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TITLE: **Glutamate Neuroexcitotoxicity in GWI**

PRINCIPAL INVESTIGATOR: **Kathleen Holton, PhD, MPH**

CONTRACTING ORGANIZATION: **American University**
Washington, DC 20016

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The objective of the proposed research is to examine whether dietary exposure to food additives containing glutamate may be contributing to symptoms in Gulf War Illness (GWI). The rationale for proposed study comes from data in the fibromyalgia field which suggests that reducing the consumption of dietary glutamate can reduce over-excitation in the nervous system, leading to symptom improvement. Since there is almost complete symptom overlap between fibromyalgia and GWI, it is of utmost importance to test this diet as a low-cost treatment option in GWI patients. Thus far, we have enrolled 16 subjects into the study and have 4 more people scheduled for their initial visit in the upcoming months. Overall, we are still on pace to recruit a total of 40 subjects in the timeline indicated in our SOW.

15. SUBJECT TERMS Gulf War Illness, GWI, glutamate, diet, nutrition, intervention					
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INTRODUCTION: This is a treatment grant being completed to examine the effect of using a low glutamate diet as a low-cost treatment option for Gulf War veterans who are suffering from Gulf War Illness (GWI). We are recruiting 40 subjects from across the US who are currently suffering from symptoms according to the Kansas City criteria for GWI. We have completed the first year of the 3-year grant and are on target to complete enrollment on time according to our SOW.

KEYWORDS: Gulf War Illness, GWI, multi-symptom illness, neurological symptoms, glutamate, diet, intervention, nutrients, nutrition

ACCOMPLISHMENTS: We currently have 16 people enrolled in the study, 13 people have completed their participation, and we have scheduled 4 additional subjects in the upcoming months. Overall, we are accomplishing our goal of timely recruitment in the first year of the study. We should be half way done with recruitment by January 2019.

What were the major goals of the project?

The major goals of the project for year 1, as stated in the approved SOW, included:

1. Getting IRB approvals – 100% completion
2. Registering the study with clinicaltrials.gov – 100% completion
3. Recruiting, scheduling, and collecting data on 15 subjects – we have enrolled 16 subjects to date, so we are ahead of schedule.

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 – included getting IRB approvals, registering the study with clinicaltrials.gov, recruiting/scheduling subjects from across the US into the study, and collecting data on participants.
2. Specific Objectives – our objective was to recruit 15/40 subjects by the end of year 1
3. Significant Results - thus far, we have enrolled 16 subjects, so we are slightly ahead of schedule for recruitment.

   Due to the second part of the study being a double blind, placebo controlled, crossover challenge, we cannot yet look at that data. However, below is some preliminary data on the improvements we are seeing when comparing baseline to post-diet measures (Figure 1). These examples are focusing on pain and symptoms. At baseline, subjects are reporting over 20 symptoms on average, and these been reduced by half after one month on the diet. The total myalgic score and number of tenderpoints have also been significantly reduced, and the average dolorimetry (the amount of pressure they can withstand before feeling pain) has significantly increased. Figure 2 shows changes in abdominal symptoms after one month on the diet, and Figure 3 shows changes in

neurological symptoms reported after one month on the diet. Overall, this preliminary data is very promising and we look forward to analyzing the other measures including EEG, cognitive testing, and measures of brain glutamate using MRS; as well as analyzing the results of the challenge period.

Figure 1.

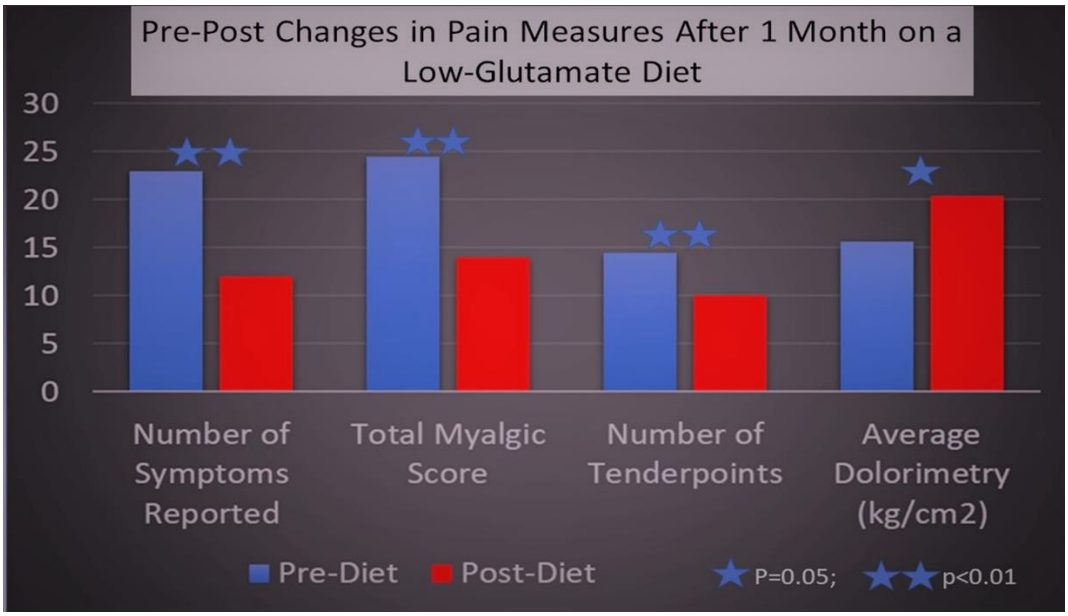


Figure 2.

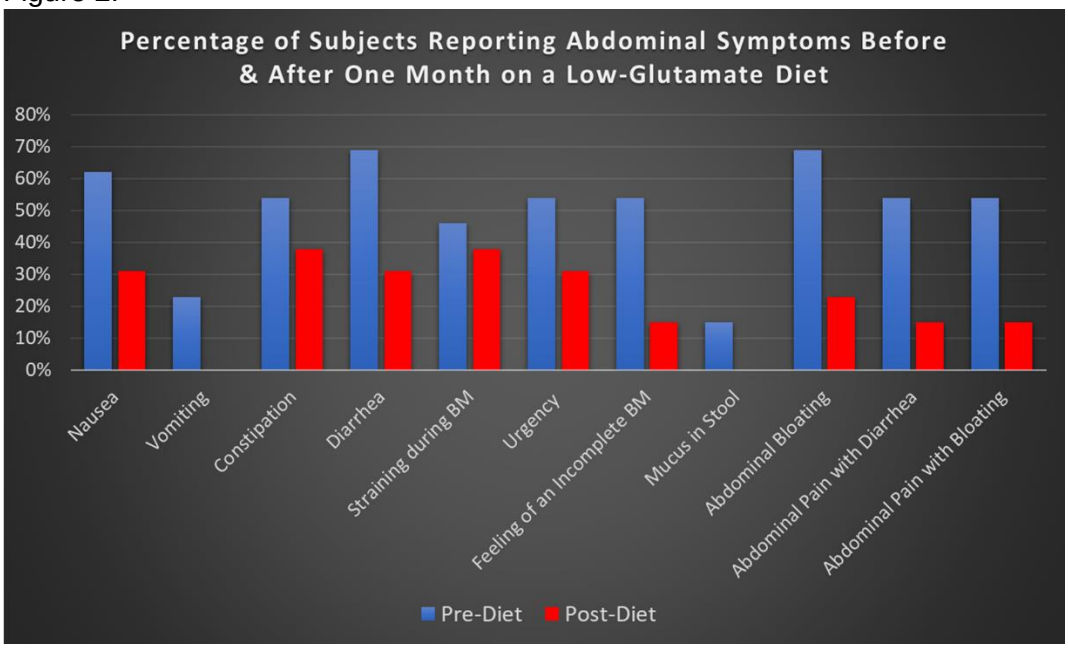
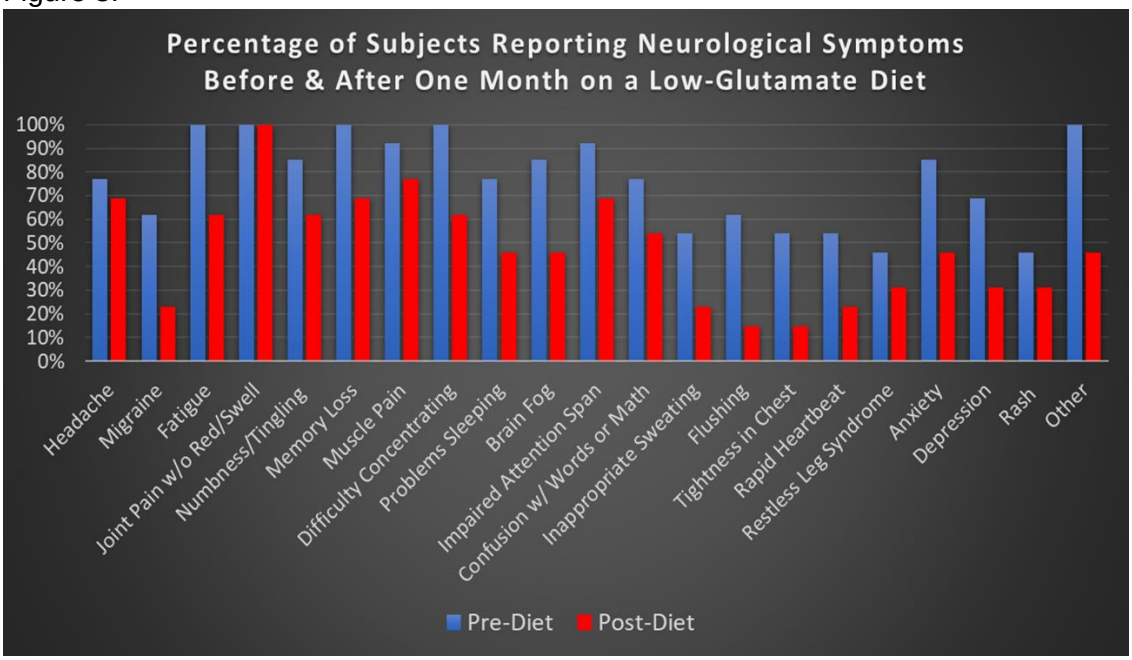


Figure 3.



What opportunities for training and professional development has the project provided?

The project was not intended to provide training and professional development opportunities.

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?

During the next reporting period, I plan to continue recruiting subjects and collecting data with the goal of having 35/40 subjects recruited by the end of year 2.

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?

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?

If this diet is found to be significantly impactful on symptoms of GWI, then this could make a significant impact on patients who suffer from these symptoms. This diet could be used as a low-cost treatment option for GWI patients, and could ultimately be distributed through VA dietitians.

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

We have experienced a delay due to Georgetown University upgrading their MRI machine. The imaging lab is currently closed for ~1 month to do the upgrade, which is limiting our ability to schedule subjects during this time. However, due to the fact that we were ahead of schedule with our recruitment, this delay does not look like it will cause a problem in achieving our goals for the year.

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

Nothing to report for any of the below items.

Significant changes in use or care of human subjects

Significant changes in use or care of vertebrate animals.

Significant changes in use of biohazards and/or select agents

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
Nothing to Report.

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)
Not applicable.

Technologies or techniques
Nothing to Report.

Inventions, patent applications, and/or licenses
Nothing to Report.

Other Products
None.

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	Kathleen Holton, PhD, MPH
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	0000-0003-2619-7983
Nearest person month worked:	5
Contribution to Project:	Oversight of all aspects of the study.
Funding Support:	

Name:	James Baraniuk, MD
Project Role:	Co-I
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	Medical oversight for safety of participants during challenges.
Funding Support:	

Name:	John VanMeter, PhD
Project Role:	Co-I
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	Oversight of collection of MRI and MRS data for the study.
Funding Support:	

Name:	Meissa Jones, MS; Elizabeth Brandley, MS (see explanation below)
Project Role:	Research Coordinator Position
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	12 (combined time after Elizabeth took over for Meissa)
Contribution to Project:	Marketing, recruitment, scheduling, data management
Funding Support:	

Name:	Anna Kirkland
Project Role:	Research Assistant
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	3
Contribution to Project:	Collecting data during subject visits, data entry
Funding Support:	

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

The research coordinator for the project, Meissa Jones, went on maternity leave, and then decided to only work as a part-time hourly employee going forward. Elizabeth Brandley was hired to take over for her as the research coordinator for the project.

What other organizations were involved as partners?

Organization Name: Georgetown University

Location of Organization: Washington, DC

Partner's contribution to the project includes medical oversight for the challenges and collection of MRI data for the study.

Financial support;

In-kind support None

Facilities MRI facility is used.

Collaboration Both Co-Is work at GU.

Personnel exchanges None.

Other. None.

SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: Not applicable.

QUAD CHARTS: I was told that this does NOT need to be included.

APPENDICES: None.