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Pathophysiology of Concussion

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Disclosure

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- No Financial or other disclosures

Sports Concussion

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Post Concussive Symptoms

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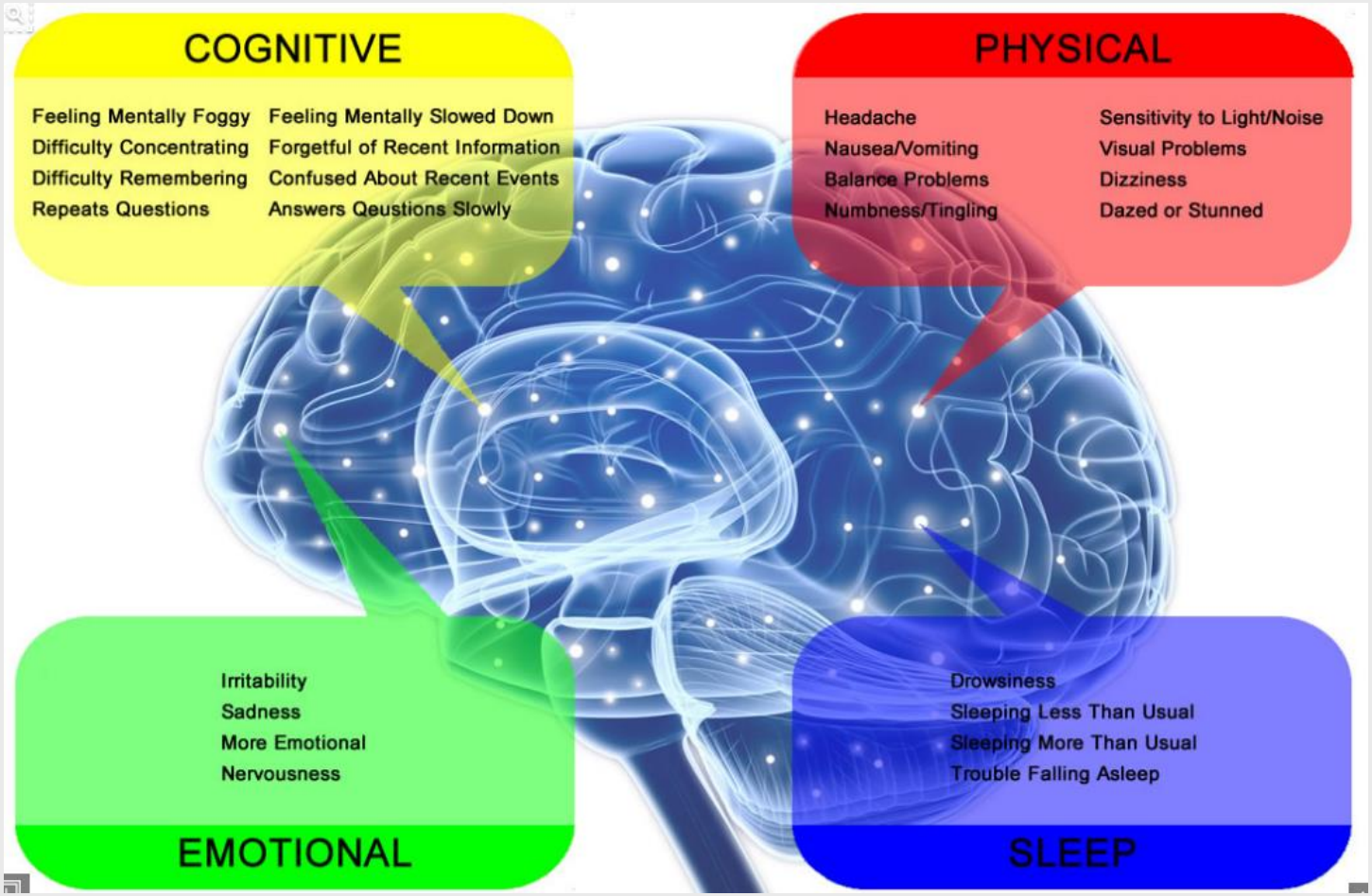

Post Concussion Symptoms: Cognitive

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- Memory Difficulties (inefficiency)
- Attentional/Multi-tasking Difficulties
- Slowed Information Processing
- Word Finding Difficulties
- Confused
- Mental “Fogginess”
- Cognitive Fatigue
- Decision Making Difficulties (due to decreased attention and processing speed)
- Other Cognitive Difficulties (No Profound/Non-Credible Deficits)

- Cicerone & Kalmar, 1995

Post Concussion Symptoms: Physical

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- Smell/Taste Changes
- Noise Sensitivity
- Light Sensitivity
- Ocular-Motor/ Vestibular
- Visual Disturbance
- Poor Coordination
- Fatigue/loss of energy
- Headaches (post traumatic Migraine)
- Dizziness
- Poor Balance
- Vertigo
- Nausea
- Appetite Problems
- Sleep Disturbance

- Cicerone & Kalmar, 1995

Post Concussion Symptoms: Emotional

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- Depression
- Anxiety
- Irritability/Anger
- Poor Frustration Tolerance
- Affective Lability/More Emotional
- Decreased Libido
- Changes in Self-Image/Identity
- Feeling Overwhelmed

- Cicerone & Kalmar, 1995

Post Concussion Symptoms: Behavioral

- Impatience
- Impulsivity
- Anger outbursts
- Demanding behavior

Neurometabolic Cascade (Giza & Hovda, 2014; Levine, 2017)

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- **Initial phase**
- **Indiscriminant release of neurotransmitters and unchecked ionic fluxes**
  - Outpouring (efflux) of K+ (potassium) and influx of Ca2 (calcium)
  - Initial depolarization release of Glutamate (excitatory) which increases K+ efflux
- **Na+-K+ pump tries to restore equilibrium**
  - Increasing demand for adenosine triphosphate (ATP; carries energy) triggers jump in glucose metabolism (hypermetabolic state).
- **Increased demand for energy with decreased CBF + decreased intracellular energy supply leads to a cellular Energy Crisis**

Neurometabolic Cascade (Levine, 2017)

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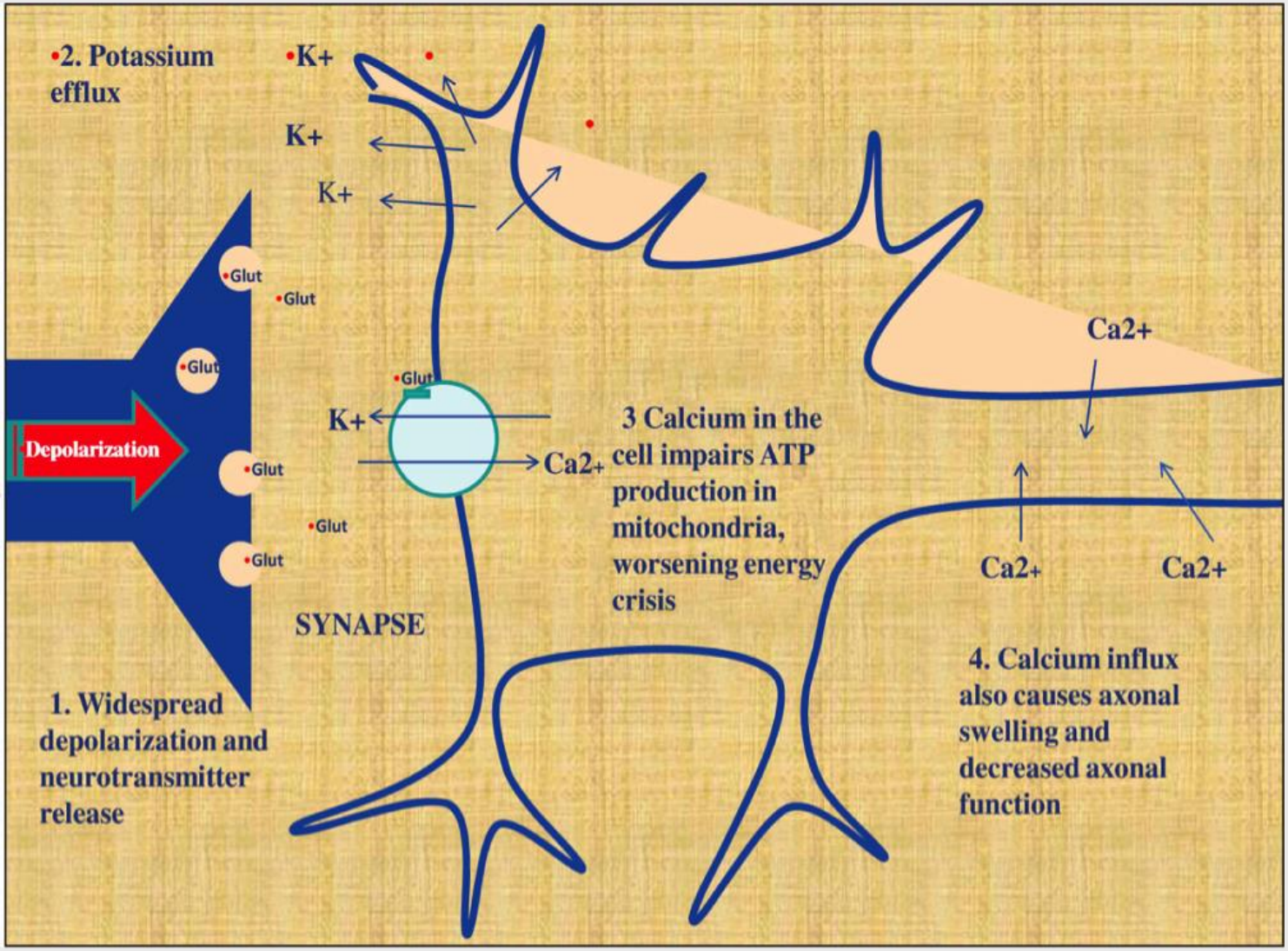

Neurometabolic Cascade (Giza & Hovda, 2014; Levine, 2017)

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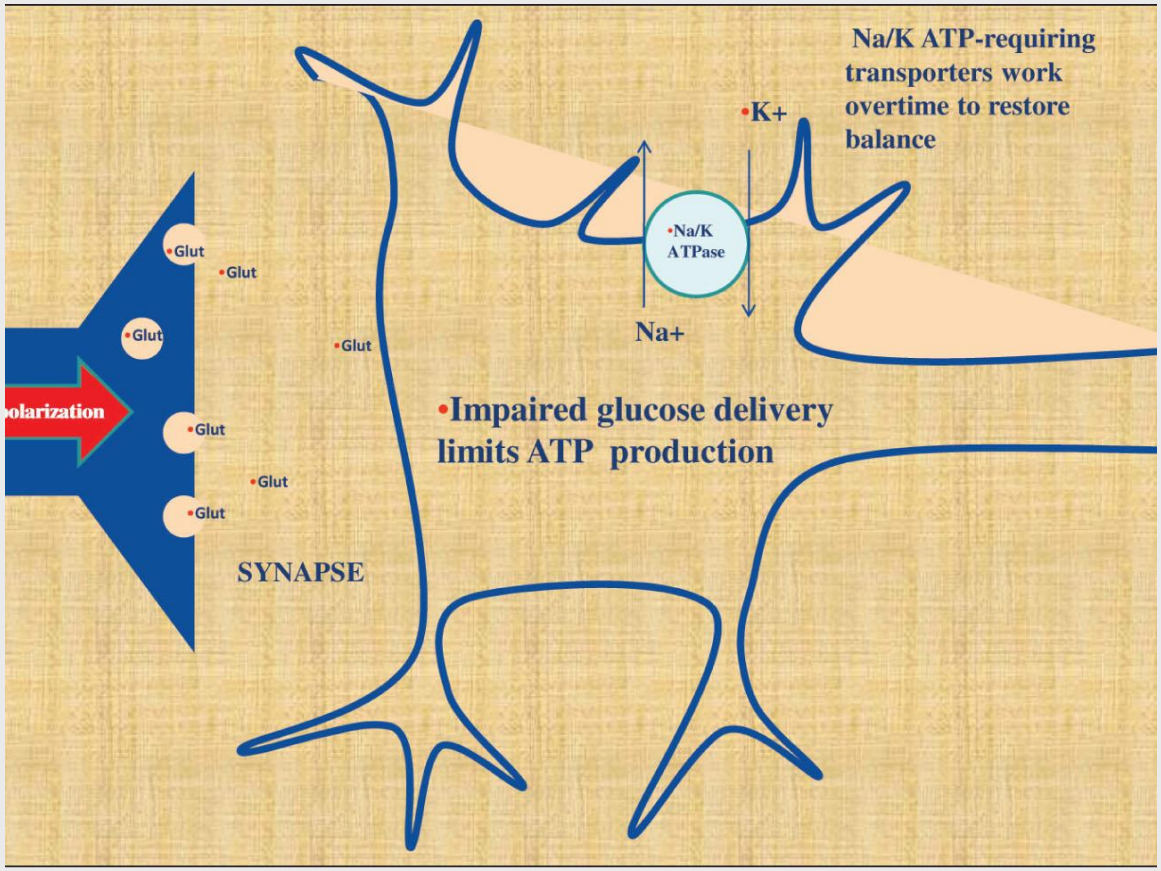
- **Period of depressed metabolism:**
- **Next phase**
  - Persistent increases in Ca2 impairs mitochondrial metabolism (which produces ATP) which worsens the energy crisis (can also cause permeability of the Blood Brain Barrier and cerebral edema (swelling of the brain)
  - Unchecked Ca2 accumulates in activated pathways and can cause cell death
  - Intra-axonal Ca2 flux causes impaired neuronal connectivity
- **Other processes**
  - Generation of lactic acid→vulnerability to secondary ischemic injury
  - Decreased intracellular magnesium→ lasts days and correlates with neurologic deficits-Magnesium essential for ATP, protein synthesis, and maintenance of cellular membrane potential
  - Inflammatory response
  - Altered neurotransmission

Neurometabolic Cascade (Levine, 2017)



Decreased bioavailability of fuel sources that generate ATP: Glucose / Amino acids

Neurocellular Changes

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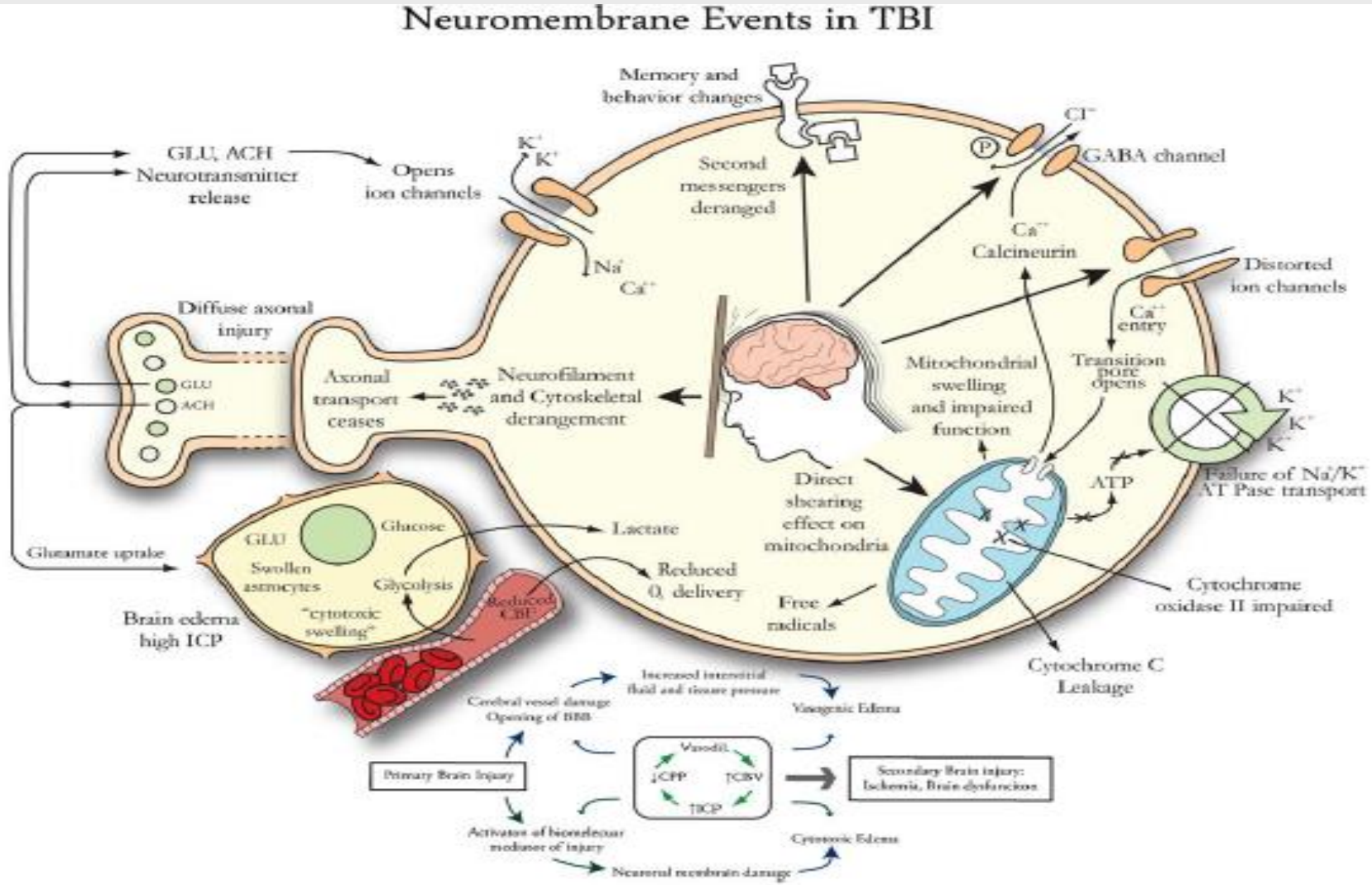

Fig. 7 Cartoon demonstration showing the complex cellular and vascular physiological and pathological interactions that occur following TBI and the central role of mitochondrial failure that relates to all neuromembrane events that occur in TBI. Note the schematic of the head striking a fixed object in the center of the illustration, which would produce similar motion and strain as depicted in the head/brain impact shown in Fig. 6. Adapted from Mazzeo et al. (2009) and Elsevier, with permission

Neurometabolic Cascade Timeline

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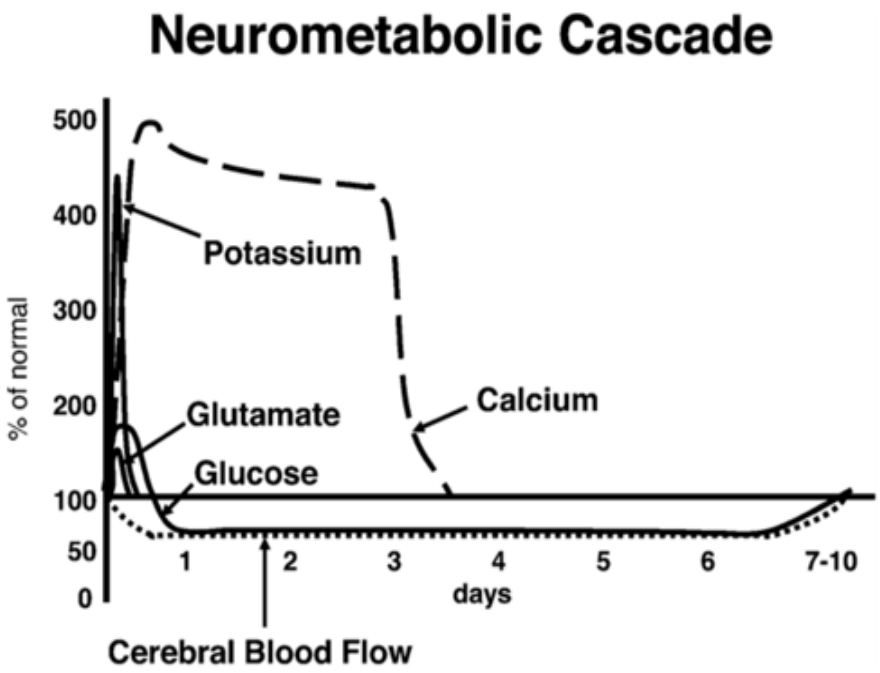

Time course of the neurometabolic cascade of concussion.

From: **The New Neurometabolic Cascade of Concussion**

Giza CC, Hovda DA. Neurosurgery. 2014;75(suppl_4):S24-S33. doi:10.1227/NEU.0000000000000505

Neurometabolic Cascade

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- Shortly after a concussion, the cerebral blood flow and the delivery of those fuel sources is also decreased and is prolonged
- Metabolic mismatch: High metabolic demand vs. decreased availability
- Energy crisis may increase vulnerability to greater severity following a repeat concussion during the recovery period (Giza & Hovda, 2014)
- Structural changes in integrity of axons, axonal transport, and other cell microstructures

Proposed Relationship Between Neurophysiology and Symptoms (Giza & Hovda, 2014)

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Neurophysiology

- Ionic Flux
- Energy Crisis
- Axonal Structural Changes
- Changes in Neurotransmission

Symptoms

- Migraine, light sensitivity, noise sensitivity
- Vulnerability to 2nd impact
- Impaired processing speed, reaction time, and cognition

Other areas of disturbance

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- Vestibular system: inner ear and connections to cerebellum, brain stem, cortex, and ocular system
  - Vestibulo-ocular: dizziness; visual stability
  - Vestibulo-spinal: poor balance
- Ocular motor: Present as dizziness, blurred vision, headache, and visual instability
- Vestibular and ocular motor disruption may delay recovery

Other Blood Tests: No/Very Poor Evidence to Support Use (CDC, 2016)

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- S100B: Not useful in determining mTBI vs No mTBI
- Serum Tau: Not useful in determining mTBI vs No mTBI
- Serum Potassium (K), Sodium (Na), Glucose (Glu), WBC: Not useful in determining mTBI vs No mTBI
- Autoantibodies against Glutamate (Glut) receptors and Nitritic Oxide metabolites: Low evidence – *Possible* useful in determining mTBI vs No mTBI (study had no controls)

Brain CT or No Brain CT (CDC, 2016)

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- Not routinely recommended BUT Risk Factors:
  - Age <2
  - Vomiting
  - Loss of Consciousness
  - Severe Injury Suspected
  - Severe or Worsening Headache
  - Amnesia
  - Non-frontal scalp hematoma
  - GCS <15
  - Suspected Skull Fracture
  - Other Complicating Factors

Second Impact Syndrome (Bey & Ostick, 2009)

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- Controversial; Rare
- Initial concussion neurometabolic changes set stage for vulnerability
- A second concussion in close proximity to initial injury brain is unable to regulate intracranial pressure can lead to diffuse edema, herniation, rapid decline and death
- Management: If suspect more serious injury do CT or MRI; Immediate stabilization (airway/intubation, neurosurg consult)
- Prevention: Do not return to play if symptoms persist.

Chronic Traumatic Encephalopathy

(Perrine, Helcer, Tsiouris, Pisapia, Stieg, 2017)

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- A neurodegenerative condition that results from repetitive head trauma
- Characterized by p-tau deposition noted post-mortem
- Many problems with studies to date due to bias sampling, lack of controls, pathology has been found in non-symptomatic cases, and overlap pathology with other conditions
- Clinical descriptions are significantly varied, overlap significantly with many other conditions and there are no specific Dx criteria
- CONCLUSION: We don’t know but multiple blows to the head are a problem

Resources

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Knee Surg Sports Traumatol Arthrosc
DOI 10.1007/s00167-013-2791-6

SPORTS MEDICINE

A comprehensive, targeted approach to the clinical care of athletes following sport-related concussion

Michael W. Collins · Anthony P. Kontos ·
Erin Reynolds · Christopher D. Murawski ·
Freddie H. Fu

Perrine K, Helcer J, Tsiouris AJ, Pisapia DJ, Stieg P, The Current Status of Research on Chronic Traumatic Encephalopathy, *World Neurosurgery* (2017), doi: 10.1016/j.wneu.2017.02.084.

The New Neurometabolic Cascade of Concussion

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Since the original descriptions of postconcussive pathophysiology, there has been a significant increase in interest and ongoing research to study the biological underpinnings of concussion. The initial ionic flux and glutamate release result in significant energy demands and a period of metabolic crisis for the injured brain. These physiological perturbations can now be linked to clinical characteristics of concussion, including migrainous symptoms, vulnerability to repeat injury, and cognitive impairment. Furthermore, advanced neuroimaging now allows a research window to monitor postconcussion pathophysiology in humans noninvasively. There is also increasing concern about the risk for chronic or even progressive neurobehavioral impairment after concussion/mild traumatic brain injury. Critical studies are underway to better link the acute pathobiology of concussion with potential mechanisms of chronic cell death, dysfunction, and neurodegeneration. This "new and improved" article summarizes in a translational fashion and updates what is known about the acute neurometabolic changes after concussive brain injury. Furthermore, new connections are proposed between this neurobiology and early clinical symptoms as well as to cellular processes that may underlie long-term impairment.

KEY WORDS: Metabolism, Mild traumatic brain injury, Neurodegeneration, Pediatric, Physiology

Neurosurgery 75:S24–S33, 2014 DOI: 10.1227/NEU.0000000000000505 www.neurosurgery-online.com

10.88 in

Resources: CDC

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Report From the Pediatric Mild Traumatic Brain Injury Guideline Workgroup:

Systematic Review and Clinical Recommendations for Healthcare Providers on the Diagnosis and Management of Mild Traumatic Brain Injury Among Children

https://www.cdc.gov/injury/pdfs/bsc/systematicreviewcompilation_august_2016.pdf

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QUESTIONS