

10  
celebrating  
YEARS

VOLUME II | 2020

# FORCE READINESS THROUGH RESEARCH



Walter Reed  
National Military  
Medical Center

 **NICoE**  
NATIONAL INTREPID CENTER OF EXCELLENCE

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*Research at the National Intrepid Center of Excellence contributes to force readiness by evaluating promising treatments, sharpening our understanding of traumatic brain injury effects on service members and their families, and exporting this knowledge to the Military Health System.*

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## **Mission**

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We improve the lives of patients and families impacted by TBI through excellence and innovation



## **Vision**

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To be a global leader in TBI care, research, and education



## **Guiding Principles**

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Excellence, Innovation, Compassion, Honor, and Collaboration

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## List of Acronyms

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**APD** - Acquired Auditory Processing Deficits

**CAREN** - Computer Assisted Rehabilitation Environment

**CES** - Cranial Electrical Stimulation

**CNRM** - Center for Neuroscience and Regenerative Medicine, USU, Bethesda, MD

**CRSR** - Center for Rehabilitation Sciences Research

**DoD** - Department of Defense

**DVBIC** - Defense and Veterans Brain Injury Center, Silver Spring, MD

**EEG** - Electroencephalogram

**FBCH** - Fort Belvoir Community Hospital, Fort Belvoir, VA

**HJF** - Henry M. Jackson Foundation, Bethesda, MD

**ICT-rTMS** - Individual Connectome-Targeted Repetitive Transcranial Magnetic Stimulation

**IOP** - Intensive Outpatient Program

**ISC** - Intrepid Spirit Center

**mTBI** - Mild Traumatic Brain Injury

**MHS** - Military Health Systems

**3MDR** - Motion-assisted, Multi-modular Memory Desensitization and Reconsolidation

**NCPTSD** - National Center for Posttraumatic Stress Disorder

**NICoE** - The National Intrepid Center of Excellence, Bethesda, MD

**NIH** - National Institutes of Health, Bethesda, MD

**NHT** - Normal-to-Near-Normal Hearing Thresholds

**NRAP** - National Research Action Plan

**PET** - Positron Emission Tomography

**PTSD** - Posttraumatic Stress Disorder

**PTS** - Posttraumatic Stress Symptoms

**rTMS** - Repetitive Transcranial Magnetic Stimulation

**TBI** - Traumatic Brain Injury

**TMS** - Transcranial Magnetic Stimulation

**USU** - Uniformed Services University of the Health Sciences, Bethesda, MD

**WAMC** - Womack Army Medical Center, Fort Bragg, NC

**WRNMMC** - Walter Reed National Military Medical Center, Bethesda, MD



## Introduction

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### **Treven C. Pickett, Psy.D.**

*Department Chief, Research  
National Intrepid Center of Excellence,  
Walter Reed National Military Medical Center*



This year has been one in which profound changes have affected many aspects of life. Amidst the uncertainty and stress brought about by a global pandemic, as well as social and economic unrest, we find ourselves now more than ever discovering latent strengths and ingenuity to adapt to challenges. On March 16, 2020, NICoE leadership made a careful decision to suspend all face-to-face research activities as part of a multi-faceted effort to reduce the risk of infection to patients, participants, and staff.

In the months that followed, our research teams found innovative ways to adapt to ever-evolving environmental circumstances. They have incorporated virtual platforms in study procedures to the fullest extent possible and secured personal protective equipment, all while navigating regulatory channels. I have been both humbled and inspired by our study teams' intelligence, adaptability, and unwavering commitment to the advancement of science.

As of the printing of this booklet and after careful examination of each team's proposed risk mitigation plans, more than half of our active studies have been approved to resume face-to-face research activities at the NICoE. We are committed to proceeding thoughtfully, incrementally, and with an abundance of caution for participants and staff.

Within this booklet is a brief account of the NICoE's current research portfolio, which comprises a wide range of studies aimed toward characterizing TBI and associated psychological health conditions and, in some cases, addressing their long-term impacts. These studies employ a host of tools and techniques to assess patient outcomes, including biomarker discovery, advanced neuroimaging, and an array of cognitive and emotional assessments.

An emerging finding that is particularly relevant to service members with a history of TBI, the population we most immediately serve, is that the presence of PTS in these men and women may be associated with adverse long-term neurobehavioral outcomes. In alignment with this finding are various interventional studies for PTS in service members with a history of TBI. Examples of such research include the exploration of CES for anxiety; TMS and 3MDR therapy studies for PTSD; and analyses of the Biopsychosocial Effect of Service Dog Training on PTS and Post Concussive Symptoms. In addition to investigating the complex comorbidity of PTS and TBI, NICoE's research portfolio includes several interventional studies targeting other common neurobehavioral and mental health sequelae following TBI, such as posttraumatic headaches and depression.

NICoE study teams' external partnerships with federal, academia, and industry organizations are critical to furthering scientific work. As the NICoE and ISC Network evolves, so do the interdisciplinary research teams interested in exploring the more pressing symptoms affecting service members with a history of TBI. In alignment with the NRAP and the Warfighter Brain Health initiative, we ultimately intend to continue translating research findings into contributions that inform clinical practice, improve care for service members and their families, and promote warfighter readiness.

We hope you enjoy reading about the NICoE's active research studies and that this booklet leaves you informed, inspired, and eager to learn more.



# Imaging [18F]AV-1451 and Florbetaben F18 in Military Service Members with Blast-Related Mild Traumatic Brain Injury

## Grant Bonavia, M.D., Ph.D., Principal Investigator

Service Chief, Imaging and Measurement, NICoE  
Staff Radiologist and Nuclear Medicine Physician, WRNMMC



### RESEARCH HIGHLIGHT

This interdisciplinary study aims to develop an understanding of the molecular imaging features of blast-related mTBI in military personnel while helping to establish assessment tools that may be of use in the diagnosis, determining prognosis, and in future therapeutic clinical trials. Of particular interest is the relationship between mTBI and chronic neurodegeneration in active duty military service members with a history of blast-related mTBI. The study is one of the first to use PET imaging to investigate tau and amyloid in active duty military service members with a history of blast exposure, to determine whether these individuals are at risk for developing chronic traumatic encephalopathy (CTE).

### KEY STUDY TEAM

*Co-Principal Investigator:*

Dara Dickstein, Ph.D. (USU)

*Associate Investigators:*

John Ollinger, Ph.D. (NICoE)

Thomas DeGraba, M.D. (NICoE)

### STUDY SITE(S)

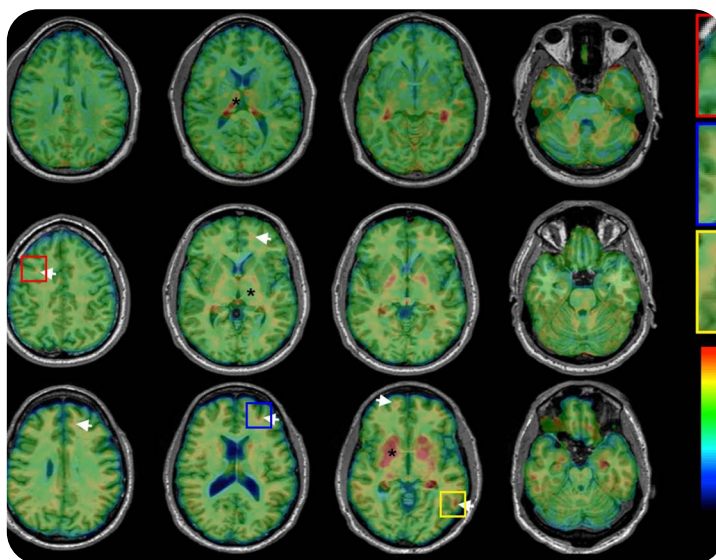
- NICoE, WRNMMC, Bethesda, MD
- USU, WRNMMC, Bethesda, MD

### FUNDING

CNRM, USU, Bethesda, MD

### STUDY IMPACT

This study's results may aid in the delineation of the cognitive and neurobiological profile of blast-related mTBI in the military population and may provide currently unavailable and crucial information with regard to the risk of developing CTE-like dementia. Additionally, findings from this study may be useful in the development of adequate intervention, new treatments, and improved long-term care planning.





# A Randomized, Sham-Controlled, Blinded Study of Bilateral Prefrontal Individual Connectome- Targeted Repetitive Transcranial Magnetic Stimulation (ICT-rTMS) to Treat the Symptoms of Depression Associated with Concussive TBI

**David Brody, M.D., Ph.D., Principal Investigator**

*Director, CNRM, USU*



## RESEARCH HIGHLIGHT

This multi-site study sponsored by the CNRM at the USU investigates the efficacy and tolerability of ICT-rTMS treatment to improve symptoms of depression that are often associated with concussive TBI.

Up to ninety subjects will be block randomized to active ICT-rTMS or sham treatment. Subjects will receive 20 sessions of ICT-rTMS over approximately five weeks. Treatment sessions will consist of high-frequency left dorsolateral prefrontal cortex (DLPFC) stimulation for 3,000 pulses followed by low-frequency right DLPFC stimulation for 1,000 pulses for a total stimulation time of approximately one hour per session. The primary outcome will be a change in depression severity from baseline to post-treatment.

This study aims to develop a novel, effective treatment for depressive symptoms associated with concussive TBI by using a coordinate-based computer system to deliver a more precise and individualized intervention. Depression after TBI increases the risk of developing other neuropsychiatric problems that may contribute to morbidity and functional disability after TBI, including increased suicidality, cognitive dysfunction, and aggressive behavior. Posttraumatic depression also interferes with physical and cognitive rehabilitation, making depressive symptoms one of the strongest correlates of poor recovery and quality of life after injury.

## STUDY IMPACT

If successful, findings from this study will speed the development of a novel, nonpharmacologic treatment for depression for service members with a history of concussion.

## KEY STUDY TEAM

*Associate Investigators:*

Charline Simon, M.A. (CNRM, USU)

Diana Nora, B.S., CNA (CNRM, USU)

Alexander Koosman, B.S. (CNRM, USU)

Xochitl Ceniceros, Ph.D., RN (CNRM, USU)

## STUDY SITE(S)

- WRNMMC, Bethesda, MD
- FBCH, Fort Belvoir, VA

## FUNDING

CNRM, USU, Bethesda, MD

## SELECTED PUBLICATION

1. Siddiqi, S. H., Trapp, N. T., Hacker, C. D., Laumann, T. O., Kandala, S., Hong, X., ... & Brody, D. L. (2019). Repetitive Transcranial Magnetic Stimulation with Resting-State Network Targeting for Treatment-Resistant Depression in Traumatic Brain Injury: A Randomized, Controlled, Double-Blinded Pilot Study. *Journal of neurotrauma*, 36(8), 1361-1374

FIND OUT MORE: <https://clinicaltrials.gov/ct2/show/NCT03523507>



# Rehabilitation of Acquired Auditory Processing Disorders – Low-Gain Hearing Aids

## Douglas S. Brungart, Ph.D., Principal Investigator

Chief Scientist, National Military Audiology and Speech Center, WRNMMC  
Chief Scientist and Associate Director, Research Coordination Branch, Hearing Center of Excellence



### RESEARCH HIGHLIGHT

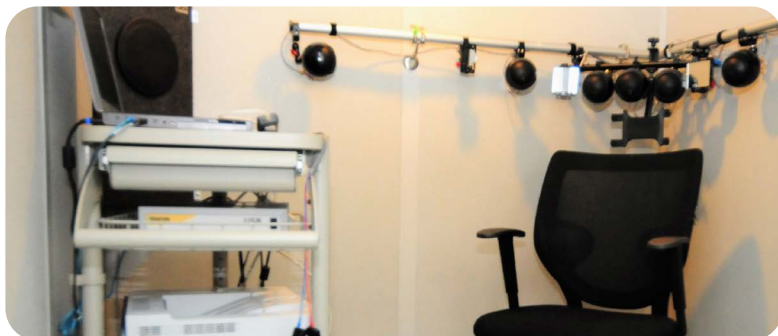
Adult patients diagnosed with APD are often offered low-gain hearing aids (LGHAs) as a treatment option despite the presence of NHT. This treatment, arguably becoming the standard of care in the private sector and military medical system, is based primarily on anecdotal patient reports with minimal published research.

While peripheral hearing loss remains a pervasive problem among service members, injury to the military's peripheral and central auditory system is increasingly related to TBI and blast exposure. The functional communication and hearing deficits subjectively reported by these individuals often occur in the absence of elevated pure-tone thresholds and have been identified as APD. While these service members often receive treatment in the form of LGHAs, limited systematic evaluation of treatment efficacy is available, despite common reports of subjective benefit.

This work aims to examine the efficacy of LGHAs in an active duty military population with a history of mild TBI and blast exposure who have been diagnosed with APD in the presence of NHT. This research addresses the limited evidence to support fitting LGHAs in this population by comparing aided and unaided outcomes using both subjective and objective measures. In addition, the potential "hidden" peripheral damage associated with the functional presentation of these deficits, despite NHTs, will be examined as it relates to subjective and objective outcomes.

### STUDY IMPACT

Results from this study will influence the standard of care received by adult TBI patients diagnosed with APD in the presence of NHT, thus improving the ability to treat and limit associated functional impairments.



### KEY STUDY TEAM

Associate Investigators:

Melissa Kokx-Ryan, Au.D., Ph.D. (NICoE)

Shoshannah Russell, Au.D. (WRNMMC)

Mary Barrett, Au.D. (WRNMMC)

### STUDY SITE(S)

WRNMMC, Bethesda, MD

### FUNDING

US Army Medical Research and Materiel Command – Award Number: W81XWH-16-1-0026

### SELECTED PRESENTATION

1. Kokx-Ryan, M. (2020) Evaluation of low-gain hearing aids as a treatment for auditory processing deficits in Service Members with normal hearing thresholds and history of mTBI [Doctoral dissertation, Gallaudet University]. ProQuest Dissertation Publishing.
2. Kokx-Ryan, M. (2017, April) Low-gain hearing aids as a treatment option for patients with normal-hearing thresholds who exhibit auditory processing deficits. Oral Presentation, eAudiology Web Seminar.





# Assessing the Impact of mTBI on Multi-Sensory Integration While Maneuvering on Foot

## Douglas S. Brungart, Ph.D., Principal Investigator

Chief Scientist, National Military Audiology and Speech Center, WRNMMC  
Chief Scientist and Associate Director, Research Coordination Branch, Hearing Center of Excellence



### RESEARCH HIGHLIGHT

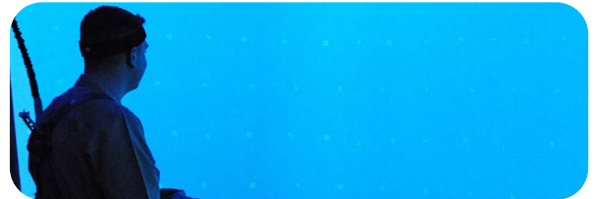
Service members' success in combat operations is largely dependent on their ability to shoot, move, and communicate on the battlefield. These critical tasks require the execution of numerous complex subtasks that involve processing simultaneous inputs from the auditory, visual, vestibular, tactile, and proprioceptive senses.

This project uses an aurally-aided visual search (AAVS) paradigm to examine the impact that unimodal and multi-sensory deficits have on the functional performance of sensory-impaired service members. Experiments are conducted using the CAREN, which was modified for this study to include a 64-speaker audio array behind the system's screen. The CAREN makes it possible to measure how well participants perform audio-visual integration tasks while standing still or maneuvering on foot using the system's embedded treadmill.

Two groups of participants were recruited: 1) healthy controls and 2) those with blast-related mTBI. Preliminary results show that the mTBI group responds about 15% slower in the AAVS task and that both groups respond faster while walking without any reduction in accuracy. With further testing, the researchers hope to validate whether the AAVS paradigm is sensitive enough to detect subtle multimodal integration problems that are not apparent in more traditional unimodal sensory tasks.

### STUDY IMPACT

Information obtained from this study will have near- and long-term positive impacts, both in defining return-to-duty standards for service members with brain injuries and developing rehabilitation strategies for impaired patients.



### KEY STUDY TEAM

Associate Investigator:

Sarah E. Kruger, M.S. (NICoE)

### STUDY SITE(S)

- NICoE, WRNMMC, Bethesda, MD
- National Military Audiology and Speech Center, WRNMMC, Bethesda, MD

### FUNDING

- US Army Medical Research and Material Command - FY11 CDMRP Psychological Health/Traumatic Brain Injury Applied Neurotrauma Research Award - Project Number: W81XWH-12-2-0068
- US Army Medical Research and Material Command - FY14 CDMRP Neurosensory and Rehabilitation Research Award - Project Number: W81XWH-16-1-0026

### SELECTED PUBLICATIONS

1. Brungart, D., Kruger, S., Kwiatkowski, T., Heil, T., Highland, K. B., Cohen, J., ... & Zion, D. (2019). The Effects of Blast-Related Neurotrauma on Aurally Aided Visual Search While Standing and Walking. *Journal of neurotrauma*.
2. Brungart, D. S., Kruger, S. E., Kwiatkowski, T., Heil, T., & Cohen, J. (2019). The effect of walking on auditory localization, visual discrimination, and aurally aided visual search. *Human factors*, 0018720819831092.



# Rehabilitation of Acquired Auditory Processing Deficits – Mobile Application-Based Computerized Auditory Training

## Douglas S. Brungart, Ph.D., Principal Investigator

*Chief Scientist, National Military Audiology and Speech Center, WRNMMC  
Chief Scientist and Associate Director, Research Coordination Branch, Hearing Center  
of Excellence*



### RESEARCH HIGHLIGHT

The auditory system is among the most frequently damaged in modern warfare, second only to the musculoskeletal system. While sensorineural hearing loss from noise exposure continues to be a pervasive problem in the military force, recent evidence suggests that blast and/or noise exposure without permanent hearing loss can have significant negative ramifications previously undetected.

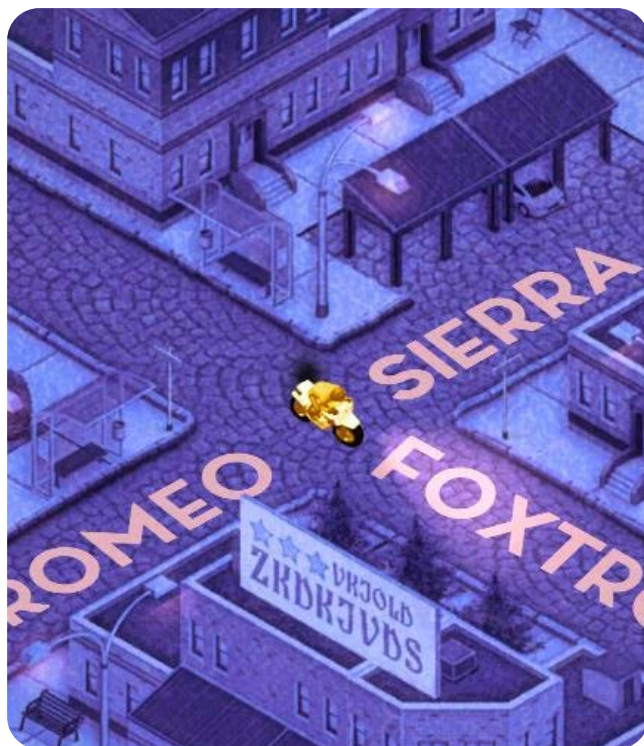
Despite the significant prevalence of patients with APD in the presence of normal hearing thresholds, professionals do not agree on the course of treatment. Management can range from receiving diagnosis of normal hearing with no additional follow-up to implementation of auditory training, counseling strategies, or management of acoustic conditions including hearing aids or frequency modulated system, or a combination of these strategies.

While there is ample research that supports the use of auditory training via software-based training programs, compliance with software-based auditory training is low. Furthermore, auditory training efficacy in service members with a history of significant noise exposure, blast injury, and/or TBI has not been evaluated.

The specific aim of this study is to provide evidence regarding the effectiveness of computerized auditory training as a treatment option for adults with normal-to-near-normal hearing thresholds and APD, who have a history of blast exposure and/or TBI.

### STUDY IMPACT

Analysis from this data may influence the standard of care that service members impacted by TBI receive, in order to improve our ability to treat functional hearing problems, which directly correlate to their quality of life.



### STUDY SITE(S)

WRNMMC, Bethesda, MD

### FUNDING

US Army Medical Research and Material Command –  
Award Number: W81XWH-16-1-0026

### KEY STUDY TEAM

*Associate Investigators*

Shoshannah Russell, Au.D. (WRNMMC)

Mary Barrett, Au.D. (WRNMMC)

Melissa Kokx-Ryan, Au.D., Ph.D. (NICoE)

Shannon Auxier, M.S. (NICoE)



# Integration of Image and Clinical Measurements of TBI Patients Using Machine Learning Techniques

## Jesus J. Caban, Ph.D., Principal Investigator

Chief for Clinical and Research Informatics, NICoE, WRNMMC



### RESEARCH HIGHLIGHT

The TBI military patient population is a high-risk group with more than 60% of active duty service members diagnosed with a TBI showing signs of depression and other behavioral health conditions within a year following their first brain injury. Currently, across the MHS, providers don't have the tools to quickly identify patients at risk of developing mental health conditions or the capabilities to model different clinical trajectories a patient can follow.

This retrospective study uses a large longitudinal clinical dataset of more than 100,000 mTBI patients to create machine learning and artificial intelligence models that can be used to automatically identify clinical trajectories, sub-categories of mTBI, and risk factors associated with the onset of mental health conditions. Through this study, a number of advanced predictive models have been developed, including models to estimate the probability of a patient returning to active duty, forecast models for retention post-injury, machine-learning models to identify the likelihood of developing clinical conditions, and predictors of healthcare utilization post-injury.

### STUDY IMPACT

The use of machine learning and artificial intelligence with large longitudinal retrospective clinical datasets will allow us to model the progression of mTBI, impacting our understanding of the short- and long-term effects of traumatic brain injuries.

### KEY STUDY TEAM

Associate Investigators:

Joseph Bleiberg, Ph.D. (NICoE)

Thomas DeGraba, M.D. (NICoE)

Donna Neuges, RN (NICoE)

### STUDY SITE(S)

NICoE, WRNMMC, Bethesda, MD

### SELECTED PUBLICATIONS

1. Dabek, F., Hoover, P., & Caban, J. (2018, December). DeepDx: A Deep Learning Approach for Predicting the Likelihood and Severity of Symptoms Post Concussion. In International Conference on Brain Informatics (pp. 381-391). Springer, Cham.
2. Dabek, F., Hoover, P., & Caban, J. (2018, December). Evaluating Mental Health Encounters in mTBI: Identifying Patient Subgroups and Recommending Personalized Treatments. In International Conference on Brain Informatics (pp. 370-380). Springer, Cham.
3. Dabek, F. J., & Caban, J. J. (2016). A k-reversible approach to model clinical trajectories. In AMIA Annual Symposium Proceedings (Vol. 2016, p. 460). American Medical Informatics Association.
4. Dabek, F., & Caban, J. J. (2015). Leveraging big data to model the likelihood of developing psychological conditions after a concussion. *Procedia Computer Science*, 53, 265-273.



# A Retrospective Study of the Natural History of Traumatic Brain Injury and Psychological Health Outcomes in Military Personnel Through Analysis of the NICoE Clinical Research Database

**Thomas J. DeGraba, M.D., Principal Investigator**

*Chief Innovations Officer, NICoE, WRNMMC*



## STUDY IMPACT

This systematic approach to collecting information on TBI and other psychological health conditions will advance the ability to evaluate, diagnose, and treat these conditions in both military and civilian populations. Additionally, this study is designed to enhance clinical practice guidelines, leveraging evidence-based analysis to identify best treatment practices for complex patient subpopulations cared for within the MHS.

## RESEARCH HIGHLIGHT

A central strategy to the NRAP is to develop a more precise staging and criteria for clinical subpopulations with combat-related TBI and comorbid psychological health conditions. This improved characterization of the heterogeneous injury state will lead to more rapid and earlier identification of brain disturbances and a more accurate selection of targeted treatment strategies.

This protocol is designed to leverage nine years of comprehensive data collected in the NICoE's IOP for service members with TBI and associated comorbidities. Synchronized collection of clinical data from this integrative program provides an opportunity to identify patterns of symptom clusters and corresponding neural network disruption to understand which treatment modalities are successful in specific subgroups of patient populations.

Preliminary data obtained from patients' self-report scales revealed a significant improvement in posttraumatic stress, anxiety, depression, sleep disturbances, and satisfaction in life from admission to discharge, with improvements lasting at least six months after participation in the program.

Continuing research aims to identify specific treatment strategies in the 17 different disciplines utilized in the NICoE IOP. Future goals include the ability to share information with other MHS TBI treatment facilities, such as the ISCs, to standardize best practices across the spectrum of injury severity.

## SELECTED PUBLICATIONS

1. Kaimal, G., Walker, M. S., Herres, J., Berberian, M., & DeGraba, T. J. (2020). Examining associations between montage painting imagery and symptoms of depression and posttraumatic stress among active-duty military service members. *Psychology of Aesthetics, Creativity, and the Arts*. Advance online publication. <http://dx.doi.org/10.1037/aca0000316>
2. Kaimal G, Walker MS, Herres J, French LM, DeGraba TJ (2018) Observational study of associations between visual imagery and measures of depression, anxiety and post-traumatic stress among active-duty military service members with traumatic brain injury at the Walter Reed National Military Medical Center. *BMJ Open* 2018;8:e021448. doi: 10.1136/bmjopen-2017-021448.
3. Walker M.S., Kaimal G., Gonzaga A.M.L., Myers-Coffman K.A., DeGraba T.J. (2017) Active-duty military service members' visual representations of PTSD and TBI in masks. *International Journal of Qualitative Studies on Health and Well-being*: 12(1), 1267317.
4. Dretsch MN, Williams K, Staver T, Grammer G, Bleiberg J, DeGraba T, Lange RT. (2016) Evaluating the clinical utility of the Validity-10 for detecting amplified symptom reporting for patients with mild traumatic brain injury and comorbid psychological health conditions. *Appl Neuropsychol Adult*. 2016 Aug 24:1-5.

## KEY STUDY TEAM

*Associate Investigators*

Louis French, Psy.D. (NICoE)

Chandler Rhodes, Ph.D. (NICoE)

Treven Pickett, Psy.D. (NICoE)

Donna Neuges, RN (NICoE)

## STUDY SITE(S)

NICoE, WRNMMC,  
Bethesda, MD





# Genomic Determinants Pre- and Post-NICoE Skills-Based Training: Measuring Relaxation Response in Service Members with Post-Traumatic Stress Disorder (PTSD) and Traumatic Brain Injury (TBI)

**Thomas J. DeGraba, M.D., Principal Investigator**

*Chief Innovations Officer, NICoE, WRNMMC*



## RESEARCH HIGHLIGHT

The need for effective treatments and reliable outcome measures for PTSD and TBI is a top priority for the MHS.

The study aims to measure quantifiable biological and clinical responses to integrative and conventional medicine treatments used in NICoE's four-week IOP, which targets service members recovering from TBI and behavioral health comorbidities.

Preliminary outcomes indicate that time spent in the creative arts, particularly art therapy, is associated with a reduction of PTS and anxiety. Additionally, the implementation of integrative medicine that includes mind-body treatments correlated with decreased anxiety and improved autonomic function and cerebral blood flow.

Furthermore, the initial analysis of genomic expression reveals a reduction of inflammatory gene activation during the four-week period. By the third and fourth weeks of the IOP, activation of genes involved in neuronal repair were noted to be up-regulated and closely-correlated with time spent in art therapy.

Ongoing recruitment for this study aims to validate initial findings. The study is a partnership with Harvard Medical School/Beth Israel Deaconess Medical Center for blood specimen analysis of genomic expression and the NIH for protein marker identification.

## STUDY IMPACT

The goal of this study is to develop definitive diagnostic biomarkers for TBI and comorbid PTSD and associated psychological health conditions.

### KEY STUDY TEAM

*Associate Investigators*

Donna Neuges, RN (NICoE)

Manoj Bhasin, Ph.D. (Emory)

Herbert Benson, M.D. (Harvard)

### STUDY SITE(S)

NICoE, WRNMMC, Bethesda, MD

## SELECTED PRESENTATIONS

1. MHSRS 2020 (Poster): Effect of combat and mission related repetitive blast and blunt force TBI on cerebral autonomic injury and response to integrative medicine therapies. Thomas DeGraba, MD, Nicholas Carter, MD, E Marshall Gregg MD, Sorana Raiciulescu
2. MHSRS 2018 (Poster): Gene expression and cerebral autonomic markers the recovery in an interdisciplinary integrative care model for service members with combat related TBI and PTSD. Thomas DeGraba, Mukta Joshi, Donna Neuges, Manoj Bhasin
3. National Capitol Area TBI Symposium 2019 (Poster): PTSD Symptom Reduction Among Combat Veterans with Co-Morbid TBI: Regression Analysis Investigating PCL-M Score Change as a Function of Time Engaged In Art Therapy. E. Marshall Gregg, Donna Neuges, Sorana Raiciulescu, Melissa S. Walker, Thomas J. DeGraba





# Expanding Our Understanding of Computer-Based Cognitive Rehabilitation in the Military Population – a Longitudinal Brain Fitness Center Database

## Louis M. French, Psy.D., Principal Investigator

Deputy Director for Operations, NICoE, WRNMMC  
Site Director, DVBIC; Associate Professor of Neurology and Rehabilitation, USU



### RESEARCH HIGHLIGHT

Cognitive dysfunction can occur from a variety of brain insults, including TBI. These deficits can have a significant impact on service members' functioning and quality of life. Unfortunately, there is a limited range of treatment options to address these concerns. Technology provides an additional method of treatment delivery that can increase access to rehabilitation. While computer-based cognitive rehabilitation is heavily marketed commercially, understanding of its efficacy, applicability in sub-populations, and other treatment characteristics are limited.

The purpose of this study is to improve understanding of the efficacy of computer-based cognitive rehabilitation tools and their utilization in the Brain Fitness Center (BFC) by developing a data repository.

The data repository consists of data, such as demographic information, objective cognitive assessments, self-report questionnaires, and participation data from individuals who use the computer-based cognitive rehabilitation tools in the BFC at WRNMMC and FBCH.



### STUDY IMPACT

This study will improve the understanding of the population, the utilization, and the efficacy of the BFC through retrospectively analyzing data from a pre-existing and pre-approved data collection protocol.

### KEY STUDY TEAM

Associate Investigators:

Katherine W. Sullivan, M.S. (NICoE)

Wendy Law, Ph.D. (NICoE)

Madeline Hartman, B.S. (NICoE)

Brett Theeler, M.D. (WRNMMC)

Dan Shub, Ph.D. (WRNMMC)

### STUDY SITE(S)

WRNMMC, Bethesda, MD

### FUNDING

CNRM, USU, Bethesda, MD



### SELECTED PUBLICATIONS

1. Sullivan, K. W., Law, W. A., Loyola, L., Knoll, M. A., Shub, D. E., & French, L. M. (2020). A Novel Intervention Platform for Service Members with Subjective Cognitive Complaints: Implementation, Patient Participation, and Satisfaction. *Military medicine*, 185(Supplement\_1), 326.
2. Sullivan, K. W., Solomon, N. P., Pramuka, M., Quinn, J. E., Teixeira, K. A., & French, L. M. (2015). Computer-based cognitive rehabilitation research in a military treatment facility: Recruitment, compliance, and lessons learned. *Work*, 50(1), 131-142.
3. Sullivan, K. W., Quinn, J. E., Pramuka, M., Sharkey, L. A., & French, L. M. (2012). Outcomes from a pilot study using computer-based rehabilitative tools in a military population. *Studies in health technology and informatics*, 181, 71-77.



## The 15-Year Studies

### Louis M. French, Psy.D., Principal Investigator

*Deputy Director for Operations, NICoE, WRNMMC  
Site Director, DVBIC; Associate Professor of Neurology and Rehabilitation, USU*



#### RESEARCH HIGHLIGHT

Walter Reed National Military Medical Center serves as the core site for this multi-site, longitudinal study into the long-term implications of traumatic brain injury (TBI) in military service members. This Defense and Veterans Brain Injury Center supported study was developed to respond to a congressional mandate (Sec721 NDAA FY07). It has two components:

1. The Natural History Study, which employs a host of clinical, behavioral, cognitive, sensory-motor, blood biomarker, and imaging assessments to identify issues that may make TBI recovery more difficult.
2. The Caregiver Study, which examines caregiver outcomes such as physical and mental health, employment, finances, family functioning, relationship satisfaction, and quality of life, as well as the impact on the health and behavior of the caregiver and service member's children.

#### STUDY IMPACT

These studies focus on the long-term physical and mental health outcomes and the effects on service members and their families following TBI with the goal of improving treatments and services for those affected.

#### KEY STUDY TEAM

*Associate Investigators:*

Rael T. Lange, Ph.D. (DVBIC)

Tracey A. Brickell, Psy.D. (DVBIC)

#### STUDY SITE(S)

- WRNMMC, Bethesda, MD
- FBCH, Fort Belvoir, VA

#### FUNDING

Defense and Veterans Brain Injury Center (DVBIC)

#### SELECTED PUBLICATIONS

1. Lange, R. T., Lippa, S. M., French, L. M., Bailie, J. M., Gartner, R. L., Driscoll, A. E., ... & Holzinger, J. B. (2019). Long-term neurobehavioural symptom reporting following mild, moderate, severe, and penetrating traumatic brain injury in US military service members. *Neuropsychological rehabilitation*, 1-24.
2. Lippa, S. M., Yeh, P. H., Gill, J., French, L. M., Brickell, T. A., & Lange, R. T. (2019). Plasma tau and amyloid are not reliably related to injury characteristics, neuropsychological performance, or white matter integrity in service members with a history of traumatic brain injury. *Journal of neurotrauma*.



# The Investigation of Cranial Electrical Stimulation (CES) to Reduce Anxiety in Service Members with a History of Mild TBI

**Linda Fuller, D.O., M.P.H, Principal Investigator**

*Psychiatrist, NICoE, WRNMMC*



## RESEARCH HIGHLIGHT

Service members with a history of mild TBI are at an increased risk for developing anxiety, which has secondarily been implicated in extended recovery timelines and poorer outcomes. This study's primary purpose is to determine the efficacy of non-invasive CES in conjunction with an integrative treatment program for improving symptoms of anxiety associated with TBI.

Sixty participants will be recruited from the NICoE IOP and will be randomly assigned to one of four treatment groups: an active or sham treatment group using CES applied to the scalp, or an active or sham treatment group using CES applied to the ear. Self-report assessments (BAI, GAD7, PSQI, PCL-5, NSI, HIT6, PHQ9, and ESS) administered pre and post two weeks of daily CES usage will be used to assess the primary outcome measure of anxiety as well as secondary outcome measures of depression, headache, and sleep.

## STUDY IMPACT

Findings of this study may support the use of CES as an adjunctive therapy to reduce persistent postconcussive and psychological health symptoms.

### KEY STUDY TEAM

*Co-Principal Investigator:*

Chandler Rhodes, Ph.D. (NICoE)

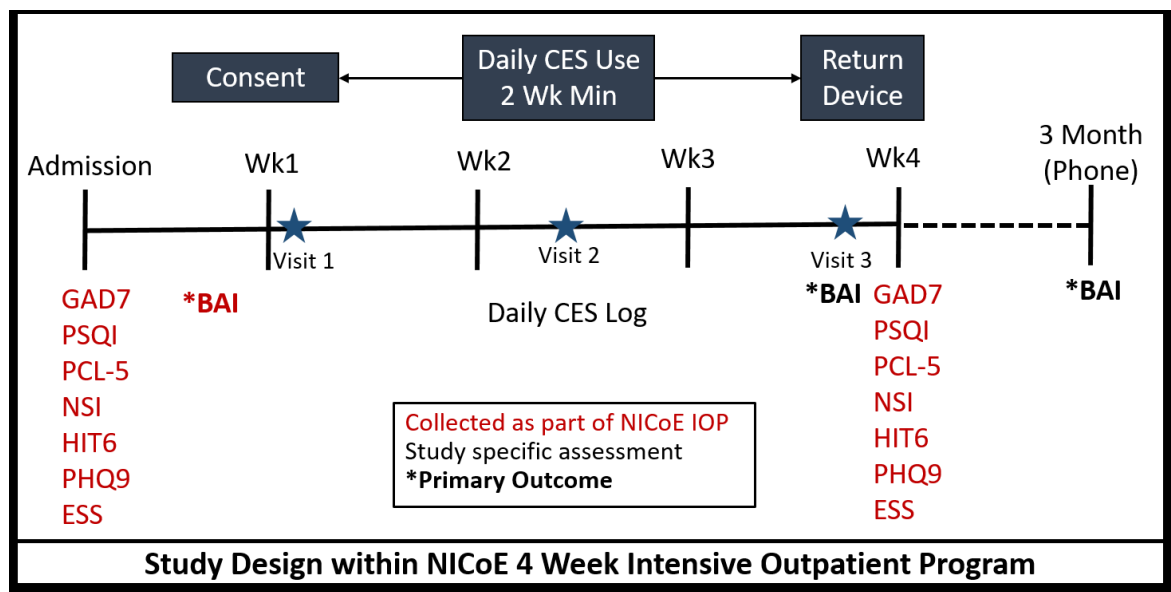
*Associate Investigators:*

Tara Staver, Psy.D. (NICoE)

Tamara McKenzie-Hartman, Psy.D. (NICoE)

### STUDY SITE(S)

NICoE, WRNMMC, Bethesda, MD



# NICoE TBI Magnetoencephalography (MEG) Core Project

## John D. Hughes, M.D., Principal Investigator

*Behavioral Biology Branch, Walter Reed Army Institute of Research (WRAIR)*



### RESEARCH HIGHLIGHT

Brain function is determined by the coordinated activity of ensembles of neurons bound together by virtue of neuronal oscillations (brainwaves) of various frequencies at various spatial scales (local, global). Brain dysfunction can be conceptualized fundamentally as an alteration of these oscillations and disorganization of these neuronal networks. Such alterations can only be assessed by methodologies, such as MEG, which record brain activity at a time scale of milliseconds.

This research provides neurophysiological data that will help understand the neurobiology of TBI and psychological health conditions, such as PTSD and depression. Our researcher scientists are mapping brain activity by noninvasively recording the magnetic fields produced when brain cells communicate with one another while participants are at rest or performing cognitive tasks.

By understanding the associations between functional impairments and neurophysiological derangements, such as between memory deficits and alterations in oscillatory brain activity, this study aims to further inform and evaluate treatment strategies to improve cognitive and emotional functioning in those affected by TBI and associated psychological health conditions.

### STUDY IMPACT

This study hopes to advance the understanding of the relationship between specific symptoms that affect those with TBI and the brain activity changes that underlie them. The physiologic changes associated with these symptoms may provide increased insight to tailor specific therapies and treatments for TBI and psychological health concerns.

### KEY STUDY TEAM

*Associate Investigators:*

Mihai Popescu, Ph.D. (NICoE)

Anda Popescu, Ph.D. (NICoE)

Thomas DeGraba, M.D. (NICoE)

Rebecca Sandlain, B.S. (NICoE)

Andrew Bryant, CNMT (NICoE)

### STUDY SITE(S)

WRNMMC, Bethesda, MD

### COLLABORATING SITE(S)

- WRAIR, Silver Spring, MD
- Washington DC VA Medical Center, Washington, DC
- USU, Bethesda, MD

### FUNDING

- Henry M. Jackson Foundation, Research Development Testing and Evaluation (RDT&E) funds

### SELECTED PUBLICATIONS

1. Popescu, M., Popescu, E. A., DeGraba, T. J., & Hughes, J. D. (2020). Altered modulation of beta-band oscillations during memory encoding is predictive of lower subsequent recognition performance in posttraumatic stress disorder. *NeuroImage: Clinical*, 25, 102154.
2. Popescu, M., Popescu, E. A., DeGraba, T. J., Fernandez-Fidalgo, D. J., Riedy, G., & Hughes, J. D. (2019). Posttraumatic stress disorder is associated with altered modulation of prefrontal alpha-band oscillations during working memory. *Clinical Neurophysiology*. 130(10), 1869-1881.
3. Popescu, M., Hughes, J. D., Popescu, E. A., Mikola, J., Merrifield, W., DeGraba, M., ... & DeGraba, T. J. (2017). Activation of dominant hemisphere association cortex during naming as a function of cognitive performance in mild traumatic brain injury: Insights into mechanisms of lexical access. *NeuroImage: Clinical*, 15, 741-752.
4. Popescu, M., Hughes, J. D., Popescu, E. A., Riedy, G., & DeGraba, T. J. (2016). Reduced prefrontal MEG alpha-band power in mild traumatic brain injury with associated posttraumatic stress disorder symptoms. *Clinical Neurophysiology*, 127(9), 3075-3085.



## Nutrition for Post-Traumatic Headache Study

### Kimbra Kenney, M.D., (Overall) Principal Investigator

*Service Chief, Research Operations, NICOE, WRNMMC*

*Professor, Neurology, USU*



### RESEARCH HIGHLIGHT

This is a multi-site, double-blind, two-arm, randomized clinical trial (NCT03272399) of a dietary intervention to treat chronic post-traumatic headache (PTH), funded by CDMRP.

The purpose of the study is to examine whether a targeted alteration of dietary essential fatty acids can improve headache-related quality of life among TBI survivors with PTH that also fulfill International Classification of Headache Disorders-3 criteria for migraine headache disorder as measured by the following primary study endpoints: 1) Overall headache burden, i.e. PTH frequency and severity (primary clinical outcome); and 2) changes in circulating fatty acid lipid mediators (primary biochemical outcome) as a result of the 12-week dietary intervention.

Chronic PTH is more prevalent among active duty military than civilian populations, and has recently been shown to be more difficult to treat than PTH among civilian TBI survivors. Additionally, it significantly adversely impacts force readiness (Metti A et al. *Neurology* 2020; doi: 10.1212/WNL.0000000000008935).

Traditional migraine therapies (pharmacologic and behavioral) have limited effectiveness in many PTH sufferers. This study investigates food alone as a novel PTH treatment through a dietary manipulation of essential fatty acids that have been linked to migraine pain propagation and pathogenesis. It is based on a pilot study of a similar dietary intervention in chronic migraine and chronic daily headache (CDH) patients that showed significant reduction in headache burden, headache medication use, as well as overall pain measures in patients randomized to the high omega-3/low omega-6 diet (Ramsden C et al. *Pain* 2013; doi: 10.1016/j.pain.2013.07.028).

### STUDY IMPACT

If successful, this study will support a safe, non-medicinal, dietary ("food as medicine") therapy that reduces chronic PTH burden, decreases PTH medication use and may reduce overall pain medication use.

#### KEY STUDY TEAM

*Site Principal Investigators:*

Kimbra Kenney, M.D. (WRNMMC)

Hee-Chin Chae, M.D. (FBCH)

Wes Cole, Ph.D. (WAMC),

Kim Faurot, Ph.D. (UNC)

Doug Mann, M.D. (UNC)

Christopher Ramsden, M.D. (NIH)

*Associate Investigators:*

Ruth Clark, RD (NICOE)

J. Kent Werner, M.D., Ph.D. (WRNMMC)

Ann Nothwehr, M.P.H., RD (WRNMMC)

Cora Davis, B.A. (WRNMMC)

Carole Moore, M.S. (USU)

Margaret Dunlap, M.S. (FBCH)

Wanda Rivera, R.D. (FBCH)

Brittney Roberson, M.S. (WAMC)

Jacques Arrieux, M.A. (WAMC)

Beth MacIntosh, M.P.H., RD, LDN (UNC)

Michelle Bean, RD (UNC)

#### STUDY SITE(S)

- WRNMMC, Bethesda, MD
- FBCH, Fort Belvoir, VA
- NIH, Bethesda, MD
- Womack Army Medical Center (WAMC), Fort Bragg, NC
- University of North Carolina (UNC), Chapel Hill, NC

#### FUNDING

CDMRP

*FIND OUT MORE:*  
<https://clinicaltrials.gov/ct2/show/NCT03272399>





## Oculomotor Assessment of Traumatic Brain Injury

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### John E. King, Ph.D., Principal Investigator

*Audiologist, NICoE, WRNMMC*



#### RESEARCH HIGHLIGHT

Oculomotor testing, a subcomponent of vestibular testing, is a broad term for a number of tests that evaluate a patient's eye movements with specialized camera systems. Historically, oculomotor testing is used to rule out central vestibular disorders that contribute to dizziness or imbalance; however, it is reasonable to expect that functional deficits in the oculomotor system are sensitive indicators of insult in TBI.

The purpose of the study is to compare the sensitivity and specificity of three oculomotor testing devices. Data from each device will undergo area-under-the-curve analysis to determine the ability of each to correctly identify control subjects versus subjects with confirmed history of TBI.

The study is designed as a prospective research project in which a group of 120 normal controls without a history of TBI will be compared to another group of 120 participants who have a confirmed history of TBI. Each participant (total of 240) will complete the TBI assessment protocol for all three aforementioned devices.

#### STUDY IMPACT

The military will utilize results from this study for further development of a deployable oculomotor test for use in theater.

#### KEY STUDY TEAM

Louis French, Psy.D. (NICoE)

Saafan Malik, M.D., M.B.A. (DHA)

#### STUDY SITE(S)

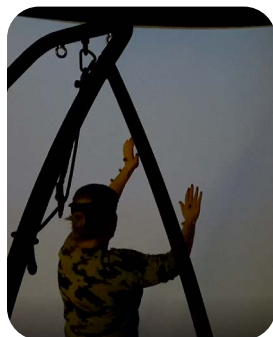
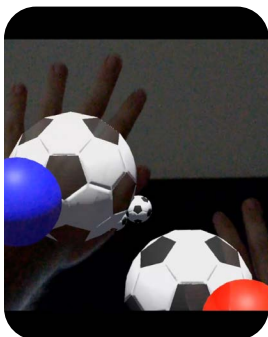
Robinson Clinic, WAMC, Fort Bragg, NC



# Comparison of Visual and Auditory Technologies in Large Scale and Mobile Virtual Reality Systems

## Sarah E. Kruger, M.S., Principal Investigator

Biomedical Engineer, NICOE, WRNMMC



### STUDY IMPACT

This study seeks to validate a mobile system that combines visual and audio technologies and has the potential to improve the current standard of care. This advancement in the field of concussion research may benefit service members who experience persistent sensory systems injury.

### RESEARCH HIGHLIGHT

The MHS has made substantial investments to develop sophisticated multimodal virtual reality (VR) systems to address the challenges faced by service members who experience vestibular and sensory issues related to traumatic brain injury. Thus, VR-based systems have emerged as tools that can be used independently or as an adjunct to traditional assessment and rehabilitation. VR has been shown to improve outcomes in patients with clinical presentations of multisensory dysfunction as well as improve balance and confidence in those affected by vestibular dysfunction. At the NICOE and NHRC, the CAREN, a VR-based system, is often utilized as an adjunct to traditional vestibular physical therapy (VPT).

Although there are benefits to using the CAREN, the systems are fixed, large in size, and expensive to install and maintain. These constraints can severely limit the number of patients who have access to them. However, with recent advances in VR and augmented reality (AR) head-mounted display technology, in conjunction with 3D spatial audio ("virtual audio"), alternatives to larger-scale VR-based systems like the CAREN may finally be possible.

The purpose of this study is to replicate CAREN-based VPT by leveraging new technologies, combining visual and auditory inputs into a mobile system that can be used in a variety of settings. It is expected that the mobile system will have sufficient detail and function to provide similar feedback to participants, comparable to those received while utilizing the CAREN. Additionally, participant performance outcomes should be similar between the two systems.

This is a multi-site study in collaboration with the Naval Health Research Center (NHRC) and Naval Medical Center San Diego (NMCS). Up to 60 participants (40 healthy, 20 mTBI) will be recruited at both sites.

### KEY STUDY TEAM

Associate Investigators:

Douglas S. Brungart, Ph.D.  
(WRNMMC)

Pinata H. Sessoms, Ph.D. (NHRC)

### STUDY SITE(S)

- NICOE, Bethesda, MD
- NHRC, San Diego, CA
- NMCS, San Diego, CA

### FUNDING

US Army Medical Research and Materiel Command –  
Award Number: CDMRPL-17-0-PT160118



## NICoE Traumatic Brain Injury Neuroimaging Core Project

### John Ollinger, Ph.D., Principal Investigator

Biomedical Engineer, NICoE, WRNMMC



### RESEARCH HIGHLIGHT

Despite ongoing research, there remains a critical knowledge gap of the relationship between blood-based exosome biomarkers and neuroimaging biomarkers in chronic TBI. The goal of this study is to develop a database of advanced neuroimaging measurements, along with relevant blood-based biomarkers, to clarify these relationships.

This project is being done in collaboration with scientists at the NIH and the CNRM. Structural, resting-state, and multishell diffusion magnetic resonance imaging data are being collected at the NICoE, along with clinical variables and detailed injury information. Blood data will be analyzed at the NIH for biomarkers reflecting axonal, neuronal, and vascular injury as well as astrogliosis/neuroinflammation and synaptic activity. Finally, these data will be analyzed jointly using advanced statistical methods.

### STUDY IMPACT

Findings from this study will be used to develop neuroimaging and blood biomarkers that can provide objective evidence of TBI and differentiate them from psychological health issues.

### STUDY SITE(S)

NICoE, WRNMMC, Bethesda, MD

### KEY STUDY TEAM

*Associate Investigators:*

Ping-Hong Yeh, Ph.D. (NICoE)

Andy Srikanthana, Ph.D. (NICoE)

Wei Liu, Ph.D. (NICoE)

Chihwa Song, Ph.D. (NICoE)

Kimbra Kenney, M.D. (NICoE)

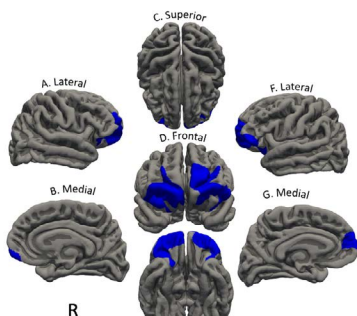
Jessica Gill, Ph.D. (NIH)

Pashtun Shahim, M.D., Ph.D. (CNRM, USU)

Thomas DeGraba, M.D. (NICoE)

### SELECTED PUBLICATIONS

1. Eierud, C., Nathan, D. E., Bonavia, G. H., Ollinger, J., & Riedy, G. (2019). Cortical thinning in military blast compared to non-blast persistent mild traumatic brain injuries. *Neuroimage: clinical*, 22, 101793.
2. Liu, W., Yeh, P. H., Nathan, D. E., Song, C., Wu, H., Bonavia, G. H., ... & Riedy, G. (2019). Assessment of Brain Venous Structure in Military TBI Patients Using Susceptibility Weighted Imaging and Quantitative Susceptibility Mapping. *Journal of neurotrauma*.
3. Tchopov, Z. N., Yeh, P. H., Morgan, G. W., Meyer, E., Wolf, J. M., Ollinger, J. M., ... & Young, L. C. (2018). Acquired sleep-related hyper motor epilepsy with disrupted white matter tracts assessed by multishell diffusion magnetic resonance imaging. *Frontiers in neurology*, 9, 6.
4. Yeh, P. H., Guan Koay, C., Wang, B., Morissette, J., Sham, E., Senseney, J., ... & Liu, W. (2017). Compromised Neurocircuitry in Chronic Blast-Related Mild Traumatic Brain Injury. *Human brain mapping*, 38(1), 352-369.



# Treating mTBI and PTSD with Bilateral Prefrontal Transcranial Magnetic Stimulation (TMS)

## Paul F. Pasquina, M.D., Principal Investigator

*Chair of Physical Medicine and Rehabilitation, USU*



### STUDY IMPACT

This study may shed light on the ability of rTMS to reduce the symptoms associated with PTSD and mTBI to improve the overall quality of life for injured service members.

### KEY STUDY TEAM

*Associate Investigators:*

Louis French, Psy.D. (NICoE)

Navneet Atwal, M.D. (WRNMMC)

Megan Tsui, B.S. (WRNMMC)

Jerika Taylor, M.A. (WRNMMC)

### STUDY SITE(S)

WRNMMC, Bethesda, MD

### FUNDING

CRSR

### RESEARCH HIGHLIGHT

Numerous reports have shown a high association between war-related PTSD and mTBI. The NICoE, in collaboration with the CRSR at the USU, has set out to assess the efficacy of using rTMS to reduce the frequency and severity of symptoms associated with PTSD and mTBI.

rTMS involves non-invasive stimulation of specific cortical regions and is FDA approved for treatment-resistant depression, migraines, and obsessive-compulsive disorder. Common off-label and experimental uses include PTSD, anxiety, and various other behavioral health conditions. TMS may offer a highly tolerable, non-invasive, and nonpharmacological treatment option for many patients who currently suffer from posttraumatic stress, PTSD, and mTBI.

This study seeks to determine the efficacy and tolerability of TMS as a treatment for mTBI with PTSD symptoms and correlate treatment response with anatomical and biological factors unique to each service member. Exploratory work will examine neuronal and biological changes that may occur over the course of TMS treatment.

FIND OUT MORE: <https://clinicaltrials.gov/ct2/show/NCT02458521>



# Biopsychosocial Effect of Service Dog Training on Post-Traumatic Stress (PTS) and Post Concussive Symptoms

## Paul F. Pasquina, M.D., Principal Investigator

*Chair of Physical Medicine and Rehabilitation, USU*



### RESEARCH HIGHLIGHT

Preliminary anecdotal evidence suggests that service members with symptoms of PTS report improved physical, social, and psychological symptoms after participation in the NICoE's Service Dog Training Program (SDTP).

The SDTP teaches service members how to train dogs to become service dogs, to provide support to veterans with mobility impairments and mood disorders. The program's purpose is to help service members develop skills such as effective communication and emotion regulation that are translatable to other social settings. This research assesses various biological, psychological, and sociological outcomes to evaluate the effectiveness of the SDTP.

As many as 104 participants will be recruited. Half of these participants will be randomized to participate in the SDTP, while the other half will serve as a control group. Participants randomized to the SDTP group will collaborate with professional service dog trainers for one hour, twice a week, for three weeks to train service dogs that will be gifted to a veteran once fully trained. Each group will continue to receive standard-of-care rehabilitation and treatment. Participants will complete self-report assessments of behavioral symptoms weekly throughout participation in the study. Biological samples will be collected at the baseline, during the Week 3 post-training visit, and during an optional three-month follow-up appointment to examine genetics and changes in stress hormones post-SDTP.

Additionally, by volunteering to help train service animals for veterans, participants may develop a restructured commitment to service post-injury.



### STUDY IMPACT

Findings from this study will inform the efficacy of implementing the SDTP as a complementary program for service members undergoing treatment for symptoms of PTS and traumatic brain injury. If this study's results are positive, it could lead to more service members and veterans being offered access to the SDTP to augment their ongoing care.

### KEY STUDY TEAM

*Associate Investigators:*

Louis French, Psy.D. (NICoE)

Jerika Taylor, M.A. (WRNMMC)

Kiara H. Buccellato, M.A. (WRNMMC)

Michelle J. Nordstrom, OT (WRNMMC)

Lauren Chin, B.S. (WRNMMC)

### STUDY SITE(S)

- WRNMMC, Bethesda, MD
- FBHC, Fort Belvoir, VA

### FUNDING

Congressionally Reprogrammed Research Development Testing and Evaluation Funds

FIND OUT MORE: <https://clinicaltrials.gov/ct2/show/NCT03907254>





# Psychometric Evaluation of the Clinician Administered PTSD Scale for DSM-5 (CAPS-5) and the PTSD Symptom Scale Interview for DSM-5 (PSSI-5) in an Active Duty and Military Veteran Sample

**Treven C. Pickett, Psy.D.**

*Department Chief, Research, NICoE, WRNMMC*



## STUDY IMPACT

The knowledge gained from this study will directly impact the ability of clinicians to reliably diagnose PTSD and assess PTSD symptom severity. It will also directly impact the likelihood of future clinical trials' technical and regulatory success in the development of novel treatments for PTSD.

## KEY STUDY TEAM

*Principal Investigators:*

Kathleen Chard, Ph.D. (CVAMC)

Brian Marx, Ph.D. (NCPTSD)

*Associate Investigators:*

Sarah Lippa, Ph.D. (NICoE)

Kimbra Kenney, M.D. (NICoE)

Thomas DeGraba, M.D. (NICoE)

Theresa Woo, Ph.D. (NICoE)

Paul Frimpong, M.S. (NICoE)

## STUDY SITE(S)

- Cincinnati VA Medical Center (CVAMC), Cincinnati, OH
- Tripler Army Medical Center, Honolulu, HI
- NICoE, WRNMMC, Bethesda, MD

## FUNDING

US Army Medical Material Development Activity (USAMMDA)

## RESEARCH HIGHLIGHT

The CAPS-5 and PSSI-5, the two most utilized clinical assessment tools for diagnosing and treating PTSD, need to be evaluated for their utility and reliability, especially in military service members.

The latest edition of the DSM-5 included changes to the diagnostic criteria for PTSD. To align with these changes, updated tools (CAPS-5 and PSSI-5) have been developed. Clinician-administered (e.g., CAPS and PSS-I) and patient-reported assessment tools (e.g., PTSD checklist [PCL]) are used for the diagnosis and assessment of the severity of PTSD symptoms. Evaluating the psychometric properties of these and any new assessment tool(s) in the population in which they will be used is a crucial step to ensure their utility and reliability.

This study will evaluate the psychometric properties of the CAPS-5 and PSSI-5 assessment tools in active duty military personnel and veterans. Biomarkers believed to be related to PTSD (e.g., biofluid biomarkers, cognitive and physiological markers, and neural activity as measured by EEG) will be collected to inform targeted interventions in specific groups of patients and other large-scale biomarker discovery efforts in the field.

In addition, many PTSD treatment trials have likely failed, at least in part, due to the biological heterogeneity underlying PTSD (i.e., the disruption of many different neurobiological systems can lead to a common set of symptoms consistent with a PTSD diagnosis). Evaluation of biomarkers thought to be related to PTSD (e.g., biofluid biomarkers, cognitive and physiological markers, and neural activity as measured by EEG) will help identify subgroups of patients with common biological abnormalities who may be more likely to respond to certain types of interventions targeted to normalize those specific abnormal systems or circuits.

FIND OUT MORE: <https://clinicaltrials.gov/ct2/show/NCT02458521>



# Evaluation of qEEG During Art Therapy in Service Members with Co-morbid TBI and Posttraumatic Stress Symptoms

## Chandler Rhodes, Ph.D., Principal Investigator

*Service Chief, Treatment and Rehabilitation, NICoE, WRNMMC*



### RESEARCH HIGHLIGHT

The complex presentation of comorbid mTBI and behavioral health symptoms experienced by service members returning from deployment remains a challenge to the Military Healthcare System. Although there is great anecdotal evidence of the benefits of art therapy at the NICoE, there is a gap in knowledge regarding this therapy's underlying neurobiological mechanisms. The purpose of this pilot project is to conduct a longitudinal study collecting mobile, quantitative EEG (qEEG) directly before, during, and after art therapy sessions to assess the impact of art therapy on brain networks and associated behavioral health symptoms.

Up to 15 service members with comorbid mTBI and significant posttraumatic stress symptoms will participate in eight sessions over the course of ten weeks. These will include two assessment visits that will collect information on a variety of symptoms, experiences, and personality traits pre- and post-art therapy, and six art therapy sessions conducted by a certified art therapist.

The goal of this study is to investigate brain signals associated with the art therapy process as well as generate preliminary data for the efficacy of art therapy in a population of service members with comorbid mTBI and posttraumatic stress symptoms.



### KEY STUDY TEAM

*Associate Investigators:*

Melissa Walker, M.A. (NICoE)

Hannah O'Malley, B.A. (USU, NEA Creative Forces)

Adrienne M. Stamper, M.A. (HJF, NEA Creative Forces)

Thomas DeGraba, M.D. (NICoE)

### STUDY SITE(S)

NICoE, WRNMMC, Bethesda, MD

### FUNDING

Creative Forces®: National Endowment for the Arts (NEA) Military Healing Arts Network

### STUDY IMPACT

Findings from this study will provide novel evidence of neurobiological changes associated with the treatment benefits of art therapy. These may be used to guide future research in the creative art therapies and offer creative art therapists greater insight into the mechanisms of action of this therapy, allowing them to further refine their therapeutic techniques and continue to personalize treatment.



# Clinical Trial of 3MDR to Treat PTSD After mTBI, With and Without Eye Movement

## Michael J. Roy, M.D., M.P.H., Principal Investigator

Recruitment Corps, CNRM, USU  
Director, Division of Military Internal Medicine, Professor of Medicine, USU  
Staff, Internal Medicine, WRNMMC



### RESEARCH HIGHLIGHT

PTSD and mTBI are persistent and frequently comorbid complications of combat. There is no proven treatment for mTBI, and standard treatments for PTSD often achieve only transient, modest impact. Motion-assisted, Multi-modular Memory Desensitization and Reconsolidation (3MDR) is a novel treatment for PTSD combining aspects of virtual reality exposure therapy and eye movement desensitization and reprocessing treatment within the Computer Assisted Rehabilitation Environment (CAREN). The purpose of this pilot study is to 1) obtain an initial estimate of the efficacy of 3MDR in service members with comorbid PTSD and mTBI and 2) determine the impact of eye movement (EM) on treatment response.

Up to 20 participants with comorbid PTSD and mTBI, randomized to either EM+ or EM-, receive ten sessions (three preparatory, six 3MDR treatment, and one conclusion). In preparatory sessions, the therapist and participant select songs and pictures. During treatment sessions, participants walk on the CAREN's embedded treadmill as the 3MDR environment projects on the screen. Sessions begin with a song to bring participants back to the time of their trauma. Subsequently, they walk toward a series of emotionally-evocative pictures (4-7 each session) while engaging in a form of "walk and talk" therapy. For each picture, keywords are superimposed over the picture and spoken aloud. Then for ~30 seconds, participants either follow a red ball across the screen in front of the picture (EM+) or continue walking toward the picture without any ball (EM-). A second song is used to bring participants back to the present day and plays to close each session.

To date, interim results have been compiled for the first nine participants who have completed the intervention. Overall, the average PCL5 score declined from 55.9 at baseline to 30.4 post-intervention, a highly clinically significant improvement on average. Five of the nine completers no longer meet the criteria for PTSD. Additionally, there has been no obvious difference between the EM+ and EM- groups at this point.

### STUDY IMPACT

Findings from this study may support the use of 3MDR in the CAREN as an enhanced therapy to significantly impact the care of individuals with PTSD and mTBI.



### KEY STUDY TEAM

Associate Investigators:

Sarah E. Kruger, M.S. (NICoE)

Paula G. Bellini, M.A. (USU)

Hannah O'Malley, B.A. (USU, NEA Creative Forces)

### STUDY SITE(S)

- NICoE, WRNMMC, Bethesda, MD
- CNRM, USU, Bethesda, MD

### FUNDING

USU, CRSR

FIND OUT MORE: <https://clinicaltrials.gov/ct2/show/NCT03796936>





## **The National Intrepid Center of Excellence**

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