relationship between visuospatial processing and WM (Kavanagh et al., 2001; Lilley et al., 2009). Taken together, examining WM domains is a critical avenue of research to better understand susceptibility to PTSD symptom clusters, especially re-experiencing symptoms.

Little is known about the relationship between WM deficits and re-experiencing symptoms. A WM deficit may be a pre-existing vulnerability factor that contributes to the risk of developing PTSD (Verwoerd et al., 2011), or a cognitive symptom correlated with PTSD (Honzel et al., 2014; Koso & Hansen, 2006). Thus, our cross-sectional study sought to further evaluate the association between PTSD and impaired WM. We examined measures of (1) negative affect (e.g., depression, anxiety, and stress), (2) emotion dysregulation, and (3) non-WM cognitive variables (Kashdan et al., 2010; Klemanski et al., 2012; Price et al., 2006; Tull et al., 2007) as other relevant variables that may influence the PTSD-WM relationship.

Negative affect significantly impedes WM performance (Lee et al., 2012; Moran, 2016; Schoofs et al., 2008), and is elevated in PTSD (Ehring & Quack, 2010; Etkin & Wager, 2007; Vujanovic et al., 2013). Although WM deficits in PTSD are partially attributed to anxiety and depressive symptoms (Dretsch et al., 2012), research has shown that after controlling for these emotional variables, there was a significant association between cognitive control deficits and re-experiencing symptoms, which was not observed for other PTSD symptoms (Bomyea et al., 2012; Dretsch et al., 2012). Therefore, it is important to control for negative affect to accurately evaluate the PTSD-WM relationship.

Negative affect and emotional dysregulation are highly overlapping, yet considered clinically distinct (Bradley et al., 2011). Emotion dysregulation is significantly associated with PTSD symptoms (Aupperle et al., 2012; Badour & Feldner, 2013) and viewed as a distal vulnerability factor, which may lead to the development of PTSD after traumatic exposure (Lanius et al., 2010). Physiological indices are insightful indicators of emotion dysregulation (Beauchaine et al., 2007; Davies et al., 2015) as visceral reactions are promising biomarkers of having experienced a traumatic event (Schuettler & Boals, 2010). Heart rate variability (HRV) is a recognized physiological index of self-regulatory capacity (Applehans & Luecken, 2006; Reynard et al., 2011) with diminished HRV indicating emotional dysregulation (Chalmers et al., 2014; Godfrey et al., 2019). Decreased HRV is evident in PTSD (Gillie & Thayer, 2014) and associated with poor performance on cognitive control tasks (Gillie & Thayer, 2014; Nagpal et al., 2013; Norte et al., 2013). Therefore, HRV is employed in this study as a valuable psychophysiological tool to evaluate emotional dysregulation.

In terms of non-WM cognitive variables, research has shown that cognitive control measures like inhibition and hyper-vigilance toward threat are related to PTSD symptomology (Aupperle et al., 2012; Pineles et al., 2009). Difficulty with attention disengagement from threat may be related to executive dysfunction in PTSD and can contribute to maintenance of the disorder (Aupperle et al., 2012). Specifically, researchers have suggested that re-experiencing and hyperarousal symptoms may interfere with inhibitory control, or pre-existing inhibitory control deficits may exacerbate PTSD symptoms (Aupperle et al., 2012; DeGutis et al., 2015). Researchers should examine whether the observed association is merely attributable to general cognitive control deficits that do not directly reflect WM processes. In particular, cognitive control in the emotional context is an important covariate to consider in elucidating the PTSD-WM association (Gray, 2004). The term affective control refers to the ability to attend and respond to goal-relevant information, while inhibiting distracting emotional information (Schweizer et al., 2020). The emotional Stroop (eStroop) task is an established measure of affective control, which assesses the ability to attend to the target while disregarding emotional distracters (Aupperle et al., 2012; Tipples & Sharma, 2000). Importantly, the eStroop does not directly tap into WM processes unlike other well-known WM tasks (e.g., n-back; Song et al., 2017; Malhi et al., 2005; Rahm et al., 2013). Therefore, the eStroop can serve as a useful instrument of affective control, which will allow us to account for other non-WM cognitive features that may influence the PTSD-WM relationship.

More research is needed to better understand whether PTSD is characterized by general WM deficits or whether such deficits are limited to trauma-related emotional cues. Regarding this issue, existing research is mixed. Some studies demonstrate that WM deficits are more pronounced toward trauma-related emotional cues (Zhang et al., 2013; Schweizer & Dalgleish, 2011, 2016; Dolcos, 2013), while other studies show that PTSD is associated with general WM deficits in a non-emotional context (Hale et al., 2011; Kanstrup et al., 2020; Kessler et al., 2020; Morey et al., 2009; Nejati et al., 2018). In terms of the use of emotional stimuli on WM tasks, research has shown that those exposed to trauma demonstrate poorer performance to negative emotional cues during WM tasks (Zhang et al., 2013; Schweizer et al., 2017; 2017), enhanced activity in ventral emotional processing regions (Morey et al., 2009), and increased memory for emotionally charged events increasing distraction away from goal-relevant tasks (Dolcos, 2013). However, there is also evidence suggesting the presence of non-emotional, general WM deficits associated with PTSD. The dorsolateral prefrontal cortex, associated with WM and attention, was disrupted by distractors independent of trauma content (Morey et al., 2009). Experiments have shown positive training findings using non-emotional stimuli such as Tetris (Kanstrup et al., 2020; Kessler et al., 2020; Bomyea & Amir, 2011). Those with PTSD showed inferior WM compared to controls, but no significant differences in WM performance for emotional and non-emotional stimuli (Nejati et al., 2018). Taken together, our study sought to address whether non-trauma related general WM deficits would be found across specific WM domains in association with PTSD symptom clusters, which has yet to be examined. This is an important

question to lay the groundwork for examining how WM processes in PTSD are modulated by trauma-related affective cues in future investigations.

We examined the PTSD-WM association while controlling for relevant covariates, including anxiety and depressive symptoms, emotional dysregulation, and non-WM-related affective control deficits. We hypothesized that lower levels of WM would be significantly associated with PTSD severity, especially re-experiencing symptoms, while controlling for these covariates. We also aimed to evaluate the association between PTSD symptom clusters and WM domains (verbal, operational, and visuospatial).

2. Method

2.1. Participants

Seventy-six veterans were recruited for a larger randomized control trial investigating WM training from the Milwaukee Veterans Affairs (VA), University of Wisconsin – Milwaukee (UWM), and surrounding Milwaukee region. Inclusion criteria were as follows: spoke fluent English, had access to internet, and scored >38 on the PTSD Checklist for DSM-5 (PCL-5; Weathers et al., 2013). Exclusion criteria included suicidality, substance use disorder within the past three months, psychotic disorders, unmanaged bipolar disorder, brain injury, neurocognitive disorder, organic mental disorder, or a neurological disorder diagnosis. Eligibility was assessed based on the Mini International Neuropsychiatric Interview 6.0. (MINI; Sheehan et al., 1998), chart review, and self-report. Of the 76 prescreening responders, 30 were eligible for the study.

2.2. Materials and procedure

The current study was reviewed and approved by the Institutional Review Boards of both the Milwaukee VA and UWM Human Research Protection Program. Participants completed self-report measures, and physiological and computerized tasks (see below).

PTSD symptoms. The PTSD Checklist (PCL-5; Weathers et al., 2013) measures PTSD symptoms across four clusters: Re-experiencing, Avoidance, Negative alterations in cognition and mood, and Hyperarousal. The measure consists of 20 items rated on a 5-point scale from 0 ("not at all") to 4 ("extremely"). The PCL-5 has good test-retest reliability (r = 0.82–0.84), internal consistency (a = 0.94–0.96), and convergent/discriminant validity in trauma exposed veterans and college students (Blevins et al., 2015; Bovin et al., 2016).

General Anxiety and Depression Symptoms. The Depression Anxiety and Stress Scale (DASS-21) is a 21-item measure on a 4-point scale from 0 ("did not apply to me at all") to 3 ("applied to me very much or most of the time"). The DASS-21 has good internal consistency and convergent/discriminant validity (Henry & Crawford, 2005).

Physiological measure of emotional dysregulation. Emotion dysregulation was measured by comparing HRV prior to (resting baseline) and during (exposure) a stress challenge task (i.e., Dysregulation index = Baseline – Exposure). Prior to monitoring, participants chose 12 of 60 words that were rated as most relevant to their trauma. A BioHarness strap and sensor (Zephyr Performance Systems) was positioned tightly across the chest to monitor the electrocardiogram using OmniSense 5.1 software. Monitoring commenced at baseline, with participants sitting at rest wearing a headset without audio recording and watching a slideshow of generic nature pictures for 3 min. During the 3-min exposure task, participants closed their eyes to focus on each of the selected words, which were randomly repeated three times. Kubios HRV 2.2 software was used to analyze the electrocardiogram data using the time-domain method. The root mean square of successive difference (RMSSD) was used to measure short-term variability (Shaffer & Ginsberg, 2017). RMSSD is an appropriate HRV index related to emotion regulation (Godfrey et al., 2019) and psychophysiology (Bigger et al., 1988; Owen & Steptoe, 2003), is preferred for its statistical characteristics (Buccelletti et al., 2009), and accurately represents parasympathetic activity (Chalmers et al., 2014).

Affective Control. The Emotional Stroop Task (eStroop) was used to measure affective control (Schweizer et al., 2020). Participants were presented with a series of colored words with emotional or neutral valence (Williams et al., 1996). Subjects were to identify the word color by pressing the appropriate key on a computer keyboard. Participants were to ignore the word content and respond quickly while maintaining accuracy. The task lasted approximately 4 min, and two index scores, using all positive, negative, and neutral words, were computed (i.e., Positive Interference Bias = Positive RT – Neutral RT; Negative Interference Bias = Negative RT – Neutral RT).

Working memory tasks. The Automated Complex Span Tasks (Oswald et al., 2015) assessed operational (O-Span), reading/verbal (R-Span), and symmetry/visuospatial (S-Span) WM abilities and took approximately 20–25 min to complete. The tasks capture the multifaceted functioning of WM more effectively than simple span tasks (e.g., digit span; Redick et al., 2012). The main structure of these three tasks consists of a processing component (e.g., a simple arithmetic operation) and a storage component (i.e., the to-be-remembered letter) to measure individual differences in WM (Oswald et al., 2015).

The O-Span instructs the participant to view simple arithmetic problems, determine whether the presented answer is correct, and remember a letter for future recall (e.g., 5 + 3 = ?, 8, S). Once the sequence of math problems and letter presentations was complete, participants recalled items on a 4 × 3 matrix of letters in the order presented. These steps (arithmetic operation, storage and recall) were presented on sequential display screens to reduce verbal rehearsal of the items (Oswald et al., 2015). The number of items gradually increased, after a correct recall, to reflect the maximum WM capacity. The set sizes ranged from 3 to 7 items and were repeated three times for each set.

The R-Span and S-Span had a similar procedure. The R-Span involves reading a sentence consisting of 10–15 words and determining whether the sentences make sense (approximately half of the sentences make sense). The R-Span set sizes ranged from 3 to 7 items per set. The S-Span is a test of visuospatial WM and requires the participant to remember locations of grids in a serial order. Participants were first presented with a series of red squares shown on a 4 × 4 matrix and instructed to remember the sequence at the recall phase. Participants were then presented with black and white squares on an 8 x 8 matrix and asked to decide whether the black squares were symmetrical along the vertical axis. Finally, participants were instructed to recall the location of the red squares. Set sizes ranged from 2 to 5 items and were repeated three times. In total, the O-Span and R-Span included 30 items to be recalled, and the S-Span included 24 items.

Complex span tasks are interpreted in two ways. First, researchers must decide whether to use absolute or partial scores. The absolute score is the sum of all trials where all items are recalled in the correct serial order (Redick et al., 2012). The partial score is the sum of items recalled in the correct serial order, regardless of whether the entire trial is recalled correctly (Redick et al., 2012). Research has advocated for the use of partial scores when evaluating complex span results because of its higher internal consistency, and preservation of incomplete trials (Conway & Pleydell-Pearce, 2000; Friedman & Miyake, 2005; Redick et al., 2012). Second, researchers must determine whether to use non-weighted or weighted scoring. In non-weighted scoring, the number of items remembered are treated equally regardless of the length of the set they belong to (Đokić et al., 2018). Correctly recalled items from individual sets are calculated as a proportion and the final result is the average of all the sets combined (Đokić et al., 2018). In weighted scoring, longer sets are given more weight in the final result. (Đokić et al., 2018). We used the weighted partial score for each WM task by dividing the partial span score by the total possible score (i.e., [partial span score/30] for O-Span and R-Span or [partial span score/24] for S-Span).

Although the span tasks are moderately inter-correlated (r = 0.36 to 0.68), particularly for O-Span and R-Span (Redick et al., 2012), the literature has differentiated their utility. The R-Span assesses WM for semantic processing of sentences while retaining letters, and a meta-analysis also showed that the R-Span is a stronger predictor of reading comprehension than the O-Span (Daneman & Merikle, 1996). In contrast, the O-Span utilizes the arithmetic calculation as the primary task while retaining letters, and thus tap into more operational aspect of WM. Other studies have used these WM span tasks to assess the multi-faceted aspects of WM (Larsen et al., 2019; Bomyea & Amir, 2011).

2.3. Data analysis

Hierarchical regression analyses were conducted using the total and subscale scores of the PCL-5 as the dependent measure, with covariates in Step 1. Step 1 included self-report indices of general emotional distress. We expected emotion variables to explain most of the variance in PTSD symptomology and clusters. We also entered the RMSSD HRV index and the eStroop (i.e., the Positive Interference Bias and Negative Interference Bias indices) in Step 1. In Step 2, the three WM indices were entered into the model (i.e., O-Span, R-Span, and S-Span) as main predictors.

3. Results

3.1. Descriptive statistics

Table 1 presents the demographic and clinical characteristics of the sample.

3.2. Correlations

The results, shown in Table 2, suggest a significant correlation between the DASS-21 and the PCL-5 symptom clusters, $p < 0.05$. There was also a significant correlation between the PCL-5 Re-experiencing cluster and S-Span, such that greater re-experiencing symptoms was associated with lower S-Span performance, $r = -0.56$. There was no association between the PCL-5 symptom clusters and the RMSSD or eStroop tasks, p > 0.5.

3.3. PTSD symptom clusters and working memory performance

Various indices supported the statistical assumptions for regression analysis, including the homogeneity of variance (no systematic relationship between the variability of the residuals and outcomes), the overall linear Q-Q plot showing few/negligible outliers with a small Cook's distance (<1), and no evidence of multicollinearity (i.e., Tolerance >0.1, VIF <10).

Total PCL-5 Symptom Severity Score. In Step 1, DASS-21, eStroop, and HRV data accounted for 56.5% of the variance in the PCL-5 Total, $F(6, 21) = 4.55$, $p = 0.004$. In Step 2, the WM tasks did not significantly explain additional variance in overall PTSD severity, $F(3, 18) = 1.34$, $p = 0.29$, $R^2\Delta = 0.079$.

Cluster B: Re-experiencing Cluster. The Step 1 covariates explained 41.90% of the variance in re-experiencing symptoms, $F(6, 21) = 2.53$, $p = 0.053$. In Step 2, the WM tasks explained an additional 29.70% of the variance, $F(3, 18) = 6.29$, $p = 0.004$, $R^2\Delta = 0.30$. Notably, the S-Span task was the only WM task that significantly explained PCL-5 re-experiencing symptoms ($\beta = -0.50$, $t = -4.27$, $p < 0.001$), unlike R-Span ($\beta = 0.13$, $t = 1.18$, $p = 0.25$) and O-Span ($\beta = 0.08$, $t = 1.11$, $p = 0.28$). Multicollinearity was not indicated for this analysis (VIF = 1.34–1.82).

Cluster C: Avoidance. The Step 1 covariates did not significantly explain the variance, $F(6, 21) = 1.44$, $p = 0.25$, $R^2 = 0.29$. In Step 2, the WM tasks additionally explained only 9.0% of the variance in avoidance symptoms, $F(3, 18) = 0.87$, $p = 0.47$, $R^2\Delta = 0.09$.

Cluster D: Negative Cognition and Mood. The Step 1 covariates significantly explained 56.5% of the variance, $F(6, 21) = 4.54$, $p = 0.004$. The WM tasks did not explain additional variance, $F(3, 18) = 0.09$, $p = 0.94$, $R^2\Delta = 0.007$.

Cluster E: Arousal. The Step 1 covariates significantly explained the variance, $F(6, 21) = 2.56$, $p = 0.05$, $R^2 = 0.42$. The addition of the WM tasks did not significantly explain the variance, $F(3, 18) = 1.50$, $p = 0.25$, $R^2\Delta = 0.12$.

Table 1
Baseline demographic, clinical, and computerized task characteristics of the sample.

Demographic	
Age *(M, SD)*	49.93 (13.38)
Gender (% Male)	66.67%
Ethnicity (% Hispanic, *n*)	3.3% (*n* = 1)
Race	**(%, *n*)**
White	53.33% (*n* = 16)
African American	33.33% (*n* = 10)
Native American	3.33% (*n* = 1)
Multiracial	10% (*n* = 3)
Education	**(%, *n*)**
Some High School	3.3% (*n* = 1)
High School Diploma	6.7% (*n* = 2)
Some College	53.5% (*n* = 16)
Bachelor's Degree	16.7% (*n* = 5)
Master's Degree	20.0% (*n* = 6)
Marital Status	**(%, *n*)**
Never married	16.7% (*n* = 5)
Married	50.0% (*n* = 15)
Divorced/Annulled	30.0% (*n* = 9)
DASS-21	***M* (*SD*)**
DASS-21 Total	58.53 (23.35)
Depression	20.87 (9.46)
Anxiety	16.2 (9.85)
Stress	21.47 (8.25)
PCL-5	***M* (*SD*)**
PCL-5 Total	52.97 (11.89)
Cluster B	12.87 (3.87)
Cluster C	5.63 (2.16)
Cluster D	18.77 (5.42)
Cluster E	15.70 (3.37)
RMSSD	***M* (*SD*)**
Baseline	68.34 (73.17)
Exposure	37.65 (31.05)
Dysregulation index (Baseline – Exposure)	30.68 (62.25)
Emotional Stroop (eStroop)	***M* (*SD*)**
eStroop Negative RT	968.96 (393.77)
eStroop Positive RT	960.96 (410.34)
eStroop Neutral RT	954.74 (352.60)
eStroop Negative Interference Bias (Neg. RT-Neut. RT)	19.54 (124.83)
eStroop Positive Interference Bias (Pos. RT-Neut. RT)	12.58 (98.28)
Automated Complex Span Tasks	***M* (*SD*)/%**
R-SPAN_Partial Weighted Score	17.76 (5.86)
R-SPAN Overall Accuracy	59%
S-SPAN_Partial Weighted Score	10.52 (5.69)
S-SPAN Overall Accuracy	45%
O-SPAN Partial Weighted Score	15.14 (8.06)
O-SPAN Overall Accuracy	50%

Note: DASS-21 = Depression, Anxiety, Stress Scale-21 Items; PCL-5 = PTSD Checklist for DSM-5; RMSSD = Root Mean Squared of the Successive Differences (Heart Rate Variability); eStroop = Emotional Stroop Task; RT = Reaction Time; R-Span = Reading Complex Span Task; S-Span = Spatial Complex Span Task; O-Span = Operation Complex Span Task; Overall Accuracy Scores = partial span/total of span task (i.e., 30 or 24).

3.4. Association between Re-experiencing symptoms and visuospatial WM

To further assess the magnitude of S-Span's association with re-experiencing symptoms, we conducted a regression analysis to examine the proportion of variance uniquely explained by S-Span. Thus, we repeated the analysis, entering the DASS-21 factors, eStroop and HRV variables in Step 1, O-Span and R-Span in Step 2, and S-Span in Step 3. After controlling all these relevant variables, S-Span explained an additional 28.7% of the variance in re-experiencing symptoms (R^2 =

Table 2
Correlations of PTSD symptom clusters and PTSD covariates.

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. O-SPAN													
2. R-SPAN	.44[b]												
3. S-SPAN	.42[b]	.48[b]											
4. PCL-5 Total	-.21	-.17	-.37										
5. Cluster B	-.12	-.14	-.56[a]	.83[a]									
6. Cluster C	.20	-.01	-.25	.71[a]	.63[a]								
7. Cluster D	-.21	-.05	-.12	.85[a]	.51[a]	.50[a]							
8. Cluster E	-.38	-.34	-.32	.74[a]	.56[a]	.34	.47[b]						
9. RMSSD	-.21	-.20	-.31	.37	.37	.09	.27	.38[b]					
10. Depression	-.20	-.06	-.19	.64[a]	.53[a]	.15	.64[a]	.51[a]	.37				
11. Anxiety	-.07	-.07	-.14	.56[a]	.54[a]	.34	.50[a]	.32	.27	.44[b]			
12. Stress	-.14	.05	-.06	.40[b]	.47[a]	.01	.33	.34	.18	.64[a]	.65[a]		
13. Negative	.10	.17	-.12	-.02	.02	-.06	.10	-.24	-.14	.16	-.08	.10	
14. Positive	-.13	-.03	-.24	-.15	-.14	-.20	-.11	-.06	-.18	-.15	-.10	-.14	.41[b]

Note: O-SPAN = Operation Complex Span; R-SPAN = Reading Complex Span; S-SPAN = Symmetry Complex Span; PCL-5 Total = PTSD Checklist for DSM-5 Total; Cluster B = PCL-5 Re-experiencing; Cluster C = PCL-5 Avoidance; Cluster D = PCL-5 Negative Cognition and Mood; Cluster E = PCL-5 Hyperarousal; RMSSD = Root Mean Squared of the Successive Differences (Heart Rate Variability); Depression = DASS-21 Depression; Anxiety = DASS-21 Anxiety; Stress = DASS-21 Stress; Negative = eStroop Negative Bias; Positive = eStroop Positive Bias.

[a] Correlation is significant at the 0.01 level (2-tailed).

[b] Correlation is significant at the 0.05 level (2-tailed).

0.72, $F(1,18) = 18.25$, $p < 0.001$; $\beta = -0.50$, $t = -4.27$, $p < 0.001$, large effect size; See Fig. 1).

4. Discussion

Researchers have identified a relationship between heightened trait-anxiety and WM deficits (Bishop, 2007; Moran, 2016; Stout et al., 2013), yet little research has evaluated the association between WM domains (i.e., verbal, operational, and visuospatial) and PTSD symptoms (Schweizer & Dalgleish, 2011; Shaw et al., 2009; Weber et al., 2005). We evaluated re-experiencing symptoms, which are central to PTSD and more frequently endorsed than other PTSD symptom clusters (e.g., avoidance, mood/cognition, hyperarousal; Durham et al., 1985; Genest et al., 1990; Matthijssen et al., 2017; Laposa et al., 2012). We sought to determine whether WM is a cognitive correlate of PTSD symptom severity while considering other important variables including negative affect, emotional dysregulation, and non-WM affective control processes. An additional aim was to evaluate the relationship between PTSD symptom clusters and WM domains.

Our data revealed that the visuospatial WM index is significantly associated with re-experiencing symptoms, even after controlling for other PTSD-relevant variables. The visuospatial WM index explained a large amount of variance (approximately 26%) in re-experiencing symptoms, which suggests that the level of visuospatial WM functioning is a useful cognitive correlate of the re-experiencing symptom cluster. Despite the theoretical relevance of the HRV-based dysregulation index and the general eStroop-based affective control index, they were not significant predictors of PTSD symptom clusters in our sample. Negative affect, as assessed by the DASS-21, was significantly associated with PTSD symptoms, but visuospatial WM emerged as the cognitive variable most strongly associated with PTSD re-experiencing symptoms among all study variables.

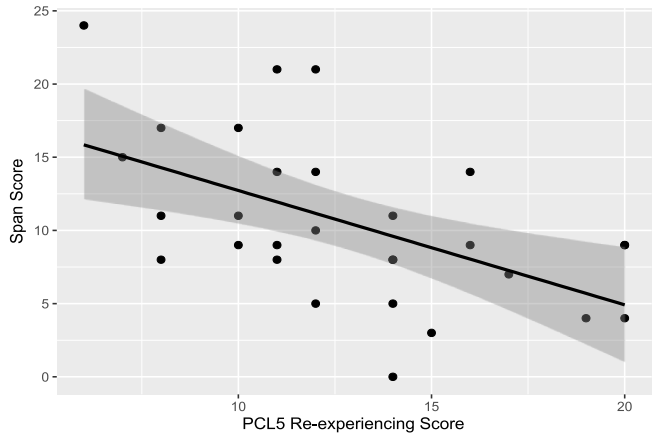

Fig. 1. Correlation between S-Span and Re-experiencing Symptoms. Gray zone indicates the 95% confidence interval of the regression line.

Our findings align with previous research showing that repeated trauma exposure was positively associated with poorer visuospatial memory function (Smith et al., 2015; Tempesta et al., 2012. There are a few reasons why this may be. First, visuospatial WM deficits may be linked to re-experiencing symptoms because many of these symptoms occur in the form of visual recollections (Ehlers et al., 2002; Hackmann et al., 2004). Second, re-experiencing involves frequent and repeated visual intrusions that may be triggered by real or imaginary events, which can be highly distressing (Brewin et al., 2010). Further, re-experiencing can be maintained by avoiding environmental/visual triggers, which contributes to the inability to filter out threatening cues (Lissek & van Meurs, 2015). Taken together, visual intrusions are commonly experienced in PTSD and re-experiencing symptoms may reflect concurrent deficits in visuospatial WM.

Further investigations are needed to understand why associations were not found between deficits in other WM domains (e.g., verbal and operational) and other PTSD symptom clusters (e.g., hyperarousal, avoidance, negative alterations in mood). While some studies have found impairments in verbal memory (Johnsen & Asbjørnsen, 2008), and executive function deficits (Polak et al., 2012) in PTSD samples, our data showed that operational and verbal WM was not significantly correlated with any PTSD symptoms. There are a few potential explanations for these findings. First, it is possible that R-Span and/or O-Span do not adequately capture verbal and operational deficits relevant for PTSD. In other words, solving math problems and determining semantic congruency may be unrelated to PTSD symptoms as compared to visuospatial processes. Second, impaired visuospatial WM may be associated with the diminished ability to filter out irrelevant visuospatial trauma cues, which would make the affected individual more vulnerable to elevated re-experiencing symptoms. As mentioned, visual memories are the most commonly experienced form of intrusive symptoms (Ehlers et al., 2002), and visuospatial WM deficits may play a greater role in PTSD symptoms, relative to other domains of WM. Third, PTSD symptoms may display negligible associations with WM indices except for the re-experiencing symptom cluster. Recent work in visuospatial WM

training, such as the visual n-back, showed reduced intrusions in thought suppression tasks, improved WM, and reduced PTSD symptoms (Bomyea & Amir, 2011; Larsen et al., 2019). Though few studies have evaluated WM training, our preliminary results support the link between visuospatial WM and PTSD.

Our sample did not display a significant relationship between re-experiencing symptoms and affective control. Research suggests that individuals with PTSD demonstrate difficulty with attention disengagement from salient emotional cues due to difficulties with affective control (Bardeen & Orcutt, 2011; El Khoury-Malhame et al., 2011; Khanna et al., 2017; Schweizer, Samimi, et al., 2017). While the eStroop task controls for emotional stimuli interference, it does not directly assess WM processes and may not be as relevant for PTSD symptomatology, which may explain the lack of an association between eStroop and PTSD symptoms. In our study, even compared to other WM tasks (i.e., verbal, operational), the visuospatial WM task was the only cognitive domain to correlate with re-experiencing symptoms, which suggests that visuospatial WM deficits are more specifically linked to re-experiencing symptoms. Another consideration is the type of stimuli used in the tasks. The eStroop task used valanced words (verbal stimuli), while the visuospatial WM task used patterns and designs (visuospatial stimuli). Thus, the results suggest that re-experiencing symptoms are more closely linked to cognitive deficits in the visuospatial, rather than verbal, modality. Clarke and colleagues (2003) found that individuals with PTSD excessively relied on visuospatial coding of information on a WM updating task (i.e., a visuo-verbal target detection task), relative to verbal, phonological, and symbolic representations of the stimuli. A reliance on nonverbal WM and a shift away from verbal processing has been found in other studies evaluating PTSD and is important to further understand the nature of intrusive traumatic memories (Bremner et al., 1999; Clark et al., 2003; Rauch et al., 1996). Considering the reliance on nonverbal WM in PTSD, it is conceivable that cognitive deficits in visuospatial WM are more strongly associated with PTSD symptoms, particularly re-experiencing symptoms, compared to deficits in verbal cognitive processing. Taken together, our findings contribute to the literature by suggesting that visuospatial WM deficits are associated with increased PTSD symptoms (De Bellis et al., 2010; Li et al., 2020; Mirabolfathi et al., 2020; Morey et al., 2009). However, affective control across different modes of stimuli related to traumatic experiences (e.g., affective go/no-go based on words vs. faces/pictures; Amick et al., 2013; Sadeh et al., 2018) should be assessed.

Although HRV, an established indicator of emotional dysregulation, is significantly lower in those with PTSD compared to controls and associated with poor cognitive control (Gillie & Thayer, 2014; Nagpal et al., 2013; Norte et al., 2013; Tan et al., 2011), our study did not find a significant relationship between HRV and any PTSD symptom clusters. HRV was evaluated in a stress-challenge by auditory presentation of salient trauma words. Enhancement of the impact and duration of the challenge may be necessary to generate a meaningful context for PTSD-related emotional dysregulation (Hauschildt et al., 2011), as HRV indices can be sensitive to task demands, situational factors, and random variation (Maestri et al., 2007; Pinna et al., 2007).

This study is not without limitations. First, a relatively small sample of individuals may increase the potential for false positives and reduced measurement precision (Sandercock, 2007). Therefore, the results are preliminary and require further research to corroborate these findings. Nonetheless, a large effect size of the association between visuospatial WM and re-experiencing symptoms is noteworthy. Future research should use a large clinical sample as the currently underpowered study may have missed a meaningful pattern in other aspects of the WM-PTSD relationship. Second, participants were all veterans. Thus, the generalizability of our findings cannot be established without examining individuals presenting with diverse demographic characteristics and traumatic experiences. Third, we did not measure WM filtering directly in this study, as the Automated Complex Span tasks are primarily focused on the retention and operation of information presented across different stimulus domains. Future work may consider a task that directly evaluates filtration of irrelevant information from WM (e.g., emotional change detection task; Stout et al., 2013; Stout et al., 2015). Fourth, we did not gather data related to the length/course of illness. Future research should evaluate the relationship between chronic re-experiencing symptoms and visuospatial WM. Fifth, our findings are cross-sectional and do not allow for causal inference regarding the WM-PTSD relationship. To this end, further investigation is needed to assess whether visuospatial WM deficits lead to greater re-experiencing problems or vice versa. Future studies should include non-PTSD anxious controls to examine whether the observed PTSD-WM relationship is attributable to general anxiety psychopathology, as opposed to the association with a particular PTSD symptom cluster.

Despite these limitations, our study contributes novel findings to the existing literature by presenting a specific pattern of the PTSD-WM relationship. First, visuospatial WM deficits may be a specific cognitive deficit substantially correlated with re-experiencing symptoms in PTSD. Second, it appears unlikely that PTSD is characterized by generalized WM deficits across all domains. Third, only a certain facet of PTSD symptoms (re-experiencing) may be strongly associated with WM deficits. Given the current findings, visuospatial WM is expected to have incremental validity in explaining re-experiencing symptoms in PTSD even when considering other important variables related to negative affect, emotional dysregulation, and general affective control. Continuing research is warranted to better understand the nature and role of WM processes in PTSD psychopathology.

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Declaration of interest

The authors of the current manuscript have no conflict of interest to report.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jbtep.2021.101714.

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