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TITLE: Control Network Neuromodulation to Enhance Cognitive Training in Complex Traumatic Brain Injury (The CONNECT-TBI Trial)

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CONTRACTING ORGANIZATION: University of New Mexico Albuquerque, NM

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14. ABSTRACT

The objective of this application is to conduct a clinical trial of APT-3 combined with targeted neuromodulation to treat cognitive control deficits in complex mTBI. Veterans and Servicemembers with mTBI and cognitive symptoms will be recruited from the New Mexico and Minneapolis VA Polytrauma clinics. Participants will undergo baseline demographic, neuropsychological, and quality of life testing, as well as resting/task-related fMRI. They will be randomized to 4 weeks of computer-based APT with concurrent rTMS, HD-tDCS, or sham stimulation delivered to the dorsolateral prefrontal cortex (DLPFC). Lastly, they will repeat all baseline tests, and report on 3- and 6-month recovery levels. Our central hypotheses are: (Aim 1) targeted neuromodulation applied to the DLPFC, when paired with APT-3, will facilitate the greatest improvement in cognitive control for the rTMS group (rTMS>HD-tDCS>sham); (Aim 2) these interventions will result in improvements in functional measures and quality of life; (Aim 3) fMRI will identify changes in CCN activation associated with cognitive control deficits and recovery.

15. SUBJECT TERMS

Traumatic brain injury; cognitive rehabiliation; transcranial direct current stimulation; transcranial magnetic stimulation

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TABLE OF CONTENTS

INTRODUCTION:

Our long-term goal is to develop safe, effective treatments for complex mild traumatic brain injury (mTBI) that improve functioning. Focal noninvasive neuromodulation such as high definition transcranial direct current stimulation (HD-tDCS) and repetitive transcranial magnetic stimulation (rTMS) have been found beneficial in small trials for attention, working memory, and postconcussive headaches after TBI. The objective of this application is to conduct a clinical trial of Attention Process Training (APT-3) combined with targeted neuromodulation to treat cognitive control deficits in complex mTBI. 108 Veterans and Servicemembers with mTBI and cognitive symptoms will be recruited from New Mexico and Minneapolis VA Polytrauma clinics. Participants will undergo baseline demographic, neuropsychological, and quality of life testing, as well as resting/task-related functional magnetic resonance imaging (fMRI). They will then be randomized to 4 weeks of computer-based APT with concurrent rTMS, HD-tDCS, or sham stimulation delivered to the dorsolateral prefrontal cortex (DLPFC), a primary node of the cognitive control network (CCN). Lastly, they will repeat all baseline tests, and report on 3- and 6-month recovery levels. Our central hypotheses are: (Aim 1) targeted neuromodulation applied to the DLPFC, when paired with APT-3, will facilitate the greatest improvement in cognitive control for the rTMS group (rTMS>HD-tDCS>sham); (Aim 2) these interventions will result in improvements in functional measures and quality of life; (Aim 3) fMRI will identify changes in CCN activation associated with cognitive control deficits and recovery.

1. KEYWORDS:

Traumatic brain injury, cognitive rehabilitation, transcranial direct current stimulation, transcranial magnetic stimulation, attention process training

2. ACCOMPLISHMENTS:

What were the major goals of the project?

	Timeline	% Completed
Major Task 1: Prepare Protocol for Submission and Approvals	(Mos.)	
Subtask 1: Prepare Regulatory Documents and Research Protocol		100%
Coordinate with Sites for Data Use Agreements (DUAs) clinical trial agreements (CTAs) submission, nondisclosure agreements (NDAs) a) The reliance agreement between the University of Minnesota and the University of New Mexico was fully executed on 10/05/2021. The UNM HSC IRB is currently onboarding the University of Minnesota as a participating site.	1-3	100%
Finalize eligibility, exclusions, screening, master consent and protocol a) Protocol and consent documents were drafted, vetted by all site investigators, finalized, and submitted, along with all other study materials, to each local IRB with oversight of the study activities, ie. Minneapolis VAHCS, New Mexico VAHCS, and University of New Mexico (overseeing Mind Research Network and University of Minnesota).	1-3	100%
Coordinate with Sites for local IRB submission/review a) UNM: Initial committee review by the UNM HSC HRRC occurred on 02/12/2021, with a follow-up review occurring on 04/16/2021. Final approval by the UNM HSC IRB was obtained on 04/29/2021. b) NMVAHCS: Initial IRB committee review by the NMVAHCS IRB occurred on 02/09/2021, with approval being granted on 04/02/2021. R&D committee review by the NMVAHCS ACOS/R&D committee occurred on 04/21/2021, with approval being granted on 05/17/2021. c) Minneapolis VAHCS: Initial committee review by the Minneapolis VAHCS IRB occurred 04/05/2021, with a follow-up committee review occurring on 05/03/2021. Initial IRB approval was granted on 05/06/2021. R&D committee review by the Minneapolis VAHCS ACOS/R&D committee occurred in late May, with approval being granted on 05/24/2021. d) U. Minnesota: The University of Minnesota submitted the study materials to their IRB in the third quarter, indicating the use of an external IRB. On 09/08/2021 the University of Minnesota Human Research Protection Program approved pursuing IRB review from an external IRB for this study.	1-3	100%
Coordinate with Sites for Military 2nd level IRB review (ORP/HRPO) a) DoD HRPO: Study documents were uploaded to the EBRAP system for the DoD HRPO second level review on 06/21/2021. The DoD HRPO granted initial approval of the study on 09/10/2021.	4-6	90%
Submit amendments, adverse events and protocol deviations as needed	As needed	100%
Coordinate with Sites for annual IRB report for continuing review	Annually	0%
Milestone Achieved: Local IRB and ORP/HRPO approval for all protocols.	6	95%
Major Task 2: Harmonize Sites and Establish Cores for MRCTN		
Subtask1: Hiring and Training of Study Staff a) NMVAHCS: Tiana Maple and Joann Harner were both hired as study staff and added to the IRB as study team members. b) U. Minnesota/Minneapolis VAHCS: Sloan Davidson, Rebecca Hiltner, and Alana Lieske were hired as study staff and added to the IRB as study team members.		95%

c) UNM/MRN: Cidney Robertson-Benta and Sharvani Reddy were added to the IRB as study team members. d) Data Safety Monitoring Board: DSMB members have been identified and confirmed: Dr. Jeremy Hogeveen (University of New Mexico), Dr. Kelvin Lim (University of Minnesota), and Dr. Madeleine Goodkind (New Mexico VAHCS). A DSMB charter has been finalized and approved by the UNM HSC IRB.		
Coordinate with Sites for job descriptions, advertising, interviewing	1-4	100%
Coordinate for space and equipment allocation for new staff	1-4	100%
Milestone Achieved: Research staff hired	4	95%
Subtask 2: Coordinate Study Initiation Visits #1 and #2, with in-person trainings for NRC Core Technicians and Coordinators a) Site initiation visit #1 was held on August 30th, 2021.	5-6	100%
Subtask 3: Conduct human phantom imaging tests, disseminate methods and scripts, create and test pipelines for data capture, storage, and analysis a) Human phantom studies were conducted on August 30th, 2021 during the Minneapolis site visit, and in Albuquerque over the month of September, 2021. b) Purchasing of equipment: All necessary and pending equipment purchases have been completed at all sites, including the StarStim 8 HD tDCS device, Attention Process Training (APT-3) materials, TMS and TDCS materials, computer analysis tools, and neuropsychological testing tools.	5-6	90%
Milestone Achieved: Trained and maintained Study Staff, equipment, and analytic tools throughout duration of clinical trial	6	90%
Major Task 3: Protocol Setup, Recruitment, Scanning, Assessments, Neuromodulation, Cognitive Training, Followup		
Subtask 1: Establish Protocol Structure		
Coordinate with Sites to map out all study steps, data collection, data transfer, and analytic tasks Analysis pipeline testing has taken place from August to October, 2021.	4-6	95%
Finalize screening tool, assessment measures, sequence of tests a) Testing battery was finalized at Site Initiation Visti #1 on August 30th, 2021.	1-6	100%
Milestone Achieved: 1st participant consented, screened and enrolled	6-36	0%
Subtask 2: Run Protocol, Submit Regular Reports	6-36	
Participants complete baseline testing (surveys, cognitive testing, fMRI)	6-36	0%
Participants complete intervention (training + sham/rTMS/HD-tDCS)	6-36	0%
Participants complete post-testing (surveys, cognitive testing, fMRI)	6-36	0%
Participants complete follow-up assessments (symptoms, quality of life, function surveys) 3, 6 months after completion of post-testing	12-36	0%
Submit quarterly safety reports to DSMB, scientific reports to CDMRP, annual continuing reviews to IRBs/HRPO	6-36	50%
Milestone Achieved: Met recruitment and protocol completion goals	34-36	15%
Major Task 4: Data Analysis, Dissemination, Uploading		
Subtask 1: Report all analyses according to specifications, share output and finding with all investigators	36-48	0%
Work with MRCTN team members to disseminate findings (abstracts, presentation, publications, DOD)	36-48	0%

Upload data to FITBIR for data sharing a) The process of FITBIR upload pipeline construction has been initiated with Rakib Zaman. Both the New Mexico and the Minnesota teams have experience with FITBIR upload processes from previous federally funded TBI grants. The sites participated in a training with Mr. Zaman in the second quarter. FITBIR account creation is pending necessary documentation and institutional approval. The study measures will be sent upon study account creation for data definition and validation.	36-40	0%
Milestone Achieved: Report results from data analyses	36-48	0%

What was accomplished under these goals?

1. Major Activities

a) **Administrative**: Investigator meetings occur virtually on Zoom teleconference platform on a weekly basis, with attention to the following:

1. Subawards: Subawards have been structured, finalized, and awarded for Year 1.

2. Protocol dissemination and IRB submission: Protocol and consent documents were drafted, vetted by all site investigators, finalized, and submitted, along with all other study materials, to each local IRB with oversight of the study activities, ie. Minneapolis VAHCS, New Mexico VAHCS, and University of New Mexico (overseeing Mind Research Network and University of Minnesota). Initial IRB committee review of the study documents by each IRB occurred in the second quarter.

    a. UNM: Initial committee review by the UNM HSC HRRC occurred on 02/12/2021, with a follow-up review occurring on 04/16/2021. Final approval by the UNM HSC IRB was obtained on 04/29/2021.

    b. NMVAHCS: Initial IRB committee review by the NMVAHCS IRB occurred on 02/09/2021, with approval being granted on 04/02/2021. R&D committee review by the NMVAHCS ACOS/R&D committee occurred on 04/21/2021, with approval being granted on 05/17/2021.

c. Minneapolis VAHCS: Initial committee review by the Minneapolis VAHCS IRB occurred 04/05/2021, with a follow-up committee review occurring on 05/03/2021. Initial IRB approval was granted on 05/06/2021. R&D committee review by the Minneapolis VAHCS ACOS/R&D committee occurred in late May, with approval being granted on 05/24/2021.

d. U. Minnesota: The University of Minnesota submitted the study materials to their IRB in the third quarter, indicating the use of an external IRB. On 09/08/2021 the University of Minnesota Human Research Protection Program approved pursuing IRB review from an external IRB for this study. The subsequent reliance agreement between the University of Minnesota and the University of New Mexico was fully executed on 10/05/2021. The UNM HSC IRB is currently onboarding the University of Minnesota as a participating site.

e. DoD HRPO: Study documents were uploaded to the EBRAP system for the DoD HRPO second level review on 06/21/2021. The DoD HRPO granted initial approval of the study on 09/10/2021. The Minneapolis VAHCS and New Mexico VAHCS sites are currently seeking local IRB approval for the DoD requested modifications to the protocol and consent documents. Once these modifications have been approved by the local VAHCS IRBs, the study materials with local context information will be submitted and reviewed by the DoD HRPO, at which point all necessary review/approval to begin recruitment and enrollment will be completed.

3. Purchasing of equipment: All necessary and pending equipment purchases have been completed at all sites, including the StarStim 8 HD tDCS device, Attention Process Training (APT-3) materials, TMS and TDCS materials, computer analysis tools, and neuropsychological testing tools.

4. FITBIR: The process of FITBIR upload pipeline construction has been initiated with Rakib Zaman. Both the New Mexico and the Minnesota teams have experience with FITBIR upload processes from previous federally funded TBI grants. The sites participated in a training with Mr. Zaman in the second quarter. FITBIR account creation is pending necessary documentation and institutional approval. The study measures will be sent upon study account creation for data definition and validation.

5. Data Safety Monitoring Board: DSMB members have been identified and confirmed: Dr. Jeremy Hogeveen (University of New Mexico), Dr. Kelvin Lim (University of Minnesota), and Dr. Madeleine Goodkind (New Mexico VAHCS). A DSMB charter has been finalized and approved by the UNM HSC IRB. The VA sites will submit the charter for review to their respective IRBs as a modification.

6. Site Initiation Visit: After significant delays due to COVID-19 travel restrictions, PI Quinn and UNM clinical research manager Cesar Ojeda were able to travel to Minneapolis from 08/30/2021 to 09/01/2021 for a site initiation visit with study collaborators at the University of Minnesota.

a. Imaging: During the visit, three human phantom scans of the study imaging protocol were conducted to compare imaging data collected at the Mind Research Network in Albuquerque for fidelity. The UMN study team provided a tour of the imaging resources at the Center for Magnetic Resonance Research.

b. Neuromodulation: Demonstrations of study protocols in Dr. Chen's Non-invasive Neuromodulation Lab at the UMN Department of Psychiatry were conducted. The study team conducted a trial/demonstration of the digitization of electrode placement for the tDCS arm of the study protocol with imaging data collected the previous day. The visit served as an opportunity to compare neuromodulation equipment and accessories as well.

c. Assessment: The visit concluded with a tour of the Minneapolis VA and detailed discussion of the study assessments, where the study team was able to determine the final battery components.

b) **Personnel**:

1. NMVAHCS: Tiana Maple and Joann Harner were both hired as study staff and added to the IRB as study team members. A third personnel is currently in the process of being hired.

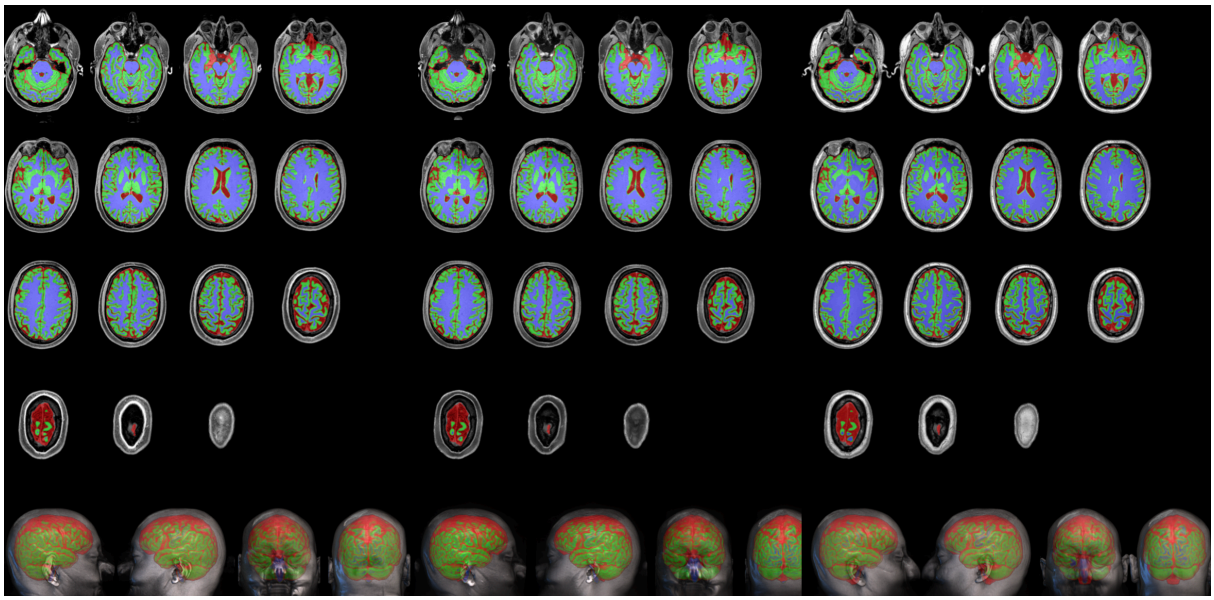
2. U. Minnesota/Minneapolis VAHCS: Sloan Davidson, Rebecca Hiltner, and Alana Lieske were hired as study staff and added to the IRB as study team members.

3. UNM/MRN: Cidney Robertson-Benta and Sharvani Reddy were added to the IRB as study team members.

4. All key personnel, site PIs, and collaborators have completed necessary trainings and certifications to perform study tasks, including CITI, HIPAA, and FCOI certifications, MRI performance and safety training.

5. Certifications: All study staff have been granted access to study databases such as COINS. Study staff are currently completing brain stimulation performance and safety training, and neuropsychological testing, assessment, and rehabilitation task training.

c) **Scientific**: Our study team has been productive with regard to generating preliminary data and harmonization of study protocol methods.



Segmentation Dice Coefficients

$$D = \frac{3|A \,\&\, B \,\&\, C|}{|A| + |B| + |C|}$$

$$D_{\{subset\}} = \frac{2|A \,\&\, B\,|}{|A| + |B|}$$

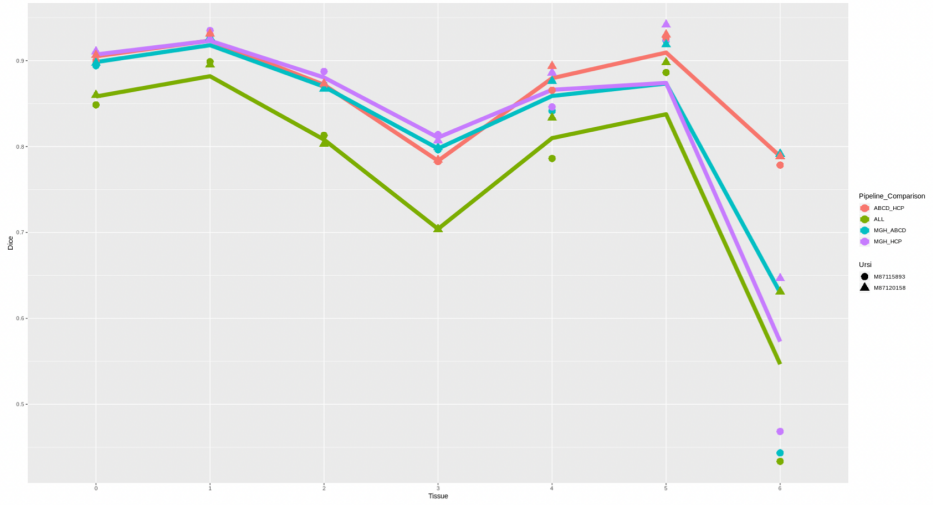


Figure 1. Top: Segmentation of a human phantom scan into scalp, skull, CSF, white matter, and grey matter using the three candidate image sequences (left: ABCD; center: HCP; right: MGH). Bottom: analysis of the DICE coefficients for different tissue layers between the candidate image sequences.

1. Image Sequence Testing and Selection: A series of computational modeling experiments were conducted on pilot healthy controls with three different imaging sequence protocols. Results of these tests were used to inform the selection of the final imaging sequences to use for both modeling of electric current as well as assessment of post-intervention brain changes. A standard operating procedure (SOP) manual for imaging has been created and revised.

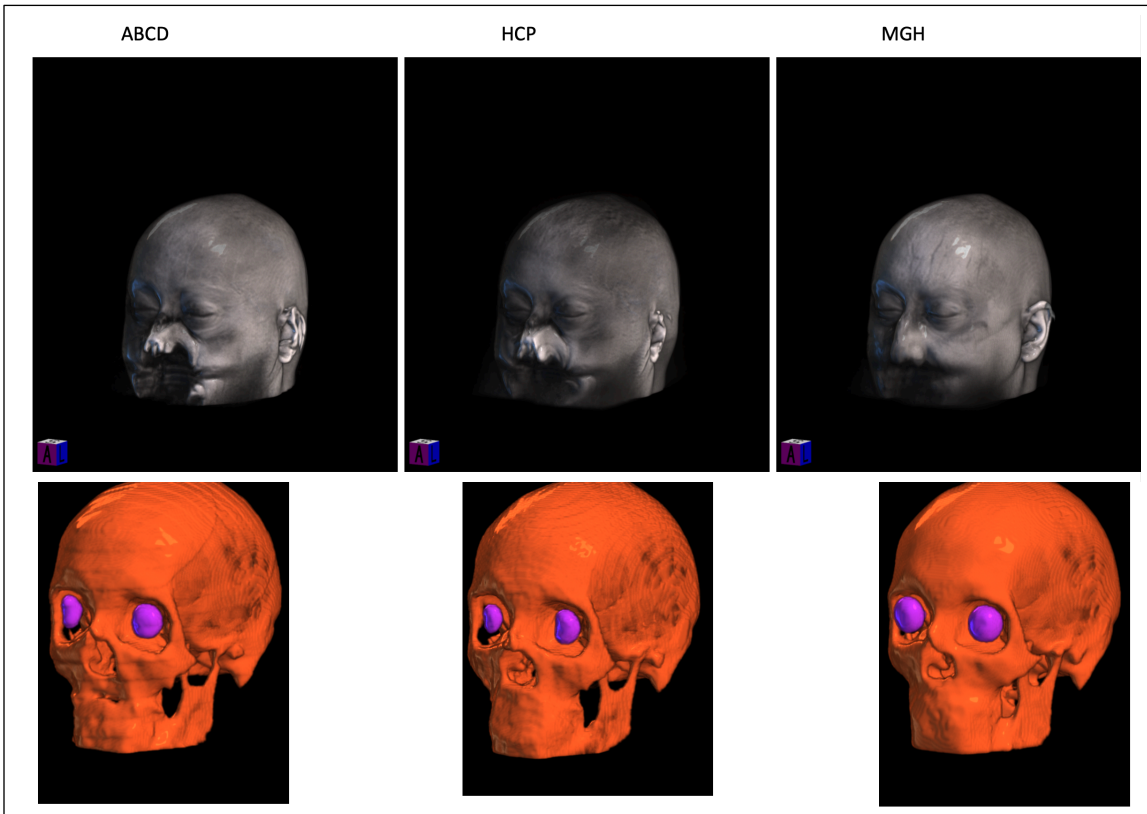


Figure 2. Top: 3D reconstruction of head with different scan sequences (left: ABCD; center: HCP; right: MGH). Bottom: skull layer reconstruction.

2. Imaging Harmonization: At the site initiation visit at U. Minnesota as well as through work with study staff at MRN, 2 complete sets of imaging data were obtained on human phantoms at both sites. Quality control checks were performed on the sequences to ensure identical settings of scanners. The images were analyzed independently by both the Minneapolis and Albuquerque data analysis teams, to ensure that identical behavioral and imaging results were produced by each site when given identical data to analyze.

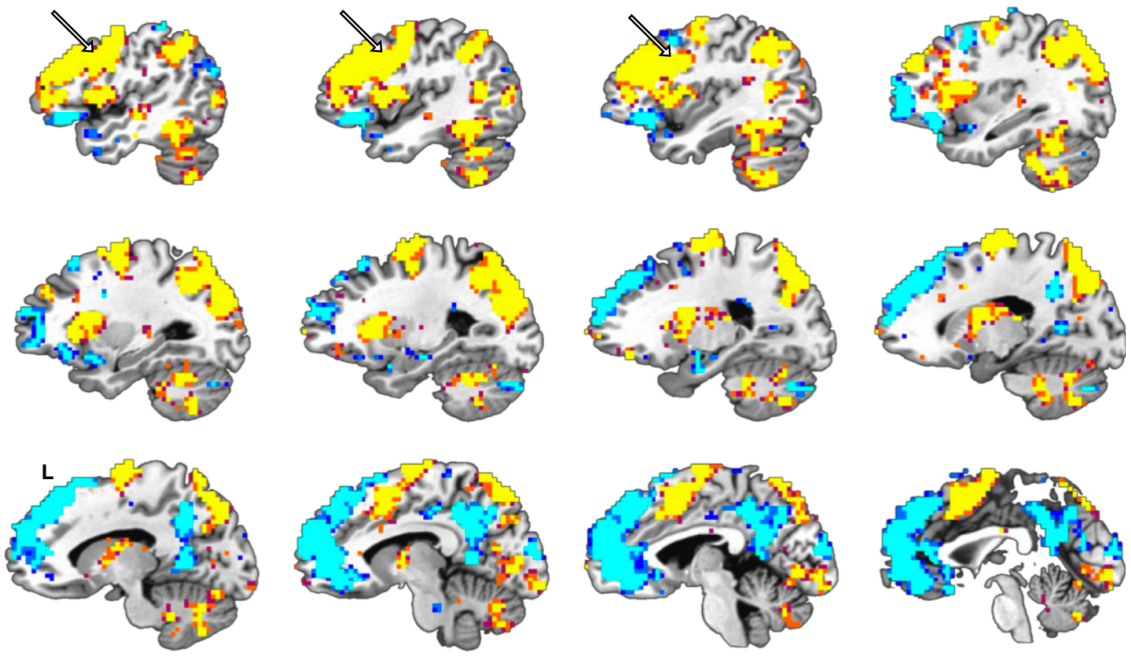


Figure 3. Blood oxygen level-dependent signal (BOLD) in a single human pilot subject using the multimodal attention task developed by Co-I Mayer to target brain stimulation. The arrow indicates the point of maximal signal to which stimulation would be directed.

3. Analytic Pipeline Construction and Testing: The Imaging and Assessment Core data analysis teams at both Minneapolis and Albuquerque collaborated to construct the computational pipeline to preprocess the structural and functional imaging data and analyze the individual BOLD signal activations in the region of interest for each subject for local maxima. The Core then created a virtual container for processing of imaging data to identify the DLPFC target, so that the study teams in both sites will be sure to conduct identical processing using identical scripts.

4. Modeling Pipeline Construction and Testing: A second virtual container was constructed to house the code that was written to conduct finite element modeling of electrical current density in the brain for the TDCS arm and determine the optimal placement of electrodes. Determination of this process involved testing and comparing several programs, troubleshooting compatibility and replicability issues, and the Minnesota team has successfully replicated the results of the New Mexico team on updated computers. Next step validation will be conducted on the 2 data sets that were obtained at the 2 sites.

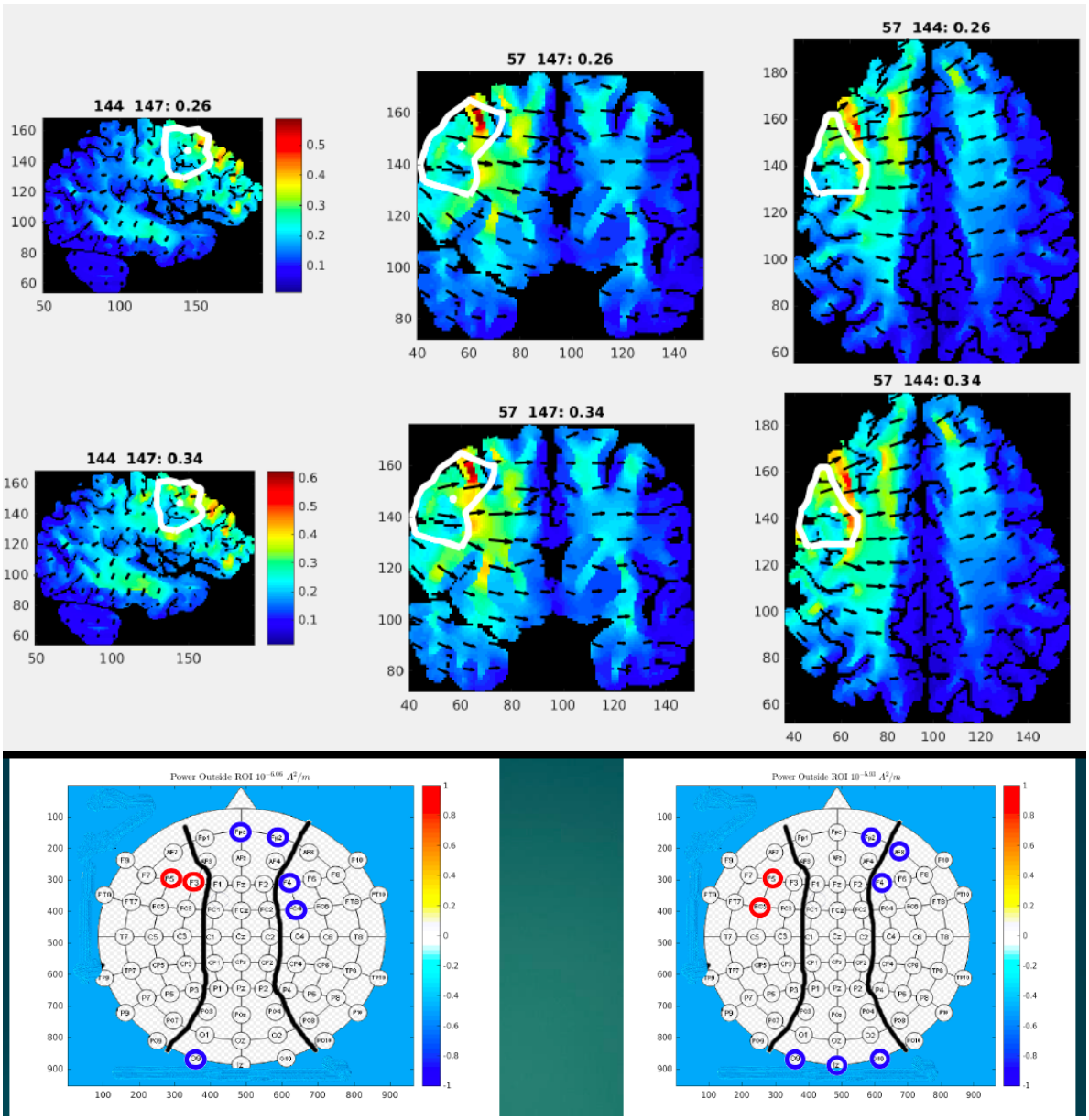


Figure 4. Comparison of the possible modeling optimization algorithms (automated electrode placement vs subject-specific methods), demonstrating differential maximum electric current density in the region of interest (white outline) and differential electrode placements.

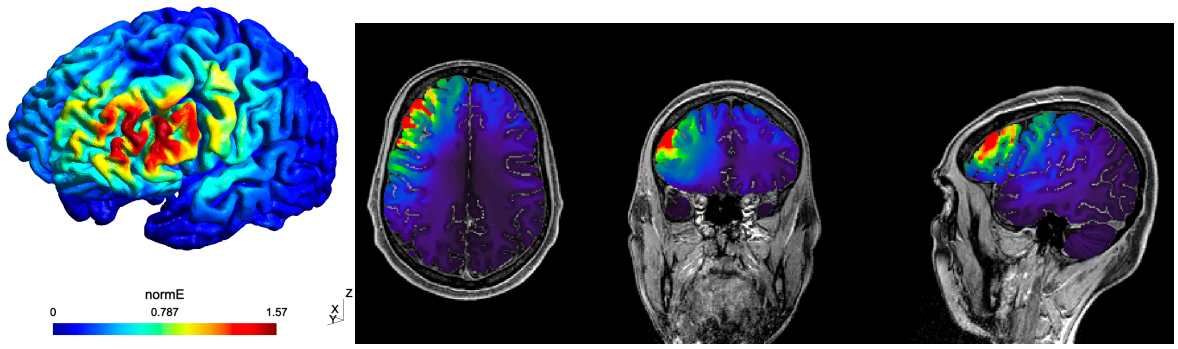
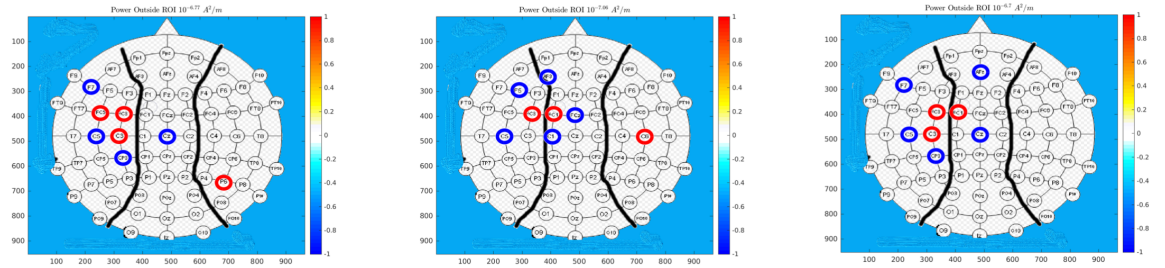


Figure 5. Modeled induced electric field density of TMS in the left DLPFC of a human phantom subject, using the ABCD imaging protocol and SIMNIBS software.



FC3	1mA
FC5	0.46 mA
C3	0.49mA
C5	-0.52 mA
Cz	-0.62 mA
F7	-0.47 mA
CP3	-0.39 mA
P6	0.05 mA

FC3	1mA
FC1	0.97 mA
CP3	-0.89mA
C5	-0.4 mA
C1	-0.53 mA
F5	-0.2 mA
AF3	-0.22 mA
C6	0.03 mA

FC3	1mA
C3	0.64mA
FC1	0.36mA
CP3	-0.66 mA
Cz	-0.46 mA
C5	-0.34 mA
F7	-0.33 mA
AFz	-0.21 mA

Figure 6. Stimulation solutions for HD-tDCS generated by the SIMNIBS pipeline using structural and functional data obtained from a human phantom with the three different image sequences (left: ABCD; center: HCP; right: MGH).

5. Attention Process Training Standardization: The APT-3 is a manualized, computerized form of cognitive rehabilitation that is designed to be delivered at an optimal level of difficulty for each patient, through individualized components. Our team has constructed an algorithm based on prior studies using the APT-3 to allow for adjustment of the difficulty and speed of the training tasks, but within certain parameters, in order to achieve the best balance between variability and consistency. A standard operating procedure manual was created, so as to harmonize the administration of this component of the intervention across sites.

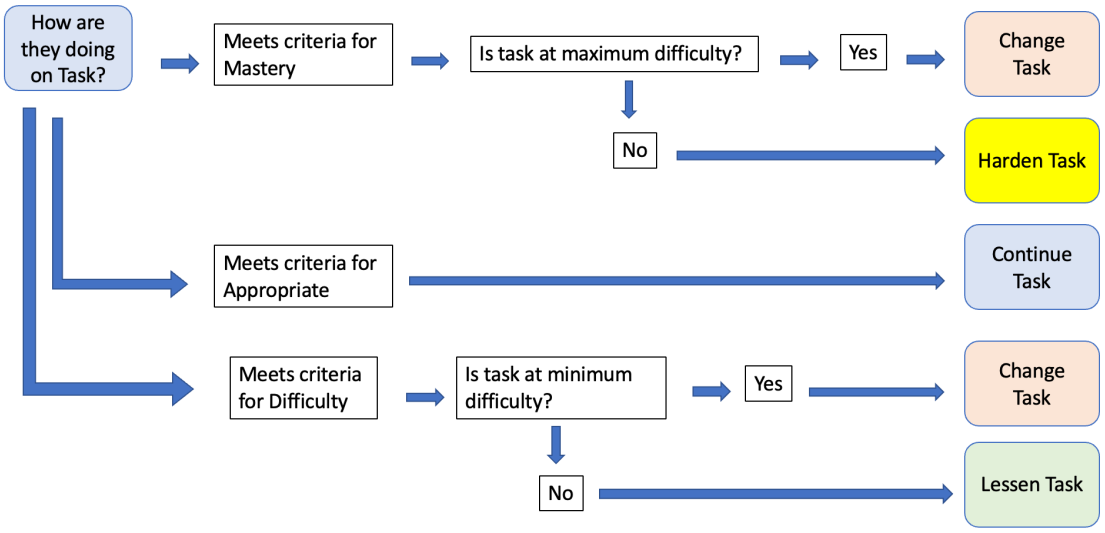


Figure 7. Attention Process Training algorithm as recommended by user manual and speech language pathologist input.

6. Data Collection and Curation: All study data collection tools including surveys, instruments, and interviews were constructed by the New Mexico team in the COINS database, and training and certification in use of COINS was performed by all Minneapolis team members. A single data collection database can now be used at both sites for demographic, history, and symptom data. Training in the various assessments is now ongoing on a biweekly basis.

2. Specific Objectives

CONNECT-TBI is a randomized, double-blinded, sham-controlled clinical trial of neuromodulation to accelerate cognitive training in military mTBI. There are three treatment arms: 36 patients will receive rTMS + training; 36 patients will receive HD-tDCS + training; and 36 patients will receive sham + training. As outlined above, the specific objectives of the study are:

Aim 1 (HD-tDCS): To assess the efficacy of APT-3 combined with HD-tDCS to improve subjective PCS, objective cognitive control, and quality of life in Veterans and Active Duty Personnel with complex TBI.

Aim 2 (rTMS): To assess the efficacy of APT-3 combined with rTMS to improve subjective PCS, objective cognitive control, and quality of life in Veterans and Active Duty Personnel with complex TBI.

Aim 3 (Imaging): To identify baseline characteristics and longitudinal changes in activity within the CCN that correlate with clinical recovery and predict response to the interventions.

3. Significant Results or Key Outcomes

Nothing to Report.

4. Other Achievements

Nothing to Report.

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

Nothing to Report.

How were the results disseminated to communities of interest?

Nothing to Report.

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

In the next reporting period, the following activities will take place:

a) Recruitment: Flyers, advertisements, and letters to clinicians will be distributed to the staff at the Minneapolis VAHCS and NMVAHCS. Informational sessions will be held to describe the study, answer questions, and provide information about how to refer subjects.
b) Protocol: The study protocol will begin, and the first subjects will be screened, consented, and enrolled. Standard Operating Procedures will be reviewed and adjusted based on feedback from study staff.
c) Data Quality Assurance: As data is collected, the study team and its Cores will meet regularly to ensure that data being collected is in the appropriate form and is usable.
d) Regulatory: Continuing Review, Audit Compliance, and reporting of anticipated and unanticipated adverse events will occur as needed and as directed by the IRBs overseeing the study.

3. IMPACT:

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

Nothing to Report

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

4. **CHANGES/PROBLEMS:**

Changes in approach and reasons for change

Nothing to Report

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

Three main challenges occurred in the past year that significantly delayed study start-up activities:

1) Due to the ongoing COVID-19 pandemic and travel restrictions imposed on faculty and staff in Minneapolis and Albuquerque throughout the past year, site initiation visit was delayed until the fourth quarter of the reporting period. As a result, the harmonization activities were not able to be carried out until August 30th. Three human phantom studies were conducted, and two of the phantoms were re-scanned in Albuquerque after the visit. As a result of the comparison of the scan results, important decisions and adjustments were able to be made to the scan protocol, including how to position subjects within the scanner and which settings to select for optimal image acquisition. We now have a high degree of confidence the imaging data obtained has been harmonized to the degree possible. The imaging sequences have been finalized, and the analytic studies of the image processing and modeling using the code devised by the study team are now being carried out to ensure identical results are derived when each site performs them with the same data.

2) In addition to the imaging harmonization, during the site visit the study team also reviewed and examined the neuromodulation equipment at Minneapolis to ensure the intervention procedures could be carried out, and whether there needs to be site specific changes to the protocol to account for the different brands of transcranial magnetic stimulators. During the visit it was discovered that the current Magstim TMS (in Minneapolis) is not able to achieve the same maximum intensity of stimulation with the protocol as the Magventure TMS (in Albuquerque). While this is only a potential issue for subjects with abnormally high motor thresholds, the study team has corresponded with the two device companies, and has arrived at a solution to obtain a more powerful stimulator from Magstim for the Minneapolis site. As Co-I Chen has maintained a close working relationship with the Magstim manufacturer for many years, the module will arrive within a few weeks and will not have negative impact on the subaward budget due to support from the institution.

3) Regulatory delays: Initial IRB submissions were delayed due to difficulty in determining whether a Single IRB arrangement would be possible for the involved study sites. It was finally determined in 11/2020 that the most expeditious model going forward would be a hybrid model, with some institutions (MRN, U. New Mexico, U. Minnesota) relying on a Single IRB (UNM), and the other institutions (New Mexico VA, Minneapolis VA) would use their own IRBs. Initial IRB reviews took longer than anticipated, with each site's IRB requesting modifications to the study materials. This resulted in several committee reviews of the submission materials at each site, particularly at U. New Mexico. Once initial approvals by the local IRBs involved were obtained, the U. Minnesota was able to submit the study materials to their IRB indicating the use of an external IRB (U. New Mexico). It wasn't until the UMN review was completed that The U. New Mexico and U. Minnesota were able to execute the necessary reliance agreement for this model of regulatory oversight. The required review of the reliance documentation by each institution's research leadership took longer than expected. The DoD second level review took place in the fourth quarter of the reporting period. The DoD requested modifications to the study materials had to be submitted to the local site IRBs for approval before being sent back to the DoD for final approval. This multi-layer process of reviews took longer than expected. The VA site IRBs are currently reviewing the DoD requested modifications, local approval is expected this month, with DoD approval quickly following soon after.

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

5. PRODUCTS:

- **Publications, conference papers, and presentations**
  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

6. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name	**Davin Quinn, MD**
Project Role	Coordinating PI (New Mexico), AOC Co-Director
Research Identifier	**0000-0002-1613-8018**
Nearest person month worked	**12**
Contribution to Project	Dr. Quinn is a Neuropsychiatrist at the University of New Mexico. With Dr. Nicholas Davenport, he is Co-Director of the Administration and Oversight Core, and runs meetings and conference calls, and assists the site PIs and Core Co-Directors in oversight and training of study staff. Dr. Quinn with Dr. Davenport oversees the creation and management of regulatory binders, written updates, progress reports,

	data safety and monitoring reports, and random audits of the research data performed by the USAMRMC Human Research Protection Office, and maintains compliance with the IRBs of record for the study.

Name	**Nicholas Davenport, PhD**
Project Role	Co-PI (Minnesota), AOC Co-Director
Research Identifier	
Nearest person month worked	**12**
Contribution to Project	As the Minneapolis site PI, Dr. Davenport will be responsible for carrying out the study tasks at UM/MAVHCS, and will coordinate closely with Dr. Quinn and collaborators regarding protocol harmonization, IRB submission, data management, and results dissemination. With Dr. Quinn, he will co-direct the Administration and Oversight Core (AOC).

Name	**Andrew Mayer, PhD**
Project Role	Co-PI, IAC Co-Director (New Mexico)
Research Identifier	
Nearest person month worked	**12**
Contribution to Project	Dr. Mayer is the Director of Trauma and En-route Care, as well as a Professor of Translational Neuroscience at The Mind Research Network (MRN) and an Adjunct Professor of Neurology at the University of New Mexico. He will assist in the development of the study and will be involved in all aspects of the neuropsychological and imaging components, including data quality assurance and analysis of data. He will work with Drs. Quinn, Pirio Richardson, Davenport, Chen, and Sponheim, to interpret results of MRI in relation to cognition, attention processing performance and behavioral data. He will serve as the co-Director of the Imaging and Assessment Core (IAC), along with Dr. Sponheim, and will provide oversight and leadership in the harmonization and consistency of the multi-site imaging component of the protocol.

Name	**Scott Sponheim, PhD**
Project Role	Co-I, IAC Co-Director (Minnesota)

Research Identifier	
Nearest person month worked	**12**
Contribution to Project	Dr. Sponheim is a Professor of Psychiatry at the University of Minnesota, and a Staff Psychologist at the Minneapolis VAHCS. He will provide input on the recruitment, imaging, and neuropsychological testing components of the planned clinical trial. He will co-direct, with Dr. Mayer, the Imaging and Assessment Core (IAC).

Name	**Sarah Pirio Richardson, MD**
Project Role	Co-PI, NRC Co-Director (New Mexico)
Research Identifier	
Nearest person month worked	**12**
Contribution to Project	Dr. Pirio Richardson is a Neurologist and an Attending Physician in the Neurology Section at the New Mexico VAHCS. She will provide expertise on harmonization of stimulation techniques, safety and individualization of stimulation, and clinical trial design and management. Along with Dr. Mo Chen, Dr. Pirio Richardson will be co-Director of the Neuromodulation and Rehabilitation Core (NRC).

Name	**Mo Chen, PhD**
Project Role	Co-Investigator, NRC Co-Director
Research Identifier	
Nearest person month worked	**12**
Contribution to Project	Dr. Chen is a Research Scientist in the University of Minnesota Department of Psychiatry, and Manager of the Noninvasive Neuromodulation Laboratories. He will contribute his expertise in neuromodulation methods and safety, as well as inform the targeting of cognitive control networks with rTMS. With Dr. Pirio Richardson, he will co-direct the Neuromodulation and Rehabilitation Core (NRC).

Name	**Orrin Myers, PhD.**
Project Role	Biostatistician

Research Identifier	
Nearest person month worked	**12**
Contribution to Project	Dr. Myers is the Director of Biostatistics in Department of Family and Community Medicine and a faculty member in the Biostatistics, Epidemiology and Research Design Core of the UNM Clinical and Translational Sciences Center. He will provide biostatistical consultation and input for the CONNECT-TBI MRCTN, including for study design and sample size calculations, data analysis approaches and safety monitoring. He will coordinate closely with Drs. Quinn and Davenport as a member of the Administration and Oversight Core, as well as with Drs. Mayer and Sponheim as a member of the Imaging and Assessment Core.

Name	**Cesar Ojeda, MBA**
Project Role	Clinical Program Manager
Research Identifier	
Nearest person month worked	**12**
Contribution to Project	Mr. Ojeda, as the Clinical Research Manager (CRM), will assist the AOC Co-Directors Drs. Quinn and Davenport in ensuring site integration and harmonization. Weekly AOC meetings run by the CRM will review each component of the study, discussing updates, modifications, protocol deviations or violations, expected and unexpected study-related events, regulatory reporting, recruitment, and data capture. Monthly meetings with all six Core Co-Directors and all study staff will review each of these components, as well as data analysis updates and plans for dissemination, presentations, and publications.

Name	**Elijah Lahud**
Project Role	Study Coordinator (Minnesota)
Research Identifier	
Nearest person month worked	**9**
Contribution to Project	As the site study coordinator, Mr. Lahud is responsible for regulatory submissions and reporting, personnel management, participant payments, recruitment, consenting, and coordination between the Minnesota and New Mexico teams.

Name	**Joann Harnar**
Project Role	Study Coordinator (New Mexico Va)
Research Identifier	
Nearest person month worked	**9**
Contribution to Project	As the site study coordinator, Ms. Harnar is responsible for regulatory submissions and reporting, personnel management, participant payments, recruitment, consenting, and coordination between the New Mexico and Minnesota teams.

Name	**Sloan Davidson, MS**
Project Role	Study Coordinator (U. Minnesota)
Research Identifier	
Nearest person month worked	**9**
Contribution to Project	As the site study coordinator, Ms. Davidson is responsible for regulatory submissions and reporting, personnel management, participant payments, recruitment, consenting, and coordination between the New Mexico and Minnesota teams.

Name	**Rebecca Hiltner**
Project Role	Recruitment Coordinator (U. Minnesota)
Research Identifier	
Nearest person month worked	**9**
Contribution to Project	As the recruitment coordinator, Ms. Hiltner is responsible for coordinating recruitment efforts at the UMN site. This will entail creation/dissemination of recruitment materials, acting as liaison/point of contact for patient referrals between the UMN site and the Minn. VAHCS, screening potential subjects, tracking all recruitment efforts, and coordination between the New Mexico and Minnesota teams.

Name	**Alana Lieske**
Project Role	Research Assistant (U. Minnesota)

Research Identifier	
Nearest person month worked	**4**
Contribution to Project	As a research assistant, Ms. Lieske is responsible for the administration of the study interventions at the University of Minnesota, including TMS, tDCS, and APT. Ms. Lieske will assist Dr. Chen in his lab with all parts of the neuromodulation component of the research protocol. Ms. Lieske will also provide comprehensive training to the study team on the StarStim 8 HD tDCS device.

Name	**Tiana Maple**
Project Role	Study Coordinator (New Mexico VAHCS)
Research Identifier	
Nearest person month worked	**3**
Contribution to Project	As the study coordinator, Ms. Maple is responsible for the administration of the study interventions at the New Mexico VAHCS, including TMS, tDCS, and APT. Ms. Maple will assist Dr. Pirio Richardson in her lab with all parts of the neuromodulation component of the research protocol.

Name	**Cidney Robertson-Benta**
Project Role	Study Technician (MRN)
Research Identifier	
Nearest person month worked	**1**
Contribution to Project	As a study technicia, Ms. Robertson-Benta is responsible for the administration of the study interventions at the MRN, including consent, baseline demographic, symptom, and cognitive assessment, and MRI.

Name	**Sharvani Reddy**
Project Role	Study Technician (MRN)
Research Identifier	

Nearest person month worked	**1**
Contribution to Project	As a study technician, Ms. Reddy is responsible for the administration of the study interventions at the MRN, including consent, baseline demographic, symptom, and cognitive assessment, and MRI.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

The only change to the active other support of PI Quinn is an increase, for involvement as Co-Investigator for "Multimodal Imaging of Neuropsychiatric Disorders (MIND)," PI: Mayer AR. FTE: 0.05/0.6 calendar months. Role: administrative core member.

For Co-PI Mayer, the only change to his active other support is an increase, for involvement as Co-Investigator for "Healthy Brain and Child Development (HBCD) Study", PI: Bakhireva L. FTE: 0.10/1.2 calendar months. Role: imaging core director.

For Co-PIs Pirio Richardson and Davenport, and Co-Is Chen and Sponheim there have been no significant changes to their active other support.

What other organizations were involved as partners?

Organization Name	**University of New Mexico Health Sciences Center**
Location of Organization	Albuquerque, New Mexico, USA
Partner's Contribution to Project	Financial support; in-kind support; facilities; collaboration.

Organization Name	**University of Minnesota**
Location of Organization	Minneapolis, Minnesota, USA
Partner's Contribution to Project	Financial support; in-kind support; facilities; collaboration.

Organization Name	**Mind Research Network**
Location of Organization	Albuquerque, New Mexico, USA
Partner's Contribution to Project	Financial support; in-kind support; facilities; collaboration.

Organization Name	**New Mexico VA Health Care System**
Location of Organization	Albuquerque, New Mexico, USA
Partner's Contribution to Project	Financial support; in-kind support; facilities; collaboration.

Organization Name	**Minneapolis VA Health Care System**
Location of Organization	Minneapolis, Minnesota, USA
Partner's Contribution to Project	Financial support; in-kind support; facilities; collaboration.

7. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

8. APPENDICES: