



Polytrauma, TBI and Dementia: The Latest Terrible Triad

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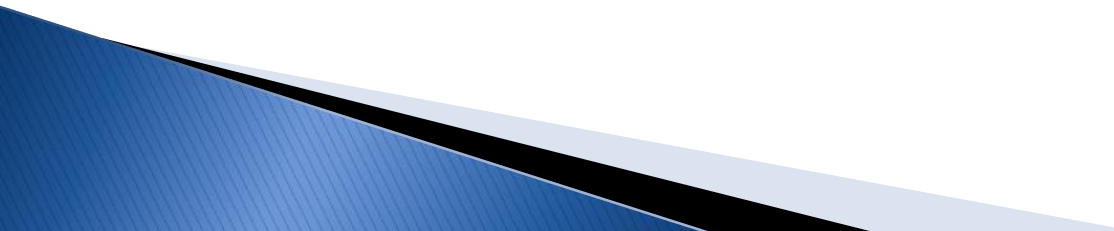
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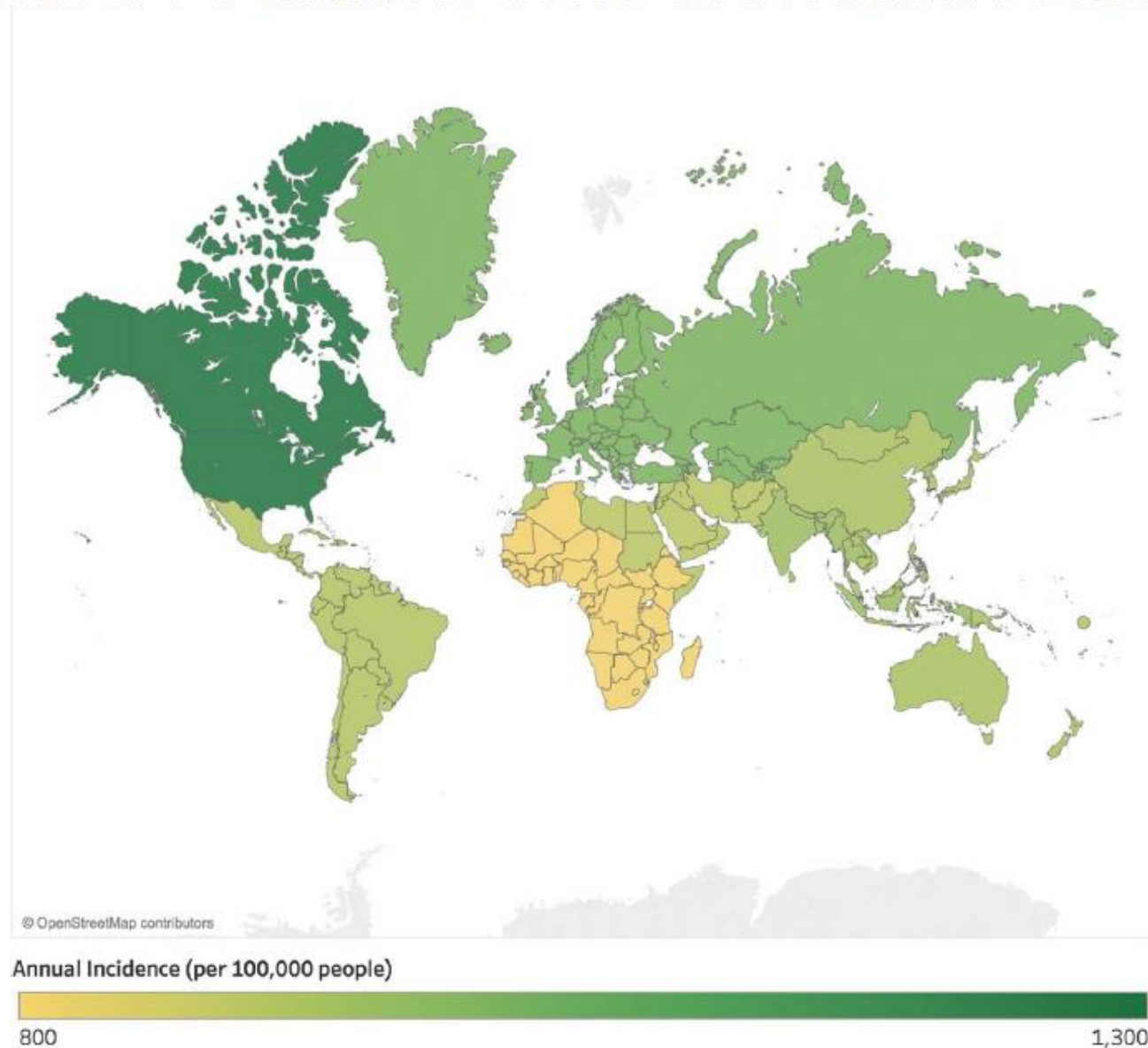
Presentation Overview

1. Chronology of disorders with unexplained symptoms and war
 2. Critical review of CTE, blast and mild TBI
 3. Update on ongoing VA, DoD and Academic Multi-Center, Longitudinal Studies of repetitive mild TBI and blast exposure, including the CENC Longitudinal Study
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How Did We Get Here?

- ▶ Humans have been sustaining mild TBI's (and experiencing PTSD) for millions of years, and yet we have no significant reports of related long-term effects in any great amount until the last 20 years.
 - ▶ High-contact athletes have been known to develop cognitive-behavioral issues for 100 years.
 - ▶ Combat-exposed Veterans have been known to develop behavioral issues for centuries.
 - ▶ NFL + OEF/OIF + \$\$\$ + Fame = Perfect Storm
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Estimated 70 Million TBIs Worldwide Each Year



Estimate based on road traffic injuries, systematic review, and meta-analysis of TBI literature. Dewan et al, *J Neurosurg*, 2018.

TBI: Incidence in U.S. 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

'00 '01 '02 '03 '04 '05 '06 '07 '08 '09 '10 '11 '12 '13 '14 '15 '16

Calendar year

Mild

Moderate

Severe

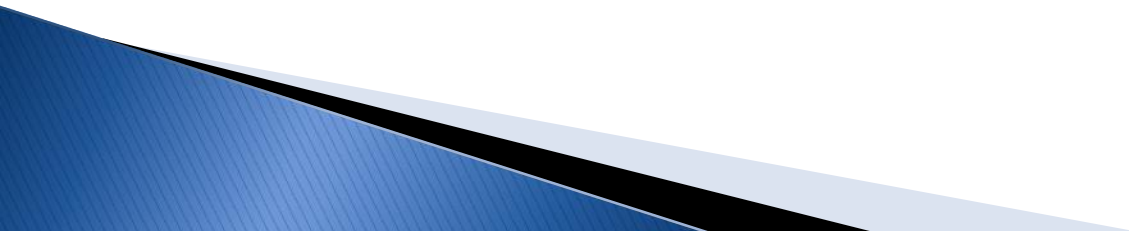
Penetrating

Unclassified

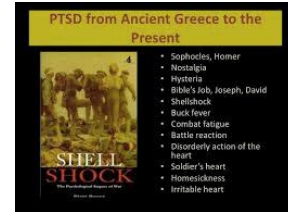
Source: Defense Medical Surveillance System (DMSS), Theater Medical Data Store (TMDS)
provided by the Armed Forces Health Surveillance Branch (AFHSB).
Prepared by the Defense and Veterans Brain Injury Center (DVBIC)

2000-2016 as of May 10, 2017

Chronology of disorders with unexplained symptoms and war



BATTLE FATIGUE

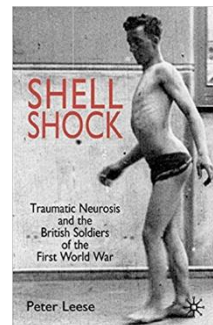
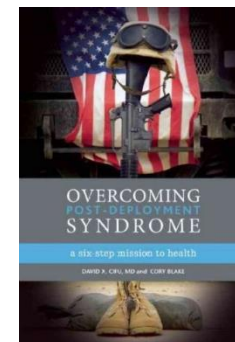


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SOLDIER'S HEART

Being the Story of the Enthusiasm and Day Service of the Boy Chaspy Goldend in the First Minnesota Volunteer

GARY PAULSEN



Concussions

Concussion = mTBI

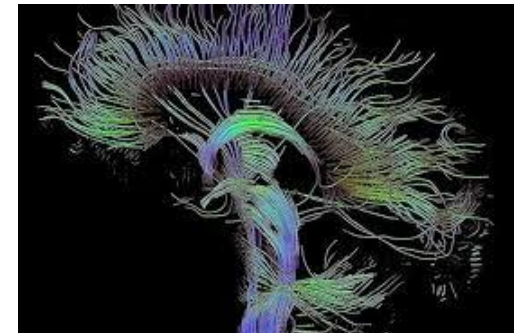


- ▶ **Concussion** (= mild TBI) is a complex pathophysiologic process induced by traumatic forces secondary to direct or indirect impulsive forces to the head that disrupts the function of the brain.
- ▶ Concussion is defined as an alteration or loss of consciousness for up to 30 minutes with associated loss of memory surrounding the event (post-traumatic amnesia) for up to 24 hours.
- ▶ Transient (<24 hours) neurologic sequelae may also be present, including numbness, dizziness, cognitive deficits, discoordination, and alterations in special senses.
- ▶ This disturbance of brain function is typically associated with normal structural neuroimaging findings.



Challenges to Management

- ▶ Uncertainty of diagnosis
 - Gold standard test is question concerning AOC
 - Imaging (CT Scan) normal >95% of time or high false positive rate (50%) or poor clinical correlations.
 - Few clinicians specialty trained
 - Carpenters like to use wood for everything!
 - Overlap of symptoms with pain, depression, fatigue, stress and life.



Challenges to Management

- ▶ Range of Treatment Options
 - Benign neglect successful >90% of the time
 - Majority of complaints are related to either musculoskeletal or stress-related factors.
 - Army of “specialists” and charlatans
 - Musculoskeletal
 - Vision
 - Vestibular
 - Cognitive
 - Catalogues full of remedies



Persistent Symptoms After Concussion



Post-Concussive Symptoms



- ▶ Acute symptoms resolve in $>85\%$ by 2 weeks
- ▶ As with any mild traumatic injury, patients who are acutely and uniformly treated by experienced clinicians respond rapidly ($>90\%$ musculoskeletal origin), however benign neglect can also get some/many better.
- ▶ Symptoms presenting >2 weeks post-injury are not related to injury

Post-Concussive Symptoms

- ▶ “Post-Concussive Syndrome”
 - Label used if symptoms persist for 3+ months
 - May be seen in 15–30% of concussions and continue for >1 year in 5%.
- ▶ No clear central physiologic reason for symptoms after 2–6 weeks.
 - Axonal disconnection of <5% of white matter tracts
- ▶ ? Chronic pain, anxiety, learned behavior

Common signs of concussion:



Dizziness



Nausea



Headaches



Light
Sensitivity



Confusion

Challenges to Management

- ▶ Individuals bring beliefs, fears and biases
 - Media is replete with concussion and dementia stories
 - Anxiety, misunderstanding, variable compliance, and symptom attribution affect efficacy
 - Differing opinions, prior experiences and outside influences (internet!) affect level of self-efficacy
 - Healthcare system favors testing and illness



Post-Concussive Management – Integrative Medicine

▶ Education

- Diagnosis – explain multiple contributors
- Prognosis – optimism, self-actualization
- Health Management – Fitness, Sleep, Diet, Mind/Body

▶ Interventions

- Sleep – sleep hygiene, medications
- Pain – pain management, non-narcotic medications (short term)
- Behavior – counseling, mood stabilizers (at full dosing)
- Cognition – adaptive strategies, assistive technology
- Fatigue – sleep, fitness, diet, counseling

▶ Goals

- Normalization
- Deinstitutionalization
- Return to productivity and activity
- Reintegrate into social roles and activities



Blast-Related Concussion

One Explosion/Blast has Multiple Mechanisms of Injury



Wall of Air (Primary)



Blast Wind (Primary)



Flying Debris
(Secondary)

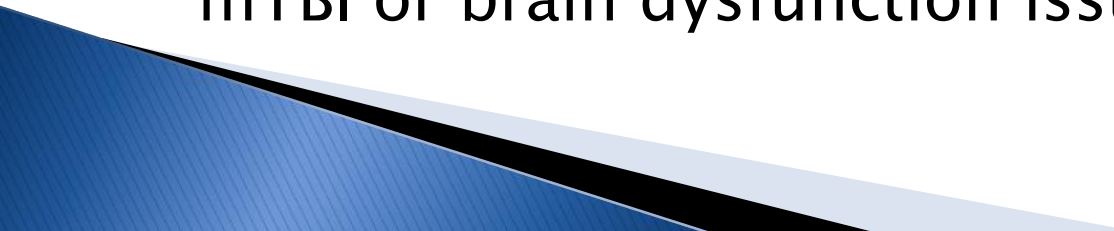


Displacement
(Tertiary)



Collapse Building
(Quaternary)

What is a blast-related mTBI?

- ▶ Per DoD, there have been approximately 10 “pure” blast mTBI from OEF/OIF, but it’s not clear what this even means.
 - ▶ No definitive literature supporting the existence of a blast-related mTBI without physical forces on head.
 - ▶ The head and/or body are moving in >99% of blasts.
 - ▶ Breacher research (munitions experts) that features repeated blast exposure has NOT revealed definitive mTBI or brain dysfunction issues.
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Combat Concussions



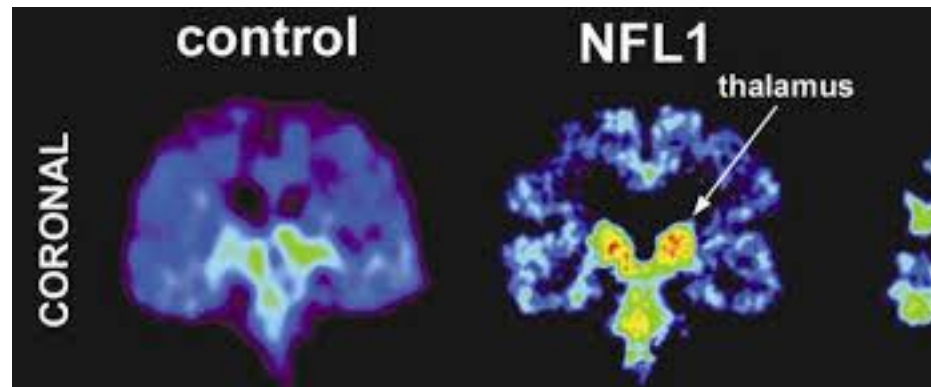
- ▶ 16–20% of OEF–OIF–OND Veterans who received VA medical care have confirmed TBI and 8% were still symptomatic when initiating care at VA
 - ~200,000 total (>1,100,000 screened) in VA
 - 90,000 symptomatic
 - >98% mild
 - <2% moderate–severe
 - >50% due to MVC
- ▶ 75% of Veterans with symptomatic mild TBI also have at least one mental health diagnosis, most commonly Post Traumatic Stress Disorder (PTSD)
- ▶ 90% will have either PTSD or chronic pain disorder



How is blast-related mTBI unique?

- ▶ Definitive research findings identifying the presence of any blast-specific contributions to mTBI without blast forces (i.e., head acceleration-deceleration) is lacking. Similarly, no blast-related PCE research findings!
- ▶ No literature supporting the existence of a blast-related mTBI without physical forces on head.
- ▶ Psychologic stressors of concussion resulting all or in part from a blast exposure must be considered.
- ▶ Unclear if further research is needed?

Chronic Traumatic Encephalopathy



ALZHEIMER'S DISEASE IS THE
6TH LEADING
CAUSE OF
DEATH
IN THE UNITED STATES

MORE THAN
5 MILLION
AMERICANS ARE LIVING WITH ALZHEIMER'S

1 IN 3 SENIORS
DIES WITH ALZHEIMER'S
OR ANOTHER DEMENTIA



IN 2015, MORE
THAN 15 MILLION
CAREGIVERS
PROVIDED AN
ESTIMATED

18.1 BILLION
HOURS OF
UNPAID CARE

ALZHEIMER'S COSTS CAREGIVERS
MORE THAN THEIR TIME

FAMILY CAREGIVERS SPEND MORE THAN
\$5,000 A YEAR
CARING FOR SOMEONE WITH ALZHEIMER'S

FOR SOME FAMILIES THIS MEANS
MISSING A VACATION

BUT FOR OTHERS, IT MAY MEAN
GOING HUNGRY

EVERY
66 SECONDS

SOMEONE IN THE UNITED STATES
DEVELOPS THE DISEASE



IN 2016, ALZHEIMER'S AND OTHER
DEMENTIAS WILL COST THE NATION

\$236 BILLION

IT
KILLS
MORE
THAN

BREAST AND
PROSTATE CANCER
COMBINED





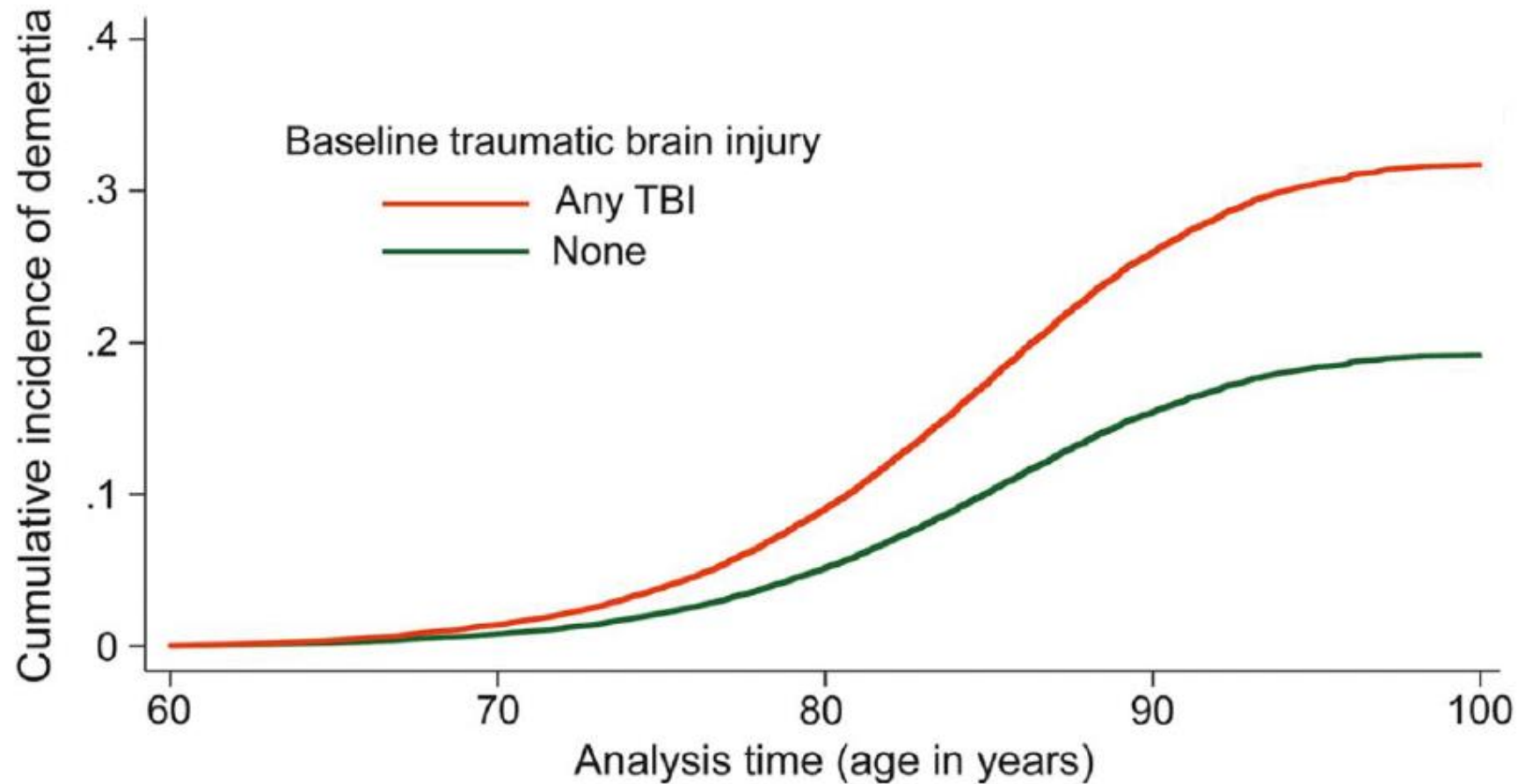
Iraq War combatants (U.S.) with mTBI
report 1–150 mTBIs (~4 average).

NFL players sustain 3,000–8,000
concussions during a lifetime of sports.

Your speaker has sustained 5–6
concussions in his timid, little life



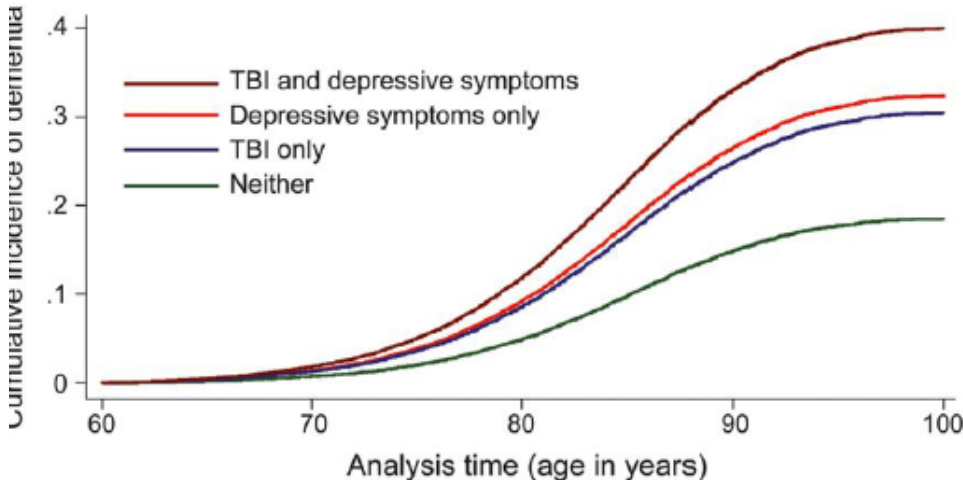
60% Increased Risk of Dementia with TBI



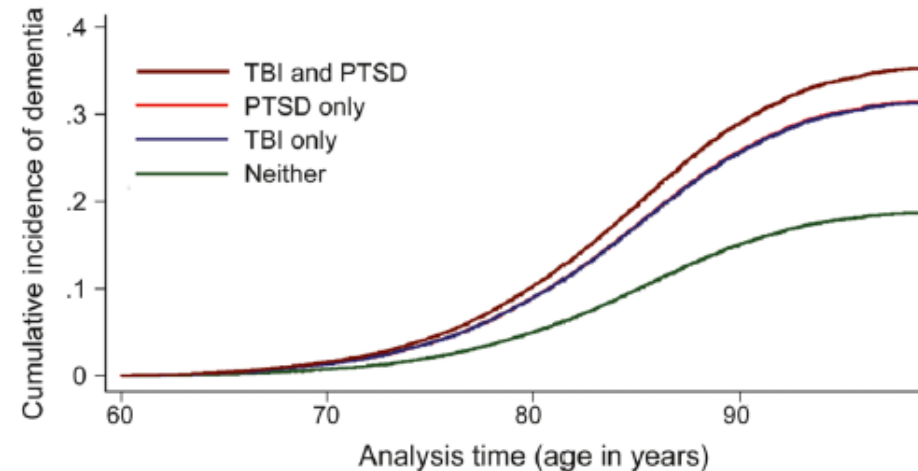
Adjusted HR:1.57; 95% CI (1.35–1.83)

Comorbidities Have an Additive Effect on Dementia Risk

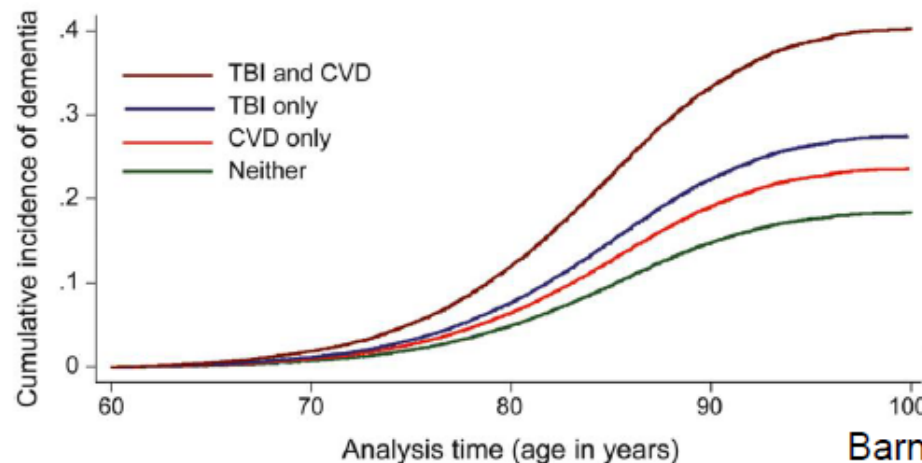
Depression



PTSD



Cerebrovascular Disease



Chronic Traumatic Encephalopathy

- ▶ CTE (Punch Drunk, Dementia Pugilistica) begins insidiously, usually many years (5–20) after the patients have stopped playing sports, with inattention, mood and behavior disturbances, confusion, and memory loss, and progresses over many years (5+) to a stage of full blown dementia and Parkinsonism.
- ▶ The brain, in CTE, shows atrophy, dilatation of the lateral and third ventricles, and thinning of the corpus callosum.
- ▶ Microscopic examination reveals neuronal loss and **tau deposition** in neurons (**neurofibrillary tangles–NFTs**) and in astrocytes. This pathology involves the cerebral cortex (perivascular areas, deep), white matter, deep nuclei, and the brainstem.
- ▶ Beta amyloid deposition in the form of diffuse and less frequently neuritic plaques is seen inconstantly (unlike AD)

Update on ongoing VA, DoD and Academic
Multi-Center, Longitudinal Studies of
repetitive mild TBI and blast exposure,
including the Chronic Effects of NeurTrauma
Consortium (CENC) Longitudinal Study





Chronic Effects of Neurotrauma Consortium

CENC Sites

Barrows Neurological Institute, Phoenix, AZ

Baylor College of Medicine, Houston, TX

Boston University, Boston, MA

Brigham Young University, Provo, UT

Duke University School of Medicine,
Durham, NC

Dwight D. Eisenhower Army Medical Center,
Fort Gordon, GA

Fort Belvoir Community Hospital,
Alexandria, VA

Hunter Holmes McGuire VA, Richmond, VA

James A. Haley Veteran's Hospital, Tampa, FL

Iowa City VA Health Care Center

Medical College of Wisconsin, Milwaukee, WI

Medical University of South Carolina,
Charleston, SC

Michael E. DeBakey VA Medical Center,
Houston, TX

Milwaukee VA Medical Center,
Milwaukee, WI

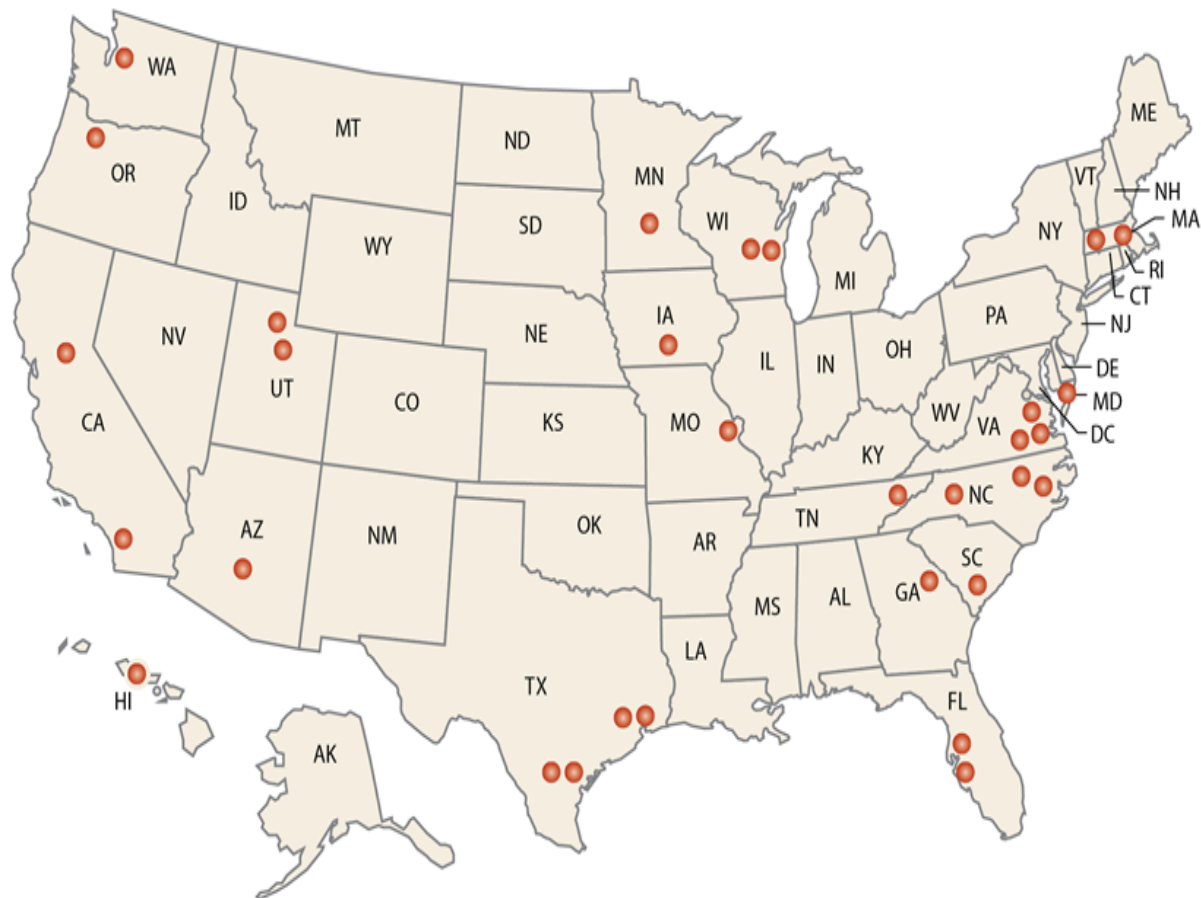
Minneapolis VA Health Care System

Mountain Home VA Medical Center,
Mountain Home, TN

Northern California Institute of Research
and Education, San Francisco, CA

Roskamp Institute, Sarasota, FL

RTI International, Durham, NC



San Antonio Military Medical Center,

San Antonio, TX

San Francisco VA Medical Center,

San Francisco, CA

South Texas Veterans Healthcare Center,

San Antonio, TX

Uniformed Services University of the Health Sciences,

Bethesda, MD

University of Missouri St. Louis, St. Louis, MO

University of Hawaii, Manoa, HI

University of Utah, Salt Lake City, UT

University of Washington, Seattle, WA

VA Boston Healthcare System

VA Portland Health Care System

VA San Diego Health Care System,
San Diego, CA

Virginia Commonwealth University,
Richmond, VA

WG Hefner VA Medical Center, Salisbury, NC

CENC Findings

- ▶ More than two-thirds of Servicemembers and Veterans with persistent difficulties after combat concussions and related issues are high functioning, employed and managing well in the community more than 7 years after injury.
- ▶ One-third are demonstrating ongoing and increasing difficulties that are requiring significant health care utilization.
- ▶
- ▶ None of the subjects is exhibiting signs of dementia on average 9 years from last mTBI.
- ▶ Female subjects have greater symptoms than male.
- ▶ Servicemembers and Veterans with combat-related concussions and associated conditions (PTSD, pain, depression, substance use, elevated suicide risk) represent a unique and high-risk population.

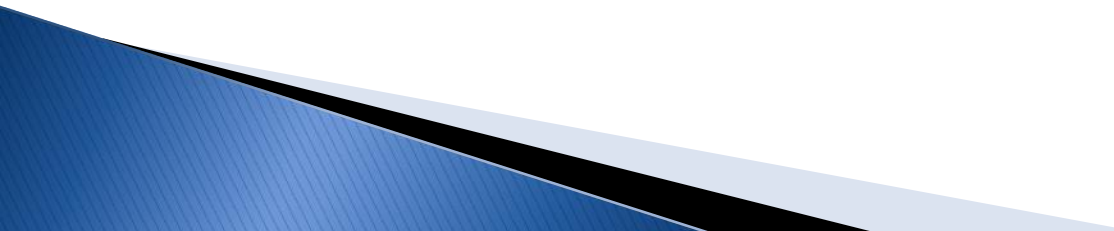
CENC Findings

- ▶ Linkages have been identified between elevated lifetime risks for neuro-degeneration, including Alzheimer's dementia and Parkinson's disease, chronic pain, opioid misuse, and PTSD in Servicemembers and Veterans who have experienced TBI.
- ▶ Multi-modal research assessment techniques have been developed that allow for more accurate diagnoses and clinical characterization. As of yet, these techniques and technologies (e.g. biomarker, imaging, eye-tracking, qEEG) are not appropriate for every day, clinical usage, and the existing diagnostic, assessment and intervention protocols that exist in the VA Polytrauma System of Care are state-of-the-art and clinically appropriate.

CENC Findings

- ▶ While evidence-based, comprehensive clinical services for the care of Servicemembers and Veterans with persistent difficulties due to military service and combat-related concussion exist across VA's Polytrauma System of Care, a number of individuals are not aware and/or accessing these services.
- ▶ While there exist a range of novel techniques and technologies (e.g., hyperbaric oxygen, transcranial magnetic stimulation, neurofacilitation) that are being either advocated or researched for the clinical care of Servicemembers and Veterans with military service and combat-related concussions, none of these newer treatments are yet appropriate for recommended for this population.
- ▶ The comprehensive, symptom-based, team-directed care provided through the VA Polytrauma System is the gold standard.

Clinical Practice Guideline–directed,
comprehensive approach to the clinical
management for individuals with
combat–related exposure to blast
and/or repetitive mild TBI who believe
they are at risk for or have CTE.

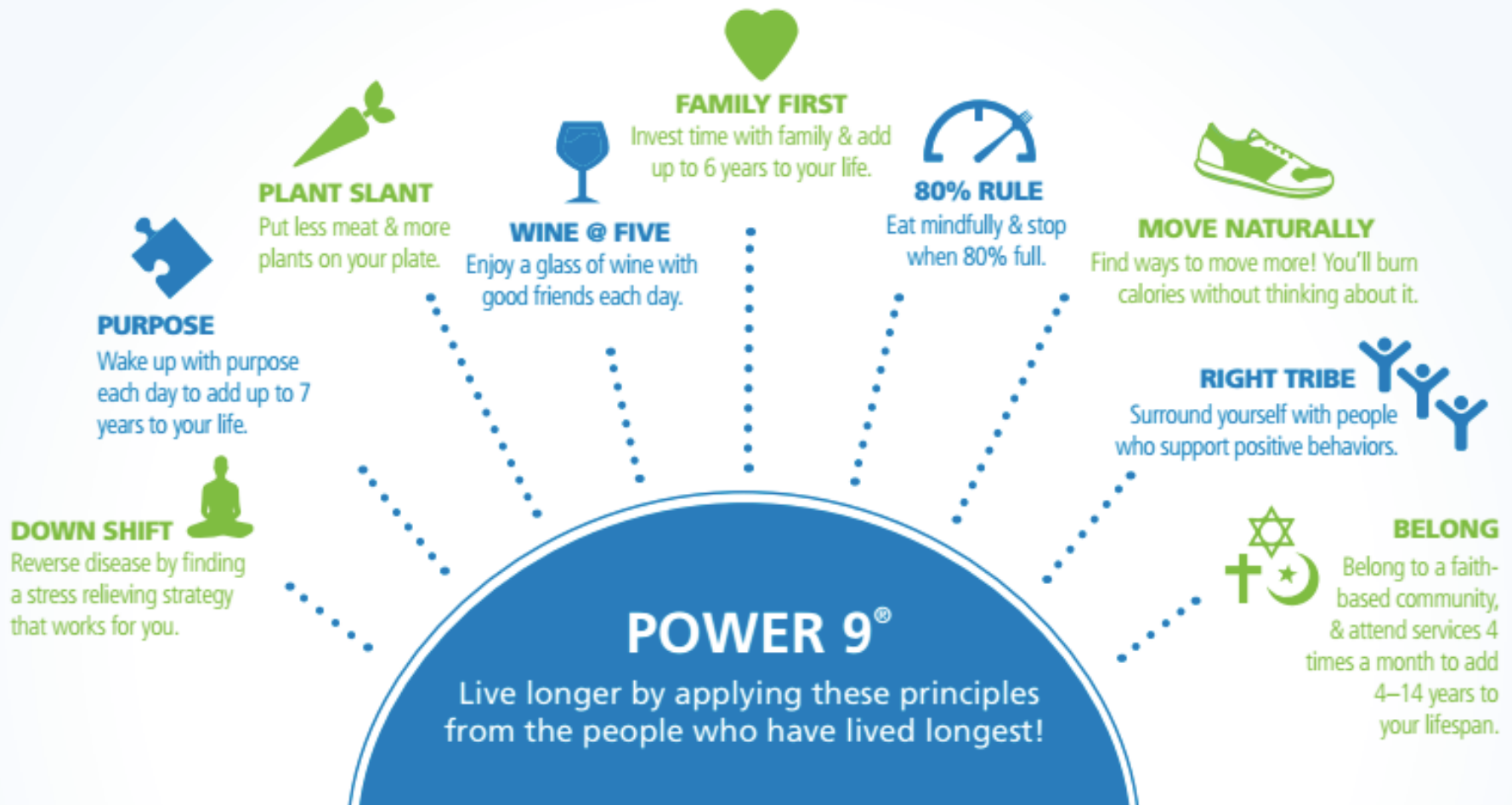


Dementia-related Factors

- ▶ Nine modifiable lifestyle factors account for up to 50% of all cases of dementia
 - Limited education in early life
 - hearing loss
 - Hypertension
 - Obesity
 - Smoking
 - Depression
 - Physical inactivity
 - Social isolation
 - Diabetes
- ▶ No single risk or protective factor is dominant.

Ashby-Mitchell: Alzheim Res Ther 2017

Norton: Lancet Neurology 2014



75% of chronic diseases preventable
One-third of dementias preventable

**Diet, Exercise, Sleep, Stress Management, Pain Care,
Productivity, Social Integration, Family, Faith-Based Community**

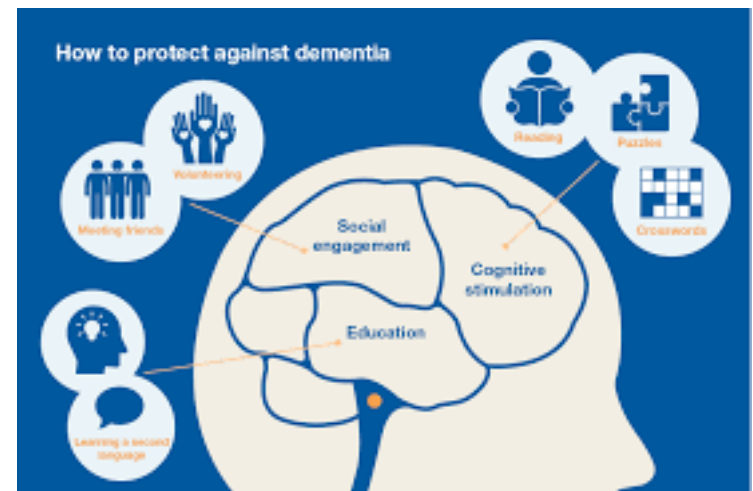
Dementia-related Factors

- ▶ Repeated TBI's may play a small role (1%) in increasing the risk for dementia.
- ▶ The presence of the apolipoprotein E (APOE) $\epsilon 4$ allele may increase AD risk by 8%.
- ▶ In addition to depression, intermittent or persistent mental illness likely increases risk.
- ▶ Spending enough time getting tests and seeing doctors likely also increase the risk for dementia (? in the doctors)

Managing “Dementia”



- ▶ Dementia is a 20–60 year prodromal disease
 - We are seeing the effects in the last 5 years of life
 - We are attempting to intervene in the last 2 years of life
- ▶ Even though 99% of the folks we see will NOT have classic dementia, they all likely have elevated risks.
- ▶ And we wonder why we are failing??



Counseling on TBI and CTE

- ▶ Acknowledge their issues and concerns.
- ▶ Don't over explain or hedge your answer.
- ▶ The risk of developing dementia from a single concussion is zero. The risk of developing dementia from 10 concussions is just barely above zero.
- ▶ Undertreated symptoms (post-concussion, mental health, pain) may be a more relevant risk factor for dementia.
- ▶ Lifestyle factors, general wellness, and integration into society are biggest risk factors

