TRAUMATIC BRAIN INJURY: FROM PHYSIOLOGY TO TREATMENT

Presented by: Dr. J. Brandon Brock, DC, MSN, RN, NP-C, DAAIM, DACNB, BCIM, FICC

https://www.facebook.com/drbrandonbrock/
Dr. Brandon Brock is a Certified Family Nurse Practitioner and a Board Certified Chiropractor and Chiropractic Neurologist. In Dallas, Texas, he serves as a staff clinician at Cerebrum Health Centers, Foundation Physician’s Group, and Innovative Health and Wellness Group. Dr. Brock is also the co-owner, creator and educator at Functional Neurology Seminars and he is the sole owner and operator of Dr. Brock Lectures along with his wife Tara. Dr. Brock has a passion for lecturing and helping others develop didactic and academic skills in a way that is easy to digest when learning. He has developed thousands of hours of curriculum pertaining to the academic categories of neurology, nutrition, physical diagnosis, pharmacology, immunology, endocrinology and students of all types and disciplines have utilized his lecture material. He currently enjoys teaching for Apex Energetics as well as providing education and support to facilitate learning for multiple groups and agencies. This includes state association meetings to governmental panels.

Dr. Brock has received the most outstanding functional neurology teacher of the year from the ACA council of Neurology for five years straight and two times from IAFNR (International Association of Functional Neurology and Rehabilitation). He recently received the humanitarian award from IAFNR as a result of his research on Injured Military Veterans with PTSD and traumatic brain injury. Dr. Brock was also the recent honorable recipient of the prestigious Living Legacy Award from Samford Universities Ida Moffett School Nursing.

Currently Dr. Brock is working on a Doctorate of Nursing Practice from Duke University along with being a global clinical research scholar from Harvard Medical School. He is planning upon completion of the doctoral program at Duke, starting a conjointed PhD program with a major in nursing and a minor in behavioral neuroscience. Dr. Brock’s unique blend of clinical and teaching experience along with a background in medicine, chiropractic, neurology and nutrition has created a very unique clinical background that has helped him treat difficult cases from many different academic, clinical and professional perspectives. He truly loves integrative care.
The Problem!!!
What are We Dealing With?

• What happens with TBI?
  – In the last ten years the average annular number of traumatic brain injuries in the United States has been 1.7 million incidents, 52,000 deaths, 275,000 hospitalizations, 1,365,000 emergency room visits, and 30.5% of all injury related deaths
  
  • (Injury Prevention & Control: Traumatic Brain Injury & Concussion, Centers for Disease Control and Prevention).
What are We Dealing With?

• **What happens with TBI?**
  
  – The current cost of TBI annually is $76.5 billion with an average lifetime annual cost of $85,000. Both suicide and depression have an increased prevalence after TBI and an estimated 25% of those impacted had an increase of both

  • *(Research America, An Alliance for Discoveries in Health).*
Changes in the cell
We have to Change Cellular Function

• **What happens with TBI?**
  – Organelles
  – Mitochondria
  – Membranes
  – Cytokines and glial cells
  – Receptors
  – Barriers
  – Synaptic Function
  – Plasticity
Cutting your nerve changes your brain

Keri S. Taylor,1,2 Dimitri J. Anastakis2,3,4 and Karen D. Davis1,2,3

Figure 5  Summary of findings and possible causes. Nerve conduction measures remain abnormal 1.5 years following peripheral nerve transection and microsurgical repair, indicative of cell death and/or incomplete re-myelination. Incomplete peripheral nerve regeneration may cause: (i) long-term sensory abnormalities; (ii) grey matter and white matter atrophy in key somatosensory regions; (iii) functional changes in key somatosensory regions. In addition, structural and functional changes may impact sensory recovery. Finally, functional and structural changes may influence each other.
Changes in the cell
The Fundamental’s Come Together

Functional Neurology, Rehabilitation, and Ergonomics

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Changes in the cell

- Cell Death
  - Direct damage
- Vascular sensitization
- Glial Priming
- Cellular excitotoxicity
- Intracellular damage
- Axonal Damage
- Brain swelling
- BBB Breakdown

Traumatic Brain Injury
Changes in the cell

Brain Damage Structure damage

- Changes in Neurofilament and microtubules
- Changes in synaptic capacity
- Changes in mitochondrial function
- Changes in secretory vesicles
- Changes in protein replication and epigenetic factors
- Changes in lysosomes
Figure 1 A simplified schematic illustration of the interaction between the trios of neurons, astrocytes, and microglia in the CNS under the normal (a) and pathological conditions (b). Healthy neurons are able to tightly regulate the activation of their neighboring glial cells. Meanwhile both astrocytes and microglia help maintain the neuronal activity. Under various diseased conditions, this homeostasis is broken so that neurons lose their controlling ability but instead deliver damage signals to glial cells, which in turn may exacerbate neuronal damage through inflammation. The cross-talk among astrocytes and microglia themselves and its aftermath on neurons is currently not very clear.
Factors that Matter

Life Timeline

Genetic Risk Factors
- Maternal care
- Exercise, Omega-3 Fatty Acids, Diet
- Antidepressants, exercise, diet, and cognitive therapy

Environmental Factors
- BDNF
- BDNF (and other factors)
- BDNF
- BDNF (and other factors)

Healthy

Depressed

Genetic Risk Factors
- e.g., BDNF Val66Met
- Early life stress
- Adult stress or trauma

BDNF

K.T. Ota, R.S. Duman / Neurobiology of Disease 57 (2013) 28–37
The Growing Cellular Story

Neuron Adaptation to Cellular Insult
- Production of neurotrophic factors and cytokines, expression of various cell survival-promoting proteins
- Antioxidant enzymes
- Protein chaperones
- Bcl-2 and inhibitor of apoptosis proteins

Glial cell activation
- Can adapt to cellular insult
  - Mobilization of neural stem cells to replace damaged neurons and glia.
  - Preservation of genomic integrity by telomerase and DNA repair proteins
- Cannot adapt to cellular insult

Neuron Degeneration
Factors that Matter
Mechanisms to consider

1. Excitotoxicity
2. Resting membrane potential / CIEG
3. Free radical / DNA damage
4. Mitochondrial / energy failure
5. Inflammation
6. Cellular wall / structure damage
7. Apoptosis
8. Damage to surrounding tissue
9. Secondary plastic changes
10. Efficiency of damage
11. Resultant seizure disorder
12. Future metabolic failure
13. Perpetuation of autonomic damage
14. Damage to adrenal regulation
15. Disruption of gut function
16. Perpetuation of inflammation
17. Perpetuation of energy failure
18. Loss in cortical volume / integrity
19. Cyclic relapse
Figure 4 | Scheme summarizing the pathophysiological events that lead from CNS injury to infection and worsening of patient outcome. CNS injury (1a) induces a disturbance of the normally well balanced interplay between the immune system and the CNS. By inducing the local release of immune modulators (2), such as interleukins, CNS injury activates the hypothalamo–pituitary–adrenal axis, and the sympathetic and parasympathetic nervous systems. Through the release of noradrenaline, glucocorticoids and acetylcholine, a systemic anti-inflammatory response is mounted that negatively affects the function and composition of the innate and adaptive immune systems. As a consequence of the resulting immunodepression (3) and breakdown of immunological barriers (4), infection develops (5). The risk of infection is further increased because these patients are hospitalized under intensive care conditions and the CNS lesion itself may lead to dysphagia, aspiration, bladder dysfunction and so on (1b). Systemic infection increases morbidity and mortality in patients with CNS injury, and leads to worsening of outcome (6). IFN, interferon; IL-4/10, interleukin-4/10; MHC II, major histocompatibility complex class II; NO, nitric oxide.
The Great Breach

Trauma → BRAIN

- BBB disruption
- Spleen
- Liver
- Thymus

Peripheral organs

Neuronal Death

- Reactive Astroglisis
- Microglial activation

Chemokines

Cytokines: TNF α, IL6, IL4, ROS

Anti-inflammatory cytokines

Immune cells

Hyperinflammation

Immune suppression

Post Traumatic Infection

Neuronal Recovery

Das et al. Journal of Neuroinflammation 2012, 9:236
http://www.jneuroinflammation.com/content/9/1/236
The Great Breach

- Small Intestine Bacteria Overgrowth
- Enteric Nervous System Degeneration
- Blood-Brain Barrier Breakdown
- Intestinal Permeability
- NEUROINFLAMMATION
- Loss of Immunological Tolerance
- Food Protein Reactivity
- Immune Cross-Reactivity
- Chemical Immune Reactivity
Factors that Matter

TABLE 37-1
Pathophysiological Consequences of Impaired Cerebral Perfusion

<table>
<thead>
<tr>
<th>Consequences</th>
<th>Timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depletion of oxygen</td>
<td>10 sec</td>
</tr>
<tr>
<td>Depletion of glucose</td>
<td>2–4 min</td>
</tr>
<tr>
<td>Conversion to anaerobic metabolism</td>
<td>2–4 min</td>
</tr>
<tr>
<td>Exhaustion of cellular ATP</td>
<td>4–5 min</td>
</tr>
<tr>
<td>Consequences</td>
<td></td>
</tr>
<tr>
<td>Efflux of potassium</td>
<td></td>
</tr>
<tr>
<td>Influx of sodium</td>
<td></td>
</tr>
<tr>
<td>Influx of calcium</td>
<td></td>
</tr>
</tbody>
</table>

FEATURE REVIEW

Brain-immune interactions and disease susceptibility

A Marques-Deak\(^1\), G Cizza\(^2\) and E Sternberg\(^3\)

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Issues of Treatment
What Do We Need to Change?

• Treatment Considerations
  – Acute phase
  – Cellular stability – Glial priming
  – Inflammation management
  – Barrier integrity
  – Gut function
  – Endocrine function
  – Glandular function
  – Reduce comorbidities
Changes in the cell

- Systemic Inflammation
  - Damage to BBB - Presentation of Brain Self-Antigenic Markers to Systemic Immune System
  - Hormonal issues
    - Progesterone in TBI Neuronal Thyroid Requirements
    - NFkB inhibition by estrogen Adrenal/Cortisol Inhibition of Inflammation
  - Multiple Connections

- Redox Chemistry Issues Leading to Neuronal Necrosis Instead of Apoptosis

- Promotion of Pro-Inflammatory Cytokines or other Signaling Molecule Changes / Increased ON Signals, Decreased OFF Signals

- Changes in Microglia / Neuron Relationship and/or Excitotoxic Status of Brain Environment Favoring Death of Neurons / Loss of Cortical Integrity

- IL-6 causes NTIS...
  - ↓ T4 & T3; ↑ rT3 ⇒ ↓ Metabolism including Neuronal Metabolism

- Death of Vestibular, Cerebellar, Mesencephalic, PM, Vagal and other neurons & Alteration of Total Brain Integrity

- IL-6 Elevation

- Increased Mesencephalic / Sympathetic Activation

- Death of Cortical Neurons & Alteration of Total Brain Integrity

- Has Neuroprotective Aspects

- Central Nervous System-Induced Immunodepression Syndrome (CIDS) & Shift Toward Th2 Dominance in Brain & Body

- Increased Perivascular Vascular Resistance - Affects Brain O2?

- Faster Use of Glucose

- Diminished Th1 Surveillance & Diminished Innate Immune Response

- Hepatic Biotransformation Issues
  - Altered biotransformation of endogenous compounds (cortisol, sex hormones, etc.)
  - Haptens
  - Chemicals

- Inflammatory Promotion of MDSC-Based Immune Suppression

- Fuel:
  - O2
  - Glucose

- Neuronal Fuel Exhaustion ⇒ Low FOF

- Insulin Resistance ⇒ Inflammation

- Glycation ⇒ Induction of Inflammatory and AI Potential

- Systemic Pathogens
  - Respiratory Infection
  - UTI
  - GI Dysbiosis
  - Viral Infections

- Neuropsychiatric Consequences

- Diminished Th1 Surveillance & Diminished Innate Immune Response