

AWARD NUMBER: W81XWH-14-C-0091

TITLE: BRAVEMIND: Advancing the Virtual Iraq/Afghanistan PTSD Exposure Therapy for MST

PRINCIPAL INVESTIGATOR: Dr. Albert Rizzo

CONTRACTING ORGANIZATION: University of Southern California
Los Angeles, CA 90089

REPORT DATE: June 2016

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE June 2016		2. REPORT TYPE Annual		3. DATES COVERED 27 May 2015 - 26 May 2016	
4. TITLE AND SUBTITLE BRAVEMIND: Advancing the Virtual Iraq/Afghanistan PTSD Exposure Therapy System for MST				5a. CONTRACT NUMBER W81XWH-14-C-0091	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Dr. Albert Rizzo E-Mail: rizzo@ict.usc.edu				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) UNIVERSITY OF SOUTHERN CALIFORNIA 3720 S. FLOWER STREET LOS ANGELES, CA 90089-0001				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT PTSD can result from exposure to actual or threatened death, serious injury or sexual violation. Military Sexual Trauma (MST) has been recognized as a significant risk factor for the development of PTSD. This has become an issue of grave concern within the military, as reports of sexual violations and assaults have been on the rise over the last ten years, and have garnered significant popular media attention. The current project proposes to develop content for inclusion in the BRAVEMIND virtual reality exposure therapy (VRET) system that will provide new customizable options for persons who have experienced MST and to run a pilot RCT with a sample of 20 persons diagnosed with PTSD due to MST. The effort in the second year focused on enrollment and treatment of subjects for the RCT. A no-cost extension was granted for one year until May 26, 2017 to allow completion of the RCT.					
15. SUBJECT TERMS PTSD, Virtual Reality, Prolonged Exposure, Military Sexual Trauma					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT Unclassified	18. NUMBER OF PAGES 46	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT Unclassified	b. ABSTRACT Unclassified	c. THIS PAGE Unclassified			19b. TELEPHONE NUMBER (include area code)

Table of Contents

	<u>Page</u>
1. Introduction	4
2. Keywords	4
3. Accomplishments	4
4. Impact	12
5. Changes/Problems	12
6. Products	14
7. Participants & Other Collaborating Organizations	16
8. Figures	18
9. References	20
10. Special Reporting Requirements	20
11. Appendices	21
12. Journal Publications	29

1. **INTRODUCTION:** The major goals of this project are to create VR content to extend our VR PTSD Exposure Therapy system to address the clinical needs of those with PTSD due to Military Sexual Trauma and to test the efficacy of the system in a pilot clinical trial.
2. **KEYWORDS:** PTSD, Virtual Reality, Prolonged Exposure, Military Sexual Trauma
3. **ACCOMPLISHMENTS:**
 - **What were the major goals of the project?**
 - Specific Aim 1 – To extend and evolve the BRAVEMIND (BM) system to enhance the relevance, functionality, and usability of a VRET system for persons with PTSD due to MST (Months 1-6, 100% completion)
 - Specific Aim 2: We will test the clinical efficacy of the VRET system in an initial feasibility and waitlist clinical trial of 20 users diagnosed with PTSD due to MST (Months 1-24, 30% completion).
 - **What was accomplished under these goals?**
 - **Specific Aim 1, Major Task 1 – Develop Working MST VRET System for Study**

All of the below Subtasks have been completed and the system was delivered to the RCT site at Emory University in Mid-February 2015.

 - **Subtask 1: Review existing feedback and collect and organize new feedback from patients, clinicians, and consultants on MST contexts for design input.**

This was the initial step where our subject matter experts (SMEs) consultants, Barbara Rothbaum, JoAnn Difede and Chris Reist participated in conference calls that explored and discussed the possible desired VR contexts and functionalities that would be useful for this application. This input drew from their previous clinical expertise in both treatment and research in the area of civilian sexual trauma. The biggest concern involved finding the best balance between what the budget would support and the creation of content that would provide the widest range of exposure contexts needed to address the diverse experiences that MST victims present with. This was an iterative process that involved frequent and regular email and phone conversations between ICT and the SMEs. As well, a review of key literature ranging from government reports (cf. DoD Sexual Assault Prevention and Response Program (SAPR) (DoD, 2012)) to comprehensive journalism reports that provided great detail on the sexual trauma experiences of those in the military (cf. Moffeit & Herdy, 2004) further informed initial design directions. These various inputs formed the basis for the design work in Subtask 2.
 - **Subtask 2: Design and specify settings, stimuli and features based on input.**

From the results of Subtask 1, the team (ICT and SMEs) determined that since most MST occurs on or around US military bases, we would need to create a significant amount of US civilian contexts and relevant trigger stimulus input functionality. It was also determined that some of the existing BRAVEMIND (BM) Iraq/Afghanistan content could be reused as developed initially (when the contexts were relevant to the user's experience of MST—for example, in abandoned buildings, vehicles, outdoor spaces, etc.), but that the remote Forward Operating Base scenario was most ideally suited as a context, that with modification, would provide the best setting for spending resources to evolve specific communal, shared space areas—the types of areas where in-theatre MST has often been reported to occur. Thus, multiple MST scenarios were agreed upon and designed: 1) a remote Forward Operating Base that had shared barrack areas, primitive sheltered offices, remote outdoor spaces, shower areas, and latrines. And, 2) a US Base and Small Town scenario that included a bar area, back lots, alleys, streets, strip mall, motel and car ride. Other related US Base scenes were designed that included: apartment

and motel bedrooms/bathrooms/living spaces, a land-based office and a shipboard office. A wide range of indwelling functionality was designed in collaboration with the clinical partners such as: the user experience of walking and laying down, ambient lighting controls, perpetrator customization and behavior, car ride controls, and the creation of a diverse range of audio trigger stimuli clips relevant to the VR scenarios and contexts.

- **Subtask 3: Design and develop extended BRAVEMIND (BM) functionality as needed.** All of these elements of the design were iteratively evolved over the first year of the project where the clinical team could examine early prototype builds and provide input on the layout, lighting and content in the scenarios as they had the opportunity to review evolving instances of content development via video and still image captures, in addition to initial compiled versions of the VR simulation sections and prototype as they became available. See **Figure 1** for example images of some of the content developed for the VR MST scenarios.
- **Subtask 4: Produce needed art and related assets.** This occurred in parallel with Subtask 3 and it was the task of the ICT art and development group. Daily meetings were held to review the status of art creation and critiques of various iterations of the art by the team. While the remote Forward Operating Base had already been created and only required additive art assets to expand the content and functionality for MST relevance, a completely new set of contextual 3D art was required to create the US Base and Small town scenario.
- **Subtask 5: Integration of assets into BRAVEMIND (BM) system.** As the art assets were created for both scenarios, all team members (ICT and SMEs) provided feedback on the graphic art appearance/quality and upon consensual approval, the art (and necessary functionality to present the art and events) was integrated into the BM software architecture. The architecture consisted of the actual simulated VR worlds AND a clinical “wizard of oz” type interface. This point and click clinical interface is the control panel that clinicians use to select scenarios, place users in strategic locations within the scenarios, adjust ambient atmospheric, weather, lighting, and audio settings, in addition to the introduction of strategic trigger stimuli, all within the standard clinical protocol for appropriately delivering VRET (note—the VRET therapy process is detailed in the original proposal). Layout of the controls of the interface was based on the template created from the original BM combat-related PTSD VRET system (user-tested for usability) with slight modifications for the delivery of content unique to the MST system (e.g. Perpetrator appearance and behavior customization controls, individual room lighting effects, door controls, etc.). **Figures 2 and 3** present the front end interface layout for both major scenario components.
- **Subtask 6: Bug test Q&A.** After the scenarios were integrated into the BM architecture, Q&A and bug testing occurred internally at ICT in order to deliver an optimized and usable system to the clinical SME group for a final round of iterative feedback. The Q&A was completed by early December 2014 and was then sent out to the clinical SMEs for their feedback that would then be used to inform the creation of the final deliverable system to be used in the clinical trial in the next phase of the project. Although this was delivered right before the hectic time of the holiday season, the clinical SMEs tested the system over the next month and returned their feedback to us in January of 2015. Due to the tight collaboration that ICT and the SMEs had going on throughout the early design and development process, with numerous cycles of iterative feedback, the issues reported to ICT for modification were relatively small and easily addressed. One example of this involved the addition of a quick interface key to eliminate the presence of the

perpetrator rapidly, as the “following perpetrator” function (where the character would follow the user wherever they navigated in the scenario, akin to the “Terminator” character in the classic Si-Fi movies) was deemed to be more provocative when actually implemented in the scenario than had been anticipated during the design phase. Clinical SMEs wanted the capability to instantly eliminate its presence to better pace the VRET process. Other examples included the addition of various sound effects such as the sound of door locks being shut in the car and sounds of zippers, heavy breathing, clothes being torn, were requested. As well, additional content that made the car experience more diverse and flexible was added. The setting for the car ride to have the additional option of emulating the back seat of a taxi was requested as well as the ability to put the user in either the front or back of the car and to easily add or take away the perpetrator from the front or back seat was also requested. All of the requested adjustments were implemented by ICT and another round of bug testing occurred, whereupon what turned out to be an acceptable and final deliverable system was made available to the clinical site. Upon approval of the system by the clinical team, the PI visited the clinical site at Emory to work with the clinical team to sort out any training or use issues as needed for the clinical use of the system. With the system, delivered the next major Specific Aim of the project could commence.

○ **Specific Aim 2, Major Task 1 – Conduct Study**

Subtasks 1 and 2 have been completed. As of the end of the reporting period, Subtasks 3 through 6 are underway. Subtasks 7 through 10 are not yet due. See Appendix 1 for a full report of study enrollment and completion.

▪ **Subtask 1: IRB and Administrative Approval Process**

- 07/14/2014—IRB granted approval upon minor corrections
- 08/05/2014—IRB approval granted following minor corrections
- 09/02/2014—IRB approved “sensitive study status”
- 10/13/2014—Amendment approval, including changes to informed consent form and changes to study team
- 12/03/2014—Amendment approval, including waiver of signature for phone screen content, Emory added as a study site, protocol update, oral consent form, and changes to informed consent
- 02/13/2015—Amendment approval, including change to informed consent, protocol, and application for NIMH Certificate of Confidentiality
- 03/05/2015—Amendment approval, including changes to study team and changes to recruitment materials (i.e., internet ad, MST clinician handout, MST flyer, and PTSD screen card)
- 03/19/2015—Emory declared designated IRB, on which USC will rely for review and continued oversight of human subjects research for this study
- 04/06/2015—Amendment approval, including changes to consent form, changes to study team, changes to protocol document, and changes to questionnaires and surveys (addition of SimSensei Questionnaire, removal of PCL-5 and PSSI-5)
- 04/13/2015—Amendment approval, including changes to study team, changes to protocol document, changes to informed consent, addition of Certificate of Confidentiality, changes to questionnaires (added PCL-5).

- **Subtask 2: Hire and Train Study Personnel.** All study personnel completed the web-based Collaborative IRB Training Initiative (CITI) Program in the Protection of Human Subjects in Research. All investigators have completed training in

Conflict of Interest and Key Concepts in Clinical Research for Investigators through the Emory University Office for Clinical Research. All study personnel received additional training specific to study roles, including training in obtaining informed consent and administering study assessments. On 2/17/2015, Emory initiated its study kickoff meeting. In attendance were all Emory and USC study team personnel. Recruitment, screening and enrollment procedures were outlined and reviewed and training was given for administering SimSensei.

Psychophysiological data collection, which Dr. Rothbaum and her team collect for other studies, was outlined and reviewed as well. All therapists will have been trained in Prolonged Imaginal Exposure therapy (PE) followed by training in VRET, and will be supervised by psychologists experienced in providing VRET. Under the clinical guidance of Dr. Rothbaum, therapists and assessors receive weekly supervision. All treatment sessions are videotaped to ensure reliability.

- **Subtask 3: Subject Recruitment.** See Appendix 2 for list of recruitment efforts. Participants are self-referred from advertisements, community outreach, or referred by professionals. Advertisements include flyers around the Atlanta area, radio and television coverage, postings on websites such as craigslist, and social media outreach through <http://emoryhealthcare.org/veterans-program/index.html>, Facebook, and Twitter. Veteran Outreach Coordinators actively engage in outreach efforts by attending military/veteran events such as Veteran's Day functions, military family resource fairs, career fairs, Female Veterans and Active Duty Female Summit, VA Town Hall Meetings and other relevant events (see Appendix 2). Patients may be referred from both VA personnel and non-VA sources. Procedures have been established with the VA to ease the referral process between the VA and Emory. Phone screening is conducted by a member of the study team to determine appropriateness of this study for each participant and to inform the participant of study procedures. Basic inclusion and exclusion criteria, including psychological history, suicidality, and alcohol/substance abuse/dependence, and ability to wear VR headset is briefly reviewed according to a structured telephone screening interview. The investigators have been granted an IRB waiver of documentation of consent/HIPAA authorization for the various pre-randomization screening activities, including the telephone screening process.

During the reporting period, 13 people have been assessed for eligibility, with 8 being eligible and agreeing to participate in the study.

- **Subtask 4: Assessment of Participants (n=20).** See Appendix 3 for a full review of assessment measures. Enrolled participants will complete a pre-treatment assessment, 6-week post randomization assessment, post-treatment assessment if treatment continues beyond 6-week post randomization assessment, and a 3-month follow up assessment. Following the initial screen, an initial evaluation will be scheduled for individuals that are potentially eligible and interested in participating. Potential subjects will be asked to provide a copy of their DD214 to verify their military service record. Participants will meet with the study assessor who is trained in obtaining informed consent and all study assessments. The assessor will discuss all study procedures with the subject and inform them that the research is sponsored by the DoD. They will answer any questions they may have. The assessor will decide if the participant has the capacity to consent. To determine eligibility (detailed below), participants will be interviewed using the CAPS and MINI assessments. All assessments will be conducted by independent assessors

who will be blinded to treatment condition once randomization occurs, individually and in person. Once a participant is determined to be eligible for the study, the assessor will assign them a study number. Each study number will have a sealed containing the randomized condition. At assignment the day of the pre assessment visit, the assessor will open the envelope and inform the participant of their study group. They will then either schedule the participant to begin therapy or for the post-waitlist assessment in six weeks. In addition to the information gathered for eligibility, participants will also complete several other self-report and clinician administered measures as listed in Appendix 3. We will collect a one-time 2mL saliva sample to be used for the purpose of DNA extraction. DNA extraction is optional and will be presented to participants under a separate consent. Psychophysiological data will be collected including 4 cortisol samples.

During this reporting period, 8 participants completed the pre-assessment, all of whom were randomized to either waitlist or treatment conditions (see Appendix 1 for further details).

- **Subtask 5: Treatment of Participants (n=20).** Participants will be randomized to receive VRET immediately or wait 6 weeks during which time they will continue to receive usual care. VRET treatment will be delivered in a minimum of 6 sessions and a maximum of 12 sessions, based upon reaching criterion of 70 % symptom improvement as indicated on the PCL-5 from baseline, or an agreement between clinician and participant that maximum treatment response has been achieved. All sessions will be individual and weekly or twice weekly. Consistent with traditional Prolonged Exposure therapy, the first session will be spent in information gathering, treatment planning, and explaining the treatment rationale to the patient. Information gathering will consist of reviewing the history of PTSD and their military service and will include a brief psychosocial history, including review of prior treatment. Additionally, a rationale for VRET will be provided and breathing retraining will be introduced and practiced in session. Session 2 will review common reactions to trauma, provide a rationale for in vivo exposure, and include construction of the hierarchy for in vivo exposure. VR exposure begins in Session 3. The VRET sessions will last 90-minutes each and will consist of 15 minutes of checking in with the patient about their functioning and anxiety and homework completion since the last session, up to 45 minutes of exposure to their traumatic memories and the virtual stimuli, followed by processing and discussion about the material from the exposure, and ending with homework assignment. During VRET sessions patients will wear a head-mounted display with stereo earphones that will provide visual and audio cues consistent with Iraqi or Afghan military scenarios or other base-related scenarios or US scenarios as appropriate for the individual patient. The therapist simultaneously views on a video monitor all of the virtual environments in which patients are interacting and therefore is able to comment appropriately and is attempting to match stimuli that the patient is describing to the virtual stimuli, as much as possible. The therapist will make appropriate comments and encourage continued exposure until anxiety has habituated. During exposure, information will be gathered on the participant's anxiety level through the use of a 0-100 SUDs scale. As the number of sessions is limited, we are limiting exposure to the identified index trauma, and in some cases, a second traumatic event.

During this reporting period, 3 participants have completed the treatment phase and 3 participants are actively engaged in treatment. Those active in treatment all have completed more than 6 treatment sessions and intend to complete the study.

- **Subtask 6: Follow-up Assessments (Post-Treatment/3-month Follow-up).** During this reporting period, 3 participants completed the follow up phase, including both the post-treatment and 3-month follow up assessments.
- **Subtask 7: Conclude Study Enrollment.** Study enrollment is ongoing through August 12, 2016 (month 27).
- **Subtask 8: Conclude 6 Week Post Randomization Assessments.** 6 week post randomization assessments are ongoing through September 30, 2016 (month 28).
- **Subtask 9: Conclude Treatment and Post-Treatment Assessments.** Treatment and post-treatment assessments ongoing through December 26, 2016 (month 31).
- **Subtask 10: Conclude Follow Up Phase.** Follow up phase ongoing through 3/26/2017 (month 34).

○ **Specific Aim 2, Major Task 2 – Analyze Data and Report**

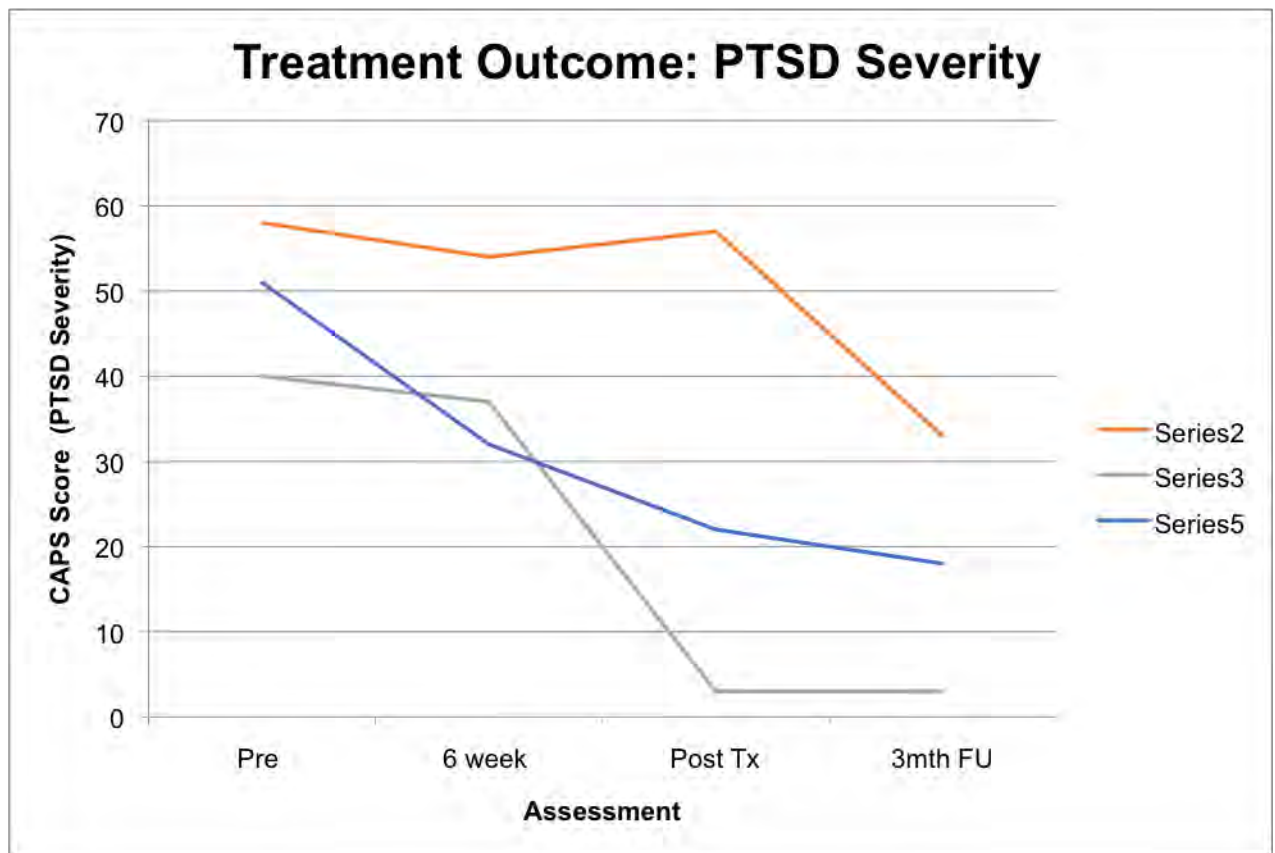
Subtasks 1, 2, and 4 are scheduled for months 35-36 and are not yet due.

- **Subtask 1: Data Analysis**
- **Subtask 2: Write up paper and results for publication**
- **Subtask #3: Submit Annual Report #2.** See data for first five participants below. All participants who engaged in treatment are considered study completers, as they completed the minimum of 6 sessions and all assessment through the follow up phase. From pre-assessment to 3-month follow up, all study completers demonstrated a reduction in PTSD symptom severity ranging from 25 to 37 points on the CAPS PTSD severity rating. Therefore, the use of VRET for the treatment of PTSD due to MST appears promising. Depressive symptoms, as measured by the PHQ-9, remained elevated for some but not all participants. This is not surprising given that the assaults for many of our patients occurred many years or decades prior to presenting for treatment and has caused widespread impairments that may not be ameliorated in a brief research protocol treatment. The primary challenge in study implementation has been related to recruitment rather than retention. CAPS scores for the 3 treatment completers from these first 5 patients randomized is represented in the graph following the table below.

ID	1	2	3	4	5
Treatment					
Condition	Waitlist	Treatment	Treatment	Waitlist	Treatment
Total # of Sessions	0	6	11	0	12
CAPS					

Pre	30	58	40	46	51
6 Week	--	54	37	--	32
Post-Tx	--	57	3	--	22
3 Month	--	33	3	--	18
PCL-5					
Pre	53	52	32	--	43
6 Week	--	53	30	--	--
Post-Tx	--	55	1	--	27
3 Month	--	56	2	--	21
PHQ-9					
Pre	--	18	12	--	24
6 Week	--	--	7	--	--
Post-Tx	--	19	3	--	19
3 Month	--	18	2	--	17
Comments	Participant was experiencing health problems at time of pre assessment and was awaiting surgery at time of 6-week post randomization assessment. Participant was unreachable after this time.	Participant and therapist agreed to discontinue treatment after 6 sessions due to patient's report of ongoing distress and difficulty engaging in treatment sessions. Participant left 6-week assessment early and did	Participant did well in treatment	Participant experienced high levels of distress during the pre-tx assessment and did not complete all self-report measures. Despite follow up efforts, she did not complete measures as discussed. At 6-week post	Participant left 6-week post randomization assessment early and did not complete all self-report measures. Participant's depressive symptoms remained high and overlapped with most endorsed PTSD symptoms at

		not complete all self-report measures.		randomization, patient indicated treatment was not an option for her at this time.	3-month follow up.
--	--	--	--	--	--------------------



- **Subtask #4: Submit Final Report to include efficacy rates with 95% confidence intervals.** The first 5 randomized subjects may be included in the final analyses. The report should include a complete feasibility report that addresses any future feasibility issues for any larger hypothesized/proposed RCT. [not due at this time]
- **What opportunities for training and professional development has the project provided?**
 - The clinical providers were trained in the operation of the software in January, 2015.
 - A Standard Operating Procedures clinical manual was created to train clinical staff in the conduct of the RCT.
 - Training and ongoing supervision in implementation of Virtual Reality Exposure Therapy.
 - Training and ongoing supervision in the conduct of clinical trials
 - Training and ongoing supervision in recruitment

- **How were the results disseminated to communities of interest?**
 - no results reported to date
- **What do you plan to do during the next reporting period to accomplish the goals?**
 - We will continue to recruit, assess and treat clinical research participants. Recruitment efforts continue to increase, including increased social media presence, on hold messaging for all Emory Healthcare offices, and increased outreach in military, veteran and community programs and organizations. Monthly ongoing contact with VA clinics. See additional efforts in Appendix 2.
 - We recently engaged a VA liaison to bridge communication between the Atlanta VAMC and Emory Healthcare Veterans Program. The liaison is assisting in recruitment efforts for the BraveMind MST study.
 - We have established goals to recruit 5 participants in the month of June, 6 in the month of July, and 4 in the month of August. We continue to evaluate and address recruitment progress and challenges each week and adjust efforts accordingly.

4. IMPACT:

- **What was the impact on the development of the principal discipline(s) of the project?**
 - Although it is still in an early state of clinical efficacy testing, we have received many requests to use the system by other clinical sites. This is the first immersive VR system to be created and to be undergoing clinical tests in the area of Military Sexual Trauma and if clinical results are positive, we expect wide dissemination of the system for both military and civilian treatment.
- **What was the impact on other disciplines?**
 - Nothing to Report.
- **What was the impact on technology transfer?**
 - Nothing to Report.
- **What was the impact on society beyond science and technology?**
 - Nothing to Report.

5. CHANGES/PROBLEMS:

- **Changes in approach and reasons for change**
 - The sample size has been reduced to 20 from the original 34 outlined in the SOW. Informed by current recruitment rates, changes reflect a more realistic estimate of the patients that can be recruited and treated in the NCE period and yield results that are publishable and can inform the field.
 - Established SOP and consent procedures with VA to increase study referrals and communication between providers (12/15/2016)
- **Actual or anticipated problems or delays and actions or plans to resolve them**
 - A one-year no-cost extension for the project was requested and granted. The revised end date is now May 26, 2017.
 - Recruitment for the MST study has been slower than anticipated despite vigorous outreach efforts. We were overly optimistic to propose a clinical trial to be completed within 18 month for PTSD resulting from MST using virtual reality (VR) exposure therapy. Recruitment challenges are part of any RCT, and particularly for PTSD. PTSD is a disorder of avoidance. There likely are thousands of sufferers within driving distance of our program that we could help that won't come in for treatment. There often is reluctance to report MST due to fear of reprisal, concern for military career, or shame. Recruitment always progresses more slowly than hoped until it reaches a tipping point and we reach our recruitment goals. We also face some challenges using VR for

this population, as the first reaction providers often have is to cringe until we explain that we are not presenting anything threatening in the VR. Unfortunately, but not unexpectedly, that is where we find ourselves with the BRAVEMIND MST trial now.

To address this problem, we continue to implement new outreach efforts and maintain those already in place. Our media and outreach efforts are increasing every month, with increasing numbers of assessments in response to these efforts, and include recruitment for MST survivors with PTSD of all eras (for this study). The face page of our website (<http://emoryhealthcare.org/veterans-program/index.html>) lists MST under “What we Treat” with a full page devoted to MST. Our VOCs attend events specifically for MST survivors to recruit. Our staff attended a program at Atlanta SHARP Program (Sexual Harassment/Assault Response & Prevention) in April 2016. The Atlanta VA has agreed to refer us MST survivors with PTSD for treatment within this study and our study coordinator has regular contact with their team, although referrals have not kept pace with their promises. We understand there are several MST studies at the Atlanta VA that are under recruiting and this may contribute to the low referral rate. Please see Appendix 4 for the letter from Dr. Patel, the leader of the Atlanta VA’s MST team, estimating that they will refer us approximately 20 patients/year for this study.

The MST study is under the umbrella of the Emory Healthcare Veterans Program. Emory’s Veterans Program offers post-9/11 veterans expert care that combines behavioral health care, including psychiatry and neurology, with rehabilitative medicine, wellness, and family support to help heal the invisible wounds of war. Emory’s Veterans Program takes a collaborative approach to healing, beginning with a comprehensive assessment conducted by top specialists in the fields of psychiatry, neurology, rehabilitative medicine, and wellness. Assessment results inform treatment planning and may include treatment for PTSD (Posttraumatic Stress Disorder), TBI (Traumatic Brain Injury), MST (Military Sexual Trauma), Anxiety, and Depression. Through a \$15.7 million grant from the Wounded Warrior Project, we can provide care at no cost to the veteran. We have over 20 staff on the Emory Veterans Program, many of whom are veterans, and include Veteran Outreach Coordinators (VOCs). We opened our doors for clinical care September 1, 2015 and have seen a steady increase in calls, assessments, and patients entering treatment. We have assessed 133 patients since September 1, 2015 and currently have 70 patients enrolled in our services.

We treated an MST survivor during our second 2-week intensive outpatient program in March who completed the program and announced that she will spread the word. It is this spreading of the word by veterans we have treated that will bring in more veterans, but this requires a bit of time to reach a tipping point for more active recruitment. We are close but not to that tipping point yet. Our patients who have completed have improved significantly, so we have every reason to believe it will be successful. It will just require more patience and time. We have listed below some of the MST specific recruitment activities.

- Unanticipated delays in study completion have occurred, as scheduling conflicts have occurred for some patients (e.g., health issues, death in family). These challenges have prolonged treatment initiation and or consistency between appointments. However, once engaged in treatment, all participants have followed through with completion or continuation.

- **Changes that had a significant impact on expenditures**
 - A one-year no-cost extension is being financed by funds remaining in the project.
- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**
 - Nothing to report.
- **Significant changes in use or care of vertebrate animals.**
 - Not applicable
- **Significant changes in use of biohazards and/or select agents**
 - Not applicable

6. PRODUCTS:

- **Publications, conference papers, and presentations**
 - **Journal publications.**
 - Rizzo, A.A., Cukor, J., Gerardi, M., Alley, S., Reist, C., Roy, M., Rothbaum, B.O., & Difede, J. (2015). Virtual Reality Exposure Therapy for PTSD due to Military Combat and Terrorist Attacks. *Journal of Contemporary Psychotherapy*. 45: Early Online. DOI 10.1007/s10879-015-9306-3
 - Rizzo, A.A., Hartholt, A., Grimani, M., Leeds, A. & Liewer, M. (2014). Virtual Reality Exposure Therapy for Treating Combat-Related PTSD. *IEEE Computer*. July, 2014. 31-37.
 - **Books or other non-periodical, one-time publications.**
 - Safir, M., Wallach, H. & Rizzo, A.A. (2014). *Future Directions in Post-Traumatic Stress Disorder: Prevention, Diagnosis, and Treatment*. Springer, Inc., NY, NY.
 - **Other publications, conference papers, and presentations.**
 - Rizzo, A.A., Roy, M., Hartholt, A., Costanzo, M., Highland, K.B., Jovanovic, T., Norrholm, S.D., Reist, C., Rothbaum, B.O., & Difede, J. (in press). Virtual Reality Applications for the Assessment and Treatment of PTSD. In Bowles, S. & Bartone, P.T. (eds.): *Military Psychology: Clinical and Organizational Practice*. Springer, Inc., NY, NY.
 - Roy, M.J., Rizzo, A.A., Difede, J. & Rothbaum, B.O. (in press). Virtual Reality Exposure Therapy. In: D. Benedek, and G. H. Wynn (Eds), *Complimentary and Alternative Approaches to the management of PTSD*. Oxford University Press.
 - Cukor, J., Gerardi, M., Alley, S., Reist, C., Roy, M., Rothbaum, B.O., Difede, J., & Rizzo, A.A. (2015). Virtual Reality Exposure Therapy for Combat-Related PTSD. In Ritchie, E.C. (Ed). *Post-Traumatic Stress Disorder and Related Diseases in Combat Veterans: A Clinical Casebook*. Springer Science: Arlington, VA.
 - Rizzo, A.A. (2016). The Next Big Things in Technology: A Preview. Milken Institute Global Conference. Los Angeles, CA. May 4, 2016.
 - Rizzo, A.A. (2016). Virtual Reality Goes to War: Advances in the Prevention of Posttraumatic Stress. Invited Keynote at NATO Summit on Resilience and PTSD. Bucharest, Romania. April 12, 2016.
 - Rizzo, A.A. (2016). Beyond Video Games: A Virtual Reality Revolution in Behavioral Health. Laval Virtual Reality International Conference. Laval, France. March 23, 2016.
 - Rizzo, A.A. (2016). Clinical VR: A Visit to the Future of Therapy Practice. Psychotherapy Networker Conference. Wash.D.C. March 18, 2016.
 - Rizzo, A.A. (2016). Clinical Virtual Reality Applications to Address the Wounds of War. Workshop presented at the Tampa VA. Tampa Fl. Jan. 19, 2016
 - Rizzo, A.A. (2015). Virtual Reality Goes to War: Advances in the Prevention, Assessment, and Treatment of Posttraumatic Stress. Invited presentation at ETH Zurich, Swiss Federal Institute for Technology. Dec. 8, 2015.

- Rizzo, A.A. Buckwalter, J. G, John, B., Roy, M., Difede, J., Rothbaum, B.O., Reist, C., Kwok, D., Leeds, A., Hartholt, A. (2015). Applications to Prevent, Assess and Treat PTSD. Presented at the 2015 International Society of Traumatic Stress Studies Convention. New Orleans. LA. Nov. 6, 2015.
- Rizzo, A.A. (2015). Virtual Reality Goes to War: Advances in the Prevention of Posttraumatic Stress. Invited Keynote at TNO: Netherlands Organisation for Applied Scientific Research. Eindhoven, Netherlands. November 3, 2015.
- Rizzo, A.A. (2015). Virtual Reality Goes to War and Beyond. Invited presentation at the Sydney Disrupt conference, Sydney Australia. September 24, 2015.
- Rizzo, A.A. (2015). Virtual Reality Goes to War. Invited presentation to MITRE/Red Sox, My Homebase Vets Support Program. Boston, MA. Sept. 8, 2015.
- Rizzo, A.A. (2015). Clinical Virtual Reality: A Brief Review of the Future. LA StoryCode Event. August 19, 2015.
- Rizzo, A.A. (2015). Virtual Reality Goes to War: Application for the Prevention, Assessment, and Treatment of PTSD. Invited presentation at Stanford University. July 13, 2015.
- Rizzo, A.A. (2015). Virtual Reality Goes to War: Innovations in Veteran Behavioral Healthcare. Invited presentation at the Los Angeles VA Medical Center. March 23, 2015.
- Rizzo, A.A. (2015). Clinical Virtual Reality: Application to Address the Wounds of War. Invited Colloquium Talk at the Binghamton University Psychology Dept. Binghamton, NY, March 16, 2015.
- Rizzo, A.A. (2015). Using Virtual Reality Simulation Technology to Support Military Mental Health and Resilience. West Point Human Performance Optimization Workshop. West Point, NY. Feb. 26, 2015.
- Rizzo, A.A. (2014). Virtual Reality goes to War: New Tools for preventing, assessing and treating PTSD. Invited presentation at the Naval Health Research Center – San Diego, CA. December 4, 2014.
- Rizzo, A.A. (2014). Virtual Reality goes to War: Simulation Tools for preventing, assessing and treating PTSD. Invited Talk at West Point, West Point, NY, November 21, 2014.
- Rizzo, A.A. (2014). Virtual Reality goes to War: The Future use of VR to Prevent and Treat PTS. Invited address to the Summa Healthcare Network. Akron, Ohio, November 13, 2014.
- Rizzo, A.A. (2014). Virtual Reality goes to War: Advances in the Assessment and Treatment of Posttraumatic Stress. Invited opening talk at the Web Summit. Dublin Ireland. November 4, 2014.
- Rizzo, A.A. (2014). Virtual Reality and Treatment of Posttraumatic Stress. Invited speaker at L.A. Library's Odyssey Project: The Warriors Return: From Surge to Suburbia With David Finkel and Skip Rizzo. Los Angeles, CA. October 27, 2014.
- Rizzo, A.A. (2014). Virtual Reality goes to War: Advances in the Assessment and Treatment of Posttraumatic Stress. The 2nd Annual Infinite Hero's Foundation Veterans Summit. Irvine, CA., September 15-16, 2014.
- Rizzo, A.A. (2014). Update and Expansion of the Virtual Iraq/Afghanistan PTSD Exposure Therapy System. The 122nd Annual Convention of the American Psychological Association. Washington D.C. August 7, 2011.
- **Website(s) or other Internet site(s)**
 - The ICT Website provides information on the overall research program. <http://ict.usc.edu/>
 - http://psychiatry.emory.edu/research/clinical_trials/ptsd/rothbaum_MilitarySexTrauma.html

- **Technologies or techniques**
 - This is the first immersive VR system to be created and to be undergoing clinical tests in the area of Military Sexual Trauma and if clinical results are positive, we expect wide dissemination of the system for both military and civilian treatment. At that point this content would be bundled with the standard BRAVEMIND software package. The current BRAVEMIND system is located at approximately 40 sites.
- **Inventions, patent applications, and/or licenses**
 - None.
- **Other Product**
 - None
- **Identify any other reportable outcomes that were developed under this project.**
 - None.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

- **What individuals have worked on the project?**

Name:	Dr. Albert Rizzo
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	skiprizzo (eRA Common)
Nearest person month worked:	1
Contribution to Project:	Dr. Rizzo has led the project and provided scenario and study design from a clinical psychology perspective.
Funding Support:	N/A

Name:	David Kwok
Project Role:	Special Project Manager
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1
Contribution to Project:	Mr. Kwok oversaw project operations, maintained the budget and the milestone schedule, and assisted with purchasing of equipment, travel, and supplies. He also supported the project team and consultants.
Funding Support:	N/A

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**
 - Nothing to Report.

- **What other organizations were involved as partners?**
 - **Organization Name:** Emory University
 - **Location of Organization:** Atlanta, GA
 - **Partner's contribution to the project:** IRB approval process, hire and train study personnel, recruit subjects, assess participants, treat participants, provide follow-up assessments, assist with data analysis, and assist with write-up of paper and results for publication.
 - **Financial support:** Subcontract
 - **In-kind support:** None
 - **Facilities:** RCT will take place at Emory University.
 - **Collaboration:** Emory University provided subject matter expertise in scenario design and is running the RCT.
 - **Personnel exchanges:** None

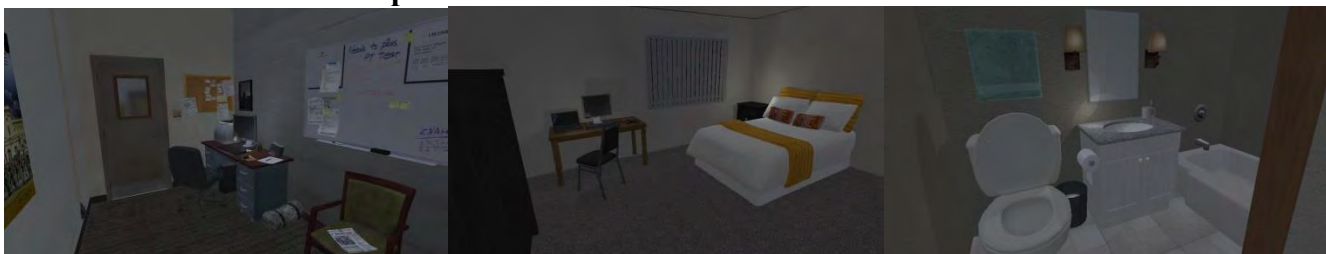
8. FIGURES

Figure 1. Bravemind Military Sexual Trauma PTSD Virtual Reality Exposure Therapy System Images

US Base and Town Outdoor Content:



US Base and Town Indoor Spaces:



Forward Operating Base Content:



Figure 2. Forward Operating Base Scenario Clinician Interface.



Figure 3. US Base and Town Scenario Clinician Interface.



Created by the USC Institute for Creative Technologies. PI: Skip Rizzo

9. REFERENCES

- DoD. (2012). Strategic Direction to the Joint Force on Sexual Assault Prevention and Response. Downloaded from: [http://www.jcs.mil/content/files/2012-05/050812085404_Joint_Strategic_Direction_on_Sexual_Assault_\(7_May_12\).pdf](http://www.jcs.mil/content/files/2012-05/050812085404_Joint_Strategic_Direction_on_Sexual_Assault_(7_May_12).pdf)
- Moffeit, M. and Herdy, A. (2004). Betrayal in the ranks. Denver Post, Downloaded from: http://extras.denverpost.com/justice/tdp_betrayal.pdf

10. SPECIAL REPORTING REQUIREMENTS:

- **COLLABORATIVE AWARDS:** None
- **QUAD CHARTS:** Revised Quad Chart below.

BRAVEMIND: Advancing the Virtual Iraq/Afghanistan PTSD Exposure for Military Sexual Trauma
 Proposal Log Number: 13210024
 Award Number W81XWH-14-C-0091



PI: Albert "Skip" Rizzo

Org: USC Institute for Creative Technologies

Award Amount: \$1,442,307

Study/Product Aim(s)

- **Specific Aim 1** - Extend and evolve the BRAVEMIND system to enhance the relevance, functionality, and usability of a VRET system for persons with PTSD due to MST
- **Specific Aim 2** - Test the feasibility/clinical efficacy of the system in a pilot randomized clinical trial.

Approach

Military Sexual Trauma (MST) has been recognized as a significant risk factor for the development of PTSD. This has become an issue of grave concern within the military, as reports of sexual violations and assaults have been on the rise over the last ten years, and have garnered significant popular media attention. The current project proposes to develop content for inclusion in the BRAVEMIND virtual reality exposure therapy (VRET) system that will provide new customizable options for persons who have experienced MST and to run a pilot RCT (in collaboration with Barbara Rothbaum at Emory University) with a sample of 20 persons diagnosed with PTSD due to MST.



Four VR contexts for conducting Virtual Reality Exposure for PTSD due to Military Sexual Trauma: (a) Civilian Bar Town; (b) Barracks Bathroom; (c) Bedroom; (d) Forward Operating Base.

Timeline and Cost

Activities	FY	14	15	16	17
• VRET System Development for use in RCT					
• Preparations for Conducting RCT					
• Conduct pilot RCT					
• Data Analysis and write up results for publication.					
Estimated Budget (\$K)		\$306	\$864	\$163	\$109

Updated: USC-ICT: June 20, 2016

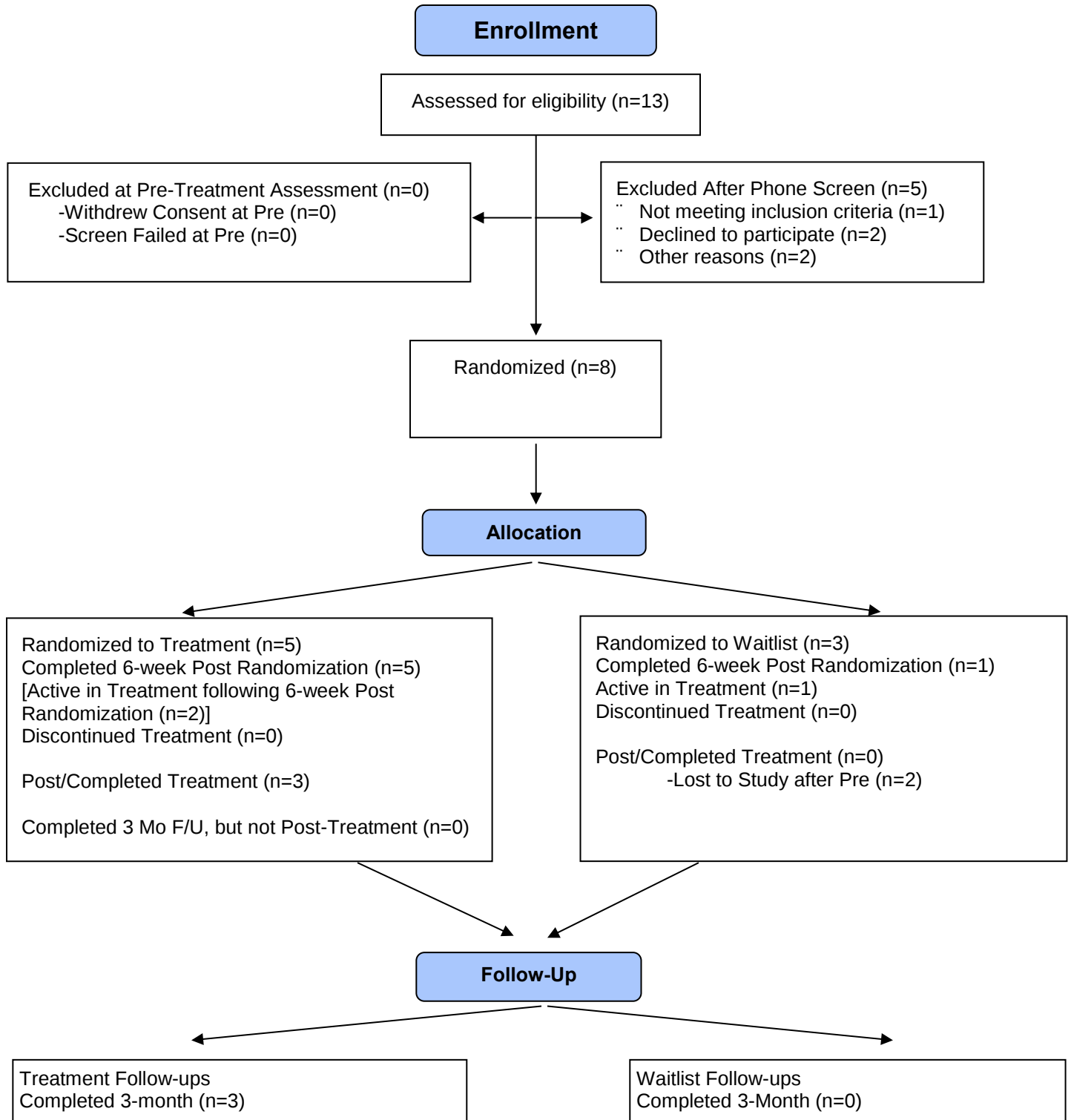
Goals/Milestones

- FY14 Goals** – VRET System Development and Preparation for RCT
- ☒ Build out VR content based on literature and clinical feedback
 - ☒ Preparations for RCT: Hire staff, Study set-up, IRB approval, etc.
- FY15 Goal** – Conduct pilot RCT
- ☒ Continue VRET System Development
 - ☒ Subject Recruitment, Assessment, Treatment, Follow-up.
- FY16 Goal** –
- ☒ Continue RCT.
- FY17 Goal** –
- ☐ Complete RCT, Compile/Analyze data, Write up results for publication and presentation.
- Comments/Challenges/Issues/Concerns**
- ☐ A one-year NCE was requested to allow additional time for recruitment and treatment of subjects for RCT.
 - ☐ Study size was reduced from n=34 to n=20.
- Budget Expenditure to Date**
 Projected Expenditure: \$1,442,307; Actual Expenditure: \$1,295,487

11. APPENDICES

Appendix 1. Consort Table

BRAVEMIND MST Consort Table



Appendix 2. Recruitment Efforts

Advertisements:

- \$3000/month social media
- \$2100/month search marketing (MST keywords)
 - Search “military sexual trauma treatment” on google, we are the first ad

Websites Links:

- http://www.psychiatry.emory.edu/research/clinical_trials/ptsd/rothbaum_MilitarySexTrauma.html
- http://emoryhealthcare.org/veterans-program/conditions/mst.html?gclid=CjwKEAiAmNW2BRDL4KqS3vmqgUESJABiiwDTuYEOPAeQ6kmQZ91lnKmGa0NpNfjrTK71_InAArsdGxoCRYPw_wcB

News Media:

- Fox 5 Atlanta (9/4/2015)
 - <http://www.fox5atlanta.com/health/fox-medical-team/16280151-story>
- 90.1 WABE Atlanta’s NPR Station (12/23/2015)
 - <http://news.wabe.org/post/emory-uses-virtual-reality-treat-military-sexual-trauma-survivors>

Community and Provider Outreach:

- Atlanta VAMC
 - Visit with PE/CPT team: 9/25/2015
 - Visit with MST team: Summer 2015, 10/29/2015
 - Established SOP and consent procedures with VA to increase study referrals and communication between providers (12/15/2016)
 - Ongoing monthly email communication regarding study progress with Trauma Recovery Program
 - Email outreach with Women’s Clinic: 12/15/15, 1/19/2016, 5/26/2016
 - Email outreach with General Mental Health Clinics in Atlanta Area: 4/25/2016, 5/25/2016
 - Phone and email communication with employee assistance programs serving Atlanta area (5/25/2016)
- WWP Veteran Dinner (2/22/2016)
- Kennesaw State Purple Heart Day (4/21/2016)
- Pat Tillman Run (4/23/2016)
- Emory University Veterans Day Events
 - EHVP booth at Emory Veterans Day event (flyers, brochures)
 - Emory campus: November 11, 2015

Veteran and Military Events:

- Atlanta Metropolitan College 335th Signal Command (Theater) HHC Holiday Party (12/5/2015)
- Military Family Resource Fair (Kennesaw, GA) (12/14/2015)
- Gwinnett Technical College Wellness Wednesdays for Veterans (1/20/2016)
- Atlanta Army’s SHARP Program (Sexual Harassment/Assault Response & Prevention):
 - Program leaders visited our program (2/1/2016)
 - Presented at SHARP for Sexual Harassment Awareness Day (4/13/16)
- DAV Career Fair at GA Dome (2/4/2016)
- Gwinnett Coalition for Health & Human Services (2/9/2016)
- WWP Veteran Dinner (2/22/2016)
- 3rd Annual Female Veterans and Active Duty Female Summit (2/29/2016)
- Ft Benning Women’s Summit March 2016

- Veteran Transition Training at Chattahoochee (3/24/2016)
- Monthly: Red Cross Veteran Outreach
- Monthly: Gwinnett Coalition for Health & Human Services

Flyers:

- Distributed at Veterans Day and Memorial Day parades, Pat Tillman Memorial Day 5k Run/Walk
- Lt. Dan Band concert at the Atlanta Aquarium (6/18/2016)
- Flyers posted throughout Atlanta metro and surrounding area businesses

Recruitment through Emory Healthcare's Veterans Program

- Ongoing: Eligible veterans with MST who enroll in Emory Healthcare Veterans Program are offered the MST study as a treatment option

Social Media

- Ongoing advertisement for study on Twitter and Facebook
- Ongoing advertisement through Emory Healthcare Veterans Program and Emory Healthcare Facebook page

Appendix 3. Patient Assessment

Pre-Treatment Assessment

Potential subjects will be asked to provide a copy of their DD214 to verify their military service record. Once a potential participant has met all screening inclusion and exclusion criteria and consented to participate, the CAPS will be administered to determine current PTSD status.

The Clinician Administered PTSD Scale (CAPS; Blake et al., 1990, 1995; updated for DSM V) is an interviewer-administered diagnostic instrument that measures PTSD. The CAPS provides a diagnostic measure of PTSD and a continuous measure of the severity, frequency, and intensity of the three symptom clusters (intrusion, avoidance, and arousal) and overall PTSD. If positive for current PTSD on the CAPS, and all other eligibility criteria are fulfilled, the rest of the pre-treatment measures will be administered.

Standardized Trauma Interview (STI; Foa & Rothbaum 1998): The STI was modified for this study and will be used to gather information on relevant aspects of the trauma and demographic information to be used in exploratory analyses to predict response to treatment.

The Demographics Questionnaire covers demographics, family composition, personal psychiatric history, and income and education information to obtain a *Hollingshead Four Factor Scale of Socioeconomic Status*.

The Childhood Trauma Questionnaire (CTQ; Bernstein, et al., 2003) is a self-report measure which assesses history of childhood trauma employing a Likert-scale format with 5 responses per item.

The Emory Treatment Resistance Interview for PTSD (E-TRIP) is a structured interview that assesses prior trials of pharmacology and psychotherapy PTSD treatments and provides a quantitative indicator of PTSD treatment resistance.

PTSD Checklist for DSM-5 (PCL-5): The PCL-5 is a 20-item self-report measure that assesses the 20 DSM 5 symptoms of PTSD. The PCL-5 has been shown to be equivalent to the well-validated PCL-S.

The MINI International Neuropsychiatric Interview (M.I.N.I.; Sheehan, D. V. et al., 1998) will be administered to screen axis 1 disorders and to establish co-morbid diagnosis.

The Beck Depression Inventory-II (BDI; Beck, Steer, & Brown, 1996) is a 21-item measure of cognitive and vegetative symptoms of depression is widely used in a variety of populations, including trauma victims and is sensitive to treatment effects on depression.

Deployment Risk and Resiliency Inventory (DRRI; King, King, & Vogt, 2003) is a self-report measure of pre-deployment, deployment and post-deployment experiences and trauma specific to the veteran population. The scale employs yes-no and Likert scale format responses ranging from 1-5.

The Quality of Life Inventory (QOLI; Frisch et al., 1992) The QOLI consists of 16 items selected to include all areas of life that have been empirically associated with life satisfaction. Respondents rate how important each of the 16 domains is to their overall satisfaction and happiness; they then rate how satisfied they are in the area. The total score reflects one's satisfaction in areas that one considers important to them. The QOLI's sensitivity to treatment-related change has been demonstrated with clinical samples of depressed, socially anxious/phobic, and chemically-dependent patients.

Clinical Global Impressions Scale, Severity of Illness (CGI-Severity; Guy & Bonato, 1970). This is a study personnel rated measure of severity of illness ranging from 0 (not assessed) to 7 (among the most extremely ill patients).

The Columbia–Suicide Severity Rating Scale. (Columbia; Posner et al., 2011). The Columbia–Suicide Severity Rating Scale was initially designed to assess suicidal ideation and behavior in clinical trials. It assesses occurrences, types, and severity of suicidal ideation and all types of behavior.

Neurobehavioral Symptom Inventory (NBI; Mererko et al., 2012). This is a 22 item measure designed to assess postconcussive symptoms following deployment-related mild traumatic brain injury among veterans.

Patient-Reported Outcomes Measurement Information System 8a and 4a -Satisfaction with Social Roles and Activities (PROMIS 4a, PROMIS8a, (Cella et al., 2010). The PROMIS item bank assesses satisfaction with performing one’s usual social roles and activities.

The Patient Health Questionnaire (PHQ-9; Kroenke, Spitzer, & Williams 2001). The PHQ-9 is assesses each of the 9 DSM-IV criteria for depression as “0” (not at all) to “3” (nearly everyday).

The Alcohol Use Disorders Identification Test—Consumption (AUDIT-C; Frank, Danielle et al. 2008). The AUDIT-C is a brief validated self-report screen for risky drinking and alcohol abuse and dependence (alcohol misuse). It has three questions that ask the frequency and amount of alcohol consumed.

Psychophysiological Patient Report: This is a brief self-report administered following each psychophysiological assessment. Using a Likert scale (Not at all to Very/Severe) participants rate the assessment VE as to 1. How closely the video matched their experience and 2. How distressing they found the video.

Intent to Attend (Leon et al., 2007) is a short, two question survey asking participants how likely they are to complete all of the study and how likely they are to attend the next session.

Update Interview. Assessment interview of treatment involvement, medications, and impact of trauma since the pre-assessment interview.

Oragene DNA Collection (optional). If the participant agrees, they will provide a 2mL sample of saliva for DNA analysis.

Psychophysiological Reactivity Assessment: Acoustic startle response, skin conductance, and heart rate will be assessed during a viewing of three VR scenes. The VR scenes will be presented through a head-mount display for 15 minutes. Psychophysiological data collection is described below.

SimSensei Rating Scale: This is a brief questionnaire assessing how comfortable and engaged the patient feels about interacting with a virtual human in the SimSensei video.

Measures at Therapy Session

State Trait Anxiety Inventory (STAI; Spielberger et al., 1970). The STAI-State is a 20-item self-report scale employing a Likert scale format with 4 responses per item (1-4). Ten of the STAI items measure feelings of stress and anxiety, while the remaining ten items measure feelings of relaxation.

Expectancy of Therapeutic Outcome Questionnaire (ETOQ) assesses how logical the treatment appears and the expectancy of success for the patient and for others. This measure is administered after session 1 only.

Clinical Global Impressions Scale, Severity of Illness (CGI-Severity; Guy & Bonato, 1970). This is a study personnel rated measure of severity of illness ranging from 0 (not assessed) to 7 (among the most extremely ill patients). This measure is administered after sessions 1–12.

Clinical Global Impression – Improvement (CGI-Improvement; Guy & Bonato, 1970). This is a study personnel rated measure of patient's improvement since start of study ranging from 1 (very much improved) to 7 (very much worse). This measure is administered after sessions 2-12.

Clinical Global Improvement Scale, Patient Report (CGI - Self Report; Guy & Bonato, 1970). This is a self-reported global measure of change in severity of symptoms, ranging from 1 (*very much improved*) to 4 (*unchanged*) to 7 (*very much worse*). This measure is administered after sessions 1-12.

PTSD Checklist for DSM-5 (PCL-5): The PCL-5 is a 20-item self-report measure that assesses the 20 DSM 5 symptoms of PTSD. The PCL-5 has been shown to be equivalent to the well-validated PCL-S.

Subjective Units of Discomfort (SUDs) will be gathered during each exposure session. Participants will be asked to rate their level of discomfort on a scale of 0 (no anxiety) to 100 (panic levels of anxiety) every 5 minutes during the VR exposure.

Intent to Attend (Leon et al., 2007) is a short, two question survey asking participants how likely they are to complete all of the study and how likely they are to attend the next session.

Psychophysiological Assessment:

Pre-treatment, 6 weeks post-randomization, and 3 month follow up. Psychophysiological data will be acquired at a sampling rate of 1kHz, amplified and digitized using the EMG module of the Biopac MP150 for Windows (Biopac Systems, Inc., Aero Camino, CA).

- The acoustic startle response (eye blink component) will be measured via electromyographic (EMG) recordings of the right *orbicularis oculi* muscle. Two 5 mm Ag/AgCl pre-gelled disposable electrodes will be positioned approximately 1 cm under the pupil and 1 cm below the lateral canthus. The startle probe (noise burst) will be a 108-dB (A) SPL, 40-ms burst of broadband noise with a near instantaneous rise time.
- Skin conductance level and skin conductance response will be acquired at a sampling rate of 1 kHz using the GSR module of the Biopac system. Two 5 mm Ag/AgCl disposable electrodes filled with isotonic paste will be attached to middle phalanges of the second and fourth finger of the non-dominant hand.
- Heart-rate and heart-rate variability (HRV) will be measured using the ECG module of the Biopac system at a sampling rate of 1 kHz. One 5mm Ag/AgCl electrode will be placed on the chest above the right clavicle; another electrode will be placed on the chest under the left side of the ribcage.
- Four saliva samples will be obtained from participants for measuring cortisol.

SimSensei sessions:

Participants will be interviewed by a virtual human for approximately 15 minutes. Psychophysiological measures will be collected during the presentation of the SimSensei using Biopac MP150 System EMG, GSR and ECG modules as described above. These measures are non-invasive and will provide minimal interference with the SimSensei presentation, yet will provide objective measures

of both arousal and valence. EMG of the corrugator muscle will provide an index of negative facial expressions, while skin conductance will measure arousal and sympathetic nervous system activity. The ECG data will provide measures of heart rate (HR) and heart rate variability (HRV) as an index of vagal control of cardiovascular function. All of these measures are associated with emotion regulation and have been associated with PTSD symptoms.

	Study Timepoint				
	Pre	6 Weeks Post Randomization	Therapy	Post Treatment	3 Month Follow Up
CAPS	x	x		x	x
STI			x		
Update Interview		x		x	x
Demographics	x				
CTQ	x				
E-TRIP	x				
PCL-5	x	x	x	x	x
MINI	x				
BDI	x	x		x	x
STAI	x	x		x	x
DRRI	x				
QOLI	x	x		x	x
ITA	x	x	x	x	
Columbia	x				
NBI	x	x			
PROMIS	x	x			
PHQ-9	x	x			
Audit-C	x	x			
DNA	x				
ETOQ	x				
CGI-Severity	x	x	x	x	x
CGI-Clinician		x	x	x	x
CGI- Patient		x	x	x	x
SUDS			x		
Psychophys	x	x			x
Psychophys- SR	x	x			x
SimSensei	x	x			x
SimSensei SR	x	x			x

Appendix 4. VA MST Letter

March 29, 2016

Barbara O. Rothbaum, Ph.D., ABPP
Professor in Psychiatry
Director, Emory Healthcare Veterans Program and Trauma and Anxiety Recovery Program
Paul A. Janssen Chair in Neuropsychopharmacology
Associate Vice Chair of Clinical Research
Emory University School of Medicine
12 Executive Park Drive, 3rd Floor
Atlanta, GA 30329
(404) 712-8866
(404) 727-3700 fax
brothba@emory.edu

RE: Military Sexual Trauma treatment study at Emory University

Dear Barbara:

I am happy to have you and your team at Emory as a resource for our patients. I serve as the team lead for the Military Sexual Trauma/Dialectical Behavior Therapy team at the Atlanta VA. We currently treat approximately 250 veterans who have experienced military sexual trauma (MST) per year. Of these, approximately 90% are suffering from PTSD and of these, approximately 70% would be appropriate for trauma focused therapy. Therefore, we could estimate that we would refer you approximately 20 patients/year for treatment through your MST study.

Thank you for our ongoing collaborations in treating our veterans and training our providers.

Sincerely,



Meghna Patel, PhD, ABPP
Clinical Psychologist
Team Leader of Military Sexual Trauma (MST)/Dialectical Behavior Therapy (DBT) Team
Atlanta VA Medical Center
Assistant Professor, Dept. of Psychiatry & Behavioral Sciences
Emory University

12. JOURNAL PUBLICATIONS ATTACHED BELOW



Virtual Reality Exposure Therapy for Combat-Related Posttraumatic Stress Disorder

Albert Rizzo, Arno Hartholt, Mario Grimani,
Andrew Leeds, and Matt Liewer,
USC Institute for Creative Technologies

Virtual reality (VR) technology is rapidly evolving to support prolonged exposure (PE) therapy, a proven treatment for combat-related posttraumatic stress disorder. Building on the successful 2007 Virtual Iraq/Afghanistan VRET system, a team of behavioral scientists, software engineers, and virtual artists has created Bravemind, a flexible VR system that offers significantly enhanced PE treatment possibilities.

In the early 1990s, behavioral healthcare professionals began to envision using virtual reality (VR) simulations for clinical intervention, particularly as a means to deliver exposure therapy in treating specific phobias, but were limited by the rudimentary systems then available. Over just two decades, dramatic advances in underlying VR technologies—computational speed, 3D graphics rendering, audiovisual and haptic displays, user interfaces and tracking devices, voice recognition capabilities, intelligent agents, and authoring software—have greatly expanded treatment opportunities. Driven in part by the digital gaming and entertainment industries, these advances have led to the emergence of sophisticated yet

cost-effective VR systems that run on commodity-level personal computers and provide interactive, immersive experiences and scenarios that open many doors for psychological research and behavioral health applications in the 21st century.

More specifically, the spike over the last 10 years in the number of US service personnel returning from battlefields in Afghanistan and Iraq with traumatic injuries has driven an intense focus on marshaling computer technology to enhance, expand, and extend clinical care methodologies. The US Department of Defense (DoD) and Department of Veterans Affairs (VA) have responded to this urgency with substantial funding to foster innovations in behavioral healthcare technology for purposes of treatment as well as to reduce “barriers to care.”¹ This support is evident most dramatically in the resources now devoted to research on traumatic brain injury, posttraumatic stress disorder (PTSD), and comorbid health conditions, with a special focus on clinical VR technology that can help assess, treat, and optimally prevent PTSD.

COMBAT-RELATED PTSD

The physical, emotional, cognitive, and psychological demands military personnel face in combat create enormous stress for even the best prepared. The particular challenges characterizing the ground wars in Iraq and Afghanistan have produced significant numbers of active service members and veterans at risk for developing PTSD and other psychosocial and behavioral health conditions.



As of December 2012, the DoD's Defense Medical Surveillance System database reported 131,341 active-duty service members diagnosed with PTSD.² In a meta-analysis across studies since 2001, 13.2 percent of operational infantry units met overall criteria for PTSD, with PTSD incidence rising dramatically from 25 to 30 percent in those units experiencing the highest levels of direct combat.³ During this same period, the prevalence of PTSD among discharged veterans receiving treatment at VA clinics has been reported at 29 percent.² These findings make a compelling case for a continued focus on developing and enhancing diverse evidence-based treatment options for combat-related PTSD.

Anticipating a need for behavioral therapies appropriate to serve Gulf War combatants, the USC Institute for Creative Technologies in 2004 developed a prototype Virtual Iraq VRET system for initial user feasibility testing.

PROLONGED EXPOSURE THERAPY

Among the many approaches used to treat people diagnosed with PTSD, prolonged exposure (PE) therapy⁴ has significant scientific evidence supporting its therapeutic efficacy.¹ Such treatment typically involves a patient's graded and repeated imaginal reliving and narrative recounting of the traumatic event within a therapeutic setting.

Although PE therapy relies primarily on sensory memory and imagination, the exposure process is not passive. Patients are asked to recount their trauma verbally in the first person with their eyes closed, as if it were happening again, with as much attention to sensory detail as they can. Based on his or her clinical judgment, the therapist might prompt the patient with questions about the experience or provide encouraging remarks to facilitate recounting the trauma narrative. This approach provides a low-threat context in which a patient can confront and therapeutically process trauma-relevant memories and emotions as well as de-condition the cycle associated with the disorder via a process known as habituation/extinction.

VR AS A PE THERAPY TOOL

While PE therapy's efficacy has been established in multiple studies with diverse trauma populations, many patients are unwilling or unable to effectively visualize the traumatic event, an occurrence that may result in treatment failure. In fact, avoiding reminders of the trauma is a cardinal symptom of PTSD. To address this problem, researchers have explored VR as a tool for delivering exposure therapy (such as VRET). The rationale for this is

clear and compelling. Used as part of an evidence-based PE protocol, VR can provide a way to immerse users in simulations of the traumatic experience. Moreover, the clinician can precisely control the scene's emotional intensity and customize the pace and relevance of the exposure for the individual patient.

VRET effectively circumvents the natural tendency to avoid traumatic memories by directly delivering multi-sensory and contextual cues that help the patient retrieve, confront, and process these experiences. VR also provides the therapist with an objective and consistent format for documenting the sensory stimuli to which a patient is exposed and the resulting reactions; this is not possible when the therapy operates exclusively within the unseen world of the patient's imagination.

Success using VRET for patients with non-PTSD anxiety disorders such as specific phobias has been documented in multiple independent literature meta-analyses, most recently by David Opris and his colleagues.⁵ In addition, multiple studies report positive outcomes using VRET for patients diagnosed with PTSD unrelated to combat in Iraq and Afghanistan, who were unresponsive to a previous course of imaginal-only PE treatment.^{6,7}

Using VR as a delivery system for PE therapy in cases of combat-related PTSD could also help break down barriers to care by improving treatment appeal, acceptability, and adherence among those most at need.⁸ Although perhaps reluctant to seek out traditional talk therapies, the current generation of military service members and veterans, most of whom grew up with digital gaming technology, might perceive less stigma attached to VR therapy, and so be more attracted to and comfortable with this treatment option.

THE VIRTUAL IRAQ/AFGHANISTAN VRET SYSTEM

Anticipating a need for behavioral therapies appropriate to serve Gulf War combatants, the USC Institute for Creative Technologies in 2004 developed a prototype Virtual Iraq VRET system for initial user feasibility testing. Supported by a clear theoretical rationale and the current literature, this prototype was followed by a full Virtual Iraq/Afghanistan VRET system, developed between 2005 and 2007 with funding from the US Office of Naval Research.

To maximize its clinical relevance, the system combined theory-driven design with iterative user-centered feedback cycles involving military personnel who served in Iraq and Afghanistan. Pre-clinical testing was conducted at Fort Lewis, Washington, and with a US Army Combat and Operational Stress Control unit stationed in Iraq.⁸ This feedback from service members not diagnosed with PTSD, and from later clinical users, has provided essential input for the system design's ongoing evolution in content and usability.

The 2007 system consists of four customizable scenarios representing relevant contexts for treating combat-related PTSD: three Humvee driving scenarios—set respectively in Iraq, Afghanistan, and the US—and a navigable dismounted patrol scenario set in a 24-block Middle Eastern city. General driving navigation uses a standard Logitech F310 game pad; for interactions in the dismounted foot patrol, an Ion GoPad thumb mouse affixed to a user-held mock M4 carbine rifle supports travel. The simulation's real-time 3D scenes use Emergent's Gamebryo as the rendering engine, and visual stimuli are presented within an orientation-tracked Emagin Z-800 head-mounted display (HMD). (We developed the system with an HMD component based on the idea that immersing users more fully in these controlled stimulus environment, enhances the emotional engagement required for therapeutic exposure; we should note, however, that no studies have compared the relative effectiveness for PTSD patients of delivering simulation content via a less immersive large-screen display.)

Directional 3D audio, vibrotactile, and olfactory stimuli relevant to the scene can also be delivered to users, controlled and modified in real time by the clinician via a separate *Wizard of Oz*-type interface. A key feature, this interface lets clinicians customize each therapy experience to the patient's individual needs, placing users in VR scenario locations that resemble the settings where traumatic events occurred. The clinician can modify ambient lighting and sound conditions to match the patient's description of the experience, and then gradually introduce and control real-time trigger stimuli—gunfire, explosions, insurgent attacks, and the like. This clinician control, customized to an individual's past experience and overall treatment progress, fosters the anxiety modulation necessary for the patient's therapeutic habituation to and emotional processing of the past traumatic experiences.

The 2007 Virtual Iraq/Afghanistan VRET system has so far been disseminated to over 60 early-adopter sites including VA medical centers and military, university, and private clinics for use as a PE therapy tool and to collect further data regarding outcome effectiveness.

VRET TREATMENT PROCEDURE

VRET treatment follows the standard evidence-based protocol for imaginal-only PE therapy⁴ and consists of weekly 90- to 120-minute individualized, patient-driven sessions over 10 weeks.

During the first session, the clinician generally aims to develop a working therapeutic alliance with the patient as is standard for most clinical approaches. The clinician might attempt to identify and discuss some of the patient's traumatic experiences, provide psychoeducation on trauma and PTSD, and present instruction on a deep breathing technique for general stress management.

The second session follows up on topics from the first, as needed, and then focuses on providing the patient with a clear explanation and rationale for PE. In some cases, the patient is engaged in light practice with imaginal exposure that focuses on the less provocative elements of his or her traumatic experience.

The third session introduces the rationale for VRET. The patient is encouraged to explore a personally relevant scenario within the Virtual Iraq/Afghanistan environment for approximately 25 minutes, without recounting any trauma narrative and with no provocative trigger stimuli. This enables the participant to learn how to navigate the system, and functions as a bridge from imaginal exposure alone to imaginal exposure combined with VRET.

During the fourth through tenth sessions, full VRET therapy is conducted: the participant engages in a Virtual Iraq/Afghanistan environment while verbally recounting his or her trauma narrative. The goal during these active exposure sessions is for patients to experience moderate yet manageable anxiety levels while, with the therapist's encouragement, they activate, confront, and process difficult trauma memories and emotions they likely avoid elsewhere—and often have never discussed with anyone before. When this process is conducted in a safe, supportive clinical setting at a pace the patient can handle, the patient's anxiety typically habituates by way of a learning process known as “extinction.” As this occurs, the patient is encouraged to confront additional, more provocative elements within the VR scenarios, which the therapist can introduce in real time via the clinician control panel.

Treatment throughout also includes homework; for example, during the week following a session the therapist might have the participant listen to an audiotope of his or her trauma narrative from that session, providing further exposure to help the patient continue processing the trauma outside the treatment setting. Assessing status over the course of treatment typically involves a combination of patient self-report symptom questionnaires and structured interviews with the therapist; active psychophysiological reactivity tests are sometimes used as well.

A more detailed description of this system, general PTSD assessment procedures, and the methodology for a standard VRET clinical protocol is provided elsewhere.⁹

RESEARCH OUTCOMES

Initial clinical tests of the Virtual Iraq/Afghanistan VRET system conducted with active-duty service members produced encouraging results. Three early case report studies documented the system's feasibility and safety, and showed positive clinical outcomes.^{10–12} Two later open clinical trials with active-duty service members reported similar outcomes.^{13,14}

In one trial involving an average of 11 sessions with 20 active-duty service members (19 male and 1 female, with

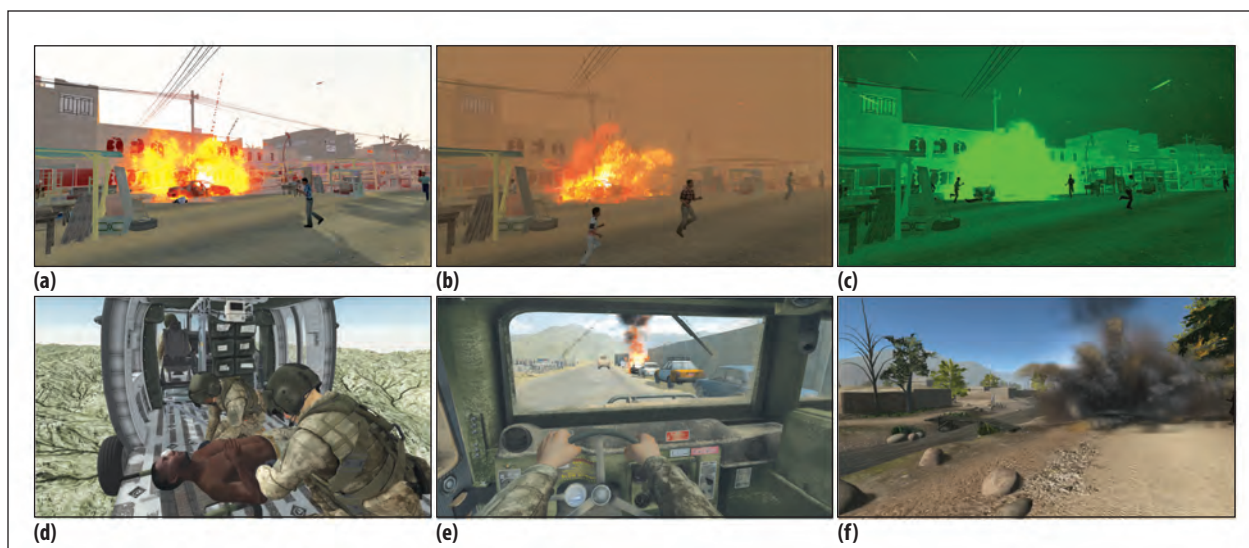


Figure 1. Images from 4 of the 14 scenario settings available in Bravemind, a virtual reality system for delivering prolonged exposure therapy (VRET) in cases of patients with combat-related posttraumatic stress disorder (PTSD). (a, b, c) A vehicle-borne improvised explosive device (IED) in an Iraq city showing three customizable views: a daytime setting, an evening setting with a sandstorm, and a perspective with night-vision goggles. (d) A helicopter extraction scenario. (e) A checkpoint explosion. (f) An IED in an Afghan village.

a mean age of 28) who completed treatment, results using the diagnostic PTSD checklist–military version (PCL-M) showed scores decreasing pre- and posttreatment in a statistically and clinically meaningful fashion from 54.4 (standard deviation: 9.7) to 35.6 (standard deviation: 17.4).¹³ Paired pre- and post-*t*-test analysis showed these differences to be significant ($t = 5.99$, $df = 19$, $p < .001$), with 16 of the 20 completers no longer meeting the PCL-M criteria for PTSD after treatment and an average 50 percent decrease in symptoms among all completers. Beck Anxiety Inventory scores significantly decreased (33 percent), and mean Patient Health Questionnaire depression scores decreased even more (49 percent). Treatment gains were maintained at a posttreatment follow-up three months later, and anecdotal patient reports suggested that participants saw improvements in everyday life functioning.

Another open clinical trial conducted with 24 active-duty soldiers produced significant pre- and posttreatment reductions in PCL-M scores and a large treatment effect size (Cohen's $d = 1.17$).¹⁴ After an average of seven sessions, 45 percent of those treated no longer screened positive for PTSD, and 62 percent had reliably improved. In a small preliminary quasi-randomized controlled trial,¹⁵ 7 of 10 participants with PTSD showed a 30 percent or greater improvement with VR, while only 1 of 9 participants in a usual PE treatment group showed similar improvement.

Five randomized clinical trials (RCTs) are currently ongoing using the Virtual Iraq/Afghanistan VRET system with both current active-service member and veteran populations. Two of these focus on comparing treatment efficacy

between VRET and imaginal PE. Another is comparing VRET to VRET along with a supplemental care approach. Two more RCTs are investigating the additive value of supplementing VRET and PE with a cognitive enhancer called D-Cycloserine (DCS). DCS, an N-methyl-D-aspartate partial agonist, has been shown to facilitate extinction learning in laboratory animals when infused bilaterally within the amygdala (the “fight or flight” conditioning center in the brain) prior to extinction training. Recent evidence of both VRET and DCS effectiveness has been reported by JoAnne Difede and her colleagues.¹⁶ Significant funding for these RCTs underscores the interest the DoD and VA have in exploring innovative VRET approaches.

BRAVEMIND

Based on these encouraging clinical outcomes using VRET to treat combat-related PTSD and an urgent need to provide the best care for active-duty and veteran service members who increasingly report PTSD symptoms, in 2011 the US Army funded development of an updated and expanded Virtual Iraq/Afghanistan system called Bravemind. Among this effort's primary goals are to increase the original system's VR scenario content diversity and improve stimulus delivery customization to better address the needs of clinical users reporting a wide range of traumatic experiences. Bravemind draws on the large body of patient and clinician feedback from those who used the previous 2007 VRET system.

The system has been rebuilt from the ground up using the state-of-the-art Unity game engine. The four original

2007 environments have been completely redesigned, and 10 additional scenario settings have been added, including separate Iraq and Afghanistan cities with both slum and residential areas, a rural Afghan village, an industrial zone, a roadway checkpoint, a mountainous forward operations base, and a simulated Bagram Airfield, the largest US military base in Afghanistan. Figure 1 shows some images from these new scenario settings.

New system features include the choice of Humvees, MRAP (mine-resistant ambush-protected) vehicles, or helicopters; vehicle-to-foot patrol transitioning; expanded weather and time-of-day controls; customizable sound trigger profiles; and an updated clinician interface designed to improve usability based on professional feedback. The Unity engine's higher-fidelity graphic art and animation have enhanced the stimulus content's realism and credibility, and present an experience uniquely different from commercial videogames. The system has also been designed to use off-the-shelf components—standard laptop/PC, head-mounted display, and tracking/interface technology, for example—aimed at reducing costs to well under \$5,000.

The Bravemind system, shown in Figure 2, is now being distributed to clinical sites and provides a flexible software architecture that can support efficiently adding new content to expand and diversify functionality as novel clinical needs are specified.

BRAVEMIND SYSTEM EVOLUTION

Bravemind was designed specifically to support customizable options for a range of relevant traumatic experiences with new functionalities. Currently, for example, the system is evolving to address the unique therapeutic needs of combat medics and hospital corpsmen as well as active-duty service members and veterans with PTSD who have also experienced military sexual trauma. In addition, the software has been reconfigured to provide a VR tool currently under testing for cognitive assessment purposes and to provide psychological resilience training prior to combat deployment.¹⁷

We consider these first two emerging applications here.



Figure 2. Sample Bravemind system components. (a) A clinician interface for modifying VR settings in real time to match user experiences. (b) VR head-mounted display and traditional gamepad used by a seated participant in a driving scenario. (c) Rifle-mounted mini-gamepad used in a walking scenario.

VRET for combat medics and corpsmen

Our prior clinical work and recent government reports indicate a growing need to address PTSD in Navy and Marine medics and Army and Air Force corpsmen, those service members whose primary role is providing medical treatment to the wounded.

Combat medics and corpsmen represent a unique population among deployed military ranks, serving double duty both professionally and psychologically. In addition to bearing full soldiering responsibilities, medics must also calmly and efficiently care for the devastating injuries of modern warfare, and are more exposed than other soldiers to seriously wounded and dying comrades. Unlike hospital doctors or nurses, who rarely know their patients personally, medics face the added pressure of camaraderie with the patients they are trying to keep alive. And when one patient dies, medics often experience self-doubt—an emotion they must hide, or risk losing their platoon's confidence.

Treating these men and women requires specialized VR content relevant to their experiences, providing emotionally challenging situations fundamentally different from what has proven effective with other service members. For this reason, Bravemind scenarios have been tailored with significant new graphic art, motion-capture animation, and airborne vehicle integration, as well as a library of virtual human content to emulate the range of wounds, burns, and other injuries and manifest realistic injury behaviors common to combat environments. In addition, we have developed helicopter insertion and extraction scenarios and a Bagram Air Force Base hospital setting for medic and corpsmen “first receivers.”



This system is currently nearing completion and will be available for clinical use in mid-2014.

VRET for military sexual trauma

In addition to witnessing death and experiencing life-threatening injury, sexual violation can be a trigger for PTSD. Service members who suffer actual or threatened sexual violation or assault from within the ranks or in a military context may exhibit a psychological condition known as military sexual trauma (MST). MST places soldiers already undergoing the trauma inherent in combat at especially high risk for developing PTSD.

Ultimately, we believe clinical VRET has potential civilian applications well beyond treating military service personnel for PTSD. In fact, over the last century, war has provided an impetus for many advances in clinical care.

A 2012 report issued by the Joint Chiefs of Staff, together with the DoD's Sexual Assault Prevention and Response Program,¹⁸ specifies the need for improvements in "advocacy coordination, medical services, legal support, and [behavioral health] counseling for the victim" of military sexual assault. This issue poses grave concern in the military as reports of sexual violation and assault have risen over the last decade and also garnered significant media and congressional attention. Overall, 6.1 percent of female and 1.2 percent of male active-duty service members indicated they experienced unwanted sexual contact in 2012. For women, this rate is statistically significantly higher than in 2010, when it was reported at 4.4 percent.¹⁸

A bleaker picture emerges when we consider reports from postdischarge veteran surveys. In a nationwide randomly selected sample of women seeking care through VA medical centers, approximately one in four reported experiencing sexual trauma while on active duty.¹⁹ Prevalence rates of MST in women were 20 to 25 percent for sexual assault and 24 to 60 percent for sexual harassment. Thus, even though the DoD is mobilizing to reduce MST incidence with new education and prevention programs, a significant effort is also required to develop and disseminate effective treatments to address the needs of those already experiencing PTSD due to MST. While both men and women can experience MST, the growing number of women transitioning to a full combat role underscores this work's urgency.

Content currently in development for the Bravemind system will provide customizable options to conduct VRET with persons who have experienced MST. This

novel component involves embedding within existing Bravemind scenarios new settings such as barracks, tents, latrines, work quarters, and other contexts that MST victims have reported as locations where sexual assault occurred. The system will not attempt to re-create actual sexual assaults; rather it will set up contexts surrounding such assaults that can support users in therapeutic confrontation and processing of MST memories in accordance with the protocol established to implement PE using the simulations.⁹

Following projected completion of the new content in summer 2014, we plan a pilot RCT with 34 male and female participants. Nothing like this has been attempted previously with immersive VRET, and the challenges for such unique and sensitive content are significant.

Ultimately, we believe clinical VRET has potential civilian applications well beyond treating military service personnel for PTSD. In fact, over the last century, war has provided an impetus for many advances in clinical care. During World War I, the Army Alpha and Army Beta tests emerged as systems to assess and classify cognitive ability; these served as prototypes for later widely used civilian psychometric tests. Clinical psychology as a treatment-oriented profession was born from the need to provide care to the many veterans returning from World War II with "shell shock" or "battle fatigue." The Vietnam War drove recognition of PTSD as a definable and treatable clinical disorder outside the context of war alone.

Similarly, the US military's current support for research and development advancing clinical systems to treat PTSD that leverage new interactive and immersive technologies such as VR could have a lasting influence on civilian healthcare long after the last Afghanistan war veteran has returned home. ■

References

1. Inst. Medicine, *Treatment for Posttraumatic Stress Disorder in Military and Veteran Populations: Initial Assessment*, Nat'l Academies Press, 2012.
2. H. Fischer, *United States Military Casualty Statistics: Operation New Dawn, Operation Iraqi Freedom, and Operation Enduring Freedom*, Congressional Research Service, 5 Feb. 2013; www.fas.org/sgp/crs/natsec/RS22452.pdf.
3. B.C. Kok et al., "Posttraumatic Stress Disorder Associated with Combat Service in Iraq or Afghanistan: Reconciling Prevalence Difference between Studies," *J. Nervous and Mental Disease*, vol. 200, no. 5, 2012, pp. 444–450.
4. E.B. Foa, E. Hembree, and B.O. Rothbaum, *Prolonged Exposure Therapy for PTSD: Emotional Processing of*

- Traumatic Experiences, Therapist Guide*, Oxford Univ. Press, 2007.
5. D. Opris et al., "Virtual Reality Exposure Therapy in Anxiety Disorders: A Quantitative Meta-Analysis," *Depression and Anxiety*, vol. 29, no. 2, 2012, pp. 85–93.
 6. J. Difede et al., "Virtual Reality Exposure Therapy for the Treatment of Posttraumatic Stress Disorder following September 11, 2001," *J. Clinical Psychiatry*, vol. 68, no. 11, 2007, pp. 1639–1647.
 7. B.O. Rothbaum et al., "Virtual Reality Exposure Therapy for Vietnam Veterans with Posttraumatic Stress Disorder," *J. Clinical Psychiatry*, vol. 62, no. 8, 2001, pp. 617–622.
 8. G.M. Reger et al., "Soldier Evaluation of the Virtual Reality Iraq," *Telemedicine and e-Health*, vol. 15, no. 1, 2009, pp. 100–103.
 9. B.O. Rothbaum, J. Difede, and A. Rizzo, *Therapist Treatment Manual for Virtual Reality Exposure Therapy: Posttraumatic Stress Disorder in Iraq Combat Veterans*, Virtually Better, Inc., 2008.
 10. M. Gerardi et al., "Virtual Reality Exposure Therapy Using a Virtual Iraq: Case Report," *J. Traumatic Stress*, vol. 21, no. 2, 2008, pp. 209–213.
 11. G. Reger and G. Gahm, "Virtual Reality Exposure Therapy for Active Duty Soldiers," *J. Clinical Psychology*, vol. 64, no. 8, 2008, pp. 940–946.
 12. A. Rizzo et al., "Initial Case Reports from a VR Exposure Therapy Application for Combat-Related Posttraumatic Stress Disorder," *Proc. 2007 IEEE Int'l Conf. Virtual Rehabilitation (ICVR)*, 2007, pp. 124–130.
 13. A. Rizzo et al., "Virtual Iraq/Afghanistan: Development and Early Evaluation of a Virtual Reality Exposure Therapy System for Combat-Related PTSD," *Annals NY Academy of Sciences*, vol. 1208, 2012, pp. 114–125.
 14. G.M. Reger et al., "Effectiveness of Virtual Reality Exposure Therapy for Active Duty Soldiers in a Military Mental Health Clinic," *J. Traumatic Stress*, vol. 24, no. 1, 2011, pp. 93–96.
 15. R.N. McLay et al., "A Randomized, Controlled Trial of Virtual Reality Exposure Therapy for Posttraumatic Stress Disorder in Active Duty Service Members with Combat-related Posttraumatic Stress Disorder," *Cyberpsychology, Behavior, and Social Networking*, vol. 14, no. 4, 2011, pp. 223–229.
 16. J. Difede et al., "D-Cycloserine Augmentation of Exposure Therapy for Posttraumatic Stress Disorder: A Pilot Randomized Clinical Trial," *Neuropsychopharmacology*, 12 Nov. 2013; doi:10.1038/npp.2013.317.
 17. A. Rizzo et al., "Virtual Reality Applications to Address the Wounds of War," *Psychiatric Annals*, vol. 43, no. 3, 2013, pp. 123–138.
 18. US Dept. of Defense, *Strategic Direction to the Joint Force on Sexual Assault Prevention and Response*, 7 May 2012; www.sapr.mil/public/docs/directives/Strategic_Direction_on_SAPR.pdf.
 19. K.M. Skinner et al., "The Prevalence of Military Sexual Assault among Female Veterans Administration Outpatients," *J. Interpersonal Violence*, vol. 15, no. 3, 2000, pp. 291–310.
- Albert Rizzo** is a clinical psychologist and director of Medical Virtual Reality at the USC Institute for Creative Technologies and is also a research professor in the USC Department of Psychiatry and the USC Davis School of Gerontology. He conducts research on VR systems for clinical assessment, treatment, and rehabilitation across the psychological, cognitive, and motor functioning domains, focusing on PTSD, autism, ADHD, Alzheimer's disease, and stroke. Rizzo received a PhD in clinical psychology from the State University of New York at Binghamton. He is a member of IEEE and the American Psychological Association. Contact him at rizzo@ict.usc.edu.
- Arno Hartholt** is project leader of the Integrated Virtual Humans group and the Art Group at the USC Institute for Creative Technologies. His research and professional software engineering work focus on task modeling, natural language processing, and knowledge representation in virtual humans. Hartholt received an MA in computer science from the University of Twente, the Netherlands. Contact him at hartholt@ict.usc.edu.
- Mario Grimani** is a research programmer at the USC Institute for Creative Technologies. His research interests include clinical VR artificial intelligence, multiagent systems, game theory, and virtual world creation. Grimani received an MS in computer science from Texas State University. Contact him at grimani@ict.usc.edu.
- Andrew Leeds** is a technical project specialist at the USC Institute for Creative Technologies, where his work focuses on medical and training application software development and technologies for novel, multisensory VR systems. Leeds received a BA in film and video from Columbia College Chicago. Contact him at leeds@ict.usc.edu.
- Matt Liewer** is the technical art lead in the Art Group at the USC Institute for Creative Technologies. He received a BFA from the University of Oregon. Contact him at liewer@ict.usc.edu.



Selected CS articles and columns are available for free at <http://ComputingNow.computer.org>.

Virtual Reality Exposure for PTSD Due to Military Combat and Terrorist Attacks

Albert Rizzo¹ · Judith Cukor² · Maryrose Gerardi³ · Stephanie Alley⁴ ·
Chris Reist⁴ · Mike Roy⁵ · Barbara O. Rothbaum³ · JoAnn Difede²

© Springer Science+Business Media New York 2015

Abstract Humans exposed to war and terrorist attacks are at risk for the development of posttraumatic stress disorder (PTSD). Numerous reports indicate that the incidence of PTSD in both returning Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) military personnel and survivors of the 9/11 World Trade Center (WTC) attacks is significant. These situations have served to motivate research on how to better develop and disseminate evidence-based treatments for PTSD and other related psychosocial conditions. Virtual reality (VR) delivered exposure therapy for PTSD is currently being used to treat combat and terrorist attack related PTSD with initial reports of positive outcomes. This paper presents an overview and rationale for the use of VR exposure therapy with anxiety disorders and PTSD and describes the status of two systems (Virtual Iraq/Afghanistan and Virtual World Trade Center) developed for this purpose.

Keywords Posttraumatic stress disorder · Anxiety disorders · Virtual reality · Prolonged exposure

Introduction

War is perhaps one of the most challenging situations that a human being can experience. The physical, emotional, cognitive and psychological demands of a combat environment place enormous stress on even the best-prepared military personnel. Thus, it is no surprise that the stressful experiences that have been characteristic of the Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) combat theatres have produced significant numbers of SMs and Veterans at risk for developing PTSD and other psychosocial/behavioral health conditions. In a meta-analysis across studies since 2001, 13.2 % of OEF/OIF operational infantry units met criteria for PTSD with the PTSD incidence rising dramatically (ranging from 25 to 30 %) in infantry units with the highest levels of direct combat (Kok et al. 2012). During this same time period, the prevalence of PTSD among discharged veterans receiving treatment at VA clinics has been reported to be 29 % (Fischer 2013). These findings make a compelling case for a continued focus on developing and enhancing the availability of diverse evidence-based treatment options to address this military behavioral healthcare challenge.

Similarly, trauma experienced from acts of terror can have a significant effect on the psychological well-being of the civilian population. The World Trade Center (WTC) attacks of September 11, 2001 were unprecedented in their unique impact, with the loss of almost 3000 lives, more than 10,000 eyewitnesses in New York, and thousands of disaster workers who were exposed on that day (and in the aftermath at Ground Zero) to the massive devastation and loss of life. Unsurprisingly, the psychological effects were substantial. Screenings 1–2 months following 9/11 found rates of probable PTSD ranging from 7.5 % in Manhattan residents (Galea et al. 2002) to nearly 40 % in individuals in the area of

✉ Albert Rizzo
rizzo@ict.usc.edu

¹ Institute for Creative Technologies, University of Southern California, Los Angeles, CA, USA

² Department of Psychiatry, Weill Cornell Medical College, New York, NY, USA

³ Department of Psychiatry, Emory University, Atlanta, GA, USA

⁴ Long Beach VA Medical Center, Long Beach, CA, USA

⁵ Uniform Services University of the Health Sciences, Bethesda, MD, USA

the attacks (Rosenczweig et al. 2002). The WTC Health Registry found estimated PTSD prevalence at 12.4 % among almost 29,000 rescue and recovery workers two to three years after 9/11 (Perrin et al. 2007) and a rate of 23 % estimated PTSD among over 43,000 participants screened in three waves over 10 years (Ghuman et al. 2014). The World Trade Center Worker and Volunteer Medical Screening Program reported probable PTSD in 11 % of over 10,000 workers in the 5 years following the attacks. In our own studies of almost 3,000 non-rescue workers deployed to Ground Zero, we found rates of 8 % with full PTSD and an additional 9 % with sub threshold PTSD 10–34 months following the attacks (Cukor et al. 2011).

These dramatic geopolitical events (OEF/OIF/WTC) put a high profile on the impact of trauma on its human victims. This provided an impetus for innovative efforts to develop and evaluate the use of Virtual Reality simulations of the Afghanistan/Iraq combat zones and the WTC attack as tools for delivering trauma-focused exposure therapy to treat PTSD. It is within this historical context that this paper will discuss two efforts to apply VR technology for the treatment of PTSD. This includes a short review of the previous literature, descriptions of the system components and the treatment protocol, discussion of the initial research and results, and the presentation of two cases that have been treated with each of these systems.

The Rationale for Virtual Reality Exposure

Prolonged Exposure (PE)

Prolonged exposure (PE) is a form of individual psychotherapy based on the Foa and Kozak (1986) emotional processing theory, which posits that phobic disorders and PTSD involve pathological fear structures that are activated when information represented in the structures is encountered. Emotional processing theory purports that fear memories include information about stimuli, responses, and meaning and that fear structures are composed of harmless stimuli that have been associated with danger and are reflected in the belief that the world is a dangerous place. This belief then manifests itself in cognitive and behavioral avoidance strategies that limit exposure to potentially corrective information that could be incorporated into and alter the fear structure. As escape and avoidance from feared situations are intrinsically (albeit, temporarily) rewarding, phobic disorders can perpetuate without treatment. Consequently, several theorists have proposed that conditioning processes are involved in the etiology and maintenance of anxiety disorders often invoking Mowrer's (1960) two-factor theory in the acquisition of fear and avoidance behavior. Successful treatment requires emotional processing of the

fear structures in order to modify their pathological elements so that the stimuli no longer invoke fear, and any method capable of activating the fear structure and modifying it would be predicted to improve symptoms of anxiety. Imaginal PE entails engaging mentally with the fear structure through repeatedly revisiting the feared or traumatic event in a safe environment. The proposed mechanisms for symptom reduction involves activation and emotional processing, extinction/habituation of the anxiety, cognitive reprocessing of pathogenic meanings, the learning of new responses to previously feared stimuli, and ultimately an integration of corrective non-pathological information into the fear structure (Bryant et al. 2003; Foa et al. 1996).

When PE is used for PTSD the approach typically involves the graded and repeated imaginal reliving and narrative recounting of the traumatic event by the client within the therapeutic setting. Clients are asked to verbally recount their trauma experience in the first person with their eyes closed, as if it were happening again with as much attention to sensory detail as they can. Using clinical judgment, the therapist might prompt the client with questions about their experience or provide encouraging remarks as deemed necessary to facilitate the recounting of the trauma narrative. This approach is believed to provide a low-threat context where the client can begin to confront and therapeutically process trauma-relevant memories and emotions as well as de-condition the learning cycle of the disorder via an extinction learning process.

Virtual Reality Exposure (VRE)

VR can be seen as an advanced form of human–computer interaction (Rizzo et al. 1997) that allows the user to “interact” with computers and digital content in a more natural or sophisticated fashion relative to what is afforded by standard mouse and keyboard input devices. Immersive VR can be produced by combining computers, head mounted displays (HMDs), body tracking sensors, specialized interface devices and real-time graphics to immerse a participant in a computer-generated simulated world that changes in a natural/intuitive way with head and body motion. One common configuration employs a combination of a HMD and head tracking system that allows delivery of real-time images and sounds of a simulated virtual scene rendered in relation to user movements that corresponds to what the individual would see and hear if the scene were real. Thus, an engaged virtual experience creates the illusion of being immersed “in” a virtual space within which the user can interact.

The use of VR to address psychological disorders began in the mid-90s with its use as a tool to deliver exposure therapy targeting anxiety disorders. Primarily targeting specific phobias (e.g., heights, flying, spiders, enclosed spaces), virtual environments could be created that provided views from tall

buildings, aircraft interiors, spiders in kitchens, elevators, etc. In general, the phenomenon that users of VR could become immersed in digital 3D graphic rendering of a feared environment provided a potentially powerful tool for activating and modifying relevant fears in the PE treatment of specific phobias. From this starting point, a body of literature evolved that suggested that the use of virtual reality exposure (VRE) therapy was effective. Case studies in the 1990s initially documented the successful use of VR in the treatment of acrophobia (Rothbaum et al. 1995), fear of flying (Rothbaum et al. 1996), spider phobia (Carlin et al. 1997), and claustrophobia (Botella et al. 1998). For example, in an early wait list controlled study, VRE was used to treat the fear of heights, exposing clients to virtual footbridges, virtual balconies, and a virtual elevator (Rothbaum et al. 1995). Clients were encouraged to spend as much time in each situation as needed for their anxiety to decrease and were allowed to progress at their own pace. The therapist saw on a computer monitor what the participant saw in the virtual environment and therefore was able to comment appropriately. Results showed that anxiety, avoidance, and distress decreased significantly from pre- to post-treatment for the VRE group but not for the wait list control group.

Since that time, an evolved body of controlled studies targeting specific phobias has emerged and two meta-analyses of the available literature (Parsons and Rizzo 2008; Powers and Emmelkamp 2008) concurred with the finding that VR is an efficacious approach for delivering PE, that it sometimes outperformed imaginal PE and was as effective as in vivo exposure. A newer meta-analysis and a systematic review of this literature expand on the findings (Opris et al. 2012; Scozzari and Gamberini 2011) and further support the notion that VR is an effective method for delivering exposure within an evidence-based CBT protocol to treat these types of anxiety disorders.

Virtual Reality Exposure for Posttraumatic Stress Disorder

In the late 1990s researchers began to test the use of VRE for the treatment of posttraumatic stress disorder (PTSD) by systematically immersing users in simulations of trauma-relevant environments. While the efficacy of imaginal PE for PTSD has been established in multiple studies with diverse trauma populations (Bryant 2005; Rothbaum and Schwartz 2002), it is reported that some clients are unwilling or unable to effectively visualize the traumatic event (Difede and Hoffman 2002). This is a crucial concern since avoidance of cues and reminders of the trauma is one of the cardinal symptoms of the DSM 5 (American Psychiatric Association 2012) diagnosis of PTSD. In fact, research on this aspect of PTSD treatment suggests that the inability to emotionally engage (*in imagination*) is a

predictor for negative treatment outcomes (Jaycox et al. 1998). Similar to its use in treating specific phobias, the rationale for using VR as a tool to deliver PE for PTSD is straightforward. Clients can be immersed in simulations of trauma-relevant environments in which the emotional intensity of the scenes can be precisely controlled by the clinician to customize the pace and relevance of the exposure for the individual client. In this fashion, VRE offers a way to circumvent the natural avoidance tendency by directly delivering multi-sensory and context-relevant scenes and cues that aid in the retrieval, confrontation, and processing of traumatic experiences.

The first effort to apply VRE for PTSD began in 1997 when researchers at Georgia Tech and Emory University began testing the *Virtual Vietnam* VR scenario with Vietnam veterans diagnosed with PTSD (Rothbaum et al. 2001). This occurred over 20 years after the end of the Vietnam War. During those intervening years, in spite of valiant efforts to develop and apply traditional psychotherapeutic and pharmacological treatment approaches to PTSD, the progression of the disorder in some veterans significantly impacted their psychological well-being, functional abilities and quality of life, as well as that of their families and friends. This initial effort yielded encouraging results in a case study of a 50-year-old, male Vietnam veteran meeting DSM 4-r criteria for PTSD (Rothbaum and Hodges 1999).

Results indicated post-treatment improvement on all measures of PTSD and maintenance of these gains at a 6-month follow-up, with a 34 % decrease in clinician-rated symptoms of PTSD and a 45 % decrease on self-reported symptoms of PTSD. This case study was followed by an open clinical trial with Vietnam veterans (Rothbaum et al. 2001). In this study, 16 male veterans with PTSD were exposed to two HMD-delivered virtual environments, a virtual clearing surrounded by jungle scenery and a virtual Huey helicopter, in which the therapist controlled various visual and auditory effects (e.g. rockets, explosions, day/night, and shouting). After an average of 13 exposure therapy sessions over 5–7 weeks, there was a significant reduction in PTSD and related symptoms.

The Implementation of VRE Therapy for PTSD: Technical Development

Development of the Virtual Iraq/Afghanistan VRE System

In anticipation of the impending military behavioral health needs, the USC Institute for Creative Technologies developed an initial prototype Virtual Iraq VRE system in 2004 for running initial user tests to determine feasibility. This

was followed by the creation of a full Virtual Iraq/Afghanistan VRE system developed during 2005–2007, funded by the U.S. Office of Naval Research. This early version system was the product of both theory-driven design and iterative user-centered feedback cycles with OEF/OIF service members to maximize its ultimate relevance for clinical users. Pre-clinical user-testing was conducted at Ft. Lewis, Washington and within an Army Combat Stress Control Team in Iraq (Reger et al. 2009). This feedback from non-diagnosed SMs (and later by clinical users) has provided essential input for an iterative design process that has served to continuously evolve the content and usability of the clinical VRE system to the current day.

The 2007 system consisted of four customizable scenarios designed to represent relevant contexts for VRE: three Humvee driving scenarios within Iraq, Afghanistan and USA-themed settings and a 24-block middle-eastern city that was navigable in a dismounted patrol format. General navigation for driving used a standard game pad and when interacting in the dismounted foot patrol, a thumb mouse affixed to a user-held mock M4 gun supported travel. The visual stimuli presented within an orientation-tracked *Emagin Z-800* head mounted display (HMD). Directional 3D audio, vibrotactile and olfactory stimuli of relevance could also be delivered to users. Such stimuli could be controlled and modified in real time by the clinician via a separate “Wizard of Oz”-type clinician interface. This interface is a key feature that allows clinicians to customize the therapy experience to the individual needs of the client. Using the interface, clinicians can place users in various VR scenario locations that resemble the settings in which the client’s trauma-relevant events had occurred. Ambient lighting and sound conditions can be modified to match the client’s description of their experience and the clinician can then gradually introduce and control real time trigger stimuli (e.g., gunfire, explosions, insurgent attacks, etc.). This level of clinician control is required to foster the anxiety modulation needed for therapeutic exposure and emotional processing in a fashion customized to the client’s past experience and treatment progress. The use of a VR HMD to immerse the user within these controlled stimulus environments is believed to help support user engagement with typically avoided trauma-relevant experiences as required to activate the emotions needed for therapeutic exposure to occur. This system was been disseminated to over 60 early-adopter clinical sites (e.g., VA Medical Centers, military, university and private clinics) for use as a tool to deliver PE and to collect outcome data as to its effectiveness.

In 2011, the U.S. Army funded the development of an updated and expanded version of Virtual Iraq/Afghanistan system. Now referred to as *BRAVEMIND*, one of the

primary goals for this effort was to increase the diversity of the VR scenario content and improve the customizability of stimulus delivery to better address the needs of clinical users who have had a diverse range of trauma experiences. This effort was supported by drawing on the vast amount of user feedback generated from both clients’ and clinicians’ feedback from use of the previous 2007 VRE system. The system was rebuilt from the ground up using the state-of-the-art current software. The four original 2007 environments have been completely rebuilt and ten additional scenarios have been added for a total of 14, including: separate Iraq and Afghanistan cities, a rural Afghan village, an industrial zone, a roadway checkpoint, slum and high-end residential areas, a mountainous forward operating base, and a Bagram Air Force Base setting. New features include selectable Humvee/MRAP/Helicopter vehicles, vehicle-to-foot patrol transitioning, expanded weather and time of day controls, customizable sound trigger profiles, and an updated clinical interface designed with clinician feedback to enhance usability. The system was also designed to use off the shelf components with the aim to reduce equipment costs to under \$5000 and a detailed equipment/software manual is available from the first author.

Development of the World Trade Center VRE System

In the months immediately following the World Trade Center attacks, a collaboration between Dr. JoAnn Difede at Weill Cornell Medical College and Dr. Hunter Hoffman of the Human Interface Technology Laboratory at University of Washington set out to develop a virtual reality environment and protocol that would address the needs of the anticipated thousands of disaster workers and civilians who would develop PTSD related to 9/11. This early virtual setup utilized MultiGen-Paradigm Inc. Vega VR software coupled with a 1024 × 768 resolution Kaiser XL-50 VR helmet, with 40° horizontal field of view. Users viewed the virtual environment through two goggle-sized miniature LCD computer screens embedded in the helmet. Immersion in the environment was enhanced by the use of the PolhemusTM Fastrak position tracking system, which tracked the movement and position of the user’s head. Thus as the users turned their heads in the environment, their visual field would change, displaying different city blocks and buildings.

The World Trade Center virtual environment was designed to enable the therapist to introduce progressively more intense and detailed stimuli with the push of a button. Visual stimuli mirrored the actual landscape of lower Manhattan and simulated the events of that day. Auditory stimuli were based upon audio recordings made by national

news networks. Throughout, the therapist observed the same stimuli as the participant on a computer monitor. The user began in downtown New York City on a sunny day with a clear view of the towers. At the therapist's touch of pre-programmed computer keys, an airplane could fly by or into the towers. Progressively more detailed scenes would approximate the events of September 11th, including planes hitting the North and South towers with sounds of explosions, the towers burning accompanied by falling debris and screams, distant avatars in the towers and falling from them, and finally the collapse of each of the towers followed by blinding dust clouds. Clients would describe their experiences on the day of 9/11, as visual and audio stimuli would be introduced to match their experiences. Guidelines in the treatment protocol detailed a graded hierarchical exposure such that clients would progress in the intensity of stimuli only once they showed a significant reduction in distress to the existing sensory experience. This was carefully constructed to prevent overwhelming the client and to follow the principals of graded exposure therapy utilized in other exposure treatments.

Research Outcomes

Initial positive results were reported in a case study by Difede and Hoffman (2002) for PTSD related to the terrorist attack on the World Trade Center (WTC) using VRE with a client who had failed to improve with traditional imaginal exposure therapy. The authors reported a 90 % reduction in PTSD symptoms as measured by the "gold standard" Clinician Administered PTSD Scale (CAPS), and an 83 % reduction in depressive symptomatology as measured by the Beck Depression Inventory (Beck et al. 1988). This research group later reported positive results from a wait-list controlled study using the same WTC VR application (Difede et al. 2007). The VR group demonstrated statistically and clinically significant decreases on the CAPS relative to both pre-treatment and to the wait-list control group with a between-groups post treatment effect size of 1.54. Seven of ten people in the VR group no longer carried the diagnosis of PTSD, while all of the wait-list controls retained the diagnosis following the waiting period and treatment gains were maintained at 6-month follow-up. Also noteworthy was the finding that five of the 10 VR clients who had previously participated in imaginal PE with no clinical benefit, showed a 25–50 % improvement following VRE.

Initial clinical tests of the Virtual Iraq/Afghanistan system also produced promising results. Three early case studies reported positive results using this system (Gerardi et al. 2008; Reger and Gahm 2008; Rizzo et al. 2007). In the first open clinical trial, analyses of 20 active duty

treatment completers produced positive clinical outcomes (Rizzo et al. 2010). For this sample, mean pre/post PCL-M (Blanchard et al. 1996) scores decreased in a statistical and clinically meaningful fashion: 54.4 (SD = 9.7) to 35.6 (SD = 17.4). Paired pre/post *t* test analysis showed these differences to be significant ($t = 5.99$, $df = 19$, $p < .001$) and 16 of the 20 completers no longer met PCL-M criteria for PTSD at post treatment. Mean Beck Anxiety Inventory (Beck et al. 1988) scores significantly decreased 33 % from 18.6 (SD = 9.5) to 11.9 (SD = 13.6), ($t = 3.37$, $df = 19$, $p < .003$) and mean PHQ-9 (Kroenke and Spitzer 2002) depression scores decreased 49 % from 13.3 (SD = 5.4) to 7.1 (SD = 6.7), ($t = 3.68$, $df = 19$, $p < .002$). These improvements were also maintained at three-month post-treatment follow-up.

Other reports have also indicated positive outcomes including an open clinical trial with active duty soldiers ($n = 24$) which produced significant pre/post reductions in PCL-M scores and a large treatment effect size (Cohen's $d = 1.17$) (Reger et al. 2011). After an average of seven sessions, 45 % of those treated no longer screened positive for PTSD and 62 % had reliably improved. In a small preliminary quasi-randomized controlled trial (McLay et al. 2011) 7 of 10 participants with PTSD showed a 30 % or greater improvement with VR, while only 1 of 9 participants in a "treatment as usual" group showed similar improvement. The results are limited by small size, lack of blinding, a single therapist, and comparison to a set relatively uncontrolled usual care conditions, but it did add to the incremental evidence suggesting VR to be a safe and effective treatment for combat-related PTSD.

The overall trend of these positive findings (in the absence of any reports of negative findings) is encouraging for the view that VRE is safe and may be an effective approach for delivering an evidence-based treatment (PE) for PTSD. Three randomized controlled trials (RCTs) are currently ongoing using the Virtual Iraq/Afghanistan system with SMs and Veteran populations. One RCT is focusing on comparisons of treatment efficacy between VRE and imaginal PE (Reger and Gahm 2010) and another is testing VRE compared with VRE + a supplemental care approach (Beidel et al. 2010). Another RCT is investigating the additive value of supplementing VRE and PE with a cognitive enhancer called D-cycloserine (DCS) (Difede et al. 2010). DCS, an *N*-methyl-D-aspartate partial agonist, has been shown to facilitate extinction learning in laboratory animals when infused bilaterally within the amygdala ("fight or flight" conditioning center in the brain) prior to extinction training. Recent evidence of both VRE and DCS effectiveness has been reported by Difede et al. (2013) in a clinical trial with WTC PTSD clients. In a double-blinded controlled comparison between VRE + DCS and VRE + Placebo, both groups had clinically meaningful

and statistically significant positive outcomes with the DCS group achieving equivalent gains with fewer sessions. Significant funding support for these RCTs underscore the interest that the DOD/VA has in exploring this innovative approach for delivering PE using VR.

The Implementation of VRE for PTSD: Clinical Delivery

General VRE Treatment Procedures

The VRE treatment procedure follows the standard evidence-based protocol for “imagination-only” PE therapy (Foa et al. 2007) and consists of weekly, 90–120 min individualized and client-driven sessions over 10 weeks. During the first session, the clinician generally aims to develop a working therapeutic alliance with the client as is standard for most clinical approaches. The clinician may attempt to identify and discuss some of the client’s trauma experiences, provide psychoeducation on trauma and PTSD, and present instruction on a deep breathing technique for general stress management purposes. The second session follows up on topics from session 1 as needed and then focuses on providing the client with a clear explanation and rationale for PE. In some cases, the client is engaged in light practice with imaginal exposure that focuses on less provocative elements of their trauma experience. In session 3 the rationale for VRE is introduced and the client is encouraged to explore a personally relevant area of the simulation environment without recounting any trauma narrative for approximately 25 min, with no provocative trigger stimuli introduced. The purpose of this is to allow the participant to learn how to navigate the system, and to function as a “bridge session” from imaginal alone to imaginal exposure combined with VRE. Sessions four through ten is when the VRE proper is conducted with the participant engaging in the VR while verbally recounting the trauma narrative. The treatment also includes homework, such as requesting the participant to listen to an audiotope of their exposure narrative from the most recent session and in vivo exposure activities for processing the trauma outside of the treatment setting. Assessment of PTSD status is typically done with a combination of self-report symptom questionnaires, structured interview methods, and sometimes active psychophysiological reactivity tests. A more detailed description of this system, PTSD assessment procedures, and the methodology for a standard VRE clinical protocol can be found elsewhere (Rothbaum et al. 2008).

Virtual Iraq/Afghanistan Case Study

John was a 30 year old Army veteran of the war in Iraq. He deployed twice during his military service, and had been

home for 3 years at the time of treatment. John was married with a young child, and attending school to learn a trade. He reported experiencing intrusive thoughts, especially at night when trying to fall asleep, nightmares, very strong startle reaction to any loud or unpredictable noise, irritable mood, impatience with a “short fuse”, and tension and distance in his marriage. He also had some difficulty with concentration in school, and described being easily angered by the comments of fellow students who he saw as “clueless”, sometimes resulting in him having to leave class. John was very avoidant of any situation he perceived as dangerous, such as being in crowds, and only attended mandatory events such as classes. He also kept a weapon at home, and was extremely vigilant when night fell. He acknowledged drinking too much, as he reported that it was the only thing that helped him stop thinking about events in Iraq and allowed him to eventually fall asleep. He reported being tired of hearing family and friends tell him that they are worried about him and that he is not the guy he was before he deployed. He came to treatment with the understanding that he needed to do something to keep his marriage intact, although he was ambivalent about the relationship, stating, “I just don’t seem to care”. He reported that he doesn’t engage much with his daughter, and that he did feel bad about that.

During the first session, John’s symptoms of PTSD and their impact on his life were discussed, and the rationale for exposure therapy was explained, along with a description of the immersive nature of VRE therapy. John was also taught a breathing/relaxation technique to use between sessions. He was asked to identify and describe his index (most distressing) trauma in detail, in order to prepare for the VR therapy to follow. John had not spoken about the event previously, and was wary of doing so, but managed to follow through. The identified event occurred while John was driving the lead Humvee vehicle in a convoy going through a city area of Iraq, late in the afternoon on a sunny day. John described noticing the people on the street starting to thin out as he drove, and then an insurgent holding an AK-47 suddenly coming around a corner up ahead, holding a young woman in front of him as a shield. John kept driving, yelled out to alert others in the vehicle, hesitated briefly, and then shot the insurgent, also killing the woman. He recalled looking in his side view mirror as he drove, and seeing her lying on the street, receding in his view. The therapist later matched the most appropriate VR scenario and available cues to John’s reported traumatic event.

John began the VRE seated in the Humvee driver position, feeling the vibration under his feet and using the controller to drive ahead down a Baghdad-like city street. Humvee radio sounds were introduced, and John described his thoughts and feelings in the first person as he moved down the street (for example, beginning to suspect

something was wrong as the crowd thinned out, feeling a sense of apprehension and feeling his heart start to pound). He then described the sudden appearance of the insurgent, and this image was introduced. John continued to describe his experience of disbelief and then his training “kicking in” as he took action, simultaneously making a split-second decision around saving the hostage and taking the chance that the insurgent (and possible accomplices) would then take out the following trucks in the convoy, vs. eliminating the threat. The sound of John’s weapon was also introduced into the VR scenario. John’s subjective units of distress (SUDS) ratings were monitored via a self-reported 1–100 level scale throughout his repeated recounting of the event. After going through the event multiple times, John then processed the experience, expressing exhaustion, surprise at all of the details he remembered as he went through the repetitions, and commenting on the realistic nature of the virtual environment leading him to feel as if he was “there, but safe here”.

Subsequent sessions focusing in on the “hot spots” of the memory allowed John to put the event in context, identify emotional reactions which were put aside out of necessity at the time, and realizing the complexity of the “no-win” situation he was placed in. He was able to both express and feel sorrow over the loss of an innocent life, and to acknowledge all of the factors which came together at that moment which were not in his control, especially the decision of the insurgent to place the woman’s life in such grave danger. As he progressed in treatment, John was able to acknowledge the fact that his decision likely resulted in the saving of lives, and that he had done the best that he could in that moment. He began to talk with his wife about what was happening in treatment, and reported that she was feeling more included and more able to understand some of what he had been through. John also noticed a softening of feelings toward his daughter, which pleased him. Additionally John reported improvement in his ability to sleep without nightmares waking him, and began challenging some of his fears around going to restaurants, movies, etc. At follow-up, John’s symptoms continued to decrease in frequency and intensity, and he reported improved ability to be comfortable in public situations.

Virtual World Trade Center Case Report

David was a 45 year-old firefighter who first sought treatment for PTSD 5 years after the World Trade Center attacks. David had just gone through a divorce and had shared custody of his son who was experiencing significant issues in school himself. David was still working with the fire department but was in trouble with superiors for his verbal explosiveness and for breaking protocols and putting himself in danger more than once. The threat of potential dismissal

spurred him to pursue treatment which he had avoided until that point because, as he stated, “I help other people, I don’t ask for help.” Though he had experienced numerous traumas throughout the course of his career, David identified the index trauma of 9/11 as “the one that just broke me”. He met criteria for PTSD related to the attacks of 9/11 as well as a comorbid Major Depressive Disorder. An assessment of daily activity revealed that David took numerous work shifts, spending as many hours at the job as his superiors would allow, but was otherwise socially isolated and avoided family and friends. He reported nightmares daily and avoided sleep as much as possible since his dreams were so unpleasant. Content of the nightmares alternated between individuals who died on 9/11 blaming him for not helping them, and watching his own loved ones in danger. Other prominent symptoms included frequent intrusive thoughts, avoidance of thoughts, feelings, and reminders of the trauma, emotional numbing, anhedonia, feelings of detachment, and increased startle and hypervigilance.

David had never revealed the details of his trauma experience to others, and he successfully removed himself emotionally from the retelling when describing the event during the assessment. On September 11, he had responded to the attacks immediately, arriving at the buildings soon after the second plane had collided with the South Tower. He stood frozen at the devastation and the sight of individuals hanging from windows and jumping from the buildings. The North Tower collapsed as he was preparing to enter and he ran for his life, choking on the debris and dust and finally jumping beneath a vehicle. David described the moments when he realized the devastating loss of life that was occurring and how many of his firefighter brethren had died. He did not return home for days after 9/11 and only after being forced by his superiors to do so. Still, he returned to the site soon after and spent weeks digging there. David’s composure broke as he described some of the sights he saw when working on “the pile.” The bodies or body parts and the personal items that gave glimpses into the lives of those who had died left indelible marks in his memory. He left Ground Zero for short periods of time, often to go to funerals or wakes, of which he attended dozens. David blamed himself for not doing enough to save people on that day and for not running into the towers like so many others. The fact that he was alive served as a constant reminder to him of his failure to help. At the same time he faulted himself for the destruction of his family, for ignoring them during this difficult time, for bringing the ugliness home when he did return, and for in essence, causing them to lose a husband and father on that day as well.

A treatment plan was set with an emphasis on the use of exposure therapy with the virtual WTC environment. David was notably moved during his first immersion in the environment. He commented on the blueness of the sky, “It really was that blue” and began narrating his experience on that day.

Over the course of ten sessions, David told his experience repeatedly. By the third exposure session, he began to work on “hot spots”—identifying the most intense parts of his experience and focusing on them individually and repeatedly. David was very engaged in the exposure exercise, weeping openly as he spoke about the loss of life and the fear of losing his own. He slowly progressed through the virtual reality sequences. In initial sessions he narrated his event while simply looking at the towers from a distance without auditory stimuli. As he habituated to stimuli, the therapist began to match the elements of his experience more closely. He was placed in the virtual environment at closer proximity to the towers as he had been on that day, and auditory and visual elements were added to reflect his experience. The towers were shown with gaping holes in flames, accompanied by sounds of screams and fear. As he described seeing the South Tower collapse, the virtual environment displayed the South Tower crumbling, accompanied by the rumbling sound, as he was virtually overrun by the dust cloud. Slowly he habituated to each of the sensory elements as well. Processing of the event was conducted after each exposure exercise and focused on his grief and guilt. Over time David began to display habituation to the retellings of the events. He was able to describe his experience with significantly less overwhelming emotion. He began to express a realization that there was simply no right way to deal with this horrible situation. He began to replace his thoughts of “I should have saved people” to “I wish I could have saved people but the situation did not allow for it”. He was able to forgive missteps with his family and recognize he was a fallible person in a difficult situation.

As treatment end approached, David reported that he felt as if a load had been lifted off his shoulders. By telling his experience and habituating to the details, the event became a tragedy that saddened him, rather than an event that defined his life and made him feel overwhelmed by emotion. He began to engage more with those around him, both physically and emotionally, especially his son. He increased his level of activity outside of work and reported slowly gaining enjoyment from these efforts. His nightmares decreased significantly, and he no longer avoided reminders of the trauma. David began to look forward to a future instead of focusing on the past. Though he knew he would always be changed by his experience on 9/11, David reported that through treatment he had learned not to live in the shadow of the trauma, defined by his symptoms from it, but to embrace life and look to the future.

Conclusions

Interest in using VR technology to deliver exposure therapy for PTSD has grown in recent years as positive outcomes have been reported with its initial implementation.

When clinicians were surveyed as to interventions predicted to increase in the next decade, VR ranked 4th out of 45 options with other computer-supported methods occupying four out of the top five positions (Norcross et al. 2013). VR for exposure-based treatment may have particular appeal to clinicians in that it uses the latest advances in human–computer interaction to deliver consistent, controllable, and immersive trauma-relevant stimulus environments that do not rely exclusively on the variable nature and ultimately hidden world of a client’s imagination. VR also provides an objective and consistent format for documenting the sensory stimuli that the client is exposed to that can be precisely linked to physiological and self-reported reactions for treatment documentation and research. In addition to these functional stimulus/response quantification assets, the use of VR as a PE delivery system may also be found to break down barriers to care by improving treatment appeal, acceptability and adherence by those in need of care. The current generation of young military SMs and veterans, many having grown up with digital gaming technology, may be more attracted to and comfortable with participation in a VR therapy approach (Wilson et al. 2008) and this could lead to increased accessing of care by those in need. Thus, more research is needed to determine if VRE is perceived with less stigma by “digital generation” SMs and Veterans relative to what they perceive as traditional talk therapies.

While it can be said that VR simply provides a novel and engaging mechanism for delivering an already endorsed, evidence-based approach (CBT with exposure), more research is needed to provide scientific support for that claim. Although the current state of the literature is promising (especially with the solid evidence for VRE effectiveness in the treatment of specific phobias), the existing research for VRE therapy with PTSD provides only preliminary evidence for its efficacy. Positive results from three published case reports, two open trials, two waitlist controlled studies and one small RCT have formed the initial basis for support thus far, but RCTs with larger sample-sizes are still needed to provide confirmatory evidence for the efficacy of VRE with PTSD. As well, it will be important to conduct dismantling studies to better specify what elements of VRE are crucial for differentiating VRE from standard CBT exposure approaches, for improving the treatment, and for providing a better understanding of the mechanisms that may predict who this treatment may appeal to and who will benefit from it. Subject variables including gender, age, video game experience, number of deployments, and past trauma history may provide useful covariates to support better prediction as to who might benefit from what form of exposure. As well, research on variations from the standard protocol delivery of VRE in terms of the frequency and duration of

sessions, the additive value of multisensory stimuli—i.e., olfaction, and the addition of pharmacological agents (D-cycloserine) or CNS focused procedures (vagal nerve stimulation), could also be usefully studied for their impact on treatment outcomes within the controlled stimulus environment that a VR simulation provides. Such clinical research efforts are now more feasible, with the rapid advances in the technology that have driven the recent availability of off-the-shelf VR equipment that is cheaper, less complex and of higher quality than what was available just two years ago. Thus, it is likely that VRE interventions for PTSD will continue to drive novel research and address the significant clinical and social welfare challenges that exist with those who suffer from the experience of trauma. For an extensive collection of videos on this project (simulation videos, patient interviews, media reports) the reader is directed to: http://www.youtube.com/watch?v=2wmM2aCZ3JA&list=PLMuMO5eoYy_BDmAfZrFSLBLIniAtvAdad.

References

- American Psychiatric Association. (2012). *Diagnostic and statistical manual of mental disorders* (revised 5 ed.). Washington, DC: American Psychiatric Association.
- Beck, A. T., Epstein, N., Brown, G., Steer, R. A. (1998). An inventory for measuring clinical anxiety: Psychometric properties. *Journal of Consulting and Clinical Psychology*, 56(6), 893–897.
- Beidel, D. C., Frueh, B. C., & Uhde, T. W. (2010). *Trauma management therapy for OIF/OEF veterans*. Department of Defense United States Army Military Operational Medical Research Program. Retrieved April 10, 2015 from http://www.psych.ucf.edu/faculty_beidel.php.
- Blanchard, E. B., Jones-Alexander, J., Buckley, T. C., & Forneris, C. A. (1996). Psychometric properties of the PTSD checklist (PCL). *Behaviour Research and Therapy*, 34(8), 669–673.
- Botella, C., Banos, R. M., Perpina, C., Villa, H., Alcaniz, M., & Rey, A. (1998). Virtual reality treatment of claustrophobia: A case report. *Behavior Research and Therapy*, 36, 239–246.
- Bryant, R. A. (2005). Psychosocial approaches of acute stress reactions. *CNS Spectrums*, 10(2), 116–122.
- Bryant, R. A., Moulds, M. L., Guthrie, R. M., Dang, S. T., & Nixon, R. D. V. (2003). Imaginal exposure alone and imaginal exposure with cognitive restructuring in treatment of posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology*, 71, 706–712.
- Carlin, A. S., Hoffman, H. G., & Weghorst, S. (1997). Virtual reality and tactile augmentation in the treatment of spider phobia: A case report. *Behavior Research and Therapy*, 35, 153–158.
- Cukor, J., Wyka, K., Jayasinghe, N., Weathers, F., Giosan, C., Leck, P., et al. (2011). Prevalence and predictors of posttraumatic stress symptoms in utility workers deployed to the World Trade Center following the attacks of September 11, 2001. *Depression and Anxiety*, 28(3), 210–217. doi:10.1002/da.20776.
- Difede, J., Cukor, J., Jayasinghe, N., Patt, I., Jedel, S., Spielman, L., et al. (2007). Virtual reality exposure therapy for the treatment of posttraumatic stress disorder following September 11, 2001. *Journal of Clinical Psychiatry*, 68(11), 1639–1647.
- Difede, J., Cukor, J., Wyka, K., Olden, M., Hoffman, H., Lee, F. S., & Altemus, M. (2013). D-cycloserine augmentation of exposure therapy for posttraumatic stress disorder: A pilot randomized clinical trial. *Neuropsychopharmacology*, 2013(39), 1052–1058.
- Difede, J., & Hoffman, H. G. (2002). Virtual reality exposure therapy for World Trade Center posttraumatic stress disorder: a case report. *Cyberpsychology & Behavior*, 5(6), 529–535.
- Difede, J., Rothbaum, B. O., & Rizzo, A. (2010–2015). Enhancing exposure therapy for PTSD: Virtual reality and imaginal exposure with a cognitive enhancer. Randomized controlled trial. Retrieved April 10, 2015 from <http://clinicaltrials.gov/ct2/show/NCT01352637>.
- Fischer, H. (2013, February 5). *United States military casualty statistics: Operation New Dawn, Operation Iraqi Freedom, and Operation Enduring Freedom*. Congressional Research Service 7-5700: RS22452. Retrieved April 10, 2015 from <http://www.fas.org/sgp/crs/natsec/RS22452.pdf>.
- Foa, E. B., Franklin, M. E., Perry, K. J., & Herbert, J. D. (1996). Cognitive biases in generalized social phobia. *Journal of Abnormal Psychology*, 105(3), 433–439.
- Foa, E. B., Hembree, E., & Rothbaum, B. O. (2007). *Prolonged exposure therapy for PTSD: Emotional processing of traumatic experiences. Therapist Guide*. New York: Oxford University Press.
- Foa, E. B., & Kozak, M. J. (1986). Emotional processing of fear: Exposure to corrective information. *Psychological Bulletin*, 99(1), 20–35.
- Galea, S., Ahern, J., Resnick, H., Kilpatrick, D., Bucuvalas, M., Gold, J., & Vlahov, D. (2002). Psychological sequelae of the September 11 terrorist attacks in New York City. *New England Journal of Medicine*, 346(13), 982–987.
- Gerardi, M., Rothbaum, B. O., Ressler, K., Heekin, M., & Rizzo, A. A. (2008). Virtual reality exposure therapy using a virtual Iraq: Case report. *Journal of Traumatic Stress*, 21(2), 209–213.
- Ghuman, S. J., Brackbill, R. M., Stelman, S. D., Farfel, M. R., & Cone, J. E. (2014). Unmet mental health care need 10–11 years after the 9/11 terrorist attacks: 2011–2012 results from the World Trade Center Health Registry. *BMC Public Health*, 14, 491.
- Jaycox, L. H., Foa, E. B., & Morral, A. R. (1998). Influence of emotional engagement and habituation on exposure therapy for PTSD. *Journal of Consulting and Clinical Psychology*, 66, 186–192.
- Kok, B. C., Herrell, R. K., Thomas, J. L., & Hoge, C. W. (2012). Posttraumatic stress disorder associated with combat service in Iraq or Afghanistan: reconciling prevalence difference between studies. *Journal of Nervous and Mental Disorders*, 200(5), 444–450.
- Kroenke, K., & Spitzer, R. L. (2002). The PHQ-9: A new depression and diagnostic severity measure. *Psychiatric Annals*, 32, 509–521.
- McLay, R. N., Wood, D. P., Webb-Murphy, J. A., Spira, J. L., Weiderhold, M. D., Pyne, J. M., et al. (2011). A randomized, controlled trial of virtual reality exposure therapy for post-traumatic stress disorder in active duty service members with combat-related post-traumatic stress disorder. *Cyberpsychology, Behavior, and Social Networking*, 14, 223–229.
- Mowrer, O. A. (1960). *Learning and behavior*. New York: Wiley.
- Norcross, J. C., Pfund, R. A., & Prochaska, J. O. (2013). Psychotherapy in 2022: A Delphi poll on its future. *Professional Psychology: Research and Practice*, 44(5), 363–370.
- Opris, D., Pintea, S., García-Palacios, A., Botella, C., Szamosközi, S., & David, D. (2012). Virtual reality exposure therapy in anxiety disorders: A quantitative meta-analysis. *Depression and Anxiety*, 29(2), 85–93.
- Parsons, T., & Rizzo, A. A. (2008). Affective outcomes of virtual reality exposure therapy for anxiety and specific phobias: A

- meta-analysis. *Journal of Behavior Therapy and Experimental Psychiatry*, 39, 250–261.
- Perrin, M. A., DiGrande, L., Wheeler, K., Thorpe, L., Farfel, M., & Brackbill, R. (2007). Differences in PTSD Prevalence and associated risk factors among World Trade Center Disaster Rescue and Recovery Workers. *American Journal of Psychiatry*, 164, 1385–1394. doi:10.1176/appi.ajp.2007.06101645.
- Powers, M., & Emmelkamp, P. M. G. (2008). Virtual reality exposure therapy for anxiety disorders: A meta-analysis. *Journal of Anxiety Disorders*, 22, 561–569.
- Reger, G., & Gahm, G. (2008). Virtual reality exposure therapy for active duty soldiers. *Journal of Clinical Psychology*, 64, 940–946.
- Reger, G., & Gahm, G. (2010). Comparing virtual reality exposure therapy to prolonged exposure. Randomized controlled trial. Retrieved April 10, 2015 from <http://clinicaltrials.gov/ct2/show/NCT01193725?term=Reger&rank=2>.
- Reger, G. M., Gahm, G. A., Rizzo, A. A., Swanson, R. A., & Duma, S. (2009). Soldier evaluation of the virtual reality Iraq. *Telemedicine and e-Health Journal*, 15, 100–103.
- Reger, G. M., Holloway, K. M., Rothbaum, B. O., Difede, J., Rizzo, A. A., & Gahm, G. A. (2011). Effectiveness of virtual reality exposure therapy for active duty soldiers in a military mental health clinic. *Journal of Traumatic Stress*, 24(1), 93–96.
- Rizzo, A. A., Buckwalter, J. G., & Neumann, U. (1997). Virtual reality and cognitive rehabilitation: A brief review of the future. *The Journal of Head Trauma Rehab*, 12(6), 1–15.
- Rizzo, A., Difede, J., Rothbaum, B. O., & Reger, G. (2010). Virtual Iraq/Afghanistan: Development and early evaluation of a virtual reality exposure therapy system for combat-related PTSD. *Annals of the New York Academy of Sciences*, 1208, 114–125.
- Rizzo, A. A., Graap, K., Mclay, R. N., Perlman, K., Rothbaum, B., Reger, G., et al. (2007). Initial case reports from a VR exposure therapy application for combat-related post traumatic stress disorder. In *IEEE XPlore virtual rehabilitation conference* (pp. 124–130).
- Rosenczweig, C. C., Kravitz, J., & Delvin, M. E. (2002). The psychological impact of helping in a disaster-The New York City experience, September 11th, 2001. *Academic Emergency Medicine*, 9(5), 502.
- Rothbaum, B., Difede, J., & Rizzo, A. (2008). *Therapist treatment manual for virtual reality exposure therapy: Posttraumatic stress disorder in Iraq combat Veterans*. Atlanta: Virtually Better Inc.
- Rothbaum, B. O., & Hodges, L. F. (1999). The use of virtual reality exposure in the treatment of anxiety disorders. *Behavior Modification*, 23, 507–525.
- Rothbaum, B. O., Hodges, L. F., Kooper, R., Opdyke, D., Williford, J. S., & North, M. (1995). Effectiveness of computer-generated (virtual reality) graded exposure in the treatment of acrophobia. *American Journal of Psychiatry*, 152, 626–628.
- Rothbaum, B. O., Hodges, L., Ready, D., Graap, K., & Alarcon, R. (2001). Virtual reality exposure therapy for Vietnam veterans with posttraumatic stress disorder. *Journal of Clinical Psychiatry*, 62, 617–622.
- Rothbaum, B. O., Hodges, L., Watson, B. A., Kessler, C. D., & Opdyke, D. (1996). Virtual reality exposure therapy in the treatment of fear of flying: A case report. *Behaviour Research and Therapy*, 34(5–6), 477–481.
- Rothbaum, B. O., & Schwartz, A. (2002). Exposure therapy for posttraumatic stress disorder. *American Journal of Psychotherapy*, 56, 59–75.
- Scozzari, S., & Gamberini, L. (2011). Virtual reality as a tool for cognitive behavioral therapy: a review. In Brahnham S., & Jain L. C. (Eds.) *Advanced computational intelligence paradigms in healthcare*, SCI 337 (Vol. 6, pp. 63–108). Berlin: Springer.
- Wilson, J., Onorati, K., Mishkind, M., Reger, M., & Gahm, G. A. (2008). Soldier attitudes about technology-based approaches to mental healthcare. *Cyberpsychology and Behavior*, 11, 767–769.