

AWARD NUMBER: W81XWH-19-C-0093

TITLE: Optimizing Attention Bias Modification for Post-traumatic Stress Disorder: An Entirely Remote Study

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CONTRACTING ORGANIZATION:
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14. ABSTRACT Our overall goal is to optimize mobile app-based threat-related attentional training for posttraumatic stress symptoms (PTSS). This report summarizes work completed on the project during the second year of the award (09/01/2020-08/31/2021). In summary, we have obtained regulatory approval at our institution, obtained Human Research Protection Office (HRPO) approval, have designed, developed, and bug tested our application and online application-management backend. We have also established our study team and have finalized all standard operating procedures and protocols, including for advertising, recruitment, automated inclusion/exclusion review and randomization, patient management, team communication, documentation of participant engagement, and data management. Delays in application development took place due to the COVID-19 pandemic and transitions in managers at the development company for our mobile app, but our core team has picked up the slack, developing internal systems for bug testing, reviewing and critiquing biweekly builds of the app to ensure full functionality of all features, meeting with developers weekly or more often, creating numerous videos and documents to clarify complex features of the app and backend, and documenting all components of the app to be used in future publications. Beyond the work on the app, the core team has completed all other study preparation work, including creating all systems and codes for automatization of screening, randomization, study management, and data management, developing the study website for recruitment and dissemination, and developing protocols for all study procedures.		

15. SUBJECT TERMS Posttraumatic stress disorder (PTSD), attention bias modification (ABM), attention control training (ACT), cognitive training, mobile application			
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1. INTRODUCTION:

New treatments for posttraumatic stress symptoms (PTSS) are desperately needed because existing treatments are limited by high costs, low uptake, poor adherence and retention, negative side effects, and ineffectiveness for a large proportion of patients. Moreover, among active component service members and military veterans, stigma remains a significant barrier to traditional mental health care. Computerized cognitive training programs such as attention bias modification (ABM) target the threat-related attention biases underlying PTSS and have potential to overcome many of these issues. If effective, such applications may be particularly desirable for contexts where access to traditional mental health care is difficult or impossible (e.g., during deployment). However, there are two critical knowledge gaps that limit progress. First, emerging data indicate that PTSS may be characterized by increased attention bias variability (i.e. rapid fluctuations in attention towards and away from threat), not mere individual differences in aggregate bias towards threat. A variant of ABM called attention control training (ACT) targets such attention bias variability and may be more effective than ABM in reducing PTSS. However, only a few small studies and no remote studies have examined the effectiveness of ACT. Second, ABM and ACT either use threatening words or threatening faces as stimuli. Although some evidence indicates that words may be the optimal stimuli for ABM, few studies have actually compared ABM with words and faces and thus, critical decisions about stimuli are not evidence based. We propose to recruit individuals with clinically significant PTSS who are demographically matched to the post-9/11 military population (N = 1,056 completers; 85% male; ages 18-55) in order to test two active interventions (ABM and ACT) and optimize mobile threat-related attentional training for PTSS. People interested in taking part in the study will complete the PTSD Checklist-5 (PCL-5) and report age and gender online. We will randomize eligible participants to one of four active conditions to include ABM with words or images and ACT with words or images, or to one of two control conditions to include matched attentional training with only neutral words or images (176 participants per group). Participants will complete 14 days of training during a 4-week period. PTSS severity and threat-related attention biases (aggregate bias and variability) will be assessed at baseline, after 1 week and 2 weeks of training, and at 8 weeks. Our aims are to determine the effects of both ABM and ACT on threat-related attentional biases and PTSS severity, to determine if any positive effects are durable at eight weeks, and to compare words and faces as stimuli.

2. KEYWORDS:

Posttraumatic stress symptoms (PTSS), mobile application, remote study, attention bias modification (ABM), attention control training (ACT)

3. ACCOMPLISHMENTS:

a. What were the major goals of the project?

Major Task 1: Study Preparation and Regulatory Approval

Subtasks include: hire and train study coordinator (Completed 9/01/19); buy relevant study supplies (Completed 10/01/19); receive UCSF Institutional Review Board approval of study protocol (Completed 6/7/20); receive HRPO approval of study protocol (Completed 9/20/20); initiate for UCSF IT Risk Assessment of finalized mobile app (Completed 9/25/21).

Timeline: Months 1-4; Actual Completion: 99%

SITE: SFVAMC, PI's: Woolley, O'Donovan

Major Task 2: Complete development of study software

Subtasks include: begin upgrade of mobile application (Completed 3/17/20); provide detailed analysis of app functioning and data requirements to developers (Completed 10/31/2020); test successful functioning of study protocol in app across full two-month cycles (Completed 6/1/2021 and 8/1/2021); crash test the app across different devices (Completed 8/20/21); completed troubleshoot and debugging of the mobile application (Completed 9/1/2021); contract and construct clinical trial management system, Ripple Science (Completed 5/13/21); create code to automatically determine inclusion/exclusion and randomize participants to allow for faster participant enrollment (Completed 7/30/21); create iOS and Android developer accounts to upload

mobile app (Completed 9/15/21); finalize app and make available for future researchers (Month 36)

Timeline: Months 1-7; Actual Completion: 100%

SITE: SFVAMC+UCSF, Collaboration of all PI's: Woolley, O'Donovan, Anguera

Major Task 3: Recruit and enroll participants

Subtasks include: develop study-specific website for recruitment (Completed 08/31/21); creation of advertisements for online platforms (Completed 3/30/20); contact local organizations that can post advertisements in newsletters and develop plan for circulating flyers (Completed 6/30/21); finalize study website (Completed 8/30/21); created social media accounts for recruitment (Completed 10/25/20); place ads on social media and begin recruitment and enrollment (Predicted 10/1/2021)

Timeline: Months 7-30; Actual Completion: 10%

SITE: UCSF, Site-PI: Anguera (Collaboration with PIs Woolley and O'Donovan)

Major Task 4: De-identify and transfer data

Timeline: Month 30

SITE: UCSF, Site-PI: Anguera (Collaboration with PIs Woolley and O'Donovan)

Major Task 5: Analyze data, present poster, begin manuscript preparation

Timeline: Months 31-33

SITE: SFVAMC, PI's: Woolley, O'Donovan

b. What was accomplished under these goals?

1. Contracted a clinical trial management system, Ripple Science, and created/customized participant management console for protocol (FY2, Qtr 2-4)
 - a. Site: UCSF
2. Develop the online backend and mobile application (FY2, Qtr 4)
 - a. Site: SFVAMC
3. Initiated final review of mobile app by UCSF IT Risk Management to ensure proper safety measures to guard data have been utilized in the app (FY2, Qtr 4)
 - a. Site: UCSF
4. Finalized recruitment methods and resources by creating all materials including website, posters, ad language, and animated videos as well as finding organizations to help post advertisements in national newsletters (FY2, Qtrs 1-4)
 - a. Site: SFVAMC & UCSF

c. What opportunities for training and professional development has the project provided?

Nothing to report.

• How were the results disseminated to communities of interest?

Nothing to report.

• What do you plan to do during the next reporting period to accomplish the goals?

We plan to accomplish the following goals in our next reporting period:

1. Begin recruitment and data collection, aiming to recruit approximately 150 participants per month. Based on previous experience as well as the extensive research we have conducted regarding recruitment techniques, this is a realistic goal to reach our recruitment target by the end of the project.
 - a. Site: UCSF

4. IMPACT:

a. What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

b. What was the impact on other disciplines?

Nothing to report.

c. What was the impact on technology transfer?

The final mobile application and online backend will be delivered to the Department of Defense to allow for use by other investigators that may be able to deploy the app for future studies.

d. What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:

a. Changes in approach and reasons for change

Nothing to report.

b. Actual or anticipated problems or delays and actions or plans to resolve them

The continuing and evolving COVID-19 pandemic caused delays for the project due to unforeseeable circumstances surrounding the development of the mobile application. Specifically, the development group Code Brew Labs has had significant turnover of personnel leading to delays in the final development. Due to reduced availability of the developers, the core study team had to take over significant responsibility for bug testing, troubleshooting programming issues, and communicating across time to new developers. Now that the mobile app and online backend are completed, we will be able to recruit and run participants. We utilized the extra time we had while the development was delayed in order to strengthen and enhance our protocols and procedures, including the addition of a clinical trial management system from Ripple Science that will allow for automated participant tracking, allowing us to track hundreds of participants simultaneously. Additionally, we utilized the time to research the most effective recruitment strategies and practices, and have created all the necessary resources, including a website and animated videos that will allow us to quickly recruit our sample.

c. Changes that had a significant impact on expenditures

Due to delays associated with COVID-19, we were unable to start recruiting participants during the second year of this award. For this reason, our expenditure is less than expected as no participant costs have incurred. We expect to use these funds in the next year of the award as we will enroll a greater number of participants in the coming up year to compensate for the delay. We are fortunate in that we are planning an entirely remote study, and have enhanced our recruitment protocols over the past year. Therefore we do not expect delays in recruitment.

d. Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report.

e. Significant changes in use or care of human subjects

Nothing to report.

f. Significant changes in use or care of vertebrate animals

g. Significant changes in use of biohazards and/or select agents

6. PRODUCTS:

a. Publications, conference papers, and presentations

i. Journal publications.

1. Nothing to report

ii. Books or other non-periodical, one-time publications.

1. Nothing to report

iii. Other publications, conference papers, and presentations.

1. Nothing to report

b. Website(s) or other Internet site(s)

1. We have developed a study website to facilitate recruitment and screening as well as appropriate dissemination of study information and data.

c. Technologies or techniques

i. Both the mobile application as well as the online backend will be given to the DoD upon the completion of this project. The backend allows researchers to customize questions, duration of cognitive training, and the specific protocol for cognitive training. The mobile app collects all pertinent data. All code that is necessary to run either the application or the backend will be sent to the proper administrator as requested. Further, we will provide a written description of all functionalities of the app and backend.

d. Inventions, patent applications, and/or licenses

1. Nothing to report

e. Other Products

1. Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

a. What individuals have worked on the project?

Name: Paige Tripp
Project Role: Study Coordinator
Nearest person month worked: 22
Contribution to Project: No change

Name: Aoife O'Donovan
Project Role: Co-PI
Nearest person month worked: 13
Contribution to Project: No change

Name: Joshua Woolley
Project Role: Co-PI
Nearest person month worked: 9
Contribution to Project: No change

Name: Jennifer Mitchell
Project Role: UCSF Site PI
Nearest person month worked: 2
Contribution to Project: Dr. Mitchell has recently taken on a new role at the SFVAMC and is no longer available to work on the project. Her role as site-PI has been reassigned to Dr. Joaquin Anguera (approval received 5/14/2020).

Name: Joaquin Anguera
Project Role: UCSF Site PI
Nearest person month worked: 6
Contribution to Project: Dr. Anguera has taken over all roles and responsibilities previously held by Dr. Jennifer Mitchell

Name: Thomas Neylan
Project Role: Co-I
Nearest person month worked: 8
Contribution to Project: No change

Name: Phillip Quartana
Project Role: Co-I
Nearest person month worked: 4
Contribution to Project: No change

b. 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.

c. What other organizations were involved as partners?

1. **Organization Name:** University of California, San Francisco
2. **Location of Organization:** San Francisco, CA
3. **Partner's contribution to the project**
 - a. **Financial support;**
 - b. **In-kind support**
 - c. **Facilities:** All study procedures and activities involving identifiable participant data will be collected and accessed at the UCSF site. Only de-identified data will be transferred back to the SFVAMC for final data analysis.
 - d. **Collaboration:** Dr. Joaquin Anguera (UCSF site-PI) has provided his expertise in mobile application development and studies to ensure optimal results of the technology and protocols. All study PI's (Woolley, O'Donovan, Anguera) and the Study Coordinator collaborate to ensure the progression of preparation and oversight.
 - e. **Personnel exchanges:** The Study Coordinator will have access to Dr. Anguera's UCSF facilities while running participants through the study protocols.

f. **Other**

8. SPECIAL REPORTING REQUIREMENTS

a. **COLLABORATIVE AWARDS:**

b. **QUAD CHARTS:**

9. **APPENDICES:** *None.*