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Principal Investigator: Jamie Mayo, PhD, RN

Contracting organization:

The Assistant Secretary of Defense for Health Affairs endorsed by the Department of Defense

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14. ABSTRACT Frontotemporal dementia (FTD) is a group of disorders that occur when there is a degeneration in the frontal and temporal lobes of the brain. Unlike Alzheimer's disease, FTD usually does not involve memory impairments, instead exhibit a variety of behavioral symptoms and language problems. Clinical presentation of the disease is heterogeneous and based on the phenotype of FTD. Understanding the epidemiology of FTD and its clinical phenotypes in a population, and the risk factors associated, play an important role in the accurate diagnosis, appropriate management of, and in identifying those at risk for the disease. Our study has two main aims: first to identify the clinical phenotypes of Frontotemporal dementia (FTD) through natural language processing aided detailed medical chart reviews of post-9/11 era U.S military veterans in Veterans Health Administration care between fiscal years 2002-2015 diagnosed with FTD. Second: Evaluate if the clinical phenotypes of FTD among the post-9/11 era U.S. military veterans diagnosed with FTD vary by exposure to traumatic brain injury (TBI), spinal cord injury and by occupational risk to blast injury. This knowledge is critical for the clinical care of FTD and for planning of health and preventive services as this cohort of Post-9/11 Veterans ages.								
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1. INTRODUCTION AND BACKGROUND

The proposed project will identify clinical phenotypes of Frontotemporal dementia (FTD) disease among post-9/11 era United States Veterans and identify the association of military exposures with the FTD disease characteristics using data from the Departments of Defense (DoD) and Veterans Affairs (VA). Existing research from animal and human studies suggests that symptomatic FTD patients, both familial and sporadic, can be clinically heterogeneous. Occurrence of FTD and its clinical presentation among military populations is not well studied. While prior studies have examined the associations between Traumatic Brain Injury (TBI) and dementia broadly speaking, little is known about the association of military exposures and injuries to FTD—which is a subtype of the broad category of dementia. This study will address this gap in knowledge through two specific aims. In Aim 1, we will identify cases of FTD from a cohort of all Post-9/11 era Veterans who received VA care (2 or more years 2002-2019); obtain VA and DoD health care system data for these cases; and identify the diverse disease characteristics associated with FTD diagnosis using chart reviews and natural language processing (NLP) in VA data. The NLP software that we are using is called Moonstone. It has been used to assess function before in a VA dataset and is based on semantic, grammar based rules. In Aim 2, we will identify whether FTD risk and clinical phenotypes vary by exposure to TBI, spinal cord injury or high risk of blast injury. Together these aims address the DoD FY19 PRMRP Topic Area of Frontotemporal Lobe Degeneration by examining FTD disease characteristics among post-9/11 era Veterans in relation to specific military exposures.

KEYWORDS

Frontotemporal dementia, traumatic brain injury, epidemiology, natural language processing

2. AIMS MAJOR TASKS & ACCOMPLISHMENTS

Aim 1: Identify the clinical phenotypes of FTD through detailed medical chart reviews in post-9/11 era U.S military Veterans receiving VHA health care during FY 2002-2019.

- **Major Task 1:** Complete Regulatory Requirements for Study
 - **Subtask 1:** prepare regulatory Documents and Research protocol

Anticipated completion: Months 0-24
Actual completion: University of Utah IRB approval on 07-04-2020, SLC VA IRB approval 13-04-2020, HRPO approval 06-10-2020. Continuing maintenance throughout the active study period.
- **Major Task 2:** Identify cohort, cases, controls and exposures
 - **Subtask 1:** Obtain VA data for Post 9/11 Era Veterans
 - **Subtask 2:** Identify cases, controls, exposures and other variables in FY02-FY19 cohort

Anticipated completion: Current completion- 75%
Identified cases, controls, and exposures in cohort; completed June of 2020. Need to request and receive TIU notes for cohort; expect to complete this by July 2021
- **Major Task 3:** Identify and abstract clinical characteristics of FTD among cases
Anticipated completion: Months 9-20; Have manually reviewed a portion of cases to define cognitive dysfunction and poor psychosocial function at a sentence level in order for the NLP programing to identify these concepts in free text notes from the cases. Current completion- 40%
- **Major Task 4:** Identification of clinical phenotypes of FTD
Anticipated completion: Months 18-20; Current completion- 0%

Aim 2: Evaluate whether the FTD clinical phenotypes in post-9/11 era U.S. military Veterans diagnosed with FTD vary by exposure to traumatic brain injury (TBI), spinal cord injury, and occupational risk to blast injury

- **Major Task 5:** Matched case control analysis
Anticipated Completion: Months 18-20; Current completion- 0%
- **Major Task 6:** Complete manuscripts
Anticipated completion: Months 21-24; Current completion- 0%

Accomplishments during this annual reporting period

Major Tasks 1 and 2: We have completed the regulatory process for this study and have created a cohort with cases and matched controls.

Major Tasks 3 and 4: We have made progress towards the goal of training the NLP software in that we have identified the gold standard cases and begun extracting their associated free form text notes. We have created a training protocol for annotators and developed a training protocol for NLP software validation. We have brought on and begun training of two new team members who will work as annotators for NLP software training. We have also organized the existing software ontology and created new ontology as needed to incorporate the concepts necessary for this study. Furthermore, we have modified the current software to work more efficiently with large numbers of documents across many varied concepts. As of now, we have finalized our initial training of Moonstone on the neuropsychiatric and psychosocial free form text notes of the gold standard cases. This will allow Moonstone to assess both the cognitive and more subtle, and possibly earlier detected, interpersonal impacts of cognitive dysfunction.

Major Tasks 5 and 6: No progress was made on Major Task 5 this year. We have begun to write the introduction and methods section in preparation for our first manuscript as progress towards Major Task 6.

Methods

Over the past quarter we have not advanced the analysis for Aim 1 or 2.

Opportunities for Training and Personal Development

While the project was not intended to provide training/professional development, we have provided opportunities for professional development on the team. Jamie Mayo and Lee Christensen provided training for new staff and graduate students, to prepare them for NLP development and case analysis in year two.

Dissemination to Communities of Interest

Nothing to report this quarter.

Plans for Next Reporting Period

Major Tasks 3 and 4: We will complete abstraction of clinical characteristics of FTD among cases and develop FTD phenotypes based on these clinical characteristics.

Major Tasks 5 and 6: We will complete analysis of contributing factors that are unique to specific phenotypes and complete manuscripts in order to disseminate these findings.

4. IMPACT

Impact On The Development Of The Principal Disciplines Of The Project

None to report this quarter

Impact On Other Disciplines

None to report this quarter

Impact On Technology Transfer

None to report this quarter

Impact On Society Beyond Science And Technology

None to report this quarter

5. CHANGES/PROBLEMS

Changes in approach and reasons for change

There were no problems that arose during this reporting period.

Actual or anticipated problems or delays and actions or plans to resolve them

There were no problems that arose during this reporting period.

Changes that had a significant impact on expenditures

There were no problems that arose during this reporting period.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

In our initial application we stated that we would obtain and compile VA inpatient, outpatient, and pharmacy data, to identify a cohort of Post-9/11 era Veterans receiving two or more years of VA care during 2002-2019 from the sources listed in Table 1 of the project narrative. Our group has created a repository of inpatient, outpatient, and pharmacy data to identify post-911 Veterans in the past called the Characterizing Health Outcomes in Post-9/11 Veterans (CHOP) repository. We would like to identify our cases of frontotemporal dementia and the case matched controls from this CHOP repository as it has already been compiled, cleaned and verified to ensure of post-911 veterans that are applicable to this study

6. PRODUCTS

Conference Papers and Presentations

None to report this quarter

Papers Submitted

None to report this quarter

Website

We updated our university website to include information on our study and resources for Veterans and Service Members https://medicine.utah.edu/internalmedicine/epidemiology/research_programs/torch/.

7. PARTICIPANTS AND OTHER COLLABORATING ORGANIZATIONS

Organization Name:		Location of Organization:		Organization Contributions:
University of Utah		Salt Lake City, Utah		Collaboration & Facilities
Name:	Project Role:	Researcher Identifier (ORCID):	Percent Effort:	Person Month(s) Worked this Year:
Jamie Mayo	Principal Investigator	0000-0003-4259-4938	50%	6

Mary Jo Pugh	Co-PI	0000-0003-4196-7763	23%	2.76
Lee Christenson	Programmer		45%	5.4
Tyler Cooper	Graduate Research Assistant		50%	6
Samin Panahi	Graduate Research Assistant		50%	6
Sreekanth Kamineni	Research Analyst		10%	1.2

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?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

Quad Chart Attached