

# Traumatic Brain Injury

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# Disclosures

- None
- Funding: Washington University Institute of Clinical and Translational Sciences NIH grant UL1TR002345

# Outline

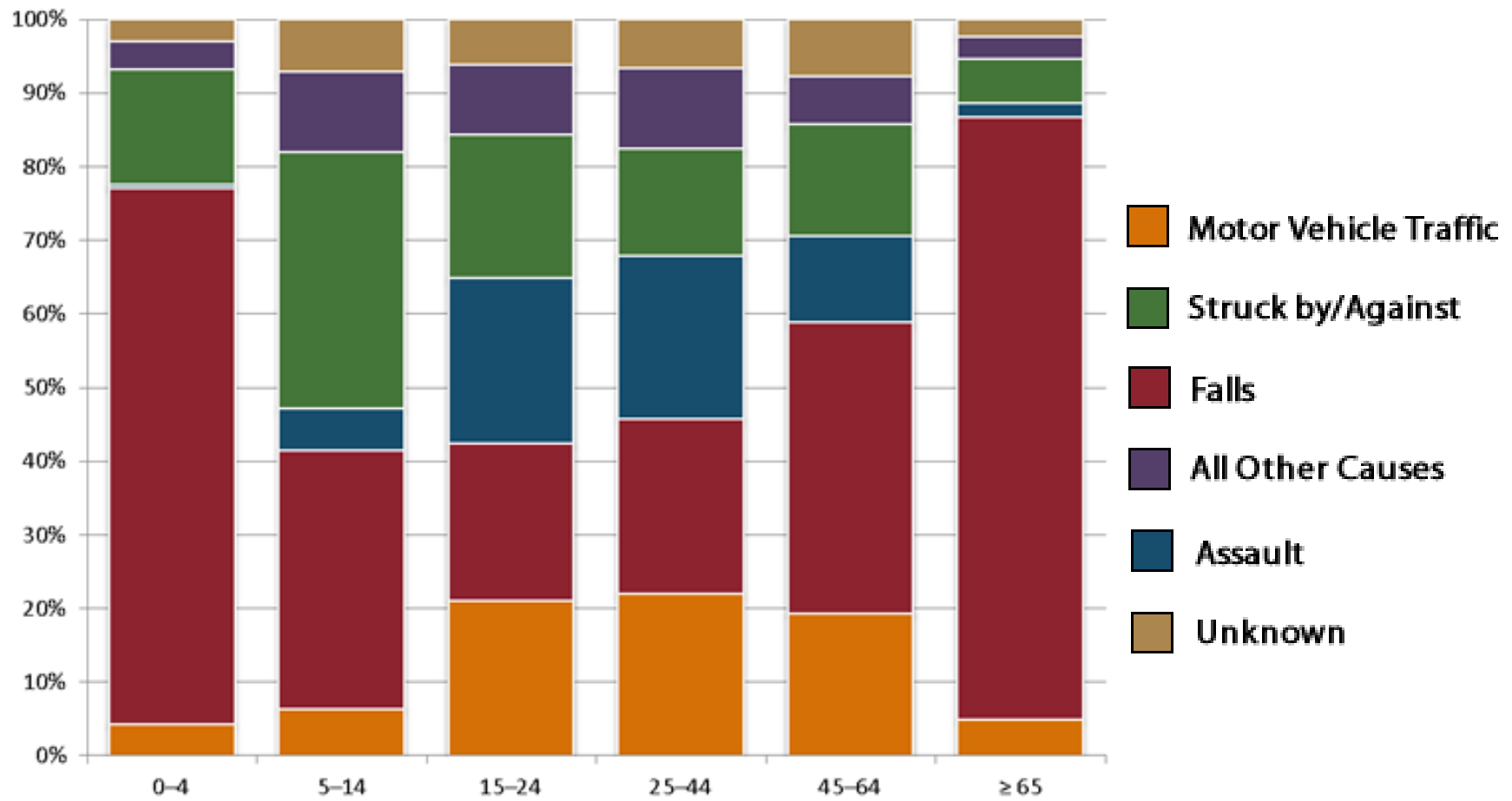
- Introduction
  - Epidemiology, mechanisms and pathophysiology of injury
- Factors that predict and influence outcome
  - Moderate-severe TBI
    - Secondary injuries
  - Mild TBI/concussion
    - Diagnosis and management
- Chronic Traumatic Encephalopathy

# Epidemiology

- 2013:
  - 2.5 million ED visits
  - 282,000 TBI-related hospitalizations
  - 56,000 TBI-related deaths
- 80 hospitalizations & 6 deaths per 100,000 kids

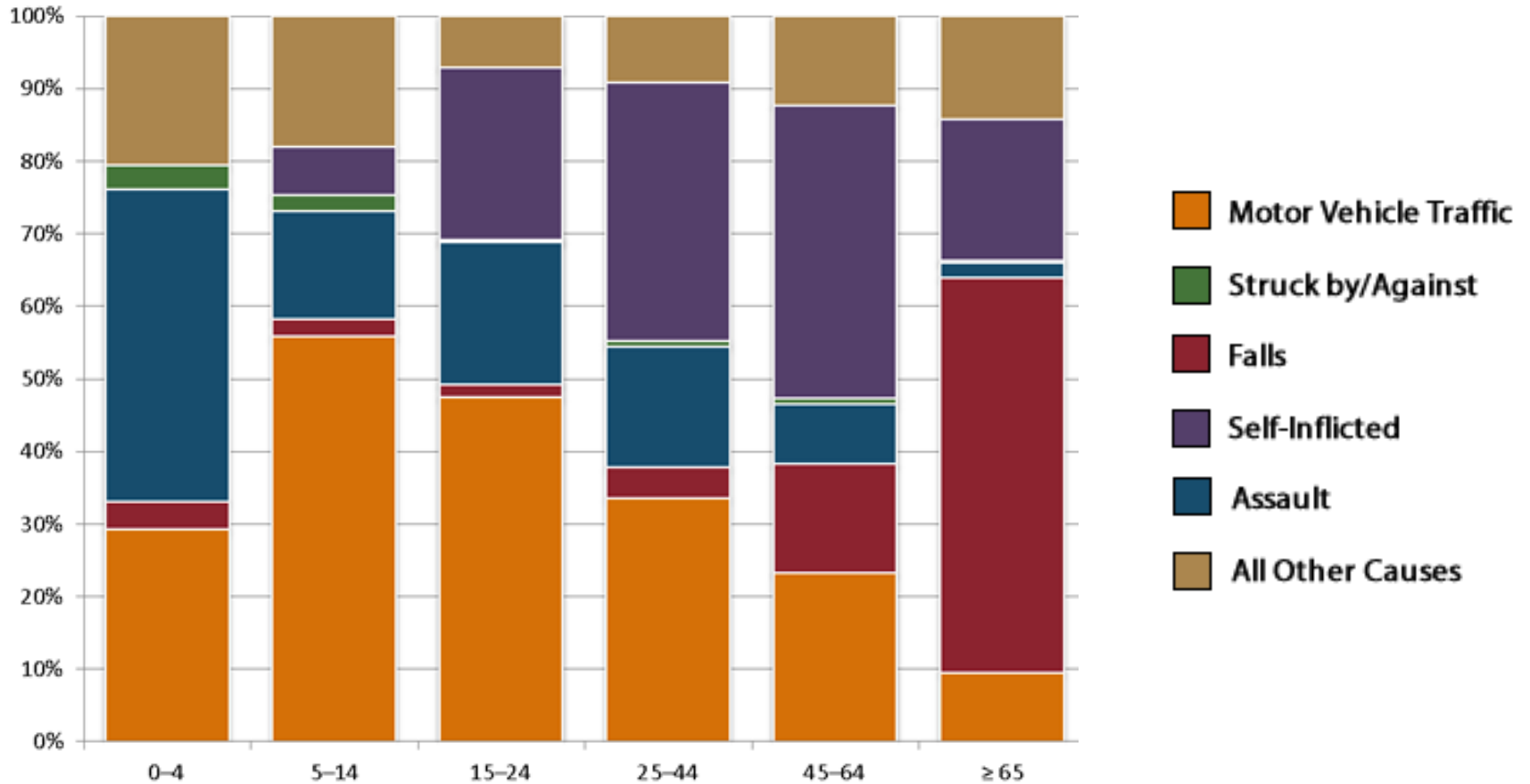
Taylor, et al. *Morbidity and Mortality Weekly Report. Surveillance Summaries*, 2013. 66(9), 1–16.

# Mechanism varies by age

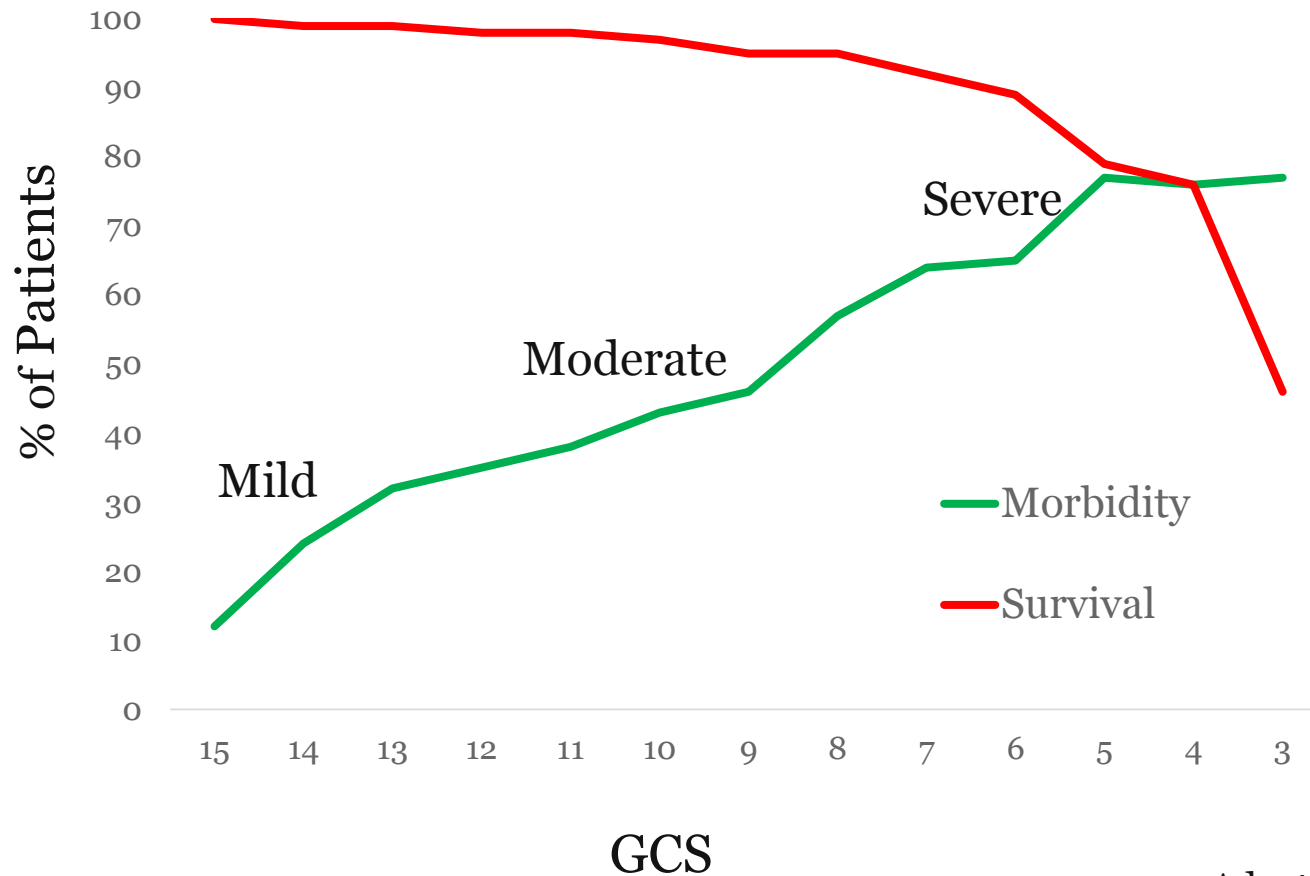


[cdc.gov/traumaticbraininjury/data/dist\\_ed](https://cdc.gov/traumaticbraininjury/data/dist_ed)

# Mortality varies by age



# GCS: Morbidity and Survival



Adapted from: Cicero, M. X., & Cross, *Ped Emerg Care*, 2013. 29(1), 43–48.

# Pediatric GCS

| Best eye opening     | Spontaneously       | 4 |
|----------------------|---------------------|---|
|                      | To verbal stimuli   | 3 |
|                      | To painful stimuli  | 2 |
|                      | No eye opening      | 1 |
| Best verbal response | Appropriate coo/cry | 5 |
|                      | Irritable Cry       | 4 |
|                      | Inconsolable        | 3 |
|                      | Grunts              | 2 |
|                      | No verbal response  | 1 |
| Best motor response  | Normal spontaneous  | 6 |
|                      | Withdraws to touch  | 5 |
|                      | Withdraws to pain   | 4 |
|                      | Flexion to pain     | 3 |
|                      | Extension to pain   | 2 |
|                      | No motor response   | 1 |



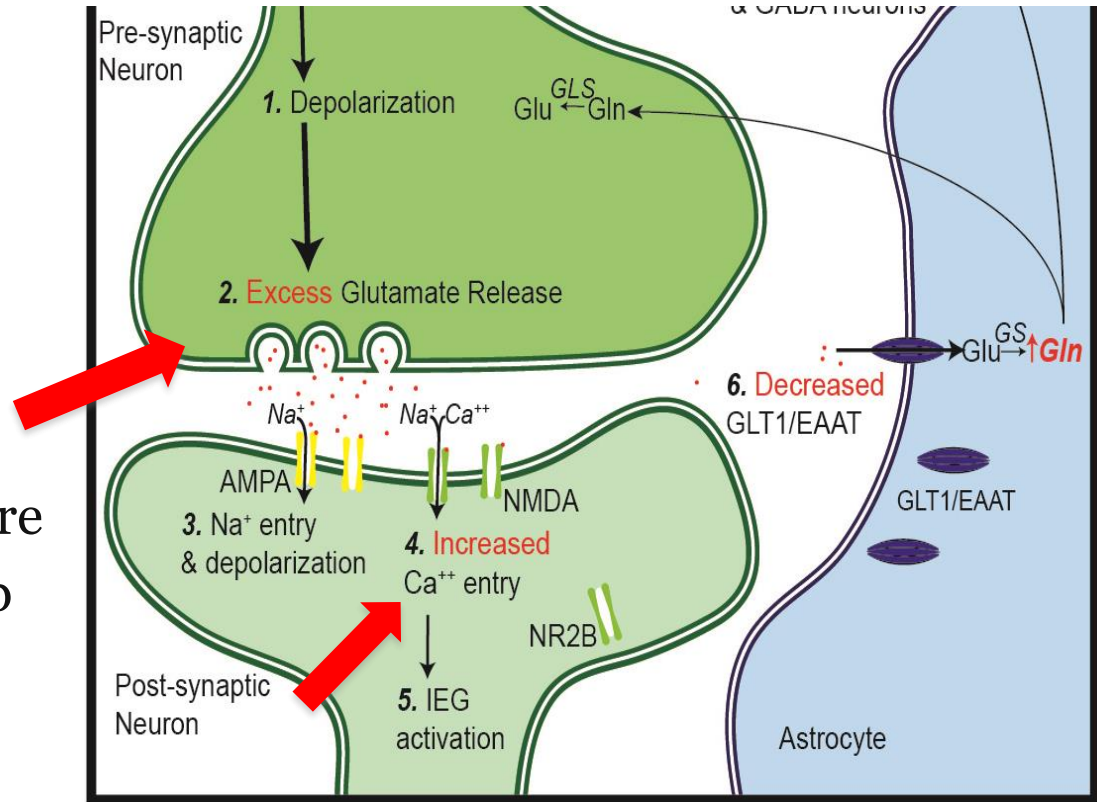
# Story

- Jack, 19 years old and his sister Jill, 16 years old were driving too fast down a hill when the car went off the road and hit a tree.
- Jack (the unrestrained driver) sustained moderate TBI with a contusion and diffuse axonal injury.
- Jill (restrained passenger) sustained a whiplash injury.

# Moderate TBI: Jack

# Acute Injury

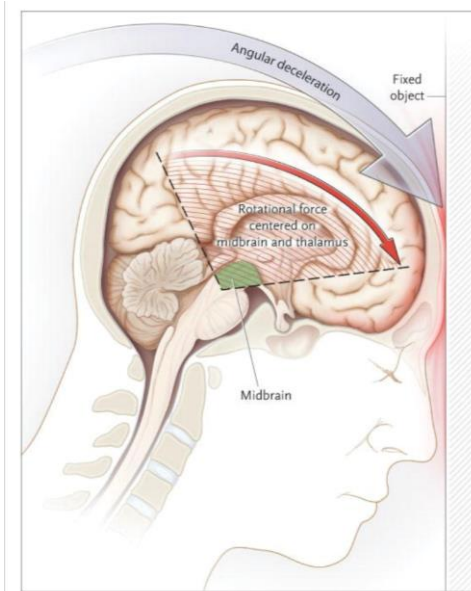
- Direct tissue damage
  - Swelling, ischemia, hemorrhage
- Glutamate increases
  - Cell membrane rupture
  - Failure of Na/K pump
  - Activation of post-synaptic neurons & Ca<sup>++</sup> toxicity



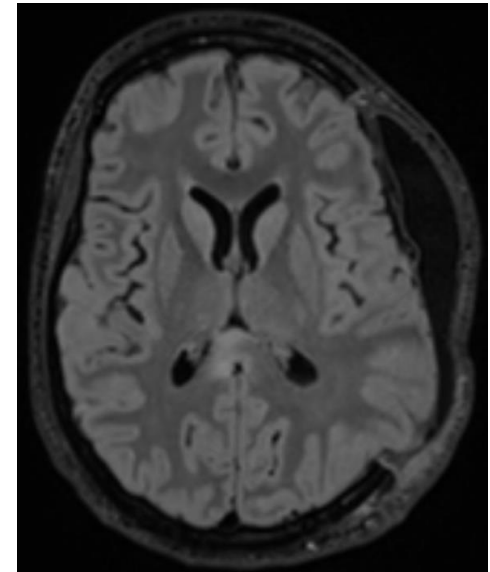
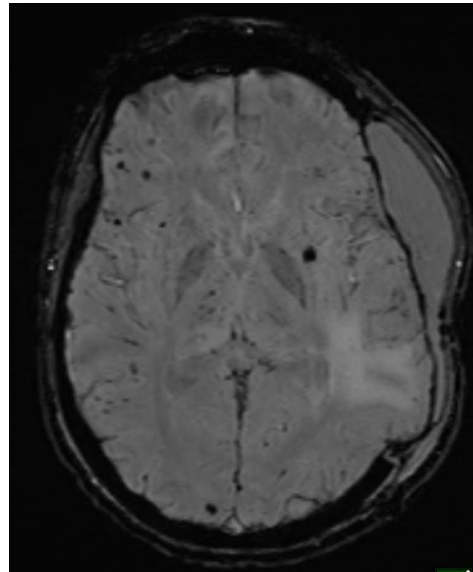
Vespa, et al. *J. Neurosurg*, 1998. 89(6), 971–982.  
Chamoun, et al. *J Neurosurg*, 2010 113(3), 564–570.  
Reviewed in: Guerriero, Giza, & Rotenberg. *Current Neuro & Neurosci Reports*, 2015. 15(5), 27–11.

# Diffuse Axonal Injury (DAI)

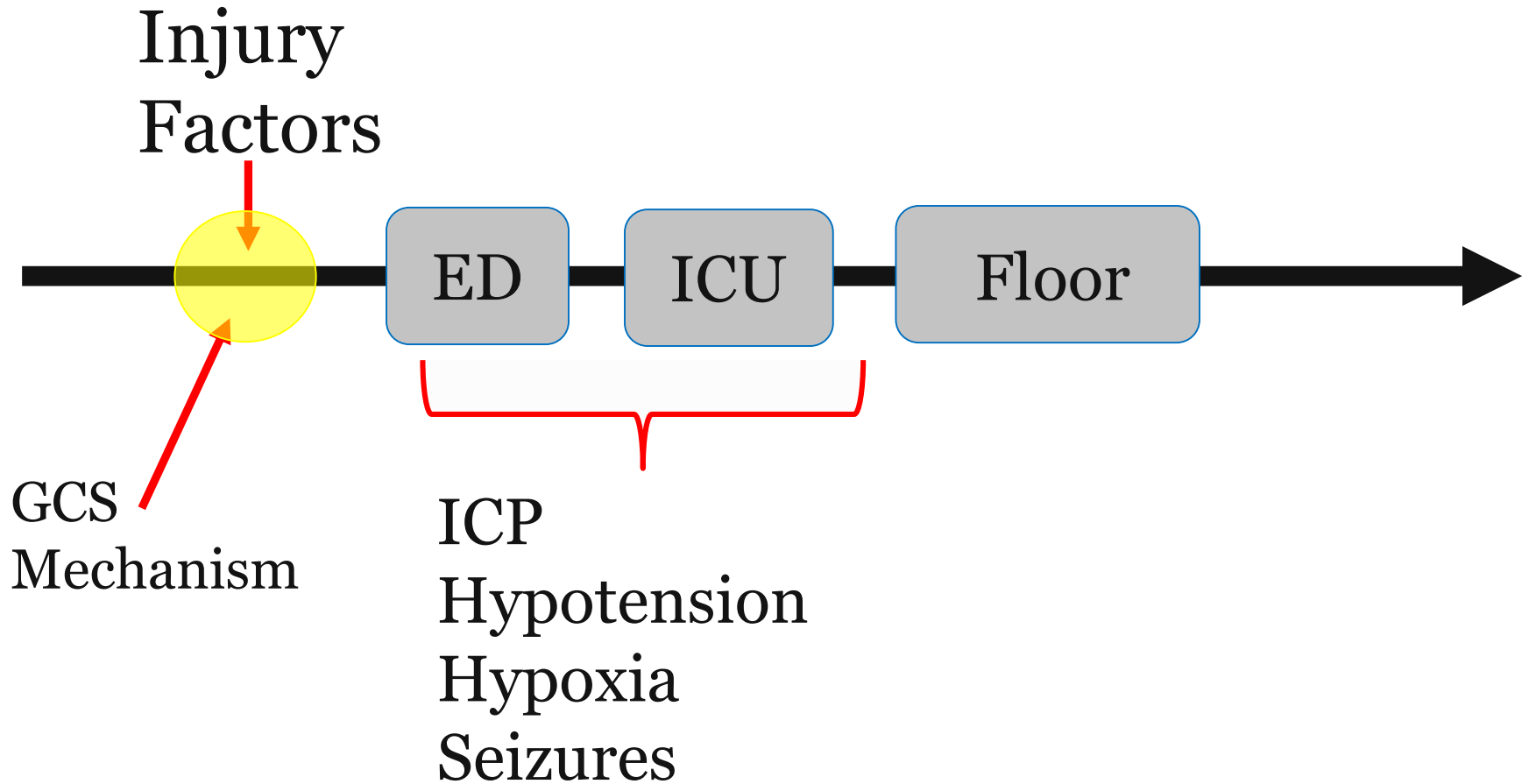
- Spectrum of MRI negative to profound
- Shearing injury to axons with local swelling
- Microhemorrhages



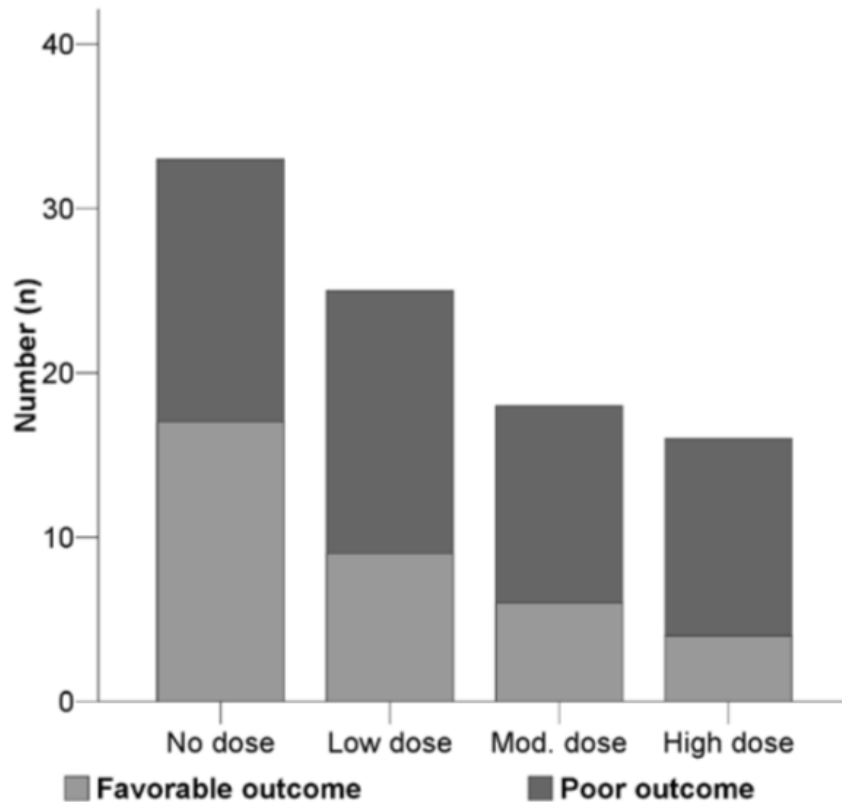
Ropper, & Gorton, Concussion. NEJM. 2007



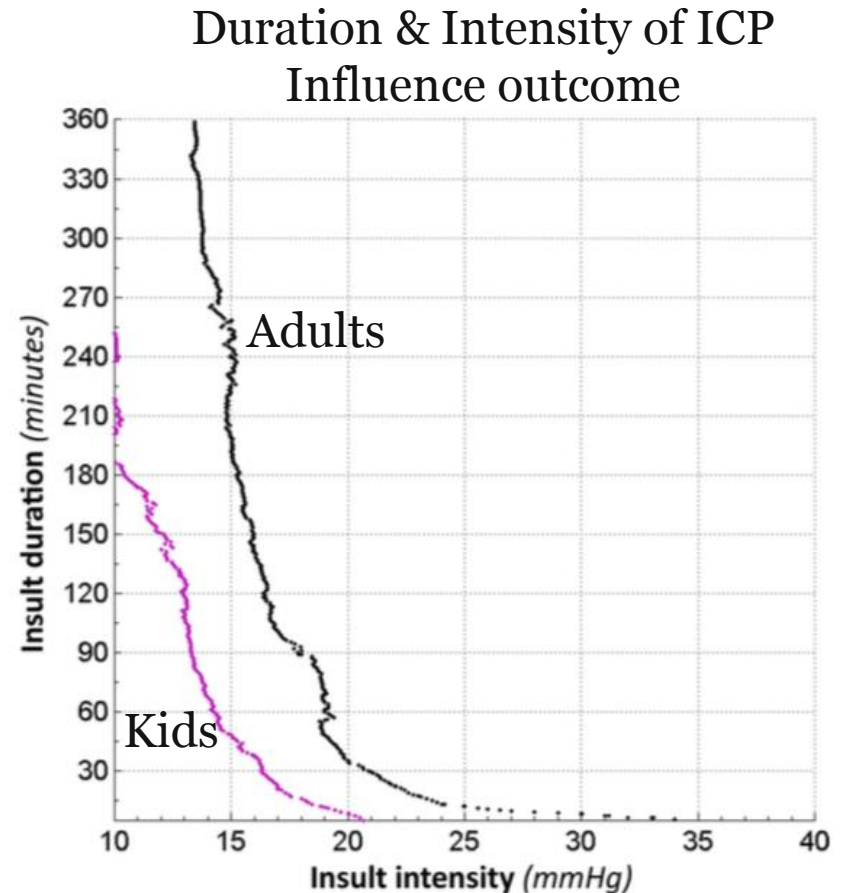
# Primary versus Secondary Factors



# Dose of ICP influences outcome

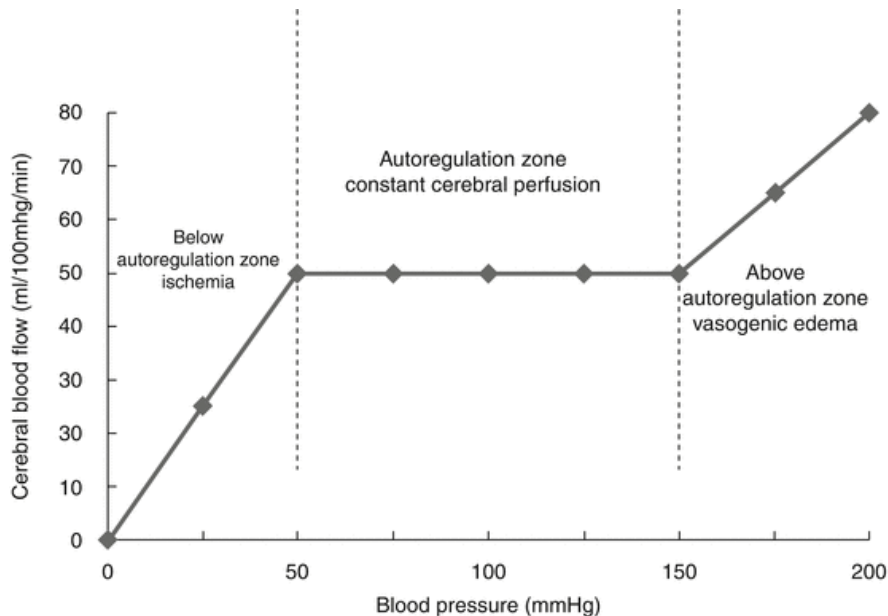


Vik, A., et al. *J Neurosurgery*, 2008.  
109(4), 678–684.



Güiza, F., et al. *Intensive Care Medicine*,  
2015 41(6), 1067–1076.

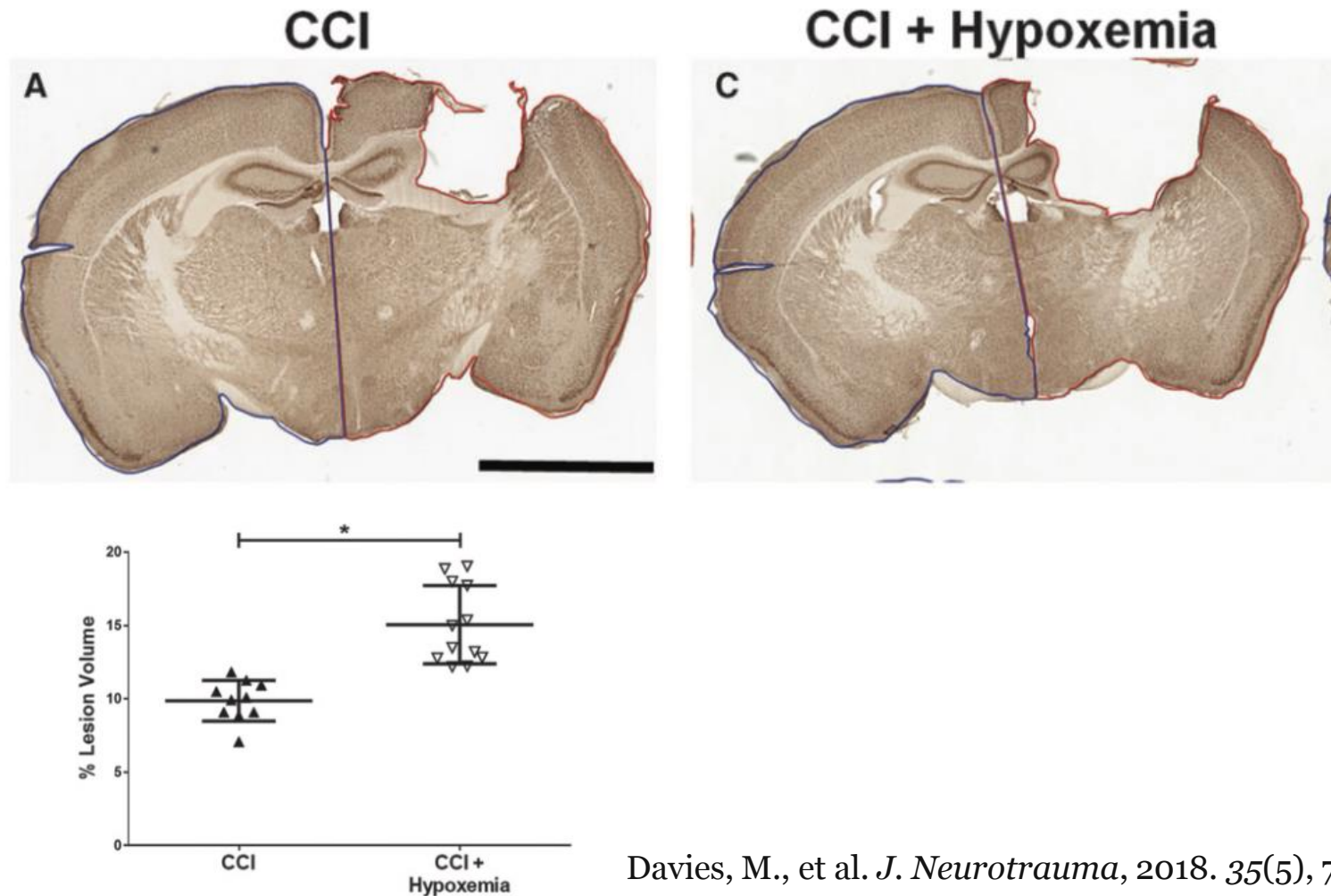
# Blood Pressure



$$CPP = MAP - ICP$$

$$MAP = [2/3 \text{ diastolic}] + [1/3 \text{ systolic}]$$

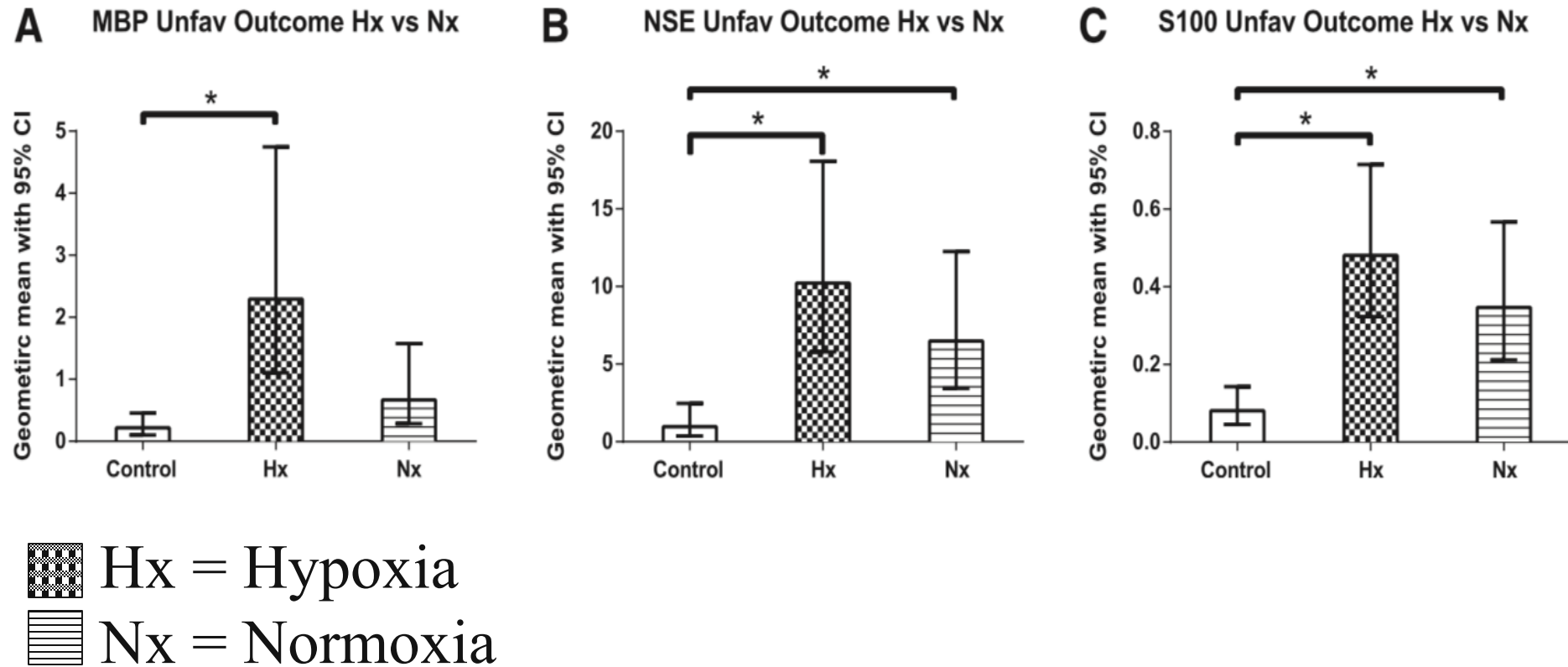
# Hypoxia worsens outcomes



Davies, M., et al. *J. Neurotrauma*, 2018. 35(5), 790–801.



# Hypoxia worsens outcomes



Yan, E. et al. *J. Neurotrauma*. 2014

# Seizures

- Adults: 94 patients
  - 22 % had seizures, 6/94 with SE
  - 52 % with nonconvulsive seizures
- Kids: 189 patients
  - 30 & 43 % had seizures
  - 7 & 40 % with subclinical only seizures
- Risk factors
  - Younger age
  - AHT
  - Intraaxial blood

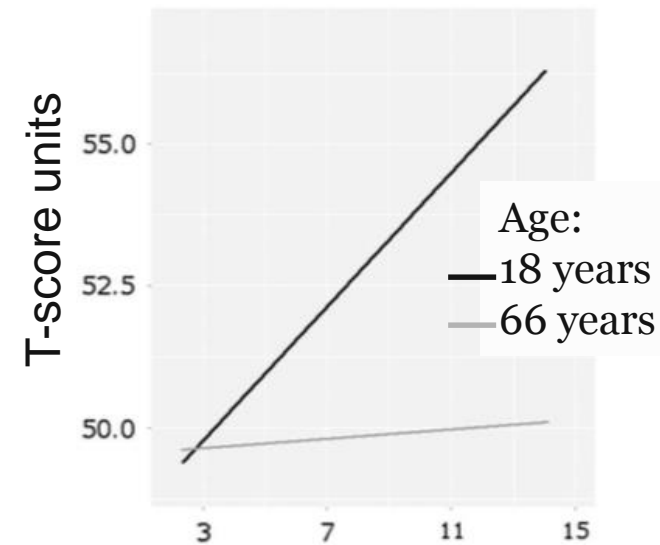
Vespa, et al. *J Neurosurgery*, 1999; 91(5), 750–760.

Arndt, et al. *Epilepsia*, 2013. 54(10), 1780–1788.  
O'Neill, et al. *J. Neurosurg: Peds*, 2015. 16(2), 167–176.

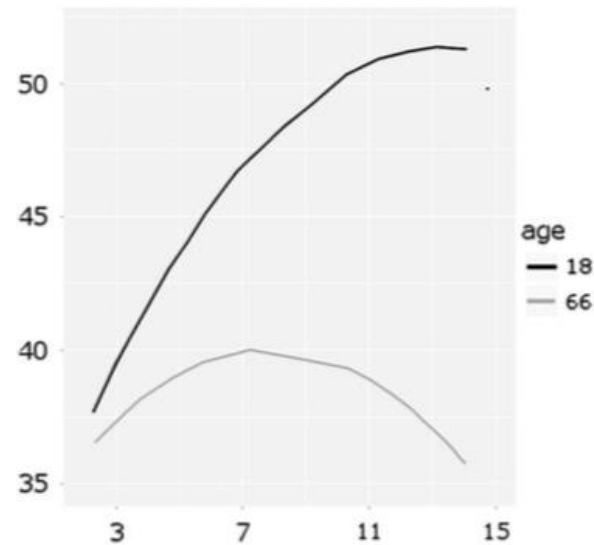
# How is Jack going to do?

# Age impacts neurocognitive outcome

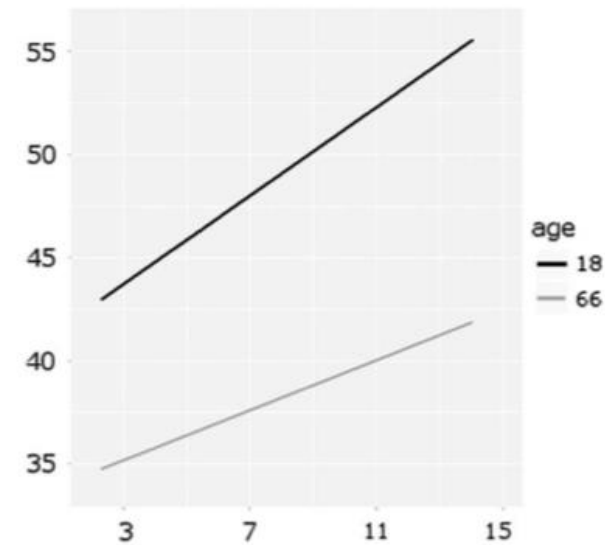
Executive Function



Processing Speed



Verbal learning

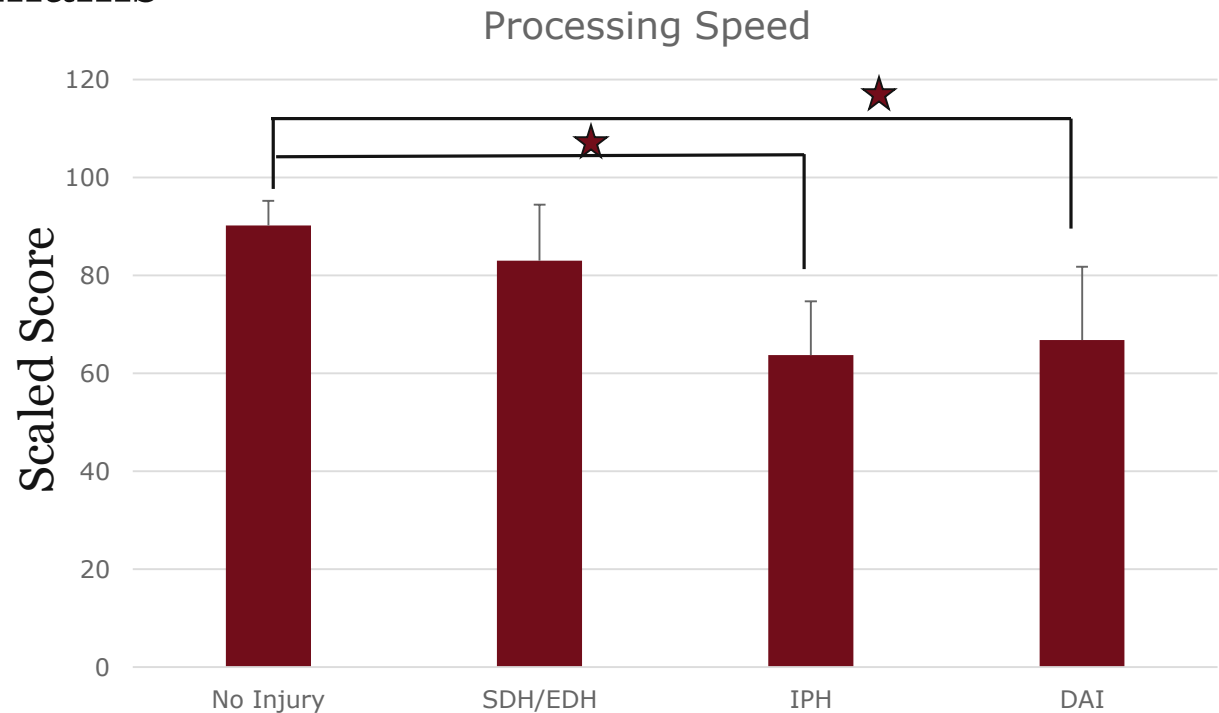
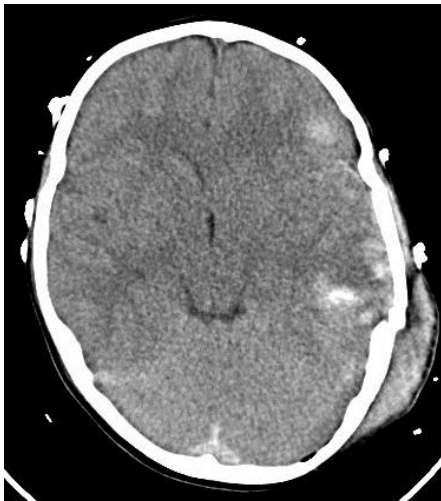


Months After injury

Rabinowitz, et al. *JINS*, 2018; 24(3), 237–246.

# Injury severity impacts outcome

- DAI and IPH leads to reduced processing speed, but not IQ and other domains



Guerriero, Dodd, Pineda in preparation

# Outcomes

- Post-traumatic epilepsy: 10 – 20 %
  - Risk: Younger age and severity of injury

Park & Chugani. *Ped Neuro*, 2015  
Liesemer, et al. *J Neurotrauma*, 2011

- Sleep disturbance associated with increased depression, anxiety and apathy 12 months post-injury

Rao, et al. *Brain Injury*, 2013

- Affective disorders, ADHD and Anxiety
  - Mild: Anxiety decreases
  - **Severe: Anxiety increases**

Keenan, et al. *J Neurotrauma*, 2018

# Therapeutic options

- Cognitive
- Headache
- Affective
- Sleep dysfunction
- Motor
  - Gross Motor -> PT
  - Fine Motor -> OT
  - Speech/communication -> Speech

# What happened to Jill?

- In the ED, Jill complains of a headache and dizziness



# Concussion

- Transient neurologic symptoms
- Complex pathophysiologic process
- No traditional brain imaging correlate



Giza C.C. et al. *Neurology* 2013. (80), 2250-2257.

# History

- Hit to the head or body with transient neurologic symptoms
- Mechanism of injury
- Additional history

# Recovery

Injury

Full Recovery

Course -> 7 - 28 days



# Symptoms

- General
- Cognitive
- Neurologic
- Emotional

# Symptoms

- General

- Headache
- Dizziness
- Nausea
- Vomiting
- Fatigue
- Sleep difficulties

- Cognitive

- Disorientation
- Memory loss
- Feeling “foggy”, “dazed”
- Attention problems
- Difficulty concentrating
- Slow to respond

- Neurologic

- LOC
- Balance problems
- Visual disturbances
- Sensitivity to light or noise
- Seizures

- Emotional

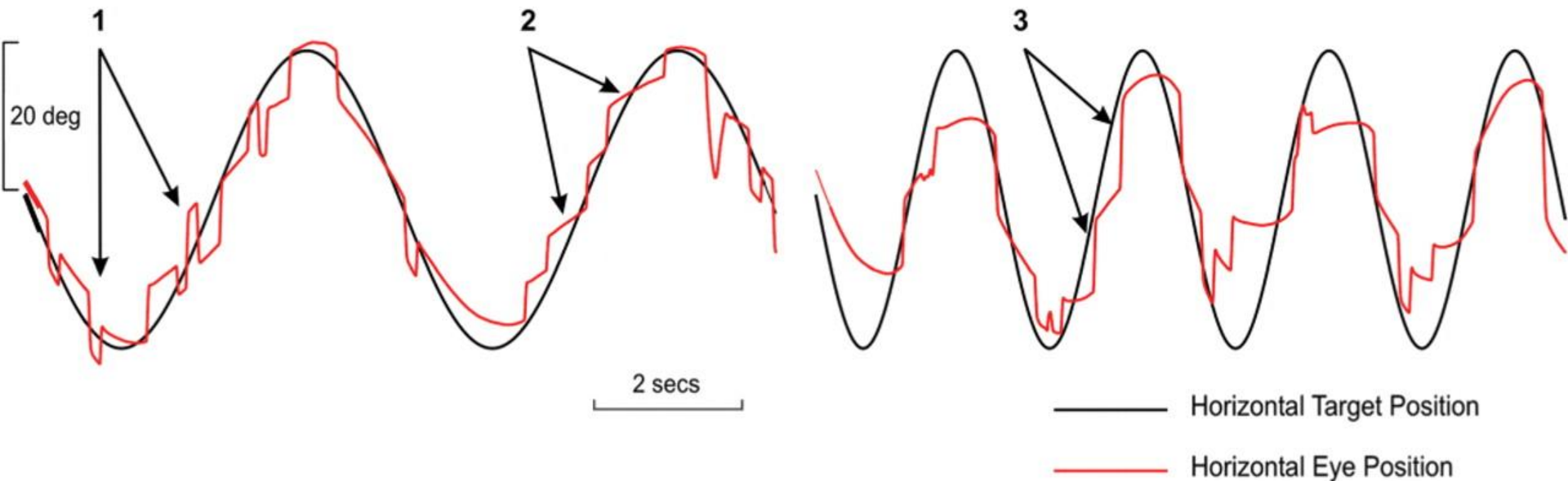
- Irritability
- Emotional lability
- Sadness
- Anxiety

# Physical Exam

- General and Neurologic Exams
  - Mental Status Exam
  - Focal findings = Red Flag
- 
- And some specifics -

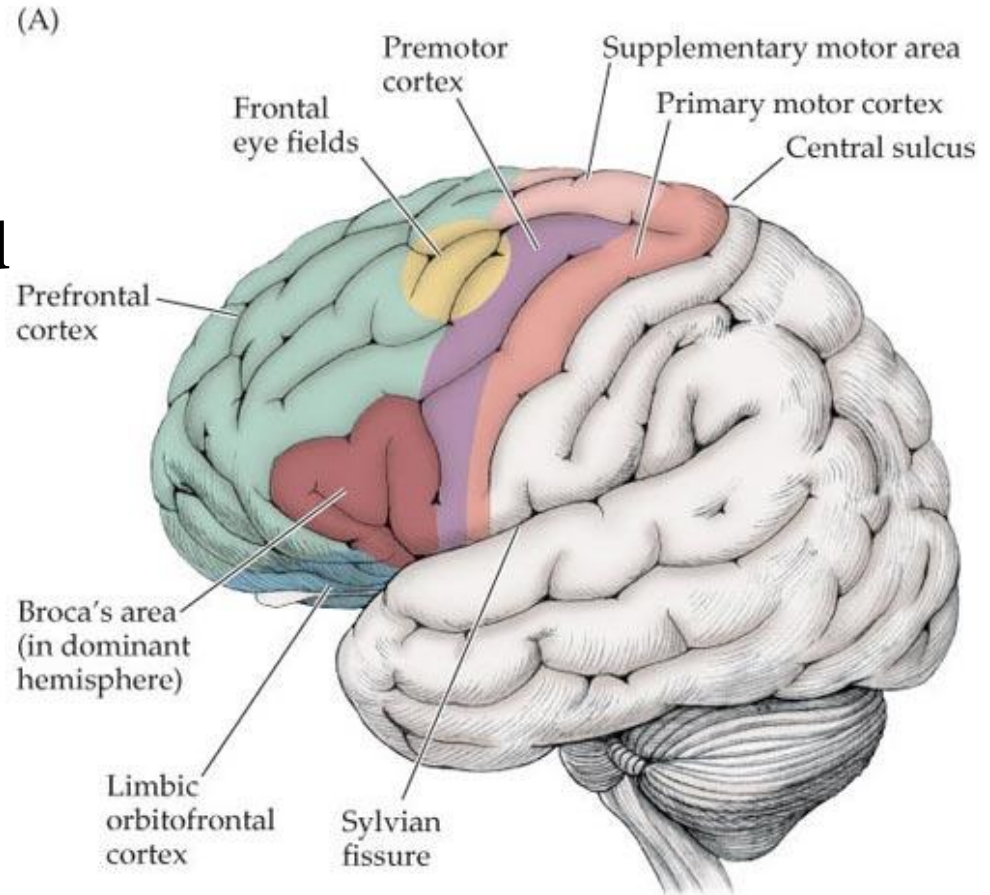
# Physical Exam

- General appearance
- Saccadic intrusions or difficulties with visual pursuit
- Balance problems



# Neuroanatomy

- Frontal Eye Fields
  - Guide attention and saccades





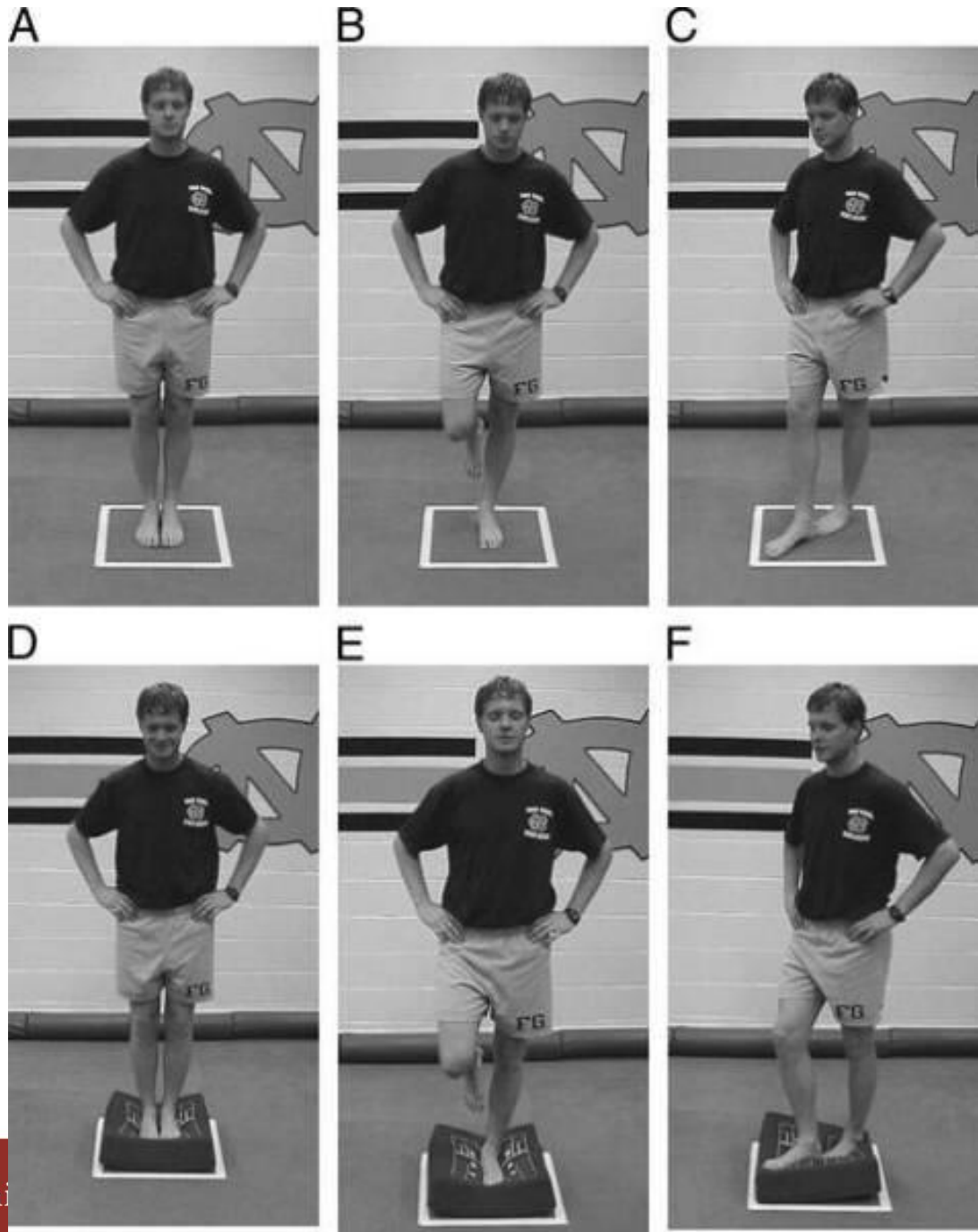
# Physical Exam

- General appearance
- Saccadic intrusions or
- Balance problems

## BESS

Double leg stance Single  
(non-dom)

Tandem (non-dom in back)  
20 secs & Record errors



# What's Jill's course going to be?

# Recovery

Injury

Full Recovery

Course -> 7 - 28 days

Susceptibility &  
Risk

Post-concussive  
syndrome

# Outcomes

- Kids: 13– 29% of mild TBI have persistent somatic, cognitive, sleep, and psychological symptoms 3 months following injury
- Adults: Litigation status and disability seeking status were significant predictors of prolonged concussion

Stein, et al. *Brain Injury*, 2017. 31(13-14), 1736–44.  
Hanks, et al. *J Neurotrauma*, 2018. Sep 6.

# Psychological and behavioral outcomes

- Higher rates of **ADHD** in:
  - Hospitalized vs not hospitalized
  - Injured vs noninjured (healthy) controls
- **Depression:** Children 6 months post-mTBI 9.3 x more likely vs orthopedic injury
- **Anxiety:** Higher rates 0-6 months after injury, but not by 1 year

Emery, et al. *Canadian Journal of Psychiatry*, 2016 61(5), 259–269.

# Will Jill have prolonged symptoms?

- Premorbid factors
- Number of injuries
- Genetic predisposition
- Resiliency factors
- Recovery strategy

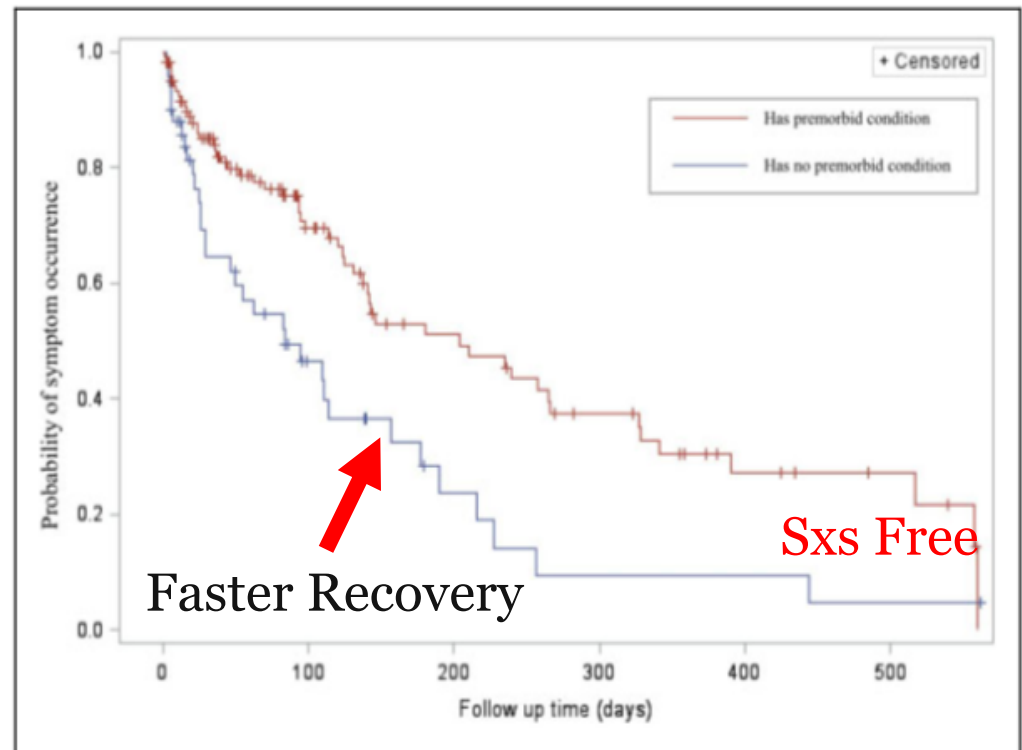
# Risk factors for prolonged recovery

- Symptom severity
- Multiple concussions
- Female sex
- Preexisting conditions:
  - Anxiety
  - Mood disorders
  - ADHD
  - Migraine

Giza, Kutcher and Ashwal, Neurology 2013.

# Premorbidities

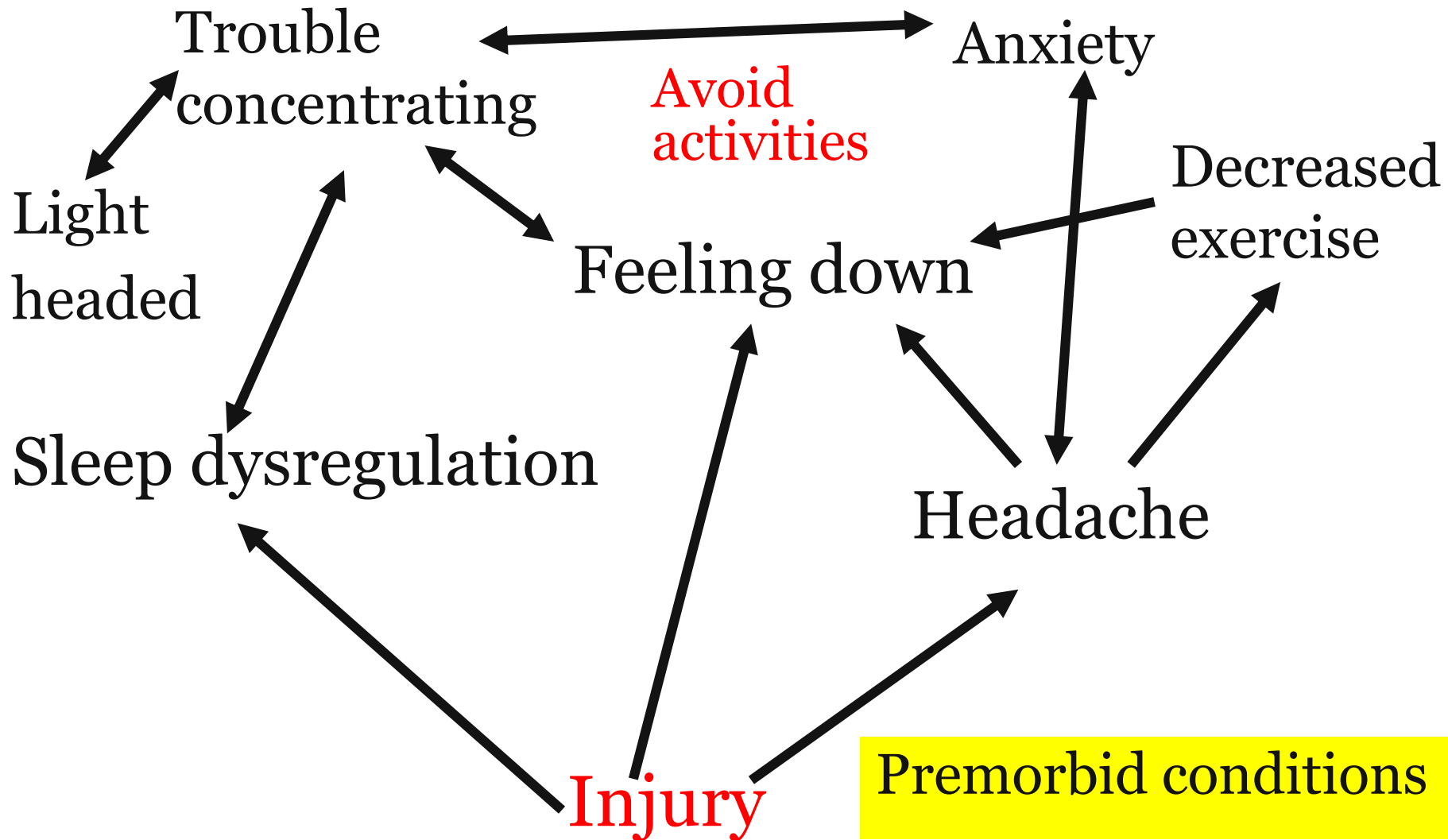
- Children < 12 with premorbid conditions
- Adolescents +/- premorbid conditions
- Life stressors
- Family history:
  - Mood disorders
  - Psychiatric history
  - Migraines



Guerriero, et al. *J Child Neurology*, 2018; 33(2), 168–173.  
Yeates, et al. *Int J Dev Neurosci*. 2012; 30(3):231-237.  
Morgan et al. *J Neurosurg Pediatr*. 2015; 15(6):589-598.



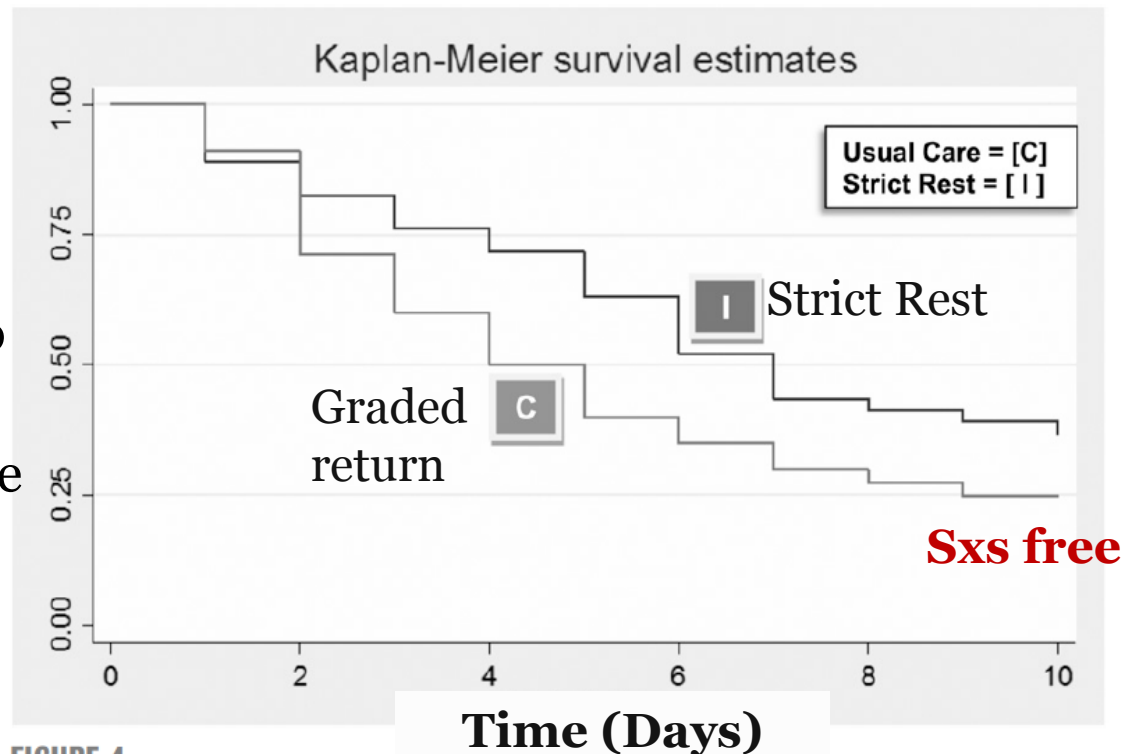
# Cycle



# How do we break the cycle?

# Rest

- Benefit of 5 days of strict rest over conventional recommendations (1-2 days rest, graded return to activities)
- **Outcome:** Neurocognitive performance and balance at 10 days.



**FIGURE 4**

Proportion of patients reporting symptom resolution (PCSS  $\leq 7$ ) over time. It took longer for 50% the intervention group to report symptom resolution. However, the difference in overall proportion of patient reporting symptom resolution did not meet statistical significance ( $P = .08$ ).

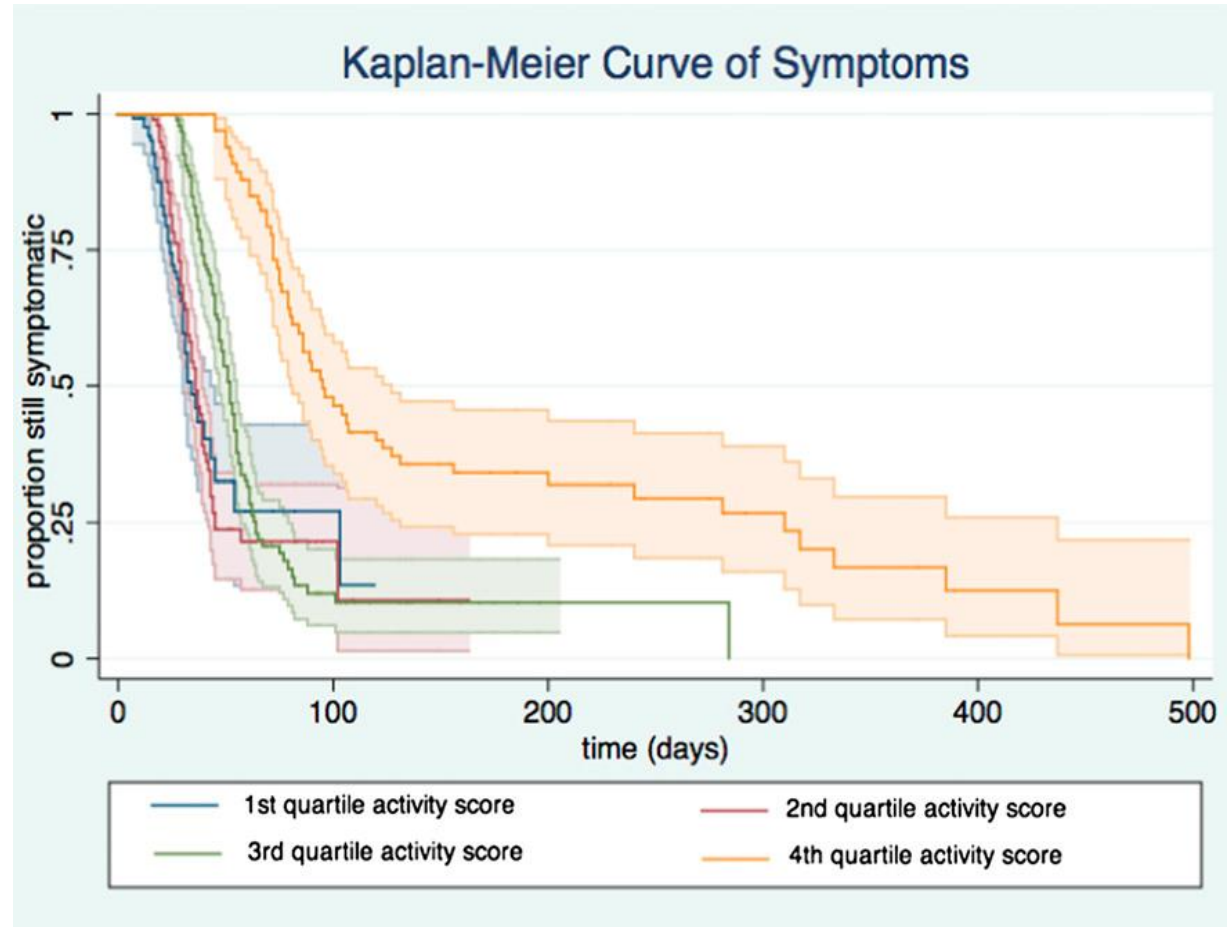
Thomas, et al. *Pediatrics*, 2015; 135(2), 213–223.

Schneider, et al. *Brit J Sports Med*, 2013; 47(5), 304–307.

Broglia, et al. *Clin in Sports Med*, 2015; 34(2), 213–231.

# How much screen time is too much?

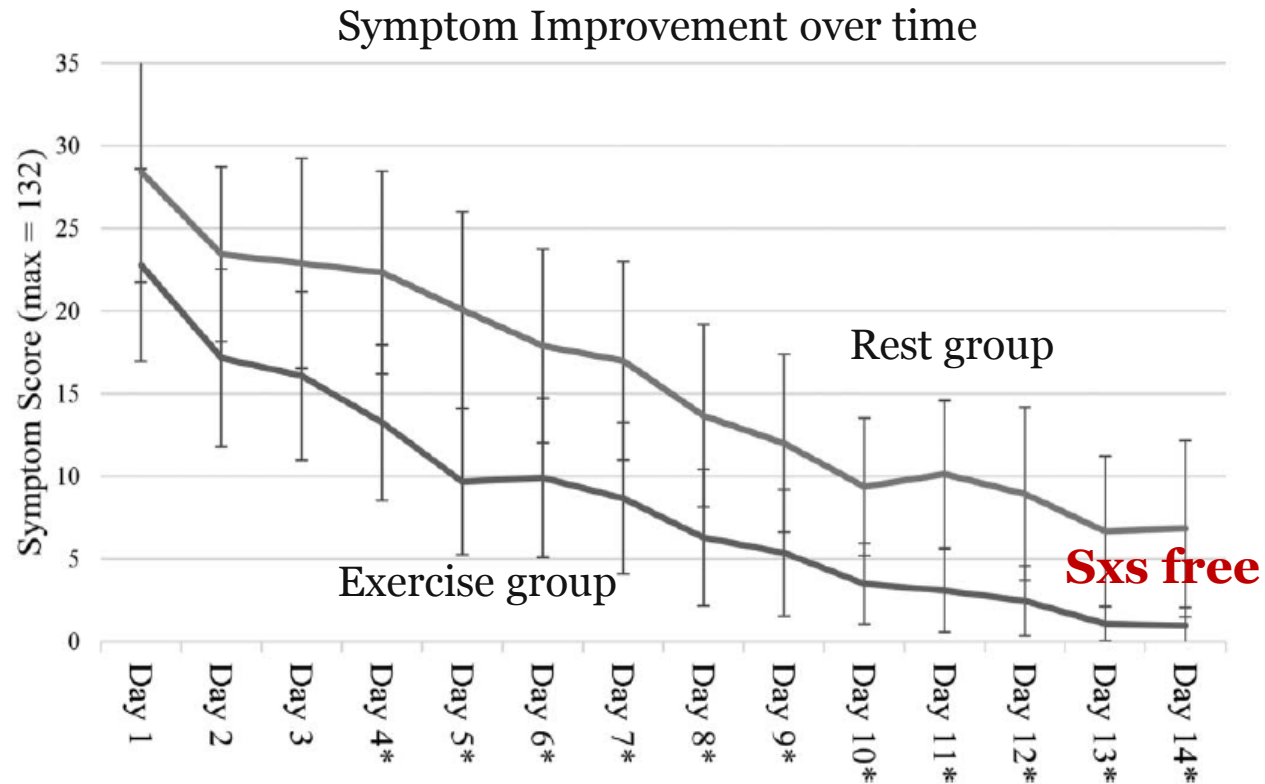
- Individuals with greatest cognitive activity had longest symptom duration.



Brown, NJ, et al. *Pediatrics*; 2014

# Does exercise help or hurt?

- Subthreshold exercise
- 80% of heart rate threshold for symptoms



Leddy, et al. *Clin J Sport Med*, 2018 epub1–8.

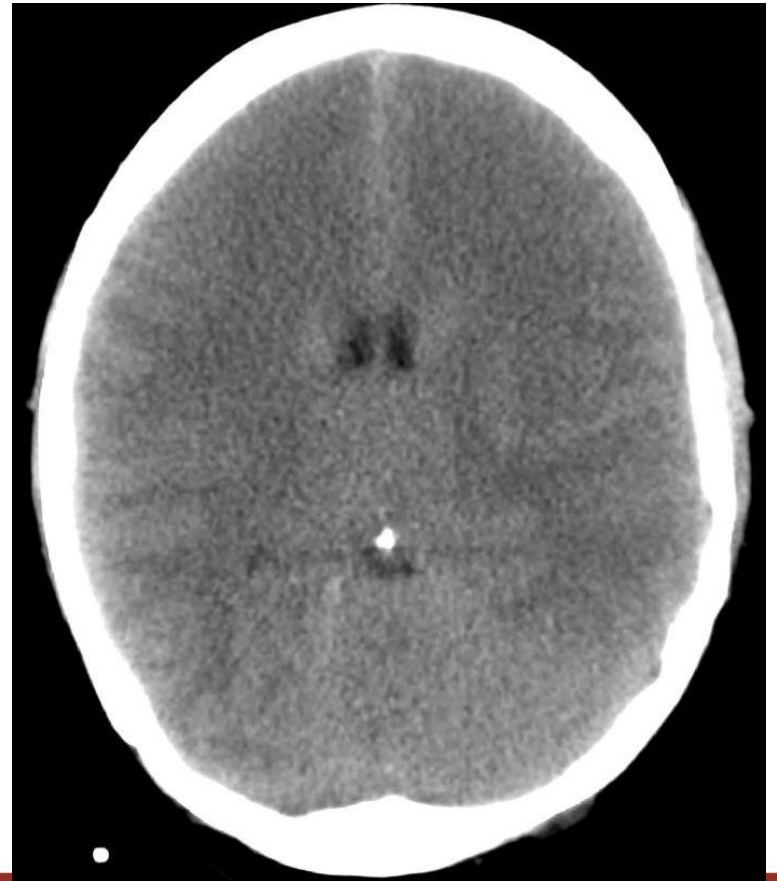
# Pharmacologic treatments

- Post-traumatic headache
  - Acute: ibuprofen or naproxen
  - If migraine: triptans
  - Preventive: amitriptyline > topiramate/zonisamide
- Nausea
  - ondansetron, prochlorperazine, metoclopramide
- Attention
- Depression/Anxiety
- Sleep dysfunction

# Can Jill go home from the ER?

# When to suspect more than a concussion

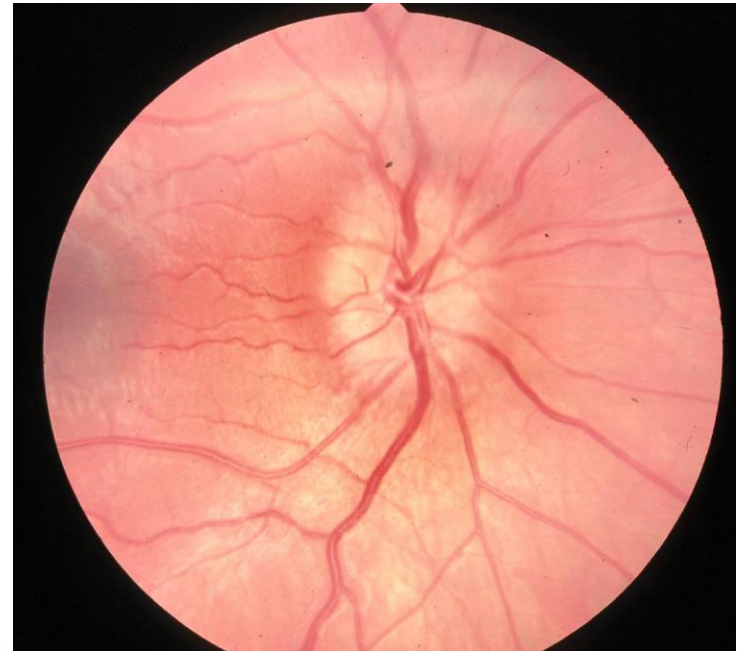
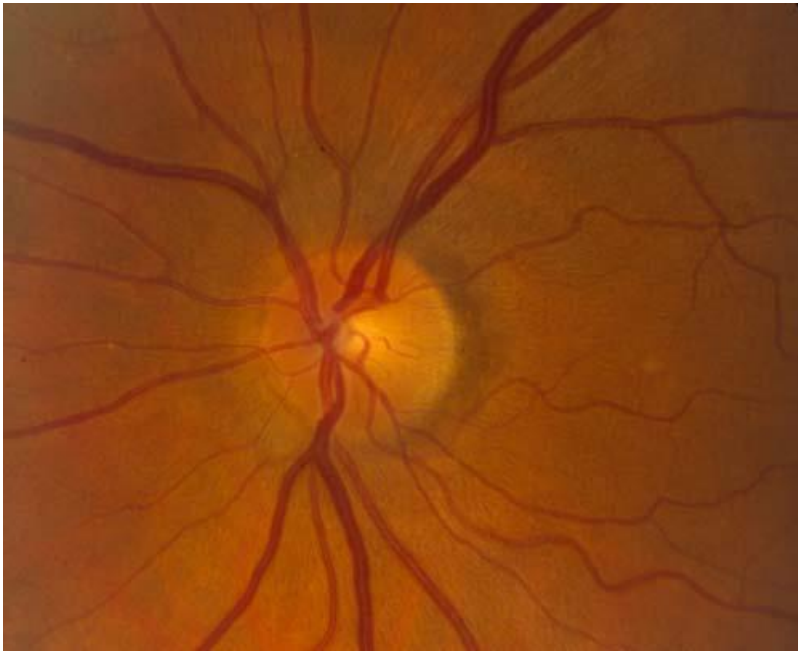
- Differentiating:





# Signs of Increased ICP

- Progressively decreasing mental status
- Papilledema (although may be normal early)



# Signs of Increased ICP

- Worsening headaches
- Focal neurologic deficits
- Cushings triad
  - Hypertension
  - Bradycardia
  - Decreased respiratory rate

# Lucid interval

- Typically 5 – 60 mins
- More often in younger kids (< 24 months)
- Can be as long as a 3 hours
- Case reports only of 12 hours and 48 hours (with arterial dissection)

Arbogast, et al. Pediatrics. 2005 Jul;116(1):180-4.

Plunkett. Am J Forensic Med Pathol. 2001 Mar;22(1):1-12.

# If concerned..

- Observe for some period of time

...6 months later

- Jill and parents come into you office
- Soccer season is coming up and Jill is working



# CTE found in former soccer players, study shows

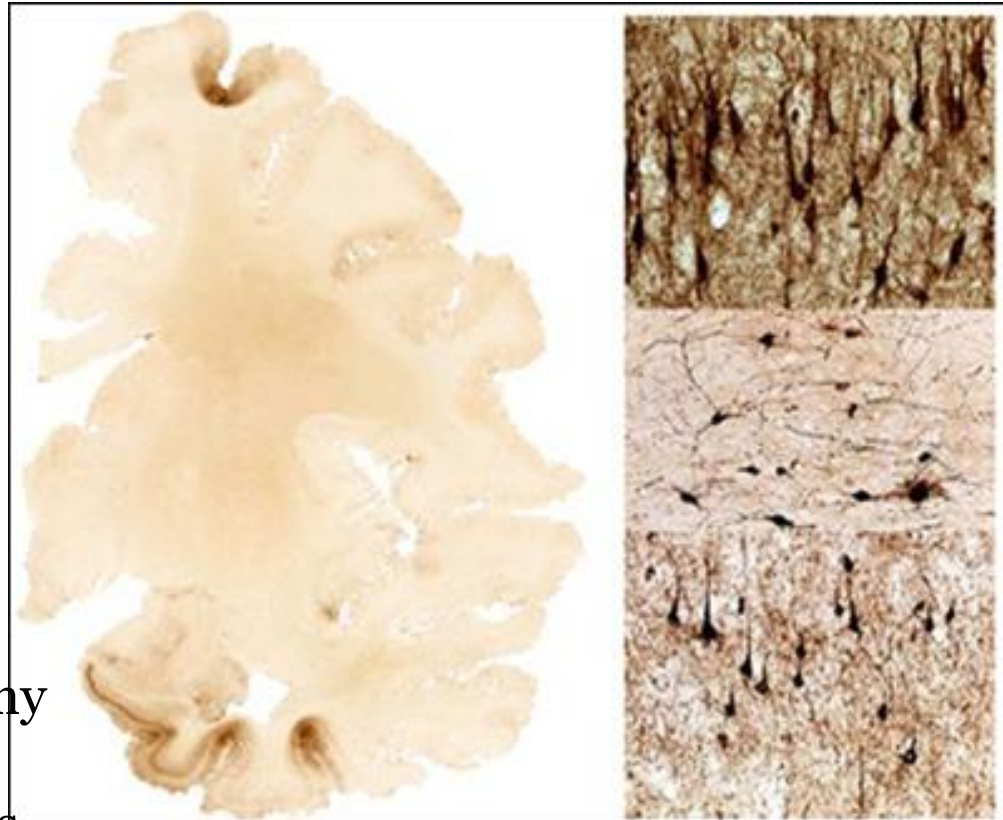
By Meera Senthilingam and Nadia Kounang, CNN

🕒 Updated 9:58 AM ET, Wed February 15, 2017



# Chronic Traumatic Encephalopathy (CTE)

- Neuropathologically
  - Atrophy of the cerebral hemispheres, medial temporal lobe, thalamus, mammillary bodies, and brainstem
- Microscopically
  - Tau-immunoreactive neurofibrillary tangles
  - Preferential involvement of superficial cortical layers, patchy distribution in frontal and temporal cortices, sulcal depths and perivascular regions

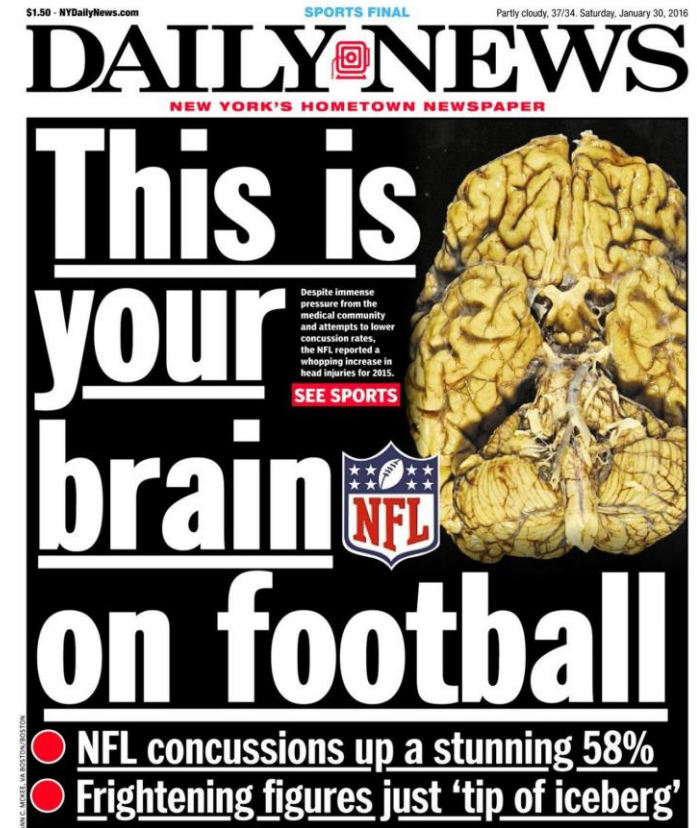




By **CHRIS CHAVEZ** July 25, 2017

A new study by Boston University researcher Dr. [unclear] brains of 202 deceased football players and four of former NFL players had chronic traumatic encephalopathy. The results were published in the Journal of the American

- 110 of 111 of NFL players
- Brains donated by concerned family members



Mez, J, et al. *JAMA*, 2017; 318(4)



# Case series

- 14 retired soccer players with dementia
  - 4 had CTE
  - 6 had Alzheimer's disease
  - 5 cerebral amyloid angiopathy
  - 5 other (Lewy body, vascular pathology)

Ling, et al. *Acta Neuropath*, 2017; 1–16.



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McKee, et al. *Brain*, 2013; 136, 43–64.

# Clinical features of CTE?

- CTE in the brains of 21 of 66 former contact sports athletes, but not in the brains of 198 without contact sports exposure
- No difference in premortem clinical characteristics

Bieniek, et al. A. E., et al. *Acta Neuropath*, 2015 130, 877–899.

# Are contact sports bad for your health?

- 3,400 NFL retirees
- Mortality rates due to cardiovascular disease, suicide, and cancer are dramatically reduced
- Suicide rate: 41% of expected
- Death rates due to AD and ALS were higher than expected, but only in "skill/speed" positions
- "Speed" position players were found to be generally healthier and live longer, therefore they would be at increased risk of late life neurodegenerative disease

Lehman, et al. *Neurology*, 2012; 79, 1970–1974.

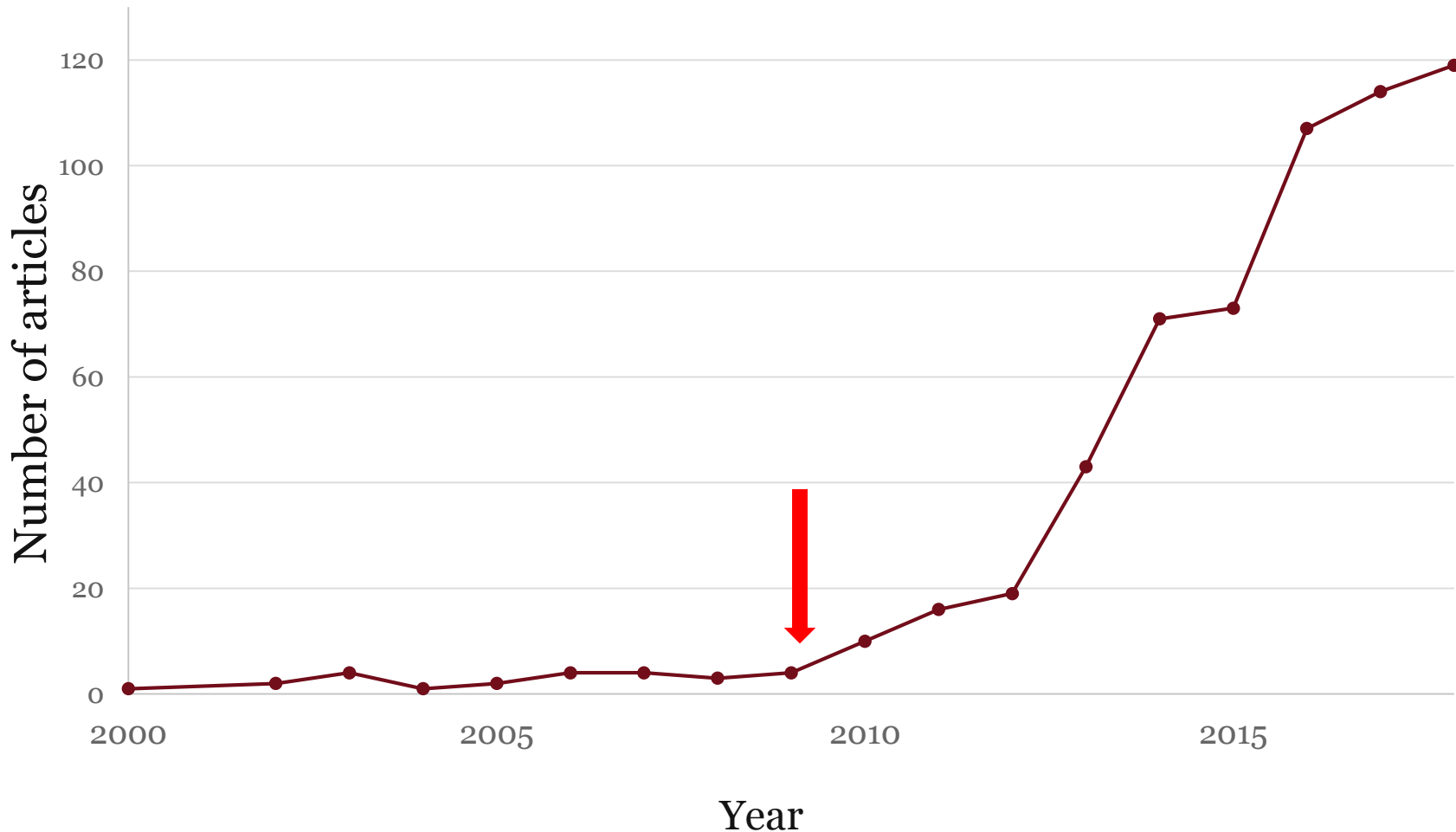
For review see: Randolph, *Arch of Clin Neuropsych*, 2018; 33; 644–648

# Suicide rates in retired NFL players

- 1920–2015
- 26,702 athletes
- 26 suicides
  - 46 % of those occurred since 2009

Webner & Iverson. *Brain Injury*, 2016: 30, 1718–1721

# Annual Pubmed articles on CTE



# Some conclusions

- TBI is an environmental risk factor for cognitive decline or dementia

- So is:

- Alcohol abuse

Schwarzinger, et al. *The Lancet Public Health*, 2018

- Anabolic steroid use

Kaufman, et al. *Drug & Alcohol Depend*, 2015; 152

- Drug use

Hulse, et al. *Int Psychogeriatr*, 2005; 27

- Marijuana

Auer, et al. *JAMA int Med*, 2016; 176(3)

- And - air pollution, aluminum, silicon, selenium, pesticides, vitamin D deficiency, and electric and magnetic fields

Killin, et al. *BMC Geriatrics*, 2016; 16, 175

# Summary

- Moderate TBI – Avoid secondary injuries
- Mild TBI
  - ~ 75 % will be recover by 28 days
  - Early rehabilitation, particularly for those with premorbid conditions
- To date there is no causal relationship between head impacts and CTE

# Collaborators

**Neurology:** Chris Smyser, Chris Gurnett, Jon Zempel, Mike Morrissey, Stuart Tomko, Jen Griffith, Sarah Bauer-Huang, Susan Hibits, Mike Noetzel, Brad Schlaggar

**Critical Care:** Julie Bubeck-Wardenburg, Mary Hartman, Jose Pineda, Stuart Friess, Erin Murphy

**Neurosurgery:** Dave Limbrick, Jen Strahle, Sean Mcvoy

**NCFP:** Jon Dodd, Chris Bosworth Sara Small, Celine Zidar



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