

**AWARD NUMBER:** W81XWH-21-1-0173

**TITLE:** Quantitative Ambulatory Assessment and Prognosis of the Impact of Severe Upper Limb Injuries on Real-World Behavior

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**CONTRACTING ORGANIZATION:** Curators of the University of Missouri, Columbia, MO

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<b>14. ABSTRACT</b> Military personnel are at particularly high risk for severe upper limb injuries (SULIs)—often involving damage to the peripheral nerves—that adversely impact quality of life, limit occupational and recreational participation, and present major economic and readiness burdens on the military system. We predict that individuals with SULIs are at increased risk of developing chronic one-handedness through the mechanism of learned disuse of the injured limb. We deploy a novel, high spatio-temporal resolution, wireless accelerometry technique to evaluate this central hypothesis over multiple days of real-real-world activity.					
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## 1. INTRODUCTION:

Military personnel are at particularly high risk for severe upper limb injuries (SULIs)—often involving damage to the peripheral nerves—that adversely impact quality of life, limit occupational and recreational participation, and present major economic and readiness burdens on the military system. The majority of these patients develop chronic neuropathic pain. Though rarely fatal, these injuries are associated with a 23% increased risk of attrition from duty. During acute recovery, SULI patients are forced to adopt unnatural, one-handed patterns of limb use due to the injury itself as well as bracing, bandaging and acute pain associated with post-surgical healing. If this ‘one-handedness’ becomes chronic, however, SULI patients are at greatly increased risk of developing long-term pain and disability. Successful functional recovery depends on unlearning this one-handed pattern and resuming more normal bimanual movements. The overarching hypothesis of this project is that *individuals with SULIs are at increased risk of developing chronic one-handedness through the mechanism of learned disuse of the injured limb*. We deploy a novel, high spatio-temporal resolution, wireless accelerometry technique to evaluate this central hypothesis over multiple days of real-world activity.

**2. KEYWORDS:** severe upper limb injury, rehabilitation, upper extremity, ecological momentary assessment, longitudinal cohort, accelerometry.

## 3. ACCOMPLISHMENTS:

### What were the major goals of the project?

#### Major Task 1: Prepare Regulatory Documents, Maintain Compliance, and Other Administrative Tasks

- Subtask 1: Submission of human subjects research materials to local IRB and DoD HRPO. Continual maintenance of human research materials, including: compliance with annual reviews & submission of amendments, adverse events, and protocol deviations as needed; management of all study research records, ensure regulatory compliance, and maintain regulatory mind.
  - University of Missouri received local IRB approval (#2036363) with expedited status on 03/23/2021.
  - Washington University (WUSM) was added to the University of Missouri Single IRB as a site via Amendment #325020 on 07/01/2021.
  - Ohio State University (OSU) was added to the University of Missouri Single IRB as a site via Amendment #325515 on 07/20/2021.
  - Johns Hopkins University (JHU) was added to the University of Missouri Single IRB as a site via Amendment #311476 on 09/20/2021.
  - University of Missouri submitted regulatory package to DoD HRPO on 09/21/2021.
  - Received University of Missouri approval (E02020.1a) from HRPO on 10/29/21.
  - Received WUSM (E02020.1b), JHU (E02020.1c), and OSU (E02020.1d) approvals from HRPO on 11/17/21.

- Our Statement of Work goal was to obtain initial approval by Month 5 of the award. We obtained HRPO approval for University of Missouri in Month 6 of the award, and full approval for the rest of the study sites in Month 9 of the award.
  - As of the end of Year 2, all regulatory approvals are current and up to date.
- Subtask 2: MU team conducts training visits to subaward sites to train teams on administration of behavioral tasks.
    - The WU team was trained in person by Research Coordinator Nick Henigman on February 24, 2023. Mr. Henigman met with two WU site coordinators and trained all on-site staff in all relevant tests (e.g. ARAT, Monofilament, Two-point Discrimination).
    - Research Coordinator Nick Henigman trained the OSU team virtually over zoom on February 28, 2023. Mr. Henigman trained the OSU team on all relevant tests (e.g. ARAT, Monofilament, Two-point Discrimination).
    - The JHU team has not yet been trained but will be in the next quarter (Year 3, Quarter 1). This reflects that WU and OSU are closer to data collection than JHU.
- Subtask 3: Organize and participate in biweekly teleconferences between sites to ensure timely progress on all SOW goals and discuss scientific aims.
    - Bi-weekly teleconferences between sites was halted during summer of 2022 as Ms. Buchanan (previous Research Coordinator at MU) took a different job. During this time, Dr. Davis-Stober transitioned from Co-I to Co-PI on the project. The bi-weekly teleconferences soon resumed at the beginning of Year 2 Quarter 3 (September) and have been ongoing since. The hiring of new lead coordinator Nick Henigman to replace Ms. Buchanan occurred in Year 2, Quarter 3. Mr. Henigman was trained and brought up to speed on the project during Year 2 Quarters 3-4.
- Subtask 4: Provide assistance, support, and corrective feedback to subaward sites as needed through email, phone and in-person.
    - University of Missouri maintains close email contact with all sites to aid, support, and provide corrective feedback as needed. Phone and in-person assistance is available when necessary.

#### Major Task 2: Data collection

- Subtask 1 (subaward sites): recruit and enroll cohort of participants (N=20 per site) and conduct initial in-clinic behavioral testing. 5 participants per site in Year 1, Quarter 3, Months 5-6; 7 participants per subaward site in Year 1, Quarter 3, Months 7-9; and 8 participants per subaward site in Year 1, Quarter 4, Months 10-12. MU's task: enroll all participants (entire cohort; N=20) in remote actigraphy testing and ecological momentary assessment.
  - At the conclusion of Year 2, Quarter 4, WU and OSU are actively recruiting. Data collection has been slowed by staff turnover at all three sub-award sites and general disruption due to COVID-19 pandemic.
  - No participants have yet been successfully enrolled in the study.

#### Major Task 3: Data analysis and Prognostic Model Development

- Subtask 1: Establish factors related to use and disuse of the injured side through various analysis techniques. Refine existing analysis techniques for actigraphy data analysis and visualization/data representation techniques.
  - Not yet applicable.
- Subtask 2: Develop and apply advanced statistical methods (e.g., p=median clustering) to detect subgroups of individuals who have meaningfully different patterns of real-world upper limb use.
  - Not yet applicable
- Subtask 3: Utilize machine learning techniques to develop a prognostic model that will guide evidence-based decisions on severe upper limb injury care.
  - Not yet applicable.

#### Major Task 4: Manuscript Preparation and Dissemination of Results

- Subtask 1: Manuscript preparation and submission to journals based on cross-sectional and longitudinal analyses.
  - Not yet applicable.
- Subtask 2: Presentation of data at academic conferences.
  - Not yet applicable.
- Subtask 3: Attend DoD-sponsored scientific meeting.
  - Not yet applicable.
- Subtask 4: Attend DoD-sponsored In-Progress Review meeting.
  - Dr. Frey attended the March 23, 2022 In-Progress meeting.

#### **What was accomplished under these goals?**

Please see above for progress on 1) Major Activities and 2) Specific Objectives organized by Statement-of-Work tasks. Overall, effort on the second year of the project was directed towards hiring (especially the replacement of Ms. Buchanan as lead coordinator), training new staff (both at MU and sub-sites), and identifying, and resolving, additional recruitment hurdles. All sites worked to develop professional working relationships and engaged in frequent communication regarding the project and its progress. MU continues to provide support and monitor timely progress at all sites.

3) Significant results or key outcomes.  
Not yet applicable.

4) Other achievements.  
Not yet applicable.

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

On December 7<sup>th</sup>, 2022, Mr. Henigman attended the “Clinical Research Study Coordinator Bootcamp” sponsored by the University of Missouri System and received training on many aspects of government sponsored research trials.

**How were the results disseminated to communities of interest?**

Nothing to report.

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

In Year 3 of this award, we will continue tasks related to Major Tasks 2, 3, and 4. Data collection will continue with the recruitment of the study cohort (n = 20 per site). MU will enroll all participants in the remote protocol that involves actigraphy monitoring and ecological momentary assessment of daily pain levels. Initial data processing will take place. MU will provide continual support and corrective feedback to the study subaward sites. If necessary, the MU team, in collaboration with the sub-sites, will consider additional recruitment strategies (e.g., sending recruitment letters in addition to cold calls).

**4. IMPACT:**

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

Nothing to report.

**What was the impact on other disciplines?**

Nothing to report.

**What was the impact on technology transfer?**

Nothing to report.

**What was the impact on society beyond science and technology?**

Nothing to report.

**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**

Problems/Delays

As described in Section 2, data collection has been significantly slowed. This has been due to myriad factors. All three subaward sites experienced significant staffing issues in Year 2. This resulted in time lost due to training/onboarding, etc. At MU, Ms. Buchanan left her position as lead coordinator to take a different job. This resulted in delays, as the MU team hired and trained her replacement (Mr. Nick Henigman, hired in October, 2022). The staffing issues have now been largely resolved. Recruitment remains a challenge. WU reports that potential participants are unresponsive to cold calls. OSU reports that their list of potential participants is relatively narrow based on the project exclusion criterion of smoking.

Plans

The staffing and training issues at the sites have now been largely resolved. We will be examining different approaches for improving recruitment. This may include pre-cold call informative flyers, emails, etc. On a positive note, 2 of the 3 sub-sites (WU and OSU) are fully trained in the behavioral measures and all regulatory hurdles are taken care of. Recruitment is expected to continue during the next quarter.

**Changes that had a significant impact on expenditures**

See above. Since no participants have yet been enrolled, our expenditures have been less than expected.

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

**Significant changes in use or care of human subjects**

Nothing to report. See p. 4 for all IRB / HRPO approval dates.

**Significant changes in use or care of vertebrate animals**

Not applicable, no use or care of vertebrate animals in this project.

**Significant changes in use of biohazards and/or select agents**

Not applicable, no use of biohazards or select agents in this project.

**6. PRODUCTS:**

- **Publications, conference papers, and presentations**

Nothing to report.

**Journal publications.**

Nothing to report.

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

Nothing to report.

**Other publications, conference papers and presentations.**

Nothing to report.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

The project team created a survey designed to measure pain at multiple timepoints throughout the day. The survey captures emotional and functional aspects of pain as well as the present pain rating. This survey will be deployed using the ecological momentary assessment data capture system utilized in this project.

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

### What individuals have worked on the project?

University of Missouri School of Medicine (MU)

Name: Scott Frey, PhD, EdM  
Project Role: Co-Principal Investigator  
Nearest person month worked: 2

Contribution to Project: Dr. Frey is the lead investigator for this project. He oversees all project activities. He developed the scientific approach for the study and monitors progress. He is available to provide corrective feedback to subaward sites as needed.

Name: Clinton Stober, PhD

Project Role: Co-Principal Investigator

Nearest person month worked: 1

Contribution to Project: Dr. Stober lends his statistical expertise to the project. He develops novel statistical methods to develop a prognostic model that will guide evidence-based decisions in severe upper limb injury care.

Name: Kelli Buchanan, MPH

Project Role: Lead Coordinator

Nearest person month worked: 2

Contribution to Project: Ms. Buchanan is the lead coordinator for this project. She manages regulatory approvals for this project (MU is the Single IRB of Record for this project, DoD HRPO oversees the MU IRB of Record), is the primary contact for subaward sites, leads bi-weekly coordinator meetings, assists with technical report writing, and completes other misc. tasks as needed to support the timely completion of project goals.

Name: Nicholas Henigman

Project Role: Research Coordinator

Nearest person month worked: 4

Contribution to project: Mr. Henigman has replaced Ms. Buchanan as the lead program coordinator. He took over all responsibilities that Ms. Buchanan had.

Name: Binal Motawar, PhD

Project Role: Post-doctoral fellow

Nearest person month worked: 3

Contribution to Project: Dr. Motawar worked to develop an automated pipeline to export and clean data from our data capture systems.

## Washington University School of Medicine (WUSM)

Name: David Brogan, MD

Project Role: Principal Investigator, Washington University.

Researcher Identifier (e.g. ORCID ID): 0000-0001-6259-4885

Nearest person month worked: 1

Contribution to Project: Dr. Brogan oversees all project activities at WUSM. In particular, Dr. Brogan provides expertise in selecting medical codes that will identify potential participants.

Name: Carrie Burk

Project Role: Research Coordinator

Researcher Identifier (e.g. ORCID ID): 0000-0002-8233-5001

Nearest person month worked: 2

Contribution to Project: Carrie is the coordinator for WUSM. Her duties include, but are not limited to, attending bi-weekly coordinator meetings with the lead site, managing local regulatory acknowledgements, coordinating the space and materials needed to conduct the space at WUSM, and leading recruitment efforts.

Name: Yosita Beamer

Project Role: Research Assistant

Nearest person month worked: 1

Contribution to Project: Yosita has contributed to the project by attending coordinator meetings and screening/recruiting for the study.

## Ohio State University School of Medicine (OSU)

Name: Amy M. Moore, MD, FACS

Role on project: Principal Investigator – The Ohio State University

Nearest person month worked: < 1 person month

Contribution to project: Dr. Moore is the principal investigator at The Ohio State University site. She oversees all activities of the study and research staff.

Name: Irene Kapsan, MACPR

Role on the project: Clinical Research Coordinator – The Ohio State University

Nearest month worked: 2 person months

Contribution to project: Ms. Kapsan is part of the research study staff at The Ohio State University site. She is the primary contact for this site, completing site-specific documents (such as reliance agreements, ICF, etc). Over the past year, she worked on study start-up activities, such as outcome measure testing and CRF completion.

Name: Emily Rice, RDN, LD

Role on the project: Clinical Research Coordinator – The Ohio State University

Nearest month worked: < 1 person month

Contribution to project: Ms. Rice was hired in 2022 by The Ohio State University as a research coordinator. She is currently helping Ms. Kapsan with regulatory processes and will be administering tests to participants when recruitment begins.

Name: Tiam Mana Saffari, MD PhD MSc

Role on the project: Outcomes Evaluator – The Ohio State University

Nearest month worked: < 1 person month

Contribution to project: Dr. Saffari is part of the research study staff at The Ohio State University site. She will be conducting the outcome measures indicated in the protocol.

## Johns Hopkins University School of Medicine (JHU)

Name: Gerald Brandacher, MD

Role on project: Site PI

Nearest person month worked: < 1 month

Contribution to project: Dr. Brandacher is overseeing the study team and ensuring that all necessary regulatory approvals are secured.

Name: Jaimie Shores, MD

Role on project: Co-I

Nearest person month worked: <1 month

Contribution to project: Dr. Shores is available to advise the team on local standard care processes and practicality of protocol implementation locally.

Name: Carisa M. Cooney, MPH

Role on project: Co-I

Nearest person month worked: < 1 month

Contribution to project: Ms. Cooney, who is the site expert in regulatory processes (e.g., IRB, HRPO), is working with Ms. Kelli Buchanan and Nicholas Henigman at MU to secure regulatory approvals at MU and Hopkins in order to start the study at Johns Hopkins. She liaises between Ms. Buchanan and the Hopkins Team to accomplish study tasks and milestones.

Name: Jonathan Vullier

Role on the project: Clinical Research Coordinator – Johns Hopkins University School of Medicine

Nearest person month worked: < 1 month

Contribution to project: Mr. Vullier was hired by JHU in 2022 and is currently helping Ms. Cooney on regulatory processes. He will be administering tests to participants when recruitment begins.

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

University of Missouri School of Medicine– Nothing to report.

Washington University School of Medicine– Nothing to report.

Ohio State University School of Medicine– Dr. Moore devotes 15% on a DoD project (Promoting Healing of Nerves through Electrical Stimulation; W81XWH1920065) effective June 2021. This project does not impact Dr. Moore’s effort on this project.

Johns Hopkins University School of Medicine- Nothing to report.

**What other organizations were involved as partners?**

Organization Name: Washington University School of Medicine

Partner’s contribution to the project:

- Facilities (e.g., project staff use the partner’s facilities for project activities);
- Collaboration (e.g., partner’s staff work with project staff on the project);

Organization Name: Ohio State University School of Medicine

Partner’s contribution to the project:

- Facilities (e.g., project staff use the partner’s facilities for project activities);
- Collaboration (e.g., partner’s staff work with project staff on the project);

Organization Name: Johns Hopkins University School of Medicine

Partner’s contribution to the project:

- Facilities (e.g., project staff use the partner’s facilities for project activities);
- Collaboration (e.g., partner’s staff work with project staff on the project);

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:**

**QUAD CHARTS:**

**9. APPENDICES:**