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

REPORT DATE: October 2022

TYPE OF REPORT: Annual Report

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

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2022	Annual	30 Sep 2021 - 29 Sep 2022

4. TITLE AND SUBTITLE

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

5a. CONTRACT NUMBER
W81XWH-16-1-0521

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Dr. John Hart Jr.
E-Mail: jhart@utdallas.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
The University of Texas at Dallas
800 W Campbell RD
Richardson TX 75080-1407

8. PERFORMING ORGANIZATION REPORT NUMBER

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

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

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

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, maintained approval of all regulatory documents for the study, and established recruiting procedures. We have recruited 77 subjects for the study and enrolled 27 out of 80 subjects. Twenty-one subjects have completed treatment.

15. SUBJECT TERMS
Gulf War Illness; High Definition Transcranial Direct Current Stimulation; word finding; semantic memory

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	9	19b. TELEPHONE NUMBER *(include area code)*

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

TABLE OF CONTENTS

1. INTRODUCTION:

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:

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

3. ACCOMPLISHMENTS:

What were the major goals of the project?

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 – 64% complete (77 patients recruited and screened out of 120 goal)
    b. Screening of patients – 64% complete (77 patients recruited and screened out of 120 goal)
3. Performing Pre-Treatment Assessments
    a. Perform pre-treatment neuropsychological assessments - 34% completed (have completed 27 out of 80 goal)
    b. Perform pre-treatment EEGs - 34% completed (have completed 27 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 - 28% completed (have completed 22 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 - 26% completed (have completed 21 out of 80 goal)

5. Perform Follow-up Neuropsychological and EEG Studies of Treatment Effect
    c. Perform post-treatment neuropsychological assessments – 26% completed (have completed 21 out of 80 goal)
    d. Perform post-treatment EEG tests of word retrieval - 26% completed (have completed 21 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?

We have established the research team and laboratory settings, maintained continued approval of all regulatory documents for the study, and refined recruiting procedures.

We have recruited 77 subjects for the study and enrolled 27 out of 80 subjects. Twenty-one subjects have completed treatment. To increase enrollment and completed treatment numbers, we received a no cost extension for the project until 29 September 2023.

The COVID-19 pandemic continuous to impact recruitment. However, we continue to grow our recruiting network and social media presence. We have reconnected with VSOs in the area and are active with the Dallas VA. This year we successfully launched ad campaigns to promote other studies on Facebook and Instagram which has increased visibility of the lab and this study. Three participants were screened this year and two are pending pre-treatment assessments.

<u>Participants Screened, Consented, Enrolled, and Tested during this reporting period</u>
Screened: 3
Consented, enrolled, and tested: 0
Completed: 0

<u>Stated Goals Not Met</u>

Recruitment continues to be an issue. We resumed human subject research in September 2020, but the pandemic continues to have an impact on enrollment. We are working with other Veteran Research labs and organizations to share ideas and seeking new avenues to recruit.

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 focus on recruiting efforts by actively pursuing partnerships with VSOs and seeking other avenues of recruitment. We are considering utilizing a targeted recruitment strategy via Facebook and Instagram that has proven successful for other Veteran studies in our lab.

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?

We have made presentations to various agencies about our project and Gulf War Illness to create awareness of both.

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

Covid-19 pandemic has impacted recruitment, and we are realistic about the lasting effects of the pandemic. We are constantly working to improve recruitment and reach our overall recruitment goals.

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

Nothing to Report.

Significant changes in use or care of vertebrate animals

Nothing to Report.

Significant changes in use of biohazards and/or select agents

Nothing to Report.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications.

Nothing to Report.

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

Nothing to Report.

- **Other publications, conference papers and presentations.**

Nothing to Report.

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

Nothing to Report.

- **Technologies or techniques**

Nothing to Report.

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

Nothing to Report.

- **Other Products**

Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: John Hart, Jr., MD, Principal Investigator – no change

Name: Michael Motes, PhD, Co-Investigator, PhD – no change

Name: Jeffrey Spence, PhD, Co-Investigator – no change

Name: Elizabeth Ellen Morris, PhD, Project Coordinator – no change

Name: Kelsey Watson, Research Assistant – no change

Name: Jared Brooks, Veteran Outreach Coordinator – no change

Name: Jill Ritter, Coordinator – no change

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

Nothing to Report.

What other organizations were involved as partners?

Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *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.*