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TITLE: Neuromodulation and Neurorehabilitation for Treatment of Functional Deficits after mTBI plus PTSD

PRINCIPAL INVESTIGATOR: Theresa Pape, DrPH

CONTRACTING ORGANIZATION:
Chicago Association for Research and Education in Science
Hines, IL

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6. AUTHOR(S)

Dr. Theresa Pape

E-Mail: Theresa.BenderPape@va.gov

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

Chicago Association for Research and Education
5000 South 5th Avenue
Bldg. One C347
Hines, IL 60141

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USA MED Research Acquisition Activity
820 Chandler St.
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14. ABSTRACT

This study will determine (i) the magnitude of immediate and sustained effects of a current clinical standard interactive computer attention processing training (APT) when combined with intermittent theta burst stimulation (iTBS), a type of repetitive transcranial magnetic stimulation (TMS) and (ii) determine how APT + iTBS changes the neurocognitive system of attention in individuals with persistent attention deficits related to mTBI and PTSD. Previous studies have shown that iTBS can produce alterations in cerebral function that facilitate learning and recovery from neurologic injury.

15. SUBJECT TERMS

Neurobehavioral, intermittent Theta Burst Stimulation(iTBS), Attention Processing Training (APT), Mild Traumatic Brain Injury (mTBI), Post-traumatic Stress Disorder (PTSD)

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1. **INTRODUCTION:** The purpose of this study is to determine the magnitude of immediate, sustained and long term effects of the current clinical standard interactive computer attention processing training (APT)1 combined with intermittent theta burst transcranial magnetic stimulation (iTBS) in Veterans, Active Duty Military Personnel and Civilians with persisting attention deficits related to Mild Traumatic Brain Injury (mTBI) and Post Traumatic Stress Disorder (PTSD) and to determine how APT + iTBS changes the neurocognitive system of attention in these individuals. This study is a randomized clinical trial (RCT) that directly addresses the intent of the Neurosensory and Rehabilitation Research Award program announcement (W81XWH-14-CRMRP-NSRRA), specifically the Clinical Trial Research Focus Area of Neuromusculoskeletal Rehabilitation. The proposed work will impact the health care needs of Active Duty Military Personnel and Veterans with mTBI and PTSD (mTBI + PTSD) because the anticipated findings will advance our understanding of long-term remediation of attentional deficits and how this translates to improved functioning in everyday life. This research is also likely to provide new avenues for treatment research for all TBI, fundamentally advancing the field of TBI neurorehabilitation.

2. **KEYWORDS:**

   Attention Processing Training (APT), Intermittent Theta Burst Stimulation (iTBS), Mild Traumatic Brain Injury (mTBI), Post-Traumatic Stress Disorder (PTSD), Randomized Clinical Trial (RCT)

3. **ACCOMPLISHMENTS:**

What were the major goals of the project?

Major Goal 1: Regulatory Requirements (Months 1-6)

Milestones Achieved: Local IRB approval for VA and NMH;

Milestones Achieved: 2nd level IRB approval by HRPO/ORP;

Initial IRB approvals have been obtained from both Northwestern University and Hines VA IRB. HRPO has reviewed and approved the study at Northwestern University as of December 21, 2017. HRPO reviewed and approved the study at Hines VA as of 11-23-2018. Local IRB approved requested changes with an effective date of 11-26-2018.

Major Goal 2: Coordinate Study Staff and Logistics for Study (Months 1-6)

Subtask 2a: Hiring and Training of Study Staff

Milestones Achieved: Study staff hired and trained at both study sites;

Subtask 2b: Development of study related materials and finalize logistics

Milestones Achieved: All study materials and procedures finalized at both study sites; All study staff have been hired at Hines VA and Northwestern. Training of staff to administer neuropsychological evaluations is almost complete. Training of staff to do iTBS and finalizing procedures are in progress. This training of iTBS and final procedures were previously on hold due to the COVID-Administrative Hold and remote working environments. Training has resumed on intervention and testing batteries to prepare for resuming in person research activities.

Major Goal 3: Participant Recruitment, iTBS/APT Intervention and Follow-up (Months 6-45):
Study Cohort data has been acquired through the use of the VA Data Access Request Tracker (DART). Vetting of cohort data for recruitment is ongoing (approximately 30,000 records remained after initial vetting process). Screening of civilians has been bolstered by initiating services of Patient Wing, a web-based recruitment platform. During the current reporting period, 42 new screenings have been completed with a total of 641 potential subjects screened to date. At the time of this report, 404 of those potential subjects were excluded and we were unable to achieve contact with 78 potential subjects to screen for participation. 287 letters have been sent to potentially eligible participants, with 92 individuals declining participation or opting out of being contacted. An additional 67 individuals are in the process of being contacted for telephone screening after screening of the electronic medical record or Patient Wing application has indicated possible eligibility. Fifty-one telephone screenings have been completed to date, with 9 individuals pending a Diagnostic Confirmation Screening once the COVID-Administrative hold is lifted. No participants have been enrolled to date, however we have received approval to lift the administrative hold at Hines pending a final IRB approval, and are awaiting a decision from Northwestern to lift the hold at that site.

Major Goal 4: Data Analysis (Months 4-48): Nothing to report.

What opportunities for training and professional development has the project provided?
Nothing to report.

How were the results disseminated to communities of interest? Nothing to report.

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

During the next reporting period, we will continue remote recruitment efforts and hope to progress subjects who have passed Telephone Screening to Diagnostic Confirmation Screening. We are working with leadership at Hines and Northwestern on appropriate procedures and timing to resume enrollment of participants at Northwestern and Hines VA following the administrative hold due to COVID-19. We have preliminary approval to resume in-person research activities at Hines and have submitted necessary documents to lift the hold to Hines IRB. We have approval from the Clinical Research Unit to resume in person research activities at Northwestern, and are awaiting approval of the Pandemic Research Plan that is a final requirement for reactivation. We will continue training of staff to use TMS equipment, deliver iTBS protocol and administer active and sham APT. Hines and Northwestern IRBs have approved our most recent protocol revision to reduce treatment days and increased compensation to decrease the burden on participants and facilitate improved enrollment for this study.

4. **IMPACT:** Nothing to report.

5. **CHANGES/PROBLEMS:**

Changes in approach are **not** anticipated at this time.

Problems: The only problem encountered during this period has been with recruitment and enrollment. We have heard from several possible participants that the time commitment required for participation in this study is too burdensome. As mentioned previously, we have plans to revise the study in order to reduce that burden on participants.

6. **PRODUCTS:** We currently have two manuscripts in press, including Cognitive Capacity and WHODAS Function and a first paper for Mayo Portland Participation Index in press, with a 2nd follow up paper under review. A previously unreported manuscript, Psychometric measurement properties of the world health organization disability assessment schedule 2.0 (WHODAS) evaluated among veterans with mild traumatic brain injury and behavioral health conditions Herrold et al., was published in Disability and Rehabilitation in September 2019. Additional manuscripts are in development to describe the basis for iTBS and APT as interventions, and APT standardization. We are also in the process of developing a manual for APT administration.

7. PARTICIPANTS AND OTHER COLLABORATING ORGANIZATIONS:

What individuals have worked on the project?

Name: Ann Guernon, MS, CCC-SLP, CCRC No Change

Name: Theresa Pape, DrPH, MA, CCC-SLP No Change

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period? Nothing to report.

What other organizations were involved as partners?

Organization Name: Northwestern University
Location of Organization: Chicago, IL, USA
Partner's Contribution to the Project: Collaboration

8. **SPECIAL REORTING REQUIREMENTS:** None.

9. **APPENDICES:** Quad chart attached.