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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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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 third 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: Much of this year, and most especially the past few months have been dedicated to first transferring the grant to Dr. Ansley Stanfill, establishing clear communication and developing a plan for next steps between her and members of the NHRC and between her, Dr. Tsao, and the program officer Dr. Heroux, and then securing new subawards for Dr. Tsao's continued involvement through New York Harbor Veteran's Affairs and for Dr. Yu's through University of Memphis. Drs. Tsao and Stanfill have met at a minimum of weekly since the grant was transferred; both have met or otherwise communicated with the NHRC group on roughly a biweekly basis and with the program officer Dr. Heroux on roughly a monthly basis. After establishing communication, Dr. Stanfill's next task as new PI was to address the continued roadblocks with the IRB reliance agreement between UTHSC and the VA Memphis, and with the CRADA. It was determined that the VA Memphis could no longer support the research with Dr. Tsao's move, and the IRB protocols needed to be submitted anew to the New York Harbor VA, which also necessitated establishing new WOC appointments at the New York Harbor VA for Dr. Stanfill and the research staff at UTHSC. This paperwork was filed, and approval is pending. Simultaneously, the new IRB protocol was submitted by Dr. Tsao to the New York Harbor VA and has been in review approximately 3 weeks. Dr. Stanfill has been working closely with the reliance agreement officer at UTHSC IRB to ensure that all necessary items are in place to avoid the challenges of the past agreement. All paperwork has been drafted and as soon as the approval comes from the New York Harbor VA IRB, the reliance agreement and data sharing agreements will be submitted for approval by UTHSC.

One other issue needed to be resolved as well. It was also found that there was a pilot clinical trial that was added into the scope of the project after peer review. This information was included in the SOW that was submitted with the PI transfer documents. However, working together with Drs. Stanfill, Tsao, Heroux, and Fontaine it was determined that the SOW needed to be revised to remove this piece as it was not peer reviewed, and to plan out the remainder of the work in the NCE period. This revised statement of work is expected to be submitted for approval in the coming week.

Meanwhile, the NHRC completed their preparation of the individual data files. This includes: (1) career records for those who were at least 45 years old by 2020 (primarily dating back to ≈1980s), (2) medical records during active-duty service (inpatient records dating back to ≈1980, outpatient records dating back

to ≈2000), and (3) medical records for retirees from the Military Health System Medical Data Repository (dating back to ≈2000). All data have been analyzed; sample size is ≈6.1M service members, which includes ≈1.2M retirees. An 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)" was submitted and is currently in review for the International Brain Injury Conference. Drs. Stanfill, Tsao, and Belding have also drafted a manuscript (working title: "Associations between concussion and more severe traumatic brain injuries, mild cognitive impairment, & dementia among military retirees over 40 years") and this will be submitted in the coming months.

Impact

Nothing to report

Changes/Problems

All research activities are delayed at the UTHSC/New York Harbor VA sites due to the IRB change and SOW alterations 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