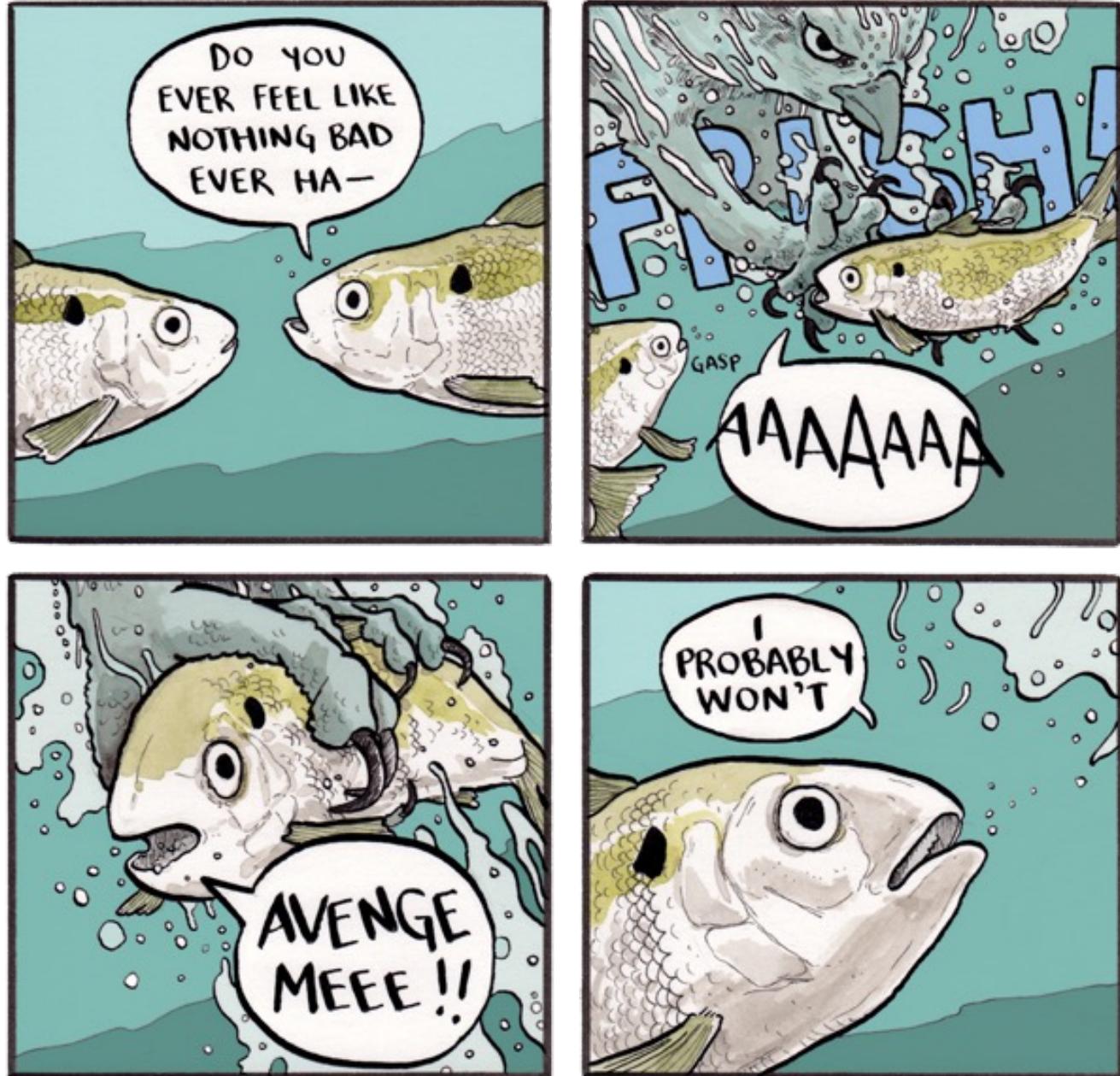


# PSYC301: (Some) Causes of brain dysfunction

Jay Hosking, PhD



# Lecture overview: part I

Brain tumours

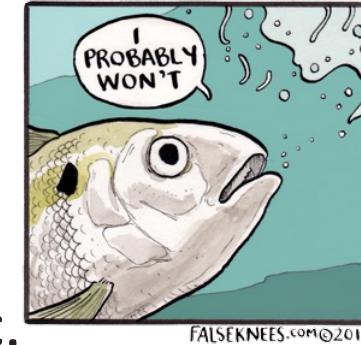
Strokes

Head injuries



FALSEKNEES.COM ©2018

# Learning objectives part I



1. Describe these terms as related to tumours:  
encapsulated vs. infiltrating, benign vs. malignant, metastatic.
2. Identify and describe one encapsulated and one infiltrating tumour we discussed.
3. What should the doctor be trying to save in a stroke?
4. Identify regions in stroke, types of stroke, and causes of stroke.
5. Describe and compare two methods of dealing with an aneurysm.
6. What is excitotoxicity? What causes it? How is it related to this lecture?  
(For the future:) How is it related to other topics?
7. Describe these terms in head injuries: closed vs. open, contusion vs.  
mTBI, concussive vs. subconcussive mTBI.
8. What is CTE? What causes it? What is one marker of CTE? How does  
this marker relate to other diseases? Why is diagnosis currently a  
problem in CTE?

# Encapsulated tumours

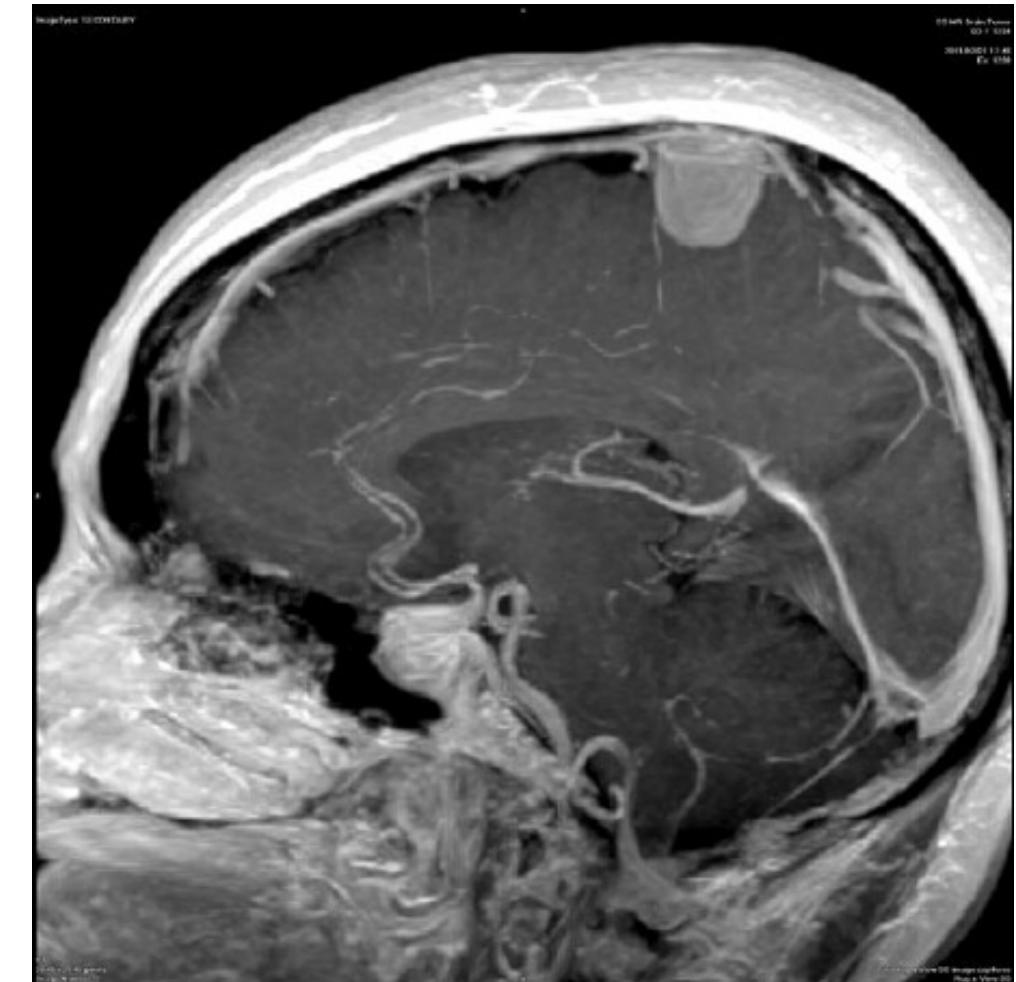
Tumours, aka neoplasms

Here: meningioma

Grow between the meninges

Encapsulated

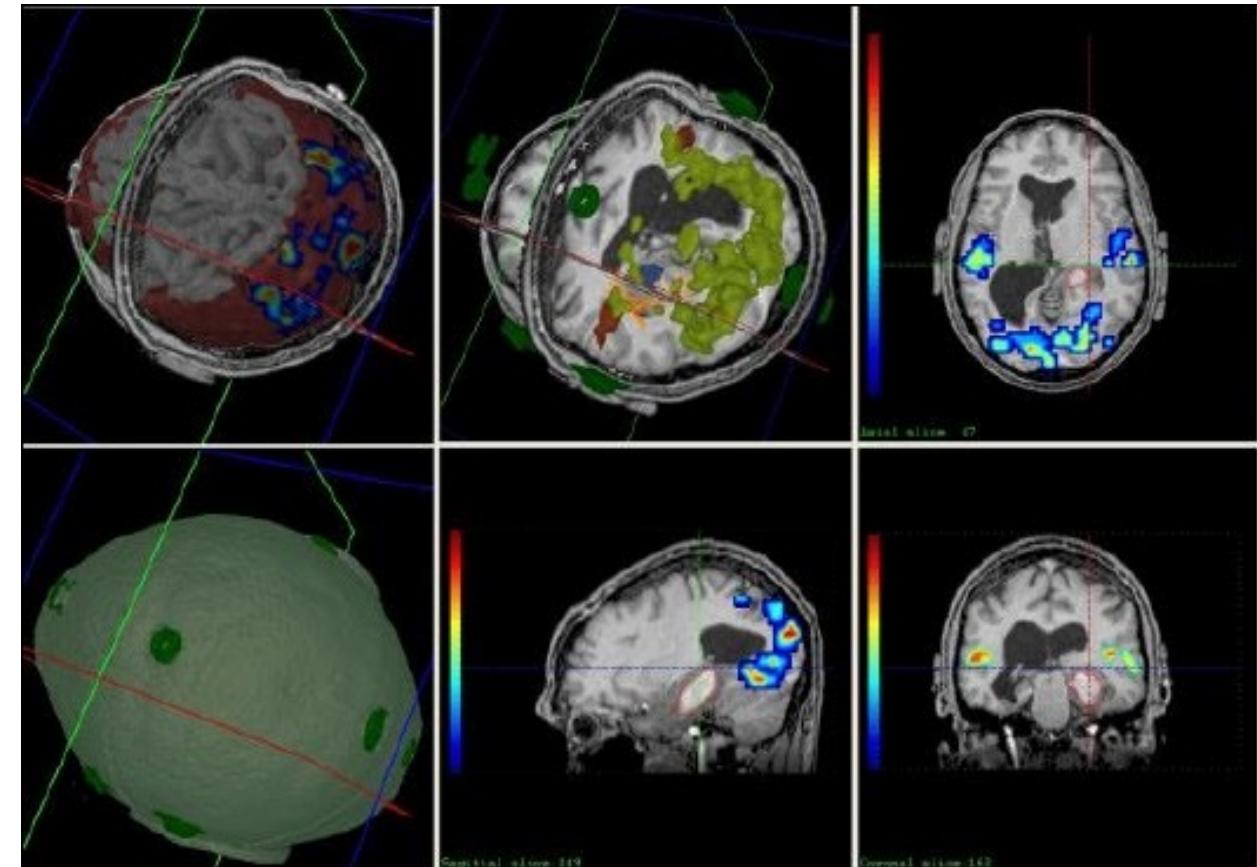
Benign



# Infiltrating tumours

Grow diffusely through surrounding brain tissue

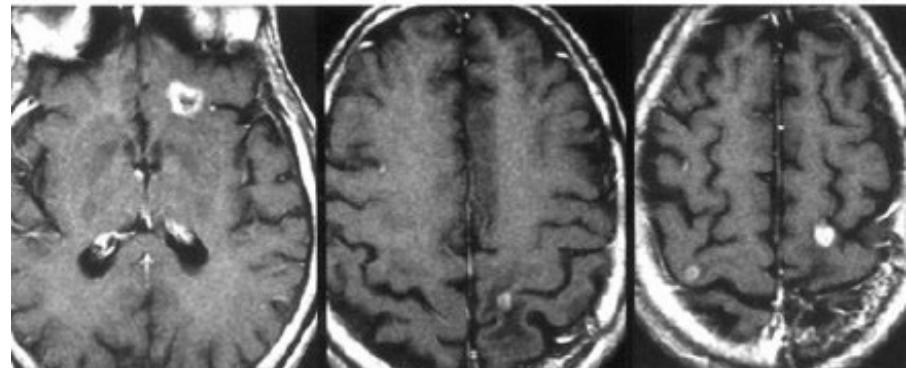
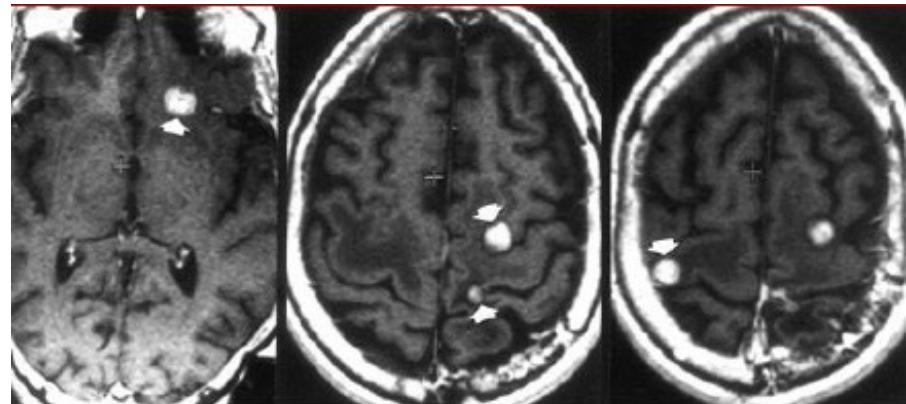
Malignant



# Metastatic tumours

Some infiltrating brain tumours grow from tumour fragments carried to the brain from another body part via the bloodstream

Commonly originate from a breast cancer or a lung cancer



# Glioblastoma



Gord Downie

Bob Moog

Brain tumours

## Box 1 | WHO classification of brain tumours

### Astrocytic tumours

- Diffuse astrocytoma (grade II)
- Anaplastic astrocytoma (grade III)
- Glioblastoma (grade IV)

### Oligodendroglial tumours

- Oligodendrogioma

### Mixed gliomas

- Oligoastrocytoma

### Ependymal tumours

- Ependymoma

### Neuronal and mixed tumours

- Gangliocytoma

### Neuronal/glial tumours

- Dysembryoplastic neuroepithelial tumour
- Ganglioglioma

### Embryonal tumours

- Medulloepithelioma
- Ependymoblastoma
- Neuroblastoma

### Primitive neuroectodermal tumours

- Medulloblastoma

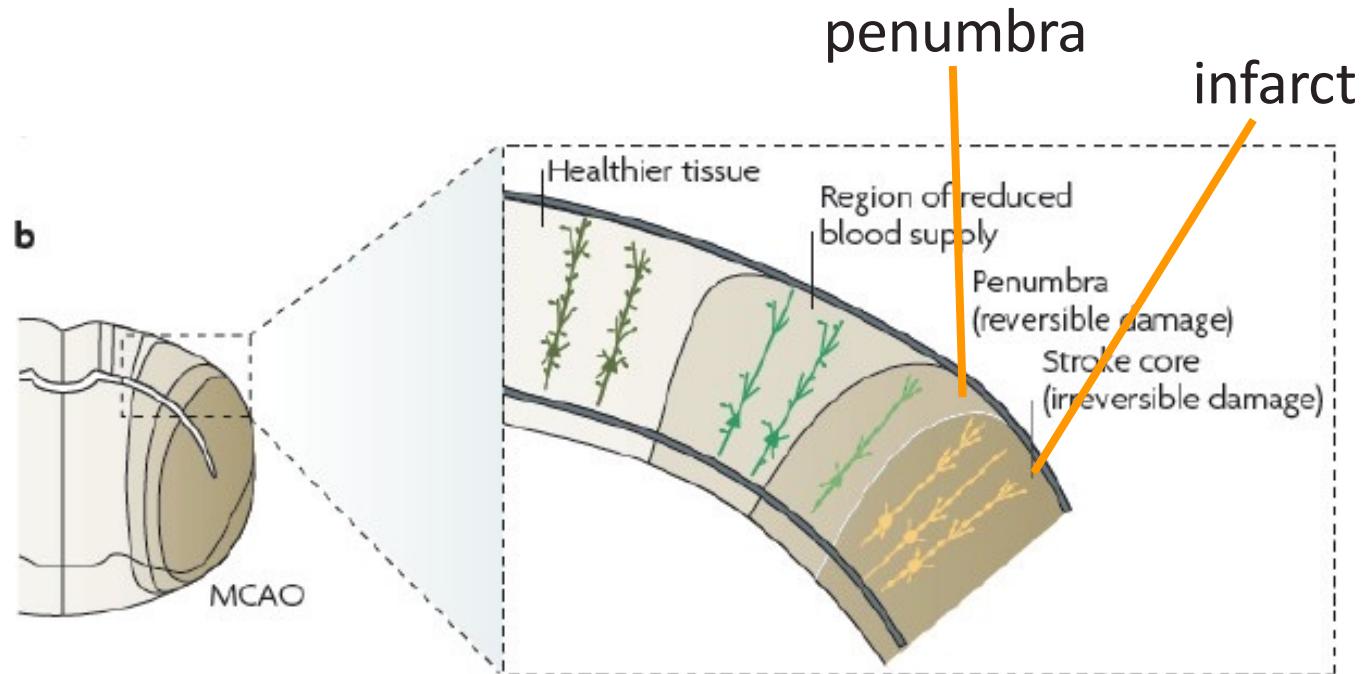
most common type  
of malignant brain  
tumour in adults  
(aka: glioma)

Most malignant  
Short survival rate

Strokes are sudden-onset cerebrovascular disorders that cause brain damage

Infarct: area of dead/dying tissue

Penumbra: dysfunctional area surrounding the infarct; tissue in penumbra may either recover or die



Strokes

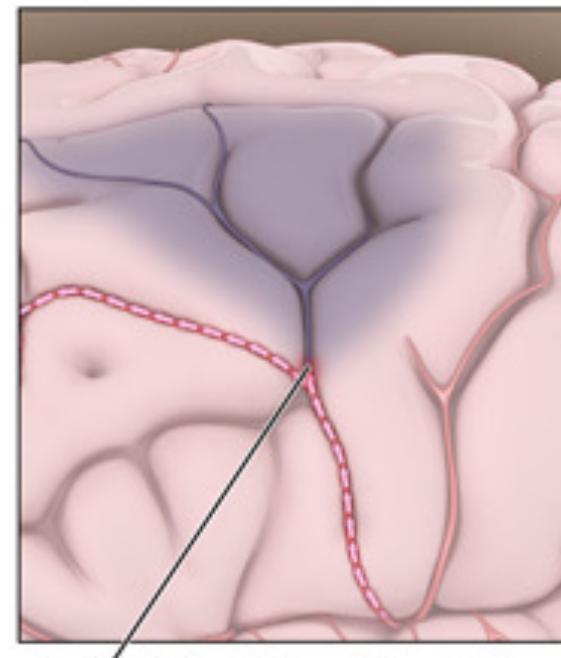
from Murphy & Corbett, 2009

# Types of stroke

Ischemic, i.e. resulting from cerebral ischemia

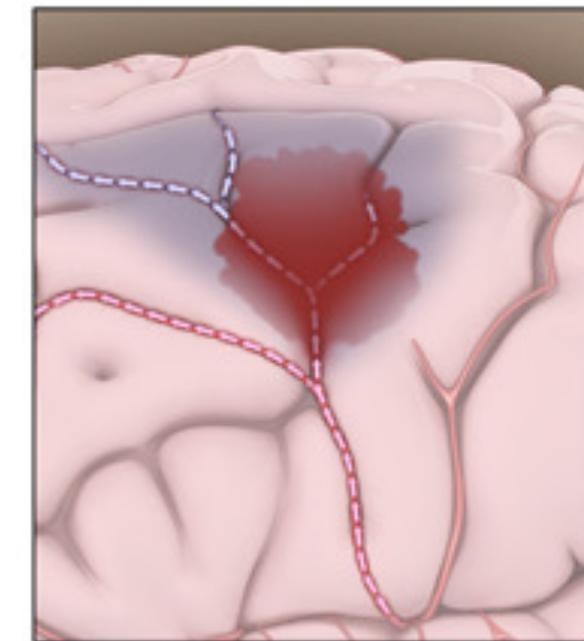
Hemorrhagic, i.e. resulting from cerebral hemorrhage

Ischemic stroke



A clot blocking blood flow  
to an area of the brain

Hemorrhagic stroke



Bleeding inside or around  
brain tissue

# Cerebral hemorrhage: aneurysm

Can be congenital or develop later

Commonly at base of brain  
(e.g. Circle of Willis)

Risk factors: diabetes, hypertension,  
smoking cigarettes, alcoholism, **aging**

Usually artery

Two common treatments:

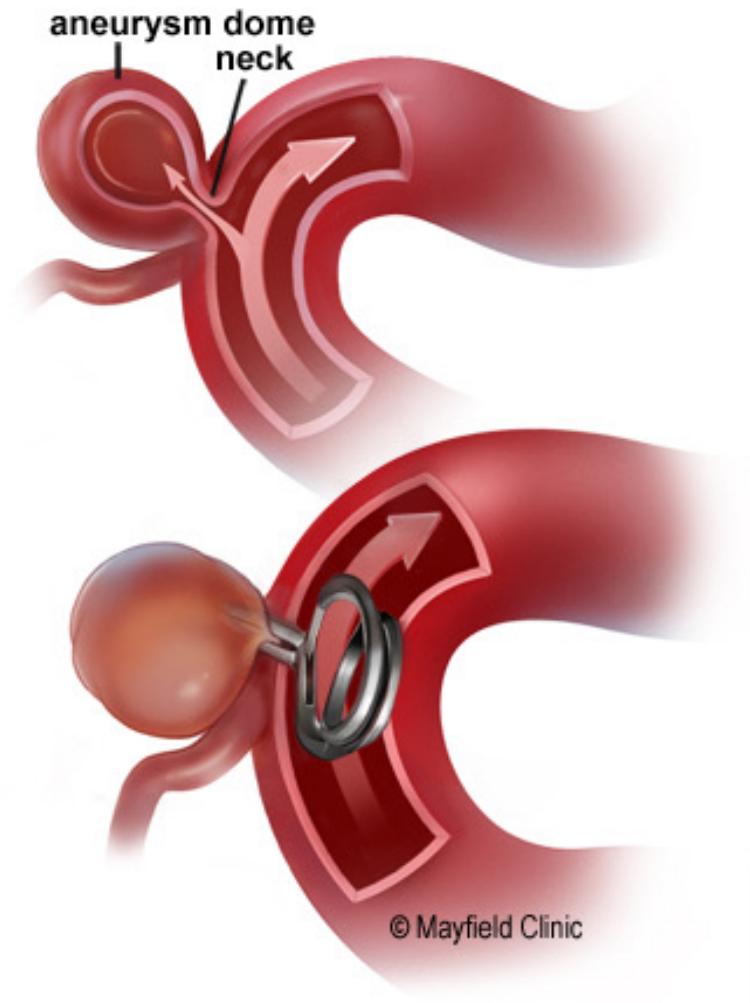
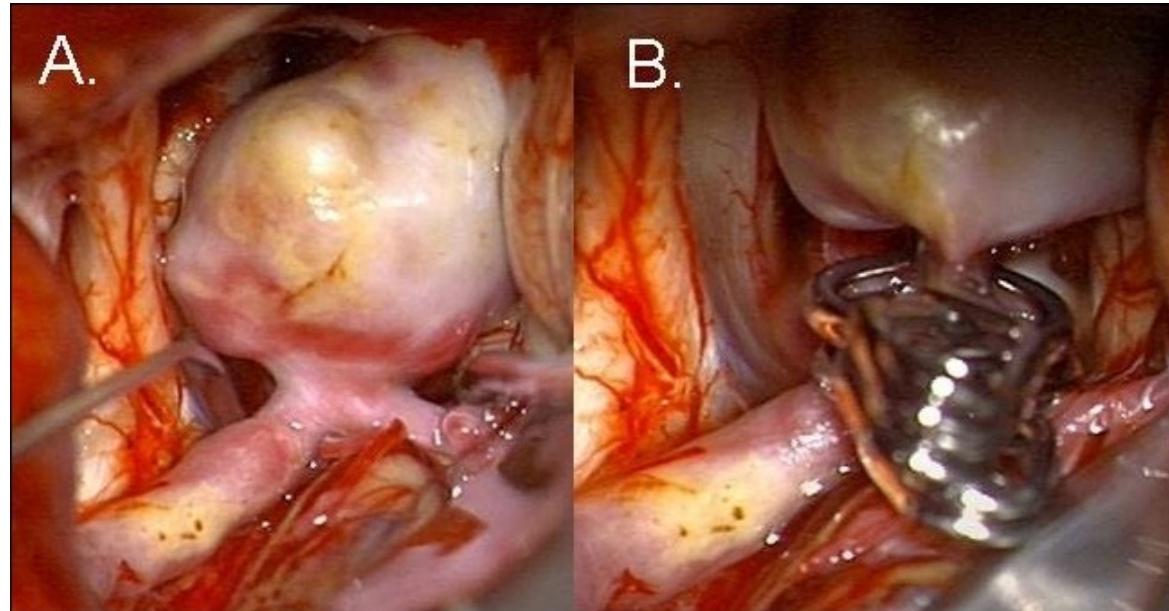


# Cerebral hemorrhage: aneurysm

Treatment option 1:

Clipping

Requires craniotomy, but slightly lower rate of recurrence than option 2



# Cerebral hemorrhage: aneurysm

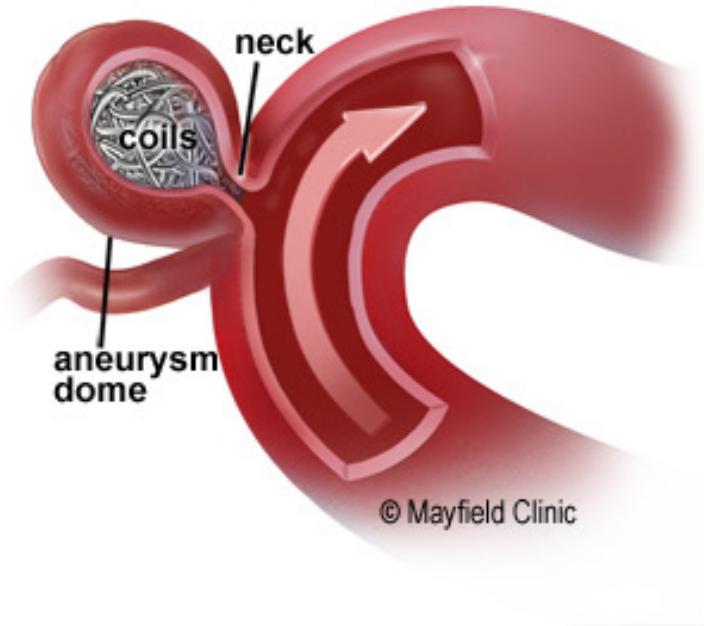
Treatment option 2:

Endovascular coiling

Much less invasive, but slightly higher rate of recurrence than option 1



Strokes



Femoral artery

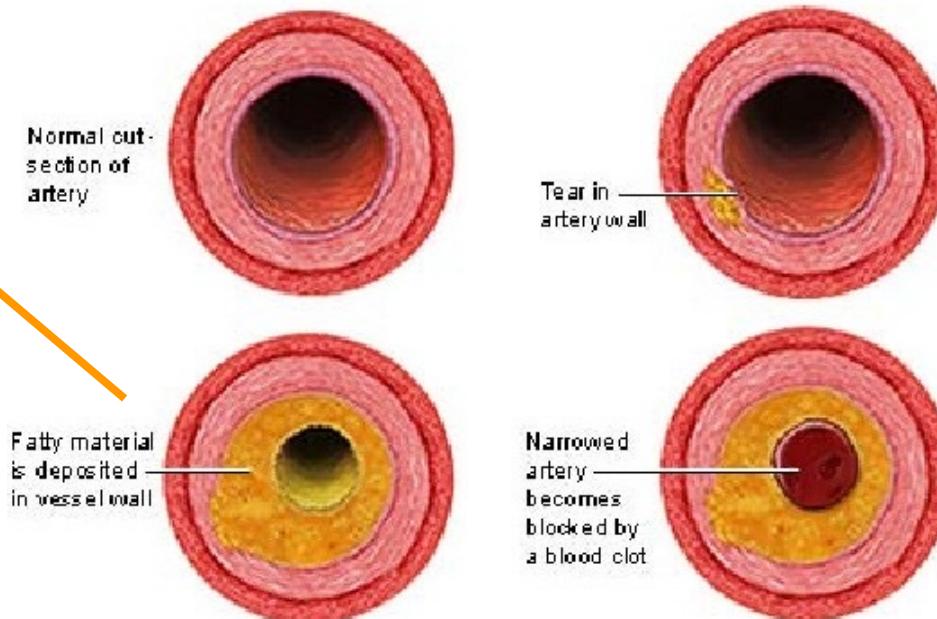
# Cerebral ischemia

A disruption of blood supply to some area of the brain

Three main causes:

1. Thrombosis: a plug
2. Embolism: a moving thrombosis
3. Arteriosclerosis

3 can interact with 1 or 2!



# Cerebral ischemia

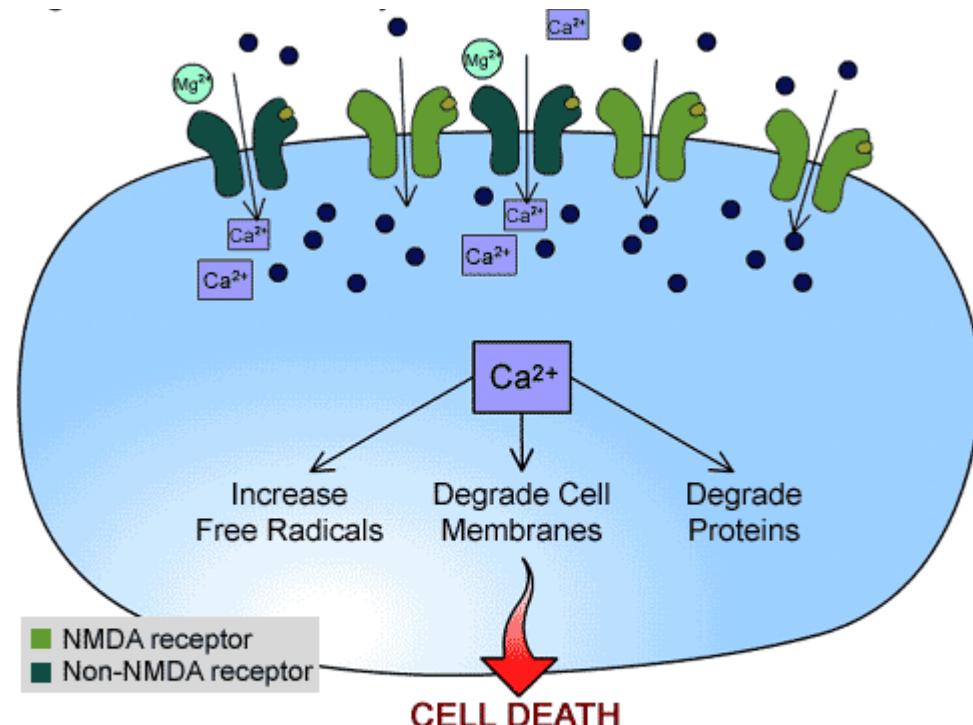
Ischemia-produced brain damage has three important properties:

1. It takes a while to develop (can be days)
2. Damage is more likely in some parts of the brain (e.g. hippocampus)
3. The mechanisms of ischemia-induced damage vary between brain structures (one example: excitotoxicity and apoptosis)

Target NMDARs for stroke?  
(Unfortunately not yet)

Hang on to excitotoxicity and NMDARs,  
as we'll keep seeing them

Strokes



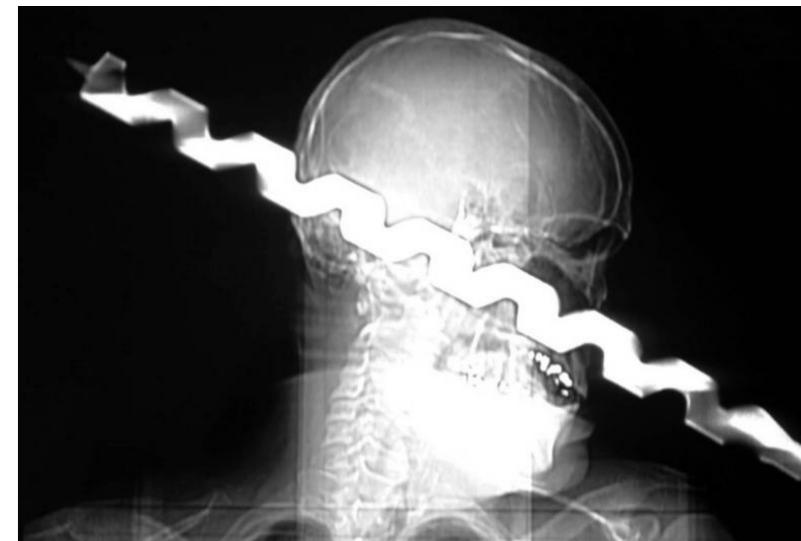
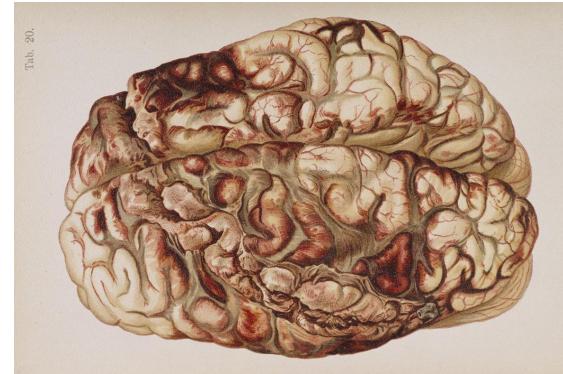
# Open-head injuries

aka Penetrating or perforating head injuries

Typically very severe

High risk of infection, complications

High velocity worse than low



Head injuries

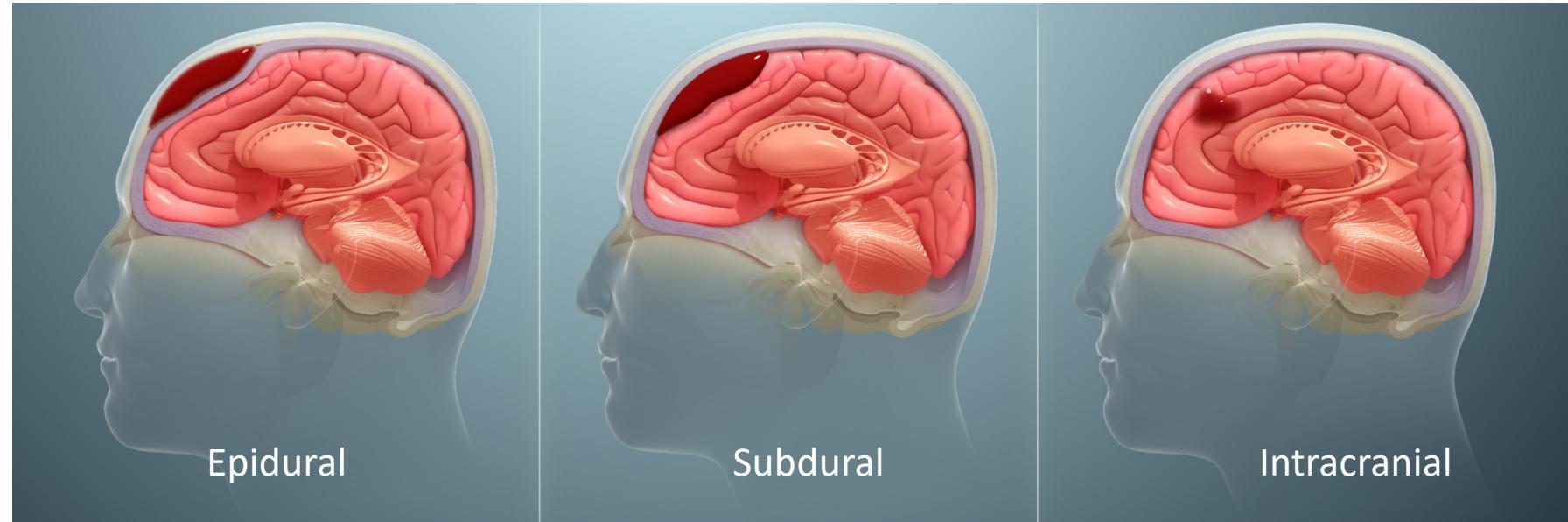
# Closed-head injuries: contusion

Well, contusion essentially just means “bruise”

Closed-head injuries that involve damage to the cerebral circulatory system, producing internal hemorrhaging and a resultant **hematoma**

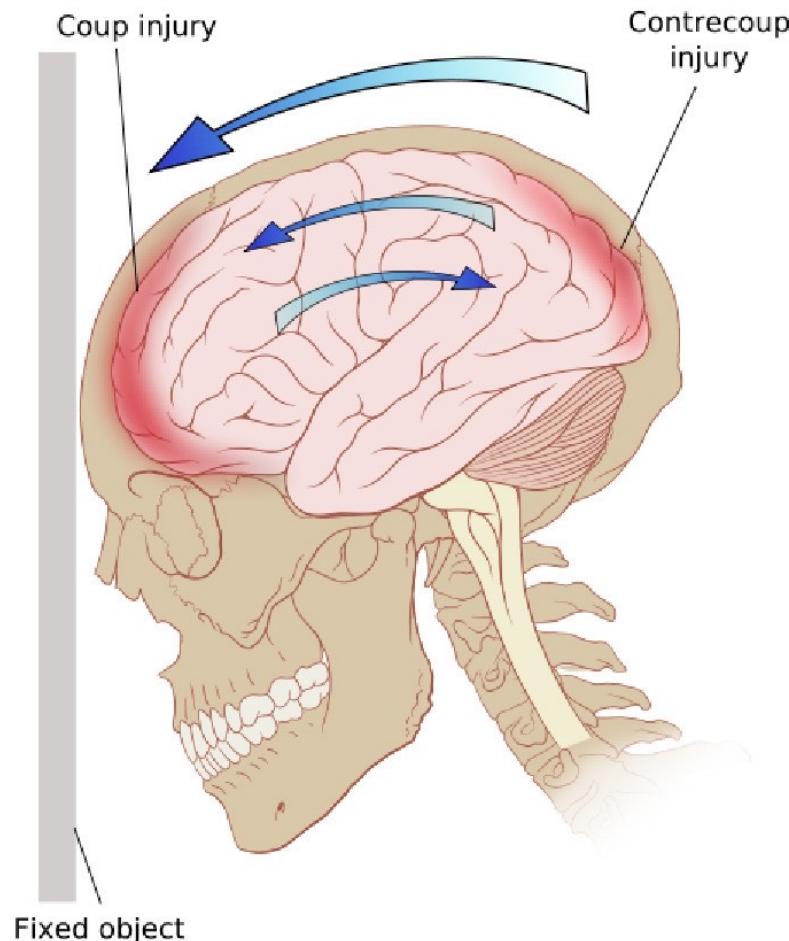
Occurs where the brain slams against the skull

Many types of  
hematomas, e.g.:



# Closed-head injuries

Contusions (and closed-head injuries in general) are frequently **coup contrecoup** injuries



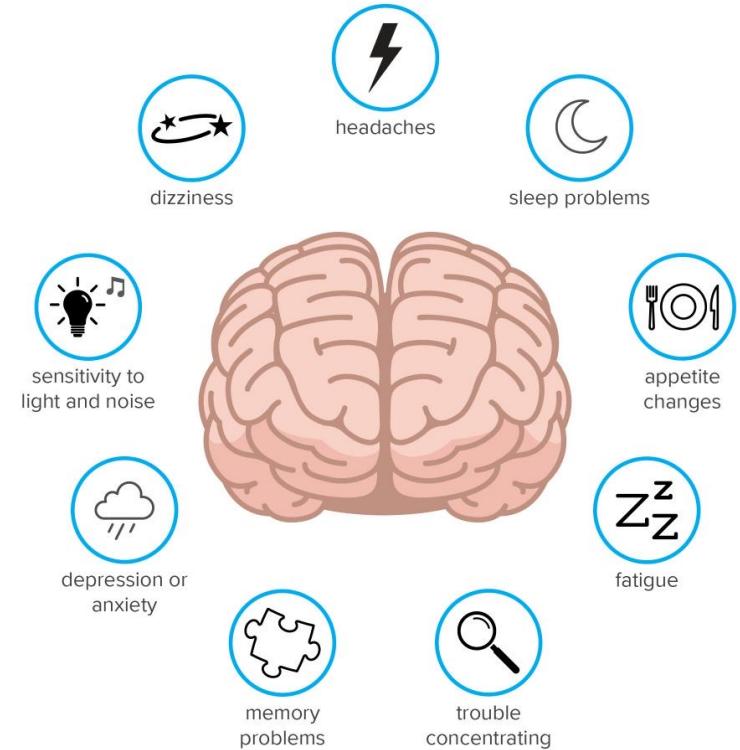
# Mild traumatic brain injury (mTBI)

When there is a blow to the head but no evidence of contusion or other structural damage

Typically synonymous with **concussion**, which is a syndrome,

**but you can injure your brain without getting a concussion (subconcussive mTBIs)**

## Post-Concussion Syndrome



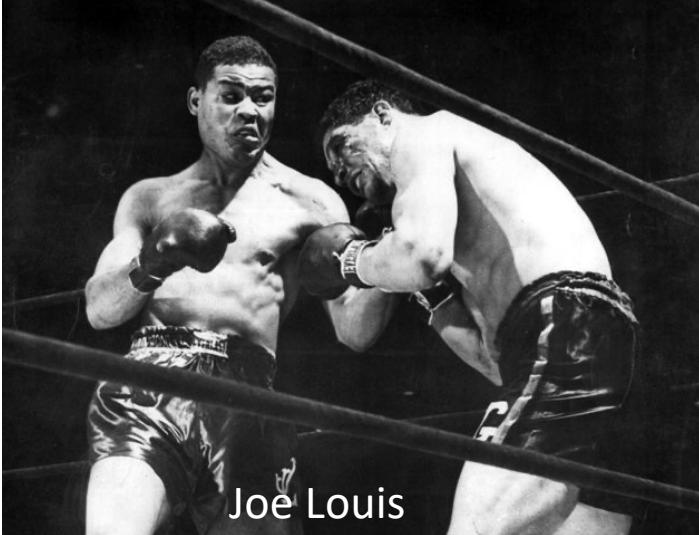
# Chronic traumatic encephalopathy (CTE)

aka Dementia pugilistica, punch-drunk syndrome

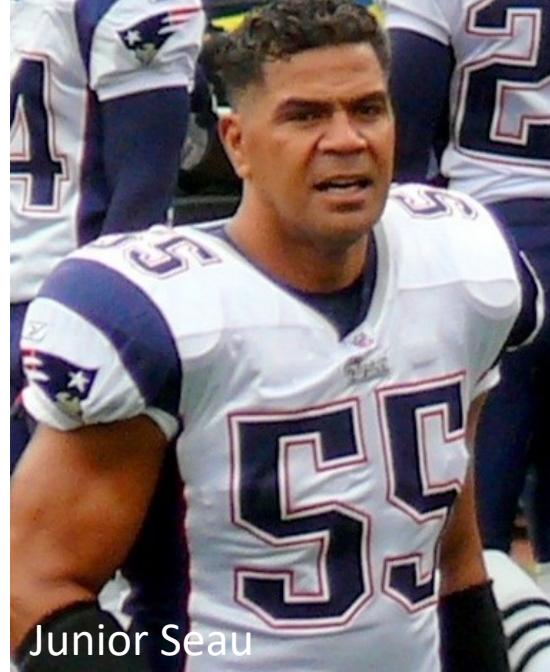
A progressive, irreversible neurodegenerative disease

Caused by repeated blows to the head

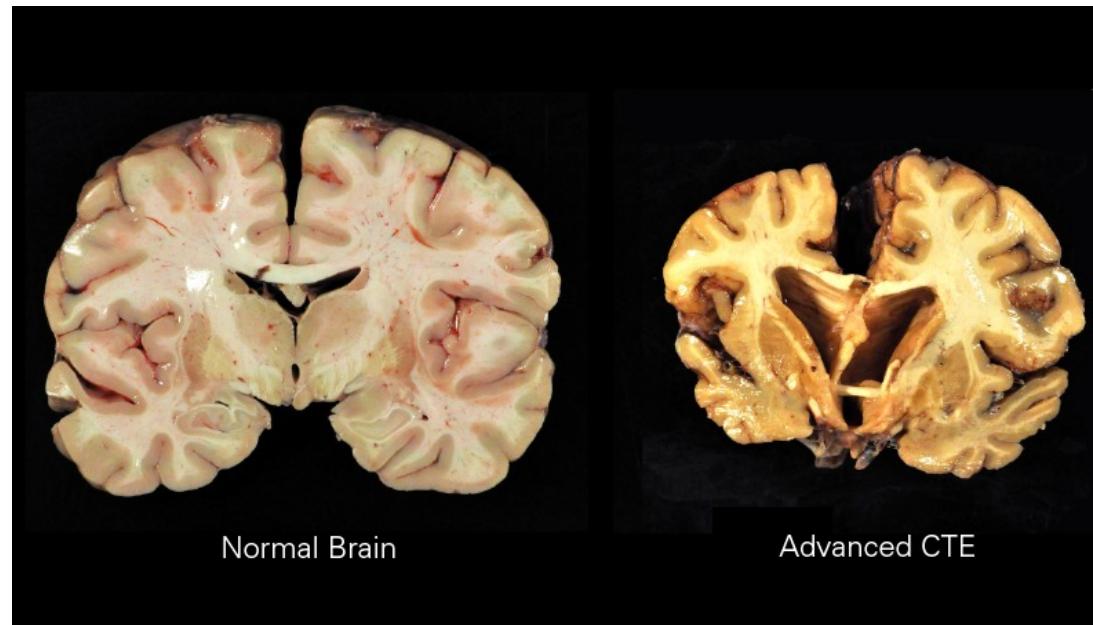
Not just professional athletes!



Head injuries



Junior Seau



<https://www.youtube.com/watch?v=d9Vlc7kBUW8>

# CTE

Stage 1: confusion, disorientation, headaches

Stage 2: lapses in memory, social norms, impulsivity, judgement

Stage 3/4: progressive dementia, movement disorders  
(esp. Parkinsonism), speech disorders, depression, suicidality

<https://www.youtube.com/watch?v=NsZ1kYv6hXw>  
<https://www.youtube.com/watch?v=HZy8xGOzsUA>



Pathological aggression, jealousy, and paranoia are common

Not just concussion  
Not just professional athletes

# CTE

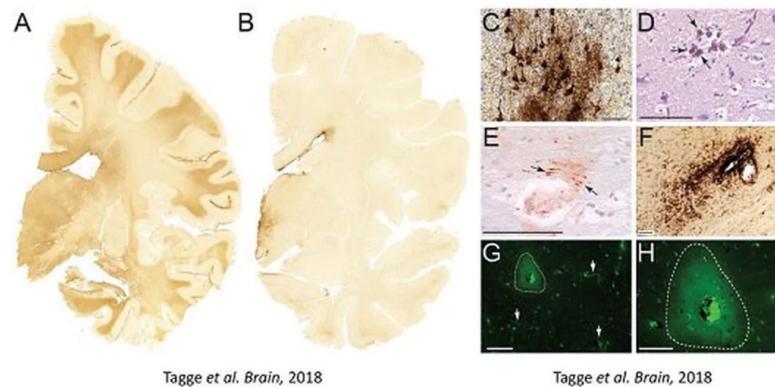
Early Lead

## A new study shows that hits to the head, not concussions, cause CTE

By Cindy Boren January 18 Email the author

### TBI-CTE Pathology in Teenage Athletes After Mild Head Injury

*Rare brains from teenagers in acute-subacute period after sports-related TBI*



<https://www.youtube.com/watch?v=St3dzliCWS4>

Head injuries

From [https://www.washingtonpost.com/news/early-lead/wp/2018/01/18/a-new-study-shows-that-hits-to-the-head-not-concussions-cause-cte/?utm\\_term=.e603dc4dd10f](https://www.washingtonpost.com/news/early-lead/wp/2018/01/18/a-new-study-shows-that-hits-to-the-head-not-concussions-cause-cte/?utm_term=.e603dc4dd10f)

21

### Most Read

1 Perspective At the Harper — at I

2 2018 and s need

3 Natic an er its pr

4 At All wins free a

5 The E hard roll fr

# CTE: Tau & neurofibrillary tangles

Tau stabilizes cytoskeleton

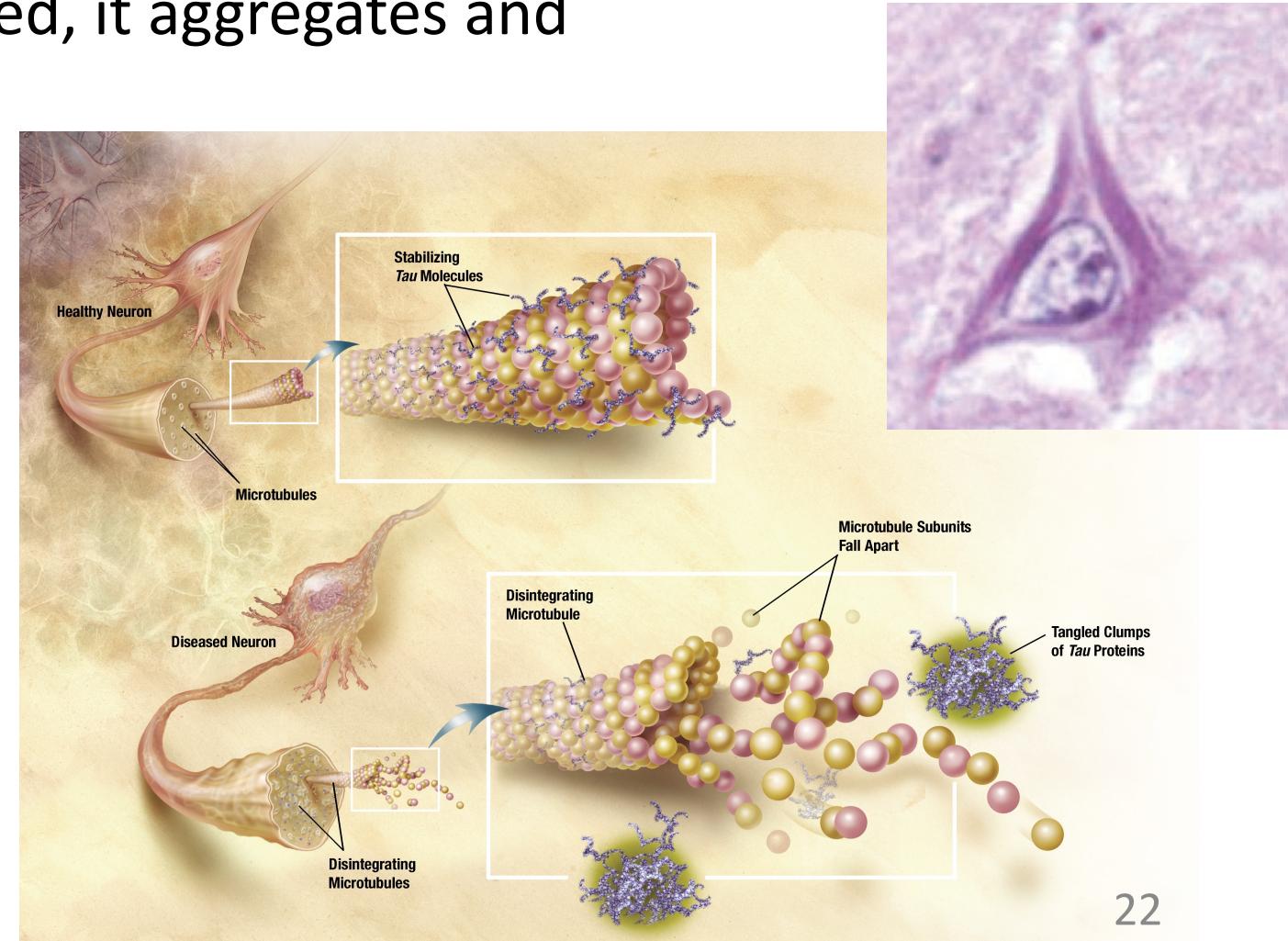
When tau is hyperphosphorylated, it aggregates and cytoskeleton becomes unstable

Not necessarily cause of CTE

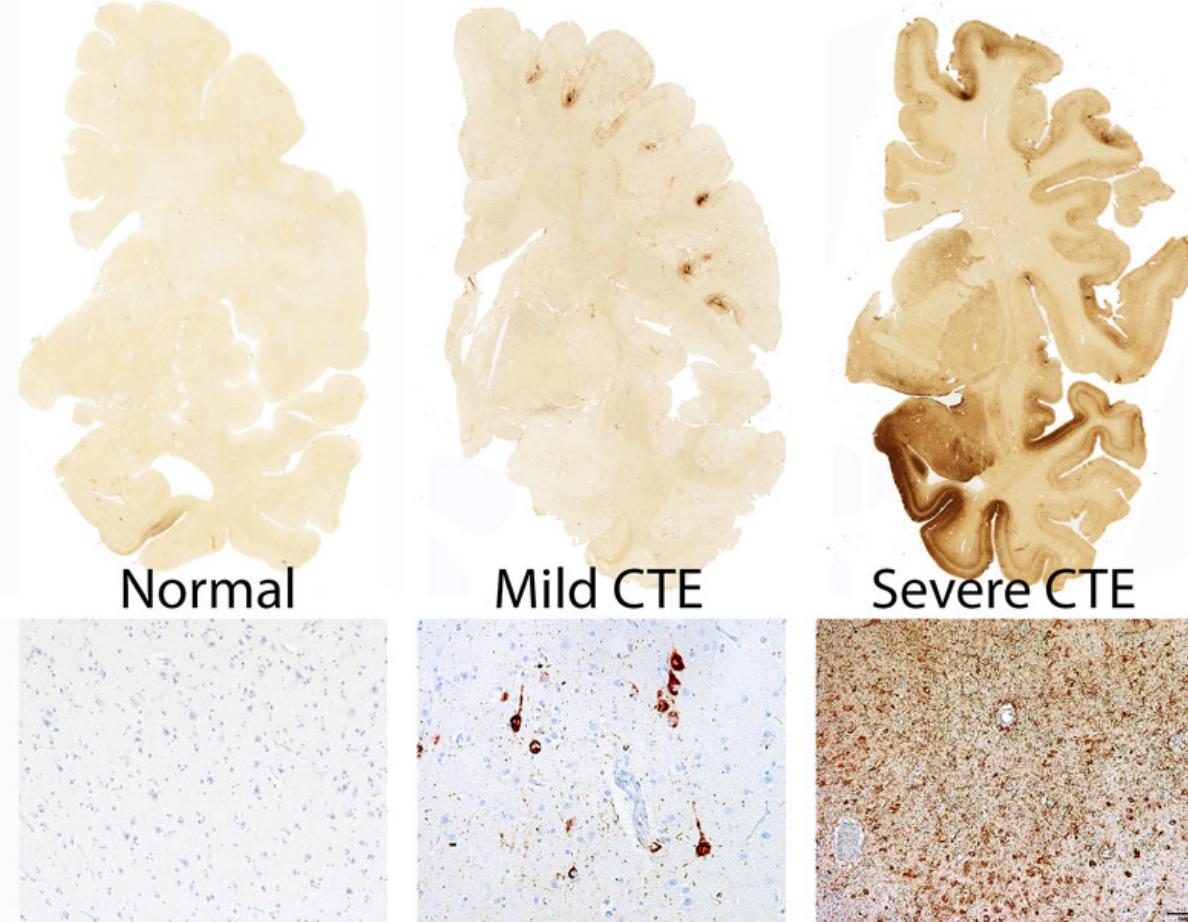
Also seen in AD, PD

A clear marker of CTE, but relies on postmortem staining

Head injuries



# Tau progression



Sulci first (?): iron deposits from hemorrhage?

Tau progression is different for CTE vs. AD  
Head injuries

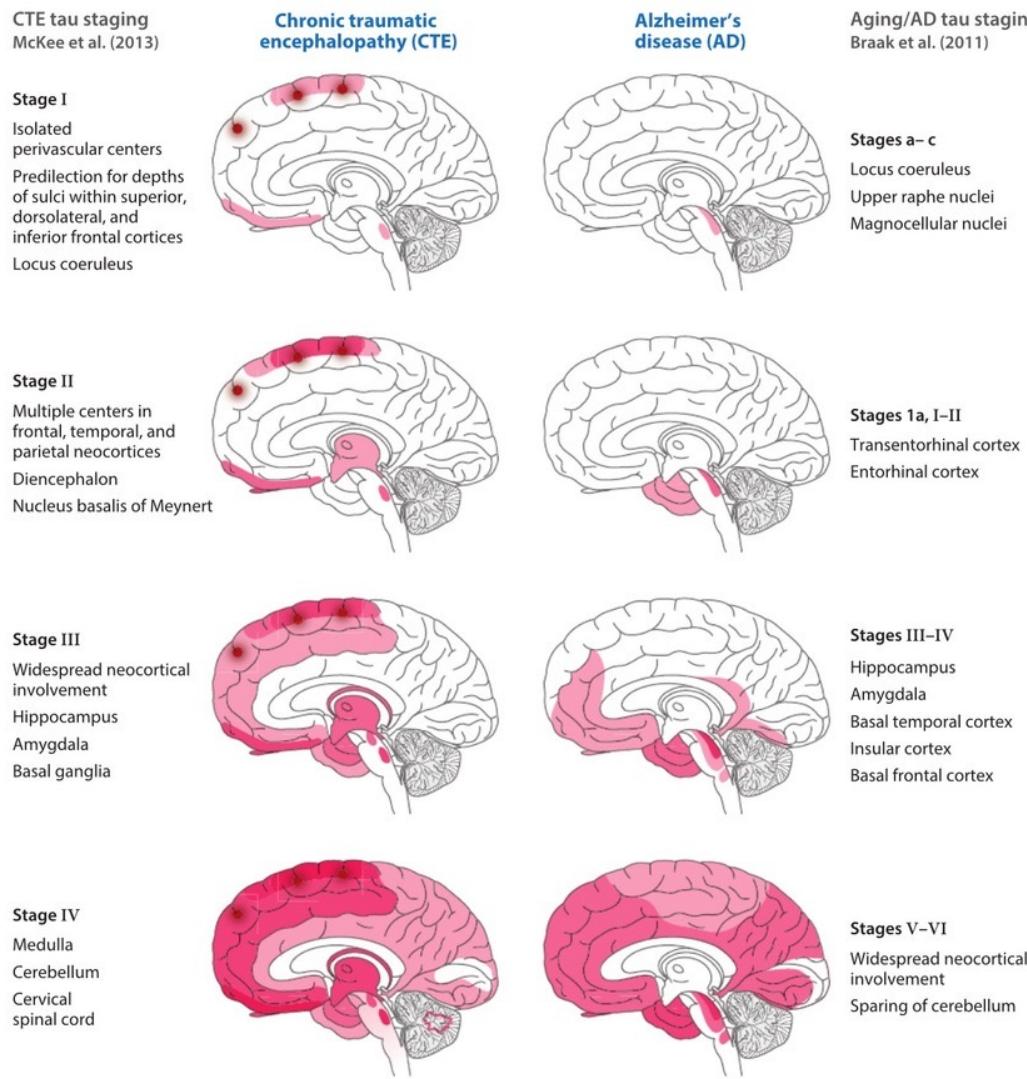
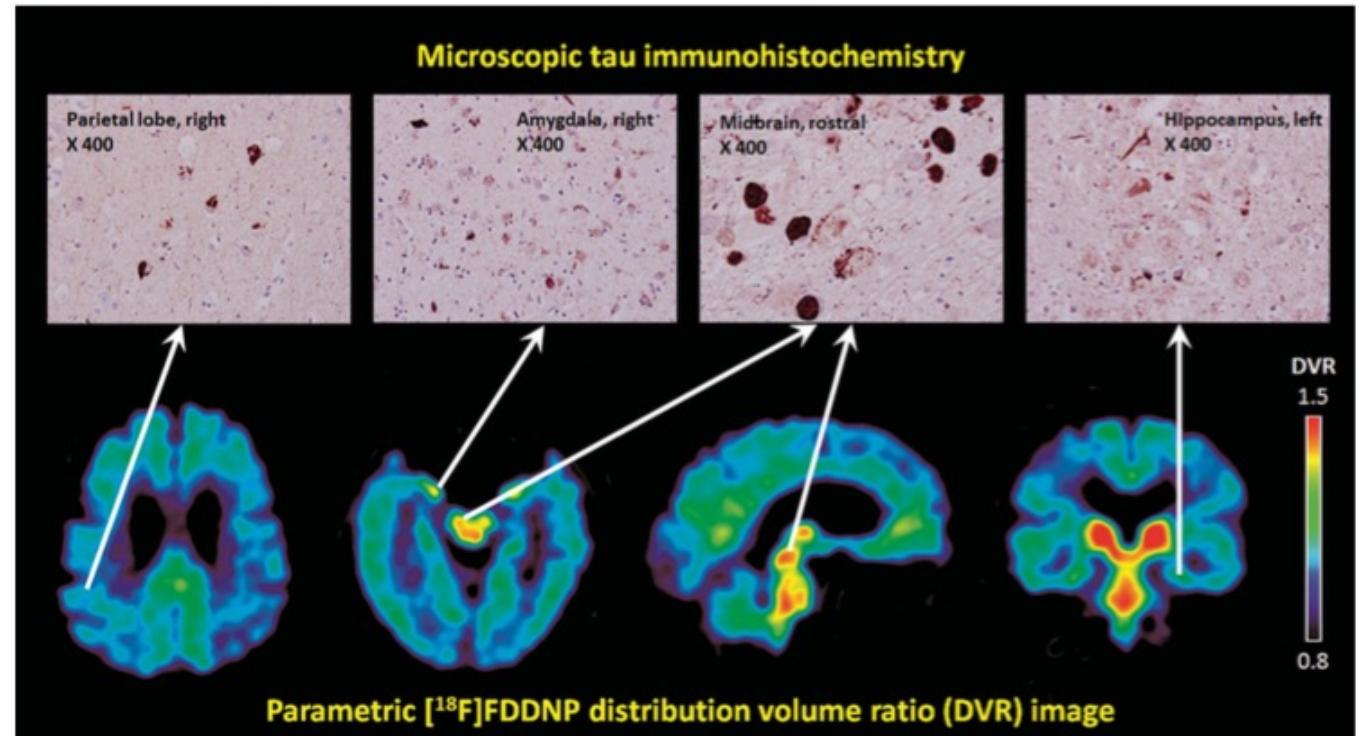
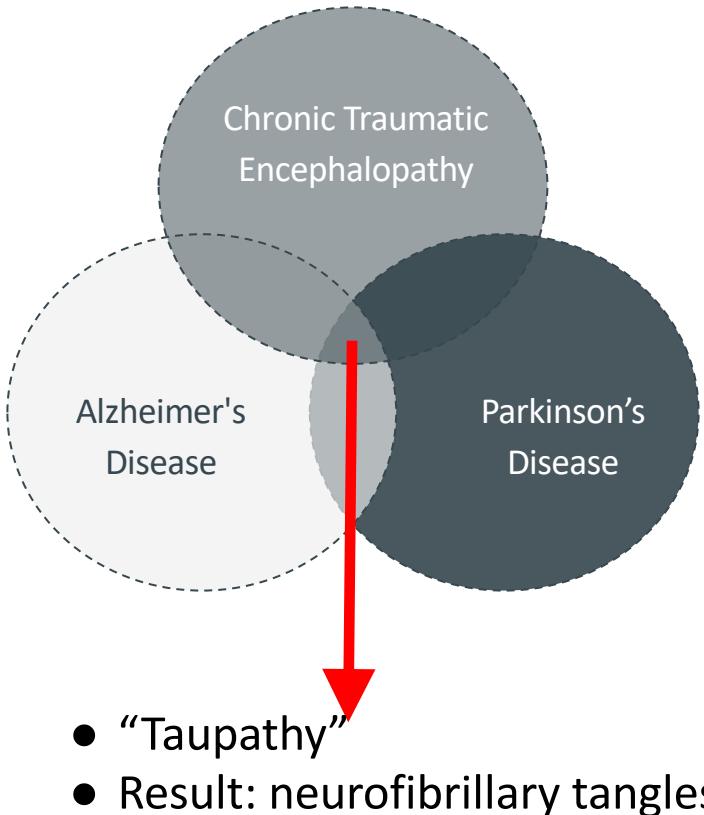


Figure 3

Comparison of hyperphosphorylated tau progression. In chronic traumatic encephalopathy (CTE) the abnormal accumulation of hyperphosphorylated tau first appears in the neocortex and locus coeruleus (CTE stage I), then involves the diencephalon (CTE stage II), next the medial temporal lobe (CTE stage III), and finally is widespread throughout the neocortical, brainstem, and cerebellar regions (CTE stage IV). This is in contrast to Alzheimer's disease (AD), where the tau pathology first occurs in the brainstem (Braak stages a-c), next involves the entorhinal cortex (stages 1a, 1b, I-II), then more widespread involvement of the medial temporal lobe (stages III-IV), and finally widespread involvement of the neocortex (stages V-VI). This schematic figure is based on information reported in Braak et al. (2011), McKee et al. (2013), and Stein et al. (2014).

# Taupathies



Omalu et al. 2017

Trying to develop PET tracer for CTE diagnosis in the living, but not there yet



<https://www.cbc.ca/sports/hockey/nhl/henri-richard-cte-1.6876247>

# Knowledge changes you (well, me)

Preliminary results (Mez, 2022):

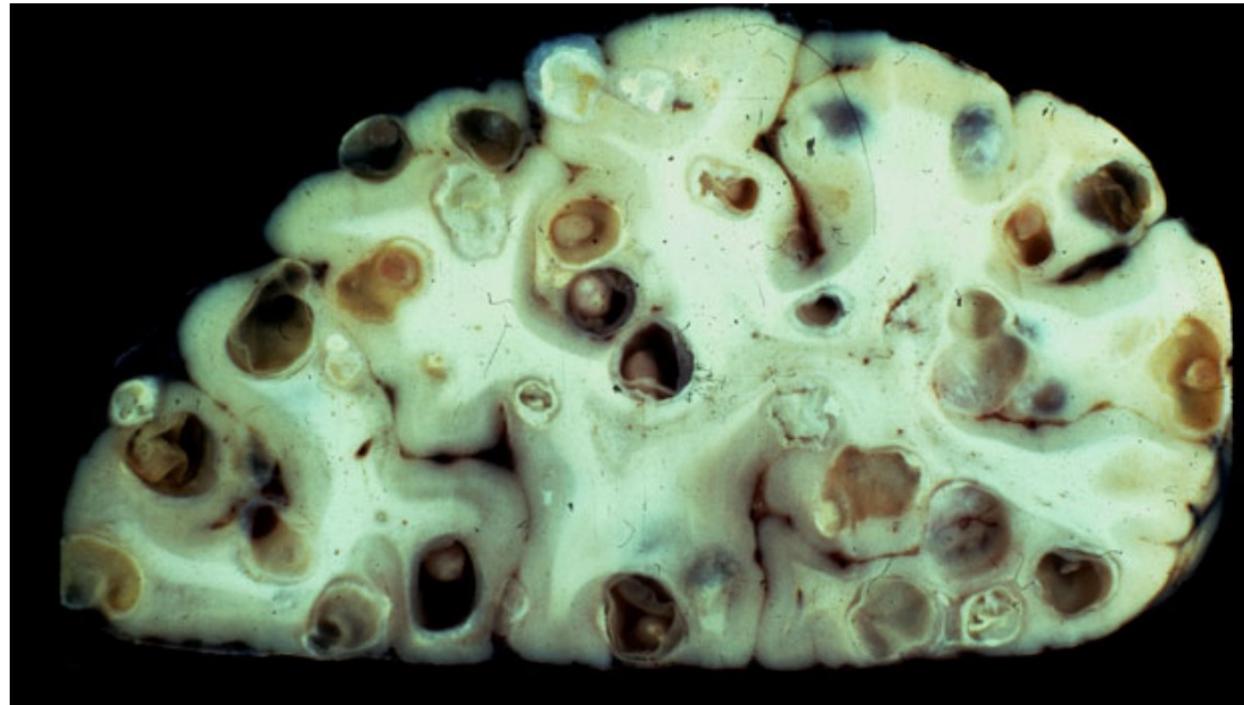
- 74 post-mortem hockey players
- (7 youth, 25 high school, 22 junior or college, 19 professional)
- 54% of their brains showed signs of CTE
- “We found each year of ice hockey play may increase the odds of developing CTE by 23%.”

<https://www.bumc.bu.edu/camed/2022/03/04/additional-years-of-ice-hockey-play-may-be-linked-to-greater-chance-of-cte/>



“We listen to the medical opinions on CTE, and I don't believe there has been any documented study that suggests that elements of our game result in CTE.”  
- Gary Bettman, National Hockey League Commissioner

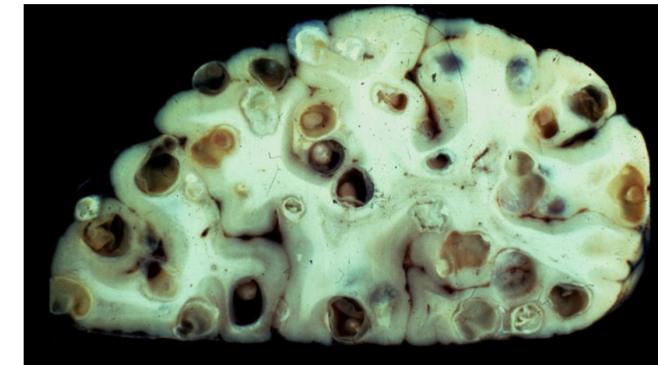
# Lecture overview: part II



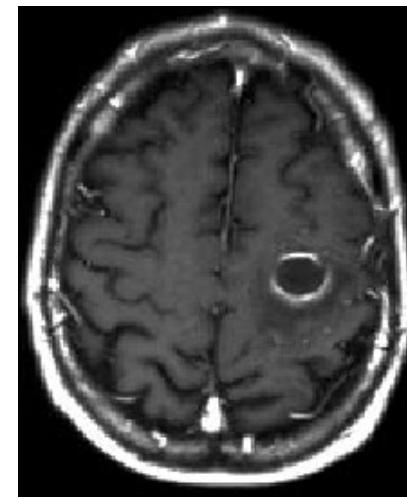
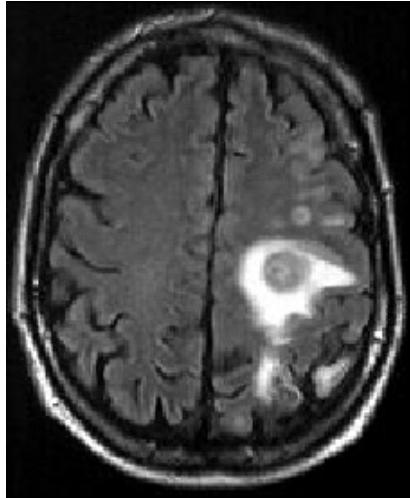
- A. Infections of the brain
- B. Neurotoxins
- C. Multiple sclerosis

# Learning objectives part II

1. Discuss three types of brain infections, including their cause and severity.
2. Discuss two types of neurotoxin-induced brain dysfunction.
3. Are vaccines dangerous? Describe their relationship to toxicity and to autism.
4. Describe the symptoms of multiple sclerosis (MS).
5. Discuss the two theories of MS.  
What evidence is there to suggest that  
MS is not simply an auto-immune disorder?
6. Read the paper by Bjornevik *et al.* 2022. Some of the molecular details will be outside of your knowledge base, so don't worry about them as much. Instead, focus on the longitudinal design of the study, and why it is particularly convincing in seeing Epstein-Barr virus as causal to MS. Be sure to also know the general results, e.g. time course of EBV and MS.



# Bacterial infections

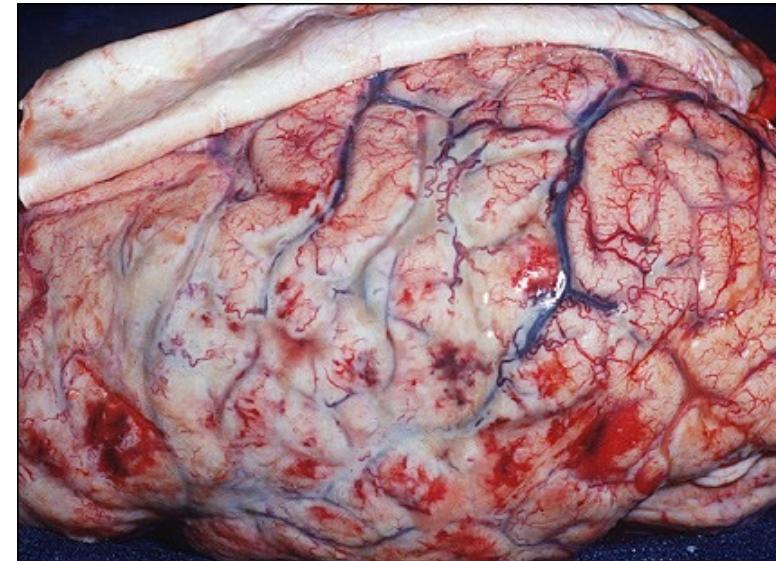


Can cause inflammation of the brain (**encephalitis**).

When bacteria attack the brain they often lead to the formation of cerebral **abscesses** (pus pockets).

# Bacterial infections

Bacteria often attack the meninges, producing an inflammation known as **meningitis**.



# Bacterial infections

In the news:

**Convicted for using natural remedies to treat dying son, father back promoting alternative medicine**

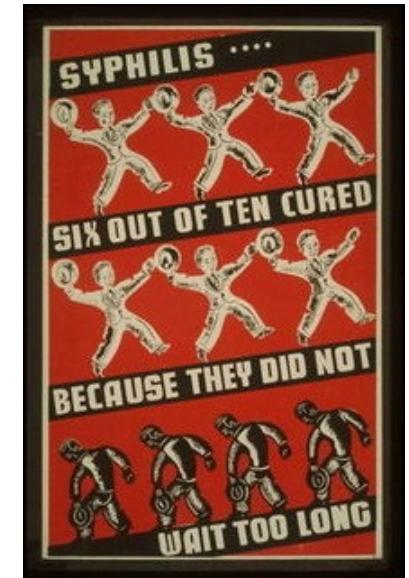
GRAEME HAMILTON 01.11.2017 |



# Bacterial infections: syphilis

A type of bacteria that can attack the brain.

**General paresis:** The syndrome of psychosis/dementia that results from a syphilitic infection of the brain.

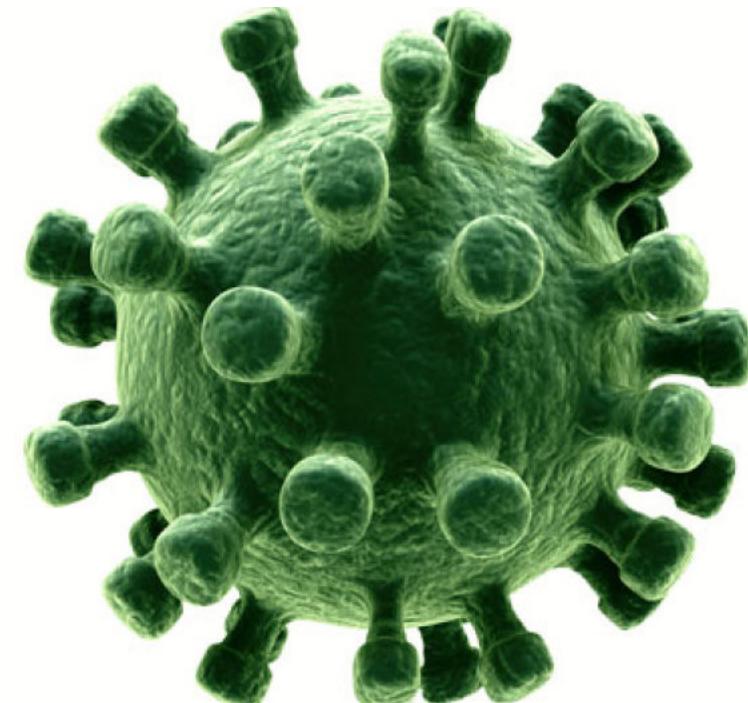


# Viral Infections

Two types:

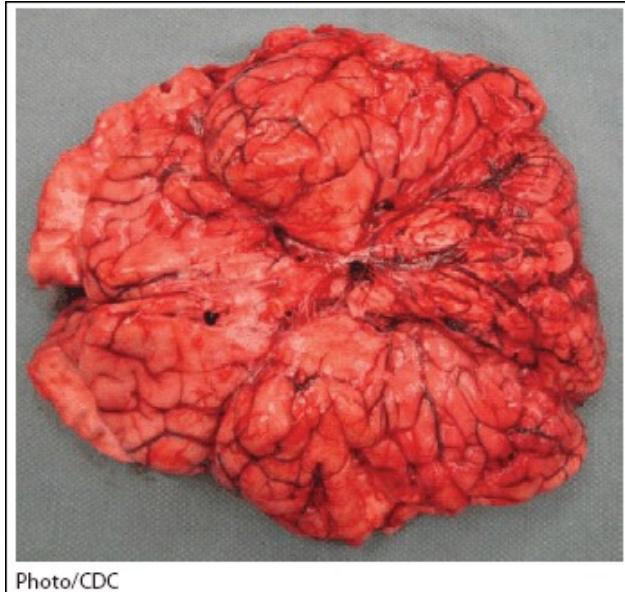
1. Those that have a particular affinity for neural tissue (e.g. rabies)
2. Those that attack all tissues indiscriminately, including nervous tissue (e.g. herpes simplex)

Viral infections of the brain can cause encephalitis and meningitis.

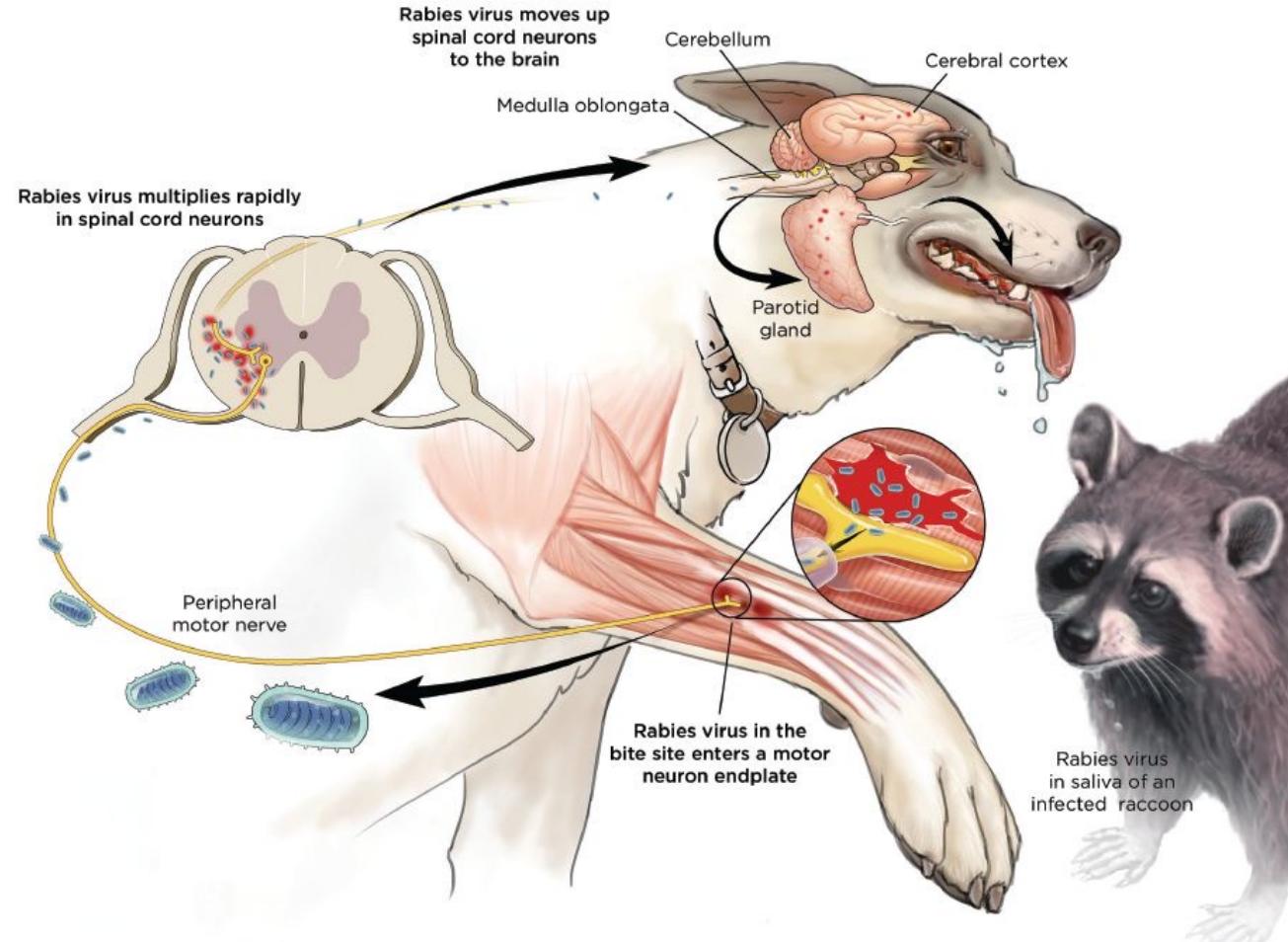


# Viral Infections: Rabies

The rabies virus has an affinity for the nervous system.

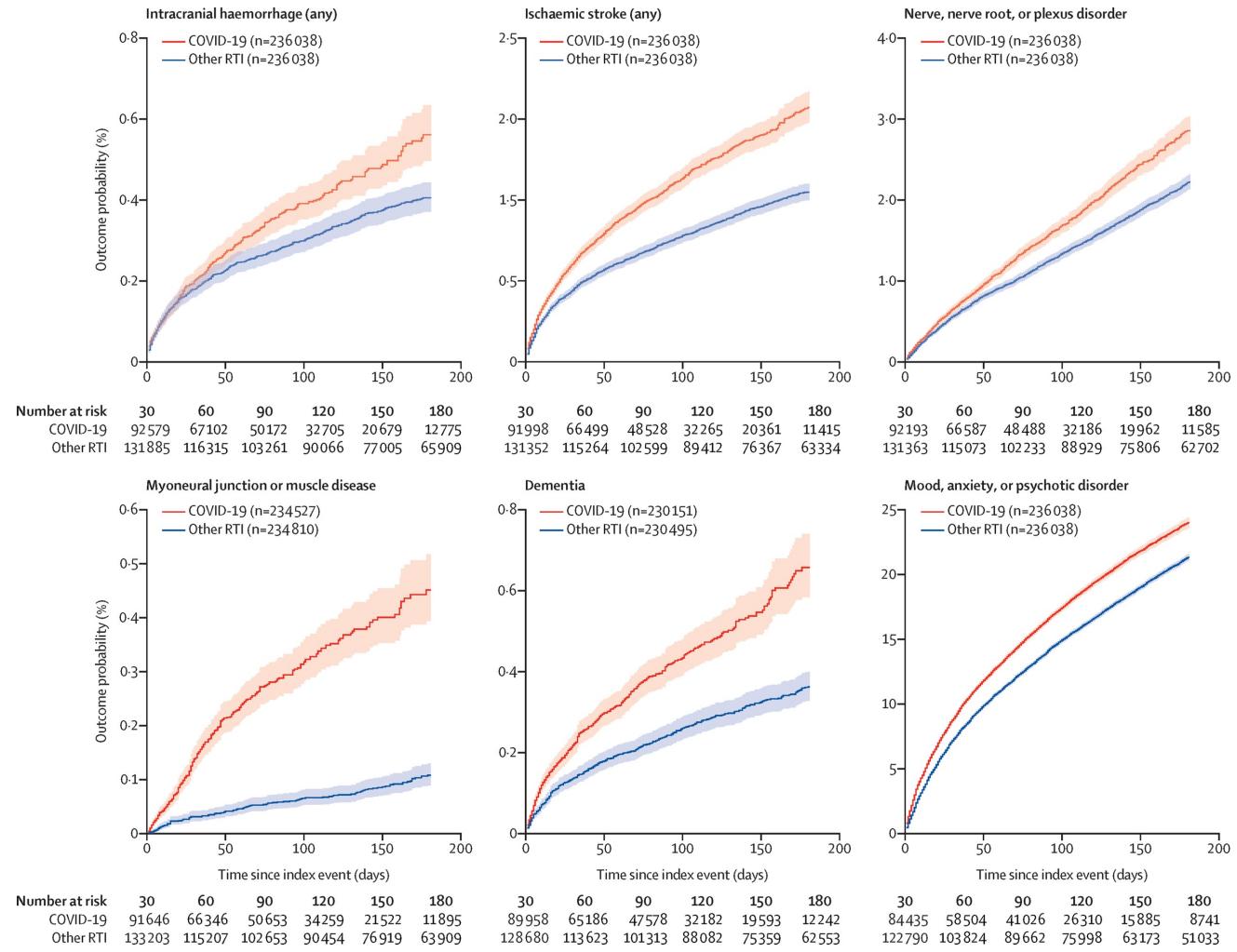


This is a human brain!



# What about COVID-19?

- Caveat: not all of us symptomatic, new topic, other complications to studying
- ~35% of those symptomatic have neurological symptoms (Koralnik & Tyler 2020, Mukerji & Solomon 2021)
- Often detected in olfactory neurons, likely rare in CNS (Soung *et al.* 2022)
- Often markers of inflammation
- Most dangerous issue seems to be cerebrovascular (i.e. blood flow) leading to hypoxia



Taquet *et al.* 2021

# What about COVID-19?

- Douaud *et al.* 2022: longitudinal design, 401 people's brains, before and after COVID-19
- Effects on brain small but significant: decreased grey matter in OFC and parahippocampal gyrus, global reductions in brain size
- Also saw greater cognitive decline vs. controls
- Effects largest on oldest participants

Infections

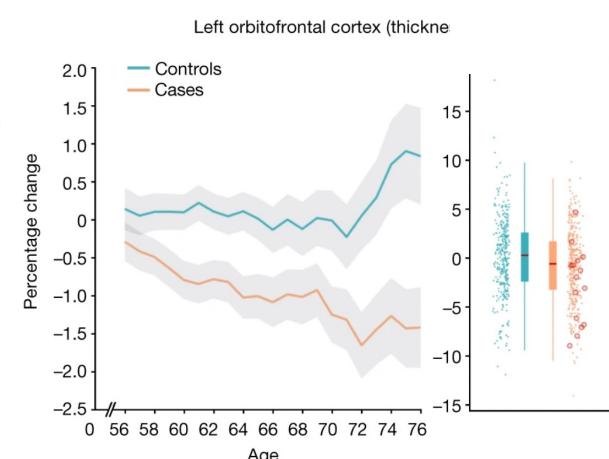
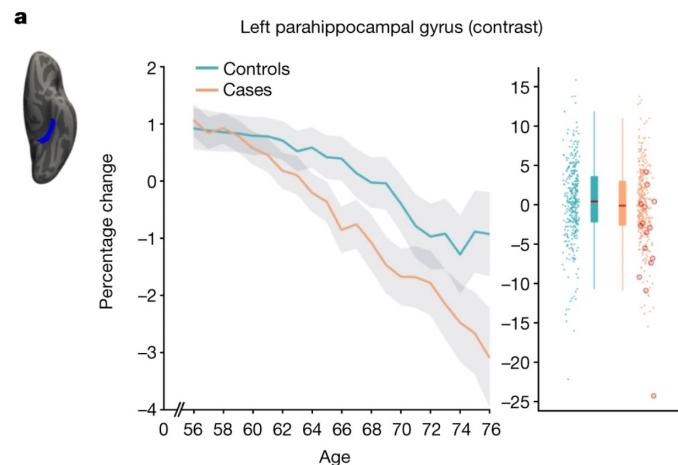


Fig. 3: Significant longitudinal differences in cognition.

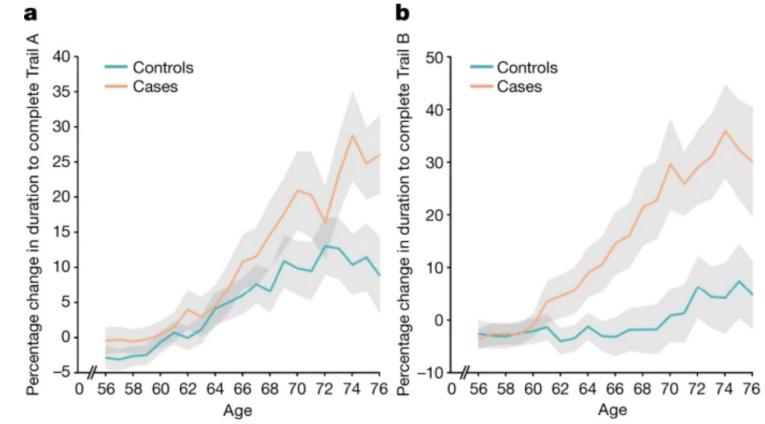
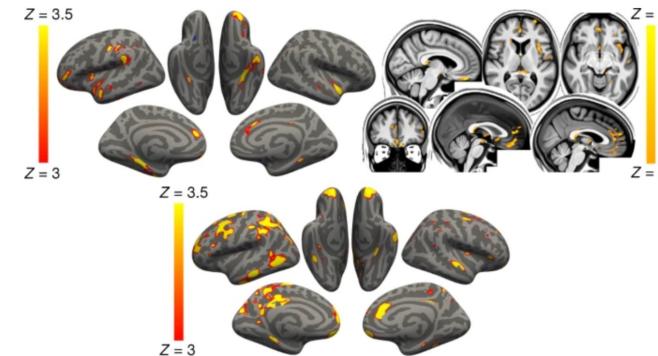


Fig. 2: Vertex-wise and voxel-wise longitudinal group differences in grey matter thickness and mean diffusivity changes.



Douaud *et al.* 2022

# Parasite infections

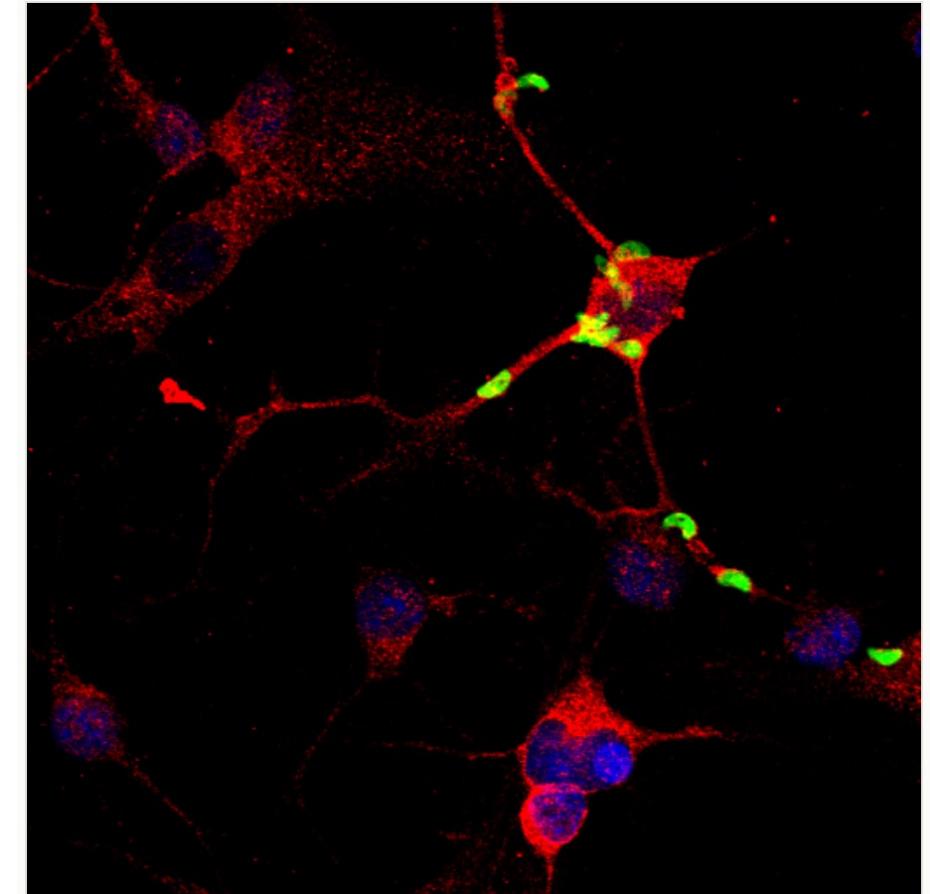
## **Toxoplasma gondii:** eukaryotic parasite



Stanford Report, August 17, 2011

Parasite uses the power of sexual attraction  
to trick rats into becoming cat food

<https://news.stanford.edu/news/2011/august/catrat-081711.html>



Individual *Toxoplasma* parasites (green) are shown invading neurons (red) grown in a petri dish in the lab. The blue areas are fluorescently tagged cell nuclei.

# In the news



NBC News

@NBCNews

Follow

A mind-controlling parasite found in cat feces may give people the courage they need to become entrepreneurs, researchers reported.



A mind-controlling parasite found in cat feces may give people the courage they need to become entrepreneurs, researchers reported Tuesday.

They found that people who have been infected with the *Toxoplasma gondii* parasite are more likely to major in business and to have started their own businesses than non-infected people.

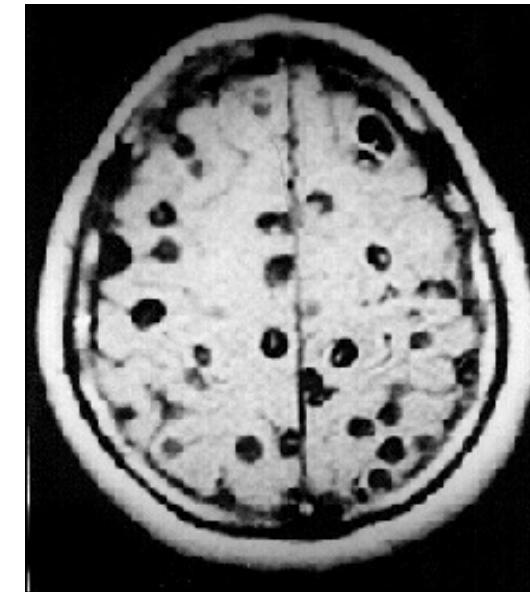
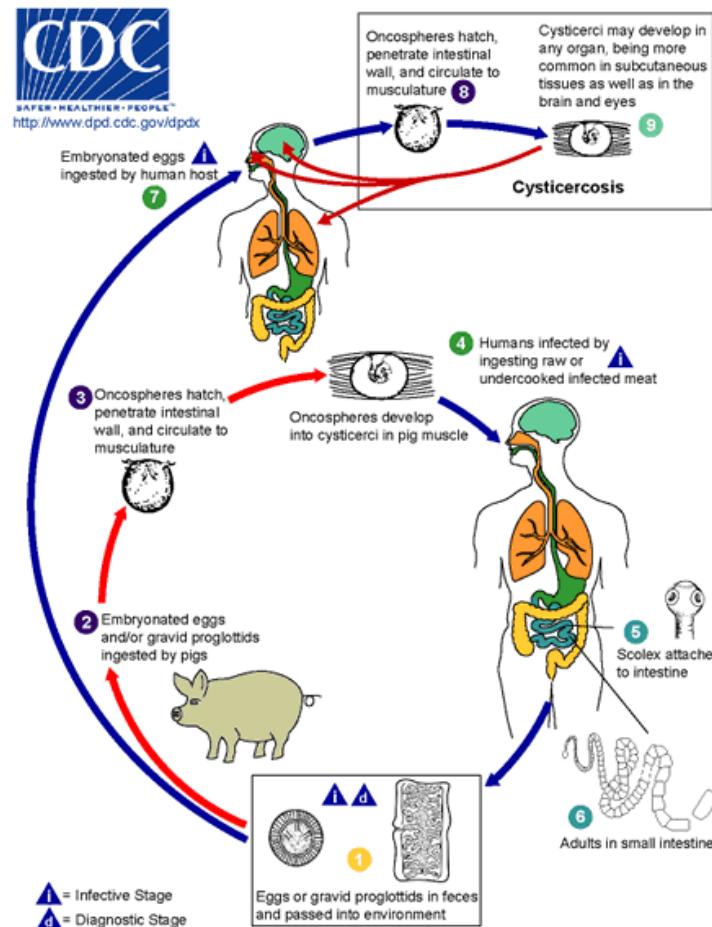
The parasite, which makes rodents unafraid of cats, may be reducing the fear of failure in people, Stefanie Johnson of the University of Colorado and colleagues said.

**They haven't actually shown that.** But toxoplasma does get into the brain, and it's been linked to a variety of mental effects in mice and people alike. And fear of failure could be a good thing, Johnson said.

[https://www.nbcnews.com/health/health-news/parasite-cat-poop-could-be-reducing-our-fear-failure-study-n894221?cid=sm\\_npd\\_nn\\_tw\\_ma](https://www.nbcnews.com/health/health-news/parasite-cat-poop-could-be-reducing-our-fear-failure-study-n894221?cid=sm_npd_nn_tw_ma)

# Parasite infections

## Neurocysticercosis: Tape worm in the brain.



<https://www.youtube.com/watch?v=kNP3JInUcxg>

# Heavy Metals

Mercury can accumulate in the brain and permanently damage it--producing a **toxic psychosis**.



# Heavy Metals

Minamata disease: caused by severe methylmercury poisoning; ataxia, numbness, muscle weakness, damage to vision/hearing/speech, paralysis, coma, death; congenital effects



# Heavy Metals

Methylmercury poisoning is thankfully rare in North America, now, but still sometimes occurs

**CNN health** Food Fitness Wellness Parenting Vital Signs • LIVE TV Edition ▾ Q

**A woman was permanently injured from a skin-lightening cream tainted with an extremely toxic form of mercury - the first such case in the US**

By Scottie Andrew, CNN

① Updated 11:01 AM ET, Thu December 26, 2019



EMBODIMENT COUNTY DEPARTMENT OF HEALTH SERVICES

# Heavy Metals

Small amounts of ethylmercury are present in vaccines as a preservative, BUT no evidence whatsoever to suggest harmful neurological effects.

Aside:

Relationship between vaccines and autism?

NO

Neurotoxins



Wakefield

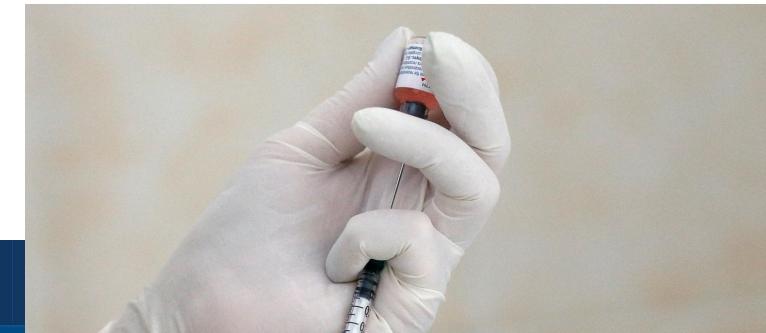
WORLD NEWS DECEMBER 5, 2019 / 10:08 AM / 2 MONTHS AGO

WHO decries 'collective failure' as measles kills 140,000

Kate Kelland

4 MIN READ

LONDON (Reuters) - Measles infected nearly 10 million people in 2018 and killed 140,000, mostly children, as devastating outbreaks of the viral disease hit every region of the world, the World Health Organization said on Thursday.



World Canada Local Politics Smart Living Money Entertainment Health Video Podcast T

HEALTH February 9, 2019 5:12 pm

Updated: February 9, 2019 8:37 pm

Health officials confirm measles case in Vancouver area

By Simon Little  
Online Journalist Global News



# Heavy Metals

Lead can also lead to toxic psychosis (origin of “crackpots”).



Free time: *Cosmos* episode 7

# Comparing Canadian water to Flint, Michigan

## Prince Rupert

Prince Rupert (no LSLs) versus Flint (including 12% that have LSLs)

Samples first drawn after 6 hours of stagnation			
	Median (ppb)	Average (ppb)	% above 5 ppb
Prince Rupert (15 samples)	9.9	14.1	80%
Flint (277 samples)	3.5	10.5	40.4%

Samples include 1-minute flush from Flint and 45 second flush from Prince Rupert after 6 hours of stagnation			
	Median (ppb)	Average (ppb)	% above 5 ppb
Prince Rupert (15 samples)	3.9	4.0	26.7%
Flint (277 samples)	1.4	10.2	24.9%

Samples include 3-minute flush from Flint and 2-minute flush from Prince Rupert after 6 hours of stagnation			
	Median (ppb)	Average (ppb)	% above 5 ppb
Prince Rupert (15 samples)	2.3	2.8	13.3%
Flint (277 samples)	0.5	3.7	12.6%

Credit: Data obtained and analyzed by the Institute for Investigative Journalism

©Global News

# Heavy Metals

However, lead is toxic at much lower levels as well. Lead poisoning is especially deleterious to children, where it impairs physical and mental development. It can also cause a variety of neurological problems in adults.

## Tainted Water

INVESTIGATIONS

### Is Canada's tap water safe? Thousands of test results show high lead levels across the country

BY GLOBAL NEWS, TORONTO

Posted November 4, 2019

Updated November 5, 2019

INVESTIGATIONS

In Metro Vancouver, you may not know if you have lead in your water. Here's why



By [Ainslie Cruickshank](#) Star Vancouver  
Thu., Nov. 21, 2019 | 7 min. read

# Multiple Sclerosis (MS)

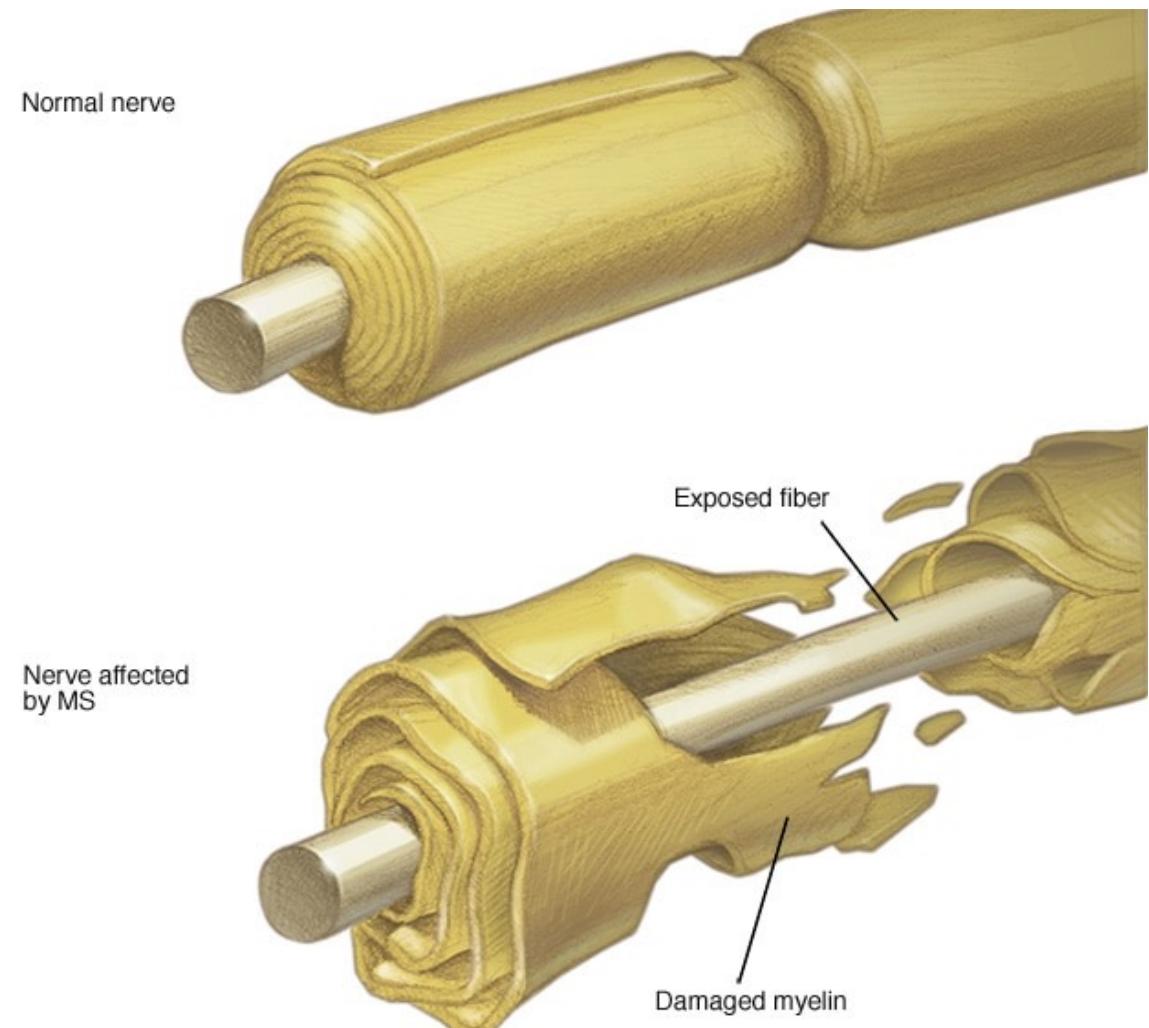
Progressive disorder that primarily attacks the myelin of axons in the CNS, but there is also cell loss.

**Common symptoms in advanced cases:** visual disturbances, muscular weakness, numbness, tremor, and loss of motor coordination.

The immune system often appears to attack the CNS myelin as if it were a foreign substance.

Multiple forms: e.g. relapsing-remitting, secondary progressive, primary progressive

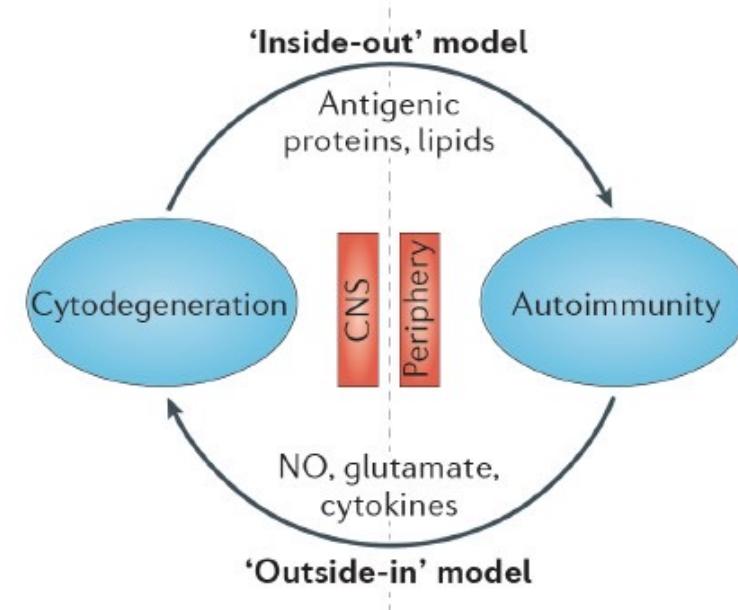
Multiple Sclerosis



# Theories of Pathogenesis

1. Primarily an autoimmune disease (“outside-in” theory).
2. Primarily a neurodegenerative disease, with inflammation in some patients (“inside-out” theory).

Evidence to suggest that it isn't simply an autoimmune disease (3)



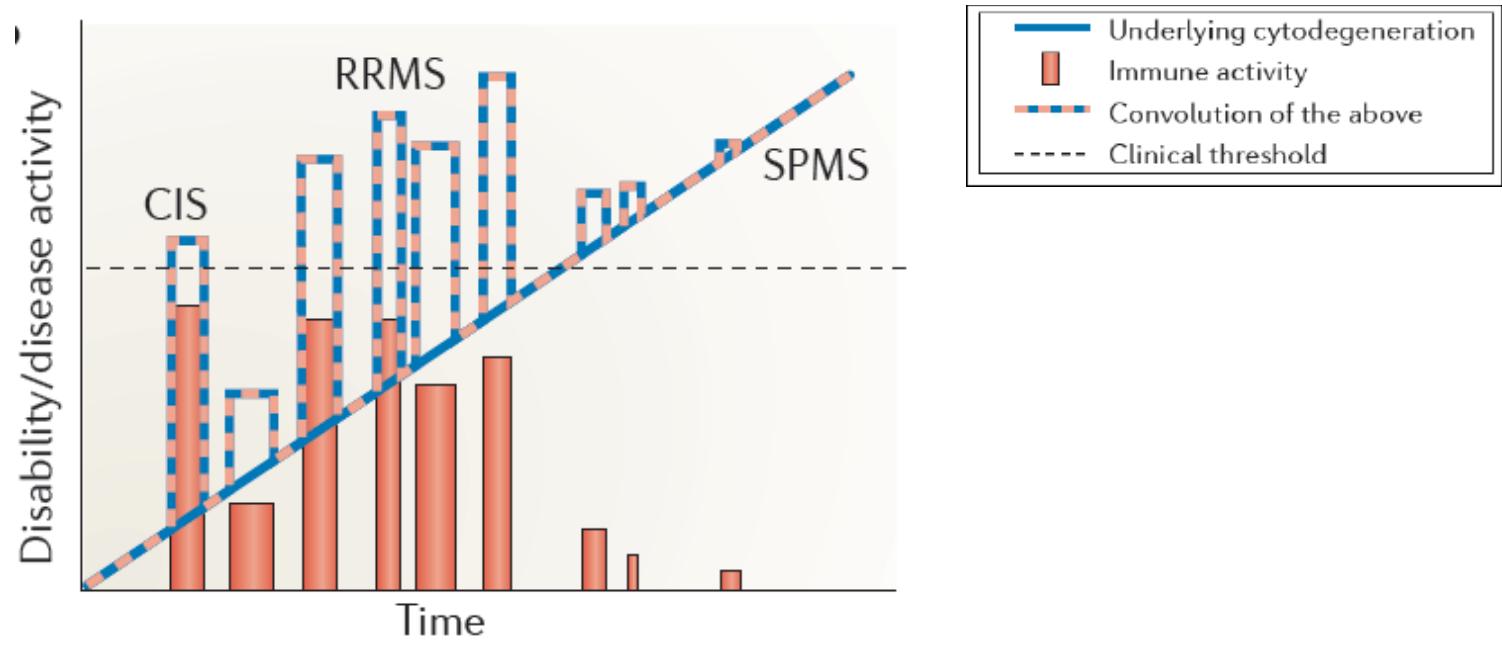
from Stys et al., 2012

# Progression: relapsing-remitting form

CIS = clinically isolated syndrome

RRMS = Relapsing-remitting MS

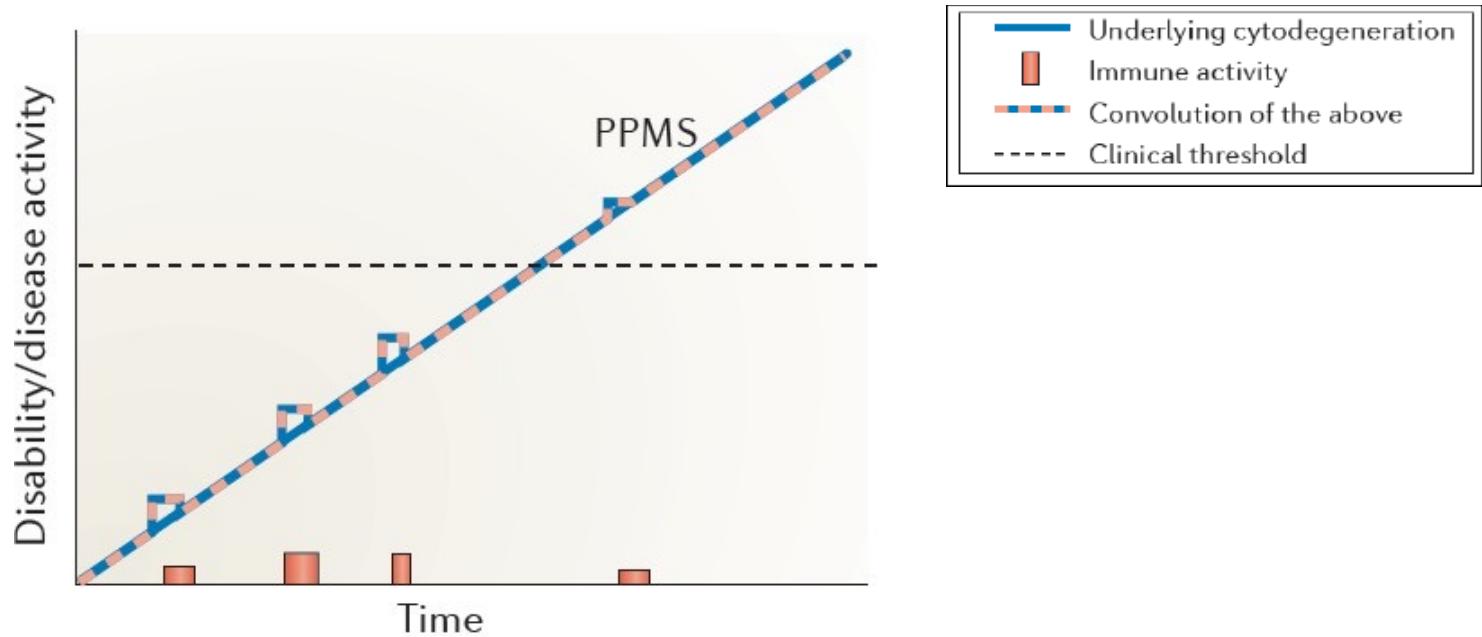
SPMS = Secondary progressive MS



from Stys et al., 2012

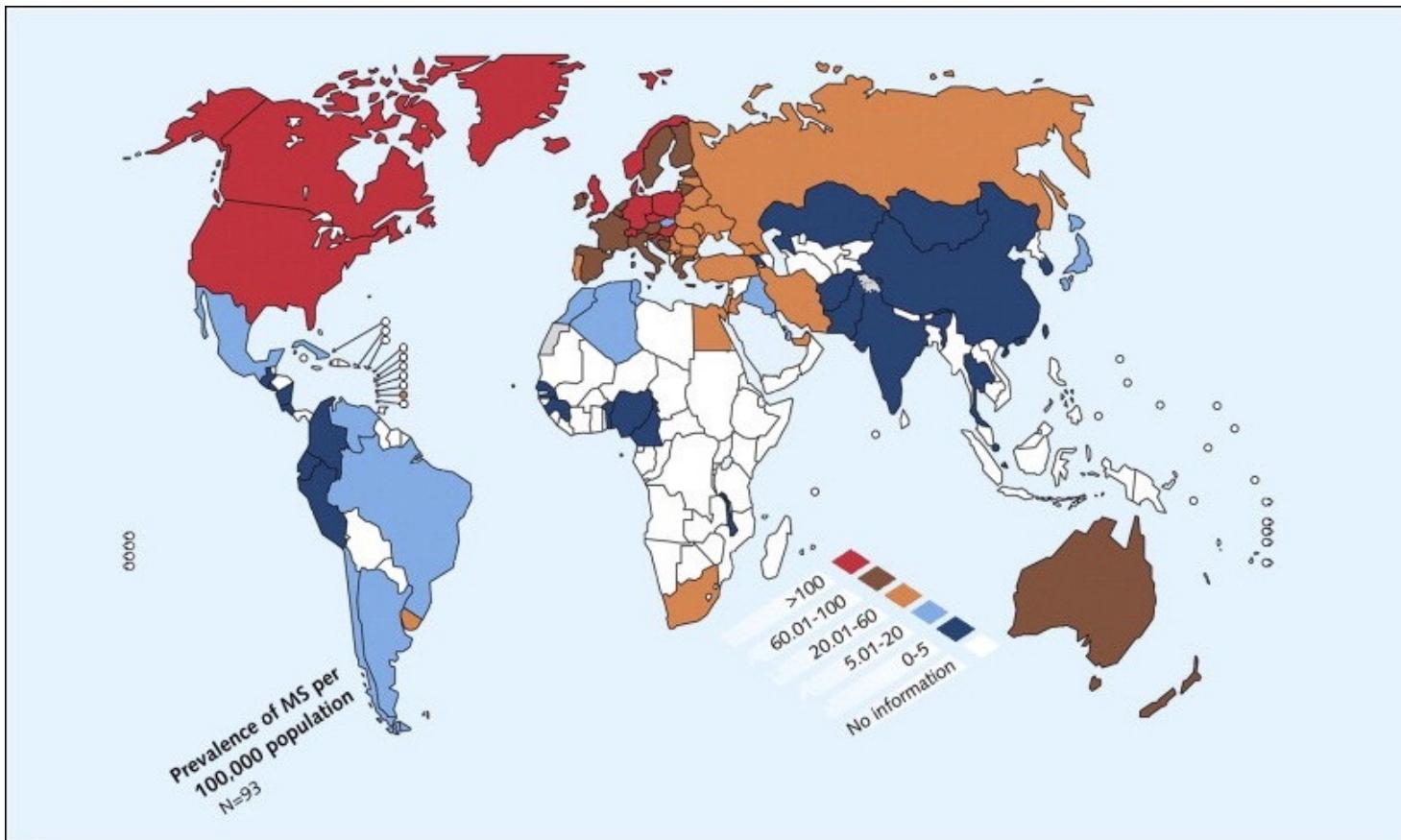
# Progression: primary progressive form

PPMS = Primary progressive MS

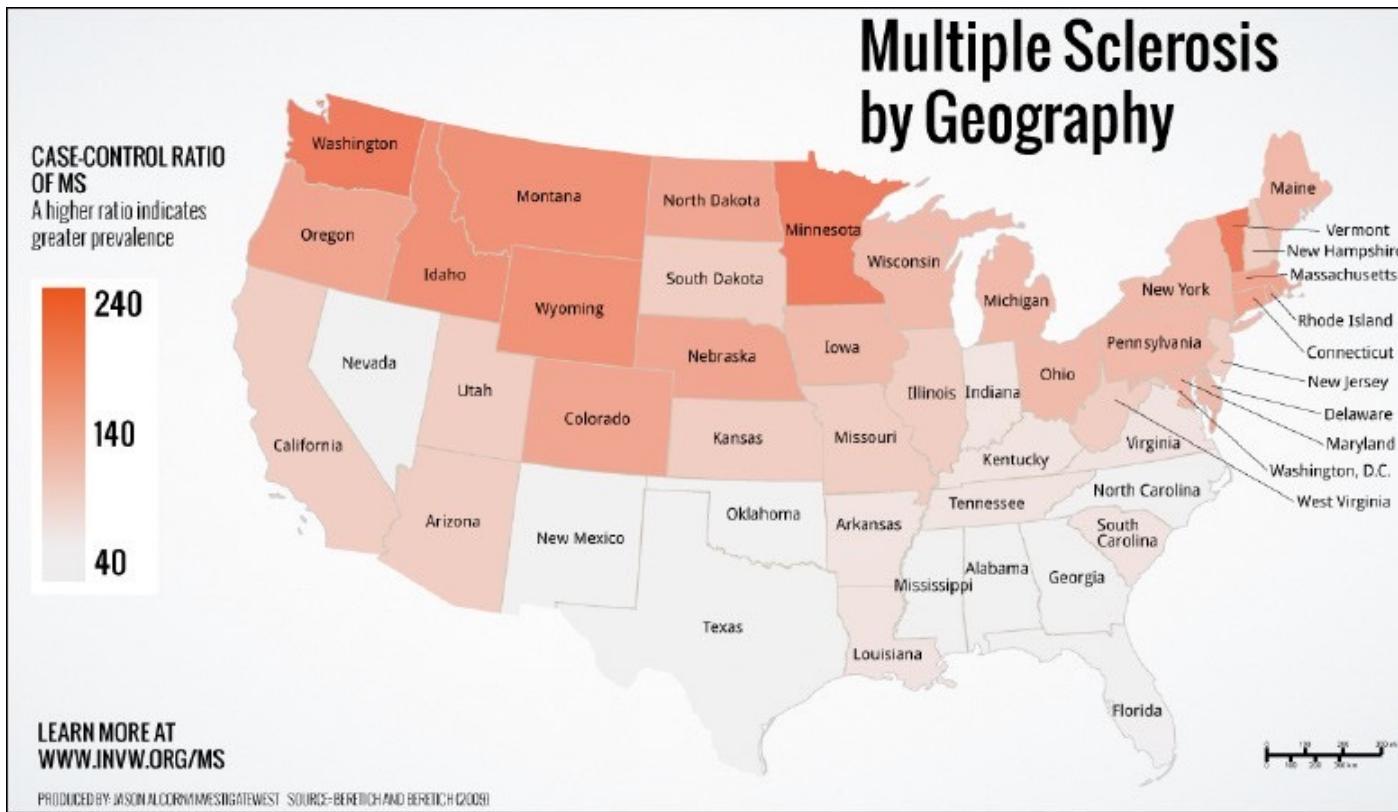


from Stys et al., 2012

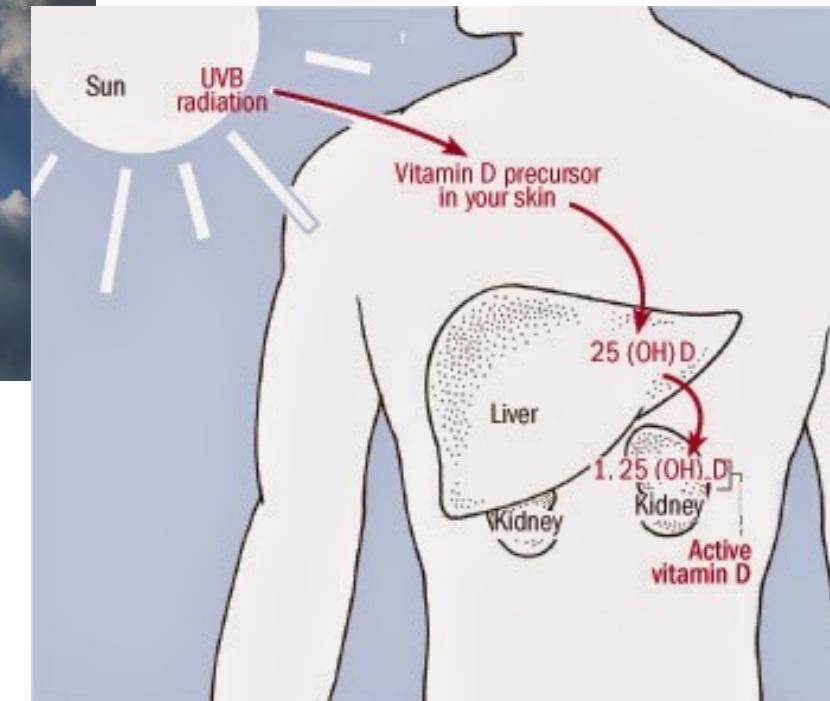
# Geography of MS



# Geography of MS

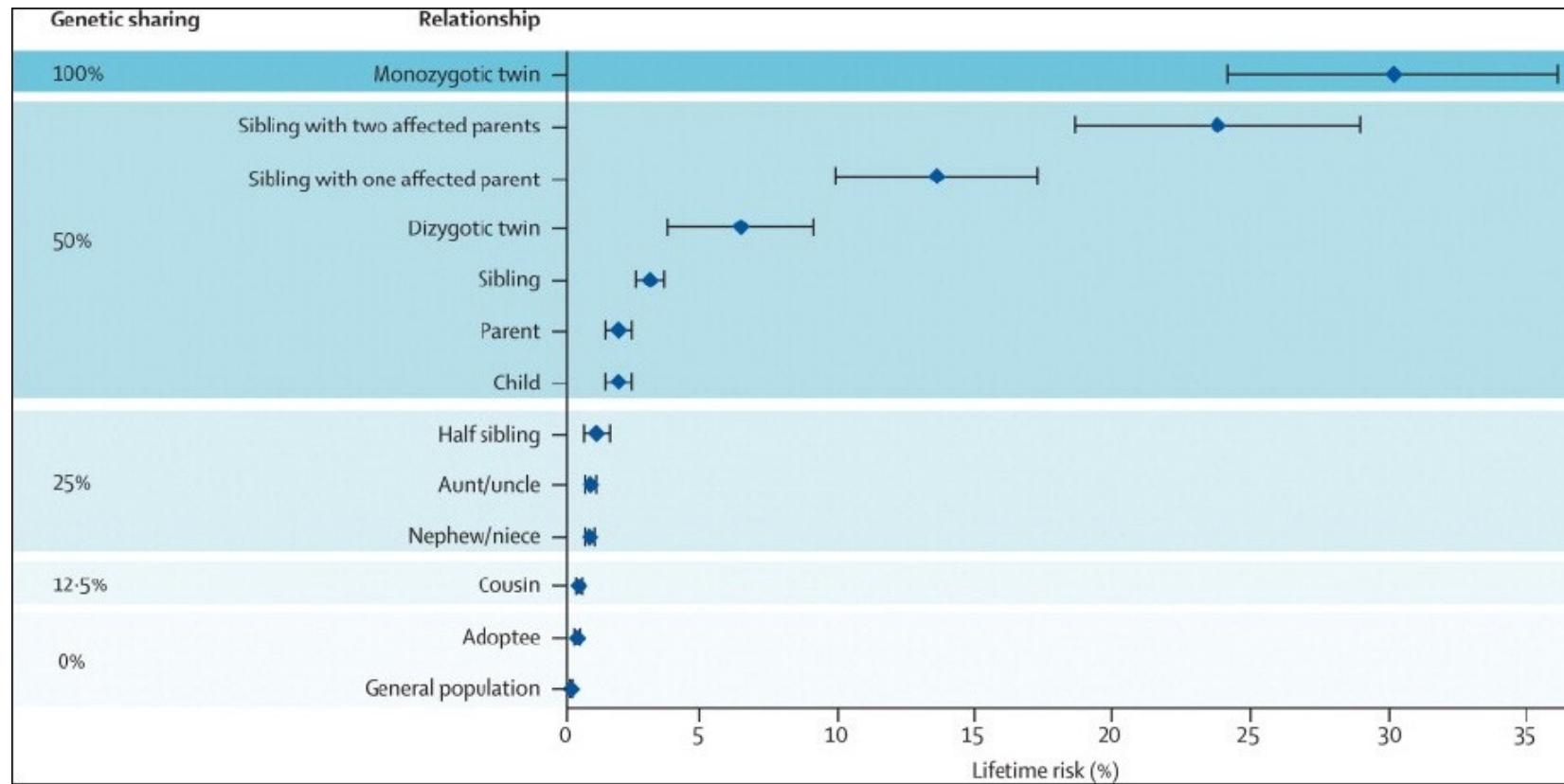


# Vitamin D

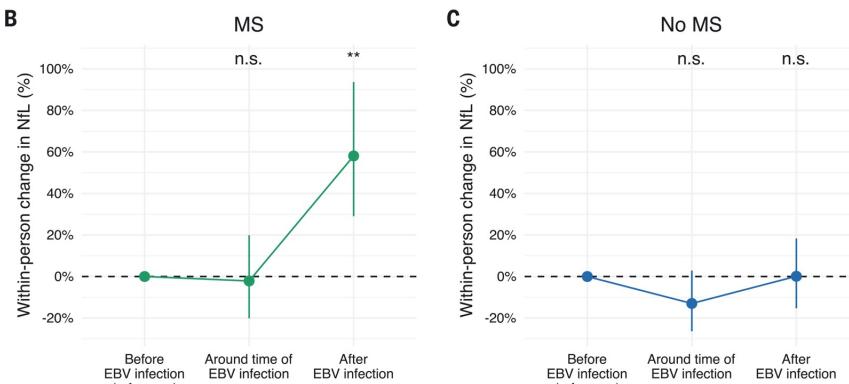


Some evidence for relationship between vitamin D and MS.

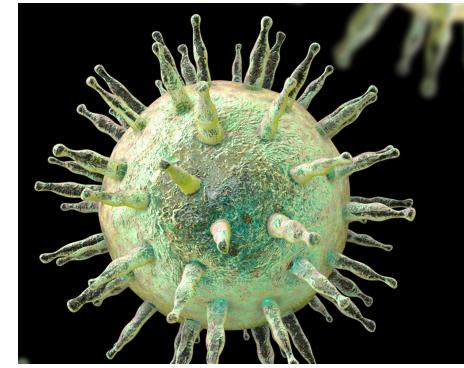
# Genetics



# What's causing MS?



Strong link to **Epstein-Barr virus (EBV, Herpes virus 4)**  
 Same virus that causes “mono”  
 Also associated with various cancers



Bjornevik *et al.* 2022: 10 million participants in the military!  
 All have blood sampled (HIV screening)  
 They selected EBV-negative participants and followed them  
 Can see screenings over time, plus onset of MS years later  
 i.e. longitudinal design

Findings: Epstein-Barr Virus increases risk of MS by 32x!

Only 1 of 801 new MS patients did not have EBV!

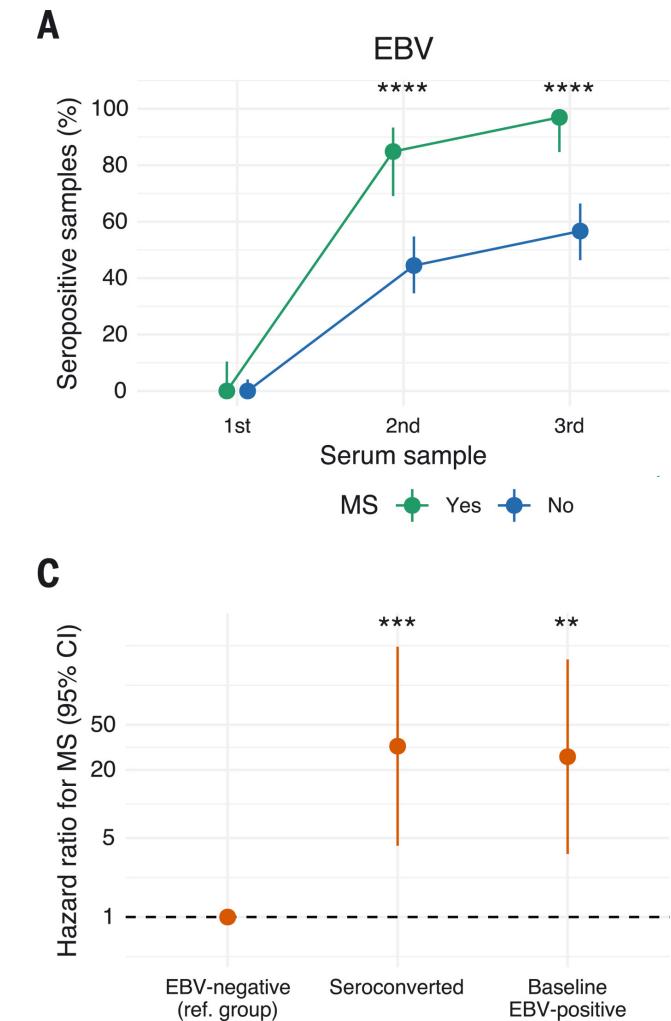
EBV preceded increase in markers of MS

Other virus exposure did not increase MS risk

Complication: most of us have EBV

Implication for MS prevention?:

## Multiple Sclerosis



Bjornevik *et al.* 2022

# Treatment / prevention?

1. Vitamin D supplements? (lack of is more a risk factor)
2. Corticosteroids
3. Immune system modulators
4. Cannabis (Sativex)
5. Physical therapy
6. Muscle relaxants
7. “Liberation treatment” of the veins? (No)
8. High-dose biotin? (Modest)
9. Hematopoietic stem cell transplantation? (Maybe)
10. Hopefully more/better soon
11. Hopefully EBV vaccine soon  
(not treatment, though)



WORKING TOGETHER TO ADVANCE BRAIN HEALTH  
THROUGH RESEARCH AND TREATMENT

MENU

- Home
- About
- Research
- Clinics
- News & Events
- Newsroom
- Events
- Brain Matters Newsletter
- Neuroscience Research Colloquia
- Donate
- Contact

**CLINICAL TRIAL RESULTS PUT LIBERATION THERAPY CONTROVERSY TO REST**

