AWARD NUMBER: W81XWH-17-1-0384

TITLE: Direct Current Stimulation for Pain Treatment of Gulf War Illness

PRINCIPAL INVESTIGATOR: Sven Vanneste, PhD

CONTRACTING ORGANIZATION: University of Texas at Dallas

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The purpose of this research is to study the pain modulation pathways that are thought to be the active in Gulf War Illness veterans with pain symptoms. By studying these pathways, the study aims to find a pain treatment that can improve the pain symptoms of patients diagnosed with GWI and to better understand the mechanism of action of the pain indicators. We intend to achieve this by applying non-invasive transcranial direct current stimulation (tDCS) to patients that will be randomly assigned to active/sham groups and by using behavioral and electrophysiological measures to assess the outcome of the experiments. These measures include a test battery to depict level of pain, electroencephalogram (EEG) and resting state functional magnetic resonance (rsfMRI). We plan to consent and enroll 60 patients that will undergo the entire procedure, which consists of pre-assessments, neurostimulation, post-assessments, and follow up visits at 4 weeks, 12 weeks and 24 weeks

15. SUBJECT TERMS

Gulf War Illness, transcranial Direct Current Stimulation, pain symptoms.

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
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Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

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

The aim of our study is to develop a pain treatment that can improve the pain symptoms in patients diagnosed with Gulf War Illness veterans and to better understand the mechanism of action of the pain indicators. We intend to achieve this by applying non-invasive transcranial direct current stimulation (tDCS) to participants that will be randomly assigned to active/sham groups and by using behavioral and electrophysiological measures to assess the outcome of the experiments. These measures include a test battery to depict level of pain, electroencephalogram (EEG) and resting state functional magnetic resonance (rsfMRI). We planned to consent and enroll 60 patients that will undergo the entire procedure, which consists of pre-assessments, neurostimulation, post-assessments, and follow up visits at 4 weeks, 12 weeks and 24 weeks.

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

Gulf War Illness, transcranial direct current stimulation, pain symptoms.

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.

1. Study Approval of Regulatory Documents for use of tDCS in Therapeutic Setting
2. Recruiting and Screening Patients for the Study
3. Performing Pre-Treatment Assessments
4. Performing tDCS vs. Sham tDCS Treatment.
5. Perform Follow-up Neuropsychological and EEG assessment of Treatment Effect
6. Data Analyses
7. Dissemination of Findings - Manuscript and Report Preparation

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.

1. Recruiting and Screening Patients for the Study
    - Recruiting methods included expansive in-person and digital efforts
    - We were able to screen 48 out of the 120 planned target number of subjects to screen

2. Subject Enrollment, Performing Treatment, and Completing Pre/Post-Assessments
    - Subject enrollment continued to be a problem throughout the duration of the study despite extensive recruitment efforts. It was difficult to find participants that were willing to commit to attend all study visits and were eligible for study enrollment (veterans of the Persian Gulf war, not taking tDCS contradictory medication, MRI eligible, no substance abuse or dependency in last six months, and matching inclusion criteria based off Kansas, CDC, and Haley gulf war illness descriptions) We were only able to enroll 6 the desired 60 participants to complete this study. 2 participants were discontinued from the study after enrollment and did not complete data collection.

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.

All lab staff received professional training on the following topics: Applying tDCS in a therapeutic setting, use of EEG system, regulatory patient recruiting and screening, etiquette for interaction with patients. All lab staff also learned how to process EEG and fMRI data. Additionally, opportunities for professional speaking engagements and participation at veteran community outreach events were provided to lab staff throughout the recruitment process.

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.

Due to the number of participants enrolled in the study, we were not able to acquire enough data to have conclusive results on the viability of tDCS to improve pain symptoms in veterans with Gulf War Illness.

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).

We were able to enroll and complete data collection in four participants. All participants handled the stimulation procedure well and did not report any adverse effects. Participants reported a reduction in pain sensations after receiving treatment suggesting that some positive effect may be a result of the tDCS procedure but without more participants we are not able to draw more broad conclusions.

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.*

Throughout our efforts to recruit participants, lab staff was able to spread information to veteran and civilian populations about Gulf War Illness such as disease symptoms and current efforts in the research community to treat veterans afflicted with GWI. We were able to host lunches to spread information about GWI in Waco and around the Dallas area at which members of the veteran community could ask researchers questions. Additionally a informational segment discussing GWI was broadcasted on KWTX local news to inform others on how GWI is affecting veterans and how to support veteran clinical research.

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:*

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.

As mentioned above, there were problems with recruiting participants for this study.
Additionally recruitment was negatively impacted by COVID-19.

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

Nothing to Report.

Significant changes in use of biohazards and/or select agents

Nothing to Report.

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).*

Nothing to report.

  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.

- **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.

Nothing 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.*

Nothing to report.

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: Sven Vanneste
  Project Role: Principal Investigator
  Research Identifier: 2-9906-1836 (ORCID)
  Nearest person month worked: no change
  Contribution to project: Oversees the project, data analysis, manuscript
- Name: John Hart, Jr.
  Project role: Co-PI
  Research identifier: 3-3919-8125
  Nearest person month worked: no change
  Contribution to project: Oversees medical aspects of the study.

- Name: Jeffrey Spence
  Project role: Co-I
  Research identifier:
  Nearest person month worked: no change
  Contribution to project: Statistical support

- Name: Robert Haley
  Project role: Sub-contract PI
  Research identifier: 1-8849-9579
  Nearest person month worked: no change
  Contribution to project: Subject classification and recruitment.

- Name: Wing Ting To
  Project role: Study coordinator
  Nearest person month worked: no change
  Contribution to project: In charge of general study administration, i.e. monitors recruiting, screening and enrollment, progress of data collection, and data quality, performs assessment (questionnaires, rsfMRI, and EEG)

- Name: Alison Luckey
  Project role: Research assistant
  Nearest person month worked: 6
  Contribution to project: Recruiting and screening, administering tDCS, data processing.

- Name: Sarah Lauren McLeod
  Project role: Research assistant
  Nearest person month worked: 5
  Contribution to project: Recruiting, screening and enrollment, performs assessment (questionnaires, rsfMRI, and EEG)

- Name: Brenda Villasana
  Project role: Research assistant
  Nearest person month worked: 5
  Contribution to project: Monitors general study administration, administration of tDCS, data processing.

- Name: Anusha Mohan
  Project role: Research assistant
  Nearest person month worked: no change
  Contribution to project: Administering tDCS

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:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (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.*

- Organization: UT Southwestern Medical Center – AIRC
  Location: 5323 Harry Hines Blvd, Dallas, TX 75390
  Contribution: Facilities (facilitation of the MR equipment, MR mock room, changing room for patients).

- Organization: UTSW Department of Epidemiology
  Location: 6000 Harry Hines Blvd, Dallas, TX 75235
  Contribution: Subject recruiting and enrollment.

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.*