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CONTRACTING ORGANIZATION: The Leland Stanford Junior University

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14. ABSTRACT Traumatic brain injury (TBI) is a leading cause of death and disability in the United States, and the incidence of mild TBI among military members has increased since 2000. Oculomotor deficits have been identified as a phenotypical subtype post mTBI and it has been shown to be associated with clinical symptoms after injury. Vision-related symptoms include reading difficulties, blurred or double vision, difficulty switching focus from near to far, photophobia, discomfort in busy and dynamic environments, and visual attention deficits. It has also been shown that individuals have increased symptoms if they also have an additional phenotype, such as vestibular dysfunction. The addition of the vestibulo-ocular phenotype may account for increased visually related symptoms, including movement-related dizziness and blurred vision, as individuals would not only be symptomatic to moving objects, but they would also have additional symptoms as they move their head while trying to fixate on stationary objects. This study directly addresses the focus area 'Visual dysfunction as related to a military-relevant traumatic event' and will address the critical gaps in understanding the myriad of visual symptoms, corresponding vision related deficits, and their associations with motion sensitivity and visual attention following mTBI.					
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TABLE OF CONTENTS

Table of Contents	3
1.0 INTRODUCTION	4
2.0 KEYWORDS	5
3.0 ACCOMPLISHMENTS	6
4.0 IMPACT	10
5.0 CHANGES/PROBLEMS	11
6.0 PRODUCTS	12
7.0 PARTICIPANTS AND OTHER COLLABORATION ORGANIZATIONS.....	13
8.0 SPECIAL REPORTING REQUIREMENTS	14
Appendices.....	Error! Bookmark not defined.

1.0 INTRODUCTION

Traumatic brain injury (TBI) is a leading cause of death and disability in the United States, and the incidence of TBI among military members has increased since 2000. TBI is rated as being mild, moderate, and severe based upon the severity and time of associated coma and impaired consciousness, with mild TBI (mTBI, i.e., concussion) being the most common type. While the term ‘mild’ is used to classify the severity of the injury, the term ‘mild’ does not classify the severity of symptoms as many individuals with mTBI have prolonged and often debilitating symptoms that may last weeks, months, and even years. Oculomotor deficits have been identified as a phenotypical subtype of post-concussion syndrome and it has been shown to be associated with clinical symptoms after injury. Vision-related symptoms include reading difficulties, blurred or double vision, difficulty switching focus from near to far, photophobia, discomfort in busy and dynamic environments, and visual attention deficits. Convergence and/or accommodative disorders are the most common vision diagnoses reported after mTBI but it is unlikely that these disorders account for the myriad and severity of vision symptoms, particularly symptoms related to visual motion sensitivity and visual discomfort in busy and dynamic environments. It has also been shown that individuals have increased symptoms if they also have an additional phenotype, such as vestibular dysfunction. The addition of the vestibulo-ocular phenotype may account for increased visually related symptoms, including movement-related dizziness and blurred vision, as individuals would not only be symptomatic to moving objects but they would also have additional symptoms as they move their head while trying to fixate on stationary objects. This study directly addresses the focus area ‘Visual dysfunction as related to a military-relevant traumatic event’ and will address the critical gaps in understanding the myriad of visual symptoms, corresponding vision related deficits, and their associations with motion sensitivity and visual attention following mTBI.

2.0 KEYWORDS

Mild Traumatic Brain Injury, oculomotor, accommodation, vergence, vestibular

3.0 ACCOMPLISHMENTS

What were the major goals of the project?

Our major goals include: (Aim1) to test the hypothesis that a moving stimulus induces an increase in visual symptoms and is associated with decreased vergence and accommodation performance in young adults with a history of concussion, (Aim2) to test the hypothesis that visual motion sensitivity and visual attention deficits are associated with abnormal dynamic vergence and accommodation, and (Aim3) to test the hypothesis that the presence of an abnormal vestibulo-ocular reflex will result in a relative increase in visual symptomatology even in the absence of vergence or accommodative deficits.

What was accomplished under these goals?

- 1) *Major Task 1: Prepare Standardized Research Protocols for Aims 1-3*
 - a. *Objectives: Goals met in Quarter 1, nothing new to report*
 - b. *Significant results or key outcomes: nothing to report*
 - c. *Other achievements: nothing to report*

- 2) *Major Task 2: Coordinate Study Staff for Data Collection*
 - a. *Subtask 1*
 - i. *Objective: Hire and train study staff: Study staff has been hired and trained for Aims 1, 2, and 3. As reported in the quartley reports, we have been waiting for our expert vision scientist to arrive from Iran for Aim 2. He was delayed for nearly a year due to Visa processing, but arrived in Q4. Despite his absence throughout the vast majority of Year 01, we were able to develop the protocols for all aims and train study personnel by Q4.*
 - ii. *Significant results or key outcomes: Despite the project's key scientist, we made new collaborations in the meantime for another vision scientist to complete Aim 2's study set-up according to protocol. This was completed in the beginning of Q4. We have been delayed on Major Task 4 (beginning recruitment) due to the delay in the arrival of our vision scientist from Iran and needing to pivot to collaborate with*

other scientist in developing the Aim 2 protocol. Participant recruitment was supposed to begin at the beginning of Q3 (anticipated in month 6) but was delayed until Q4 (we have started participant recruitment). Despite the delay in starting recruitment, we capitalized on the additional time to further refine our protocols for Aims 1 and 3 by adding additional dimensions and automation to our data collection and data processing procedures.

iii. Other achievements: Nothing to report.

b. Subtask 2: Facilitate and Coordinate with personnel for training, supervision and fidelity checks as needed for attrition.

i. Objectives: All research staff, except for our vision scientist have been trained on protocols 1, 2, and 3. Our vision scientist arrived at the beginning of Year 02, Q1 so he is being trained on the protocol for Aims 1-3.

ii. Significant results or key outcomes: nothing to report

iii. Other achievements: nothing to report

3) Major Task 3: Prepare Research for Aims 1-3

a. Objectives: Protocols for Aims 1 and 2 developed in Q1.

b. Significant results or key outcomes: We made temporary collaborations in the meantime for another vision scientist at Stanford to complete Aim 2's study set-up. This was completed in Q4. We have also taken the time in our delay of the set-up in Aim 2 to further refine our protocols adding additional dimensions and automation to our data collection and data processing procedures for Aims 1 and 3.

c. Other achievements: nothing to report

4) Major Task 4: Participant Recruitment, Therapy, Participant Evaluation

a. Subtask 1:

i. Objectives: Coordinate with study personnel for flow chart for all study steps, data collection and database requirements

ii. Significant results or key outcomes: Study flow charts have been developed and are being used for recruitment.

iii. *Other achievements: Nothing to report.*

b. *Subtask 2:*

i. *Objectives: Participant recruitment.*

ii. *Significant results or key outcomes: As noted above we were delayed in developing and deploying Aim 2 because the delay in our vision scientist. However, we started recruitment at the end of Q4 and have recruited 6 participants thus far. We expect the delay in recruitment to only be a minor setback.*

iii. *Other achievements: Nothing to report*

5) *Major Task 5: Data Analysis*

a. *Objectives: Coordinate with study personnel for monitoring data collection rates and data quality. Perform all analyses according to specifications, share output and finding with all investigators and study team.*

b. *Significant results or key outcomes: Recruitment began at the end of Q4. We are monitoring data collection rates and performing data quality checks as participants are recruited.*

c. *Other achievements: nothing to report*

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

Nothing to Report.

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?

In Year 02, we expect to continue recruitment and begin developing data analysis scripts using Matlab.

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.

4.0 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.

5.0 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

There was been a delay with hiring our vision scientist due to his Visa. He arrived at the very end of Q4 and is currently being trained on all protocols. Despite his delay, we have used existing staff to work on the development of the protocol in his absence and begin recruitment. We are currently behind in recruitment, however, once we started recruitment we have been recruiting steadily and I do not expect to remain behind throughout Year 02.

Changes that had a significant impact on expenditures

Due to delays in hiring our scientist and being able to begin recruitment, we functioned on the lowest expenditures as we could so that we will be able to dedicate all financial resources to catching

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

No deviations to report.

Significant changes in use or care of human subjects

Nothing to Report.

Significant changes in use or care of vertebrate animals.

Nothing to Report.

Significant changes in use of biohazards and/or select agents

Nothing to Report.

6.0 PRODUCTS

Nothing to Report

7.0 PARTICIPANTS AND OTHER COLLABORATION ORGANIZATIONS

What individuals have worked on the project?

Name:	<i>Tawna Roberts</i>
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	0000-0002-6835-5559
Nearest person month worked:	<i>1.4</i>
Contribution to Project:	<i>Dr. Roberts has developed protocols, and overseen scientists/collaborators, and research assistants, and coordinators.</i>
Funding Support:	NIH/NEI, Research to Prevent Blindness
Name:	Amber Hu
Project Role:	Research assistant/study coordinator
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	1.4
Contribution to Project:	Develop data forms, recruit participants, store collected data
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?

Nothing to report.

What other organizations were involved as partners?

Nothing to report.

8.0 SPECIAL REPORTING REQUIREMENTS

Nothing to report.