AWARD NUMBER: W81XWH-18-1-0707

TITLE: Rehabilitation 2.0: Addressing Neuroplasticity in the Musculoskeletal Rehabilitation Model

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REPORT DATE: October 2020

TYPE OF REPORT: Annual

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

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
Oct 2020	Annual	15 Sep 2019 - 14 Sep 2020

4. TITLE AND SUBTITLE

Rehabilitation 2.0: Addressing Neuroplasticity in the Musculoskeletal Rehabilitation Model

5a. CONTRACT NUMBER

5b. GRANT NUMBER
81XWH-18-1-0707

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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

Ohio University
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8. PERFORMING ORGANIZATION REPORT NUMBER

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

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

10. SPONSOR/MONITOR'S ACRONYM(S)

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

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Musculoskeletal injuries such as to the knee's anterior cruciate ligament (ACL) degrade the operational readiness of our U.S. Service members. These injuries cause decreased physical ability that leads to reduced performance and high re-injury risk. Changes in brain activity as the result of the injury is directly related to the decreased physical performance, affecting the Service member's motor performance capability in complex or highly reactive military training and operations environments. Unfortunately, current treatments do not restore post-injury Service member's physical performance, especially when under stress. This deficit has clear consequences for military personnel, as the intense stress and constant need of situational awareness can impair physical performance when returned to active duty. To that end, new therapies are needed to restore Service member performance after injury. Thus, the purpose of this proposal is to quantify how the brain changes after injury across the typical 6-month window of physical therapy. We are also testing new functional assessments that target the brain changes that limit Service member performance. These assessments will support the transition of this research to clinical practice. This applied research award will provide the knowledge of the time course of brain changes that influence function to implement these new impactful interventions. These synergistic outcomes provide an immediate product that can be clinically implemented and propel further investigations to ensure truly restored functional capacity of our nations Service members.

15. SUBJECT TERMS

None Listed

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	7	19b. TELEPHONE NUMBER *(include area code)*

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1. Introduction

Musculoskeletal injuries such as to the knee's anterior cruciate ligament (ACL) degrade the operational readiness of our U.S. Service members. These injuries cause decreased physical ability that leads to reduced performance and high re-injury risk. Changes in brain activity as the result of the injury is directly related to the decreased physical performance, affecting the Service member's motor performance capability in complex or highly reactive military training and operations environments. Unfortunately, current treatments do not restore post-injury Service member's physical performance, especially when under stress. This deficit has clear consequences for military personnel, as the intense stress and constant need of situational awareness can impair physical performance when returned to active duty. To that end, new therapies are needed to restore Service member performance after injury. Thus, the purpose of this proposal is to quantify how the brain changes after injury across the typical 6-month window of physical therapy. We are also testing new functional assessments that target the brain changes that limit Service member performance. These assessments will support the transition of this research to clinical practice. This applied research award will provide the knowledge of the time course of brain changes that influence function to implement these new impactful interventions. These synergistic outcomes provide an immediate product that can be clinically implemented and propel further investigations to ensure truly restored functional capacity of our nations Service members.

2. Keywords

Neuroimaging, lower extremity, biomechanics, knee injury, anterior cruciate ligament, tactical performance, neural control of movement, neuromuscular control, cognitive motor interaction

3. Accomplishments

Project Goals
The project is split into 2 primary goals\aims.

<u>Goal 1: To determine when the maladaptive neuroplastic sensory reweighting occurs following ACL injury.</u>

Local IRB Approval: Achieved – Year 2 Continuing Review Approved
HRPO Approval: Achieved – Year 2 Continuing Review Approved
Equipment preparation: Achieved
New technology integration (virtual reality and sensorimotor monitoring during neuroimaging): achieved
Participant recruitment: Ongoing
Injured cohort Neuroimaging data collection: Ongoing (n=4 completed, ~n=15 enrolled and recruited participants are now lost to follow-up due to COVID (as the study requires specific data collection in time windows were missed, and recruitment is also on hold)
Control cohort Neuroimaging data collection: Ongoing (n=8 completed)

<u>Goal 2: To determine the functional correlates of neuroplastic sensory reweighting for motor performance.</u>

Local IRB Approval: Achieved – Year 2 Continuing Review Approved
HRPO Approval: Achieved – Year 2 Continuing Review Approved
Equipment preparation: Achieved
New technology integration (virtual reality, proprioception, reactive motor control): achieved
Participant recruitment: Ongoing
Injured cohort Biomechanical data collection (muscle strength, proprioception, postural control, neuromuscular control and patient outcomes): Ongoing (n=4 completed, ~n=15 enrolled and recruited participants are now lost to follow-up due to COVID)
Control cohort Biomechanics data collection (muscle strength, proprioception, postural control, neuromuscular control and patient outcomes): Ongoing (n=8 completed)
ROTC cohort tactical neuromuscular control performance data collection: Completed (n=33)

4. Impact

Work has completed development stage, as well as completed the ROTC arm of the study and is in currently in data collection for the ACL injured cohort. Nothing to report at this time.

5. Changes/Problems

No changes to the deliverables, general scope of work, expenditures or human subject experience was made during this reporting period. Work is ongoing to modify the protocol via a required local IRB amendment on new procedures secondary to the COVID pandemic. This amendment once approved by the local IRB will be submitted to the HPRO office. The local University IRB has shutdown all research and is requiring full-board review of all protocols and their COVID containment plans before allowing any research activity to resume. We are working with the local IRB to determine what precautions and procedures will be required to engage in data collection again and are planning submission to the next IRB full board meeting in November for review of the new protocol with COVID precautions.

We did have to change personnel due to the project manager leaving the University in August. Mr. Haggerty was offered a position with the Navy at much higher salary and benefits then we could compete with and he resigned his position with the University on the project effective August 21st. We have reposted the position, completed interviews and offered the position to an exceptional candidate that we anticipate starting by November 1st 2020. The position rehire will coincide with the timing of hopeful resumption of data collection and limit impact to the project.

Due to COVID resulting in no allowed laboratory research activity with human subjects since March 2020, we have reduced charges to the grant and reduced personnel effort to allow for increased effort and charges to resume once research is restarted. We foresee this potentially requiring a no-cost extension to ensure the human participant enrollment targets are met.

Before COVID we did complete data collection on the tactical performance assessments with our ROTC cohort arm of the study and have prepared manuscripts for journal submission.

As the patient arm of the study is longitudinal, we had 7 participants on the protocol and engaged in the study that were lost to follow-up due to COVID shutdown and will now require new data collections to replace and we lost another 8 recruited participants that postponed their surgery or otherwise could not participate also due to the COVID shutdown. Our University IRB has finally begun adopting and approving new safety procedures to allow a gradual restart to research. Overall, we have lost 15 ongoing or recruited participants, which is 40% of the projected patient cohort sample size that will require new participants to replace.

It is difficult to determine how this will affect the study timeline and objectives at this time as so many unknowns still exist regarding when the volume of orthopedic surgery will reach normal levels again and how open participants and patients will be to participating once research is allowed to start again. Once allowed to begin again, we are planning to maximize recruitment, however at this point a no-cost extension might be needed to allow for data collection to make up for all the loss in the critical summer window of high surgery volume in our area. Though we are hopeful that once the COVID issues pass we can catch up rapidly. The longitudinal nature of this study while a great experimental and clinically impactful strength has resulted in this COVID-19 situation being particularly troublesome due to the forced loss of follow-up.

6. Products

Work has completed development stage and is in currently in data collection on the primary longitudinal patient arm of the study.

Data from the initial development arm of the work is in review at Frontiers in Neuroscience, and the ROTC arm of the study is in review at Medicine Science in Sport and Exercise. 5 Abstracts have been presented or accepted at national scientific meetings related to the work

1. McCarren GA, Grooms DR, Yom J, Simon JE. Dual Cognitive-Tactical Performance on Knee Kinematics and Kinetics. *National Athletic Training Association 65th Annual Meeting;* Atlanta, GA. June 2020
2. Brazalovich PJ, Simon JE, Yom J, Grooms DR. The Effects of Virtual Reality Immersion on Drop Landing Biomechanics. *National Athletic Training Association 65th Annual Meeting;* Atlanta, GA. June 2020
3. Buckley ST, Simon JE, Yom J, Grooms DR. Effects of a Cognitive Load on Marksmanship Performance in ROTC Members. *National Athletic Training Association 65th Annual Meeting;* Atlanta, GA. June 2020
4. Wohl TR, Criss CR, Haggerty A, Simon JE, Grooms DR. Visual Perturbation-Augmented Neuromuscular Training Enhances Knee Motor Neural Efficiency and Real-Time Landing Mechanics. Combined Sections Meeting of the American Physical Therapy Association; Virtual. Feb 2021 National
5. Haggerty A, Simon JE, Grooms DR, Russell J. Effects of Limb Weighting on Knee Joint Position Sense Measured with a Smartphone Inclinometer. Great Lakes Athletic Trainers' Association 52nd Annual Meeting and Symposium. Wheeling, IL. March 2020

7. Participants & Other Collaborating Organizations

Name: Dustin Grooms
Role: PI
Research identifier:
Person month worked: 3
Contribution: Coordinate overall project, IRB\HRPO approval, hire and train research assistants\project manager, secure technologies, patient and participant recruitment and data collection\analysis
Funding support: This award and university research release time (in-kind)

Name: Adam Haggerty
Role: Project manager\research associate
Research identifier: *NA*
Person month worked: 8
Contribution: Undergo training in all data collection methods and CITI training for human subject interaction. Facilitate participant recruitment, data collection\analysis and manage research equipment.
Funding support: This award

Name: Janet Simon
Role: Co-I
Research identifier: *NA*
Person month worked: 1
Contribution: Data analysis and experimental design, patient outcomes management
Funding support: This award and university research release time (in-kind)

Name: Meredith Chaput
Role: Research assistant\PhD student
Person month worked: 6
Contribution: Data analysis, reporting and manuscript preparation on the phase 1 initial study data.
Funding support: This award and university

Name: Sergio Ulloa
Role: Physician
Person month worked: 0.5
Contribution: Patient recruitment
Funding support: This award and university and clinical practice

Changes: Adam Haggerty project manager resigned for a better position with the US Navy August 21st, his replacement has been offered the position and plans to start November 1st. Hopefully coinciding with a research restart approval from the local IRB. Reduced effort of investigator faculty to reduce grant cost during COVID related research limitations with hope to increase effort on data collection when human subject research operational again.

8. Special Reporting Requirements

Updated quad chart included

9. Appendices

No appendices