Chronic Traumatic Encephalopathy and the Athlete

Update from the Boston University Center for the Study of Traumatic Encephalopathy

CSTE

Boston University Center for the Study of Traumatic Encephalopathy

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Center for the Study of Traumatic Encephalopathy

A Collaboration Between Sports Legacy Institute
and Boston University School of Medicine
Established September 2008

Goal of CSTE: To study the long-term effects of sports-related brain trauma

1. Establishment of Brain Donation Registry (C.O.N.T.A.C.T.)
   - Current or retired athletes (pro and college), with and without history of concussion, to agree to donate brain and spinal cord tissue following death and to be interviewed by phone annually.
2. Conduct Longitudinal Clinical Research
   - In-depth examinations of retired athletes, including neuropsychological, psychiatric, and neurological assessments, as well as brain MRI (DTI, fMRI) and lumbar punctures (to measure proteins in cerebrospinal fluid), electrophysiological studies, and genetics. Study longitudinally and examine brains following death.
3. Create a Brain Bank
   - Brain and spinal cord tissue repository (at the Bedford VAMC) for the examination of the underlying neuropathology associated with repetitive brain trauma in athletes.

Non-Amyloid AD?

- We propose that some (perhaps, many) cases hitherto diagnosed both clinically and neuropathologically as AD are, in fact, examples of CTE.
- Furthermore, the reported and widely accepted increased risk of AD following TBI is actually due to the inclusion of such CTE cases that were erroneously diagnosed as AD.
- Interestingly, in a recent report, Nelson and colleagues (2009) at the University of Kentucky ADC queried the 5108 cases in the NACC Neuropathology Registry and found that ~5% demonstrated medial temporal lobe NFTs in the presence of little or no amyloid plaques.
- Is it possible that some (perhaps many) of these cases may have had CTE (head trauma history for these cases would not have been available and, of course, were not reported)?

Dementia Pugilistica

First described in boxers by Martland in 1928

– *Martland HS: Punch drunk.* ***JAMA*** *91:1103–1107, 1928.*

Harrison S. Martland

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

Chronic Traumatic Encephalopathy (CTE)

- Believed to be caused by repeated trauma to brain, including mild concussions and subconcussive blows.
- Progressive neurodegenerative disease, distinct from Alzheimer's.
  - Tauopathy
- Early Symptoms:
  - memory and cognitive difficulties
  - depression
  - impulse control problems and behavior change
- Symptoms begin months or years after concussions and continue to worsen
- Eventually leads to full-blown dementia
- Perhaps the only fully preventable cause of dementia

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CSTE Brain Bank (n=21)

October 2009

Bedford Veterans Administration Medical Center

#	age	sex	highest level of sport	reference
1	75	M	Professional Boxing	Journal of Neuropathology and Experimental Neurology, July 2009
2	80	M	Professional Boxing	
3	45	M	NFL Football	
4	45	M	NFL Football	
5	18	M	High School Football	
6	66	M	NFL Football	
7	49	M	NFL Football	
8	40	M	College Football	
9	75	M	Professional Boxing	
10	35	M	NFL Football	
11	80	M	NFL Football	
12	70	M	NHL Hockey	


CTE in Football players (11)

5 reported in literature (1 from BU); our 6 additional cases

- 8 died suddenly in middle age (8/11 = 73%):
  (age at death, 36-80 years; m = 45 years)
- 7 of the 11 experienced tragic deaths (64%):
  3 from suicide
  2 substance abuse
  1 during a high-speed police chase
  1 accidental gunshot while cleaning his gun

10 years of professional football

Death in his 80s with dementia

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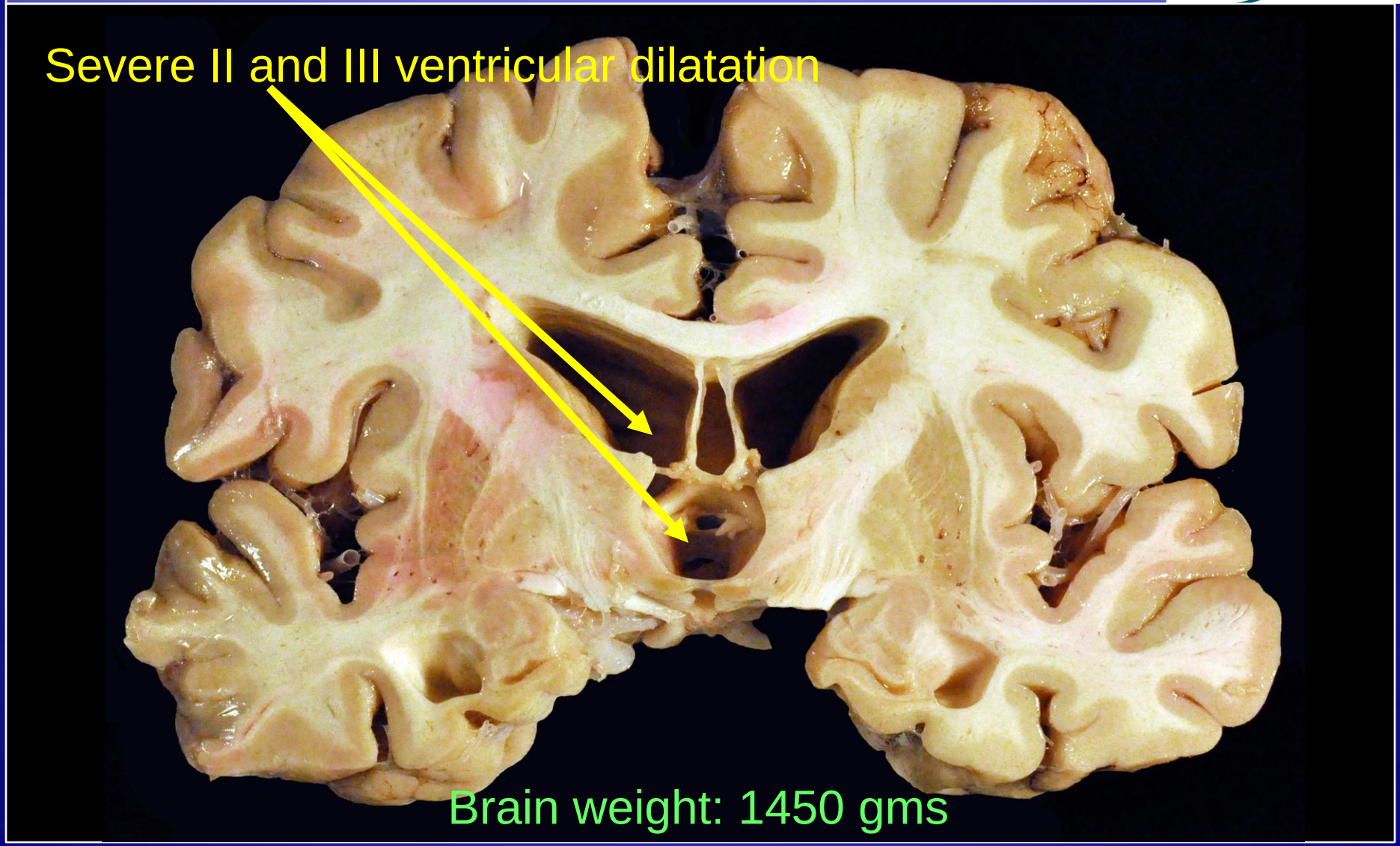

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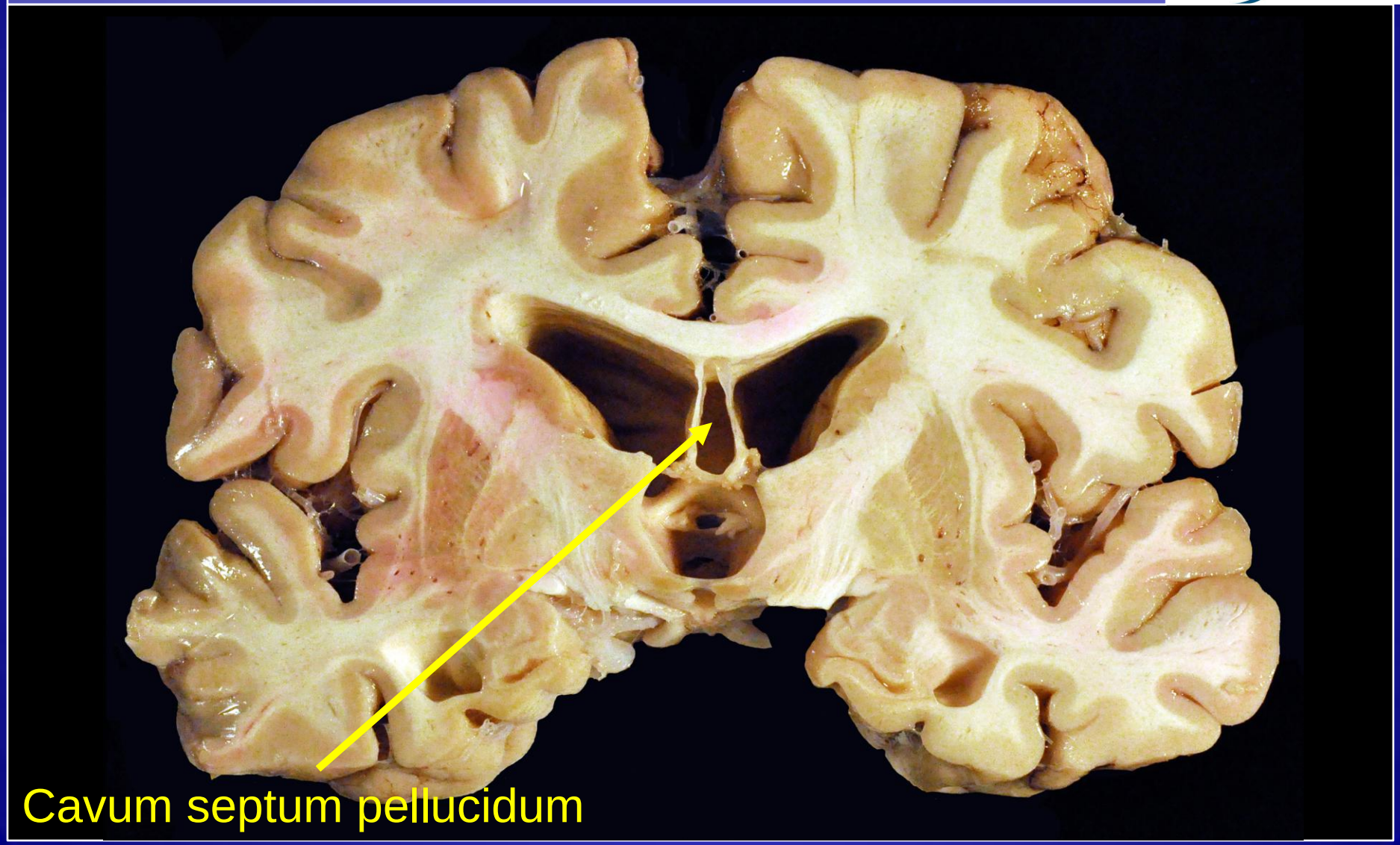

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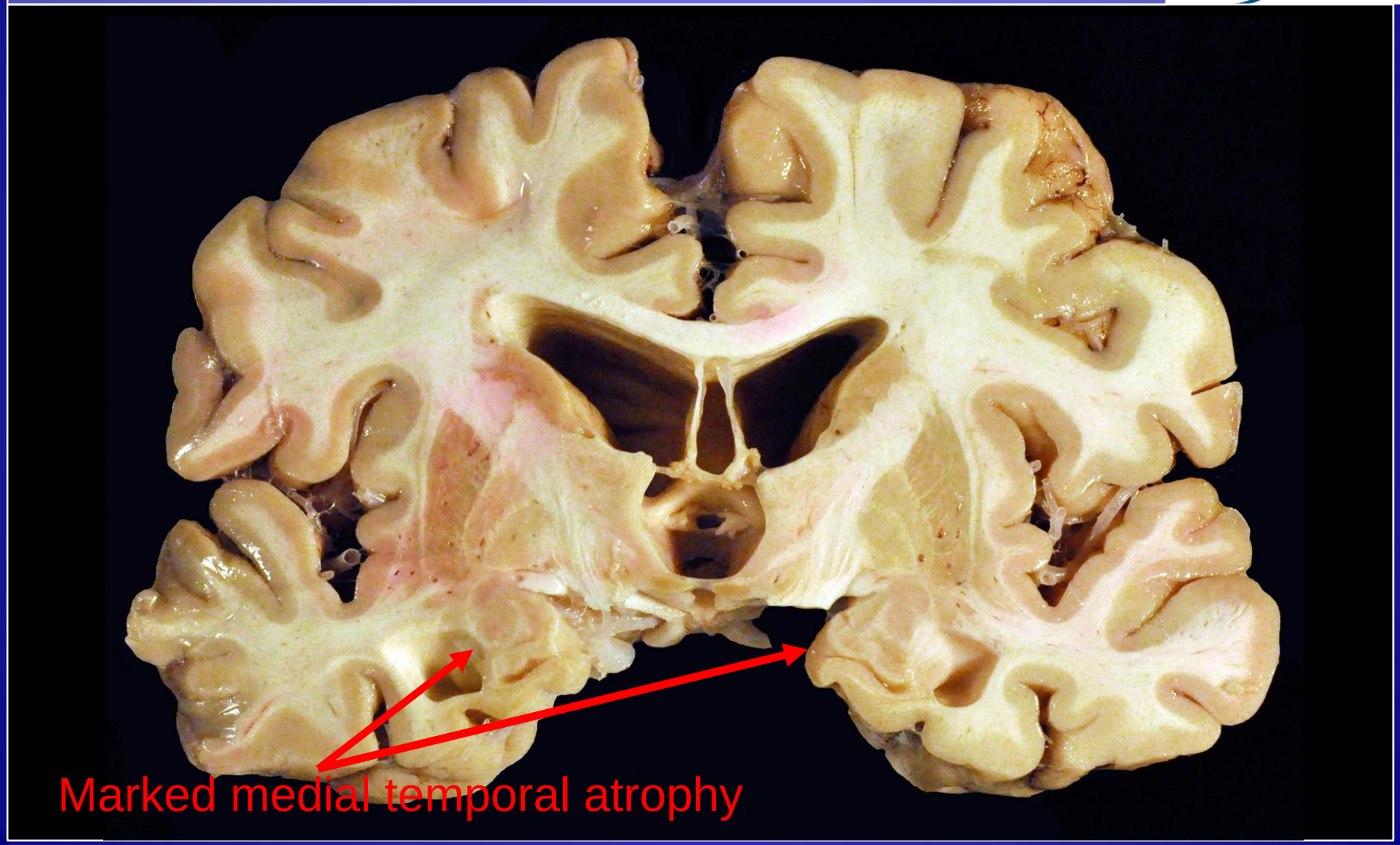
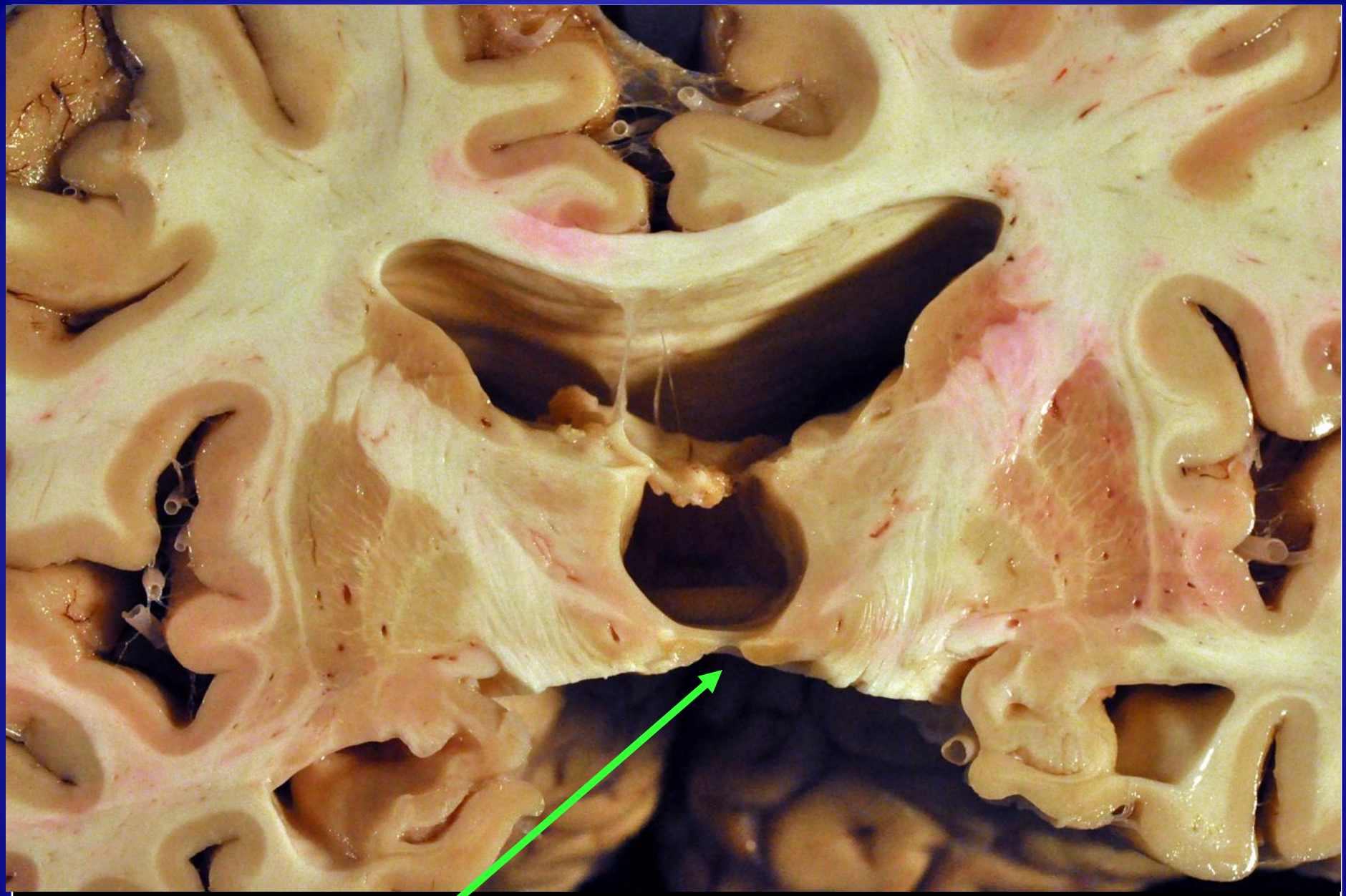
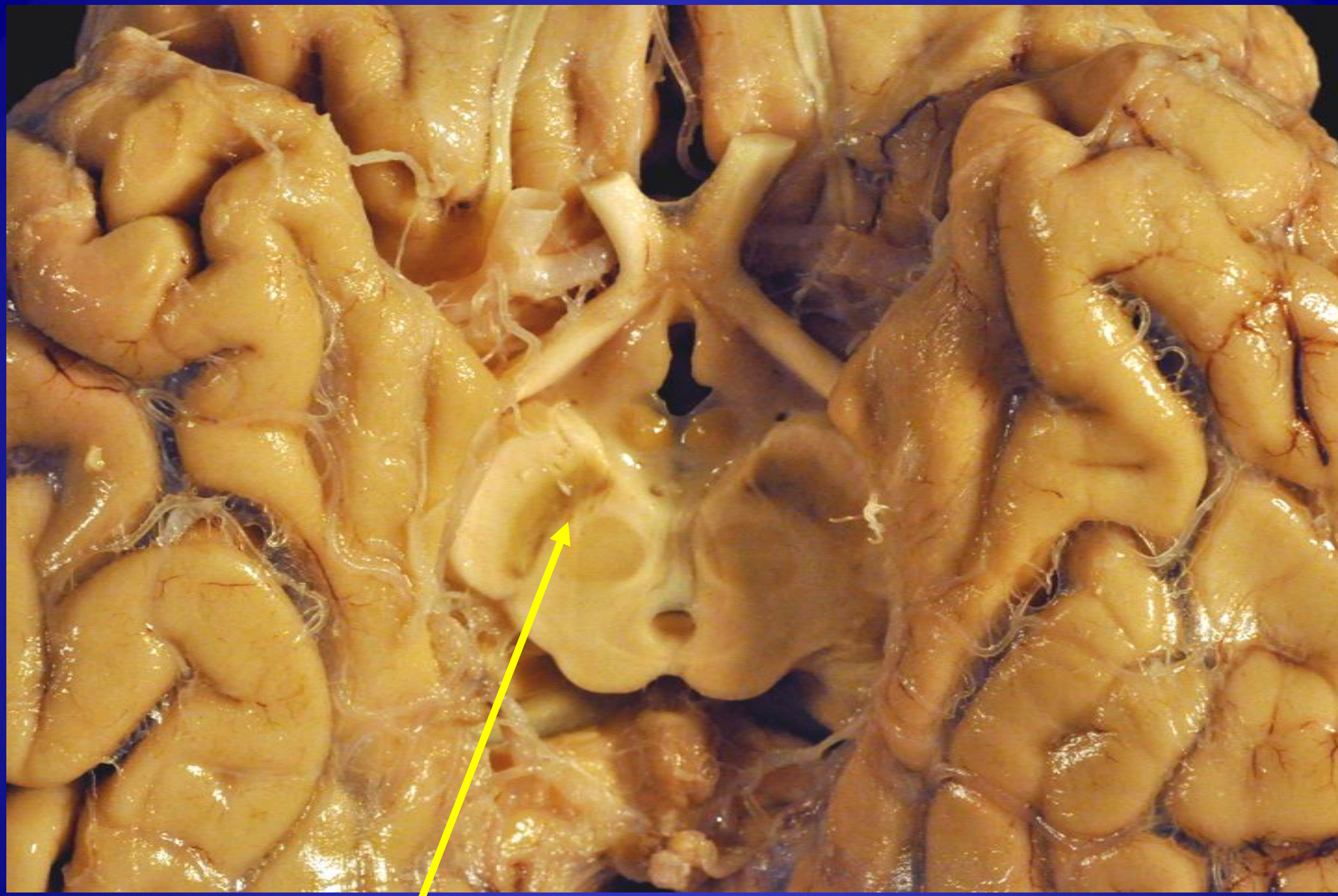




Shrinkage of the mammillary bodies


pallor of the substantia nigra

Microscopic Pathology of CTE

Neurofibrillary degeneration

Extensive tau-immunoreactive NFTs, glial tangles, and neurites throughout the brain

Widespread distribution:

- Cerebral cortex – frontal and temporal lobes
- Medial temporal lobe – amygdala, hippocampus, entorhinal cortex
- Subcortical white matter
- Thalamus, hypothalamus, mammillary bodies
- Brainstem
- Spinal cord

Microscopic Pathology of CTE

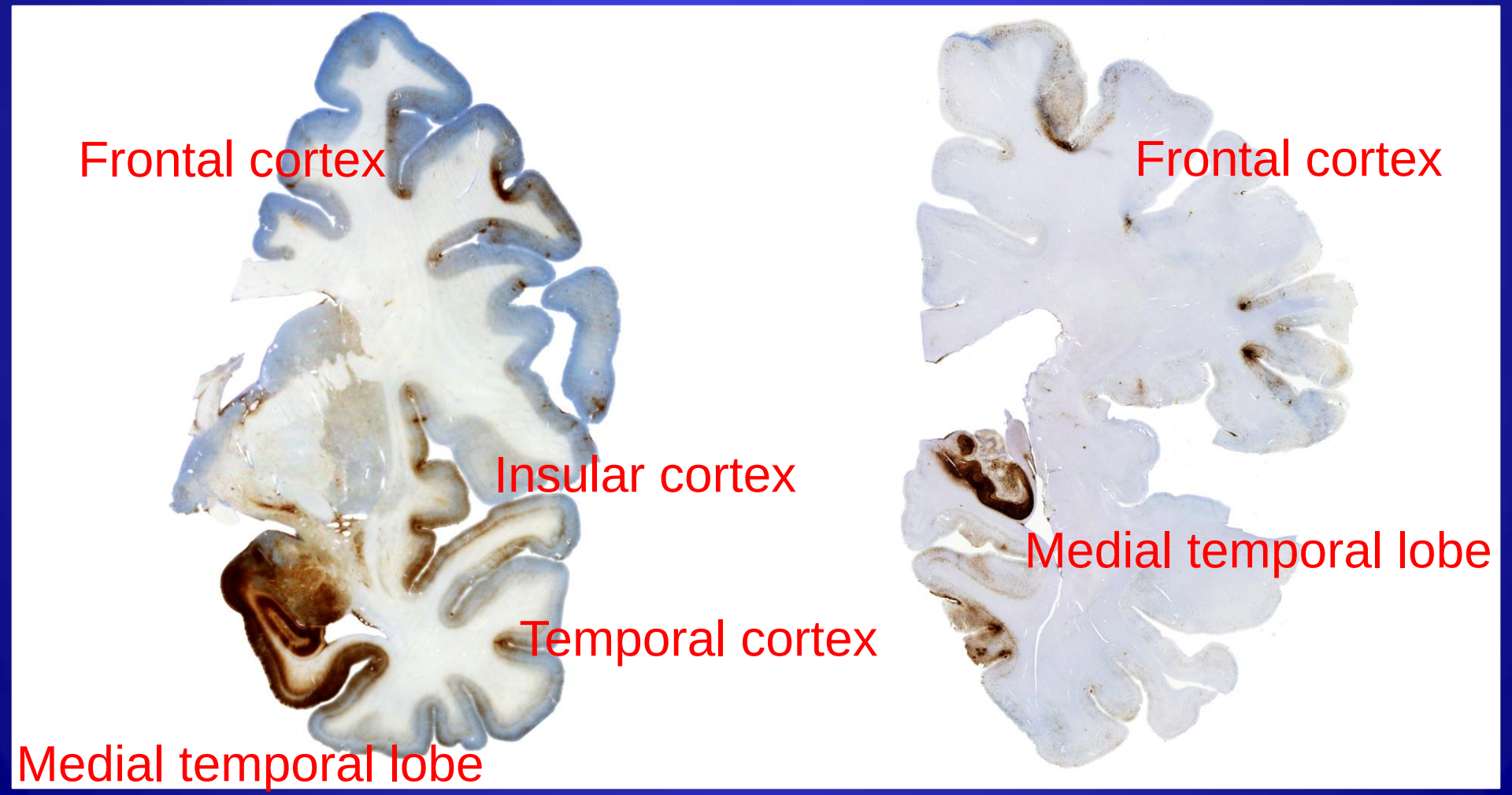
Unique pattern of involvement:

- Superficial cortical laminae: layers II and III
- Perivascular
- Patchy, irregular
- Prominent glial tangles
- Often greatest at sulcal depths
- Dotlike, spindle-shaped neurites
- Subcortical white matter

CTE: Tau immunoreactive NFTs

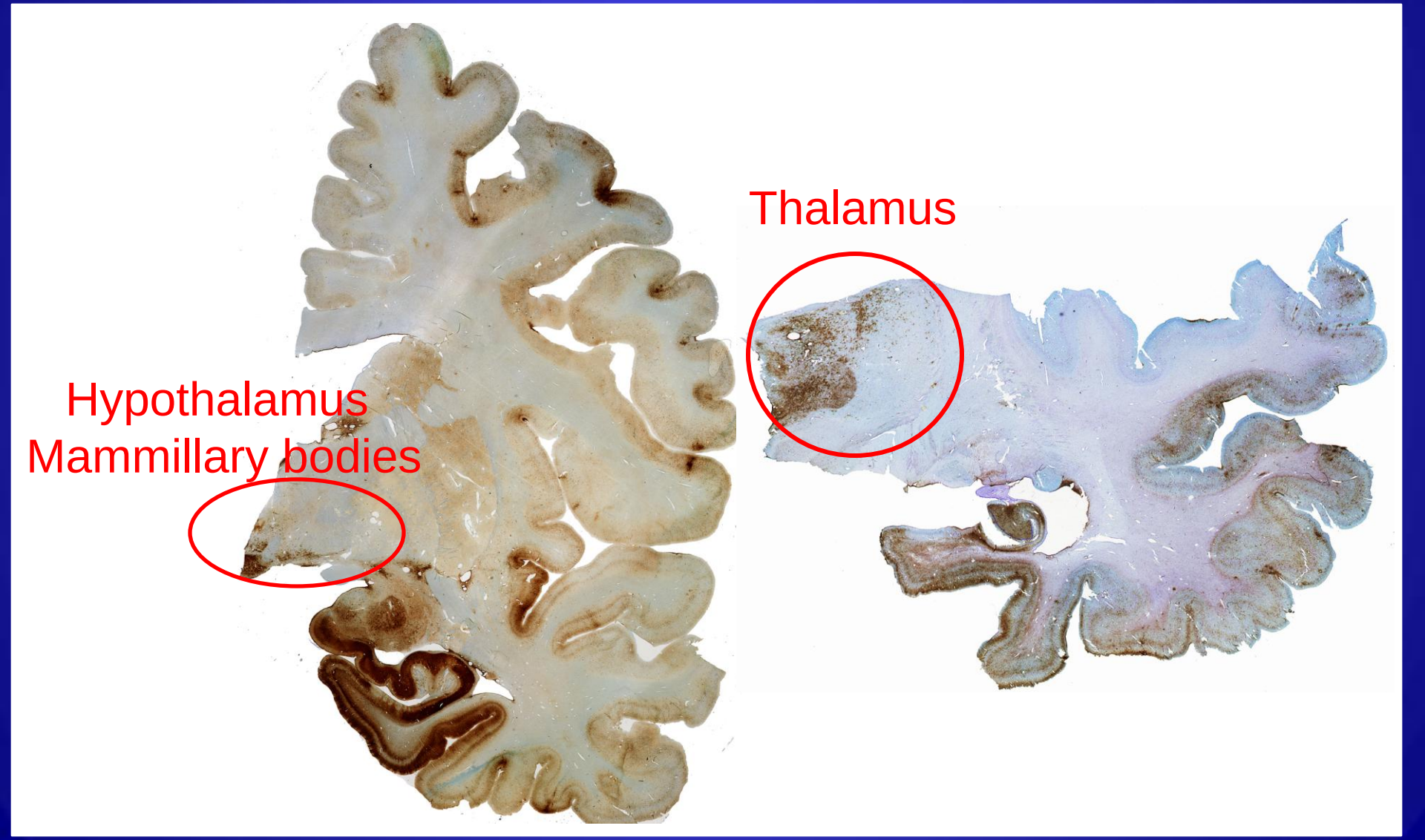
Cerebral cortex – primarily the frontal and temporal lobes

Medial temporal lobe – amygdala, hippocampus, entorhinal cortex



CTE: Tau immunoreactive NFTs

Subcortical Nuclei



CTE: Tau immunoreactive NFTs

Brainstem and Spinal cord

Substantia Nigra

Locus ceruleus

Midbrain

Pons

Medulla

Cord

World Champion Boxer

death at age 73 years, profoundly demented

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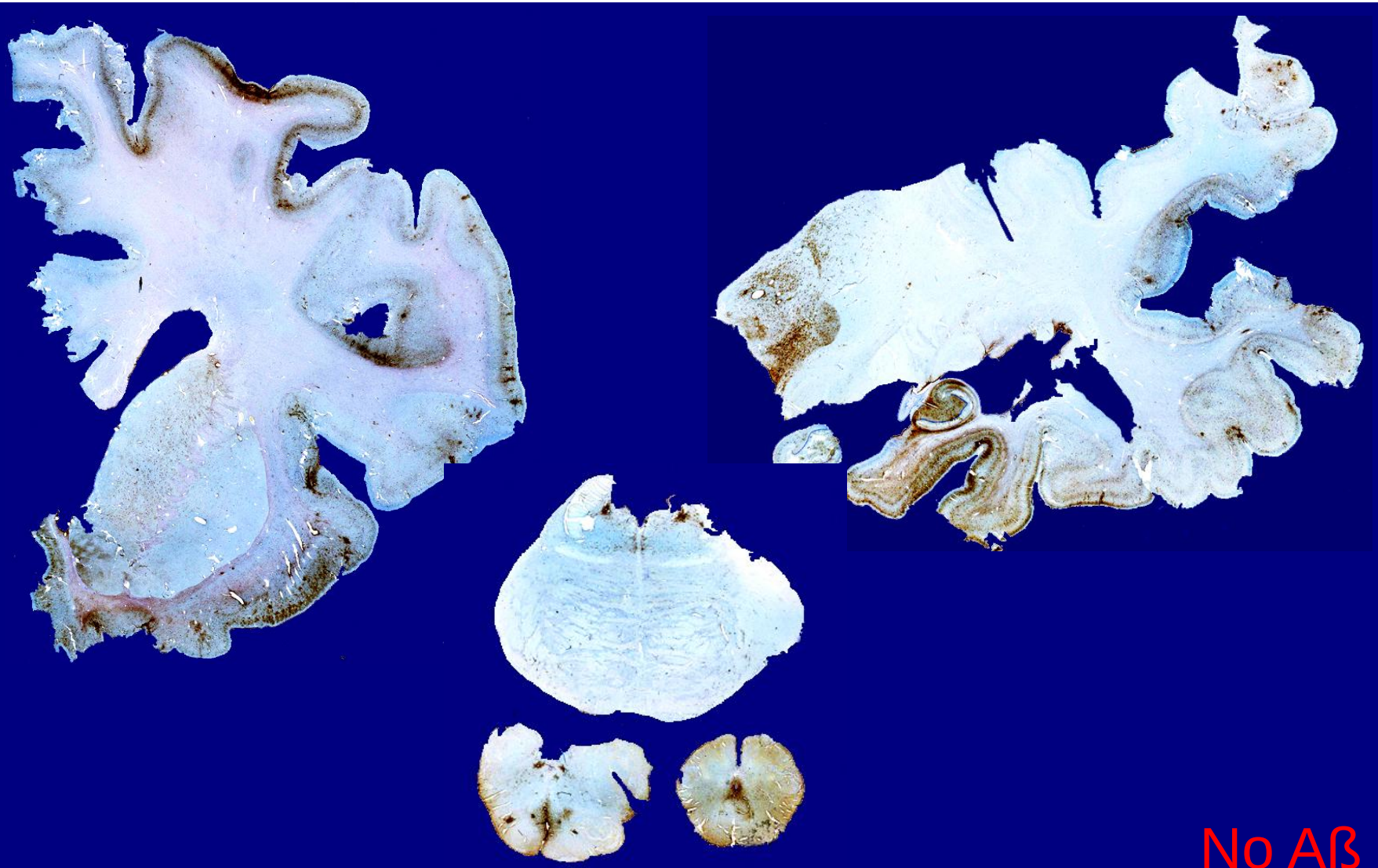
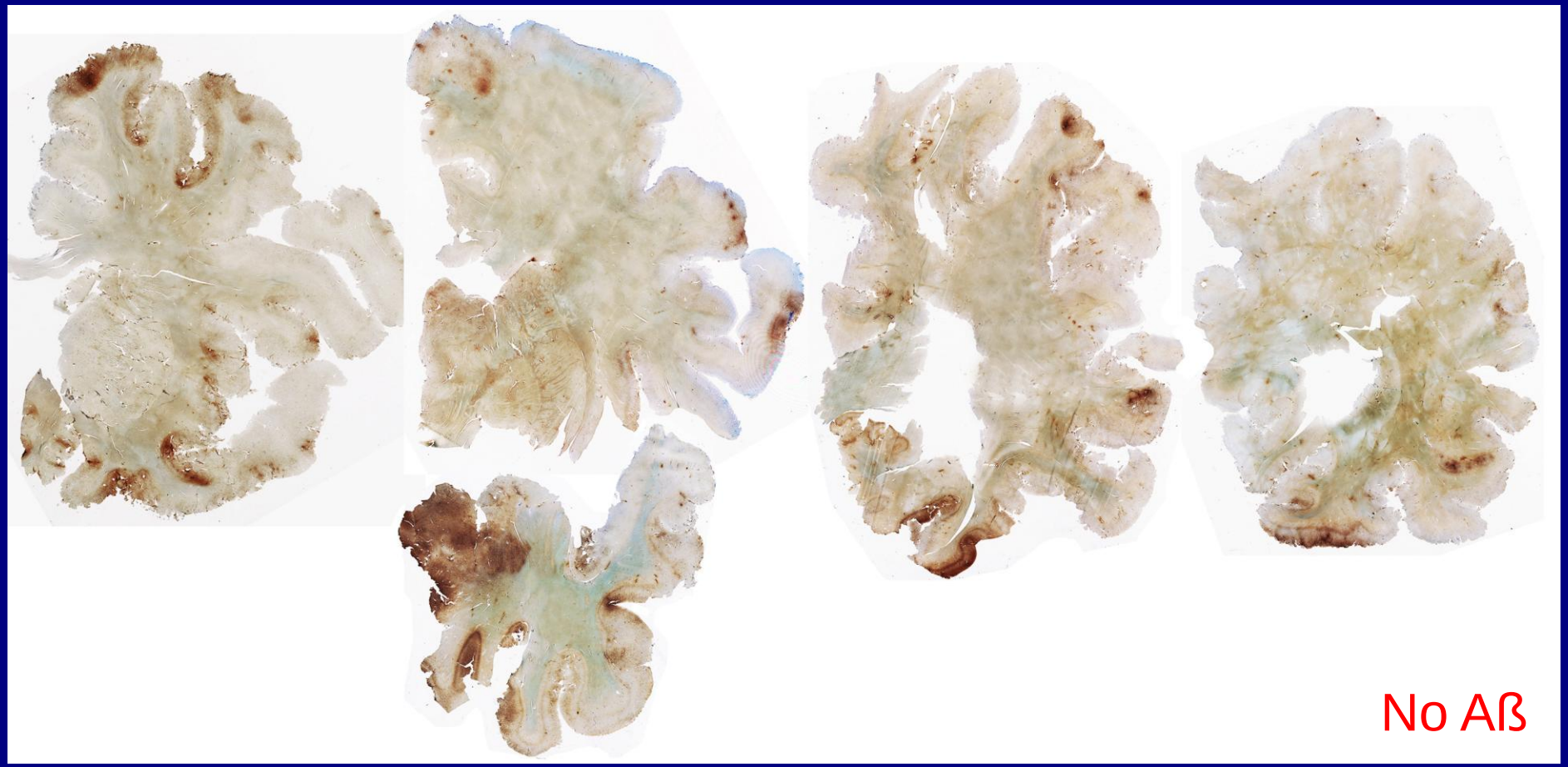


Tau immunohistochemistry

No Aß

Football player: 10 years in NFL

death at age 45 years: memory loss, confusion, executive dysfunction



Tau immunohistochemistry

Football player: 16 years in NFL

death at age 66 years: memory loss, confusion, executive dysfunction, profound apathy

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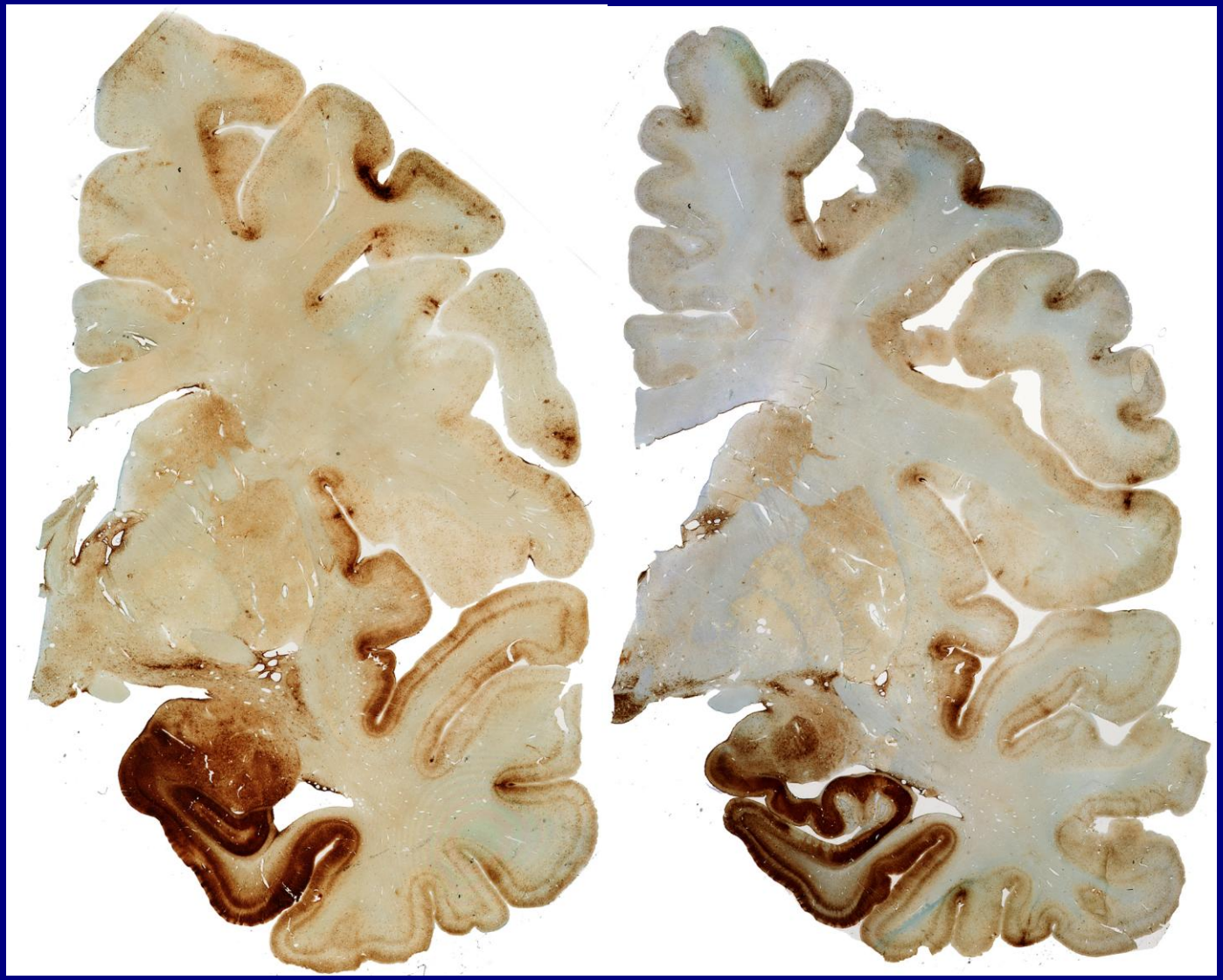

No Aß

Football player: 9 years in NFL

death at age 45 years: depression, poor decision making, substance abuse

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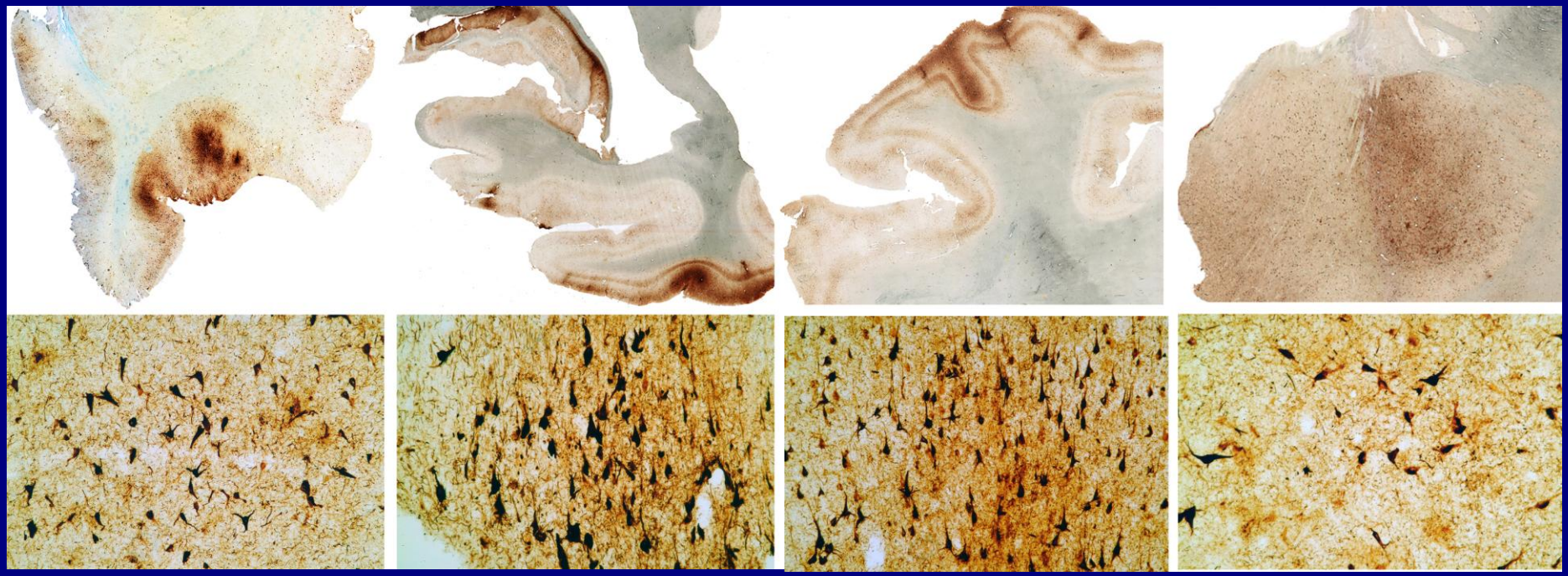
Orbital frontal | Hippocampus | Temporal | Amygdala



Aß: rare diffuse plaques

High school football player

Death at age 18. Cognitively intact. Focal evidence of perivascular tau

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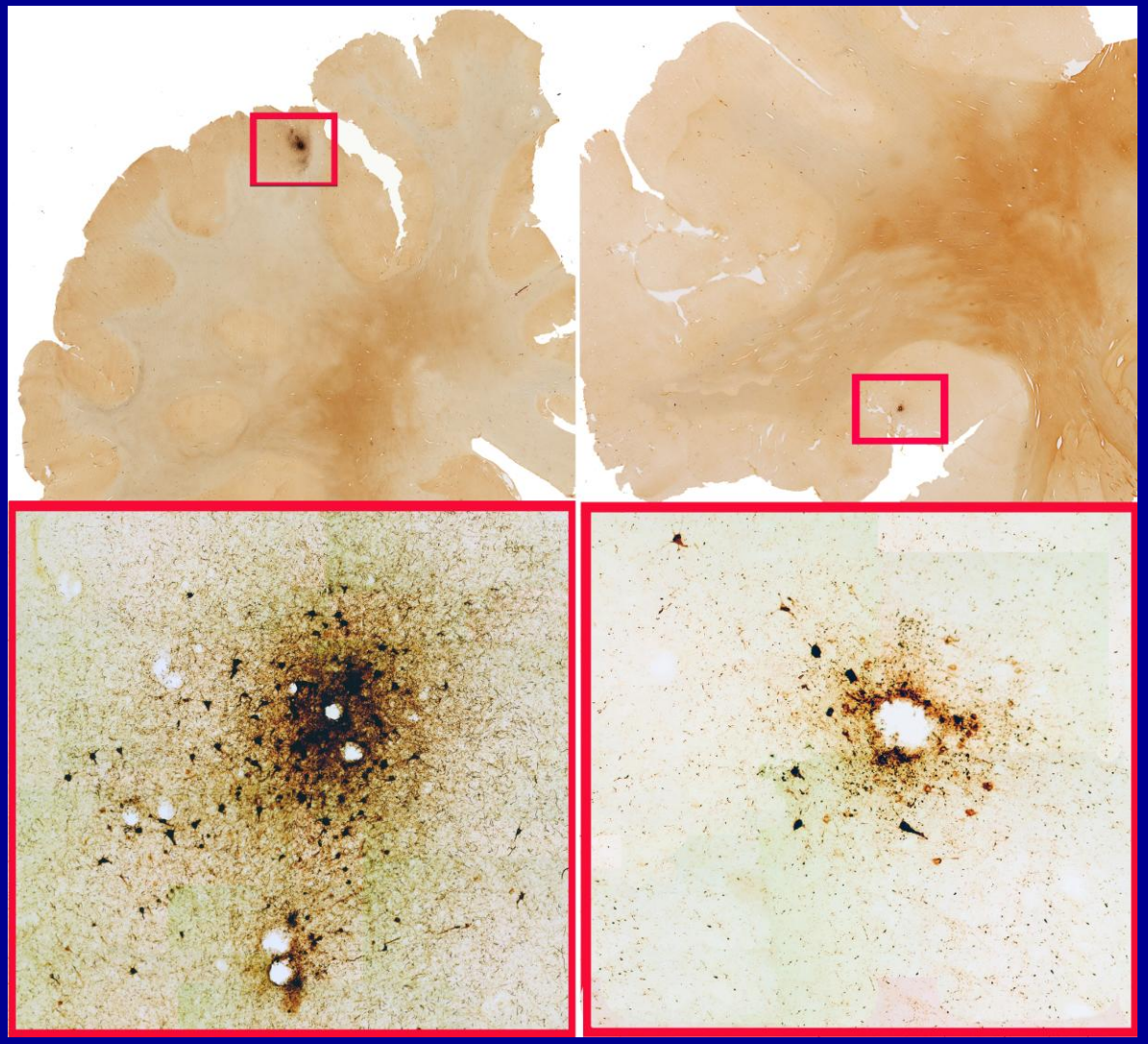
Tau immunohistochemistry



No Aß

Chronic Traumatic Encephalopathy in Football Players

- To date, all 11 brains from college and professional football players that we have studied have shown evidence of CTE

Not Just Athletes…

- Although CTE is most commonly found in athletes, many individuals are susceptible: epileptics, persons who suffer falls, accidental blows from moving objects, motor vehicle accidents, and military veterans (blast injuries)

Collaborators Wanted

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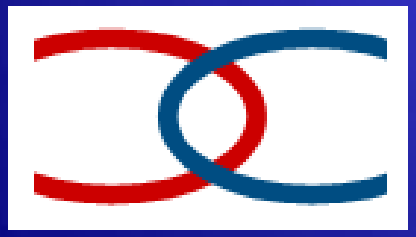

Boston University School of Medicine

NIA: Boston University Alzheimer's Disease Center

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supplements

National Operating Committee on Standards in Athletic Equipment (NOCSAE)

Department of Veteran's Affairs