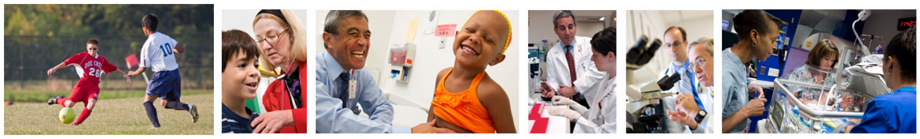

Chronic Traumatic Encephalopathy (CTE)

Jorge E. Gomez, MD, MS

Sports Medicine

Associate Professor

Texas Children's Hospital

Baylor College of Medicine

Sports Medicine

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Disclosure

- I have no conflicts of interest to disclose related to this presentation

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Learning Objectives

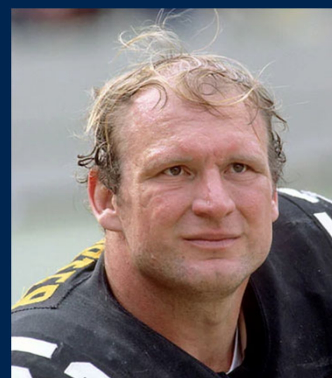
- Be familiar with the basics of CTE pathology
- Learn how assessment of CTE incidence is limited
- Be familiar with the results of long-term studies of repeated head impacts
- Have the knowledge to advocate for prevention strategies

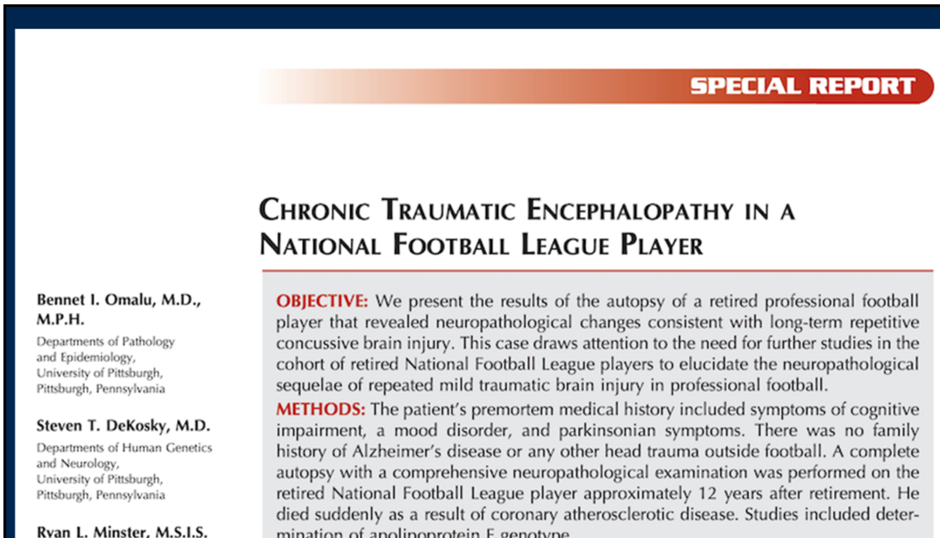
Definition

- CTE is a neurodegenerative disease that has been associated with repetitive head impacts (RHI) sustained in a wide variety of contact sports, such as American football, ice hockey, rugby, wrestling, soccer, and boxing.
- Previously known by "punch drunk syndrome", "Dementia Pugilistica

Cases Studies

- Impulsivity
- Aggression
- Depression
- Impaired memory
- Impaired executive function





SPECIAL REPORT

Chronic Traumatic Encephalopathy in a National Football League Player

Bennet I. Omalu, M.D., M.P.H.
Departments of Pathology and Epidemiology, University of Pittsburgh, Pittsburgh, Pennsylvania

Steven T. DeKosky, M.D.
Departments of Human Genetics and Neurology, University of Pittsburgh, Pittsburgh, Pennsylvania

Ryan L. Minster, M.S.I.S.

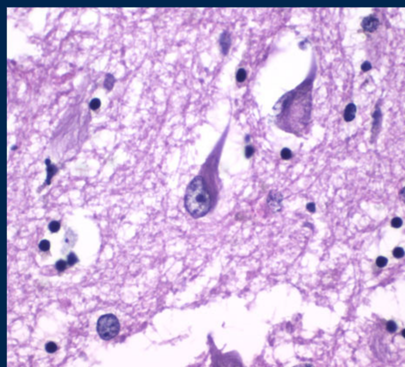
OBJECTIVE: We present the results of the autopsy of a retired professional football player that revealed neuropathological changes consistent with long-term repetitive concussive brain injury. This case draws attention to the need for further studies in the cohort of retired National Football League players to elucidate the neuropathological sequelae of repeated mild traumatic brain injury in professional football.

METHODS: The patient's premortem medical history included symptoms of cognitive impairment, a mood disorder, and parkinsonian symptoms. There was no family history of Alzheimer's disease or any other head trauma outside football. A complete autopsy with a comprehensive neuropathological examination was performed on the retired National Football League player approximately 12 years after retirement. He died suddenly as a result of coronary atherosclerotic disease. Studies included determination of apolipoprotein E genotype.

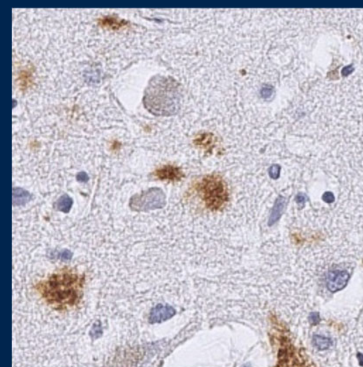
Neurosurgery 57:128-134, 2005

Microscopic Findings in CTE

NFTs



Amyloid Plaques



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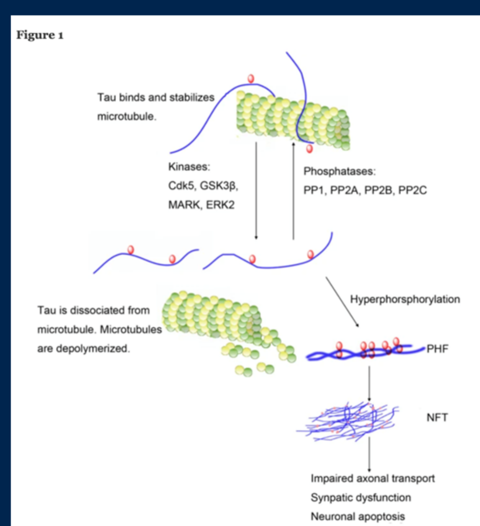
Tau Protein (ptau)

- Primarily found in axons where it promotes microtubule stabilization
- 6 types (351-442 AA)
- Hyperphosporylation reduces ptau affinity to microtubles causing cytoskeleton destabilization, leading to neuron death
- Also leads to neurofibrillary tangle (NFTs)



Duan Y, et al. *Translational Neurodegeneration*, 2012

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CTE Pathology

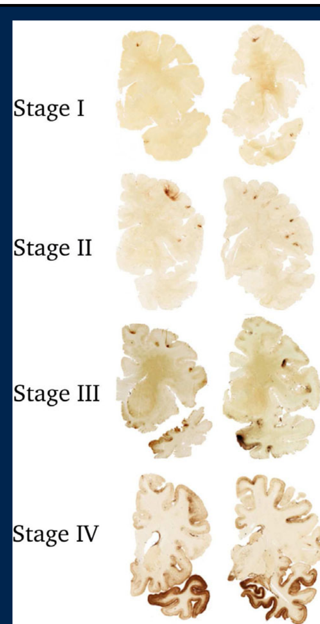
ptau deposits (NFTs) in the neocortex, along blood vessels.

In more advanced cases the deposits are found in the sulci.

Deposits spread from the superior-lateral cortex to other areas.

There are also gross changes more pronounced in advanced cases

McKee AC, et al. *Brain Pathology*, 2015



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CTE as a Unique Entity

- Establishing cause and effect is not straightforward
  - Brains of patients with suspected CTE show similarities with other neurodegenerative diseases, esp Alzheimers
  - Other disease and injury processes may lead to similar pathologic changes
  - Other diseases may cause similar cognitive and behavior features
  - Patients may have co-morbid conditions

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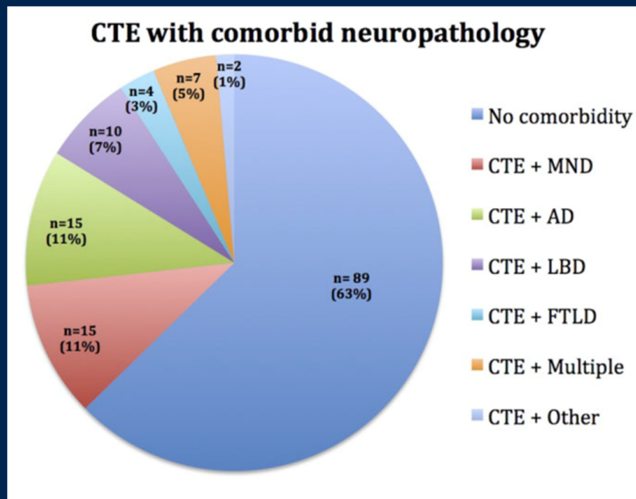


McKee AC, et al. The neuropathology of chronic traumatic encephalopathy. 2015. Brain Pathology 25: 350-364.

CTE found in nearly 90 percent of brains donated by football players

Data Base for CTE

- Relying so far primarily on retrospective studies, that are subject to selection/ascertrainment bias
- Long-term, prospective studies are lacking
- CTE has only been described in individuals with a history of repetitive brain injury

Ascertainment Bias in NFL CTE Studies

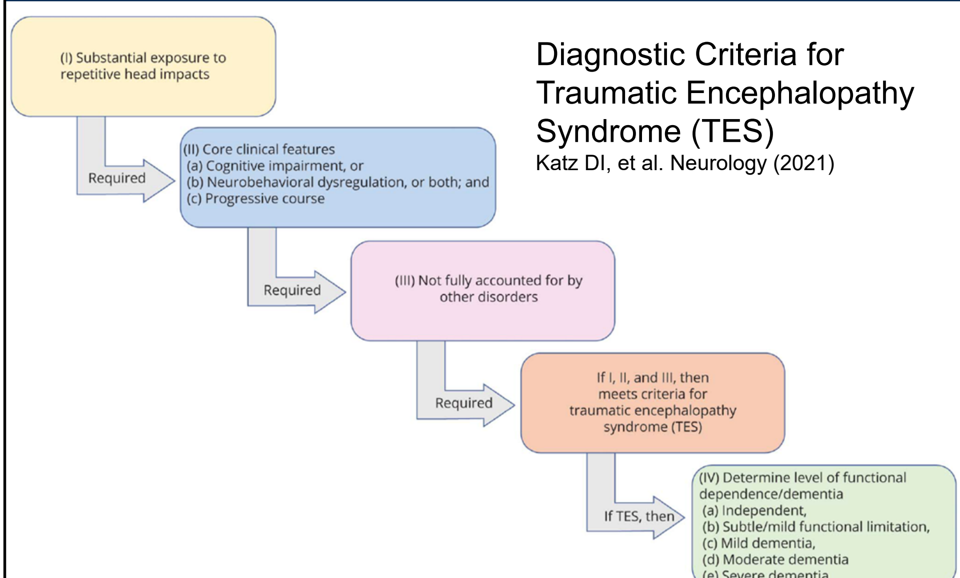
Traumatic Encephalopathy Syndrome (TES) vs Chronic Traumatic Encephalopathy (CTE)

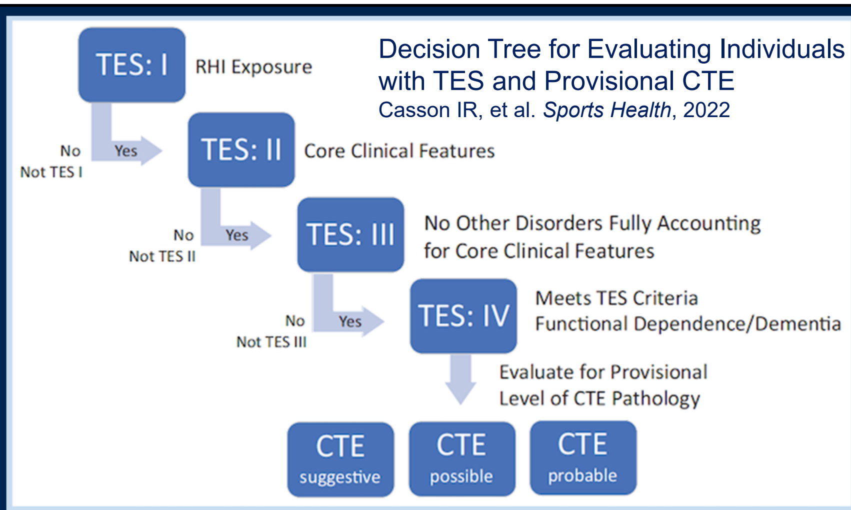
- **CTE** is a ***pathologic diagnosis*** (diagnosis made by looking at brain tissue)

- **TES** is a ***clinical diagnosis***, a syndrome comprising the clinical features of CTE

Diagnostic Criteria for Traumatic Encephalopathy Syndrome (TES)

Katz DI, et al. Neurology (2021)





Suggestive: meets criteria for TES
Possible: TES + 5 yrs RHI + cognitive impairment (TES II) + add'l features
Probable:TES + 11 yrs RHI + 5 add'l features (NBD & dementia)

Questions

- How common is this?
- How many years of football are too many?
- How young is too young?
- How much do genetics determine risk?
- "Why do some players not have evidence of this disease despite long playing years?
- What other lifestyle habits might contribute -- alcohol, drugs, steroids, diet?

Biomarkers of Brain Injury

- Certain biomarkers may be sensitive to diffuse axonal injury (DAI), which appears to reflect the number & magnitude of subconcussive head impacts
  - pTau
  - NF-L (neurofilament polypeptide – light)

- Less expensive, less time intensive, easier to obtain that MR imaging

Oliver JM, et al. *J Neurosurg* 2019

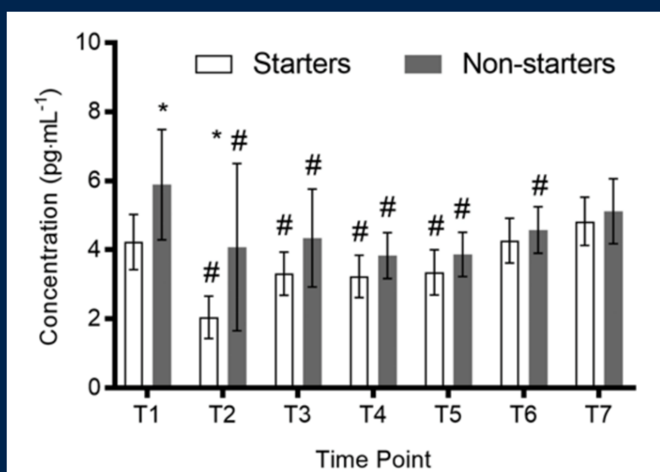


FIG. 2. Plasma concentrations of tau over the course of the season in American football athletes. *Asterisk* indicates significant difference by starter status ($p \leq 0.05$); *pound sign* indicates significant difference from T1 ($p \leq 0.05$).

Oliver JM, et al. *J Neurosurg* 2019

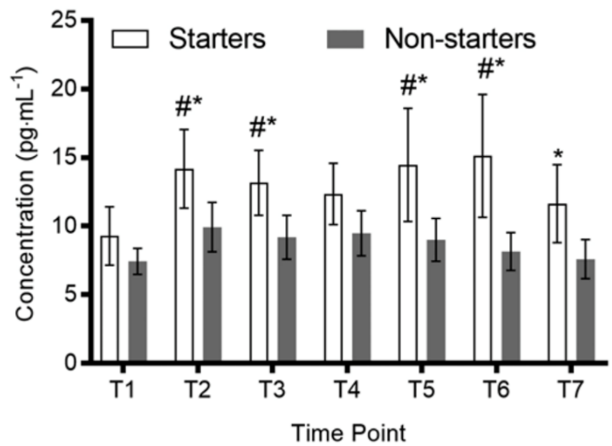


FIG. 3. Serum concentrations of NF-L over the course of the season in American football athletes. *Asterisk* indicates significant difference by starter status ($p \leq 0.05$); *pound sign* indicates significant difference from T1 ($p \leq 0.05$).

Cumulative Head Impacts - College

- McAllister TW. *Neurology* 2012
- Prospective study, 214 Div I FB & hockey, 46 controls, repeated head impacts (RHI), 1 season
- Mixed results. Generally, contact sport athletes did not do worse. A higher % performed more poorly on a verbal learning test (24% vs 3.4%, p<.006

Cumulative Head Impacts - Soccer

- Guskiewitz KM. *AJSM* 2002
  - 187 college athletes (91 soccer) over 1 season. The soccer athletes did not demonstrate impaired cognitive fxn c/w non-soccer athletes or non-athletes
- Stephens R. *J Neuropsych & Clin Neurosci* 2010
  - 185 male HS athletes, soccer & rugby. Neither soccer or rugby players showed NP decrement c/w noncontact sport athletes

Age at First Exposure (AFE) & CTE Risk

Iverson GL, et al. *Frontiers in Neurology*, 2021

- 21 studies
- The largest study of retired NFL players (N = 3,506) suggested there was not a significant association between earlier AFE and worse cognitive functioning, depression, or anxiety
- No study of current players showed an assoc of AFE & cognitive or behavioral problems
- All studies judged to be at high risk of bias

Playing High School Football

- Deshpande SK. *JAMA Neurology* 2017
- 2692 men, age 64.4, 834 played HS FB. No diff in multiple socioeconomic variables
- Cognitive & depression outcomes later in life were found to be similar for FB players & non-FB players

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They Don't Make Players Like They Used To

- Today's children are definitely bigger than they used to be, but they are not as fit as they used to be.
- Declines in performance of running, jumping, and neuromotor tests, as well as tests of strength, have been documented in children and youth in several industrialized countries over the past 20-30 yrs
- Rates of obesity in children have also climbed in that same period

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Does improved strength, fitness reduce concussion risk?

- A recent meta-analysis (Garret JM, et al. *JOSPT* 2023) found greater neck strength and/or motor control reduced concussion incidence
- Another recent meta-analysysis (Daly E, et al. *J Functional Morph Kinesiol* 2021) no reduction in incidence of concussion or neck injuries with neck strengthening programs in adult athletes.
- Studies in youth and studies looking at other aspects of fitness are lacking
- NMT has been shown in 3 studies to reduce concussion in youth and adult rugby union players

Safe Tackling

- Swartz EE. *J Athletic Train* 2016
  - RCT. College FB players. Head impacts/AE decreased by end of season
- Swartz EE, et al. *J Sci Med Sport* 2019
  - 115 FB players ages 14-17. Reduced frequency of head impacts initially, but diff between experimental & control diminished by end of season

"Safe Tackling is Good Tackling"

Hirase T, et al. *OJSM* 2023

- Video analysis of 1000 solo tackle attempts in 8 SEC member schools
- Tackles with head-up tackles, at or above the offensive player's waist, and inside-shoulder had the highest success rates
- Tackles with head-down and helmet-to-helmet had lower success rates

CTE Take-Home Points

- CTE is clearly associated with head trauma
- So far, studies have been retrospective, subject to selection bias
- Prospective studies are mixed in terms of effects of RHI on cognitive function
- Limited data from retrospective studies of living people fail to show significant long-term effect of American football on cognitive function
- Teaching helmetless tackling shows promise in reducing head impacts

Prevention Strategies

- Reducing contact practice
- Teaching heads-up tackling
- NMT (rugby)
- Mouthguards (ice hockey)

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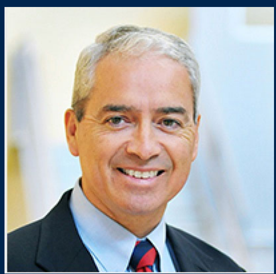
Thank you for your attention



jxgomez@texaschildrens.org

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Resources

•ANSWERING QUESTIONS ABOUT Chronic Traumatic Encephalopathy (CTE)

•https://www.cdc.gov/traumaticbraininjury/pdf/CDC-CTE-FactSheet-508.pdf

•Helmetless Tackling Training (HuTT)

•http://huttprogram.com