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Motion-Assisted, Multi-Modal Memory Desensitization and Reconsolidation Therapy for Posttraumatic Stress Disorder in Women with a History of Sexual Trauma

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ABSTRACT

Background: Women military service members (SMs) are more likely to have posttraumatic stress disorder (PTSD) related to sexual assault, highlighting a need for the development and validation of therapies. A new exposure-based therapy called motion-assisted, multi-modal memory desensitization and reconsolidation (3MDR) uses participant-chosen music and images and an eye movement (EM) task in a virtual environment. Motion-assisted, multi-modal memory desensitization and reconsolidation has shown effectiveness in treating treatment-resistant male veterans; thus, this paper focuses expressly on the utility of 3MDR in female study participants, who were 50% of the full study population.

Methods: Participants with probable PTSD and mild traumatic brain injury (mTBI) completed 10 sessions of 3MDR. They provided songs and images representative of their trauma(s). While walking on a treadmill, participants confronted up to 7 of their trauma images while keywords were superimposed over the images. Half the participants were randomized to an eye movement task (EM+). The primary outcome was the change in posttraumatic stress disorder checklist for DSM-5 (PCL-5) score from pre- to post-intervention, with 3- and 6-month follow-ups.

Results: All women participants had a history of sexual trauma and showed statistically and clinically significant improvement in symptom severity. The decline in mean PCL-5 scores was greater for women than for men (none of whom reported sexual trauma), though the difference was not statistically significant. Although a small sample size, the results suggest clinically meaningful sex differences.

Conclusion: Motion-assisted, multi-modal memory desensitization and reconsolidation is an effective and powerful intervention for female SMs and veterans with a history of sexual trauma. Further investigation with larger sample sizes is needed.

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INTRODUCTION

Posttraumatic stress disorder (PTSD) and mild traumatic brain injury (mTBI) are common, and often comorbid, in military service members (SMs) and veterans.[1] In recent years, the number of women serving in the U.S. Armed Forces has progressively increased, to nearly 1 in 5 SMs.[2] Nationally, rates of PTSD are higher for women than men overall[3] and female veterans have more than twice the rate of PTSD as males.[4] More than half of women veterans report having experienced at least 1 traumatic life event prior to starting their military career, and women veterans nearly universally report experiencing a traumatic event in their lifetime, including their military service.[5] A contributing factor to the marked prevalence of PTSD for women in the military is the disproportionate rates of sexual assault reported by females compared to males, ranging from 20% to 70% for women compared to 2% for men.[6-8]

Studies consistently document a significant gap in the treatment of military sexual trauma (MST) and adult sexual trauma (AST) for women veterans. Women veterans who have reported MST and AST experience reduced treatment efficacy for both PTSD and depression, as well as decreased maintenance of symptom reduction.[9,10] Previous research indicates that intensive outpatient programs offer an effective intervention for MST-related PTSD.[10] However, these programs require a significant time commitment and are not widely available to veterans, with limitations related

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to geography, program space, and healthcare coverage. Moreover, the literature suggests that when trauma-focused interventions are the centerpiece of such programs, they are less effective in treating MST-related PTSD, with smaller effect sizes and lower rates of remission than for combat-related PTSD.[10,11] This highlights a need for therapies that have proven efficacy in sexual trauma-related PTSD.

Virtual reality exposure therapy (VRET) is a unique and innovative approach to PTSD intervention. Virtual reality exposure therapy employs visual and auditory cues to facilitate the participant's recall of the traumatic experience. Previous research has shown that VRET is a safe and effective therapy for PTSD related to MST, with high treatment completion rates and statistically significant drops in self-reported PTSD and depression symptoms.[12]

Motion-assisted, multi-modal memory desensitization and reconsolidation (3MDR) is a novel PTSD therapy based on dual-task processing and working memory theory;[13,14] Motion-assisted, multi-modal memory desensitization and reconsolidation methods have been previously described.[15] Briefly, 3MDR is delivered via the revolutionary Computer Assisted Rehabilitation Environment (CAREN) with the intent to decrease cognitive avoidance and increase engagement. The CAREN features a motion platform with an embedded treadmill, surrounded by a 180-degree panoramic screen to display virtual environments (VEs) that are synchronized to the speed of the treadmill. Two published randomized control trials compared 3MDR to a non-specific treatment control group and a waitlist control, respectively, for veterans with PTSD; both found 3MDR reduced PTSD symptom severity.[15,16] However, those study populations were almost exclusively male, and it is important to assess whether 3MDR is also efficacious in women, who are more likely to have MST-related PTSD.

Recent research on women with a history of complex trauma emphasizes the significant negative impact sexual assault and harassment have on one's self-esteem and sense of empowerment, often fueling isolation, self-harming, and sabotaging behaviors.[17] Motion-assisted, multi-modal memory desensitization and reconsolidation allows the patient to take the initiative, confront their past and present fears, and mitigate feelings of helplessness.[18] As such, 3MDR would seem to have the potential to effectively treat PTSD related to sexual trauma, with specific benefits derived from the unprecedented combination of VE immersion, a "walk and talk" therapeutic approach, pronounced individualization and collaboration with the patient, and lateral eye movement (EM), integrated in a more engaging manner than traditional Eye Movement Desensitization and Reprocessing.

MAIN POINTS

- There is a need for novel trauma therapies to help women in the military with post-traumatic stress disorder (PTSD) and a history of sexual assault.
- Motion-assisted, multi-modal memory desensitization and reconsolidation is an innovative, engaging, and empowering exposure therapy for PTSD in service members and veterans.
- Motion-assisted, multi-modal memory desensitization and reconsolidation appear to be an effective intervention for women in the military with PTSD due to sexual assault.

MATERIAL AND METHODS

Participants and Setting

A total of 20 participants with probable PTSD and a comorbid history of mTBI were enrolled. Due to the lack of research on women in the military with PTSD, this pilot study intentionally recruited 50% females. All participants met a score of at least 34 on the Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5), indicating a probable diagnosis of PTSD. There was no specification for the type of trauma to be enrolled and participants' traumas ranged from childhood sexual abuse to military combat-related traumas. Interestingly, all the female participants reported a history of sexual trauma, whereas all the male participants disclosed combat trauma and none reported a history of sexual trauma. A full description of all inclusion and exclusion criteria is detailed in the overall report of this pilot study.[19] The protocol was approved by the institutional review boards at Uniformed Services University and Walter Reed National Military Medical Center, both in Bethesda, Maryland, USA (protocol number WRNMMC-2018-0201).

Procedures

The protocol procedures have been previously described in the 2022 manuscript,[19] and the 3MDR procedures are consistent with those previously indicated and published.[14,20] To briefly review the details pertinent to the findings, all participants were required to attend 10 sessions: 3 preparatory, 6 intervention, and 1 consolidation. Preparatory sessions focused on trauma selection(s), education on 3MDR and PTSD, picture and music selections, and comfortability with the virtual environment. Picture selection is an integral part of the 3MDR therapy, and for the purposes of this paper, the focus will be on this process for the female participants, who, as previously mentioned, all reported sexual traumas. The types of sexual traumas the female participants disclosed included childhood sexual trauma, intimate partner violence, MST, and sexual assault or rape. In order to find images that best represented these incredibly sensitive experiences, participants selected images ranging from the location of the sexual assault all the way to an image of their perpetrator or assailant. Each image was rated on its emotional intensity according to a Subjective Unit of Distress Scale (SUDS) of 1-10. Table 1 provides examples of images that participants used for sexual assault-related traumas, and the initial SUDS that were associated with them.

Table 1. Types of Sexual Traumas Among Female Participants and Examples of Pre-Selected Participant Images

Type of Sexual Trauma	Example of Images
Military sexual trauma	Image of perpetrator (SUDS - 10) Entry to military base (SUDS - 4) Barracks where assault occurred (SUDS - 7) Participant in uniform before general court martial (SUDS - 9)
Childhood sexual trauma	Childhood home (SUDS - 5) Family photos (SUDS - 9)
Intimate partner sexual violence	Couch (SUDS - 4) Bed (SUDS - 7) Device used in assault (SUDS - 10)

SUDS, Subjective Units of Distress Scale.

Participants completed 6 intervention sessions, during which the therapist and participant worked through the images selected to represent the trauma(s). Each intervention session had 3 phases: warm-up, intervention—where the participant's images are displayed and associations are identified, and cool-down. During the warm-up, participants walked on the treadmill without interruption, listening to the first piece of music selected to take them back emotionally and mentally to the time of the trauma. For example, a participant who experienced intimate partner violence selected a song that she and her and partner listened to often. A maximum of 7 pre-selected images were used in each intervention session, where the therapist queried about the memories associated with the images, superimposed key words or associations over the images, and conducted the EM task (if applicable). To complete the virtual environment portion of the session, participants continued walking on the treadmill to a preselected song that brought them back to the present while they continued walking to bring down their psychophysiological reactions to the exposure work. Each intervention session ended with a debrief period where the participant was able to journal about her experience of confronting her trauma images and discuss them.

The final consolidation session was conducted with the therapist and principal investigator. The participant was asked to complete a battery of questionnaires. The therapist reviewed the progress made by the participant, highlighting significant improvements in symptoms, changes in associations, and SUDs with select pictures, as well as quotes from their written entries. Finally, there was a discussion of what additional therapy, if any, might be helpful to supplement the gains made during the study, and how it might be obtained.

Measures

The primary outcome measure was the PCL-5, which is used to evaluate self-reported PTSD symptom severity. The PCL-5 was conducted at various time points to assess progress: midway through the intervention, post-intervention, and during 3- and 6-month follow-ups. Secondary measures included various self-report questionnaires to assess commonly associated issues with PTSD: the Neurobehavioral Symptom Inventory (NSI) for post-concussive symptoms, the Patient Health Questionnaire Depression module (PHQ-9) for depression symptoms, and the Insomnia Severity Index (ISI) for insomnia and sleep issues. These secondary measures were administered at baseline, after therapy, and during 3- and 6-month follow-ups.

Analytic Plan

We focus here on 2 sets of analyses: 1) changes in measures over time with respect to gender using permutation tests, and 2) changes in measures over time in the female cohort using paired t-tests as well as linear mixed-effects models (LMM). Analyses were conducted using Base SAS and SAS/STAT 14.1 packages of SAS Version 9.4 and the standard R base packages of R software Version 4.2.1.

RESULTS

Demographics

The study was designed to include an equal number of males and females. Table 2 shows the demographic information for the female participants, including comparisons between those who completed the study and those who withdrew. Nine of the 10 females completed the study (compared to only 7 of 10 males).

Given the small sample size, permutation tests (1000 iterations) were conducted to compare differences between male and female participants for the 4 primary outcome variables (PCL-5, NSI, ISI, and PHQ-9) at Visit 2, Visit 3, and Visit 4 with respect to Visit 1 (baseline). Two-sided tests and a significance level of 0.05 were assumed to assess significant differences by gender. In analyses that included female participants only, paired *t*-tests were used to assess changes in the means of the 4 primary outcome variables, respectively, for Visit 2 v. Visit 1, Visit 3 v. Visit 1, and Visit 4 vs. Visit 1. A significance level of 0.05 was

Table 2. Female Participant Demographics

	All Participants	Completers	Withdrawals
Sex			
Female	10	9	1
Race			
White	6	6	0
Black	3	2	1
Hispanic	1	1	0
Age, Mean (SD), years	41.1 (11.5)	41.1 (12.2)	41
Branch of Service			
Army	6	5	1
Navy	2	2	0
Air Force	1	1	0
Coast Guard	1	1	0

Table 3. Permutation Test of Mean Difference of Change in Outcome Measures (Follow-Up Vs. Baseline) in Females Compared with Males (Negative Values Indicate That Females' Scores Decreased More Than Those of Males)

	Mean Difference	SE*	95% CI*	*P***
PCL-5				
Visit 2 v. baseline	−4.94	10.58	(−25.68, 15.80)	.640
Visit 3 v. baseline	−11.54	11.30	(−33.69, 10.61)	.345
Visit 4 v. baseline	−13.76	11.28	(−35.87, 8.35)	.247
ISI				
Visit 2 v. baseline	−2.30	3.10	(−8.38, 3.78)	.471
Visit 3 v. baseline	−3.19	2.99	(−9.05, 2.67)	.319
Visit 4 v. baseline	−1.63	6.11	(−13.61, 10.35)	.625
NSI				
Visit 2 v. baseline	2.57	5.73	(−8.66, 13.80)	.677
Visit 3 v. baseline	0.54	6.80	(−12.79, 13.87)	.955
Visit 4 v. baseline	0.33	7.02	(−13.43, 14.09)	.975
PHQ-9				
Visit 2 v. baseline	2.35	3.05	(−3.63, 8.33)	.479
Visit 3 v. baseline	1.89	3.27	(−4.52, 8.30)	.578
Visit 4 v. baseline	1.05	3.31	(−5.44, 7.54)	.771

ISI, Insomnia Severity Inventory; NSI, Neurobehavioral Symptom Inventory; PCL-5, PTSD Checklist; PHQ-9, Patient Health Questionnaire; SE, Standard Error.
*SE and 95% CIs based on the observed data across gender.
***P*-value based on the observed mean difference with respect to a distribution from a random sorting (i.e. permutations) of differences in scores across gender.

assumed for the different tests. Additionally, the mean changes in these variables were examined using LMM to evaluate whether the scores at Visits 2, 3, and 4 differed significantly from their respective scores at baseline. Given the limited sample size, standard error and 95% CI estimates were derived based on bootstrap sampling (500 iterations) to provide more robust measures of precision of the LMM estimates. *P*-values were calculated from these estimates using available methods.[21]

ANALYSIS

Analysis of Mean Change in Measures by Gender

We ran permutation tests, which allowed us to assess the actual observed differences between women and men for the different outcomes (Visit 2 vs. Visit 1, Visit 3 v. Visit 1, Visit 4 vs. Visit 1), compared with a random sorting (i.e. permutation) of the difference scores across the sexes. The differences indicated a larger decrease in PCL-5 over time in women vs. men; however, these were nonsignificant (Visit 2 vs. Visit 1: mean difference = −4.94, *P*-value = .640; Visit 3 vs. Visit 1: mean difference = −11.54, *P*-value = .345; Visit 4 vs. Visit 1: mean difference = −13.76, *P*-value = .247). Similarly, nonsignificant differences were observed for the remaining measures, NSI, ISI, and PHQ, between the sexes at Visit 2, Visit 3, and Visit 4 vs. Visit 1 (Table 3). Although nonsignificant differences were observed between women vs. men, the results nonetheless suggest potentially important clinical differences between the sexes. For example, the difference in mean change in PCL between Visit 3 and Visit 1 and Visit 4 and Visit 1 for women vs. men was −11 and −14, respectively.

Analysis of Mean Change in Measures in Women Only

Figure 1 provides a visual representation of the change in scores over time and between-subject variability of PCL, ISI, NSI, and PHQ among the 9 female participant completers.

For the paired t-tests, for Visit 2 v. Visit 1, Visit 3 v. Visit 1, and Visit 4 v. Visit 1, a statistically significant drop in PCL-5 was observed (Table 4). A similar significant drop was observed for NSI at each of the follow-up visit times (Visit 2, Visit 3, Visit 4) v. Visit 1. For ISI, a significant drop was observed only for Visit 4 v. Visit 1. No significant changes were observed for PHQ-9. Figure 2 provides a visual representation of the changes in the overall mean PCL-5, ISI, NSI, and PHQ-9 over time in the 9 participants.

Based on the LMM (Tables 5-8), there was a positive effect of the intervention on the PCL-5, ISI, and NSI outcome measures. Between the baseline and post-intervention assessments, there was a statistically significant improvement in PCL-5, ISI, and NSI for the female participants both after intervention (Visit 2) and 3 months after intervention (Visit 3). For the PHQ-9, there was no statistically significant improvement.

QUALITATIVE RESULTS

Qualitative analysis reveals interesting changes in word associations across the intervention sessions. Table 9 displays examples of women who had various types of sexual trauma and the comparison of word associations when a particular image was first used versus when the image was shown again in a later session. One can see a dramatic perspective shift in the characterization of these images, often leading to a positive descriptor rather than the original quite negative or self-contempt descriptor. Figures 3 and 4 present word clouds that compare the negative and positive word associations over the course of the intervention.

Qualitative interpretation of the participant associations led the researchers to discern several important themes among the participants, the most significant being empowerment and self-worth. Reviewing the associations made during sessions, you see words and phrases such as "disempowerment" and "hidden and separated from the world" evolving to "internal power" and "I want to be part of the solution." As previously mentioned in the methods of the 3MDR intervention, participants are asked

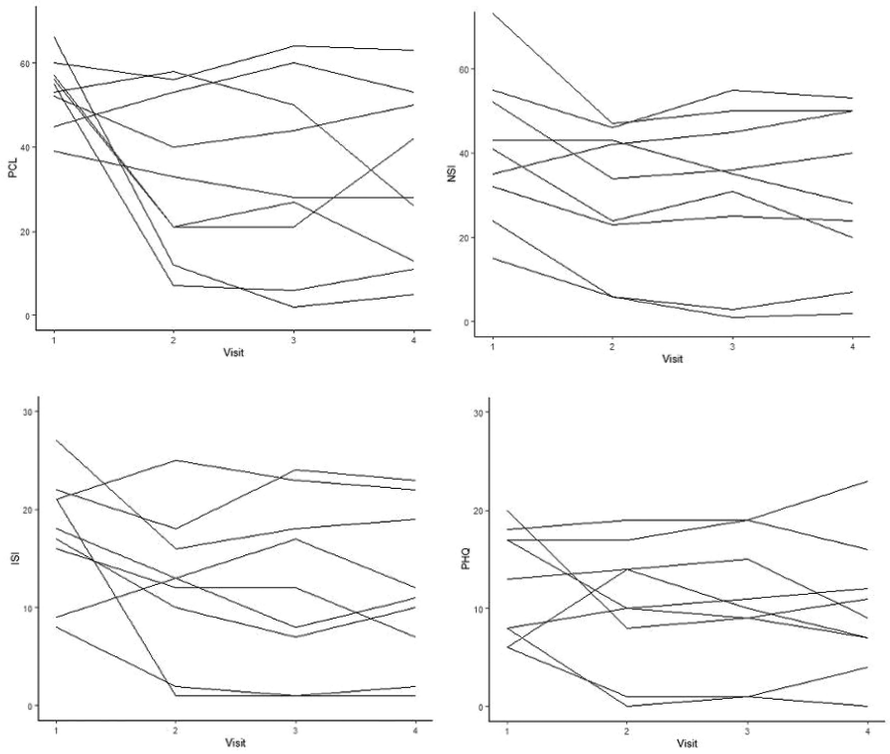

Figure 1. Plots for primary outcome variables in PCL (PTSD Checklist), ISI (Insomnia Severity Index), NSI (Neurobehavioral Symptom Inventory), and PHQ (Patient Health Questionnaire) among the 9 female participants.

to write a brief journal-style entry at the conclusion of each intervention session. Participants are simply asked to reflect on the session and elaborate on any lingering thoughts or emotions. In addition to the word associations in session discussed above, therapists found participants expressing these themes in their journal entries. Below are examples pulled from participants' later sessions as their expression of self-worth and empowerment becomes more evident in their journal entries.

"That makes me a powerhouse, and such powerhouses can choose to be positive, kind, fun, disciplined, and protective of the vulnerable."

-Participant who had experienced childhood sexual trauma

Table 4. Paired *t*-Test of Mean Differences in Outcome Measures (Female Participants Only)

	Mean Difference	SE	95% CI	*P*
PCL-5				
Visit 2 v. baseline	−20.22	7.77	(−38.14, −2.31)	.032
Visit 3 v. baseline	−20.11	8.67	(−40.11, −0.11)	.049
Visit 4 v. baseline	−21.33	8.01	(−39.81, −2.86)	.029
ISI				
Visit 2 v. baseline	−5.44	2.44	(−11.07, 0.18)	.056
Visit 3 v. baseline	−5.33	2.36	(−10.77, 0.10)	.054
Visit 4 v. baseline	−5.78	2.19	(−10.83, −0.73)	.030
NSI				
Visit 2 v. baseline	−11.00	3.37	(−18.76, −3.24)	.011
Visit 3 v. baseline	−9.89	3.45	(−17.83, −1.94)	.021
Visit 4 v. baseline	−10.67	3.85	(−19.54, −1.79)	.024
PHQ-9				
Visit 2 v. baseline	−2.22	6.20	(−6.99, 2.54)	.314
Visit 3 v. baseline	−2.11	5.99	(−6.71, 2.49)	.321
Visit 4 v. baseline	−2.67	1.58	(−6.31, 0.98)	.130

ISI, Insomnia Severity Inventory; NSI, Neurobehavioral Symptom Inventory; PCL-5, PTSD Checklist for DSM-5; PHQ-9, Patient Health Questionnaire; SE, standard error.

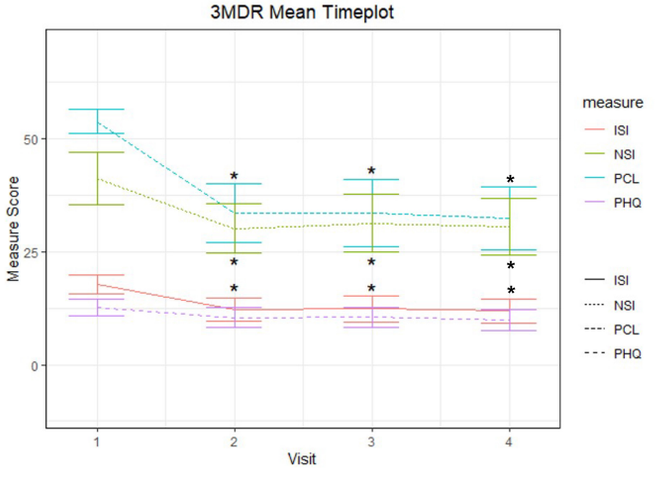

Figure 2. Mean time plots for primary outcome variables. Mean ± SE: Significance labels (*) in the time plot are determined from the bootstrapped 95% CIs in Tables 5-8. If the 95% CI does not cross 0, then the change from that time point and baseline is statistically significant.

Table 5. Posttraumatic Stress Disorder Checklist for DSM-5 Linear Mixed Effects Model Results of Mean Differences (Female Participants Only)

	β	SE*	95% CI*	*P***
Intercept	53.67			
Visit 2	−20.22	7.65	[−34.73, −5.38]	.008
Visit 3	−20.11	8.50	[−36.63, −3.67]	.018
Visit 4	−21.33	7.70	[−36.12, −5.22]	.006

Intercept coefficient (**β**) represents the mean PTSD Checklist for DSM-5 at baseline. Coefficients for Visits 2,3, and 4 represent the difference in mean PCL-5 at these visits compared to the mean PCL-5 at baseline, respectively.
PCL-5, PTSD Checklist for DSM-5; SE, standard error.
*SE and 95% CIs were derived by bootstrap (500 samples).
***P*-values were calculated using available methods.[21]

Table 6. Insomnia Severity Index Linear Mixed Effects Model Results of Mean Differences (Female Participants Only)

	β	SE*	95% CI*	*P***
Intercept	17.67			
Visit 2	−5.44	2.35	[−9.95, −1.00]	.020
Visit 3	−5.33	2.23	[−9.67, −1.16]	.017
Visit 4	−5.78	2.10	[−10.01, −1.44]	.006

Intercept coefficient (**β**) represents the mean ISI at baseline. Coefficients for Visits 2, 3, and 4 represent the difference in mean ISI at these visits compared to the mean ISI at baseline, respectively.
ISI, Insomnia Severity Inventory; SE, standard error.
*SE and 95% CIs were derived by bootstrap (500 samples).
***P*-values were calculated using available methods.[21]

Table 7. Neurobehavioral Symptom Inventory Linear Mixed Effects Model Results of Mean Differences (Female Participants Only)

	β	SE*	95% CI*	*P***
Intercept	41.11			
Visit 2	−11.00	3.07	[−16.73, −5.11]	.001
Visit 3	−9.89	3.20	[−15.46. −3.28]	.002
Visit 4	−10.67	3.56	[−16.89, −2.88]	.003

Intercept coefficient (**β**) represents the mean NSI at baseline. Coefficients for Visits 2,3, and 4 represent the difference in mean NSI at these visits compared to the mean NSI at baseline, respectively.
NSI, Neurobehavioral Sleep Inventory; SE, standard error.
*SE and 95% CIs were derived by bootstrap (500 samples).
**P*-values were calculated using available methods.[21]

"I am ready to go back to work again. I am living again. I am grateful in life to be back. Thank you. The perspective I have gained is amazing."

-Participant who had experienced sexual assault

"Therefore, the anger was suppressed and repressed because of punishments and threats to remain passive and not be angry enough to take action to tell authorities who would help protect me from them. I believe this intervention/activity helps me purge and release the anger as I now have 'permission' that I never got from abusers/family to feel and release anger."

-Participant who had experienced sexual assault

Table 8. Patient Health Questionnaire Linear Mixed Effects Model Results of Mean Differences (Female Participants Only)

	β	SE*	95% CI*	*P***
(Intercept)	12.56			
Visit 2	−2.22	1.97	[−6.11, 1.89]	.263
Visit 3	−2.11	1.89	[−5.50, 2.12]	.268
Visit 4	−2.67	1.47	[−5.28, 0.39]	.069

Intercept coefficient (**β**) represents the mean PHQ at baseline. Coefficients for Visits 2,3, and 4 represent the difference in mean PHQ-9 at these visits compared to the mean PHQ-9 at baseline, respectively.
SE, standard error.
*SE and 95% CIs were derived by bootstrap (500 samples).
**P*-values were calculated using available methods.[21]

DISCUSSION

There is an urgent need for better PTSD treatment options overall, and especially for women with a history of sexual trauma. In this study, 3MDR showed statistically and clinically significant PTSD symptom reduction in the women participants, who universally had histories of MST.

Table 9. Examples of Changes in Associations for Repeated Images

Trauma Type	First Time Image Used	Second Time Image Used
Childhood sexual trauma	Disempowered Self-loathing Fear Embarrassed	Empathy Internal power He's pathetic Relief
Sexual assault Combat	Injustice Gaslighting Stuck	Misdirected anger I want to be part of the solution I am now an artist
Childhood sexual trauma Interpersonal sexual violence	Unsafe	Angry
Domestic abuse	Out of control Isolation Inadequate Anxious anger	Grateful Closure Calm Emotional security
MST Suicide attempt	Stab in the heart Worthless	Annoyance Disappointed
MST	Despair Vulnerable Pain Hurt	Hope I feel whole Faith Determination
Sexual assault	Hidden and separated from the world	Always positives if you choose to look for them

MST, military sexual trauma.

Figure 3. Word cloud of negative associations at beginning sessions.

Of the 9 cisgender female participants who completed the study, all had sexual trauma-related PTSD. For the female participants alone, there was, on average a 20-point reduction in symptoms, based on the PCL-5. Six participants experienced a clinically significant drop in symptoms, reporting at least a 10-point reduction, and 5 participants no longer met the criteria for PTSD by the end of the intervention sessions, providing significant quantitative evidence of the value of 3MDR in women. Qualitative data analysis adds further value by demonstrating marked improvements in the associations and perceptions of the traumatic events that female participants had over the course of their participation in the study. Furthermore, it demonstrates improvements in individual self-esteem, sense of empowerment and belonging, and existential perspective.

Further, only 1 of 10 women withdrew from the study (compared to 3 of 10 men), which is remarkably better than the ~50% drop-out rates reported, for example, in the largest study to date assessing current "first-line" PTSD therapies Prolonged Exposure and Cognitive Processing Therapy.[22] Moreover, the dropouts that occurred were all prior to the initiation of the CAREN phase involving the self-selected music and pictures, suggesting that there is something particularly engaging about this treatment approach. The impressive levels of symptom reduction and remission were also achieved in a relatively short amount of time, namely with 6 weekly sessions. While corroboration in future larger studies is needed, it appears that there may be something especially empowering in the 3MDR approach, likely both through enabling women to choose music and pictures that recall their trauma, as well as affording them the opportunity to actively confront these trauma reminders by walking on the treadmill throughout each session and facing down their pictures, that enables them to make rapid, dramatic improvements in their symptom severity and put their PTSD behind them.

There are a few limitations to acknowledge with this pilot study. Most significantly, this was a small pilot study with only 20 enrolled participants, 10 of whom were women.

Figure 4. Word cloud of positive associations at final sessions.

Moreover, it was by chance rather than by design that all female participants had experienced some form of sexual assault or violence. It will be important for future studies to have larger sample sizes and to prospectively and deliberately study participants, both female and male, with a history of sexual assault. Secondly, while the PCL-5 compares favorably to the structured diagnostic interview, CAPS-5, since the CAPS-5 is widely considered a gold standard for PTSD diagnosis, it may be worthwhile for future studies to corroborate the results by using the CAPS-5. Finally, the CAREN system is extremely expensive and is only available in select locations around the world. Therefore, future research should assess the efficacy of using a less expensive delivery modality to allow 3MDR to be available to more populations and settings.

To address many of these limitations, the research team has started a new clinical trial, "Computer Monitor versus Augmented Reality: Expanding 3MDR Therapy for PTSD: A Randomized" Controlled Trial (CARE4PTSD), which seeks 60 participants, includes CAPS-5 assessments and employs a standard treadmill with comparatively inexpensive delivery mechanisms. The latter include the Microsoft Hololens2 augmented reality head-mounted display ($3500) and a high-definition, curved-screen computer monitor ($400).

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of Uniformed Services University and Walter Reed National Military Medical Center, Bethesda, Maryland, USA (Reference no.: 906495; Date: January 11, 2019).

Informed Consent: Written informed consent was obtained from participants who agreed to take part in the study.

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Author Contributions: Concept – EV, MJR.; Design – EV, MJR; Supervision – EV, MJR Resources – MJR; Materials – MJR; Data Collection and/or Processing – PB, ALR, MJR; Analysis and/or Interpretation – PB, ALR, AF, TH, EV, MJR; Literature Search – PB, ALR, MJR; Writing – PB, ALR, MJR; Critical Review – PB, ALR, AF, TH, EV, MJR.

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