The Molecular Pathology of Chronic Traumatic Encephalopathy & Chronic Traumatic Encephalomyelopathy

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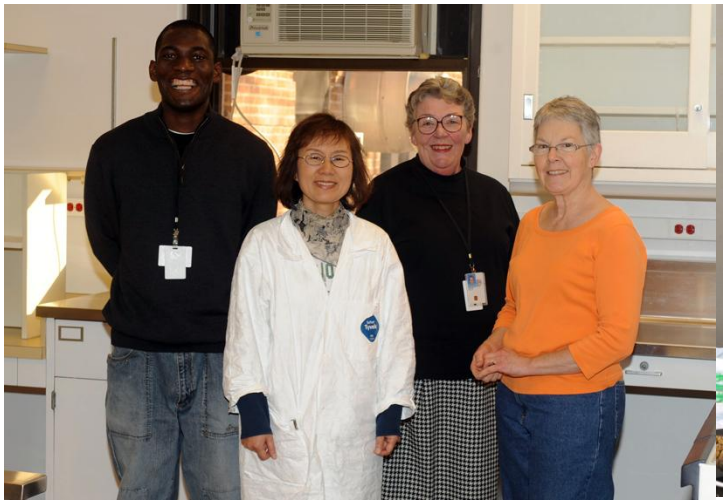
CSTE Brain Bank

mTBI Brain Bank




Over the past 3.5 years, the the brains and spinal cords
Of 107 athletes and military veterans who experienced mTBI
have been donated to the CSTE Brain Bank

Chronic Traumatic Encephalopathy

or Dementia Pugilistica

First reported by Martland in 1928 in Boxers *Punch drunk.* ***JAMA*** *91:1103–1107, 1928*

Martland described the spectrum of abnormalities found in

"nearly one half of the fighters who have stayed in the game long enough"

In 2009, in the worlds literature: 51 cases of CTE including 3 cases from BU

Harrison S. Martland
(1883-1954)
First full time paid pathologist
Newark city Hospital 1909-1927
Chief Medical examiner Essex county

Chronic Traumatic Encephalopathy in Athletes:
Progressive Tauopathy following Repetitive Head Injury.
McKee et al. J Neuropath Exp Neurol, 2009 68(7): 709-735

Symptoms of CTE

- Emotional / Behavioral changes
  - Short fuse
  - Irritability
  - Aggressive or violent behavior
  - Impulse control problems
  - Mood changes, usually depression
  - Confusion
  - Suicidality
  - Erratic dangerous behavior
  - Paranoia
  - Drug and Alcohol abuse
- Cognitive changes
  - Short-term memory problems
  - Executive dysfunction (e.g., poor planning, organization, multitasking, judgment)
  - Dementia
- Other abnormalities
  - Gait problems
    - Parkinsonism
    - Speech abnormalities
- Subset (~10%)
  - Motor Neuron Disease

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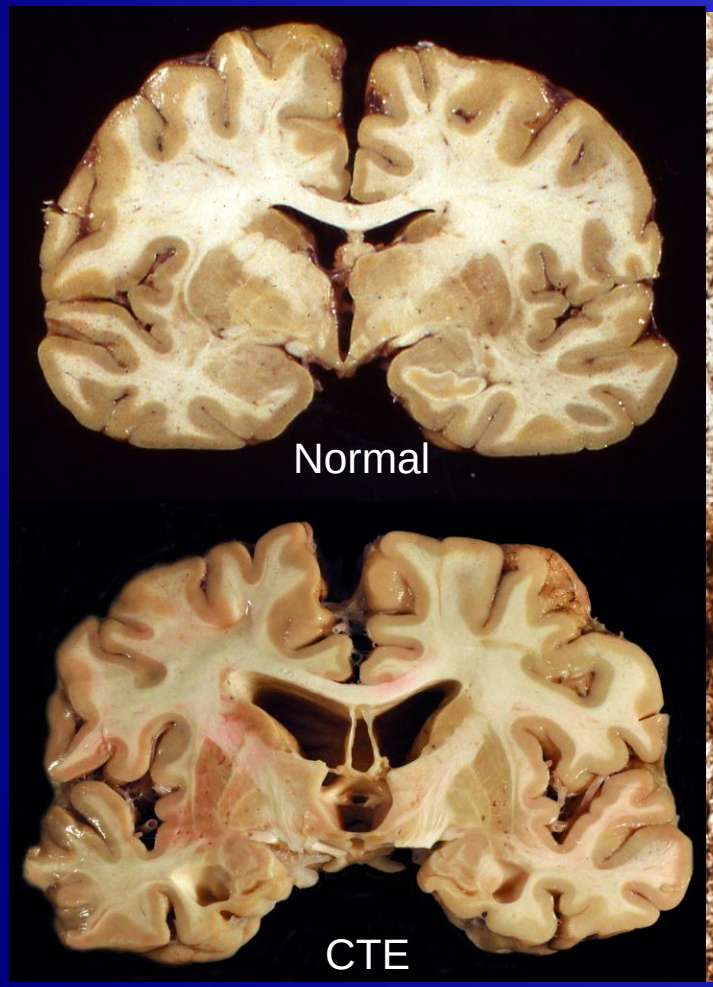
Pathology of CTE

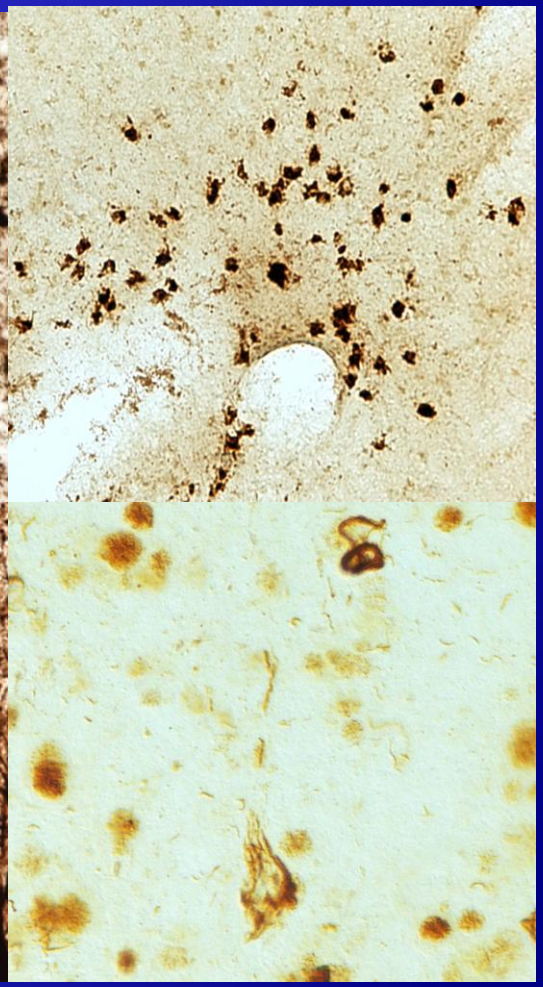
Brain Atrophy



Abnormal tau protein

Neurofibrillary tangles

TDP-43



Inclusions and neurites

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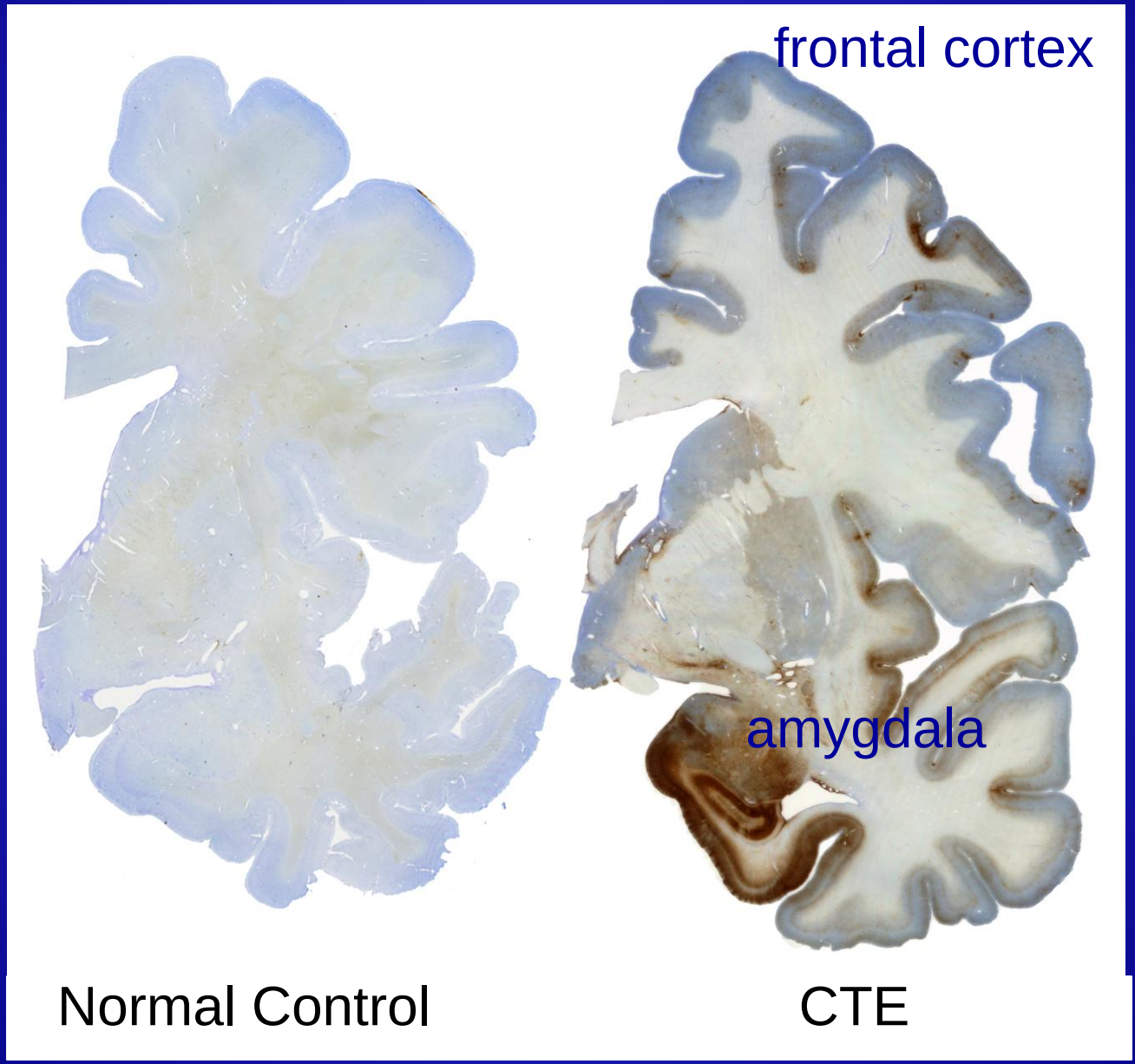
Hyperphosphorylated tau protein



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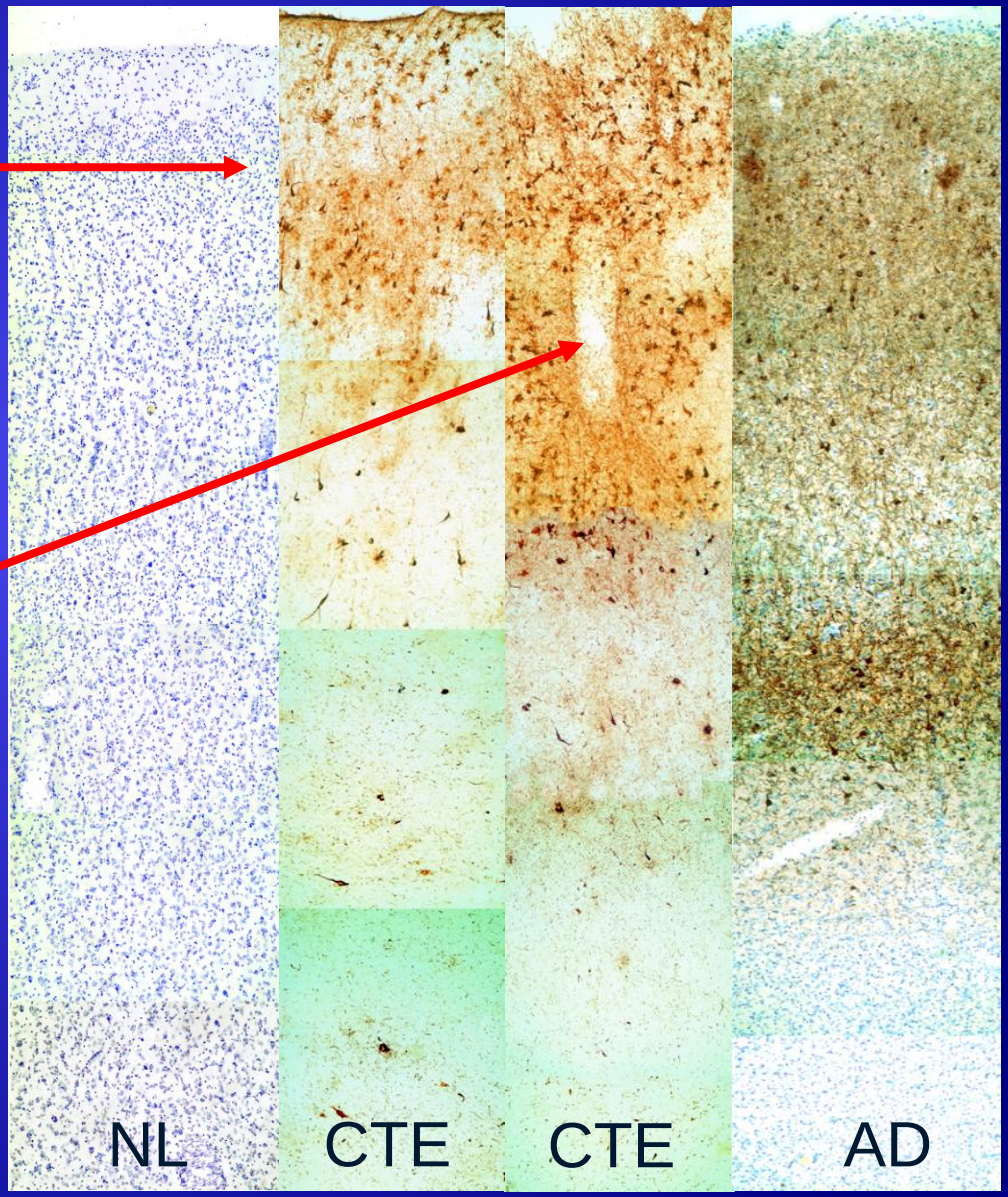
Superficial layers

CORTICAL LAYERS

Perivascular



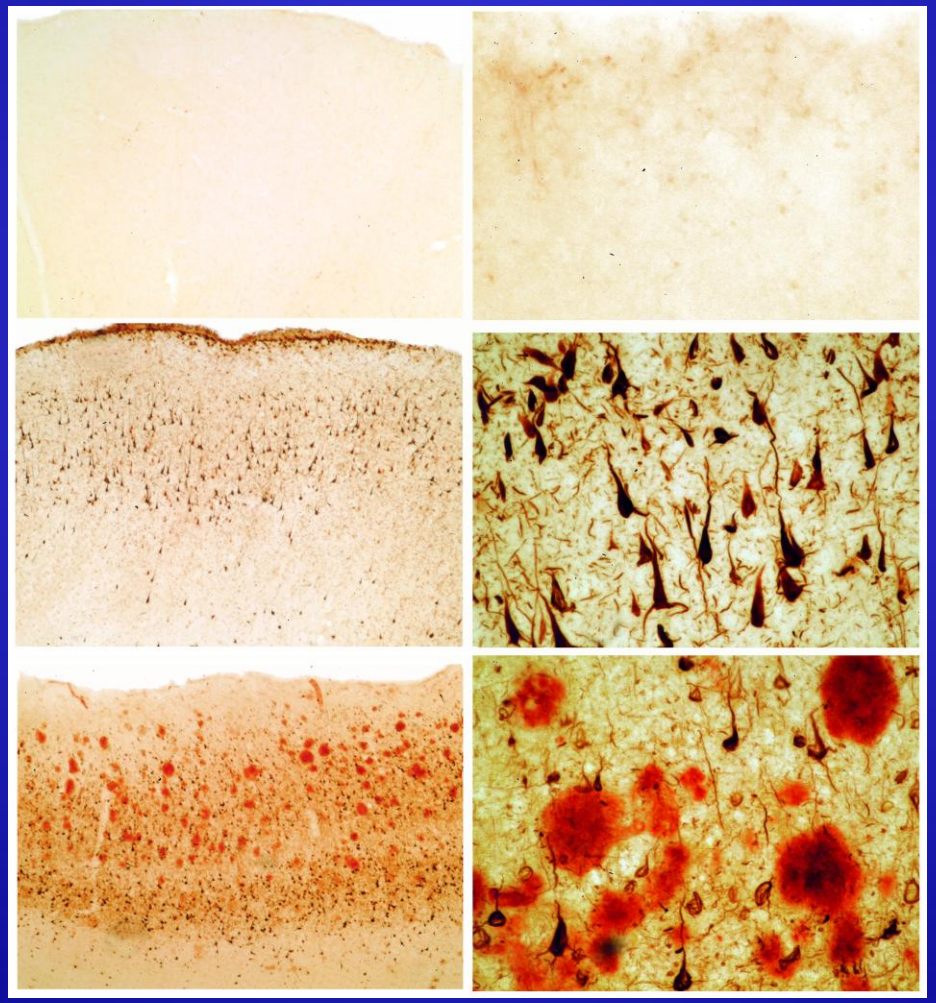
Immunostaining for phosphorylated TAU

Pathologically CTE is entirely distinct from AD

Normal

CTE

Alzheimer's disease



No Tau, no Aß

Tau, no Aß

Tau and Aß

Dave Duerson

Death at age 50 years

Began playing football at age 8
- 24 total seasons, safety in college and pro
- 10 concussions

11-year NFL career

Post-NFL, very successful in food supply industry (Duerson Foods)

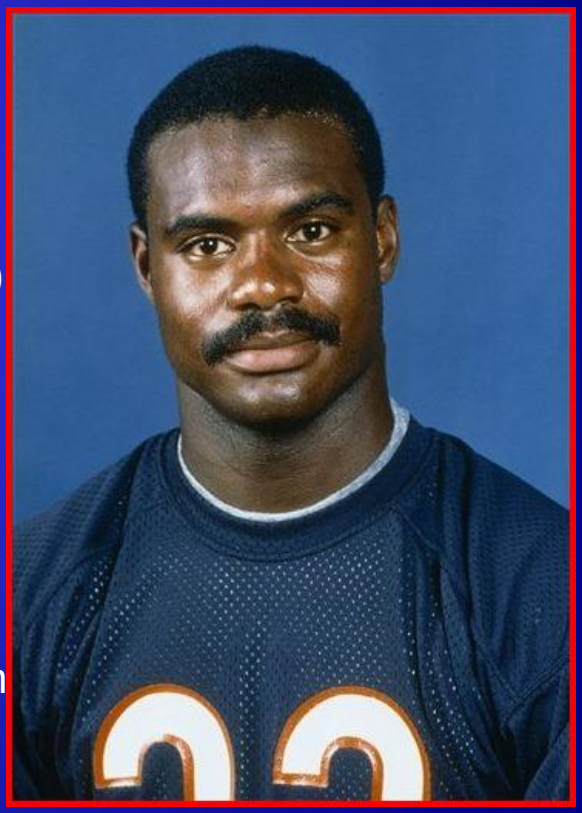
Very active in NFLPA; Benefits Board

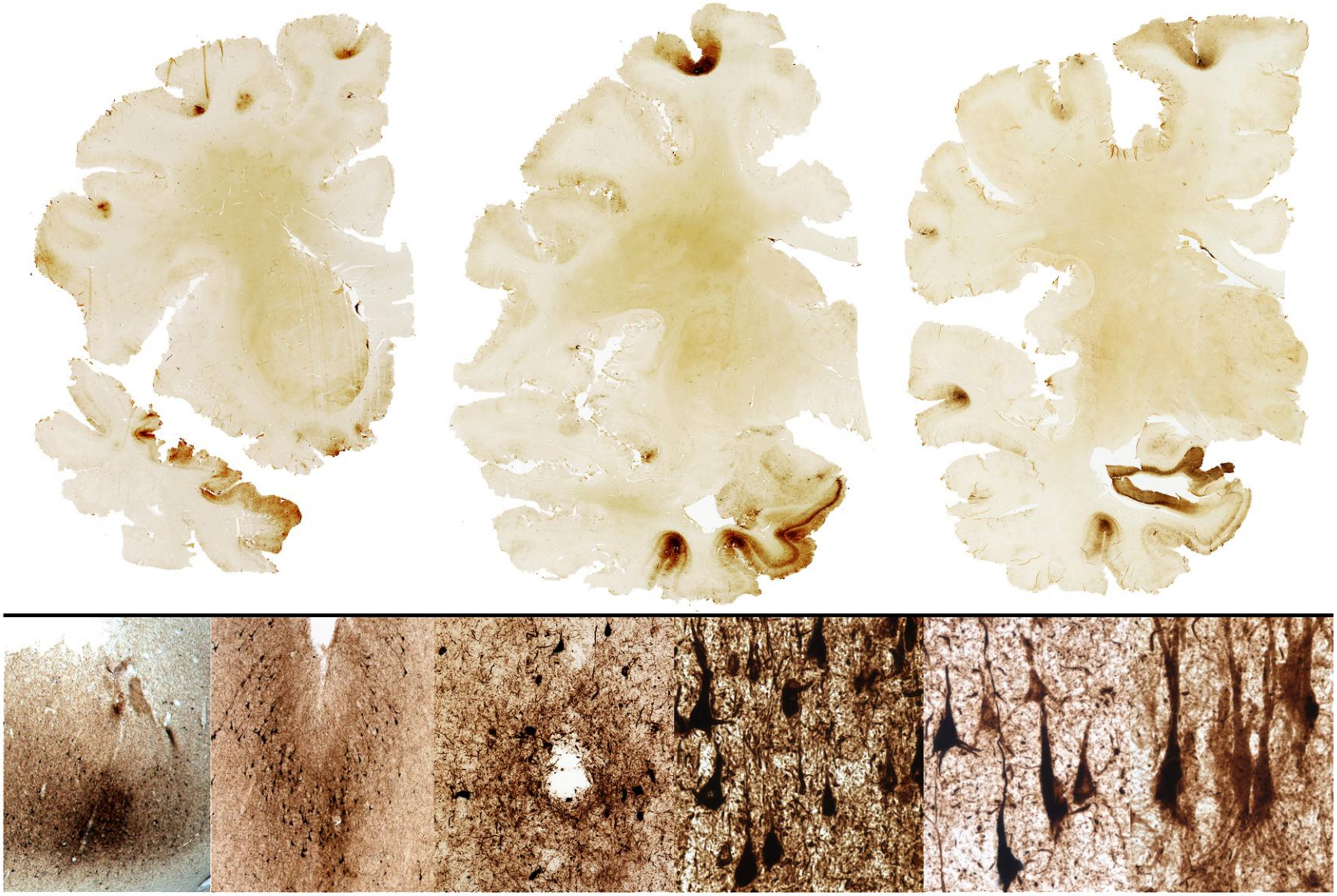
Work and financial difficulties began in 2007

Long-standing complaints of headaches since NFL and onward.

Over the ~5 years prior to death, he had worsening short-term mem
difficulties, as well as problems with language and “vision”

Increasingly out of control:
Short fuse, hot tempered, physically abusive, verbally abusive





Dave Duerson

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Derek Boogaard

Death at 28 Professional Hockey Player

- Played for the Minnesota Wild from 2005-2010, New York Rangers 2010-2011
- Considered to be a tough fighter in the NHL
- In 277 NHL games, he scored 3 goals, 589 penalty minutes and participated in 61 regular season fights.
- He reportedly had 174 career fights in professional hockey
- Had not played since December 2010 due to injuries sustained during a fight, including a reported concussion
- He died at age 28 from an accidental overdose of oxycodone mixed with alcohol

Derek Boogaard

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Chronic traumatic encephalopathy (CTE)

So what do we know?

- CTE is a progressive neurodegenerative disease distinct from Alzheimer's disease, that we are finding in the brains of many professional football players, boxers, veterans and hockey players.
- CTE is a tauopathy and TDP-43 proteinopathy associated with repeated mTBI that most commonly occurs in an individual's teens and early twenties.
- Once triggered, the neurodegeneration progresses slowly over decades to involve widespread degeneration of many brain structures.
- The symptoms of CTE are often insidious and begin in mid-life with prominent early personality and behavioral changes (short fuse, depression, suicidal ideations, impulsivity) and memory loss. There is a slow deterioration that progresses to include dementia, parkinsonism, gait and speech disorders.

CTE/CTEM

What do we need to know?

- We do not understand what triggers CTE/CTEM in some individuals
- We cannot diagnose these disorders during life
- We cannot treat these disorders
- Preventative education and increased awareness concerning management of mTBI in sports and military will decrease the frequency of CTE/CTEM
- We need to understand the basic mechanisms of CTE/CTEM pathobiology in order to treat it effectively
- Current work includes reproducing the injury in experimental model systems and beginning preclinical therapeutic trials

Victor Alvarez
Christine Baugh
Andrew Budson
Kerry Cormier
Dan Daneshvar
Brandon Gavett.
Lee Goldstein
Garth Hall
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Carol Kubilus
Lisa McHale
David Riley
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Sydney Wojtowicz

all individuals from:
Boston University CSTE

Boston University
Framingham Heart Study

Boston University
Alzheimer's Disease Center

And all the veterans, athletes and families who participated in our research