#### CHRONIC TRAUMATIC ENCEPHALOPATHY (CTE)

MEGHAN L GEISS, PHD, LCP REHABILITATION NEUROPSYCHOLOGIST

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## DISCLAIMER

 The views expressed in this presentation are solely those of the presenter and do not represent those of the Veterans Health Administration, the Department of Defense, or the United States government





### OBJECTIVES

- Define Chronic Traumatic Encephalopathy (CTE) and Traumatic Brain Injury (TBI) including mechanisms of injury and severity levels.
- 2. Review updated CTE research including what is known and where additional research is needed.
- **3.** Explore clinical features of CTE including possible cognitive and behavioral correlates.
- **4.** Review clinical implications in working with adults presenting with brain injury and behavioral dysfunction.

### CHRONIC TRAUMATIC ENCEPHALOPATHY (CTE)

CTE is a degenerative brain disease caused in part by repeated traumatic brain injuries, which include concussions and sub-concussive impacts.



## **BRAIN INJURY**



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#### TRAUMATIC BRAIN INJURY (TBI)



- An alteration in brain function or other evidence of brain pathology caused by an external force and characterized by the following:
- a. Any period of loss or decreased consciousness
- b. Any loss of memory for events immediately before (retrograde) or after (posttraumatic) the injury
- **c.** Any neurological deficits and/or
- d. Any alteration in mental state at the time of injury

(National Institute for Neurologic Disorders and Stroke [NINDS] Common Data Elements [CDE] for TBI)

### TYPES OF TBI: OPEN

#### Penetration to the brain

-Causes localized brain damage

-Result in discrete and relatively predictable disabilities

Common Causes

-Assaults

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-Severe falls

-Accidents

Abuse

-Surgery

## EASIER TO DETECT USING



#### TYPES OF TBI - CLOSED

Internal damage to the brain; no open head wound -Causes diffuse tissue damage -Result in generalized and highly variable disabilities **Common causes:** -Falls -Vehicle accidents -sports accidents



#### CAUSES OF TBI

- Motor Vehicle Crashes
- Falls

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- Gunshot Wounds
- Sports Injuries
- Workplace Injuries
- Child Abuse
- Domestic Violence
- Military Actions
- Other injuries caused by trauma



#### CAUSES OF BRAIN INJURY

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#### HOW IS TBI ASSESSED?

## THE CLASSIFICATION OF BRAIN INJURIES

#### **CLASSIFICATION OF BRAIN INJURY**

Mild	LOC less than 30 minutes	GCS 13-15	PTA less than 24 hours
Moderate	LOC greater than 30 minutes, but less than 24 hours	GCS 9-12	PTA 24 hours to 7 days
Severe	LOC greater than 24 hours	GCS 8 or less	PTA more than 7 days

Injuries are classified according to mild, moderate and severe injuries.

#### EPIDEMIOLOGY OF TBI

- Every **23** seconds, one person in the United States sustains a traumatic brain injury.
- More than **50,000** people die every year as a result of traumatic brain injury.
- 284,000 people are hospitalized each year with traumatic brain injury.
- 80,000-90,000 Americans experience the onset of a long-term disability following traumatic brain injury each year.

(CDC, 2011)

#### TBI PREVALENCE

- An estimated 2.5 million TBIs occur in the United States annually
- Of the 2.5 million TBIs occurring, 2.2 (88%) were emergency department visits.



#### TBI PREVALENCE



#### Of hospitalized cases

- 19% are classified as severe (GCS 8 or below)
- 21% as moderate (GCS 9-12)
- 52% as mild (GCS 13-15)
   (CDC, 2011)

#### EPIDEMIOLOGY OF TBI

 After one traumatic brain injury, the risk for a second injury is three times greater; after the second injury, the risk for a third injury is eight times greater.



### WHO IS AT HIGHEST RISK FOR TBI

- Males are about 1.5 times as likely as females to sustain a TBI
- Males have higher rates of Hospitalization, Death, and Emergency Department Visits
- The three age groups at highest risk for TBI are
  - 0 to 4
  - 15 to 19
  - 75+

#### INCIDENCE & AGE

- Incidence of TBI is highest in the 0-4 age group (1121 per 100,000)
- Deaths from TBI are highest in the 75 or older age group (51 per 100,000)
- Emergency Department visits are highest in the 0-4 age group

(1035 per 100,000)



#### WHO IS AT HIGHEST RISK FOR TBI

- A high proportion of individual who sustain TBI have a criminal history
- One study found that 19.5% of 327 consecutive admissions for TBI had a preinjury criminal record (Kreutzer, Marwitz, and Witol, 1996).
- Learning disabilities, emotional problems, and attention deficits (Woodward et al., 1999).

#### TBI - INMATES

Across various TBI studies examining offender populations, 25% to 87% of offenders reported having a TBI. (Shiroma et al., 2012; Farrer & Hedges, 2011)

 These estimates suggest that TBI appears more frequent in offender populations (i.e., prisons) than in general population.

#### PROBLEMS ASSOCIATED WITH BRAIN INJURY: ALCOHOL/SUBSTANCE USE

- Strong link between intoxication and incurring TBI
- Incidence of positive blood alcohol findings (>50% and BAC >.08) in motor vehicle crashes and violence-related TBI (Kraus & McArthur, 1998)
- Hospitalized for TBI– 21% (BAC .08) ( Whiteneck et al., 2001)
- Receiving rehab for TBI 37% (BAC .10) (Corrigan et al., 2003).





PROBLEMS ASSOCIATED WITH BRAIN INJURY: SUBSTANCE ABUSE/ALCOHOL

- Those who had substance use issues prior to TBI are likely to return to substance use following injury.
- Alcohol use can be a risk factor for TBI, particularly among older adults. (Dams-O'conner et al., 2016; Bombardier et al., 2002)
- 10%-20% of those with no prior substance use have developed substance abuse disorder following TBI

#### MILITARY TBI

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#### **TBI Severity**



**DoD Numbers for Traumatic Brain Injury Worldwide – Totals** 

#### 2000 - 2018 Q1

Penetrating5,215Severe4,067Moderate37,424Mild315,897Not Classifiable21,344

#### Total - All Severities 383,947

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

Prepared by the Defense and Veterans Brain Injury Center (DVBIC) "Percentages do not odd up to 100% due to rounding



2000 - 2018 Q1, as of June 21, 2018

#### TBI Incidence by Armed Forces Branch





## TBI AND VETERANS



- The relative incidence of penetrating head injuries is especially high compared with civilian population
- The incidence of TBI among US military personnel deployed to Iraq and Afghanistan is reportedly the highest of any military conflict in US history (Okie, 2005; Warden, 2006)
- "Signature Wound"

#### TBI AND VETERANS

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- Approximately one out of five OIF/OEF Veterans screen positive for TBI.
- An estimated 20% of Veterans who have served since 2001 report experiencing a probable Traumatic Brain Injury (Mathias & Alvaro, 2012)
- Most VA patients with a TBI diagnosis also carried a mental health diagnosis, with PTSD being the most common.

## COMBAT INJURIES

- Blast exposure
- The majority of OEF-OIF injuries during combat are caused by <u>blasts</u>, and most are <u>mild in severity</u>
- Motor vehicle accidents
- Falls



#### WHAT HAPPENS IN A CONCUSSION?

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## IMMEDIATE SYMPTOMS OF A CONCUSSION

Acting confused, feeling spacey, or not thinking straight
Being drowsy, hard to wake up, or similar changes
Loss of consciousness
Memory loss (amnesia) of events before the injury or right after
Nausea and vomiting
Seeing flashing lights
Feeling like you have "lost time"

### **CONCUSSION - PROGNOSIS**

- Chronic symptoms from concussion are RARE
- Most patients return to normal baseline in days to up to 3 months
- Ongoing symptoms after concussion are likely cooccurring conditions and not direct symptoms

 Symptoms are most severe in the hours to days following injury and gradually improve to the degree possible

## POST CONCUSSION SYNDROME

 A complex disorder in which various symptoms (e.g., headaches, dizziness, fatigue, irritability, etc.) persist for weeks, months, or a year (although rare) following mTBI/concussion.

•Not the same as CTE





## SYMPTOM OVERLAP

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# LAYMAN'S VIEW OF HOW THE BRAIN WORKS...



# AND HOW IT MIGHT LOOK AFTER A TBI...

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### MECHANISM OF DAMAGE



- Bruising of brain due to forward/backward movement against skull
- Twisting of nerve fibers due to twisting of brain within skull
- Nerve fibers are broken or stretched = temporary or permanent brain damage



#### **Neuron Following Concussion**

Metabolic dysfunction results in ENERGY CRISI Massive release of neurotransmitters interferes with cell communications

It may take many days for the nerve cells to return to their normal condition.

Sports Legacy Institute 2013

#### CHRONIC EFFECTS OF BRAIN INJURY

- Greater risk for Alzheimer's Disease, Parkinson's Disease, and ALS.
- Veterans with severe TBI were 4 times more likely to have AD, whereas veterans with moderate TBI were twice as likely to have AD in late life compared with controls

#### CHRONIC EFFECTS OF BRAIN INJURY

- In a cohort study of >350,000 veterans, even concussion/mild TBI without LOC was associated with a 2-fold increase in risk of dementia diagnosis (Barnes et al., 2018)
- Concussion/mTBI was associated with 56% increased risk of Parkinson's disease, even after adjusting for demographics and medical/psychiatric comorbidities (Gardner et al., 2018

### CHRONIC TRAUMATIC ENCEPHALOPATHY (CTE)

CTE is a degenerative brain disease caused in part by repeated traumatic brain injuries, which include concussions and sub-concussive impacts.

#### SUB-CONCUSSIVE IMPACTS

- Repeated head impacts that do not manifest in overt symptoms
  - Contact sports

- CTE has been identified in athletes with no known history of concussion
- Sub-concussive events are believed to be the driving force behind CTE (wear and tear vs. single trauma)

## CHRONIC TRAUMATIC ENCEPHALOPATHY: HISTORY

- 1928- First described in boxers
   "Punch-Drunk" syndrome by Dr. Harrison Martland
- "Dementia Pugilistica"
- 2005- A pathologist (Dr. Bennet Omalu) published first evidence of CTE in American football players, including Pittsburgh Steeler Mike Webster.



### CHRONIC TRAUMATIC ENCEPHALOPATHY: HISTORY

2008- UNITE/VA-BU-CLF Brain Bank was established. Led by Dr. Ann McKee

-Currently has >1300 donated brains



Paul Pender World Champion Boxer Marine

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Death at age 73 Severe Dementia



#### 45 year old ex-NFL players



#### Tom McHale

Lineman, 9 years NFL Retired from NFL at age 32 Age 40: business failed, painkillers, short-term memory problems, depression, Irritability Ace 45: depth - overclose



Linebacker, 9 years in NFL Retired from NFL at age 32 Age 40: short term memory problems, attention, concentration, judgment, multitasking alfficuities Age 45: death - accidential GSW

### BRAIN BANK RESEARCH FINDINGS

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- 87% of the brain donors were diagnosed with CTE using strictly defined criteria, including:
- 110 of 111 NFL (99%)
- 48 of 53 college football (91%)
- 3 of 14 high school football (21%)

#### McKee et al., 2017

## CTE BRAIN BANK

- American football players
- Boxers
- Ice hockey players
- Rugby players
- Soccer players
- Veterans

McKee et al., 2017



#### HOW IS CTE DIAGNOSED?

 Currently CTE CANNOT be diagnosed in living people and can only be definitively diagnosed by autopsy after death via neuropathological examination.



### CTE PREVALANCE

- Diagnostic limitations limit a clear understanding.
- Studies suggest possibly 1-3% of the population has CTE

### CTE IN VETERANS

• Research is limited

Of the 110 cases diagnosed with CTE at the Boston VA TBI Brain Bank, CTE has been diagnosed in 23 veterans.

Sixteen veterans with CTE were accomplished athletes

- 9 former NFL players,
- > 1 former semiprofessional football player,
- 3 former professional boxers,
- 1 former army rugby player
- > 1 former army boxer
- 1 amateur hockey player.





### CTE IN VETERANS

- The New England Journal of Medicine study examined 225 brains from deceased service members:
  - <5% showed evidence of CTE
  - 6.7% of 45 brains of those w/ blast exposure were diagnosed with CTE
  - All brains with CTE were from those with history of contact sports
  - (Priemer et al., 2022)

# CLINICAL SYMPTOMS OF CTE: MOOD AND BEHAVIOR

#### Among individuals with CTE some report:

- Impulse control problems
- Mood swings/emotional dysregulation
- Aggression
- Depression
- Paranoia
- Anxiety
- Sleep problems

Can appear as early as the patients 20s



# CTE SYMPTOMS: COGNITION



- Executive dysfunction
- Variable judgement
- Memory impairment
- Dementia
- Tend to appear later in life – more frequently in 60's and 70's.

## CTE SYMPTOMS: SLEEP

- Problems with sleep may be related to CTE
- REM Behavior Disorder (Stein et al., 2020)



## CTE: PROGRESSION

- 4 Stages
- Although clinical symptoms appear to be slowly progressive in most individuals diagnosed with CTE, CTE may not progress, may not progress at the same rate, in all individuals with the disease.
- 11-14 years between stages

#### **CTE: STAGES**

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#### McKee et al.'s (2013) **CTE Tau Staging**

STAGEI · Isolated perivascular epicenters · Predilection for depths of sulci · Neocortex: superior, dorsolateral and inferior frontal . Locus coeruleus (66% of cases)

STAGE II Multiple epicenters in frontal, temporal cortex, and parietal neocortices Diencephalon

STAGE III · Widespread neocortical involvement Hippocampus Entorhinal cortex Amygdala Nucleus basalis of Meynert

STAGE IV Thalamus Basal ganglia Brain stem Cerebellum



CTE











Braak et al.'s (2011) Aging/AD Tau Staging

#### STAGE a-c

· Locus coeruleus Upper raphe nuclei Magnocellular nuclei



AD





Basal temporal

Transentorhinal cortex

STAGE 1a, 1b, I-II

STAGE III-IV Hipppocampus Amygdala



## CTE: STAGES

- <u>Stage I</u>-Clinical symptoms include headaches and attention and concentration deficits
- <u>Stage II</u> Expand to include depression, explosivity and short-term memory impairment

(McKee et al., 2013)



### **CTE: STAGES**

- Stage III- Cognitive impairment and problems with executive functions, specifically planning, organization, multitasking and judgement
- Stage IV- Dementia
  (McKee et al., 2013)



Greater years of football, higher level of play predict:

- Increased CTE severity
- Greater p-tau burden
- Greater inflammation

(Cherry et al., 2017; Mez et al., 2017)

• Lewy Body Disease (LBD)

(Adams et al., 2018)

- More severe white matter degeneration (Alosco et al., 2018)
- Every 1-year younger participants began to play football resulted in earlier cognitive and behavioral/mood symptom onset by 2.4-2.5 years (Alosco et al., 2018)

### CTE

### WHAT HAS BEEN DONE?

#### Development of a Concussion protocol:

- Immediate removal from playing field or battlefield – without return
- Examination by neurological consultant
- Concussion "protocol" including stepwise return to previous activity

#### 6-STEP RETURN-TO-PLAY PROTOCOL

PHASE	REHABILITATION	OBJECTIVE
Phase 1	Baseline	Patient must be on physical and cognitive rest with no symptoms for at least 24 hr.
Phase 2	Increase heart rate	The goal is to increase heart rate for 5-10 min through mild activity such as walking, light jogging, or an exercise bike.
Phase 3	Moderate exercise	In this phase the goal is limited body and head movement through more moderate intensity activities such as brief running or moderate weight lifting.
Phase 4	Noncontact exercise	The goal is to increase intensity but avoid contact. Activities could include more intense running, stationary biking, or noncontact sport-specific drills.
Phase 5	Practice	Reintegrate into full contact practice.
Phase 6	Play	Return to competition.

#### TREATMENT FOR CTE

- Limited studies on how to treat clinical symptoms CTE
- This is partially based on CTE not being diagnosed with known level of statistical accuracy in living patients.
- Treatments targeting symptoms associated with CTE can be pursued to improve quality of life.

## WHAT NEEDS TO HAPPEN TO

- Brain bank currently has ~1300 donated brains and in need of more from other populations (i.e., women, domestic abuse survivors)
- Diagnostic advances (e.g., CTE in the living [PET scan, etc.])
- Identify genetic susceptibility factors
- Develop therapies and treatments
- Prevent this disease in future generations



## CLINICAL IMPLICATIONS

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### SCREENINGS

#### TBI

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#### Anxiety

#### Depression

#### PTSD

#### Etoh/SA

- Has there been an event that had the potential to cause a significant force to the head?
  - If yes, was this force to the head immediately followed by:
    - A. Any period of loss of or a decreased level of consciousness
    - B. Any loss of memory for events immediately before or after the injury (post traumatic amnesia).
    - Alteration in mental state at the time of the injury (mental confusion, disorientation, slowed thinking, etc.)

## MH TREATMENT

- Individual
- Group (psychoeducation, TBI, caregiver support)
- Couples/family
  - Communication skills
  - Interpersonal skill building



# CONSIDER FURTHER EVALUATION

#### Neuropsychological evaluation

- Help identify cognitive deficits/strengths, possible changes 2/2 TBI
- Provide specific recommendations regarding accommodations for school and/or work to support vocational aspirations
- Recommendations regarding additional therapies (e.g., speech therapy, occupational therapy, etc.)



# VA POLYTRAUMA/TBI SYSTEM OF CARE



- VA has a Polytrauma/TBI national system of care composed of four components:
- <u>Polytrauma Rehabilitation Centers</u> (<u>PRCs</u>) are regional referral centers for acute inpatient medical and rehabilitation care
- Polytrauma Network Sites
   (PNS) provide post-acute
   rehabilitation and coordinate
   polytrauma services within the
   Veterans Integrated Service Networks
   (VISNs)
- Polytrauma Support Clinic Teams (PSCT) provide outpatient interdisciplinary rehabilitation evaluation and treatment services within their catchment areas
- <u>Polytrauma Point of Contact (PPOC)</u> at each VA facility deliver a more limited range of rehabilitation services and facilitate referrals to other PSC programs, as necessary

#### Polytrauma System of Care Locations

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#### RESOURCES



- Brain Injury Association (<u>https://www.biausa.org</u>)
- Brainline (<u>https://www.brainline.org</u>) Brain Injury and PTSD, especially helpful for caregivers
- <u>Homepage | Concussion Legacy Foundation</u> (concussionfoundation.org) – Concussion Legacy Foundation
- <u>https://msktc.org/tbi</u> TBI Model Systems Knowledge Translation Center
- <u>https://www.polytrauma.va.gov/concussioncoach</u>
   <u>.asp</u> (concussion coach app)

## RESOURCES (TBI SCREENING FOR VETERAN)

<u>TBI Screening: DVBIC (3 questions)</u>

- <u>https://www.mirecc.va.gov/docs/visn6/5</u>
   <u>TBI 3 Question Screening Tool.pdf</u>
- Brief ABI Screen
- The Ohio State University Traumatic Brain Injury(TBI) Identification Method
- <u>https://wexnermedical.osu.edu/neurologic</u> <u>al-institute/neuroscience-research-</u> <u>institute/research-centers/ohio-valley-</u> <u>center-for-brain-injury-prevention-and-</u> <u>rehabilitation/osu-tbi-id</u>


## QUESTIONS

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## **Contact:**

## Meghan Geiss, Ph.D. <u>Meghan.Geiss1@gmail.com</u>