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14. ABSTRACT

This study will evaluate Constraint-Induced Movement (CI) therapy for promoting motor recovery in veterans and civilians with traumatic brain injury (TBI). This form of physical rehabilitation has been shown to substantially improve motor function after brain injury not due to trauma and to provoke a widespread neuroplastic response in the brain. This study (N = 80) is a single blind, randomized controlled trial that compares CI therapy for improving use of the more-affected arm in adults with TBI to a holistic fitness program named Lakeshore Enriched Fitness Training (LEFT). In addition to assessing changes from pre-treatment in more-affected arm motor function at post-treatment and 1-year afterwards, changes will be examined in white matter, grey matter, and functional brain activity. Products at the end of the first year of this blinded study are a manual of procedures and a method for generating synthetic neuroimaging data for the purpose of evaluating the sensitivity of the techniques proposed for quantifying changes in grey matter.

15. SUBJECT TERMS
Constraint-Induced Movement therapy, neurorehabilitation, traumatic brain injury, upper-extremity, hemiparesis, neuroplasticity

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1. INTRODUCTION

The purpose of this study is to determine the value of Constraint-Induced Movement (CI) therapy for promoting motor recovery in veterans and civilians with traumatic brain injury (TBI). CI therapy is a family of physical rehabilitation interventions derived from basic research in behavioral neuroscience and behavioral psychology. Each of the members of the family has four main components: (a) extensive, intensive training; (b) organization of the training following shaping principles, a well-known method in psychology for teaching new behaviors; (c) constraint of compensatory behaviors; and (d) a package of behavioral techniques designed to transfer therapeutic gains from the treatment to everyday setting. CI therapy has been shown in controlled studies to produce substantial improvement in function in motor disorders produced by several types of damage to the central nervous system and to produce widespread plastic changes in the organization and structure of the brain. Preliminary data suggest that CI therapy has an equivalent positive effect for motor deficit produced by TBI in military and civilian populations. This study is a rigorous, single blind, randomized controlled trial that compares the efficacy of CI therapy for improving use of the more-affected arm in adults with TBI to a holistic fitness program named Lakeshore Enriched Fitness Training (LEFT). Forty adults with TBI will be randomly assigned to each group. Participants in each group will receive 35 hours of training over two weeks, although the type of training, i.e., CI therapy vs. LEFT, will vary depending on group assignment. Assessment of more-affected arm motor function will be conducted at pre- and post-treatment and at 1-year afterwards. At the same occasions, magnetic resonance imaging (MRI), diffusion tensor imaging (DTI), and functional MRI (fMRI) of the brain will be carried out to determine changes in white matter, grey matter, and functional brain activity. If these neuroplastic changes parallel the changes in the more-affected arm expected, then the neuroimaging data will confirm the clinical data. In addition, the nature of the results from the neuroimaging studies may provide suggestions as to which types of neuroplasticity-inducing pharmacological agents when combined with CI therapy are most likely to yield a superior treatment outcome compared to CI therapy alone.

2. KEYWORDS

Constraint-Induced Movement therapy
neurorehabilitation
occupational therapy
physical therapy
traumatic brain injury
arm
hand
upper extremity

hemiparesis
neuroplasticity
magnetic resonance imaging
diffusion tensor imaging
fMRI

3. ACCOMPLISHMENTS

What were the major goals of the project?

1. To compare the effect of CI therapy and LEFT training on motor function in TBI patients.
2. To determine whether the initial clinical treatment effect, if any, persists over time.
3. To ascertain whether plastic brain changes accompany whatever clinical changes that may result from CI therapy and LEFT, and whether the magnitude of the clinical and plastic brain changes are correlated.
4. To evaluate the effects of CI therapy and LEFT on return to work and quality of life on a preliminary basis.

Table 1. Year 1 Milestones

Milestones	*Date Completed or Percent of Task Completed*
IRB approval for UAB and Lakeshore Foundation sites	Pre-award (3/26/14)
HRPO approval for these two sites	Pre-award (9/8/15)
IRB approval for VA recruitment sites	
Birmingham VAMC	Month 1 (10/22/14)
Richmond VAMC	Month 2 (11/11/14)
Denver VAMC	Month 4 (1/9/15)
HRPO approval for VA recruitment sites	
Birmingham VAMC	Month 6 (3/31/15)
Richmond VAMC	Month 6 (3/31/15)
Denver VAMC	Month 7 (4/2/15)
All personnel on board	Month 1
Data system set-up	Month 2
Treat & pre- and post-test first 24 participants	11 enrolled, 9 completed (37.5%)

A small number of changes to the methods have been made since our application was submitted. All have already been described in our pre-award correspondence or quarterly progress reports and been reviewed with and approved by the Science Officer for this project or the HRPO or both. The changes are listed below.

- The original design for this RCT was a 2 x 2 factorial: Type of Therapy (CI therapy vs. LEFT) X Severity of Arm Motor Impairment (Mild-to-moderate vs. Moderate). A third factor was added after the award was made: Provision of

Transfer Package (Standard vs. Enhanced). The Transfer Package is a set of behavioral techniques designed to transfer gains from the treatment to everyday setting.

- Collection of data on the presence of variants of the gene that codes for BDNF was added. Animals with different variants of this gene have varying neuroplastic responses to training. We want to test whether the response to rehabilitation will vary among study participants with different variants of this gene.
- Housing of participants was split between the Lakeshore Foundation and our institution, the University of Alabama at Birmingham (UAB). All participants were originally to have been housed at the Lakeshore Foundation.
- The makeup of the VA recruitment sites was changed. Subcontracts were negotiated with the Birmingham VAMC, Denver VAMC, and Richmond VAMC.
- The option of collecting MRI data using a 1.5T scanner was added for participants for whom a 3T scanner is contraindicated but 1.5T is safe.
- The option of giving participants with anxiety about scanning a mild sedative agent was added.

What was accomplished under these goals?

The specific objectives this year were to obtain IRB and other regulatory approvals for the project, hire and train new personnel needed to round out the project team, refine and make final the study protocol, and recruit, enroll, treat, and test 24 participants.

Major activities were in accord with these objectives. Table 1 shows that we obtained IRB and HRPO approval for study activities in Birmingham before the start of the award. Although applications for approval of recruitment activities at our VA recruitment sites were submitted to their respective IRBs two-three months before the start of the award, IRB and HRPO approval was not obtained for the last VA recruitment site until Month 7 of the project. The study was registered with clinicaltrials.gov in Month 4. All study personnel were on board before the end of Month 1. Training and verification that personnel had appropriate knowledge of and skill in the study procedures was completed by end-Month 3. In addition, the protocol for the LEFT intervention was refined and an enhanced version of the set of behavioral techniques used in CI therapy for transferring therapeutic gains from the therapeutic setting to the everyday life was developed. The key aspects of the database that warehouses the study data were completed by end-Month 2. In Months 4-6, three practice participants were treated and tested to ensure that coordination of the complex array of treatment and testing procedures was in order. In addition, in this quarter, step-by-step instructions were written up for all the study procedures and assembled in a manual of procedures (MOP; see Section 6). In Months 7-9, a method was developed for generating synthetic neuroimaging data to permit evaluation of the sensitivity of the different types of

structural MRI analyses proposed on the study (see Section 6). Treatment and pre-and post-testing were completed with 9 participants in Months 6-12. A total of 11 were enrolled. One participant withdrew after being randomized to the LEFT intervention. The other was withdrawn by mutual consent of the project and the mother of the participant because the participant missed several treatment sessions. Entry of the testing data collected to date has been completed.

Recruitment of candidates for the study proceeded in parallel to these efforts. Since IRB and HRPO approval for recruitment of veterans with TBI at our VA sites was not yet granted, we initiated a major effort to recruit veterans in Alabama in Month 1 with the assistance of Admiral Clyde Marsh, Commissioner, Alabama Department of Veterans Affairs. Admiral Marsh directed his team to distribute this project's recruitment materials to all 67 county offices in Alabama of AlaVetNet. In Month 2, UAB did a press release in connection with Veterans Day, which was followed by interviews with two local television stations about the project and opportunities for veterans to take part in it. In Month 3, a brief recruitment interview was taped with Admiral Marsh for airing on TV in Central Alabama on the program Veterans Affairs. We also placed color, 1/8 page ads in the Spring and Summer issues of US Veterans Magazine. Regrettably, these substantial efforts yielded only a handful of contacts. It appears that outreach to the general community of veterans is too diffuse to reach our specific, target audience: veterans with TBI with motor impairment of one or both arms.

HRPO approval for recruitment activity at our three VA sites was received in Months 6 & 7. Recruitment efforts at these sites began shortly afterwards. The investigators at the three sites queried their electronic medical record system for the contact information of veterans with diagnostic and procedural codes reflecting a history of TBI and motor impairment of one or both arms. A cover letter, brochure, card to indicate interest, and stamped, addressed return envelope were mailed in batches of 100 to 500 to veterans who fit these criteria. The Birmingham VAMC site mailed materials to 554 veterans. The Richmond VAMC site database search yielded 2,325 records, out of which 161 were determined to be likely enough candidates to mail a letter after review. The Denver VAMC site mailed materials to 1800 veterans. In addition, in Month 6, the Director of the TBI Model Systems Center at UAB, Thomas Novack, PhD, who is an investigator on this project, mailed materials to approximately 100 civilians with TBI. (Dr. Novack has also directed patients under his care who appeared to be likely candidates to the study.) This recruitment strategy, targeted mailings, has proven to be most productive.

The recruitment efforts above have resulted in 145 unique contacts of candidates with the project over Year 1 in total. Out of this number, telephone or videoconference screens were completed with 107 by end-Year 1; contact had not yet been made or

preliminary screening was in still in process for 38. Out of 107, comprehensive, on-site screening was conducted with 19, out of which 11 were enrolled.

The reasons that enrollment fell short of the target number are discussed in Section 5 under the heading “Actual or anticipated problems or delays and actions or plans to resolve them.”

Both the investigators and testing personnel on this project are blinded to exclude the possibility of experimenter bias from influencing the study results. Hence, none of the data collected have been analyzed to date with respect to the scientific questions reflected in the four main study goals. The data will be unblinded with respect to assignment to intervention group in the third year of the project. Analysis of the data with respect to the questions reflected in the study goals and write-up of these results in our progress and annual reports, along with dissemination of these results to the scientific, healthcare, and patient communities will take place then.

What opportunities for training and professional development did the project provide?

This project does not have a formal training and professional development component. Training in the study procedures and in the conduct of research, however, has been provided to several staff members and students. Laura Reder, PTA, the blinded tester, has been trained to conduct the motor testing on a blinded basis. This testing includes the Motor Activity Log and Wolf Motor Function Test, which are widely used in neurorehabilitation research. Ms. Reder has also received training in the ethical conduct of research with humans. Brice Lambert, the data manager, has received training in processing the data from the movement monitors used to track changes in amount of movement of the more-affected arm in study participants and in searching the electronic medical records system in use at our University’s health system and elsewhere. Michele Haddad, one of the graduate students who works on the analysis of the neuroimaging data, has received further mentoring in voxel-based morphometry, a method for quantifying changes in grey matter. Brent Womble, the other graduate student who works on the analysis of the neuroimaging data, has received mentoring in tract-based spatial statistics and Freesurfer, which are methods for quantifying changes in white matter and grey matter, respectively. Ms. Haddad and Mr. Womble have also received mentoring in experimental strategy, study design, and interpretation and writing up of data. In addition, 3 undergraduate volunteers have received training in selected components of one or more of these methods and in the ethical conduct of research with humans. Six undergraduates, two on a work study basis and four on a volunteer basis, have received training in the ethical conduct of research with humans, the data

entry and processing procedures, and in selected components of the study testing and treatment procedures.

How were the results disseminated to communities of interest?
As noted, both the investigators and testing personnel on this project are blinded to exclude the possibility of experimenter bias from influencing the study results. Hence, analysis of the efficacy of the interventions tested and the write-up and dissemination of these results to the scientific, healthcare, and patient communities will have to wait until Year 3, when the study will be unblinded.

In the meantime, our recruitment efforts have increased awareness among veterans and the general public that impairment in the motor function of the arms after TBI may be amenable to treatment. Regrettably, little attention by healthcare professionals is paid to rehabilitation of motor function, particularly of the arms, after TBI because of the prominent nature of the cognitive impairments present after TBI. Hence, impairment of upper-extremity motor function often goes untreated and survivors live with persistent deficits. As noted, the project has been featured in several local television broadcasts and in a nationwide podcast. In addition, letters and recruitment brochures have been mailed to approximately 2,500 veterans and 5,000 brochures have distributed across the state of Alabama by AlaVetNet county offices. We believe these efforts are starting to change the view of patients with TBI, at least in Alabama, from nothing can be done to something needs to and can be done about upper-extremity motor impairment after TBI.

What do you plan to do during the next reporting period to accomplish the goals?
In the next quarter, we plan to recruit, screen, enroll, test, and treat 6 participants. (See our response under the heading “Actual or anticipated problems or delays and actions or plans to resolve them” in Section 5 for a discussion of this enrollment rate. Six rather nine will be enrolled next quarter because of Thanksgiving in November and Christmas and other holidays in December.) Entry of the motor, quality of life, and other self-report data will continue, as will processing of the movement monitor data. Work on processing and analysis of the neuroimaging data, i.e., MRI, DTI, and fMRI scans, will also continue.

To ensure an adequate flow of participants, we plan to expand our recruitment efforts at our current VA sites and add new recruitment sources. At the Denver VAMC, the catchment area for candidates will be expanded from the Denver VAMC to the entire VISN. At the Richmond VAMC, the original search of their electronic medical records limited the period to examined to 2005-2015; the search will now be expanded to 2001-2005. We are not renewing the subcontract with our recruitment site at the Birmingham

VAMC because we are confident that we have made outreach to all or close to all of the candidates from that source. We will seek new VA recruitment sites with those funds, e.g., the Tampa VAMC and San Antonio VAMC, which both host Polytrauma Rehabilitation Centers. In addition, we plan to work with the Alabama Brain Injury Foundation and several TBI Model Systems Centers, first in the South and then elsewhere, to help recruit civilian candidates.

4. IMPACT

What was the impact on the development of the principal discipline of the project?

Nothing to report. Please see explanation in the last paragraph of our response under the heading "What was accomplished under these goals?**"** in Section 3**.**

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?

Please see the second paragraph of our response under the heading "How were the results disseminated to communities of interest?**"** in Section 3**.**

5. CHANGES

Changes in approach and reasons for change

Nothing to report. There have been no changes in our approach since the third quarter progress report.

Actual or anticipated problems or delays and actions or plans to resolve them

We reported in our third quarter and previous progress reports that enrollment was proceeding slower than planned because of a long delay in gaining approval to recruit through our three VA recruitment sites because of multiple and lengthy administrative and regulatory hurdles to clear. Recruitment at the last VA site in Denver did not begin until May 18, 2015. These delays resulted despite our submitting the initial application for approval of this project to the IRB at UAB in January 2014, nine months before the start date of the award, and submitting initial versions of the applications for approval of recruitment activity at our three VA sites in June-July 2014, two-three months before the award start date. As reported previously, we initiated recruitment independently of our VA sites through the Department of Veterans Affairs in Alabama in October 2014 but

that large effort, which involved distribution of recruitment brochures to all 67 AlaVetNeT county offices, among other measures, did not yield any candidates.

To address these unanticipated delays, we submitted a revised projection for quarterly enrollment with our second quarter progress report. The target for end-Year 1 in that report was 24 participants. We actually enrolled 11 by that date. We now anticipate that we can enroll 9 participants per quarter going forward rather than 14 as projected. After allowing for 4 weeks each year during which enrollment cannot take place because of holidays, this rate will permit enrollment of 76 participants by the end of the project, i.e., end-Year 3. We had planned to enroll 80 participants by end-Year 2. The power analysis in our application estimated that adequate power was available to address all the primary aims even after 20% attrition, i.e., 64 participants. Thus, the plan presented here will permit evaluation of all of the primary aims with adequate power. One-year follow-up testing will be conducted with participants treated in Year 3 in the next year. This work will be funded by filing a no-cost extension, if any funds remain at end-Year 3, or other funds available to the laboratory, or a combination of these sources. A revised SOW that accords with this plan is enclosed in the Appendix.

We plan to expand our recruitment efforts at our current VA recruitment sites and add new recruitment sources to ensure an adequate flow of participants. At the Denver VAMC, the catchment area for candidates will be expanded from the Denver VAMC to the entire VISN. At the Richmond VAMC, the original search of their electronic medical records limited the period to examined to 2005-2015; the search will now be expanded to 2001-2005. We are not renewing the subcontract with our recruitment site at the Birmingham VAMC because we are confident that we have made outreach to all or close to all of the candidates from that source. We will seek new VA recruitment sites with those funds, e.g., the Tampa VAMC and San Antonio VAMC, which both host Polytrauma Rehabilitation Centers. In addition, we are seeking the assistance of the Alabama Brain Injury Foundation and several TBI Model Systems Centers, first in the South and then elsewhere, to help recruit civilian candidates. The Alabama Brain Injury Foundation and the TBI Model Systems Centers have patient registries that include mailing addresses. We have found that the most successful form of outreach is mailing a cover letter and brochure, along with a stamped, addressed return envelope, to candidates.

Changes that had a significant impact on expenditures

We reported in our third quarter and previous reports that funds were being expended at a slower rate than planned because of the delays that resulted in enrollment at a lower rate than projected. As of end-Year 1, expenditures registered for total costs were $681,325, with approximately $60,000 in charges still pending. The amount budgeted

was $1,024,724. We plan to carry forward the unexpended funds, and use them to supplement the amount budgeted originally for Year 3, which was $544,230. This shift will allow enrollment, treatment, and testing to continue at the rate projected above until end-Year 3. As noted, this plan will permit enrollment of 76 participants, which is close to the original number projected.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report. There have been no significant changes since the third quarter progress report. There have been no serious adverse events since the inception of the project. The risk-to-benefit ratio of the study has not changed. The Data & Safety Monitor for this project did not recommend any changes in the conduct of the study at our meeting in the fourth quarter.

6. PRODUCTS

Publications, conference papers, and presentations

Nothing to report. As noted, both the testing personnel and investigators are blinded to assignment to intervention group until the last year of this project.

Website or other Internet Site

We have developed a website for the purpose of recruiting participants. As noted, our recruitment activities have the benefit of increasing public awareness about the effects of TBI on motor function of the upper-extremities and the possibility of remedying those impairments. The website address is: **www.tbirehabtherapy.net.**

Technology or techniques

1. *A manual of procedures that describes the treatment and testing procedures in detail has been completed.* It was submitted along with our second quarter progress report. Work on a manuscript that introduces the protocol is underway. It will be submitted for publication to a high impact neurorehabilitation journal along with the manual of procedures before the end of the second year of the project. Dissemination of the manual of procedures will permit researchers to replicate our study and clinicians to implement the interventions tested, if found to be efficacious, in their practices.
2. *A method was developed for generating synthetic data to permit evaluation of the sensitivity of the different types of structural MRI analyses proposed on the study.* Longitudinal structural analyses attempt to detect use-dependent structural neuroplasticity at a gross anatomical level. Longitudinal voxel-based morphometry (VBM) is traditionally used to detect changes in volume or density of grey matter relative to other tissue. Surface-based morphometry (e.g. Freesurfer) reconstructs the edge of the grey matter and white matter into 3-dimensional surfaces, then

measures geometric values, e.g. distance (thickness), surface area, volume, and curvature (gyrification). These two methods will be used on this project to study if and what types of neuroplastic change CI therapy and LEFT induce in veterans and civilians with TBI.

Longitudinal VBM and surface-based morphometry may be differentially sensitive to different types of cellular and gross anatomical changes taking place in use-dependent structural reorganization of the brain. Hence, a method was developed by our laboratory in the last year for generating synthetic data to permit evaluation of the sensitivity of these two structural MRI analysis methods to the different types of structural changes that we anticipate in the brain as a result of the study interventions.

We synthetically generated 3 longitudinal datasets with changes in each dataset isolated to a single gross anatomical (expansion or increased gyrification) or cellular (increased density) feature. All changes were made in the right superior frontal gyrus, using the anterior tip of the corpus callosum as a landmark. We used a point-based deformation technique to manually alter the shape of a gyrus. For cortical expansion, we pushed multiple points along the selected gyrus outward (**Fig. 1a**). For increased gyrification, we pushed two points along the selected gyrus inward, while keeping the overall shape of the gyrus intact (**Fig. 1b**). For increased density, we made a spherical region of the gyrus darker, with the change restricted to the grey matter (**Fig. 1c**). Finally, we processed these synthetic datasets using surface-based morphometry (Freesurfer 5.3), and we have begun to process the datasets using VBM (SPM12). Freesurfer accurately reconstructed the edge of the grey and white matter as the gyrus expanded and folded (**Fig. 1a-b**). Freesurfer did not detect the change in density (**Fig. 1c**). Preliminary VBM results suggest that SPM12 is more sensitive to changes in density than Freesurfer.

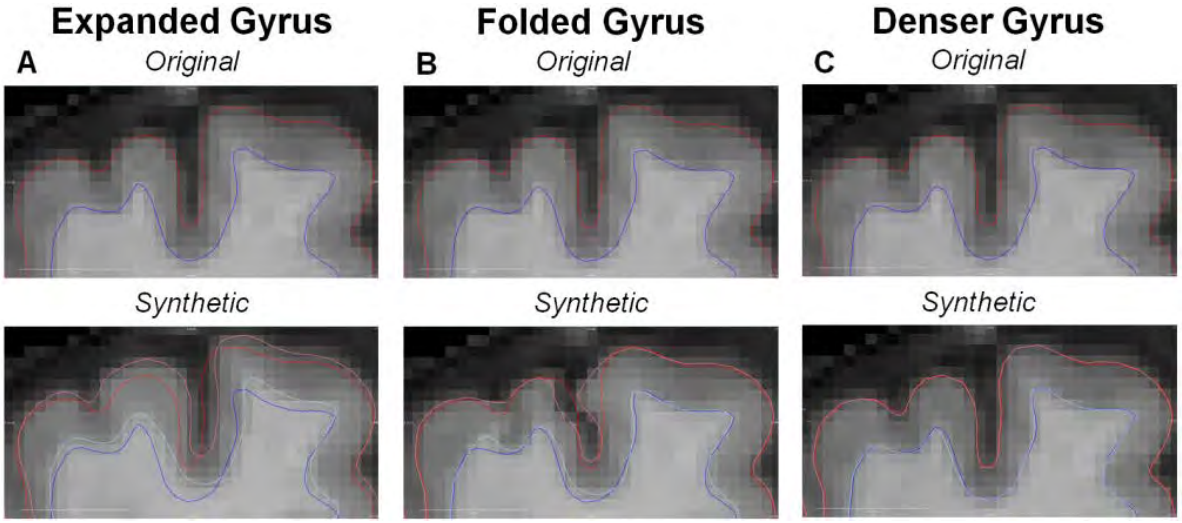

Figure 1. Freesurfer reconstruction of grey and white matter edges. The edges in the original brain are traced in red and blue. In the synthetic brains, the grey and white matter edges are traced in pink and light blue and are shown alongside the original traces.

This type of evaluation of imaging analysis methods has not been done to date. When this work is completed, a manuscript will be submitted to a high impact neuroimaging journal describing the method for generating synthetic data and its application to evaluating the sensitivity of voxel-based morphometry and measurement of cortical thickness using Freesurfer. We expect that the manuscript will be submitted before the end of Year 2.

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: Edward Taub, PhD
Project Role: Principal Investigator, UAB
Researcher Identifier: n/a
Nearest person month worked: 3
Contribution to project: He supervised the design, implementation, and conduct of all aspects of the project.

Name: Victor Mark, MD
Project Role: Medical Director, UAB
Researcher Identifier: ORCID ID 0000-0002-9468-7952
Nearest person month worked: 1
Contribution to project: He was responsible for the general medical supervision of participants in project procedures, carried out medical evaluations on all prospective participants, and supervised the administration of cognitive testing by project staff. He also participated in the design of the cognitive testing and the setup of the collection of neuroimaging data.

Name: Jerzy Szaflarski, MD, PhD
Project Role: Investigator/Neuroimaging Supervisor, UAB
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: Dr. Szaflarski designed the procedures for collection of structural magnetic resonance imaging (MRI) and resting state functional MRI.

Name: Jane Allendorfer, PhD
Project Role: Investigator, Neuroimaging Expert, UAB
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: Dr. Allendorfer designed the procedures for the collection of the diffusion tensor imaging (DTI) scans.

Name: David Morris, PhD
Project Role: Investigator, CIMT Training & Scoring Supervisor, UAB
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: Dr. Morris trained the Tester and ensured that she and others were able to perform the study procedures with adequate fidelity. He played in a major role in the design, implementation, and supervision of the LEFT intervention protocol. In addition, he wrote the manual of procedures in conjunction with the PI.

Name: James Rimmer, PhD
Project Role: Investigator, LEFT Intervention Supervisor, UAB
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: Dr. Rimmer designed the fitness testing procedures and assisted with the design of the LEFT intervention protocol.

Name: Gitendra Uswatte, PhD
Project Role: Investigator, Accelerometry & Data Analysis Supervisor, UAB
Researcher Identifier: ORCID ID 0000-0003-4507-7098
Nearest person month worked: 2
Contribution to project: He trained the Data Manager to collect and process the data from the movement monitors worn by participants and supervised the construction of the database for the study. He also took part in the design of the testing and treatment procedures, design and implementation of the recruitment procedures, and in the preparation of the regulatory documents for the study.

Name: Gary Cutter, PhD
Project Role: Investigator, Data Analysis Supervisor, UAB
Researcher Identifier: ORCID ID 0000-0002-8455-980X
Nearest person month worked: 1
Contribution to project: Dr. Cutter supervised the design of the randomization scheme and the construction of the database for the study.

Name: Thomas Novack, PhD
Project Role: Investigator, Recruiting & Cognitive Testing Supervisor, UAB
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: He assisted with the recruitment of patients and design of the cognitive and post-traumatic stress disorder testing procedures.

Name: Stephen Mennemeyer, PhD
Project Role: Investigator, Economic Analyst, UAB
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: He designed the procedures for collection economic and quality of life data.

Name: Staci McKay
Project Role: Trainer, UAB
Researcher Identifier: n/a
Nearest person month worked: 12
Contribution to project: She helped to design the enhanced Transfer Package procedures and has conducted recruitment and provided CI therapy in addition to coordinating work on the project on a day-to-day basis.

Name: Andrea Taylor
Project Role: Research Assistant, UAB
Researcher Identifier: n/a
Nearest person month worked: 12
Contribution to project: She helped to design the enhanced Transfer Package procedures and has conducted recruitment and provided CI therapy.

Name: Terrie Adams
Project Role: Trainer, UAB
Researcher Identifier: n/a
Nearest person month worked: 2
Contribution to project: She delivered the physical and mental fitness components of the LEFT intervention.
Source: Department of Psychology, UAB

Name: Jennifer Zimmerman
Project Role: Research Assistant, UAB
Researcher Identifier: n/a
Nearest person month worked: 6
Contribution to project: She delivered the massage therapy component of the LEFT intervention.

Name: Laura Reder
Project Role: Research Assistant, UAB
Researcher Identifier: n/a
Nearest person month worked: 6
Contribution to project: She conducted the blinded motor and other clinical testing of the participants and conducted on-site screening of participants in conjunction with the Medical Director.

Name: Michelle Haddad
Project Role: Graduate Student, UAB
Researcher Identifier: n/a
Nearest person month worked: 6
Contribution to project: She assisted with collection of the neuroimaging data and development of a method for evaluating the sensitivity of the neuroimaging methods proposed for assessing changes in grey matter.

Name: Brent Womble
Project Role: Graduate Student, UAB
Researcher Identifier: n/a
Nearest person month worked: 6
Contribution to project: He assisted with collection and processing of the neuroimaging data and developed a method for evaluating the sensitivity of the neuroimaging methods proposed for assessing changes in grey matter.
Source: Department of Psychology, UAB

Name: Ameen Barghi
Project Role: Research Assistant, UAB
Researcher Identifier: ORCID ID 0000-0001-5233-7279
Nearest person month worked: 3
Contribution to project: He assisted with the collection and processing of the neuroimaging data.

Name: Brice Lambert
Project Role: Data Manager, UAB
Researcher Identifier: ORCID ID 0000-0003-1947-1569
Nearest person month worked: 6
Contribution to project: He constructed the database that holds the data from this project, set-up the movement monitors to collect data and processed the data collected, and conducted random assignment of participants to the study groups.

Name: Ezekiel Byrom (until 10/19/14)
Project Role: Research Assistant (regulatory documents, recruitment), UAB
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: He helped to prepare and maintained the regulatory documents, ordered equipment and supplies, and assisted with recruitment, including design of the website and recruitment materials for the study.

Name: Ayushe Sharma (effective 10/20/14)
Project Role: Research Assistant (regulatory documents, recruitment), UAB
Researcher Identifier: n/a
Nearest person month worked: 9
Contribution to project: Ms. Sharma replaced Mr. Byrom. She performed the same activities.

Name: Jeff Underwood
Project Role: Subcontract Principal Investigator, Lakeshore Foundation
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: Oversight of activities at the Lakeshore Foundation. The LEFT intervention was conducted on the campus of the Lakeshore Foundation. In addition, participants in the LEFT group were housed there.

Name: Laurie Berenotto
Project Role: Cottage Coordinator, Lakeshore Foundation
Researcher Identifier: n/a
Nearest person month worked: 2
Contribution to project: She facilitated the stay of the study participants on the campus of the Lakeshore Foundation.

Name: Marca Alexander, PhD
Project Role: Subcontract Principal Investigator, VISTAR
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: Oversight of activities at the Birmingham VAMC recruitment site.

Name: Nazaren Hartman Mindingall
Project Role: Recruitment Coordinator, VISTAR
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: She helped to assemble the mailing list and mail out letters to study candidates, answered telephone calls from candidates with questions about the mailing, and assisted with preparation of the regulatory documents for this site.

Name: Lisa Brenner, PhD
Project Role: Subcontract Principal Investigator, Denver Research Institute
Researcher Identifier: ORCID ID 0000-0002-2629-214X
Nearest person month worked: 1
Contribution to project: Oversight of all activities at the Denver VAMC recruitment site.

Name: Kelly Stearns
Project Role: Recruitment Coordinator, Denver Research Institute
Researcher Identifier: ORCID ID 0000-0002-2629-214X
Nearest person month worked: 1
Contribution to project: She assembled the mailing list, mailed out letters to study candidates, answered telephone calls from candidates with questions about the mailing, and assisted with preparation of the regulatory documents for this site.

Name: Treven Pickett, PsyD
Project Role: Subcontract Principal Investigator, McGuire Research Institute
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to project: Oversight of all activities at the Richmond VAMC recruitment site.
Source: Richmond VAMC

Name: David Rothman
Project Role: Recruitment Coordinator, McGuire Research Institute
Researcher Identifier: n/a
Nearest person month worked: 3
Contribution to project: He reviewed the medical records, assembled the mailing list, mailed out letters to study candidates, answered telephone calls from candidates with questions about the mailing, and assisted with preparation of the regulatory documents for this site.

Has there been a change in the active other support of the PI or senior/key personnel since the last report period?

Edward Taub, PI
Compative Effectiveness of a Low-cost Virtual Reality Gaming Platform for Neurorehabilitation of Hemiparesis (Uswatte, PI, UAB clinical site, subcontract from The Ohio State University lead site)
0.18 academic months, 0.42 summer months
Patient-Centered Outcomes Research Institute
Geri Gunman, MBA
1828 L Street, NW, 9th Fl
Washington, DC 20006
Performance Period: 11/01/15 – 10/30/18
Annual Direct Costs: $124,000
The general objective of this project is to refine and test a video game delivery model of CI therapy against standard delivery of CI therapy and typical neurorehabilitation for rehabilitating use of the more-affected arm after stroke.
Aim 1. To compare the effectiveness of video game delivery CI therapy in the home to that of one-on-one, face-to-face delivery of CI therapy in the clinic and of one-on-one, face-to-face delivery of conventional neurorehabilitation.
Aim 2. To determine the patient characteristics that differentially influence response to the three interventions.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Gitendra Uswatte, Investigator
Compative Effectiveness of a Low-cost Virtual Reality Gaming Platform for Neurorehabilitation of Hemiparesis (Uswatte, PI, UAB clinical site, subcontract from The Ohio State University lead site)
0.9 academic months, 0.9 summer months
Patient-Centered Outcomes Research Institute
Geri Gunman, MBA

1828 L Street, NW, 9th Fl
Washington, DC 20006
Performance Period: 11/01/15 – 10/30/18
Annual Direct Costs: $124,000
The general objective of this project is to refine and test a video game delivery model of CI therapy against standard delivery of CI therapy and typical neurorehabilitation for rehabilitating use of the more-affected arm after stroke.
Aim 1. To compare the effectiveness of video game delivery CI therapy in the home to that of one-on-one, face-to-face delivery of CI therapy in the clinic and of one-on-one, face-to-face delivery of conventional neurorehabilitation.
Aim 2. To determine the patient characteristics that differentially influence response to the three interventions.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

David Morris, Investigator
Compative Effectiveness of a Low-cost Virtual Reality Gaming Platform for Neurorehabilitation of Hemiparesis (Uswatte, PI, UAB clinical site, subcontract from The Ohio State University lead site)
0.6 calendar months
Patient-Centered Outcomes Research Institute
Geri Gunman, MBA
1828 L Street, NW, 9th Fl
Washington, DC 20006
Performance Period: 11/01/15 – 10/30/18
Annual Direct Costs: $124,000
The general objective of this project is to refine and test a video game delivery model of CI therapy against standard delivery of CI therapy and typical neurorehabilitation for rehabilitating use of the more-affected arm after stroke.
Aim 1. To compare the effectiveness of video game delivery CI therapy in the home to that of one-on-one, face-to-face delivery of CI therapy in the clinic and of one-on-one, face-to-face delivery of conventional neurorehabilitation.
Aim 2. To determine the patient characteristics that differentially influence response to the three interventions.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Victor Mark, Investigator
Rehabilitating Extremity Use after Multiple Sclerosis (Mark)
1.72 calendar
National Multiple Sclerosis Society
Nicholas G. LaRocca, Ph.D.
Vice President, Health Care Delivery and Policy Research
National Multiple Sclerosis Society
733 Third Avenue
New York, NY 10017
Performance Period: 10/01/09 – 09/30/14
Annual Direct Costs: $200,762
Compare CI Therapy and Complementary and Alternative Medicine treatments to determine their changes in the extent of more-affected arm use in the life setting and maximal movement ability in the laboratory for individuals with multiple sclerosis.
Role: Principal Investigator
Overlap: none.
This project has ended. Dr. Mark is no longer committing any time to this project.

Evolution of Learned Nonuse in Stroke Hemiparesis
2.07 calendar
NIH
Beth Ansel, Ph.D.
6705 Rockledge Drive
Room 2207, MSC 7987
Bethesda, MD 20892-7987
12/01/09 – 11/30/11
Annual Direct Costs: $50,000
Performance Period: 12/10/2010-11/30/2012
To determine whether learned nonuse occurs in the acute-subacute period after hemiparetic stroke, how often it occurs, and test hypotheses concerning its modulation by neurologic factors.
Role: Principal Investigator
Overlap: none.
This project has ended. Dr. Mark is no longer committing any time to this project.

fMRI of Language Recovery Following Stroke in Adults (Szflarski)
.60 calendar
NIH
Annual direct costs: $303,325
Performance Period: 8/1/08-7/31/13

The goals are to evaluate trajectories of aphasia recovery after ischemic stroke using fMRI and neuropsychological measures of aphasia and on evaluating Constraint-Induced Aphasia therapy as an intervention in patient with chronic aphasia after ischemic stroke.
Role: Co-Investigator
Overlap: none.
This project has ended. Dr. Mark is no longer committing any time to this project.

Post-stroke Aphasia and rTMS Treatment (PART) Study (Szaflarski)
.90 calendar months
National Institutes of Health
9000 Rockville Pike
Bethesda MD 20892
Annual Direct Costs: $319,473
Performance Period: 1/1/12-12/31/16
The goal of this study is to assess in a blinded, randomized, and sham controlled trial the efficacy of fMRI-guided rTMS for the management of post-stroke aphasia.
Role: Co-Investigator.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Long-Term Neuroplasticity after Rehabilitation for Progressive MS. (Mark)
1.46 calendar months
Consortium of Multiple Sclerosis Centers
3 University Plaza Drive, Suite 116
Hackensack NJ 07601
Performance Period: 11/01/2014-4/30/2016:
Annual Direct Costs: $36,363
This project aims to evaluate 5-year follow-up on structural MRI and clinical motor testing persons with multiple sclerosis who had undergone either Constraint-Induced Movement therapy or a program of Complementary and Alternative Medicine.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Dose-Response Effects of Transformative Exercise in Improving Health and Function in Adults with Spinal Cord Injury and Multiple Sclerosis (Rimmer)
0.36 calendar months
Department of Education
400 Maryland Avenue SW
Washington DC 20202

Performance Period: 10/1/2013-9/30/2018
Annual Direct Costs: $475,000
This study will randomize ambulatory persons either with multiple sclerosis or spinal cord injury to a program either of yoga or dance-based therapy.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Compative Effectiveness of a Low-cost Virtual Reality Gaming Platform for Neurorehabilitation of Hemiparesis (Uswatte, PI, UAB clinical site, subcontract from The Ohio State University lead site)
1.2 calendar months
Patient-Centered Outcomes Research Institute
Geri Gunman, MBA
1828 L Street, NW, 9th Fl
Washington, DC 20006
Performance Period: 11/01/15 – 10/30/18
Annual Direct Costs: $124,000
The general objective of this project is to refine and test a video game delivery model of CI therapy against standard delivery of CI therapy and typical neurorehabilitation for rehabilitating use of the more-affected arm after stroke.
Aim 1. To compare the effectiveness of video game delivery CI therapy in the home to that of one-on-one, face-to-face delivery of CI therapy in the clinic and of one-on-one, face-to-face delivery of conventional neurorehabilitation.
Aim 2. To determine the patient characteristics that differentially influence response to the three interventions.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

James Rimmer, Investigator
Rehabilitation Engineering Research Center on Recreational Technologies and Exercise Physiology Benefiting Persons with Disabilities
.6 calendar
Department of Education
DED H133E110007 (Rimmer)
Performance Period: 10/01/07 – 9/30/14
Annual Direct Costs: $1,147,093
The major goal of this project is to develop and operate a rehabilitation engineering and research center focused on improving the health, wellness, and quality of life of people with disabilities by promoting and facilitating increased participation in physical activity and recreation. Role: Principal Investigator

This project has ended. Dr. Rimmer is no longer committing any time to this project.

Creating a Community Health Inclusion Index (CHII)
1.44 calendar
Centers for Disease Control and Prevention
000HCUB-2011-0365(Rimmer)
Performance Period: 01/03/12 – 8/21/14
Annual Direct Costs: $38,802
The primary goal for this project is to develop a Community Health Inclusion Index that is valid and reliable and a solutions database to provide criteria-based solutions to building healthy communities for people with disabilities. Role: UAB Principal Investigator
This project has ended. Dr. Rimmer is no longer committing any time to this project.

National Center on Health, Physical Activity and Disability (Rimmer, PI)
1.8 calendar months
Centers for Disease Control and Prevention (CDC)
Dr. Arlene Vincent-Mark, Project Officer
National Center for Chronic Disease Prevention and Health Promotion
1825 Century Blvd NE, Mailstop E-88
Atlanta, GA 30341 Period of Performance: 04/01/15-03/31/16
Award# HHS U59DD000906-04
Annual Direct Cost: $906,013
The primary focus of this one year application is to develop the infrastructure to support the inclusion of people with disability in existing and future public health promotion programs in physical activity, nutrition and healthy weight management.
Dr. Rimmer's effort on this project has increased. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

UIC Obesity Research Project on Prevalence, Adaptations and Knowledge Translation in Youth and Young Adults with Disabilities (Rimmer, PI)
.6 calendar months
Department of Health and Human Services
Dr. Margaret Campbell
Administration for Community Living
One Massachusetts Avenue
Washington, DC. 20201-1401 Period of Performance: 04/01/12-09/29/16
Award# 90DP0048-01-00
Annual Direct Cost: $348,380

This project addresses significant gaps in the literature related to prevalence, risk factors and consequences of obesity; successful and promising community-based strategies for obesity prevention; and knowledge translation issues that limit access to important research findings in youth and young adults with disabilities.
Dr. Rimmer's effort on this project has decreased. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Interactive Exercise Technologies and Exercise Physiology for People with Disabilities (Rimmer, PI)
3.6 calendar months
Department of Health and Human Services
Dr. Margaret Campbell
Administration for Community Living
One Massachusetts Avenue
Washington, DC. 20201-1401 Period of Performance: 09/30/15-09/29/16
Award# 90RE5009-02-00
Annual Direct Cost: $1,509,833
This project will conduct an advanced engineering research and development program using new and emerging technologies to address the high rates of physical inactivity in youths and adults with disabilities
Dr. Rimmer's effort on this project has increased. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Dose-Response Effects of Transformative Exercise in Improving Health and Function in Adults with Spinal Cord Injury and Multiple Sclerosis (Rimmer, PI)
1.8 calendar months
Department of Health and Human Services
Dr. Margaret Campbell
Administration for Community Living
One Massachusetts Avenue
Washington, DC. 20201-1401 Period of Performance: 09/30/15-09/29/16
Award# 90DP0059-02-00
Annual Direct Cost: $435,935
This project consists of three overlapping studies focused on developing and implementing sustainable and effective approaches to improving health and function in people with spinal cord injury (SCI) and multiple sclerosis (MS).
Dr. Rimmer's effort on this project has increased. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Personalized Telehealth Weight Management System for Overweight Adults with Disability (Rimmer, PI)
.12 calendar months
National Institute of Diabetes and Digestive and Kidney Diseases
BrightOutcome Inc.
Dr. Dershung Yang
1110 Lake Cook Road Ste. 167
Buffalo Grove, IL 60089-1998 Performance Period: 5/20/13-4/30/16
Award# NIH 1R43DK097972-01
Annual Direct Cost: $73,504
The central goal of this project is to develop a personalized telehealth weight management system for overweight adults with spinal cord injury.
Dr. Rimmer's effort on this project has decreased. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

POWERSforID A Telehealth Weight Management System for Adults with ID (Rimmer, PI)
1.08 calendar months
Department of Health and Human Services
Univ. of Illinois at Chicago
Dr. Tamar Heller
436 Disability, Health, and Social Policy Building
1640 W. Roosevelt Road
Chicago, IL 60608-6904 Period of Performance: 09/30/15-09/29/16
Award# DHHS
Annual Direct Cost: $65,217
The aim of this study is to develop a customized physical activity, nutrition and behavioral intervention for obese adults with intellectual disability.
Dr. Rimmer's effort on this project has increased. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Quad-Rider Accessible Handcycle (Rimmer, Subcontract PI)
1.2 calendar months
National Institutes of Health
NIH
Invotek, Inc
Mr. Thomas Jacobs
1026 Riverview Drive
Alma, AR 72921-7780 Performance Period: 06/12/14-06/11/2016
Award# NIH 1R43HD080283-01

Annual Direct Cost: $45,057
This project will create a brake and derailleur gear-changing mechanism named Quad-Rider that enables individuals with limited hand function to safely operate a handcycle. InvoTek engineers will create four prototype Quad-Riders that enable riders with C5-C8 tetraplegia to safely propel, steer, and stop using arm, shoulder, and wrist musculature, which are still functionally intact at this level of SCI/D. The evaluation plan will ensure that the design is safe and effective for our target population, ensure that participants with C5-C8 SCI/D can safely operate Quad-Rider; and measure the health benefits to riders.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Jerzy Szaflarski, Investigator
FMRI of language recovery following stroke in adults
6.0 calendar
National Institutes of Health
Grants Officer: Donna James
NSC BG Rm. 3249
6001 Executive Blvd
Rockville, MD 20852
R01 NS048281 (Szaflarski)
08/01/2008-07/31/2014
$303,325
Abstract: This study focuses on evaluating trajectories of aphasia recovery after ischemic stroke using fMRI and neuropsychological measures of aphasia and on evaluating constraint-induced aphasia therapy as an intervention in patient with chronic aphasia after ischemic stroke.
Aim 1: In young and old adults we will map longitudinal changes in language activation patterns and determine language localization and lateralization using fMRI after LMCA stroke; Aim 2: In dextral and non-dextral LMCA stroke patients, we will map changes in language activation using fMRI, assess the differences in post-stroke language recovery between these groups, and determine whether non-dextral patients exhibit a) more symmetric or right-lateralized language distribution as compared to dextral patients, b) whether the changes in lateralization correlate with recovery from aphasia, and c) whether these patients activate additional language processing and production areas; Aim 3: We will demonstrate via a pilot study that CIAT administered 1 year after the incident stroke positively influences recovery of chronic aphasia after stroke when compared to traditional care.
This project has ended. Dr. Szaflarski is no longer committing any time to this project.

Post-stroke aphasia and rTMS treatment (PART) (Szaflarski, PI)
3.0 calendar months
National Institutes of Health
Grants Officer: Alesia Brody
BT 6100 Rm. 8A17C
6100 Executive Blvd
Rockville, MD 20852
Performance Period: 01/01/2012-12/30/2016
Annual Direct Cost: $319,473
Abstract: The goal of this study is to conduct randomized, blinded, sham controlled trial of excitatory rTMS for the treatment of post-stroke aphasia
Aim 1: To determine the comparative efficacy and optimal dosing of nerTMS on aphasia recovery using a randomized, double-blind, sham-controlled study design; Aim 2: To use fMRI to assess changes in language lateralization in response toner TMS; Aim 3: To explore the possible synergistic effect of constraint induced aphasia therapy (CIAT) plus nerTMS on aphasia recovery in a group of 20 LMCA stroke patients.
Calendar months have been reduced from 3.6 to 3. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Glutamate, brain connectivity and duration of untreated psychosis (Lahti, PI)
0.24 calendar months
National Institutes of Health
Performance Period: 04/01/2014-03/31/2019
Annual Direct Cost: $631,795
Role: Co-Investigator
The goals of this study are to evaluate neuroimaging biomarkers of treatment response in patients with new onset schizophrenia and untreated psychosis.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

The UAB Cannabidiol Program (Standaert, PI)
3.0 calendar months
Alabama Department of Commerce
Period of Performance: 04/01/2014-09/30/2016
Annual Direct Cost: $1,000,000/year
Role: Co-Investigator
The goal is to establish a program for cannabidiol treatment of seizures.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

Human Epilepsy Project (HEP) (Bebin, PI)
0.24 calendar months
Epilepsy Study Consortium
Period of Performance: 08/06/2013-08/05/2018
Annual Direct Cost: $211,300
Role: Subcontract Co-PI
The goal is to identify clinical characteristics and biomarkers predictive of disease outcome, progression, and treatment response in participants with new onset or recently diagnosed focal epilepsy.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

RNS System Post-Approval Study in Epilepsy (Szaflarski, PI)
0.24 calendar months
NeuroPace, Inc.
Period of Performance: 05/08/2015-05/17/2022
Direct Costs: $197,127
The primary objective is to follow patients prospectively over 5 years in the real-world environment to gather data on the long-term safety and effectiveness of the RNS System at qualified Comprehensive Epilepsy Centers by qualified neurologists, epileptologists, and neurosurgeons trained on the RNS System.
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

An Open-label Study to Evaluate the Safety, Efficacy, and Pharmacokinetics of SAGE-547 Injection as Adjunctive Therapy for the Treatment of Super-Refractory Status Epilepticus (Szaflarski, PI)
0.12 calendar months
Sage Therapeutics
Period of Performance: 03/26/2015-03/25/2018
Annual Direct Costs: $ 66,941
The primary objective is to evaluate the safety and tolerability of SAGE-547 Injection (SAGE-547) in subjects in super-refractory status epilepticus (SRSE)
This is a new project. There is no overlap. Participation in the project that is the subject of this report will not be impeded by this activity.

What other organizations were involved as partners?

Organization Name: Alabama Department of Veterans Affairs
Location of Organization: 1815 Cogswell Ave #132, Pell City, AL 35125
Partner's contribution to the project: Collaboration. This partner posted recruitment materials in all of their county offices.

Organization Name: UAB TBI Model Systems
Location of Organization: 529 Spain Rehabilitation Center,1717 6th Avenue South Birmingham, AL 35249-7330
Partner's contribution to the project: Collaboration. This partner mailed recruitment materials to candidates for this study to adults with TBI in their patient registry.

Organization Name: Alabama AHEC
Location of Organization: 930 20th Street South, Room 307, Birmingham, AL 35205
Partner's contribution to the project: Facilities. This partner permitted project staff to host a booth promoting our study at a community fair for veterans and the organizations that provide services to veterans in Birmingham, AL.

Organization Name: Greater Birmingham Republican Women
Location of Organization: P.O. Box 43922, Birmingham, AL 35243
Partner's contribution to the project: Other. This partner hosted a presentation about the project by the PI and Co-investigator Uswatte at their monthly meeting with the aim of galvanizing community resources to support the project.

8. SPECIAL REPORTING REQUIREMENTS

None.

9. APPENDICES

Appendix A. Revised Statement of Work

Appendix A

Revised Statement of Work

STATEMENT OF WORK – 10/26/2015
START DATE September 30, 2014

Site 1: University of Alabama at Birmingham (UAB)
1720 2nd Avenue South
Birmingham, AL 35294
PI: Edward Taub, PhD (ET)
Neuroimaging Supervisor: Jerzy Szaflarski, MD (JS)
Neuroimaging Supervisor: Jane Allendorfer, PhD (JA)
Recruitment, NP Testing Supervisor: Thomas Novack, PhD (TN)
Medical Director: Victor Mark, MD (VM)
Treatment and Testing Fidelity: David Morris, PT, PhD (DM)
Mental & Physical Fitness Training Supervisor: James Rimmer PhD (JaR)
Biostatistics Supervisor: Gary Cutter, PhD (GC)
Data Management Supervisor: Gitendra Uswatte, PhD (GU)
Employment and QOL Analysis: Stephen Mennemeyer, PhD (SM)

Site 2: Lakeshore Foundation (LF)
4000 Ridgeway Drive
Birmingham, AL 35209
Supervisor Housing OoT Participants: Jeff Underwood, MPA (JU)

Site 3: Richmond VAMC (RVAMC)
1201 Broad Rock Blvd
Richmond, VA 23224
Recruit. Director: Treven Pickett, PsyD (TP)

Site 4: Birmingham VAMC (BVAMC)
700 19th Street South
Birmingham, AL 35233
Recruit. Director: Marca Alexander, MD (MA)

Site 5: Denver VAMC (DVAMC)
1055 Clermont St, MIRECC
Denver, CO 80220
Recruit. Director: Lisa Brenner, PhD (LB)

Abbreviations: VAMC= Veterans Administration Medical Center; PI= Primary Investigator; NP= Neuropsychological; QOL=Quality of Life; OoT=Out-of-Town; CIMT= Constraint-Induced Movement therapy; LEFT= Lakeshore Enriched Fitness Training; TP=transfer package.

Study 1 Specific Aims: (1) To compare the effect of CIMT and LEFT on motor function, fitness & QOL in TBI patients; (2) To determine whether the initial clinical treatment effect, if any, persists over time; (3) To ascertain whether plastic brain changes accompany whatever clinical changes that may result from CIMT and LEFT, and whether the magnitude of the clinical and plastic brain changes are correlated; and (4) To evaluate the effects of CIMT and LEFT on return to work and quality of life on a preliminary basis.

Study 1 Specific Aims 1-4: (1) To compare the effect of CIMT and LEFT training on motor function in TBI patients; (2) To determine whether the initial clinical treatment effect, if any, persists over time; (3) To ascertain whether plastic brain changes accompany whatever clinical changes that may result from CIMT and LEFT, and whether the magnitude of the clinical and plastic brain changes are correlated; and (4) To evaluate the effects of CIMT and LEFT on return to work and quality of life on a preliminary basis.

Research Sites

	Timeline (Months)	**UAB**	**LF**	**RVAMC**	**BVAMC**	**DVAMC**
Major Task 1: Set-up Project						
Subtask 1: Prepare Regulatory Documents & Complete Setup						
Submit documents for HRPO* review	Pre	ET				
Submit documents for local IRB** review	Pre	ET	JU	TP	MA	LB
Submit amendments, adverse events and protocol deviations as needed	As Needed	ET	JU	TP	MA	LB
Coordinate with Sites for annual IRB report for continuing review	Annually	ET	JU	TP	MA	LB
Hire any personnel needed	1-2	ET/GU				
Set-up data collection system	1-2	GC/GU				
Milestones achieved: Local IRB approval & HRPO approval obtained	Pre	ET	JU	TP	MA	LB
Milestone achieved: All personnel on board, Data system set-up	2	ET	JU	TP	MA	LB

	Timeline (Months)	**UAB**	**LF**	**RVAMC**	**BVAMC**	**DVAMC**
Major Task 2: Conduct Study						
Subtask 1: Recruit, Screen, and Treat Participants						
Recruit 76 participants	1-36	ET/TN		TP	MA	LB
Screen all participants	1-36	VM/TN				
Treat first 11 participants with either CIMT or LEFT. Half in each group will get enhanced TP.	3-12	ET/DM/JaR/VM	JU			
Treat last 65 participants with either CIMT or LEFT. Half in each group will get enhanced TP.	13-36	ET/DM/JaR/VM	JU			
Milestones achieved: 76 participants recruited, screened, & treated	36	ET/DM/JaR/VM/ TN	JU	TP	MA	LB
Subtask 2: Test All Participants Before and After Treatment and 12-months Afterwards						
Conduct clinical tests to evaluate any change in motor function (Specific Aims 1 & 2)	3-48	GU/ET/DM/VM/ TN				
Conduct neuroimaging to examine potential neuroplastic change (Specific Aim 3)	3-48	JS/JA/VM/ET				
Conduct employment, QOL evaluation to test for expected improvements (Specific Aim 4)	3-48	SM/GU/ET				
Conduct neuropsychological tests to examine possible relationship between pre-existing conditions and treatment outcome (Secondary Aim)	3-48	TN/VM				
Milestone achieved: 76 participants tested	48	GU/ET/DM/VM/ TN/JS/JA/SM				

	Timeline (Months)	**UAB**	**LF**	**RVAMC**	**BVAMC**	**DVAMC**
Major Task 3: Process & Analyze Data						
Subtask 1: Process data on a blinded basis	3-48	GU/GC/JS/JA				
Milestone achieved: All data processed	48	GU/GC/JS/JA				
Subtask 2: Analyze data	37-48	GU/GC/JS/JA/SM				
Milestone achieved: All data analyzed	48	GU/GC/JS/JA/SM				
Major Task 4: Write-up & Disseminate Results and Procedures						
Subtask 1: Write-up Data for Presentation & Publication	37-48	ET				
Milestone achieved: Data written up	48	ET				
Subtask 2: Disseminate Results & Procedures	37-48	ET/DM/GU/VM				
Milestone achieved: Results & procedures disseminated	48	ET/DM/GU/VM				

This space has been left blank on purpose. The Statement of Work continues on the next page.

Projected Quarterly Enrollment

	Year 1				Year 2				Year 3****				Year 4			
Target Enrollment	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**
UAB***	0	1	5	5	6	9	9	9	6	9	9	8	0	0	0	0

** HRPO = Human Research Protection Office; review and approval by HRPO office of protocols involving human subjects is required of all DoD-funded awards.*

*** IRB = Institutional Review Board; committee formally designated to approve, monitor, and review human subjects research.*

****UAB is the only site at which participants will be enrolled and be treated and tested. The other sites will refer potential participants to UAB for screening and enrollment, if appropriate.*

*****All enrollment will be completed by end-Year 3; Year 4, which will be on a no-cost extension basis, is for follow-up and analysis and writing up of data for publication*