AWARD NUMBER: W81XWH-19-1-0381

TITLE: Autonomic Dysfunction, Brain Blood Flow, and Cognitive Decline in Veterans with Gulf War Illness

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CONTRACTING ORGANIZATION: University of Wisconsin-Madison

REPORT DATE: JULY 2021

TYPE OF REPORT: Annual

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
JULY 2021	Annual Report	1 JULY 2020 - 30 June 2021

4. TITLE AND SUBTITLE

Autonomic Dysfunction, Brain Blood Flow, and Cognitive Decline in Veterans with Gulf War Illness

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-19-1-0381

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

University of Wisconsin-Madison
Madison, WI 53715

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 incidence of multi-symptom illness or Gulf War Illness (GWI) in the Veterans deployed during the Gulf War is estimated to be 25-32%. The primary goal of this project is to examine cerebral blood flow responses to chemical and metabolic stress in Veterans with GWI compared with age and deployment-matched Veterans. We hypothesize that GWI is associated with both vascular dysfunction in the cerebral circulation and autonomic dysfunction. Participants will take part in a laboratory visit for autonomic function testing, and a magnetic resonance imaging scan (MRI) visit to determine brain structure and intracranial blood flow measurements at rest and in response to physiological stress. These experiments represent a novel and comprehensive approach and address fundamental and significant unresolved physiological questions in how GWI affects the human brain, with relevance to GWI symptoms.

15. SUBJECT TERMS
Gulf War Illness; Middle Aged; Neuroimaging; Autonomic; Cerebral Blood Flow

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
Unclassified	Unclassified	Unclassified	Unclassified	7	19b. TELEPHONE NUMBER *(include area code)*

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1. Introduction

The incidence of multi-symptom illness or Gulf War Illness (GWI) in the Veterans deployed during the Gulf War is estimated to be 25-32%. As Veterans from the Gulf War grow older, they may develop age-related conditions earlier and have a premature onset of disability. Importantly, many of the pathophysiological changes associated with GWI may increase the risk of developing Alzheimer's disease (AD) or other dementias. Altered regulation of cerebral blood flow is likely a key mechanism underlying the cognitive complaints in Veterans with GWI. In addition, autonomic dysfunction has been associated with GWI and this may be functionally linked to the impairment in cerebral blood flow regulation. Cerebral blood flow responses to chemical and metabolic stress will be measured in Veterans with GWI compared with age and deployment-matched Veterans. This project will be the first step in providing critical information and establish a proof-of-concept regarding the pathophysiology of GWI.

2. Keywords

Gulf War Illness; Middle Aged; Neuroimaging; Autonomic; Cerebral Blood Flow

3. Accomplishments

The major goals of this project include: (1) to determine if Veterans with GWI demonstrate vascular dysfunction in the cerebral circulation and impaired neurovascular coupling of blood flow with metabolic demand, compared with controls (n=30); (2) to determine if Veterans with GWI (n=30) demonstrate autonomic dysregulation compared with controls (n=30); (3) to determine if impaired cerebrovascular and autonomic variables in Veterans with GWI are associated with neuroimaging biomarkers of cognitive decline.

Our first major task on the Statement of Work for this project was to obtain the necessary human subject approvals. This project has obtained local IRB approval, HRPO approval along with ClinicalTrials.gov registration. This first major task is 100% complete. As we were beginning to prepare for our next two major tasks, training in study-specific protocols for trainees and students and initiating participant recruitment, our institution suspended all face-to-face human subjects research due to the COVID-19 pandemic. It is estimated that we are 70% complete in training on study-specific protocols and on physiological measurements. We are 20% complete in participant recruitment as recruitment flyers and documents have been prepared along with a list of organizations to contact to initiate recruitment.

Due to the COVID-19 pandemic, laboratory polices have been revised in terms of use of personal protective equipment (PPE), social distancing, and preparation, use and cleaning of equipment. Obtaining PPE supplies and the revision of polices has taken a significant amount of time due to the availability of resources. In addition, the laboratory obtained a revised system to use disposable, single-use masks for participant visits. The use of this device requires specialized training for proper use. We are currently in the process of training laboratory staff. The laboratory was approved to restart human subjects research procedures on March 25, 2021. The research team was approved to return to regular work in the laboratory in June 2021. We expect to initiate participant recruitment in September 2021.

During the next reporting period, we plan to complete training of students and staff, initiate participant recruitment and begin data collection. This will allow continued progress in working towards the major goals of the project.

4. Impact

This study received local IRB approval and HRPO approval in late February 2020. The University of Wisconsin-Madison shut down research laboratories and suspended all face-to-face human subject research in early March 2020. We received approval to restart human subjects research on March 25, 2021. We expect to initiate participant recruitment in September 2021. Therefore, at this time, there are no results or significant impacts to report.

5. Changes/Problems

Due to the COVID-19 pandemic, there has been a delay in training of laboratory staff and initiating participant recruitment. The laboratory was shut-down due to the COVID-19 pandemic from March 13, 2021 to March 25, 2021. On March 25, 2021, we were approved to resume human subject research processes and laboratory staff were allowed to return to work in the laboratory in June 2021. We are currently in the process of purchasing necessary PPE, laboratory supplies, training of laboratory staff and performing pilot testing. Because of the length of time that the laboratory was shut down, we have also had to recalibrate all equipment. While it is our goal to initiate recruitment in September 2021, it will take some time to obtain supplies that are now necessary due to the COVID-19 pandemic (particularly PPE and disposable supplies such as respiratory filters). It will also take time to train members new to the laboratory on procedures and practices, before initiating participant recruitment.

As mentioned above, due to new COVID-19-related requirements for safe research participant testing, we now need more disposable supplies per participant study visit. In the past, we could sterilize and re-use equipment such as respiratory masks, but now we are required to move to single-use masks and tubing, which comes at a significant supply cost.

6. Products

Nothing to Report.

7. Participants & Other Collaborating Organizations

Name:	Jill Barnes, PhD
Project Role:	PI
Researcher Identifier:	0000-0001-6317-4153
Nearest person month worked:	Effort: 2 months Funding: 1 month
Contribution to Project:	Dr. Barnes has performed work in the area of obtaining local IRB approval, HRPO approval, equipment calibration, and training of trainees and students.
Funding Support:	Funding for protected research time provided by the University of Wisconsin-Madison

Name:	Anna Howery, MS
Project Role:	Research Associate
Researcher Identifier:	
Nearest person month worked:	Effort: 3 months Funding: 3 months
Contribution to Project:	Ms. Howery has performed work in the area of obtaining local IRB approval, HRPO approval, revising study-specific protocols to comply with COVID-19-related regulations, performing equipment calibration, ordering PPE and supplies, and training of trainees and students.
Funding Support:	University of Wisconsin-Madison

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

Yes. The PI had a previously active grant close (Alzheimer's Association 17-499398, closed 12/31/2020) and a pending grant (NIH/NINDS RF1 NS117746) was awarded with the PI effort at 25% effort.

What other organizations were involved as partners?

Nothing to Report.

8. Special Reporting Requirements

None.

9. Appendices

None.