Head injuries, dementia and the brain

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THE HUMAN BRAIN

- The brain is the most complex organ in the body.
- **“Powerful computer”**
  - Controls how we think and move
  - Stores our memories
  - Influences our emotions – fear, anxiety, happiness, sadness, etc.

DID YOU KNOW?

The brain contains **billions** of nerve cells that send and receive information around the body.

Information can go in between parts of your brain at a **speed of >400 kmh.**

DID YOU KNOW?

The brain of an adult human weighs around 3 lbs.

Although it makes up just 2% of the body's weight, it uses around **20% of its energy.**

WHAT ABOUT PROTECTION FROM INJURY?

Brain is protected by the **skull (cranium)**, a protective casing made up of 22 bones that are joined together.

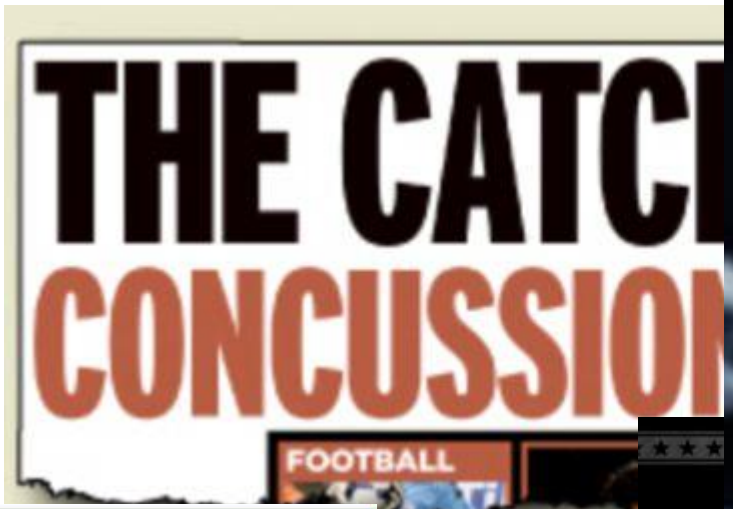
The brain is **suspended in fluid**, effectively floating in liquid that acts as both a cushion to physical impact and a barrier to infections.

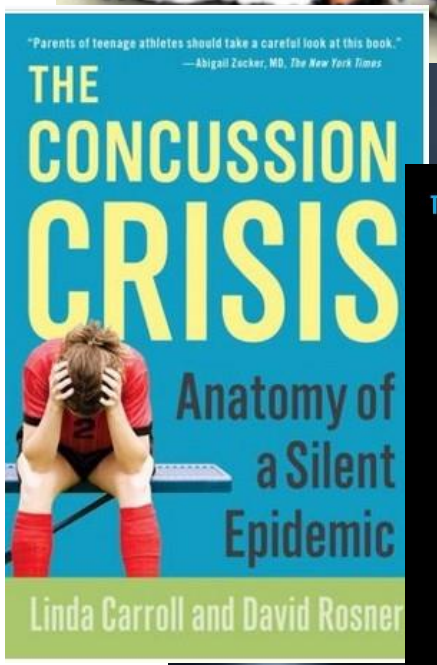
THE RISK OF INJURY

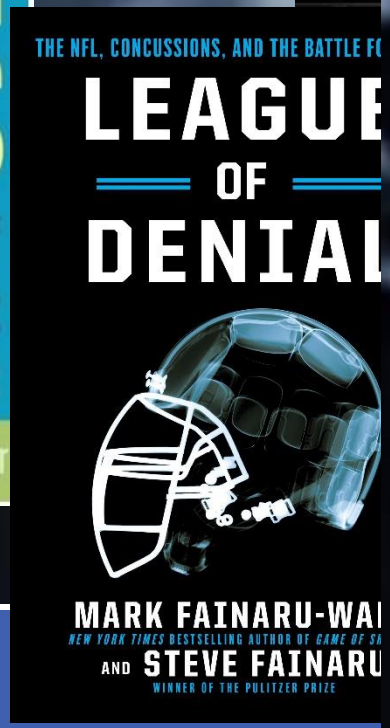
- Physical activity / sport has **numerous benefits**
  - Prevent / manage health problems
  - Improve your mood
  - Boosts your energy / improves your sleep
  - Social benefits – working together, communication, etc.

- Unfortunately, there is a risk for injury

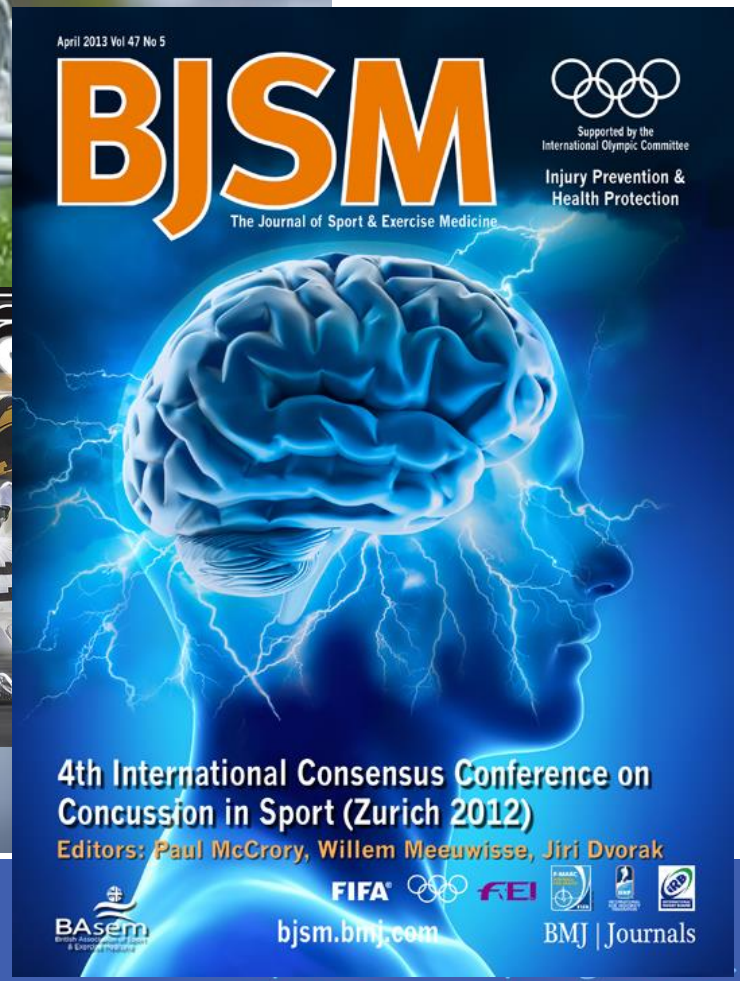
- What about mild injury – Concussions?



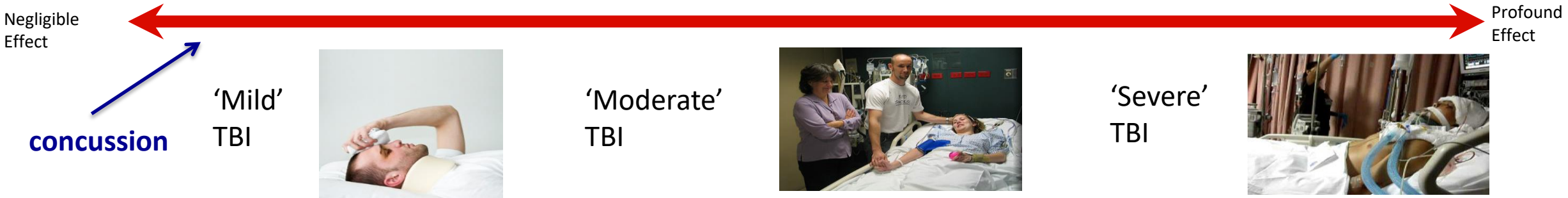




research organizations



The Continuum of Traumatic Brain Injury



- Concussion
  - a brain injury and is defined as a complex pathophysiological process induced by biomechanical forces.

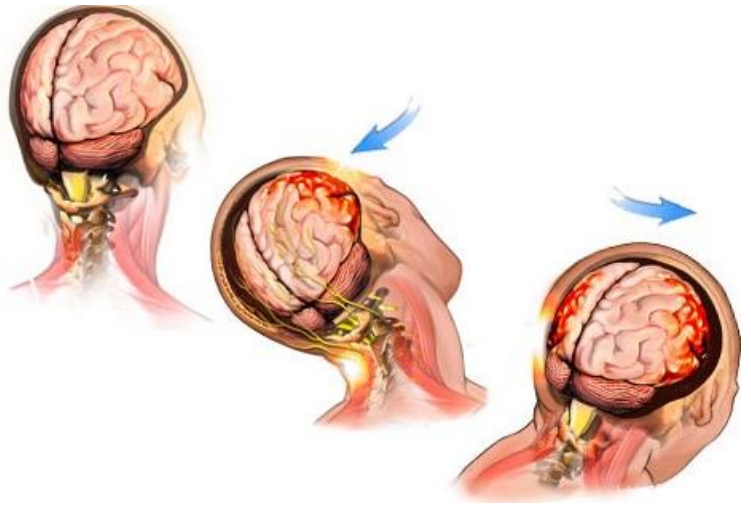
(Concussion in Sport Consensus Statement, 2013)

- *Operationally defined* by …

Event (Acc. of Head) + **[Signs +/or Symptoms]**

RISK OF INJURY

- It is important to recognize **concussion = brain injury**
  - "mild" traumatic brain injury



- How do they happen?
  - **Rapid acceleration / deceleration**
    - Meaning how quickly an individual or object changes
    - Its speed with respect to time
    - Coup and Contrecoup Injury

- One of the most common neurologic conditions worldwide, with over 4 million cases/year in North America

Skull Base

GENERAL FEATURES OF CONCUSSIONS

- Majority direct head trauma (85%+)
- < 10% - probable or possible LOC (“knocked out”), majority no LOC
- 15-20% Amnesia (Pre and/or Post)

Clinical syndrome

- Reliance on symptoms and observations of others

SYMPTOMS OF CONCUSSION

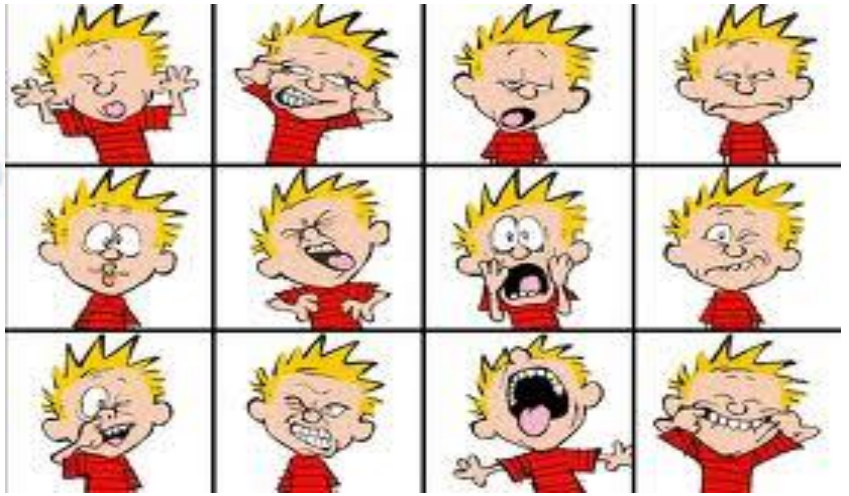
Physical

- Headache
- Nausea, feel like vomiting
- Neck / head pain
- Difficulty with balance
- Sleep disturbances

Cognitive

- Feeling “off” or “in a fog”
- Disorientation/dazed
- Difficulty concentrating
- More forgetful

Emotional & Sensory



- Irritable
- Sadness/Depression
- Fatigue
- Anxiety
- Sensitive to light and sound

WHAT SYMPTOM IS MOST COMMON?

DIFFICULTY WITH READING

HEADACHE

FATIGUE

DIFFCULTY WITH BALANCE

WHAT'S THE MINIMUM NUMBER OF SYMPTOMS FOR A CONCUSSION?

3

2

1

4

WHAT TO DO IF YOU SUSPECT A CONCUSSION?

1. Remove yourself from the activity = **INITIAL REST**.
2. Tell someone!

DANGEROUS SIGNS & SYMPTOMS OF A CONCUSSION

- One pupil larger than the other.
- Drowsiness or inability to wake up.
- A headache that gets worse and does not go away.
- Slurred speech, weakness, numbness, or decreased coordination.
- Repeated vomiting or nausea, convulsions or seizures (shaking or twitching).
- Unusual behavior, increased confusion, restlessness, or agitation.
- Loss of consciousness (passed out/knocked out). Even a brief loss of consciousness should be taken seriously.

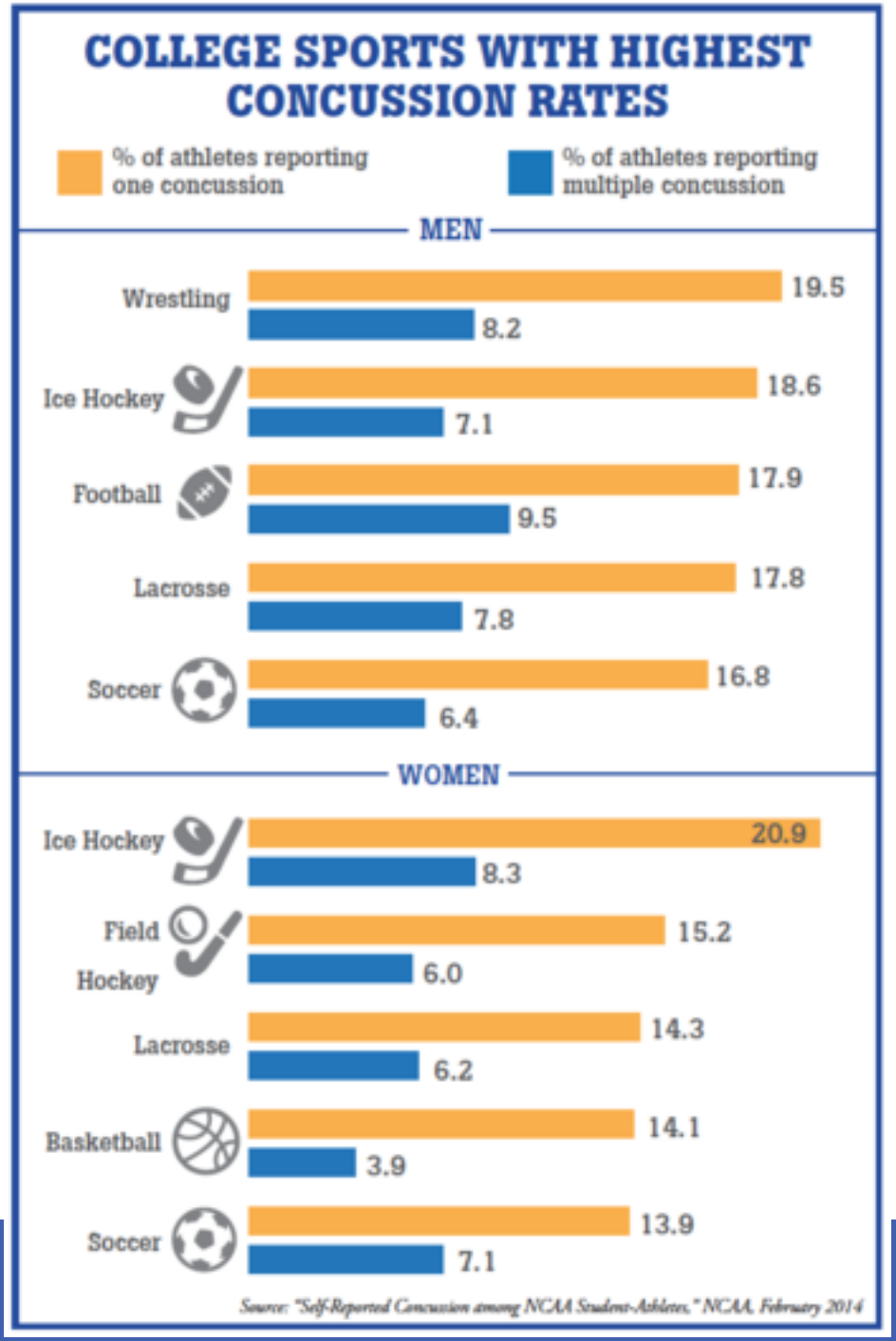
MILD TBI - CONCUSSION

- Among individuals 15 to 24 years of age, sports are second only to motor vehicle crashes as the leading cause of concussions.

- The most common mechanisms of injury were player-player contact (70.3%) and player–playing surface contact (17.2%).

Marar et al., 2012

COLLEGE SPORTS WITH HIGHEST CONCUSSION RATES



Source: "Self-Reported Concussion among NCAA Student-Athletes," NCAA, February 2014

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What about older adults?

TBI – Older Adults (65+)

- TBIs in adults 65 years and older is estimated at 237,844/year
- More than 80,000 emergency department (ED) visits each year
- ¾ of these visits result in hospitalization.
  - Falls are the leading known cause representing 2/3 of the total.
  - motor vehicle traffic–related TBI (8%), struck by or against objects (6%), assaults (1%)

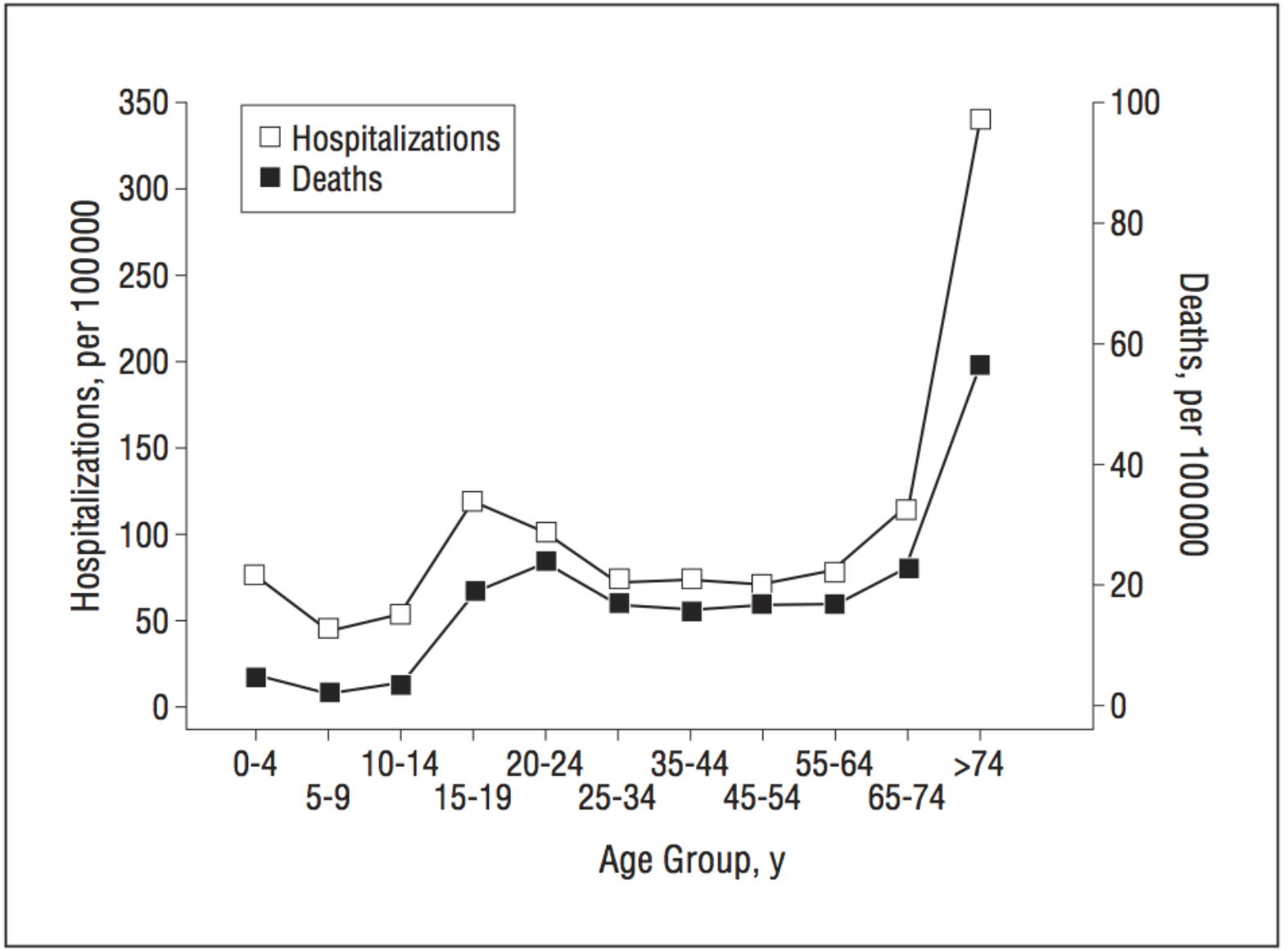
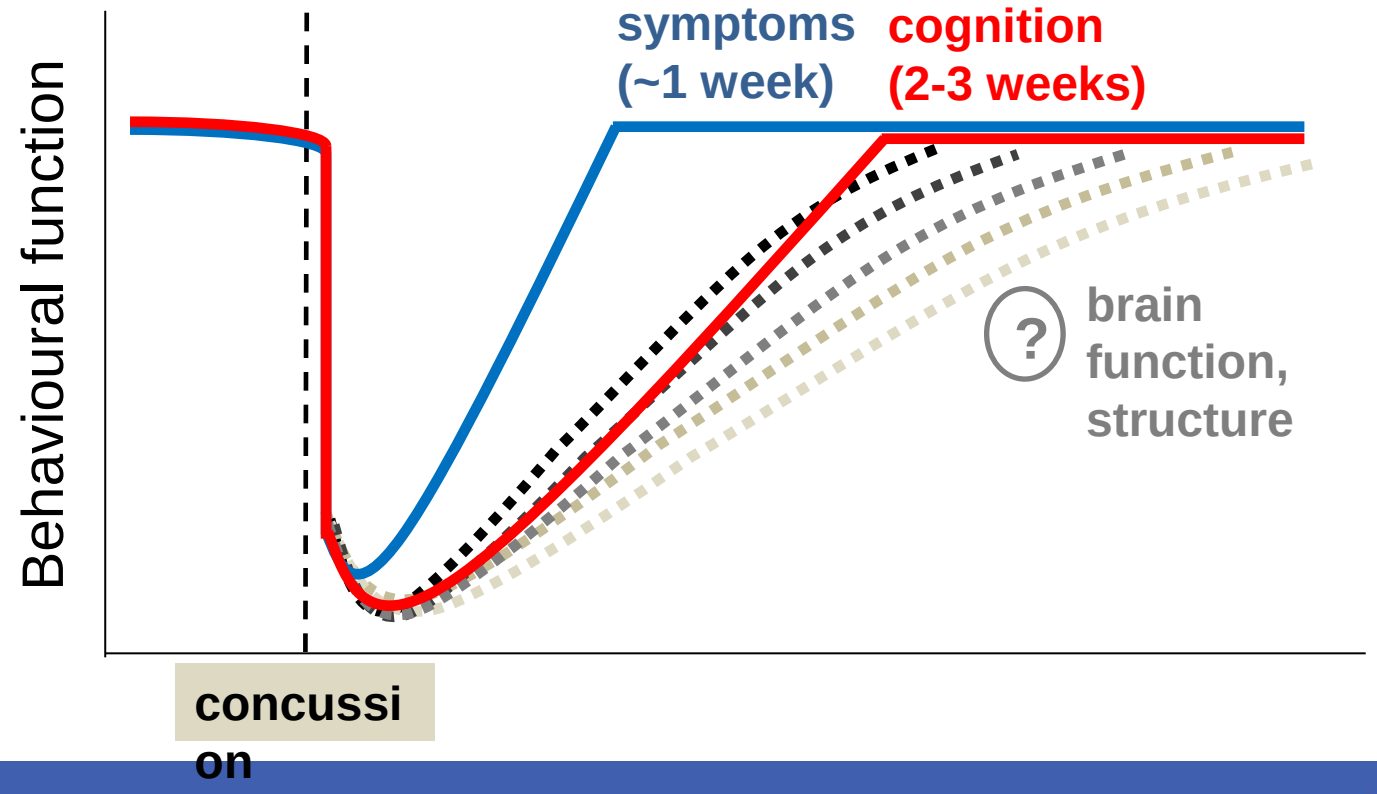


Figure 1. Annual rate of traumatic brain injury–related hospitalizations and deaths, by age. Adapted from Faul et al.[5]

THE SCIENCE BEHIND CONCUSSION AND RECOVERY AFTER BRAIN INJURY

MAPPING THE TRAJECTORY OF RECOVERY

- Clinical recovery based on clinical symptoms and brief cognitive tests (SCAT, ANAM)
- Indirectly related to the (unknown) course of brain recovery



GAPS IN OUR UNDERSTANDING OF SPORT CONCUSSION

When is brain recovery complete?

- Symptoms recover before cognition and brain function, (Hutchison et al., 2009; McCrea et al., 2010)
- Can we improve clinical guidelines for RTP?

COLLABORATION

Strong partnership between St. Michael's Hospital and University of Toronto Sports Medicine Clinic

Progress to Date:

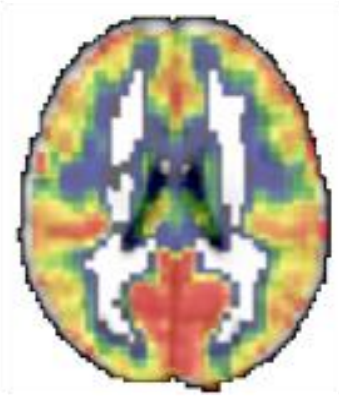
- Scanned athletes over the course of concussion recovery (along with 218 uninjured athlete controls):
- The first week after injury (100 athletes)
- At time of medical clearance (86 athletes)
- 1-month after medical clearance (45 athletes)
- 1-year after medical clearance (36 athletes)

SMH-MRI PROTOCOL

- Athletes scanned during a 1-hour Magnetic Resonance Imaging (MRI) session
- Collected multiple different measures of brain structure, function and metabolism

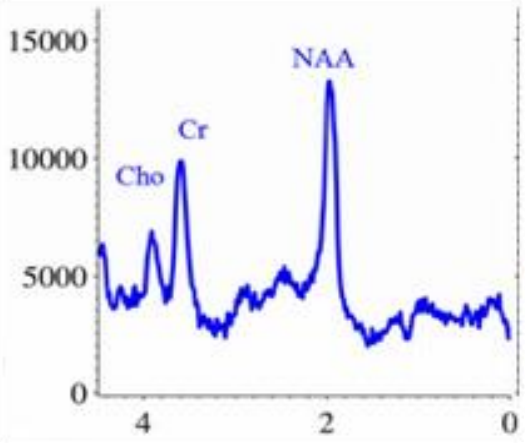
Neuroanatomy
T1, FLAIR, SWI

Brain function
Functional MRI



Blood flow
Arterial Spin Labelling

White matter
Diffusion Tensor Imaging



Brain metabolites
Single-voxel spectroscopy

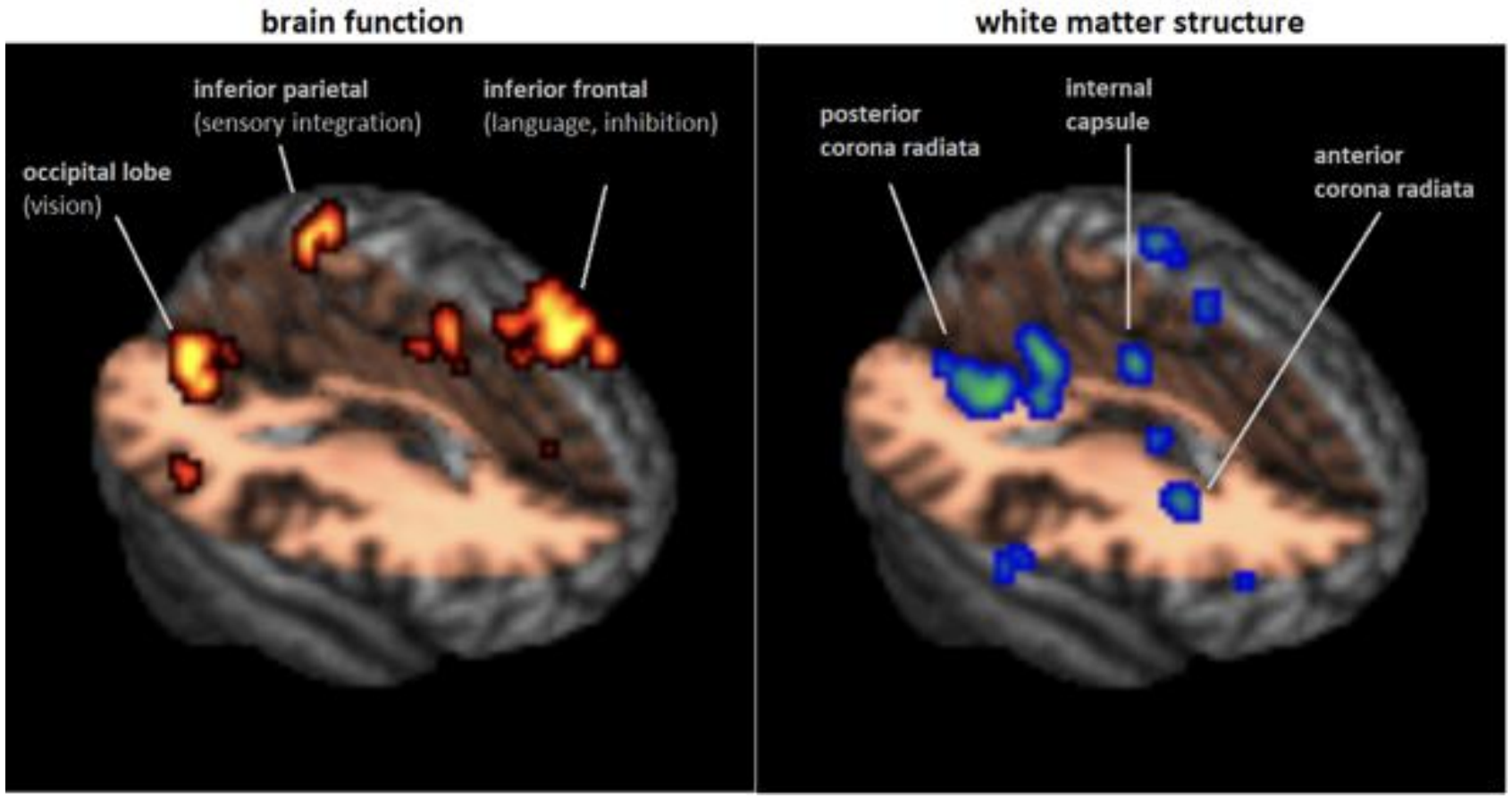
GAPS IN OUR UNDERSTANDING OF SPORT CONCUSSION

When is brain recovery complete?

- Symptoms recover before cognition and brain function, (Hutchison et al., 2009; McCrea et al., 2010)
- Can we improve clinical guidelines for RTP?

- **What does the brain look like at the time of RTP compared to uninjured control athletes?**

- Significant differences in brain activity and white matter remain at the time of medical clearance (return to play)



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HEALTH August 24, 2017 4:00 am Updated:

University athletes with concussio show changes in the brain after m clearance to play

By Dani-Elle Dubé
National Online Journalist, Smart Living Global News

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BREAKING Census: Education rates, commute times and time at work all growing

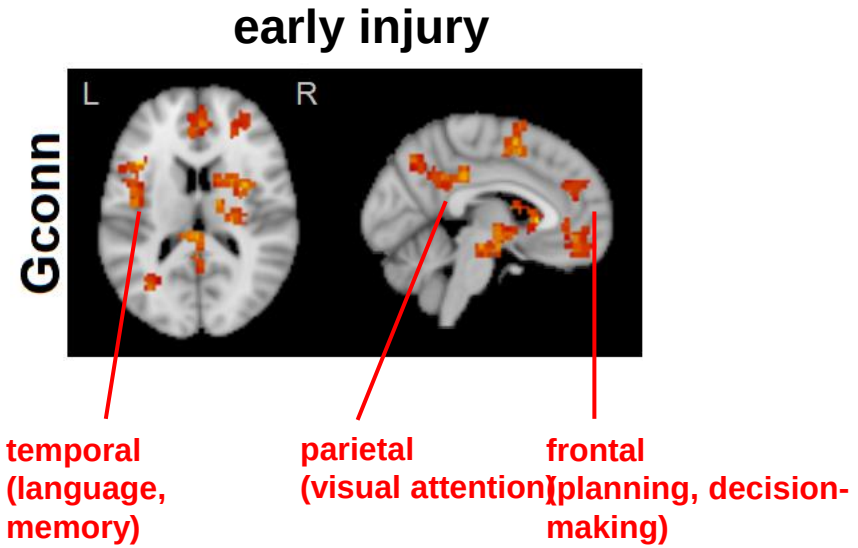
Brain recovery 'lagging' after sports concussion

AFP

Published Thursday, August 24, 2017 3:08PM EDT

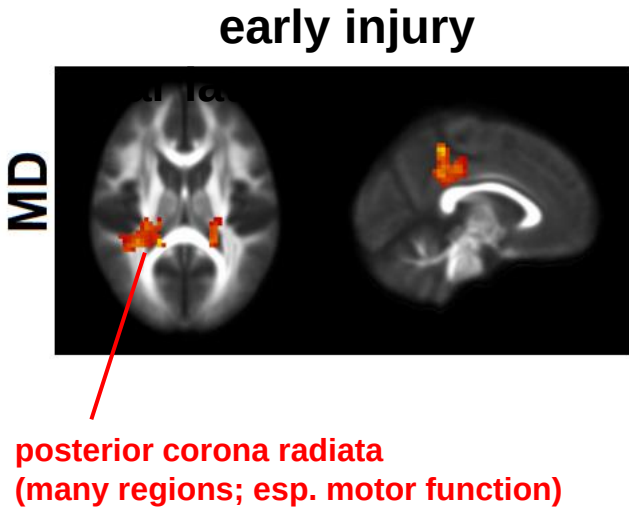
Rs-fMRI AND BRAIN RECOVERY

- Brain areas show higher connectivity after injury – “hyper-communication” between areas
- Possible causes: may be an adaptive mechanism (more redundancy) to protect against re-injury



DTI AND BRAIN RECOVERY

- White matter has high diffusivity after injury – signs of tissue swelling
- Possible causes: disrupted cell environment, injury to blood-brain barrier, inflammation



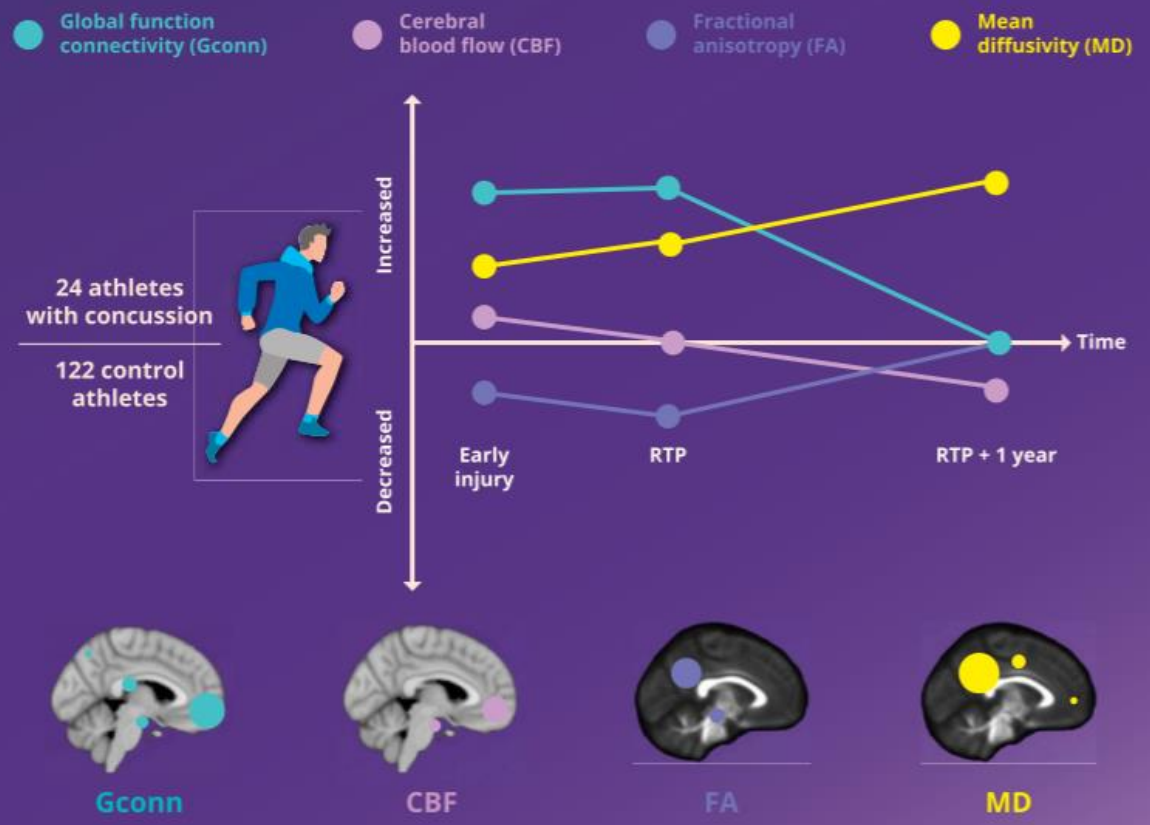
The Physiology of Concussion Recovery

Diagnosis and prognosis (i.e. return to play [RTP] decisions) of concussion are mainly determined by symptom evaluation

However, the underlying injury and course of recovery remain unknown

Study question

Does brain recovery lag clinical recovery postconcussion?



Different physiologic aspects of the brain have different concussion recovery times, which can be observed using MRI

doi:10.1212/WNL.0000000000008523

Neurology®

Churchill NW, Hutchison MG, Graham SJ, Schweizer TA. **Neurology**. 2019 Nov 19;93(21):e1980-e1992.

GAPS IN OUR UNDERSTANDING OF SPORT CONCUSSION

Long-term health consequences of contact exposure in sport

- What is the risk of repeated exposure on brain health?

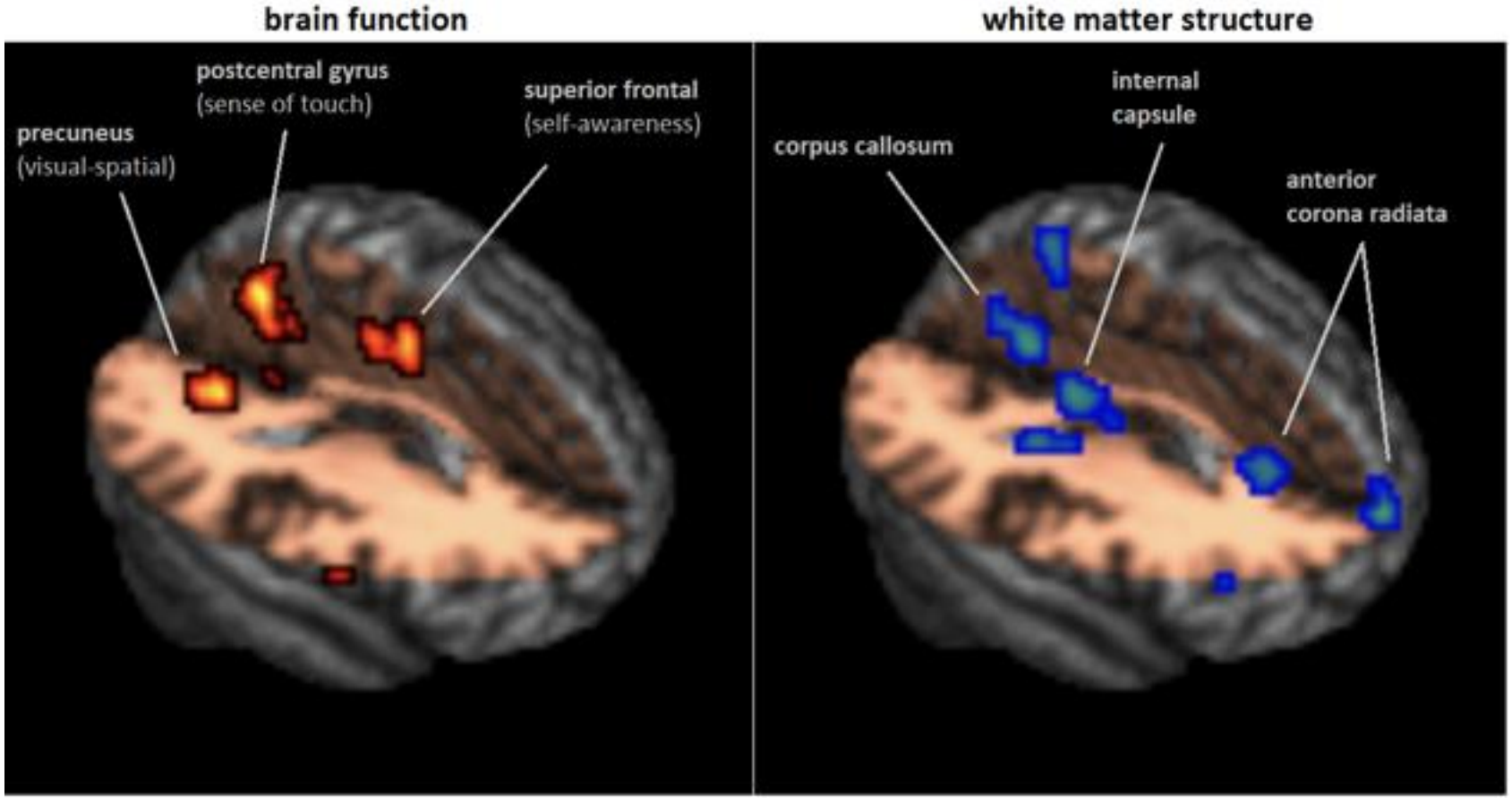
CONTACT VS NON-CONTACT

- Scanned the brains of 65 athletes at the start of their season

- Including non-contact sports (volleyball), limited contact (soccer, basketball, field hockey) and higher-risk collision sports (ice hockey, football, rugby)

- Examined differences in brain activity and white matter structure between different contact sport groups

- Athletes in higher-risk collision sports showed changes in brain activity and white matter, despite no acute injury



CONCUSSIONS

Brain scans reveal impact of contact sports even on young, healthy athletes: study

Contact sports are causing noticeable brain changes in otherwise healthy young athletes, a new study shows

By Abigail Miller For Dailymail.com
04:41 22 Aug 2017, updated 11:37 22 Aug 2017

What about older adults?

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 7, 2019 VOL. 381 NO. 19

Neurodegenerative Disease Mortality among Former Professional Soccer Players

Daniel F. Mackay, Ph.D., Emma R. Russell, M.Sc., Katy Stewart, Ph.D., John A. MacLean, M.B., Ch.B., Jill P. Pell, M.D., and William Stewart, M.B., Ch.B., Ph.D.

Former Professional Soccer Players

Table 2. Primary Cause of Death among Former Soccer Players and Matched Controls.

Primary Cause of Death	Former Soccer Players (N = 7676)	Matched Controls (N = 23,028)	Hazard Ratio for Death (95% CI)	P Value*
	number (percent)			
Any cause†	1180 (15.4)	3807 (16.5)	0.87 (0.80–0.93)	<0.001
Ischemic heart disease	173 (2.3)	568 (2.5)	0.80 (0.66–0.97)	0.02
Lung cancer	74 (1.0)	362 (1.6)	0.53 (0.40–0.70)	<0.001
Neurodegenerative disease	134 (1.7)	120 (0.5)	4.10 (2.88–5.83)‡	<0.001

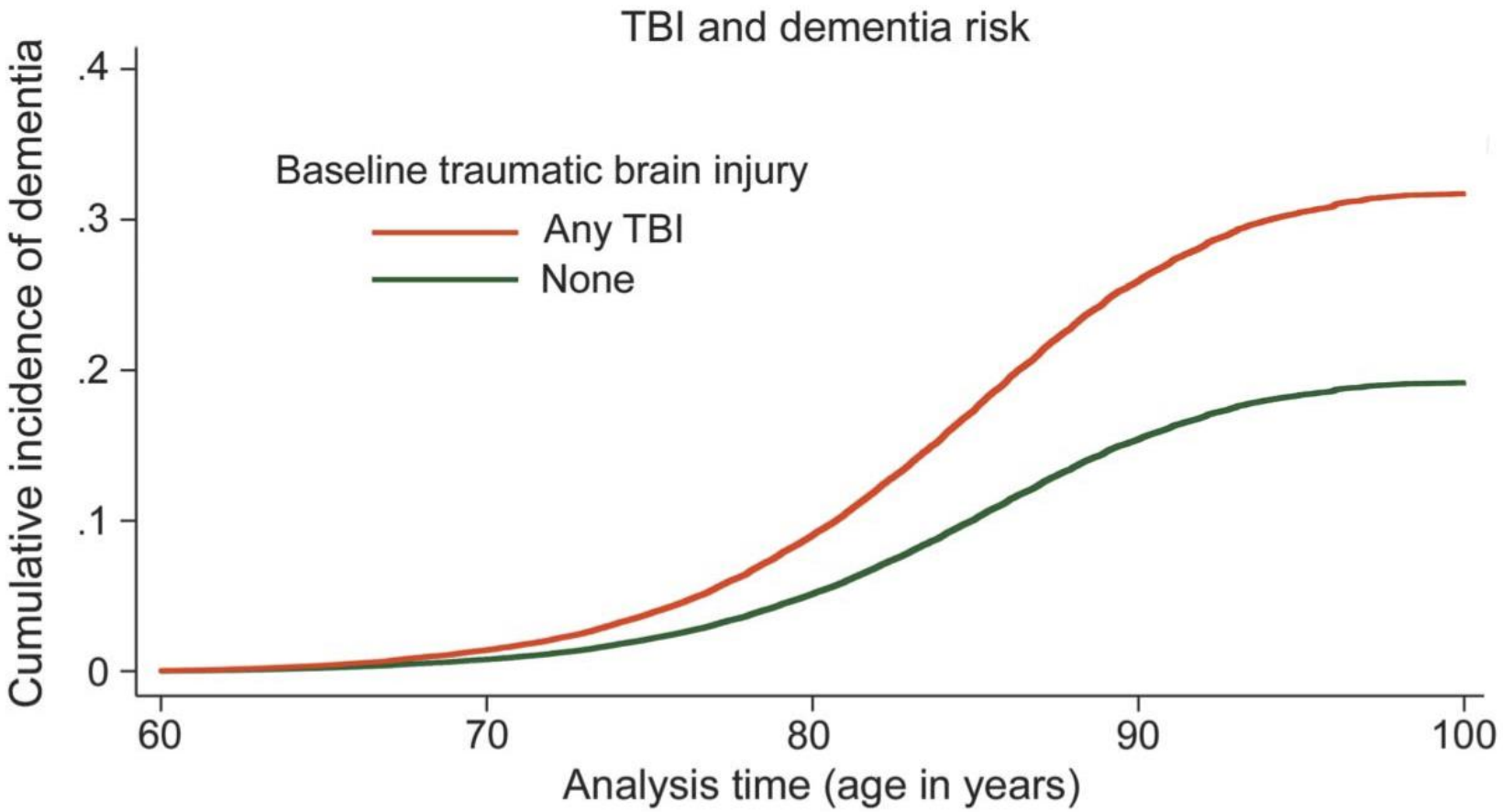
Dementia and TBI – Older Adults

- Past 30 years, research has linked moderate and severe TBI to a greater risk of developing AD or another dementia years after the original head injury.
- Older adults with history of moderate TBI had a 2.3 times greater risk of AD
- Severe TBI had a 4.5 times greater risk
- There’s no DIRECT evidence that a single mTBI increases dementia risk.

Dementia and TBI – Older Adults

- However, repeated mTBIs, may be linked to a greater risk of dementia.
- History of TBI may accelerate the age of onset of cognitive impairment by two or more years
- Might be associated with an earlier age of onset in people with mild cognitive impairment and Alzheimer's disease.

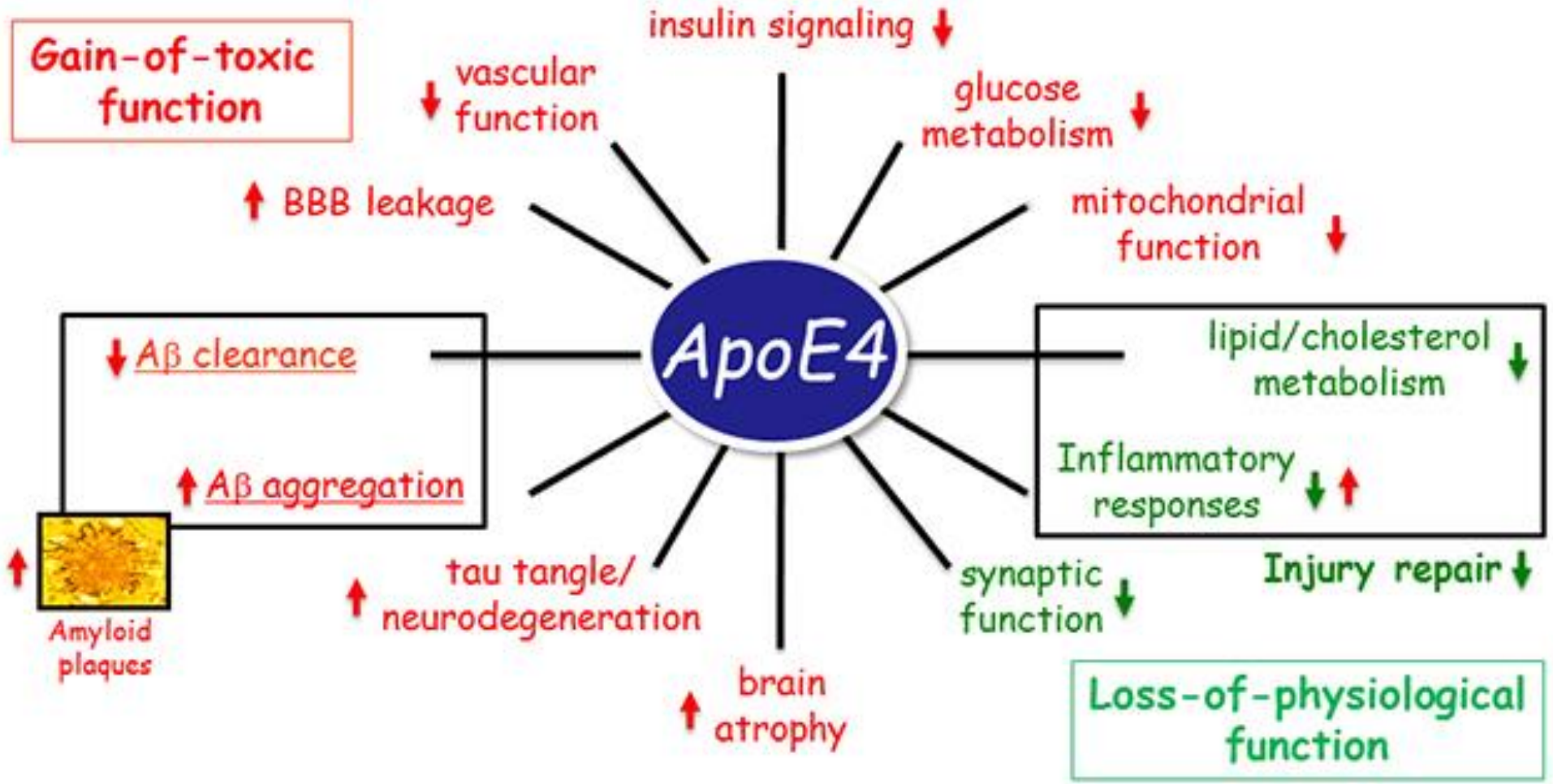
Figure 1 **Age at dementia diagnosis in veterans with and without TBI, accounting for mortality**



The cumulative incidence of dementia is shown for veterans with traumatic brain injury (TBI) at baseline (orange) and without TBI at baseline (green), accounting for the competing risk of mortality. Age is used as the time scale to indicate age at dementia diagnosis.

Is APOE a factor?

- The APOE gene makes a protein that helps carry cholesterol and other types of fat in the bloodstream
- APOE ε4, present in approx. 10-15% of people, increases the risk for Alzheimer's and lowers the age of onset.
- Having one copy of E4 (E3/E4) can increase your risk by 2 to 3 times while two copies (E4/E4) can increase the risk by 12 times



Is APOE a factor?

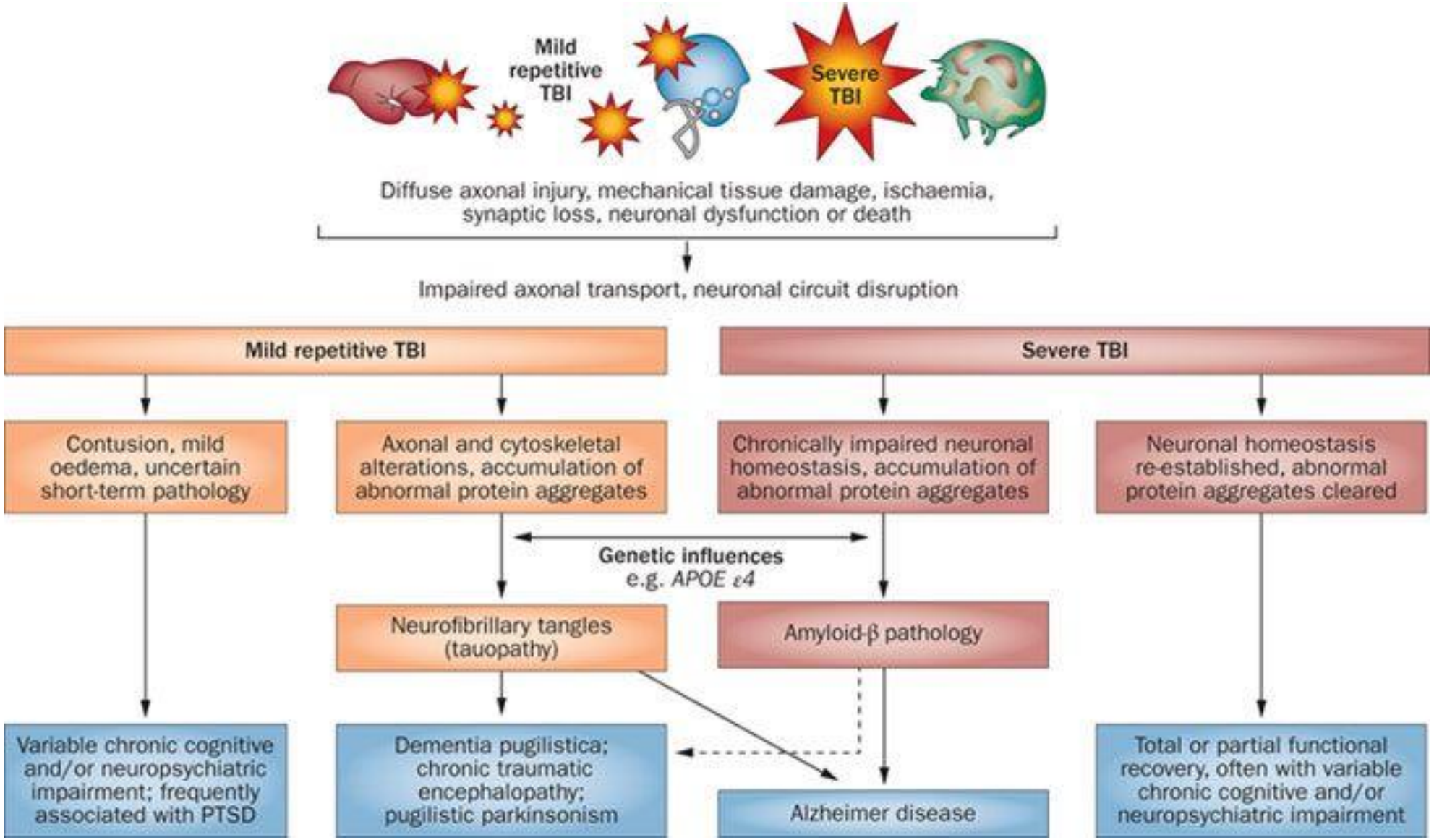
- Some research suggests that TBI may be more likely to cause dementia in individuals who have a variation of the gene for apolipoprotein E (APOE) called APOE-e4.
- Genetic testing for APOE or other genetic variants cannot determine an individual's likelihood of developing AD—just which risk factor genes a person has.

APOE and mTBI history

Table 2. Odds ratios of dementia by *APOE* genotype and past mild head injury

HEAD INJURY	APOE ε4 STATUS (CARRIER)	DEMENTIA	CONTROLS	OR (95% CI)
No	No	82	231	1.0 (ref.)
No	Yes	74	85	3.0 (1.9–4.7)*
Yes	No	12	36	0.9 (0.4–1.8)
Yes	Yes	13	10	5.2 (2.0–14.0)*

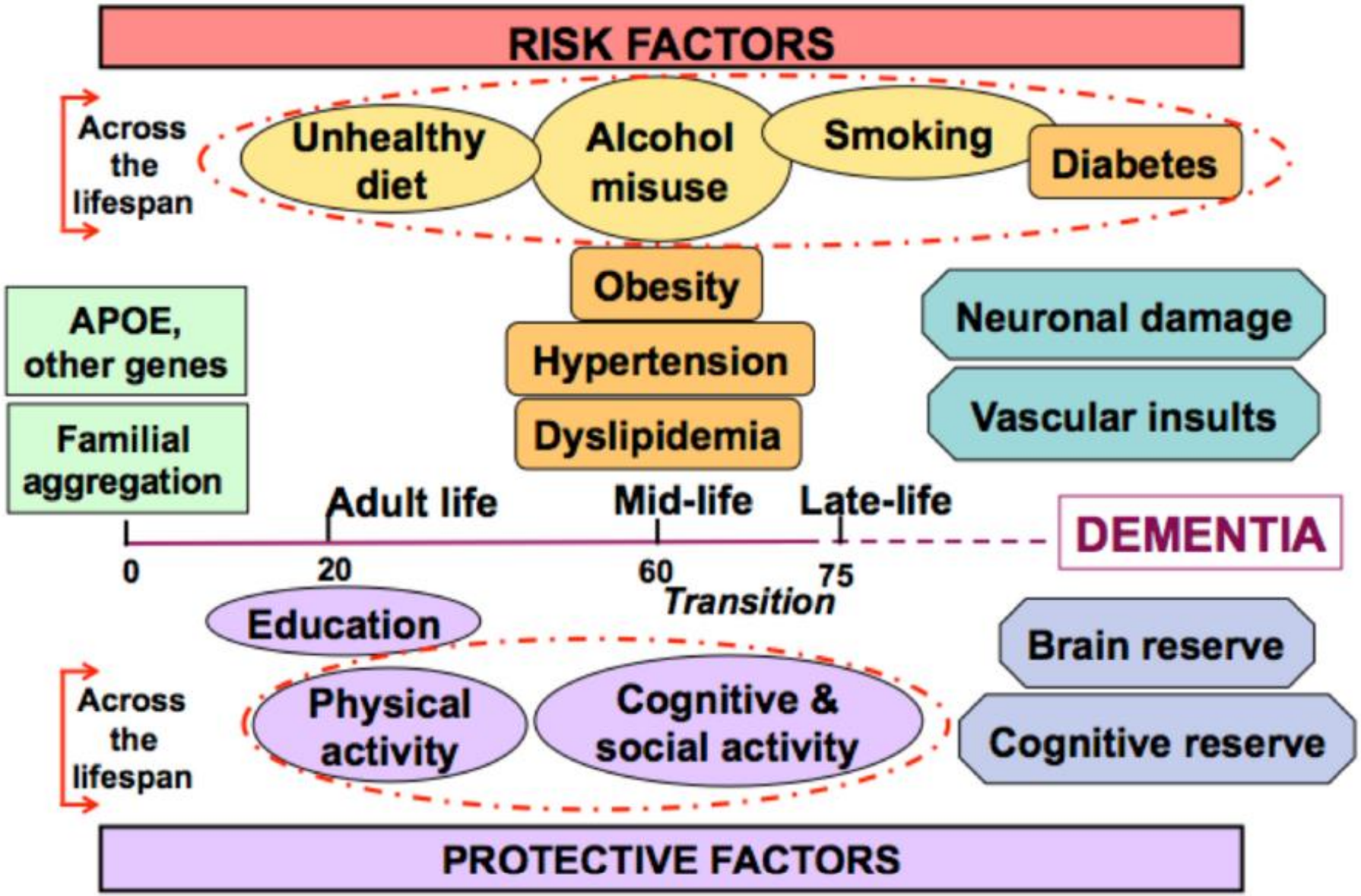
APOE = apolipoprotein E; OR = odds ratio; CI = confidence interval. *$p < 0.001$.



Federico Grosso (2014)

Other Risk Factors to Consider?

It’s Complicated……



Sindi et al., 2015

Conclusions

- The effects of concussion can be long-lasting – MRI data 1-year post!
- Moderate to severe TBI is a risk factor for dementia
- Repeated mTBI **may** increase risk
- Other important factors to consider:
  - APOE status
  - Diabetes
  - Hypertension
  - Smoking, Diet etc…..

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