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TITLE: Does Military Traumatic Brain Injury Increase the Risk for Developing Early-Onset Dementia and Mild Cognitive Impairment?

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CONTRACTING ORGANIZATION: University of Tennessee Health Science Center

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14. ABSTRACT This project seeks to examine whether traumatic brain injury sustained during military service increases the risk for early-onset of neurodegenerative conditions.					
15. SUBJECT TERMS Traumatic brain injury, mild cognitive impairment, dementia, early-onset					
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Introduction

This is the fourth annual report. The grant seeks to examine whether traumatic brain injury of any severity sustained during military service increases the risk of early-onset of neurodegenerative disorders, including dementia and mild cognitive impairment.

Keywords

Traumatic brain injury, dementia, mild cognitive impairment, early-onset

Accomplishments

Our primary hypothesis is that having sustained a single or multiple TBIs during military service is associated with an increased risk for early-onset of dementia (EOD), including AD, and early-onset MCI and that this relationship is correlated with the severity of the TBI.

This research will occur in two phases corresponding to the following specific aims:

1. To determine and compare the baseline prevalence of EOD, including AD and other dementia types, and early-onset MCI in a Veteran population with a history of single and multiple TBIs of any severity sustained during military service to a demographically-matched Veteran population without a history of TBI. We will use Department of Veterans Affairs databases and obtain military medical records through a proprietary database held at the Naval Health Research Center in San Diego, CA to verify that a clinician-diagnosed concussion, moderate, severe, or penetrating TBI occurred during military service.
2. To identify a cohort of veterans diagnosed with single or multiple TBIs of any severity and a matched cohort of unexposed veterans that will be leveraged to study the association between TBI of any severity and EOD, including AD and other types of dementia, and early-onset MCI longitudinally to determine the incidence of these conditions. We will include the presence or absence of co-occurring conditions such as hypertension, diabetes, hypercholesterolemia, sleep disturbances and mental health sequelae as co-variates in the analyses.

Specific Accomplishments:

The team is happy to report that much progress was made this year, especially in the roadblocks that had previously plagued this award in relation to regulatory approvals and credentialing. Note that only the major milestones of this year are presented here; more granular details were provided in previous quarterly reports.

- UTHSC received a new Notice of Award document on 12/22/22, removing the pilot clinical trial that had been added into the scope of the project after peer review.
- On 2/7/23, Dr. Stanfill received a notice from OHRO to complete the delinquent post-approval compliance monitoring, from the original OHRO approval (dated 1/15/21) prior to Dr. Tsao's departure from UTHSC. The protocol was then officially closed by OHRO on 3/9/23, with the understanding it would be reopened under the new site of the New York Harbor VA.
- The NHRC team presented the abstract titled "Concussions during U.S. military service and subsequent diagnoses of dementia, mild cognitive impairment, and memory loss: A Career History Archival Medical and Personnel System Study (1980-2020)" at the International Brain Injury Conference in Dublin, Ireland on 3/29/23.
- VA IRB approval was received on 5/2/23 and signed by the R&D committee and ACOS on 6/14/23.
- UTHSC IRB approval was received on 6/15/23.
- OHRO approval was received on 6/26/23, with OHRO Log Numbers E00963.1d (VA) and E00963.1e (UTHSC).
- Dr. Stanfill, Drew Prescott, and Leah Somerville were approved for WOC appointments at the New York Harbor VA by 7/14/23. Dr. Stanfill received her PIV card on 10/11/23. Drew and Leah have appointments to receive theirs in early November to begin to access the records.
- Dr. Tsao filed the paperwork on 10/23/23 to release a VA laptop to access the records for Dr. Stanfill. She is awaiting the approval and delivery of that equipment from the New York Harbor VA.
- The paper "Associations between concussion and more severe traumatic brain injuries, mild cognitive impairment, & dementia among military retirees over 40 years" was unfortunately rejected by *JAMA Neurology* in April 2023. The manuscript was then submitted to *Journal of Neurotrauma* 5/16/23, and a request was received for major revisions and several additional analyses. These were completed on 10/26 and returned to the remaining co-authors for final approval. Once approved, this will be resubmitted to the *Journal of Neurotrauma*.

Drs. Tsao and Stanfill have continued to meet at a minimum of weekly throughout the time covered in this annual report. They have also continued to communicate with the NHRC group on a biweekly basis for the first portion of year 4, and then on roughly a monthly basis since their project period ended in February 2023. The NHRC team and Drs. Stanfill and Tsao have also discussed rebudgeting possibilities to allow their work to be resumed after the completion of Aim 1.

Impact

Nothing to report – abstract was presented as described and a manuscript is in review.

Changes/Problems

As described above.

Products

Nothing to report

Participants & Other Collaborating Organizations

Ansley Stanfill – PI – UTHSC – 2.4 cal. Mo.

Jack Tsao – AI – Manhattan VAMC – 2.4 cal. Mo. (uncompensated- sub-award pending)

Jeffrey, Metter – AI – UTHSC – 0.6 cal. Mo.

Xinhua Yu – AI – University of Memphis – sub-award pending

Leah Somerville – Graduate Student – UTHSC – 12 cal. Mo.

Drew Prescott– Graduate Student – UTHSC – 3 cal. Mo.

Cynthia J. Thomsen – PI – NHRC – 0.6 cal. Mo.

Jennifer Belding – AI – NHRC – 3.6 cal. Mo.

James Bonkowski – Database Manager – NHRC – 9 cal. Mo.

Robyn Englert – Epidemiologist & Project Coordinator – NHRC – 3.6 cal. Mo.

Special Reporting Requirements

Nothing to report

Appendices

Nothing to report