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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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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 rehabilitation; transcranial direct current stimulation; transcranial magnetic stimulation

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Contents

1. Accomplishments

	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)	1-3	100%
Finalize eligibility, exclusions, screening, master consent and protocol	1-3	100%
Coordinate with Sites for local IRB submission/review	1-3	100%
Coordinate with Sites for Military 2nd level IRB review (ORP/HRPO)	4-6	100%
Submit amendments, adverse events and protocol deviations as needed	As needed	100%
Coordinate with Sites for annual IRB report for continuing review	Annually	100%
Milestone Achieved: Local IRB and ORP/HRPO approval for all protocols.	6	100%
Major Task 2: Harmonize Sites and Establish Cores for MRCTN		
Subtask1: Hiring and Training of Study Staff		100%
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	100%
Subtask 2: Coordinate Study Initiation Visits #1 and #2, with in-person trainings for NRC Core Technicians and Coordinators	5-6	100%
Subtask 3: Conduct human phantom imaging tests, disseminate methods and scripts, create and test pipelines for data capture, storage, and analysis	5-6	100%
Milestone Achieved: Trained and maintained Study Staff, equipment, and analytic tools throughout duration of clinical trial	6	100%
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	4-6	100%
Finalize screening tool, assessment measures, sequence of tests	1-6	100%
Milestone Achieved: 1st participant consented, screened and enrolled	6-36	100%
Subtask 2: Run Protocol, Submit Regular Reports	6-36	
Participants complete baseline testing (surveys, cognitive testing, fMRI)	6-36	24%
Participants complete intervention (training + sham/rTMS/HD-tDCS)	6-36	20%
Participants complete post-testing (surveys, cognitive testing, fMRI)	6-36	19%
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	100%
Milestone Achieved: Met recruitment and protocol completion goals	34-36	24%
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	36-40	0%
Milestone Achieved: Report results from data analyses	36-48	0%

1.1 Major Activities

1.1.1 Administrative: All-Investigator meetings and Core meetings occur virtually on Zoom teleconference platform on a weekly basis, with attention to the following:

A) Budgetary: Subawards were structured, finalized, and awarded in Year 3. There were no significant changes to subawards. A no-cost extension was requested to continue data collection for an additional year and was granted in September 2023.

B) Protocol and Consent modifications and IRB submissions: Protocol and consent documents for each site have undergone several modifications to add study team members, and make minor amendations to inclusion and exclusion criteria in order to improve enrollment rates of study participants without sacrificing scientific integrity. Each of these modifications was drafted with vetting by the Administration and Oversight Core (AOC), approved by all site investigators, and submitted along with all other relevant 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).

C) Testing, quality assurance, and maintenance of equipment: TMS equipment operated without issue at both NMVAHCS and University of Minnesota sites. The StarStim 8 HD tDCS device at University of Minnesota was found to have a minor malfunction with its Bluetooth connection, and was recommended to be replaced by the device manufacturer. The MRI scanner at UNM/MRN underwent a software upgrade recommended by the device manufacturer, which resulted in significant delays in administering the protocol due to unforeseen operational difficulties with the new software.

D) FITBIR: The process of FITBIR upload pipeline construction has been continued with Rakib Zaman and the CONNECT study coordinator.

E) Data Safety Monitoring Board: The DSMB continued to meet throughout the year on a quarterly schedule, with discussion of adverse events, safety monitoring procedures, and methods to present safety data in the DSMB report. The CONNECT study statistician Dr. Orrin Myers and the Study Coordinator delivered all Closed Session reports to the DSMB. The DSMB reviewed all prepared reports at each meeting and approved the continued performance of the study.

F) Recruitment and retention: Recruitment of participants was overall successful, with the volume of qualified participants identified, screened, and enrolled at both sites meeting goal rates with use of recruitment methods described in previous reports. However, turnover of staff at both sites resulted in delays to provide necessary training and certification in study procedures for newly hired staff.

1.1.2 Personnel:

A. NMVAHCS: Tiana Maple

B. U. Minnesota/Minneapolis VAHCS: Ciara Allen, Kayla Edmundson, Alana Lieske Mia Kellman and Cassie Nelson

C. UNM/MRN: Lindsay Worth, Jessica McQuaid, Samuel Miller, Upasana Nathaniel

D. Trainings: 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.

E. Certifications: All study staff have been granted access to necessary study databases such as COINS. Study staff are all trained in brain stimulation performance and safety training, neuropsychological testing, assessment, and rehabilitation task training.

1.1.3 Scientific:

A) In the first year of performance for CONNECT-TBI, scientific advancements were predominantly centered around standardization and harmonization of site imaging protocols, targeting pipelines, and stimulation parameters. In the second year of performance, optimization of different intervention components was accomplished while the first set of participants were administered the protocol. This included refinement of the targeting pipeline and management of outliers, as well as fine-tuning the individualization algorithm for APT-3, which had never been described before. In this third year of performance, we generated preliminary blinded data on side effects, behavioral and cognitive benefits, and neuroimaging changes associated with the intervention, in particular the APT-3 component. Several posters presenting preliminary data on the APT-3 individualization algorithm, side effect profiles, neuropsychological outcomes, and neuroimaging outcomes of CONNECT-TBI were presented at regional conferences and the 2022 MHSRS conference in Orlando, FL.

Abstract #1: With regard to the APT-3 individualization algorithm, our study team recognized early on that a reproducible procedure for selecting tasks and adjusting their difficulty up or down was needed, in order to ensure that the APT-3 was being delivered at the optimum difficulty level for each participant's cognitive capabilities. Therefore, we operationalized the APT-3 adjustment rules and created if-then contingencies based on accuracy, perceived effort, boredom, and non-progression. We adapted and standardized metacognitive strategy sessions and created session tracking sheets and instructional videos. Graphs of participant progress over 16 APT-3 sessions demonstrate expected variability in individualized pathways.

Abstract #2: With regard to side effects, preliminary results from CONNECT-TBI indicate that side effects with tDCS and rTMS are common but overwhelmingly mild, indicating that both types of brain stimulation are tolerable and feasible in a Veteran polytrauma population. There is variability between participants with regard to reported side effect burden, with baseline mBIAS score (indicating greater implausible somatic complaints) correlating positively with reported number of side effects. However, even low mBIAS-scoring Veterans with mTBI reported numerous side effects, confirming this as an expected part of the experience of receiving noninvasive neuromodulation.

Abstract #3: With regard to neuropsychological outcomes, cognitive and behavioral outcomes were assessed before and after 16 sessions of Attention Process Training-3. Scores on the Digit Span were significantly improved after 1 month, with specific improvements in Sequencing and Digit Span Forward, indicating that APT-3 is effective for rehabilitating executive functions. However, improved Digit Span Total and Backward performance were associated with increased Pain Interference and decreased Ability to Participate in Social Roles and Activities, suggesting that the

intervention may be overly time-consuming and arduous. This is a known liability of cognitive rehabilitation paradigms in general and was a motivation for pairing APT-3 with neuromodulation to improve pace of improvement.

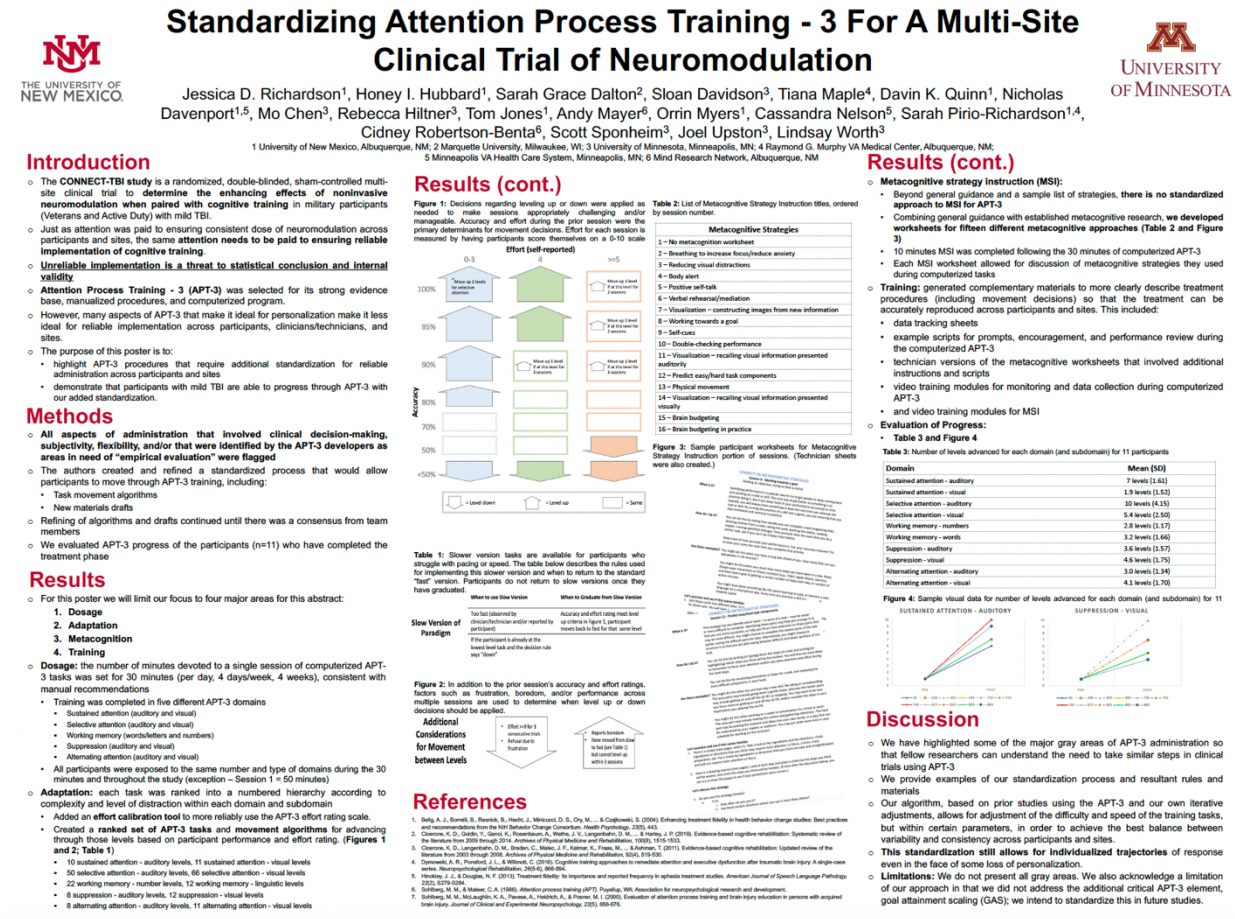
Abstract #4: Functional MRI is utilized in CONNECT-TBI not only to target neuromodulation to the dorsolateral prefrontal cortex, but also to assess changes in brain activation during executive function tasks associated with the intervention. Preliminary data in 10 participants demonstrated trend-level improvements in reaction time on the fMRI working memory task from pre- to post-intervention. Over the same interval, brain activation in posterolateral prefrontal cortex and bilateral caudate nuclei decreased, but after correction for false discovery rate, these changes were no longer significant. This finding is consistent with the theory of cognitive training improving neural efficiency, in which cognitive performance improves as brain activations stays the same or reduces.

Please see below for complete descriptions of the poster presentations contents. In the context of the scientific progress made in the CONNECT-TBI study, these preliminary results provide early validation of key conceptual underpinnings of the study: 1) that cognitive rehabilitation is effective, but arduous; 2) that cognitive training can improve the efficiency of the brain; and 3) that noninvasive neuromodulation is a well-tolerated and synergistic adjunct for cognitive training. Future analysis of the complete dataset for CONNECT-TBI over the next 12 to 18 months will permit unblinding of condition and determination whether cognitive performance and brain activation changes are greater with active stimulation compared to sham.

B) Update to APT-3 standardization procedure: As the APT-3 is intended to be optimized for each subject according to effort, performance, and challenge level, the algorithm to guide this optimization process continues to be refined by the Neuromodulation/Rehabilitation Core, to account for cases where participant performance falls outside expected ranges for accuracy and effort.

C) Updates to Image acquisition, processing, and targeting: The Imaging/Assessment Core continued its work of refining its targeting algorithms, to account for outlier cases in which no significant activation was identified in the bounding region.

Poster #1:



Standardizing Attention Process Training - 3 For A Multi-Site Clinical Trial of Neuromodulation

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Introduction

- The **CONNECT-TBI study** is a randomized, double-blinded, sham-controlled multi-site clinical trial to **determine the enhancing effects of noninvasive neuromodulation when paired with cognitive training** in military participants (Veterans and Active Duty) with mild TBI.
- Just as attention was paid to ensuring consistent dose of neuromodulation across participants and sites, the same **attention needs to be paid to ensuring reliable implementation of cognitive training**.
- **Unreliable implementation is a threat to statistical conclusion and internal validity**
- **Attention Process Training - 3 (APT-3)** was selected for its strong evidence base, manualized procedures, and computerized program.
- However, many aspects of APT-3 that make it ideal for personalization make it less ideal for reliable implementation across participants, clinicians/technicians, and sites.
- The purpose of this poster is to:
  - highlight APT-3 procedures that require additional standardization for reliable administration across participants and sites
  - demonstrate that participants with mild TBI are able to progress through APT-3 with our added standardization.

Methods

- **All aspects of administration that involved clinical decision-making, subjectivity, flexibility, and/or that were identified by the APT-3 developers as areas in need of "empirical evaluation" were flagged**
- The authors created and refined a standardized process that would allow participants to move through APT-3 training, including:
  - Task movement algorithms
  - New materials drafts
- Refining of algorithms and drafts continued until there was a consensus from team members
- We evaluated APT-3 progress of the participants (n=11) who have completed the treatment phase

Results

- For this poster we will limit our focus to four major areas for this abstract:
  1. **Dosage**
  2. **Adaptation**
  3. **Metacognition**
  4. **Training**
- **Dosage:** the number of minutes devoted to a single session of computerized APT-3 tasks was set for 30 minutes (per day, 4 days/week, 4 weeks), consistent with manual recommendations
  - Training was completed in five different APT-3 domains
    - Sustained attention (auditory and visual)
    - Selective attention (auditory and visual)
    - Working memory (words/letters and numbers)
    - Suppression (auditory and visual)
    - Alternating attention (auditory and visual)
  - All participants were exposed to the same number and type of domains during the 30 minutes and throughout the study (exception – Session 1 = 50 minutes)
- **Adaptation:** each task was ranked into a numbered hierarchy according to complexity and level of distraction within each domain and subdomain
  - Added an **effort calibration tool** to more reliably use the APT-3 effort rating scale.
  - Created a **ranked set of APT-3 tasks** and **movement algorithms** for advancing through those levels based on participant performance and effort rating. (**Figures 1 and 2; Table 1**)
    - 10 sustained attention - auditory levels, 11 sustained attention - visual levels
    - 50 selective attention - auditory levels, 66 selective attention - visual levels
    - 22 working memory - number levels, 12 working memory - linguistic levels
    - 8 suppression - auditory levels, 12 suppression - visual levels
    - 8 alternating attention - auditory levels, 11 alternating attention - visual levels

Results (cont.)

Figure 1: Decisions regarding leveling up or down were applied as needed to make sessions appropriately challenging and/or manageable. Accuracy and effort during the prior session were the primary determinants for movement decisions. Effort for each session is measured by having participants score themselves on a 0-10 scale

Table 2: List of Metacognitive Strategy Instruction titles, ordered by session number.

Metacognitive Strategies
1 – No metacognition worksheet
2 – Breathing to increase focus/reduce anxiety
3 – Reducing visual distractions
4 – Body alert
5 – Positive self-talk
6 – Verbal rehearsal/mediation
7 – Visualization – constructing images from new information
8 – Working towards a goal
9 – Self-cues
10 – Double-checking performance
11 – Visualization – recalling visual information presented auditorily
12 – Predict easy/hard task components
13 – Physical movement
14 – Visualization – recalling visual information presented visually
15 – Brain budgeting
16 – Brain budgeting in practice

Figure 3: Sample participant worksheets for Metacognitive Strategy Instruction portion of sessions. (Technician sheets were also created.)

Table 1: Slower version tasks are available for participants who struggle with pacing or speed. The table below describes the rules used for implementing this slower version and when to return to the standard "fast" version. Participants do not return to slow versions once they have graduated.

	When to use Slow Version	When to Graduate from Slow Version
Slow Version of Paradigm	Too fast (observed by clinician/technician and/or reported by participant)	Accuracy and effort rating meet level up criteria in figure 1, participant moves back to fast for that same level
	If the participant is already at the lowest level task and the decision rule says "down"	

Figure 2: In addition to the prior session's accuracy and effort ratings, factors such as frustration, boredom, and/or performance across multiple sessions are used to determine when level up or down decisions should be applied.

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Results (cont.)

- **Metacognitive strategy instruction (MSI):**
  - Beyond general guidance and a sample list of strategies, **there is no standardized approach to MSI for APT-3**
  - Combining general guidance with established metacognitive research, **we developed worksheets for fifteen different metacognitive approaches (Table 2 and Figure 3)**
  - 10 minutes MSI was completed following the 30 minutes of computerized APT-3
  - Each MSI worksheet allowed for discussion of metacognitive strategies they used during computerized tasks
- **Training:** generated complementary materials to more clearly describe treatment procedures (including movement decisions) so that the treatment can be accurately reproduced across participants and sites. This included:
  - data tracking sheets
  - example scripts for prompts, encouragement, and performance review during the computerized APT-3
  - technician versions of the metacognitive worksheets that involved additional instructions and scripts
  - video training modules for monitoring and data collection during computerized APT-3
  - and video training modules for MSI
- **Evaluation of Progress:**
  - **Table 3 and Figure 4**

Table 3: Number of levels advanced for each domain (and subdomain) for 11 participants

Domain	Mean (SD)
Sustained attention - auditory	7 levels (1.61)
Sustained attention - visual	1.9 levels (1.52)
Selective attention - auditory	10 levels (4.15)
Selective attention - visual	5.4 levels (2.50)
Working memory - numbers	2.8 levels (1.17)
Working memory - words	3.2 levels (1.66)
Suppression - auditory	3.6 levels (1.57)
Suppression - visual	4.6 levels (1.75)
Alternating attention - auditory	3.0 levels (1.34)
Alternating attention - visual	4.1 levels (1.70)

Figure 4: Sample visual data for number of levels advanced for each domain (and subdomain) for 11

Discussion

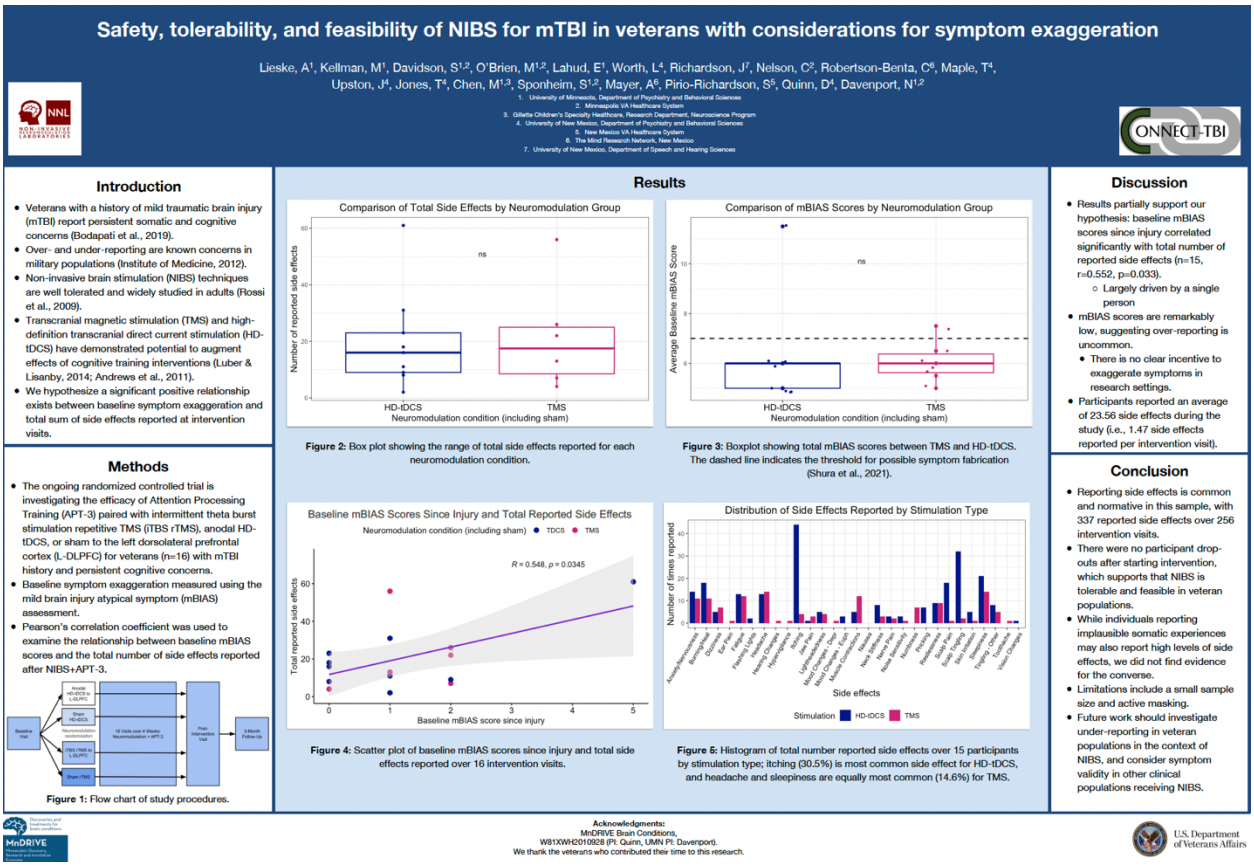
- We have highlighted some of the major gray areas of APT-3 administration so that fellow researchers can understand the need to take similar steps in clinical trials using APT-3
- We provide examples of our standardization process and resultant rules and materials
- Our algorithm, based on prior studies using the APT-3 and our own iterative adjustments, allows 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 across participants and sites.
- **This standardization still allows for individualized trajectories** of response even in the face of some loss of personalization.
- **Limitations:** We do not present all gray areas. We also acknowledge a limitation of our approach in that we did not address the additional critical APT-3 element, goal attainment scaling (GAS); we intend to standardize this in future studies.

Standardizing attention process training-3 for a multi-site clinical trial of neuromodulation

Background: The CONNECT-TBI study is a randomized, double-blinded, sham-controlled multi-site clinical trial to determine the enhancing effects of noninvasive neuromodulation when paired with cognitive training in military participants (Veterans and Active Duty) with mild TBI. To make this determination, the same attention paid to ensuring consistent dose of neuromodulation across participants and sites must also be paid to ensuring reliable implementation of cognitive training. Unreliable implementation is a threat to statistical conclusion and internal validity, which increases the chance of Type I or Type II error, or the additional error ("Type III") of concluding significance or nonsignificance of enhancement when in fact the paired cognitive training was not correctly administered. Attention Process Training - 3 (APT-3) is commonly used in clinical trials of cognitive rehabilitation, due to its strong evidence base, manualized procedures, and computerized program. However, many aspects of APT-3 that make it ideal for personalization make it less ideal for reliable implementation across participants, clinicians/technicians, and sites, especially for studies seeking to determine adjunctive effects of neuromodulation. The purpose of this abstract is to highlight APT-3 procedures that require additional standardization for reliable administration, to provide examples of standardization, and to demonstrate that with these efforts, participants with mild TBI are able to progress through APT-3.
Methods: The APT-3 manual and computerized program were carefully scrutinized by two licensed speech-language pathologists (SLPs) with clinical and research expertise in cognitive training in adults with TBI and other neurological disorders. Any aspect of administration that involved clinical decision-making, subjectivity, flexibility, and/or that were identified by the APT-3 developers as areas in need of "empirical evaluation" were flagged. These "gray areas" were presented to the project executive committee and study technicians for discussion and solution-finding. We then initiated an iterative

standardization process where solutions, algorithms, and material drafts were created and refined over multiple rounds of testing. Final standardized rules and materials represented consensus of relevant study team members and were also heavily influenced by treatment fidelity and replicability guidelines. We evaluated APT-3 progress of the participants who have completed the treatment phase of this study.
Results: Many gray areas were identified, but we will limit our focus to four major areas for this abstract: 1) dosage, 2) adaptation, 3) metacognition, and 4) training. Regarding dosage, the number of minutes devoted to a single session of computerized APT-3 tasks was set for 30 minutes (per day, 4 days/week, 4 weeks), consistent with manual recommendations. However, because different tasks vary in their duration of instructions and duration of task (with some tasks requiring a decision regarding number of trials per task), additional rules were developed to ensure all participants were engaged with APT-3 computerized tasks for 30 minutes each session. The dosage of exposure to the five different APT-3 domains (sustained attention, selective attention, working memory, suppression, and alternating attention) was also standardized across participants, so that all were exposed to the same number and type of domains during the 30 minutes and throughout the study. With regard to adaptation, the manual provides many examples of personalized adaptive programs as well as sampler starter sets focusing on areas of greatest deficit. The manual also encourages extensive interview and pre-assessment, and emphasizes that programming should be dynamic and clinician-guided. For clinical trials like ours and many others, this guidance was too flexible for replication or to be carried out by study technicians. We thus first ranked each task into a numbered hierarchy according to complexity and level of distraction within each domain and subdomain (e.g., sustained attention – auditory v. – visual). We created a starter set of APT-3 tasks and created algorithms for moving through those levels (to harder tasks, to easier tasks, to slower presentation speed). In addition, because effort ratings impact movement decisions, we added an effort calibration tool for participants to more reliably use the APT-3 effort rating scale. Metacognitive strategy instruction (MSI) is considered to be a critical APT-3 component and is the primary contributor to any findings of generalization following APT-3. However, beyond general guidance to areas of metacognition to target, references to the literature, and a sample list of strategies, there is no standardized approach to MSI. Combining the general guidance in the manual with established metacognitive research, we developed worksheets for fifteen different metacognitive approaches to be used in MSI with participants for 10 minutes following the 30 minutes of computerized APT-3. Each MSI worksheet also allowed for discussion of metacognitive strategies they were observed to be using during computerized tasks, which were tracked by the technician. Established guidelines for treatment replicability and fidelity shaped development of training materials and procedures. We generated complementary (to the APT-3 manual and computerized program) materials to more clearly describe treatment procedures (including movement decisions) so that the treatment can be accurately reproduced. This included: data tracking sheets; example scripts for prompts, encouragement, and performance review during the computerized APT-3; technician versions of the metacognitive worksheets that involved additional instructions and scripts; video training modules for monitoring and data collection during computerized APT-3; and video training modules for MSI. This allows monitoring of multiple treatment fidelity components (i.e., clinician training, treatment delivery, and treatment receipt) to increase the likelihood that treatment implementation in the first days and months of the project is the same as in the last days and months of the project. The number of levels advanced for each domain (and subdomain) for participants (N=11) to date is as follows: sustained attention – auditory, M=7 levels (SD=1.61); sustained attention – visual, M=1.9 levels (SD=1.52); selective attention – auditory, M=10 (SD=4.15); selective attention – visual, M=5.4 (SD=2.5); working memory – numbers, M=2.8 (SD=1.17); working memory – words, M=3.2 (SD=1.66); suppression – auditory, M=3.6 (SD=1.57); suppression – visual, M=4.6 (SD=1.75); alternating attention – auditory, M=3 (SD=1.34); and alternating attention – visual, M=4.1 (SD=1.70).
Discussion: In this abstract, we have highlighted some of the major gray areas of APT-3 administration and our rationale for the need for additional standardization so that fellow researchers can understand the need to take similar steps in clinical trials using APT-3. We provide examples of our standardization process and resultant rules and materials; additional materials will be provided at time of presentation. We successfully constructed an algorithm, based on prior studies using the APT-3 and our own iterative adjustments, 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 across participants and sites. We document here that this standardization still allows for individualized trajectories of response even in the face of some loss of personalization. We do not present all gray areas in this brief abstract. We also acknowledge a limitation of our approach in that we did not address the additional critical APT-3 element, goal attainment scaling (GAS); we intend to standardize this in future studies.

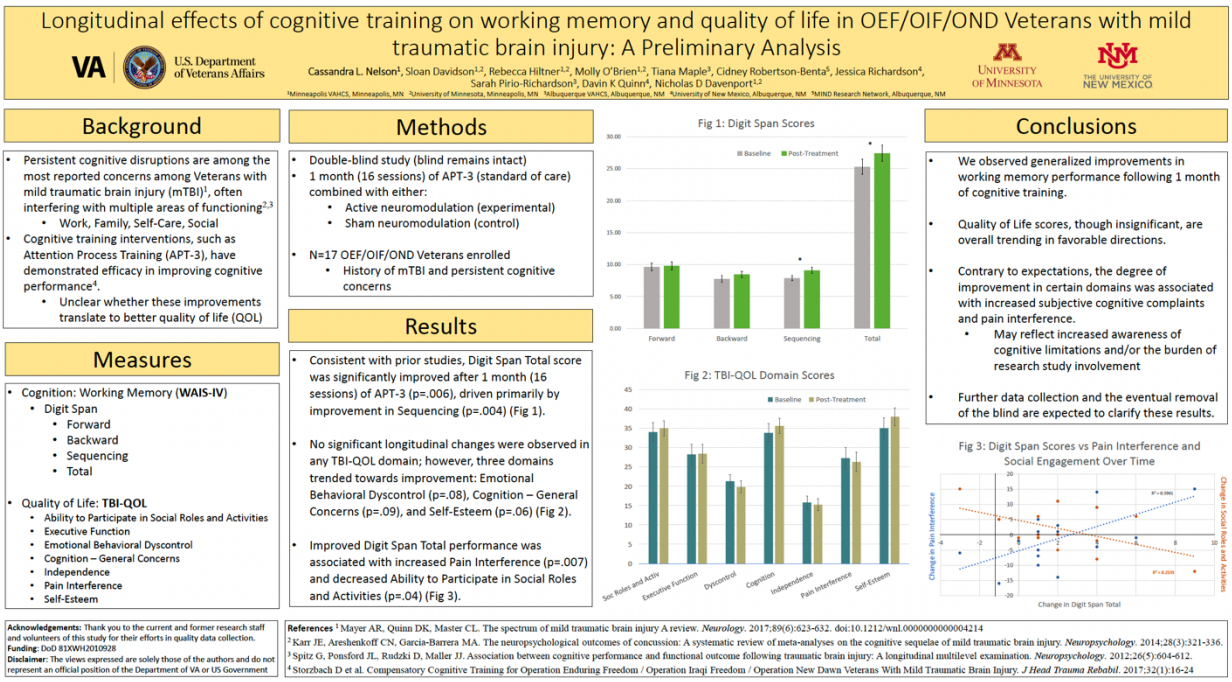
Poster #2:



Safety, tolerability, and feasibility of NIBS for mTBI in veterans with considerations for symptom exaggeration

Background: Veterans who report a history of mild traumatic brain injury (mTBI) often also report persistent somatic and cognitive concerns, though both over-reporting and under-reporting are known concerns in military populations. Conventional cognitive training interventions have shown short term efficacy but are limited in durability and generalization of benefits. Non-invasive brain stimulation (NIBS) techniques, such as transcranial magnetic stimulation (TMS) and high-definition transcranial direct current stimulation (HD-tDCS), have demonstrated potential to augment effects of cognitive training when delivered in tandem. While NIBS is generally well tolerated, participants report a wide range of side effects that must be monitored. Better characterization of side effect reporting rates, and their predictors, in this population could inform clinical decision-making when implementing NIBS interventions.
Methods: The ongoing randomized controlled trial reported here investigates the efficacy of Attention Processing Training (APT) paired with intermittent theta burst TMS, HD-tDCS, or sham for Veterans (n=16) with mTBI history and persistent cognitive concerns. Validity of symptom reporting is assessed using the Mild Brain Injury Atypical Symptoms (mBIAS) scale. We computed Pearson's correlation coefficients between mBIAS scores and total number of reported side effects to test the hypothesis that baseline mBIAS measures would predict frequency of side effect reporting.
Results: Baseline mBIAS scores correlated significantly with the number of reported side effects (n=15, r=0.552, p=0.033), though this was largely driven by a single person. Closer inspection reveals that mBIAS scores were remarkably low, suggesting over-reporting was uncommon, while reports of up to 25 side effects (over 16 sessions) was typical.
Conclusion: Reporting side effects is common and normative, with 337 reported side effects over 256 intervention visits. While individuals reporting implausible somatic experiences may also report high levels of side effects, we did not find evidence for the converse.

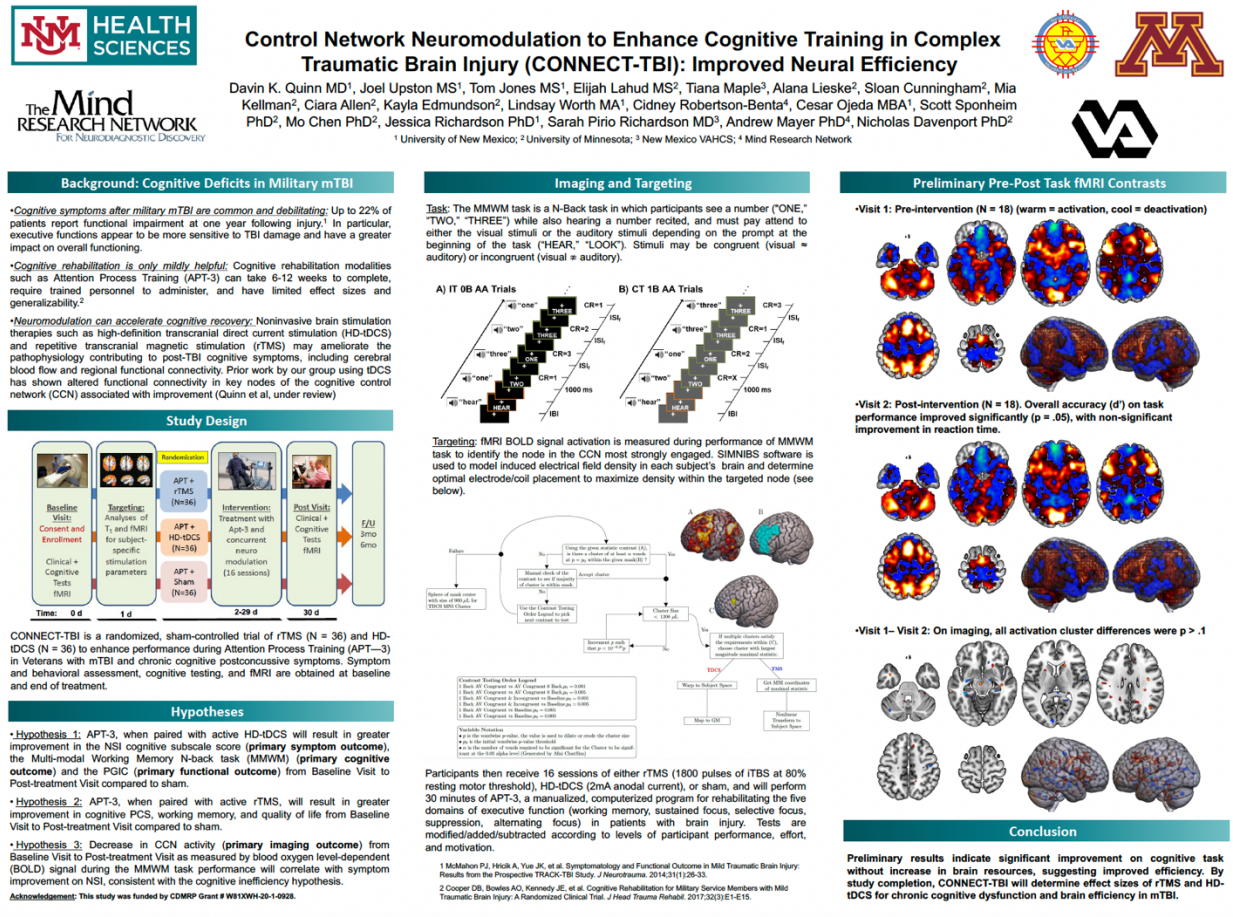
Poster #3:



Longitudinal effects of cognitive training on working memory and quality of life in OEF/OIF/OND Veterans with mild traumatic brain injury: A Preliminary Analysis

Background: Persistent cognitive disruptions are among the most commonly reported concerns among Veterans with mild traumatic brain injury (mTBI), often interfering with multiple areas of functioning (e.g., job, family, self-care, social). Cognitive training interventions, such as Attention Process Training (APT-3), have demonstrated efficacy in improving cognitive performance, but it is less well established whether these improvements translate to better quality of life.
Methods: As part of an ongoing study of OEF/OIF/OND Veterans with a history of mTBI and persistent cognitive concerns, 11 participants completed a baseline assessment, one month (16 sessions) of APT-3 combined with either Active or Sham neuromodulation, and a post-treatment assessment. At both the baseline and post-treatment visits, working memory was assessed using the Digit Span, and 7 domains of quality of life were assessed using modules from the TBI-QOL battery. Longitudinal changes in each measure were evaluated using paired t-tests, and relationships between changes in cognition and changes in quality of life were evaluated using Pearson correlation coefficients.
Results: Consistent with prior studies, Digit Span total score was significantly improved after 1 month (16 sessions) of APT-3 (p=.03), driven primarily by improvement in Sequencing (p=.051) and Digit Span Forward (p=.11). No longitudinal changes were observed in any TBI-QOL domain; however, increases in Cognition - General Concerns were significantly correlated with improvement in Digit Span Forward (p=.025) and, to a lesser extent, Backward (p=.079). Similarly, improved Digit Span Total and Backward performance was associated with increased Pain Interference and decreased Ability to Participate in Social Roles and Activities (all p<.02).
Conclusion: We observed generalized improvements in working memory performance following a month of cognitive training. Contrary to expectations, the degree of improvement in certain domains was associated with increased subjective cognitive complaints and pain interference, along with decreased participation in social activities. This may reflect increased awareness of cognitive limitations and/or the additional physical burden and life disruption of completing a research visit four days per week for a month.

Poster #4:



Control-Network Neuromodulation to Enhance Cognitive Training in Complex TBI (The CONNECT-TBI Study): fMRI Evidence of Improved Neural Efficiency with APT-3

Background: United States Veterans with mild traumatic brain injury (mTBI) sustained in recent conflicts frequently report cognitive postconcussive symptoms (PCS), particularly in the domains of executive function, attention, and processing speed. Prior findings of our scientific team suggest that symptoms arise from a problem of inefficiency in the cognitive control network (CCN) responsible for executive functions, such as set shifting, response inhibition, and working memory, and that cognitive training combined with neuromodulation can accelerate improvement. We report pilot data from the multi-center CONNECT-TBI study (W81XWH-20-1-0928), a randomized, sham-controlled trial of individually targeted non-invasive neuromodulation interventions, including high-definition transcranial direct current stimulation (HD-tDCS) and repetitive transcranial direct current stimulation (rTMS) paired with Attention Process Training (APT-3) for the treatment of chronic cognitive PCS in mTBI. In particular, we present task-based functional magnetic resonance imaging (fMRI) data indicating improvement in neural efficiency in key nodes of the CCN after 16 sessions of APT-3, across stimulation types.
Methods: In CONNECT-TBI, participants ages 18-59 with documented mTBI and chronic cognitive PCS are recruited from the New Mexico Veterans Affairs Health Care System (VAHCS) and Minneapolis VAHCS Polytrauma Network Clinics. All subjects undergo demographic and behavioral assessment, neuropsychological testing, and fMRI. Scans are collected at the Mind Research Network (MRN) in Albuquerque and the University of Minnesota's Center for Magnetic Resonance Research (CMRR) in Minneapolis. A multimodal attention task (MMAT) that queries both working memory and selective attention during functional MRI is used to characterize the CCN. The participants undergo 16 daily sessions of Attention Process Training (APT-3), a manualized, computerized program of cognitive training designed to be individualized for a patient's level of impairment, effort, and coping style. APT-3 is

combined with active/sham HD-tDCS (2mA current in 2 anodes + 6 cathodes for 30 minutes) or active/sham rTMS (intermittent theta burst, 1800 pulses, 80% resting motor threshold for 10 minutes) delivered to each subject's individualized target. Following the 16th stimulation session, the initial assessment battery, including functional MRI, is repeated.
Task: The MMAT task performed in the scanner is a multisensory working memory and attention task that assesses three domains of cognitive control: set shifting, working memory, and response inhibition. During the task, participants watch a screen that displays a number (1, 2, or 3) every two seconds. Simultaneously, they hear a voice reciting a number (1, 2, or 3) every two seconds. The instructions at the beginning of each block direct them to attend to the visual data only ("LOOK") or auditory data only ("HEAR") and press a button corresponding to the number. If the instructions are displayed on a black background, the participants must press a button corresponding to the attended number displayed/recited on each trial (0-back). If the instructions are displayed on a grey background, they must press a button corresponding to the previously attended number (1-back). Participants complete trial blocks in which the visual and auditory numbers are identical (congruent) or different (incongruent). Inside the scanner, they complete three runs of the task, five blocks of each of the eight trial types per run (0- vs 1-back; congruent vs incongruent; visual vs auditory). Reaction time (RT) and accuracy (d') are calculated for each trial type.
Imaging: During each MRI scan task-based fMRI [repetition time (TR) of 800 ms] with multi-band capabilities is obtained and preprocessed using AFNI including despiking, slice-time correction, temporal auto-correlations correction, motion correction at the slice and volume level, and distortion correction. Preprocessed datasets undergo spatial normalization to MNI space for group analysis. Images with high frame-wise displacement (> 0.3) are excluded from fMRI analyses. Activation contrast beta weight maps reflecting working memory load were calculated with 3dREMLfit in AFNI between the 0-back and 1-back conditions for all subjects at both Visit 1 and Visit 2. Change in activation beta weight maps from Visit 1 to Visit 2 are calculated and averaged across all subjects from both sites. Cluster correction is applied to the associated contrast statistical maps to correct for multiple comparisons.
Results: Ten patients were included in this preliminary analysis. Psychometrics and MMAT performance at baseline were comparable between both sites. From Visit 1 to Visit 2 there was a trend-level improvement in reaction time on trials involving incongruent stimuli. Otherwise there were no significant changes in RT and d' for any other trial types. From Visit 1 to Visit 2 there was a significant reduction ($p<0.005$) in activation during working memory trials within the Congruent 1-back vs Congruent 0-back contrast in a postero-lateral region of the prefrontal cortex, adjacent to lingual and premotor areas, as well as in bilateral caudate nuclei. However, only the prefrontal cluster remained after cluster correction (FPR=0.1).
Conclusion: Cognitive PCS following mTBI are a significant clinical problem in military personnel. APT-3 is a validated method of cognitive rehabilitation, but the mechanism of improvement is not known. Our preliminary data suggests that CCN activation decreases over time with sixteen sessions of APT-3, without compromised performance in working memory reaction time and accuracy, and possibly improved performance with incongruent stimuli. This supports the theory of improved neural efficiency with cognitive training. Future analysis will quantify effect sizes of specific neuromodulation types paired with APT-3 on brain activation.

1.2 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.

1.3 Significant Results or Key Outcomes

Nothing to report.

1.3.1 Other Achievements

Nothing to report.

Stated Goals Not Met

To date, the only study goals not met at the time of this annual report are the stated recruitment goals: we are aiming for recruitment of 108 mTBI subjects. To date we have enrolled 28 subjects across the sites. This lag in recruitment is attributable to several factors:

a) Delays in full HRPO approval to begin the study, due to required modifications to UNM, Minneapolis VA, and NM VA IRB protocols.
b) Delays in equipment acquisition, underperformance of existing equipment needing to be replaced, and troubleshooting of equipment leading to need for the manufacturer to design software fixes.
c) Lack of published standards for conduct of Attention Process Training-3 in research and in clinical care, necessitating the study team to review literature, consult with experts, and build algorithms for this purpose.
d) Slower than expected intake of potential patients from the Minneapolis VAHCS and NMVAHCS Polytrauma Support Clinics.

Since the previous annual report, our recruitment efforts have been successful, resulting in enrollment rates approximating the initial planned rate of recruitment. Please see next section for description of efforts to meet this goal.

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

Nothing to report.

1.5 How were the results disseminated to communities of interest?

Nothing to report.

1.6 Planning

During the next reporting period, we plan to accomplish the following goals:

1) Continue recruitment, enrollment, and conduct participants through the protocol.
2) Continue successful recruitment efforts via expanded inclusion/exclusion criteria, polytrauma registry review, polytrauma team engagement, allied health service team engagement, monthly research tables, targeted social media advertisements.
3) Maintain study staff necessary to perform the protocol at each site.
4) Begin planning for end of study and data analysis of unblinded data.

2. Impact

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

Nothing to report.

2.2 What was the impact on other disciplines?

Nothing to report.

2.3. What was the impact on technology transfer?

Nothing to report.

2.4 What was the impact on society beyond science and technology?

Nothing to report.

3. Changes/Problems

3.1 Changes in approach and reasons for change

None at this time.

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

Three actual problems occurred in the past year that significantly delayed study activities:

A) Staff Turnover: Several staff members at each state left the study team, owing to professional advancement opportunities. The recruitment, hiring, and training of new staff members necessitated pausing of participants being conducted through the protocol.

B) MRI Scanner Upgrade: The MRI scanner at UNM/MRN underwent a recommended software upgrade, resulting in unforeseen problems with running the CONNECT-TBI imaging sequences. These problems were ultimately solved, but resulted in a pause to protocol administration. The MRI Scanner is now functioning at normal capacity and capability.

C) Brain Stimulation Performance: A minor device malfunction occurred with the tDCS device at University of Minnesota, in which Bluetooth connectivity between the programming computer and the stimulation unit was lost and current ramp down did not occur as expected. Based on this, the device manufacturer recommended replacement of the unit, resulting in a pause in protocol administration. The device replacement has been ordered and will arrive within the next week.

D) Recruitment lag: Recruitment of participants between October 2022 and October 2023 has been at the approximate projected rate in the Scope of Work. Efforts to bolster recruitment since the last Annual Report were successful, including monthly research tables at the VAHCS sites; direct engagement of polytrauma clinicians via face to face meetings; targeted advertising strategies using social media channels such as Facebook; review of disqualifying factors and relaxation of inclusion/exclusion criteria.

Anticipated Problems/Issues

Given the ongoing post-pandemic effects on workforce health, staff availability, and participant retention, and ongoing economic challenges and hardships affecting attitudes about participation in research, we anticipate that achieving enrollment rates sufficient to meet our scientific goals will be the top challenge that our study team will face.

A) Staff/workforce health: Each team has redundancies built into staff roles, so that sickness or absence of any one team member does not lead to inability to conduct the protocol at the particular site. Standard operating procedures and automated scripts will ensure that centralized Core functions can be carried out even if data analysts or principle/site investigators must be absent from work. COVID symptom screening and ad hoc testing will continue to be carried out according to each institution's local guidelines. Recruitment, consenting, and follow-up methods will be contactless and virtual whenever possible.

B) Economic/travel hardship: Feedback from potential participants who were unable to enroll has revealed that costs associated with study participation (gas costs, parking costs, housing costs) have been negatively impacting enthusiasm to enroll in the study. Therefore we are allotting available study budget to reimburse participants for mileage according to the federal approved rate, as well as providing support for accommodations when participants are traveling long distances to the study sites.

C) Retention rates: In addition to the above outreach activities to spread awareness of the study and recruit Veterans from the community, we have also honed our study procedures to account for a small percentage of participants for whom we are not able to successfully generated MRI-based targets for brain stimulation. In these cases, we now have a generic target/montage that is situated in the anatomic DLPFC.

3.3 Changes that had a significant impact on expenditures

A no-cost extension was requested and approved to continue data collection and data analysis for an additional year.

3.4 Significant changes in use or care of human subjects, vertebrate animals, biohazards, or select agents.

Nothing to report.

3.5 Other Achievements

None at this time.

Human Use Regulatory Protocols

TOTAL PROTOCOLS: 3

PROTOCOL (1 of 3 total):
Protocol [HRPO Assigned Number]: UNM HRRC #: 21-026

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

Target required for clinical significance: 108 (combined from both NM and MN sites)

Target approved for clinical significance: 108 (combined from both NM and MN sites)

SUBMITTED TO AND APPROVED BY:
- **Submitted: 12/11/2020**
- **Reviewed: 02/12/2021**
- **Approved: 04/29/2021**

STATUS:
See "Protocol 2 & 3" for recruitment and enrollment numbers.

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:

Type of Submission	Summary of Submission	Site	Date of Approval
Modification	Changed ramp up and down time for all protocols; changed consent and protocol to reflect receipt of CoC	UNM	7/12/2022
Modification	Adding study team member McQuaid	MRN	8/22/2022
RNI	Older version of consent used on 07/28/22 and 08/10/22; Both participants reconsented with correct version of consent at post-treatment visit. No further action needed.	MRN	10/02/22
Modification	Adding study team member Richardson	UNM	9/19/2022
Modification	Following completion of the Baseline Visit, participants will receive 16 total sessions of either active HD-tDCS, active rTMS, or sham stimulation to the left DLPFC for a total of 30 minutes, approximately 4 sessions/week, over a period of 4 to 6 consecutive weeks. For participants for whom an individualized montage cannot be generated, generic targeting methods will be used. For tDCS participants, a generic high-definition electrode montage based on the Montreal Neurological Institute brain atlas will be used to target the left DLPFC. For TMS participants, the Beam F3 method will be used to determine a target for the left DLPFC based on scalp measurements.	MRN	12/22/2022

Modification	Adding study team member Ann Hittson	MRN	4/18/2023
Modification	Adding study team members Samuel Miller and Upasana Nathaniel	MRN	10/03/2023

Submissions for Minnesota Site through the University of New Mexico

Type of Submission	Summary of Submission	Site	Date of Approval
Initial Approval	UNM IRB Site Approval for Minnesota Participating Site	UMN	12/22/2021
Modification	Changed ramp up and down time for all protocols; changed consent and protocol to reflect receipt of CoC	UMN	7/12/2022
Modification	The following changes are being made to the study: -Increasing age range from 18-59 to 18-69 -Including military conflicts since 1990 (to include Desert Storm and Desert Shield) - Increasing time since injury from occurring since 2001 to Injury is within the last 35 years -Changing exclusion criteria of substance / alcohol dependence with past 2 years to past 6 months -Deleted "warfighters" in the protocol in the few places it was not deleted in previous submission. This submission also includes a new document, "CONNECT, Thank you Letter" for review. This letter will be sent to participants by MRN staff after they complete the study (i.e., follow-ups are complete).	UMN	11/4/2022
Modification	Following completion of the Baseline Visit, participants will receive 16 total sessions of either active HD-tDCS, active rTMS, or sham stimulation to the left DLPFC for a total of 30 minutes, approximately 4 sessions/week, over a period of 4 to 6 consecutive weeks. For participants for whom an individualized montage cannot be generated, generic targeting methods will be used. For tDCS participants, a generic high-definition electrode montage based on the Montreal Neurological Institute brain atlas will be used to target the left DLPFC. For TMS participants, the Beam F3 method will be used to determine a target for the left DLPFC based on scalp measurements.	UMN	12/22/2022

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:

None to report

PROTOCOL (2 of 3 total):

Protocol [HRPO Assigned Number]: NMVAHCS IRB #: H3588

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

Target required for clinical significance: 54

Target approved for clinical significance: 54

SUBMITTED TO AND APPROVED BY:

- **Submitted: 12/04/2020**
- **Reviewed: 02/09/2021**
- **Approved: Main IRB approval on 04/02/2021, R&D and IT approval on 05/14/2021**

STATUS:

(i) Number of subjects recruited /original planned target: 992/250
Number of subjects screened/original planned target: 78/250
Number of patients enrolled/original planned target: 15/54
Number of patients completed/original planned target: 10/54

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:

Type of Submission	Summary of Submission	Site	Date of Approval
Initial Approval		NMVAHCS	5/12/2021
Modification	Adding study team member Tiana Crabbe (Maple), use of non-VA Laptop and Non-VA Software (ATP3 Standard Encryption) to be used off network	NMVAHCS	9/30/2021
Modification	Reduction in participant payment from $660 to $590. ICF language changed to clarify protection of identifiers. Removed the COWAT test from protocol and replaced with DKEFS. GCS now exclusion criteria instead of inclusion criteria. Added to protocol info regarding COINS use. Updated multiple questionnaires. Created DSMB charter.	NMVAHCS	10/12/2021
Continuing Review/Progress Report	Progress report, protocol changes 9_23_2021, Combined consent HIPAA 09_21_2021, modified letter to clinicians, letter to participants, recruitment flyer, UNM newspaper and online advertisement	NMVAHCS	2/2/2022
Modification	Expanding inclusion criteria from 5 years to 21 years post injury. Advertisements, recruitment letters and protocol were all modified	NMVAHCS	3/28/2022
Modification	Adding study team member Davin Quinn, Cesar Ojeda & Dana Allsop	NMVAHCS	4/7/2022
Modification	Changed magnetic field strength from 120% RMT to 80 % RMT, removed 7 questionnaires/surveys, added 8 new questionnaires/data collection forms	NMVAHCS	6/17/2022
Modification	Protocol change - HD-tDCS ramp up/down changed to 1 min for both real and sham treatments, updated CoC language on protocol & consent, changed consent form language	NMVAHCS	9/13/2022
Modification	Adding study team member, Worth and removing study team member - Allsop	NMVAHCS	9/14/2022
Modification	Adding study team member Smith	NMVAHCS	10/4/2022
Adverse Event Report	Unexpected Adverse Event: On 9/7/22 at approx. 9 pm, participant was broadsided by another car while driving through an intersection. Participant did not sustain major injuries and he declined to be transported to the ER at time of accident. On 9/8/22, he developed a severe headache and dizziness and went to Presbyterian ER where he was diagnosed with mild concussion. Acknowledged 10/11/2022.	NMVAHCS	10/11/2022

Modification	The following changes are being made to the study: -Increasing age range from 18-59 to 18-69 -Including military conflicts since 1990 (to include Desert Storm and Desert Shield) - Increasing time since injury from occurring since 2001 to Injury is within the last 35 years -Changing exclusion criteria of substance / alcohol dependence with past 2 years to past 6 months -Deleted "warfighters" in the protocol in the few places it was not deleted in previous submission. These changes impact the protocol, consent and HIPAA, newspaper and online advertisements, recruitment flyer, letters to potential participants and clinicians, and phone screen (all attached to this submission). This submission also includes a new document, "CONNECT, Thank you Letter" for review. This letter will be sent to participants after they complete the study (i.e., follow-ups are complete).	NMVAHCS	11/17/2022
Continuing Review	Continuing review documents and progress report	NMVAHCS	12/13/2022
Modification	Request to expand the intervention length from 4 weeks to 4-6 weeks, to add general targeting methods for tDCS and TMS, to expand on participant compensation language	NMVAHCS	1/10/2023
Adverse Event Report	Unexpected Adverse Event: Fall 2/12/2023, reported to NMVAHCS IRB 2/21/23, IRB determined serious, unanticipated, unrelated	NMVAHCS	3/14/2023
Modification	Adding study team member Reyes	NMVAHCS	5/5/2023
Protocol Deviation	M87105968, M87146536, M87177832 - Participants were reconsented without IRB approval on 01/18/2023, 01/24/2023, 02/01/2023. All participants continued/completed study participation. Discovered during consent audit. Submitted deviation report to IRB on 5/15/2023.	NMVAHCS	6/13/2023
Protocol Deviation	Participant did not complete consent quiz prior to signing consent form. Participant decided not to participate due to schedule. Participant was not randomized and did not participate in any study related procedures. Discovered during consent audit. Submitted deviation report to IRB on 5/16/2023.	NMVAHCS	6/13/2023
Action Plan	Submitted Action Plan to IRB in response to audit findings & protocol deviation reports (submitted 6/6/2023)	NMVAHCS	6/13/2023
Modification	Removing study team member Ojeda and Smith	NMVAHCS	Pending
Modification	Changed inclusion criteria to include mild cognitive symptoms	NMVAHCS	9/12/2023

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:

New Mexico Adverse Events

PT ID	Site	Event Term	AE Onset Date	AE Stop Date	Reported to IRB?	IRB Determination	Study Period	Severity	Related to Study?	Unanticipated?	Outcome	Action Taken
M8718 7742	NMVA HCS	MVA	9/7/2022	Unkn own	Yes	No increase d risk, no action needed	Interve ntion	Mild	No	Yes	Unkno wn	Discont inued study interve ntion perma nently, but comple ted post-interve

												ntion visits
M8714 6536	NMVA HCS	Fall	1/22/202 3	Unkn own	No	N/A	Pre-Interve ntion (after baselin e visit & before interve ntion)	Mild	No	Yes	No fractur e, fully recover ed	No actions taken
M8710 5968	NMVA HCS	Fall	2/12/202 3	Unkn own	Yes	Serious, Unantici pated, Not related - No actions needed to be taken	Interve ntion	Sev ere	No	Yes	Unkno wn	Discont inued study interve ntion perma nently, but comple ted post-interve ntion visits
M8711 5840	NMVA HCS	Increas ed anxiety/ overwh elm	6/16/202 3	Unkn own	Pendi ng	Pending	Interve ntion	Mild	Yes	Yes	Discont inued	Particip ant request ed a break from study visits on 6/20/23
M8717 7688	NMVA HCS	Fall	9/16/202 3		CR		Pre-Interve ntion (after baselin e visit & before interve ntion)	Mild	No	Yes	Vetera n reporte d fall/"fai nting spell" to provide r - provide r had no concer ns	Vetera n reporte d event to study coordin ator during sessio n #5 (9/27/2 3). Event was reporte d to PI on 9/28/23 .

Narrative of AE's:

M87187742 NMVAHCS 09/07/2022: Before beginning treatment Session 15 on Thursday 9/8/2022, participant reported he was involved in a motor vehicle accident at approximately 9:00 p.m. on 9/7/2022. He reported severe headache, dizziness, and less than 2 hours of sleep. Study Coordinator referred the participant to the ER and reported the incident to the P.I., Dr. Pirio-Richardson. The participant was seen

at ER on 9/8/2022 and told that he had experienced a concussion, and he was instructed to rest for 7 days. The PI met with the study team and determined that it was not safe to continue the study intervention. The incident was reported to the NMVAHCS IRB, and no further action is required per IRB. The participant will complete research post-intervention visits.

M87146536 NMVAHCS 01/22/2023: Participant called study coordinator on 1/23/23 to report ER visit on 1/22/23 due to fall. Participant stepped over dog, skipping 4 steps landing on rt foot on concrete. Participant was treated at ER and released with referral to orthopedics due to possible fracture/bone bruise. Participant decided to begin intervention. The incident was not reported to NMVAHCS IRB.

M87105968 NMVAHCS 02/12/2023: Participant sustained mTBI due to fall at friend's house with LOC on 2/12/22. Intervention discontinued on 2/13/23. Participant did not complete sessions 12 – 16. The incident was reported to NMVAHCS IRB 2/21/23 and no actions needed to be taken to eliminate immediate hazards to participants.

M87115840 NMVAHCS 06/16/2023: On 6/16/2023, this participant was a no-show to study visit. The study coordinator received a call from the participant's provider on 6/16/23 stating that the participant arrived at scheduled clinical visit on 6/16/23 with significant agitation and anger due to work and home stress. The provider walked the participant to Beacon services (psychiatric urgent care clinic) to be assessed for suicidality; the participant denied suicidal ideation during this assessment. On 6/20/23, the participant attended the next scheduled study visit and requested to withdraw from study due to increased anxiety and overwhelm; the participant expressed a desire to continue study visits at a later date.

M87177688 NMVAHCS 09/16/2023 - Participant reported fall/"fainting spell" to study coordinator on 9/27/23. The fall occurred on 9/16/23 after baseline visit & before intervention. Participant was not injured during the fall and did not report LOC. Participant mentioned to clinical provider during a subsequent visit for unrelated issue. Participant reported provider had no concerns. Event was reported to PI on 9/28/23 and determined unrelated to study intervention.

PROTOCOL (3 of 3 total):

Protocol [HRPO Assigned Number]: Minneapolis VAHCS IRB #
Title: **Control Network Neuromodulation to Enhance Cognitive Training in Complex Traumatic Brain Injury (The CONNECT-TBI Trial)**
Target required for clinical significance: 54
Target approved for clinical significance: 54

SUBMITTED TO AND APPROVED BY:

- **Submitted: Feb. 2021**
- **Reviewed: 04/05/2021**
- **Approved: Main IRB approval on 05/06/2021, R&D and IT approval on 05/24/2021**

STATUS:

(i) Number of subjects recruited/original planned target: 438/250
Number of subjects screened/original planned target: 40/250
Number of patients enrolled/original planned target: 13/54
Number of patients completed/original planned target: 10/54

(ii) Report amendments submitted to the IRB and USAMRMC HRPO for review:

Type of Submission	Summary of Submission	Site	Date of Approval
Initial Approval		Minneapolis VAHCS	5/24/2021
Continuing Review		Minneapolis VAHCS	4/11/2022
Modification	Edit protocol language, add questionnaires	Minneapolis VAHCS	8/19/2022
Modification	Adding study team member, Cassie Nelson	Minneapolis VAHCS	10/20/2022
Modification	Adding study team members Kellman, Edumndson, and Byrd	Minneapolis VAHCS	11/15/2022
Modification	The following changes are being made to the study: ~~-Increasing age range from 18-59 to 18-69~~ -Including military conflicts since 1990 (to include Desert Storm and Desert Shield) - Increasing time since injury from occurring since 2001 to Injury is within the last 35 years -Changing exclusion criteria of substance / alcohol dependence with past 2 years to past 6 months -Deleted "warfighters" in the protocol in the few places it was not deleted in previous submission. -Following completion of the Baseline Visit, participants will receive 16 total sessions of either active HD-tDCS, active rTMS, or sham stimulation to the left DLPFC for a total of 30 minutes, approximately 4 sessions/week, over a period of 4 to 6 consecutive weeks. -For participants for whom an individualized montage cannot be generated, generic targeting methods will be used. For tDCS participants, a generic high-definition electrode montage based on the Montreal Neurological Institute brain atlas will be used to target the left DLPFC. For TMS participants, the Beam F3 method will be used to determine a target for the left DLPFC based on scalp measurements.	Minneapolis VAHCS	12/19/2022
Modification	Update age range in consent to reflect new criteria (omitted from previous submission), updating IRB records that CPRS note is required	Minneapolis VAHCS	pending
Modification	Changed inclusion criteria to include mild cognitive symptoms	Minneapolis VAHCS	pending

(iii) Adverse event/unanticipated problems involving risks to subjects or others and actions or plans for mitigation:

Minnesota Serious Adverse Events

PT ID	Site	Event Term	AE Onset Date	AE Stop Date	Reported to IRB?	IRB Determination	Study Period	Severity	Related to Study?	Unanticipated?	Outcome	Action Taken
6005	MN	Suicide Attempt	04/06/23	04/11/23	Yes	No increased risk, no action needed	Follow-Up	Serious	No	Yes	Resolved	None

Minnesota Adverse Events

PTID	Site	Event Term	AE Onset Date	AE Stop Date	Reported to IRB?	IRB Determination	Study Period	Severity	Related to Study?	Unanticipated?	Outcome	Action Taken
6001	MN	Amnesia	6/12/22	6/13/22	Yes	No increased risk, no action needed	Intervention	Mild	No	Yes	Resolved	None
6009	MN	Skin Irritation	2/8/23	Unknown	Yes	No increased risk, no action needed	Intervention	Mild	No	Yes	Unknown	None

Minnesota AE Narratives

6001 MN 06/12/2022: Before beginning Treatment Session 14 on Tuesday 6/14/2022, Participant 6001D reported experiencing amnesia for 8 hours on Sunday 6/12/2022. He reported that he and his girlfriend watched a movie, and he does not remember the next 8 hours after that. He was told by his girlfriend that he drove to the store alone to buy bacon and eggs, came home, and cooked for himself and his girlfriend, and then fell asleep. His girlfriend told him that he was acting normally but was sweating profusely while he was asleep. He reported that he was not under the influence of alcohol or drugs.

Once the participant reported this to study staff, the Study Coordinator, immediately called the site PI, Dr. Davenport to report this incident. Based on the information provided, Dr. Davenport determined that the reported experiences were unlikely to be causally linked to the neuromodulation intervention, especially considering no stimulation had occurred in the 5 days prior to the event, and that the participant should be allowed to continue participation if willing and interested in doing so. Dr. Davenport discussed this adverse event with the full multi-site study team, including Drs. Pirio Richardson, Chen, and Quinn, who concurred that this event was not consistent with common or rare side effects of transcranial direct current stimulation.

Dr. Davenport recommended that the participant be reminded that all participation is voluntary and given the opportunity to discontinue or delay subsequent visits if concerned about safety. The Study Coordinator communicated this to the participant, who said “I’m here aren’t I?”. The participant reported no concern about safety issues, and that he felt that we should know about amnesia. The visit proceeded without further incident.

This was reported to the UNM IRB, and it was determined that this did not increase the overall risk and no further action was required (06/13/22).

6009 MN 2/8/2023: During Treatment Session 10, the participant reported some skin irritation on the left side of his forehead. Study staff examined the participant’s forehead and observed that the skin was red, raised, and swelling. The participant reported no changes in lotions or skin care products that could explain an allergic reaction. He also reported no pain or itching, and that he has been using antibiotic anti-inflammatory creams to control the swelling. The participant stated that he would like to continue with the session. The skin irritation was reported to the study PI’s and Co-I’s.

During Treatment Session 13 on 2/13/23, study staff noticed that the irritated skin was still present and that the irritated area had broken skin. The participant reported that over the weekend his left eye was swollen shut. At this session, minor swelling was present over his left eyelid. The participant also reported that he has lost 15 lbs. since January 12th (his first stimulation session was on January 18th) and has

had no changes in his diet or exercise habits. Study staff reminded the participant that his participation in the study is voluntary, and asked if he would like to continue. He opted to continue with the session. Study PI's and Co-I's were informed of the changes in the participant's condition. Study staff were instructed to pause the participant's future stimulation sessions.

The skin irritation was discussed extensively among the local site team as well as with the Neuromodulation/ Rehabilitation Core Directors, the Coordinating PI, and the full investigator team. Based on the characteristics of the skin irritation, their location away from the center of the coil and in an area not touching the coil, their pattern of distribution, and the fact that the irritation and swelling was improving spontaneously without any intervention by the team, it was determined that this is most likely not related to the study intervention or to any aspect of the intervention such as cleaning products used to disinfect the coil or to gloves or materials used by the study staff. This is most likely an unrelated minor condition of skin irritation or mild infection that is resolving spontaneously. It was also felt by the study team that continuing to participate in the study with this skin irritation would not place the participant at any greater risk than he would otherwise experience without this skin condition.

6005 MN 04/06/2023: After completing the 3-month follow-up on 04/12/23, participant M87124880 reported to the site RA that he was involuntarily hospitalized on 04/06/23 and placed on a 72-hour psychiatric hold. The participant's medical chart indicates that while intoxicated, the participant attempted suicide. Emergency services were alerted by family members and were able to intervene. The participant was discharged on 04/11/23 and his medical chart indicates there is a care plan in place as well as a scheduled outpatient visit. The PI's discussed this event and determined it is unrelated to participation in research or study intervention. Note the participant completed intervention on 12/29/22.

Use of Human Cadavers for Research Development Test & Evaluation (RDT&E), Education or Training

TOTAL ACTIVITIES: *No RDT&E, education or training activities involving human cadavers will be performed to complete the Statement of Work (SOW).*

ACTIVITIES: *No RDT&E, education or training activities involving human cadavers will be performed to complete the Statement of Work (SOW).*

Animal Use Regulatory Protocols

TOTAL PROTOCOL(S): *"No animal use research will be performed to complete the Statement of Work."*

4 Products

4.1 Journal Publications
Nothing to report.

4.2 Books or other non-periodical, one-time publications
Nothing to report.

4.3 Other publications conference papers and presentations

Quinn DK, Maple T, Lieske A, Cunningham S, Hiltner R, Worth L, Ojeda C, Jones TR, Upston J, Lehud E, Chen M, Pirio Richardson S, Sponheim S, Mayer AR, Davenport N. Control network neuromodulation to enhance cognitive training in complex traumatic brain injury (CONNECT-TBI). Poster abstract accepted at the Military Health System Research Symposium, Kissimmee, FL, September 12-15, 2022.

Lieske, A., Kellman, M., Davidson, S., O'Brien, M., Lahud, E., Worth, L., Richardson, J., Nelson, C., Robertson-Benta, C., Maple, T., Upston, J., Jones, T., Chen, M., Sponheim, S., Mayer, A., Pirio-Richardson, S., Quinn, D., & Davenport, N. (2023, April 21). *Safety, tolerability, and feasibility of NIBS for mTBI in veterans with considerations for symptom exaggeration* [Poster session]. MN Neuromodulation Symposium, Minneapolis, MN, United States.

Lieske, A., Kellman, M., Davidson, S., O'Brien, M., Lahud, E., Worth, L., Richardson, J., Nelson, C., Robertson-Benta, C., Maple, T., Upston, J., Jones, T., Chen, M., Sponheim, S., Mayer, A., Pirio-Richardson, S., Quinn, D., & Davenport, N. (2023, June 13). *Safety, tolerability, and feasibility of NIBS for mTBI in veterans with considerations for symptom exaggeration* [Poster session]. MINDS Post-Baccalaureate Poster Symposium, Minneapolis, MN, United States.

Jessica D. Richardson, Honey I. Hubbard, Sarah Grace Dalton, Sloan Davidson, Tiana Maple, Davin K. Quinn, Nicholas Davenport, Mo Chen, Rebecca Hiltner, Tom Jones, Andy Mayer, Orrin Myers, Cassandra Nelson, Sarah Pirio-Richardson1, Cidney Robertson-Benta, Scott Sponheim, Joel Upston, Lindsay Worth. Standardizing Attention Process Training – 3 For A Multi-Site Clinical Trial of Neuromodulation. 2023.

Refereed Conference Abstracts, Articles, and Presentations

Quinn, D.K., Upston, J., Jones, T., Lahud, E., Maple, T., Lieske, A., Cunningham, S., Robertson-Benta, C., Hiltner, R., Smith, C., Kellman, M., Nelson, C., Hubbard, H., Worth, L., Ojeda, C., Chen, M., Pirio-Richardson, S., Sponheim, S., Richardson, J.D., Mayer, A., & Davenport, N. (2023, Aug 14-17). *Control-network neuromodulation to enhance cognitive training in complex TBI (The CONNECT-TBI study): fMRI evidence of improved neural efficiency with APT-3.* Poster presented at the 2023 Military Health System Research Symposium.

Nelson, C.L., Richardson, J.D., Pirio-Richardson, S., Quinn, D.K., & Davenport, N.D. (2023, Aug 14-17). *Longitudinal effects of cognitive training on working memory and quality of life in OEF/OIF/OND Veterans with mild traumatic brain injury: A preliminary analysis.* Poster presented at the 2023 Military Health System Research Symposium.

Richardson, J.D., Hubbard, H.I., Dalton, S.G., Davidson, S., Maple, T., Quinn, D.K., Davenport, N., Chen, M., Hiltner, R., Jones, T., Mayer, A., Myers, O., Nelson, C.L., Pirio-Richardson, S., Robertson-Benta, C., Sponheim, S.R., Upston, J.A., & Worth, L. (2023, Aug 14-17). *Standardizing attention process training-3 for a multi-site clinical trial of neuromodulation.* Poster presented at the 2023 Military Health System Research Symposium.

Lieske, A., Kellman, M., Davidson, S., O'Brien, M., Lahud, E., Worth, L., Richardson, J.D., Nelson, C., Robertson-Benta, C., Maple, T., Upston, J., Chen, M., Sponheim, S., Mayer, A., Pirio-Richardson, S., Quinn, D., & Davenport, N. (2023, Apr 20-21). *Safety, tolerability, and feasibility of NIBS for mTBI in veterans with considerations for symptom exaggeration.* Poster presented at the 10th Annual Minnesota Neuromodulation Symposium – Neuromodulation of Homeostatic Mechanisms, Minneapolis, MN.

Contributed (un-refereed) Abstracts and/or Oral Presentations at Professional Meetings

4.4 Websites or other Internet sites

Nothing to report.

4.5 Technologies or techniques
The study team developed a containerized, virtual method of processing MRI images and determining ideal targets in the region of interest for individual subjects based on a novel task developed by the study investigators. The team also developed an algorithm for standardized Attention Process Training-3 individualization based on rules for increasing/decreasing difficulty across separate cognitive domains. These will be described in separate research papers to be published in 2023.

4.6 Inventions, patent applications, and/or licenses
Nothing to report.

4.7 Other products
Nothing to report.

5 Participants & Other Collaborating Organizations

Name	**Davin Quinn, MD**
Project Role	Coordinating PI (New Mexico), AOC Co-Director
Research Identifier	**0000-0002-1613-8018**
Nearest person month worked	**36**
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	**36**
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	**36**
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	**36**
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	**36**
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	**36**
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	**36**
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	**Lindsay Worth**
Project Role	Clinical Program Manager
Research Identifier	
Nearest person month worked	**16**
Contribution to Project	Ms. Worth, 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	**21**
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	**Sloan Davidson, MS**
Project Role	Study Coordinator (U. Minnesota)
Research Identifier	
Nearest person month worked	**21**
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	**21**
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	**28**
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	**Mia Kellman**
Project Role	Research Assistant (U. Minnesota)
Research Identifier	
Nearest person month worked	**14**
Contribution to Project	As a research assistant, Ms. Kellman is responsible for the administration of the study interventions at the University of Minnesota, including TMS, tDCS, and APT. Ms. Kellman will assist Dr. Chen in his lab with all parts of the neuromodulation component of the research protocol. Ms. Kellman will also provide comprehensive training to the study team on the StarStim 8 HD tDCS device.

Name	**Alana Lieske**
Project Role	Research Assistant (U. Minnesota)
Research Identifier	
Nearest person month worked	**28**
Contribution to Project	As a research assistant, Ms. Nelson is responsible for the administration of the study interventions at the University of Minnesota, including TMS, tDCS, and APT. Ms. Nelson will assist Dr. Chen in his lab with all parts of the neuromodulation component of the research protocol. Ms. Nelson 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	**27**
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	**Jessica McQuaid**
Project Role	Study Technician (MRN)
Research Identifier	
Nearest person month worked	**15**
Contribution to Project	As a study technician, Ms. McQuaid 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?

Davin Quinn, MD

New Support Starting

Site Principal Investigator, "Eye Recovery Automation for Post-Injury Dysfunctions (iRAPID)" (PI: Yaramothu). Department of Defense CDMRP FY21 TBIPHRP Clinical Trial Award. FTE: 0.10/1.2 calendar moths. Total Costs: . 09/01/2022-08/31/2026. Purpose: to conduct a clinical trial of VERVE, a virtual reality platform for delivering automated vision therapy for post-concussion convergence insufficiency in Veterans with mild traumatic brain injury.

Co-Investigator, "A Prospective Observational Study on Therapeutic and Adverse Effects of Medical Cannabis for Chronic Traumatic Brain Injury." Department of Defense CDMRP FY221 TBIPHRP Clinical Research Award. FTE: 0.05/0.6 calendar months. Total Costs: . 10/01/2022-09/30/2025. Purpose: To use advanced neuroimaging techniques to quantify changes in brain function in Veterans with traumatic brain injury taking medical cannabis.

Coordinating Principal Investigator, "Multimodal Image Analysis and Guidance of Neuromodulation for Trauma-Related Symptoms (MAGNETS)." DoD USAMRAA HT9425-23-1-1038. (PI: Quinn) FTE: 0.20/2.4 calendar months. Total costs: 09/30/2023-09/29/2027. Purpose: to conduct a randomized controlled trial of fMRI-guided accelerated intermittent theta burst stimulation for PTSD in Veterans.

Old Support Ended

Coordinating Principal Investigator on "High-Definition Transcranial Direct Current Stimulation for Sensory Deficits in Complex Traumatic Brain Injury." W81XWH-17-1-0432, "Department of Defense, Congressionally Directed Medical Research Programs: Complex Traumatic Brain Injury Rehabilitation Research Award." PI: Quinn. FTE: 0.3/3.6 calendar months. 11/1/2017-9/30/2022. Purpose: to characterize and ameliorate cognitive control deficits underlying multisensory postconcussive symptoms using magnetoencephalography and high-definition transcranial direct current stimulation in Veterans and Servicemembers with mild traumatic brain injury.

Co-Principal Investigator on "Individualized Targeting and Neuromodulation of Late Life Depression." Mind Research Network CoBRE Pilot Program. PI: Quinn/Abbott. FTE: 0.01 FTE/0.12 calendar months. 10/01/2020 – 04/30/2022. Purpose: a pilot study of structural and functional MRI (sfMRI) to identify individual-specific targets for TMS to treat late life depression.

Nicholas Davenport

New Support
None

Decrease in Support
Co-Investigator Advancing Mechanisms of Resilience (decrease of .6 calendar months)

Andrew Mayer

New Support
None

Old support ended:

Co-Investigator on “High-Definition Transcranial Direct Current Stimulation for Sensory Deficits in Complex Traumatic Brain Injury.” W81XWH-17-1-0432, “Department of Defense, Congressionally Directed Medical Research Programs: Complex Traumatic Brain Injury Rehabilitation Research Award.” PI: Quinn. FTE: 0.1/1.2 calendar months. 11/1/2017-9/30/2022. Purpose: to characterize and ameliorate cognitive control deficits underlying multisensory post concussive symptoms using magnetoencephalography and high-definition transcranial direct current stimulation in Veterans and Servicemembers with mild traumatic brain injury.

Scott Sponheim

New Support
None

Old Support Ended
***Title: 5/5 Cognitive Neurocomputational Task Reliability & Clinical Applications**
***Major Goals: Multisite study to develop new cognitive tasks that can be resolved computationally in patients with SMI.
***Status of Support: ACTIVE
Project Number: R01MH084861
Name of PD/PI: MacDonald, Angus
***Source of Support: NIH
***Primary Place of Performance: University of Minnesota
Project/Proposal Start and End Date: (MM/YYYY) (if available): 09/01/2019 – 06/30/2023
***Total Award Amount (including Indirect Costs):
***Person Months (Calendar/Academic/Summer) per budget period.

Mo Chen

New support starting
None

Old Support Ended
*Role: Co-I.
*Title: Transcranial magnetic stimulation to augment behavior therapy for tics
*Major Goals: using non-invasive neuromodulation technique as a treatment to tics
*Status of Support: active
*Project Number: R61MH123754
*Name of PD/PI: Christine Conelea
*Source of Support: NIH-NIMH
*Primary Place of Performance: University of Minnesota
*Project/Proposal Start and End Date: (MM/YYYY) (if available): 11/2020-08/2023
* Total Award Amount (including Indirect Costs):
*Person Months (Calendar/Academic/Summer) per budget period: Year (YYYY) Person Months (##.##):
4. 2023 0.2

Sarah Pirio-Richardson

New Support
DOD 13767423 Quinn (PI) 9/1/23-8/31/27
DOD TBI/PHRP/CTA “Multimodal Image Analysis and Guidance of Neuromodulation for Trauma-Related Symptoms (MAGNETS)” The project will examine neuromodulation for the treatment of posttraumatic symptoms and assess functional and structural connectivity features.
Role: Co-I (0.10 FTE)

R01 NS133569-01 Ryman (PI) 8/1/23-7/30/27

“Microbiome-gut-brain dysfunction in prodromal and symptomatic Lewy body diseases”
The current project will evaluate specific aspects of microbiome-gut-brain dysfunction in prodromal and symptomatic patients to identify potential early disease mechanisms.
Role: Co-I (0.10 FTE)

R21 TR0044220-01 Peterson (PI) 4/1/23-3/31/25
“Synergistic clinical outcome assessments for cervical dystonia”
This project will provide important information about CMOR’s validity and a quantitative basis for sample size estimates for future clinical trials in CD.
Role: Consultant

Old Support Ended
Dystonia Coalition Pilot Project 8/1/22-7/31/23
Martino (PI)
“MOODSCREEN for Dystonia: a diagnostic accuracy study of depression and anxiety in people with adult-onset isolated dystonia”
Role: Site PI

Jessica Richardson

New Support
Combining cerebellar tDCS in CILT in non-fluent aphasia: A novel approach to discourse
Role: Consultant (PI: Samargia-Grivette)
NIH National Center of Neuromodulation for Rehabilitation (NM4R)
Award period: 6/12/23 – 4/30/24

Translating educational brain injury materials into American Sign Language
Role: PI
State of New Mexico, Governor’s Commission on Disability, Brain Injury Advisory Council
Award period: 4/1/23 – 6/30/23

Group singing to improve communication and wellbeing for persons with aphasia or Parkinson disease
Role: PI
SingWell Canada
Award period: 4/1/22 – 3/31/24

Old Support Ended
Investigating the benefits of remotely supervised neuromodulation in primary progressive aphasia
Role: Consultant (PI: Henry)
UCSF, Private Gift
Gift: 2023

Speech profiles and cue responsiveness in primary progressive aphasia
Role: Co-I (PI: Haley)
NIH NIDCD, 3R01 DC018569-02S1
Award period: 4/1/2021 – 3/31/2023

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.

6 Special Reporting Requirements

Quad Charts: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

7 Appendices

None.