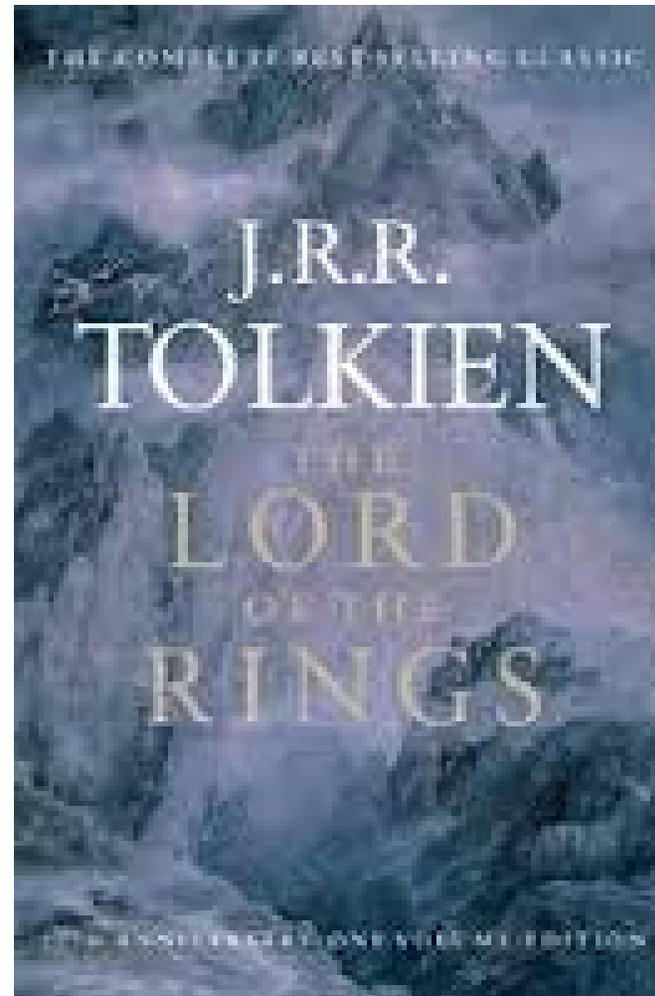


- "A day may come when the courage of men fails....but it is not THIS day."
- All that is gold does not glitter, not all those who wander are lost; The old that is strong does not wither, Deep roots are not reached by the frost.





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BOARD CERTIFICATIONS

Functional Neurology (FACFN)

Neurology Diplomate (DACBN)

Vestibular Rehabilitation (FABVR)

Brain Injury Rehabilitation (FABBIR)

- Special thanks to:

Dave Rosenthal
Brandon Brock
Datis Kharrazian
Frederick Carrick
Jeff States
Arthur Croft

3 Potentially Fatal Myths about TBI

(That everyone **who treats TBI should know**)

Introduction, Pathophysiology, Clinical Considerations,
Neuroplasticity

Jason L. Smith, DC, FABVR, FACFN, DACBN, FABBIR

Thursday – November 3, 2016

Provo, Utah – Utah Trauma Academy

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You need to be hit your the head to sustain a concussion.

Fact: Concussions can occur with any movement or jostling of the head as in whiplash injuries (front to back) or rotational force (side to side).

If you didn't lose consciousness, there is no concussion.

Fact: Concussions can occur with any movement or jostling of the head as in whiplash injuries (front to back) or rotational force (side to side).

Concussions are far less serious than mild traumatic brain injury.

Fact: Concussion, by definition, is mild traumatic brain injury.

A true concussion is a rare event that usually happens to people that don't wear proper head protection.

Fact: No equipment can completely protect from concussion.

- mTBI injury can be caused by straight-on impact, rotation with impact, whiplash **without** impact and sideways **without** impact.
- Helmets, mouth guards and other protective devices **may lower the risk** or offer more information for the trainer and doctor, but no equipment eliminates the risk of concussion.
- Newer products with rubber padding and different materials **may reduce the chance** of concussion in one model (such as straight-on impact) but not change the risk in another model (such as rotation with impact).

My Objectives today

- Share common myths and facts about concussion.
- Inspire you to be able to gain confidence in recognizing and treating TBI.
- Provide you with simple tools to screen all trauma patients

Journal of Vestibular Research

Does Vestibular Damage Cause Cognitive Dysfunction in Humans?

- Paul F. Smith, Yiwen Zheng, Arata Horii, Cynthia L. Darlington
- ...evidence...has suggested that damage to the vestibular system leads to deficits in spatial navigation which are indicative of impaired spatial learning and memory.
- ...humans with vestibular disorders exhibit a range of cognitive deficits that are not just spatial in nature, but also include non-spatial functions such as object recognition memory.

Epidemiology & Facts (cont.)

- mTBI symptoms typically include difficulties in speed of processing, attention & memory.
- **Most patients show recovery within 6 months.**
- **Most with mTBI return to work within first 30 days.**
- A small portion of complicated mTBI patients can have persistent symptoms 12 months or longer.
- mTBI is associated with the onset of psychiatric disorders including depression and PTSD.
- (see slide 128 or 129)
- **What if you or your family or your are not one of the “most” that recovers?**

One of the most troubling aspects
of TBI...

*“The person we have always known
is strangely missing.”*

Concussion Epidemiology

- 3-10 million affected individuals annually in the United States, many of whom do not obtain immediate medical attention. (Langlois)
- 475,000 children included in the above number
- 90% of all TBI is mTBI.
- 85% resolve in 1-3 months. Up to 15% experience long term effects, including disability. (1.5M). (Hartlage)
- Some providers opinion – “you won’t get any better—after two years, no one ever does.”

One of the most troubling aspects of TBI...

- We suspect may contribute to the increased risk of suicide.
- ... We have in many ways, already lost that which makes us human.
- ...hundreds of other cognitive changes that are less easy to define.

One of the most troubling aspects of TBI...

A dangerous combination:

- A concussive may feel that to a large extent he has already died.
- There is a longing to return home, to be human again.

- At some juncture, usually after the first 2 years have passed, he will finally approach the realization that in *this* life anyway, he is *never* going home again.
- ...pondering suicide might have nothing to do with a depressed and painful mental state, or being a cry for help, but rather a giving in, a simple final acknowledgement of what really, inside, has already happened. It is a walking *to*, instead of a walking *from*.

(Elliott)

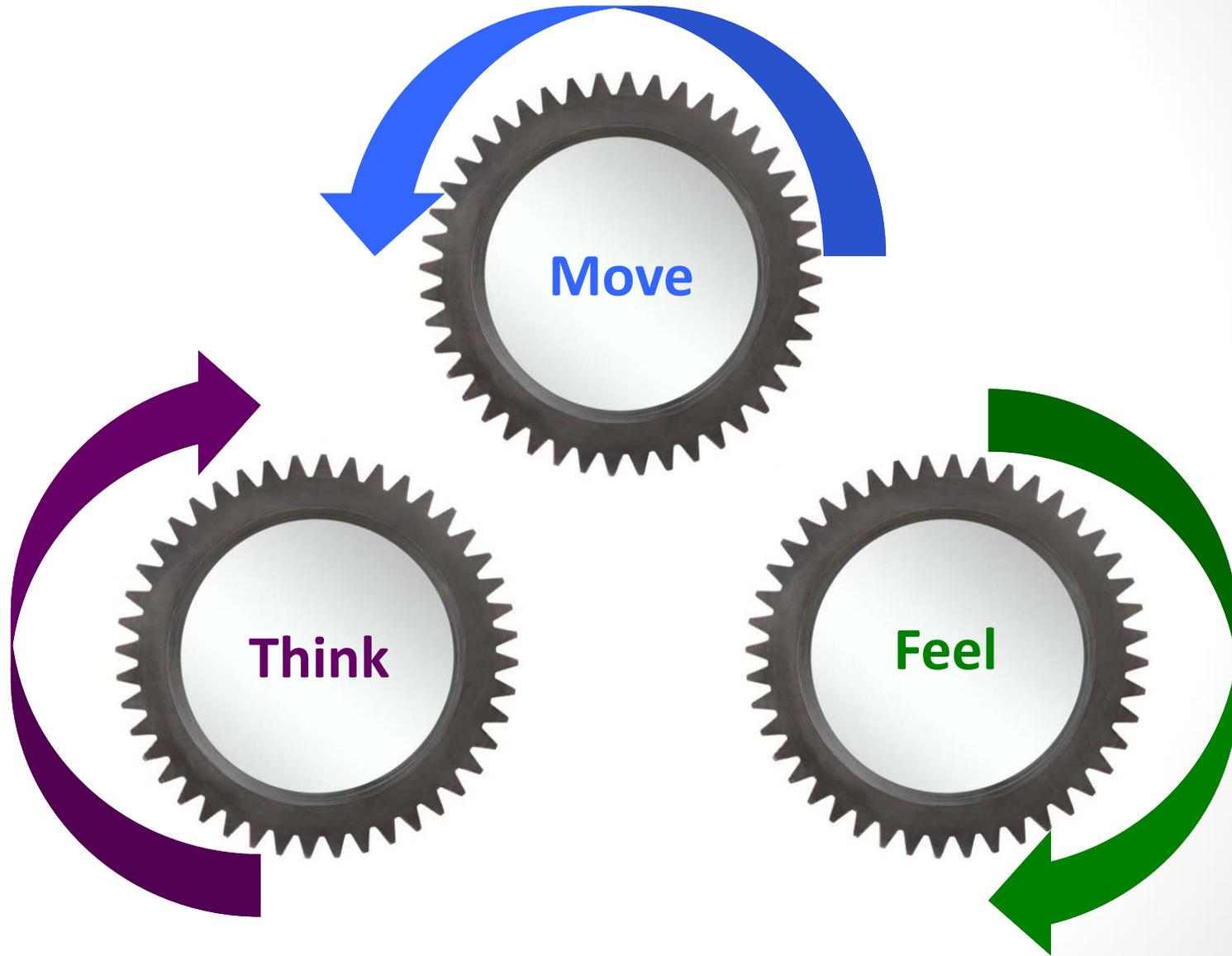
Functional Neurology Considerations

- Observe the patient.
- Do a thorough history and physical examination.
- Always make a diagnosis, know the differentials.
- Treat the findings, NOT just the ICD-10.
- The diagnosis has a greater likelihood of resolving when you appropriately treat YOUR clinical findings.
- If you just treat the diagnosis the clinical findings may not resolve (i.e. not every paresthesia is a paresthesia).

Neuroplasticity

- “The brain is not just a stagnant, nonpliable, round mass, submersed in a fluid and surrounded by a durable case. It is not finished in its development once we reach adulthood. The brain changes over time, and with that change, end organs such as the eye (and its very function) can be cortically changed, show improvement after insult and injury, and be remediated and enhanced. ” [Taube 2012].

The Brain- How it all works



Patient Presents with a Neurological Lesion

Physiological Functional lesion

Ablative Pathology

Labs

Previous medical treatment

Imaging and other diagnostics
ie: EEG, EMG, NCV, MRI

Subjective Objective Outside records

Peripheral Nerve

Infectious Disease

Autoimmune

Vascular

Inflammatory

Mitochondrial failure

Ventral Horn Cell
Nerve Root

Plexus Lesion
Mono neuropathy
Polyneuropathy

Central or peripheral nervous system.
Viral, bacterial, parasitic, fungal

Peripheral or central nervous system
Th polarization
Th surveillance

Basilar
Upper - lower - Midline

Glial priming
Excitotoxicity

Energy pumps
CIS / Ox phos

Which level

Upper - superior - lower inferior - Rib, scalene or pec minor

Motor or sensory
Fiber type

Brainstem

Anterior or posterior circulation

BBB issues
IL-6 / NFkB

Caspase
PON / INOS

Bulbar or spinal

Cortex

Fiber type.
Cause of lesion

Basal Ganglionic

Mesencephalon
Pons
Medulla

Cerebellar

Extrinsic
Intrinsic

End Organ Receptor

Is the lesion left, right or bilateral hemisphere pathology

Is the lesion anterior or posterior cortex

Is the lesions superior or inferior related to cortex

Is the lesion medial wall or lateral convexity

Is the lesion Striatal

Is the lesion pallidal

Is the lesion sub-thalamic

Is the lesion Nigral

Vermal Fastigial

Int. Globose Emboliform

Lateral Detate

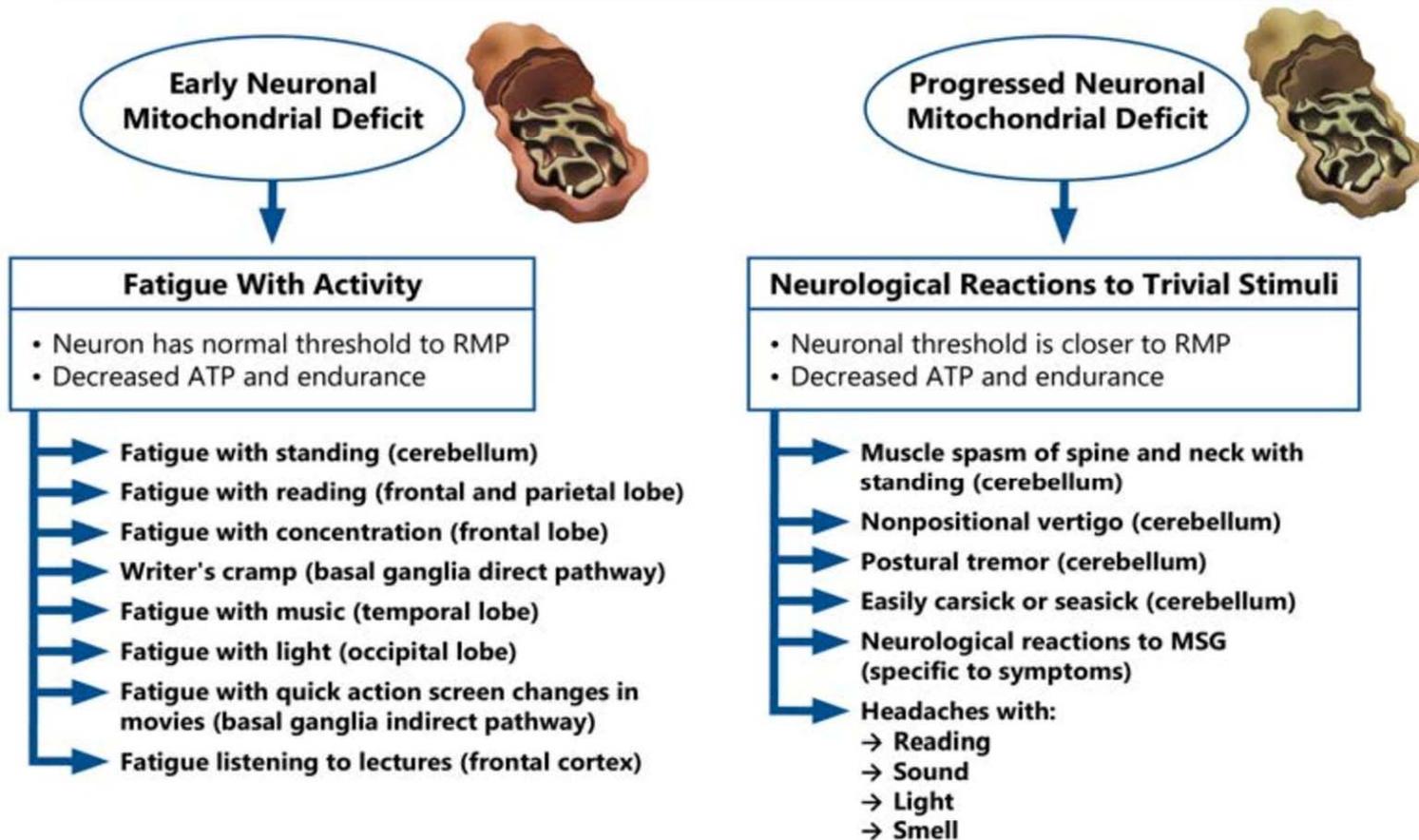
Anterior or posterior lobe

Floculonodular

Myopathy
Joint dysfunction

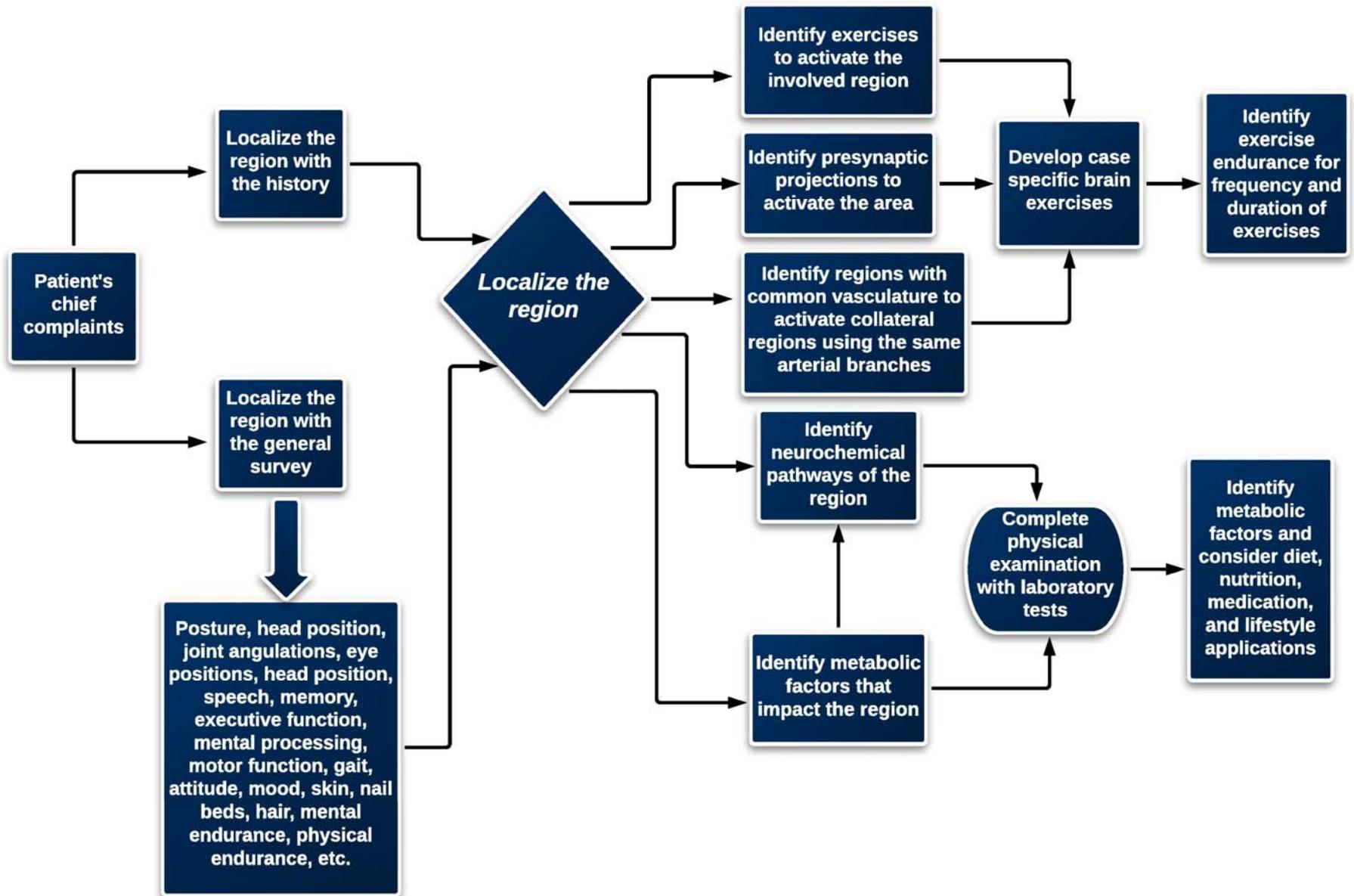
NMJ disorder

Clinical Presentations of Impaired Neuronal Mitochondria

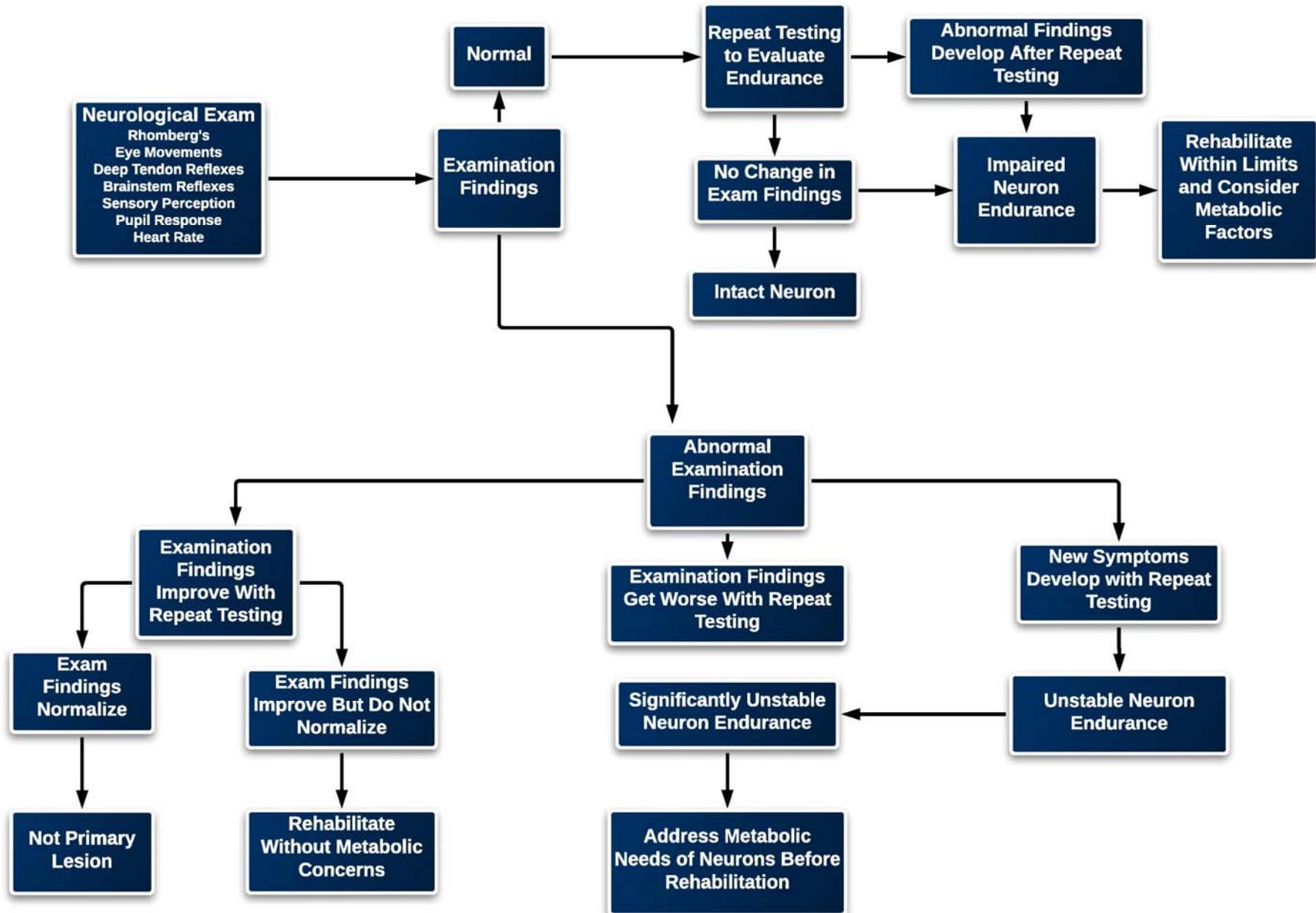


Abbreviations: ATP, adenosine triphosphate; MSG, monosodium glutamate; RMP, resting membrane potential.

Clinical Decision Process in Functional Neurology



Identifying Neuron Fatigue Mechanisms in Clinical Practice



ON DISCOVERIES

- Just as the hand, held before the eye, can hide the tallest mountain, so the routine of everyday life can keep us from seeing the vast radiance and the secret wonders that fill the world.

Chasidic saying, 18th century

ON RECOVERIES

- Life is short, and Art long; opportunity fleeting, experience misleading, and decision difficult. It is the duty of the physician not only to provide what he himself must do, but to enable the patient, the attendants, and the external circumstances to do their part as well.

Hippocrates, father of medicine, 460-735 BC

What function is lost/affected?

- Memory (Declarative, episodic, procedural, semantic)
- Executive function
- Muscle strength & tone
- Balance & Gait (reaction time, limits of stability)
- Extraocular reflexive control of gaze, pursuits, saccades.

What function is lost/affected?

- Sensory discrimination (pain/temperature, anterolateral cord, brainstem, parietal lobe)
- Proprioception (GTO, spindle, dorsal column pathways, cerebellum, parietal lobe)
- Visual Acuity (retinal, optic, LGN of thalamus, occipital / parietal)
- Hearing Acuity (cochlea, CN VIII, pons, temporal)
- Sleep (midbrain, circadian)
- Digestion/ cardiac / respiratory function (vagus, Medulla)



Frontal lobe

Executive functions, thinking, planning, organising and problem solving, emotions and behavioural control, personality

Motor cortex

Movement

Sensory cortex

Sensations

Parietal lobe

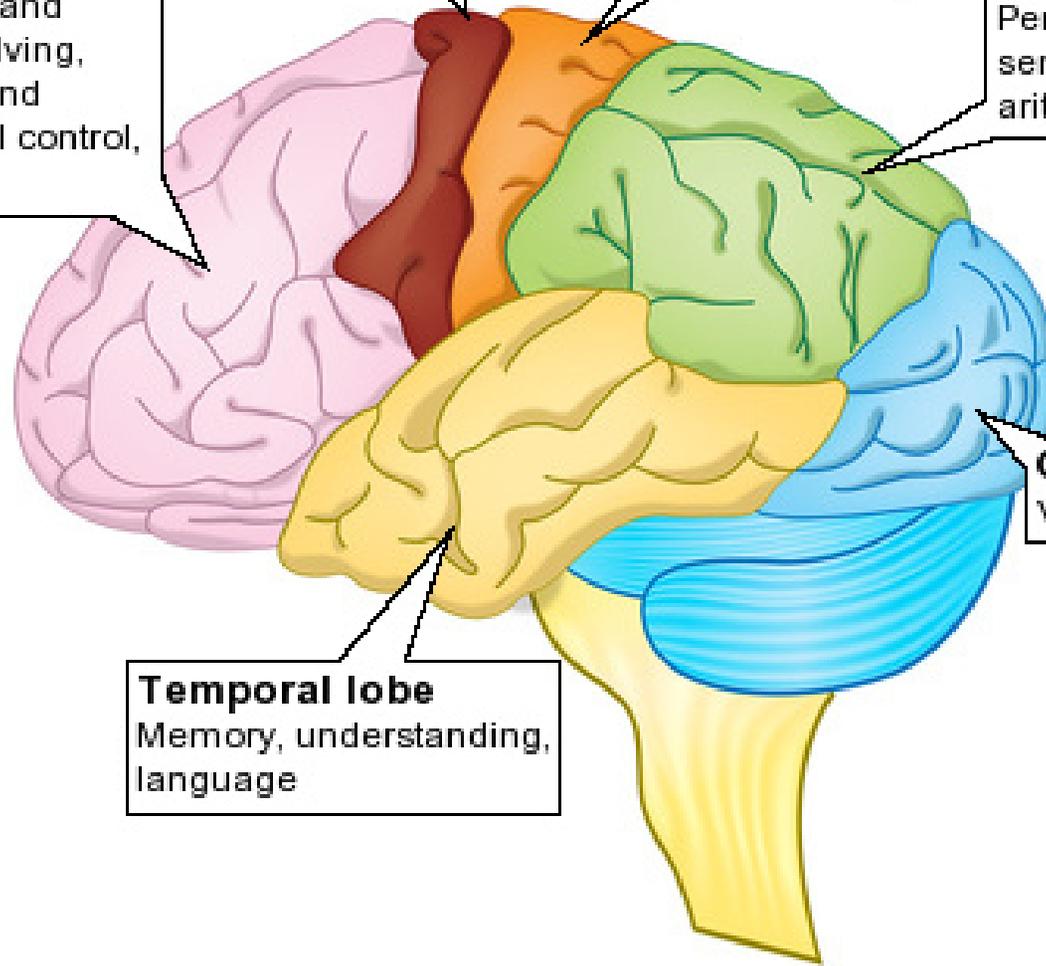
Perception, making sense of the world, arithmetic, spelling

Temporal lobe

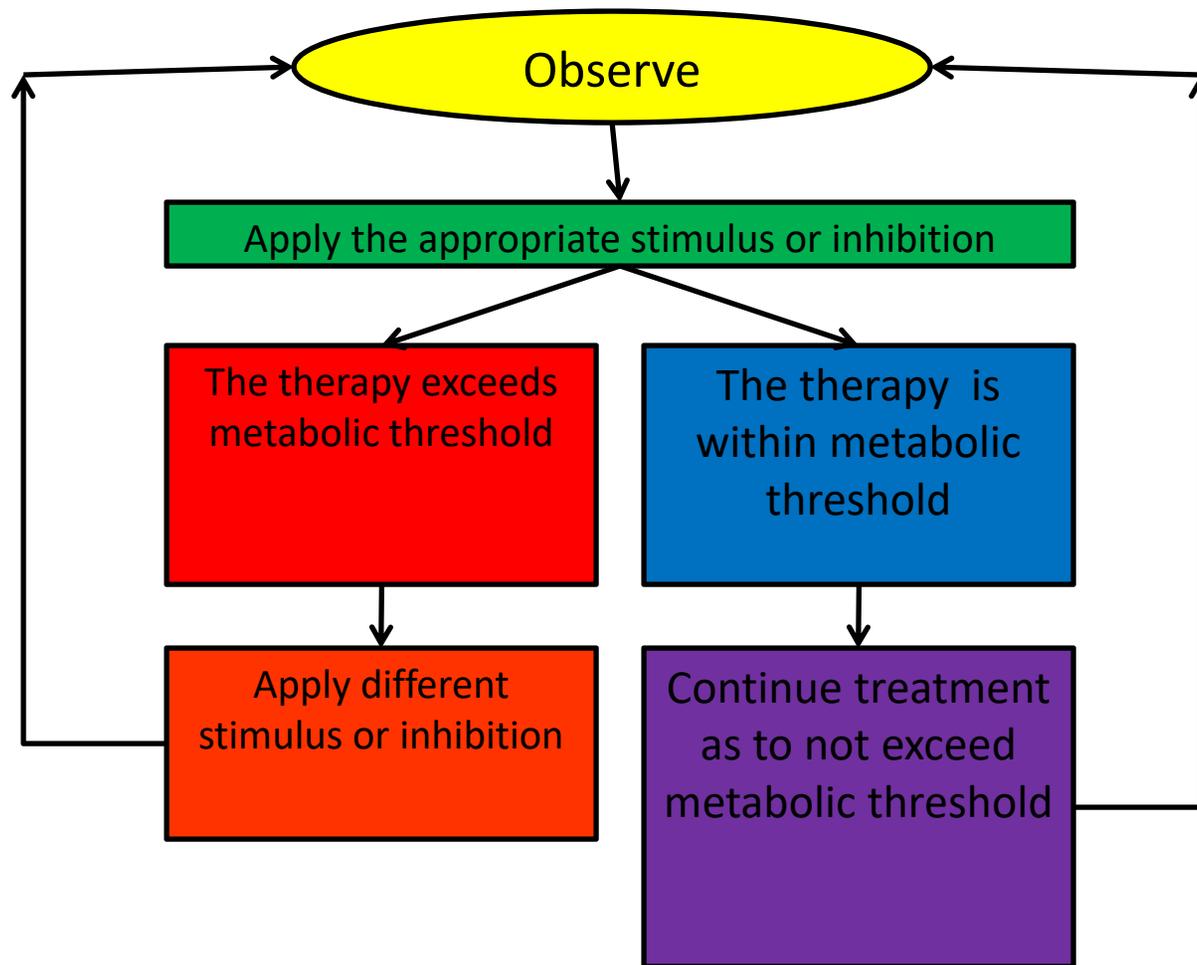
Memory, understanding, language

Occipital lobe

Vision



What is the functional neurological treatment algorithm?



Questions to ask yourself

- What is the Longitudinal Level of the Lesion (LLL)?
- Is it ablative or physiologic?
- Is it Left or Right?
- Is this a crossed pathway (if so, where)?
- Is it motor or sensory dysfunction?
- Are there autonomic concomitants / dysregulation (fuel delivery issues)?

Longitudinal Level of the Lesion

- Cortex / Internal Capsule
- Basal Ganglia (subcortical nuclei)
- Brainstem
- Cerebellum
- Spinal Cord
- Peripheral Nerve
- Receptor / End Organ (muscle, gland)

BUT ALL ARE FUNCTIONALLY CONNECTED!

Neural plasticity – Diagnosis

“... different approaches (to the same patient) have often produced different research results and and researchers with different backgrounds often arrive at different results . . . and thus instate different treatments. It is almost like the old story about six blind men and the elephant . [Moller, 3].”

Neural plasticity – Diagnosis

“They all came to different results from their examination. [Moller, 3].”



Neural plasticity – Diagnosis



“We are sorry, but we cannot agree on what an elephant is like. We each touched the same animal. But to each of us the animal is completely different.’ The prince spoke gently, ‘the elephant is a very large animal. Its side is like a wall. Its trunk is like a snake. Its tusks are like spears. Its legs are like trees. Its ears are like fans. And its tail is like a rope. So you are all right. But you are all wrong, too. For each of you touched only one part of the animal. *To know what an elephant is really like, you must put all those parts together*’ [Moller, 3].”

Ask yourself –

How do I diagnose a
concussion?

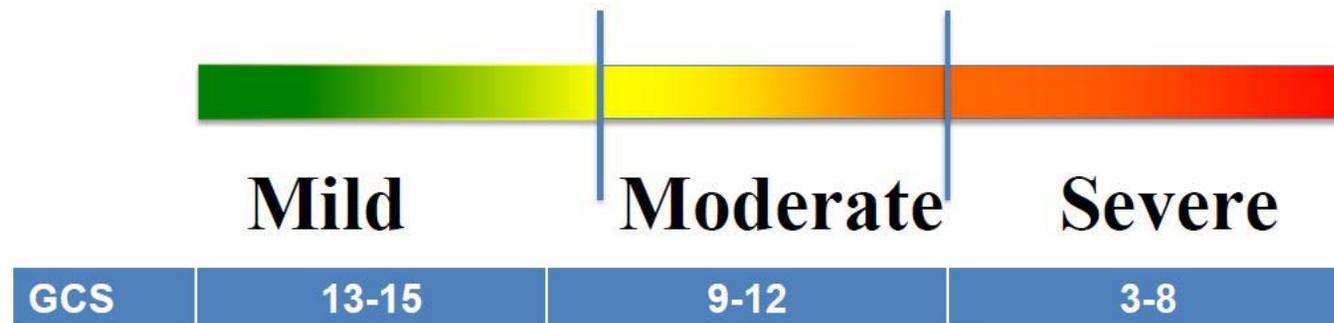
How does proper diagnosis
change or save this individual's
life?

Concussion Diagnosis

- History – GCS 13-15
- Majority resolve within 7 days
- Approximately 15% of concussions have prolonged /intractable symptoms.
- Look at all four symptom categories:
 - 1- Physical
 - 2- Cognitive
 - 3- Emotional
 - 4- Sleep

Forms really help you remember to ask the correct questions.

Traumatic Brain Injury Scale



Concussion is likely different than mild TBI

Concussion Symptoms

- **Physical** – headache, nausea, vomiting, balance problems, tinnitus, visual problems, light/sound sensitivity, loss of coordination
- **Cognitive** – brain fog, dazed, slow, difficulty concentrating, remembering, making decision
- **Sleep** – too much, too little, fatigue
- **Behavioral** – anxiety, depression, irritability, aggressive without provocation, social inappropriateness, apathy

Post-Concussion Syndrome

- Variable symptoms (at least 3) that persist for 4 or more weeks following a head injury
- Symptoms of PCS include: chronic headaches, fatigue, sleep disturbances, personality changes, sensitivity to light and noise, dizziness, and deficits in short-term memory (cognitive).
- Often results in significant disruption of / withdrawal from school, employment, military service.

Injury Stratification

| Criteria | Mild Concussion | Moderate | Severe |
|---|-------------------------|---------------------------|-------------------------------------|
| Structural Imaging | Typically Normal | Normal or abnormal | Normal or abnormal |
| Loss of Consciousness LOC | 0-30 mins | >30 mins & <24 hrs. | >24 hrs. |
| Alteration of consciousness/ mental state | A moment or <24 hrs. | >24 hrs. | Severity based on other criteria |
| Post Traumatic Amnesia PTA | < or equal to 1 day | ➤ 1 day but ➤ < 7 days | > 7 days |
| Glasgow Coma Score in first 24 hrs. GCS | 13-15 | 9-12 | 3-8 |

Glasgow Coma Scale

- I think I remember hearing about it in school...
- It is stored in the same place that the APGAR rating scale for infants is.
- There are often no reliable witnesses as to their state of consciousness (MVC, slip and falls.)

Glasgow Coma Scale (GCS)

GCS scores range from 3-15

| Category | Response | Value |
|----------------------|-----------------------------|-------|
| Eye Opening | Spontaneous | 4 |
| | Response to verbal command | 3 |
| | Response to pain | 2 |
| | No eye opening | 1 |
| Best verbal response | Oriented | 5 |
| | Confused | 4 |
| | Inappropriate words | 3 |
| | Incomprehensible sounds | 2 |
| Best motor response | No verbal response | 1 |
| | Obeys commands | 6 |
| | Localizing response to pain | 5 |
| | Withdrawal response to pain | 4 |
| | Flexion to pain | 3 |
| | Extension to pain | 2 |
| Total | No motor response | 1 |
| | | 3-15 |

Outcome Assessments

- Acute Concussion Evaluation (ACE) form
- Rivermead Concussion Form - 0 to 4 rating on each symptom
- Nordhoff – Concussion symptom impact form
- Epworth Sleepiness scale / Pittsburgh Sleep Quality Index (PSQI)
- Folstein Mini-mental status Exam



ACUTE CONCUSSION EVALUATION (ACE)

PHYSICIAN/CLINICIAN OFFICE VERSION

Gerard Gioia, PhD¹ & Micky Collins, PhD²
¹Children's National Medical Center
²University of Pittsburgh Medical Center

Patient Name: _____
 DOB: _____ Age: _____
 Date: _____ ID/MR# _____

A. Injury Characteristics Date/Time of Injury _____ Reporter: Patient Parent Spouse Other _____

1. Injury Description _____

- 1a. Is there evidence of a forcible blow to the head (direct or indirect)? Yes No Unknown
 1b. Is there evidence of intracranial injury or skull fracture? Yes No Unknown
 1c. Location of Impact: Frontal Lt Temporal Rt Temporal Lt Parietal Rt Parietal Occipital Neck Indirect Force
 2. Cause: MVC Pedestrian-MVC Fall Assault Sports (specify) _____ Other _____
 3. **Amnesia Before (Retrograde)** Are there any events just BEFORE the injury that you/ person has no memory of (even brief)? Yes No Duration _____
 4. **Amnesia After (Anterograde)** Are there any events just AFTER the injury that you/ person has no memory of (even brief)? Yes No Duration _____
 5. **Loss of Consciousness:** Did you/ person lose consciousness? Yes No Duration _____
 6. **EARLY SIGNS:** Appears dazed or stunned Is confused about events Answers questions slowly Repeats Questions Forgetful (recent info)
 7. **Seizures:** Were seizures observed? No Yes Detail _____

B. Symptom Check List* Since the injury, has the person experienced any of these symptoms any more than usual today or in the past day?

Indicate presence of each symptom (0=No, 1=Yes).

**Lovell & Collins, 1998 JHTR*

| PHYSICAL (10) | | COGNITIVE (4) | | SLEEP (4) | |
|--|-----|------------------------------------|-----|---|---------|
| Headache | 0 1 | Feeling mentally foggy | 0 1 | Drowsiness | 0 1 |
| Nausea | 0 1 | Feeling slowed down | 0 1 | Sleeping less than usual | 0 1 N/A |
| Vomiting | 0 1 | Difficulty concentrating | 0 1 | Sleeping more than usual | 0 1 N/A |
| Balance problems | 0 1 | Difficulty remembering | 0 1 | Trouble falling asleep | 0 1 N/A |
| Dizziness | 0 1 | COGNITIVE Total (0-4) _____ | | SLEEP Total (0-4) _____ | |
| Visual problems | 0 1 | EMOTIONAL (4) | | Exertion: Do these symptoms <u>worsen</u> with: Physical Activity <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A Cognitive Activity <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> N/A Overall Rating: How <u>different</u> is the person acting compared to his/her usual self? (circle) Normal 0 1 2 3 4 5 6 Very Different | |
| Fatigue | 0 1 | Irritability | 0 1 | | |
| Sensitivity to light | 0 1 | Sadness | 0 1 | | |
| Sensitivity to noise | 0 1 | More emotional | 0 1 | | |
| Numbness/Tingling | 0 1 | Nervousness | 0 1 | | |
| PHYSICAL Total (0-10) _____ | | EMOTIONAL Total (0-4) _____ | | | |
| (Add Physical, Cognitive, Emotion, Sleep totals) | | | | | |
| Total Symptom Score (0-22) | | | | _____ | |

C. Risk Factors for Protracted Recovery (check all that apply)

| Concussion History? Y ___ N___ | √ | Headache History? Y ___ N___ | √ | Developmental History | √ | Psychiatric History |
|--|---|---|---|--|---|-------------------------------------|
| Previous # 1 2 3 4 5 6+ | | Prior treatment for headache | | Learning disabilities | | Anxiety |
| Longest symptom duration Days__ Weeks__ Months__ Years__ | | History of migraine headache __ Personal __ Family_____ | | Attention-Deficit/ Hyperactivity Disorder | | Depression |
| If multiple concussions, less force caused reinjury? Yes__ No__ | | | | Other developmental disorder_____ | | Sleep disorder |
| | | | | | | Other psychiatric disorder _____ |

List other comorbid medical disorders or medication usage (e.g., hypothyroid, seizures) _____

D. RED FLAGS for acute emergency management: Refer to the emergency department with sudden onset of any of the following:

- * Headaches that worsen
- * Looks very drowsy/ can't be awakened
- * Can't recognize people or places
- * Neck pain
- * Seizures
- * Repeated vomiting
- * Increasing confusion or irritability
- * Unusual behavioral change
- * Focal neurologic signs
- * Slurred speech
- * Weakness or numbness in arms/legs
- * Change in state of consciousness

E. Diagnosis (ICD): ___ Concussion w/o LOC 850.0 ___ Concussion w/ LOC 850.1 ___ Concussion (Unspecified) 850.9 ___ Other (854) _____
 ___ No diagnosis

F. Follow-Up Action Plan Complete *ACE Care Plan* and provide copy to patient/family.

- ___ No Follow-Up Needed
- ___ Physician/Clinician Office Monitoring: Date of next follow-up _____
- ___ Referral:
 - ___ Neuropsychological Testing
 - ___ Physician: Neurosurgery ___ Neurology ___ Sports Medicine ___ Physiatrist ___ Psychiatrist ___ Other _____
 - ___ Emergency Department

ACE Completed by: _____

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This form is part of the "Heads Up: Brain Injury in Your Practice" tool kit developed by the Centers for Disease Control and Prevention (CDC).

Rivermead Post Concussion Symptoms Questionnaire

Modified (Rpq-3 And Rpq-13)⁴² Printed With Permission: Modified Scoring System From Eyres 2005 ²⁸

Name:

Date:

After a head injury or accident some people experience symptoms that can cause worry or nuisance. We would like to know if you now suffer any of the symptoms given below. Because many of these symptoms occur normally, we would like you to compare yourself now with before the accident. For each symptom listed below please circle the number that most closely represents your answer.

- 0 = not experienced at all
- 1 = no more of a problem
- 2 = a mild problem
- 3 = a moderate problem
- 4 = a severe problem

Compared with **before** the accident, do you **now** (i.e., over the last 24 hours) suffer from:

| | not experienced | no more of a problem | mild problem | moderate problem | severe problem |
|------------------------|--------------------|-------------------------|--------------|---------------------|-------------------|
| Headaches | 0 | 1 | 2 | 3 | 4 |
| Feelings of dizziness | 0 | 1 | 2 | 3 | 4 |
| Nausea and/or vomiting | 0 | 1 | 2 | 3 | 4 |

| | | | | | |
|--|---|---|---|---|---|
| Noise sensitivity (easily upset by loud noise) | 0 | 1 | 2 | 3 | 4 |
| Sleep disturbance | 0 | 1 | 2 | 3 | 4 |
| Fatigue, tiring more easily | 0 | 1 | 2 | 3 | 4 |
| Being irritable, easily angered | 0 | 1 | 2 | 3 | 4 |
| Feeling depressed or tearful | 0 | 1 | 2 | 3 | 4 |
| Feeling frustrated or impatient | 0 | 1 | 2 | 3 | 4 |
| Forgetfulness, poor memory | 0 | 1 | 2 | 3 | 4 |
| Poor concentration | 0 | 1 | 2 | 3 | 4 |
| Taking longer to think | 0 | 1 | 2 | 3 | 4 |
| Blurred vision | 0 | 1 | 2 | 3 | 4 |
| Light sensitivity (easily upset by bright light) | 0 | 1 | 2 | 3 | 4 |
| Double vision | 0 | 1 | 2 | 3 | 4 |
| Restlessness | 0 | 1 | 2 | 3 | 4 |

Are you experiencing any other difficulties? Please specify, and rate as above.

| | | | | | |
|----|---|---|---|---|---|
| 1. | 0 | 1 | 2 | 3 | 4 |
| 2. | 0 | 1 | 2 | 3 | 4 |

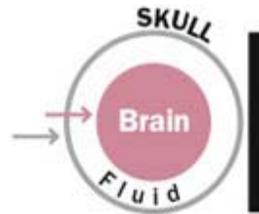
Administration only:

| | |
|--|--|
| RPQ-3 (total for first three items) | |
| RPQ-13 (total for next 13 items) | |

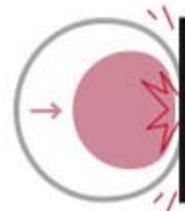
PRIMARY MECHANICS OF BRAIN INJURY

ROOM TO MOVE

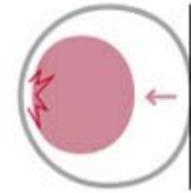
The brain does not sit snugly in the skull but is set off by an intracranial space. Skull and brain thus don't move in tandem



The head in motion stops suddenly ...



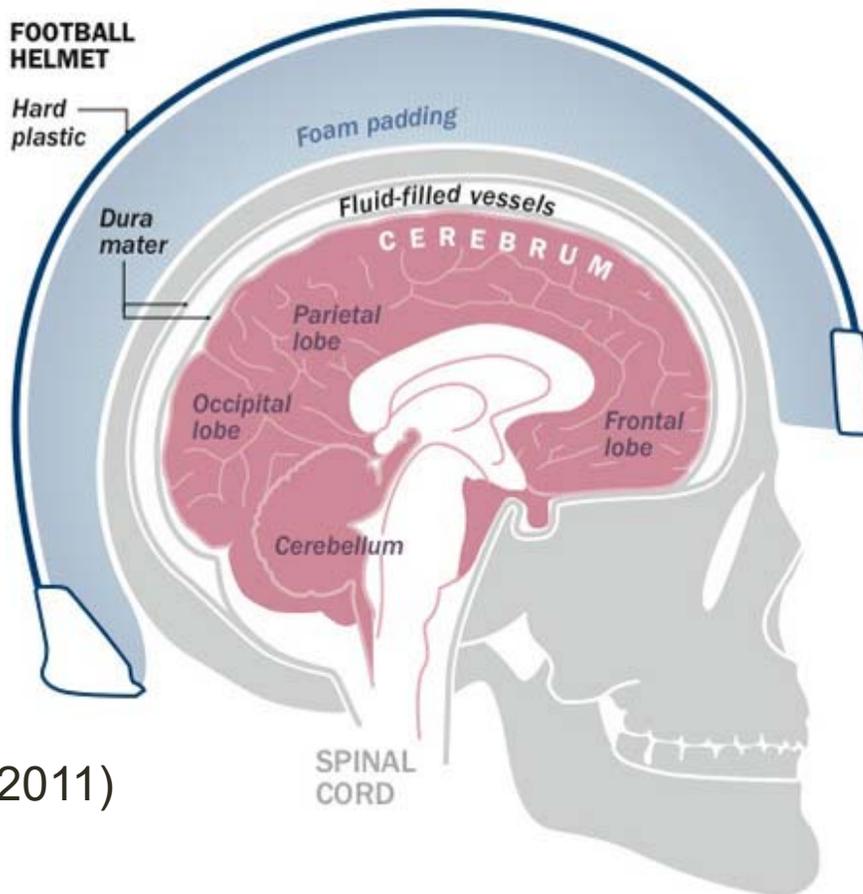
... the brain compresses into the skull ...



... and compresses again as it rebounds

FOOTBALL HELMET

Hard plastic



SIMPLE CONCUSSION

Brain swelling, axonal damage and metabolic disruption lead to classic concussion symptoms

HEMATOMA

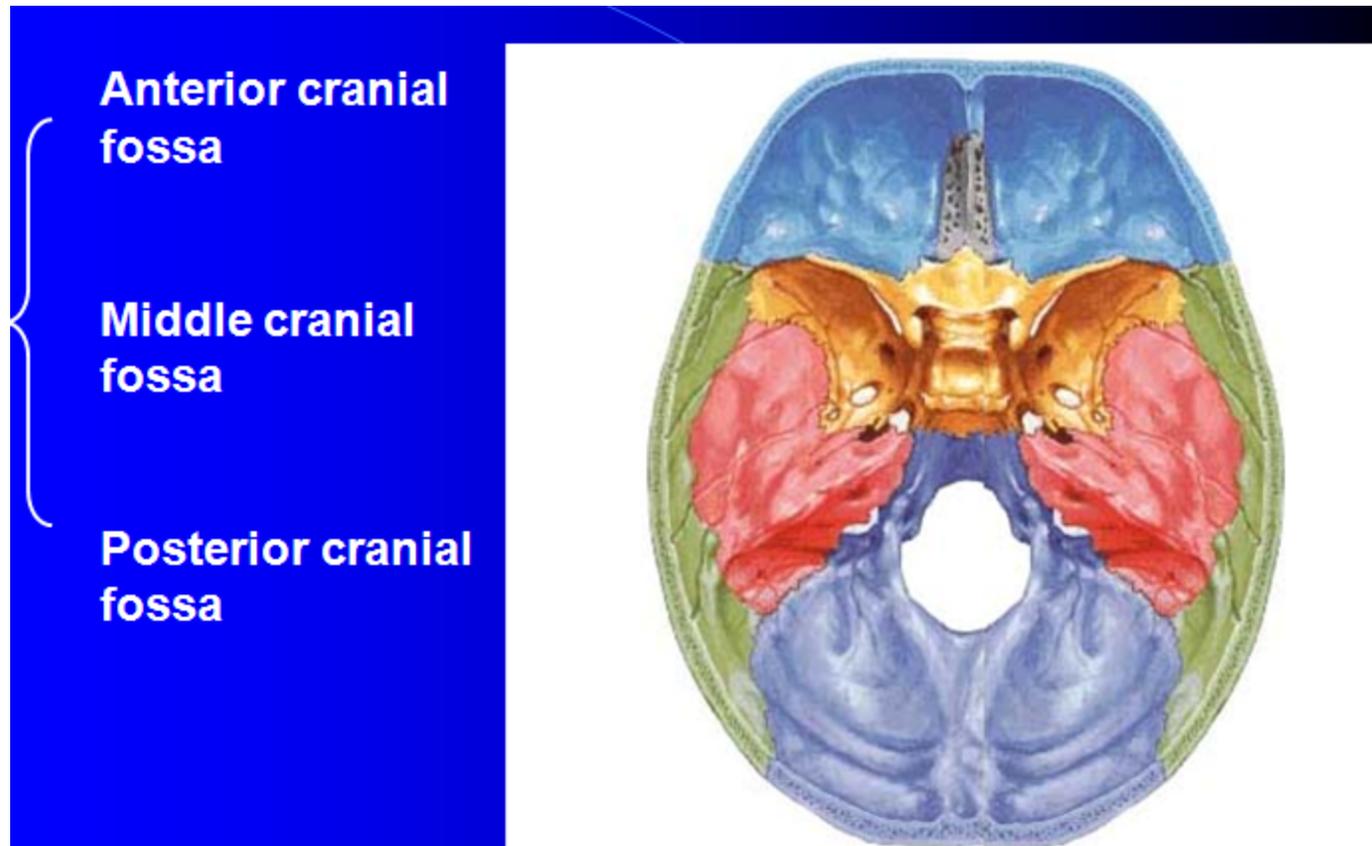
Damaged vessels can cause blood to collect above or below the dura, a much more serious injury than a simple concussion

FRACTURE

Uncommon for players wearing football helmets. A fracture can leave bone shards in the brain or otherwise damage soft tissue

(Kluger, 2011)

Primary Mechanics of Brain Injury



<http://medicinembbs.blogspot.com/2011/02/skull-anatomy.html>

Axonal Injury



Figure 3.5 *Small focal area of yellow stained scarring in the dorsolateral quadrant of the rostral pons in a case of DAI with several months survival.*

Axonal Injury (retraction bulbs)

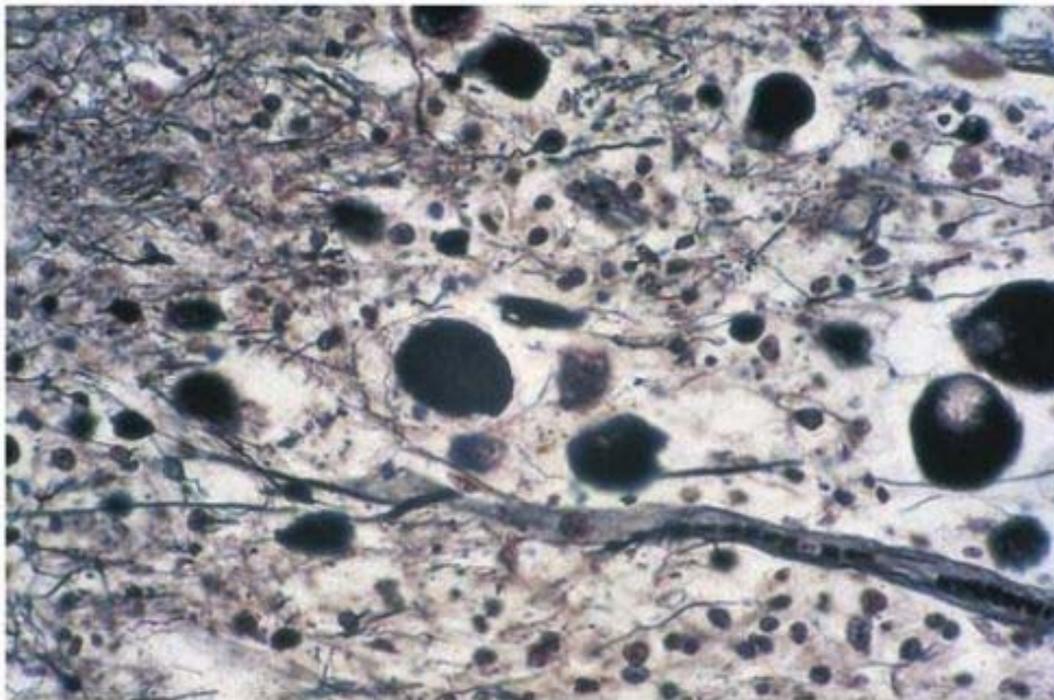


Figure 3.1 Axonal retraction bulbs. *Glees and Marsland silver technique* $\times 400$.

Axonal Injury (magnified x 1000)

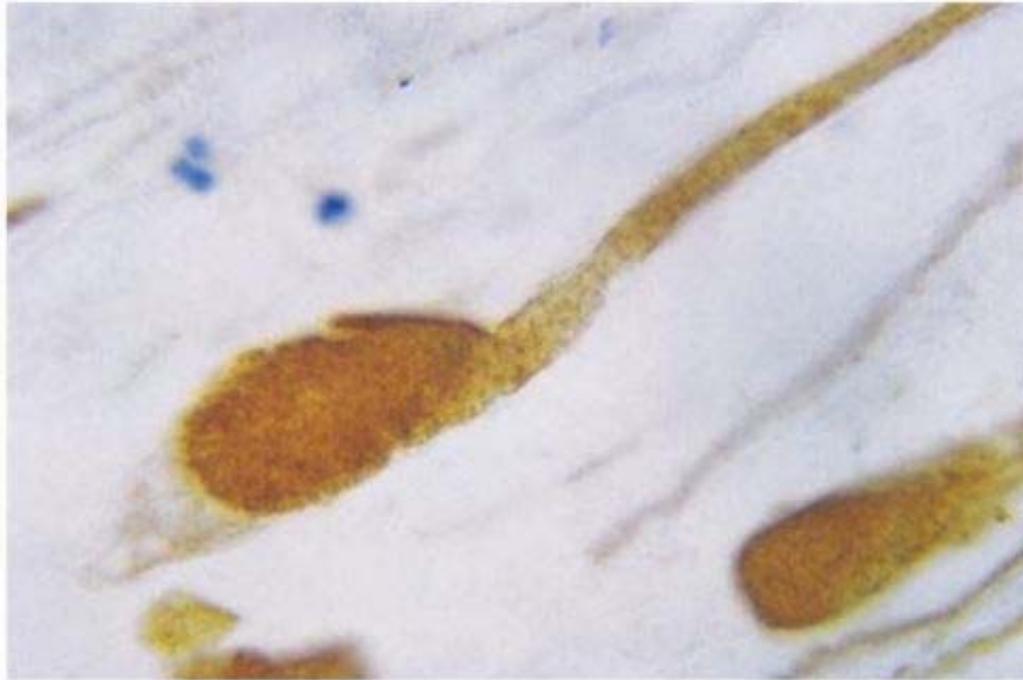


Figure 3.7 *Axonal retraction bulb. APP immunostain × 1000.*

Concussion Update: Immunoexcitotoxicity, the Common Etiology of Postconcussion Syndrome, Chronic Traumatic Encephalopathy and Posttraumatic Stress Disorder

Joseph C. Maroon · Jeff Bost · Austin Amos · Robert Winkelman · Christina Mathyssek

Department of Neurosurgery, University of Pittsburgh Medical Center, Pittsburgh, Pa., USA

Abstract

A conservatively estimated 1.6–3.8 million people experience sport- and recreation-related concussions annually in the USA. In addition, it has been estimated that an average of 300 mild traumatic brain injuries (mTBI), more commonly referred to as concussion, occur per month among US active military members, accounting for tens of thousands of affected soldiers during the last two wars. The diagnosis and management of concussions has become a major healthcare crisis. The degree of altered neuronal function and degeneration associated with concussion varies significantly, from no long-term sequelae protracted to postconcussion syndrome, posttraumatic stress disorder and the pathologic diagnosis of chronic traumatic encephalopathy. The pathway from head injury to neurodegeneration and its associated clinical sequelae has recently been linked to a unifying cause known as immunoexcitotoxicity. In this chapter, we will discuss the common etiology of these three neurological conditions as well as the immunoexcitotoxicity pathway, and introduce potential prevention and metabolic treatment strategies based on the new concept of immunoexcitotoxicity.

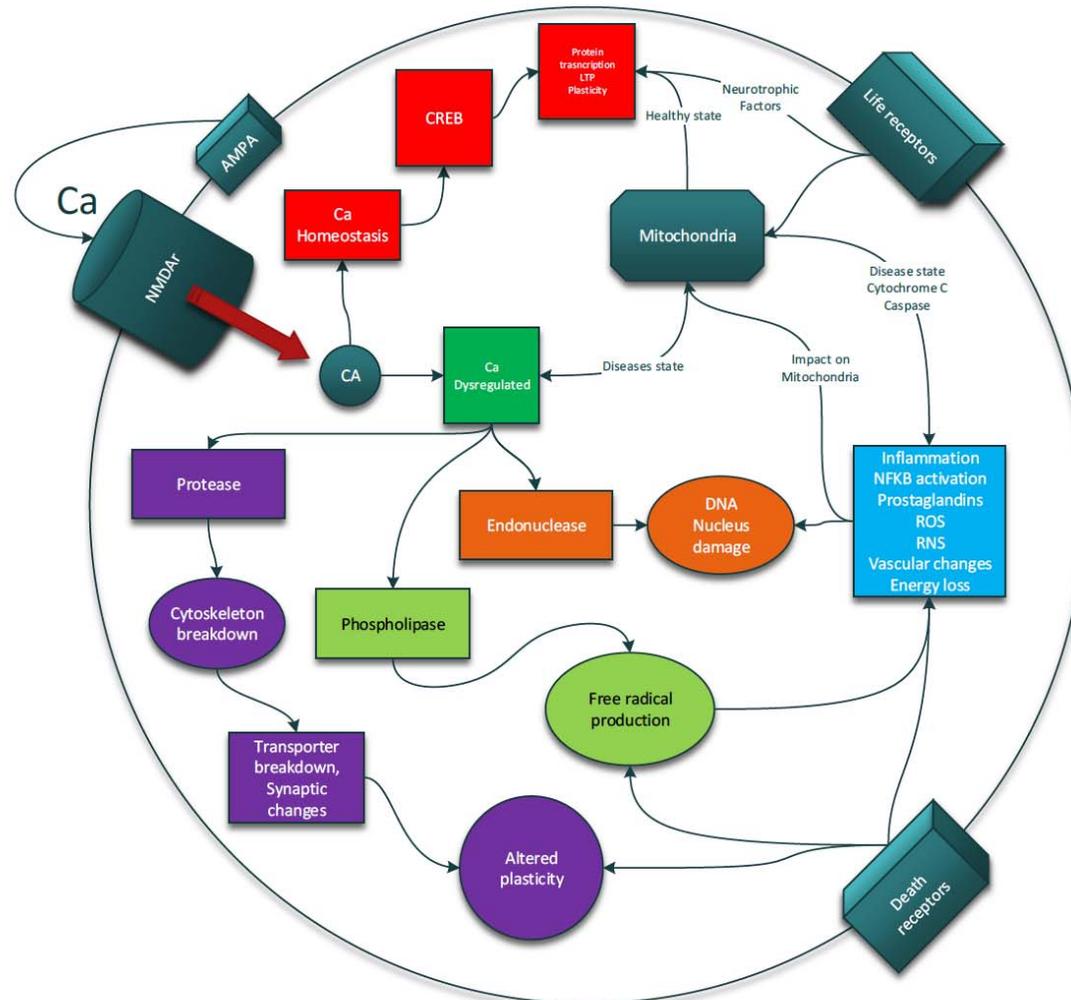
Altered neuronal function and degeneration associated with symptoms of postconcussion syndrome (PCS) and posttraumatic stress disorder (PTSD) and the pathologic diagnosis of chronic traumatic encephalopathy (CTE) and its associated clinical sequelae have been linked to a unifying cause known as immunoexcitotoxicity. First described by Blaylock and Maroon [1] in 2011, this hypothesis links mild traumatic brain injury (mTBI) to two separate inflammatory pathways mediated by brain-based reactive microglia and the neurotoxic effects of extracellular glutamine. This chapter highlights the common etiology of these three neurological conditions and introduces potential preventative and metabolic treatment strategies based on the new concept of immunoexcitotoxicity.

Background on PCS, PTSD and CTE

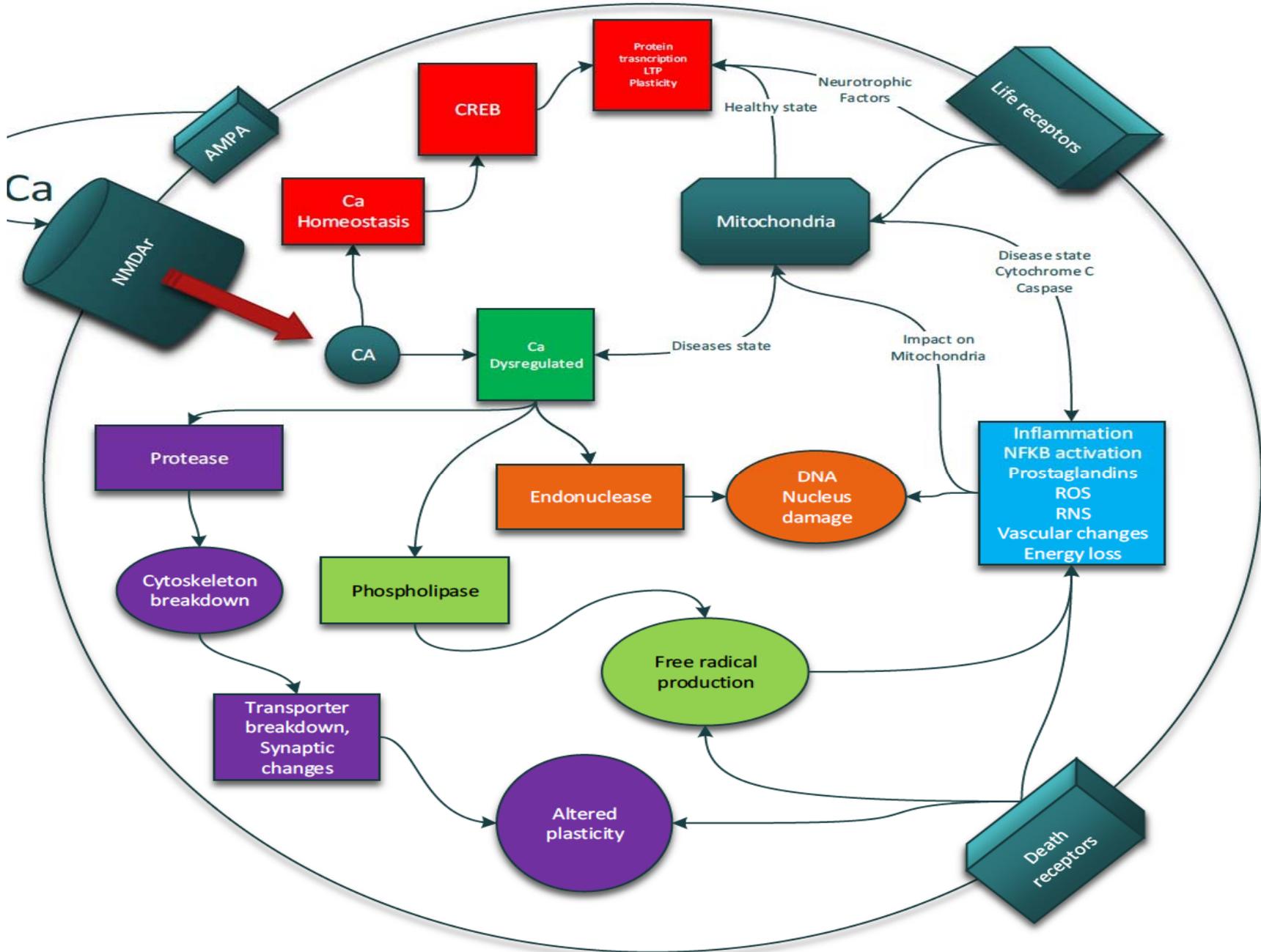
Postconcussion Syndrome

A conservatively estimated 1.6–3.8 million people experience sport- and recreation-related concus-

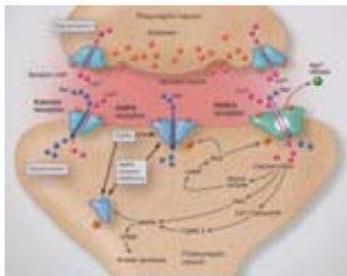
THE POTENTIAL IMPACT OF VARIOUS PHYSIOLOGICAL MECHANISMS ON OUTCOMES IN TBI, mTBI, CONCUSSION AND PPCS



Brock 2013



mTBI/
concussion



Excitotoxicity

CTE and abnormal CSF pressure

Microglial (immune)
activation

Acute microglial activation
inflammatory mode

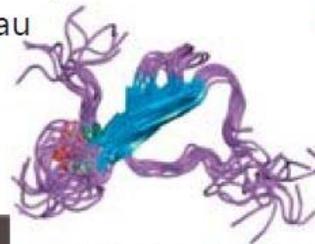
Released:

- Predominant proinflammatory cytokines
- Cytokines (TNF- α , IL-1 β , IL-6)
- Chemokines (MAP-1, MCP-1)
- Excitotoxins (glutamate, aspartate, and quinolinic acid)

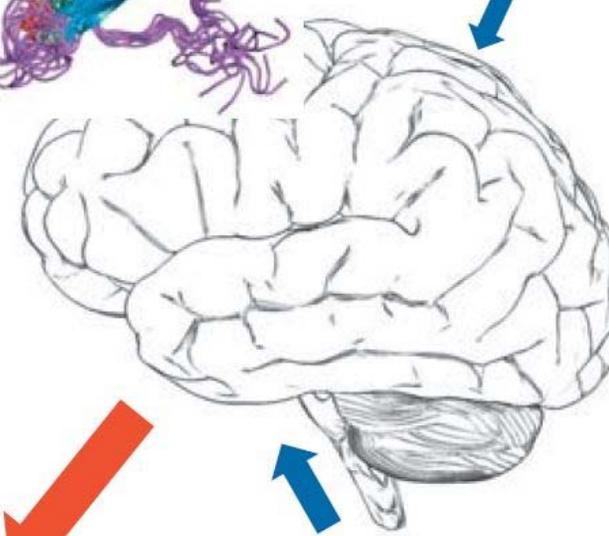
Acute microglial activation

Immunoexcitotoxicity (failure to switch into
reparative mode)

1. Phosphorylated
tau



2. Opening VRS
channels



3. Cervical
stenosis
 \uparrow CSF pressure

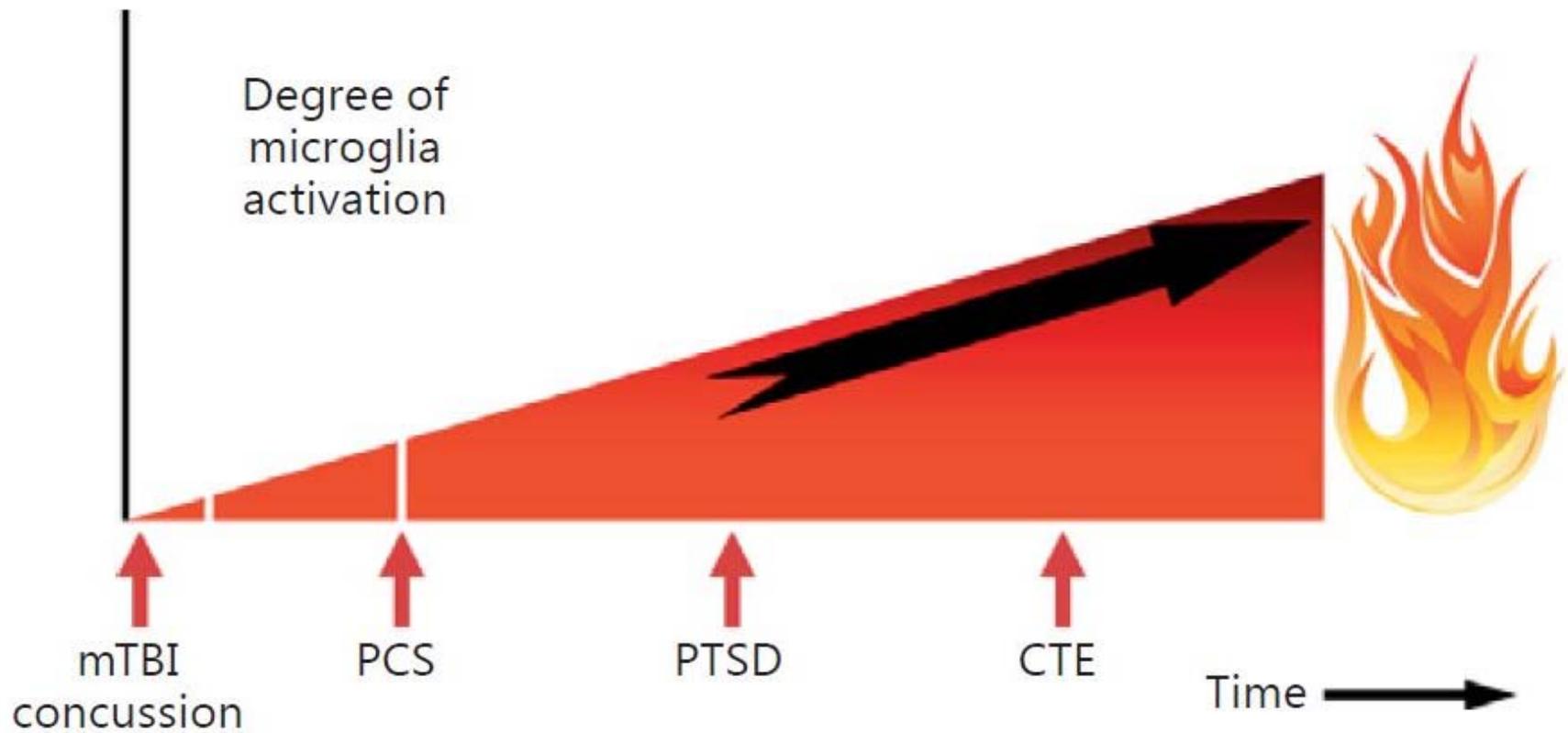
CTE



Blaylock, R., Maroon, J, July 2011
Damadian RV, Chu, D, Sept. 2011

Concussion: Pathophysiology

- Axonal Injury
 - Rarely see small hemorrhages
 - Most detailed imaging studies are normal
- Recurrent concussion and CTE
- Immunoexcitotoxicity
- Glutamate – excessive release and delayed reuptake eventually can cause neuron death.
- Microglia – macrophages that release cytokines to initiate healing and repair, but may not turn off and cause chronic inflammation.



Spectrum of Immunoexcitotoxicity

Inflammation

- Inflammation is a double – edged sword
- We need the microglia to be active to remove and metabolize damaged neurons
- The lack of regulatory immune cells in the brain cause this smoldering fire to burn indefinitely and may delay recovery, and sometimes burn chronically waiting for the chance to burst into a wildfire in the brain.

Inflammation= Brain on fire



Post-Traumatic Stress Disorder

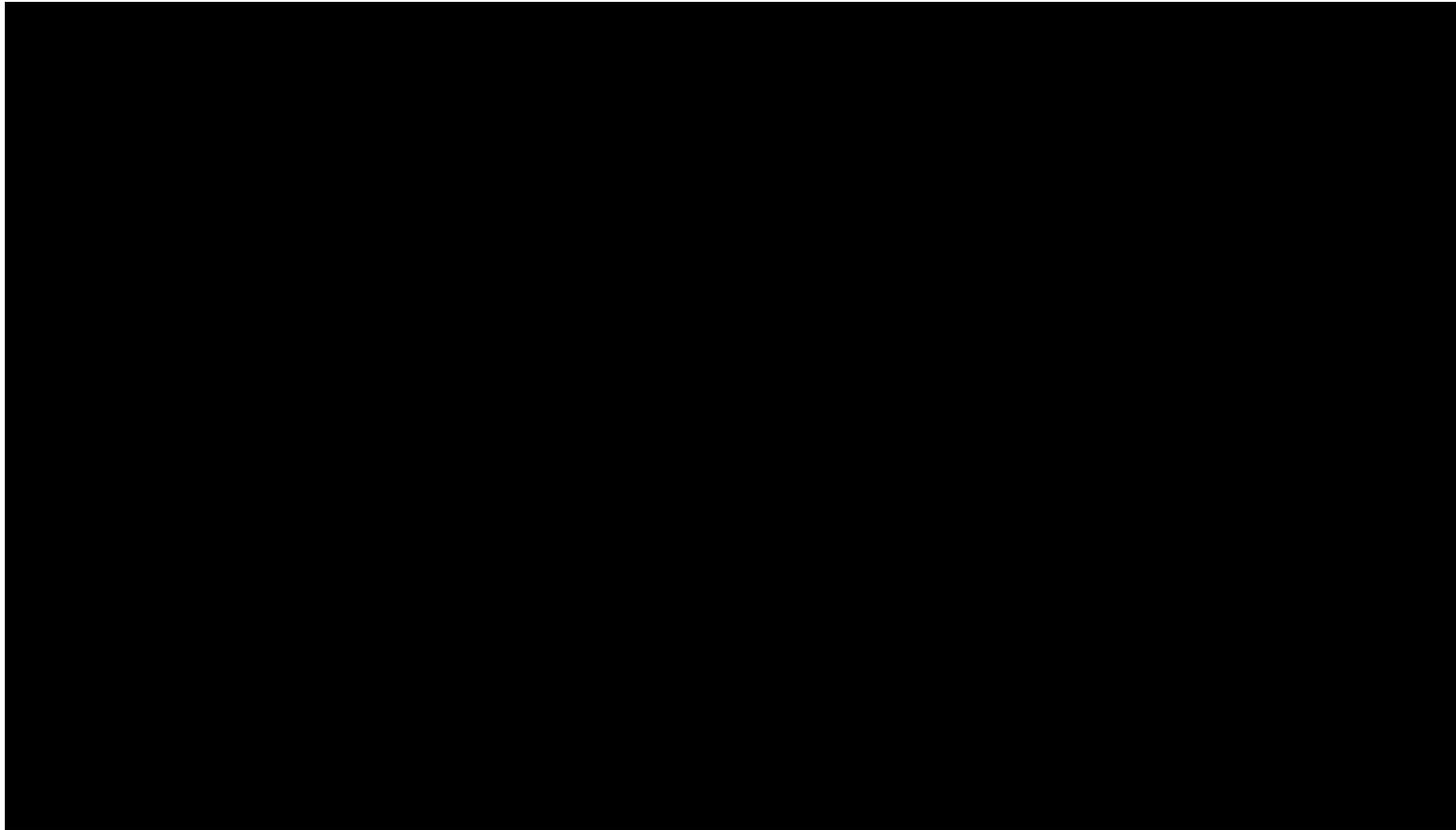
- Both psychological and behavioral changes following a traumatic event (abused children, military personnel, victims of violent crime or natural disasters)
- Symptoms may include – flashbacks, hyper-responsiveness, emotional lability, increased autonomic reactivity, sleep disturbances.
- Up to 30% of returning veterans
- May be linked to rising rates of suicide
- May occur with or without history of concussion
- Neurochemical and inflammatory changes



“OK, Mrs. Dunn. We’ll slide you in there, scan your brain, and see if we can find out why you’ve been having these spells of claustrophobia.”

TREATMENT CONSIDERATIONS

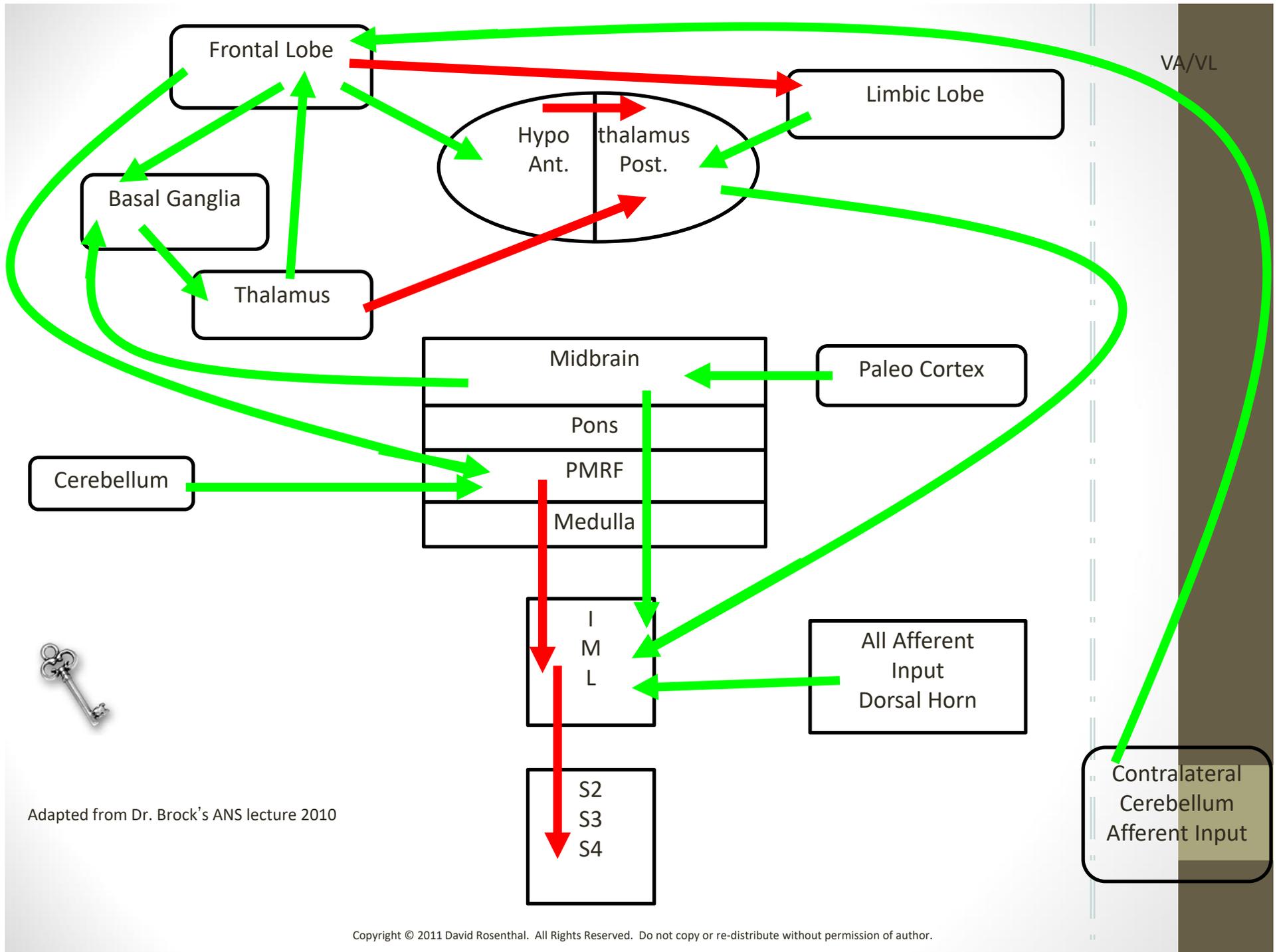
What do you observe?



Neural plasticity – Treatments

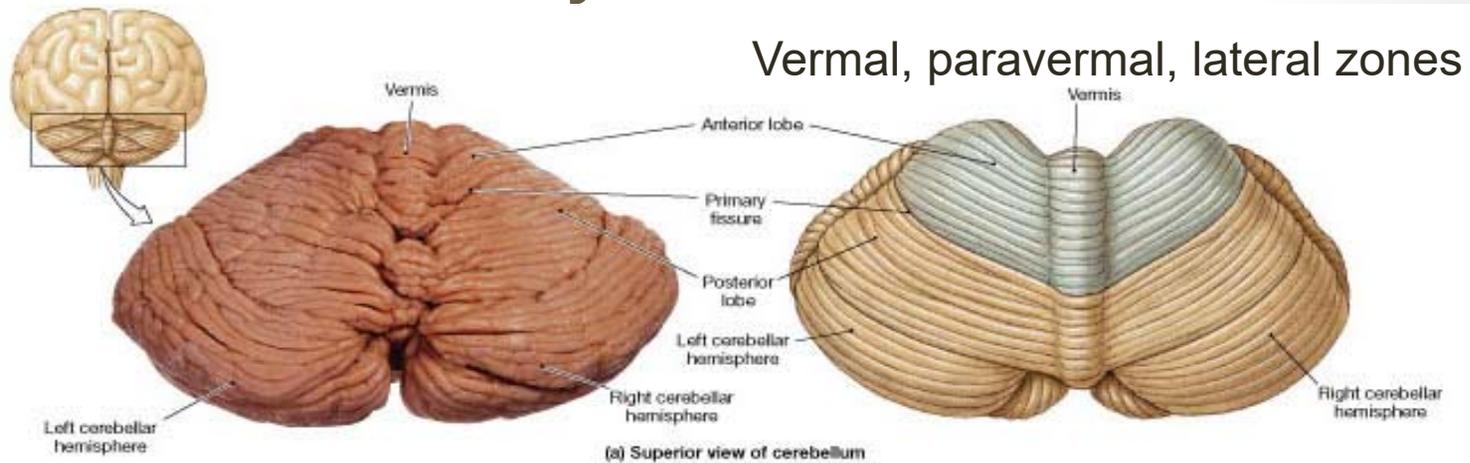
- “More focus on understanding of the pathophysiology of neurological disorders and greater focus on the role of functional changes in disorders of the nervous system would benefit diagnosis and treatment of many diseases. [Moller, 2].”



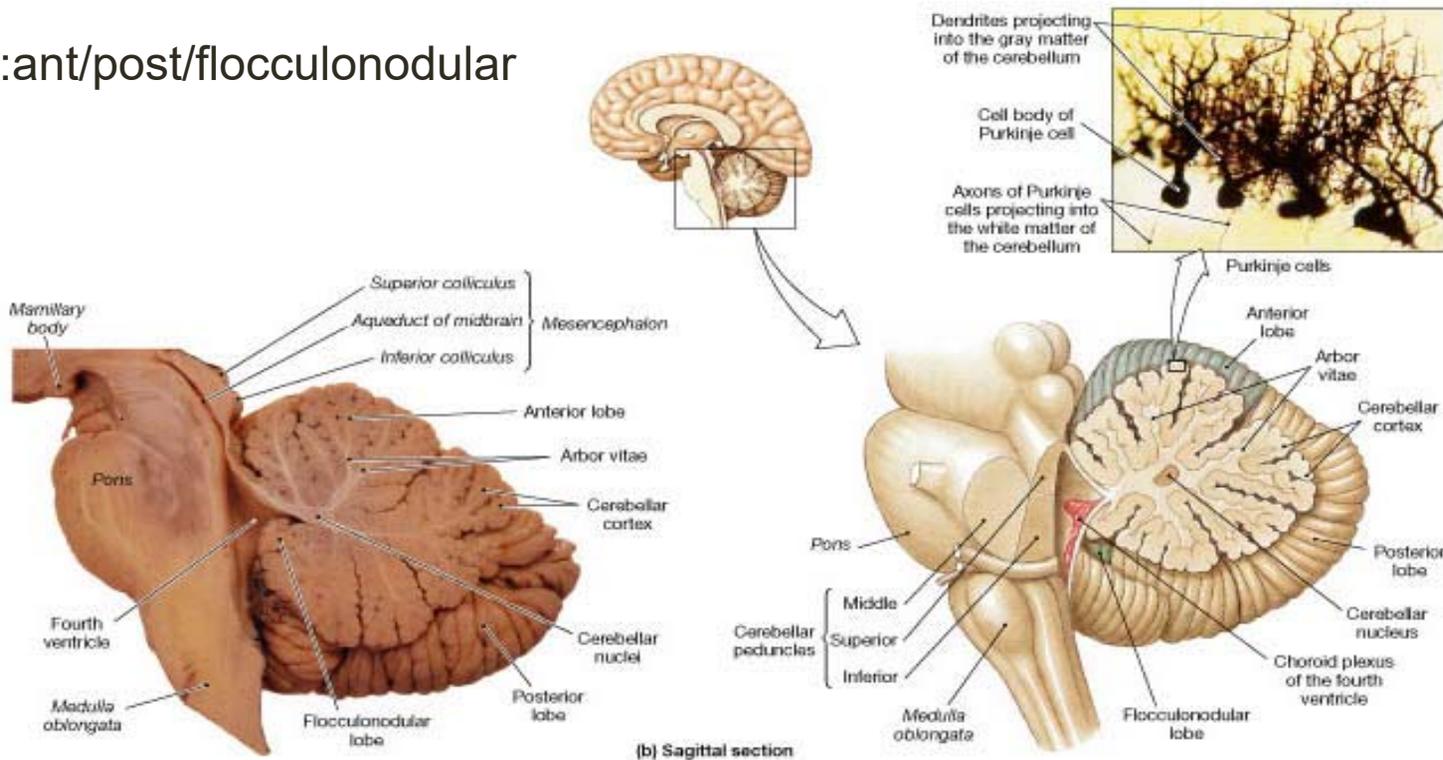


Adapted from Dr. Brock's ANS lecture 2010

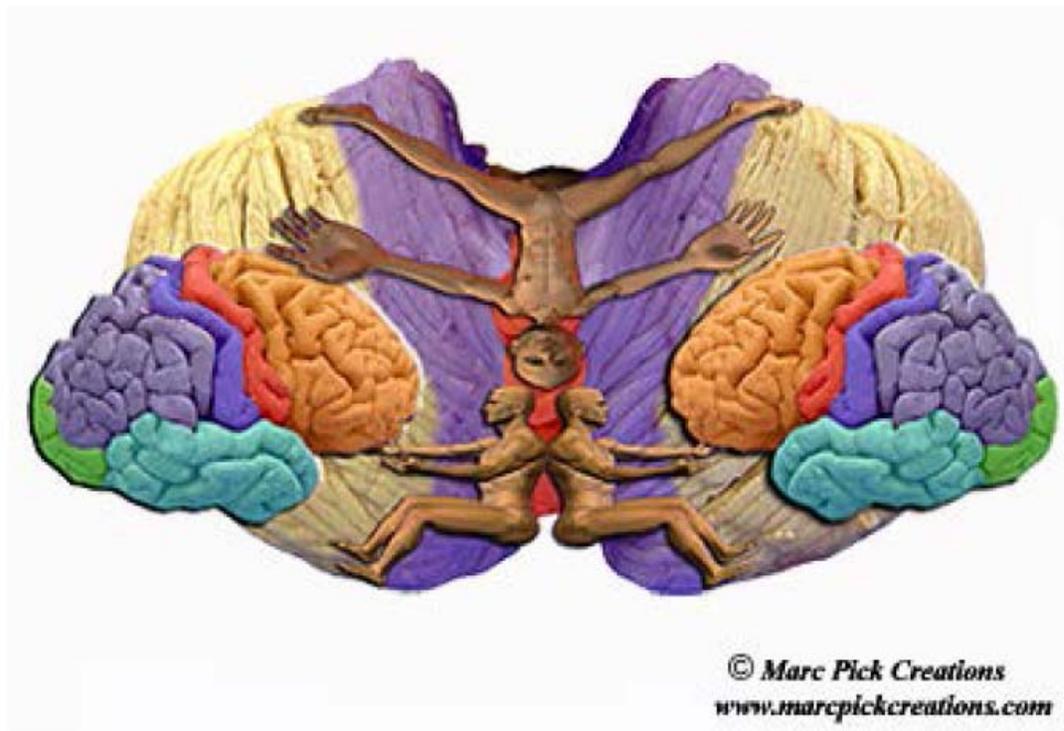
Cerebellum – many triads



3 lobes: ant/post/flocculonodular



Cerebellar Functional Zones



Spinocerebellum, Cerebrocerebellum, Vestibulocerebellum

Key Functional Neurologic tests

- 45 second or 8 minute Cranial nerve exam (but do it!)
- Corneal Blink test – CN V sensory, CN 7 motor
- Palate elevation inspection, gag reflex.
- Rib expansion test – O2 delivery, all patients
- Eyes Closed Finger to nose – CB, look for tremor, titubation
- Rapid alternating forearm motions – ipsi CB
- Sharpened Romberg's – Midline CB
- Finger tap – rapid 10x – contra FL, ipsi lateral CB
- Hand open/close - contra FL, ipsi CB (post lobe)
- Heel tap/toe tap – rapid 10x, ant lobe CB

Common Exam Findings

- Exophoria on convergence, intolerance of convergence
- Lack of gag reflex (even in nauseated patients)
- Palatal elevation asymmetry
- Unilateral or Bilateral Decrease in Corneal Blink reflex
- Myerson's sign (on glabellar tap)
- Refixation saccade on head impulse test
- Intention tremor on finger to nose test
- Large truncal titubations on tandem stance test
- Dysdiadochokinesia on rapid alternating movements of hand and forearm
- Choppy horizontal / vertical pursuits with catchup and refixation saccades

Rib expansion test

- **Chest expansion**—This should be measured by a uniform method. Using a cloth tape measure the change in circumference of the patients chest at the level of the 4th intercostal space is recorded.
- Patients should be asked to inspire and exhale maximally using standard breathing instructions. This is done a minimum of twice and the greater excursion recorded.
- Patient instructions **Please take a deep breath in as far as you can and then breathe out as far as you can and continue to breathe out until I tell you to stop”**
- Limitation of chest expansion is where the patient’s measure recorded in centimeters is less than the average normal value by a minimum of 2.5cm correcting for age and gender.

Chest Expansion Normal Data

Chest expansion—This should be measured by a uniform method. Using a tape measure the change in circumference of the patient's chest at the level of the 4th intercostal space is recorded.

Patients should be asked to inspire and exhale maximally using standard breathing instructions. This is done a minimum of twice and the greater excursion recorded.

Patient instructions **“Please take a deep breath in as far as you can and then breathe out as far as you can and continue to breathe out until I tell you to stop”**

Limitation of chest expansion is where the patient's measure recorded in centimetres is less than the average normal value by a minimum of 2.5cm correcting for age and gender.

Normal Average Values for circumferential Chest Expansion

| Age | 18-24 | | 25-34 | | 35-44 | | 45-54 | | 55-64 | | 65-74 | | 75+ | |
|-----------|-------|-----|-------|-----|-------|-----|-------|-----|-------|-----|-------|-----|-----|-----|
| Sex | M | F | M | F | M | F | M | F | M | F | M | F | M | F |
| Mean (cm) | 7.0 | 5.5 | 7.5 | 5.5 | 6.5 | 4.5 | 6.0 | 5.0 | 5.5 | 4.0 | 4.0 | 4.0 | 3.0 | 2.5 |

Treatment Considerations:

- Avoid exceeding metabolic capacity
- Low stimulation environment (visual, auditory, vestibular, cognitive)
- Vestibular - Gaze stabilization fails, saccade velocity slows, pursuits become choppy
- Lab values – look for biomarkers of chronic inflammation

When can I return to play?

- **Return to Activity Considerations**
- (Reintroduce exercise slowly)
- Start with slow jogging.
- Introduce intervals - 30 seconds intense: 90 seconds easy
- Practice with no contact
- Practice with light contact
- Practice with contact at full intensity
- Return to game play only if no symptoms are exacerbated by the above trials of activity.
- I require parents to sign affidavit and communicate with me that they have followed the above sequence and it did not cause symptoms over the subsequent 24 hours.

When can I return to play?

- If multiple concussions with no resolution of symptoms, RETIRE
- Look at the long view
- Would you rather play in one or two more games or be able to read to your children?
- How will your life be impacted if a second or third impact causes permanent damage?
- The cornerstone of concussion management is physical and cognitive rest until symptoms resolve and then a graded program of exertion prior to medical clearance and RTP. (McCroory 2008.)

Memory

- Memories are not stored in a single part of the brain. They are stored globally across the brain.
- The hippocampus is important for transferring declarative memory from short-term memory to long-term memory, but not for procedural memories (e.g., riding a bike).

Anterograde amnesia is memory loss of any memories after the onset of the amnesia. For example, if someone has damage to the hippocampus. They may have difficulty forming new memories, but they will be able to remember the memories formed before the damage to the hippocampus.

Retrograde amnesia is the memory loss of memories formed prior to the onset of the amnesia.

Clinical gem - Use n-back app to challenge and exercise patient's working memory.

Labs can show “silent” inflammation

- Inflammation (and subsequent healing) is an immune event.
- CRP > 0.5
- ESR > 6
- Ferritin > 100 should raise red flags
- Lipids
- Homocysteine (Hcys) > 7
- Elevated TSH (possible post-traumatic hypothyroidism)
- Elevated reverse T3 (rT3)
- Anemia – will delay healing
- Infection – will delay healing
- Dysglycemia – will delay healing (hypo or hyperglycemia)
- Autoimmune disease – will delay healing

What to tell patients

- Hydrate, maintain electrolyte levels (not Gatorade)
- Decrease calories (to minimize the digestive load)
- No sugar or grains for 7 days, then reintroduce slowly as symptoms fade.
- Take Anti-oxidants (curcumin, glutathione, NAC is the precursor)
- Take Omega 3's (EPA/DHA) to increase BDNF, build and maintain cell membrane flexibility. Take coconut oil.
- Take Vitamin D to decrease inflammation
- Take Magnesium – most people are deficient

What to tell patients (cont.)

- Sleep 10-12 hours a night for 7-14 days
- Avoid excitotoxins – msg, artificial sweeteners (sucralose, saccharin, aspartame)
- Avoid Ceramides – found in alcohol, nitrites in processed meats. These increase the risk of insulin resistance in the brain.
- Avoid vehicles if motion sick, (hyperbarics before air travel may be beneficial).
- Avoid cell phones – light/screen and EMF of phone
- Avoid strong smells, bright lights, loud sounds (temporary sensory deprivation)
- Limit prolonged stress/concentration 4-7 days (school/work)



Surgeons prepare for the world's first loopendectomy. Objective: Remove that part of the brain that plays the same snippet of music over and over and over.

Reversal of cognitive decline:

- Nine of the 10 displayed subjective or objective improvement in cognition beginning within 3-6 months,
- with the one failure being a patient with very late stage AD. Six of the patients had had to discontinue working or were
- struggling with their jobs at the time of presentation, and all were able to return to work or continue working with
- improved performance. Improvements have been sustained

- (Bredesen 2014)

Chronic Traumatic Encephalopathy

Current Issue:

March 2016

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The Big Idea: Brain Trauma

Published: February 2011



Lasting Impact

New research suggests that even small hits to the head may lead to brain deterioration over time. So what can be done?

By Luna Shyr

Photographs by Ann C. McKee, Boston University/Bedford Veterans Hospital

Football draws as much attention lately for the knocks that players take as it does for

Concussion Expert: Over 90% of NFL Players Have Brain Disease

Sean Gregory @seanmgregory | Dec. 22, 2015



TIME talks to Bennet Omalu, the doctor portrayed in the film *Concussion*, about his research, the future of football, and more

Bennet Omalu, a Nigeria-born neuropathologist, first discovered chronic encephalopathy (CTE) in an NFL player when he saw the debilitating disease in the brain of Mike Webster, the Hall of Fame center for the Pittsburgh Steelers who died in 2002. This finding sparked a chain of events that ultimately forced the NFL to settle a class-action lawsuit from retired players and raised unprecedented awareness of the dangers of football head trauma.



Jim Spellman—Getty Images

Dr. Bennet Omalu attends the "Concussion" premiere on Dec. 16, 2015 in New York City.

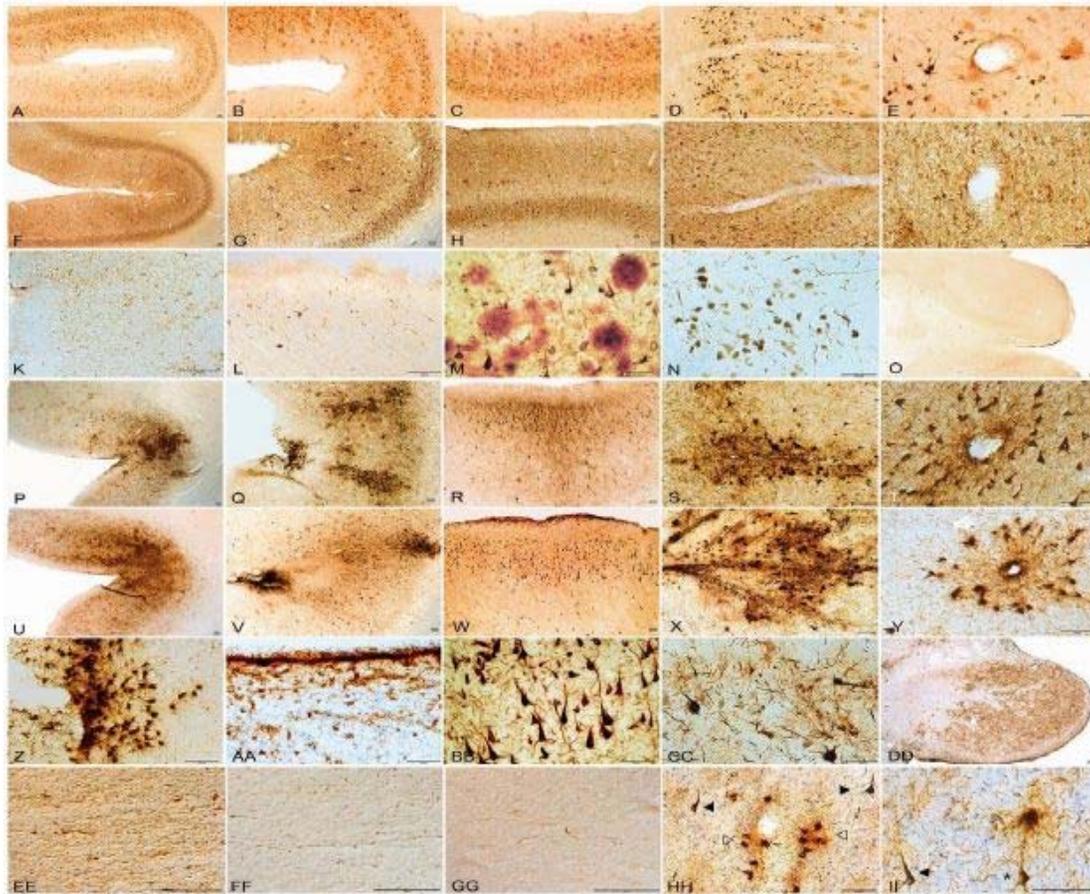
Chronic Traumatic Encephalopathy

- Pathologic post-mortem changes AND clinical syndrome of cognitive, memory and behavioral decline
- Omalu at U of Pittsburgh med center published first autopsy report

Chronic Traumatic Encephalopathy

- **Gross neuropathological findings** - atrophy of cortex, temporal lobe, diencephalon, mammillary bodies, enlarged ventricles and septum pellucidum.
- **Clinical symptoms** – irritability, impulsivity, aggression, depression, short-term memory loss, suicidal ideations.
- Most cases (67%) involve former boxers, football players, multiple concussions, repetitive blows to the head.

Distinctive p-tau pathology of CTE compared with Alzheimer's disease.



McKee A C et al. Brain 2013;136:43-64

Neuroplasticity

Stages of Neuroplastic Healing

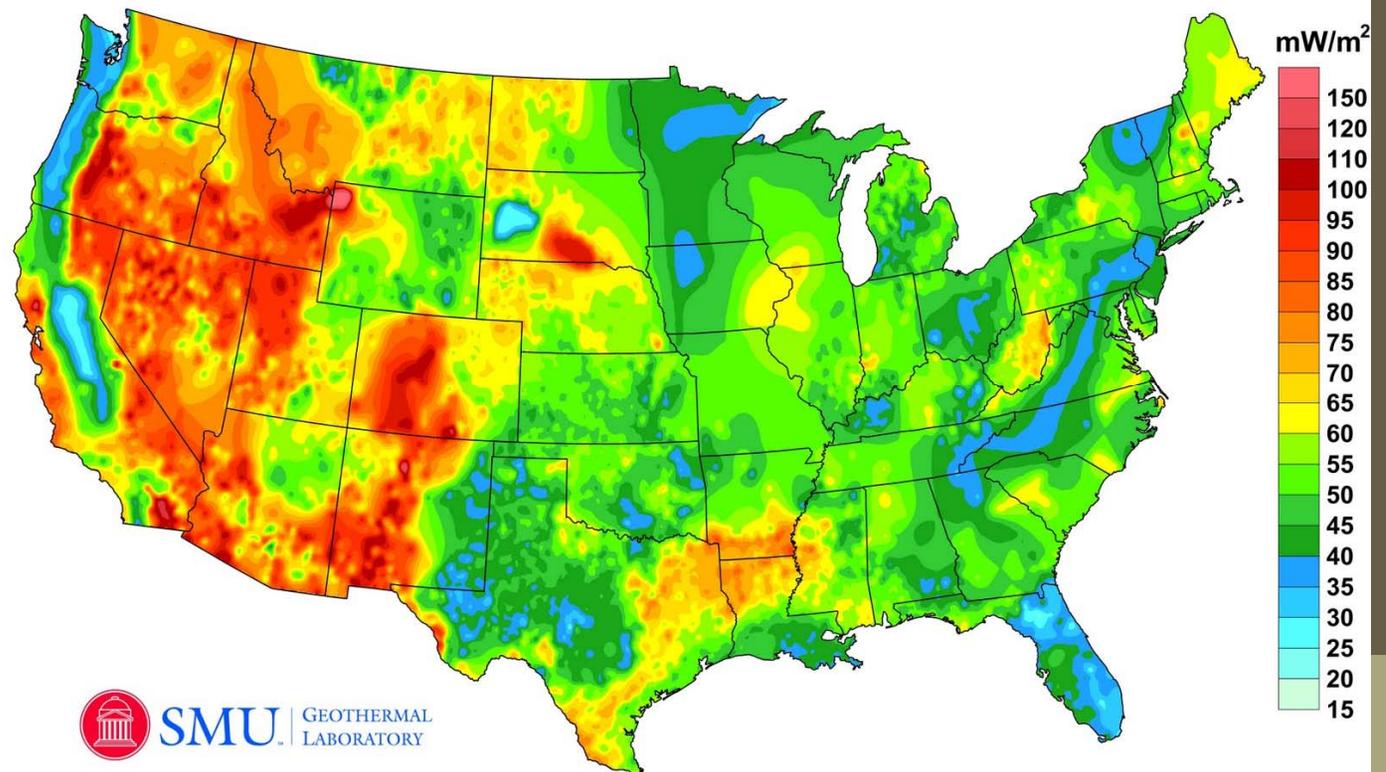
- 1-Correction of general function of neurons and glia
- 2-Neurostimulation – light, sound, electricity, movement, thought
- 3-Neuromodulation – brain contributes to its own healing by controlling RAS, and ANS (sympathetic suppression)
- 4 – Neurorelaxation – accumulate and store energy
- 5- Neurodifferentiation and learning – brain is rested and quiet and can learn and relearn functions.

- (Doidge – Brain's Way of Healing)

Key points on neurogenesis and synaptogenesis:

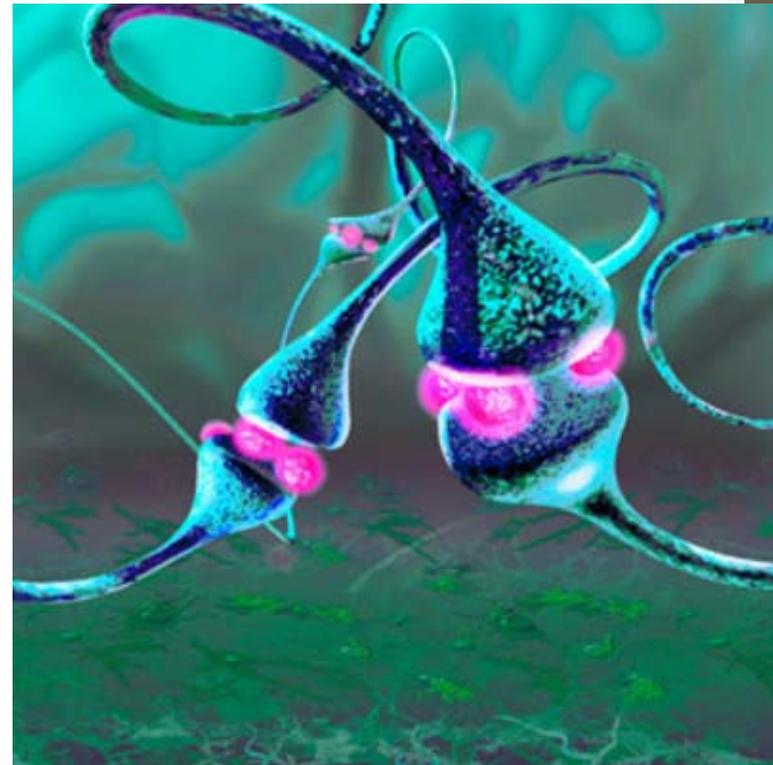
- A newborn enters the world with about 100 billion neurons, which is an average of 250,000 per minute averaged over 9 months in utero. Most of this is finished by the 18th week after gestation.
- After the 15th week after conception a body map appears in the brainstem, then the thalamus, the precursor to the somatosensory cortex which begins to be solidified at birth when cerebellum and thalamus become myelinated.

- It is like an axon growing from New York to a specific address in Seattle, WA – requires genetic code and trophic factors.



Synaptogenesis

- Neurons are pruned from 200 to 100 billion at birth; Synapses must be pruned even more vigorously, because each cortical neuron forms 15,000 connections. Estimated that 20 billion synapses are pruned every day between childhood and early adolescence. (Survival of the busiest)



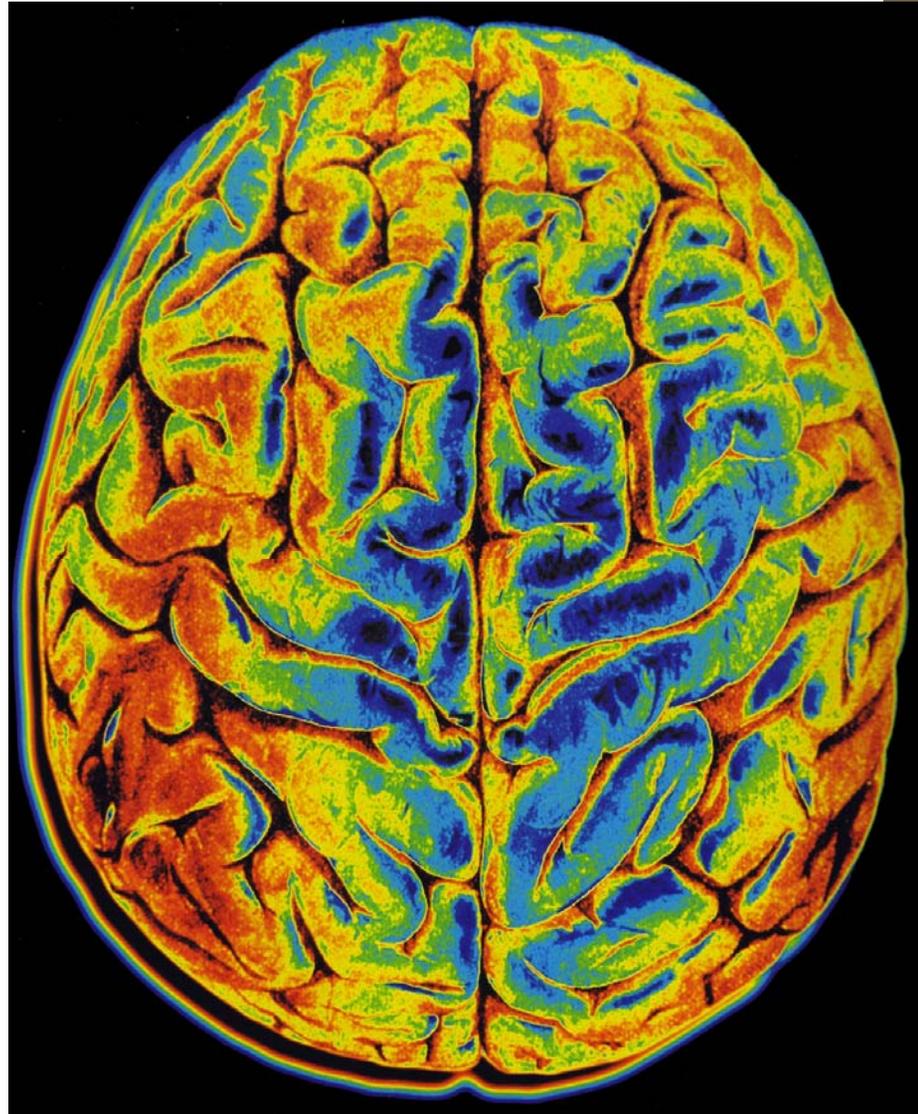


- “The hardware of the brain is far from fixed at birth... it is dynamic and malleable.”



Synaptogenesis

- Second wave of synaptogenesis may not be complete until early twenties (Jay Giedde of National Institute of Mental Health.)

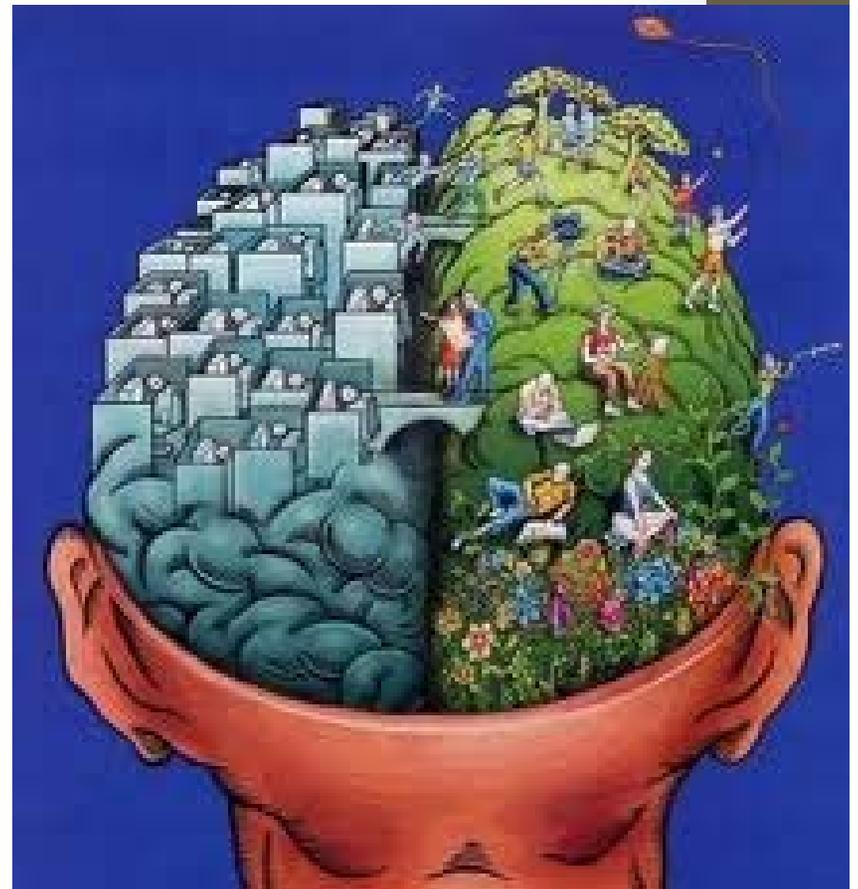


“The adult has the ability not only to repair damaged regions but also to grow new neurons.” Willful activity has power to shape the brain (A working principle for early brains and adult brains.)



Neurogenesis & Neuroplasticity

- “It can grow new cells. It can change the function of old [cells].” It can rezone an area... change the circuitry that weaves neurons into the networks that allow us to see and hear, remember, feel, suffer, think, imagine, and dream.





Key points learned from the Silver Springs Monkeys:

A REPORT BY AT LARGE

THE RAID AT SILVER SPRING

Edward Taub claims that he was conducting legitimate private experiments in ground-breaking neurological studies, but critics charged that he was needlessly torturing monkeys. Their experimental legal battle gave rise to the American animal rights movement, and called into question the morality of the people on both sides of the issue.

BY CAROLYN TRAVIS



During the raid, pictures provided to *Life* (clockwise right), the Maryland police seized the monkey lab of Edward Taub (left), who said, "The experiment, although, was blocked by this. There is no point in these experiments. It's completely unethical pain."

There were seven Chimps, Allens, Rappins, Harbys, Montagues, Liberians, Big Ben, Augustus, Tino, Sam, Charlie, Fred Thoms, Brooks, Billy, Paul, Albin, and Sarah. They were monkeys. Over a decade ago, an animal researcher performed an experiment on some of them, applying their ears. The monkeys had to run from a small wooden building in Silver Spring, Maryland—a building that the researcher called the Behavioral Biology Center. In October of 1981, he was charged with numerous counts of animal cruelty and became the only researcher ever cited and arrested on that charge in the country. Twelve of the creatures Silver Spring monkeys are now dead. But they are arguably the most famous experimental animals in the history of science.

A few things were handled less so: In doing the run test again and three months of these monkeys were confined to the month for the police. The first of the millions of animals—some 100,000, 100,000, 100,000, and 100,000—experimented on. Many of the monkeys attacked have helped save the public consciousness gaps in the Silver Spring monkeys have. Millions of

American have seen the monkeys' faces on posters and pamphlets, and on the morning news. To hundreds of these people, the monkeys became individuals with names and personalities, political positions to be argued from their laboratory jail. They became the most real to what they did for us—yet for us this is not to wonder they protest—yet for other was done nothing.

Except for Sarah, who is a female human surrogate, all the monkeys were male and young, energetic. These are small brown monkeys with a coat of white skin around their eyes. Collecting managers are harder to the Philippines, Malaysia, and Indonesia, may be over three and much smaller than other species. The most often torturous prisoners, these managers live in colonies and are intensely social, they are strong bonds between members and offspring. Local support who have the monkeys—they get the separation of two of these dollars per animal in the marketplace—generally look for a mother and young, about the mother and again the child as a stage in her body. The Silver Spring monkeys was caught in jungles, Edward Taub, the man who experimented on them.

Thought there, for you finished William, then it didn't even a period of three years during the last session.

Edward Taub is now a professor in the Department of Psychology of the University of Baltimore in Baltimore. Since the day the police seized the Maryland laboratory, he has been dismissed in the University of animal rights groups as a torturer of the animals he had in his care. He has been married to the first chimp Fred Monique. When you meet him, he doesn't let up on the matter that passes time has been passed of him. He is a small man, thin and slapping his walls with a rocky complexion and he has a strong Brooklyn accent. Although his reputation on the charge of animal cruelty was ultimately overturned, he has never been granted the opportunity on the funding to perform research on animals. Taub has ultimately denied any wrongdoing in his treatment of his animals, and scientific societies have questioned him, but the journals that once published his work reject his work, and the institutions that once gave him grants have done his application. Taub has spent thousands of hours defending himself, but photographs of his laboratory speak for him.

Lessons Learned

- Institute for Behavior Research, Silver Springs, Maryland.
- Lead researcher was Edward Taub.
- 16 male macaque and 1 female rhesus monkey.
- Animal rights movement (PETA)
- Taub was exonerated in 3 separate trials

Lessons Learned

- After surgical deafferentation (sensory nerve, not motor) of one arm, the adolescent monkey never learns that the limb is potentially useful. (Principle of learned non-use, not motor incapacity. 1980.)



Lessons Learned

- Bilaterally deafferentated monkeys were able, soon after surgery, to use both arms to grasp, walk, and climb, almost normally (Taub & Berman 1968)
- Smaller lesion was more crippling than a lesion twice the size.



Lessons Learned

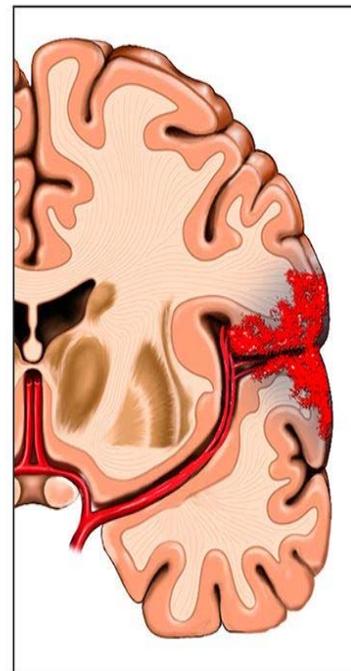
- Monkey can learn to use their “bad” arm, only if their good arm is constrained (3 months), and they are forced to not use the good arm. Eventually use arms to climb and pick up raisins.
- Fetal experiments were abysmal failures, but Taub concluded that volitional movement is preloaded into animal’s brain like Windows XP on a laptop.



Lessons Learned

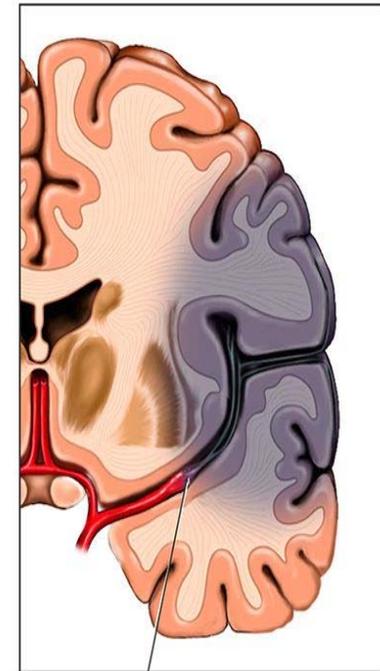
- 1980- just started to apply monkey research to stroke and brain injury patients.
- It is impossible to have a central injury without a peripheral consequence. And it is also impossible to have a peripheral injury without a central consequence.

Hemorrhagic Stroke



Hemorrhage/blood leaks into brain tissue

Ischemic Stroke



Clot stops blood supply to an area of the brain

How long to change Neural Maps?

- Somatosensory cortex was reorganized after amputation of raccoon 5th digit.
- Severed median nerves in squirrel monkeys – within 4.5 months the new maps were as refined as the originals, in that the radial and ulnar nerves had moved into the medians cortical territory.
(Kaas and Merzenich)

Nervous System Organization

- Takes in sensory information
 - Peripheral nervous system via receptors for vision, hearing, smell, taste, vestibular
- Provides fuel – autonomic nervous system
- Creates the PERCEPTION of the world
- Allows MOVEMENT in your world- frontal lobes, basal ganglia, thalamus, cerebellum

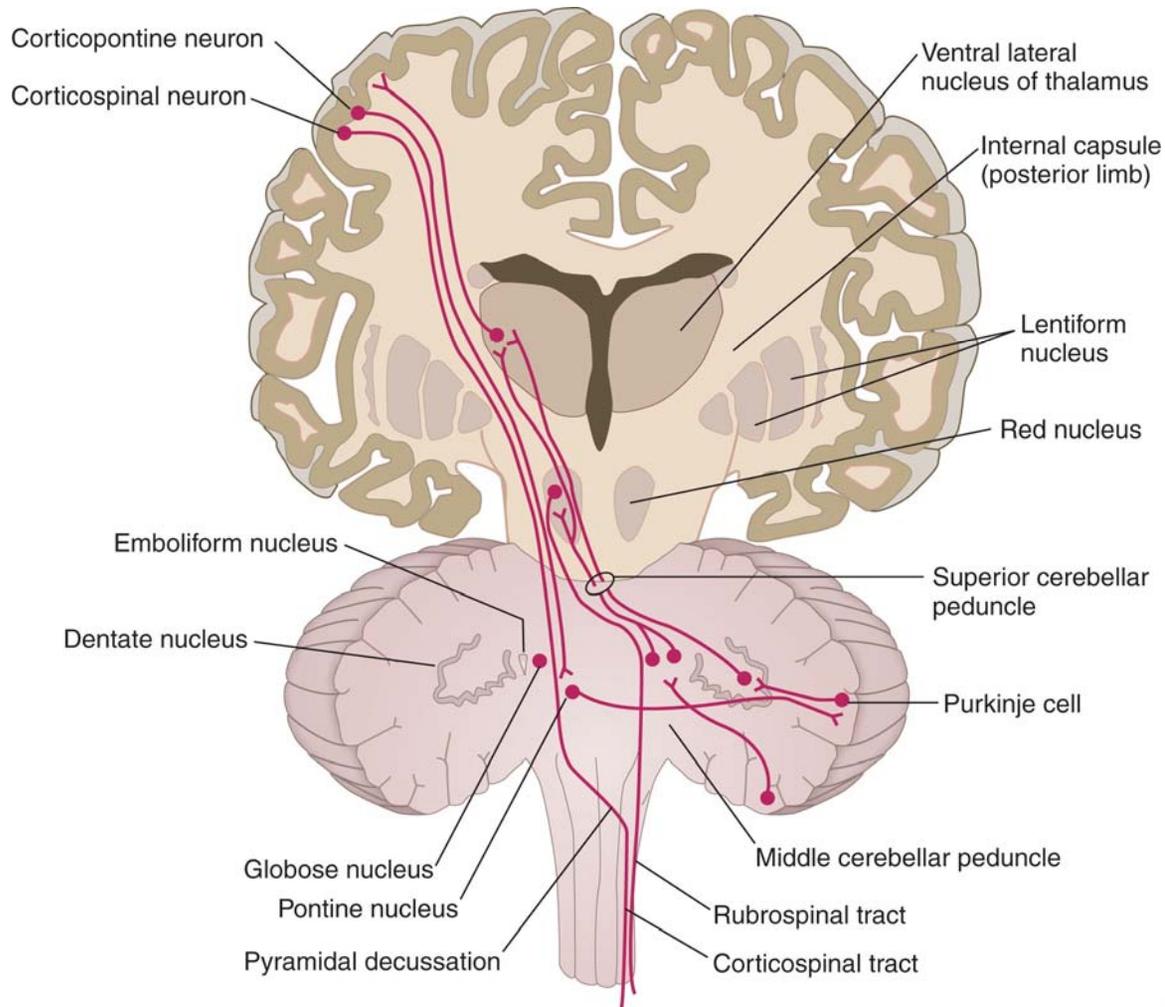
Nervous System Organization

- Cerebellum processes all brain activity, makes the sensory-motor interface smooth, accurate and coordinated (including visceral)
- Basal Ganglia influences ALL motor output, including emotional

Cerebellar input pathways

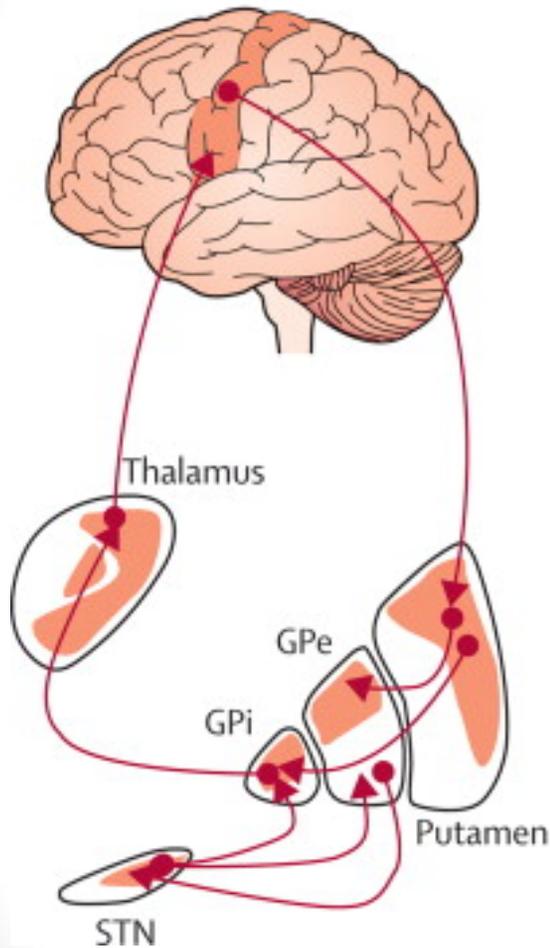
- Pontocerebellar fibers
- Spinocerebellar pathways
(dorsal SC tr,
Cuneocerebellar tr, ventral
spinocerebellar tr, rostral
SC tr)
- Climbing fibers (red
nucleus, cortex, brainstem,
spinal cord,
olivocerebellar)
- Vestibular inputs

Cerebellar input pathways

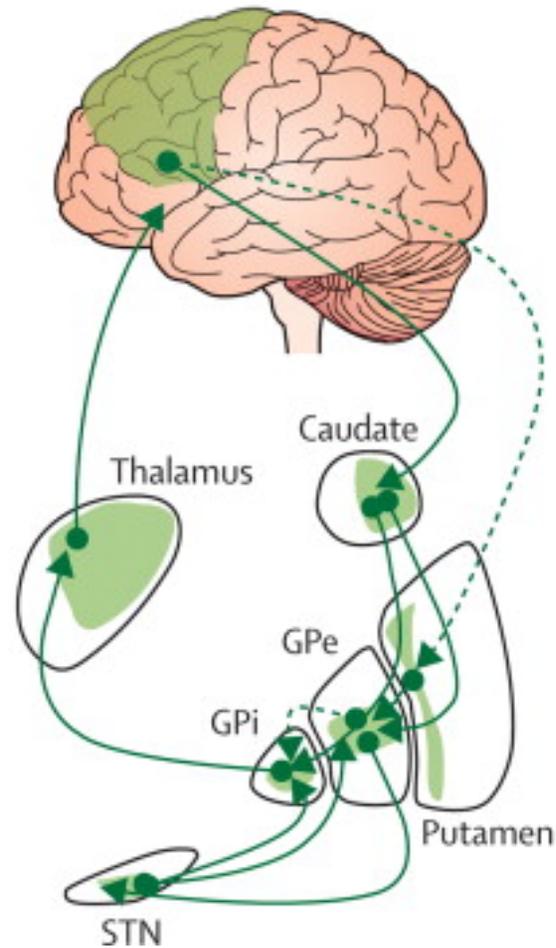


Basal Ganglia Circuits

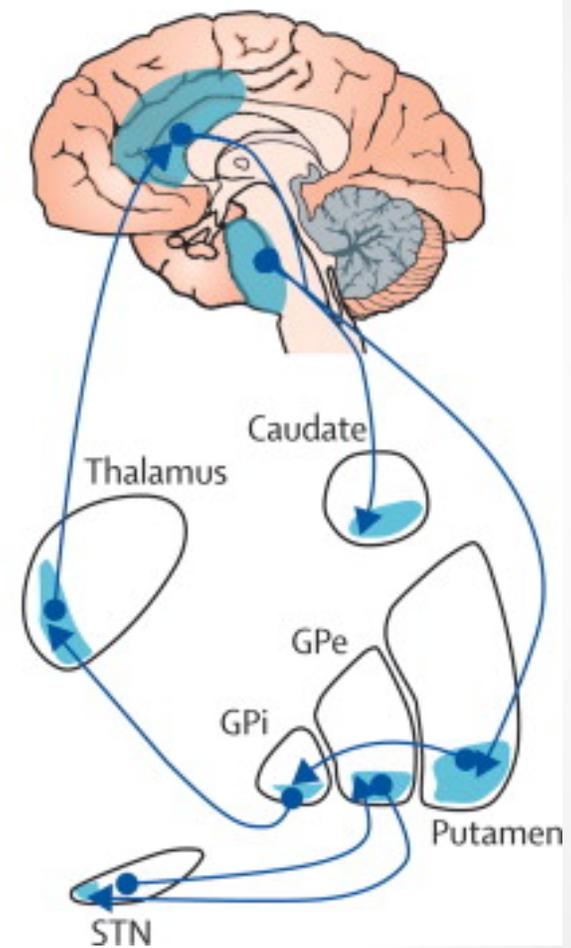
A Motor circuit



B Associative circuit



C Limbic circuit



Human Neural Plasticity

Thomas Elbert (Univ of Konstanz, Germany) summarized 4 basic principles:

1- Disuse (or deafferentation via damage) leads to invasion of unused cortical area by neurons from nearby areas (stroke/tbi)

2- Increased use leads to expansion of cortical map (musical training)

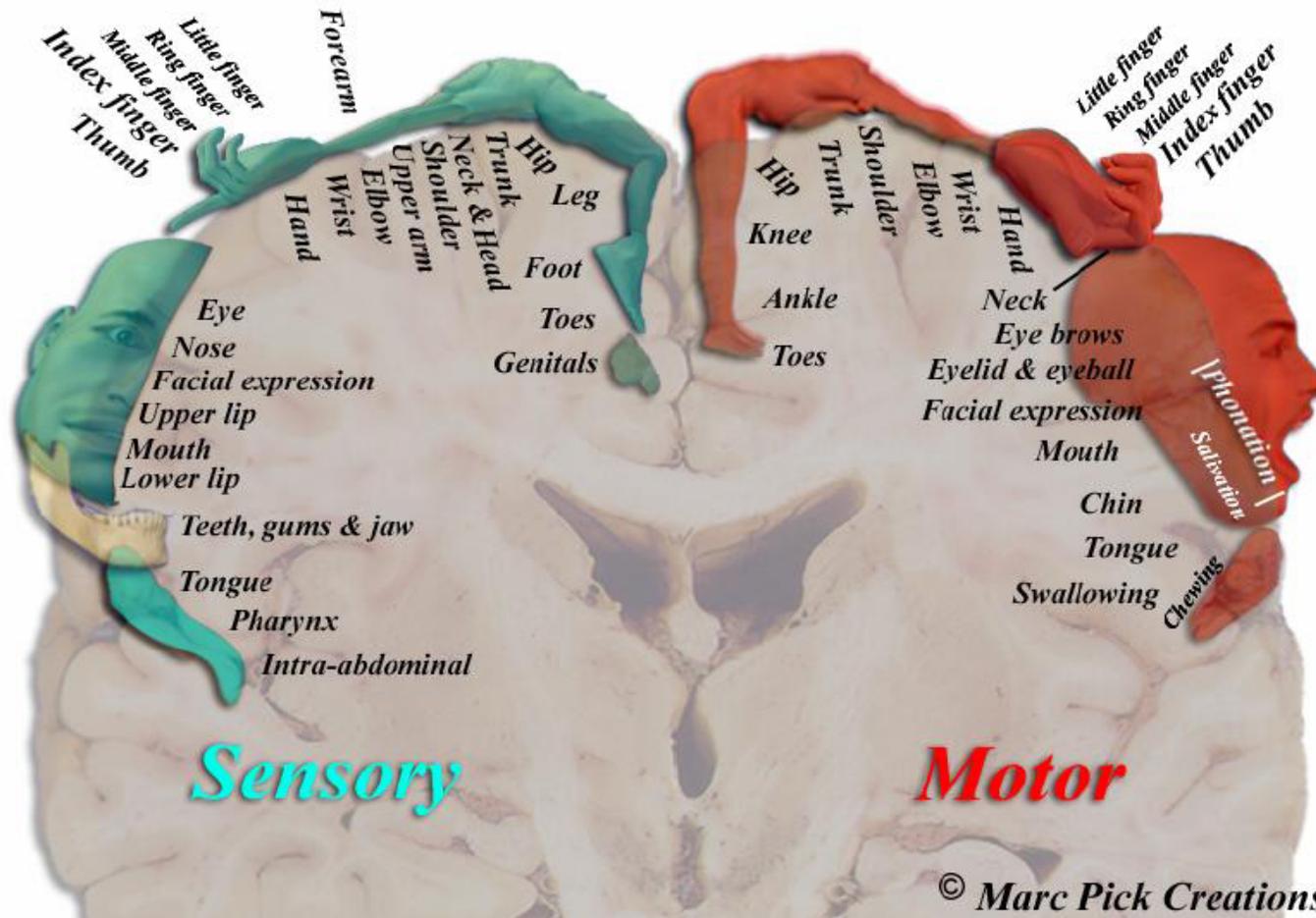
Human Neural Plasticity

3 - Synchronous inputs lead to fusion of cortical zones representing those inputs

4 - Asynchronous inputs lead to segregation of cortical zones representing those inputs

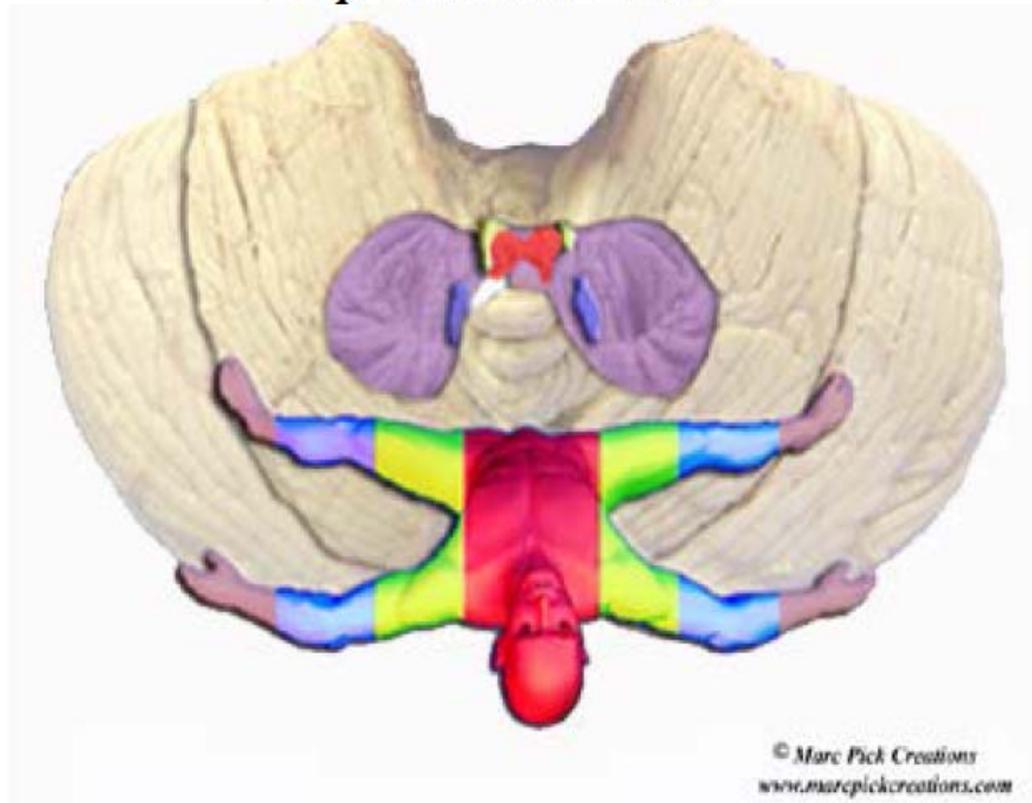
Brain Maps

Somatotopic Organization of the Sensorimotor Cortex



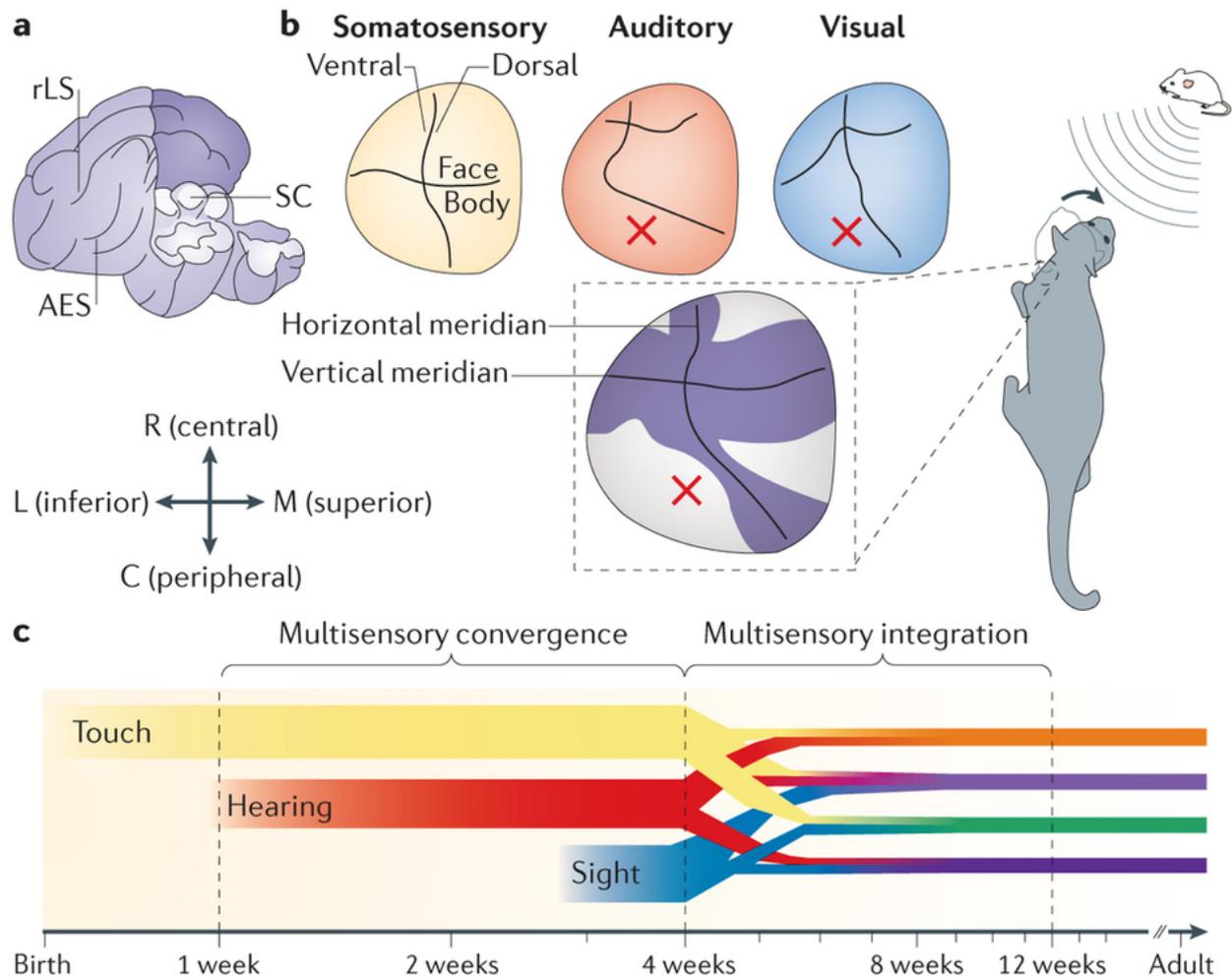
Brain Maps

Deep Cerebellar Nuclei



Fastigial, Interposed (globose, emboliform), Dentate

Superior Colliculus maps



Neural plasticity – Treatments

“Directing treatments toward correcting the abnormal function that causes the symptoms and signs of disease is more beneficial to the patient, than attempts to treat the abnormal test results.”

This requires a thorough knowledge of not only the normal physiology that makes up a given system, but also its pathophysiology – a topic that is sparsely taught in medical schools [Moller, 2].”



Neural plasticity - Objective Testing

The focus on so-called objective tests, which mainly detect gross morphological abnormalities, has been a distraction in searching for accurate diagnoses and treatments for many disorders of the nervous system.

The fact that induction of neural plasticity can reverse or correct certain pathologic conditions of the nervous system means that induction of neural plasticity is a valuable addition to the medical arsenal of treatment [Moller, 2]."

Neural plasticity – Treatments

“Increase in understanding how functional changes in the nervous system can cause symptoms and signs of diseases has already led to more efficient treatments, with fewer side effects.

And it seems likely that we have just seen the beginning of a development that focuses on functional changes in the nervous system as a cause of symptoms and signs of disease.

Fully utilization of these advancements in diagnosis and treatment of disorders of the nervous system will lead to better treatment of many disorders of the nervous system. [Moller, 2].”

DEFINITIONS

Definition: Traumatic Brain Injury

- **TBI is defined as an alteration in brain function or other evidence of brain pathology, caused by an external force.**
- **Alteration in brain functioning is defined as one or more of the following signs:**
 - Any period of loss or of decreased LOC
 - Any loss of memory for events immediately before or after the injury
 - Neurologic deficits (weakness, loss of balance, change in vision, dyspraxia paralysis, sensory loss, aphasia, etc.)
 - Any alteration in mental state at the time of the injury (confusion, disorientation, slowed thinking, etc.)
- **Other evidence of brain pathology may include:** visual, neuroradiologic , or laboratory confirmation of damage to the brain.

Another definition of concussion



Definition: Traumatic Brain Injury

- **Caused by an external force may include any of the following events:**
 - -The head being struck by an object
 - -The head striking an object
 - -The brain undergoing an acceleration/deceleration movement without direct external trauma to the head.
 - -A foreign body penetrating the brain
 - -Forces generated from events such as a blast or explosion
 - **-Or other force yet to be defined**
- **Broader to include mild TBI and delayed clinical manifestation of symptoms.**
- (Menon, et al, 2010)



OPEN ACCESS

Concussion is confusing us all

David J Sharp, Peter O Jenkins

Computational, Cognitive, and Clinical Neuroimaging Laboratory, Division of Brain Sciences, Faculty of Medicine, Imperial College London, Hammersmith Hospital Campus, London, UK

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ABSTRACT

It is time to stop using the term concussion as it has no clear definition and no pathological meaning. This confusion is increasingly problematic as the management of 'concussed' individuals is a pressing concern. Historically, it has been used to describe patients briefly disabled following a head injury, with the assumption that this was due to a transient disorder of brain function without long-term sequelae. However, the symptoms of concussion are highly variable in duration, and can persist for many years with no reliable early predictors of outcome. Vague terminology for post-traumatic problems leads to misconceptions and biases in the diagnostic process, producing uninterpretable science, poor clinical guidelines and confused policy. We propose that the term concussion should be avoided. Instead neurologists and other healthcare professionals should classify the severity of traumatic brain injury and then attempt to precisely diagnose the underlying cause of post-traumatic symptoms.

INTRODUCTION

As neurologists, we often see patients who have persistent neurological problems after head injuries. Many of us are happy to reassure them that they have had a concussion and are suffering from transient 'postconcussion syndrome'. These labels provide reassurance, both to the neurologist and patient, that the injury is benign and reinforce the view that nothing can be done to help. But what does concussion mean, and is such therapeutic nihilism justified? Although a 'light touch' to mild traumatic brain injury (TBI) is often appropriate, many patients go on to have persistent problems that would benefit from more precise neurological assessment.

TBI is a common problem. There are estimated to be at least 1 million emergency department attendances each year in the UK due to head injuries, 90% of which have been considered to be mild.¹ Mild TBI is often considered relatively harmless. The assumption is that any neurological dysfunction is short-lived,

usually in the region of minutes. However, long-term effects can be surprisingly common. The resolution of obvious confusion is often followed by a constellation of symptoms that include headache, dizziness, fatigue, irritability, reduced concentration, sleep disturbance, memory impairment, anxiety, sensitivity to noise and light, blurred vision and depression. Most patients suffering a mild TBI recover in the first 3 months,²⁻⁴ but a significant minority (up to a third) report symptoms persisting beyond 6 months.⁵⁻⁷ The presence of a more severe initial injury, pre-existing psychological problems, older age, female sex and previous head injuries all increase the likelihood of persistent symptoms.⁸ In addition, involvement in a compensation claim can also be a significant factor in perpetuating symptoms.^{9,10}

TBI can also lead to long-term effects including epilepsy and neurodegeneration. There is an increased risk of Alzheimer's disease, Parkinson's disease and chronic traumatic encephalopathy.¹¹⁻¹³ Since the early 20th century, repetitive brain trauma sustained from boxing was recognised to produce a progressive neurological deterioration. Originally termed 'dementia pugilistica', there has recently been renewed interest in what is now termed chronic traumatic encephalopathy, a condition defined by neuropathological findings including the presence of neurofibrillary tangles in the depths of sulci.¹⁴ Epidemiological studies also show increased mortality rates even after mild TBI. One large cohort study tracked patients with TBI of all severities attending emergency departments in Glasgow, UK, in 1995 and 1996.^{15,16} Thirteen years after injury the mortality rate of the group had reached over 40%, with increased mortality even in young patients after mild TBI (~15 vs 2 per 1000 per year in community controls).¹⁵ This did not simply reflect non-specific lifestyle factors associated with those exposing themselves to likely injury, as



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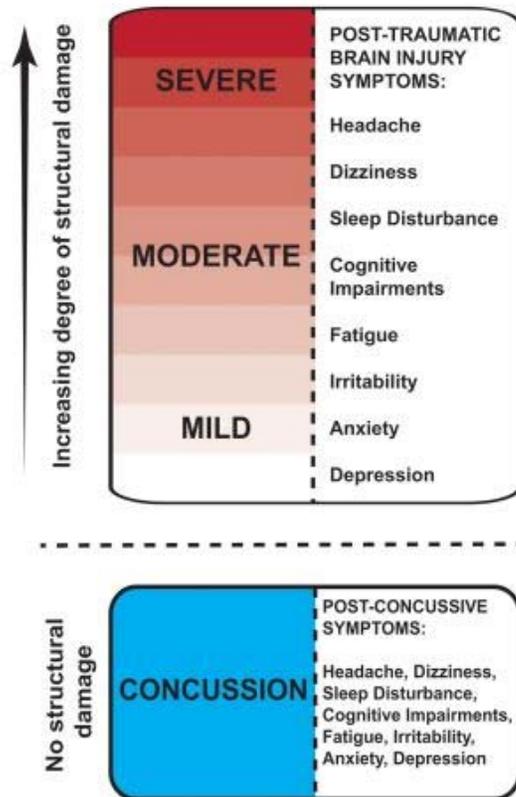
“Concussion” is confusing us all

- The 2013 Zurich Consensus Statement on Concussion in Sport
- “Concussion and mild TBI should be viewed as distinct entities. The group defined concussion as a “complex pathophysiological process affecting the brain”, and allowed for the presence of neuropathological damage. “

Concussion definitions (cont.)

- American Academy of Neurology guidelines for sports concussion (2013)
- They do not separate concussion from mild TBI
- Concussion is defined as “a clinical syndrome of biomechanically induced alteration of brain function, typically affecting memory and orientation, which may involve loss of consciousness”.

A Concussion as a separate entity to Traumatic Brain Injury Classification



B Combined Traumatic Brain Injury Classification using the Mayo criteria and separating post-injury symptoms

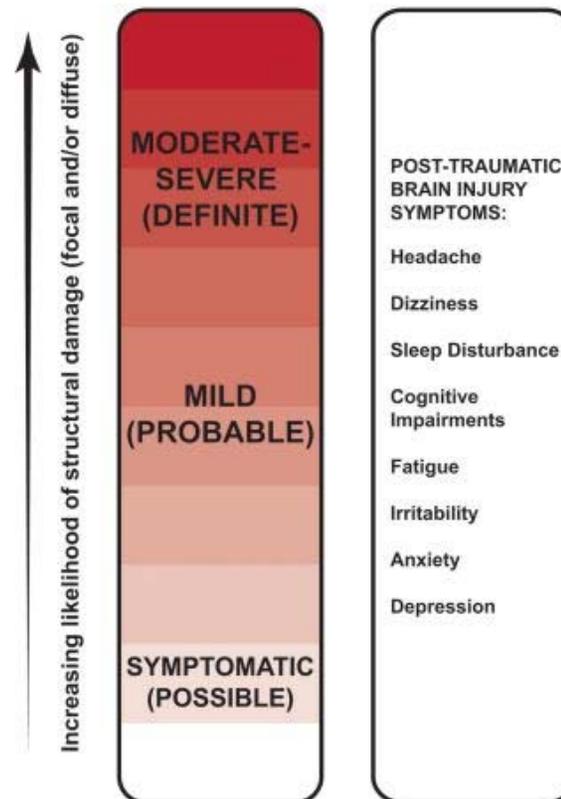


Figure 2 Two potential classification systems for traumatic brain injury and concussion.

Concussion definitions (cont.)

- Concussion is used to describe both a pathophysiological condition and a constellation of symptoms arising from mTBI. (Croft A, 2015.)

Mayo Clinic Version

- **A. Classify as Moderate–Severe (Definite) TBI** if one or more of the following criteria apply:

1. Death due to this TBI

2. Loss of consciousness of 30 min or more

3. Post-traumatic anterograde amnesia of 24 h or more

4. Worst Glasgow Coma Scale full score in first 24 h < 13 (unless invalidated upon review eg, attributable to intoxication, sedation, systemic shock)

5. One or more of the following present: ▶ Intracerebral haematoma ▶ Subdural haematoma ▶ Epidural haematoma ▶ Cerebral contusion ▶ Haemorrhagic contusion ▶ Penetrating TBI (dura penetrated) ▶ Subarachnoid haemorrhage ▶ Brainstem injury

Mayo Clinic Version

- B. If none of Criteria A apply, classify as **Mild (Probable) TBI** if **one or more** of the following criteria apply:
 1. Loss of consciousness momentarily to less than 30 min
 2. Post-traumatic anterograde amnesia momentarily to less than 24 h
 3. Depressed, basilar or linear skull fracture (dura intact)

Mayo Clinic Version

- C. If none of Criteria A or B apply, classify as **Symptomatic (Possible) TBI** if one or more of the following symptoms are present:
 - ▶ Blurred vision
 - ▶ Confusion (mental state changes)
 - ▶ Daze
 - ▶ Dizziness
 - ▶ Focal neurological symptoms
 - ▶ Headache
 - ▶ Nausea

Definition: Acquired Brain Injury (ABI)

- In 1997, the Brain Injury Association of America adopted a definition of ABI beyond that only produced by trauma:
 - “An acquired brain injury is an injury to the brain that has occurred after birth and is not hereditary, congenital or degenerative. The injury commonly results in a **change in neuronal activity**, which affects the physical integrity, the metabolic activity, or the **functional ability of the cell**. The term does not refer to brain injuries induced by birth trauma.”

Definition: Acquired Brain Injury (cont.)

- Includes not only injuries caused by the trauma of external physical force applied to the head and/or neck (TBI), but also internal insults to the brain.
- Causes include:
 - Tumors - blood clots - strokes - seizures
 - Toxic exposure (e.g., substance abuse, ingestion of lead, inhalation of volatile agents)
 - Infections (encephalitis, meningitis)
 - Metabolic disorders (insulin shock, diabetic coma, liver and kidney disease), - neurotoxic poisoning
 - Lack of oxygen to the brain (airway obstruction, strangulation, cardiopulmonary arrest, **carbon monoxide poisoning**, drowning).

Sex Differences in Concussion Symptoms of High School Athletes

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Context: More than 1.6 million sport-related concussions occur every year in the United States, affecting greater than 5% of all high school athletes who participate in contact sports. As more females participate in sports, understanding possible differences in concussion symptoms between sexes becomes more important.

Objective: To compare symptoms, symptom resolution time, and time to return to sport between males and females with sport-related concussions.

Design: Descriptive epidemiology study.

Setting: Data were collected from 100 high schools via High School RIO (Reporting Information Online).

Patients or Other Participants: Athletes from participating schools who sustained concussions while involved in interscholastic sports practice or competition in 9 sports (boys' football, soccer, basketball, wrestling, and baseball and girls' soccer, volleyball, basketball, and softball) during the 2005–2006 and 2006–2007 school years. A total of 812 sport concussions were reported (610 males, 202 females).

Main Outcome Measure(s): Reported symptoms, symptom resolution time, and return-to-play time.

Results: No difference was found between the number of symptoms reported ($P = .30$). However, a difference was seen in the types of symptoms reported. In year 1, males reported amnesia (exact $P = .03$) and confusion/disorientation (exact $P = .04$) more frequently than did females. In year 2, males reported more amnesia (exact $P = .002$) and confusion/disorientation (exact $P = .002$) than did females, whereas females reported more drowsiness (exact $P = .02$) and sensitivity to noise (exact $P = .002$) than did males. No differences were observed for symptom resolution time ($P = .40$) or return-to-play time ($P = .43$) between sexes.

Conclusions: The types of symptoms reported differed between sexes after sport-related concussion, but symptom resolution time and return-to-play timelines were similar.

Key Words: epidemiology, mild traumatic brain injuries, symptom resolution, return to play

Key Points

- After a sport-related concussion, male and female high school athletes presented with different types of symptoms.
- Males reported more cognitive symptoms, whereas females reported more neurobehavioral and somatic symptoms.
- Symptom resolution time and time to return to play did not differ between sexes.

There are an estimated 7.3 million high school students participating in organized interscholastic athletics in the United States each year.¹ An estimated 1.6 to 3.8 million sport-related concussions are sustained every year,² with an average of 21% occurring in high school athletes.^{3,4} More than 5% of all high school athletes who participate in contact sports such as football, lacrosse, and hockey sustain a concussion each year.^{5–8} Although males continue to participate in sports at a higher rate than females, in 2008, 3.01 million (or 41%)¹ of high school athletes were female, up from 2.4 million 10 years earlier.⁹ Injury incidence among females has increased with increased female sport participation, and now females have a higher incidence rate of sport-related concussions than do males.^{3,10,11} However, the female response to concussion has not been well described, and similarities in male and female sport-related concussion symptoms remain largely anecdotal.

Diagnosing sport-related concussions is one of the most elusive tasks of sports medicine clinicians. No biological markers exist to detect this relatively mild injury, and

diagnosis largely depends on a patient's report.¹² Assessment is further complicated by the tendency of many athletes to underreport or hide symptoms from clinicians, coaches, and parents.¹³

Research^{14–16} on more severe closed head injuries and traumatic brain injuries (TBIs) indicates that females may respond to concussions differently than males. Authors¹⁴ of a meta-analysis of postconcussion outcome sex differences identified 8 studies that provided data by sex, citing worse overall outcomes in females. Twenty outcomes were compared, including variables such as postconcussive symptoms at 6 weeks, days of posttraumatic amnesia, length of hospitalization, inability to return to work, and presence of headache, dizziness, and insomnia. Retrospective studies^{16,17} comparing males and females with TBI showed that females tended to fare worse than their male counterparts, with longer hospitalizations, longer residual disabilities, and higher mortality rates. In one pharmacologic trial,¹⁵ female patients younger than 51 years had greater frequency of brain swelling and intracranial

Epidemiology & Facts

- estimated 7.3 million high school students participating in organized interscholastic athletics in the US each year
- estimated 1.6 to 3.8 million sport-related concussions are sustained every year, with an average of 21% occurring in high school athletes (the ones who show up in the ER.)
- males and females recover differently and tend to have different symptoms (Frommer 2011.)

Epidemiology & Facts (cont.)

- mTBI symptoms typically include difficulties in speed of processing, attention & memory.
- Most patients show recovery within 6 months.
- Most with mTBI return to work within first 30 days.
- A small portion of complicated mTBI patients can have persistent symptoms 12 months or longer.
- mTBI is associated with the onset of psychiatric disorders including depression and PTSD.
- What if you or your family or your are not one of the “most” that recovers.

Risk factors for complications...

- Increased age at injury
- Premorbid psychiatric illness
- Development of psychiatric illness after injury (depression, PTSD)
- Compensation/litigation
- Repetitive injuries
- Selected genetic factors (e.g., APOE4)
- Acute abnormal imaging
- Expectation of poor outcome
- Extracranial injuries

(McAllister, 2011)

TBI in kids

- **TBI is the leading cause of disability and death in children and adolescents in the U.S.**
- Greatest risk for TBI are age 0-4 and 15-19.

Among those ages 0 to 19, each year an average of:

- 62,000 children sustain brain injuries requiring hospitalization as a result of motor vehicle crashes, falls, sports injuries, physical abuse and other causes
- 564,000 children are seen in hospital emergency departments for TBI and released.
- Among children ages 0 to 14 years, TBI results in an estimated in:
 - 2,685 deaths
 - 37,000 hospitalizations
 - 435,000 emergency department visits

TBI & Bankruptcy

- Risk of bankruptcy before and after brain or spinal cord injury (Hollingworth, et.al. August, 2007)
- Compared with pre-injury, there is a **33% increase in bankruptcy post-injury.**
- Patients with commercial insurance 2x more likely to file for bankruptcy (pre-injury mortgages, loans, debt) within 3 yrs.



Uncounted: TBI in Prisoners

- Studies indicate TBI occurs among an estimated 25 – 87% of the jail and prison population (Wald, Helgeson, Langlois, Brain Injury Professional, 2008)
- In contrast, to an estimated 8.5% of non-incarcerated adults (Silver, et al. 2001)

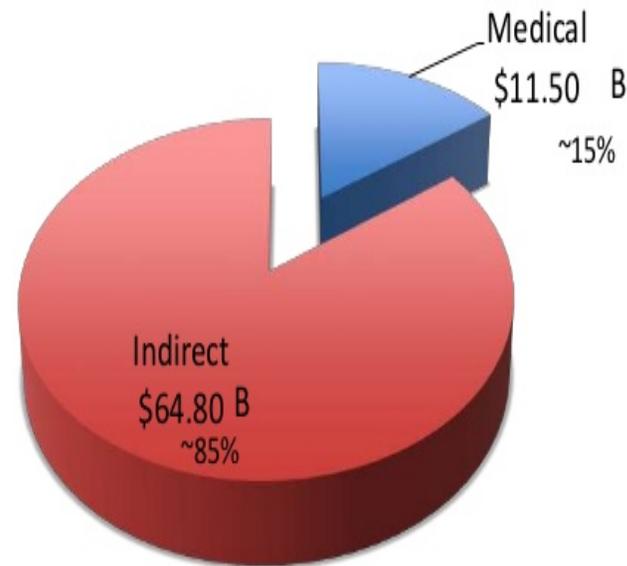


TBI National Costs: Civilians

- Indirect costs (e.g., lost wages, lost productivity, and nonmedical expenditures)
- Does not include TBIs managed in nonhospital settings nor military personnel.

(Coronado 2012)

Estimated Economic Costs of TBI \$76.3 Billion in 2010



Finkelstein, E et al. The Incidence and Economic Burden of Injuries in the United States. New York (NY): Oxford University Press, 2006 Coronado, VG et al. The epidemiology and prevention of TBI, in press, 2012

Hidden Costs of TBI

- 62.1% of all bankruptcies in 2007 were medical (Himmelstein, Thorne, Warren & Woolhandler, 2009.)
- 92% of this due to medical debts, the remainder due to loss of home, job, etc.
- Most medical debtors were well educated, owned homes and had middle-class occupations.
- $\frac{3}{4}$ had health insurance
- Medical Bankruptcies rose by 49.6% from 2001-2007
- 44% of the \$56 billion annual cost for TBI in the U.S. is for MTBI. It truly is, as the CDC characterized it, a "silent epidemic." (Belanger 2007)
- The chronicity rate for MTBI ranged from 7-33%.

Thank you for your time !

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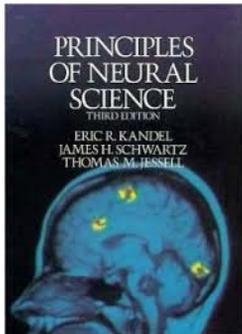
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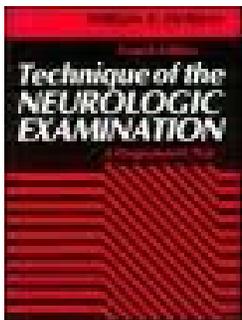
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- So much to learn, so little time!
- Learning neurology is a never-ending journey. Decide to take steps toward mastery, one at a time.

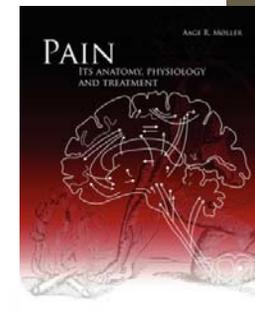
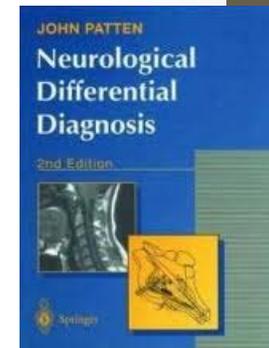
Recommended Readings



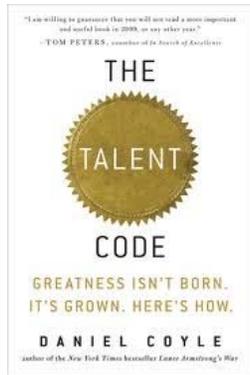
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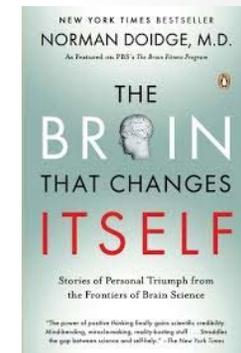
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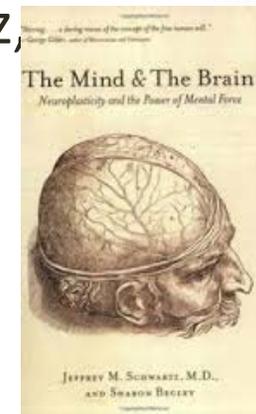
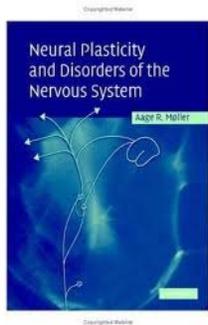
Recommended Readings (cont'd)



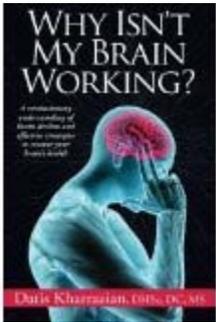
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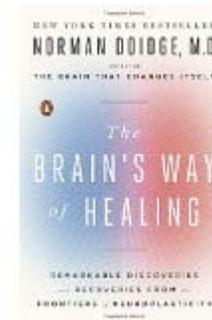


Recommended Readings (cont'd)

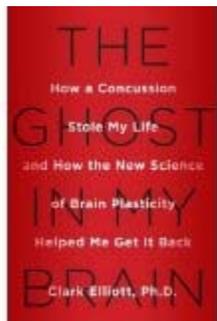


- **Why Isn't My Brain Working.** Datis Kharrazian

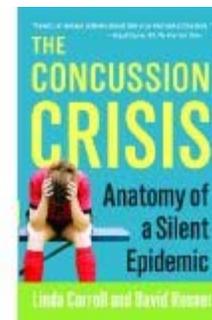
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