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TITLE: Assessing Neuroinflammation in Gulf War Illness with Whole-Brain Magnetic Resonance Spectroscopy

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CONTRACTING ORGANIZATION: University of Alabama, Birmingham, AL

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13. SUPPLEMENTARY NOTES

14. ABSTRACT
Currently, there are no targeted treatments for Gulf War Illness (GWI). In order to solve that problem, it is essential that researchers discover the cause of GWI. It is similarly important that an objective test be developed that can clearly show why individuals suffer from GWI. While many attempts at developing such a test have been made, none of them have yielded a clinically-useful tool. Our central hypothesis is that GWI involves chronic neuroinflammation. The symptoms of GWI (e.g. fatigue, musculoskeletal pain, sleep disturbances, and cognitive dysfunction) overlap heavily with classic cytokine-induced sickness responses. In the case of GWI, microglial cells in the brain can be pushed into a hypersensitized state by toxins or abnormal immune challenges, leading to chronic overproduction of pro-inflammatory factors that result in the primary symptoms of GWI.
To test the central hypothesis, it is necessary to measure neuroinflammation in humans in vivo. However, most techniques are too invasive for using in living individuals. To address that problem, we use an MRSI scan which provides metabolite concentrations in 4,000 separate voxels, giving whole-brain coverage. The scan yields measurements for: myo-inositol (a marker of glial cell proliferation), lactate (a product of anaerobic metabolism), choline (a sign of cellular breakdown), and N-acetylaspartate (a marker of neuronal health). The scan also provides absolute brain temperature, which is elevated with severe neuroinflammation.

15. SUBJECT TERMS
Gulf War Illness

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TABLE OF CONTENTS Page

1. **Introduction** 4
2. **Keywords** 4
3. **Accomplishments** 4
4. **Impact** 5
5. **Changes/Problems** 5
6. **Products** 5
7. **Participants & Other Collaborating Organizations** 6
8. **Special Reporting Requirements** 6
9. **Appendices** 6

Introduction

The primary objective of this study is to determine if Gulf War Illness (GWI) likely involves neuroinflammation. By assessing the five neuroinflammatory outcomes across the brain, we can determine if there are focal or global signs of one or more neuroinflammatory markers in brains of individuals with GWI. The magnetic resonance spectroscopy imaging (MRSi) technique may allow our group and others to detect cases of GWI neuroinflammation, which would improve treatment decisions as well as the development of new targeted therapies. It is an ideal diagnostic tool because it has low patient risk, is noninvasive, can be used repeatedly in longitudinal studies, provides whole-brain coverage, yields multiple independent markers of inflammation, and can be employed at most hospital and research neuroimaging suites.

Keywords

Gulf War Illness, neuroinflammation, neuroimaging

Accomplishments

What were the major goals of the project?
The major goal of this work is to determine if GWI involves neuroinflammation. Our milestones for study activities are as follows:

	Target Date
Agreement on eligibility criteria, screening protocol, and procedures	July 2019
Consent form and human subjects protocol finalized	July 2019
All UAB, HRPO, and other approvals granted	August 2019
Study protocol ready to begin	August 2019
First participant enrolled	December 2019
20 GWI participants enrolled	May 2022
20 control participants enrolled	June 2022
Results reports generated	August 2022
Report full results from all analyses	August 2022

What was accomplished under these goals?
We received all regulatory approval and were ready to begin enrollment in October 2020. As of now, 17 participants (11 GWI; 6 controls) have been enrolled in the study and completed the protocol. We are currently at 43% of our target enrollment goal. Our recent progress has positioned us to accomplish our enrollment goal of 40 participants by June 2022.

What opportunities for training and professional development has the project provided?
Nothing to report

How were the results disseminated to the communities of interest?
Nothing to report

What do you plan to do during the next reporting period to accomplish the goals?
We plan to conduct radio and digital advertisement campaigns to recruit both healthy and GWI participants. Currently, we have one research coordinator for the study and 2 undergraduate students assisting with the study.

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?
Nothing to report

Changes/Problems

Changes in approach and reasons for change
There have been no changes in approach

Actual or anticipated problems or delays and actions or plans to resolve them
We have recently launched a radio marketing campaign with iHeartMedia, a media company with access to more than 860 radio stations nationwide and over 150 million registered listeners on their digital streaming platform. We have had success with iHeartMedia advertising services in the past for our other clinical studies and are confident that this campaign will bolster enrollment.

Changes that had significant impact on expenditures
We are now able to use funds as originally intended, without restrictions.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Nothing to report

Products

Publications, conference papers, and presentations
Nothing to report

Books or other non-periodical, one-time publications
Nothing to report

Other publications, conference papers, and presentations
Nothing to report

Website
Nothing to report

Technologies or techniques
Nothing to report

Inventions, patent applications, and/or licenses
Nothing to report

Other products
Nothing to report

Participants and other collaborating organizations

Name	Jarred Younger, PhD	Crystal Taylor, PhD	Chloe Jones
Project Role	PI	Manager	Study Coordinator
Researcher Identifier (ORCID)	0000-0003-3616-9919	0000-0001-8359-071X	0000-0002-7288-8235
Nearest person month worked	2	1	
Contribution to project	Dr. Younger has developed protocol for execution of study	Dr. Taylor has drafted and submitted all regulatory documents for the study	Chloe has screened and scanned all participants for this study.
Funding support	AFSA, R01NS109529 (NIH/NINDS), GWI180071 (DOD),	American Fibromyalgia Syndrome Association (AFSA)	UAB

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

Yes, there has been a change in the active other support of the PI. The grant entitled “Daily Immune Monitoring in Chronic Fatigue Syndrome” (R01AI107655) ended September 1, 2020.

What other organizations were involved as partners?
Nothing to report

Special reporting requirements
Nothing to report

Appendices
Nothing to report