AWARD NUMBER: W81XWH-16-1-0610

TITLE: Improving Cognitive Function in Veterans with Gulf War Illness by Improving Cerebral Vascular Function

PRINCIPAL INVESTIGATOR: Jorge M. Serrador, PhD

RECIPIENT: Veterans Biomedical Research Institute
East Orange, NJ 07018

REPORT DATE: October 2017

TYPE OF REPORT: Annual

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

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED *(From - To)*
October2017	Annual	15 Sep 2016 - 14 Sep 2017

4. TITLE AND SUBTITLE

Improving Cognitive Function in Veterans with Gulf War Illness by Improving Cerebral Vascular Function

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-16-1-0610

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Jorge M. Serrador, PhD

Kelly Brewer, MS

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Veterans Biomedical Research Institute

385 Tremont Ave.
East Orange, NJ 07018

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel 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
As our research team received DoD HRPO approval on Jun. 21, 2017 but our lab was placed on suspension until Aug. 7, 2017, no subject research has taken place. Therefore, we are unable to provide any significant findings during this research period.

15. SUBJECT TERMS None listed

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

TABLE OF CONTENTS

Page No.

INTRODUCTION. 4
KEYWORDS. 4
ACCOMPLISHMENTS. 4
IMPACT 7
CHANGES/PROBLEMS 8
PRODUCTS 9
PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS 11
SPECIAL REPORTING REQUIREMENTS 13
APPENDICES 13

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

The purpose of this study is to investigate a relationship between cognitive impairment in Veterans with Gulf War Illness (GWI) and reduced vasodilatory function. One of the multiple symptoms reported by Veterans with Gulf War Illness is cognitive impairment. Though it has been shown that proper blood flow is necessary for good cognitive function, little is known about blood vessel function in the brain of those Veterans who report cognitive impairments. Understanding how cognitive function is linked to cerebrovascular ability to vasodilate is potentially important in establishing vasoreactivity as a therapeutic target for treating cognitive impairments in Veterans with GWI.

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

Cerebrovascular, cognitive, neurovascular coupling, cerebral blood flow, Gulf War Illness

3. ACCOMPLISHMENTS: The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer 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.

Major Task 1: Establish Project Management System and Training Plan

Subtasks:

a) Train staff on study procedures: Kansas screening, neuropsychology battery, cerebral vascular measurements, biomarker measurements (Sept 2016-Dec 2016)
- 100% complete (Jun 2017)

b) Obtain IRB and Human Research Protection Office approvals (Sept 2016-Dec 2016)
- 80% complete

c) Develop and implement recruitment plan: Distribute flyers, recruitment mailings, contact VSOs for outreach assistance (Dec 2016 – June 2017)
- 10% complete

Major Task 2: Determine whether Cerebral Vascular Blood Flow and/or levels of 8-iso-PGF2alpha can predict cognitive and/or vascular dysfunction.

Subtasks:

a) Screen and enroll participants for initial visits (Feb 2017 – Mar 2018)
b) Neuropsychology and oxidative stress battery collection (Feb 2017 – Mar 2018)
c) Cerebral blood flow measurements and Letter/Number Sequencing Test (Feb 2017 – Mar 2018)
d) Data analysis (Feb 2017- April 2018)
e) Publish data (June 2018)

Major Task 3: Cerebrovascular function after COX inhibition via Indomethacin

Subtasks:

a) Subject testing using drug/placebo (May 2018- Mar 2019)
b) Oxidative stress battery analysis (May 2018- Mar 2019)
c) Cerebral blood flow measurements and Letter/Number Sequencing Test (May 2018- Mar 2019)
d) Data analysis (May 2018- April 2019)
e) Publish data (July 2019)

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. Major Activities:
   a) VANJ IRB approval for study including Research Monitor granted on Oct. 13, 2016.
   b) VANJ IRB documents submitted for HRPO approval on Jan. 11, 2017.
   c) HRPO approval for study granted on Jun. 21, 2017.
   d) Rutgers IRB documents submitted for approval on Sep. 7, 2017

2. Specific Objectives within this quarter
   a) Obtain IRB and Human Research Protection Office approvals for testing at Rutgers.

3. Significant Results of Key Outcomes
   a) Testing has not begun due to not having an approved IRB protocol at Rutgers. Documents will be submitted for HRPO approval once local approval is granted.

4. Other Achievements
a) Due to Dr. Serrador's expanding Gulf War Illness focus, Rutgers University has provided the lab with a newly renovated 700 square foot suite, located in the Doctors Office Complex (DOC), within the University Hospital complex. The space was specifically chosen to provide easier access to subjects and to support expansion of Veteran's programs.

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.

This project has provided training for research staff to be educated on neuropsychological testing procedures as well as enhancing competency in obtaining cerebrovascular and physiological practice measurements prior to subject data collection. The post-doctoral fellow has been able to develop skills pertaining to the regulation of human subject testing and safety documentation to be use going forward. Graduate students are receiving education and hands-on training to be able to perform physiological measurement capture and analysis of data.

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.

1) Obtain IRB and HRPO approval to begin study at Rutgers. 2) Execute recruitment strategy by initiating contact with veterans. 3) Begin recruitment and data collection. 4) Data analysis.

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 Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer 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.

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.

There were no changes in expenditures.

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 to use of care of human subjects to report. - VANJ IRB approval was granted on Oct. 13, 2016. - HRPO approval was granted on Jun. 21, 2017.

Significant changes in use or care of vertebrate animals.

No animal use research will be performed to complete the Statement of Work

Significant changes in use of biohazards and/or select agents

No biohazards and/or select agents will be used to complete the Statement of Work

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. In addition to a description of the technologies or techniques, describe how they will be 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. State whether an application is provisional or non-provisional and indicate the application number. 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;*
  - *biospecimen collections;*
  - *audio or video products;*
  - *software;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *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."

Name: Jorge Serrador, PhD
Project Role: PI
Nearest person month worked: 0.5
Contribution to Project: Dr. Serrador has been overseeing all aspects of the project including the human subject's regulatory requirements including IRB and HRPO submissions. Dr. Serrador is overseeing all aspects of data collection and analysis.

Name: Allan Knox, PhD
Project Role: Post-doctoral candidate
Nearest person month worked: 1.0
Contribution to Project: Dr. Knox has been developing the protocol for IRB submission at Rutgers University and will be involved in all aspects of data collection, analysis, and publication.

Name: Kelly Brewer, MS
Project Role: Study Coordinator
Nearest person month worked: 0.5
Contribution to Project: Kelly has been generating documents for the VA NJ IRB and HRPO submissions. She has also assisted in training staff on study procedures and will assist in data collection and analysis.

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.*

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating 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.