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TITLE: The Epidemiology of Epilepsy and Traumatic Brain Injury: Severity, Mechanism, and Outcomes

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14. ABSTRACT Our previous research has found that Post-9/11 Veterans with any kind of traumatic brain injury (TBI) were more likely to develop epilepsy than those without a prior TBI - however, its association with closed head injury such as mild TBI is as of yet unclear. To begin to rigorously evaluate this association, we have reviewed the 7238 cases of epilepsy identified using International Classification of Diseases Ninth Edition, Clinical Modification (ICD-9-CM) diagnosis codes in Department of Veterans Affairs care, finding that 4664 (64.4%) were valid cases of epilepsy. We hope to use the results of this research to identify risk factors for post-traumatic epilepsy that will enable early identification for those at risk of its development and begin to describe the impact of post-traumatic epilepsy on Veterans.				
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1. INTRODUCTION

Studies of Veterans from World War II, the Korean War, and Vietnam provided groundbreaking information regarding the understanding of combat-related traumatic brain injury (TBI) and epilepsy. Because these studies focused on penetrating TBI (pTBI), our understanding of the association of closed head injuries including mild TBI (mTBI)—the majority of TBI exposures—with posttraumatic epilepsy (PTE) is unclear. By conducting an expansive evaluation of epilepsy epidemiology in Post-9/11 Veterans deployed in support of Wars in Iraq and Afghanistan using available data from the Departments of Defense (DoD) and Veterans Affairs (VA) and primary data collection allows us to go beyond a simple incidence/prevalence study to provide a targeted evaluation of the impact of epilepsy on Post-9/11 Veterans compared to controls, and to harness the power of cutting-edge neuroimaging (and eventually biomarker) data to answer immediate questions regarding etiology and provide the foundation for longitudinal study that will ultimately identify specific aspects of mTBI/other risk factors that will allow early identification of those at greatest risk of PTE.

KEYWORDS:

Epilepsy, mild traumatic brain injury, epidemiology

2. ACCOMPLISHMENTS:

What were the major goals of the project?

- Major Task 1: Complete Regulatory Requirements for Study
- Major Task 2: Identify cohort who meet criteria for epilepsy (Aim 1)
- Major Task 3: Identify Sample for Aims 2-3
- Major Task 4: Conduct telephone interviews/surveys for Veterans with Epilepsy and Controls to conduct analyses for Aims 2 and 3
- Major Task 5: Identify TBI phenotypes
- Major Task 6: Conduct analyses comparing Veterans with epilepsy and controls on self-report measures (Aim 3)
- Major Task 7: Conduct analyses comparing Veterans with epilepsy and controls on neuroimaging and neuropsychological testing (Aim 4)

What was accomplished under these goals?

➤ Major Task 1: Complete Regulatory Requirements for Study

We have finalized consent forms, human subjects protocols, and the chart abstraction tool, survey, and interview needed to conduct all work outlined in this grant. Further, we have secured local regulatory (Department of Veterans Affairs (VA) Research and Development and Institution Review Board) approval at all sites (i.e., South Texas Veterans Healthcare System (Site 1), University of Missouri, St. Louis (UMSL; Site 2), Hunter Holmes McGuire VA Medical Center (Richmond, VA; Site 3), Tampa VA Research and Education Foundation (TVREF; Site 4); Baylor University (BU; Site 5), as well as at the additional Chronic Effects of Neurotrauma Consortium (CENC) Longitudinal Cohort Study (Study 1) sites of Portland, OR and Boston, MA. We received Human Rights Protection Office approval for Aims 1-3 (Research Activities local to the main site in San Antonio, TX) in 2016. Salt Lake City, UT was added and approved by IRB as a study site in March 2018 for Aims 2 and 3. HRPO approved all study sites as of June 2018.

➤ Major Task 2: Identify cohort who meet criteria for epilepsy (Aim 1)

➤ We secured all proposed VA data for Veterans who entered VA care FY02-12 and received care in FY04 through FY15 and who had data in DoD health system records. After removing deceased cases, those with more severe TBI, and those without DoD data available, and those with seizures/convulsions that did not meet inclusion criteria the final study population is N = 809,757 (from 928,799 total). We completed medical chart reviews and have validated 7328 cases who met epilepsy criteria based on International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) diagnosis codes. We then were able to group the overall population into four distinct sub populations to obtain our samples for Aims 2-3. (See Major Task 3.)

➤ **Major Task 3: Identify Sample for Aims 2-3**

After completing the chart reviews, our team divided the total N for analyses into sub populations from which samples were obtained as follows:

Table 1. Sample for survey

<i>Group</i>	<i>Population</i>
No TBI: No Epilepsy	694,812
No TBI: Epilepsy	2,464
mTBI: No Epilepsy	110,178
mTBI: Epilepsy	2,303
Totals	809,757

➤ **Major Task 4: Conduct telephone interviews/surveys for Veterans with Epilepsy and Controls to conduct analyses for Aims 2 and 3**

Surveys (SATX) – Invitation letters were mailed out to the samples for each of the four groups. The letters included a paper survey with instructions of how to access and complete the survey online if preferred. The study team reviewed returned and completed surveys by each study group to review recruitment to target goals to have sufficient samples for analysis. Survey boosts that oversampled for women were defined in January 2019 and the final survey batch was mailed March 2019. The survey was closed August 31, 2019. We achieved a final response rate of 27% for the overall sample.

Table 2. Survey sample and response rates

<i>Group</i>	<i>Sampled</i>	<i>Responded</i>	<i>Target Goal for Respondents</i>	<i>Percent of of total Responded</i>
mTBI: Epilepsy	781	208	200	27%
No TBI: Epilepsy	3,748	975	931	26%
mTBI: No Epilepsy	1,407	419	421	30%
No TBI: No Epilepsy	3,749	1013	931	27%
Total	9,685	2615	2483	27%

Interviews (SLC) –

A total of 2,056/2,615 (78.6%) of our survey completers agreed to participate in additional, related research and 1,679 (64.2%) agreed to a follow up telephone interview. An initial random sample of 200 interview participants were selected from each group to begin the interview process. Interviews began in March 2019. In May and August 2019, additional staff were hired and trained to be able to conduct interviews. A total of 45 interviews were completed by September 30, 2019. We are adjusting our interview schedule to account for time zones and work schedules. Most potential participants in Groups 3 and 4 have requested evening or weekend interviews.

In the coming year, we will use the survey data to identify individuals who completed the survey, indicated they were willing to be contacted for interviews, and presented particular conditions, such as LOC >30 minutes, self-reported evidence of potential mTBI + epilepsy or seizures but no diagnosis, etc. We will examine the extent to which interviews that include the Ohio State University TBI Identification (OSU TBI ID) interview improve the ability to classify lifetime TBI beyond the survey OSU TBI ID version. We will also use information revealed in the interview related to etiology of TBI (e.g. childhood abuse, intimate partner violence, blast, etc.) are associated with epilepsy and other health conditions.

Table 3. Interview sample and completed interviews by group

<i>Group</i>	<i>Opted in for interview</i>	<i>Selected for initial sample</i>	<i>Completed interviews</i>	<i>Percent of completed initial sample (N=200)</i>	<i>Percent of total opted in for interview (N=1679)</i>
mTBI: Epilepsy	147	50	24	48%	16%
No TBI: Epilepsy	244	50	15	30%	6%
mTBI: No Epilepsy	713	50	3	6%	0.4%
No TBI: No Epilepsy	575	50	3	6%	1%
Total	1679	200	45	23%	3%

➤ **Major Task 5: Identify TBI phenotypes**

We have begun analyses of the survey data to identify TBI phenotypes. We are beginning by examining concordance of diagnosed TBI with self-report TBI severity on the survey-based OSU TBI ID measure (see Table 4). Of particular interest are individuals who reported

- a) no TBI exposure but had a diagnosis or indication of TBI on the VA Comprehensive TBI Evaluation (cells highlighted yellow),
- b) those with a self-reported loss of consciousness (LOC) >30 minutes indicating a moderate or severe TBI (cells highlighted blue)
- c) those with no indication of TBI in VA based on TBI Screening or diagnosis codes, but report head/neck injury without LOC, alteration of consciousness (AOC) or post-traumatic amnesia (PTA) (cells highlighted green)

Table 4. Self-report TBI characteristics from survey-based OSU TBI Identification Measure

<i>Study Group</i>	<i>No TBI</i>	<i>Head/neck injury reported; no data on LOC/AOC/PTA</i>	<i>TBI with altered consciousness (no LOC)</i>	<i>LOC <5 minutes</i>	<i>5 minutes <= LOC <= 30 Minutes</i>	<i>LOC>30 minute</i>
mTBI:Epilepsy n=206	17 (8.25%)	2 (0.97%)	25 (12.14%)	82 (39.81%)	48 (23.3%)	32 (15.53%)
No TBI:Epilepsy n=416	151 (36.30%)	14 (3.37%)	53 (12.74%)	93 (22.36%)	74 (17.79%)	31 (7.45%)
mTBI:No Epilepsy n=972	163 (16.77%)	12 (1.23%)	176 (18.11%)	412 (42.39%)	138 (14.2%)	71 (7.3%)
No TBI:No Epilepsy n=1007	564 (55.01%)	24 (2.38%)	163 (16.19%)	171 (16.98%)	58 (5.76%)	27 (2.68%)
Total = 2601	895	52	417	758	318	161

The current survey data suggest that there may be misclassification in VA for mTBI. To evaluate this possibility and to understand the TBI exposure, we will target all individuals in the mTBI+Epilepsy group (n=17) and sample a large proportion (n_≥ 40) of those in the mTBI, no epilepsy group. We will also sample cells without highlight, but with much lower frequency depending upon findings of early interviews of individuals selected from those cells.

Table 5 shows self-reports of other TBI related characteristics of interest including blast exposure, repetitive impact and TBI earlier than age 15. There were some individuals reporting TBI earlier than age 5, however the numbers were too small to be notable.

Table 5: TBI-related characteristics for TBI phenotypes

<i>Group</i>	<i>Self-Reported Blast Exposure</i>	<i>Self-Reported Repetitive Impact</i>	<i>Self-Reported First TBI Age < 15 years</i>
mTBI:Epilepsy n=206	174 87.44%	118 59.30%	30 16.48%
No TBI:Epilepsy n=416	271 66.58%	131 32.35%	60 24.90%
mTBI:No Epilepsy n=972	848 89.74%	462 48.94%	151 19.53%
No TBI:No Epilepsy n=1007	606 61.34%	216 21.82%	128 31.68%
Total	1899 Missing = 65	927 Missing = 66	

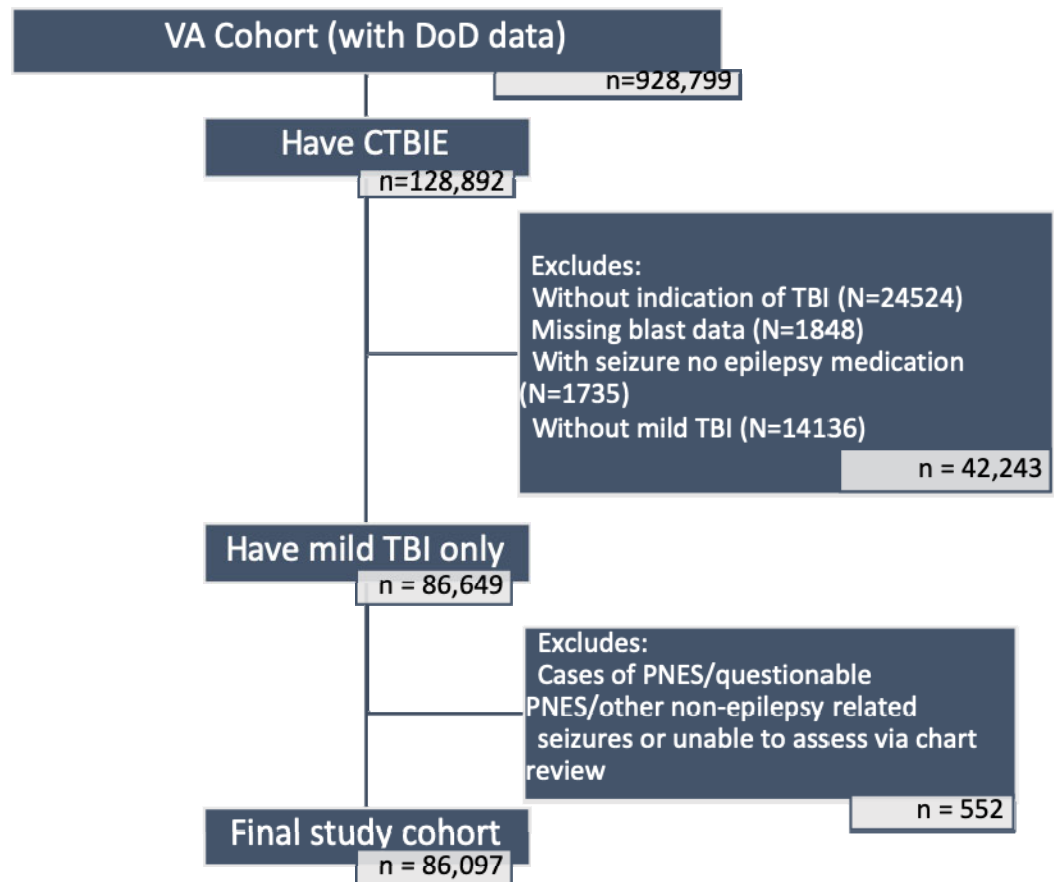
Over the next quarter our team will review self-reported TBI characteristics included in Tables 4 and 5 to develop clinically meaningful TBI phenotypes. We will also examine survey-based phenotypes with phenotypes that emerge from interview data.

➤ **Major Task 6: Conduct analyses comparing Veterans with epilepsy and controls on self-report measures (Aim 3)**

As our survey data are being cleaned and curated for analyses we have conducted analyses of self-reported symptoms in VA Comprehensive TBI evaluation data. Using the cohort described in Major Task 3.

Our cohort flow diagram is provided below.

Figure 1: Cohort: Neurobehavioral Symptoms in Veterans with mTBI by Epilepsy Status



For this cohort we calculated the four scale scores for the Neurobehavioral Symptom Inventory (Cognitive, Affective, Somatosensory, Vestibular), and calculated the mean scale score for each to allow comparison across scales and study groups. As such, the scores can be interpreted similarly to the response categories for each item:

None 0 - Rarely if ever present not a problem at all.

Mild 1 - Occasionally present but it does not disrupt activities, I can usually continue what I am doing; does not really concern me.

Moderate 2 - Often present, occasionally disrupts my activities; I can usually continue what I am doing with some effort; I am somewhat concerned.

Severe 3 - Frequently present and disrupts activities; I can only do things that are fairly simple or take little effort; I feel like I need help.

Very Severe 4 - Almost always present and I have been unable to perform at work, school, or home due to this problem; I probably cannot function without help.

To understand risk factors for severe and very severe symptom impact for each scale, we created a dichotomous measure of high and low impact using the cut-point of 3 as previously used by Iverson et al. Furthermore, as there is concern that there is significant risk for the impact of TBI and Epilepsy among women, we examined the impact on neurobehavioral symptoms of epilepsy among the cohort of Veterans with mTBI and who completed the VA comprehensive TBI evaluation.

Figure 2: High Symptoms for Neurobehavioral Symptom Inventory Scales among Veterans with mTBI by Epilepsy Status

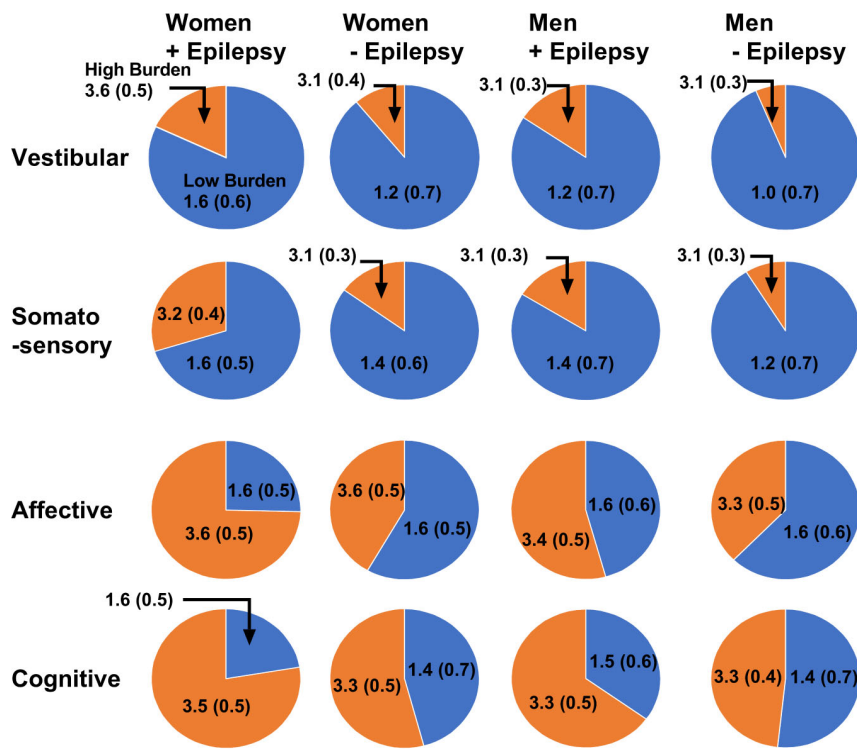


Figure 2 shows the mean scores for each scale among high and low impact symptom groups by gender and epilepsy status. We found that in bivariate analyses:

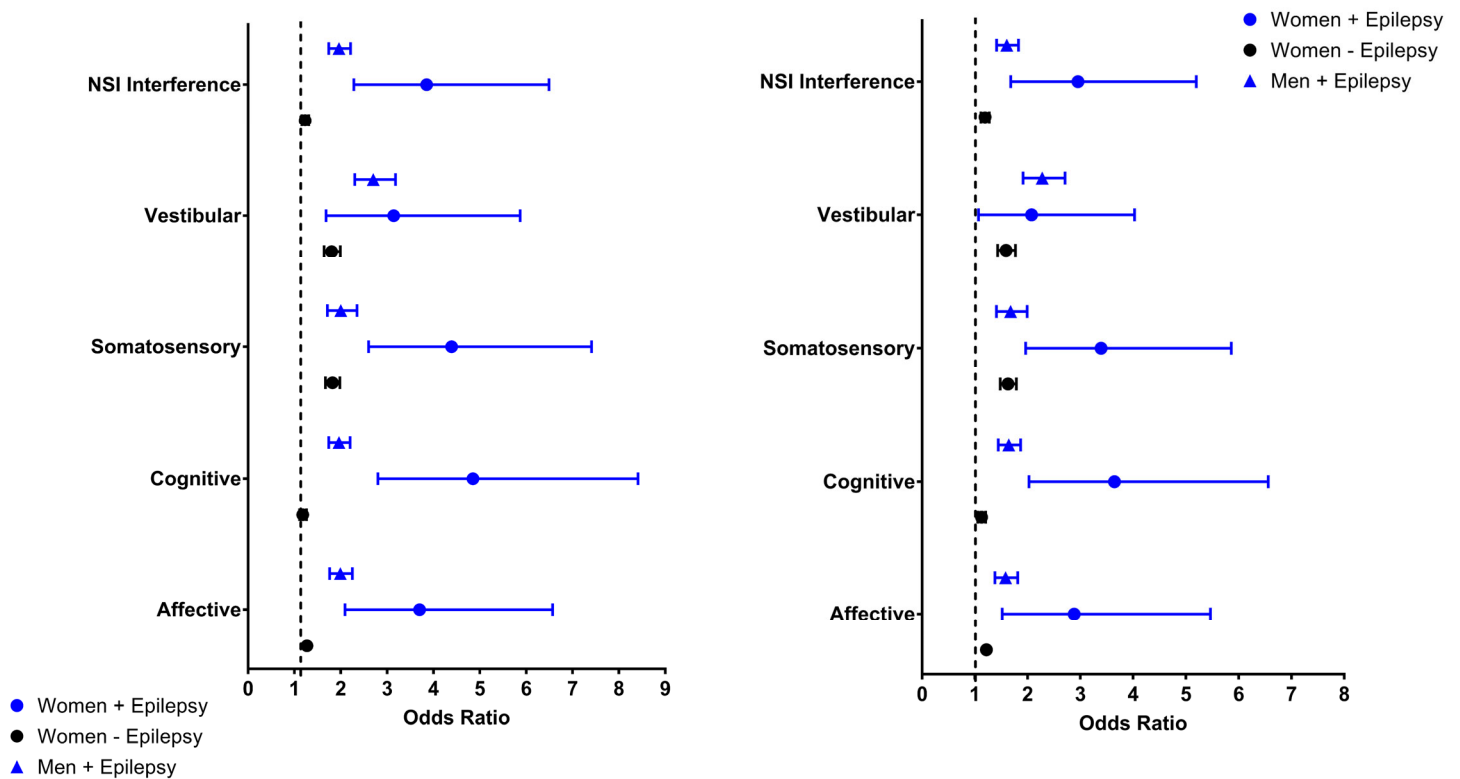
1. There was a statistically significant gender effect where women with mTBI were more likely to be high symptomology than men within their respective epilepsy categories.
2. There was a statistically significant epilepsy effect where those with epilepsy were more likely to be high symptomology than those without epilepsy within their respective gender categories.
3. There was a statistically significant interaction effect where women with epilepsy were significantly more likely to have high impact symptoms than all of the other groups.

Pie charts also show the mean score within high and low symptomology groups for each subscale. The only subscale in which women+epilepsy with high symptomology had significantly higher scores than other groups was the vestibular scale where the mean high impact group score was 3.6, while other groups each had mean high impact scores of 3.1. This suggests that even within high impact symptom groups, among women with mTBI and epilepsy, vestibular symptoms have an even higher impact compared to other groups examined in this analysis before adjusting for other conditions.

We then conducted logistic regression analyses predicting high symptomology of NSI subscale scores and overall NSI symptom interference in the past 30 days (same scoring metric as other NSI items 0-4 as described above using 3 as a cutpoint for high interference). Figure 3 shows unadjusted odds ratios for men and women with mTBI+epilepsy, and women with mTBI: no epilepsy compared to men with mTBI: no Epilepsy. Odds of being in the high symptomology group were significantly higher for women with mTBI+epilepsy than for all other groups consistent with bivariate analyses above (Figure 3a). Findings were unchanged controlling for socio-demographic characteristics. There were minor differences after controlling for multiple TBI history (Figure 3b. TBI during deployment only vs. TBI during and before; TBI during and after, and TBI before, during and after deployment)

Figure 3a: Unadjusted Odds Ratios predicting high symptomology History.

Figure 3b: Odds ratios adjusted for multiple TBI History.

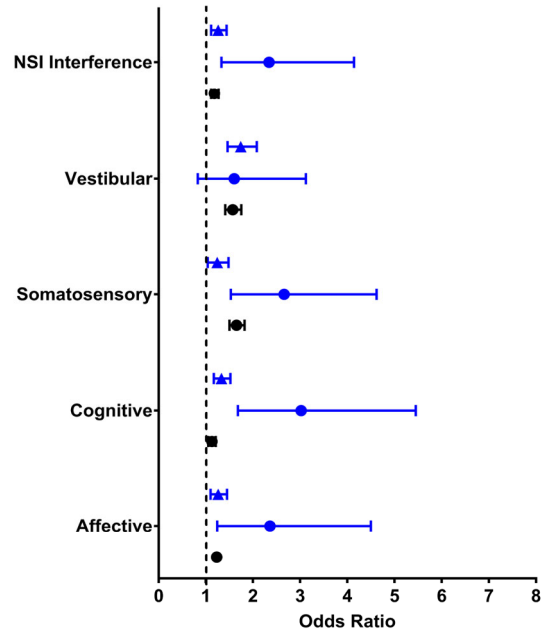
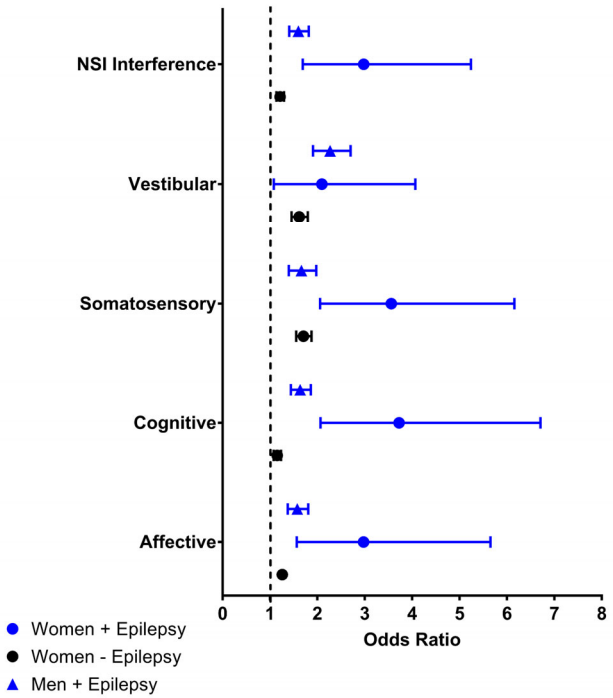


However, the most significant impact was found when controlling for previously diagnosed mental health conditions. Figures 3c and 3d show odds ratios for the groups adjusted for mental health (3c) and all characteristics (military, sociodemographic, multiple TBI exposures, blast exposure, mental

health conditions, antiepileptic drug prescription during the year of CTBIE). The findings indicate that, while the adjusted odds ratios decreased significantly, women with epilepsy remained significantly higher than all groups on the Cognitive scale, with an odds ratio of ~3. Men with no epilepsy had significantly lower scores (less impact) than women [with and without epilepsy] and men with epilepsy. Thus, while the impact of mental health comorbidity significantly reduced the impact of epilepsy on all scale scores and overall NSI symptom interference, it did not completely account for group differences, particularly for women with epilepsy.

Figure 3a: Odds Ratios controlling for previously diagnosed mental health

Figure 3b: Odds ratios adjusted for all covariates



➤ **Major Task 7: Conduct analyses comparing Veterans with epilepsy and controls on neuroimaging and neuropsychological testing (Aim 4)**

Of Veterans who indicated they would be willing to enroll in additional, related research, 234 have been referred to the six VA CENC Study 1 sites. Each of the sites collect a variety of functional tests, including neuropsychological and neuroimaging measures which are integral to Aim 4 of this study.

Table 6: CENC Study 1 referrals by location

<i>Site</i>	<i>Referred</i>
Boston	22
Houston	40
Portland	17
Richmond	55
San Antonio	61
Tampa	39
Total	234

Table 7: CENC Study 1 referrals by group

<i>Group</i>	<i>n by group</i>
mTBI+Epilepsy	21
No TBI+ Epilepsy	23
mTBI+ No Epilepsy	96
No TBI+ No Epilepsy	95
Total	234

What opportunities for training and professional development has the project provided?

With supply funds for this project, we have purchased research methods books in interview techniques, qualitative coding, and survey analysis to train junior staff for the project. The interview team includes three graduate research assistants from the University of Utah who are pursuing masters or doctoral level work, with a long-term goal to conduct health research. We have supplemented their studies by providing interview and methods training. All team members routinely attend training such as VA Cyber Seminars.

How were the results disseminated to communities of interest?

1. Dr. Pugh presented a CME course at the American Academy of Neurology Annual Meeting on Women with Epilepsy: Beyond Seizure control. Her contribution was on post-traumatic epilepsy, comorbidity and functional impact of epilepsy in women Veterans.
2. We submitted an abstract examining the unique impact of epilepsy and mTBI on neurobehavioral symptoms to the American Epilepsy Society and the VA Health Services Research and Development Annual Meeting.

3. Dr. Pugh developed a lay presentation for American Red Cross Military Caregiver Network on post-traumatic epilepsy.

What do you plan to do during the next reporting period to accomplish the goals?

Over the next year our team will review self-reported TBI characteristics included in Tables 4 and 5 to develop clinically meaningful TBI phenotypes. We will also examine survey-based phenotypes with phenotypes that emerge from interview data.

During the next year, we plan to continue analyses of all collected data to complete Major Tasks 5 and 6. The self-report survey data will be used to identify potential interview participants based on TBI characteristics, scores on specific survey scales (e.g., quality of life in brain injury scale [QOLIBRI]), specific comorbidities, and gender. We will ensure our interviews are achieving the maximum variance sampling, and anticipate interviewing a significantly larger sample than our first target of 200 participants. We will begin conduct quantitative analyses examining variation in impact of mTBI phenotypes and epilepsy on specific outcomes related to general health, QOLIBRI, mental health, and epilepsy quality of life. We will also incorporate quantitative findings from interview data examining the sufficiency of the survey based OSU TBI ID measure for population based surveys, and the impact of lifetime TBI and epilepsy on cognitive status as measured by the BTACT. We will begin analyzing the interview data for emergent themes related to TBI exposures. An initial emergent theme has come from the first 45 interviews, as participants have indicated intimate partner violence may be a factor contributing to cases of TBI. We have begun to work with CENC teams to begin analyses for Major Task 7.

3. IMPACT:

Our data on the impact of epilepsy on neurobehavioral symptoms in men and women provide new data on gender differences re: the impact of mTBI and the unique impact of epilepsy. The findings for the Cognitive Subscale, even after controlling for mental health, suggest that our interviews including the Brief Test of Adult Cognition by Telephone will provide much needed data that can examine these differences on self-reported symptoms using more objective cognitive data.

What was the impact on the development of the principal discipline(s) of the project?

Our findings to date suggest that TBI identified using health system data is not sufficient to examine the impact of deployment related mTBI on the emergence of post-traumatic epilepsy as over 15% of those with mTBI+epilepsy have self-reported moderate/severe TBI.

What was the impact on other disciplines?

Nothing to Report.

What was the impact on technology transfer?

Nothing to Report.

What was the impact on society beyond science and technology?

Our stakeholder outreach will continue, providing community education opportunities. We are specifically partnering with the TBI Warrior Foundation for outreach and dissemination of findings as they become available. We are also identifying additional stakeholder partnerships for dissemination and stakeholder input for future research and interpretation of findings.

4. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to Report.

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

Nothing to Report.

Changes that had a significant impact on expenditures

While expenditures are still below that budgeted, we are making progress by hiring staff for the large number of interviews we will be conducting.

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

Nothing to Report.

5. PRODUCTS:

Publications, conference papers, and presentations

VanCott AC, Altalib HH, Auman ME, Pugh MJ and the MINUTE Cohort Investigators.

Epilepsy in the context of TBI: Is epilepsy specialty care enough? VA Health Services Research Meeting: Poster Accepted.

Pugh MJ, Lopez MR, Amuan ME, Altalib HH, VanCott AC. Neurobehavioral symptoms and suicidality: The impact of epilepsy and gender in Post-9/11 Veterans with mild TBI. American Epilepsy Society Annual Meeting: Poster Accepted.

Journal publications.

Nothing to Report.

Books or other non-periodical, one-time publications.

Nothing to Report.

Other publications, conference papers, and presentations.

Nothing to Report.

Website(s) or other Internet site(s)

We are developing a website at the University of Utah that can be updated frequently with links to research results, other related research, and Veteran resources. We continue to maintain a project team website to provide information on the study, including an FAQ page to answer frequently asked questions by survey and interview participants (<https://torchhub.com/tbi>).

Technologies or techniques

Nothing to Report.

Inventions, patent applications, and/or licenses

Nothing to Report.

Other Products

Nothing to Report.

6. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name:	<i>Mary Jo Pugh</i>
Project Role:	<i>Principal Investigator</i>
Researcher Identifier (e.g. ORCID ID):	0000-0003-4196-7763
Nearest person month worked:	3
Contribution to Project:	<i>Dr. Pugh has overseen project staffing, management, and execution of the project across all sites.</i>
Funding Support:	

Name:	<i>Alicia Swan</i>
Project Role:	<i>Research Scientist</i>
Researcher Identifier (e.g. ORCID ID):	<i>orcid.org/0000-0003-2412-0499</i>
Nearest person month worked:	2
Contribution to Project:	<i>Dr. Swan has provided project management for the SATX site.</i>
Funding Support:	

Name:	<i>Andrea Kalvesmaki</i>
Project Role:	<i>Senior Research Analyst</i>
Researcher Identifier (e.g. ORCID ID):	<i>orcid.org/0000-0002-4282-0619</i>
Nearest person month worked:	4

Contribution to Project:	<i>Ms. Kalvesmaki leads the SLC team with scientific project management, supervision and training of staff, planning and execution for Major Task 4.</i>
Funding Support:	

Name:	<i>Brice Terpstra</i>
Project Role:	<i>Senior Research Analyst</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	3
Contribution to Project:	<i>Mr. Terpstra supervises and trains staff, and conducts research data collection and analysis for Major Task 4.</i>
Funding Support:	

Name:	<i>Charlene Humpherys</i>
Project Role:	<i>Research Analyst</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	<i>Ms. Humpherys provided analytic support and is part of the interview team.</i>
Funding Support:	

Name:	<i>Adriana Reyes Miranda</i>
Project Role:	<i>Research Analyst</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	1
Contribution to Project:	<i>Ms. Reyes Miranda has provided administrative support.</i>
Funding Support:	

Name:	<i>Silvia Padilla</i>
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Project Role:	<i>Research Analyst</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	4
Contribution to Project:	<i>Ms. Padilla provides administrative support, cleans and analyzes data, and is part of the interview team.</i>
Funding Support:	

Name:	<i>Megan Amuan</i>
Project Role:	<i>Data Scientist</i>
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	3
Contribution to Project:	<i>Ms. Amuan analyzes data for Aims 1, 2, and 3.</i>
Funding Support:	

Name:	<i>Sarah Leonhart</i>
Project Role:	Research Analyst
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	4
Contribution to Project:	<i>Ms. Leonhart provides administrative support, cleans data, and is part of the interview team.</i>
Funding Support:	

Name:	<i>Elizabeth Pulsipher</i>
Project Role:	Graduate Research Assistant
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2
Contribution to Project:	<i>Ms. Pulsipher provides administrative support and is part of the interview team.</i>
Funding Support:	

Name:	<i>Mackenzie Haller</i>
Project Role:	Graduate Research Assistant
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2
Contribution to Project:	<i>Ms. Haller provides administrative support and is part of the interview team.</i>
Funding Support:	

Name:	<i>Kelly Cronkhite</i>
Project Role:	Research Analyst
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2
Contribution to Project:	<i>Ms. Cronkhite provides administrative support and is part of the interview team.</i>
Funding Support:	

Name:	<i>Jamie Mayo</i>
Project Role:	Graduate Research Assistant
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2
Contribution to Project:	<i>Ms. Mayo analyzes data for Aim 3 and is working with Dr. Pugh to develop manuscripts using neurobehavioral symptom inventory and survey data .</i>
Funding Support:	

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

09/28/2018 -
09/27/2022

Personal Biology & Comorbidity Impact on Post-TBI Cognitive Dysfunction & Neurodegenerative Disease

Principal Investigator(s): Amy Wagner

Direct Costs: \$697,445 Total Costs: \$816,011

Department of Defense Congressionally Directed Medical Research Programs

Role: Co-Principal Investigator (5% effort)

09/28/2018 -
09/27/2021

Phenotypes of comorbidity in epilepsy: Variation by TBI severity and deployment status

Principal Investigator(s): Mary Jo Pugh

Direct Costs: \$495,169 Total Costs: \$567,672

Department of Defense Congressionally Directed Medical Research Programs

Role: Principal Investigator (12% effort)

09/28/2018 -
09/25/2020

Epidemiological Characterization and Prognostic Models for PTE: A Collaborative TBI-MS and VHA Study

Principal Investigator(s): Mary Jo Pugh; Amy Wagner

Direct Costs: \$121,154 Total Costs: \$131,419

Department of Defense Congressionally Directed Medical Research Programs

Role: Co-Principal Investigator (5% effort)

09/28/2018 -
03/31/2020

The UCD-DGMC TBI Neural Network- Precision Medicine Paradigm for Complex Trauma

Principal Investigator(s): Mary Jo Pugh; Tina Palmieri

Direct Costs: \$120,591 Total Costs: \$149,591

Department of Defense Congressionally Directed Medical Research Programs

Role: Co-Investigator (10 % effort)

Studies that accounted for 35% effort completed in FY19.

What other organizations were involved as partners?

Nothing to Report.

7. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: Not Applicable.

QUAD CHART: Attached.

8. APPENDICES: None.

The Epidemiology of Epilepsy and Traumatic Brain Injury: Severity, Mechanisms, and Outcomes

ERMS/EP150013
W81XWH-16-2-0046



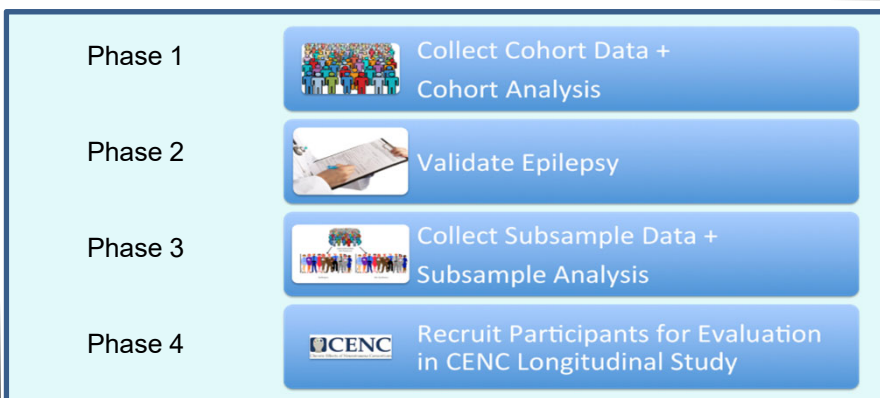
PI: Mary Jo Pugh PhD, RN **Org:** Foundation for Advancing Veterans Health Research **Award Amount:** \$2,199,189

Study Aims

- Aim 1: Identify a cohort of Post-9/11 Veterans who received VA care during at least two years (2002-2015), calculate the prevalence of epilepsy in 2015 and identify the association between mTBI and epilepsy
- Aim 2: Among a subsample of surveyed Veterans, examine the association between lifetime history of mTBI and epilepsy.
- Aim 3: Among the surveyed subsample, compare those with and without epilepsy on functional outcome measures (e.g., employment status, mental, physical and social functional status, community reintegration).
- Aim 4: Enroll 200 survey respondents in the Chronic Effects of Neurotrauma Consortium (CENC) Longitudinal study to obtain advanced clinical, cognitive, and MRI data.

Approach

This study utilizes data from existing VA and DoD data repositories, patient self-reports from surveys/interviews and data collected through the CENC longitudinal study. These unique data sources will allow us to examine population prevalence of epilepsy, identify its association of mTBI, assess outcomes associated with epilepsy, and reveal neuroimaging and biomarker correlates of mTBI and epilepsy. The longitudinal nature of the CENC longitudinal study provides an opportunity to follow this cohort beyond the course of this study to better understand the long-term impact of mTBI exposures and epilepsy among the Veterans of the Afghanistan and Iraq wars.



Accomplishments: Our team has completed Aim 1, validating 7,328 cases meeting epilepsy criteria out of a total population of 810,349. We have begun analyses for Aims 2-3. A total of 2615 surveys were received. 79% of survey respondents (2,056) agreed to an interview. Phone interviews began in April 2019. The survey data is being analyzed for TBI phenotypes, and self-report brain injury. We are using the survey data to select individuals for interview. A total of 234 respondents have been referred for CENC Study 1 (Aim 4) across the six CENC study sites.

Timeline and Cost

Activities	CY	17	18	19	20
Identify Cohort and estimate prevalence of epilepsy		█			
Examine association between lifetime mTBI and epilepsy			██████████	██████████	██████████
Compare surveyed Veterans with and without epilepsy on outcomes			██████████	██████████	██████████
Obtain clinical, cognitive, and MRI data on the select CENC subsample			██████████	██████████	██████████
Estimated Budget (\$K)		\$508	\$558	\$568	\$566

Updated: October 21, 2019

Goals/Milestones

- CY17 Goal** – Regulatory approval, data acquisition, survey design
- Gain regulatory approval and logistical readiness to execute aims
- CY18 Goals** – Survey administration, data compiling, aim 1 analysis
- Calculate epilepsy prevalence and its association with mTBI
 - Begin compiling survey data
- CY19 Goal** – Finalize survey data, chart abstractions, and commence referral to and enrollment in CENC study 1
- Execute analyses of outcomes among the surveyed Veterans with and without epilepsy and a history of mTBI
- CY20 Goal** – Complete enrollment and testing 150-200 of the surveyed subsample in the CENC Longitudinal Cohort study
- Analyze advanced clinical, cognitive and MRI data among those referred to CENC study 1

Comments/Challenges/Issues/Concerns

- No challenges, roadblocks or concerns this year

Budget Expenditure to Date

Projected Expenditure: \$1,641,469

Actual Expenditure: \$927,163