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TITLE: Effectiveness of Trauma Management Therapy and Prolonged Exposure Therapy for the Treatment of Post-Traumatic Stress Disorder in an Active Duty Sample: A Comparison Study

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14. ABSTRACT

This study will provide an evaluation of performance and suitability of the compressed versions of exposure psychotherapy to support the capability gap for the treatment of active duty service members and veterans with PTSD by comparing different exposure psychotherapy modalities. The overall objective of this study is to determine if compressed psychotherapy can be used as an effective alternative treatment for PTSD and to compare the impact of TMT and PE on social, familial, and occupational impairment. The primary objectives will be to compare 1) 3-week TMT with 12-week PE and 2) 3 week TMT with 2 week PE for the effectiveness of reducing PTSD symptoms in a gated approach or some other method to control for multiplicity. Outcomes will be determined based upon self-report, clinician ratings, as well as other aspects of psychopathology, and social/emotional functioning. The addition of the TMT group component will be assessed in particular to determine its impact on social, familial, and occupational impairment. The current status of the software and VR suite as a potential FDA-regulated medical device needs to be evaluated. The investigator or the company/supplier should request an IDE exemption for the study from the FDA. Blood samples should be collected from participants at baseline and at the end of the treatment period in order to identify PTSD biomarkers, e.g. predictors of response, biological subtypes of PTSD, and therapeutic markers. Collection, storage, and transfer of the blood samples to DoD should be performed according to standardized protocols provided by the DoD. One or more site visits may occur in order to assess adherence to standardized protocols.

15. SUBJECT TERMS: NONE LISTED

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Introduction

The purpose of this project is to identify an effective exposure psychotherapy paradigm for the treatment of Post-Traumatic Stress Disorder (PTSD) in active duty service members and veterans by comparing different exposure psychotherapy modalities. The long-term goal of exposure psychotherapy is to improve the mental health of U.S. service members and veterans with military-related PTSD. Recovery from PTSD will reduce the economic burden not only for those persons experiencing PTSD, but also for the health care system and society as a whole.

Keywords

- Post-Traumatic Stress Disorder (PTSD)
- Trauma Management Therapy (TMT)
- Prolonged Exposure (PE)
- Compressed Prolonged Exposure (CPE)
- Navy Medical Center Portsmouth (NMCP)
- Eisenhower Army Medical Center (EAMC)
- Navy Medical Center Camp Lejeune (NMCCL)

Accomplishments

Major Goals/Objectives

This project will evaluate the efficacy and suitability of the compressed versions of Prolonged Exposure Therapy (PE) and Trauma Management Therapy (TMT) for the treatment of active duty service members with PTSD. The objectives are as follows:

1. Determine if compressed formats of established interventions for PTSD (PE and TMT) are effective treatments for PTSD compared to PE when delivered in a standard treatment format. The efficacy will be determined at the end of the active treatment phase as well as at three- and six-months post-treatment.

2. Compare the impact of TMT and PE on social, familial, and occupational impairment.

3. Examine differences in attrition and the emergence of potential adverse events that may accompany intensive treatments, such as increased suicidal ideation or increased substance use.

4. Using blood samples collected at baseline, end of treatment, and three- and six-months post-treatment, identify PTSD biomarkers (e.g., predictors of response, biological subtypes of PTSD, and therapeutic markers).

Major activities

- Participants were admitted into the study protocol at NMCP in the beginning of the fourth quarter. However, patient recruitment and admissions were forced to cease due to the COVID19 pandemic. Personnel at NMCP are back on site and have resumed study operations. Staff members who have been credentialed at NMCCP are back on site and recruitment will begin this quarter. EAMC staff will return to site when permission is granted by site command. A decision regarding return is projected to be determined this week.

- One clinician at NMCCL completed the credentialing and onboarding process during the pandemic and is now on base ready to begin recruitment and treatment. The clinician at NMCCL who was hired at the end of the last quarter is going through the credentialing and onboarding process. At EAMC, one clinician resigned, and another has been hired this week to fill that position. The other clinician and research coordinator at EAMC are awaiting approval to return to post. Recruitment will begin at that time.

- During the pandemic, personnel at all study sites conducted practice assessments and treatment sessions and received clinical supervision daily. All sessions and supervision meetings took place via Zoom and were recorded for future use. During the supervision calls, study personnel reviewed each clinician's practice session. Feedback was provided immediately after each review.

- Research coordinators participated in a variety of online trainings to enhance their skills and abilities while they waited to return to their normal work schedules and locations. Training certificates are kept on file for later review if needed.

Specific objectives/Deliverables

Reporting

• Develop and Submit Quarterly Reports: The researchers will create a quarterly report that documents the project's activities.
Deliverable: Quarterly Reports.
Timeframe: Years 01-05, quarterly
Status: Quarterly reports have been submitted as required

• Submit Contractor Manpower Report (CMR): The researchers will create and submit a CMR annually.
Deliverable: Verification of Submission.
Timeframe: October 31 for the previous fiscal year
Status: The first and second CMRs were submitted as required and the submission was verified

• Develop and deliver a Contractor Recommended Surveillance Plan: The researchers will develop a recommended plan to evaluate the quality of the research effort within 5 days of contract award. This plan will include program metrics and success indicators.
Deliverable: Contractor Recommended Surveillance plan.
Timeframe: Year 01, Month 01
Status: Completed

• Provide Case Report Forms: The researchers will provide a Case Report Form Template for review within 3 months from contract award. The government will review to ensure appropriate and complete phenotypic information for each patient is being collected for correlation with the blood samples that USACEHR will analyze.
Deliverable: Case Report Forms.
Timeframe: Year 01, Month 03
Status: Completed

• Develop and deliver an Annual Progress Report: The researchers will create an Annual Progress Report that details the efforts related to the project for the year.
Deliverable: Annual Progress Report.
Timeframe: Year 01, Month 12
Status: Completed for Years 01 and 02

• Provide notification of contact with other agencies: The researchers will provide written notice of any anticipated meetings between research staff (including sub-contractors) and other government agencies.
Deliverable: Notifications of contact
Timeframe: As needed/as appropriate
Status: Will complete as needed

• Provide written communications related to the project: The researchers will provide copies of written communications between project staff (including sub-contractors) and other government agencies.
Deliverable: Copies of written communications
Timeframe: As needed/as appropriate
Status: Will complete as needed

Agreements, Subcontracts, and Surveillance

Initiate and complete subcontracts: UCF will complete the subcontract agreement with the Geneva Foundation and with Peter Tuerk, Ph.D.
Deliverable: Completed subcontracts
Timeframe: Year 01, Month 04
Status: Completed

Data Analysis Plan

• Develop a Data Analysis plan: The researchers have developed a data analysis plan (included with the original proposal).
Deliverable: Data Analysis Plan (included with proposal)
Timeframe: Year 01, Month 01
Status: Completed

Regulatory

• Initiate Human Subjects Approval: UCF will work with the three sites to submit all necessary Human Subjects documentation, and once IRB approval is granted at the sites, will submit that information to UCF IRB and HRPO for second-tier review.
Timeframe: Year 01, Month 01 through Year 01, Month 12
Status: Completed (HRPO approval no longer required).

• Develop a Draft Study Protocol: Within 2 months of contract award, the researchers will submit a draft research protocol to the government. After IRB approval, the final protocol will be submitted to HRPO. HRPO approval will be obtained prior to initiation of study recruitment.
Deliverable: Draft Study Protocol.
Timeframe: Year 01, Month 02
Status: Completed. HRPO approval is no longer required for studies with DOD IRBs.

• Determine and if necessary, obtain FDA device exemption: If the IRB makes the determination that the virtual reality system will require a device exemption from the FDA, the researchers will work with the FDA to obtain an IDE exemption. The exemption will be documented in the official meeting minutes from an FDA meeting.
Deliverable: Meeting minutes or notice from FDA, if deemed necessary by IRB.
Timeframe: Year 01, Month 01-09
Status: Completed

• Complete HRPO approval: UCF will submit approval from the sites by month 9, thereby allowing 3 months for HRPO approval.
Timeframe: Year 01, Month 12
Status: HRPO approval is no longer required for studies with DOD IRBs.

Personnel Management and Hiring

• Develop and submit job descriptions: Provide Geneva Foundation with job descriptions to begin clinical personnel recruitment at three performance sites.
Deliverable: Job descriptions.
Timeframe: Year 01, Month 02
Status: Completed

• Complete Hiring of Clinical Personnel: Personnel decisions for project personnel at the three treatment sites will be finalized.
Timeframe: Year 01, Month 03 through Year 01, Month 09
Status: One of the clinicians at EAMC resigned in late April. A new clinician has been hired and credentialing and training will commence this quarter.

• Complete Hiring of Support Personnel at UCF: Personnel decisions for project personnel at UCF finalized.
Timeframe: Year 01, Month 03 through Year 01, Month 09
Status: Completed

Study Preparation

• Develop a DSMB Charter: The researchers will provide a charter for the DSMB. This charter will include a plan or scheduled and unscheduled reviews of adverse events.
Deliverable: DSMB Charter.
Status: Completed

Timeframe: Year 01, Month 02
• Provide Training Manuals: The researchers will provide drafts of the training manuals associated with the proposed study within two months of contract award. The manuals will include recommendations for assessing treatment fidelity.
Deliverable: Draft Training Manuals
Timeframe: Year 01, Month 02
Status: Completed

• Develop a Randomization Plan: The researchers will develop a randomization plan that will describe the method by which random assignment will be achieved. This plan will be submitted within 3 months of contract award.
Deliverable: Randomization Plan
Timeframe: Year 01, Month 03
Status: Completed

• Develop a Data Management Manual: The researchers will develop and deliver a data management manual within 3 months of contract award. This manual will include a description of all phases of data management, including informed consent, data accuracy, and database audit plan.
Deliverable: Data Management Manual
Timeframe: Year 01, Month 03
Status: Completed

• Train Therapists in PE (both forms) and TMT: Therapists will complete training in both Prolonged Exposure and Trauma Management Therapy and reach approved criteria.
Timeframe: Year 01, Month 10 through Year 01, Month 12
Status: 4 of 6 therapists are fully trained. One therapist at NMCCL who started in January of 2020 is still being trained and the therapist who has been hired to fill the vacancy at EAMC has begun training this week. Training will be delivered over Zoom until face-to-face training is possible when travel restrictions are lifted (if needed).

• Project Coordinators Complete Phlebotomy Course: The three project coordinators will successfully complete a state approved phlebotomy course, allowing them to perform the blood draws specified in this protocol.
Timeframe: Year 01, Month 10 through Year 01, Month 12
Status: The Project Coordinators will not be collecting the blood samples but have been trained on how to ship the samples.

• All Research and Clinical Staff Trained in Study Protocol: All clinical staff will be trained in all aspects of the protocol, including all procedures and timelines, study assessments, and data handling.
Timeframe: Year 01, Month 10 through Year 01, Month 12
Status: 5 of 6 therapists are fully trained in the study protocol. The therapist who has been hired to fill the vacancy at EAMC has begun training in the study protocol this week.

• Project Coordinators Trained in Blood Protocol: The project coordinator will be trained in the specific procedures necessary to collect the blood samples as well as shipping requirements. All samples shall be shipped to a storage location at a time specified and according to procedures outlined by the USACEHR Director of Systems Biology.
Timeframe: Year 01, Month 10 through Year 01, Month 12
Status: As stated above, the Project Coordinators will not be collecting the blood samples but have been trained on how to ship the samples.

• Establish clinic space at each treatment site and begin recruitment: PI will travel to each site to assure project implementation. This will include meetings with leadership, site investigators, and research staff to assure that adequate space and all office equipment/computer equipment has been delivered and that clinicians have completed all necessary training at the site.
Timeframe: Year 02, Months 01 and 02
Status: Clinic space at all 3 sites has been established.

• VR equipment installed at each site and clinicians trained on use: Working with distributor, PI will ensure that VR systems are established at each site and clinicians are thoroughly trained in their use.
Deliverable: Documentation of training completion.
Timeframe: Year 02, Months 01 and 02
Status: 4 of 6 clinicians are fully trained in the use of the VR. One therapist at NMCCL who needs additional VR training will do so once allowed on base. The therapist recently hired to fill the vacancy at EAMC will also need to be trained.

Study Execution

• Admit and initiate treatment protocol: Each site will admit a minimum of three participants per month. Thus, a minimum of nine participants per month will be admitted to the study, as shown in the included Gantt chart.
Timeline: Year 02, Month 03 through Year 04, Month 12
Status: Five participants have been assessed at NMCP. Four met criteria for admission. Three participants have completed treatment and post assessment. Follow-up assessment is in progress for these participants. One participant did not start treatment due to Covid-19 but has completed an updated assessment and will begin treatment. Recruitment for additional participants is in progress, with one informational session scheduled this week.

• Initiate and continue patient follow-up: Project coordinator will track participants and arrange for 3- and 6-month follow-up assessments.
Timeline: Year 02, Month 07 through Year 05, Month 05
Status: Three-month follow-up assessments have been completed for 2 participants at NMCP.

• Finish 6-month follow-up assessments: Project coordinators will arrange final 6-month follow-up assessments.
Timeline: Year 05, Month 06
Status: Pending

Shipment of Blood Samples

• Work with the USACEHR Director of Systems Biology to develop blood sample collection and shipment protocol. This will be completed by 30 days prior to recruitment commencement.
Deliverable: Blood Sample Protocol
Timeframe: Year 01, Month 11
Status: Completed

• Send blood samples to USACEHR Director of Systems Biology and Notify Government of Shipment: On the last day of the month, samples will be sent to USACEHR Director of Systems Biology per protocol established in Year 01. This will include a detailed description of the data identifiers (as documented in the Case Report Form for each subject) as well as collection techniques. Notification of number of blood samples sent will be sent to the government with each monthly batch that is sent to USACEHR.
Deliverable: Blood samples and notification of shipment.
Timeframe: Monthly, Year 02, Month 03 through Year 05, Month 05
Status: Pending

Data Analysis

• Develop and deliver a Top Line Results report: Depending on the date of the final 6 month follow up assessment, this report will be delivered in month 07 or 08. The researchers will

create a Top Line Results report within 30 days of database lock. This report will provide a high-level summary of the research outcomes based on preliminary data analyses of the study.
Deliverable: Top Line Results report.
Timeframe: By Year 05, Month 07
Status: Pending

• Conduct data analyses: The statistician will conduct data analyses to examine the primary and secondary hypotheses per the Data Analysis Plan.
Timeframe: Year 05, Month 06 through Year 05, Month 11
Status: Pending

• Develop and deliver a final clinical results report: The researchers will create a final report that details all clinical results resulting from the study described in Task 12. The report will be submitted within 6 months of database lock.
Deliverable: Final Clinical Results

Status: Pending

Significant results or key outcomes

Nothing to report

Major findings, developments, or conclusions (both positive and negative)

Nothing to report

Results disseminated to communities of interest

Nothing to report

Other achievements

Nothing to report

Opportunities for training and professional development

Training of study procedures and assessments was held at DEAMC from 9/17/2019 to 9/19/2019 and at NMCCL from 10/8/19 to 10/10/2019 and from 1/22/2020 to 1/24/2020. As a result of the COVID19 crisis, study site personnel are currently receiving training and professional development via daily zoom calls.

Results disseminated to communities of interest

Nothing to report

Plans to accomplish the goals in the next reporting period

Resume recruitment and admission of study participants, as study site personnel can report to the study site locations and resume normal operations.

Admit a minimum of four participants per month at each site. Thus, a minimum of twelve participants per month will be admitted to the study. If possible, additional subjects will be recruited to make up time lost due to pandemic.

Personnel from UCF will conduct quarterly visits at each study site as UCF resumes approval of travel.

Collect blood samples at baseline, post-treatment and 3- and 6-month post-treatment.

The research coordinators will send blood samples to USACEHR Director of Systems for processing and analysis monthly.

As normal operations resume, Sandra M. Neer, Ph.D and Peter Tuerk Ph.D will provide weekly supervision to the clinicians to ensure each of the treatment protocols (TMT, PE, and CPE) are administered with fidelity.

Data from the assessments and treatment in Qualtrics will be uploaded daily and reviewed by the project coordinator for accuracy and quality.

Initiate and continue patient follow-up assessments at 3- and 6-month post treatment.

Impact

COVID-19 has had a significant impact on recruitment and treatment.

Changes/Problems

UCF:	Mr. Dalsemer's position as Project Manager has been completed
NMCP:	No changes
NMCCL:	LCDR Hauck will be leaving in July and LT Pelka is completing all paperwork to assume role as site PI; he will be added to IRB prior to beginning this role
EAMC:	Major Pittman has returned from deployment and will resume role as site PI

Products

Nothing new to report

Participants & Other Collaborating Organizations

Name:	Deborah C. Beidel, Ph.D., ABPP
Project Role:	Principal Investigator
Contribution to Project:	Dr. Beidel is overseeing the implementation of the project.
Name:	Sandra M. Neer, Ph.D.
Project Role:	Co-Principal Investigator
Contribution to Project:	Dr. Neer will supervise the day-to day-operations of the project and its development and will supervise Trauma Management Therapy treatment at all sites.
Name:	Clint Bowers, Ph.D.
Project Role:	Co-Principal Investigator

Contribution to Project: Dr. Bowers is developing the project's database and data analytic procedures.

Name: Amie Newins, Ph.D.
Project Role: Co-Principal Investigator
Contribution to Project: Dr. Newins will aid in supervision of treatment.

Name: Erynne Shatto, PsyD
Project Role: Clinician, NMCP
Contribution to Project: Assessment and Treatment

Name: Ladonna Hankins, PsyD
Project Role: Clinician, NMCP
Contribution to Project: Assessment and Treatment

Name: Monique Carter, MBS, CCRP
Project Role: Research Coordinator, NMCP
Contribution to Project: Oversee study site operations

Name: Alexandra Scott, PsyD
Project Role: Clinician, NMCCL
Contribution to Project: Assessment and Treatment

Name: Jacqueline Demarest, LPC
Project Role: Clinician, NMCCL
Contribution to Project: Assessment and Treatment

Name: Joe Dumayas, B.S., M.S.
Project Role: Research Coordinator, NMCCL
Contribution to Project: Oversee study site operations

Name: Sasha McCraw, LPC
Project Role: Clinician, EAMC
Contribution to Project: Assessment and Treatment

Name: Kimberley Banta, LPC
Project Role: Clinician, EAMC
Contribution to Project: Assessment and Treatment

Name: Cynthia Gilley, BSN
Project Role: Research Coordinator, EAMC
Contribution to Project: Oversee study site operations

Organization Name: Geneva Foundation
Address: 917 Pacific Ave, Tacoma, WA 98402
Contact: Brianna Drexler, Miranda Bethay
Project Role: Sub-award
Contribution of Project: Human Resource Development

Organization Name: Naval Medical Center Portsmouth
Nursing Research & Consultation Services
Address: 620 John Paul Jones Cir, Portsmouth, VA 23708

Contact:	Craig Cunningham, Ph.D., CNOR, CAPT/NC/USN
Project Role:	Study Site Co-PI
Contribution of Project:	Human subject participation site
Organization Name:	Naval Medical Center Camp Lejeune
Address:	100 Brewster Blvd, Camp Lejeune, NC 28547
Contact:	LT Pelka
Project Role:	Study Site Co-PI
Contribution of Project:	Human subject participation site
Organization Name:	Eisenhower Medical Center, Fort Gordon Dwight David Eisenhower Army Medical Center
Address:	300 E. Hospital Road, Fort Gordon, GA 30905-5650
Contact:	Demetrious L. Pittman, MAJ
Project Role:	Study Site Co-PI
Contribution of Project:	Human subject participation site

Special Reporting Requirements

Nothing to report

Appendices

None