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

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14. ABSTRACT
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.

15. SUBJECT TERMS None listed.

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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-real-world activity.

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

1. 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.

- Subtask 2: MU team conducts training visits to subaward sites to train teams on administration of behavioral tasks.
  - At the end of Year 1, training visits had not yet been conducted. This is significantly delayed from the original SOW goal to complete this task in Months 3 and 4 of Year 1. Regulatory approvals took significantly longer than anticipated, and the team decided to wait to schedule training visits until closer to the time of data collection.

- Subtask 3: Organize and participate in biweekly teleconferences between sites to ensure timely progress on all SOW goals and discuss scientific aims.
  - As discussed in our Year 1, Quarter 2 report - in lieu of biweekly teleconferences, in Quarters 1 & 2 MU communicated with the subaward teams primarily via email on a more frequent basis than biweekly. The single IRB regulatory process required close communication and coordination.
  - We started biweekly teleconferences in Quarter 3 (during our startup process, frequent email communication was efficient than meeting via teleconference). During Quarters 3 & 4, biweekly teleconferences took place as scheduled. University of Missouri follows up with team members who cannot attend or who are absent from the biweekly teleconference.

- 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.
  - Data collection did not commence in Year 1.

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.
  - Data collection did not start in Year 1. During Year 1, MU Team refined an integrated data cleaning and analysis pipeline that utilizes an automated code to process and store de-identified data in preparation for advanced analysis. This will expedite our data analysis process.

- 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 will attend the March 23, 2022 In-Progress meeting (outside of the period of reporting).

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 first year of the project was primarily directed towards obtaining full regulatory approvals. All sites worked to develop professional working relationships and engaged in frequent communication regarding the project and its progress. The research and regulatory binders (including source documents) were developed and organized on a system (Sharepoint) that is secure and accessible to all team members across sites. An automated pipeline to export and clean data was created. Recruitment efforts at WUSM and OSU started in Quarter 4 of Year 1. 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?

Nothing to report.

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 2 of this award, we will continue tasks related to Major Tasks 2, 3, and 4. Data collection will commence with the recruitment of the study cohort (n = 20 per site). The first in-clinic behavioral testing session for all participants will take place. 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.

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

As described in Section 2, regulatory approvals took longer than anticipated. Our original Statement-of-Work goal was to complete the approval process 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. This has pushed data collection back to Year 2 of the award.

Changes that had a significant impact on expenditures

See above. Data collection has not yet commenced; thus, 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**

  any other invention reporting required under the terms and conditions of an award.

  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: 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: Clintin Stober, PhD
Project Role: Co- 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: 4
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: 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.

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 Kaptsan, MACPR
Role on the project: Clinical Research Coordinator – The Ohio State University
Nearest month worked: 2 person months
Contribution to project: Ms. Kaptsan 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: 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 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.

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: