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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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#### Introduction

This is the second 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 cliniciandiagnosed 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 UTHSC and NHRC teams have continued to meet via telephone to discuss and plan logistical, theoretical, and protocol issues regarding this study. We have finally managed to access the VA central patient databases to be able to pull multiple records simultaneously. At this stage we need to write SPSS code to be able to aggregate the data for analyses. We are still working on the CRADA with NHRC. We have submitted our VA approved protocol for UTHSC IRB approval since the CRADA has to come from UTHSC which is handling the grant funds. The only missing item is a Reliance Agreement from the Memphis VA to be submitted to UTHSC IRB. This has been inexplicably delayed, and we are working to identify where it is in process.

Following receipt of initial IRB approval from NHRC, a data sharing agreement (DSA) application was submitted and approved to DHA to allow access to MDR for retiree medical data. A subsequent IRB modification was granted, and an application for modified DSA with DHA was submitted. Preliminary data were extracted from NHRC's Career History Archival Medical and Personnel System (for medical and career records while on active duty) and MDR (for retiree medical data). Following approval of an approved IRB modification, requests for a secondary extract expanding the initial diagnosis codes of interest was submitted for CHAMPS; a similar extract for MDR data will occur upon approval of the modified DSA. Active duty career records dating back to 01 Jan 1980 have been cleaned and prepared and are ready for merging with medical data. Cleaning and preparation of the medical data is underway and will facilitate timely execution upon receipt of secondary data extracts described above. The data analysis plan has been updated and is ready for timely execution upon final merging of all relevant data sets.

#### Impact

Nothing to report

#### Changes/Problems

The CRDA between NHRC and UTHSC continues to be delayed due to paperwork issues (see above). The CRADA must be fully signed and executed before data can be shared across sites and delays also affect staffing considerations. As a result, these delays directly threaten the ability to access, share, and merge VA medical data with data for active duty personnel and retirees and ultimately threaten the success of the project.

### Products

Nothing to report

### Participants & Other Collaborating Organizations

- Jack Tsao PI UTHSC 2.4 cal. Mo.
- Jeffrey, Metter AI UTHSC 0.6 cal. Mo.
- Xinhua Yu AI University of Memphis 0.6 cal. Mo.
- Leah Somerville Graduate Student UTHSC 12 cal. Mo.
- Jennifer Belding PI NHRC 3.6 cal. Mo.

### **Special Reporting Requirements**

Nothing to report

# Appendices

Nothing to report