AWARD NUMBER: W81XWH-20-1-0307

TITLE: Using an Ambulatory Technology Approach to Understand Nightmares, Nightmare Enactment, and Sleep-Related Violent Behavior: Towards Precision Diagnosis in PTSD

PRINCIPAL INVESTIGATOR: Dr. Anne Richards, MD, MPH

CONTRACTING ORGANIZATION: Northern California Institute for Research and Education

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Using an Ambulatory Technology Approach to Understand Nightmares, Nightmare Enactment, and Sleep-Related Violent Behavior: Towards Precision Diagnosis in PTSD

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6. AUTHOR(S)
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5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
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13. SUPPLEMENTARY NOTES

14. ABSTRACT

PTSD occurs in 8% to 10% of civilians, and 20% to 30% of combat veterans. Sleep problems, including distressing nightmares, are present in nearly all individuals with PTSD. The goal of this study is to characterize the sleep physiological background and clinical factors which contribute to trauma nightmares, nightmare enactment during sleep, and sleep-related violent behaviors in trauma-exposed male and female U.S. military veterans. The primary scientific aims of our study are as follows: (1) To use an ambulatory, participant-administered multi-modal approach including sleep encephalogram (EEG), sleep diary app, standard wristband actigraphy with event marker, and video-recording of sleep, to examine the sleep architectural background of nightmares, nightmare enactment, and sleep-related violent behaviors; (2) To use an ambulatory, participant-administered approach including EEG, pulse oximetry, and respiratory belts, to examine the relationship between respiratory events during sleep and nightmares, nightmare enactment, and non-nightmare distressed awakenings; (3) To use a machine learning approach, utilize the full range of demographic, clinical, trauma, sleep/wake activity, sleep architectural and sleep-associated physiological data in the sample to identify independent and interacting predictors of the target sleep disturbances in the sample.

15. SUBJECT TERMS
Sleep disturbance, Nightmares, Post-Traumatic Stress, Nightmare Enactment

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	14	**19b. TELEPHONE NUMBER** *(include area code)*

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1. INTRODUCTION:

We are aiming to characterize the sleep physiological background and clinical factors which contribute to trauma nightmares, nightmare enactment during sleep, and sleep-related violent behaviors in trauma-exposed male and female U.S. military veterans. The primary aims will be (1) to use a multi-modal approach to examine the sleep architectural background of nightmares, nightmare enactment, and sleep-related violent behaviors, (2) to examine the relationship between respiratory events during sleep and nightmares, nightmare enactment, and non-nightmare distressed awakenings, and (3) to identify independent and interacting predictors of the target sleep disturbances in the sample. Trauma-exposed male and female veterans aged 18-80, and their available and consenting bed partners, will complete a two-phase study involving 3 weeks of mobile app plus actigraphy data collection (Phase 1), followed by 1-2 weeks of multi-modal assessments (Phase 2, involving sleep diary, actigraphy, EEG recordings, and video recordings) for those meeting symptom and adherence criteria in Phase 1. In combination with physiological data obtained in Phases 1 and 2, self-report surveys and chart review will provide data on multiple clinical and demographic characteristics that will contribute to analyses for Aim 3. The sample size objective is eighty (80) veteran participant completers of multi-modal assessments (Phase 2).

2. KEYWORDS:

Sleep disturbance
Nightmares
Post-Traumatic Stress
Nightmare Enactment

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Major Goals of the Project: The Primary scientific aims of our study are as follows:
Specific Aims: (1) Using an ambulatory, participant-administered multi-modal approach including sleep EEG, sleep diary app, standard wristband actigraphy with event markers, and video-recording of sleep activity, to examine the sleep architectural background of nightmares, nightmare enactment, and sleep-related violent behaviors; (2) Using an ambulatory, participant-administered approach including EEG, pulse oximetry, and respiratory belts, to examine the relationship between respiratory events during sleep and nightmares, nightmare enactment, and non-nightmare distressed awakenings; (3) Using a machine learning approach, utilize the full range of demographic (e.g., age, sex), clinical (e.g., overweight, medication use, medical history), trauma (e.g., type of trauma; time since trauma), sleep/wake activity, sleep architectural and sleep associated physiological data in the sample to identify independent and interacting predictors of the target sleep disturbances, as well as predictors of diary-reported sleep quality characteristics (e.g., sleep efficiency, total sleep time, wake after sleep onset, subjective sleep quality) in the sample.

Major Task 1 (Months 1-5): Prepare Protocol and Perform Regulatory Procedures for Study: Complete
Milestone: Local IRB approval at UCSF and VA (Target timeline: Months 1-3)
Current status: Complete as of 6/4/2020
Milestone: HRPO approval (Target timeline: Months 2-5)

Current status: Complete as of 12/15/2020

Major Task 2 (Months 1-4): Coordinate Study Staff for Study: Complete

Milestone: Research staff hired and trained (Target timeline: Months 3-4)

Current status: Complete as of December 2020

Major Task 3 (Months 5-30): Data Collection: Pending

Milestone: Study begins (Target timeline: Month 5)

Current status: Complete as of 5/14/2021

Milestone: 1st participant consented, screened, and enrolled (Target timeline: Month 5)

Current status: Pending

Milestone: Study data collection complete (Target timeline: Month 30)

Current status: Pending

Major Task 4 (Months 5-36): Data Analysis and Dissemination of Findings: Pending

Milestone: Data analysis complete (Target timeline: Month 35)

Current status: Pending

Milestone: Results Disseminated (Target timeline: Month 36)

Current status: Pending

What was accomplished under these goals?

1. Major activities: We have finalized procedural details and study materials including consent forms, procedural manuals, and assessments. Both UCSF IRB approval and HRPO approval were received. All necessary study equipment was obtained and recruitment for the study has begun. Additionally, study staff are trained on all procedures involving recruitment and data collection.
2. Specific objectives: Our specific objectives remained consistent with our major activities. During Months 1-4, we focused on hiring and training study staff and obtaining regulatory approval for the study. After, we focused heavily on preparation for study activities and beginning recruitment.
3. Significant results or key outcomes: No results to date.
4. Other achievements: None to report

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

Given COVID-related reductions in in-person training opportunities, funds were not used for this purpose during the past year.

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 will focus heavily on Major Task 3 by continuing recruitment and beginning enrollment of participants in the study. As we enroll and guide our participants through the study procedures, we may additionally adjust procedures to increase ease of data collection based on our experience recruiting.

4. IMPACT:

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

Nothing to Report.

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

Nothing to Report.

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

Sleep Diary: Our main barrier to study initiation was finalization of our Sleep Diary App. Finalizing the Sleep Diary Application took longer than we anticipated, both because of unforeseen bugs in the software development and because of unforeseen circumstances that slowed down the software developer's work. The developer's team was significantly impacted by the COVID pandemic.

- How we addressed this: Because the Sleep Diary App is an integral resource for phase 1 of the study, we were unable to begin the study until this iteration of the mobile application was complete. To compensate for these unforeseen delays, we met regularly with the software developer team and remained in constant communication with them until the application was complete. We do not anticipate that there will be any further delays in the Sleep Diary App now that the application has been completed and released.

Interviewer trainings: Unexpected turnover of clinical interviewers within the Stress & Health Research Program resulted in much reduced access to this critical resource. Our research program responded by hiring and training new clinical interviewers. During the period between the interviewers' departure and the new interviewers being fully trained, there were limited interview slots available. This resulted in a reduction in needed resources to conduct diagnostic assessments for the study.

- How we addressed this: We held off on recruiting and enrolling participants until the new interviewers were hired and had begun training to avoid having participants begin phase 1 of the study without being able to complete the clinical interview (a necessary step to continue to phase 2 of the study).

Changes that had a significant impact on expenditures

Nothing to Report.

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 human subjects

Nothing to Report.

Significant changes in use or care of vertebrate animals

Nothing to Report.

Significant changes in use of biohazards and/or select agents

Nothing to Report.

6. **PRODUCTS:**

☐ **Publications, conference papers, and presentations**

Journal publications.

Nothing to Report.

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

Nothing to Report.

Other publications, conference papers and presentations.

Nothing to Report.

☐ **Website(s) or other Internet site(s)**

Nothing to Report.

☐ **Technologies or techniques**

Nothing to Report.

☐ **Inventions, patent applications, and/or licenses**

Nothing to Report.

☐ **Other Products**

Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Anne Richards
Project Role:	PI
Research Identifier:	
Nearest person month worked:	2
Contribution to project:	No change from previous report.
Name:	Emily Staggs
Project Role:	Lab Manager
Research Identifier:	
Nearest person month worked:	2
Contribution to project:	No change from previous report.
Name:	David Baquirin
Project Role:	Co-Coordinator
Research Identifier:	
Nearest person month worked:	8
Contribution to project:	No change from previous report.
Name:	Nikhila Udupa
Project Role:	Co-Coordinator
Research Identifier:	
Nearest person month worked:	8
Contribution to project:	No change from previous report.

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?

Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: Nothing to Report.

QUAD CHARTS: See attached.

9. APPENDICES: No appendices relevant to project status attached.

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PR191120

W81XWH-20-1-0307

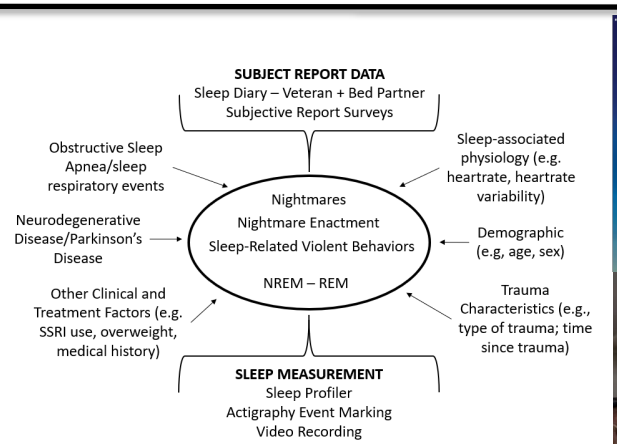
PI: Anne Richards, MD, MPH **Org:** Northern California Institute for Research and Education (NCIRE) **Award Amount: $1,816,437.00** (directs + F&A)

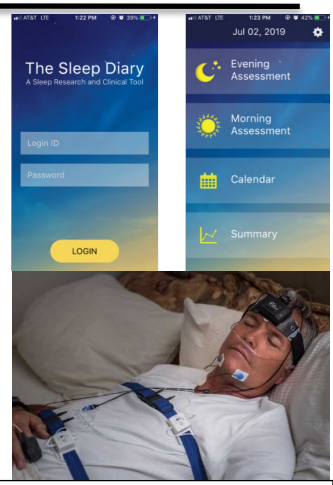
Study Aims

1. Using an ambulatory, participant-administered multi-modal approach including sleep EEG, sleep diary app, standard wristband actigraphy with event markers, and video-recording of sleep activity, to examine the sleep architectural background of nightmares, nightmare enactment, and sleep-related violent behaviors.
2. Using an ambulatory, participant-administered approach including EEG, pulse oximetry, and respiratory belts, to examine the relationship between respiratory events during sleep and nightmares, nightmare enactment, and non-nightmare distressed awakenings.
3. Using a machine learning approach, utilize the full range of in the sample to identify independent and interacting predictors of the target sleep disturbances in the sample.

Approach

Trauma-exposed male and female veterans aged 18-80, and their available and consenting bed partners, will complete a two-phase study involving 3 weeks of mobile app plus actigraphy data collection (Phase 1), followed by 1-2 weeks of multi-modal assessments (Phase 2, involving sleep diary, actigraphy, EEG recordings, and video recordings) for those meeting symptom and adherence criteria in Phase 1. In combination with physiological data obtained in Phases 1 and 2, self-report surveys and chart review will provide data on multiple clinical and demographic characteristics that will contribute to analyses for Aim 3.





Pilot work has optimized our sleep diary mobile app for collection of data on the sleep events of interest. Analysis of pilot data provides support for our primary hypothesis and compelling physiological data that will be pursued further in the current study.

Timeline and Cost

Activities CY	20-21	21-22	22-23
Prepare Protocol and Perform Regulatory Procedures			
Coordinate Study Staff for Study			
Data Collection			
Data Analysis and Dissemination of Findings			
Estimated Budget ($K)	$622,797	$629,534	$564,107

Updated: (05/28/2021)

Goals/Milestones

CY20 Goal – Perform Regulatory Procedures for Study☑
Local IRB approval at UCSF and VA
☑HRPO approval
CY20 – Coordinate Study Staff for Study
☑Research staff hired and trained
CY21-23 – Data Collection
☑Study begins
☐First participant consented, screened, and enrolled
☐Study data collection complete
CY21-23 – Data Analysis and Dissemination of Findings
☐Data analysis complete
☐Results disseminated

Budget Expenditure to Date (as of 05/21/21)
Projected Expenditure: $622,797 (directs + F&A) Actual Expenditure: $207,277 (directs + F&A)