



Alec lives in Seaside, Oregon. He was pinned down by an army truck in Iraq in 2003.

Deborah lives in New Hope, Minnesota. She was assaulted by her husband in 1979.



Olivia lives in Leesburg, Virginia. She was in a minivan when it was hit by an SUV in 2001.



Brain injury: As Diverse as We are.

No two people are alike... No two brain injuries are alike.

Joe lives in Silver City, New Mexico. He experienced a fall off of a horse in 2004.



- Every 23 seconds a brain injury occurs... It can happen to anyone.
- 1.4 million people in the United States sustain a brain injury every year
- 50,000 die, 235,000 are hospitalized, 1.1 million are treated in emergency departments
- 5.3 million Americans are now living with a disability due to a brain injury



Call BIAA's National Brain Injury Information Center's toll-free number for information and individualized help: **1-800-444-6443** or visit our website www.biausa.org

Traumatic Brain Injury

Jonathan Lifshitz, Ph.D.

Spinal Cord & Brain Injury Research Center

jlifshitz@uky.edu



Broadcast Yourself

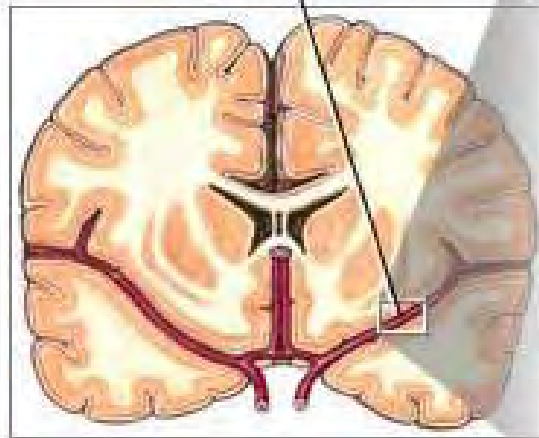
- Getting injured or the ways an injury occurs
 - <http://www.youtube.com/watch?v=RWHE3ISBJTg>
 - http://www.youtube.com/watch?v=8hb_HUY3T94
 - <http://www.youtube.com/watch?v=ZyJoPMK20Bo>
 - <http://www.youtube.com/watch?v=xLlvJqv7Mxo>
- Consequences of the injury; living with the injury
 - <http://www.youtube.com/watch?v=sAllqEwOfqk>
 - <http://www.youtube.com/watch?v=FgtHvBF4t-E>
 - http://www.youtube.com/watch?v=4m1ULS9K_4w
- Expert/professional information about the mechanisms of injury.
 - <http://www.youtube.com/watch?v=AmAML1-F2LE>
 - <http://www.youtube.com/watch?v=856rpjXDdu1M>

Traumatic vs. Atraumatic Brain Damage

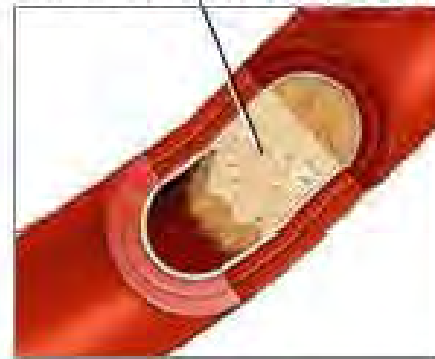
- Acquired brain injury
 - Occurs after birth
 - Not the result of genetic disorder, birth trauma, or degenerative disease
- Atraumatic: damage/forces progress over time
- Traumatic: Caused by an outside force that impacts the head hard enough to cause damage to the brain
- Outcome depends on:
 - Cause of the damage
 - Area(s) of the brain damaged
 - Extent of the damage

Atraumatic Brain Damage

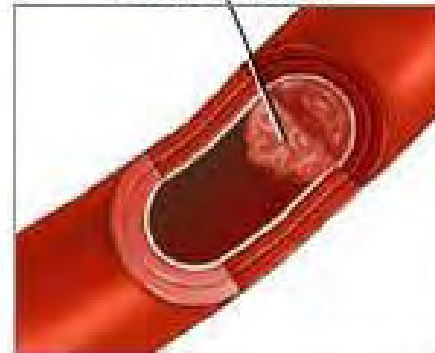
Coronal section of the brain showing middle cerebral artery



Atherosclerotic clot



Blood clot

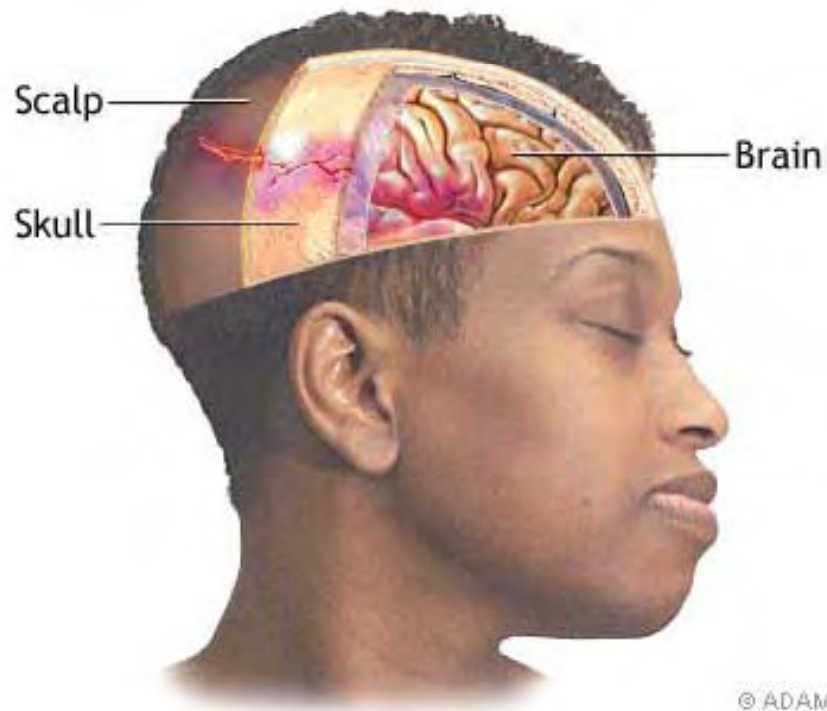




Willis McGahee – Baltimore Ravens RB
Ryan Clark – Pittsburgh Steelers DB
2009 AFC Championship
January 18th, 2009



Traumatic Brain Damage



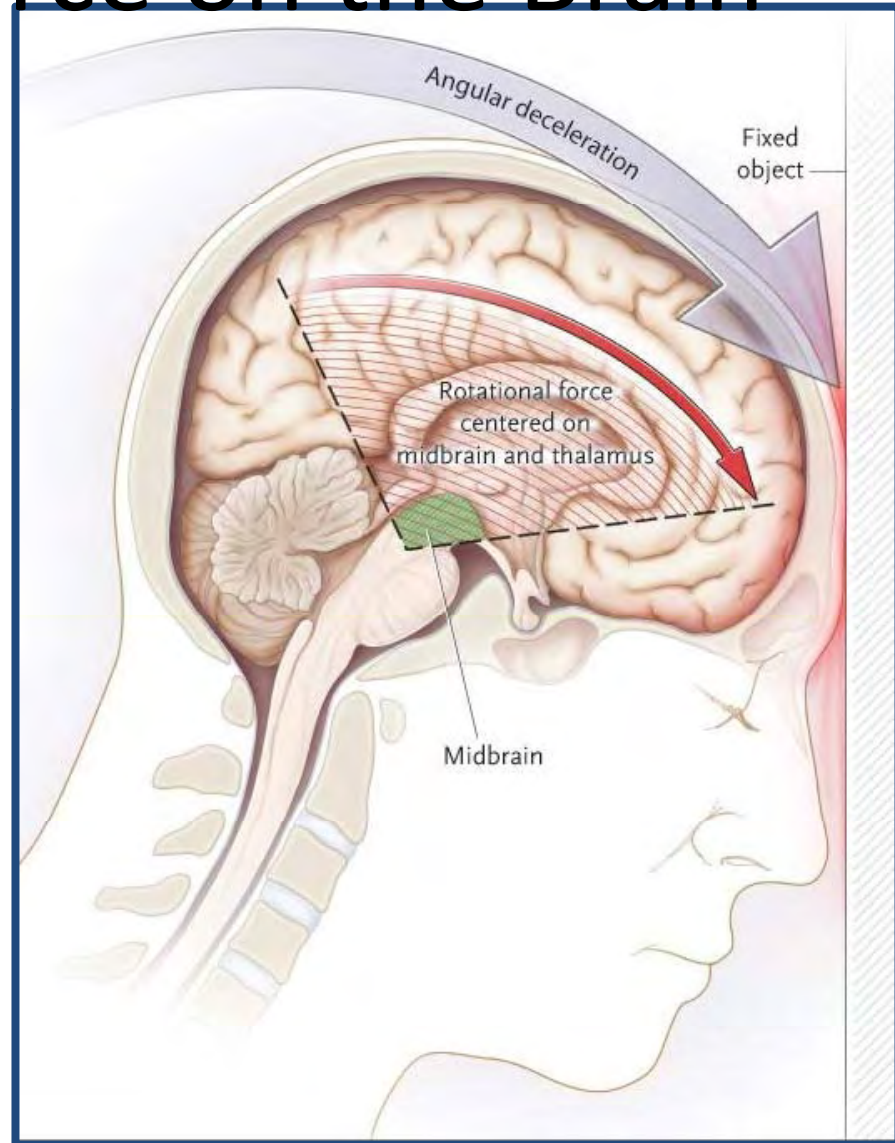
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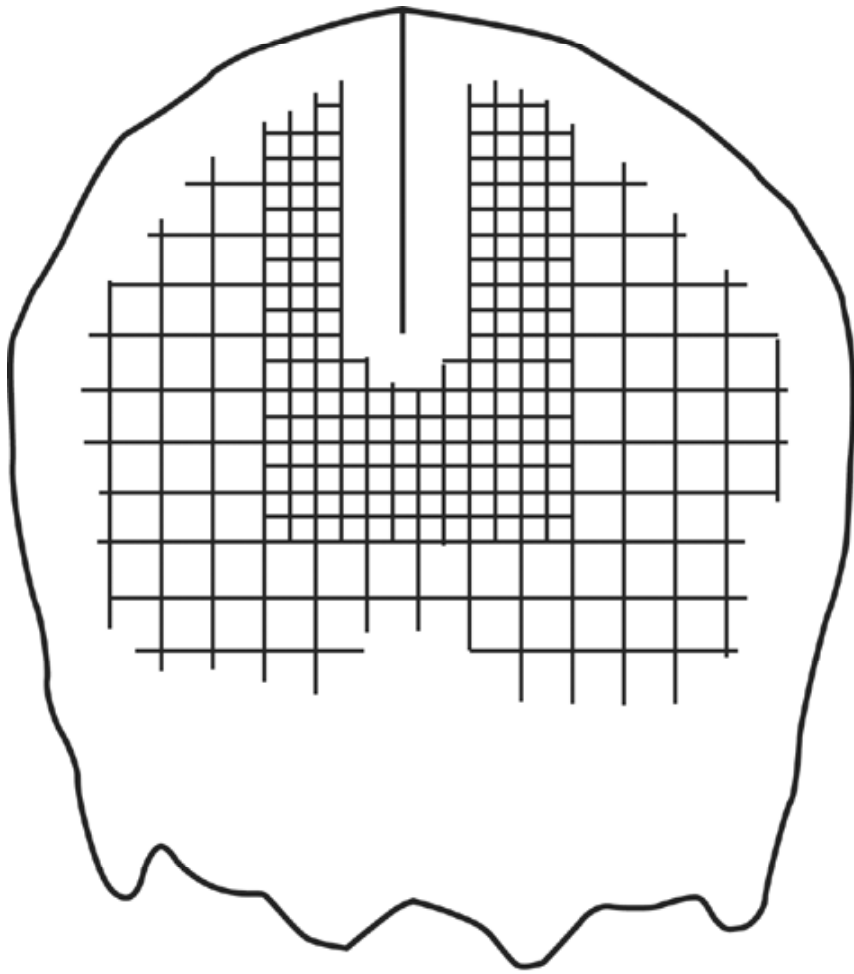


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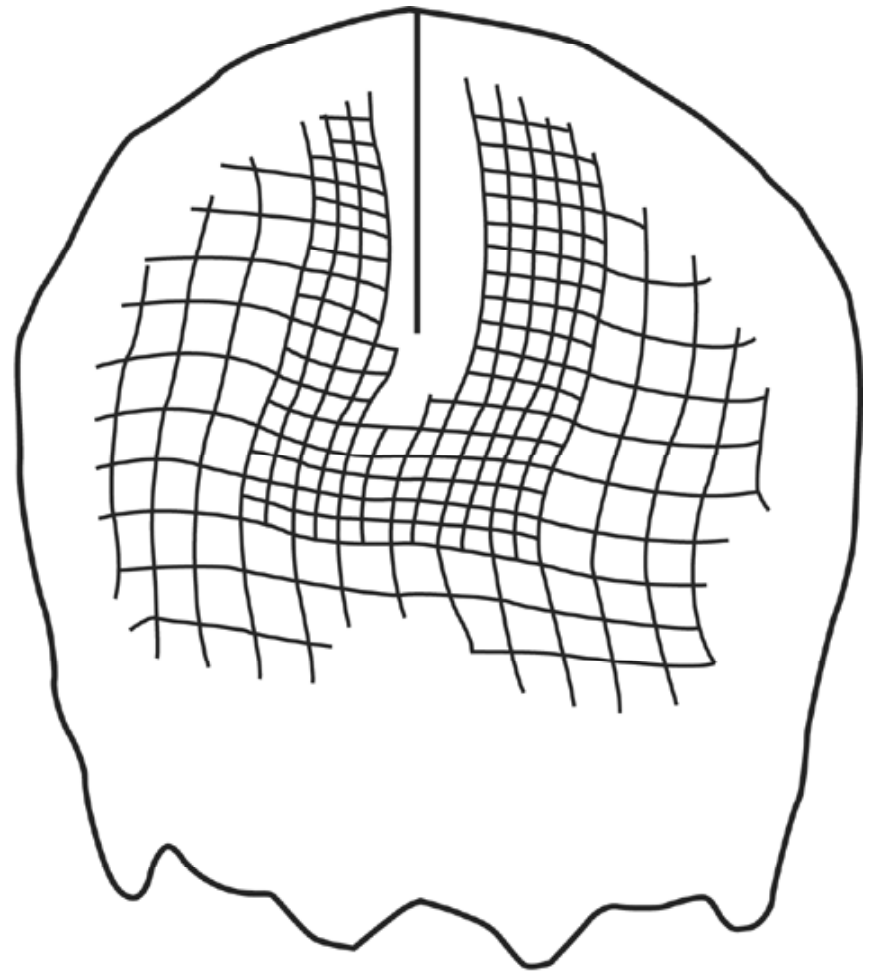
Rotational Force on the Brain

 The NEW ENGLAND
JOURNAL of MEDICINE





Undeformed

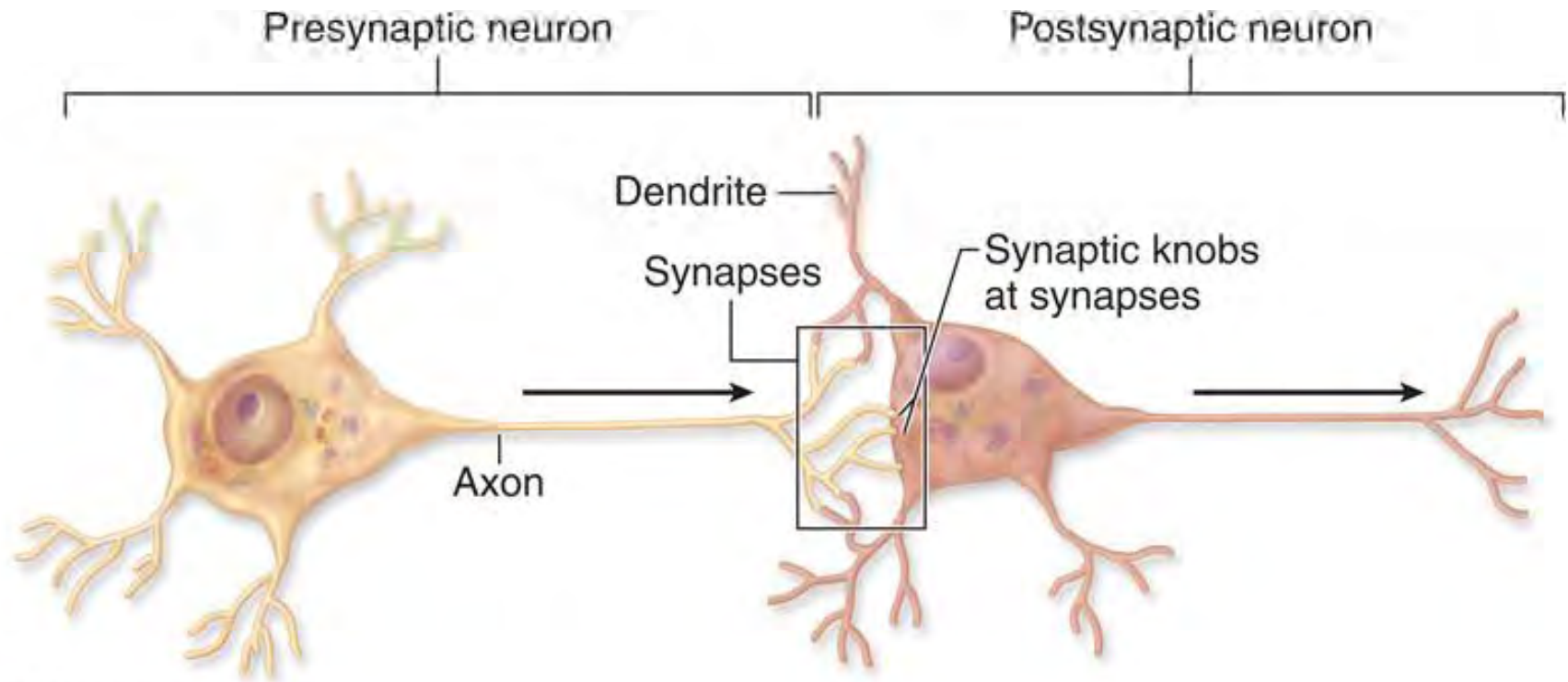


Peak acceleration

Nerve Cells neurons

- Cell body
 - Comprises gray matter
- Axon
 - Myelin forms white matter
- Dendrite
- Synapse

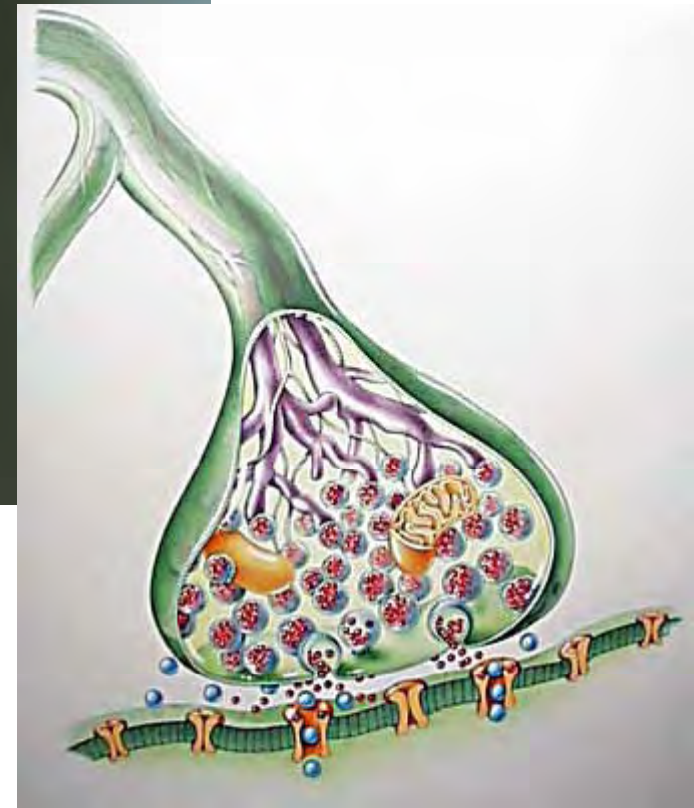
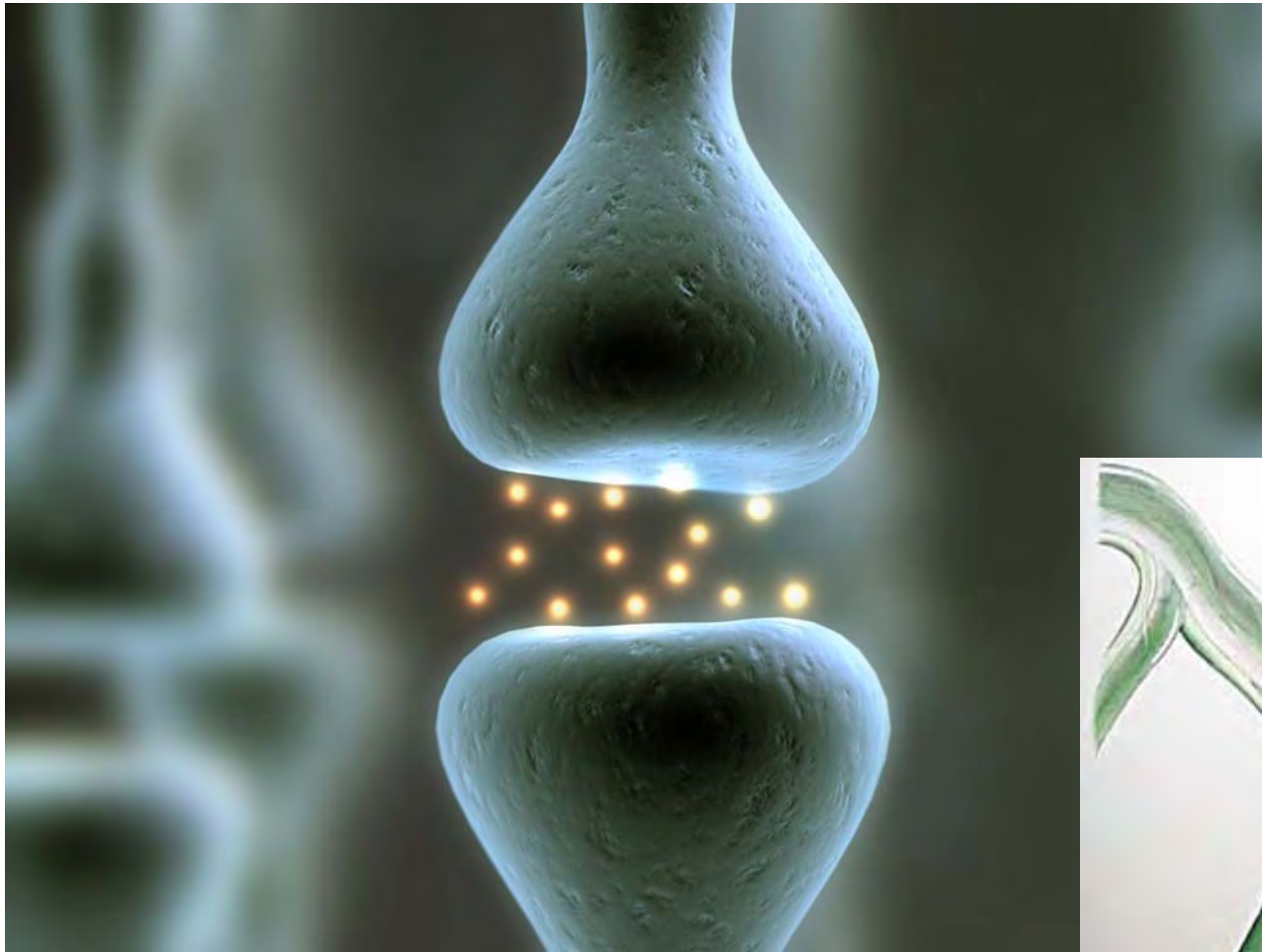


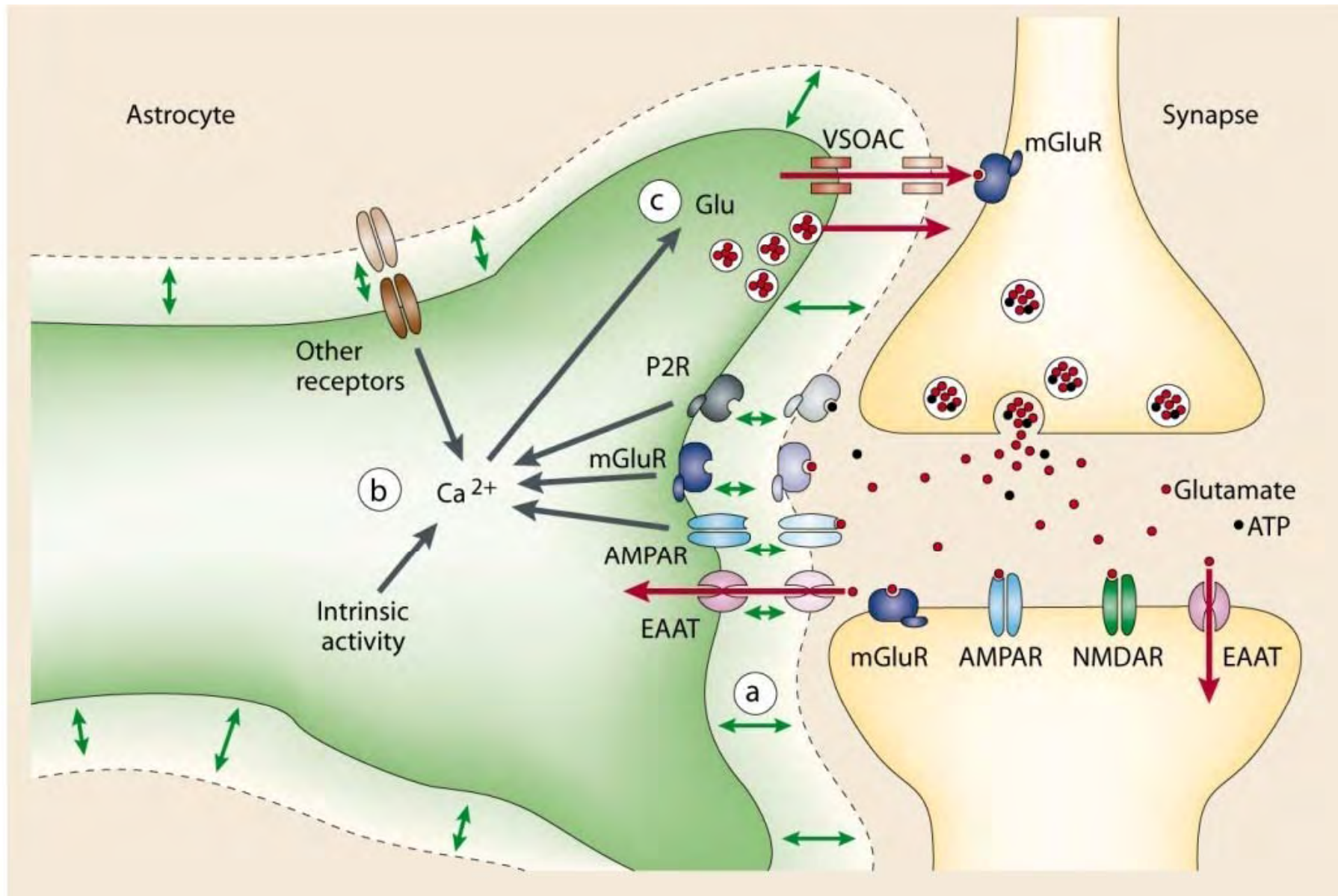


(a) Synapse



(b) Simplified representation of a synapse





Nedergaard et al. (2002) Beyond the role of glutamate as a neurotransmitter. *Nature Reviews Neuroscience* 3:748-755.

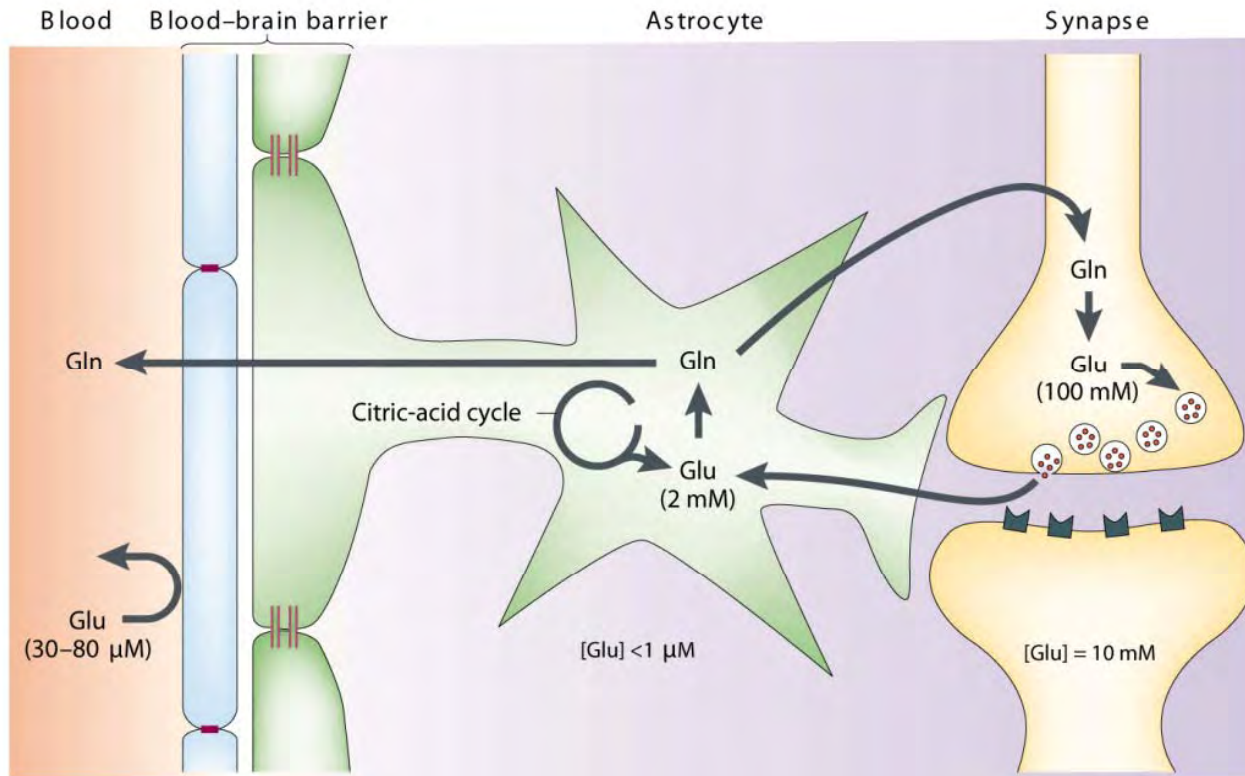
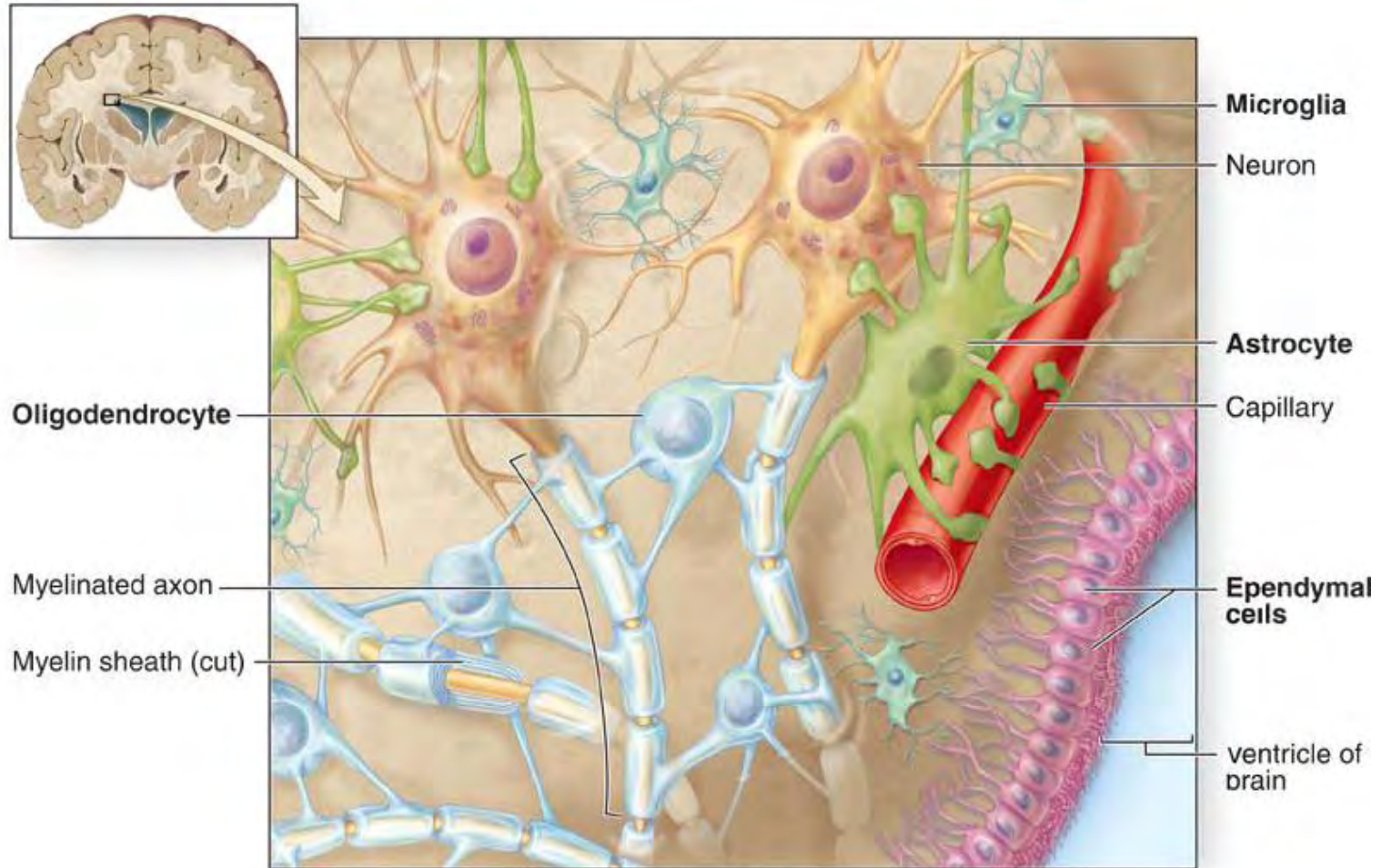
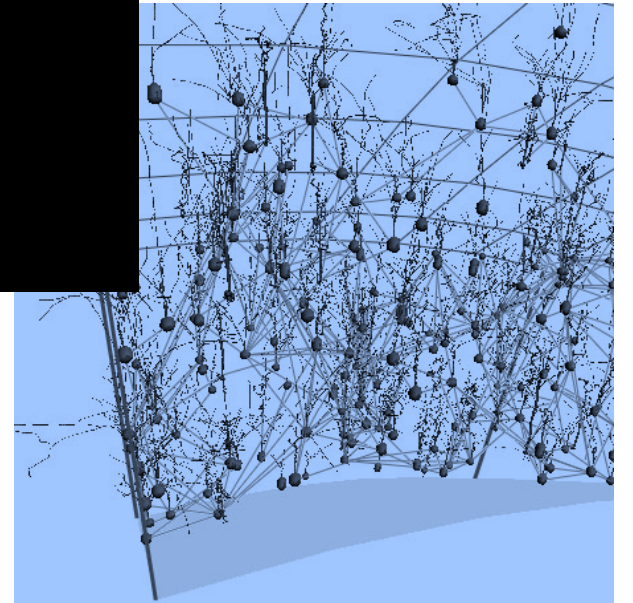
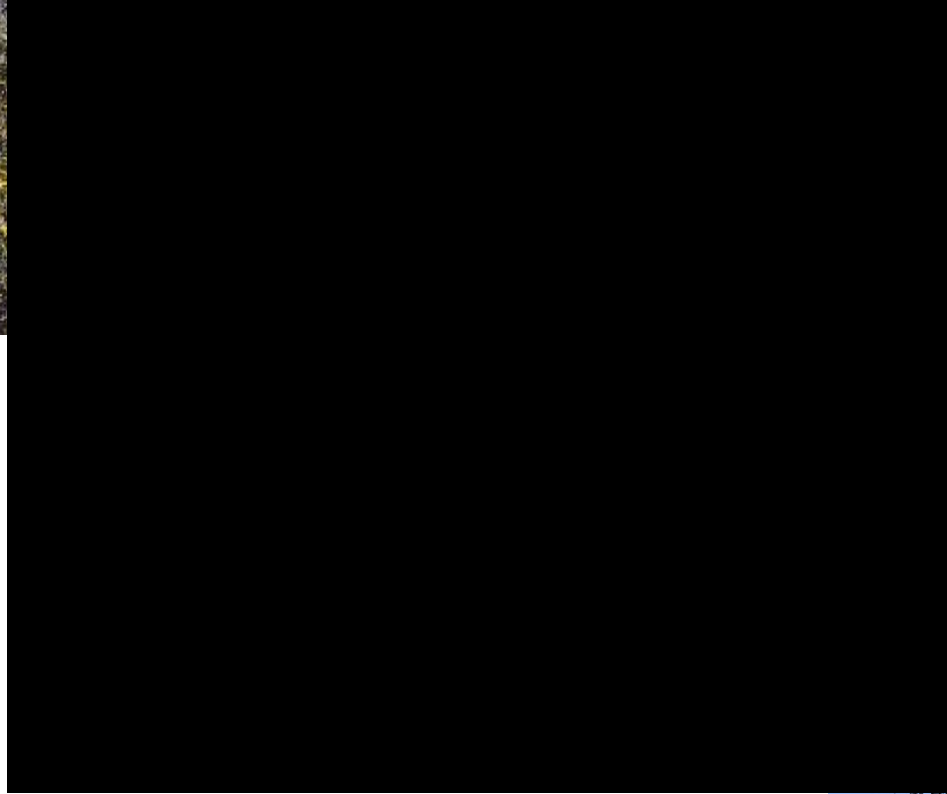
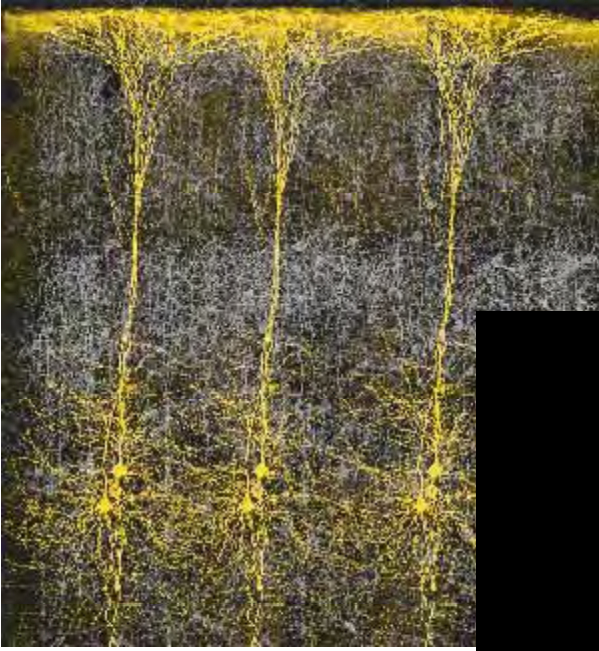


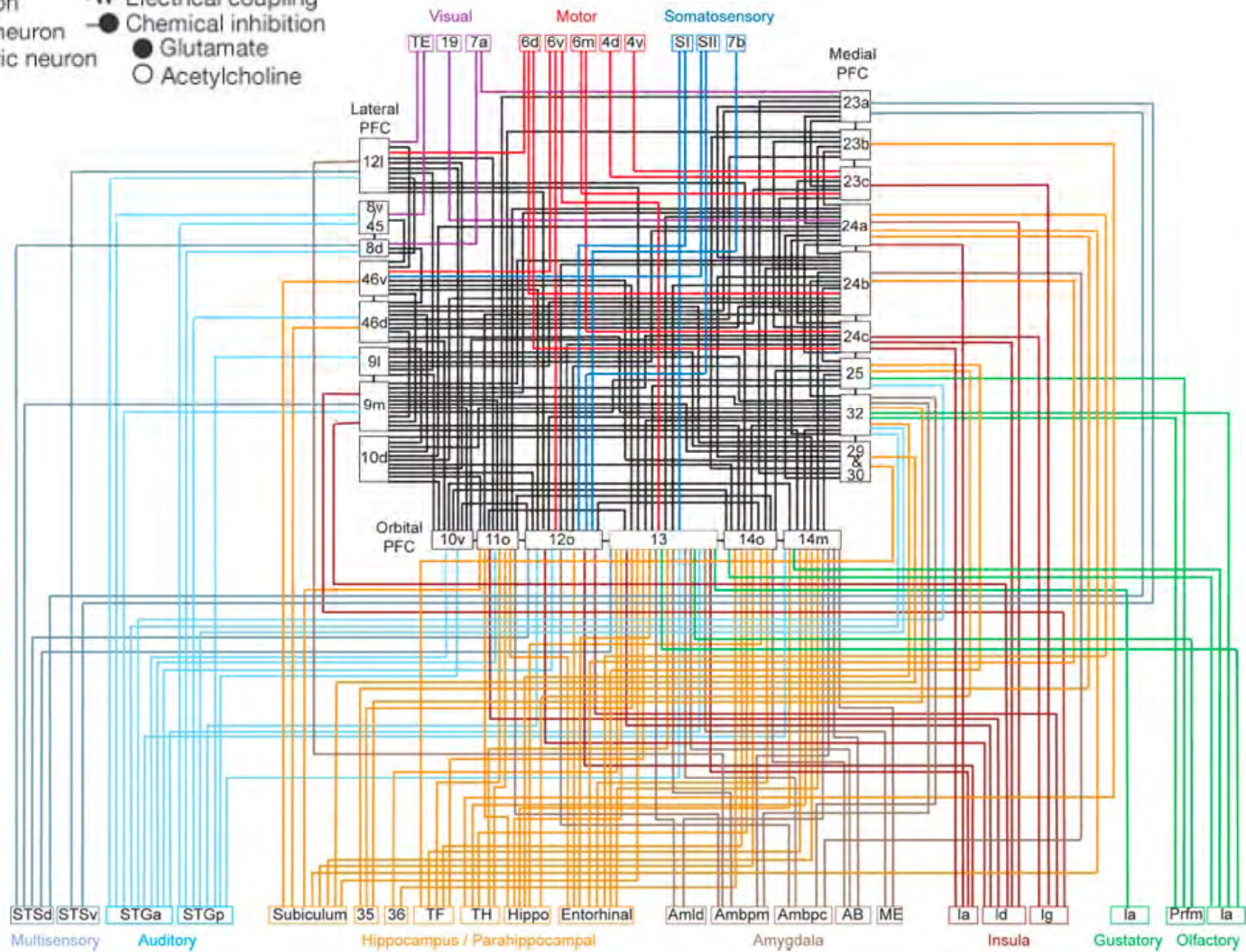
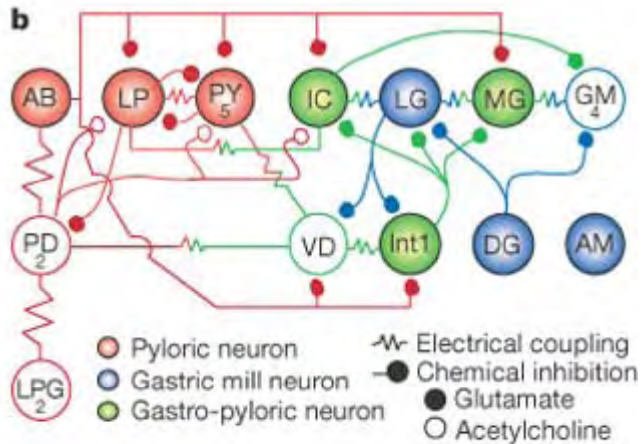
Figure 2 | Compartmentalization of brain glutamate. The blood–brain barrier has a very low permeability to glutamate (Glu). Essentially all glutamate in the brain is synthesized by transamination of α -ketoglutarate in both neurons and glia. In glial cells, glutamate is converted to glutamine (Gln) before it is released into the extracellular space. Glutamine is taken up by neurons and converted to glutamate before being packaged into synaptic vesicles. Glutamate is then recycled into the transmitter pool after uptake and conversion into glutamine by astrocytes. Glutamine also functions as a carrier of excess ammonium, and is transported across the blood–brain barrier to be disposed of by the circulation. In young animals, the blood–brain barrier has a higher permeability to glutamate, and excessive dietary uptake of glutamate can be excitotoxic¹²². The blood–brain barrier becomes impermeable to glutamate at seven days after birth¹²³, and circulating glutamate no longer represents a threat to neuronal survival after this period. The concentration of glutamate in the cerebrospinal fluid is about 1 μ M, but can increase to 20 μ M under pathological conditions that are characterized by defects in the blood–brain barrier and/or by cellular damage, such as stroke, trauma, multiple sclerosis and meningitis¹⁴.

Nedergaard et al. (2002) Beyond the role of glutamate as a neurotransmitter. *Nature Reviews Neuroscience* 3:748-755.

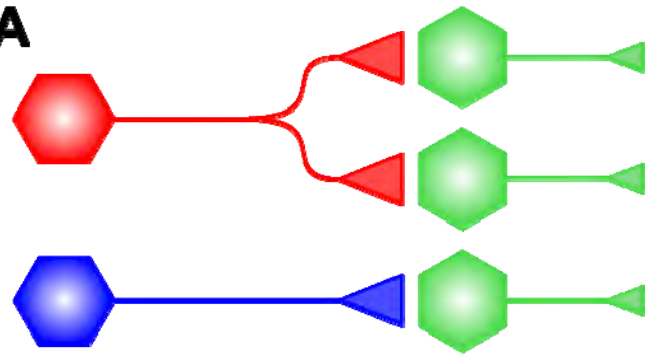
Neurovascular Unit



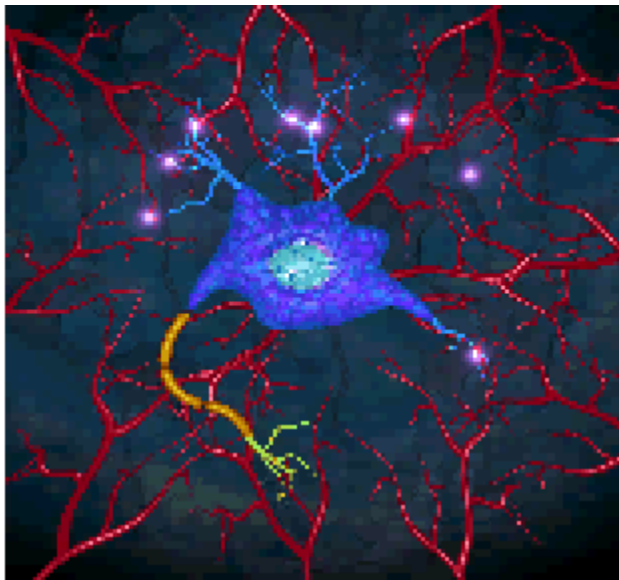




A

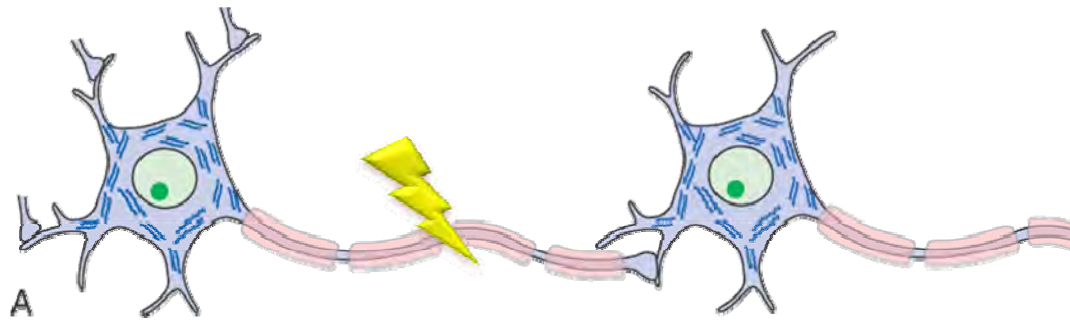


How does TBI cause the damage?

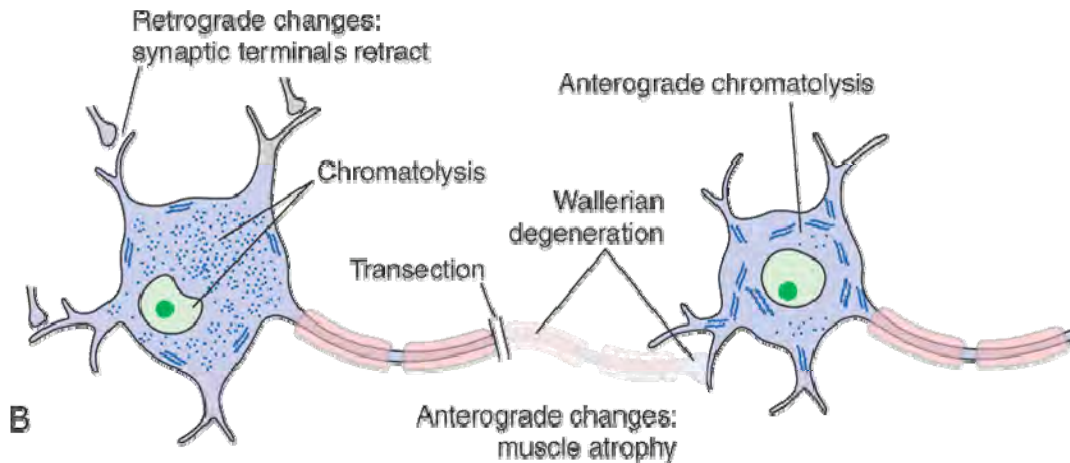


Diffuse Injury

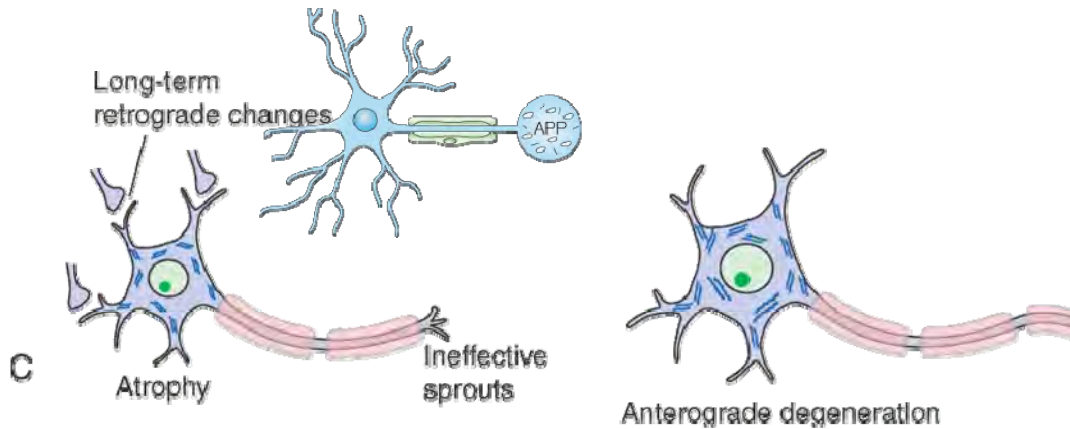
- Diffuse axonal injury
- Diffuse vascular injury
- Diffuse neuronal injury
- Diffuse glial injury
- Diffuse etcetera injury



A. Normal connection between neurons.

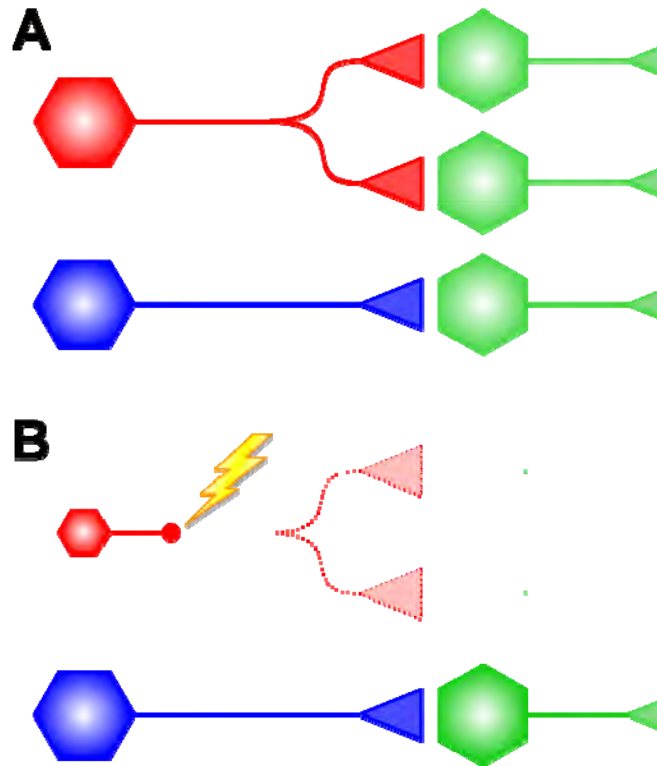


B. Wallerian degeneration and chromatolysis after axonal injury occurs together with retrograde and anterograde changes.

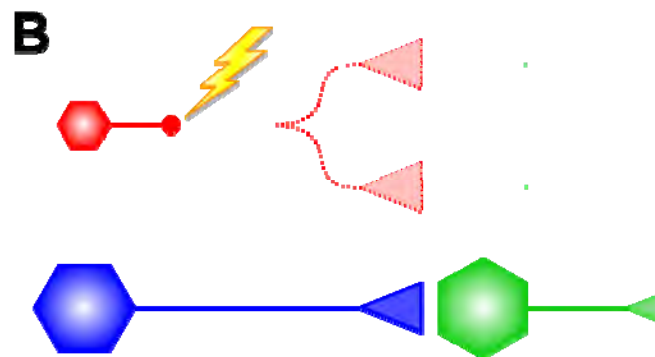
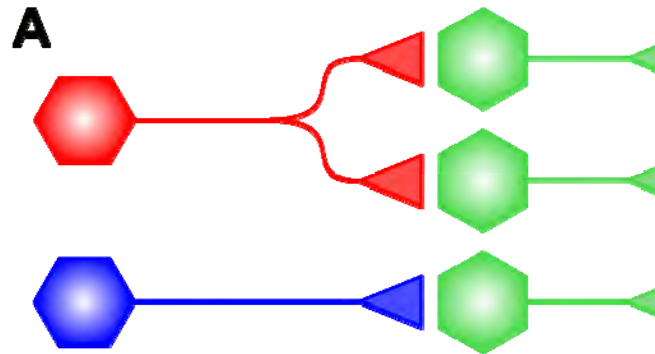


C. Surviving, axotomized neurons often atrophy and form ineffective axonal sprouts. Anterograde degeneration of the distal stump denervates post-synaptic neurons.

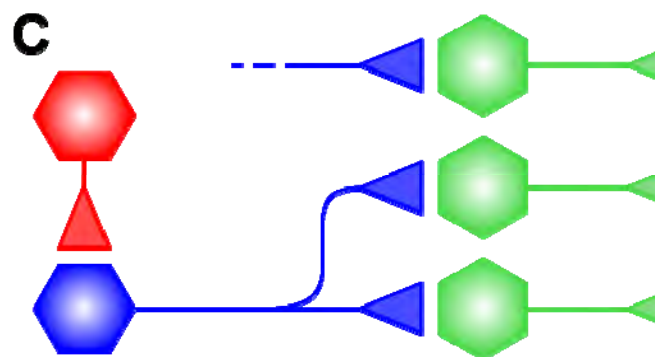
Injury-Induced Circuit Changes



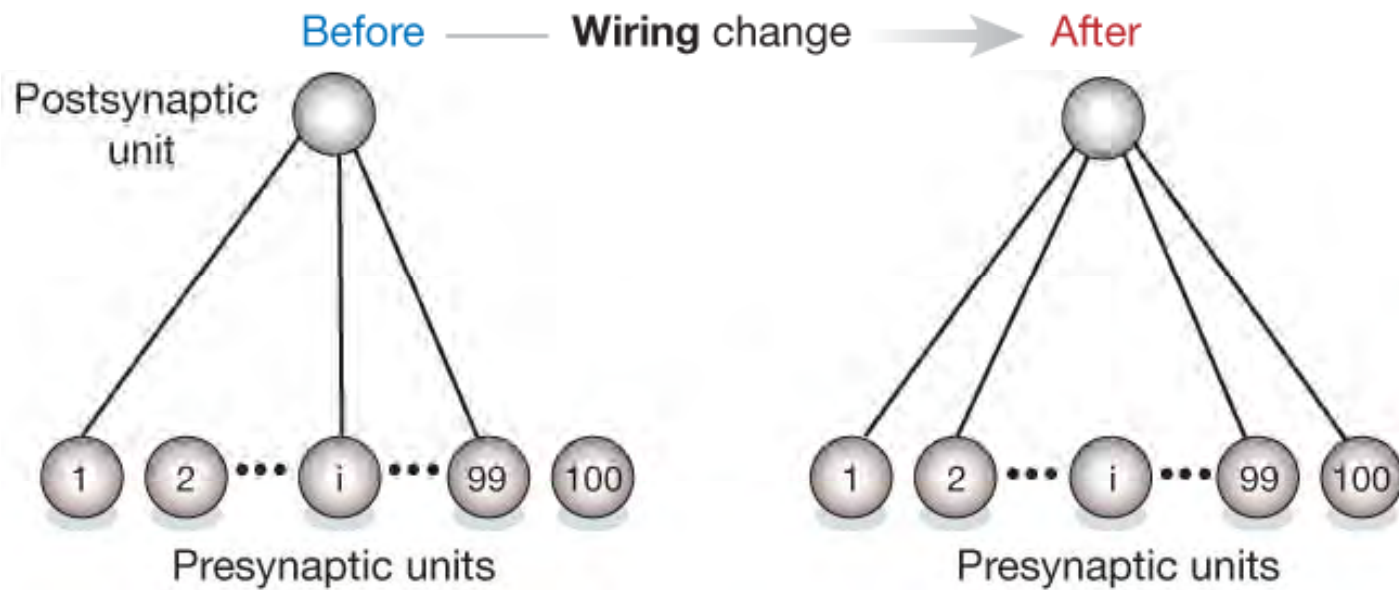
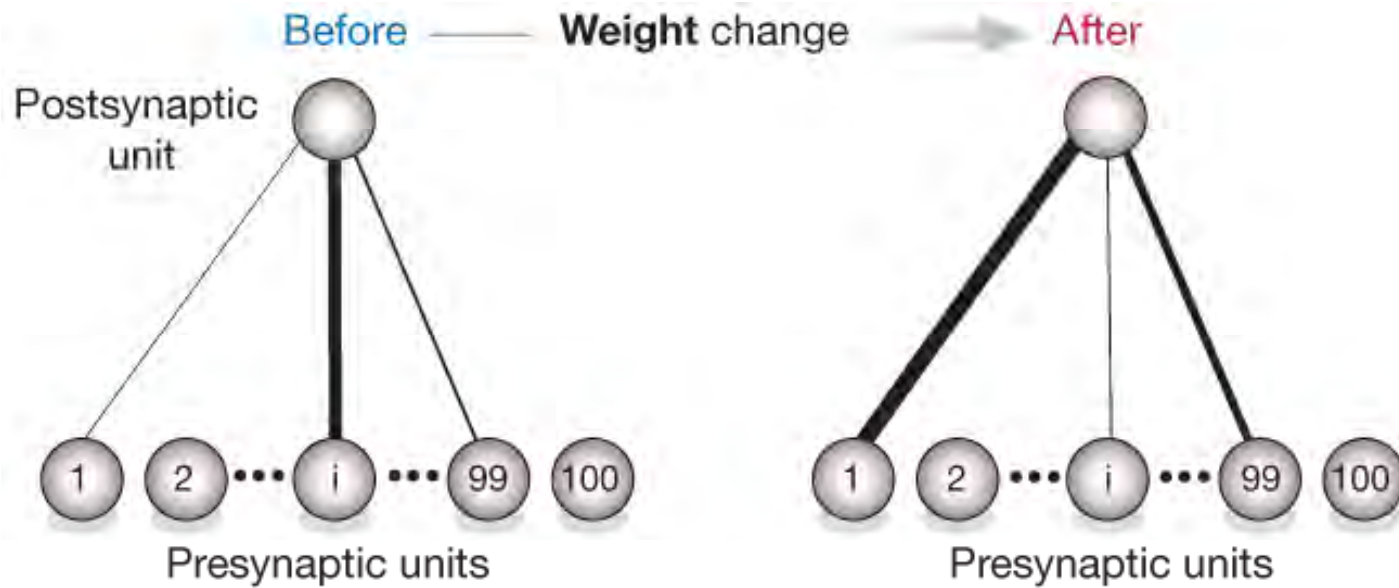
Injury-Induced Circuit Changes



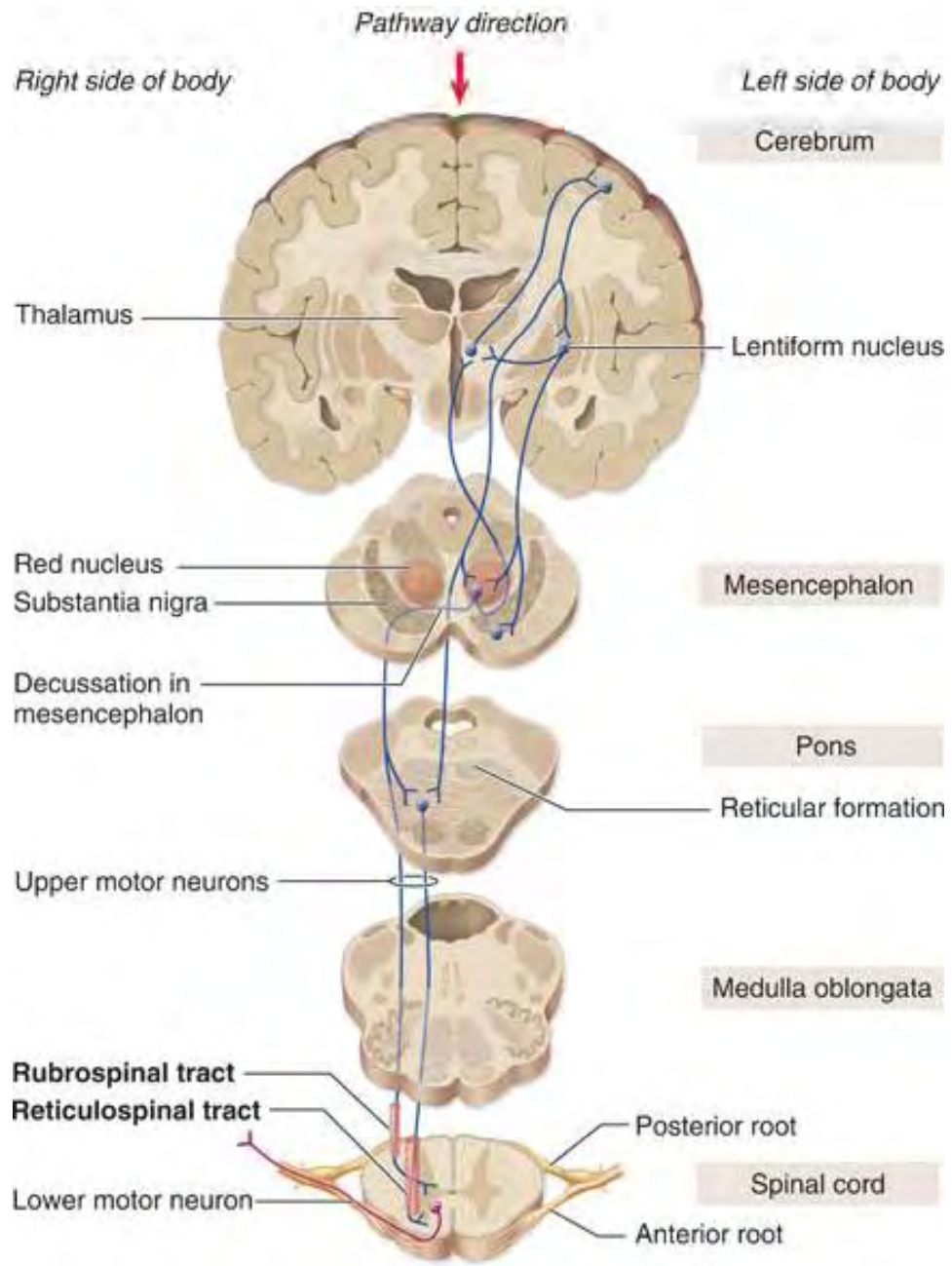
Deafferentation

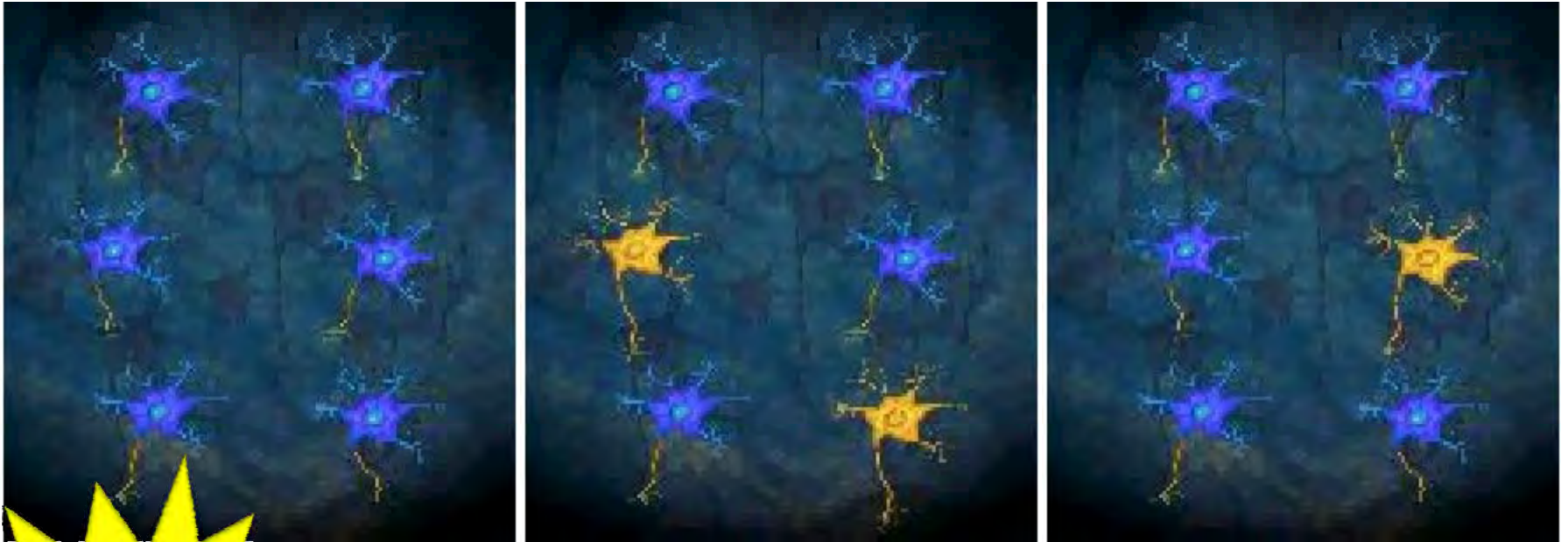


Neuroplasticity



Chklovskii et al. (2004) Cortical rewiring and information storage. *Nature* 431:782-788.





Traumatic
Brain
Injury

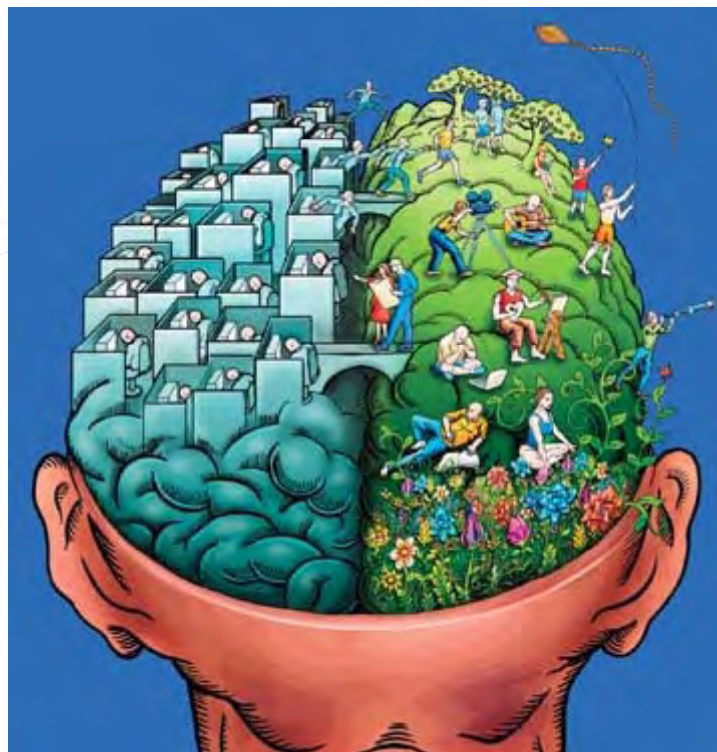
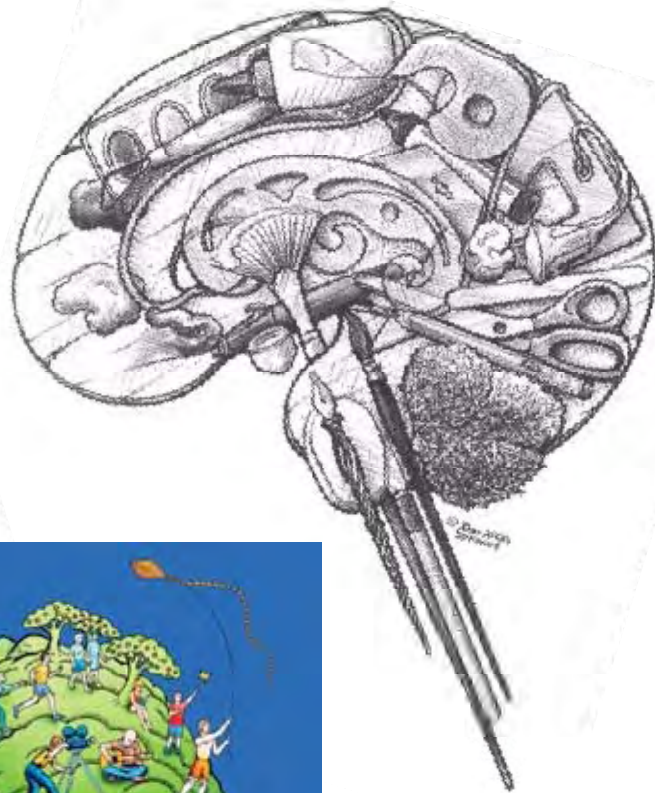
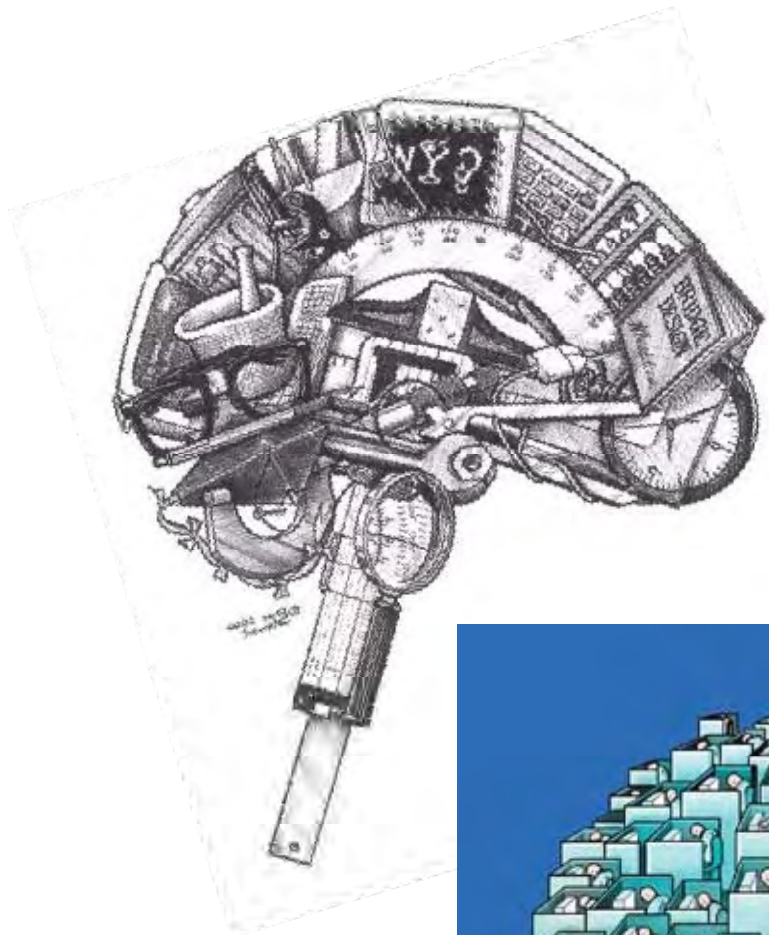
Diffuse
Brain
Pathology

Circuit
Training

Restructured
Circuit

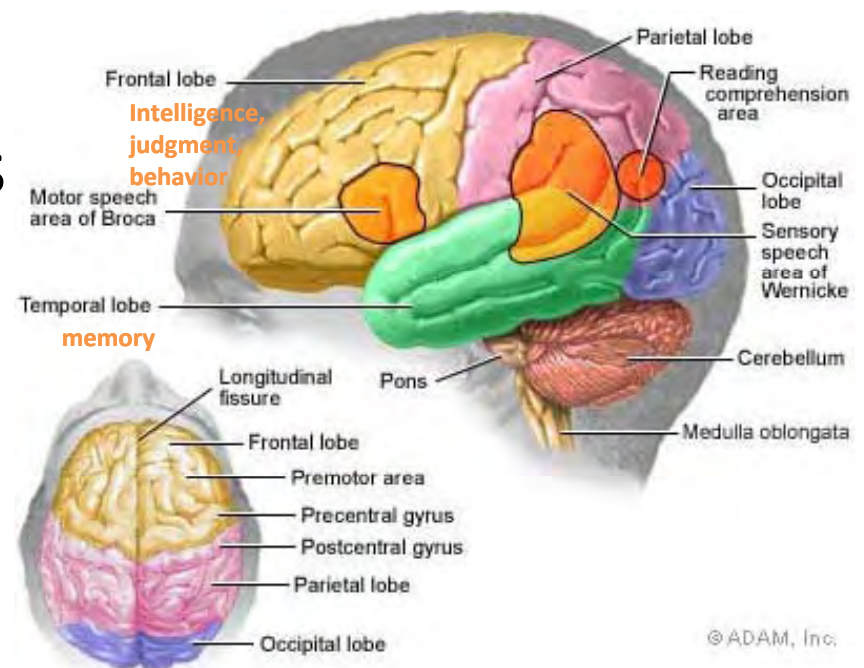
Circuit
Reorganization

Morbidity



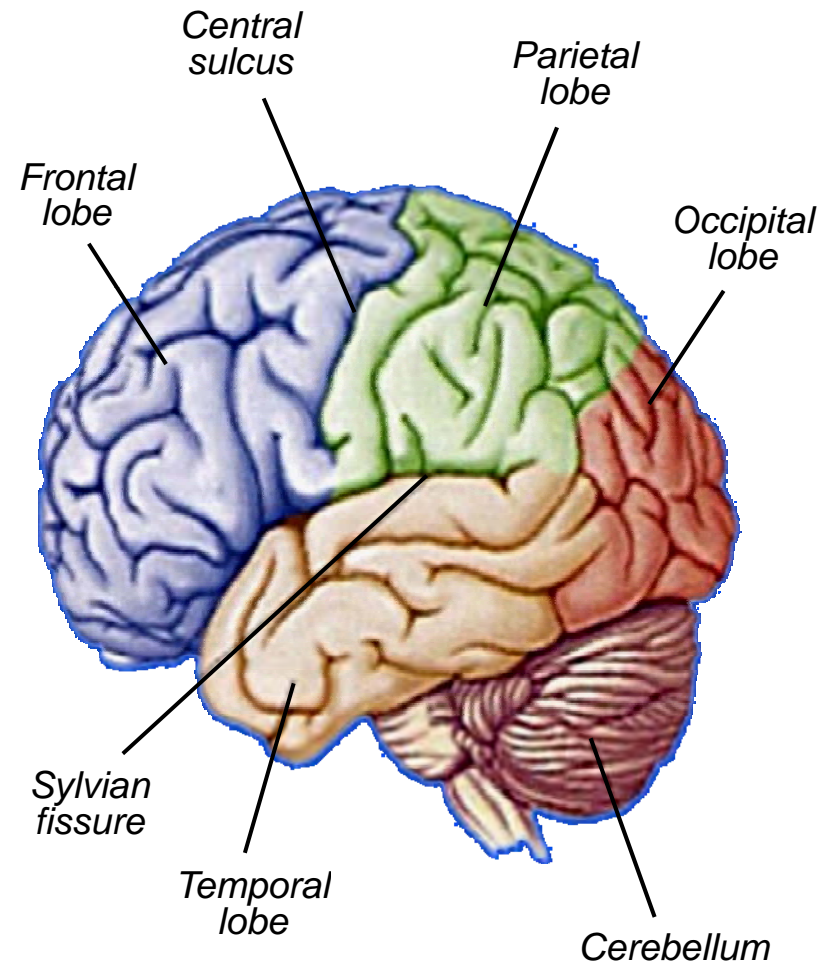
Deficits Correlate with Location of Injury

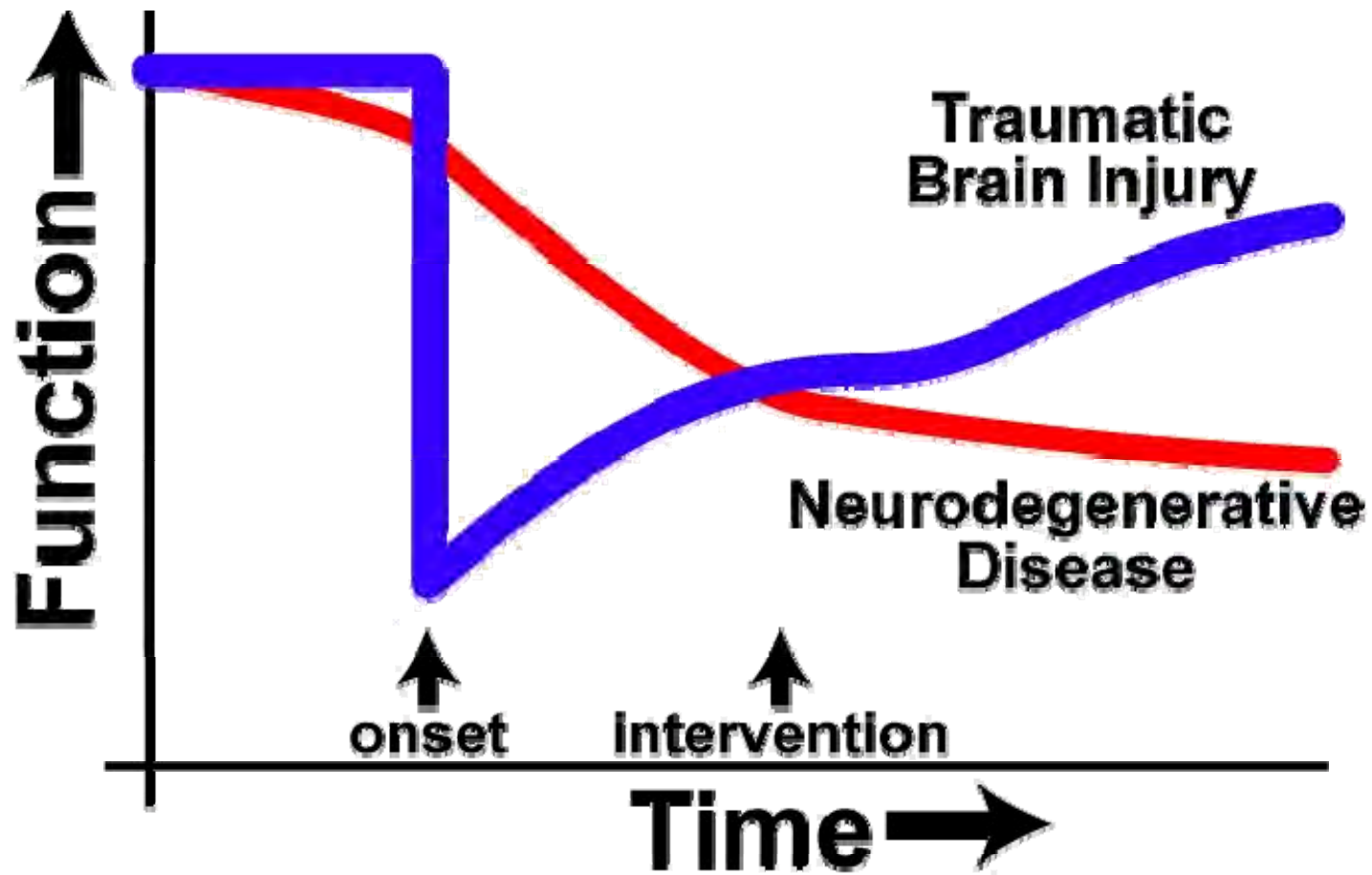
- Consequences of brain injury vary tremendously, depending on the type of injury and the area of brain damaged
 - Factors prior to and at the time of injury influence the injury and recovery
- Left vs. Right sided deficits



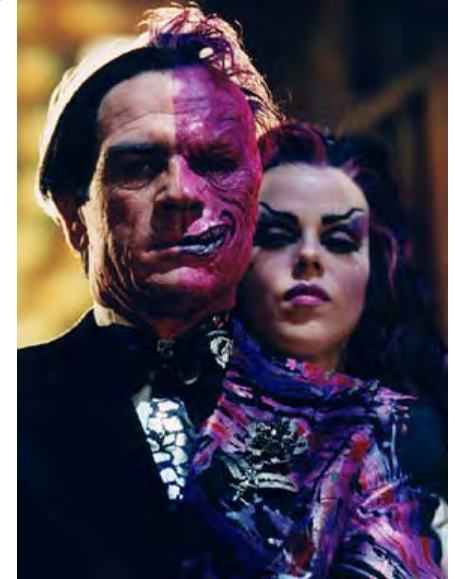
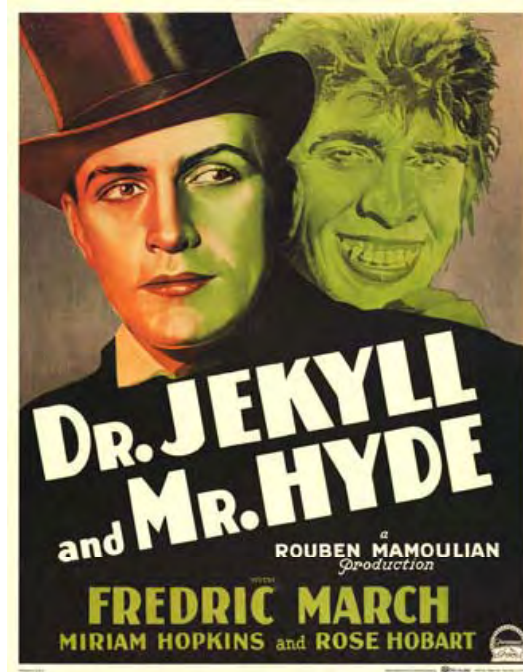
Mild Brain Injury

- Report significant
 - Headache
 - Fatigue
 - Irritability
 - Poor concentration
 - Poor attention
 - Memory problems
 - Word finding difficulty
 - Anxiety
 - Depression
 - Difficulty returning to routine, daily activities, including work





TBI Alters Personality



- Perhaps our discussions will revolve around the importance or relevance of protective gear. See the following website, for example: <http://www.headbumpa.com.au/>
- If you were to use the same search terms in Google™, the results are more than likely personal injury lawyer webpages. Would you rely on medical information provided through a law firm?

Traumatic Brain Injury

Brain injury is NOT a progressive condition.

Brain injury is, however, a lifelong disability.

*"No head injury is too severe to despair of,
nor too trivial to ignore."*

Hippocrates

****FUNCTIONAL CONSEQUENCES**

Functional Consequences of Brain Damage

- Motor control and perception
- Communication effects
- Cognitive changes
- Personality change and affective response

Functional Consequences:

Motor & Perceptual Consequences

- Movement, coordination or balance
- Visual-spatial relations
- Perception
- Vision and hearing
- Touch, taste, smell
- Eating and swallowing
- Endurance
- Bowel, bladder and sexual function

Functional Consequences: Communication Effects

- Speech
 - Physical inability to produce sounds
 - Inability to position and sequence muscle movements
- Language
 - How words are put together to convey and understand concepts

Functional Consequences: Cognitive Changes

- Memory
- Attention and concentration
- Self-awareness
- Problem solving and decision making
- Information processing and concept formation
- Judgment

Cognitive Changes: Memory

- Types of Memory
 - Immediate memory / working memory
 - Short-term memory
 - Long-term memory
- Amnesia
 - Retrograde amnesia
 - Anterograde amnesia
- Memory impairments can be the most limiting of all potential cognitive consequences of TBI, since they affect the ability to learn, store and retrieve information.
 - Ability to profit from experience

Cognitive Changes: Self-awareness

- Lack insight into the appropriateness of their behavior and may be unaware of the impact certain aspects of their behavior have on other people

Cognitive Changes: Information Processing

- More time may be needed to synthesize verbal or visual input
- ‘cognitive delay’

Functional Consequences:

Personality Change & Affective Response

- Misinterpreted by others
 - Laziness, disinterest, uncooperativeness
- Personality changes
 - Emotionally explosive, outbursts of anger or anxiety
- Anger or irritability
- Aggressive behavior – verbal or physical, active or passive
 - Decreased patience
- Nonconformance to social norms
 - Disinhibition, inadequate social skills
- Apathy and depression
- Loss of self-esteem

****FUNCTIONAL IMPLICATIONS**

Functional Implications of Brain Damage

- Psychological Issues
- Social Issues
- Lifestyle Issues
- Vocational Issues

Functional Implications:

Psychological Issues in Brain Damage

- Emotional reactivity, loss of emotional control, emotional lability
 - Depression, mood swings, psychosis
- Impulsivity

- Personality traits that were present prior to brain damage may become exaggerated after the damage has occurred, or there may be dramatic personality change, so that an individual who was quiet and passive prior to brain damage may become boisterous and aggressive after injury.
- Often because of changes in temperament, behavior and personality, there is a disruption in family cohesion and feelings of entrapment by family members.

Functional Implications: Social Issues in Brain Damage

- Family relationships are significantly altered
 - Prolonged stress of caregiving
 - Financial burden
- Neither the family nor the individual has the opportunity to prepare for the emotional and economic impact of TBI

Functional Implications: Lifestyle Issues in Brain Damage

- Implementation and acceptance of new accommodations and assistive devices
- Independence
 - Operating motor vehicle
- Eating behavior
 - Physical component
 - Planning and maintaining diet

Functional Implications:

Vocational Issues in Brain Damage

- Helping them find alternative ways to perform tasks and to develop strategies to reduce, organize, and retrieve information can reduce the disabling effects of memory impairment.
 - To overcome difficulty organizing their day and improve performance
 - Implementing structured routines
 - Using written notes or lists
 - Using audiotaped reminders
- Too much information may cause the individual to become overwhelmed and confused

****CIRCUIT REWIRING**

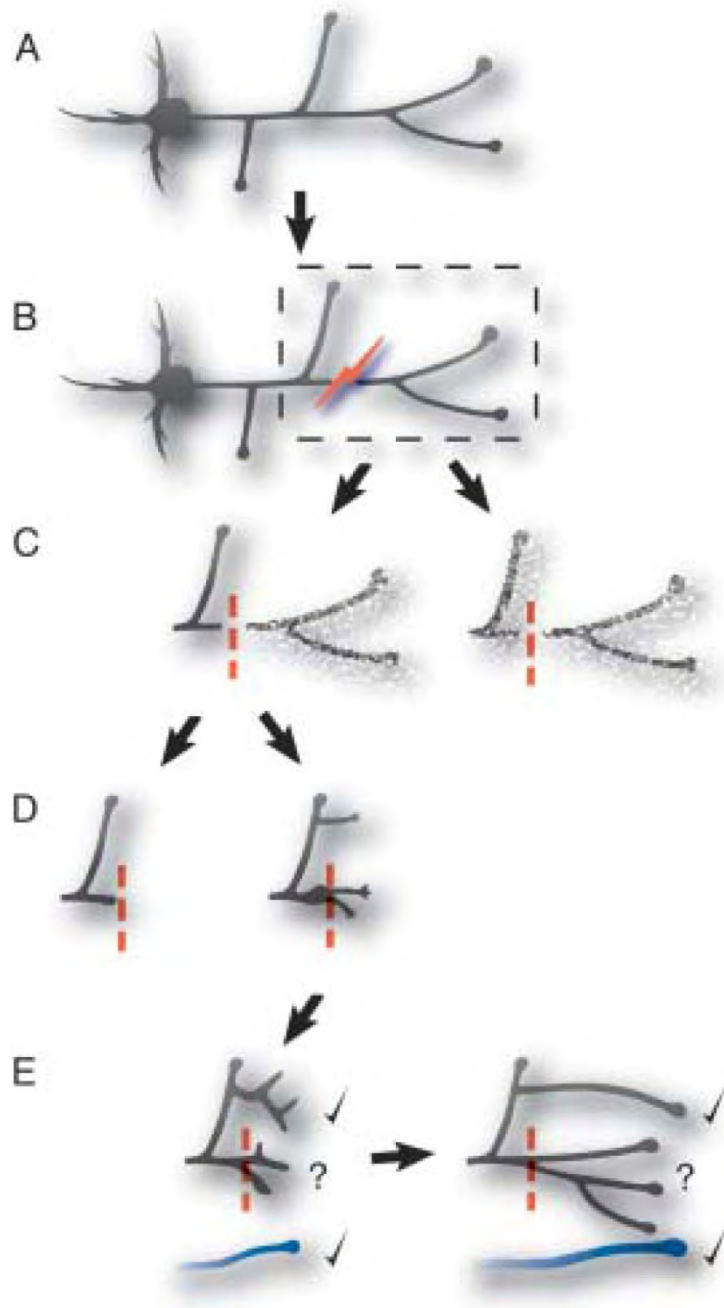


Fig. 1. Diagrammatic representation of the range of possible responses of CNS neurons to injury. A, A normal, intact cortical neuron. Axonal injury or complete transection (axotomy), as indicated in (B), may induce a cascade of reactive and regenerative alterations. Although axonal damage may induce immediate cell death (retrograde degeneration), there is also the possibility that the proximal axonal segment may seal over and survive while the disconnected distal segment degenerates (C). The proximal axonal segment may then undergo no further change or may attempt to regenerate. Attempted regeneration manifests as the formation of fine axonal protuberances or sprouts, which are often tipped by characteristic growth cones (D). Axonal sprouts may also be derived from newly generated collateral branches, either arising from undamaged branches of the injured axons or entirely uninjured axons in the vicinity of the injured axon (the latter represented by blue axons in E). In addition, though highly contentious, it is possible that axonal sprouts may be elaborated directly from the severed stump of the injured axon, albeit with sprouting limited to the local neuropil rather than extending for long distances.

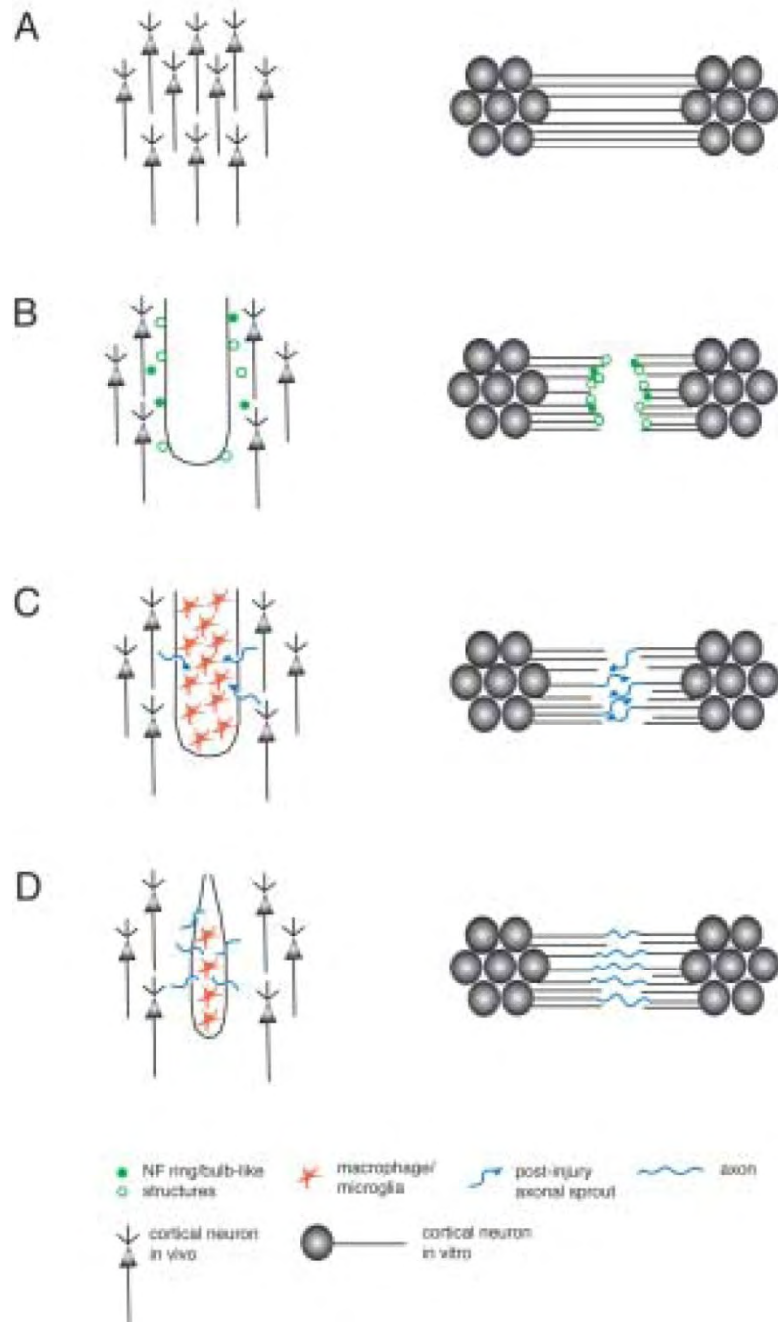
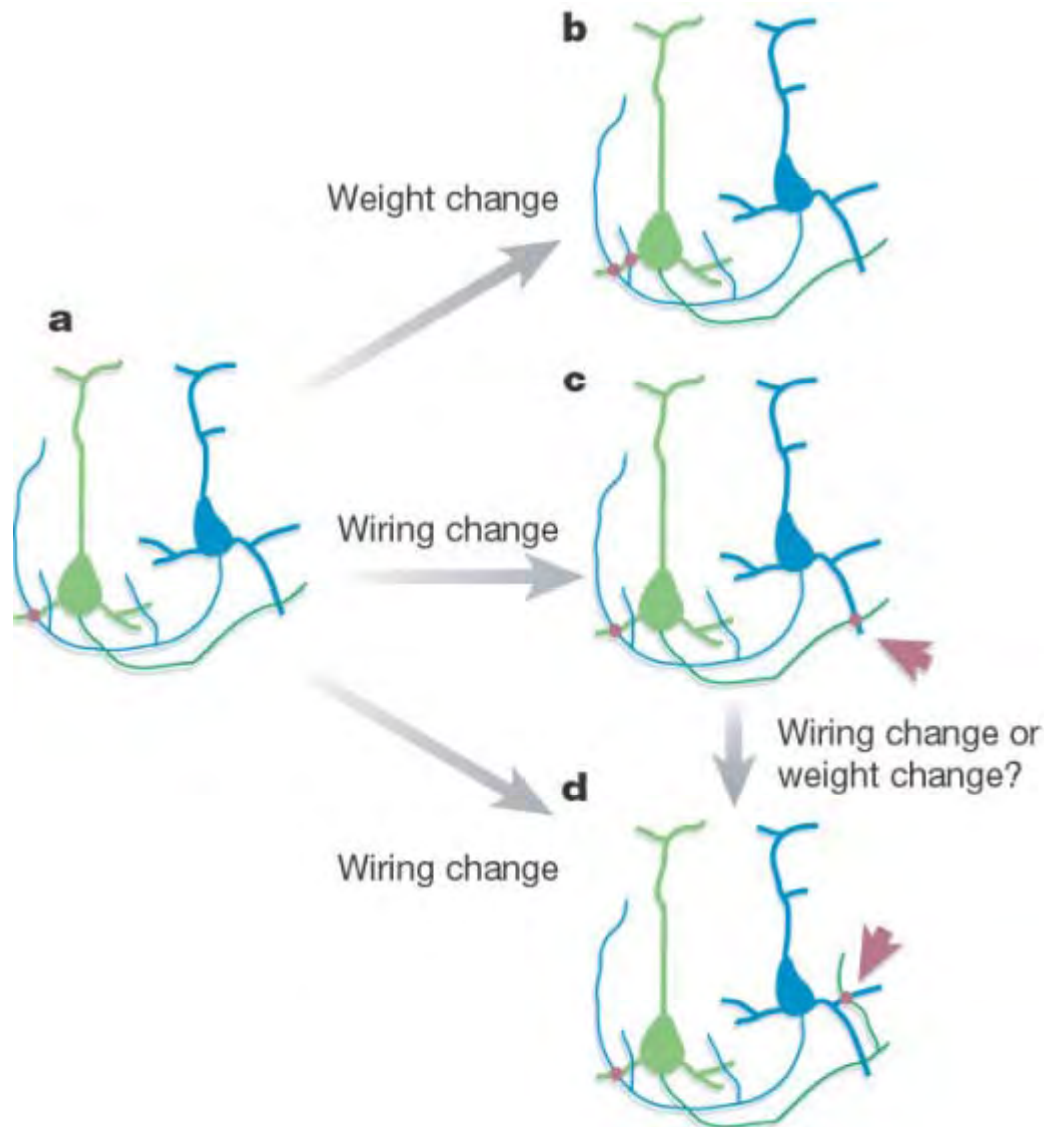


Fig. 2. Diagrammatic representation of the sequence of cellular changes following localized neuronal injury using both in vivo (King and others 1997, 2000, 2001) and in vitro (Dickson and others 1999; Chuckowree and Vickers 2003) experimental models. A, Normal cortical neurons in the intact brain (left) and cortical neurons maintained in long-term culture (right). Initially, both in vivo and in vitro injury (B) was associated with reactive changes within damaged axons, including alterations in the cytoskeleton resulting in ring- and bulb-like accumulations of neurofilaments. Reactive alterations resolve over time and are subsequently followed by regenerative sprouting (C). Notably, it is difficult to determine whether sprouting axons in vivo are derived from damaged neurites or undamaged collaterals. However, in vitro studies indicate that individually axotomized processes can give rise to regenerative sprouts. As the healing response proceeds in vivo, the needle tract largely closes over by 14 days postinjury, forming a teardrop-shaped glia remnant surrounded by a normal-appearing neuropil (D). Occasional axonal sprouts are also seen within or around this region. Abundant cortical sprouting is observed following axonal bundle transection in vitro, and by 24 h postinjury, numerous regenerating axons have traversed the lesion site.

Injury-Induced Circuit Rewiring



The schematic shows two neurons (green, blue), dendrites (thick lines), axons (thin lines) and synapses (red circles).

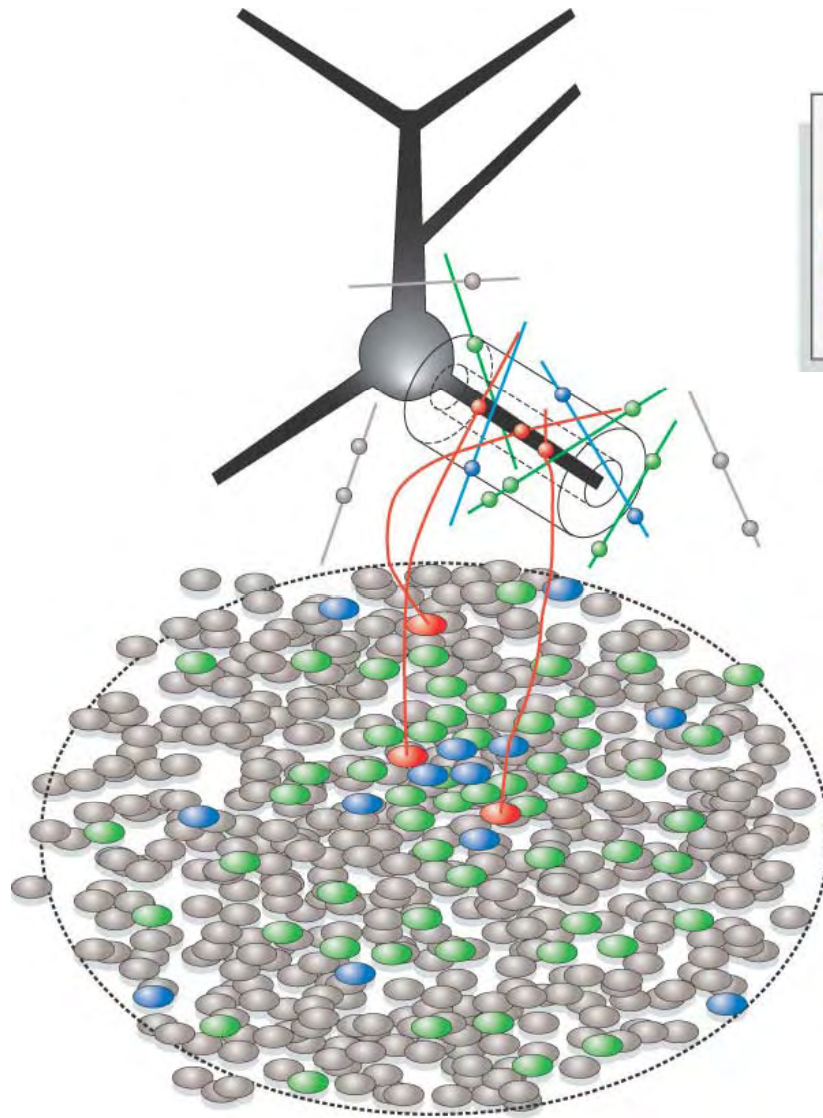
In the initial wiring diagram, signaling is from the blue neuron to the green one.

Synapse formation and elimination can result in weight changes alone (**b**) or can include a wiring change (**c**, **d**).

Wiring changes can occur with (**c**) or without (**d**) axon or dendrite growth.

In the new wiring diagram, signaling occurs from blue to green and from green to blue.

Potential for Circuit Rewiring



Presynaptic population

- Connected by actual synapse
- Connected by potential synapse
- Within reach of axonal or dendritic branch growth
- Inaccessible

Concentric cylinders surrounding the postsynaptic dendrite show the volume accessible by the spine (inner cylinder), and the volume accessible by remodelling of an axon or dendrite (outer cylinder).

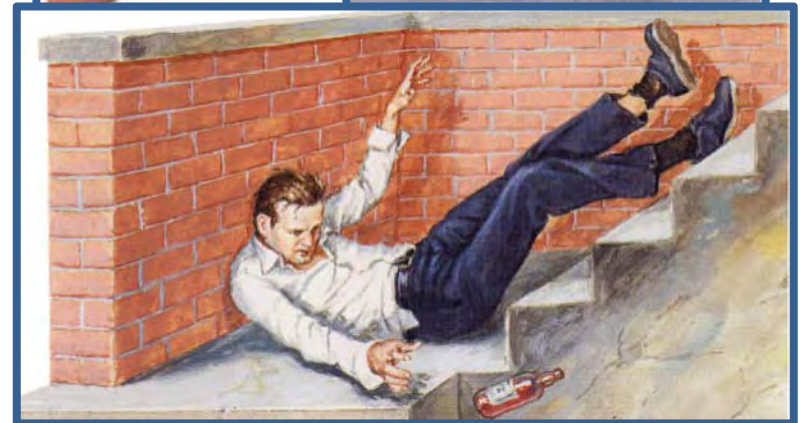
Among those presynaptic axons that cross through the inner cylinder (blue), only a small fraction form actual connections (red).

Green denotes the population of presynaptic candidates that cross through the outer cylinder.

The much larger population of inaccessible axons is shown in grey.

****TYPES OF HEAD INJURY**

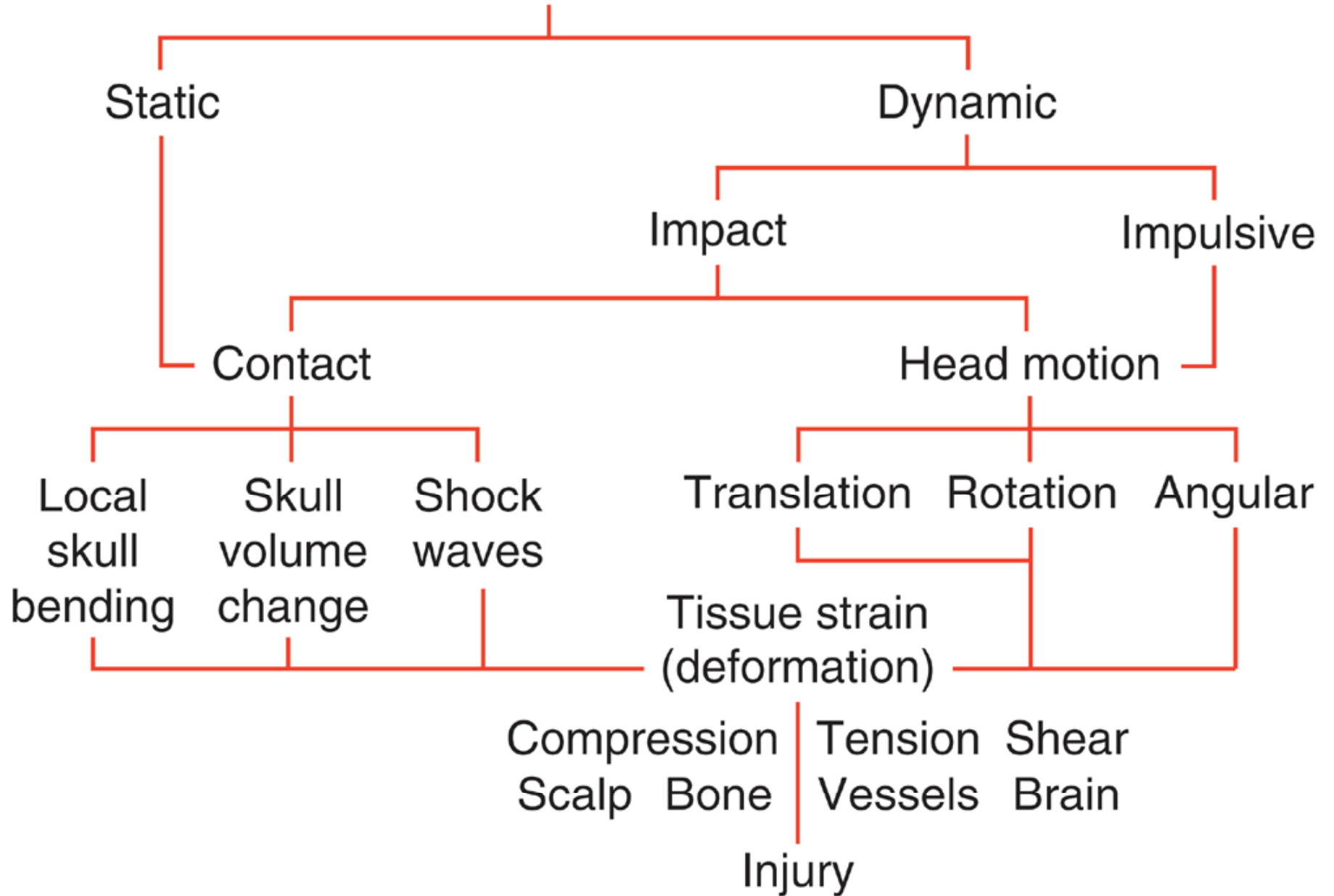
Brain Injury is a Mechanical Event



Types of Traumatic Brain Injury

- Open/penetrating injury
 - Functional impairments localized and related to function of affected brain area
- Closed head injury
 - Diffuse axonal injury (DAI)
- Edema – swelling
- Hematoma – blood

Mechanical loading



****INCIDENCE & FUNDING**



\$18,111¹

People Living With
HIV / AIDS



900,000²



\$4,635^{3,4}

People Living With
MR / DD*



4,557,000³

U.S. Federal \$ Allocated Per Person Per Year



\$295⁵

People Living With
Breast Cancer



3,000,000⁶



\$2.55⁷

People Living With A
Disability From
TBI**



5,300,000⁸

* MR / DD - Mental Retardation / Developmental Disabilities

** TBI - Traumatic Brain Injury

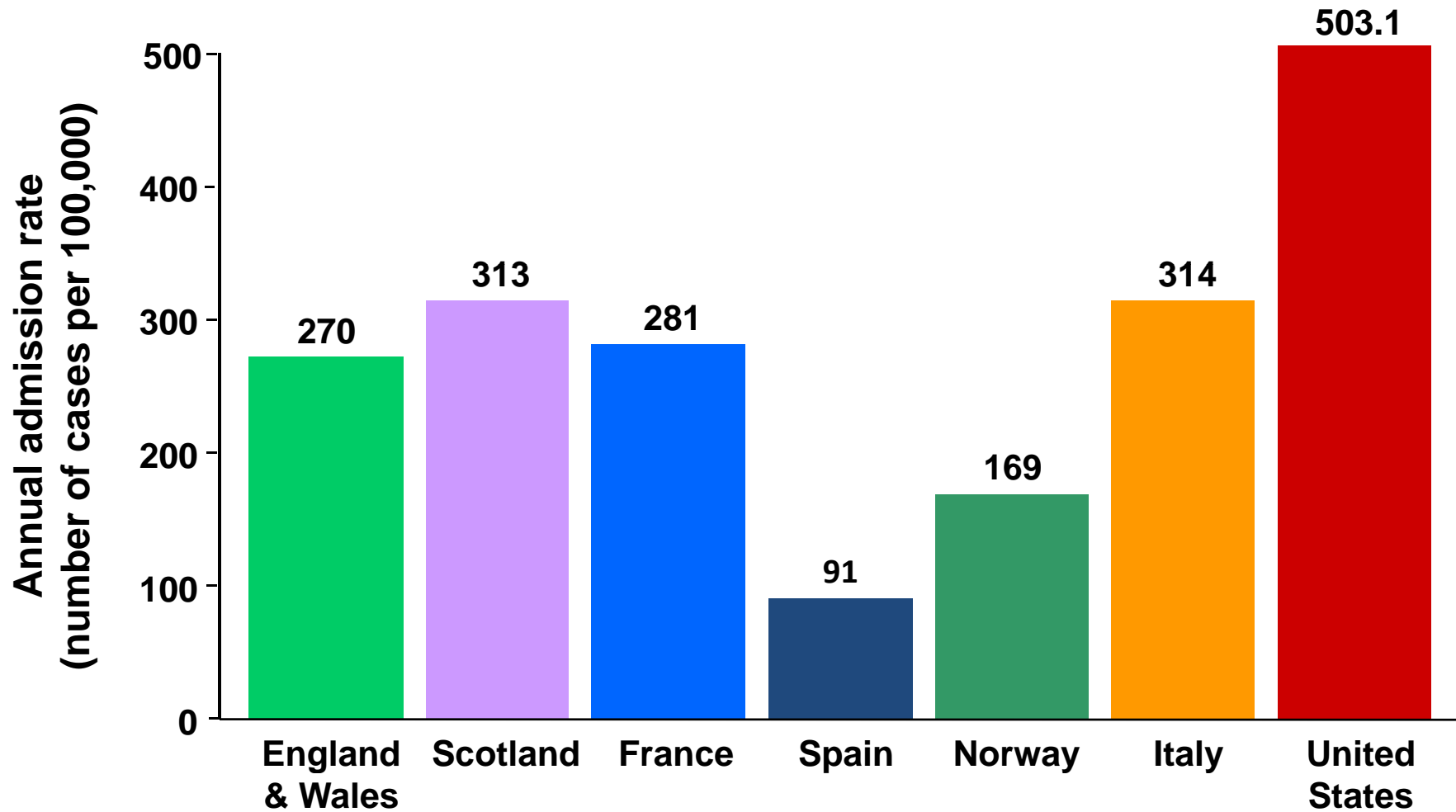
50,000
Deaths

**Direct and indirect costs
of TBI are estimated at
\$48 to \$56 billion**

VISITS

??? Receiving Other Medical
Care or No Care

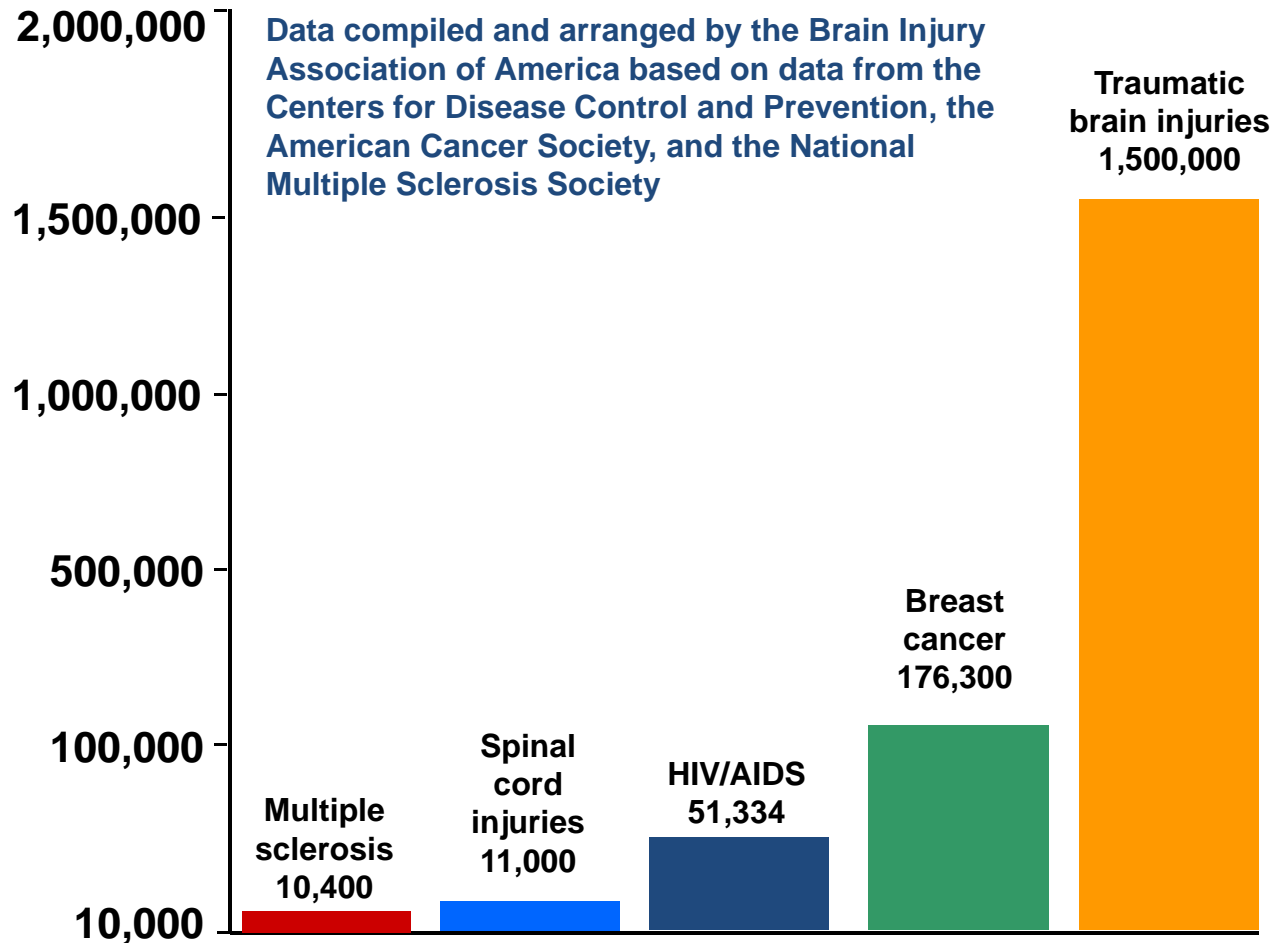
Incidence of TBI in Europe Compared to the United States



Servadei, F et al, *Neuroepidemiology*, 2002;21:297–304.

Bazarian, J et al, *Brain Injury*, 2004, 1–10.

Comparison of Annual Incidence

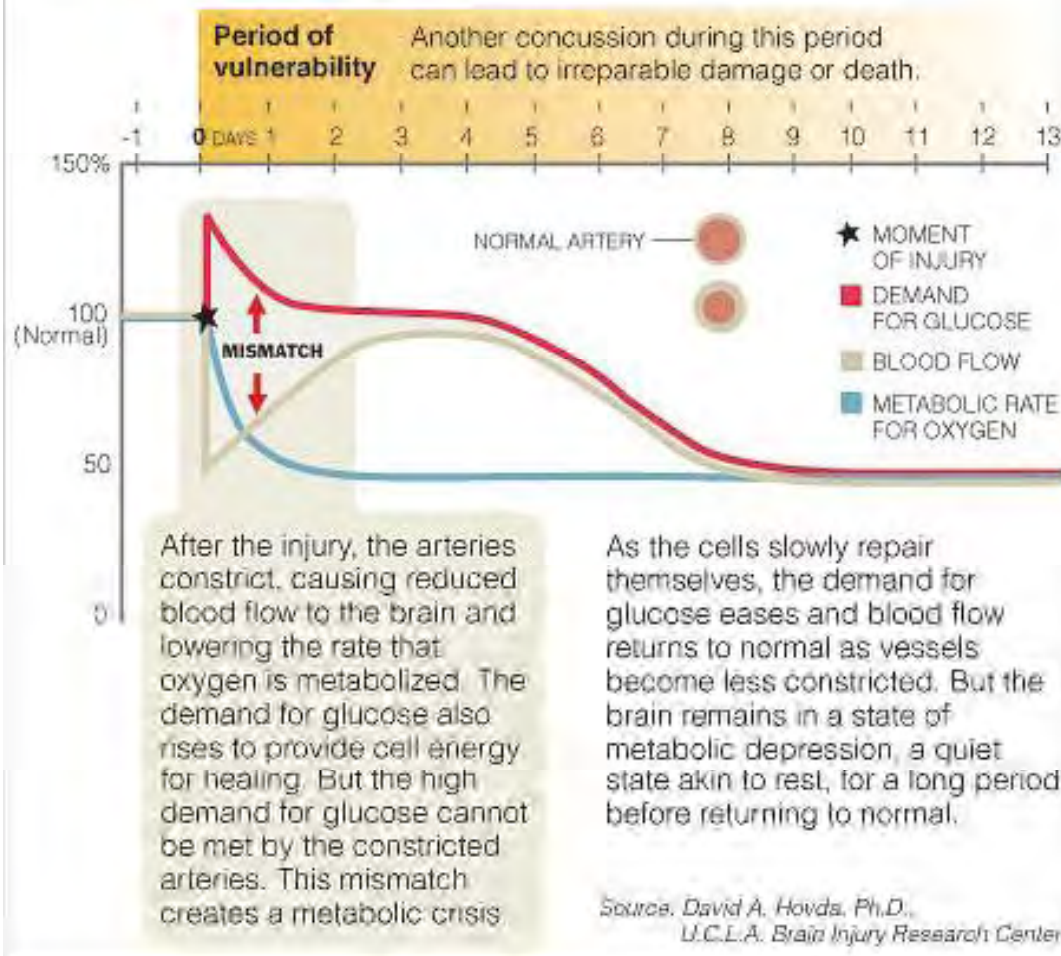


****CONSTANTLY EVOLVING DAMAGE**

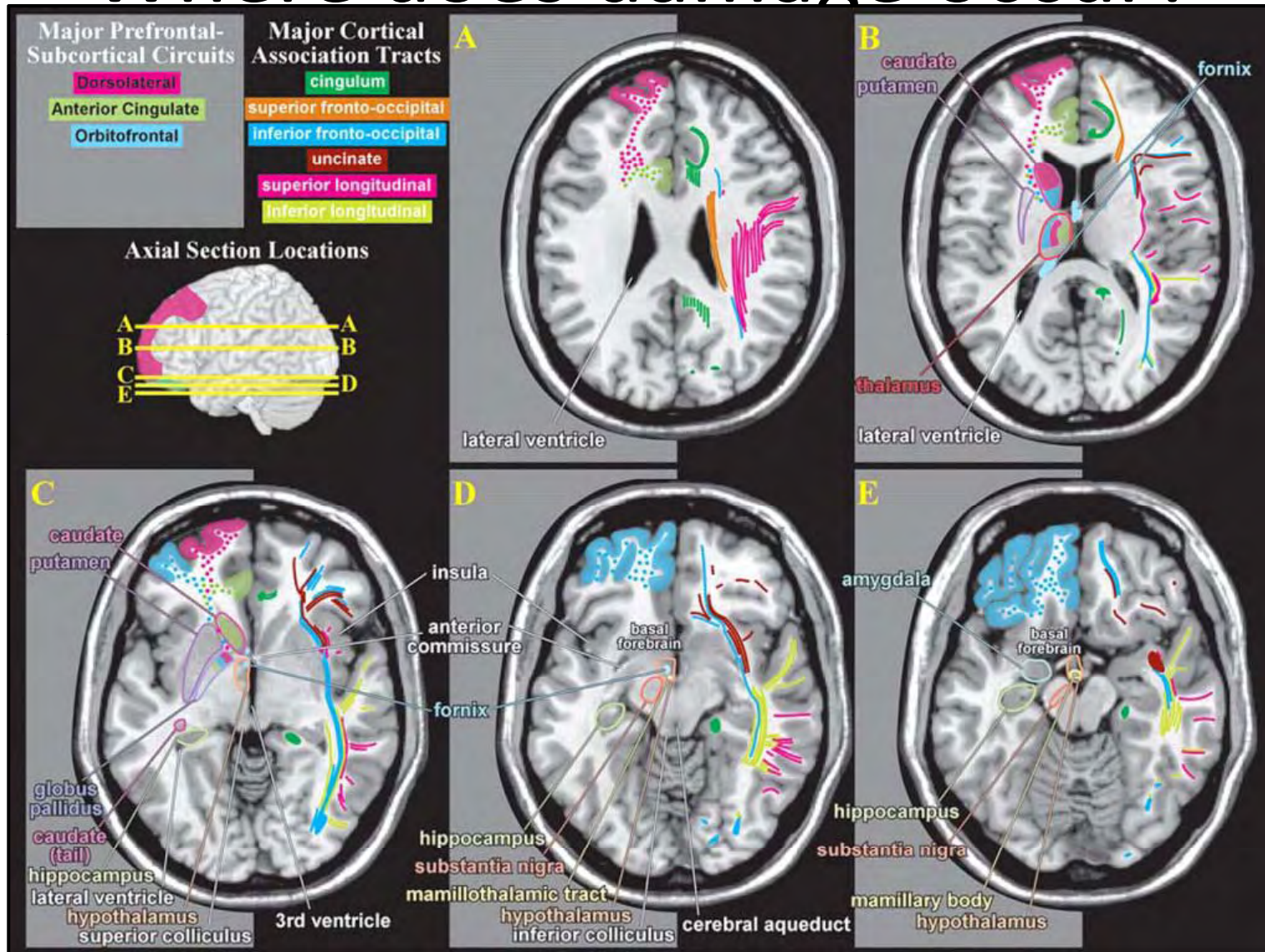
TBI: Constantly Evolving Damage

The Crisis and the Healing

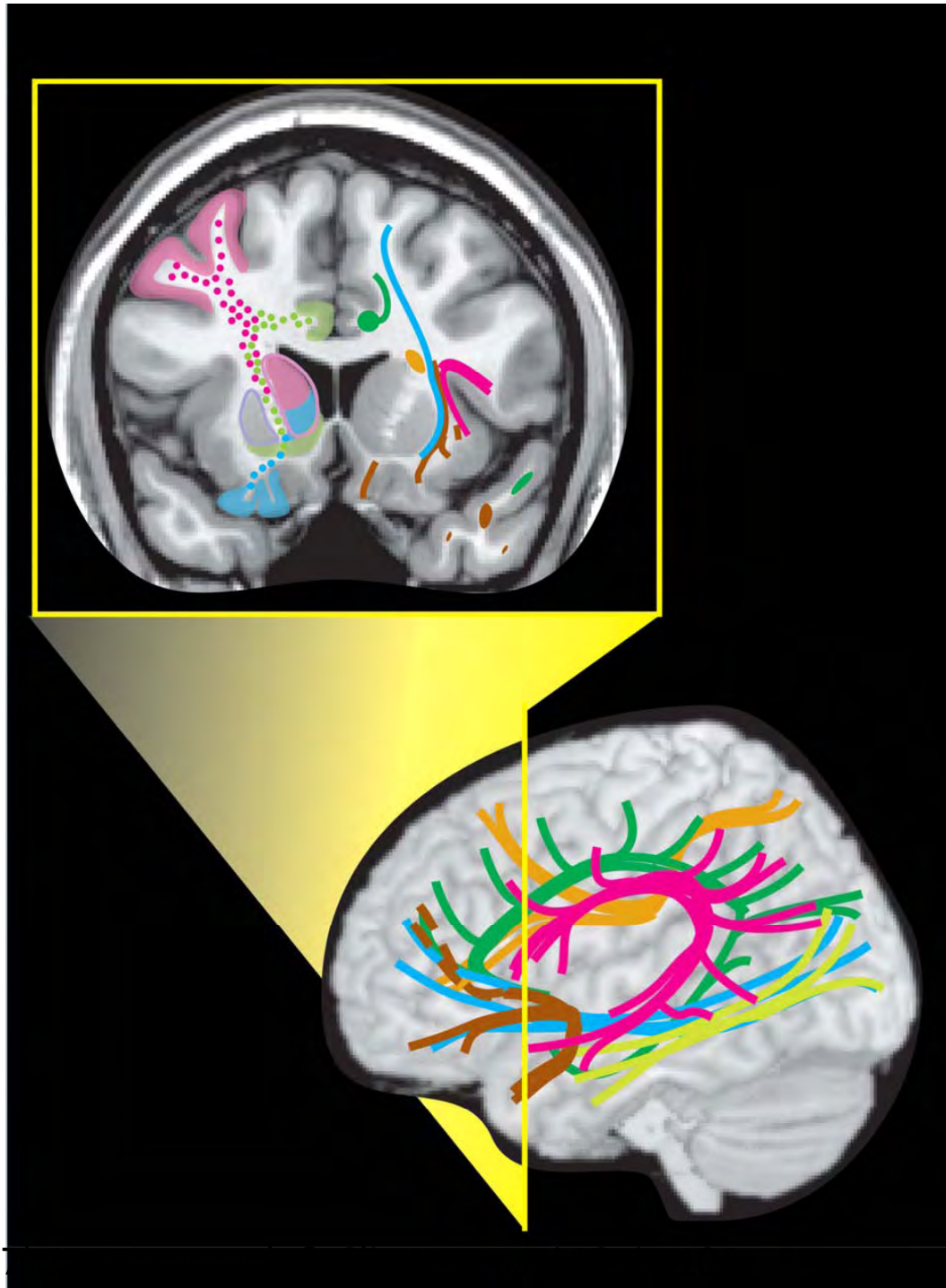
At the moment of injury, the brain goes through an initial period of crisis followed by an undetermined period of healing. The rate of recovery varies according to the severity of the injury.



Where does damage occur?



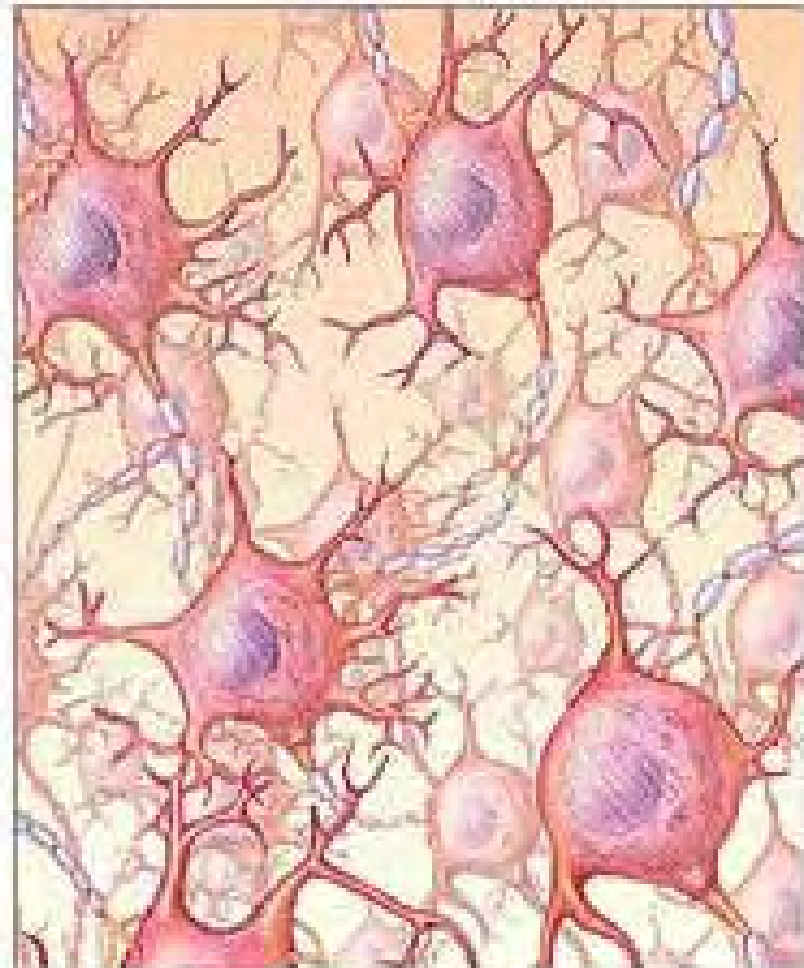
Tabor & Hurley (2007) *J. Neuropsych & Clin Neurosci* 19: iv:104.



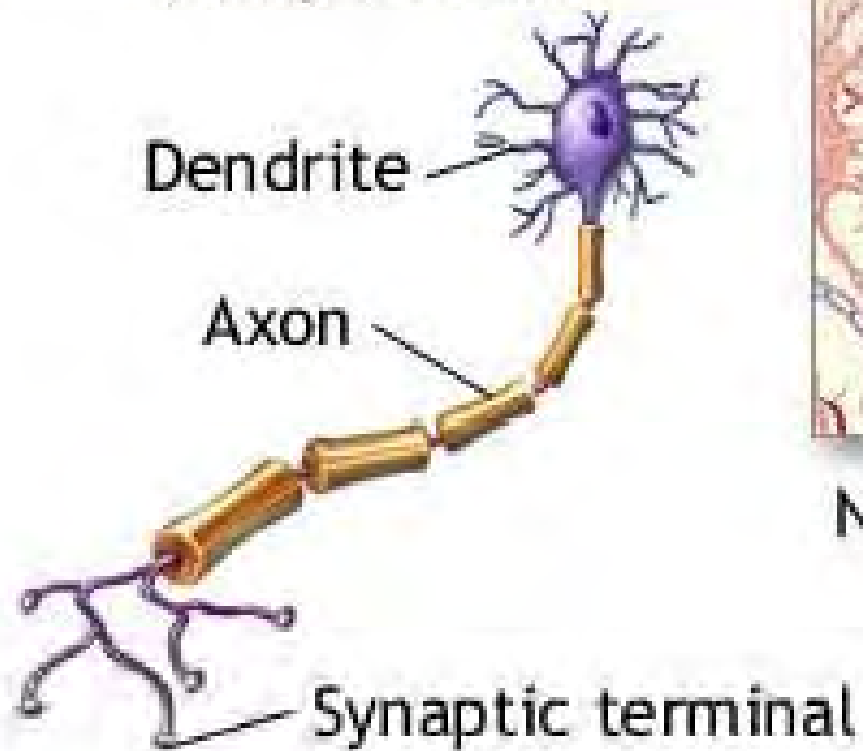
Tabor & Hurley (2007)



Younger brain



Neurons in younger brain

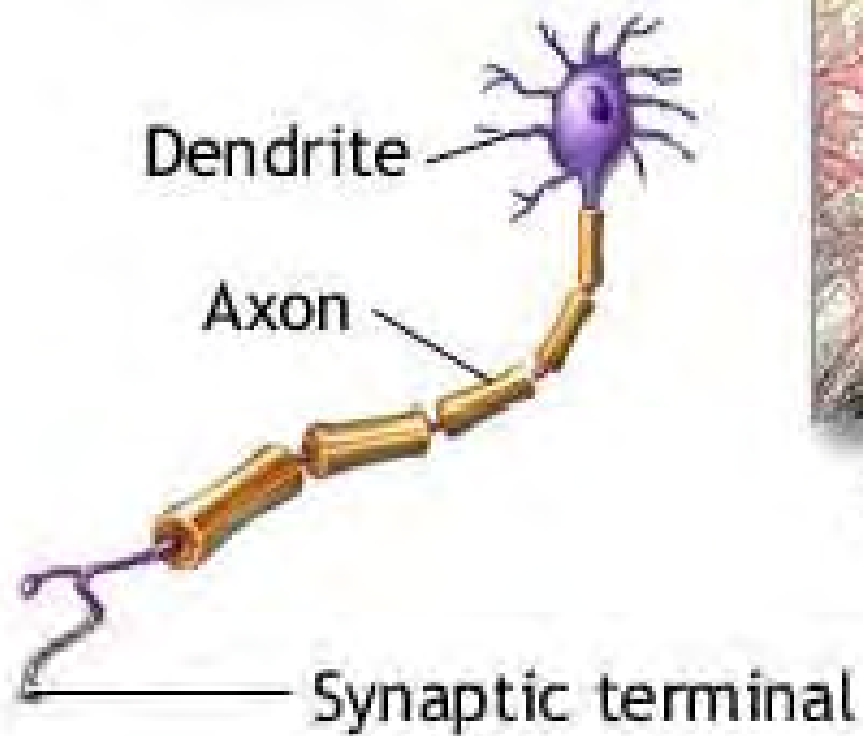




Aging brain



Neurons in aging brain

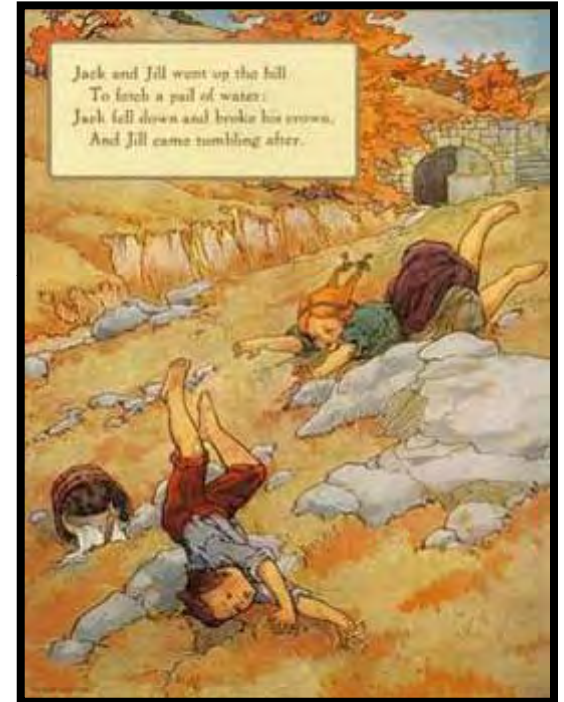


****NURSERY RHYMES**





Jack and Jill went up the hill,
To fetch a pail of water,
Jack fell down and broke his crown,
And Jill came tumbling after.



Up Jack got and home he ran,
As fast as he could caper.
There his mother bound his head,
With vinegar and brown paper.

****SECONDARY CASCADES**

