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TITLE: Sleep-Disordered Breathing in Chronic SCI: A Randomized Controlled Trial of Treatment Impact on Cognition, Quality of Life, and Cardiovascular Disease

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CONTRACTING ORGANIZATION: University of Miami

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Introduction: The impact of sleep disordered breathing (SDB) and its treatment in chronic spinal cord injury (SCI) subjects is not well known. The central hypothesis of this study was that the treatment of SDB with positive airway pressure (PAP) will improve cognitive impairment, sleep quality, and cardiovascular disease (CVD) surrogate measures in persons with chronic SCI. **Methods:** Baseline medical, sleep, demographic, and cognitive characteristics were compared between those with and without SDB. Subjects with SDB were then randomized to 4 months of PAP therapy or sham PAP (double blinded). Cognitive measures, sleep quality, mood, and inflammatory biomarkers were measured at baseline and four-month follow-up. **Results**: 63% of study participants were diagnosed with SDB. SDB was mild to moderate (AHI ≤ 15) in the majority of subjects. Insomnia symptoms were prevalent. Poor sleep quality was reported in approximately 30% of participants. There were no statistically significant differences noted in demographic, medical, and cognitive measures between those with and without SDB. There were no statistically significant, baseline or 4-month follow-up differences, in any of the cognitive outcomes in the intention to treat analysis. There was improvement in sleep quality and sleepiness in those adherent to treatment. Adherence to PAP was poor overall and a limitation that will impact effectiveness of this therapy in SCI.

15. SUBJECT TERMS
Spinal cord injury, Sleep disordered breathing, Positive airway pressure, Randomized controlled Trial, Cognitive function, Sleep Quality, Polysomnography

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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TABLE OF CONTENTS

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

There is a paucity of information on the impact of sleep disordered breathing (SDB) and its treatment in chronic spinal cord injury (SCI). Despite the increased prevalence reported in the literature, screening for SDB and its treatment are not yet standard of care. To enable change in practice, well designed randomized placebo-controlled trials (RCT) are needed to demonstrate the importance of SDB and its treatment on the health of this population. The central hypothesis of this study was that the treatment of SDB with positive airway pressure (PAP) will improve cognitive impairment, sleep quality, and cardiovascular disease (CVD) surrogate measures in persons with chronic SCI. The Specific Aims are: 1) Determine the associations between SDB and cognitive impairment and evaluate the impact of PAP therapy on cognitive measures, and 2) Determine the impact of PAP therapy on surrogate CV biomarkers, sleep quality, and mood, in a cohort with chronic SCI and SDB. This study was a four-year multi-center double blinded, placebo-controlled RCT. We objectively measured SDB in chronic SCI participants using portable unattended polysomnography, and randomized those with SDB to four months of therapeutic PAP vs. sham PAP (placebo). We measured cognitive performance (memory, attention, and executive function) using a battery of standardized neuro-cognitive tests (PASAT-primary outcome). Additionally, we measured surrogate CVD biomarkers. All measurements were done at baseline and four-month follow-up.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Spinal cord injury, Sleep disordered breathing, Positive airway pressure, Randomized controlled Trial, Cognitive function, Sleep Quality, Polysomnography

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Study Tasks

Task 1. Regulatory Approval (months 1-6)

1a. Obtain IRB approval University of Miami and Miami VA (months 1-3) **Completed**

1b. Obtain IRB approval Wayne State University and Detroit VA (months 1-3) **Completed**

1c. Obtain DoD regulatory approval (months 1-6) **Miami site Feb 25, 2014; Miami VA site April 11, 2014, Wayne State and Detroit VA: Dec 11, 2014**

1d. Obtain final project approval (month 6) **Completed for Miami site and Detroit site**

Task 2.

Elaborating Study Protocol, Training, Purchasing Equipment, and Database Design (months 1-5)

2a. Finalizing a detailed study manual explicitly outlining inclusion/exclusion criteria, protocols for recruitment, questionnaire administration, performing portable polysomnography, scoring of questionnaires, and scoring of sleep studies (months 1-5) **Completed**
2b. Design of study database (months 1-2) **Completed**
2c. Training of Research Associates in study protocol, recruitment strategies, administration of sleep and cognitive questionnaires, hook up of portable sleep study, and maintaining database (months 3-5) **Completed**
2d. Purchasing portable PSG units, auto PAP units, testing, and ensuring accurate operation (month 4-5) **Completed for University of Miami and Miami VA sites; Completed for Detroit sites March 2015.**

Task 3. Participant Recruitment, Portable Polysomnography, Randomization, Baseline Outcome Measures (months 6-40). **Participant recruitment at University Miami started in March 2014 and at the Miami VA in July 2014. Participant recruitment for Detroit site started September 2015.**
3a. Screening and recruitment of participants (months 6-40**) completed at Miami sites, completed at Detroit sites**
3b. Portable polysomnography completion (months 6-40) **completed at Miami sites, completed at Detroit sites**
3c. Polysomnography scoring and interpretation (months 6-40) **completed at Miami sites, completed at Detroit sites**
3d. Computer generated randomization (months 6-40) **completed**
3e. Completion of baseline sleep and neuro-cognitive questionnaires (months 6-40) **completed at Miami sites, completed at Detroit sites**
3f. Scoring of questionnaires (months 6-40) **completed at Miami sites, completed at Detroit sites**
3g. Medical record review to determine participant co-morbidities, and medications (months 6-40) **completed at Miami sites, completed at Detroit sites**
3h. Obtaining baseline blood and urine samples (6-40) **completed at Miami sites, completed at Detroit sites**
3i. Processing and storing of samples (6-40) **completed at all sites**
3j. Entry of results into de-identified study database (months 6-40) **completed at all sites**

Task 4. Cognitive, Sleep, Quality of Life, and Cardiovascular Outcomes (months 7-44) **completed at all sites**

4a. Completion of follow-up sleep, HRQoL, and neuro-cognitive questionnaires at 1 month (selected measures) and 4-month follow-up (months 7-44) **completed at all sites**

4b. Obtaining blood and urine samples at four-month follow-up (months 10-44) **completed at all sites**

4c. Processing and storing of follow-up samples (months 10-44) **completed at all sites**

4e. Entry of follow-up results into de-identified study database (months 7-44) **completed at all sites**

Task 5. Data Analysis, Presentations, and Manuscripts (months 40-48) **Data analysis completed. Presentations and Manuscripts in progress.**

5a. Interim baseline data accuracy and safety review (quarterly, months 6-44) **reviewed for safety and accuracy, completed**

5b. Final data analysis (months 40-48) **completed**

5c. Manuscript preparation and presentations (months 44-48) **ongoing**

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Since the last annual, and quarterly report, we have completed the study database and analyzed the data. Final analysis and write-up of a manuscript for publication is in progress. Please refer to the appendix for summary tables.

In summary, 63% of study participants were diagnosed with sleep apnea using portable polysomnography. Sleep apnea was mild to moderate (AHI ≤ 15) in the majority of subjects. However, portable polysomnography underestimates the severity of sleep apnea in the general population and likely does so in SCI population as well. Insomnia symptoms (difficulty falling asleep, early morning rising, difficulty maintaining sleep) were prevalent in study subjects regardless of diagnosis of sleep apnea (AIS score ≥ 6). Poor sleep quality was reported in both those with and without sleep apnea with 32% of those with sleep apnea and 39% of those without sleep apnea reporting fairly bad to very bad sleep quality (Table 1). There were no statistically significant differences noted in demographic and sleep characteristics (with the exception of diagnosis of sleep apnea) between those with sleep apnea (who were subsequently randomized to PAP therapy) and those without sleep apnea.

An important study conclusion (addressing Specific aim 1) was that in bivariate analyses there were no baseline differences in unadjusted cognitive function measures (Table 2) in those with and without sleep apnea. This finding held true even when controlling for age and level of education (traditionally important determinants of cognitive function). This is a negative finding, nevertheless an important

one to document. At baseline in this middle-aged population with a mean duration of injury of 13 years, no statistically significant differences in cognitive function (PASAT and other measures) was noted. Multivariable analyses also did not show sleep apnea or insomnia as an independent predictor of cognitive function in this population.

There was no statistically significant difference in baseline demographic, medical, and sleep variables in patients with chronic SCI and SDB randomized to 4 months of continuous positive airway pressure (CPAP) vs. sham therapy. There were no statistically significant, baseline or 4-month follow-up differences, in any of the cognitive outcomes in our intention to treat analysis (Table 3). In a recent 2019 publication, Berlowitz et al (*Positive airway pressure for sleep-disordered breathing in acute quadriplegia: a randomised controlled trial. Thorax. 2019 Mar;74(3):282-290*) do not report any differences in PASAT measures in acute quadriplegia after 3 months of CPAP use or usual care. Our study extends this finding to now include individuals with chronic SCI and 4 month of CPAP use. These findings hold true even after adjusting for age, level of education, adherence to CPAP, sleep apnea severity, and severity of insomnia. There was no statistically significant baseline or 4-month follow-up differences in inflammatory biomarkers in SCI patients with sleep apnea randomized to CPAP vs. Sham therapy.

Adherence to CPAP therapy (Active pressures or sham) was poor. Despite considerable effort to improve adherence through patient education, troubleshooting, mask changes, and patient motivational interviews, adherence remained poor throughout the study. This is a limitation of this study and indeed of CPAP use in the general population as well. Low PAP adherence was also reported by Berlowitz et al in acute SCI. This is likely to be more and more noted as a major limitation of sleep apnea treatment in SCI individuals. The most commonly reported complaints about CPAP in study subjects were nasal congestion, an inability to fall asleep with the mask on, no perceived benefit, and fear of suffocation with mask on, especially in those who had diminished hand function and did not have a bed partner or caregiver in the same house.

There was a clinical trend towards improvement in sleep quality and sleepiness in those subjects with sleep apnea who used CPAP more than 4 hours a night. However, due to the small sample size, no statistically significant improvement was noted. Prior studies in the general population and in SCI subjects with acute injury have concluded that in those who are adherent to CPAP, sleep quality, mood, and quality of life also improves.

In conclusion, sleep apnea, and insomnia are prevalent in subjects with SCI. These sleep disorders have a negative impact on sleep quality and perceived quality of life. In chronic SCI, no baseline cognitive differences were noted in those with and without sleep apnea. Acceptance of and adherence to CPAP was poor in all randomized subjects. We did not note any improvement in cognitive measures after 4 months of CPAP therapy. This may be due to poor adherence to therapy, small sample size, insufficient length of therapy, or indeed because neurocognitive changes noted in SCI are not significantly impacted by sleep apnea or reversible with therapy. Our study adds to the emerging body of evidence regarding the importance of sleep disorders in SCI and the challenges of therapy. Identifying the phenotype of the SCI individual with sleep apnea who would benefit from therapy is an important future area of research. Additionally, determining how CPAP adherence can be improved in this population is an important step in the effective treatment of sleep apnea in SCI.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to Report

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to Report. We are in the process of writing a manuscript for publication and abstracts for meeting presentations

If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Nothing to report.

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Many lessons learned during this study will be helpful to investigators/physicians interested in treating sleep apnea in individuals with SCI. Sleep apnea and co-morbid sleep disorders (Insomnia) are prevalent in individuals with SCI and have an impact on sleep and quality of life. Throughout the study we saw firsthand the challenges that individuals with SCI and sleep apnea face when using positive airway pressure (PAP) for treatment of sleep apnea. Adherence to PAP is poor in this population and worse than the general population. Despite educating patient about sleep apnea and PAP, encouraging patients to use PAP at several follow-up intervals, and working to troubleshoot PAP concerns, only 39% of subjects were using PAP more than 4 hours a night by end of week 1 and this number dropped to less than 30% by end of month 4. Improving adherence to this therapy in this population is an important area of future research and is a particular challenge to therapy success.

There were no baseline differences in cognitive function in those with and without sleep apnea. PAP treatment did not improve any of the baseline cognitive or cardiovascular measures during the 4 months of study therapy. Reasons for these findings are discussed elsewhere in this report.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:
- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

This study serves to increase public knowledge about sleep disorders in individuals with spinal cord injury. Sleep apnea, insomnia, and poor sleep quality are prevalent in spinal cord injury and have an impact on health and well-being. It also highlights the need to develop treatments that are more acceptable and accessible for individuals with sleep apnea and SCI as the current gold standard of therapy, positive airway pressure therapy, was poorly tolerated by many individuals in the study.

5. CHANGES/PROBLEMS: *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

No problems reported during this year. During the 4 years of the study:

- There was an initial delay in funding/project approval due to sequestration and changes in DoD regulatory personnel assigned to project. The project was approved for funding Sept 30, 2013. DoD approval of the University of Miami site occurred Feb 25, 2014 and Miami VA site April 11, 2014. Recruitment from the Miami VA was slower than anticipated One of the barriers to recruitment was transportation difficulties for subjects and lack of enthusiasm about using positive airway pressure therapy, despite education efforts.
- Subject screening and enrollment at the Detroit sites were below target. As a result, recruitment at the Detroit sites was terminated. An application for a No Cost Extension to assist in achieving target enrollment numbers at Miami site was approved Oct 2017.
- The Miami research coordinator unexpectedly left the study July 2017 with short 2 week notice to pursue other career goals. A new research coordinator was trained during the month of June and started work towards the end of July 2017.
- During the 3RD quarter in 2017, time was needed to train the new research coordinator, and obtain IRB approval for the new study personnel
- Hurricane Irma, Sept 2017, led to 2 and a half weeks where recruitment could not take place. The hurricane had a high impact on participant's ability to obtain transportation to study site even several months after the event and slowed down recruitment.
- Adherence to PAP therapy was a challenge in both study arms despite attempts at improving adherence through education, frequent subject contact and encouragement. This ultimately had the biggest impact on study conclusions

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report

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

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the

agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

No changes

Significant changes in use of biohazards and/or select agents

Not applicable

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  We are preparing a manuscript describing our findings for submission to a peer reviewed journal. In addition, we will submit an abstract of our findings for presentation at scientific meetings (American thoracic society and SCI specific meetings).

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Nothing to report

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report. Results will be available on ClinicalTrials.gov

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to Report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

None to report

- **Other Products**

  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

A de-identified database of all study variables was created and can be used for future analyses. Existing educational content for PAP was modified for this study to be more useful for individuals with SCI.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Example:

Name: *Mary Smith*
Project Role: *Graduate Student*
Researcher Identifier (e.g. ORCID ID): *1234567*
Nearest person month worked: *5*

Contribution to Project: *Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support: *The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name:	*Shirin Shafazand*
Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	4 months
Contribution to Project:	*PI, design study, responsible for overseeing all aspects of study, interpreting sleep studies*
Funding Support:	

Name:	*Daniel Samano Martin del Campo*
Project Role:	*Research Associate*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	7.5 months
Contribution to Project:	*Study coordinator, subject recruitment, responsible for conducting cognitive testing and sleep studies, data entry*
Funding Support:	

Name:	*Mark Nash*
Project Role:	*Co-investigator*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2 months
Contribution to Project:	*Assisted in study design, finalizing operations manual, database design*
Funding Support:	

Name:	*Douglas Johnson Greene*
Project Role:	*Co-investigator*
Researcher Identifier (e.g. ORCID ID):	

Nearest person month worked:	1 month
Contribution to Project:	*Training of research associates in cognitive testing, overseeing accuracy of cognitive testing*
Funding Support:	

Name:	*Safwan Badr*
Project Role:	*Co-investigator; Wayne state PI*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1 month
Contribution to Project:	*responsible for overseeing regulatory overview at Detroit sites and coordinating study procedures with Miami sites*
Funding Support:	

Name:	*Kristopher Arheart*
Project Role:	Biostatistician
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1 month
Contribution to Project:	*Assisted PI in data analysis and modelling. Responsible for generation of initial randomization code and concealment of allocation.*
Funding Support:	

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to Report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
<u>Organization Name:</u>
<u>Location of Organization: (if foreign location list country)</u>
<u>Partner's contribution to the project</u> (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ers.amedd.army.mil*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.*

9. APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*

Table 1: Subject Characteristics: Sleep Apnea vs. No sleep apnea

Baseline Characteristic	Sleep Apnea (n=47)	No Sleep Apnea (n=41)
Age, yrs*	44 ±13	40 ±13
Gender, Male, n (%)	33 (81)	43 (91)
BMI, kg/m^2*	26.2 ±5.4	25.2 ± 5.7
Level of Injury, n (%)		
C4-C7	27 (57)	15 (37)
T1-T5	12 (26)	14 (34)
T6-T12	8 (17)	11 (27)
Other		1 (2)
Duration of Injury*, years	14 ±11	13 ±11
Marital Status, n (%)		
Married/Partner	14 (30)	11 (27)
Other (Single, Divorced, Widow)	33 (70)	30 (73)
Ethnicity, Hispanic, n (%)	25 (53)	21 (51)
Race, White, n (%)	33 (70)	28 (68)
Co-Morbidities, n (%)		
Myocardial Infarction	4 (9)	3 (7)
Stroke	4 (9)	2 (5)
Diabetes	7 (2)	3 (7)
Anxiety and/or Depression	16 (3)	10 (24)
Previous History of Malignancy	1 (2)	3 (7)
Beck Depression Inventory *	10±10	8 ± 9
Beck Anxiety Inventory *	8 ± 8	6 ± 6
Insomnia (AIS)*	7 ± 5	6 ± 4
Overall Sleep Quality (PQRS)*	8.1 ± 4.5	7.9 ± 3.4
AHI *, events/hr	19.9 ±15.9	1.6 ±1.5
Sleep Duration during weekdays, hr*	6.1 ±2	6.2 ±2
Daytime Sleepiness (ESS)*	6.8 ± 4.2	6.8 ±3.9
Sleep Quality, n (%)		
Very Good	10 (21)	5 (12)
Fairly Good	22 (47)	20 (49)
Fairly Bad	11 (23)	10 (24)
Very Bad	4 (9)	6 (15)

*****Mean ± SD

Table 2: Baseline Cognitive Tests (unadjusted): Sleep Apnea vs. No Sleep Apnea

Baseline Characteristic	Sleep Apnea	No Sleep Apnea
Paced Auditory Serial Addition Test (PASAT)*, errors	17.28 ± 8.80	17.05 ± 7.56
WAIS IV- Digit span *	25.70 ± 5.59	26.65 ± 6.50
WRAT-10 (Pre-morbid intelligence) *	53.74 ±9.61	54.50 ± 11.30
Symbol digit modalities test (SDMT)*	50.09 ± 12.76	54.33 ± 8.86
Wisconsin Card Sorting Test (WCST-64)*	7.19 ±4.49	7.08 ± 4.58
Hopkin's Verbal Learning Test (HVLT) Total Recall *	22.64 ± 6.04	23.58 ± 5.48
Hopkin's Verbal Learning Test (HVLT) Delayed Recall *	7.87 ± 2.75	8.60 ± 2.71

*****Mean ± SD

Table 3: Four-month Follow-up Cognitive Function: Active vs Sham CPAP

Characteristic	Active PAP (n=19)	Sham PAP (n=15)
Paced Auditory Serial Addition Test (PASAT)*, errors	10.63 ± 7.61	15.17 ± 10.41
WAIS IV- Digit span *	26.06 ± 5.95	29.00 ± 6.76
WRAT-10 (Pre-morbid intelligence) *	54.44 ±10.11	54.08 ± 12.44
Symbol digit modalities test (SDMT)*	56.06 ± 10.31	49.54 ± 13.47
Wisconsin Card Sorting Test (WCST-64)*	6.78 ±3.32	8.42 ± 4.60
Hopkin's Verbal Learning Test (HVLT) Total Recall *	24.29 ± 4.67	22.64 ± 5.57
Hopkin's Verbal Learning Test (HVLT) Delayed Recall *	8.82 ± 2.43	7.43 ± 3.11

*****Mean ± SD