Military Risk Factors for Cognitive Aging and Dementia

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Veterans at Risk for Cognitive Aging & Dementia

- Almost 50% of veterans are older than 65 years of age
- Veterans face a unique set of military risk factors for dementia including PTSD and TBI
- In addition, veterans are at risk due to a similar set of risk factors as older adults in the general population
- But the burden of these risk factors may be even greater in veterans

Age of Veterans, 2014 and 2024 (Projected)

Rand Health, 2015.
In the next few decades, Gulf War veterans will comprise more than half of the veteran population.
The Importance of Modifiable Risk Factors for Cognitive Aging and Dementia

- Identification of modifiable risk factors can help
  - Understand the biological mechanisms associated with cognitive impairment & dementia development
  - Identify those at highest risk of developing dementia
  - Improve prevention and treatment options
- Need to understand the role of both non-military and military risk factors for aging veterans

Yaffe, *Chronic Medical Disease and Cognitive Aging: Toward a Healthy Body and Brain*, 2013.
Midlife Cardiovascular Risk Factors Increase Risk of Dementia

Multiple Cardiovascular Risk Factors Together Increase Risk of Dementia

- Metabolic syndrome:
  - ↑ blood pressure
  - ↑ cholesterol
  - ↑ triglycerides
  - ↑ blood sugar
  - ↑ body weight

- Together may be greater than individual components

- Role of inflammation

- Offer strategies to modify risk factors as a group

Cardiovascular Risk Factors in Early-Mid Adulthood & Cognition at Midlife

## Burden of Cardiovascular Risk Factors in Veterans

<table>
<thead>
<tr>
<th>Survey of Veteran Enrollees in VHA ≥65 years old</th>
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<tbody>
<tr>
<td>Hypertension</td>
<td>63.8%</td>
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<tr>
<td>Diabetes</td>
<td>27.1%</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>26.8%</td>
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<tr>
<td>Stroke</td>
<td>15.0%</td>
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</tbody>
</table>

Among VA patients ≥65 years old, an estimated 29.1% have diabetes, hyperlipidemia, and hypertension.

Mouse Model of Physical & Cognitive Activity: Use it or Lose it?

Physical activity & mental activity activity increase new brain cell development in mice

Walking and Rate of Cognitive Decline

More blocks walked associated with less decline

Exercise Improves Cognitive Function in Older Adults with Memory Complaints


170 adults
age ≥ 50 yrs

Better cognition in exercise group
Physical Activity in Veterans

Active duty members report high levels of physical activity, but veterans do not maintain those levels.

Physical activity in veterans vs non-veterans, Behavioral Risk Factor Surveillance System


Physical activity trajectories in older women veterans vs older women non-veterans, Women’s Health Initiative

Emerging evidence that sleep disturbances and poor sleep quality increase risk of developing dementia.

Diem...Yaffe et al, AJGP, 2016; Tranah...Yaffe, Annals of Neurology, 2011; Yaffe et al, JAMA, 2011.
Sleep in Veterans

• Greater than 20% of veterans report insufficient sleep and almost 35% report sleeping <7hrs/night

• Recent study of VHA users suggest diagnoses of sleep disorders are increasing

• Sleep apnea and insomnia were the most common diagnoses of sleep disorders

• Sleep disorders often comorbid with PTSD and TBI

Sleep Disturbances and Increased Risk of Dementia in Veterans

DoD Numbers for Traumatic Brain Injury
Worldwide - Incidence by Severity

No. of cases

30,000
25,000
20,000
15,000
10,000
5,000
0

Calendar year

'00  '01  '02  '03  '04  '05  '06  '07  '08  '09  '10  '11  '12  '13  '14

Mild
Moderate
Severe
Penetrating
Unclassified

Source: Defense Medical Surveillance System (DMSS), Theater Medical Data Store (TMDS) provided by the Armed Forces Health Surveillance Center (AFHSC)

Prepared by the Defense and Veterans Brain Injury Center (DVBIC) 2000 - 2014, as of May 15, 2015
Traumatic Brain Injury: 60% Increased Risk of Dementia with TBI

Adjusted HR: 1.57; 95% CI (1.35–1.83)

Barnes...Yaffe, Neurology, 2014.
Comorbidities Have an Additive Effect with TBI on Dementia Risk

Depression

PTSD

Cardiovascular Disease

Psychiatric Risk Factors & Dementia Risk

- More and more data on depression and PTSD as risk factors for dementia
- High burden of psychiatric diagnoses among veterans
- Odds of depression in Gulf War veterans is 2 times higher compared to non-deployed military personnel
- Odds of PTSD in Gulf War veterans is 3 times higher compared to non-deployed veterans

Greater Depressive Symptom Burden Over Time Increases Risk of MCI/Dementia

Odds Ratio of MCI/Dementia, 95% CI

Quartile of Depressive Symptom Burden (AUC)

* Adjusted for socio-demographics, health behaviors, co-morbidities, and use of anti-depressants

Depression Increases Risk of Dementia Among Older Veterans

Depression aHR: 2.18, 95% CI: 2.08-2.28

PTSD Increases Risk of Dementia Among Older Veterans

PTSD aHR: 1.77 95% CI 1.70-1.85

Yaffe et al, Arch Gen Psychiatry, 2010.
### PTSD & Prevalence/Incidence of Dementia

**Veterans ≥65 years old from VISN 16**

<table>
<thead>
<tr>
<th>Comparisons</th>
<th>Dementia Prevalence OR* (95% CI)</th>
<th>Dementia Incidence OR* (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>PTSD+/PH- vs PTSD-/PH-</td>
<td>2.3 (2.0–2.7)</td>
<td>2.2 (1.8–2.6)</td>
</tr>
<tr>
<td>PTSD+/PH- vs PTSD-/PH+</td>
<td>2.0 (1.6–2.5)</td>
<td>1.7 (1.4–2.2)</td>
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</tbody>
</table>

PTSD in older veterans associated with dementia prevalence and incidence compared to those without PTSD and compared to those with combat related trauma

PTSD Symptoms and Hippocampal Volume in Vietnam Twin Pairs Discordant for Warzone Service

- Hippocampal volume in non-exposed twin predicts PTSD symptom severity
- Suggests hippocampal volume loss is a pre-existing vulnerability trait

Gulf war illness shares many similar symptoms to PTSD and depression and affects multiple systems.

Need to investigate link between body and brain.

Limited data on risk of neurologic outcomes.

Too early for manifestation of neurodegenerative diseases in Gulf War veterans so more follow up needed.
Summary

• Evidence for TBI, PTSD, and other military exposures as risk factors for dementia is increasing

• In addition, veterans are at risk for accelerated cognitive aging because they have a greater burden of medical and psychiatric risk factors

• Need continued investigation of modifiable risk factors in veterans to understand the interplay of these associations

• Explore specific exposures of Gulf War veterans

• Develop a multi-domain framework for research, prevention, and intervention for cognitive aging in veterans
Acknowledgements

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