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TITLE: Abnormal Dynamic Visual Function and Associated Symptomatology in Mild Traumatic Brain Injury

PRINCIPAL INVESTIGATOR: Dr. Tawna Roberts, OD, PhD

CONTRACTING ORGANIZATION: The Leland Stanford Junior University

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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> 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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## 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.*
    - ii. *Significant results or key outcomes: This was completed in Year 01. Nothing new to report.*
    - 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. Nothing new to report.*
    - 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, and 3 were developed in Year 01. Nothing new to report.*
  - b. *Significant results or key outcomes: Nothing new to report.*
  - 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. Complete – nothing new to report.*
    - ii. *Significant results or key outcomes: Study flow charts have been developed and are being used for recruitment. Nothing new to report.*
    - iii. *Other achievements: Nothing to report.*
  - b. *Subtask 2:*
    - i. *Objectives: Participant recruitment.*
    - ii. *Significant results or key outcomes: As noted last year, we were delayed in developing and deploying Aim 2 because the delay in our vision scientist. This delayed our recruitment to the end of year 1. However, we have worked hard to recruit this year to make up for lost time. We are still behind in recruitment but we are moving in the right direction.*
    - 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:*
  - 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?**

1. We submitted a manuscript on a novel analytical approach that was developed from our data that has been collected thus far. It is currently under review.
2. Our vision scientist, Amir Norouzpour has submitted an abstract to the North American Neuro-Ophthalmology Society. If accepted, he will present preliminary results at that conference.

**What do you plan to do during the next reporting period to accomplish the goals?**

In Year 03, we expect to continue recruitment and begin writing scientific manuscripts.

**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?**

With the support of this award, Dr. Roberts was promoted to Associate Professor at the Stanford School of Medicine.

### **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 a delay with hiring our vision scientist due to his Visa in Year 01 that delayed our start in recruitment. He arrived at the very end of Year 01 Q4 and was trained on all protocols and recruitment started shortly after. We remain behind in recruitment, however, once we started recruitment, we have been recruiting steadily throughout Year 02. I expect for us to catch up by the end of Year 03.

### **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 up and recruiting. We have been mindful of our spending so that we can complete the study in a no-cost extension year, if needed.

### **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>1.0</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:	12
Contribution to Project:	Develop data forms, recruit participants, store collected data
Funding Support:	

Name:	Christabel Ameyah Baah
Project Role:	Research Assistant
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	<i>12</i>
Contribution to Project:	<i>Data collection</i>
Funding Support:	DoD
Name:	Amir Norouzpour

Project Role:	Research/Vision Scientist
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	12
Contribution to Project:	<i>Data collection, data analysis</i>
Funding Support:	
Name:	Gayathri Srinivasan
Project Role:	Research Optometrist
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	4
Contribution to Project:	Perform optometric eye exams
Funding Support:	
Name:	Min Young Lee
Project Role:	Graduate student
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	3
Contribution to Project:	Perform optometric eye exams
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.