AWARD NUMBER: W81XWH-21-1-0758

TITLE: Pilot Test of Apnea and Insomnia Relief for Veterans with Gulf War Illness

PRINCIPAL INVESTIGATOR: Linda Chao

RECIPIENT: Northern California Institute for Research and Education (NCIRE)
San Francisco, CA

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

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6. AUTHOR(S): **Linda Chao**

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7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

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8. PERFORMING ORGANIZATION REPORT

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Insomnia is a common symptom of Gulf War Illness (GWI) that can exacerbate other non-sleep GWI symptoms such as fatigue, pain, mood, cognitive dysfunction. We previously demonstrated that helping Veterans with GWI overcome insomnia with cognitive behavioral therapy for insomnia (CBT-I) not only improved sleep, but also alleviated non-sleep GWI symptoms (i.e., fatigue, cognitive failures, depression, and anxiety). We have also shown that Veterans with GWI are at greater risk for obstructive sleep apnea (OSA) compared to Veterans without GWI. Continuous Positive Airway Pressure (CPAP) is the gold standard therapy for OSA, and there is evidence that CPAP therapy can reduce symptoms of fatigue, pain, and cognitive dysfunction in Veterans with GWI and sleep disordered breathing. OSA is commonly co-morbid with insomnia and OSA together with insomnia can decrease CPAP adherence, which can negatively impact treatment and outcomes. This study will investigate whether treating OSA and insomnia in tandem will reduce GWI symptoms and improve quality of life in GW Veterans with comorbid GWI, insomnia, and OSA.

15. SUBJECT TERMS

Gulf War Illness (GWI), Obstructive Sleep Apnea (OSA), insomnia, sleep

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER	19a. NAME OF RESPONSIBLE PERSON USAMRDC
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
Unclassified	Unclassified	Unclassified	Unclassified	13	

TABLE OF CONTENTS

1. INTRODUCTION:

The goal of this project is to investigate whether treating obstructive sleep apnea (OSA) and insomnia in tandem with a behavioral intervention called Apnea and Insomnia Relief (AIR) will reduce Gulf War Illness (GWI) symptoms in Veterans with GWI and comorbid insomnia and OSA. The study's aims are to: 1) Estimate the effect size of AIR on co-primary outcomes of GWI symptoms severity, mental and physical health in Veterans with GWI and comorbid OSA and insomnia; 2) Estimate the effect size of AIR on insomnia severity and positive airway pressure (PAP) adherence in Veterans with GWI and comorbid OSA and insomnia; 3) Examine the maintenance of AIR treatment effects at 3 months.

2. KEYWORDS:

Gulf War Illness (GWI), Obstructive Sleep Apnea (OSA), insomnia, sleep

3. ACCOMPLISHMENTS:

What were the major goals of the project?

1. Obtain IRB/HRPO approval (by month 6).
2. Hire and train study staff for clinical trial (by month 6).
3. Prepare database, assessments, and randomization for trial (by month 6).
4. Recruit participants for trial (months 6-27).
5. Administer AIR and Sleep Education to study participants (months 6-27).
6. Collect study pre-, mid-, and post-intervention assessments (months7-29).
7. Analyze trial data (months 30-34).

What was accomplished under these goals?

Major activities and achievements:

1. Obtained UCSF IRB approval for protocol: 07/20/2021
2. Obtained HRPO approval for protocol: 11/02/2021
3. Finalized randomization: 01/10/2022
4. Hired and trained AIR/SE study therapist: 02/14/2022
5. Finalized sleep diary app: 02/011/2022
6. Finalized study databases and assessment measures: 02/28/2022
7. Initiated pilot Sleep Education (SE) run of trial: 03/11/2022
8. Initiated pilot AIR run of trial: 03/30/2022
9. Initiated trial proper: 06/15/2022
10. To date we have consented and enrolled 10 GW Veterans for trial; 3 participants were ineligible after clinical screening interview due to active suicidal ideation/mania/hospitalization for PTSD, 3 participants (2 AIR, 1 SE) have completed the 6-week intervention, 4 participants are currently undergoing the study interventions.

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 will continue to recruit and enroll participants for the trial, administer AIR and SE, and collect outcome data.

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

No actual or anticipated problems.

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

Significant changes in use or care of human subjects

There are no significant deviations or changes in approved protocols for the use of human subjects. The current IRB approval dates are:

Initially approved: 07/20/2021; current expiration date: 06/16/2023

Significant changes in use or care of vertebrate animals.

N/A

Significant changes in use of biohazards and/or select agents

N/A

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**

N/A

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Linda Chao
Project Role:	PI
Researcher Identifier:	0000-0002-8593-2434 (eRA Commons: lindachao)
Nearest person month worked:	1 calendar month
Contribution to Project:	Dr. Chao has been responsible for supervising all general aspects of the project, including monitoring and guiding the study progress and overseeing its direction, supervising research personnel in subject recruitment, assessment, and database management.
Name:	Thomas Metzler, M.S.
Project Role:	Study Statistician
Researcher Identifier:	N/A
Nearest person month worked:	1 calendar month
Contribution to Project:	Mr. Metzler has designed and overseen randomization of the trial. He will be responsible for the overall quality and fidelity of the data.
Name:	Dominika Swistun, Ph.D.
Project Role:	Study Interventionist
Researcher Identifier:	0000-0003-3064-8169
Nearest person month worked:	4 calendar months
Contribution to Project:	Dr. Swistun has been delivering both the AIR and the Sleep Education intervention to the pilot and the trial study participants.
Name:	Anna West, Ph.D.
Project Role:	Clinical Interview Supervisor
Researcher Identifier:	0000-0003-0390-2942
Nearest person month worked:	1 calendar month
Contribution to Project:	Dr. West has been supervising the clinical and diagnostic evaluations of all subjects recruited to establish study eligibility.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Name:	Linda Chao
Changes:	1. VA Merit grant I21CX001428 has ended. 2. VA Research Career Scientist award IK6CX002522 has been awarded to Dr. Chao (performance period 04/01/2022 – 03/31/2027). 2. Dr. Chao is now PI of VA HSR&D grant 1I0HX002764 "Preventing Loss of Independence through Exercise in Community Living Centers (PLIE-CLC)." The end date of this project is 12/31/2023. 3. DOD/CDMRP/PRAP grant W81XWH-17-1-0490 has ended. 4. Dr. Chao is now PI of DOD/CDMRP/PRAP grant W81XWH-21-1-0147 (performance period: 09/01/2021 – 09/30/2024). 5. Dr. Chao is now PI of DOD/CDMRP/GWIRP grant W81XWH-21-1-0656 (performance period: 09/01/2021-09/30/2024). 6. DOD/CDMRP/GWIRP grant W81XWH-21-1-0656 has been awarded. Dr. Chao is co-investigator. The performance period is 09/01/2022 – 08/31/2024. 7. DOD/CDMRP/GWIRP grant W81XWH-22-1-0320 has been awarded. Dr. Chao is co-investigator. The performance period is 09/01/2022 – 08/31/2025. 8. Dr. Chao's appointment with the San Francisco VA has increased from 87.5% effort to 100% effort. Her appointment with University of California San Francisco has been increased from 26.5% to 50%. Dr. Chao's combined effort may not exceed 150%.

What other organizations were involved as partners?

Name:	Lizabeth Goldstein, Ph.D.
Organization Name:	University of California, San Francisco
Project Role:	Co-investigator
Researcher Identifier:	0000-0002-2841-4120
Contribution to Project:	Dr. Goldstein has helped Dr. Chao adapt the AIR intervention for Gulf War Veterans with GWI, comorbid insomnia and obstructive sleep apnea. She has also trained and supervised the therapist in delivery of the AIR intervention.
Name:	Ashley Mason, Ph.D.
Organization Name:	University of California, San Francisco
Project Role:	Co-investigator
Researcher Identifier:	0000-0002-8744-0185
Contribution to Project:	Dr. Mason has helped Dr. Chao adapt the Sleep Education intervention for Gulf War Veterans with GWI, comorbid insomnia and obstructive sleep apnea. She has also trained and supervised the therapist in delivery of the SE intervention. She will be monitoring treatment adherence.
Name:	Rochelle Zak, M.D.
Organization Name:	University of California, San Francisco
Project Role:	Co-Investigator
Researcher Identifier:	0000-0002-8176-8622
Nearest person month worked:	calendar months
Contribution to Project:	Dr. Zak has helped to interpret HSAT results and prescribed PAP devices for study participants.

8. SPECIAL REPORTING REQUIREMENTS: N/A

9. APPENDICES: N/A