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TITLE: “Sensory Integration Balance Deficits in Complex mTBI: Can Early Initiation of Rehabilitation with Wearable Sensor Technology Improve Outcomes?”

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14. ABSTRACT

Objectives: 1) To determine the role of timing in rehabilitation of balance deficits in people with mTBI 2) To determine if home monitoring improves outcomes 3) To develop a novel feedback system using wearable sensors to provide physical therapists with real-time information about quality of head and trunk movement during exercise.

Plan: This is an interventional study on people with mTBI. Aim I examines whether initiating interventional physical therapy earlier rather than later improves outcomes. Aim II, nested within Aim I, examines whether home monitoring of vestibular rehabilitation improves outcomes. Aim III develops a system capable of delivering real-time feedback on quality to improve outcomes.

Aims and Hypotheses:
Aim I. Early Intervention: To determine the effects of early versus late rehabilitation for balance deficits in mTBI. We hypothesize that early rehabilitation will improve outcomes more than standard of care.
Aim II. Home Monitoring: To compare traditional balance rehabilitation versus balance rehabilitation with sensor-based home monitoring. We hypothesize that providing physical therapists with objective measures on performance of prescribed exercises at home will improve outcomes in rehabilitation.
Aim III. Real-time Monitoring for Training: To develop and evaluate a novel sensor system that provides real-time feedback to physical therapists. We hypothesize that real-time feedback on head and trunk movements during exercise will be feasible for use by a physical therapist.

Methods:
Aims I & II: These aims involve 160 participants who have sustained an mTBI. They will complete questionnaires to identify their perceived problems, as well as undergo clinical tests of vestibular function and balance and gait. Motion sensors, force platforms, and clinical assessments will be used to measure balance and gait.
Intervention: Participants will be randomly assigned to begin physical therapy immediately or within the standard of care timeline. During these sessions, the participant will be evaluated by the physical therapist while performing exercises around common impairments after concussion. People will perform either standard vestibular rehabilitation exercises or standard vestibular rehabilitation exercises using wearable sensors to track head movements.
Aim III: 5 physical therapists will be trained to use the biofeedback sensor system and, along with 25 people with mTBI, will be asked to provide feedback about the system. 50 people without mTBI will be asked to perform specified exercises that require head movements during standard balance and vestibular exercises to obtain normative values.

Results: For Aims I & II we have screened 83 subjects and enrolled 53 subjects in this study. There have been 22 subjects randomized to the early intervention group and 31 subjects randomized to the standard of care group. For Aim III, 45 control subjects have completed testing.

15. SUBJECT TERMS
mTBI, Rehabilitation, Brain Injury, Inertial Sensors, Balance, Central Sensory Integration, Concussion, Eye Tracking

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TABLE OF CONTENTS

1. INTRODUCTION:

Mild traumatic brain injury (mTBI) is common both in civilian and military populations and can be debilitating if symptoms do not resolve after injury. Balance problems are one of the most common complaints after sustaining an mTBI and often prevent people from returning to their previous quality of life. However, we currently lack clear guidelines on when to initiate physical therapy rehabilitation and it is unclear if early physical therapy is beneficial. We believe that the underlying problem of imbalance results from damage to parts of the brain responsible for interpreting sensory information for balance control. We hypothesize that retraining the brain early, as opposed to months after injury, to correctly interpret sensory information will improve recovery. We also believe this retraining is limited when rehabilitation exercises are performed incorrectly, and that performance feedback from wearable sensors, can improve balance rehabilitation. The researchers in this project are experts at understanding and treating complex balance problems and have developed novel and portable ways to measure balance using new technology. There are three of objectives of this proposal: 1) To determine how the timing of rehabilitation affects outcomes after mTBI 2) To determine if home monitoring of balance exercises using wearable sensors improves outcomes and 3) To develop a novel feedback system using wearable sensors to provide the physical therapist information, in real-time during training, about quality of head and trunk movements during prescribed exercises.

2. KEYWORDS:

mTBI, Rehabilitation, Brain Injury, Inertial Sensors, Balance, Central Sensory Integration, Concussion, Eye Tracking

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Goal	Target Completion Date	Percentage of Completion/ Date of Completion
Specific Aim 1 & 2 (Assessment of late vs early intervention & home monitoring)		
Major Task 1: Launch Study Activities	*March 2018*	100%
Major Task 2: Recruitment and Testing	*March 2021*	28%
Major Task 3: Randomized Interventions	*March 2021*	23%
Major Task 4: Assess Efficacy of Interventions	*March 2021*	11%

Major Task 5: Data Analysis & Publications	*September 2021*	46%
Specific Aim 3 (Real-Time Monitoring)		
Major Task 1: Develop & Evaluate the wearable system for feedback	*September 2021*	70%
Major Task 2: Launch Study Activities	*September 2020*	5%
Major Task 3: Data Collection	*September 2019*	90%
Major Task 4: Data Analysis & Publications on Interventions	*September 2021*	0%

What was accomplished under these goals?

Aim I & II

Major task 1: Launch Study Activities

Subtask 1: prepare regulatory documents and research protocol

- Prepare forms for FITBIR; Our FITBIR profile and documents have been setup on the site. We submitted our first set of data September 2019 and will continue to submit annually-100% complete

Subtask 2: prepare technology for study

- Validate sensor-based kinematics with Motion Analysis (n=10); Validation data from five subjects with mTBI and five healthy study subjects has been collected using inertial sensors and an optical motion capture system, as the reference system. Inertial data analysis is complete and results have been generated including head and trunk range of motion (ROM) and maximum velocity during assessment and training exercises. Manuscript published - 100% complete

Subtask 3: prepare research protocols- 100% complete

Subtask 4: hiring and training personnel- 100% complete

Major Task 2: Recruitment & Testing

Subtask 1: recruitment

- Make contacts with sources of referrals through OHSU Primary Care, Family Medicine, and other sites; Dr. Chesnutt and Jenny Wilhelm (PT) met with two OHSU outreach coordinators, whose main role is to connect and merge groups with mutual interests within OHSU. During this meeting they provided study flyers and brochures that could be given to physicians that frequently treat mTBI patients. In the next reporting period, we will begin to work with OHSU’s emergency room, where a triage staff member will provide mTBI patients with study information. This will be an ongoing process- 55% complete

- Meet with primary sources of referral; Our primary source of referral is utilizing OHSU’s BPA system that alerts us whenever a patient has been seen with a mTBI or related injury. This has been our most successful recruitment tool. This will be an ongoing process- 33% complete
- Meet with clinic MAs for logistics of recruitment; OHSU Concussion Clinic is aware of our recruitment process and has been providing eligible patients with study information. We will be meeting with emergency room staff members to familiarize them with this study in the next reporting period. This will be an ongoing process- 45% complete

Subtask 2: data collection & management

- Complete vestibular testing at OHSU and VA for data collection; We have tested 53 subjects out of the target 160 participants -33% complete
- Complete gait and balance testing for data collection at OHSU and VA; We have tested 53 subjects out of the target 160 participants -33% complete
- Data back-up onto server including manual data entry into Redcap; Data has been placed on the server and also manually entered into Redcap for all study participants- 25% complete
- Screen and verify data on server and check for accuracy; We did a complete data check within REDCap September 2019 - 20% complete
- Validate and submit forms to FITBIR quarterly; We submitted our first set of data to FITBIR September 2019- 20% complete

Major Task 3: Randomized Interventions on 160 mTBI Patients
Subtask 1: intervention

- Enroll Subjects in rehabilitation intervention; as subjects enroll they are being randomized in to either early or standard of care rehab- 33% complete
- Complete 6 week interventions; 29 subjects have completed the 6 week intervention- 18% complete
- PT’s document compliance, adverse events and progression of exercise for each subject; PT’s are keeping a detailed record of progression through rehab and are required to fill out a summary sheet for each visit documenting any AE’s or protocol deviations- 18% complete
- Optimize system user interface and reports based on input from users; The PT’s meet weekly with APDM staff to discuss the user interface and make necessary changes- 25% complete

Major Task 4: Assess Efficacy of Interventions
Subtask 1: intervention assessment

- Complete immediate posttest after intervention; 29 subjects have completed the posttest- 18% complete
- Complete long-term assessment 6 months later to assess retention; Seven subjects have completed the long-term assessment, however 19 subjects are currently in that 6 month waiting period and will be tested in the next few reporting periods- 4% complete

Major Task 5: Data Analysis and Publications
Subtask 1: data analysis

- Perform all analysis according to proposal and share all findings with investigators; Data is being organized in preparation for analysis, which includes eye-tracking, postural sway, gait, and mobility data from our testing sessions. We will prepare statistical analysis scripts for data analysis. We have conducted preliminary analysis on the eye-tracking and inertial sensor algorithms and these results have been shared at nine separate meetings/conferences and three manuscripts have been published (see products) - 30% complete

Subtask 2: manuscripts, presentations and other output

- Disseminate findings (abstracts, presentations, papers, DoD); We have disseminated findings through three manuscripts, platform and poster presentations, as well as community outreach events (see products below)- 10% complete
- Submit manuscript to BMC Neurology describing the protocol and intervention; This manuscript has been submitted and was recently accepted-100% complete

Aim III

Major Task 1: Technology Development
Subtask 1: technology development

- Develop real-time feedback for physical therapist; APDM completed development and verification of the algorithm to provide real-time analysis. Real-time objective measures include head and trunk range of motion and turn velocity. Collaborators at OHSU requested more objective measures to be included in the system. Specifically, coronal sway and gait speed. APDM engineers will continue development and optimization of the algorithm. This will include developing and verifying the added objective measures. Data collected for previous verification will be used to verify and optimize the updated algorithm - 90% complete
- Update and optimize user-interface framework for real-time feedback; APDM completed the first iteration of the real-time feedback system. This included developing plots for visual feedback. Based on feedback from users and investigators at OHSU, APDM will continue to develop and tune the visual biofeedback. This will include display of moving avatars and dynamic bars and digital meters- 70% complete
- Develop an array of mTBI specific gait and balance assessments; APDM continues to develop a system to monitor functional mobility during unconstrained activities of daily life. Prototypes of the instrumented socks have been developed and being tested and verified. Passive monitoring algorithms have been developed and will be verified and optimized to provided objective measures of mobility in daily life. Efforts will continue to develop and build the system to allow subjects to comfortably wear the sensors during the day, charge at night and wirelessly uploaded the data to a server for quality assurance and analysis- 50% complete

Major Task 2: Launch Study Activities
Subtask 1: train and recruit

- Identify Physical Therapists to participate and evaluate system; Physical Therapists have been collaborating with other PT’s at OHSU who may be interested in participating- 10% complete

- Identify patients from PT's to evaluate feedback system; This will begin once PT's have been identified in the next reporting period- 0% complete

Major Task 3: Data Collection
Subtask 1: normative data

- Test 50 healthy controls for normative values; 45 healthy controls have been tested for normative values and we have begun initial data checks- 90% complete

Significant Results/ Key outcomes:

At the end of September 2019, we have recruited and screened a total of 83 participants with 53 meeting inclusion criteria (Figure 1). Currently, 29 subjects have completed the rehabilitation intervention with 9 that are currently receiving rehabilitation. Seven have completed a 6-month follow up test after their rehabilitation with 19 subjects that are waiting for 6-month follow up testing. We have equally balanced our subjects between the early timed rehabilitation and standard of care time rehabilitation across multiple demographic domains with our randomization procedure (Table 1).

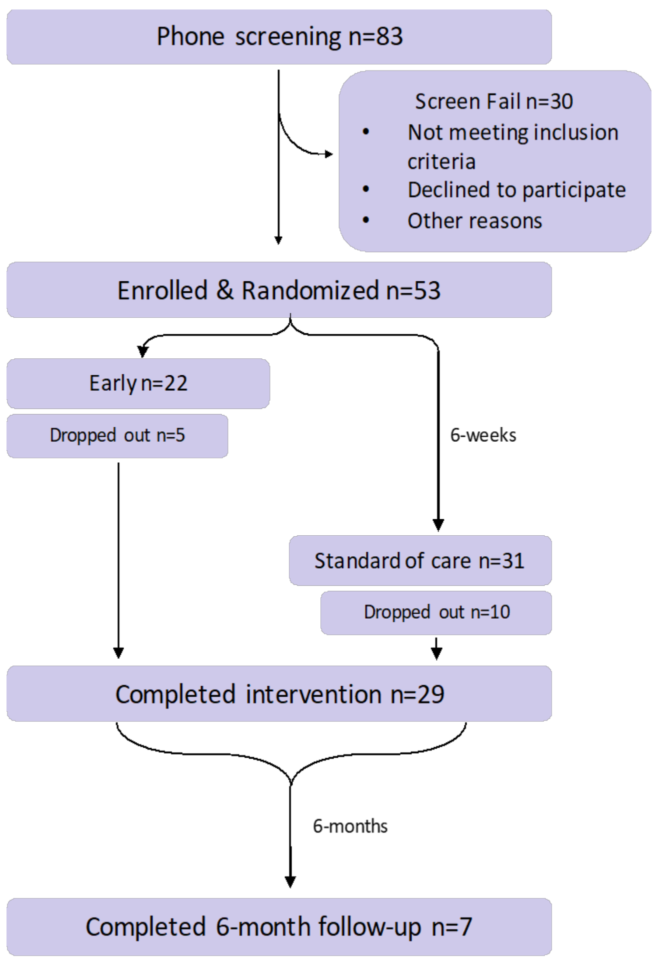


Figure 1: Subject screening and enrollment overview.

Table 1: Demographics for those subjects receiving early timed rehabilitation and for those receiving the standard of care timed rehabilitation

	Standard of Care	Early
Gender (n, % female)	25, 81%	18, 82%
Age (years)	34.1 ± 11.8	34.2 ± 12.6
Time since injury on Day 1 (days)	40.3 ± 19.2	48.6 ± 21.8
Age Group	Standard of Care	Early
18-29	13	10
30-39	8	5
40-49	6	3
50-60	4	4

Outcomes Summary:

Balance: Balance impairments are a common complaint after mTBI. Our preliminary analysis of postural sway data indicates that sway in the mediolateral plane while performing the modified Balance Error Scoring System (mBESS; Figure 2) becomes less variable over time and following rehabilitation. No changes occurred from baseline to post rehabilitation using the clinical subjective scoring of balance coordination across the mBESS testing conditions (top numbers across Figure 2). Objective measures of postural sway and balance impairments using sensors (such as APDM's Opal Sensors used in this study) are needed to quantify subtle changes in balance outcomes otherwise undetected by clinical evaluations. It is important to note, that because our research analysts are blinded to the groupings of early/ standard care, and sensor informed rehab/ no sensor informed rehab, we have not assessed whether there are differences in the postural sway data across groups.

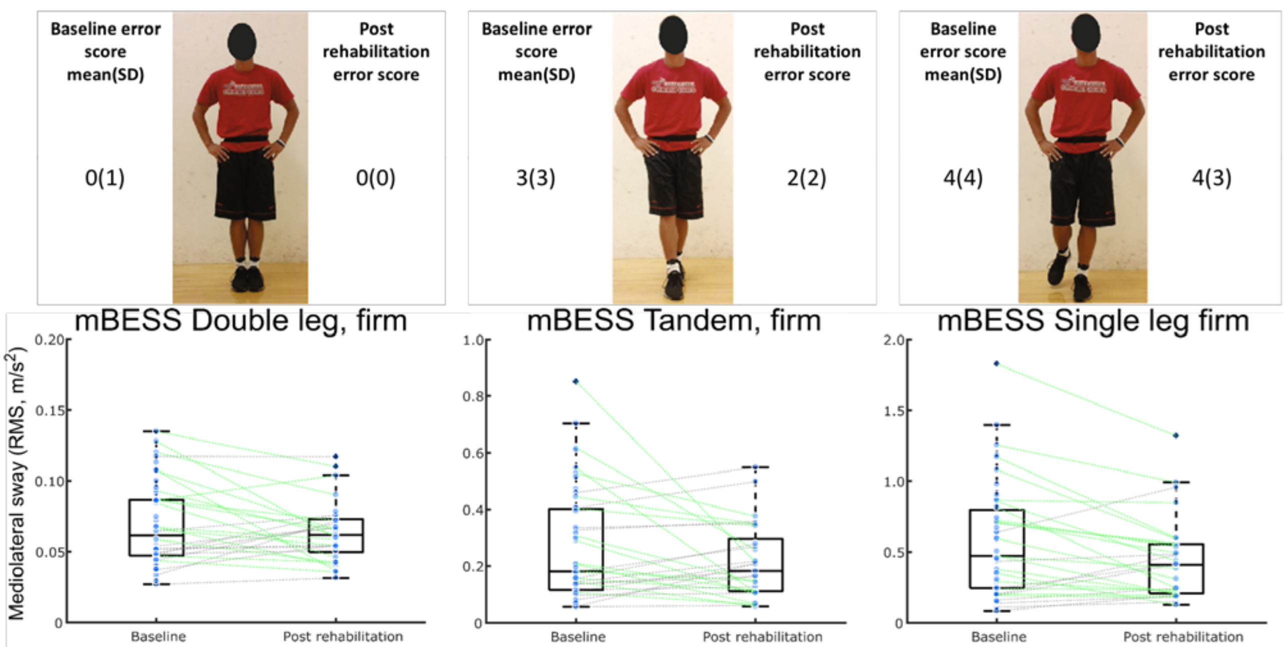


Figure 2: Modified Balance Error Scoring System (mBESS) scores at baseline and post rehabilitation across 3 different stance positions (double leg feet together, double leg tandem stance, and single leg stance). Inertial sensors worn on the head, sternum, lumbar spine, and feet recorded the mediolateral sway during each stance for baseline and post-rehabilitation sessions. Sensors were able to detect balance changes from baseline to post rehabilitation that the mBESS scores could not.

Cognition: Cognitive dysfunction is common following mTBI and our preliminary results indicate that cognitive function improves over time and following rehabilitation (Figure 3). Cognition was assessed using the Automated Neuropsychological Assessment Metric (ANAM). The ANAM assessed simple reaction time, processing speed, visual memory, working memory, and visual-spatial ability. Our participants improved their visual spatial processing ability (assessed by the match to sample task reaction time) following rehabilitation (Figure 3) and were within a normative range (indicated by the orange lines). Again, our research analysts are blinded to the groupings of early timed/ standard of care timed, and sensor informed rehab/ no sensor informed rehab. We have not assessed whether there are differences in ANAM outcomes across groups.

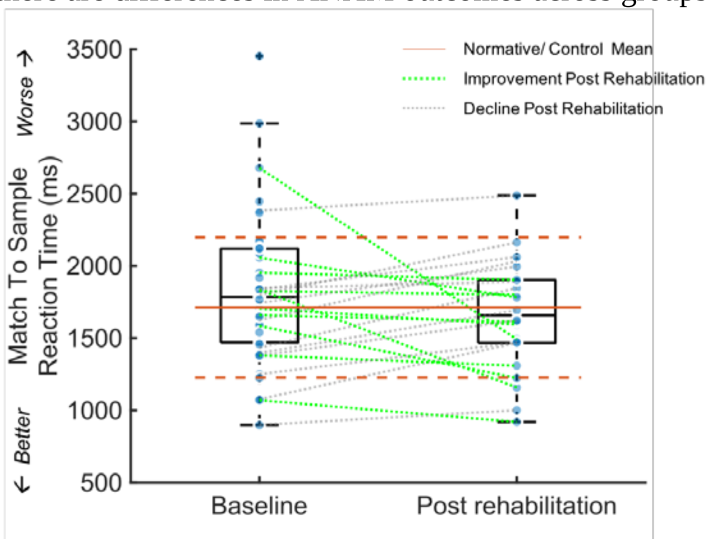


Figure 3: Visual spatial ability assessed by the Automated Neuropsychological Assessment Metric (ANAM) match to sample task reaction time between baseline and post rehabilitation sessions.

Symptoms: Our initial results indicate improvement in symptoms over time for the participants in the study, as shown by the reduction in SCAT symptom severity over time (Figure 4). It is important to note, that because our research analysts are blinded to the groupings of early/ standard care, and sensor/ no sensor data, we have not assessed whether there are differences in the recovery of these symptoms across groups.

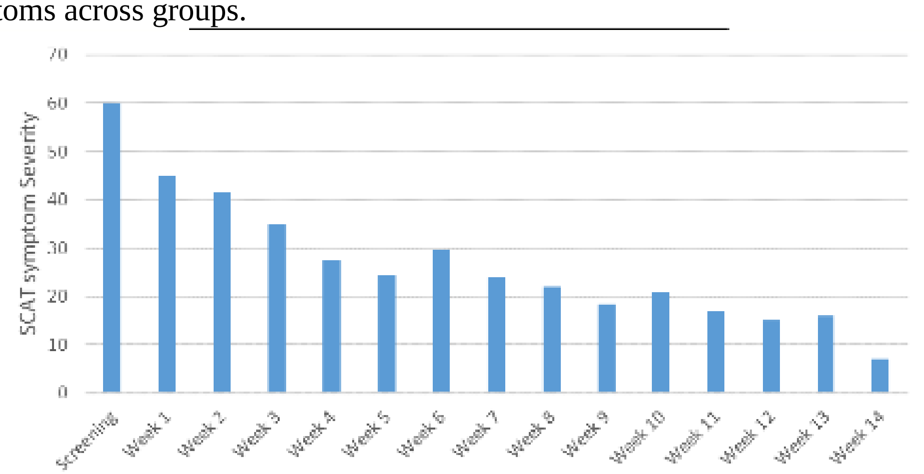


Figure 4: Median SCAT severity of all enrolled participants over time

Dizziness: We have also assessed the change in our primary outcome, the dizziness handicap inventory (DHI) total score. The change in DHI for all participants are provided in Figure 5. Preliminary qualitative assessment of descriptive data suggests a decrease in DHI following rehabilitation.

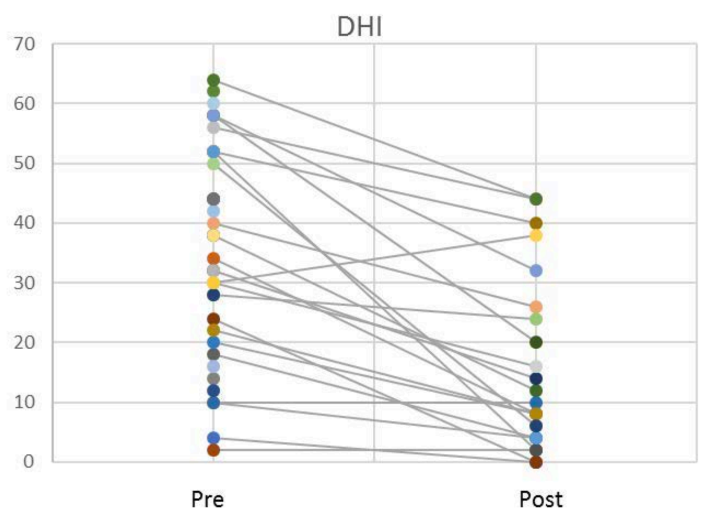


Figure 5: DHI scores for all participants tested pre-rehabilitation and post-rehabilitation. Plot represents individuals, with grey lines connecting to show the change per individual.

Preliminary retest-reliability analysis of wearable sensors measuring head movement: Eighteen healthy controls were tested at three different time points on a series of conditions involved in the rehabilitation program. A total of eight different conditions were tested:

- 2 Standing Balance: horizontal and vertical, eyes closed
- 2 Vestibular-Ocular Reflex: horizontal and vertical, eyes fixated while head moves
- 2 Visual Motion Sensitivity: horizontal and vertical, eyes and head move together
- 2 Walking (dynamic) Balance: horizontal and vertical, eyes and head move together

Participants wore an inertial sensor on their forehead and sternum, reflecting what is used during the rehabilitation program. One of our research team's physical therapists instructed participants which condition to perform for 30 seconds. For each trial, the two measures collected were the rotational velocity and range of motion (RoM) for the forehead and sternum in the primary movement axis. Intraclass correlation coefficients (ICC's) were assessed to gain an understanding of the re-test reliability of these measures. The inertial sensors had moderate to excellent retest-reliability at measuring the rotational velocity and ROM for the 8 different exercise conditions (ICC's = 0.67 to 0.96).

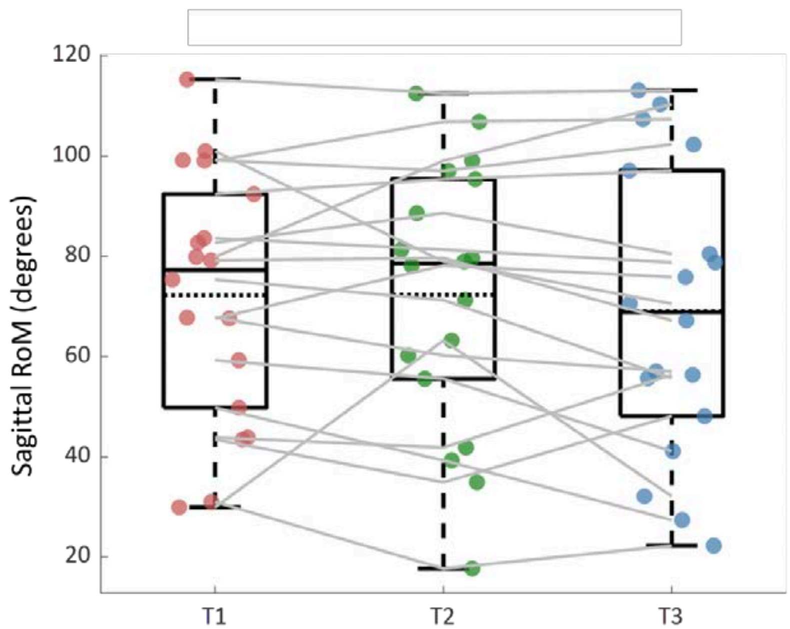


Figure 6: Box-and-scatter plot for forehead range of motion (RoM) while standing in healthy controls (n = 18), across three time points. Participants were instructed to nod their heads up and down with eyes closed for a total of 30 seconds. T1-T3 represent different time points. The dashed line represents the group mean.

Eye Tracking: Analysis for the first quarter of this annual report focused on validating an algorithm that will be used to quantify saccades (quick eye movements), which could be a potential biomarker for mild traumatic brain injury (mTBI). Eye-tracking measures such as saccades are part of our exploratory analyses within this study. As these measures are new and exploratory, we wanted to ensure we were using a valid algorithm so that we could be confident in the metrics. We validated a velocity-based algorithm for saccade detection from data collected with infrared eye-tracking glasses (Tobii Pro Glasses 2) in healthy people and people with mTBI during walking (straight ahead and while turning). The velocity- based saccade detection algorithm was validated against a ground truth reference of output from manual video inspection. The velocity-based algorithm for saccade detection had excellent agreement with video inspection across both mTBI and control groups across all conditions tested ($ICC_{2,1} > 0.9$). Overall, the algorithm correctly detected ~95% of the saccades detected via video inspection for the control group, and ~97% for the mTBI group. After validating our mobile eye-tracking algorithms to detect saccades, we performed preliminary analyses on objective eye-movements and their relationships to cognitive and gait function.

<u>Saccadic and cognitive function</u>: Cognitive dysfunction is common with mTBI and can impact saccadic eye-movements. We assessed the association between saccadic outcomes and cognitive functions on a sample of 16 people with mTBI. Participants completed anti-saccade tasks in a rotatory chair (Neuro Kinetics Inc., 100Hz), measuring 1) average anti-saccade latency (left and right), 2) number of pro-saccadic errors (left, right and overall), and 3) average pro-saccade latency (left and right). Cognitive outcomes were measured using the Automated Neuropsychological Assessment Metric (ANAM) cognitive battery and included 1) simple reaction time, 2) processing speed, 3) visual memory, 4) working memory, and 5) visual-spatial ability. Relationships between

saccadic and cognitive outcomes were assessed using partial correlations, controlling for days since injury. Poorer visual-spatial ability related to worse saccadic inhibitory control in mTBI (see Table 2). ANAM matching to sample reaction time (representative of visual-spatial ability) was associated with a greater number of pro-saccadic errors and shorter pro-saccade latency. No other cognitive functions related to saccadic outcomes. Correlations between cognitive and saccadic measures are provided in Table 2. Significant relationships are highlighted in bold font, and stronger relationships are indicated by darker hues (darker red = stronger negative relationship; darker blue = stronger positive relationship).

Table 2: Correlation table for cognitive and visual function variables.

	Attention	Processing speed	Working memory	Visual-spatial ability	Visual memory	Ave. pro-saccade latency (Left)	Ave. anti-saccade latency (Left)	Number of pro-saccadic errors (Left)	Ave. pro-saccade latency (Right)	Ave. anti-saccade latency (Right)	Number of pro-saccadic errors (Right)
Processing speed	0.09										
Working memory	-0.19	-0.03									
Visual-spatial ability	0.17	**0.52**	0.27								
Visual memory	0.11	0.37	0.31	**0.56**							
Ave. pro-saccade latency (Left)	-0.18	-0.33	-0.38	**-0.62**	-0.27						
Ave. anti-saccade latency (Left)	-0.05	-0.39	-0.12	-0.38	-0.16	0.12					
Number of pro-saccadic errors (Left)	-0.19	0.44	0.17	**0.52**	0.05	-0.48	-0.30				
Ave. pro-saccade latency (Right)	-0.18	-0.33	-0.38	**-0.62**	-0.27	**1.00**	0.12	-0.48			
Ave. anti-saccade latency (Right)	-0.24	0.33	-0.20	-0.23	-0.07	0.07	0.36	0.13	0.07		
Number of pro-saccadic errors (Right)	-0.02	0.31	0.32	**0.52**	0.13	-0.46	-0.32	**0.62**	-0.46	-0.03	
Number of pro-saccadic errors (Overall)	-0.11	0.41	0.28	**0.58**	0.11	**-0.52**	-0.34	**0.88**	**-0.52**	0.04	**0.92**

***Bold font** denotes significance	-1.00	-0.80	-0.60	-0.40	-0.20	0.00	0.20	0.40	0.60	0.80	1.00

<u>Visual exploration in mTBI and healthy controls during gait tasks:</u> As mTBI may impact visual exploration, we conducted a preliminary analysis aimed to; 1) examine visual exploration and gait when walking under single (ST) and dual-task (DT) in mTBI and controls, and 2) explore relationships between visual exploration and gait in mTBI and controls. This analysis was conducted in the same population of mTBI as above and 10 healthy controls. Participants walked for 1 minute back and forth over 10m, while wearing a mobile eye tracker (Tobii Pro Glasses 2) and five inertial sensors (APDM) under ST and DT conditions. Visual exploration outcomes included saccade frequency (sacc/sec), amplitude, peak velocity, and fixation duration, and gait outcomes included gait speed, stride length, stride time and double support time. No significant between group differences were found for either visual exploration or gait outcomes. mTBI participants Results indicated that mTBI subjects had reduced coupling of visual exploration and gait compared to controls, and reduced coupling in controls under dual-task conditions. Under ST conditions faster gait speed (rho=.642, p=.045) and stride length (rho=.718, p=.019) related to more frequent saccades, longer double support time (rho=.766, p=.010) related to faster saccade velocities, and shorter stride time related to shorter fixation durations (rho=.695, p=.026). While under DT conditions, longer double support time was related with smaller saccade amplitude (rho=-.730, p=.005) in mTBI, and double support time was related with saccade frequency (rho=.762, p=.010), and stride time with fixation duration (rho=.687, p=.028) in controls.

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

Members of the research team had the opportunity for training and professional development through attendance at specific military based conferences. Dr. Laurie King and Dr. Douglas Martini attended the Military Health System Research Symposium (MHSRS) in August 2019. MHSRS is one of the key meetings offering researchers to listen and engage with experts in the field of mTBI.

How were the results disseminated to communities of interest?

Information regarding the study has been documented on the following websites, which are available to the public:

- ClinicalTrials.gov
- ResearchMatch.org
- Fitbir.nih.gov

We have published two manuscripts and have another manuscript in press. Along with conference abstracts, platform presentations, and educational sessions we have done several oral presentations and attended a community outreach event. Also, Dr. King presented study progress to the Complex TBI Rehabilitation Research Program at the in-progress review meeting in October 2019.

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

We plan to increase Aims I & II recruitment this next reporting period to reach our projected numbers. We will do this by partnering and creating relationships with internal and external physicians that can refer mTBI patients to us. We also plan to pursue other methods such as text, email, and recruitment through MyChart. We will continue to use EPIC's Best Practice Advisory (BPA) feature that has been useful thus far. We will finish collecting healthy control data for Aim III and will begin identifying PT's and patients to evaluate the feedback system.

Engineers at APDM will continue to make progress on the remaining tasks related to technology development, verification, and validation. More specifically:

• Develop new measures for real-time algorithms based on feedback from users at OHSU
• Complete verification of the new real-time algorithms using optical motion capture data collected in the past two years
• Optimize the system real-time interface and visual biofeedback
•Complete development and testing of the system to measure functional mobility during unconstrained activities of daily life

4. IMPACT:

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

This project will influence the base knowledge and theory of physical therapy treatments for people who suffer from mTBI. This project will give insight on patient recovery for those receiving early intervention versus those receiving standard of care treatment. Clinical practice may also be impacted through the implementation of wearable sensors to more accurately measure and assess gait and balance during both at-home activity, as well as in clinical and rehabilitative settings.

What was the impact on other disciplines?

Our research team meets monthly throughout the year with a wide range of practitioners who treat patients with mTBI. These meetings allow our team to disseminate research findings, and help to translate knowledge into clinical practice. Meeting with clinicians also allows our team to gain insight and discuss how research can help influence clinical practice.

What was the impact on technology transfer?

Throughout this reporting period we have been working closely with APDM Wearable Technologies to 1) validate an algorithm capable of tracking head, neck and trunk motions, and 2) generate an easy user interface for providing objective information to physical therapists and the patient. The technology is only being used within this study and we believe this is a large step toward being able to monitor mTBI recovery in the home environment. The inertial systems in use provide information beyond the typical activity tracker, by providing information not only on quantity (eg. of steps), but on quality of movement. In the next reporting period the study team will work with physical therapists to implement this system within a clinic setting and get feedback on user experience.

What was the impact on society beyond science and technology?

Many of our research team attended the OHSU Brain Fair. At this year's annual event held at the Oregon Museum of Science and Industry (OMSI), we demonstrated several balance and gait tests and explained how this information could be used to help understand more about mTBI.

Our research team has continued to help mentor the development of young researchers completing undergraduate and high-school programs of education. Specifically, we have had students engage in projects relating to the validation of the inertial sensors, rehabilitation outcomes, and eye-tracking procedures. One student received an award from NIH Build Exito to join our lab for two years to help with this project.

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

Reported problems/delays from Year 2, Quarter 1:
1) Had to change testing locations from VA to OHSU
2) We had to hire new several new staff members and the training process for this protocol can be lengthy
<u>Resolution:</u> We were able to find a testing location at OHSU and we were able to onboard new staff members quickly

Reported problems/delays from Year 2, Quarter 2:
No actual problems or anticipated problems

Reported problems/delays from Year 2, Quarter 3:
No actual problems or anticipated problems

Problems/delays from Year 2, Quarter 4:
1) We are behind on recruitment numbers
Resolution: We are determining new recruitment methods in order to reach recruitment goals, including MyChart emails and text message options. We also plan to partner with internal and external physicians who treat mTBI patients, so they feel confident referring and providing study information to their patients. We have made significant progress on aim III through slow enrollment of aims I and II to ensure all study tasks will be completed on time.

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

Significant changes in use or care of human subjects

No significant changes have been made.

6. PRODUCTS:

Publications, conference papers, and presentations

Journal publications.

Published manuscripts:

- Parrington, L, Jehu, DA, Fino, PC, Pearson, S, El-Gohary, M, & King, LA. (2018). Validation of an inertial sensor algorithm to quantify head and trunk movement in healthy young adults and individuals with mild traumatic brain injury. Sensors, 18(12), 4501.
- Stuart S, Parrington L, Martini M, Popa B, Fino PC, King LA. Validation of a velocity-based algorithm to quantify saccades during walking and turning in mild traumatic brain injury and healthy controls." Physiological measurement 40.4 (2019): 044006.

Manuscript currently in press:

- Parrington L, Jehu, D, Fino PC, Wilhelm J, Pettigrew N, Stuart S, Murchison C, El-Gohary M, VanDerwalker J, Pearson S, Hullar T, Chesnutt JC, Peterka R, Horak FB, King LA. The

Sensor Technology and Rehabilitative Timing (START) randomized controlled trial study protocol. Submitted to the Physical Therapy Journal.

Books or other non-periodical, one-time publications.

Book Chapters:

- King, LA. Neurological Rehabilitation, 7th Ed. DA Umphred (Eds). The Emerging Role of Wearable Inertial Sensors for Neuro-rehabilitation. In Review.
- Parrington, L., Wilhelm, J., Pettigrew, N., Scanlan, K. & King, L.A. Ward, rehabilitation and clinic based wearable devices. In From A to Z: Wearables in modern medicine. Edited by S. Stuart and A. Godfrey. (Eds). In Preparation.

Other publications, conference papers and presentations.

Conference abstracts submitted:

- Pettigrew NC, Wilhelm JL, Scanlan KT, Martini DN, Chesnutt, JC, King LA. Is home exercise for dizziness after mild traumatic brain injury enough? Could wearable sensors help? Submitted to APTA Combined Sections Meeting, Denver, CO, 2020.
- Wilhelm JL, Pettigrew NC, Scanlan KT[1], Martini DN, Chesnutt, JC, King LA. Cervical proprioception and neck dysfunction in people with subacute mild traumatic brain injury. Submitted to APTA Combined Sections Meeting, Denver, CO, 2020.

Conference educational session:

- Scherer, M, King, LA, Lester, M, McCulloch, K, & Weightman, M. Functional return-to-duty decision making post mTBI and musculoskeletal injury. Presented at the Combined Sections Meeting, APTA, Jan 23-26, 2019. Washington, DC.

Platform presentations:

- Stuart, S, Parrington, L, Peterka, R, Campbell, K, Kampel, S, Putterman, D, Hullar, T, & King, L. Relationship between saccadic and cognitive function in mild traumatic brain injury. Presetned at the Military Health Systems Research Symposium (MHSRS) 2019.

Poster Presentation

- Stuart, S, Parrington, L, Fino, P, Chesnutt, J, & King, L. Comprehensive assessment of visual exploration during walking and turning in mild traumatic brain injury and controls. Submitted to the International Society of Posture and Gait (ISPGR) World Congress. June 30 - July 4, 2019. Edinburgh, Scotland.
- Scanlan KT, Pettigrew NC, Wilhelm JL, Chesnutt JC, King LA. Cervical proprioception and neck dysfunction in people with mTBI. Submitted to Oregon Health and Science University’s Research Week. Portland, OR, March 18 2019.
- Stuart, S, Popa, B, Parrington, L, Kreter, N, & King, L. Visual exploration and gait in people with mild traumatic brain injury. Submitted to the Military Health Systems Research Symposium (MHSRS) 2019.
- Popa, B, King, LA, & Stuart, S. Visual exploration during walking in people with mild traumatic brain injury. American Balance Society (ABS). February 26-27, 2019. Scottsdale, AZ.

- Wilhelm J, Scanlan K, Pettigrew N: “Cervical proprioception and neck dysfunction in people with mild traumatic brain injury”, May 13 2019, OHSU Research Week.

Oral presentation/community outreach:

- Wilhelm J, Chesnutt JC: Updates on Concussion Rehabilitation, March 15 2019, Reed College.
- Wilhelm J, Chesnutt JC: “Active Concussion Rehabilitation”, April 12 2019, Columbia Memorial Hospital.
- Wilhelm J, Pettigrew N, Stuart S: “Updates on Concussion Rehabilitation”, April 25 2019, Oregon Physical Therapy Association PT Education.
- Wilhelm J, Rockwood R: “Updates in Concussion Assessment and Rehabilitation”, June 8 2019, Oregon Athletic Training Symposium.

Website(s) or other Internet site(s)

Nothing to Report

Technologies or techniques

As outlined by the schedule of work, our team has been working with APDM Wearable Technologies in the development of a user interface for at-home implementation of vestibular therapy exercises. We are using this technology within the intervention of the study and are working closely with APDM to optimize the user experience.

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: Josh Koch, BS
Project role: Research Assistant
Nearest person month worked: 1
Contribution to project: Josh will be involved in recruitment and testing participants

Name: Lindsey Lee, BS
Project role: Research Assistant
Nearest person month worked: 1
Contribution to project: Lindsey will be involved in recruitment and testing participants

Daniel Putterman, Au.D. – no change
Natalie Pettigrew P.T, D.P.T – no change
Sam Stuart Ph.D – no change
Lucy Parrington, Ph.D – no change
Laurie King, Ph.D., P.T. – no change
Robert Peterka, Ph.D. – no change
James Chesnutt, M.D. – no change
Timothy Hullar, M.D. – no change
Jennifer Wilhelm, P.T., D.P.T., N.C.S. – no change
Shelby Martin, MA – no change
Edward King, MS – no change
Sean Kampel, Au.D – no change
Mahmoud El-Gohary – 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?

Organization Name: APDM Wearable Technologies
Location of organization: 2828 SW Corbett Avenue, Portland, OR 97201
Partner's contribution to project: Partners have developed the Opals, which are the wearable sensors that detect movement, gait, and balance. They have developed kinematic algorithms and the home exercise interface for this study.

8. SPECIAL REPORTING REQUIREMENTS

9. APPENDICES

Rehabilitation of Complex TBI with Sensory Integration Balance Deficits; Can Early Initiation of Rehabilitation with Wearable Sensor Technology Improve Outcomes?

PI: Laurie King, PhD, PT **Org:** Oregon Health & Science University **Award Amount:** $4.6 million

Study/Product Aim(s)

Our central hypothesis is that rehabilitation after mTBI is suboptimal due to late initiation of and inadequate performance of exercises that do not adequately challenge vestibular and sensory integration function. Our long-term goal is to clarify best practices for the rehabilitation of balance deficits in people with mTBI by comparing early vs late (standard of care) initiation of physical therapy with and without wearable sensors on balance deficits after mTBI.

Aim I) Early Intervention: To determine the effects of early versus late rehabilitation for balance deficits in complex mTBI. Aim II) Home Monitoring: To compare traditional balance rehabilitation versus balance rehabilitation with sensor-based home monitoring of the quality of prescribed exercises. Aim III) Real-time Monitoring for Training: To develop and evaluate a novel, wearable sensor system to provide real-time feedback to physical therapists on head and trunk movement during training.

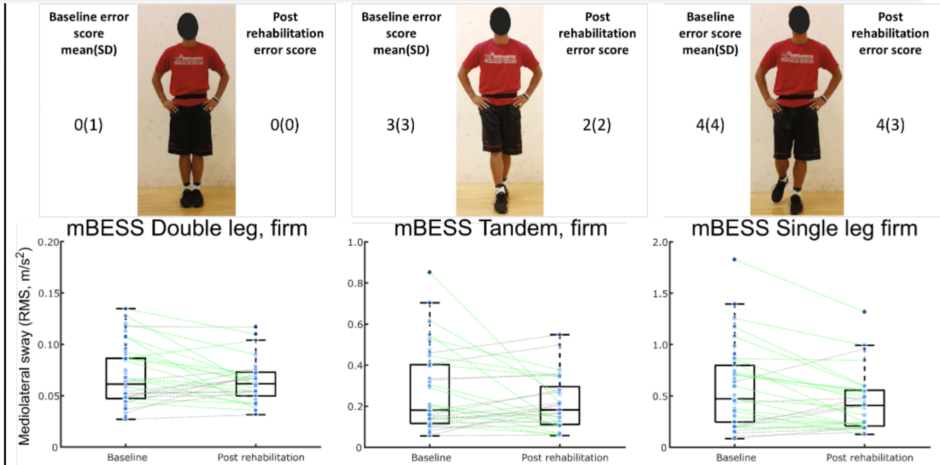
Approach

We will randomize, at the first physician visit (< 12 weeks post injury), 160 patients with mTBI to receive either early (within 2 weeks from physician visit) or late (standard of care ~60 days after physician visit) rehabilitation. People will be further randomized into either: 1) home exercise program or 2) the same home exercise program with wearable sensors worn on the forehead and trunk to monitor compliance and quality of performance during home exercises. Our primary outcome to measure efficacy of rehabilitation is the Dizziness Handicap Inventory (DHI). Secondary outcomes will be structured along the International Classification of Function and Disability (ICF) models framework and will include novel objective measures of balance and gait, central sensory integration and eye movements.

Timeline and Cost

Activities	CY	17	18	19	20
Study setup, Hiring, Training, Purchasing, IRB					
Recruitment					
Aims I and II: Balance Assessment and Rehabilitation 160 Randomized mTBI					
Aim III: Development and Evaluation of Real-time Monitoring					
Data Analysis					
Manuscript Preparation and Submission					
Estimated Budget ($K) $4,523		$1,007	$1,117	$1,148	$1,251

Updated: Portland, OR; 28 October 2019



Balance impairments are a common complaint after mTBI. We performed a preliminary analysis on modified Balance Error Scoring System (mBESS) scores and mediolateral sway (measured with inertial sensors) differences between baseline and post rehabilitation sessions. Qualitatively, mBESS scores did not change from baseline to post rehabilitation sessions. However, inertial sensors measured subtle improvements in mediolateral sway from baseline to post rehabilitation.

Goals/Milestones

CY17 Goal – Study set up and launch
☒ All IRB, finalize protocols, order and test all equipment
☒ Begin balance assessment and rehabilitation (Aims I and II)
☒ Begin development of real-time feedback monitoring system (Aim III)
CY18 Goals – Clarify best practices for mTBI balance rehabilitation
☒ Continue testing and rehabilitation of subjects with mTBI
☒ Test and evaluate prototype feedback system on mTBI and control subjects
CY19 Goal – Clarify best practice for mTBI balance rehabilitation
❑ Continue testing and rehabilitation of subjects with mTBI
❑ Continue testing/evaluating feedback system and refine as directed
CY20 Goal – Complete all testing, analysis and dissemination of results
❑ Complete rehabilitation and all long term follow up testing
❑ Analyze results and disseminate findings

Comments: We have made significant progress this reporting period with Aim III and plan to keep enrollment rates high throughout the study

Projected Expenditure: $1,550,708
Expenditures to Date: $1,429,212