Award Number: W81XWH-15-1-0442

TITLE: Sensorimotor Assessment and Rehabilitative Apparatus

PRINCIPAL INVESTIGATOR: Michael Schubert

CONTRACTING ORGANIZATION: Johns Hopkins University
Baltimore, MD 21218

REPORT DATE: October 2016

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
October 2016	Annual	15 Sept 2015 - 14 Sept 2016

4. TITLE AND SUBTITLE
''Sensorimotor Assessment and Rehabilitative Apparatus''

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-15-1-0442

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Dr. Michael C. Schubert

E-Mail: mschube1@jhmi.edu

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Johns Hopkins University, The
3400 N. Charles St.
W400 Wyman Park Bldg
Baltimore, MD 21218-2680

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

In veterans and civilians exposed to blast or blunt head trauma or those suffering from inner ear disorders, a clinical pattern of damage to the auditory, visual, and vestibular (inner ear balance mechanism) sensorimotor systems has emerged; collectively known as multi-sensory impairment (MSI). MSI related symptoms affect ~ 300-500/100000 population. The purpose of this study is to examine subjects for sensorimotor impairments within the visual and vestibular systems using a portable technology that rapidly and unobtrusively measures how these interdependent systems are functionally integrated. We call this device SARA, Sensorimotor Assessment and Rehabilitation Apparatus. The scope of the project involves recruiting n=42 Veterans from the War Related Illness and Injury Study Center (WRIISC) in East Orange NJ and n=42 civilian subjects with vestibular hypofunction from the Johns Hopkins University School of Medicine Clinics. We will also collect age-matched healthy control data. The study's duration is three years. An early, yet major finding suggests that veterans with MSI have a significant ocular misalignment in their eye position relative to healthy controls. This finding suggests that SARA may serve as an excellent proxy of more elaborate laboratory equipment that requires expertise in use, is cumbersome and impractical for many unique environments.

15. SUBJECT TERMS
Multisensory Impairment, Vestibular, Visual, Dynamic Visual Acuity, Imbalance, Mild Traumatic Brain Injury, Sensorimotor, Assessment, Portable, Sensors, Otolith, Semicircular Canal, Gait

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	27	19b. TELEPHONE NUMBER *(include area code)*

Table of Contents

1. INTRODUCTION

Exposure to brain injury via blast or blunt mechanisms disrupts multiple sensorimotor systems simultaneously in nearly 20% of veterans of the Gulf War and OIF/OEF campaigns, causing physical, sensory, cognitive, and behavioral/emotional changes. Therefore, a significant population of our wounded veterans suffer long term functional consequences including visual deficits, postural and locomotor instabilities, disorientation, dizziness, sensitivity to visual and body motion, and an impaired ability to read. A clinical pattern of damage to the auditory, visual, and vestibular (inner ear balance mechanism) sensorimotor systems has emerged, which has collectively been given the name multi-sensory impairment (MSI). In the US civilian population, MSI related symptoms are also a common sequelae of damage to the inner ear and mTBI, collectively affecting ~ 300-500/100000 population. Therefore, irrespective of the environment (military or civilian) or cause (mTBI or peripheral vestibular injury), the inner ear is commonly involved when symptoms of MSI are experienced. The purpose of this study is to examine subjects for sensorimotor impairments within the visual and vestibular systems using a portable technology that rapidly and unobtrusively measures how these interdependent systems are functionally integrated. We call this device SARA, Sensorimotor Assessment and Rehabilitation Apparatus. The scope of the project involves recruiting n=42 Veterans from the War Related Illness and Injury Study Center (WRIISC) in East Orange NJ and n=42 civilian subjects with vestibular hypofunction from the Johns Hopkins University School of Medicine Clinics (otolaryngology, rehabilitation, and neurology). We will collect age-matched healthy control subjects at the Johns Hopkins site. The duration of the study is three years.

2. KEYWORDS

Multisensory Impairment, Vestibular, Visual, Dynamic Visual Acuity, Imbalance, Mild Traumatic Brain Injury, Sensorimotor, Assessment, Portable, Sensors, Otolith, Semicircular Canal, Gait

3. ACCOMPLISHMENTS

A. Major Goals

The major goals of this project as established by the approved SOW include

I. Establish project management system to ensure success of project

This goal was projected to be completed within the 1st six months of the award, but instead took us 11 months. This goal is 100% complete. We have biweekly meetings at JHU and monthly meetings with the WRIISC (phone) in addition to 'as-needed' conversation with both JHU and WRIISC grants management offices to ensure adequate oversight from expenditure of funds, to human subjects protection, to salary support, data collection and progress towards the major goals. The PI has a monthly meeting with the JHU grant management office to go over expenditures of this award. Many meetings were necessary to secure each sites' IRB approval to perform the study and to assure the proper means were used for patient recruitment (see Goal III). Clinicians identified as possible referral sources were added to the consent forms, enabling communication between the subject and members of our study.

Per this 1st major goal, the following milestones have been achieved

i. Both sites include individuals that have been independently trained and are ready to begin data collection. Training included medical screening for vestibular pathology, balance and gait assessments, and SARA testing.

ii. Train Physical Therapist on SARA and rehabilitation program. This is complete at the JHU site. See Section 5. (Changes/Problems) regarding the Physical Therapist hire at the WRIISC.

II. Obtain Institutional Review Board approval at VA NJ and JHU

This goal was projected to be completed within the 1st six months of the award and is 100% complete.

Per this 2nd major goal, the following milestones has been achieved

1. HRPO/ACURO Approval
2. Local IRB Approval

III. Develop recruitment plan to identify and enroll Veterans with MSI. This goal was projected to be completed within the final six months of the first year of the award and is 100% complete. Completing this goal involved mailing IRB approved recruitment letters to Veterans, conducting follow up with phone calls, distributing flyers to all VA facilities and their ambulatory services including community-based outpatient clinics to publicize the study, conversing with referring physicians about the study.

Per this 3rd major goal, the following milestone has been achieved

i. Local IRB approval of the recruitment flyers and telephone scripts needed to assist with subject recruitment.

IV. Determine the effectiveness of SARA to identify vestibular function

This goal was projected to be completed within the final year of the award; after year 1 we are 10% completed at JHU and 5% completed at the WRIISC. We did have a plan to collect 32 subjects (16 each from JHU and WRIISC) by the end of the first year. Instead, we have collected data in 6 patient subjects and 5 healthy controls at JHU and 2 veterans at the WRIISC. This is 41% completion for Year 1. Please see Section 5., CHANGES/PROBLEMS for

additional information.
Per this 4th major goal, the following milestone have been achieved

i. Both sites independently trained and ready to begin data collection

B. What has been accomplished under these goals?

The major activities involved in the reporting period representing this 1st year have been extensive. Most of the effort has resolved around ensuring the portable tablets are of enough operating power, of the correct operating system, and the software can be run using the most accurate representation of true black (OLED – organic light emitting diodes). Only a few months ago (summer of 2016), was one tablet available to meet each of these criteria – the Samsung Galaxy TabPro S. Up until this summer, we were refining software, investigating wireless sensor hardware, and collecting data with multiple tablets to establish and ensure the psychomotor stability of the SARA software suite. We have chosen the sensors to be used for gait and postural assessment. Additionally, for Aim III (see below, examining how SARA can predict beneficial responders to vestibular rehabilitation), we have developed an exercise stratification program that includes three levels of difficulty (easy, moderate, hard) based on initial clinical visit. If this stratification of patients is shown to be valuable, this represents a major advance in beginning to develop predictor variables for rehabilitation benefit.

We have three Aims for this study:

> AIM I. Correlate our behavioral measure of binocular alignment symmetry (via SARA) against gold standard measures of otolith function and visual function in an mTBI, vestibular deficit, and age-matched control population.
>
> AIM II. Investigate difference in dynamic visual acuity for near versus far viewing as a means to distinguish vestibular oculomotor from visual oculomotor control dysfunction in an mTBI, vestibular deficit, and an age-matched control population.
>
> AIM III. Investigate how well our MSI test (SARA) can predict those veterans and civilians with vestibular hypofunction that respond well to vestibular rehabilitation intervention.

The SARA software and this grant involves developing and investigating 3 major sensorimotor tasks: a. Oculomotor function thru the VAN and TAN and dynamic visual acuity applications (Aim I and II); b. Examining gait via wireless sensors the size of a watch (Aim III); b) predicting those patients that may be good candidates of vestibular rehabilitation (Aim III). Accomplishments from each of these are discussed below:

a. Oculomotor function (Aim I and II)

We have developed the Vertical Alignment Nulling and Torsional Alignment Nulling tasks (VAN, TAN) to examine for any misalignment in oculomotor position. The task asks subjects to adjust a movable blue line so that it lines up horizontally with a stationary red line and both thus appear as a single line. If the right eye is elevated above the left eye (**Figure 1C**) or if the right eye is rotated (i.e. clockwise) away from the left eye (**Figure 1D**), the subject will mis-align the two lines. We test in both upright and supine position to examine differences in oculomotor position due to musculoskeletal or vestibular (otolith) injury. For example, when subjects lie supine, the vestibular contribution to an abnormal skew (vertical eye displacement as in **Figure 1C**) is abolished and the skew resolves (as in **Figure 1B**), yet a musculoskeletal or cranial nerve injury to that same eye muscle would not change and the skew would still be present.

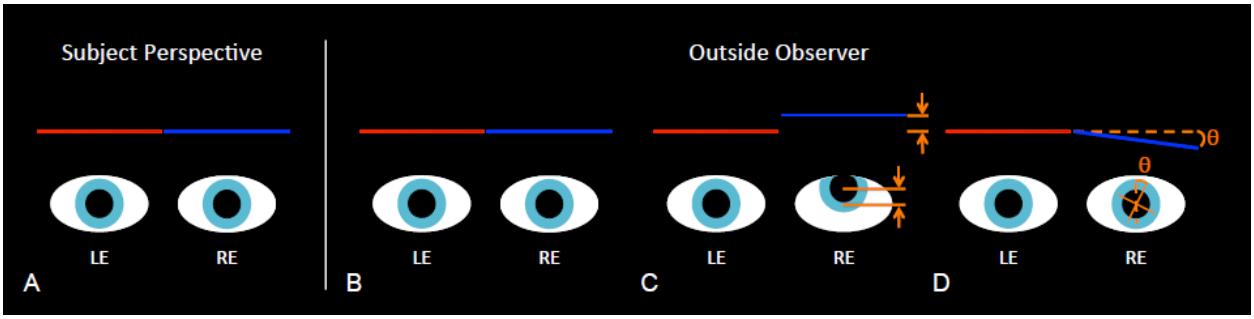

Figure 1. Examples of ocular misalignments inferred by VAN and TAN results. (A) The subject repositions the moving line (blue in this example) until it appears in line with the stationary line (red), thereby positioning each line on the center of each retina. Binocular misalignment is inferred from the relative positioning of the lines at the end of each trial. (B) If the subject has perfect binocular alignment, then the lines will be perfectly aligned at the end of the trial. (C) If the subject sets the right line above the left line during VAN, we infer that the right eye is elevated above the left eye. (D) If the subject orients the right line clockwise relative to the left line in TAN, we infer that the right eye is extorted relative to the left eye.

To date, we have measured VAN and TAN in 6 patients in both upright (seated) and supine. Four of these patients are civilians with a unilateral vestibular hypofunction and two of these subjects are veterans with MSI. Our early data suggest that the TAN test appears to uniquely identify veterans with MSI and civilians with unilateral vestibular hypofunction (VOR) from the healthy controls. In the Veterans, both TAN scores in upright and supine are significantly different from the healthy controls ($p < 0.05$). In the VOR subjects, TAN measured in supine, not upright, is 4.5x greater than healthy controls (**Figure 2**).

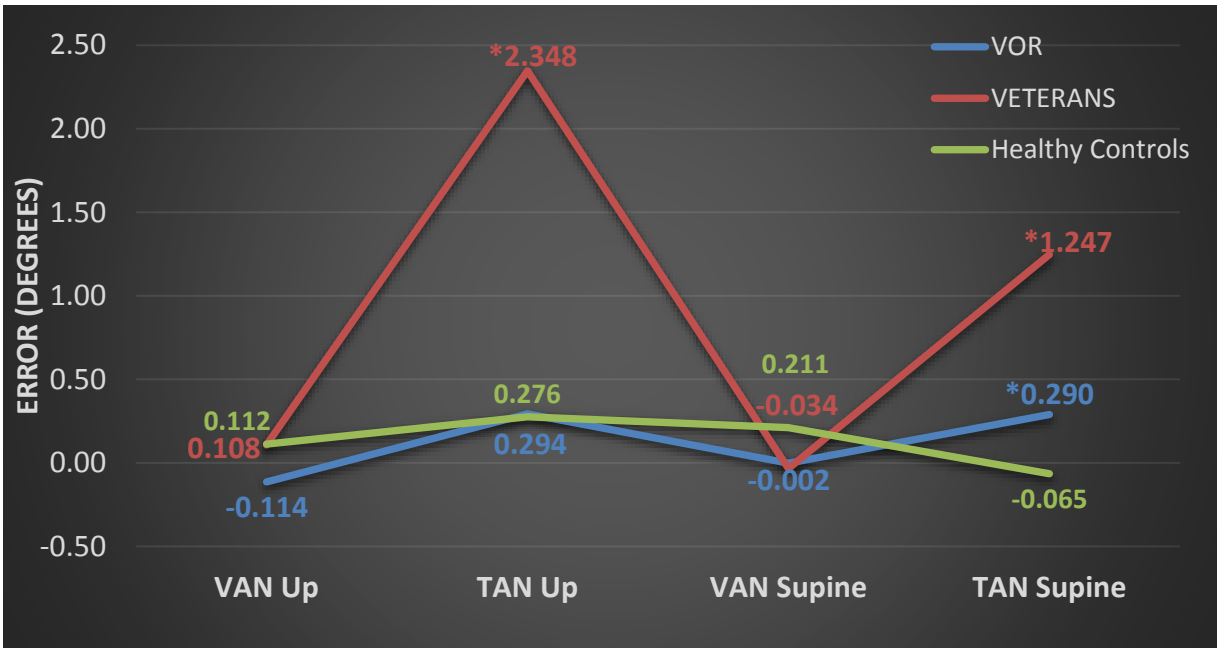

Figure 2. Differences in VAN and TAN in subjects with unilateral vestibular hypofunction (VOR), Veterans with Multisensory Impairment and healthy controls. *p< 0.05 relative to healthy controls.

We are validating the VAN and TAN test in part based on otolith vestibular function testing. Each of the VOR subjects had some abnormal VEMP testing (absent or reduced ocular or cervical VEMP testing) on the affected side. We need a greater sample size to uniquely correlate the ocular and cervical VEMP test with the VAN and TAN result. However, these early test results with VAN and TAN do appear to distinguish those patients with VOR deficits and veterans with MSI, which is very exciting. Our hypothesis may be accurate, that VAN and TAN test are valid behavioral measures of otolith function.

We developed a second measure of oculomotor function using Dynamic Visual Acuity (DVA). DVA tasks subjects to identify a letter that flashes on a monitor only when the head is moving above 120 deg/sec. We are examining DVA while looking at near (.5m) and far (2m) distances. Thus far we have only collected data in n=4 unilateral vestibular hypofunction subjects. There is not much difference between near vs. far targets in patients' ability to identify letters flashing during head motion, **Figure 3**. A score of 100 is perfect. Early results suggest DVA scores for Far target distances are worse than those compared with Near. We have collected data in healthy controls but not yet processed it.

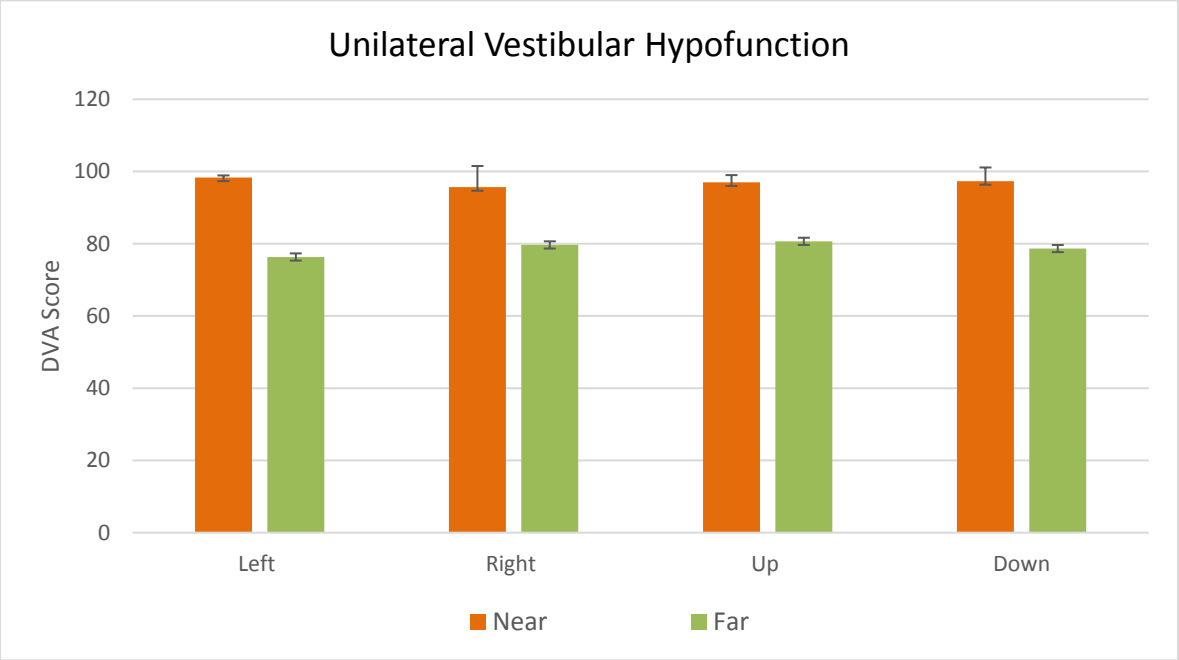

Figure 3. DVA in patients with unilateral vestibular hypofunction performing active sinusoidal right/left or up/down head rotation. Each direction is tested separately during the sinusoidal head rotation.

We are validating the DVA near and far test using the video head impulse test. We have identified VOR function in each of the semicircular canals (six) in the subjects with VOR deficit, **Figure 4**.

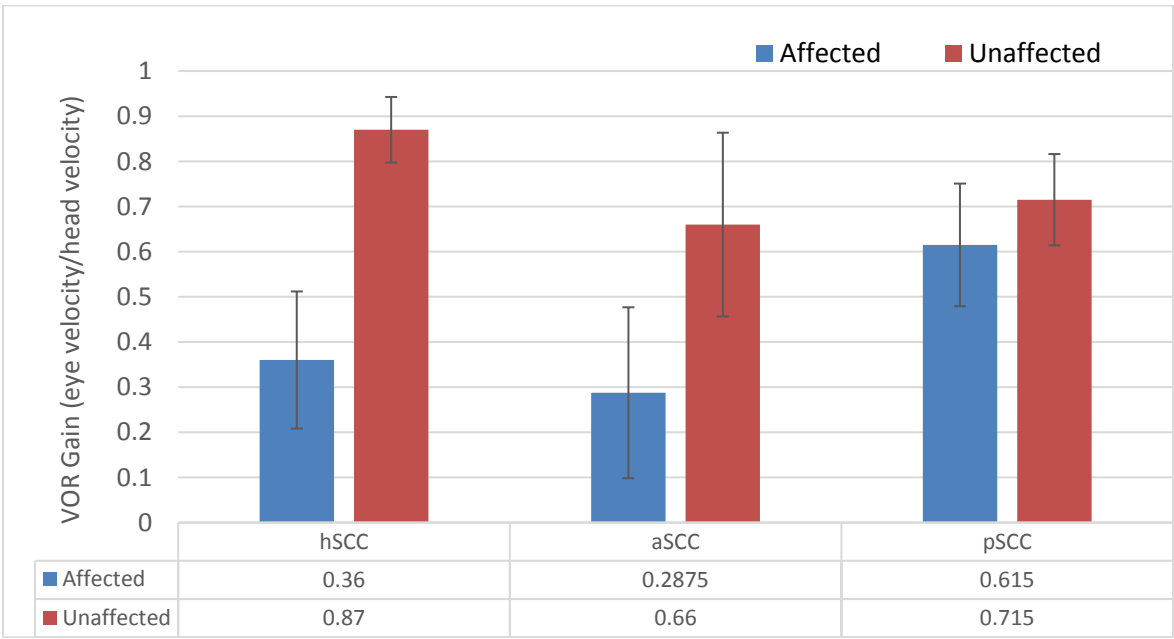

Figure 4. VOR gain during passive head impulse testing of each semicircular canal (horizontal hSCC, anterior aSCC, posterior pSCC). Function (VOR gain) within the plane of the affected canal is worse.

b. Gait (component of Aim III)

While not a direct aim or goal of our project, we will be quantifying gait using 5 wireless sensors (Aim III measures fall risk and collects outcomes related to gait) attached to each leg, the trunk, the pelvis, and the head**, Figure 5**. To process data using these sensors, we have developed new measures of balance and posture performance. We are very excited to share these measures in eventual publications.

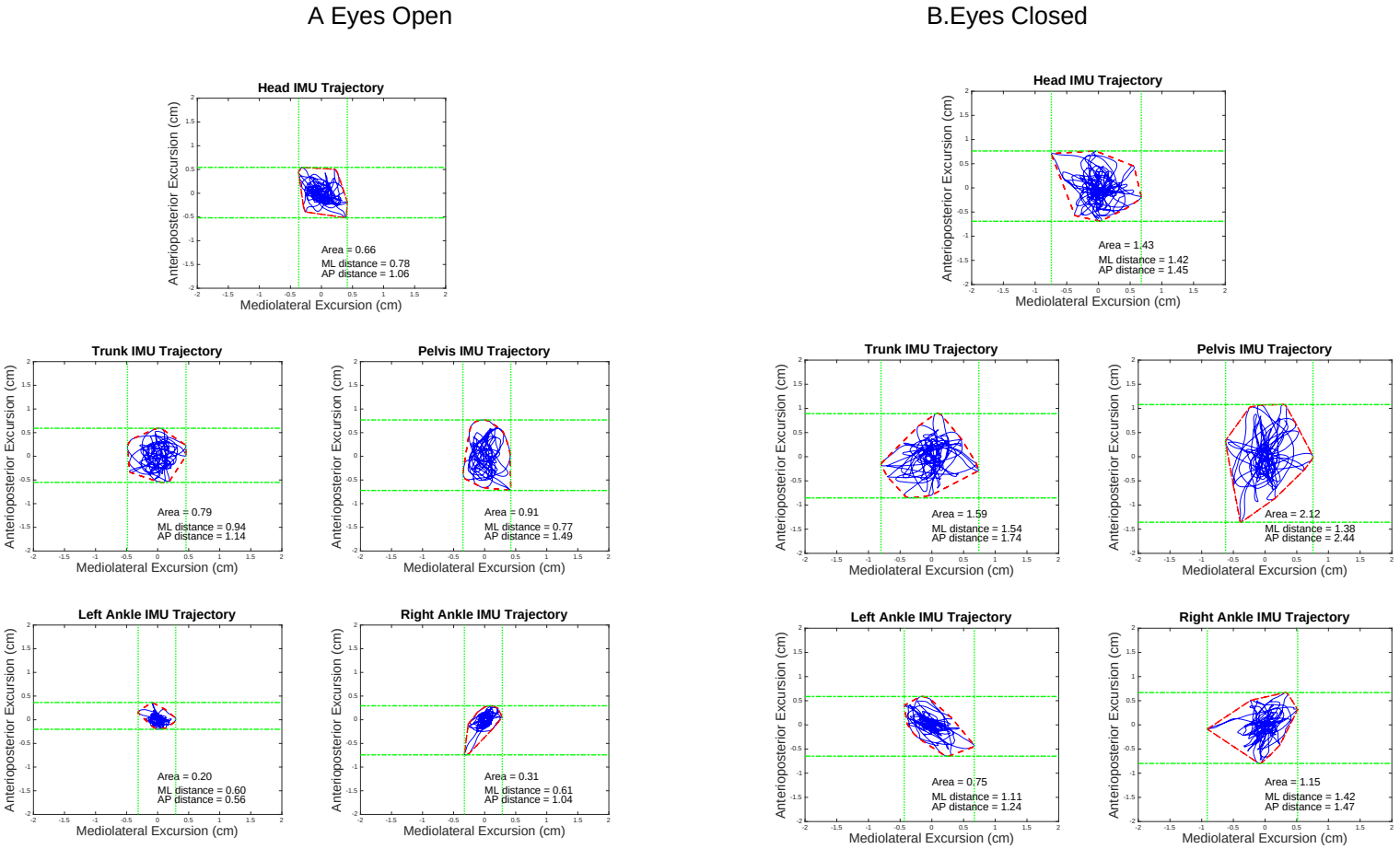

Figure 5. Five wireless sensors measure sway during quiet stance eyes open (A) and eyes closed (B).

c. Rehabilitation (component of Aim III)

Previous rehabilitation studies in several neurological populations (Ataxia, Parkinson Disease, and Vestibular Hypofunction) have shown participants who perform custom balance exercises with adequate intensity, experience statistically significant improvement in their functional performance as well as subjective outcomes. However, when studying the effect of exercise we must control for variability that custom exercises of varying intensity will incur. Therefore, we have limited how the physical therapists will choose the appropriate intensity and type of exercise in their prescription. For Aim III, we have developed a standardized treatment that ensures the subjects exercise at an intensity level to enable maximum therapeutic benefit, while limiting the amount of variability offered by the providers.

The participants will be categorized into treatment groups utilizing evidenced based on subjective and functional outcome measures treating patients with vestibular and mTBI pathologies, **Table 1**. The highest performers at baseline will be categorized into the most challenging exercise group, Group A. The moderate level performers will be categorized into Groups B, and Group C will include the easiest exercises. The study includes the subjective outcomes from the Dizziness Handicap Inventory and the Activities Balance Confidence Scale.

The functional performance measures utilized are the Timed up and Go, Dynamic Gait Index and Gait Speed.

Table 1. Stratification scheme for picking exercise program (Whitney 2004; Lajoire and Gallagher 2004; Whitney 1999; Bohannon RW 1997; Perera 2006; vanLoo & Moseley 2004)

	DHI	ABC	TUG	DGI	Gait <age 70	Gait > age 70
A	<30	>67	<11	>18	1.4m/s	1.3m/s
B	31-60	31-67	11-14	14-17	1.1	1.0
C	>60	<=30	>14	<14	0.8	0.7

C. Opportunities for training and professional development?

Over the past year, discussions with the research team and clinicians from WRIISC interested in this research project have led to the suggestion that the PI (Schubert) provide an informal continuing education training/in-service. Dr Shemoy, physiatrist expressed a strong interest to have the PI teach the clinical management of patients seeking vestibular rehabilitation to include diagnostics, pathophysiology of the vestibular system, and rehabilitation. Dr Shemoy suggested three separate days for 1-2 hours to offer this training/education. Currently, I teach at the national and international level and have been invited by many societies in many different countries to teach this content. I am honored to provide this service to clinicians at the WRIISC. There will be no charge. We plan to start this training during the 2nd year of the award.

D. Dissemination of Results to communities of interest

Nothing to report. We have submitted two abstracts to present preliminary results in a poster format and a platform presentation.

E. Plans for next reporting period

We are now ready to dedicate our efforts strictly towards patient recruitment, data collection and processing, and data dissemination. This will be the focus of our efforts during the 2nd year of the award.

4. IMPACT

The principal disciplines of this research project are to develop robust measures of sensorimotor function that can be delivered in environments that do not allow the space for cumbersome laboratory equipment, that do not require specialized training for use, and do not involve any invasive procedure to gather relevant function of multiple medical systems. Additionally, our device will provide instant results that users can compare with a normative database.

During this reporting period, most of our efforts have revolved around ensuring the proper human protection authorization, determining the most efficient hardware to adequately collect our data, and finally, developing the software with consideration given to usability (ease of use). While it is early to describe any unique contributions outside of our current laboratory, we see that this technology has relevance in paramedical disciplines (i.e. astronaut crewmembers assessing sensorimotor function after long duration space travel, epidemiologic studies on populations where status of sensorimotor function is desired). During the reporting period, the VAN and TAN software was awarded a patent (US09072481-20150707).

http://patents.uspto.gov/web/patents/patog/week27/OG/html/1416-1/US09072481-20150707.html

We believe that our stratification of intensity, based on published literature and accepted outcomes, has potential to significantly impact the management of patients with dizziness and balance disorders that seek rehabilitation. The field of rehabilitation is in need of dosing studies with rigor that can help determine meaningful change, and our stratification has potential to be used for that purpose.

5. CHANGES/PROBLEMS

Unanticipated Problem

We have had difficulty identifying a physical therapist at the WRIISC site to carry out the 3rd aim of the study (see below). In discussion with Dr Nigel Shemoy, MD we have realized that the VA does not allow salary support from grant funding to offset clinical responsibilities in order to protect time for research. This prevents us from using existing physical therapy staff at the WRIISC. Further discussion with Dr Shemoy and Dr Serrador has confirmed that many of the veterans have difficulty traveling to the WRIISC, often taking multiple bus routes all of which, in their experience, causes us to believe that we should reduce the number of visits to the WRIISC for rehabilitation. The original plan was to see the veterans for six visits, and to study them (data collect) for 3 of those 6 visits. However, given that the standard of care for delivery of vestibular rehabilitation is to participate in a home program and the average number of visits is 4 ± 2, we are satisfied that instead we can provide vestibular rehabilitation and collect our data in only 3 visits. Both Drs. Shemoy and Serrador agree this is much less burdensome on the veterans; this certainly will not affect our data collection in anyway. Therefore, this minor problem is resolved and no negative effect is anticipated on clinical care or research data.

Our 4th major goal as listed above included data collection on n=32 patients (item IV above) by the end of year one. We were delayed in data collection partly based on the time to secure HRPO approval. We secured independent IRB approval from JHU within 6 months. The IRB of the WRIISC sub-site determined that the rotary chair test (one of the clinical tests) was a greater than minimal risk to subjects given a motor is attached to the chair. Although, this is not considered a risk at any other clinic using similar equipment in the US - and is routinely used as a measure of vestibular function, this classification forced us to secure a Research Monitor at both JHU and WRIISC. We then had to identify who that would be, ensure they were appropriately trained in human subjects' research, and secure their approval. This step added another 3 months to our delay in recruiting subjects.

Changes to expenditure

We will have a significant carry-over of funds into the 2nd year of the grant. The amount of $31,490 was largely appropriated to cover the costs for the vestibular testing in the patients. However, this testing is routinely done as part of the clinical care we provide, and we are thus not able to spend that money in this manner. This favorable development, will enable a portion (~10,000) of this allocated money to be returned to the DOD; the other portion (~$20,000 total yrs 2 & 3) will be used to cover salary support of an additional co-investigator. The additional Co-I will be added for Years 2 and 3 of the award.

Changes to human subjects

There has been no change to care of human subjects.

6. PRODUCTS

As stated earlier, Aim I involves our software and technology that measures alignment between the eyes (VAN, TAN), which has been awarded a patent. The patent application was submitted before the current grant was awarded.

We have submitted 2 Abstracts for presentation at national conferences. One abstract has been accepted for a platform presentation (Combined Sections Meeting of the American Physical Therapy Associations), the fate of the other abstract has not yet been decided.

We have no journal articles, books, websites, else submitted.

7. PARTICIPANTS AND OTHER COLLABORATING ORGANIZATIONS

Ten individuals across two institutions (Johns Hopkins and the East Orange VA (WRIISC)) have worked on the project. There has not been any change in either the PI or any of the senior personnel in this reporting period. The following personnel are listed by sub-site:

Johns Hopkins

a. Michael Schubert — PI
   Identifier (era commons): mschube1
   Person Month: 5
   Contribution: Oversight and science lead for both sites, patient recruitment
   Funding Support: VBMRI (DMRDP/CDMRP)

b. Mark Shelhamer — Co-PI
   Identifier (era commons): mshelha1
   Person Month: 1
   Contribution: model development for Aim III (predictors of beneficial responders) Engineer, software development
   Funding Support: None

c. Chuck Rohde — Co-PI
   Identifier (era commons): crohde1
   Person Month: 1
   Contribution: Biostatistician
   Funding Support: NIH

d. Dan Gold — Co-PI
   Identifier (era commons): dgold7
   Person Month: 1
   Contribution: Clinician performing oculomotor exam
   Funding Support: None

e. Dale Roberts — Engineer
   Identifier (era commons): drobert7
   Person Month: 2

Contribution	hardware and software development, data analysis, data processing
Funding Support:	See Other Support Document

f. Yoav Gimmon — Post-doctoral Fellow

Identifier (era commons)	ygimmon1
Person Month	8.5
Contribution	data collection, data analysis, data processing
Funding Support:	None

g. Jennifer Millar — Physical Therapist

Person Month	4
Contribution	clinical delivery of rehab; data collection, data analysis, data processing
Funding Support:	Supported by JHH as a hospital employee

WRIISC

a. Jorge Serrador — Site PI

Identifier (era commons)	JORGESERRADOR
Person Month	1
Contribution	Oversight and science lead at VA site (WRIISC), data interpretation
Funding Support:	CDMRP/DOD, VA CSR&D, DMRDP/DOD

b. Kamila Migdal — Research Assistant

Person Month	4
Contribution	study coordinator at WRIISC, data collection, data analysis, oversight operations
Funding Support:	CDMRP/DOD, VA CSR&D, DMRDP/DOD

c. Justyna Michalik — Research Assistant

Person Month	8
Contribution	study coordinator at WRIISC, data collection, data analysis, oversight operations
Funding Support:	CDMRP/DOD, VA CSR&D, DMRDP/DOD

Change in Active Other Support

Changes in Other Support occurred for Dr. Schubert, Rohde, and Serrador. Dr. Mark Shelhamer was added as a Co-PI. Other Support documents and Dr. Shelhamer's biosketch is included in the appendix.

What other organizations were involved as partners?

Organization Name: Veterans BioMedical Research Institute

Location of Organization: 385 Tremont Ave., Bldg 11, Room 117 B, East Orange, NJ

Partner's Contribution to the project: Grant provides financial support to the subsite; Facilities, Collaboration

8. SPECIAL REPORTING REQUIRMENTS (Please see Quad Chart, pg 15)

SARA - *Sensorimotor Assessment and Rehabilitation Apparatus*

MR141166 Clinical and Rehabilitative Medicine Research Program 2014

PI: Michael Schubert **Org:** Johns Hopkins University and WRIISC East Orange NJ VA **Award Amount:1.5M**

Study/Product Aim(s)

AIM I. Correlate our behavioral measure of ocular misalignment from otolith damage (via SARA) against gold standard measures of otolith function in an mTBI, vestibular deficit, and age-matched control population.

AIM II. Investigate difference in dynamic visual acuity for near versus far viewing as a means to distinguish vestibular oculomotor from visual oculomotor control dysfunction in similar population.

AIM III. Investigate how well our multisensory impairment (MSI) test (SARA) and current standard of care variables can predict those veterans and civilians with vestibular hypofunction that respond well to vestibular rehabilitation intervention.

Approach

This is an applied research application to examine subjects for MSI using a portable technology that rapidly and unobtrusively measures how these interdependent sensorimotor subsystems are functionally integrated. We will investigate the validity of our portable measure of MSI to identify pathology and predict return to duty/function in both veteran and civilian populations. Our device (SARA) has been validated in the challenging environment of reduced gravity and shown to accurately identify misalignment in eye position due to changing gravitational force.

Left 2 panels shows the hardware (top) and bodyworn shirts/straps (bottom) of the portable MSI test known as SARA. Right panel shows SARA in use during parabolic flight measuring ocular misalignment related to altered gravity.

Timeline and Cost

Activities CY	15	16	17	18
Establish the protocol, IRB, central database, hire students				
Begin data collection, prepare MS				
Publish MS, predictor benefit model building				
Estimated Budget ($K)	**$200K**	**$500K**	**$500K**	**$300K**

Updated: June 29, 2016_Quarter 2 report

MS – manuscript; **blue square** represents % cell completed relative to size of the cell

Goals/Milestones

CY15/CY16 Goal – Obtain IRB approval, establish protocol, set up data sharing agreement. IRB approval obtained

☒ Functional tests of integrated firmware and software

☒ Subject recruitment

☒ Begin data collection

X denotes item initiated

CY16/17 Goal – Continue data collection

☐ Manuscript preparation

☐ Complete Aims I and II

CY17/18 Goal – Presentation of research and complete Aim III

☐ Statistical model building

☐ Manuscript preparation

Comments/Challenges/Issues/Concerns

- If timelines change, we will re-analyze priorities based on data collected.

Projected Expenditure: 1.5M

CURRENT/PENDING/COMPLETED SUPPORT

Schubert, Michael

ACTIVE

Title:	Sensorimotor Assessment and Rehabilitative Apparatus
Effort:	4.8 Calendar
Supporting Agency:	CDMRP (Schubert)
Grants Officer	Steven Zuraf, Department of Health and Human Services, 301-492-4855
Performance Period:	09/15/2015 -09/14/2018
Funding Amount$	1,277,882
Project Goals:	This is an applied research application to examine subjects for multisensory impairment (MSI, e.g. vision, vestibular) using a portable technology that rapidly and unobtrusively measures how these interdependent sensorimotor subsystems are functionally integrated. We will investigate the validity of our portable measure of MSI to identify pathology and predict return to duty/function in both veteran and civilian populations.
Specific Aims	Our device (SARA) has been validated in the challenging environment of reduced gravity and shown to accurately identify misalignment in eye position due to changing gravitational force, monitor gait, and measure in visual acuity
Overlap	None
Role:	PI

Title:	Treatment of Vestibular Dysfunction Using a Portable Stimulator
Effort:	3.9 calendar
Supporting Agency:	DMRDP/CDMRP, W81XWH-14-0012 (Serrador)
Grants Officer	Dr. Angella Martinelli, Program Official, CDMRP
Performance Period:	04/01/2014 -03/31/2018
Funding Amount	$212,313
Project Goals:	The goal of this work is to diagnose vestibular dysfunction in veterans with previous blast exposure and / or mild TBI history as physiological biomarker
Specific Aims	Investigate how subsensory electric stimulation can improve vestibular function in veterans
Overlap	None
Role:	Co-I

COMPLETED

Title:	Use of a Portable Stimulator to Treat GWI **(THIS GRANT RECENTLY ENDED)**
Effort:	0.90 calendar
Supporting Agency:	DMMRP/Department of Defense , W81XWH-14-0598 (Serrador)
Grants Officer	Dr. Henry Nothnagel, Grant Officer CDMRP
Performance Period:	09/01/2014 -09/29/2016
Funding Amount	$23,277
Project Goals:	Working toward the assessment of vestibular function in Veterans with Gulf War Illness
Specific Aims	Investigate how subsensory electric stimulation can improve vestibular function in GWI veterans
Overlap	None
Role:	Co-I

Title:	Research and Technology Development to Support Crew Health and Performance in Space Exploration Missions

Effort	
Supporting Agency:	National Aeronautical Space Administration, NNX10AO19G (Schubert)
Grants Officer	Libby Romaguera, NASA/Shared Services Center Bldg. 1111, C Road Stennis Space Center
Performance Period:	08/01/10 – 07/31/14
Funding Amount	
Project Goals:	The goal of this project is to develop a portable software/hardware device to enable sensorimotor testing and treatment for astronauts to use in flight.
Specific Aims	Measure multiple sensorimotor systems using a portable device
Overlap	None
Role:	PI

Title:	National Multiple Sclerosis Society
Effort:	0%
Supporting Agency:	PP1841 (Schubert and Dibble)
Grants Officer	Jan Abramson Voice: 801.587.9657
Performance Period:	01/01/13 -12/31/13 Travel only
Funding Amount	$40,000
Project Goals:	Postural and gaze stability function in person with MS at risk for falls: Characterizing deficits and response to treatment. The goal of the project is to document VCR function and improvements in patients with multiple sclerosis.
Specific Aims	Investigate vestibulo-ocular and vestibulospinal function in patients with MS Investigate how rehab can improve VOR and VSR function
Overlap	None
Role:	PI

Title:	Epidemiologic Research on Screening for Vestibular and Balance Disorders **(RECENTLY ENDED)**
Effort:	0.60 Calendar
Supporting Agency:	(NIH/NIDCD) Cohen
Grants Officer	Eric Nunn Mgmt. Specialist (301)451-5882; eric.nunn@nih.gov
Performance Period:	05/01/2015 – 04/30/2016
Funding Amount$	20,735
Project Goals:	This application continues the development of tests for use in epidemiologic studies of vestibular and balance function, and other applications in which comprehensive vestibular testing is not possible.
Specific Aims	Develop age-specific normative reference ranges for Clinical Test of Sensory Integration and Balance
Overlap	None
Role:	PI

CURRENT/PENDING/COMPLETED SUPPORT

NAME: ROHDE, CHARLES A.
TITLE: PROFESSOR

Current Support:

Title: Hopkins Center for Health Disparities Solutions
Grant Number/PI: 2P60MD000214 (LaVeist)
Time Commitments: 0.60 calendar
Supporting Agency: NIH/NIMHS
Name and Address of Funding Agency's procuring Contracting/Grants Officer:
Dorothy Castille, Program Official, 301-594-9411, dorothy.castille@nih.gov
Performance Period: 05/01/12 – 04/30/17
Level of Funding: Direct Cost: $841,410
Brief Description of project's goals:
The goal of this project is to continue our highly successful work in training health professionals to become effective addressing health disparities.

Title: Ethnic differences in endogenous pain regulation: PET imaging of opioid receptors
Grant Number/PI: 1R01MD009063-01 (Campbell)
Time Commitments: 0.06 calendar
Supporting Agency: NIH
Name and Address of Funding Agency's procuring Contracting/Grants Officer:
Nishadi Rajapakse, Program Official, 301-496-4338, chandima.rajapakse@nih.gov
Performance Period: 07/01/14-06/30/19
Level of Funding: Direct Cost: $250,000
Brief Description of project's goals:
The current proposal will measure μ-opioid binding potential and examine its role in ethnic group differences in pain sensitivity. Our overarching objective is to investigate the endogenous opioid system as the mechanism underlying the association between ethnicity and pain sensitivity, thereby enhancing our understanding of the neurobiology of ethnic differences.

Title: Alcohol & Comorbid Tobacco Use Disorders: PET Imaging of Glutamate Effects
Grant Number/PI: Wong
Time Commitments: 0.12 calendar
Supporting Agency: NIH
Name and Address of Funding Agency's procuring Contracting/Grants Officer:
John Matochik, Program Official, 301-451-7319, jmatochi@mail.nih.gov
Performance Period: 08/01/15-06/30/20
Level of Funding: Direct Cost: $3,751,640
Brief Description of project's goals:
This proposed study will set the stage for future research to directly test the therapeutic effects of mGluR5 NAMs on brain mGluR5 occupancy and behavioral outcomes in AUD (Alcohol and Tobacco Use Disorders) clinical population.

Title: Sensorimotor Assessment and Rehabilitative Apparatus (New funding)
Grant Number/PI: Schubert
Time Commitments: 1.20calendar
Supporting Agency: DOD
Name and Address of Funding Agency's procuring Contracting/Grants Officer:
Steven Zuraf, Department of Health and Human Services, 301-492-4855
Performance Period: 09/01/15-08/31/18
Level of Funding: Direct Cost: $429,484
Brief Description of project's goals:
This is an applied research application to examine subjects for multisensory impairment (MSI, e.g. vision, vestibular) using a portable technology that rapidly and unobtrusively measures how these interdependent sensorimotor subsystems are functionally integrated. We will investigate the validity of our portable measure of MSI to identify pathology and predict return to duty/function in both veteran and civilian populations. Our device (SARA) has been validated in the challenging environment of reduced gravity and shown to accurately identify misalignment in eye position due to changing gravitational force, monitor gait, and measure in visual acuity.

Pending Support:

Title: Common Symptoms of Traumatic Brain Injury and Alzheimer's Disease and Their Impact on Military Service Members' Quality of Life and Caregiver's Burden
Grant Number/PI: (Rohde)
Time Commitments: 0.94 calendar
Supporting Agency: DOD
Name and Address of Funding Agency's procuring Contracting/Grants Officer:
Steven Zuraf, Department of Health and Human Services, 301-492-4855
Performance Period: 08/01/17-07/31/18
Level of Funding: Direct Cost: $20,398
Brief Description of project's goals:
In this two-phased research project, we will first use the retrospective data from the Military Health System Data Repository to examine the epidemiology of TBI-related AD in the military. The second phase will use survey data from a random sample of service members with TBI-related AD and their caregivers to determine the impact of their symptoms on the service members' quality of life and well-being (e.g. burden, depression) of their caregivers.

Title: PET Imaging of Effects of Nicotine on a 7-nAChR in Rodent and Human Brain
Grant Number/PI: Wong
Time Commitments: 0.36 calendar
Supporting Agency: NIH/NCI
Name and Address of Funding Agency's procuring Contracting/Grants Officer:
Ying Tian, 301-427-1530, ying.tian@ahrg.hhs.gov
Performance Period: 09/01/16 – 08/31/21
Level of Funding: Direct Cost: $492,766
Brief Description of project's goals:

The purpose of this translational application is to understand the role of the α7-subunit of the nicotinic acetylcholine (α7 nAChR) in nicotine dependence. Using positron emission tomography technologies, we will compare α7 nAChR in smokers and nonsmokers. In a preclinical animal study α7 will also be compared with α4β2 to increase our understanding of the potential role of α7 as a therapeutic target and its mechanism in tobacco use disorders.

Completed Support:

Title: Tinnitus Retraining Treatment Trial Data Coordinating Center (TRTT) (GRANT RECENTLY ENDED)
Grant Number/PI: U01 DC007422 (Scherer)
Time Commitments: 0.60 calendar
Supporting Agency: NIH/NIDCD
Name and Address of Funding Agency's procuring Contracting/Grants Officer:
Gordon Hughes, Program Official, 301-435-4085, hughesg@nidcd.nih.gov
Performance Period: 09/01/09-08/31/15
Level of Funding: Direct Cost: $258,499
Brief Description of project's goals:
The Tinnitus Retraining Therapy Trial is a multi-center randomized controlled trial testing the efficacy of tinnitus retraining therapy versus usual care as a treatment for severe debilitating tinnitus in patients with functionally normal hearing.

Title: Mechanisms of Preferential Motor Reinnervation
Grant Number/PI: R01NS034484 (Brushart)
Supporting Agency: NIH/NIND
Name and Address of Funding Agency's procuring Contracting/Grants Officer:
Lyn B Jakeman, Program Official, 301-496-1447, lyn.jakeman@nih.gov
Performance Period: 04/01/09 – 06/11/13
Brief Description of project's goals:
This research uses novel in vivo and in vitro models to investigate the role played by pathway-derived growth factors in peripheral nerve regeneration.

Title: Mechanisms of Dopamine and Serotonin in Tourette Syndrome
Grant Number/PI: R01MH078175 (Wong)
Supporting Agency: NIH/NIMH
Name and Address of Funding Agency's procuring Contracting/Grants Officer:
John Matochik, Program Official, 301-451-7319, jmatochi@mail.nih.gov
Performance Period: 04/01/01 – 03/13/13
Brief Description of project's goals:
The goal of this project is to examine dopamine and serotonin aspects of Tourette Syndrome.

Title: Disparities in Cardiovascular Disease Risk: Neighborhood Segregation and Poverty
Grant Number/PI: R01HL092846 (Gaskin)
Supporting Agency: NIH/NHLBI
Name and Address of Funding Agency's procuring Contracting/Grants Officer:
Ying Tian, 301-427-1530, ying.tian@ahrg.hhs.gov

Performance Period: 09/01/09 – 06/30/12

Brief Description of project's goals:

This project will examine the social determinants of racial disparities in clinical and behavioral risk factors for cardiovascular disease.

JORGE SERRADOR, PhD

Ongoing Research Support

*W81XWH-14-GWIRP-IIRA	Serrador (PI)	09/16-08/19	1.2 months
CDMRP/Department of Defense		$638,771	

Improving Cognitive Function in Veterans with Gulf War Illness by Improving Cerebral Vascular Function

Specific Aims: Aim 1: Demonstrate the relationship between cognitive impairment in Veterans with GWI and reduced vasodilatory function of the cerebral vasculature. Aim 2: Determine if impaired cerebrovasodilatory capacity can be improved by blocking COX and as a result, improve cognitive function.

*1I01CX001329-01	Cook/Falvo (M-PI)	01/16-12/19	1.2 months
VA CSR&D Award for Research on Gulf War Veterans' Illnesses		$2,190,412	

Post Exertion Malaise in GWI: Brain Autonomic and Behavioral Interactions

Specific Aims: The proposed research studies will determine whether interactions among central nervous, autonomic, and immune systems explain symptoms at baseline and the worsening of symptoms that occur following exercise challenge (i.e., post-exertion malaise).
Role: Co-I

*W81XWH-14P1-GWIRP-IIREA	Serrador (Co-PI)	9/15-09/18	1.2 months
DMRDP/CDMRP		$850,000	

Diagnosis of Late-stage, Early-onset, Small-fiber Polyneuropathy

Specific Aims: Aim 1: Improving diagnosis: Develop and validate simpler SFPN tests for general use with Gulf War veterans. Aim 2: Developing genetic tests: Develop and validate sequencing based tests for polymorphisms in SFPN-associated genes for use in GW veterans and civilians with L/E/SFPN.
Role: Partnering PI
Grants Officer: Brett Chaney, CDMRP

W81XWH-14-CRMRP-NSRRA	Schubert (PI)	09/15-09/18	1.2 months
CDMRP		$1,500,000	

SARA - Sensorimotor Assessment and Rehabilitation Apparatus

Specific Aims: Aim 1: Correlate behavioral measure of ocular misalignment from otolith damage against gold standard measures of otolith function in an mTBI, vestibular deficit. Aim 2: Investigate difference in dynamic visual acuity to distinguish vestibular oculomotor from visual oculomotor control dysfunction. Aim 3: Predict who with vestibular hypofunction will respond well to vestibular rehabilitation intervention.
Role: Co-I

W81XWH-14-1-0598	Serrador (PI)	09/14-09/16	1.8 months
CDMRP/Department of Defense		$553,095	

Use of a Portable Stimulator to Treat Gulf War Illness

Specific Aims: Aim 1: Determine the level of vestibular dysfunction in a group of Veterans with Gulf War Illness. Aim 2: Determine the effectiveness of subsensory electrical stimulation in a population of Veterans with vestibular dysfunction to improve balance function.
Role: PI
Grants Officer: Brett Chaney, CDMRP

W81XWH-14-2-0012	Serrador (PI)	04/14-03/18	4.0 months

DMRDP/CDMRP $1,983,088

Treatment of Vestibular Dysfunction Using a Portable Stimulator

The major goal of this award is to determine if the use of stochastic noise electrical stimulation can improve vestibular function in those with vestibular loss. In addition, we will develop a portable stimulator that can be used as a new restorative device.

Role: PI

Grants Officer: Dr. Tian Wang, CDMRP

Pending Support

16045458 Serrador (PI) 04/17-03/22 3.96 months

NIH/NINDS & NHLBI $3,758,411.00

Immediate and Long Term Cardiovascular, Cerebral Hemodynamic and Hypertensive Responses to Concussive Trauma in Humans Playing Contact Sports: Effects of Age and Sex

Specific Aims: Aim 1: Determine the effect of concussion (mTBI) on blood pressure and global cerebral blood flow regulation within the first 6 hours of injury and brain tract integrity in the first 48 hours. Aim 2: Examine sex differences in the rates of concussion and the physiological response to concussion.

Completed Research Support

GW100095 Consortium Development Award Serrador (PI) 07/11-06/12

CDMRP/Dept. of Defense $254,600

Integrative Physiology of Gulf War Illness: Role of Autonomic Function, Central Neural Processing, and Sleep

The major goal of this award is to develop a consortium proposal involving 17 investigators and 7 institutions to examine the pathophysiology of Gulf War Illness.

Role: PI

R21DC009900 Serrador (PI) 09/09-08/12

N.I.H. / N.I.D.C.D. $374,203

Role of Cerebral Blood Flow in Nausea and Motion Sickness

The major goal of this award is to determine the role of changes in cerebral blood flow in the development of nausea and motion sickness to determine if cerebral blood flow changes could be used as an objective indicator of motion sickness.

Role: PI

1I21RX001079-01 Falvo (PI) 07/13-06/15

VA RR&D Merit Review Award: Pilot Projects $196,855

Effects of Deployment Exposures on Cardiopulmonary and Autonomic Function

The major goal of this award is to determine whether deployment-related exposures have affected cardiorespiratory and nervous system function.

Role: Co-I

*New awards

CURRENT/PENDING/COMPLETED SUPPORT

Shelhamer, Mark

ACTIVE

Title:	Sensorimotor Assessment and Rehabilitative Apparatus
Effort:	.60 Calendar
Supporting Agency:	CDMRP (Schubert)
Grants Officer	Steven Zuraf, Department of Health and Human Services, 301-492-4855
Performance Period:	09/01/2015 -08/31/2018
Funding Amount$	1,271,146
Project Goals:	This is an applied research application to examine subjects for multisensory impairment (MSI, e.g. vision, vestibular) using a portable technology that rapidly and unobtrusively measures how these interdependent sensorimotor subsystems are functionally integrated. We will investigate the validity of our portable measure of MSI to identify pathology and predict return to duty/function in both veteran and civilian populations.
Specific Aims	Our device (SARA) has been validated in the challenging environment of reduced gravity and shown to accurately identify misalignment in eye position due to changing gravitational force, monitor gait, and measure in visual acuity
Overlap	None
Role:	PI

COMPLETED

PENDING

None

Biographical Sketch

Provide the following information for each individual included in the Research & Related Senior/Key Person Profile (Expanded) Form.

NAME	POSITION TITLE
MARK SHELHAMER	ASSOCIATE PROFESSOR

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training).

INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY
Drexel University, Philadelphia PA	BS	1982	Electrical Engineering
Drexel University, Philadelphia PA	MS	1982	Electrical Engineering
MIT, Cambridge MA	ScD	1990	Biomedical Engineering
Johns Hopkins University, Baltimore MD	Post-doctoral	1992	

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List in chronological order the titles, all authors, and complete references to all publications during the past 3 years and to representative earlier publications pertinent to this application. If the list of publications in the last 3 years exceeds 2 pages, select the most pertinent publications. PAGE LIMITATIONS APPLY. DO NOT EXCEED 5 PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INDIVIDUAL.

Positions and Employment

1978-1979 **Cooperative Education Student**, Drexel University
1979-1980 **Research Assistant**, Ultrasonics International, Inc.
1980-1982 **Laboratory Technician**, Temple University Medical School
1985 **Volunteer Instructor**, NASA Space Life Sciences Training Program
1982-1990 **Research Assistant**, Man-Vehicle Laboratory, M.I.T.
1990-1992 **Postdoctoral Fellow**, Wilmer Institute, Johns Hopkins Univ School of Medicine
1992-1994 **Research Associate**, Biomedical Engineering, Johns Hopkins University
1994-2002 **Assistant Professor**, Otolaryngology & Biomedical Eng, Johns Hopkins School of Medicine
2002-present **Associate Professor**, Otolaryngology & Biomedical Eng, Johns Hopkins School of Medicine
2013-2016 **Chief Scientist**, NASA Human Research Program, NASA Johnson Space Center

Other Experience and Professional Memberships

Grant review panels: NASA Neurolab (1994), NIH Special Emphasis Panel (1997-2000, 2009-2013), NASA Neurobiology panel (2000-2002), NSF (2003)
IEEE Summer School in Biomedical Signal Processing (1995)
Project Leader, NASA NSBRI Vestibular Experiments (1997-2004)
NASA Workshops: Human Vestibular Adaptation (1999), Artificial Gravity (1999)
NASA Neurovestibular Integrated Product Team (IPT) (1999-2002)
NASA Clinical Status Evaluation working group (2004)
Franklin Institute brain exhibit advisory panel (2008-2010)
Commercial Spaceflight Federation – Suborbital Applications Researchers Group (2009-)
Editor, special issue of Nonlinear Dynamics in Psychology and Life Sciences (2009)
Editorial board, npj Microgravity

Honors

NASA Group Achievement Award, for Life Sciences Experiments on Spacelab-1 (1984)
Award for outstanding contributions to the MIT Man-Vehicle Laboratory (1989)
Who's Who in Science and Engineering (1999-2000)
Senior Member, IEEE

Federal Government Advisory Committees

Traumatic Injury Research Program Scientific Advisory Board (2015-)

Schubert MC, Della Santina CC, **Shelhamer M**. Incremental angular vestibulo-ocular reflex adaptation to active head rotation. *Exp Brain Res*, 2008, 191:435-446.

Scherer MR, **Shelhamer MJ**, Schubert MC. Characterizing high-velocity angular vestibulo-ocular reflex function in service members post-blast exposure. *Exp Brain Res*, 2010, 208:399-410.

Wong AL, **Shelhamer M**. Sensorimotor adaptation error signals are derived from realistic predictions of movement outcomes. *J Neurophysiol*, 2011, 105:1130-1140.

Wong AL, **Shelhamer M**. Saccade adaptation improves in response to a gradually introduced stimulus perturbation. *Neurosci Lett*, 2011, 500:207-211.

Wong AL, **Shelhamer M**. Exploring the fundamental dynamics of error-based motor learning using a stationary predictive-saccade task. *PLoS ONE*, 2011, 6:e25225.

Wong AL, **Shelhamer M**. Using prediction errors to drive saccade adaptation: the implicit double-step task. *Exp Brain Res*, 2012, 222:55-64.

Wong AL, **Shelhamer M**. A long-memory model of motor learning in the saccadic system: a regime-switching approach. *Ann Biomed Eng*, 2013, 41:1613-1624.

Wong AL, **Shelhamer M**. Similarities in error processing establish a link between saccade prediction at baseline and adaptation performance. *J Neurophysiol*, 2014, 111:2084-2093.

Shelhamer M. Life-sciences research opportunities in commercial suborbital space flight. *Acta Astronautica*, 2014, 104:432-437.

Shelhamer M. Trends in sensorimotor research and countermeasures for exploration-class space flights. *Front Syst Neurosci*, 2015, 9:115.

Shelhamer M. A call for research to assess and promote functional resilience in astronaut crews. *J App Physiol*, 2016, 120:471-472.

Shelhamer M. Parabolic flight as a spaceflight analog. *J Appl Physiol*, 2016, 120:1442-1448.