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

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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					
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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 along with HRPO approval. As we were beginning to prepare for our next two major tasks, training of trainees and students and initiating participant recruitment, our institution suspended all face-to-face human subjects research due to the COVID-19 pandemic. Therefore, we were unable to proceed in accomplishing these tasks. As data has not been collected at this time, there is nothing to report in terms of the dissemination of results to communities of interest.

During the next reporting period, we plan to complete training of students and staff, initiate participant recruitment and begin data collection. This will allow us to begin 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. Due to this, we have been unable to initiate participant recruitment and data collection. Therefore, at this time, there are no results or significant impacts to report.

5. Changes/Problems

There has been a delay in training of laboratory staff and initiating participant recruitment due to the suspension in face-to-face human subject research at the University of Wisconsin-Madison, and the move to working from home related to COVID-19 pandemic. Because of this, we were unable to spend the funds during this budget year and are planning to ask for a no-cost extension due to COVID-19. While it is our goal to initiate recruitment once the suspension is lifted, it will take some time to obtain necessary supplies (particularly PPE), train laboratory members on procedures and practices, and initiate participant recruitment.

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:	1
Contribution to Project:	Dr. Barnes has performed work in the area of obtaining local IRB approval and HRPO approval.
Funding Support:	University of Wisconsin-Madison

Name:	Anna Howery, MS
Project Role:	Research Associate
Researcher Identifier:	
Nearest person month worked:	1
Contribution to Project:	Ms. Howery has performed work in the area of obtaining local IRB approval and HRPO approval.
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 (NIH K99/R00 118154) and a pending grant (American Heart Association Innovative Project Grant 191PLOI34680015) 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.