

AWARD NUMBER: W81XWH-16-1-0521

TITLE: Treatment of Memory Disorders in Gulf War Illness with High-Definition Transcranial Direct Cortical Stimulation

PRINCIPAL INVESTIGATOR: John Hart, Jr., MD

CONTRACTING ORGANIZATION: The University of Texas at Dallas
Richardson, TX 75080

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

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| 13. SUPPLEMENTARY NOTES | | | | | |
| 14. ABSTRACT The present study consists of the application of 1 ma anodal HD tDCS over the preSMA for 20 minutes a session for 10 sessions over a two week period. The treatment is hypothesized to lead to improvement in verbal retrieval, detectable in both performance measures of verbal retrieval tasks and in ERP markers of verbal retrieval processing. Our objective is to determine if 10 sessions of 1 ma anodal HD tDCS to the preSMA for 20 minutes a session are an effective treatment for verbal retrieval deficits in GWI. We have established the research team, laboratory setting, obtained approval of all regulatory documents for the study, and established recruiting procedures. In the past year, we have screened 31 veterans for the study and enrolled 9 in the baseline testing and treatment phase of the study; 5 have completed the study, 2 have withdrawn, and the remaining 2 are currently active in the study. | | | | | |
| 15. SUBJECT TERMS Gulf War Illness; High Definition Transcranial Direct Current Stimulation; word finding; semantic memory | | | | | |
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1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

The present study consists of the application of 1 ma anodal HD tDCS over the preSMA for 20 minutes a session for 10 sessions over a two-week period will lead to improvement in verbal retrieval that will be detectable in both performance measures of verbal retrieval tasks and in ERP markers of verbal retrieval processing. Our objective is to determine if 10 sessions of 1 ma anodal HD tDCS to the preSMA for 20 minutes a session are an effective treatment for verbal retrieval deficits in GWI.

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

Gulf War Illness; High Definition Transcranial Direct Current Stimulation; word finding; semantic memory

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. Approval of Regulatory Documents for use of HD tDCS in Therapeutic Setting
 - a. UTD IRB approval – 100% complete
 - b. HRPO approval – 100% complete
 - c. Obtain lab space, purchase and set-up HD tDCS and EEG, test units – 100% complete
 - d. Train staff in EEG and HD tDCS – 100% complete
 - e. Establish recruiting procedures – 100% complete, but we continue to expand all recruiting efforts
2. Recruiting and Screening Patients for Study
 - a. Recruitment of patients – 32% complete (38 patients recruited and screened out of 120 goal)
 - b. Screening of patients – 32% complete (38 patients recruited and screened out of 120 goal)
3. Performing Pre-Treatment Assessments
 - a. Perform pre-treatment neuropsychological assessments - 13% completed (have completed 10 out of 80 goal)
 - b. Perform pre-treatment EEGs - 13% completed (have completed 10 out of 80 goal)
4. Performing HD tDCS vs. Sham HD tDCS Treatment
 - a. Randomize patients to 10 sessions of active or sham 1 ma anodal preSMA HD tDCS - 13% completed (have completed 10 out of 80 goal)
 - b. Perform 20 minutes of active or sham 1 ma anodal HD tDCS over the preSMA region for 10 daily sessions - 9% completed (have completed 7 out of 80 goal)

5. Perform Follow-up Neuropsychological and EEG Studies of Treatment Effect
 - c. Perform post-treatment neuropsychological assessments – 8% completed (have completed 6 out of 80 goal)
 - d. Perform post-treatment EEG tests of word retrieval - 8% completed (have completed 6 out of 80 goal)
6. Data Analysis
 - a. Perform longitudinal analyses of neuropsychological and EEG measures for treatment efficacy- 0% complete
7. Dissemination of Findings – Manuscript and Report Preparation – 0% complete

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.

Recruiting Efforts

In the past year, the lab website has been completed and launched. It includes information about ongoing projects and an eligibility survey (<https://www.utdallas.edu/memory/research-participation/>) for participation in this study. We also put an advertisement on Craig’s List and have been posting frequently to our lab Facebook page with both information about Gulf War Illness and other Veterans’ issues and advertisements for recruitment. We have contracted several other web sites and Reddit groups to ask for permission to post recruitment ads, but have so far been denied.

In July we hired Dr. Elizabeth Ellen Morris to act as Project Coordinator and aid in increasing our recruitment for this project. Dr. Morris was previously working in the VA North Texas Health Care System as a Lead Research Coordinator and Licensed Mental Health Professional Counselor Supervisor. Since beginning work on the project, Dr. Morris has visited the Vet Center of Mesquite and met with the Director and two counselors. This organization provides readjustment counseling and local resources. They have displayed our recruiting materials. She has also worked with Victory Therapy Center, and equine assisted therapy organization that helps Veterans. Dr. Morris has had discussions about recruitment with Patriot Anglers, a group that takes Veterans on fishing trips to reconnect with nature and learn about relaxation, and Veteran Realty Group, a Veteran-friendly realtor. She has established relationships and presented information about our project to National Veterans Outreach, 22Kill, and several VFWs.

To increase exposure, members of this research project volunteered with Carry the Load at DFW National Cemetery and followed up a week later with a meeting with National Cemetery staff members who agreed to put out recruiting materials out for this project. Dr. Morris also met with IAVA (Iraq and Afghanistan Veterans of America) and Hooves for Heroes.

Dr. Morris has attended a second workshop with Boots to Heels – Attitudes and Attire, a

nonprofit dedicated to helping women Veterans re-enter the workforce. She also attended the day-long teleconference for the Research Advisory Committee on Gulf War Illness. This committee advises the Secretary of the VA on proposed research and helps understand & treat Gulf War Illness.

In September, co-investigator, Dr. Michael Motes, spoke at The University of Texas at Dallas Center for Vital Longevity on issues facing Veterans to bring awareness to this project.

Participants Screened, Consented, Enrolled, and Tested during this reporting period

Screened: 31

Consented, enrolled, and tested: 9

Completed: 7

In progress: 2

Stated Goals Not Met

The project is behind in enrollment, but we are making multiple efforts to increase screening and enrollment. Participants are reluctant to participate due to time/monetary costs of participating in the study or because they live too far away for 10 daily sessions of HD tDCS. Veterans suffering from Gulf War Illness have also proven to be difficult to locate. This is why we have ramped up our recruiting efforts by hiring Dr. Morris, involving more Veteran Services Organizations, expanding our social media presence, and partnering with another lab at UT Dallas that is also doing research on Gulf War Illness.

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.

Under 1. Approval of Regulatory Documents for use of HD tDCS in Therapeutic Setting, Tasks 3-5 consisted of training of staff in EEG and HD tDCS usage as well as training in recruiting procedures and regulatory issues. Training in these tasks has been successfully completed.

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.

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

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.

Continue to 2. Recruit and Screen Patients, 3. Perform Pre-Treatment Assessments, 4. Perform HD tDCS vs. Sham HD tDCS Treatment, and 5. Perform Follow-up Neuropsychological and EEG Studies of Treatment Effects. These will all be performed to meet target recruitments.

4. IMPACT: Describe 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).

Nothing to 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.*

Nothing to Report.

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:*

We will continue expansion of our recruitment efforts to VSOs and social media websites in effort to increase the number of individuals screened. These efforts so far have led to a notable increase in individuals screened. What has been noted as an impediment to enrolling in the treatment phase of the study by those screened who have not yet enrolled is the number of consecutive daily sessions of the HD tDCS treatments. Ten sessions on consecutive weekdays for 2 weeks has been cited as an obstacle to enrollment. Additionally, with the number of sessions, travel time has also been noted as an issue. We are now offering flexible scheduling (including after-work hours scheduling) to facilitate ease of participation.

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.

Nothing to Report.

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 or care of vertebrate animals

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 |
| 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: John Hart, Jr.
Project Role: PI
Research Identifier: 3-3919-8125 (Orcid)
Nearest person month worked: 1
Contribution to Project: Oversees the project.

Name: Robert Haley
Project Role: Sub-contract PI
Research Identifier: 1-8849-9579 (Orcid)
Nearest person month worked: 1
Contribution to Project: Subject classification and recruitment.

Name: Sven Vanneste
Project Role: Co-I
Research Identifier: 2-9906-1836 (Orcid)
Nearest person month worked: 2
Contribution to Project: He oversees the HD tDCS stimulation aspects of the study.

Name: Jeffrey Spence
Project Role: Co-Investigator
Nearest person month worked: 2
Contribution to the Project: Statistical support

Name: Michael Motes
Project Role: Co-Investigator
Nearest person month worked: 3
Contribution to the Project: Oversees EEG aspects of the study

Name: Julie Fratatoni
Project Role: Graduate Research Assistant
Nearest person month worked: 2
Contribution to Project: Assists in the administration of testing and assessments, EEG studies, and HD tDCS administration

Name: Elizabeth Ellen Morris
Project Role: Recruiter
Nearest person month worked: 3
Contribution to Project: Developed relationships with Veterans organization, recruits participants

Name: Scott Shakal
Project Role: Study Coordinator
Nearest person month worked: 6
Contribution to Project: He performed with Drs. Hart and Vanneste the HD tDCS administration, performed the testing of the subjects (with the assistance of the graduate student), and assisted with EEGs

Name: Deborah Modesette
Project Role: Study Coordinator
Nearest person month worked: 3
Contribution to Project: Located current telephone numbers, contacted, and monitored the enrollment process for the subjects

Name: Kylee Yeatman
Project Role: Research Assistant
Nearest person month worked: 3
Contribution to Project: Screens participants, administers HD tDCS, administered EEGs

Name: Rachel O'Hair
Project Role: Research Assistant
Nearest person month worked: 3
Contribution to Project: Screens participants, administers HD tDCS, administered EEGs

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.

Ended 3/31/2018: Identifying and Characterizing Auditory Processing Disruptions in Multiple Sclerosis, National Multiple Sclerosis Society, 0.6 calendar months

Began 8/1/2018: Multi-site Confirmatory Efficacy Treatment Trial of Combat-related PTSD, Department of Defense, 1.20 calendar months

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.*

UTSW Department of Epidemiology
6000 Harry Hines Blvd.
Dallas, TX 75235
Collaboration: 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.*