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 30309-1426

REPORT DATE: September 2019

TYPE OF REPORT: Annual Report

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

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
Sept 2019	Annual	15 Aug 2018 – 14 Aug 2019

4. TITLE AND SUBTITLE

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

5a. CONTRACT NUMBER

W81XWH-16-1-0395

5b. GRANT NUMBER

SC150103

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.
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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)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

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. 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.

A total of 83 participants were expected to enroll in the study (73 expected to complete + 10 additional subjects to accommodate attrition), 58 participants with acute spinal cord injuries (>6 months post injury), 15 participants with chronic injuries (>1 year post injury). In 2018, the targeted number of participants with acute SCI was increased (with approval) from 45 to 58 due accelerated enrollment. Only clinical assessments were collected on the additional participants.

This past reporting period, we completed enrollment with 80 total participants, 7 lost to attrition, therefore meeting the goal of 73 completed participants. Data reduction has now become the primary focus of the study in anticipation of data analysis and dissemination of results.

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**		12	**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. The project will be performed in a real-world clinical setting, so that the results can be immediately relevant for application to clinical practice.

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

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

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: 10%

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 continued through the course of the study. In the past year, Marissa Mirecki MOT OTR/L joined the study team as a SCI OT fellow and was trained to take the role as the study's primary therapist and applied stimulation to participants.

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, Elizabeth (Beth) Sasso-Lance, PT and Casey Kandilakis PT completed training as backup clinical assessors for data collections.

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 July 17, 2019, all data collections were completed with a total of 80 participants, 73 of whom completed the study. The remaining 7 were not able to complete the study and were lost to attrition.

Major Task 4: Data Analysis

Milestone 8: Data analyzed
Data collections have concluded, allowing the research staff to focus efforts on data reduction in preparation for analysis. Electronic case report forms have been reviewed for finalization and clinical outcome data has been exported and sent to Matt Hyatt, biostatistician for preliminary analysis. Due to the complexity of reducing and analyzing neurophysiologic data, we expect the reduction and analysis of data to extend over 2-3 quarters. Our biomedical engineer is in the process of refining the codes needed for data reduction, and regular meetings are being conducted with the staff for data analysis planning and execution.

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 reading and interpreting data. In addition, journal clubs 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 results have been disseminated at this time.

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

During the next quarter, we plan to continue data reduction and coding in preparation for analysis. Dr. Matt Hayat is currently organizing the clinical portion of the data to analyze, and the analysis of this data is expected to begin in the upcoming quarter.

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?

The processes implemented during this study, allowing acute participants who are still inpatients at Shepherd Center to take part in the research study, has influenced and impacted Shepherd Center's approach for further studies. We now have a clear process to implement research into patients' therapy schedules, as well as buy-in from Shepherd Center therapists and staff to complete research concurrently with patients regularly scheduled therapy.

What was the impact on other disciplines?

While still emerging, the therapists at Shepherd Center are exploring ways to implement non-invasive brain stimulation into fine motor therapy groups. The research team has been available to the therapists to support the implementation and plan to provide evidence of its effectiveness when they are ready to disseminate results.

What was the impact on technology transfer?

Nothing additional to report at this time.

What was the impact on society beyond science and technology?

Nothing additional to report at this time.

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:

An updated protocol was recently approved by the Shepherd Center IRB. This updated IRB reflects minor changes in study staff as well as including a short survey about participant's engagement in therapy during their interventions. This updated protocol has been submitted to the HRPO science officer and research administrative support for the study.

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 – has transitioned from part time to PRN (as needed) status. Ms. Callahan may be brought on intermittently to assist with data analysis, reduction and dissemination of findings when additional staff is needed.

Name: Barry McKay – no change

Name: Cazmon Suri – no change

Name: Anastasia Zarkou – 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: no

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: 73 participants have completed intervention, concluding data collection phase.

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: 09/09/2019

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): $1,418,724.77

Actual Expenditure: $1,329,754.16

9. APPENDICES: none attached