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TITLE: Neuromodulatory Treatments for Pain Management in Complex TBI using Mobile Technology

PRINCIPAL INVESTIGATOR: Eric Elbogen, PhD

CONTRACTING ORGANIZATION: Duke University, Durham, NC

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E-Mail:

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The purpose of this study is to conduct a randomized controlled trial to test the efficacy of using mobile technology to deliver neuromodulatory interventions for reducing pain among Veterans with complex TBI.

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	10	**19b. TELEPHONE NUMBER** *(include area code)*

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1. INTRODUCTION:

The purpose of this study is to conduct a randomized controlled trial to test the efficacy of using mobile technology to deliver neuromodulatory interventions for reducing pain among Veterans with complex TBI.

Aim 1: Examine the effectiveness of mobile interventions for reducing pain symptoms in Veterans with complex TBI. Hypothesis 1: Given preliminary data and empirical support for neurofeedback and mindfulness, we hypothesize that Veterans in the two intervention groups will report less pain at 3 months compared to Veterans in the control group.

Aim 2: Investigate the impact of neurofeedback and mindfulness on brainwave activity in Veterans with complex TBI and chronic pain. Hypothesis 2: Given research on electroencephalogram (EEG) and pain, we hypothesize that Veterans in the two intervention groups will show increased (8–12 Hz) alpha power at 3 months compared to Veterans in the control group.

Given connections to adverse outcomes, we will explore whether neuromodulatory interventions impact: (i) risk behaviors, with a hypothesis of lower levels of suicidality, aggressiveness/ violence toward others, and use of alcohol and drugs for the neurofeedback and mindfulness groups compared to the control group; and (ii) heart rate variability (HRV), with a hypothesis of significantly greater improvements in HRV compared Veterans to the control group.

2. KEYWORDS:

- Neurofeedback
- Neuromodulatory Treatments
- Traumatic Brain Injury
- Chronic Pain
- Mobile applications
- Alpha amplitude
- Alpha frequency
- Heart Rate Variability

3. ACCOMPLISHMENTS:

- **What were the major goals of the project?**
    - Prepare for Clinical Trial (months 0-6): 100% complete
    - Baseline Interview/Data Collection (months 6-30): Ongoing
    - Implementation of Mobile Neurofeedback Intervention (months 4-30): Ongoing
    - Follow-up Interview/Data Collection (months 10-36): Ongoing
    - Data Analysis and Dissemination (months 12-36): N/A for this reporting period

- **What was accomplished under these goals?**
  - Prepare for Clinical Trial (months 0-6)
    - Not applicable.
  - Baseline Interview/Data Collection (months 6-30)
    - Recruitment efforts during this reporting period include social media boosted posts and advertisements, posting flyers and tri-fold handouts at various VA clinics and medical facilities, and contacting local college and university military associations.
    - The informed consent, initial screening, and interview processes are ongoing. As of 10/13/2020, 175 participants had completed the informed consent and initial screening/interview process with an additional 7 potential participants scheduled for baseline interviews.
  - Implementation of Mobile Neurofeedback Intervention (months 4-30)
    - Continued implementation of the 12-week intervention is ongoing. Participants were randomized into one of the three intervention groups and given an iPod Touch and instructions to practice the intervention for 12 weeks at home.
    - Individualized support calls and visits were continued during this reporting period and are ongoing. Per the study protocol, research staff visit the participant at their home (or similar location) to reinforce training related to their app, troubleshoot any difficulties, and observe participants utilizing the intervention. They also conduct support calls, per the protocol, to collect data on intervention utilization and tolerability and troubleshoot any technical difficulties.
  - Follow-up Interview/Data Collection (months 10-36)
    - Follow-up interviews and data collection are ongoing. As of 10/13/20, 133 participants had completed the 3 month follow-up interview, and 115 participants had completed the 6 month follow-up interview.
  - Data Analysis and Dissemination (months 12-36)
    - Nothing to report.

- **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?**
  - During the next reporting period, the study team will continue and expand upon recruitment efforts to continue to enroll participants in this study. Baseline interviews/data collection and implementation of the mobile neurofeedback intervention will be ongoing. Follow-up interviews/data collection will be ongoing.
  - Data analysis and dissemination will begin once data collection is completed.

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**
- Due to COVID-19 pandemic and stay-at-home orders, we began conducting study visits remotely March 2020. As such, the Duke IRB has approved the following changes to our protocol:
    - All study visits, including screening, may occur remotely via telephone, Zoom, and/or Webex, as appropriate.
    - Participants complete the informed consent process via eConsent. Study coordinators still offer ample time for reviewing the informed consent document, verbally explain the elements of informed consent, and participants are required to respond to questions to check for understanding before signing the document.
    - For remote 3-month follow-up visits, in lieu of travel reimbursement, we are reimbursing all participants $35 for returning their study equipment, to compensate for the time and travel required to ship materials back to us. Participants will still receive $100 reimbursement for completing the study visit.
    - Procedures done in person, including EEG & HRV readings, cognitive testing, and pregnancy testing are not done during remote visits during the COVID-19 pandemic. Women requiring pregnancy testing are deferred until visits can be completed in person.
- **Actual or anticipated problems or delays and actions or plans to resolve them**
    - Nothing to Report
- **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:**
    - **Significant changes in use or care of human subjects.** Nothing to Report.
    - **Significant changes in use or care of vertebrate animals.** Nothing to Report.
    - **Significant changes in use of biohazards and/or select agents.** Nothing to Report.

6. PRODUCTS:

- **Publications, conference papers, and presentations**
    - **Journal publications.** Elbogen, E.B., Alsobrooks, A.A., Battles, S., Molloy, K., Dennis, P., Beckham, J., McLean, S., Keith, J., & Russoniello, C. (2019). Mobile Neurofeedback for Pain Management in Veterans with TBI and PTSD. *Pain Medicine*.
    - **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)**
  https://psychiatry.duke.edu/BehavioralTechLab
  The lab website is used for recruitment purposes and will be used for disseminating results once the study is complete and results have been submitted for publication.

- **Technologies or techniques**
  - As part of this study, our IT manager has created three original mobile applications (relaxing nature sounds, mindfulness exercises, and neurofeedback). All mobile applications are used for study data collection with pre- and post-session ratings for pain, anger, and stress.
- **Inventions, patent applications, and/or licenses**
  - Nothing to Report.
- **Other Products**
  - Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

- **What individuals have worked on the project?**

Name:	*Eric Elbogen, Ph.D.*
Project Role:	*Principal Investigator*
Researcher Identifier (e.g. ORCID ID):	*0000-0002-8341-8028*
Nearest person month worked:	*4*
Contribution to Project:	*Dr. Elbogen has led the strategic planning and implementation of the study design, monitored the study's progress in collaboration with co-investigators, supervised the research staff, and directed instrument adaptation and development.*

Name:	*Jean Beckham, Ph.D.*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	*.5*
Contribution to Project:	*Dr. Beckham has worked to assist with recruitment of Veterans and provide consultation on IRB issues and study conceptualization.*

Name:	*Patrick Calhoun, Ph.D.*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	*.12*
Contribution to Project:	*Dr. Calhoun has worked to assist with recruitment of Veterans and provide consultation on IRB issues and study conceptualization.*

Name:	*Aatif Husain, M.D.*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	*2*
Contribution to Project:	*Dr. Husain has worked on EEG monitoring, EEG evaluation, and interpreting EEG patterns from the data collected at baseline and follow-up sessions. Currently, EEG is not being done due to the COVID-19 pandemic and stay-at-home orders.*

Name:	*Tung Tran, MS, M.D.*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	*2*
Contribution to Project:	*Dr. Tran has worked on EEG monitoring, EEG evaluation, and interpreting EEG patterns. Currently, EEG is not being done to the COVID-19 pandemic and stay-at-home orders.*

Name:	*Lana Watkins, Ph.D.*
Project Role:	*Co-Investigator*
Researcher Identifier (e.g. ORCID ID):	*0000-0003-1889-5730*

Nearest person month worked:	*2*
Contribution to Project:	*Dr. Watkins has worked with Dr. Elbogen and the research coordinators to implement, monitor, report, and interpret the heart rate variability (HRV) portion of the study. Currently, HRV is not being done due to the COVID-19 pandemic and stay-at-home orders.*

Name:	*Amber Alsobrooks, MS, MA, LPA.*
Project Role:	*Clinical Research Coordinator*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	*6*
Contribution to Project:	*Ms. Alsobrooks has conducted research interviews, interventions, data collection, documentation, and recruitment of study participants.*

Name:	*Sara Battles, MA*
Project Role:	*Clinical Research Coordinator*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	*6*
Contribution to Project:	*Ms. Battles has conducted research interviews, interventions, data collection, documentation, and recruitment of study participants.*

Name:	*Megan Lanier*
Project Role:	*Clinical Research Specialist*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	6
Contribution to Project:	*Ms. Lanier has conducted research interviews, interventions, data collection, documentation, and recruitment of study participants.*

Name:	*Alexandra Thompson*

Project Role:	*Clinical Research Specialist, Sr*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	6
Contribution to Project:	*Ms. Thompson has conducted research interviews, interventions, data collection, documentation, and recruitment of study participants.*

Name:	*Jeffrey Hertzberg*
Project Role:	*IT Manager*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	2
Contribution to Project:	*Mr. Hertzberg programmed the mobile applications and neurofeedback equipment, and ensured the data are secure and encrypted for all mobile applications.*

- **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?**
    - Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

- **COLLABORATIVE AWARDS:** N/A

- **QUAD CHARTS:** attached

APPENDICES: N/A