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AWARD NUMBER: W81XWH-16-1-0395

TITLE: Reactivating Neural Circuits with Clinically Accessible Stimulation to Restore Hand Function in Persons with Tetraplegia

PRINCIPAL INVESTIGATOR: Dr. Edelle Field-Fote

CONTRACTING ORGANZATION: Shepherd Center, Inc.
Atlanta, GA 30309

REPORT DATE: September 2018

TYPE OF REPORT: Annual

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

REPORT DOCUMENTATION PAGE

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Reactivating Neural Circuits with Clinically Accessible Stimulation to Restore Hand Function in Persons with Tetraplegia

5a. CONTRACT NUMBER

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W81XWH-16-1-0395

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)

Allison McIntyre, study coordinator
Dr. Edelle Field- Fote, Principal Investigator

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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

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

Shepherd Center, INC.
2020 Peachtree Rd NW
Atlanta GA 30309-1426

8. PERFORMING ORGANIZATION REPORT NUMBER

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

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

10. SPONSOR/MONITOR'S ACRONYM(S)

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12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This study is designed to examine arm and hand function after receiving fine motor training combined with stimulation to increase brain excitability in individuals with cervical spinal cord injuries. The project will study two types of stimulation- transcranial direct current stimulation, a type of non-invasive brain stimulation, and peripheral nerve somatosensory stimulation, which is stimulation to the median nerve. A total of 83 participants are expected to enroll in the study, 58 participants with acute spinal cord injuries (>6 months post injury) and 15 participants with chronic injuries (>1 year post injury). We estimate enrolling 10 additional participants due to attrition. The project will be performed in a real-world clinical setting, so that the results can be immediately relevant for application to clinical practice. We believe that increasing the ability of the brain to push information through the remaining spinal pathways will result in more effective therapy and larger improvements in hand function.
In this past reporting period, 46 additional participants have been enrolled into the study, bringing the total number of enrolled participants to 61. Additionally, new staff was trained to take on study roles, including a new post-doctoral fellow, a new occupational therapy & physical therapy fellow, coverage staff for primary assessor and a new biomedical engineer. Continued recruitment and enrollment is expected to run through 2019.

15. SUBJECT TERMS
Spinal cord injury; tetraplegia; rehabilitation; tDCS; somatosensory stimulation; spinal cord injury; cervical spinal cord; non-invasive brain stimulation

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
					USAMRMC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**		13	**19b. TELEPHONE NUMBER** *(include area code)*
Unclassified	Unclassified	Unclassified	Unclassified		

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1. INTRODUCTION:

This study is designed to examine arm and hand function after receiving fine motor training combined with stimulation to increase brain excitability in individuals with cervical spinal cord injuries. The project will study two types of stimulation- transcranial direct current stimulation, a type of non-invasive brain stimulation, and peripheral nerve somatosensory stimulation, which is stimulation to the median nerve. The study will supplement daily therapy, so that the results can be immediately relevant for application to clinical practice. We believe that increasing the ability of the brain to push information through the remaining spinal pathways will result in more effective therapy and larger improvements in hand function.

2. KEYWORDS:

spinal cord injury; tetraplegia; rehabilitation; tDCS; somatosensory stimulation; spinal cord injury; cervical spinal cord; non-invasive brain stimulation

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Major Task 1: Adapt Study Protocol to Facilitate Larger Trial Supported by DoD Grant

Milestone 1: IRB approval obtained
target date: 11/15/2016; completion date:07/26/2016

Milestone 2: HRPO approval obtained
target date: 03/15/2017; completion date: 09/28/2016

Major Task 2: Coordinate Study Staff for Subacute and Chronic Groups

Milestone 3: Research and clinical staff trained
target date:11/15/2016- 03/15/2017; completion date: 1/25/2017 *(ongoing as new research and clinical staff contribute to the study*)

Milestone 4: Maintain trained and available Independent Evaluators throughout duration of clinical trial
target date: 04/15/2017-02/15/2020; completion date: 1/13/2017 *(ongoing*

as new evaluators contribute to the study)

Major Task 3: Participant Recruitment, Therapy, Participant Evaluation
Milestone 5: 1st participant consented, screened and enrolled
target date:04/15/2017; completion date: 02/09/17

Milestone 6: Data collection initiated
target date:04/15/2017; completion date: 02/16/17

Milestone 7: 50% of subjects recruited and completed intervention
target date:04/15/2018; completion date: 02/08/18

Major Task 4: Data Analysis
Milestone 8: Data analyzed
target date:3/15/2020; percent completion: 0%

Major Task 5: Randomized Controlled Trial
Milestone 9: Report findings from overall studies
target date:6/15/2020- 08/15/2020; percent completion: 0%

What was accomplished under these goals?

Major Task 2: Coordinate Study Staff for Subacute and Chronic Groups
Milestone 3: Research and clinical staff trained
Initially completed in Year 1 Quarter 1, this continues to be an ongoing major task as new staff comes onto the project. Ryan Koter, DPT, and Tori Galatas, OTR/L, have completing competencies to provide stimulation during intervention sessions. Dr. Anastasia Zarkou has assumed the role of primary post-doctoral fellow on the study with Dr. Jennifer Iddings continuing to provide support. Cazmon Suri has replaced Somu Ray as biomedical engineer for the SCI research lab and this study.

(6) Milestone 4: Maintain trained and available Independent Evaluators throughout duration of clinical trial
Also initially completed in Year 1 Quarter 1, training has continued for new staff. In the past year, Dr. Anastasia Zarkou has completed training to be primary evaluator for electrophysiological evaluations. Laura Glazebrook, PT was trained as a backup clinical assessor during Ms. Callahan's maternity leave and will continue to provide ongoing support.

Major Task 3: Participant Recruitment, Therapy, Participant Evaluation

Milestone 7: 50% of subjects recruited and completed intervention
This milestone was met on February 14, 2018. On August 15, 2018, fifty participants had completed intervention with 6 additional participants actively enrolled. Five participants had dropped from the study contributing to attrition. Due to being ahead of recruitment, the total number of subjects to be enrolled has been expanded from 70 to 83, including attrition.

Major Task 4: Data Analysis

Milestone 8: Data analyzed
There will not be an interim analysis, so this milestone will remain at 0% until all participants have completed the study. Data is being collected & stored electronically in a manner that is ready for final analysis.

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

One-on-one and group mentoring has been ongoing by senior researchers to educate research staff on electrophysiological assessment measures, clinical assessment measures, and interpretation of results for data recording. In addition, weekly classes and directed readings have been held under the direction of the principal investigator to further enhance the knowledge and skills of the research lab team as related to physiology of the spinal cord, pathophysiology of spinal cord injury, mechanisms of neuroplasticity and principles underlying interventions.

How were the results disseminated to communities of interest?

Nothing to Report, no interim data analyses will be performed for this study.

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

During the next quarter, we plan to continue recruitment, enrollment, and data collection. Data will continue to be stored and managed in anticipation of data analysis at the end of data collection.

4. **IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:**

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

Nothing to report – findings & results will not be analyzed until the completion of data collection.

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: The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:**

Nothing to Report, all changes in the project have been reported to the HRPO in previous reports.

Changes in approach and reasons for change

Nothing to report.

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**
  Report only the major publication(s) resulting from the work under this award.

  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**

Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Dr. Edelle Field-Fote – no change

Name: Dr. Jennifer Iddings – no change

Name: Allison McIntyre (Ainsworth) – no change

Name: Brandon Poe – no change

Name: Sarah Callahan – no change

Name: Barry McKay – no change

Name: Saumitra (Somu) Ray – no longer affiliated with contracting organization

Name: Cazmon Suri; Research Associate/Biomedical Engineer
Nearest person month worked: 1
Contribution to Project: Provides ongoing engineering & technical support to team during data collection. Coordinates necessary repairs of study equipment.

Name: Anastasia Zarkou, PT, PhD; Post-Doctoral Research Fellow
Nearest person month worked: 2
Contribution to Project: Assumed the role of primary assessor for neurophysiological data collection. Applies stimulation (tDCS, PNSS, or sham tDCS) for intervention sessions and works on data reduction and processing of neurophysiological data in preparation for analysis.

Name: Laura Glazebrook, PT, PDT; Clinical Evaluator
Nearest person month worked: <1
Contribution to Project: Performed clinical assessments for enrolled participants (baseline, weekly, post-tests, and follow-up) as a backup assessor.

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: none

QUAD CHART:

Conditioning Neural Circuits to Improve Upper Extremity Function

Supporting Proposal: Reactivating Neural Circuits With Clinically Accessible Stimulation to Restore Hand Function in Persons With Tetraplegia
SC150103
W81XWH-16-1-0395

PI: Edelle Field-Fote, PT, PhD **Org:** SHEPHERD CENTER **Award Amount:** $1,906,189

Study/Product Aim(s)

Aim 1. Compare the effects on hand motor function of a multi-session course of stimulation-augmented functional task practice (FTP)
Aim 2. Compare changes in hand-related sensory function, self-reported function and participation, and quality of life associated with a multi-session course of stimulation-augmented FTP
Aim 3. Compare the effects on cortical and spinal excitability (spasticity) of a 3-week course of stimulation-augmented FTP
Aim 4. Compare differences in rates of conversion from passive hand function to active hand function in persons with subacute SCI among the 3 intervention groups.
Aim 5. (exploratory). In subjects with tetraplegia, compare differences in responsiveness between persons with subacute *(1-6 months post)* versus chronic (≥ 1 year post) SCI

Approach

Using commercially available forms of transcranial direct current stimulation (tDCS) and peripheral nerve somatosensory stimulation (PNSS), assessors will compare the relative value of cortical versus peripheral stimulation as adjuncts to a 4 week course of FTP. Changes will be compared as described in Aims 1, 2, and 3, and as an exploratory aim, outcomes will be compared in subacute vs chronic SCI to gather evidence regarding relative value of these approaches for early intervention (Aim 5).

Accomplishments: 50 participants have completed intervention, 6 additional participants are still completing interventions. 5 participants have dropped from the study.

Timeline and Cost

Activities	CY 16	17	18	19	20
Adapt Study Protocol to Facilitate Larger Trial Supported by DoD Grant					
Coordinate Study Staff for Subacute and Chronic Groups					
Participant Recruitment, Therapy, Participant Evaluation					
Data Analysis					
Randomized Control Trial					
Estimated Budget ($K)	**$183**	**$473**	**$468**	**$480**	**$302**

Updated: 9/10/2018

Goals/Milestones

CY16 Goal –Adapt Study Protocol to Facilitate Larger Trial Supported by DoD Grant
☑ IRB approval obtained
☑ HRPO approval obtained
☑ Research and clinical staff trained

CY17 Goal – Coordinate Study Staff for Subacute and Chronic Groups
☑ Research and clinical staff trained
☑ Maintain trained and available Independent Evaluators for duration of clinical trial

CY17 – CY 19 Goal – Participant Recruitment, Therapy, Participant Evaluation
☑ 1st participant consented, screened and enrolled
☑ Data collection initiated
☑ 50% of subjects recruited and completed intervention

CY20 Goal – Data Analysis
☐ Data analyzed

CY20 Goal – Randomized Controlled Trial
☐ Report findings from overall studies

Budget Expenditure to Date

Projected Expenditure (budgeted): $943,253.00
Actual Expenditure: $849,581.54

9. APPENDICES: none attached