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TITLE: Assessment and Rehabilitation of Central Sensory Impairments for Balance in mTBI

PRINCIPAL INVESTIGATOR: Dr. Laurie King

CONTRACTING ORGANIZATION: Oregon Health & Science University
Portland, OR 97201

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14. ABSTRACT

Objectives: Control of balance requires complex integration of sensory and motor systems. Balance measurement is often over-simplified, preventing balance deficits from being identified and treated after mTBI. Our central hypothesis is that chronic balance deficits after mTBI result from impairments in central sensorimotor integration that may be helped by rehabilitation. This research has two objectives; 1) to characterize balance deficits in people with mTBI, and 2) to use a novel auditory biofeedback device to improve measures central sensorimotor integration and balance control.

Methods: Aim I) Balance Assessment: mTBI patients with non-resolving balance deficits following injury and healthy control participants with no history of mTBI are currently being recruited and tested on a battery of vestibular, neurocognitive, and balance-related tests. Aim II) Balance Rehabilitation: mTBI patients (a subgroup from Aim 1) are randomly allocated into a standard of care balance rehabilitation program either with, or without auditory biofeedback. Both groups receive rehabilitation two times per week for six weeks. All participants are tested at baseline during Aim I testing, and are tested again following the intervention period, and again 6 weeks later to determine retention of changes.

Status: We have screened a total of 155 subjects for participation in this study. Of those screened, a total of 108 subjects have been enrolled at both sites (51 chronic mTBI and 57 controls). 101 participants have completed baseline testing (47 chronic mTBI and 54 controls) of the full protocol (Aim 1). 27 of the chronic mTBI participants have fully completed rehabilitation and the 6 week post-rehabilitation testing, and 22 have completed the 12 week retention testing (Aim 2). 10 out of the 10 control participants needed did return to complete the 6 week testing. Four chronic mTBI patients have been lost to follow up.

Findings to date: People with chronic mTBI reported worse symptoms relating to balance and vestibular dysfunction than the healthy controls. People with chronic mTBI performed worse on the ANAM neurocognitive testing battery, and were slower to respond to stimuli during the dual-task. Turning speed and coordination were slower in people with chronic mTBI. People with chronic mTBI weighted sensory information differently during the test of central sensorimotor integration.

15. SUBJECT TERMS

Balance, mTBI, Rehabilitation, Brain Injury, BESS, Dynamic Posturography, SOT, Inertial Sensors, Auditory Biofeedback, Central Sensory Integration, Concussion

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Table of contents

1. INTRODUCTION:	5
2. KEYWORDS:	5
3. ACCOMPLISHMENTS:	5
4. IMPACT:	13
5. CHANGES/PROBLEMS:	14
6. PRODUCTS:	15
7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:	18
8. SPECIAL REPORTING REQUIREMENTS:	19
9. APPENDICES:	19

1. INTRODUCTION:

Control of balance requires complex integration of sensory and motor systems. In the clinic or in the field, balance measurement is often over-simplified, preventing balance deficits from being identified and treated after mTBI. Our central hypothesis is that chronic balance deficits after mTBI result from impairments in central sensorimotor integration that may be helped by rehabilitation. There are two objectives of this proposal; the first objective is to characterize balance deficits in people with mTBI. The second objective is to use a novel auditory biofeedback (ABF) device to improve measures of central sensorimotor integration and balance control.

2. KEYWORDS:

mTBI, Rehabilitation, Brain Injury, BESS, Inertial Sensors, Balance, Auditory Biofeedback, Central Sensory Integration, Concussion

3. ACCOMPLISHMENTS:

What were the major goals and objectives of the project?

Goal	Target Completion Date	Percentage of Completion/ Date of Completion
Specific Aim 1 (Study 1: Assessment n=130 mTBI)		
Major Task 1: Launch Study Activities	30-Feb-2016	100%
Major Task 2: Recruitment and Testing (n=130)	30-Feb-2019	83%
Major Task 3: Data Analysis and Publications	30-Sep-2019	60%
Specific Aim 2 (Study 2: Rehabilitation n=40 mTBI)		
Major Task 1: Launch Study Activities	30-Feb-2016	100%
Major Task 2: Prepare Technology and Protocol for Intervention	30-Sep-2016	100%
Major Task 3: Randomized Interventions (n=40 mTBI)	30-Feb-2019	85%

Major Task 4: Assess Efficacy of Interventions (n=40)	30-Feb-2019	74%
Major Task 5: Data Analysis and Publications	30-Sep-2019	35%

What was accomplished under these goals?

Status of major activities and specific objectives:

Specific Aim 1 (Study 1: Assessment n=130)

Major task 1: Launch study activities

Subtask 1: Prepare regulatory documents and research protocol

- Prepare FITBIR forms for data reporting; The CTSIB, The Pain Location Inventory, Bucket Test, and Symptom Impact Questionnaire are still awaiting publication from FITBIR. We are currently waiting on FITBIR to finalize and publish these forms. As soon as this is completed, they will contact us; 90% complete.

Major Task 2: Recruitment and testing (n=130)

Subtask 1: Recruitment (n=130)

- Prepare brochures for subject recruitment and meet with primary sources of referral; we found that recruiting through EPIC's BPA system and OHSU's Concussion Clinic to be the most successful recruitment method. This will continue to be an ongoing process; 95% complete.
- Phone screening of subjects; screenings are being performed at OHSU by Research Assistants and Physical Therapists. This will be an ongoing procedure in the protocol; 86% complete.
- Schedule vestibular/audiogram/ocular motor, CSMI, balance and gait testing; subjects are currently being scheduled for all testing at both locations. This will be an ongoing procedure in the protocol; 83% complete.

Subtask 2: Data collection/management (n=130)

- Schedule testing sites for data collection; subjects are currently being scheduled for their vestibular/audiogram/ocular motor testing, CSMI and balance/gait testing at both OHSU and the VA. This will be an ongoing procedure in the protocol; 83% complete.
- Data collection for the 2 days of data collection for aim 1 takes place; subjects are currently completing their vestibular/audiogram/ocular motor testing, CSMI and

balance/gait testing at both OHSU and the VA. This will be an ongoing procedure in the protocol; 77% complete.

- Data back-up onto server including manual data entry; We have verified both servers and will continue to enter and back up data; 70% complete.
- Screen and verify data on server; check for accuracy; these data checks will be performed quarterly. We just completed a data check in September 2018 and are up to date on data checks; 75% complete.
- Upload data to FITBIR; We have submitted data for all published forms, for all subjects tested so far and are in compliance with reporting requirements. This was completed in December 2017, March 2018, June 2018, and September 2018. FITBIR recently changed their guidelines and now data must be reported annually, rather than quarterly. We will continue this next year to follow FITBIR guidelines; 75% complete.

Major Task 3: Data analysis and publications

Subtask 1: Data analysis

- Perform all analysis-according proposal and share all findings with investigators; we have continued analysis of data collected to date. A manuscript on the test-retest reliability of the CSMI is in preparation and due for submission in December. A methods paper aimed at improving the clinical utility of the CSMI test protocol has been submitted and is under review. As we continue analysis into the next reporting period, we are targeting further analyses and interpretation of vestibular data, neurocognitive data, and balance and gait data; 60% complete.

Subtask 2: Manuscripts and presentations

- Disseminate findings (abstracts, presentations, papers, DoD); we have had an extremely productive year, which has resulted in a number of submitted abstracts and conference presentations. Details are provided in the Products sections below; 60% complete.

Specific Aim 2 (Study 2: Rehabilitation n=40 mTBI)

Major Task 3: Randomized interventions (n=40 mTBI patients)

Subtask 1:

- PTs call subjects to schedule intervention; subjects are currently being scheduled for the 6-week intervention program; 85% complete.
- 6 week interventions at both sites; for the ease of PT and PT team member, all interventions have been and will continue to take place at OHSU; 85% complete.

- PTs document compliance, adverse events and progression of exercise for each subject; all forms have been created, entered in the database and are currently being used; 85% complete.

Major Task 4: Assess efficacy of interventions (n=40)

Subtask 1:

- Immediate post-test after intervention; 27 subjects have completed the intervention and immediate post-test. Preliminary analyses has been conducted using data from these participants; 68% complete.
- Long-term assessment 6 weeks later to assess retention of improvements; 22 subjects have completed their long-term assessment; 55% complete.

Subtask 2:

- A subset of controls will be tested at a 6 week follow up in order to determine any natural changes in the CSMI test over 6 weeks; 10 out of the planned 10 control subjects have already been assessed; 100% complete.

Major Task 5: Data analysis and publications

Subtask 1: Data Analysis

- Perform all analysis-according proposal and share all findings with investigators; we have been performing a more in depth analyses of the CSMI balance data, and are in the early stages of preparing a manuscript. Until we have finalized data capture following the intervention, we will not be completing any further analyses on Aim 2 data. We aim to complete analysis on these data during the next reporting period; 30% complete

Subtask 2: Manuscripts and presentations

- Disseminate findings (abstracts, presentations, papers, DoD), including American Physical Therapy Association and American Congress of Rehabilitative Medicine and rehabilitation journals to share with clinicians; Details are provided in the Products sections below; 40% complete.

Significant Results/ Key outcomes:

Summary of screening, enrolment and completion:

We have screened a total of 155 subjects for participation in this study. Of those screened, 108 have been enrolled (51 chronic mTBI and 57 controls). 101 participants have completed baseline testing (47 chronic mTBI and 54 controls) of the full protocol (Aim 1). Demographic information for these participants is provided in Table 1. 27 of the chronic mTBI participants have fully completed rehabilitation and the 6 week post-rehabilitation testing, and 22 have completed the 12 week retention testing (Aim 2). 10 out of 10 control participants have returned

to complete the 6 week testing, in order to check the consistency of the measures being assessed (Aim 2). Four chronic mTBI patients have been lost to follow up.

Table 1. Demographics for chronic mTBI and control groups, provided as mean (standard deviation).

	mTBI	Control	P-Value
Gender (n, %female)	52, 71%	58, 59%	--
Age (years)	40 (12)	37 (13)	0.23
Height (m)	1.70 (0.09)	1.70 (0.08)	0.80
Mass (kg)	77.8 (18.3)	76.4 (19.5)	0.71
BMI	26.7 (5.7)	25.8 (5.2)	0.40
Time since injury (years)	2.3 (2.7)	--	--

The following summary of findings are preliminary, and are subject to change with on reanalysis with a complete dataset:

People with chronic mTBI show deficits in real-world turning, but not in measures of daily activity. The chronic mTBI group were not different to healthy controls in their walking bouts per hour, bout duration, variation of bout duration or activity rate – all of which are considered measures of activity level. However, in comparison with healthy controls, mTBI participants made larger turns, had longer turning durations, and had slower peak turning speeds, as well as displaying more variation in each of these measures. These turning deficits were also related to symptom severity, suggesting that real-world turning measures may be more sensitive to mTBI symptoms than measures of daily activity.

mTBI with chronic balance problems also show signs of persistent cognitive impairment. In two different cognitive tests, chronic mTBIs have shown signs of poorer performance in comparison with healthy controls. Firstly, mTBIs performed worse overall on the ANAM computerized cognitive battery (Figure 1), and second, mTBIs were slower at responding to the cognitive task (Auditory Stroop) during dual-task walking (Figure 2). Furthermore, when dual-task cost was calculated for the cognitive task (Auditory Stroop), mTBIs showed a cost of almost 10%. Comparatively, dual-task cost on walking (Gait) was less than 3%, suggesting that mTBIs may prioritize walking over the speed of their response (Figure 3). Together these findings suggest cognitive problems may persist in this population.

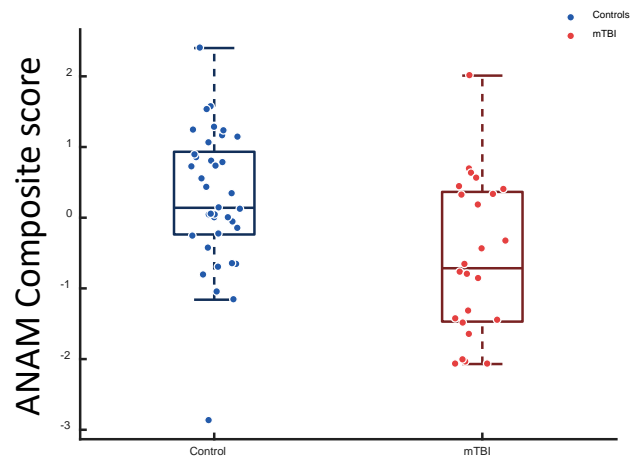


Figure 1: ANAM Composite score. mTBIs performed significantly worse overall on the ANAM.

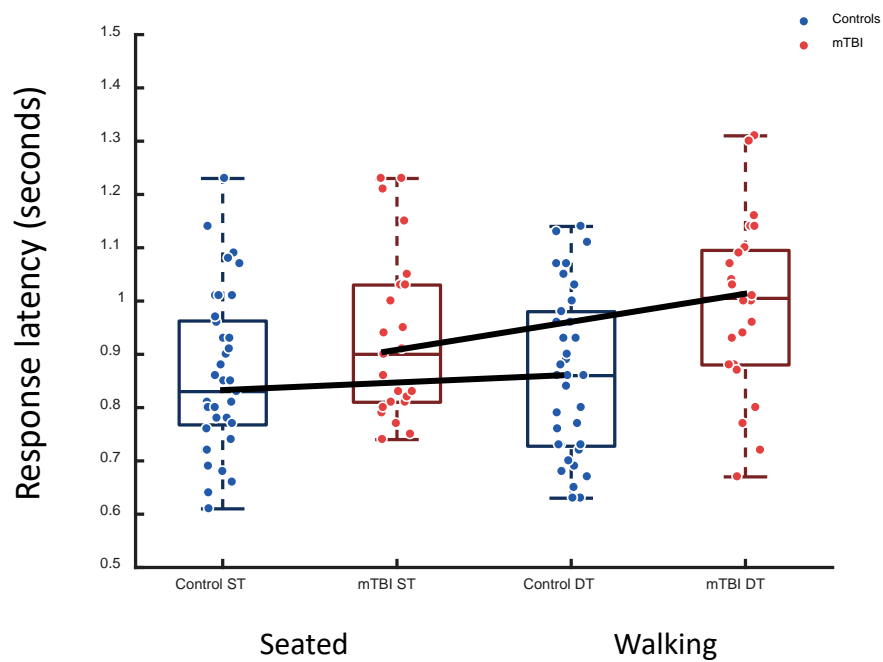


Figure 2: Response latency. mTBIs were slower to respond to the Auditory Stroop during the dual-task.

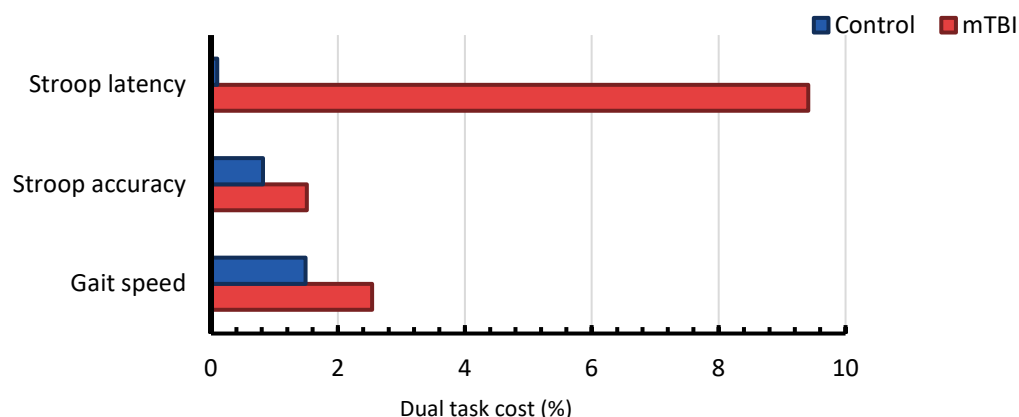


Figure 5: Dual-task costs indicating that the speed at which mTBIs were able to respond to the Auditory Stroop was limited during the dual-task.

CSMI test development:

The CSMI test can effectively be completed using a reduced time period of 2 minutes and without the use of sway rods. Our results suggested that the CSMI parameters could effectively be established under a reduced time period of 2 minutes, making the test a more practical test to be implemented in clinical settings. In addition to this, we found that a process of low-pass filtering of the center of pressure (CoP) can effectively estimate the CSMI parameters of interest. This process reduces the need for additional specialized equipment to be added to the NeuroCom Equitest system, and reduces the time needed to conduct the testing. The relationship between data collected using the Sway Rods and using a filtered CoP are provided in Figure 4.

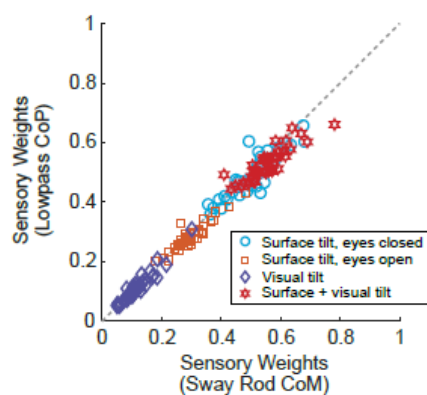


Figure 4. Scatterplot of the low-pass filter method versus the sway rod method to determine Sensory Weight for each condition.

As people with chronic mTBI progress through the intervention, they are becoming more tolerant of the exercises and able to undertake more of the exercises in the program. Results indicate that the average number of exercises performed per treatment session increase over time. In addition to this, the average patient symptom score, as measured by the SCAT, is declining as patients progress through the rehabilitation program, suggesting improvement.

The speed at which people with chronic mTBI turn improved in people with mTBI after vestibular rehabilitation. At baseline, chronic mTBIs had significantly slower peak turning speed compared with the control group. A significant group*session interaction was found for peak turning velocity, where the mTBI group increased their peak turning velocity more than controls over time – suggesting an improvement.

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

The research team has had the opportunity to attend a number of conferences and meetings in order to meet with experts in the field of research. The most important meeting and best professional development was the Military Health System Research Symposium (MHSRS).

Six members of the project team, Dr. Laurie King (PI), Dr. Lucy Parrington (post-doctoral fellow), Jim Chesnutt (Co-I), Natalie Pettigrew (PT), and Sam Stuart (postdoctoral scholar), and Dr. Peter Fino (post-doctoral fellow) each attended the MHSRS in Kissimmee, Florida, August 2018. Dr. Fino, Dr. Stuart and Dr. King were invited to orally present their findings in a platform format. Dr. Parrington presented CSMI test-retest reliability in a poster. The conference provided the opportunity for these research team members to discuss current and future work, as well as further develop networks and collaborations with other mTBI researchers. While in attendance at the MHSRS, the team also attended a meeting with researchers from across the country working in the area of mTBI to discuss return to duty decisions for military members.

Dr. King presented a summary at the in-person review at Ft. Detrick this year, as well as presenting this project at the Federal Interagency Conference on mTBI in Washington DC, 2018.

How were the results disseminated to communities of interest?

The results have been disseminated to broad communities of interest, such as:

- Other scientists (MHSRS, Federal Interagency, NASPSPA, and APTA CSM Meeting)
- Clinician audience (OHSU Grand Rounds, OHSU Primary Care Physician Group, Brain Injury Rehab Center (Portland, OR))
- Patient groups (Brain Injury Association of Oregon, International School, and Community Lab Tours)

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

We plan to finish recruitment in the two next quarters. Following this there will be a focus placed on data analysis and the dissemination of research findings through reports, conference presentations and manuscripts. Analyses of data have primarily focused on the cross-sectional data that has been collected. Once we have completed all subjects through the rehabilitation program (Aim II), we will be able to initiate analyses on the intervention data. Thus, in the next reporting period, we will begin to finalize our analysis for Aim I, and begin analysis of Aim II.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

This project is allowing researchers in the area of mTBI to understand more about the role that sensory integration plays in chronic balance deficits. Furthermore, it is creating awareness in clinicians of the need to use more objective measurements of balance deficit. As we progress through the study, we hope that this project will give insight into how audio biofeedback can be used to help the rehabilitation process, by helping to guide and recalibrate the way people use (i.e. integrate) their sensory information to balance and perform day to day tasks. We believe this research will impact clinical practice, by first, providing information on how to more objectively quantify chronic balance problems related to mTBI, and second, in guiding the standard of care to use audio biofeedback technology.

What was the impact on other disciplines?

Our research team has continued to meet once per month with mTBI treating OHSU doctors, physical therapists and athletic trainers, and affiliated clinicians from other clinics. We have found that these meetings allow an open discussion between researchers and clinicians, to discuss research findings, and work towards translating research knowledge into clinical practice. Additionally, we are working closely with the ENT Department at OHSU (Hullar) to interpret our findings as they relate to their patient population with mTBI.

What was the impact on technology transfer?

The primary impact on technology transfer is the submission of a methods-based manuscript that has been submitted to Frontiers, special edition: “Current State of Postural Research – Beyond Automatic Behavior”. Second revisions are underway. This paper provides details on how the NeuroCom Clinical Research System™ can be customized for the CSMI protocol. The paper aims to help transfer knowledge to other researchers in the field in how to program the NeuroCom for the CSMI protocol, and promote the use of this method for analyzing balance dysfunction in persons with chronic balance problems following mTBI and other balance impaired populations.

Another impact this study is generating, is in the area of home monitoring after mTBI. A postdoc on the team, Sam Stuart, is measuring quality of movement in the home after mtBI, which seems to be more sensitive to classifying people with mTBI compared to quantity of movement.

What was the impact on society beyond science and technology?

In March 2018 members of our team attended the OHSU Brain Fair, an annual event held at the Oregon Museum of Science and Industry (OMSI). The fair is open to the public and people of all ages were present. Members of our research team discussed issues around balance and gait, and reaction time in chronic mTBI, performed demonstrations and invited fair attendees to test their reaction time using our clinical reaction time test.

Our research team has provided two internships for undergraduate students from diverse backgrounds by providing them with the opportunity to learn about our study and complete independent projects to help build their knowledge in the area of mTBI, balance and gait. One student received an award from NIH Build Exito to join our lab for two years to help with this project. Another student received a grant for 3 months to work in our lab on this project from the Promoting Opportunities for Diversity in Education and Research “Build Poder”.

5. 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

In Year 3, Quarter 1: Problems taken from the quarterly report) /Resolution

- 1) Did not meet recruitment target for this month/ Increased our recruitment goals for the next quarter to ensure we hit our targeted numbers
- 2) Scheduling subjects during the holidays/ As a study team we plan to have slow enrollment during the holidays and we are able to plan for this by recruiting more people in the months prior/after
- 3) Having a difficult time recruiting mTBI subjects/ Study team members took an EPIC training course to become familiar with EPIC’s Best Practice Advisory (BPA) that alerts us when a patient is seen at OHSU with a concussion. This has been our most successful recruitment tool

In Year 3, Quarter 2: Problems taken from the quarterly report) /Resolution

- 1) IRB modification to add medical device forms stalled our project for 2 months/ Even with this delay we were able to reach our recruitment goals

In Year 3, Quarter 3: Problems taken from the quarterly report) /Resolution

- 1) IRB modification to add data storage/repository language to the consent form stalled our project for 3 weeks/ Even with this delay we were able to reach our recruitment goals

In Year 3, Quarter 4:

- 1) We had two postdocs and one RA leave the study team/ This slowed down recruitment for a short amount of time, but we have hired replacement staff and have trained them on the study protocol and methods of recruitment

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

6. PRODUCTS:

Publications, conference papers, and presentations

Publications, conference papers, and presentations submitted, accepted, and presented during the reporting period October 2017 to September 2018:

Manuscripts published:

- Mancini M, Stuart S, King LA, El-Gohary M, & Horak F. (2018). Wearable technologies: from theory to clinical practice. IEEE Conference on Biomedical and Health Informatics and Body Sensor Networks.
- Fino P, Parrington L, Pitt W, Martini D, Chesnutt JC, Chou LS, & King LA. (2018). Detecting gait abnormalities after concussion or mild traumatic brain injury: A Systematic review of single-task, dual-task, and complex gait. *Gait & Posture*, 62.
- Fino P, Wilhelm J, Parrington L, Stuart S, Chesnutt JC, & King, LA. (2018). Inertial sensors reveal subtle motor deficits when walking with horizontal head turns after concussion. *Journal of Head Trauma Rehabilitation*.
- Karim AM, Rumalla K, King LA, & Hullar TE. (2018). The effect of spatial auditory landmarks on ambulation. *Gait & Posture*, 60, 171-174.
- Fino PC, Parrington L, Walls M, Sippel E, Hullar TE, Chesnutt JC, & King LA. (2018). Abnormal turning and its association with self-reported symptoms in chronic mTBI. *Journal of Neurotrauma*.

- Fino PC, Peterka RJ, Hullar TE, Murchison C, Horak FB, Chesnutt JC, & King LA. (2017). Assessment and rehabilitation of central sensory impairments for balance in mTBI using auditory biofeedback: a randomized clinical trial. *BMC Neurology*, 17(1), 41.

Manuscript submitted:

- Peterka RJ, Murchison C, Parrington L, Fino PC, King, LA. Implementation of a Central Sensorimotor Integration Test for Characterization of Human Balance Control During Stance. *Frontiers*, special edition: “Current State of Postural Research – Beyond Automatic Behavior”.

Manuscript in preparation:

- Parrington L, Kreter N, Stuart, S, Fino PC, Peterka R, King LA. The Sensory Organization Test and a test of Central Sensory Motor Integration: Test-retest reliability in healthy adults. Due for submission December 2018

Completed conference presentations:

- Stuart S, Fino P, Parrington L, Jehu D, Chesnutt JC, & King LA. (20-23 August 2018). Free-living mobility improves with vestibular rehabilitation following mild traumatic brain injury. Military Health System Research Symposium, Kissimmee, FL. (Platform)
- Fino P, Parrington L, Stuart S, Jehu D, Chesnutt JC, & King LA. (20-23 August 2018). Improvements in turning speed but not gait speed in people with mild traumatic brain injury following vestibular rehabilitation. Military Health System Research Symposium, Kissimmee, FL. (Platform)
- King LA. (20-23 August 2018). Assessment of balance after mild traumatic brain injury: Are vestibular and ocular-motor testing capturing all balance deficits? Military Health System Research Symposium, Kissimmee, FL. (Platform)
- Parrington L, Kreter N, Fino PC, Peterka RJ, & King LA. (20-23 August 2018). Central sensorimotor integration test: Test-retest reliability and learning effects. Military Health System Research Symposium, Kissimmee, FL. (Poster)
- Wilhelm JL, Parrington L, Pettigrew NC, Chesnutt JC, & King LA. (17-19 August 2018). Exploring outcome measures after vestibular rehabilitation in chronic concussion patients. International Conference for Vestibular Rehabilitation, Chicago, IL. (Poster)
- Kreter N, Parrington L, Pettigrew N, Peterka R, & King LA. (17-19 August 2018). Test-retest reliability of systems assessing sensory contributions to balance. International Conference for Vestibular Rehabilitation, Chicago, IL. (Poster)
- Parrington L, Fino PC, Peterka RJ, Kreter N, & King LA. (8-11 August 2018). Test-retest reliability of the sensory organization test and central sensorimotor integration (CSMI) test. American Society of Biomechanics, Rochester, MN. (Poster)

- Parrington L, Duffield T, Fino PC, & King LA. (21-23 June 2018). Dual-task cost and cognition in patients with chronic mTBI. North American Society for the Psychology of Sport and Physical Activity, Denver, CO. (Platform)
- Jehu DA, Kempel S, Parrington L, Fino P, Hullar T, & King LA. (June 2018). Vestibular function following chronic mild traumatic brain injury (mTBI): Cervical vestibular-evoked myogenic potential parameters, convergence, and symptoms discriminated between mTBI patients and healthy controls. North American Society for the Psychology of Sport and Physical Activity Conference, Denver, CO. (Platform)
- Stuart S, Fino P, Parrington L, Chesnutt JC, & King LA. (11-13 June 2018) Turning the tide: Real-world turns are more sensitive to mild traumatic brain injury deficits than daily activity measures. 4th Federal Interagency Conference of Traumatic Brain Injury, Washington, DC.
- Jehu DA, Kempel S, Stuart S, Parrington L, Fino P, Hullar T, & King LA. (April 2018). Vestibular function following chronic mild traumatic brain injury: examining the association between otolith function, sensorimotor integration, and posture. Research Week at the Oregon Health & Science University, Portland, OR. (Presentation).
- Mancini M, Stuart S, King LA, El-Gohary M, & Horak FB. (March 2018). Wearable technology: from theory to clinical practice. Institute of Electrical and Electronics Engineers (IEEE) International Conference on Biomedical and Health Informatics Symposium, Las Vegas, NV. (Presentation).
- King LA. (22 February 2018). Rehabilitation and sensory reweighting in patients with chronic mTBI. APTA Combined Sections Meeting, New Orleans, LA. (Platform)

Conference workshop:

- Wearable Sensors and the Instrumented Assessment of Balance and Gait after Concussion. Laurie King & Lucy Parrington. Presented at the American College of Sports Medicine Conference, Minneapolis Minnesota, May 29-June 2, 2018.

Accepted conference abstracts:

- Scherer M, King LA, Lester M, McCulloch K, & Weightman M. (23-26 January 2019). Functional return-to-duty decision making post mTBI and musculoskeletal injury. APTA Combined Sections Meeting, Washington, DC. (2-Hour Educational Session)
- Motawar B, Wilhelm J, Jehu D, Kampel S, & King LA. (23-26 January 2019). Relationship between dizziness and oculomotor function in chronic mTBI. APTA Combined Sections Meeting, Washington, DC. (Platform)
- Parrington L, Stuart S, Jehu D, Huller T, Kampel S, & King LA. (3-7 November 2018). Sensory weighting in chronic mTBI with vestibular dysfunction. Society for Neuroscience, San Diego, CA. (Poster)

Website(s) or other Internet site(s)

Nothing to report

Technologies or techniques

Nothing to report

Inventions, patent applications, and/or licenses

Nothing to report

Other products

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:***What individuals have worked on the project?***

Name:	Sharna Donovan
Project Role:	Research Assistant 2
Researcher Identifier (e.g. ORCID ID):	N/A
Nearest person month worked:	2
Contribution to Project:	Performed data collection and data entry.

Name:	Nicholas Kreter- No Change
Name:	Daniel Putterman- No Change
Name:	Laurie King - No Change
Name:	Lucy Parrington - No Change
Name:	Shelby Martin- No Change
Name:	Robert Peterka - No Change
Name:	Jennifer Wilhelm- No Change
Name:	Sean Kampel - No Change
Name:	Samual Stuart- No Change

Name:

Natalie Pettigrew- No Change

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. SPECIAL REPORTING REQUIREMENTS

9. APPENDICES



IRB MEMO

OHSU Research Integrity Office

3181 SW Sam Jackson Park Road - L106RI
Portland, OR 97239-3098
(503)494-7887 irb@ohsu.edu

VA Research and Development Service

3710 SW U.S. Veterans Hospital Road - R&D
Portland, OR 97239-2999
(503)273-5152 pvamc-irb@va.gov

REVIEW OF REPORTABLE EVENT

October 19, 2018

[Laurie King](#)

Dear [Laurie King](#):

On 5/8/2018 7:00 AM, the IRB reviewed the following new information report:

- The VA consent form did not include banking addendum

This information is regarding:

Title:	VAPORHCS/OHSU J: Rehabilitation of Central Sensory Impairments for Balance in mTBI
Principal Investigator:	Laurie King
RNI ID:	RNI00002047
IRB ID:	STUDY00015010

This IRB determined that this event is noncompliance that is neither serious nor continuing.

Required remedial actions are now complete.

Sincerely,

The OHSU IRB office



IRB MEMO

OHSU Research Integrity Office

3181 SW Sam Jackson Park Road - L106RI
Portland, OR 97239-3098
(503)494-7887 irb@ohsu.edu

VA Research and Development Service

3710 SW U.S. Veterans Hospital Road - R&D
Portland, OR 97239-2999
(503)273-5152 pvamc-irb@va.gov

REVIEW OF REPORTABLE EVENT

May 16, 2018

[Laurie King](#)

Dear [Laurie King](#):

On 5/8/2018 7:00 AM, the IRB reviewed the following new information report:

- VA participants enrolled before VA ICF language around repository approved

This information is regarding:

Title:	VAPORHCS/OHSU J: Rehabilitation of Central Sensory Impairments for Balance in mTBI
Principal Investigator:	Laurie King
RNI ID:	RNI00002051
IRB ID:	STUDY00015010

This IRB determined that this event is noncompliance that is neither serious nor continuing. No remedial action required.

Sincerely,

The OHSU IRB office

TEST-RETEST RELIABILITY OF THE SENSORY ORGANIZATION TEST AND CENTRAL SENSORIMOTOR INTEGRATION (CSMI) TEST

^{1,2} Lucy Parrington, ^{1,2} Peter C. Fino, ^{1,2} Robert J. Peterka, ^{1,2} Nicholas Kreter, and ^{1,2} Laurie A. King

¹ Oregon Health & Science University, Portland, OR, USA

² Veterans Affairs Portland Health Care System (VAPORHCS), Portland, OR, USA
email: parringt@ohsu.edu

INTRODUCTION

The collection and integration of information from the vestibular, visual and somatosensory systems are an integral aspect of balance control. Balance dysfunction can arise from damage to sensory systems (e.g. somatosensory decline following lower limb injury) or from central integration issues (e.g. neuromotor impairment following mild traumatic brain injury). Tests such as the Sensory Organization Test (SOT), and the Central Sensorimotor Integration (CSMI) Test [1] have been developed to try to identify contributions to balance dysfunction in patients. Both of these tests collect anterior-posterior sway data under different sensory conditions (e.g. moving surface, moving visual surround, eyes open or closed). One of the key differences between the two tests, is that the surface or visual surround movement during the SOT is dependent upon an individual's sway, and thus the amplitude of surface or visual surround movement is not fixed, while movement of the surface and visual surround in the CSMI is determined by continuous pseudorandom stimuli at fixed peak-to-peak amplitudes of 2° and 4°.

Although the SOT has been recognized as a reliable tool for the assessment of sensory contribution to balance in a number of populations [2,3], one of the recognized limitations is the effect of learning with repeated exposures [4]. Comparatively, there is limited information about the test-retest reliability of the CSMI test, and whether or not the CSMI test is subject to learning effects. In this abstract we present preliminary data on the test-retest reliability of the SOT and CSMI test measures focusing on four comparable conditions across the two tests: 1) surface movement with eyes closed, 2) surface movement with eyes open, 3) visual surround movement, and 4) both surface and visual surround movement. We hypothesize that a) both the SOT and

the CSMI will have good to excellent reliability, and b) that the participants will improve on the SOT, but will not improve on the CSMI – suggesting learning effects occur in the SOT but not CSMI test.

METHODS

Participants were 14 healthy volunteers (26.3 ± 2.8 years) recruited from Oregon Health & Science University (OHSU). Exclusion criteria included any history of injury, surgery or medical condition that would impair cognition or motor ability. All participants gave written informed consent, and procedures were approved by the OHSU Institutional Review Board. Participants completed two testing sessions, conducted six-weeks apart – a timeline chosen to reflect a reasonable test-retest interval in a balance intervention program. Participants completed the SOT and the CSMI test in a custom modified SMART Balance Master (Neurocom International Inc.), adapted to collect CSMI test data (Figure 1). For the SOT, participants completed the standard SOT clinical protocol of three 20-s trials per six conditions. For the CSMI test, participants completed randomly ordered trials at amplitudes of 2° and 4°, making eight total trials. Outcome measures were the Equilibrium Score (E, SOT) and the Sensory Weight presented as sensory weight*100 (W, CSMI) per condition.

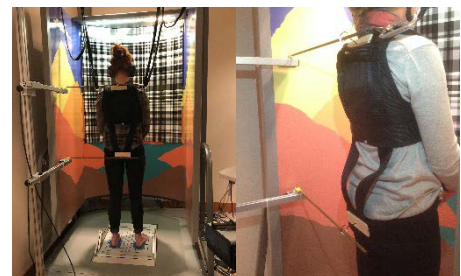


Figure 1: Custom modified SMART Balance Master

Test-retest reliability was assessed using Intraclass Correlation Coefficients (ICCs) using a 2-way mixed effects model (ICC_{3,1}) with absolute agreement. 95% confidence intervals were calculated, and interpretations (<.5=poor; .5-.75=moderate; .75-.9=good; >.9=excellent) were based off Koo & Li [5]. Paired t-tests were also assessed to evaluate any mean differences between testing sessions.

RESULTS AND DISCUSSION

Except for the 2° visual condition, the ICC values for the CSMI were on average higher than the SOT (Table 1). SOT equilibrium score significantly improved in the visual movement condition (mean±SD, E₁=92±3, E₂=94±2, $p=.041$), and the surface plus visual movement condition, (E₁=64±18, E₂=74±15), $p=.001$), but no significant changes to performance in the surface movement with eyes open condition (E₁=86±5, E₂=88±6, $p=.050$) or surface movement with eyes closed condition (E₁=66±14, E₂=72±12, $p=.168$).

Table 1: ICC values, 95% confidence intervals and interpretation of ICC for each condition tested.

		95% CI			Interpretation
		ICC _{3,1}	Lower	Upper	
SOT	S, EC	0.475	-0.46	0.83	Poor
	S, EO	0.733	0.20	0.91	Moderate
	V	0.451	-0.36	0.81	Poor
	S + V	0.867	0.10	0.97	Good
CSMI	S, EC 2°	0.854	0.55	0.95	Good
	S, EC 4°	0.655	0.03	0.89	Moderate
	S, EO 2°	0.557	-0.46	0.86	Moderate
	S, EO 4°	0.878	0.61	0.96	Good
	V 2°	0.392	-0.69	0.80	Poor
	V 4°	0.705	-0.05	0.91	Moderate
	S + V 2°	0.849	0.52	0.95	Good
	S + V 4°	0.882	0.61	0.96	Good

*S = surface movement; V = visual movement; EC = eyes closed; EO = eyes open

The only significant change in performance for the CSMI test was in the 4° visual movement condition, $W_1=5\pm3$, $W_2=3\pm1$, $p=.004$. No significant changes in performance occurred in any other condition (2° surface movement, eyes closed condition, $W_1=49\pm8$, $W_2=50\pm7$, $p=.448$; 4° surface movement, eyes closed condition, $W_1=39\pm10$, $W_2=35\pm4$, $p=.063$; 2° surface movement, eyes open condition, $W_1=72\pm4$, $W_2=72\pm5$, $p=.697$; 4° surface movement, eyes open

condition, $W_1=19\pm4$, $W_2=19\pm3$, $p=.864$; 2° visual movement condition, $W_1=10\pm5$, $W_2=8\pm2$, $p=.178$; 2° surface and visual movement condition, $W_1=53\pm7$, $W_2=54\pm6$, $p=.814$; 4° surface and visual movement condition, $W_1=44\pm9$, $W_2=41\pm7$, $p=.063$).

Our results suggest better test-retest reliability of the CSMI than the SOT for the surface movement with eyes closed condition, while being comparable for surface movement with eyes open, and surface plus visual surround movement. Test-retest reliability was low for the SOT visual condition and the low amplitude CSMI visual movement condition. Repeat test performance improved in the SOT visual movement and surface plus visual movement conditions, while for the CSMI a decrease in the sensory weight occurred in the visual movement condition. Overall reliability of the SOT and CSMI were somewhat lower than expected. This may be an outcome of the repeat trial occurring six weeks following the initial testing block. The general improvement in SOT performance is consistent with a learning effect.

CONCLUSIONS

Test-retest reliability ranged from poor to good for both the SOT and CSMI test, with the CSMI test performing slightly better overall. The observed test-retest changes in performance in healthy young adults provide a benchmark for judging whether rehabilitation interventions are effective in improving balance function in patients.

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ACKNOWLEDGEMENTS

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Central Sensorimotor Integration Test: Test-retest reliability and learning effects

Lucy Parrington^{1,2}, Nicholas Kreter^{1,2}, Peter C. Fino^{1,2}, Robert J. Peterka^{2,3}, Laurie A. King^{1,2}

- 1) Department of Neurology, Balance Disorders Laboratory, Oregon Health & Science University, Portland, USA
- 2) VA Portland Health Care System, Portland, USA
- 3) National Center for Rehabilitative Auditory Research, VA Portland Health Care System

Background: Balance and sensory integration deficits are common problems after mild traumatic brain injury and often require balance rehabilitation. Judging the effectiveness of an intervention requires practitioners to know both the retest reliability of a tool, and whether or not repeat testing is subject to learning effects. The Sensory Organization Test, a gold standard test for measuring sensory integration and balance, has been shown to be a reliable way to assess sensory contributions to balance, but is also recognized as being subject to learning effects. As an alternative, our group has utilized the Central Sensorimotor Integration (CSMI) test to identify sensory contributions to balance control. The CSMI test uses continuous pseudorandom rotations of the surface, visual surround, or paired surface and visual surround at fixed peak-to-peak amplitudes of 2° and 4° rather than the sway-evoked rotations (i.e., sway-referencing) used in the SOT. Because of the unpredictable nature of pseudorandom stimuli, it is plausible that the CSMI will not be subject to learning effects, making it a promising tool to investigate changes following rehabilitation. Also, in addition to providing measures of the relative contribution of proprioceptive, vestibular or visual systems to balance (Sensory Weights, W_s), the CSMI provides functionally meaningful sensory-to-motor transformation parameters (Stiffness, K_p and damping, K_d). The purpose of this investigation was to assess test-retest reliability and identify performance changes that may indicate learning effects in a sample of healthy controls.

Methods: Fourteen healthy participants (age: 26.3 ± 2.8 years, 9 female) were recruited from Oregon Health & Science University. Participants were excluded if they had a history of injury, surgery or medical condition that would impair cognition or motor ability. Procedures were approved by the Institutional Review Board, and all participants provided written informed consent prior to testing. Testing was comprised of two sessions completed six-weeks apart. This timeline was chosen to reflect the interval used in our vestibular rehabilitation program. The CSMI was completed in a customized SMART Balance Master (Natus Medical Inc.). Four conditions that target reliance on the 1) vestibular system (surface movement with eyes closed, SEC), 2) combined vestibular and visual systems (surface movement with eyes open, SEO), 3) combined proprioceptive and vestibular systems (visual surround movement, VEO); and 4) vestibular system with conflicting visual and proprioceptive information (paired surface and visual surround movement, S+V) were tested at 2° amplitudes in random order. Two-way mixed effects Intraclass Correlation Coefficients ($ICC_{3,1}$) with absolute agreement and 95% confidence intervals were calculated for W , K_p , and K_d . Test-retest reliability was interpreted as $ICC_{3,1} < 0.5$ =poor; $0.5-0.75$ =moderate; $0.75-$

0.9=good; >0.9=excellent. Paired t-tests were used to assess changes (learning effects) in performance between testing sessions.

Results: Test-retest reliability: Test-retest reliability was best in SEC and S+V conditions, and lowest in the VEO condition. Test-retest reliability ranged from good to excellent in the SEC condition (W, $ICC_{3,1}=0.854$, $CI=0.554, 0.953$; Kp, $ICC_{3,1}=0.922$, $CI=0.759, 0.975$; Kd, $ICC_{3,1}=0.851$, $CI = 0.534, 0.952$), and ranged from moderate to good for SEO (W, $ICC_{3,1}=0.557$, $CI=-0.457, 0.860$; Kp, $ICC_{3,1}=0.810$, $CI=0.401, 0.939$; Kd, $ICC_{3,1}=0.689$, $CI=0.044, 0.900$). In the VEO condition, test-retest reliability was poor to moderate (W, $ICC_{3,1}=0.392$, $CI=-0.692, 0.797$; Kp, $ICC_{3,1}=0.241$, $CI=-0.645, 0.717$; Kd, $ICC_{3,1}=0.677$, $CI = 0.018, 0.896$), and was good in the S+V condition (W, $ICC_{3,1}=0.849$, $CI=0.521, 0.952$; Kp, $ICC_{3,1}=0.875$, $CI=0.570, 0.961$; Kd, $ICC_{3,1}=0.814$, $CI=0.347, 0.943$). Learning effects: There were no significant changes over time to W in any of the conditions ($p=0.08$ to 0.81), however, significant changes occurred in Kp and Kd in the VEO condition (Kp, $M_{diff}=-0.098$, $p=0.031$; Kd, $M_{diff}=0.033$, $p=0.017$), and in the S+V condition (Kp, $M_{diff}=-0.051$, $p=0.044$; Kd, $M_{diff}=0.029$, $p=0.024$).

Discussion and Conclusion: Test-retest reliability was best across outcome measures in the SEC and S+V conditions, while being moderate in the SEO condition. The VEO condition had the lowest test-retest reliability. This low reliability is likely related to the very low amplitudes of sway evoked by the visual stimulus, resulting in parameters estimates with higher variability compared with the other conditions that evoked greater sway. The non-significant changes in W in each condition suggests that subjects do not alter how they use sensory information for balance over time. However, changes to Kp and Kd in VEO and S+V indicate potential changes to stiffness and damping –an indication that the mechanism of control may have adjusted in some participants. Based on these findings, SEC, which challenges the vestibular system, may be the most effective condition to monitor changes following rehabilitation. Further investigation is needed to determine the minimal detectable change for each of the CSMI conditions.

Acknowledgements: Funding was provided by the US Department of Defense (W81XWH-15-1-0620). Thank you to Ms. Alexa Beeson for her assistance with data collection.

Military Health System Research Symposium (MHSRS) Abstract

Assessment of balance after mild traumatic brain injury: Are vestibular and ocular-motor testing capturing all balance deficits?

Jehu DA^{1,2}, Fino PC^{1,2}, Parrington L^{1,2}, Kampel S³, Peterka RJ³, Hullar T⁴, King LA^{1,2}

¹ Department of Neurology, Oregon Health and Science University, Portland, Oregon

² Veterans Affairs Portland Health Care System, Portland, Oregon

³ National Center for Rehabilitative Auditory Research, Veterans Affairs Portland Health Care System, Portland, Oregon

⁴ Department of Otolaryngology-Head and Neck Surgery, Oregon Health & Science University, Portland, Oregon

Background: Mild traumatic brain injury (mTBI) has been challenging to both diagnose and treat, as symptoms are diverse in nature and subtle in presentation. Impairments post-mTBI have spanned multiple domains, such as vestibular [1], ocular-motor [2], balance [3], and sensory integration [4]. However, it is unclear whether vestibular, ocular-motor, and balance testing are redundant in identifying individuals with mTBI, or whether unique deficits can be captured across domains.

Aim and Hypothesis: The purpose of this study was to evaluate the prevalence of abnormalities in vestibular and ocular-motor testing in comparison with clinical tests of balance in people with chronic balance deficits after mTBI relative to healthy young adults. We also investigated the relationship between vestibular, ocular-motor, and balance abnormalities in people with chronic mTBI. We hypothesized that a similar prevalence of abnormalities would exist across vestibular, ocular-motor, and balance domains, and that abnormalities in vestibular and ocular-motor domains would be associated with abnormalities in balance domains.

Methods: Twenty-eight individuals with chronic mTBI (age: 39.2 ± 12.0 years, 19 females) and 51 healthy young adults (age: 35.5 ± 12.5 years, 19 females) completed a battery of 1) vestibular tests, 2) ocular-motor tests, and 3) clinical balance tests. Specifically, the vestibular examination included the evaluation of otolith function (i.e., Cervical Evoked Myogenic Potential (cVEMP), Ocular Evoked Myogenic Potential, (oVEMP)), and semi-circular canal function (i.e., Calorics, Dix-Hallpike). Ocular-motor function was evaluated via Saccade, Gaze, Smooth Pursuit, and Convergence testing. Participants were classified by an audiologist as normal or abnormal based on clinical norms. The balance assessment included the Sensory Organization Test (SOT) and the Modified Balance Error Scoring System (mBESS) test. Participants were further classified using the root mean square of medial-lateral acceleration (ML-RMS), measured by an inertial sensor worn on the lower lumbar region, when standing with feet together on a firm surface with eyes closed. ML-RMS acceleration has been previously shown to be effective for classifying individuals post-mTBI [5]. Participants were deemed abnormal on the clinical balance tests if their data were outside of 2 standard deviations from the average of the controls.

Results: Descriptively, in our participants with chronic mTBI, 7.1 % exhibited abnormalities in one or more of the vestibular tests, 3.6 % presented with abnormalities in one or more of the ocular-motor tests, 17.9 % had abnormalities in one or more of the balance tests, 0 % showed abnormalities in both vestibular and ocular-motor tests, 35.7 % displayed abnormalities in

vestibular and balance tests, 17.9 % had abnormalities in ocular-motor and balance tests, and 7.1 % revealed abnormalities across vestibular, ocular-motor and balance tests, while 10.7 % showed no abnormalities. Proportions tests demonstrated significantly more abnormalities in mTBI participants compared to controls in ocular-motor tests (mTBI: 29.6 %, Control: 9.8 %; $p=0.03$) and in clinical balance tests (mTBI: 78.6 %, Control: 9.8 %; $p<0.001$), while no differences between groups were observed for otolith tests (mTBI: 25.9 %, Control: 23.5 %; $p>0.82$) or semi-circular canal tests (mTBI: 29.6 %, Control: 27.4 %; $p=0.75$). No associations were found between vestibular function and the SOT ($r_\phi=-0.03$, $p=0.86$), the mBESS ($r_\phi=0.04$, $p=0.84$), or ML-RMS sway ($r_\phi=-0.28$, $p=0.15$). No relationships were exhibited between ocular-motor tests and the SOT ($r_\phi=0.07$, $p=0.71$), the mBESS ($r_\phi=0.19$, $p=0.33$), or ML-RMS sway ($r_\phi=-0.16$, $p=0.40$).

Conclusion: A greater proportion of individuals with mTBI presented with ocular-motor and clinical balance abnormalities relative to healthy young adults, suggesting that mTBI deficits are primarily attributed to central dysfunction. Specifically, our results did not demonstrate that tests designed to detect peripheral vestibular dysfunction were helpful in distinguishing between mTBI and controls. However, performing only ocular-motor or only balance tests will fail to detect a portion of individuals with mTBI. That is, the lack of relationships between vestibular function and clinical balance, as well as between ocular-motor function and clinical balance indicate that vestibular, ocular-motor, and balance testing offer unique information and may all be necessary to sensitively detect mTBI. These findings further the knowledge on best practices of mTBI assessment and emphasize the importance of including a multifaceted battery of tests to accurately classify mTBI.

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Key words: brain injury, vestibular function, ocular-motor function, clinical balance, accurate detection

Learning Objectives:

1. Learners will be able to identify peripheral compared to central impairments post- mild traumatic brain injury (mTBI)
2. Learners will be able to describe the prevalence of abnormalities in vestibular, ocular-motor, and balance function following mTBI
3. Learners will be able to apply the knowledge that a multifaceted testing battery may be necessary to accurately detect a mTBI into military and clinical practice

NASPSA Abstract

Exploring the relationship between otolith function, sensorimotor integration, and posture in chronic mild traumatic brain injury

Jehu DA, Kempel S, Parrington L, Fino P, Hullar T, King LA

Mild traumatic brain injury (mTBI) is common in sport contexts as well as following motor vehicle accidents and falls. Previous work has examined saccular function of the otolith organ using Cervical Vestibular-Evoked Myogenic Potential (cVEMP) in mTBI patients; however, the Ocular Vestibular-Evoked Myogenic Potential (oVEMP), a recent technique, examines utricular function and may provide further insight into the overall otolith organ function following concussion. Utricular dysfunction has been linked to poor postural control and sensorimotor integration in individuals with vestibular loss, but this has not been reported in the mTBI population. Therefore, the purpose was to measure otolith function and explore its relationship with postural sway and sensorimotor integration in chronic mTBI. Fifty-one controls and 22 chronic mTBI participants completed the cVEMP, oVEMP, Sensory Organization Test (SOT), and quiet stance as measured by an inertial sensor. Vestibular dysfunction was observed by a lower amplitude ($p<0.05$) and a trend for greater asymmetry ($p=0.07$) of the cVEMP in the mTBI compared to the control group. No differences in the amplitude or asymmetry of the oVEMP were observed between groups ($p>0.05$). Deficiencies in sensorimotor integration, as detected by the composite score of the SOT ($p<0.001$), and poor postural control, as evidenced by a trend for greater root mean square in the medial-lateral direction during standing ($p=0.06$), were apparent in the mTBI compared to the control group. Although all of the cVEMP and oVEMP parameters were correlated ($p<0.05$), and the SOT was correlated to sway ($p<0.001$), no relationship between vestibular parameters and sensorimotor integration or sway were exposed ($p>0.05$). Globally, the saccule seems to be more sensitive to damage than the utricle following head trauma. Moreover, no link between otolith function and posture or sensorimotor integration was observed, suggesting that deficits in sensorimotor integration and posture may stem from other central or peripheral mechanisms.

Key words: brain injury, vestibular function, sensorimotor integration, posture

#299 Dual-task cost and cognition in patients with chronic mTBI

Lucy Parrington, Balance Disorders Laboratory, Neurology Department, Oregon Health & Science University; VA Portland Health Care System; Tyler Duffield, Child Development and Rehabilitation Center, Oregon Health & Science University; Peter Fino, Balance Disorders Laboratory, Neurology Department, Oregon Health & Science University; VA Portland Health Care System; Laurie King, Balance Disorders Laboratory, Neurology Department, Oregon Health & Science University; VA Portland Health Care System

Dysfunction following mTBI has been previously described in cognitive and motor domains, however, limited study has been conducted across both areas in populations with persistent balance symptoms following injury. In this abstract we provide preliminary findings comparing 15 persons with chronic mTBI (10 female, 40 ± 13 years, 67 ± 3 kg, 1.7 ± 0.4 m) with 15 healthy controls (9 female, 40 ± 13 years, 67 ± 4 kg, 1.7 ± 0.5 m). Chronic mTBI participants had self-reported balance complaints persisting more than 3 months following a clinically diagnosed mTBI. Participants completed the Automated Neuropsychological Assessment Metrics (ANAM) test and a dual-task of walking while completing a continuous Auditory Stroop. Prior to undertaking the dual-task walk, baseline single-task walking and a seated Auditory Stroop condition were collected in order to calculate the dual-task cost. ANAM composite score, dual-task cost on cognition (reaction time and a throughput score of accuracy/ correct response time), and dual-task cost on gait speed were assessed. Between group differences were assessed using Cohen's d effect sizes. Medium effects suggested that the chronic mTBI group performed worse on the ANAM composite score (control = $.27 \pm 1.26$, mTBI = $-.47 \pm .99$, $d = .66$) and experienced a greater dual-task cost on cognition (reaction time [control = $-1 \pm 11\%$, mTBI = $9 \pm 22\%$, $d = -.57$] and throughput score [control = $2 \pm 5\%$, mTBI = $-6 \pm 27\%$, $d = .51$]), while a small effect suggested healthy controls may have incurred a greater dual-task cost on gait speed (control = $-4 \pm 6\%$, mTBI = $-1 \pm 6\%$, $d = -.39$). Preliminary findings suggested cognitive differences, and difficulty in dual-task function may persist in chronic mTBI patients who complain of balance impairment. Of note is the lack of dual-task cost on gait speed in chronic mTBI – although the chronic mTBI walked slower in both conditions (single-task $d = -.55$, dual-task $d = -.29$), their dual-task gait speed was not as compromised as their cognitive response. These results help explain functional deficits contributing to difficulties in complex activities in chronic mTBI patients. Funding source: This work was supported by the Assistant Secretary of Defense for Health Affairs under Award No. W81XWH-15-1-0620. Opinions, interpretations, conclusions and recommendations are those of the author and are not necessarily endorsed by the Department of Defense.