

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 ORGANIZATION: Shepherd Center, Inc.
Atlanta, GA 30309-1426**

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

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September 2017

2. REPORT TYPE

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3. DATES COVERED

15 Aug 2016 – 14 Aug 2017

4. TITLE AND SUBTITLE

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

5a. CONTRACT NUMBER**5b. GRANT NUMBER**

W81XWH-16-1-0395

5c. PROGRAM ELEMENT NUMBER**5d. PROJECT NUMBER****5e. TASK NUMBER****5f. WORK UNIT NUMBER****6. AUTHOR(S)**

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

Shepherd Center, INC.
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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

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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 70 participants are expected to enroll in the study, 45 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 our initial year, study design was refined, IRB/HRPO approval was obtained, study staff have been trained for interventions and assessments, and 15 participants have been enrolled into the study. Recruitment and enrollment is expected to continue into 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:**a. REPORT**

Unclassified

b. ABSTRACT

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c. THIS PAGE

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19a. NAME OF RESPONSIBLE PERSON
USAMRMC**19b. TELEPHONE NUMBER** (include area code)

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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; percent completion: 40%

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

Milestone 1: IRB approval obtained

Study eligibility, exclusion criteria and protocol were refined in order to support a large-scale study. Informed consent form & human subjects protocol were finalized and submitted for internal review. Shepherd Center IRB approval was obtained.

Milestone 2: HRPO approval obtained

Protocol was submitted to HRPO. The protocol was modified based on HRPO comments, and was resubmitted. Approval was obtained upon resubmission.

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

Milestone 3: Research and clinical staff trained

Research staff and clinical staff were trained through competency training, in-services and hands-on education in preparation for the study launch. Study research staff have been trained and have demonstrated competency in the following areas of assessment: cortical excitability, spinal reflex excitability, participant-perceived measures of hand-

related outcomes, hand function and motor impairment. Ongoing training has continued as new research and clinical staff are introduced to the study.

Milestone 4: Maintain trained and available Independent Evaluators throughout duration of clinical trial

Primary and secondary evaluators have been trained & competencies have been completed. Training & competency reviews for new evaluators has continued as needed.

Major Task 3: Participant Recruitment, Therapy, Participant Evaluation

Milestone 5: 1st participant consented, screened, and enrolled

In February 2017, the 1st participant was consented and enrolled in the study.

Milestone 6: Data collection initiated

Data collection was initiated in February 2017. Data is being organized & stored electronically with RedCap database system.

Milestone 7: 50% of subjects recruited and completed intervention

Fourteen subjects have been enrolled in the study and 8 have completed intervention. One participant dropped out of the study due to early discharge from the hospital. The remaining 5 are still completing interventions for the study.

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 teach members of the research lab on the physiology of the spinal cord and relevant treatment principles.

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. Due to new staff joining the Shepherd Center research lab, training of staff will continue to support the project.

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 Ainsworth – no change

Name: Brandon Poe – no change

Name: Saumitra (Somu) Ray – no change

Name: Sarah Callahan – no change

Name: Barry McKay – no change

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)

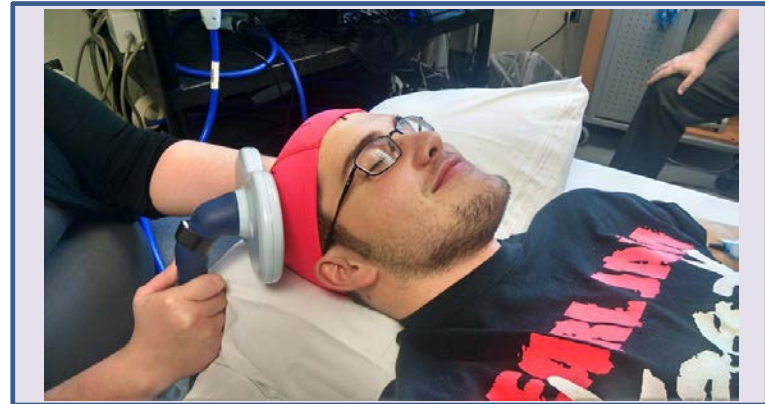
Aim 2. Compare changes in hand-related sensory function, self-reported function and participation, and quality of life associated with a multi-session course of stimulation-augmented FTP

Aim 3. Compare the effects on cortical and spinal excitability (spasticity) of a 3-week course of stimulation-augmented FTP

Aim 4. (exploratory). In subjects with tetraplegia, compare differences in responsiveness between persons with subacute (1-6 months post) versus chronic ($\geq$ 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 3 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 4).



Accomplishment: 11 participants consented, enrolled and completed intervention. 3 additional participants are completing interventions.

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: 08/31/2017

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 for Year 1): \$479,355.23

Actual Expenditure: \$411,985.87

9. APPENDICES: none attached