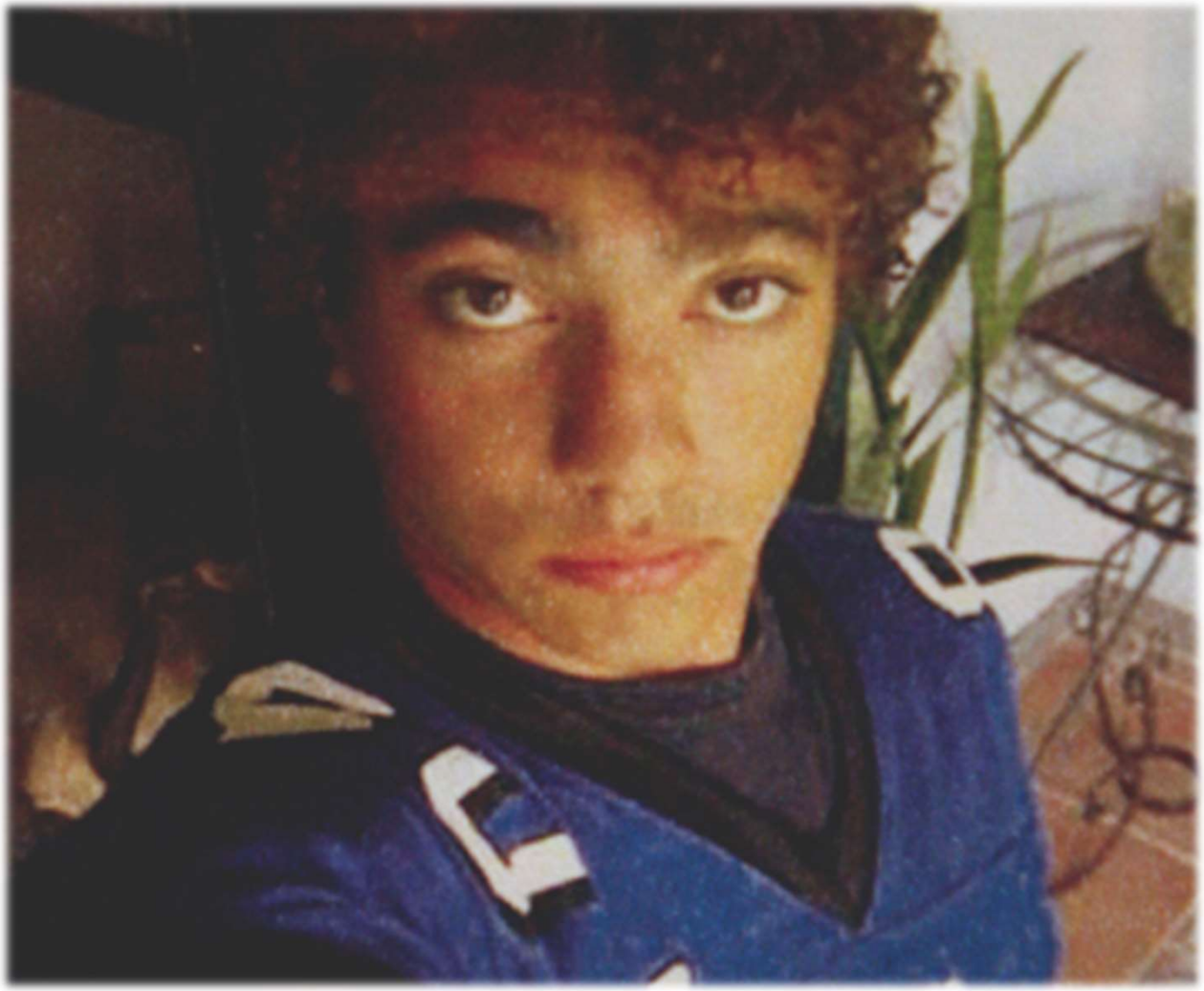
Appendices

Second Impact Syndrome

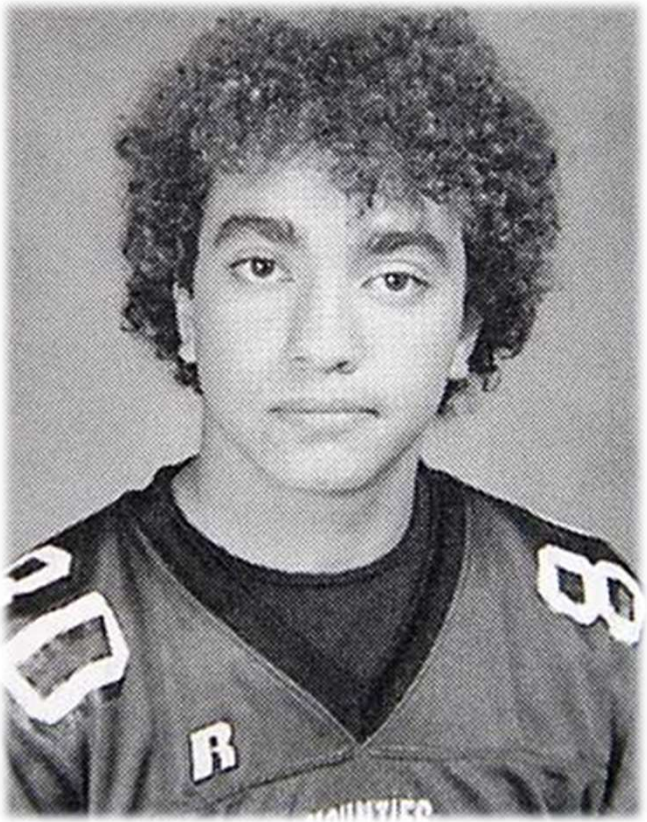
- Second concussion occurs while still symptomatic and healing from previous injury days or weeks earlier
- Second impact results in brain edema and other widespread damage

  - Can be fatal -- 50% mortality rate in most severe cases
  - Higher risk of long-term cognitive dysfunction
  - Extremely low, albeit unknown incidence

Ryne Dougherty

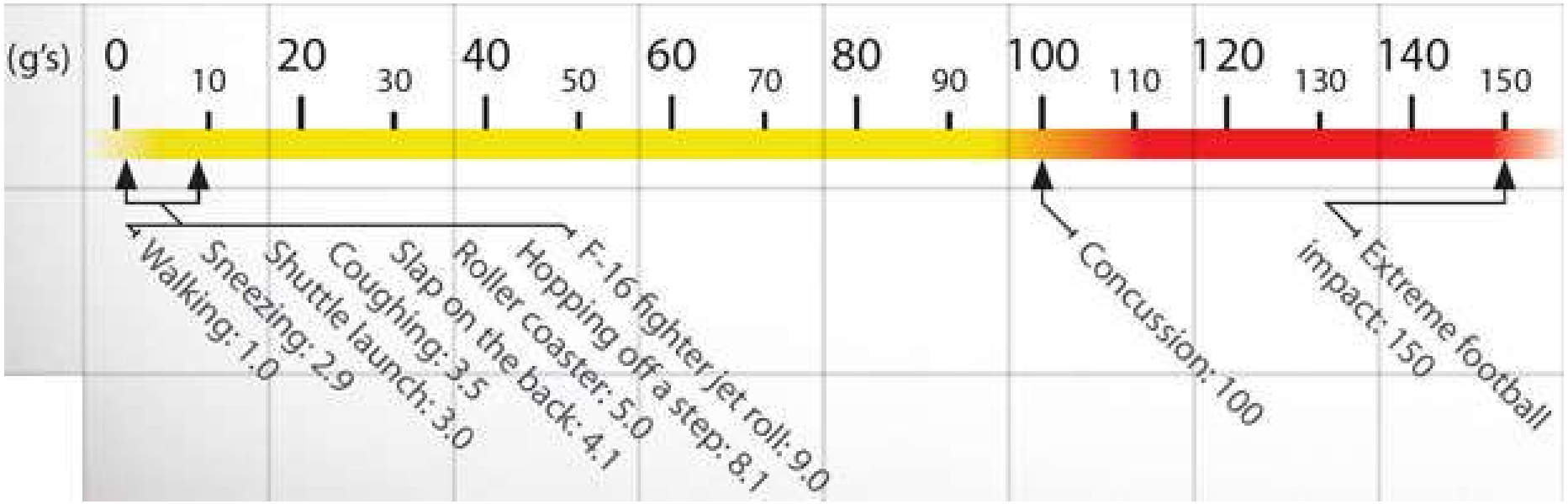


Ryne Dougherty



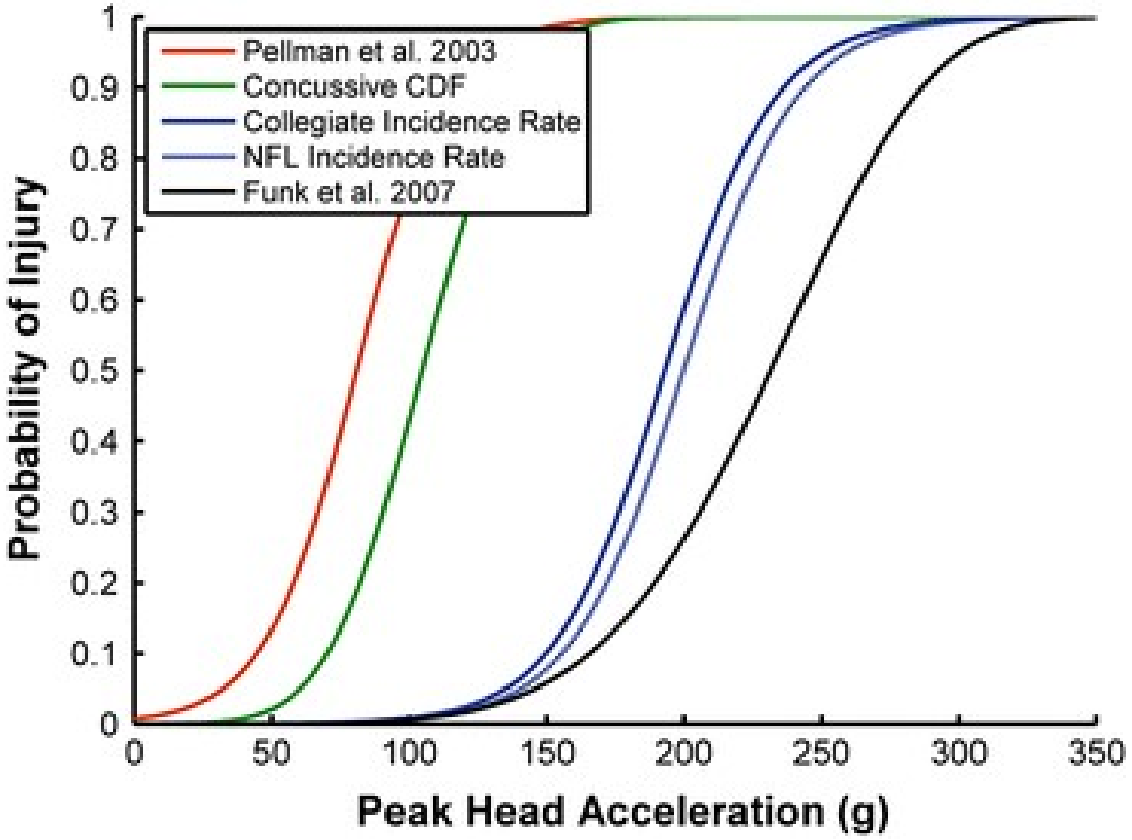
Ryne Dougherty got another concussion on October 15, 2008 less than one month after his first concussion.

g Force to Brain



Is There a Concussion Threshold?

- NO – there is only a statistical risk



Rowson & Duma 2011

Asymptomatic impacts may have consequences

- Symptomatic impacts (i.e. concussion) may only reflect part of the problem
  - Some athletes may experience 1000-1500 hits per season (>10g, median ~25g; Martini, 2013)
- Impact to brain with adequate g force to have an effect on brain cell functioning but no immediate symptoms
  - Neuropsych (Gysland, 2012; McAllister, 2012a)
  - fMRI (Talavage, 2013; Breedlove 2012)
  - DTI (McAllister, 2012b)

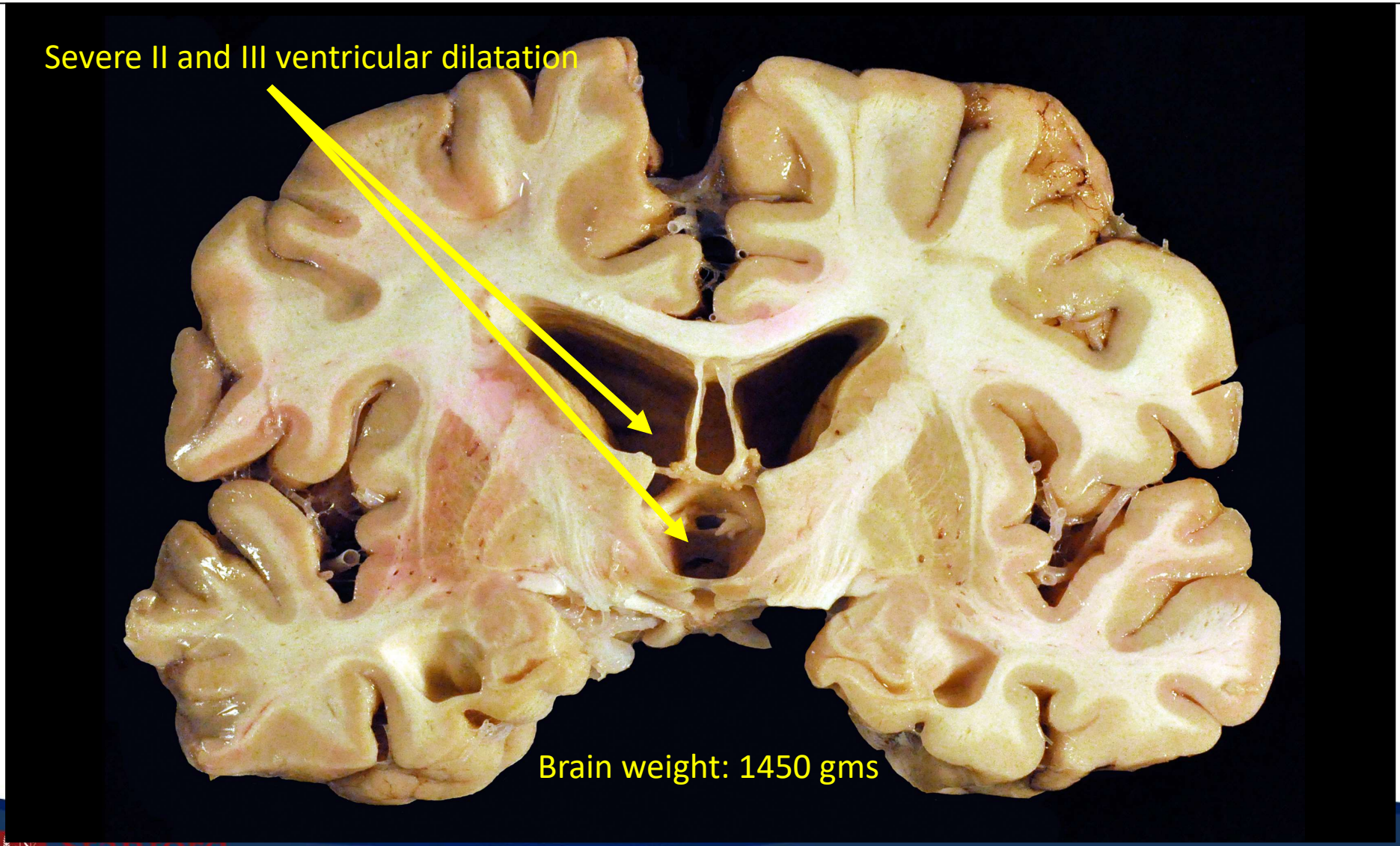
What we know: CTE and Exposure

- CTE stage significantly associated with age
  - 11-14 years between stages, $p<0.01$
- CTE stage significantly associated with duration of play
  - $p<0.01$
- What form of exposure matters most?
  - duration, intensity, frequency, cumulative

McKee et al., 2013

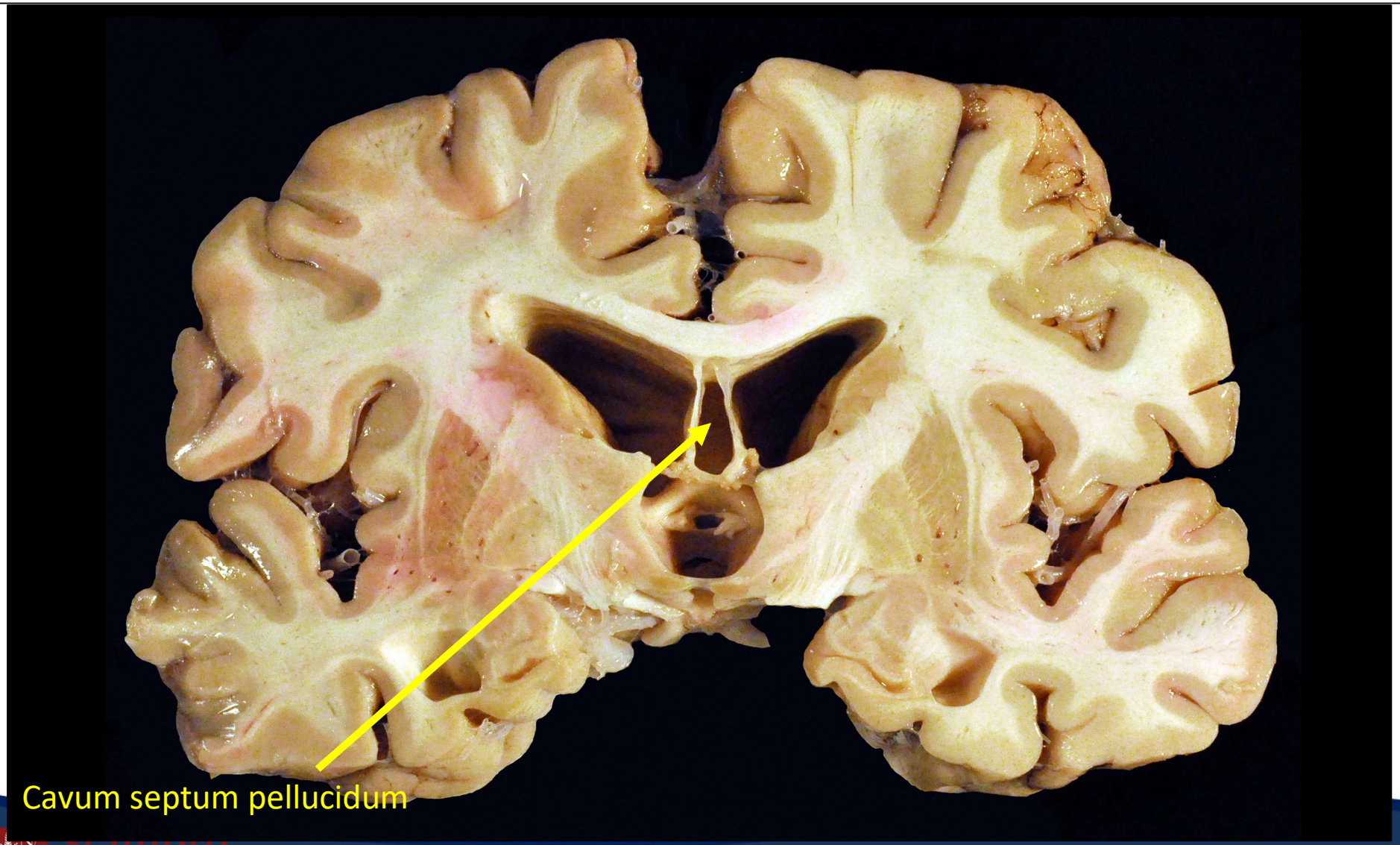
10 years of professional football

Death in his 80s with dementia



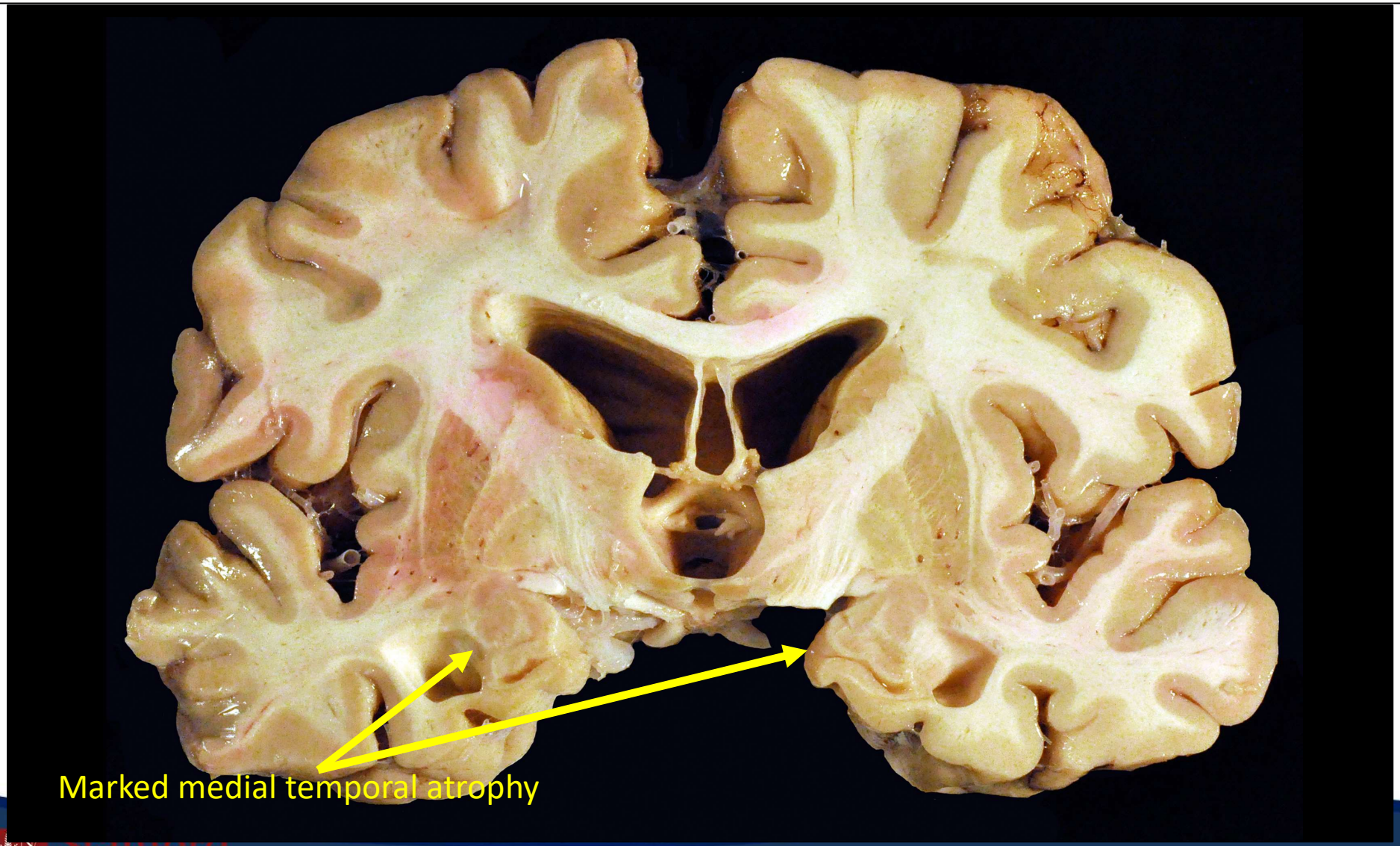
10 years of professional football

Death in his 80s with dementia



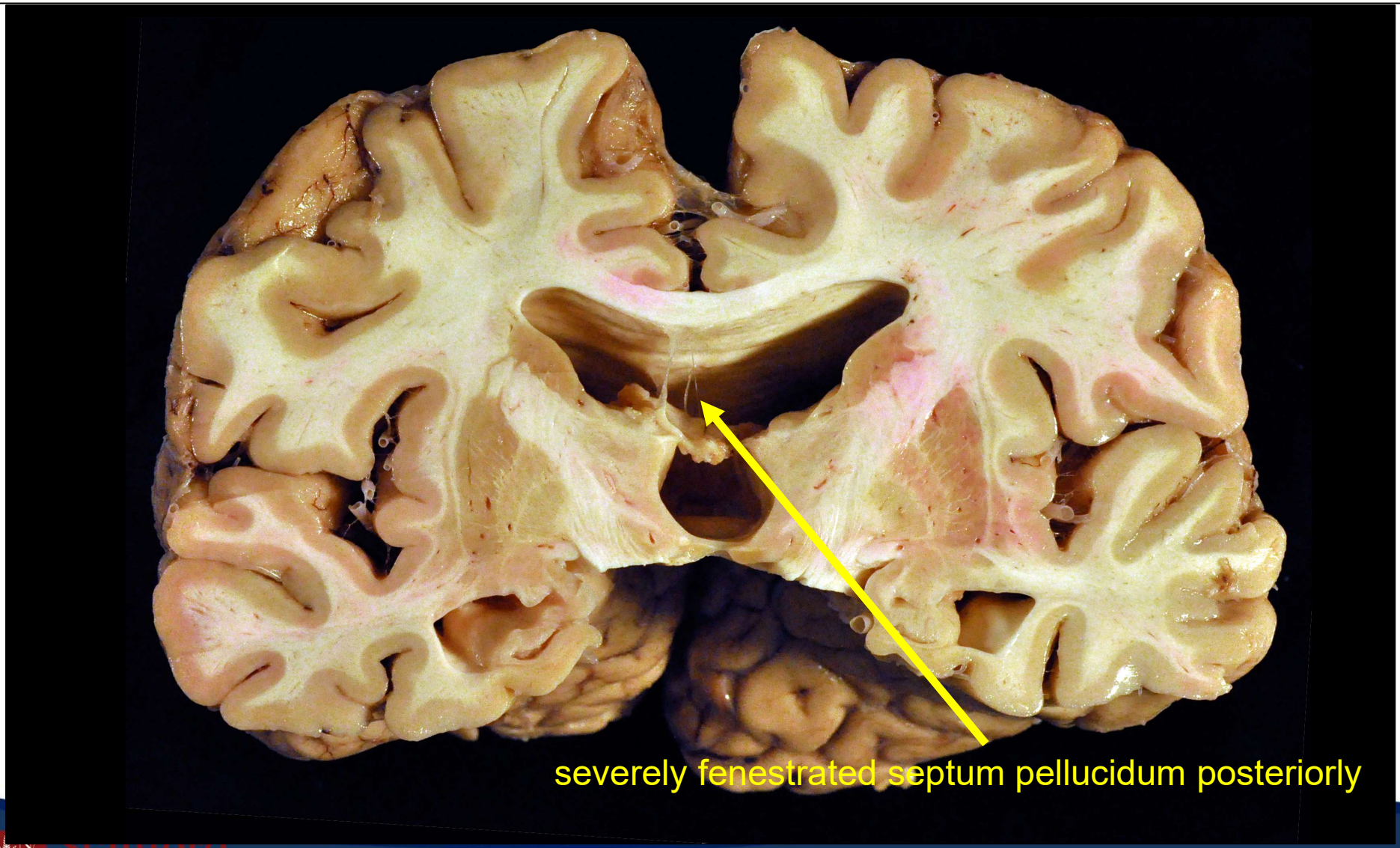
10 years of professional football

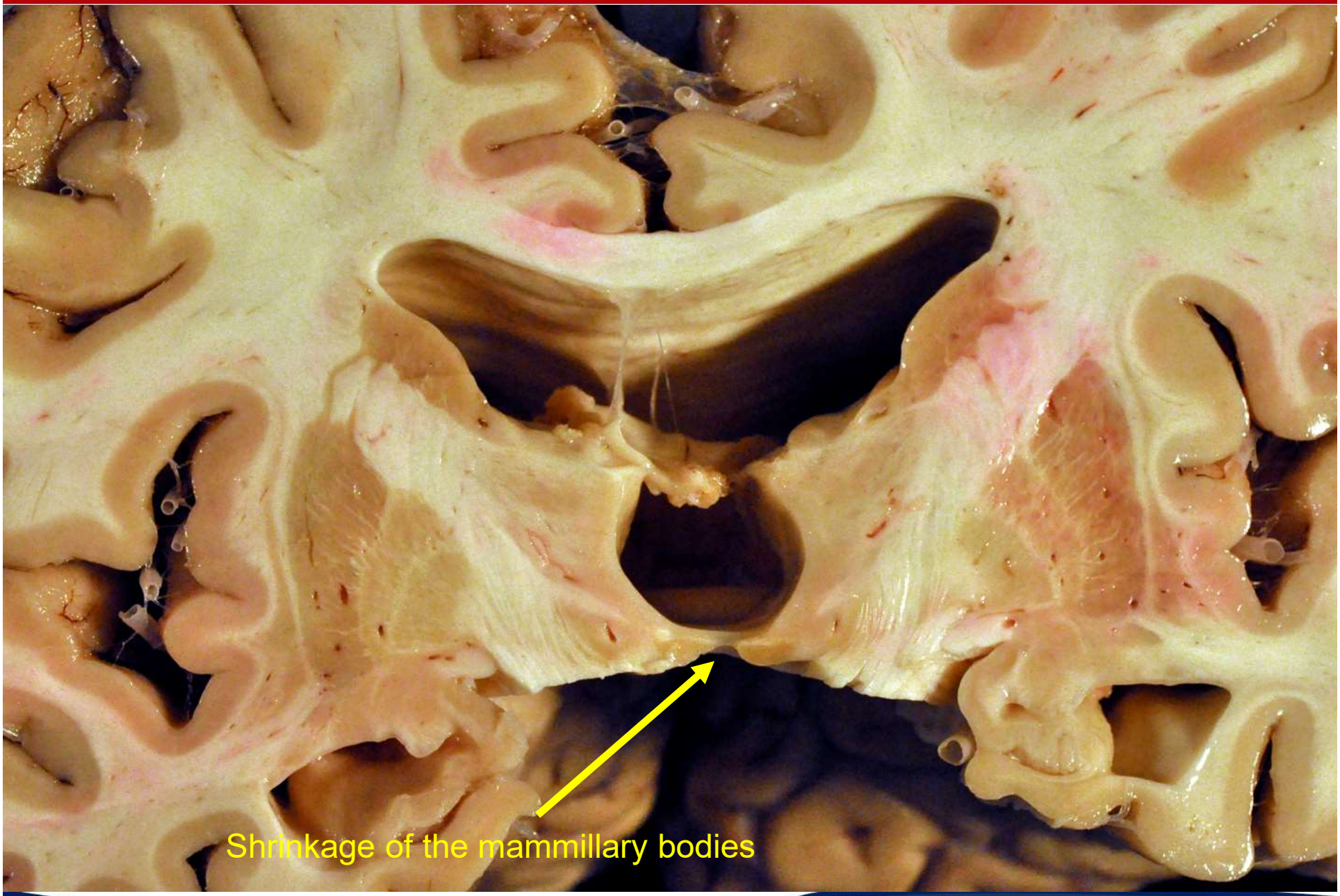
Death in his 80s with dementia

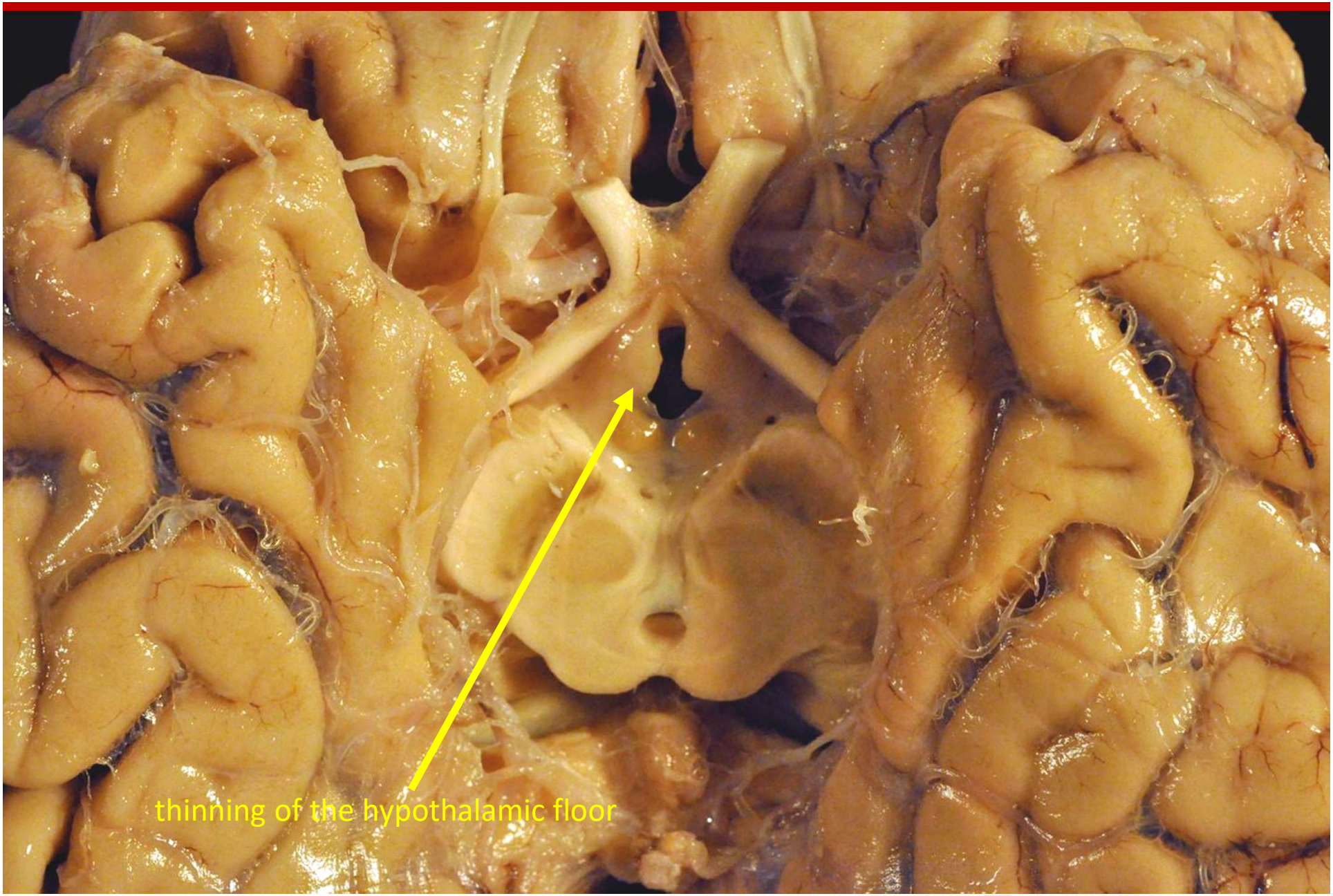


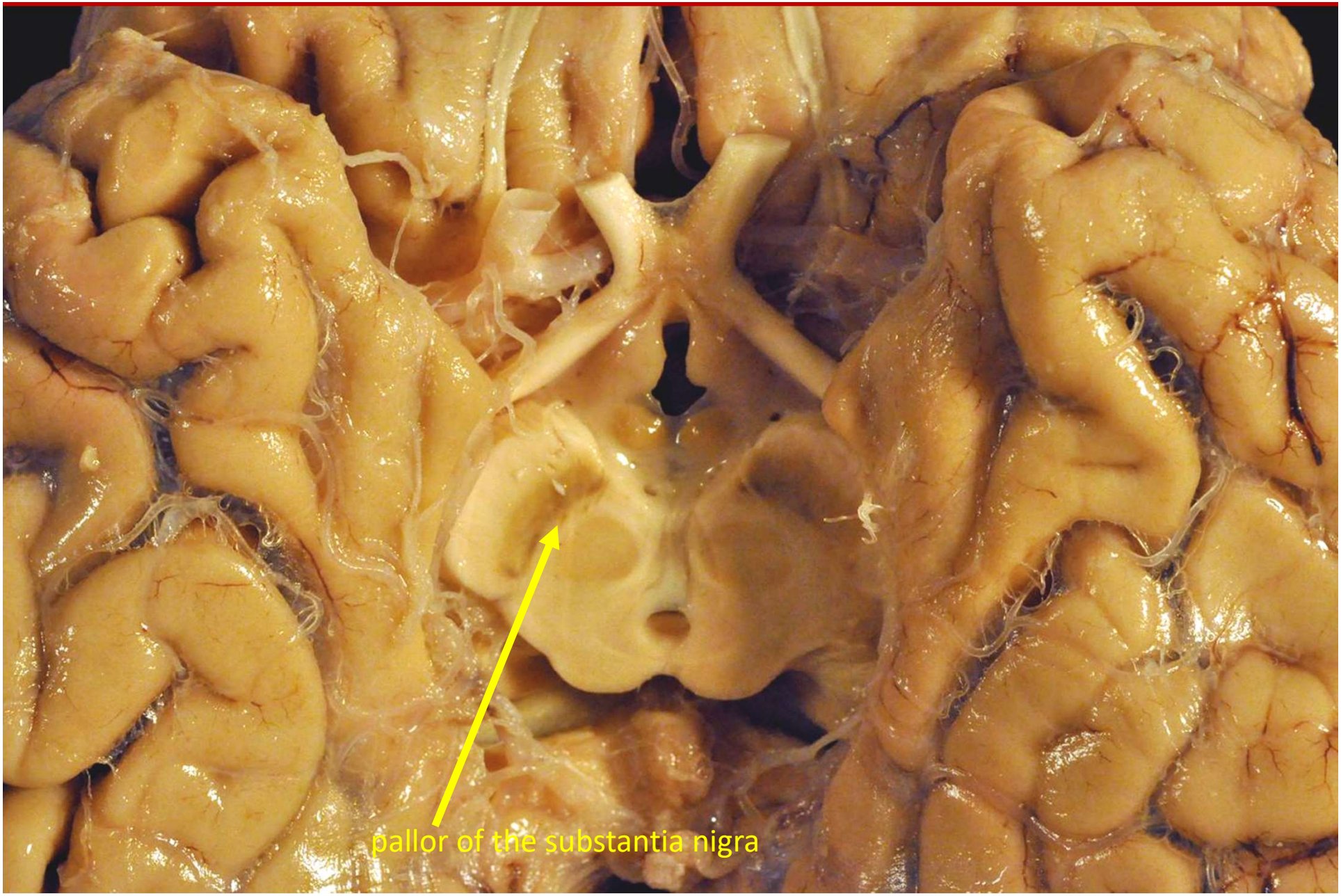
10 years of professional football

Death in his 80s with dementia




Shrinkage of the mammillary bodies


thinning of the hypothalamic floor


pallor of the substantia nigra

Lou Gehrig


4

Patrick Grange at age 29

Patrick Grange

CTE and motor neuron disease

- 100% of CTE cases have extensive tau
- 85% of CTE have extensive TDP-43 in brain
- 3 cases that had clinical ALS had extensive tau and TDP-43 in spinal cord, brain stem
- Not co-localized

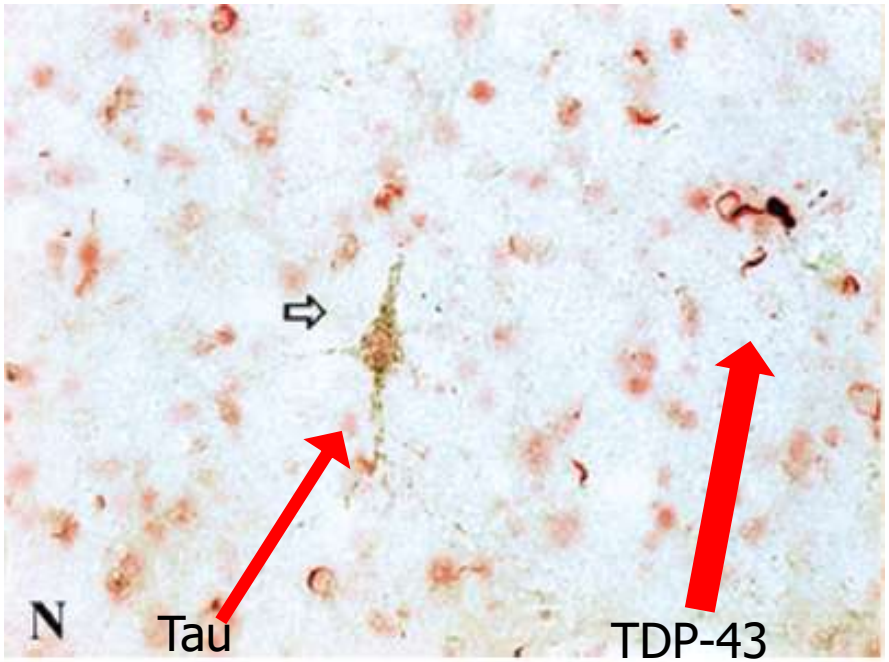


TABLE 3. TDP-43 Immunoreactivity i

Case	MND	Spinal Cord	Medulla	Midbrain
1*	Yes	+++	++	+++
2*	Yes	+++	++	+++
3*	Yes	++	+	+++
4†	No	+	+	+++
5†	No	0	+	+
6*	No	0	+	0
7*	No	0	0	+
8†	No	0	+	+
9†	No	NA	++	++
10‡	No	NA	NA	+
11‡	No	NA	NA	0
12‡	No	NA	NA	0

McKee et al., 2010

Variable	All Symptomatic Subjects (*N*=33)[1]	Behavior/Mood Group (*N*=22)[1]	Cognition Group (*N*=11)[1]
Percent with Progressive Course	90.9%	86.4%	100%
Percent with Dementia Diagnosis at Death	30.3%	18.2%*	54.5%*
Age First Clinical Feature Observed (yrs) *M* ± *SD* (range)	42.5 ± 17.8 (19-82)	34.5 ± 11.6 (19-59)*	58.5 ± 17.7 (31-82)*
Duration of Clinical Features (yrs) *M* ± *SD* (range)	14.9 ± 12.9 (0-51)	17.0 ± 14.3 (0-51)	10.7 ± 8.5 (1-30)
Clinical Domain(s) Ever Observed During Life (%)			
Cognition	93.9%	90.9%	100%
Behavior	75.8%	86.4%*	54.5%*
Mood	84.8%	95.4%*	63.6%*
Motor	30.3%	27.3%	36.4%

Variable	All Subjects (*N*=36)	Behavior/Mood Group (*N*=22)[1]	Cognition Group (*N*=11)[1]
Age at Death (*M*±*SD, range*)	56.8±21.9 (17-98)	51.4 ±18.5 (21-84)*	69.2±21.8 (34-98)*
Cause of Death	Systemic Illness = 41.8%	Systemic Illness = 49.8%	Systemic Illness = 27.3%
	Accidental OD = 13.9%	Accidental OD = 18.2%	Accidental OD = 9.1%
	Dementia-Related = 13.9%	Dementia-Related = 9.1%	Dementia-Related = 27.3%
	Suicide = 16.7%	Suicide = 18.2%	Suicide = 18.2%
	Injury = 8.4%	Injury = 4.5%	Injury = 18.2%
Years of Education (*M*±*SD, range*)	15.0±2.4 (10-20)	14.5±2.4 (10-18)	15.7±1.4 (13-18)
Neuropathological Severity Stage	Stage I = 8%	Stage I = 9.1%	Stage I = 0%
	Stage II = 28%	Stage II = 31.8%	Stage II = 9.1%
	Stage III = 31%	Stage III = 31.8%	Stage III = 36.4%
	Stage IV = 33%	Stage IV = 27.3%	Stage IV = 54.5%