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ORIGINAL ARTICLE

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Abstract
This research report describes the development of a virtual reality (VR) laboratory stressor to study the effects of exposure to stressful events. The aim of the research was to develop a VR simulation that would evoke stressor responses at a level that was tolerable for participants. Veterans with and without warzone-related posttraumatic stress disorder (PTSD) were presented with VR simulations of combat stressors. There was one complaint of feeling hot during simulations but no incidents of simulator sickness. Participants denied experiencing the simulations as overly distressing, and there were no reports of any distress or problems related to study participation when they were contacted two weeks after the VR challenge. Simulations elicited moderate levels of anxiety and mild levels of dissociation that were significantly greater in Veterans with PTSD. Simulations were less successful in eliciting differential heart rate reactivity and stress hormone secretion, though history of civilian trauma exposure was associated with elevated heart rates during the second simulation. The study demonstrated that the VR paradigm was feasible and tolerable and that it holds promise as a new method with which to conduct controlled laboratory research on the effects of exposure to stressful events.

Keywords Virtual reality · PTSD · Veterans · Research methods · Experimental psychopathology

1 Introduction

The aim of the research presented herein was to develop a virtual reality (VR) laboratory stressor that could be used to model how symptoms of posttraumatic stress disorder (PTSD) develop after exposure to adverse events. Virtual reality (VR) simulations have been used for over 20 years to augment exposure therapy for PTSD and anxiety disorders (Carl et al. 2019; Gerardi et al. 2010; Lindner et al. 2019), but they have been underutilized in clinical experimental psychopathology research. VR simulations are ideal for studying PTSD because researchers can present multisensory simulations that evoke the narrative, egocentric, and temporal aspects of exposure to stressful events (Bergouignan et al. 2014; Pause et al. 2013).

A key question in PTSD research is what mechanisms and risk factors lead to the development of PTSD. Studies that prospectively follow trauma survivors are the gold standard (Ben-Zion et al. 2018; Norris et al. 2002), but they are time-consuming and expensive. Moreover, they are limited in their ability to study how involuntary memories develop, because there is no way to verify the accuracy of memories, and because subjective reports can be biased by the severity of symptoms at the time of the assessment (Giosan et al. 2009; Roemer et al. 1998). Understanding how involuntary trauma memories develop is important because the formation of persistent, intrusive trauma memories shortly after trauma exposure is hypothesized to critical to the development of PTSD (Berntsen and Rubin 2014; Brewin 2014).

During the past decade, trauma researchers have used distressing films as a laboratory analogue to trauma exposure (Holmes and Bourne 2008; Iyadurai et al. 2019; James et al. 2016). In recent years, a few have started to utilize VR simulations instead of films (Schweizer et al. 2018). VR simulations are also an analogue of trauma exposure, but they have unique characteristics that can improve some of

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the limitations of existing research methods. Unlike films, VR simulations are experienced from the first-person perspective, which may evoke stronger emotional (Holmes and Bourne 2008; McIsaac and Eich 2004) and physiological (Wisco et al. 2015) responses than stimuli experienced from an observer perspective. The use of standardized stimuli avoids the problems of differential exposure severity and the inability to verify the accuracy of trauma memories that is inherent in field studies with trauma survivors. Responses can be assessed before, during, and immediately after exposure to stressful episodes, which allows researchers to isolate and prospectively test hypothesized mechanisms and risk factors. The ability to present stressful episodes that unfold in real time enables researchers to study the development of abnormal *episodic* emotional memories. This last feature is critical, because persistent involuntary memories, nightmares, and flashbacks have been hypothesized as developing from deficient spatial–temporal coding during traumatic episodes (Brewin 2014).

Although a variety a PTSD symptom challenge tasks have been safely used for decades to study PTSD (Blanchard et al. 1986; Carleton et al. 2019; Elzinga et al. 2003; Liberzon et al. 1999), it is important to balance the need to create ecologically validity laboratory stressors with the need to ensure that research participants do experience undue levels of distress. Hence, there is a need for careful pilot research to develop stimuli and assess participants' reactions before utilizing novel research methods.

This paper describes the authors' efforts to develop VR simulations with which to study the development of involuntary memories (Malta et al. 2008). The research grew out of extensive research on VR treatment of PTSD conducted at the Weill Medical College Program for Anxiety and Traumatic Stress Studies for nearly 20 years (Difede et al. 2007; Difede and Hoffman 2002; Reger et al. 2016). The aim was to develop the simulations and test whether they would be feasible to conduct, tolerable to participants, and capable of evoking stressor reactions. The study also tested whether PTSD and trauma history would be associated with greater dissociation and stronger emotional and physiological stress reactions to simulations.

2 Materials and methods

2.1 Participants

The Weill-Cornell Medical College Institutional Review Board approved the study. Participants provided written informed consent to participate. During consenting, they were informed that they would be exposed to warzone VR simulations and that study risks included simulator sickness (cf. Regan 1995) and a transient increase in PTSD symptoms. Participants were combat trauma-exposed Veterans of the Persian Gulf Wars recruited via advertisements and mailings. Exclusion criteria included psychosis, cognitive impairment, alcohol/substance dependence, attention deficit/hyperactivity disorder, motion sickness, and medical conditions that prevented prolonged standing. No participants were on medications for cardiovascular conditions or had a pacemaker or arrhythmia. Two participants were taking antidepressants. Participants were compensated $50.00/visit. Four participants did not show up after the diagnostic assessment, despite being contacted several times; 32 completed the study.

2.2 Instruments

1. PTSD was clinically assessed with the Clinician-Administered PTSD (CAPS) Scale (Blake et al. 1998). The CAPS is a structured clinical interview that assesses each of the 17 DSM-IV (Diagnostic and Statistical Manual of Mental Disorders 1994) PTSD symptoms, guilt, and symptoms of dissociation, depersonalization, and derealization. Each symptom is assessed on a 0–4-point frequency scale and a 0–4-point intensity scale. Item frequency and severity scores are summed to obtain individual symptom severity scores. In the present study, item scores for the three symptoms of dissociation, depersonalization, and derealization (from the associated features section of the CAPS) were summed to create a CAPS Dissociation Index, with a possible total score range of 0–24. PTSD was diagnosed according to DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 1994). Diagnostic reliability checks conducted by an independent evaluator on a random selection of 25% of assessments yielded a kappa coefficient of 1.0, $p < 0.001$.
2. PTSD checklist (PCL) (Weathers et al. 1993) is a widely used PTSD symptomatology self-report questionnaire that assessed DSM-IV symptoms of PTSD (Diagnostic and Statistical Manual of Mental Disorders 1994). The PCL was administered at each visit to assess weekly symptom severity. Items are summed to obtain a total score.
3. The Structured Clinical Interview for DSM-IV Axis I Disorders (First et al. 1997), administered by licensed clinical psychologists, was used to provide categorical diagnoses of DSM-IV disorders.
4. The attention deficit/hyperactivity disorder (ADHD) interview (Barkley and Murphy 2005) was used to obtain a diagnosis of ADHD.
5. The Beck Depression Inventory—BDI (Beck et al. 1961), a widely known 21-item self-report, was used to gauge the severity of depressive symptomatology.

6. Civilian trauma exposure was assessed with the Traumatic History Questionnaire—THQ (Green 1993). Participants reported on lifetime exposure to adverse events (excluding war-related events). Events that included threat of death or serious harm to self or others and which were reported to be very distressing were classified as traumatic events. Dichotomous variables were created to compare participants with and without a history of childhood abuse history, childhood trauma exposure (excluding abuse), and adult civilian trauma exposure.
7. Engagement in the simulations was assessed with Subjective Units of Distress (SUDS) ratings (0–100 scale) taken before, during, and after the simulations and with an (8) Immersion/Presence Questionnaire (IPQ) created for the study from existing instruments (Witmer and Singer 1998; Zimand et al. 2001). The IPQ consisted of seven items endorsed on a 7-point scale (1 = not at all; 7 = completely). An Immersion Scale was created by summing scores for four items that assessed emotional engagement, sensory–perceptual engagement, ability of simulations to evoke feelings similar to real events, and distraction level (reverse scored). A Dissociation Scale was created by summing scores for three items that assessed losing sense of time, losing track of events, and feeling emotionally numb. The IPQ was administered twice, once after each simulation. IPQ scores for each simulation were combined. Immersion and Dissociation scales were created by summing scores for eight Immersion items (four for each simulation) and scores for six Dissociation items (three for each simulation). The Immersion Scale total scores ranged from 25 to 53 (out of a possible 8–56); Cronbach's alpha = 0.76. The Dissociation Scale total scores ranged 6–35 (out of a possible 6–42); Cronbach's alpha = 0.80. The Dissociation Scale was skewed and kurtotic, and so analyses used a normally distributed percentile ranking score (1–4), where 1 = no dissociation (score of 6), 2 = mild dissociation (score of 7–10); 3 = mild-to-moderate dissociation (score of 11–14); and 4 = moderate to marked dissociation (score of 15–35).

Simulations immersed the participants in a three-dimensional, multisensory (visual/auditory/tactile) environment, where the imagery changed naturally with the participants head motion. The equipment used to achieve this was a Virtually Better VR System (http://virtuallybetter.com/buy), which included: (1) a Dell workstation with a (2) Wildcat 5110 graphics card; (3) a MultiGen-Paradigm, Inc., Vega VR software used to connect the workstation to a (4) Kaiser XL-50 VR helmet with 40-degree horizontal field of view; (5) a Polhemus Fastrak (http://polhemus.com) position tracking system to measure the users' head movements; (5) a vibrating platform on which the participants sat, which vibrated as a function of the sounds in the virtual environment (e.g., an intense, sudden, and short vibration was linked to the sound of an explosion; a mild, continuous vibration was linked to the sound of a car engine).

Warzone-related VR simulations were installed on this system. These simulations were created from the IraqWorld software (Rizzo et al. 2007) developed for VR-enhanced exposure therapy for war-related PTSD (Rizzo et al. 2009). Simulations consisted of two scenarios set in a virtual city in Iraq. Scenario 1 was a 2-min excursion through the city. Participants did not control navigation, which was automated. The second, 5.5-min scenario, was scripted into five, 45–90-s segments in order to standardize stimuli exposure. Participants navigated the environment using a keypad. They were given a background narrative (a mission to search for insurgents) and navigation instructions before each segment. During the first two neutral segments, participants perused the streets for insurgents. During the next two segments, participants took cover in a marketplace during an attack, which included the sounds of bombs and machine gunfire. During the final segment, the attack ended, and participants returned to the street to search for insurgents. Stressors in both scenarios included hearing gunfire, bombs, grenades, and improvised explosive devices and seeing vehicle damage, but no human injuries or deaths (Fig. 1).

2.3 Heart rate data

Continuous heart rate was assessed during the VR simulations with the Vivometrics LifeShirt (Ventura, CA), an ambulatory heart rate monitor, which consists of a vest outfitted with three standard electrocardiogram leads. The leads attach to disposable dry electrodes and a portable data collection unit. We used the standard deviation of normal-to-normal (NN) intervals to calculate heart rate variability (HRV). The NN intervals represented all intervals between adjacent electrocardiogram QRS complexes resulting from sinus node depolarizations (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology 1996). Due to values of artifacts greater than 10% of NN values, HRV data from two participants were excluded from the analyses. Mean heart rate was calculated for baseline, Scenario 1, and each of the five segments of Scenario 2. The scores for change from baseline, calculated by subtracting the mean baseline heart rate from the mean heart rate, were used for Scenario 1.

3 Procedures

The procedures in the present study were conducted as part of a parent study testing the effects of thought suppression on voluntary and involuntary emotional memories (Malta

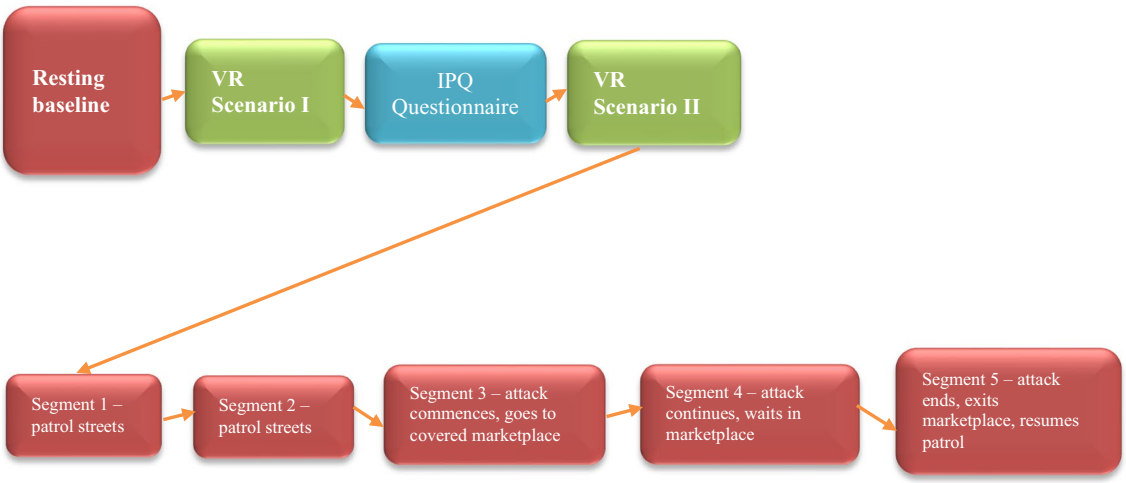


Fig.1 Diagram of the VR cues

et al. 2020). Participants completed a diagnostic evaluation and the VR challenge, administered by faculty clinical psychologists, at two separate visits. The diagnostic evaluation consisted of clinical interviews and questionnaires. Participants diagnosed with mental health conditions were provided with psychoeducation and treatment referrals.

At the second visit, participants completed the VR challenge task. Prior to the challenge, participants provided a saliva sample and completed the PCL. The VR challenge consisted of a 5-min baseline, during which participants stood and remained still, followed by the two VR scenarios. A baseline period prior to Scenario 2 was omitted to enhance immersion. For analyses, mean heart rate was calculated for the following epochs: baseline, Scenario 1 (2 min), and each of the five Scenario 2 segments (45–90 s each). Participants provided SUDS ratings immediately before and after scenarios. Upon completion of Scenario 1, participants provided a retrospective rating of peak SUDS level. For Scenario 2, participants provided SUDS rating after completing each of the five segments. Participants completed the IPQ immediately after providing final SUDS ratings for each scenario.

After the VR challenge, participants completed either a free recall memory test or a thought suppression task that were part of the parent study. They returned to the laboratory one week later to complete procedures from the parent study (memory testing, thought suppression task). At this visit, they completed another PCL to assess the severity of PSTD symptoms during the past week. Upon study completion, participants were asked (in an open-ended fashion) to provide honest feedback regarding the intensity of the simulations (i.e., too distressing, not evocative enough) and suggestions for improvement. One week after this final visit, participants were telephoned to assess for any problems related to study participation (see Figs. 1, 2).

3.1 Cortisol assessment

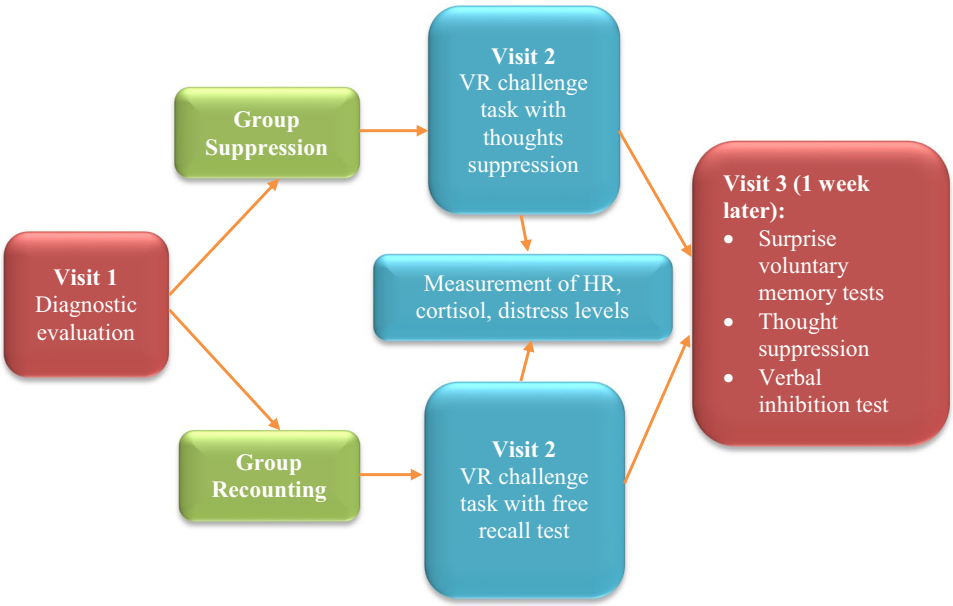
VR assessments were scheduled between 12:30 and 4:30. For two subjects, the visits commenced at 5:00 and 5:15 PM due to their tardiness. Participants were instructed to avoid eating, drinking caffeinated beverages, smoking, or exercising one hour before appointments. Saliva was collected with salivettes placed beneath the tongue for 5 min (Newton, NC: Sarstedt, Incorporated). Samples were collected before and 20–43 min after the start of Scenario 1; mean (SD) = 30.41 (4.51) s. Samples were frozen at −0°C until assayed using a commercial ELISA assay optimized for salivary samples (Salimetrics LLC, State College, PA). Samples were centrifuged after thawing from -80°C to remove solid particles. Samples were run in duplicate; the mean value for each sample was used for analysis. Intraassay variability was less than 10% for all samples.

4 Results

4.1 Participant characteristics

The sample was 84% male and 56% minority race or Hispanic ethnicity; 78% served in the current Iraq war, 16% served in the first Gulf War, and 6% served in both conflicts. The mean age was 30.28 (SD = 7.32). Eleven participants (34%) were diagnosed with PTSD of moderate severity, mean CAPS total = 59.82, SD = 10.23; and they endorsed mild symptoms of dissociation, mean CAPS dissociation score = 3.09, SD = 3.39. The remainder of the sample presented with mild symptoms of PTSD, mean CAPS total = 17.05, SD = 13.15; and absent/minimal symptoms of dissociation, mean CAPS dissociation score = 0.81,

Fig. 2 Flowchart of the method



SD = 1.99. Four participants (12.5%) were diagnosed with depression. (See Table 1 for comorbidities.)

4.2 Descriptive data

One participant reported feeling hot during Scenario 2. The simulation was terminated to prevent simulator sickness. The symptom quickly abated such that he was able to complete remaining procedures. His physiological data and IPQ data were excluded from analyses. One participant without PTSD had one combat-related nightmare during the week after the VR challenge, which was an increase for him. No other participants reported an increase in symptoms. PCL scores for PTSD symptoms during the weeks before and after the VR challenge were virtually identical: pre-challenge mean (SD) = 27.41 (11.00), post-challenge mean (SD) = 27.22 (10.57), $F(1, 31) = 0.32$, $p = 0.860$. During debriefing, 100% of participants reported that they did not find the simulations too distressing. Instead, they suggested ways to increase the intensity of the simulations, including having participants hold guns and wear flak jackets. One participant reported that being provided with a background narrative increased his ability to immerse himself in the second scenario. During the follow-up call two weeks after the VR challenge, no participant reported any distress or problems.

Immersion and Dissociation scores are shown in Table 2. SUDS ratings are shown in Table 3. Cortisol and heart rate data are shown in Tables 4 and 5, respectively. Immersion significantly correlated with Dissociation during simulations, $r = 0.478$, $p = 0.007$. There was a trend for Dissociation scores to correlate with CAPS (monthly) Dissociation scores, $r = 0.354$, $p = 0.051$. Immersion and Dissociation significantly correlated with all SUDS ratings except the initial rating (before Scenario 1). Correlation coefficients ranged from $r = 0.556$, $p = 0.001$ to $r = 0.780$, $p < 0.001$ for Immersion and $r = 0.505$, $p = 0.004$ to $r = 0.606$, $p < 0.001$ for Dissociation. Immersion and

Table 1 Comorbidities (DSM-IV diagnoses)

	Suppress (16)	Recount (16)
Current war-related diagnoses		
Full PTSD	5	6
Partial PTSD	3	2
Anxiety NOS	1	0
Major depressive disorder	1	3
Alcohol abuse	1	1
Lifetime war-related PTSD		
Full PTSD	7	6
Partial PTSD	4	3
Current non-war-related diagnoses		
MDD	1	0
Dysthymic disorder	1	0
GAD	4	0
Specific phobia	1	3
Social phobia	0	1
Substance abuse	0	1
Substance use (did not meet criteria for abuse)	1	0
OCD	1	0
Alcohol abuse	0	1
Panic disorder	0	1
Impulse control disorder NOS	0	1

Table 2 Mean (SD) Immersion and Dissociation scores

	Immersion	Dissociation raw score	Dissociation rank score[a]
PTSD ($n=10$)	38.70 (8.43)	17.10 (9.06)	3.20 (0.92)[b]
No PTSD ($n=31$)	37.10 (7.87)	9.67 (3.85)	2.10 (1.00)[b]
Adult civilian trauma ($n=8$)	38.75 (7.89)	10.00 (4.34)	2.25 (1.04)
No adult civilian trauma ($n=23$)	37.22 (8.11)	12.78 (7.48)	2.52 (1.12)
Childhood trauma ($n=12$)	38.08 (8.62)	9.75 (4.22)	2.17 (1.11)
No childhood trauma ($n=19$)	37.32 (7.73)	13.53 (7.85)	2.63 (1.07)
Childhood abuse ($n=9$)	37.78 (8.41)	12.00 (7.02)	2.56 (0.88)
No childhood abuse ($n=22$)	37.55 (7.96)	12.09 (6.96)	2.41 (1.18)

[a]Dissociation rank score: 1 = none, 2 = mild; 3 = mild to moderate; 4 = moderate to marked

[b]Significant main effect of group, PTSD > No PTSD

Table 3 Mean (SD) subjective units of distress (SUDS) scores

	Total $N=32$[a]	PTSD $N=11$[a]	Non-PTSD $N=21$
Scenario 1 Pre[b]	15.94 (16.04)	28.18 (20.03)[c]	9.52 (8.50)[c]
Scenario 1 Peak[b]	44.06 (26.89)	51.36 (28.64)	40.24 (25.81)
Scenario 1 Post[b]	36.38 (25.98)	47.91 (25.32)	30.33 (24.79)
Scenario 2 Pre[b]	25.32 (22.69)	41.50 (25.61)[c]	17.62 (16.85)[c]
Scenario 2, Mean of neutral segments 1 and 2[b]	30.44 (27.20)	47.50 (28.72)[c]	22.31 (22.88)[c]
Scenario 2, Mean of attack segments 3 and 4[b]	44.92 (28.81)	64.00 (29.63)[c]	35.83 (24.11)[c]
Scenario 2, post-segment 5[b]	41.77 (30.13)	56.50 (31.36)	

[a]For Scenario 2 variables total $N=31$; PTSD = 10

[b]Significant main effect of time, Scenario 1 ratings: Peak > Post > Pre; Scenario 2 ratings: Attack > Neutral > Pre; Pre > Post

[c]Significant main effect of group, PTSD SUDS ratings > no PTSD SUDS ratings

Table 4 Mean (SD) cortisol levels (μg/dl)

	Pre	Post
PTSD ($n=10$)[b]	0.26 (0.14)[a]	0.17 (0.07)[a]
No PTSD ($n=31$)[b]	0.16 (0.07)[a]	0.15 (0.05)[a]
Adult civilian trauma ($n=8$)	0.22 (0.15)	0.16 (0.05)
No adult civilian trauma ($n=23$)	0.18 (0.10)	0.15 (0.06)
Childhood trauma ($n=12$)	0.20 (0.17)	0.15 (0.05)
No childhood trauma ($n=19$)	0.18 (0.11)	0.15 (0.06)
Childhood abuse ($n=9$)	0.25 (0.16)	0.16 (0.08)
No childhood abuse ($n=22$)	0.16 (0.07)	0.15 (0.04)

[a]Significant main effect of time

[b]Significant main effect of group and significant time × group interaction

Dissociation did not significantly correlate with cortisol levels or heart rate during simulations.

4.3 Comparisons of experimental groups

Immersion and dissociation during simulations Four analyses were conducted to assess the effects of PTSD diagnostic status, adult non-war-related trauma history, child trauma history (excluding abuse), and history of child abuse on the dependent variables of Immersion and Dissociation scores. The first multivariate analysis of variance (MANOVA) compared between-group differences of immersion and dissociation in participants with and without PTSD. The MANOVA found significant effects of PTSD on immersion and dissociation: Pillai's Trace $F(2, 28)=4.795$, $p=0.016$. Univariate tests found that PTSD was associated with more dissociation during simulations: $F(1, 29)=8.748$, $p=0.006$. There were no differences in immersion between participants with and without PTSD. Because PTSD was associated with greater levels of dissociation, the PCL score was included as a covariate in multivariate analysis of covariance (MANCOVA) testing whether child or adult trauma history had an effect on dissociation or immersion during simulations. Neither the MANCOVA that compared participants with and without a history of childhood trauma, nor the MANCOVA that compared participants with and without a history of adult trauma found any significant effect of trauma history on dissociation or immersion during simulations.

Subjective Units of Distress Scale (SUDS) ratings Mixed Repeated Measures (Time) × Group (PTSD diagnosis vs.

Table 5 Mean (SD) heart rate

	PTSD $N=10$	No PTSD $N=21$	Adult trauma $N=8$	No adult trauma $N=23$	Child trauma $N=12$	No child trauma $N=19$	Abuse $N=9$	No abuse $N=22$
Scenario 1 mean (SD) heart rate (beats/min)								
Baseline	88.62 (11.17)	88.72 (15.92)	94.33 (12.77)	86.73 (14.63)	87.67 (11.05)	89.34 (16.38)	92.20 (9.23)	87.26 (15.96)
Scenario 1	85.79 (10.44)	84.61 (16.17)	92.90 (16.51)	82.25 (12.86)	83.98 (11.32)	85.63 (16.31)	87.55 (10.87)	83.95 (15.72)
Scenario 2 mean (SD) heart rate (beats/min)								
Segment 1 (neutral)	85.42 (8.98)	86.22 (14.65)	94.53 (12.82) [a]	82.98 (11.84) [a]	85.42 (10.78)	86.30 (14.42)	89.84 (8.85)	84.38 (14.15)
Segment 2 (neutral)	84.60 (11.62)	85.48 (14.83)	92.28 (13.60)	82.73 (13.11)	85.21 (12.26)	85.19 (14.84)	88.37 (12.09)	83.90 (14.34)
Segment 3 (attack)	85.68 (11.31)	84.57 (13.53)	93.22 (13.95) [a]	82.05 (11.12) [a]	86.27 (12.23)	84.08 (13.18)	90.07 (11.44)	82.83 (12.80)
Segment 4 (attack)	84.04 (8.50)	85.45 (14.30)	90.67 (12.08)	83.02 (12.41)	84.46 (10.55)	85.33 (14.00)	88.79 (9.33)	83.44 (13.59)
Segment 5 (post-attack)	85.32 (9.77)	86.20 (15.00)	93.44 (13.16)	83.30 (12.69)	86.64 (11.36)	85.46 (14.78)	89.53 (9.73)	84.44 (14.54)

[a]Significant main effect of group, history of adult trauma > heart rate versus no adult trauma

non) ANOVAs were conducted to test the effect of diagnostic status on SUDS levels. For all analyses, Greenhouse–Geisser adjusted degrees of freedom were used if violations of sphericity were found. The first ANOVA compared Pre-, Peak, and Post-SUDS ratings for Scenario I. The ANOVA found significant main effects of Time and Group, but no significant interaction: $F(1.433, 42.984) = 22.667$, $p < 0.001$ (Time); $F(1, 30) = 5.286$, $p = 0.029$ (Group). Analyses of the main effect of Time found that Peak SUDS ratings were the highest, followed by Post- and Pre-SUDS ratings: $F(1, 30) = 28.365$, $p < 0.001$ (pre vs. peak); $F(1, 30) = 21.065$, $p < 0.001$ (pre vs. post); $F(1, 30) = 6.350$, $p = 0.017$ (peak vs. post). Analyses of the main effect of Group found that participants with PTSD had higher pre-exposure SUDS than those without PTSD, $F(1, 30) = 13.811$, $p = 0.001$. There was a trend for higher post-ratings ($p = 0.068$) and no difference in peak SUDS.

A Repeated Measures (Time) × Group (PTSD diagnosis vs. non) ANOVA for Scenario 2 was tested for diagnostic group differences in SUDS ratings before the scenario (pre), during the patrol segments (mean of SUDS ratings after Segments 1 and 2), during the attack segments (mean of SUDS ratings after Segments 3 and 4), and post-scenario SUDS ratings (after Segment 5, resume patrol). The ANOVA also found significant main effects of Time and Group, but no significant interaction: $F(1.755, 50.891) = 20.820$, $p < 0.001$ (Time); $F(1, 29) = 7.633$, $p = 0.010$ (Group). Analyses of the main effect of time found that SUDS ratings during the attack segments were higher than those during the patrol segments, $F(1, 29) = 48.862$, $p < 0.001$. There was a trend for the attack segments SUDS ratings to be higher than post-scenario SUDS, ($p = 0.061$). Pre-scenario SUDS were also significantly lower than attack segment SUDS: $F(1, 29) = 41.874$, $p < 0.001$, and lower than SUDS for SUDS during the patrol segment SUDS, $F(1, 29) = 6.380$, $p = 0.017$, and post-scenario SUDS, $F(1, 29) = 16.200$, $p < 0.001$. Analyses of the main effect of Group found that participants with PTSD had higher SUDS ratings before and during the scenario: $F(1, 29) = 9.672$, $p = 0.004$ (pre); $F(1, 29) = 6.966$, $p = 0.013$ (patrol); $F(1, 29) = 7.980$, $p = 0.008$ (attack), with a trend ($p = 0.059$) for higher post-scenario SUDS.

Cortisol secretion and heart rate Analyses were conducted to assess the effects of PTSD diagnostic status, adult non-war-related trauma history, child trauma history, and history of childhood abuse on cortisol secretion and heart rate. Correlation analyses were conducted to identify variables that were significantly correlated with dependent variables to include as covariates in analyses. Age and gender were automatically included as covariates because of established associations between cortisol secretion and reproductive hormones (Daskalakis et al. 2014) and known changes in hormones and cardiovascular functioning with age.

For the cortisol analyses, the dependent variable was level of cortisol before (pre) and after (post) the VR simulations. Cortisol level decreased over time in 61% of participants, increased in 35%, and did not change in 3%. Depression symptoms (BDI scores), adult non-war-related trauma, and childhood trauma exposure (excluding abuse) were not significantly correlated with cortisol levels. History of childhood abuse marginally correlated with a higher cortisol level before scenarios ($p = 0.056$) and with greater decrease over time ($p = 0.070$), after controlling for PCL scores. A Time × Diagnostic Group (PTSD vs. non) ANCOVA controlling for age, gender, and abuse history found significant effects of Time, $F(1,26) = 5.058$, $p = 0.033$; Group, $F(1, 26) = 5.671$,

$p = 0.025$; and an interaction, $F(1,26) = 4.849$, $p = 0.037$. Participants with PTSD showed a greater decrease in cortisol than those without PTSD. Univariate ANCOVAs found that participants with PTSD had higher levels of cortisol before (but not after) simulations, $F(1, 26) = 7.394$, $p = 0.012$. ANCOVAs that controlled for age, gender, and PCL scores found no significant effects of history childhood abuse, adult civilian trauma exposure, or childhood trauma exposure on cortisol levels.

For the heart rate analyses, the dependent variable was mean heart rate level sampled during Scenario 1 and during each of the five segments of Scenario 2. Heart rate declined an average of 3.70 beats per minute during Scenario 1 and fluctuated approximately one beat per minute across segments in Scenario 2. Adult non-war-related trauma correlated with mean heart rate during the first segment of Scenario 2 (patrol), controlling for PCL scores, $r = 0.372$, $p = 0.043$, with trends for correlations with Scenario 2 attack ($r = 0.372$, $p = 0.053$) and post-attack ($r = 0.381$, $p = 0.087$) segments. History of childhood trauma and history of abuse history did not correlate with heart rate. A Time × Diagnostic Group (PTSD vs. non) ANCOVA that controlled for age and gender did not find any significant effects of PTSD diagnosis on heart rate during Scenario 1. For Scenario 2, a Time × Diagnostic Group (PTSD vs. non) ANCOVA that controlled for age and gender, and adult non-war-related trauma, found only a main effect of adult non-war-related trauma, $F(1,26) = 5.022$, $p = 0.034$. A one-way MANCOVA controlling for age, gender, and PCL scores found that adult non-war-related trauma was associated with higher heart rates during Scenario 2: Pillai's Trace $F(5, 22) = 4.513$, $p = 0.006$. Significant effects of trauma history were found for Segment 1 (patrol), $F(1, 26) = 5.466$, $p = 0.027$; and Segment 3 (attack), $F(1, 26) = 4.779$, $p = 0.038$; with a trend for Segment 5 (post-attack), $F(1, 26) = 3.848$, $p = 0.061$.

5 Discussion

The VR challenge elicited greater distress, dissociation, and differential cortisol secretion in participants with PTSD versus those without PTSD. Simulations elicited moderate levels of distress and mild dissociation in participants with PTSD that was significantly greater than the mild distress and dissociation endorsed by participants without PTSD. Greater immersion in the scenarios was correlated with stronger emotional engagement, and both of these variables predicted more dissociation during scenarios.

Participants with PTSD secreted more cortisol before scenarios and showed greater decrease over time, compared to participants without PTSD. There are reports of an association between PTSD and greater cortisol secretion in response to laboratory stressors in females (Elzinga et al. 2003) but not males (Liberzon et al. 1999). The results of the present study are suggestive of an over-secretion of cortisol in anticipation of a stressor followed by a return to baseline in participants with PTSD, but we would need a sample collected outside the laboratory to clearly demonstrate this was an anticipatory increase in cortisol.

There were no significant effects of diagnostic status on heart rate reactivity. Participants did show slight heart rate increases during Scenario 2′s attack segments, and those with a history of adult non-war-related trauma exposure showed elevated heart rates during portions of this simulation, compared to participants with no history of adult non-war-related trauma exposure. Null results may have been due to the small sample size. We may have erred too far on the side of caution and produced scenarios that were not evocative enough to elicit differential heart rate reactions, as the results contrast findings of increased heart rate in response to trauma cues in survivors with PTSD (Pineles and Orr 2018; Pole 2007). The VR challenge paradigm differs from those used in PTSD psychophysiology studies (Pineles and Orr 2018; Pole 2007). Scenarios were novel rather than scripts of actual events; heart rate was sampled continuously, with no intervening baselines, and not time-locked to stimuli. The VR software was not designed to permit measuring heart rate in response to discreet events during simulations, which might have revealed more subtle patterns of accelerations and decelerations in response to stressor stimuli (c.f. Bradley 2009) than we could detect in the present study. Researchers have employed fully automated VR simulations that permit events to be time-locked to physiological responses (Rumball 2013; Rumball et al. 2011) although this does sacrifice the possible benefit of having participants navigate the environment. VR researchers should continue to explore ways to balance the need for precise psychophysiological measurement with the need to engage users in VR simulations.

The results of the study suggest that prior trauma exposure may be associated with altered physiological stress responses. In addition to the finding of elevated heart rate in participants with a history of trauma exposure, history childhood abuse (but not adult or childhood trauma history) was weakly associated with greater cortisol secretion before scenarios and with greater decrease in cortisol over time. These findings were consistent with evidence that trauma exposure produces persistent changes in stress responses (McEwen 2007) and highlight the potential utility of the VR paradigm to test etiological models of PTSD and other stress-related conditions.

No participants developed full-blown simulator sickness, which may have been due to their familiarity with video games. The one participant who experienced transient discomfort during the simulation was older and did not play video games. We endeavored to develop simulations that would be evocative but not overly distressing. The scenarios

evoked moderate SUDS ratings (maximum mean score of 64 out of 100) and mild levels dissociation (low ratings on the IPQ). We found no change in PTSD symptoms assessed the week before and the week after the VR challenge. Other than the nightmare reported by one participant, there were no reports of increased PTSD symptoms during the study. We do not know whether the nightmare was due to the VR challenge or to procedures associated with the parent study, or whether this observation differs from those in other PTSD symptom challenge paradigm studies which have not followed participants after completing challenge procedures. We received no reports of any distress or problems when participants were contacted two weeks after the VR challenge. It would have been preferable to have study debriefings and follow-up calls administered by independent evaluators. However, the participants appeared to offer honest feedback, which in all cases were suggestions on how to increase the intensity of the simulations. Despite these encouraging findings, we would suggest some caution in future VR research with clinical samples with more severe PTSD, as this sample was composed of Veterans with PTSD of moderate severity and symptomatic trauma-exposed controls without PTSD. We would also recommend that researchers who plan to use VR paradigms with trauma survivors inform participants during the consenting process of the possibility of transient increase in PTSD symptoms, as well as the possibility of simulator sickness, as we did in the present study.

We have noted some of the technical limitations of the simulations. The study was also.

limited by a small, predominantly male sample. However, our prevalence of females was comparable to that reported in other research with Iraq and Afghanistan War Veterans (Katz et al. 2012; Street et al. 2009). Despite its limitations, the study introduced a novel, feasible, and well-tolerated VR challenge paradigm. Future research should continue to develop and test VR simulations and explore their potential to enhance our understanding of the emotional, cognitive, and physiological effects of exposure to trauma and adverse events.

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