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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: Three physical therapists from the study team will use the biofeedback sensor system, along with six mTBI subjects, and they 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 138 subjects and enrolled 98 subjects in this study. For Aim III, 50 healthy control subjects have completed testing.

<table>
<tr><td colspan="6">15. SUBJECT TERMS
mTBI, Rehabilitation, Brain Injury, Inertial Sensors, Balance, Central Sensory Integration, Concussion, Eye Tracking</td></tr>
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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
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*	81%
Major Task 3: Randomized Interventions	*March 2021*	55%
Major Task 4: Assess Efficacy of Interventions	*March 2021*	29%
Major Task 5: Data Analysis &	*September 2021*	73%

Publications		
Specific Aim 3 (Real-Time Monitoring)		
Major Task 1: Develop & Evaluate the wearable system for feedback	*September 2021*	90%
Major Task 2: Launch Study Activities	*September 2020*	50%
Major Task 3: Data Collection	*September 2019*	100%
Major Task 4: Data Analysis & Publications on Interventions	*September 2021*	0%

What was accomplished under these goals?

Aim I & II

Major Task 2: Recruitment & Testing
Subtask 1: recruitment (7/7 tasks completed)

Subtask 2: data collection & management (0/5 tasks completed)

- Complete vestibular testing at OHSU and VA for data collection; We have completed vestibular testing on 82 subjects out of the targeted 160 participants. Due to COVID- 19 restrictions and limitations of in-person testing we have enrolled 16 telehealth subjects, where they completed Day 1 questionnaires over the phone. Total Day 1's completed is 98- 61% complete
- Complete gait and balance testing for data collection at OHSU and VA; We have completed gait and balance testing on 79 subjects out of the targeted 160 participants. Due to COVID-19 restrictions and limitations of in-person testing we have enrolled 16 telehealth subjects, where they completed Day 2 questionnaires over the phone. Total Day 2's completed is 95- 59% 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- 61% complete
- Screen and verify data on server and check for accuracy; The last data check was completed February 2020 before OHSU was put on a research operation hold due to COVID-19. Research Assistants have returned to the lab and plan to complete the next data check within the next reporting period- 40% complete
- Validate and submit forms to FITBIR quarterly; We submitted all data thus far to FITBIR during September 2020. Data will continue to be submitted yearly, as required- 55% complete

Major Task 3: Randomized Interventions on 160 mTBI Patients
Subtask 1: intervention (1/4 tasks completed)

- Enroll subjects in rehabilitation intervention; As subjects enroll they are being randomized in to either early or standard of care rehabilitation- 57% complete
- Complete 6 week interventions; 54 total subjects (12 telehealth/42 in-person) have completed the 6 week intervention and three subjects are currently participating in the intervention. Six subjects were terminated from the study midway through the intervention due to OHSU's COVID-19 restrictions banning in-person testing- 33% complete
- Physical therapist's document compliance, adverse events and progression of exercise for each subject; Physical therapists are keeping a detailed record of progression through rehabilitation and are required to fill out a summary sheet for each visit documenting any protocol deviations and progression of exercises- 33% complete
- Optimize system user interface and reports based on input from users; APDM has corrected interface errors preventing subjects from logging data and all system kits have been updated to new compatibility standard. Ongoing work will be done to assess intermittent hardware errors- 100% complete

Major Task 4: Assess Efficacy of Interventions
Subtask 1: intervention assessment (0/2 tasks completed)

- Complete immediate posttest after intervention; Sixty-two subjects have completed the posttest- 38% complete
- Complete long-term assessment 6 months later to assess retention; Thirty-four subjects have completed the long-term assessment- 21% complete

Major Task 5: Data Analysis and Publications
Subtask 1: data analysis (0/1 task completed)

- 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 turning metrics and descriptively compared it to healthy controls collected from grant W81XWH-15-1-0620 (See significant results). Because of a 7 month shutdown of in-person testing due to COVID-19, we transitioned our project to a telehealth platform to deliver vestibular rehabilitation therapy post mTBI. We are now describing changes in symptomology as a result of rehabilitation that was delivered virtually- 43% complete

Subtask 2: manuscripts, presentations and other output (2/5 tasks completed)

- Disseminate findings (abstracts, presentations, papers, DoD); We submitted abstracts to present at the 2021 Combined Sections Meeting for the American Physical Therapist Association and the 2020 NIH Rehabilitation Research meeting (see products below)- 25% complete
- Integrate new protocols and head movement metrics into APDM Mobility Lab system; New protocols for measuring head and trunk range of motion, and velocities during gaze stabilization movements (Vestibular Ocular Reflex and Visual Motion Sensitivity) have been created and implemented into APDM Mobility Lab. These protocols in the Mobility Lab software provide real-time feedback on head movement quality in comparison to healthy normative data and deliver additional metrics offline (head velocity and range of

motion). We are continuing to monitor and address intermittent hardware and software issues that arise during data collection- 80% complete

- Submit manuscript presenting APDM algorithm and validation results; We published initial validation of an inertial sensor algorithm to quantify head movements in young healthy adults and individuals with mTBI in the journal *Sensors* in 2018 (Parrington et. al., 2018 - *Sensors*). Additionally, we have a manuscript in review detailing the reliability of inertial sensors and algorithms developed by APDM at measuring head movement metrics for vestibular rehabilitation therapy (See products)- 90% complete
- Create technical report detailing the adaptation of the Neurocom for measuring sensory weighting; We published a detailed explanation on adapting a Neurocom SMART EquiTest CRS Device for measuring central sensorimotor integration (CSMI) for balance in the journal Frontiers in Neurology in 2018 (Peterka et. al., 2018 - *Front Neurol*). The manuscript reports the equipment, software, data analysis and interpretations of the CSMI Test. For this project, we are only using 2 degree tilts (instead of 2 and 4 degree tilts) of the Neurocom's surface platform and visual surround to deliver pseudorandom perturbations for research subjects to overcome to maintain standing upright position- 100% complete

Aim III

Major Task 1: Technology Development
Subtask 1: technology development (3/4 tasks completed)

- Optimize system user interface and reports based on input from users; APDM continues to assess intermittent hardware issues that arise during data collection in the home- 95% complete
- Update and optimize user-interface framework for real-time feedback; Implemented changes to live feedback plots based on usability/readability requests from physical therapists using the system. Also implemented post exercise reporting terminology, order of results, and metrics to include 95% CI to improve physical therapist's interpretation. Completed changes to the user interface based on user (patient) feedback, updated real-time algorithms, and updated system analysis- 100% complete
    - ◊ Addition of gait speed algorithm for real-time feedback: This metric has been identified as highly valuable for physical therapy clinical use and current set up of real-time feedback may allow for this type of data collection. APDM engineers will develop the appropriate algorithm- 10% complete
    - ◊ Normative Data: Added normative data from a complete set of healthy controls ranges. Goal zones were updated with new values and goal zones were added to live and static stabilograms. Implemented trunk sway live visualization for use in exercises where a patient is required to walk- 100% complete
    - ◊ Application updates to maintain compatibility with Mobility Exchange: Fixed compatibility issues with the Mobility Exchange Server that involves testing, building, and deploying the application to physical therapist computers and the kits distributed to subjects- 100% complete

Major Task 2: Launch Study Activities
Subtask 1: train and recruit (1/2 tasks completed)

- Identify physical therapists to participate and evaluate system; (Due to impact of COVID-19) Three study team physical therapists have been identified to participate and evaluate system as the use of external clinical physical therapists is not feasible currently due to COVID- 100% complete
- Identify patients from physical therapy to evaluate feedback system; Each physical therapist (total of three) will use this on two of their patients, for a total of six mtBI subjects- 0% complete

Major Task 3: Data Collection
Subtask 1: normative data (1/1 task completed)

- Test 50 healthy controls for normative values; 50 healthy controls have been tested for normative values and we have begun initial data checks- 100% complete

Significant Results/ Key outcomes:

Aims I & 2	DoD2 In-Person Subjects	DoD2 Telehealth Subjects	Total
Screened	119	19	**138**
Enrolled	82	16	**98**
Day 1	82	16	**98**
Day 2	79	16	**95**
Posttest	46 (+4 remote visits)*	12	**62**
6-month follow up	22 (+12 remote visits)*	0	**34**

*These participants were enrolled in the study before COVID restrictions were executed. These visits were performed over the phone and no in-person data collection occurred.

Recovery of Abnormal Turning Following mTBI

Preliminary analyses indicate that turning is abnormal during the sub-acute recovery phase following mTBI, but can improve following physical therapy. Turning requires rapid, coordinated reorientation of the head, trunk, and pelvis toward a new direction of travel, and can be abnormal in people with chronic post mTBI symptoms. However, it is unknown if these abnormalities are present sub-acutely following mTBI, or how they recovery with and without rehabilitation. For this preliminary analysis, subjects (N = 52) walked a turns course – comprised of 45, 90, and 135 degree turns at a self-selected pace. Inertial measurement units (IMU) placed at the lumbar spine, sternum, and head measured transverse plane angular velocity while subjects turned. We quantified the lumbar peak angular velocity for the 135 degree turns for a group of subjects pre and post rehabilitation (Pre- Early, Post Early; N = 23), and a group that did not receive (i.e. delayed group) physical therapy for their mTBI (Pre-Delay, Post-Delay, N = 29). Both groups (early – depicted in blue in **figure 1** and delay – depicted in red in **figure 1**) demonstrated abnormal lumbar peak angular velocity at baseline (pre) in comparison to healthy control data (depicted in black in **figure 1**) acquired from grant W81XWH-15-1-0620. All subjects that received rehabilitation (post- early in

figure 1) had lumbar peak angular velocities within 2 standard deviations of the healthy control mean when tested at the post session, and on average had more similar lumbar peak angular velocities in comparison to healthy controls (**Figure 1** – Black solid line). Some subjects that did not receive intervention (post-delay) still had abnormal lumbar peak angular velocities (outside 2 standard deviations of the healthy control mean), and on average had less similar lumbar peak angular velocities in comparison to healthy controls (**Figure 1**). Future analyses will statistically analyze the effectiveness of early rehabilitation in comparison to the current standard of care on promoting improved turning coordination following mTBI.

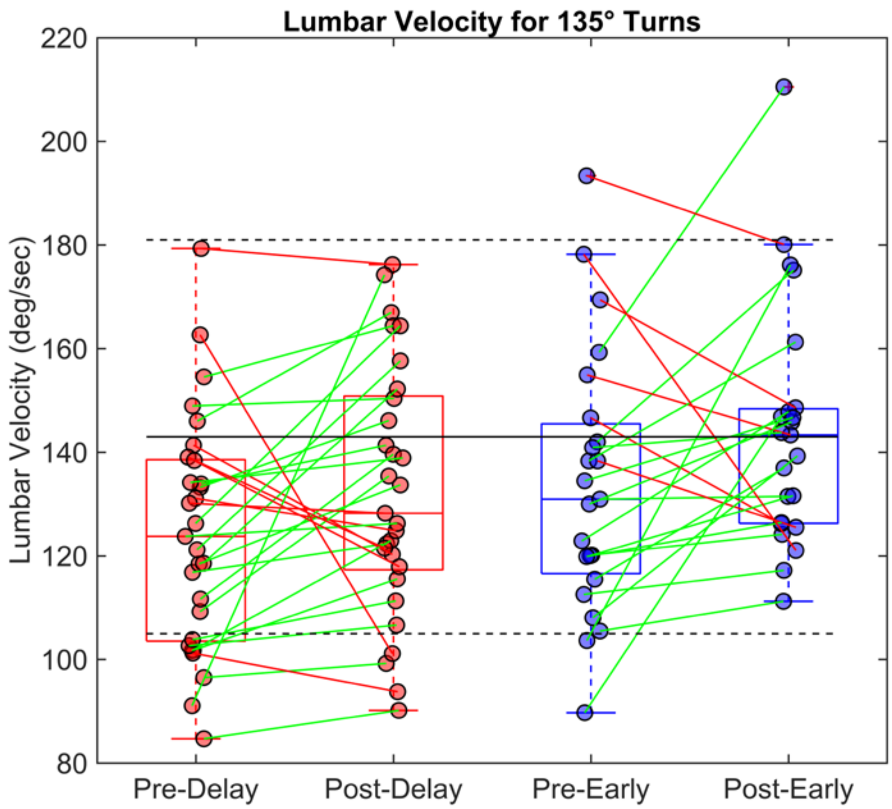


Figure 1: Lumbar peak angular velocities for subjects executing 135 degree turns while walking a turns course at pre and post rehabilitation (Early – blue), and subjects recovering naturally pre and post no interventions (Delay – red). Healthy control mean (solid black line) and 2 standard deviations (dashed black lines) are presented for comparison.

Central Sensory Integration for Balance Across the mTBI Recovery Spectrum

On average, both subacute and chronic mTBI populations utilize a larger proportion of inaccurate sensory information to maintain balance compared to healthy controls (larger mean sensory weighting values from **Table 1**). Using data obtained from our previous grant W81XWH-15-1-0620 on people with chronic mTBI, we have characterized sensory reweighting for balance control across timelines post mTBI. Our results suggest that both mTBI populations (subacute and chronic) have some abnormalities in sensory weighting for balance control. We used a 10-percentile cutoff value determined from the healthy control data to determine sensory weightings that were abnormal for the subacute and chronic mTBI groups (Percent Abnormal in **Table 1**). Interestingly, there were more abnormal sensory weighting scores in the chronic group, compared to the subacute group, suggesting a maladaptive strategy, if left to recover on their own. We will quantify the proportion of subjects within the subacute mTBI group that still have abnormal sensory weightings following rehabilitation in future analyses with additional subjects that complete rehabilitation.

Table 1: Summary of sensory weighting for balance outcomes from a central sensorimotor integration test in healthy control (CTRL), subacute mTBI (S-mTBI), and chronic mTBI (C-mTBI).

	Mean (Standard Deviation)			Range			Percent Abnormal* (Total N)	
Sensory Weighting	**CTRL**	**S-mTBI**	**C-mTBI**	**CTRL**	**S-mTBI**	**C-mTBI**	**S-mTBI**	**C-mTBI**
Proprioceptive with Eyes Closed	0.52 (0.09)	0.55 (0.09)	0.56 (0.10)	0.41	0.42	0.47	19% (68)	28% (52)
Proprioceptive with Eyes Open	0.31 (0.06)	0.33 (0.08)	0.34 (0.08)	0.30	0.43	0.48	16% (68)	16% (54)
Visual	0.12 (0.05)	0.13 (0.06)	0.17 (0.09)	0.26	0.21	0.56	23% (69)	35% (50)
Proprioceptive + Visual	0.56 (0.08)	0.57 (0.08)	0.57 (0.13)	0.38	0.37	0.71	14% (69)	21% (52)

* - Percent abnormal determined by the percentage of subjects that fell outside a 10-percentile cutoff determined from control data
CTRL – Control (Data from W81XWH-15-1-0620)
S-mTBI – Subacute mTBI (Data from W81XWH-17-1-0424)
C-mTBI – Chronic mTBI (Data from W81XWH-15-1-0620)

<u>Using the Vestibular/Oculo-Motor Screening (VOMS) Tool as an Outcome Measure after Rehabilitation for mTBI</u>

Our preliminary data suggest that the VOMS component change scores minimally decreased over time without intervention, while rehabilitation had a larger effect on decreasing symptom provocation when administering the VOMS. The VOMS tool is a commonly used screening tool to aid in mTBI diagnosis, and can provide an overview of potential impairments that require more rehabilitation. There is limited evidence that the VOMS tool can provide outcome measures to track recovery from vestibular and ocular impairments following mTBI. These preliminary analyses were to (1) determine if VOMS scores changed naturally over time without intervention, and (2) describe VOMS scores changes after rehabilitation. Due to the low sample size per group and preliminary nature of this, we calculated Hedge's G effect sizes with 95% confidence intervals (95%CI) on the magnitude of change for the VOMS change score components from two testing time points (baseline and 6 week follow up) for a group receiving rehabilitation and a group recovering naturally from mTBI. When all components of the VOMS were considered together, there was a minimal decrease in VOMS change scores that occurred naturally over a 6 week period without rehabilitation (effect size [lower 95%CI, upper 95%CI]; -0.44 [-0.64, -0.23]). Overall, there was a moderate decrease in VOMS change scores that occurred after a 6 week rehabilitation program (-0.73 [-0.95, -0.51]). Observing the individual subject change scores for the visual motion sensitivity component of the VOMS, some subjects that did not receive rehabilitation got better over six weeks (Red Data **Figure 2**). However, their recovery was more variable and not as large as compared to the group of subjects that received rehabilitation (Blue data **Figure 2**). Using symptom provocation change scores from the VOMS tool appears to be a reasonable outcome measure to track recovery of an mTBI. Future work will determine VOMS outcomes differ between rehab and non-rehab groups with larger sample sizes, and whether changes to VOMS outcomes relate to other validated measures.

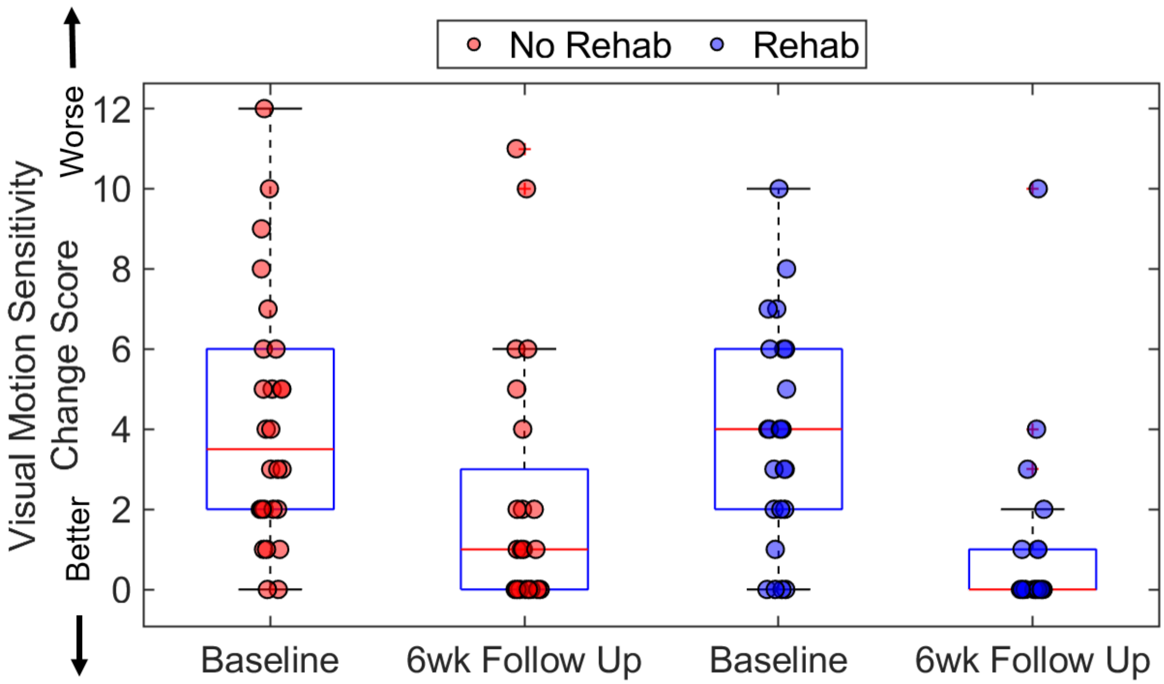


Figure 2: Visual motion sensitivity change scores at baseline and a 6 week follow up for a group of subjects with mTBI that had no rehabilitation (red) and completed a rehabilitation program (Blue).

Preliminary Results on a Wearable Sensor to Track Daily Life Mobility in the Home Environment

Preliminary analyses show that people with an mTBI in the subacute recovery phase take wider turn angles and more variable turn angles as compared to healthy controls (Figure 3). These differences may be a result of a more conservative turning pattern in an effort to not exacerbate symptoms for people with mTBI. As a result of the COVID-19 pandemic, we were unable to conduct in person laboratory assessments outlined in the grant through the 3rd and most of the 4th quarters. After consulting with the DoD we made changes to the protocol that allowed us to continue with portions of testing and intervention by phone and/or virtual visits with study participants. As part of this telehealth protocol, we had subjects wear an IMU around their waist for a period of 7 days. The wearable IMU measured acceleration and angular data, and valid algorithms quantified activities (number of steps, activity rates etc.) and movement quality (turning angle, durations, velocities, etc.). Though we are now able to bring back in-person testing at a modified operation, we will continue to measure home monitoring going forward for additional objective data in case of another in person laboratory research shutdown. Future analyses will compare mobility data changes as a result of virtual rehabilitation.

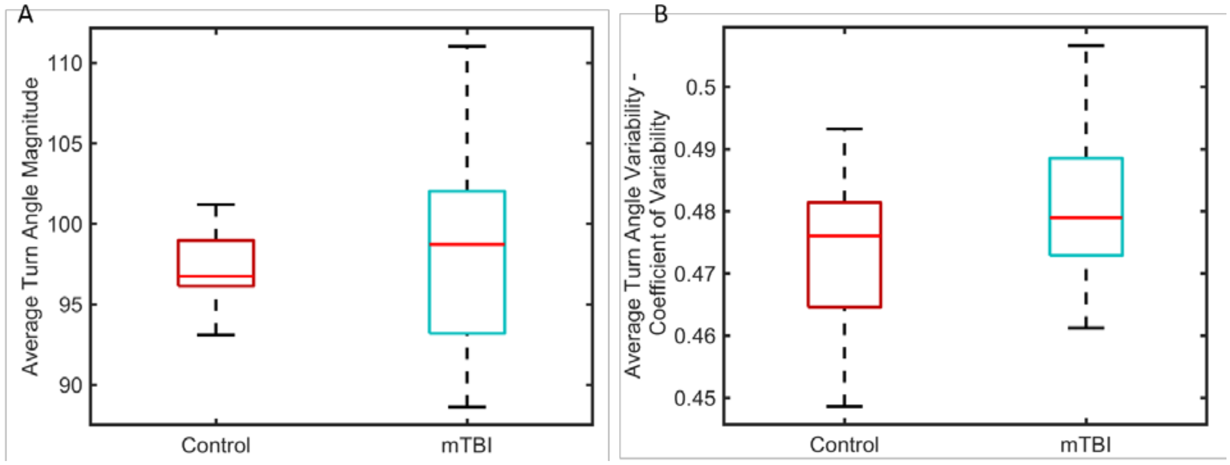


Figure 3: **Average turn angle magnitude (A) and average turn angle variability (B) for healthy controls and patients with mTBI.**

<u>**Reliability of Instrumented Vestibular Rehabilitation Therapy Exercises**</u>

IMUs may have a role in the clinic: to help objectively measure vestibular rehabilitation exercises. IMUs demonstrated good to excellent within day retest reliability (ICC[3,2] = 0.77 to 0.99)for both range of motion (ROM) and velocity for all trunk and neck movements within the vestibular rehabilitation exercises. We now have healthy normative values for ROM and velocity to help with goal setting and appropriate expectations during treatment. Vestibular rehabilitation consists of exercises involving eye-head movement and balance to stimulate the vestibular system. The implementation of IMUs can help provide objective feedback to promote more effective rehabilitation. For IMUs to be implemented in clinical rehabilitation settings, normative reference data, as well as data informing the reliability of the system across sessions is required. The purpose of these preliminary analyses were to investigate 1) normative data for healthy controls, and 2) the between-session reliability of IMUs for vestibular rehabilitation. A total of 18 (9 female, age range 8-35years) healthy participants' data were analyzed. Participants were tested on 2 separate days, an average of 11.1 (sd = 7.6) days apart. Participants performed vestibular exercises while wearing IMUs on the forehead and sternum. Each trial consisting of two, 30 second bouts of the following exercises: 1) gaze stabilization 2) visual motion sensitivity 3) static balance with head turns and 4) walking with head turns. Exercises were completed both side to side, and up and down, and ROM and maximum rotational velocity were calculated for each movement. Between session reliability was most consistent for static balance with head turns ranging from good to excellent (ICC[3,2] ≥ 0.8). For gaze stabilization, ROM and maximum rotational velocity in the side to side motions demonstrated poor reliability (ICC[3,2] < 0.3) for the trunk, but otherwise had good to excellent reliability between sessions for up-down motions at the trunk, and all head motions (ICC[3,2] > 0.8). With the exception of neck ROM during up-down motions (moderate reliability; ICC[2,3] = 0.7), visual motion sensitivity demonstrated good to excellent reliability (ICC[2,3] > 0.8). Between session reliability during gait ranged between moderate and excellent (ICC[2,3] 0.6 – 0.9). Normative data and a more detailed summary of results will be provided in our upcoming manuscript (Wearable sensors for vestibular rehabilitation: normative data and between-session reliability).

<u>Preliminary Analysis of Auditory Processing</u>

There were 42% of subjects (18/42), at the time of analysis, with subacute concussion that had abnormal auditory processing (more than 3 dB of their predicated normative spatial release- indicated by the red dots in Figure 4). This could be indicative of central auditory processing deficits that require further observation or rehabilitation. There are many neural processes needed for accurately segregating sound sources based on spatial and spectrotemporal cues. We used a validated Spatial Release (SR) task that assessed a person's ability to use spatial and spectrotemporal cues between sound sources. We plan to reanalyze this data with a larger data set over the next quarter.

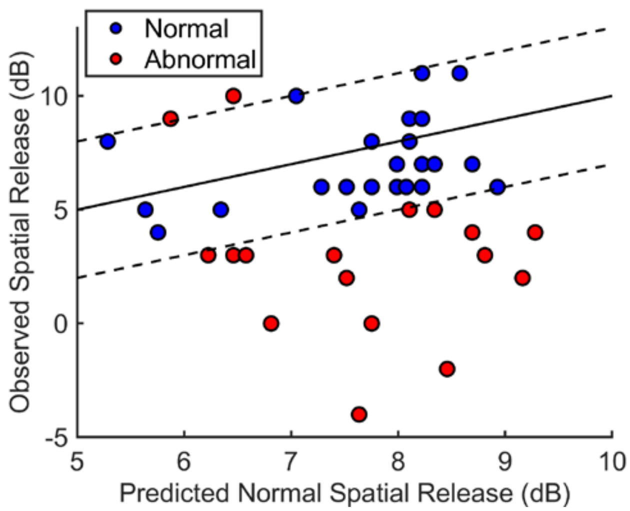


Figure 4: Observed spatial releases should fall within 3 dB (dashed lines) of a normative spatial release using a predictive linear model (solid line). Up to 42% (18/42) of our subjects had an abnormal spatial release despite a normal audiogram.

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 a military based conference, Military Health System Research Symposium (MHSRS). Due to COVID-19 restrictions this conference was canceled this year, but study team members plan to attend next year.

Members of our team meet monthly with multiple departments within our university and the Portland VA, including Family Medicine, Rehabilitation, and the National Center for Rehabilitation and Auditory Research (NCRAR) to discuss preliminary results, grant proposal and new papers in the literature.

Several members of the team attended a virtual conference where mTBI data was shared:
Brain Trust 2020 on May 1 2020: "New Research in Mild TBI Management"

Dr. Laurie King collaborated with the Portland VA on the following article and it was recently published:
Theodoroff SM, Papesh M, Duffield TC, Novak M, Gallun FJ, King L, Chesnutt J, Rockwood R, Palandri M, Hullar TE. Concussion Management Guidelines Neglect Auditory Symptoms, Clinical Journal of Sport Medicine, 2020, September 15, 2020.

Physical therapists on the team attended and presented at the National Institute of Health (NIH) "Rehabilitation Research 2020: Envisioning a Functional Future" conference October 15-16th 2020. (See products below)

One of our postdoctoral scholars, Dr. Kody Campbell, submitted a grant proposal to the Medical Research Foundation (MRF) in September 2020 titled "Can continuous monitoring of mobility with wearable sensors measure recovery after mTBI with and without rehabilitation?"

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

This reporting period we have submitted one manuscript and have one in preparation, along with conference abstracts, poster and virtual presentations, and attended a large community outreach event (see products below).

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

COVID-19 Update: Our research team was recently approved to return to the Portland VA Hospital for in-person testing, which is where our Day 1 protocol takes place. Due to this new information we will be able to enroll in-person testing again, at 25% capacity. We plan to increase enrollment over the next few reporting periods to ensure we reach study milestones.

Home Monitoring: Due to the importance of objective measures after concussion, we plan to continue to measure quality and quantity of movement in the home environment as an objective measure due to COVID restrictions. We were IRB approved to have participants wear a sensor for 7 days pre-intervention and then again 7 days post-intervention. Passive, unobtrusive monitoring in the home with wearable sensors has the untapped potential to provide quantitative measures of quality and quantity of mobility. APDM's innovative wearable technology can be unobtrusively worn during the day and may provide continuous measures of mobility that may be more sensitive markers of subtle changes, compared to standard measures of mobility during short prescribed tests. APDM will provide the additional sensors for this measure and additionally we have applied for a small local grant- MRF (see training and professional development above) for additional funds to continue measuring home mobility before and after rehabilitation. APDM will assist with data analysis.

APDM Plans:

- ◊ Provide support to analyze the home data (using instrumented wearables) and update continuous/passive data analysis and report
- ◊ Continue development of a home hub to support data collection and transfer of home data to the Mobility Exchange Server
- ◊ Development of gait speed algorithm for real-time feedback for Aim III

Aim III: Due to COVID restrictions, we have modified Aim III's evaluation of real-time monitoring and have discussed with our point of contact at the DoD for approval. We initially were approved to have five physical therapists test the system on five of their clinical patients (25 total subjects). However, due to modified operations this is not feasible to find outside physical therapists to evaluate the system during this time of modified operations due to COVID. We have three study team physical therapists that will participate and evaluate the system and each physical therapist will use two of their patients to gain feedback (six total subjects). The physical therapists have been working very closely with APDM and have weekly meetings to develop and improve this system. The working relationship our physical therapists have with APDM will allow for timely and efficient modifications and improvements to the system.

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 (e.g. 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. Two students were selected to work in our laboratory from NIH Build Exito to work on this project. Build Exito is an undergraduate training program that supports underrepresented students interested in a career in science. One student ended her term May 2020 and the other student started August 2020.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

We have modified Aim III due to COVID restrictions. (See goals for next reporting period section)

Actual or anticipated problems or delays and actions or plans to resolve them

Reported problems/delays from Year 3, Quarter 1:
No problems or delays

Reported problems/delays from Year 3, Quarter 2:
<u>*COVID-19*</u>*: With restrictions due to COVID-19 we are required to stop in-person research indefinitely as of 3/16/2020.*
<u>*Action:*</u> *After consulting with the DoD we made changes to the protocol to continue with portions of testing and intervention by phone and/or virtual visits with study participants.*

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

Problems/delays from Year 3, Quarter 4:
<u>*Low recruitment numbers:*</u> *We only recruited 6 people last quarter due COVID-19 and Oregon forest fire/smoke restrictions. The clinicians at the OHSU Concussion Clinic were not seeing many patients during these months, which influenced enrollment as the clinic is our primary source of recruitment.*
<u>*Action:*</u> *We ran a Facebook advertisement through OHSU's Social Media Department. We received some final metrics for the month this ad was posted:*

- *Impressions = 119,348*
- *Engagements = 20*

- *Link Clicks = 259*

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.

Parrington, L, Popa, B, Martini, DN, & King, LA. Instrumented balance assessment in mild Traumatic Brain Injury: Normative values and descriptive data for acute, sub-acute and chronic populations. Submitted to the Journal of Concussion.

Martini DN, Pettigrew N, Wilhelm J, Parrington L, & King LA. Wearable sensors for vestibular rehabilitation therapy: normative data and between session reliability. (Currently in preparation)

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

Other publications, conference papers and presentations.

Conference Abstracts:
Martini DN, Pettigrew NC, Wilhelm JL, Scanlan KT & King LA. Is home exercise for dizziness after mild traumatic brain injury enough? Can wearable sensors help? Vestibular-Oriented Research Meeting, Toronto Canada, May 2020. (Cancelled due to COVID)

Campbell KR, Parrington L, Hullar TE, Peterka RJ, Horak FB, & King LA. Quantifying Peripheral Vestibular and Balance Abnormalities in People with Chronic Dizziness and Imbalance Following Mild Traumatic Brain Injury. Vestibular Oriented Research Meeting. Toronto Canada, May, 2020. (Cancelled due to COVID)

Campbell KR, Parrington L, Martini DN, Wilhelm JL, Pettigrew N, Koch J, & King LA. (2020). Using the Vestibular/Oculo-Motor Screening (VOMS) Tool as an Outcome Measure after Rehabilitation for Mild Traumatic Brain Injury. 2020 Military Health Systems Research Symposium. Orlando Florida, Aug 2020. (Cancelled due to COVID)

Martini DN, Parrington L, Campbell K, Chesnutt J, & King LA. Gait variability and cognition in people with a mild traumatic brain injury. 2020 Military Health Systems Research Symposium. Orlando Florida, Aug 2020. (Cancelled due to COVID)

Pettigrew NC, Wilhelm JL, Scanlan KT, Martini DN, Chesnutt, JC, King LA Wearable sensors for vestibular rehabilitation after mild traumatic brain injury. National Institutes of Health Rehabilitation Research 2020, Oct 2020. (Virtual)

Wilhelm JL, Scanlan KS, Pettigrew NC, Chesnutt JC, & King LA. Tele-rehabilitation after mild traumatic brain injury; is it feasible? National Institutes of Health Rehabilitation Research 2020, Oct 2020. (Virtual)

Wilhelm JL, Parrington L, Pettigrew N, Scanlan K, Martini DN, Chesnutt J, & King LA. Cervical Proprioception and Neck Dysfunction in People with Subacute Mild Traumatic Brain Injury. Combined Sections Meeting, Feb 2021.

Scanlan, K, Wilhelm JL, Pettigrew N, Chesnutt J, & King LA. Is Evidenced-Based Multimodal Rehabilitation for Mild Traumatic Brain Injury Using Telehealth Possible? Combined Sections Meeting, Feb 2021.

<u>Poster Presentation:</u>
Campbell KR, Parrington L, Martini DM, Hullar TE, Peterka RJ, & King LA. (2020). Does Vestibular and Visuomotor Performance Relate to Gait in People Recovering Sub-Acutely from Concussion? 2020 Big Sky Athletic Training and Sport Medicine Conference, Feb 2019.

<u>Virtual Presentations:</u>
Pettigrew, N. OHSU Research Week on June 12 2020: "Wearable Sensors for Vestibular Rehabilitation Therapy: a Reliability Study"

King, LA. Neurology Grand Rounds on May 6 2020: "Concussion; Trends and New Directions in 2020"

Chesnutt, JC. Brain Trust 2020 on May 1 2020: "New Research in Mild TBI Management"

<u>Community Outreach:</u>
Oregon Museum of Science and Industry (OMSI): Informational handouts about the project were provided and members of our research team discussed the project with community members. March 7, 2020.

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?

Kody Campbell, PhD
Role: Kody will be lead postdoc on this project, tasks include data analysis, disseminating results, and leading subject testing sessions.

Josh Koch, BS- no change
Lindsey Lee, BS- no change
Daniel Putterman, Au.D. – no change
Natalie Pettigrew P.T, D.P.T – 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.

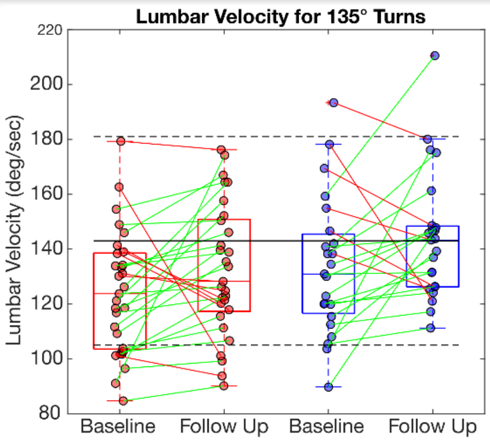
Approach

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; 27 October 2020



Turning requires rapid, coordinated reorientation of the head, trunk, and pelvis (lumbar spine) toward a new direction of travel, and can be abnormal in people with chronic post mTBI symptoms. **Preliminary analyses for this study indicate that lumbar peak angular velocity while turning is abnormal during the sub-acute recovery phase following mild traumatic brain injury, but can improve following physical therapy (Figure 1).**

Figure 1: Lumbar peak angular velocities for subjects executing 135 degree turns while walking a turns course at baseline and following a 6 week mTBI rehabilitation program (blue), and 6 weeks of no intervention (red). Healthy control mean (solid black line) ±2 standard deviations (dashed black lines) are presented for comparison. Green lines between subjects indicate faster turning speeds from baseline and red lines indicate slower turning speeds from baseline.

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 recently received approval to return to the Portland VA for Day 1 testing at 25% capacity. We will begin enrolling in-person testing subjects again.

Projected Expenditure: $3,489,093

Expenditures to Date: $2,453,939