A Multimodal, Regenerative Approach to Traumatic Brain Injury

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Disclosure

The content of this presentation has been peer reviewed for fair balance and evidence based medicine.
Learning Objectives

Define

Define the clinical, biochemical and metabolic effects from TBI

Identify

Identify mainstream and alternative treatments for TBI

Understand

Understand the regenerative model of TBI treatment
Clinical Symptoms from TBI

**Physical**
- Headache
- Fatigue
- Sleep disorders
- Vertigo or dizziness
- Tinnitus or hyperacusis
- Photosensitivity
- Anomia
- Reduced tolerance to psychotropic medications
- Disorientation
- Loss of mobility
- Seizures
- Loss of smell

**Cognitive**
- Memory decline / loss
- Slow reaction time
- Inability to pay attention
- Executive dysfunction
- Slow learning
- Interrupted speech
- Difficulty understanding
- Unable to concentrate
- Confusion
- Difficulty communicating thoughts
- Unable to plan, reason, problem-solve

**Psychological**
- Irritability
- Easy frustration
- Tension
- Anxiety
- Affective lability
- Personality changes
- Disinhibition
- Apathy
- Suspiciousness
- Suicidality
- Depression
- PTSD
Biochemical and Physiological Responses from TBI

- Disproportional proinflammatory cytokine production and release
- Increased counterregulatory hormones work against the action of insulin
Biochemical and Physiological Responses from TBI

- Hypermetabolic and catabolic states
- Severely impaired nitrogen homeostasis
- Oxidative Stress
Oxidative Stress From TBI

- Impairs cerebral vascular function
- Impairs circulation
- Impairs the energy metabolism
- Damages mitochondria and DNA
"The brain is in a **metabolic crisis** with concussion... potassium ion from inside the cell going extracellularly, calcium ions going intracellularly, neurotransmitters widely released in a **chaotic manner**.

It takes **energy** to pump that potassium back, put the neurotransmitters back on so the cell can function."

Dr Robert Cantu, MD, 2013
What Happens Metabolically with a TBI?

An Energy Crisis
Mainstream Treatments

- Occupational and physical rehabilitation
- Speech therapy
- Pharmaceutical drugs
- Cognitive maintenance exercises
- Patients simply cope with their condition
Alternative Treatments

- Do not seek to regenerate but rather simply treat symptoms
- Do not combine regenerative treatments in a multimodal manner in order to maximize patient benefit
Question 1

Which of the following are symptoms of a traumatic brain injury?

A. Headache
B. Insomnia
C. Mood changes
D. Cognitive and memory impairment
E. Sound and light sensitivity
F. All of the above
What is the most significant pathophysiologic reason why many TBI patients fail to recover?

A. Inflammation
B. Oxidative stress
C. Impaired nitrogen homeostasis
D. Impaired energy metabolism (“The brain is in a metabolic crisis.”)
It is hypothesized that the practical, effective combination of multiple regenerative TBI therapies can produce synergistic benefits to the patient that exceed the use of one particular TBI treatment.
A Multimodal, Regenerative Approach to TBI

I. Hyperbaric Oxygen Therapy

II. Intranasal Therapies

III. IV Nutrition

IV. Cranial Osteopathy

V. Ketogenic Diet and MCT Oil
Hyperbaric Oxygen Therapy (HBOT) for TBI

Part I
Hyperbaric Oxygen Therapy (HBOT)

- Allows the body to absorb about 10-15 times its normal supply of oxygen
- Stimulates the growth of tissue, bone and blood vessels, and reduces inflammation

Thom, et al., 2006
Volume rendered Brain SPECT perfusion maps of a 51-year-old woman suffering from mTBI that had occurred 2 years prior to inclusion in the study.
HBOT for TBI

• Induces neuroplasticity
• Increases tissue oxygenation
• Generates new capillary networks
• Restores blood supply
• Increases stem cells in the blood
How does hyperbaric oxygen help TBI patients?

A. HBOT reduces neuroplasticity  
B. HBOT causes vasodilation  
C. HBOT increases tissue perfusion with new capillary growth  
D. HBOT creates oxidative stress
HBOT and Stem Cells

- 2 hours of HBOT triples the patient's own circulating stem cells
- 20 sessions of HBOT increases circulating stem cells to 8 fold (800%)

Thom, et al., 2006
Mean CD34+ population in blood of humans before and after HBO2 treatments.

Data are the fraction of CD34+ cells within the gated population using leukocytes obtained from 26 patients before and after their 1st, 10th, and 20th HBO2 treatment.

Thom, et al., 2006
“[Hyperbaric oxygen therapy] is the safest way clinically to increase stem cell circulation, far safer than any of the pharmaceutical options.”

STEPHEN THOM, MD, PH.D. (2006)
Intranasal Therapies (Insulin, PRP, and Stem Cells) for TBI
Journey Through the Nose

- Through the olfactory nerves
- Bypasses the blood-brain barrier
- Into the CSF within 10 minutes
Solid arrows represent the paths of migration of cells into the brain, dashed arrows reflect possible hypothetical routes of cell delivery.
Intranasal Insulin for TBI

- Improves brain ATP production
- Decreases CSF cortisol
- Improves neuronal viability in the hippocampus
- Increases the expression of anti-inflammatory microglia
- Reduces beta-amyloid and tau protein deposition
Improved neuronal viability in the hippocampus of the insulin treated rats.

Intranasal insulin increases the expression of anti-inflammatory microglia in the hippocampus.

Brabazon, Khayrullina, Frey, & Byrnes, 2014
Intranasal insulin has the following effects:
A. Increases ATP production and utilization
B. Decreases gliosis
C. Decreases cortisol
D. Reduces amyloid and tau protein deposition
E. All of the above
Platelet Rich Plasma (PRP)

- Autologous plasma contains growth factors and cytokines to aid the injured brain:
  - VEGF, EGF increases angiogenesis
  - PDGF, TGF-p enhance collagen growth
  - IGF-1 stimulates protein synthesis
Platelet Rich Plasma (PRP)

The infusion of concentrated platelets results in an exponential increase in numerous growth factors at the sight of infusion.

Plasma cytokines control inflammatory mediators cox1, cox2 and guide stem cells to areas of injury.
Intranasal Platelet Rich Plasma (PRP) for TBI

• “Basic fibroblast growth factor infusion enhances injury-induced cell proliferation in the dentate gyrus and improves cognitive function in rats following fluid percussive injury.”

• “Other studies have found that infusion of S100β or VEGF can also enhance neurogenesis in the hippocampus and improve the functional recovery of animals following TBI.”
Peripheral Blood Based Adult Stem Cells

- Recently discovered in peripheral blood
- Behave like embryonic stem cells
- Give rise to all the cell types
- Long lifespan
- Work in combination with PRP

PLURIPOTENT adult stem cells
Intranasal Peripheral Blood Stem Cells for TBI

- Have regenerative and reparative properties
- Adult stem cells from BMA have been used to treat ischemic brain damage by reducing gray and white matter loss (Danielyan, et al., 2014).
- Downregulate neuroinflammatory cytokines
Intranasal Nutrients for TBI

- IN glutathione has been used to reduce oxidative stress and enhance cellular detoxification in Parkinson’s disease patients (Mischley, et al., 2016).

- IN methylcobalamin has been shown to improve QEEG Theta activity in ADHD and autism patients (Kurtz, 2008).
Intravenous Nutrition for TBI
IV Nutrition for TBI

- PRP
- Adult peripheral blood stem cells
- NAD+
- Myer’s cocktail with potassium, magnesium, calcium, B-complex, B5, B6, and B12, ascorbate, and glutathione
Part IV
Cranial Osteopathy for TBI
• Manual manipulation of the cranial bones and membranes to allow the cerebral spinal fluid to flow properly

• The central nervous system, including the brain and spinal cord, has a subtle, rhythmic pulsation
Cranial Osteopathy for TBI

- This rhythmic pulsation can be blocked in brain injuries - impedes CSF and blood flow
- Effective at treating vertigo and headaches associated with TBIs
▪ Time shift between peaks of TCD and B-Imp is determined by the replacement of some portion of CSF out from (or into) zone of B-Imp electrodes.

▪ This time interval represents the mobility of CSF inside the cranium during the pulse cycle.

Moskalenko, Frymann, Kravchenko, & Weinstein, 2003
Question 5

TBI patients have:

A. Reduced mobility of the CSF
B. Increased mobility of the CSF
C. Complete loss of CSF
D. No change in mobility of the CSF
Part V

MCT Oils and the Ketogenic Diet for TBI
Ketogenic Diet for TBI

- High-fat
- Low-carbohydrate
- Adequate-protein
Ketogenic Diet for TBI

**DO NOT EAT**
- Grains – wheat, corn, rice, cereal, etc.
- Sugar – honey, agave, maple syrup, etc.
- Fruit – apples, bananas, oranges, etc.
- Tubers – potato, yams, etc.

**DO EAT**
- Meats (organic, pasture-raised, sustainable)
- Above ground vegetables and leafy greens
- High fat dairy
- Nuts and seeds
- Avocado and berries
- Other fats – avocado oil, coconut oil, grass-fed ghee, high-fat salad dressing, saturated fats, etc.
Which burns more even?

Glucose/Carbohydrates = Kindling

Ketones/Fats = Logs
Ketones are like diesel fuel (Glucose is like gasoline)

• Diesel fuel has a high flash point than gasoline
• Harder to oxidize – Less flammable (excitable)
  • The brain works like a diesel engine
  • Burns more efficiently – lasts longer
What else do ketones do?

- Increases GABA
- Increases Neuroprotection
- Increases Calming
- Decreases Glutamate
- Decreases Depression, Fear, Anxiety
- Decreases Oxidative Stress
- Possible anticonvulsant effects of ketone bodies on the brain
- Increased GABA synthesis
- Decreased glutamate release by competitive inhibition of vesicular glutamate transporters.

McNally & Hartman, 2012
- Increased membrane potential hyperpolarization via KATP channels
- Decreased reactive oxygen species production from glutamate exposure
- Electron transport chain subunit transcription

McNally & Hartman, 2012
Neuroprotective Actions of the Ketogenic Diet

- Upregulates energy metabolism genes
- Stimulates of mitochondrial biogenesis
- Promotes synthesis of ATP
- Limits glutamate toxicity
The TBI Therapy Protocol
TBI Therapy HBOT Protocol

Medical Grade HBOT
- 10 - 20 before and after treatment

Home HBOT Chamber
- 5 - 7 days/wk 1 month before treatment
- 5 - 7 days/wk 2 - 9 months after treatment
<table>
<thead>
<tr>
<th>Day 1:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultation</td>
</tr>
<tr>
<td>Cranial osteopathy</td>
</tr>
<tr>
<td>HBOT</td>
</tr>
<tr>
<td>IV PRP + Nutrition</td>
</tr>
<tr>
<td>IN PRP + Insulin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Day 2:</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV pluripotent stem cells (VESLs) from the blood + NAD</td>
</tr>
<tr>
<td>IN pluripotent stem cells (VESLs) from the blood</td>
</tr>
<tr>
<td>HBOT</td>
</tr>
</tbody>
</table>
| Day 1: | Consultation  
|        | IV therapy  
|        | Cranial osteopathy  
|        | HBOT |
| Day 2: | HBOT  
|        | IV PRP + Nutrition  
|        | IN PRP + Insulin |
| Day 3: | IV pluripotent stem cells (VESLs) from the blood + NAD  
|        | IN pluripotent stem cells (VESLs) from the blood  
|        | HBOT |

**TBI Therapy 3-Day Program**
## Case Report 1: 46 year-old male

### Before Treatment:
- Memory loss
- Depression and anxiety
- Emotionally unstable
- Headaches daily
- Inability to carry on conversation
- Inability to do math or read
- Light and sound sensitivity
- Could not drive
- Insomnia

### After Treatment:
- “Memory download”
- “An awakening”
- Mood and personality improvements
- Improvements intellectually, physiologically, and psychologically
- Improved ability to read
- Able to turn on lights /electronics
- Able to drive
- Sleep normalized
TBI Therapy: 
Case Report 1

“It was like a stream of information had been let loose... I felt for the first time in a year that I had some clarity. I was excited and able to read more than 2-3 sentences without triggering a migraine... The ability to think and plan returned.”
## Case Report 2: 30 year-old female

<table>
<thead>
<tr>
<th>Before Treatment:</th>
<th>After Treatment:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Insomnia</td>
<td>• Able to travel and work</td>
</tr>
<tr>
<td>• Mood swings</td>
<td>• Light and sound sensitivity decreased</td>
</tr>
<tr>
<td>• Depression</td>
<td>• Improved mood</td>
</tr>
<tr>
<td>• Unable to work</td>
<td>• Less fatigued</td>
</tr>
<tr>
<td>• Head pressure</td>
<td>• Relief from anxiety</td>
</tr>
<tr>
<td>• Sound and light sensitivity</td>
<td></td>
</tr>
</tbody>
</table>
TBI Therapy: Case Report 2

“I felt well enough that I started saying yes again. TBI Therapy has turned me into a TBI THRIVER, not just a survivor. I’m happy. I enjoy life again, can travel and am doing work in the world that’s more aligned with myself than ever.”
Case Report 3: 48 year-old female

<table>
<thead>
<tr>
<th>Before Treatment:</th>
<th>After Treatment:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Anger</td>
<td>• Calm</td>
</tr>
<tr>
<td>• Depression</td>
<td>• No longer “reactive” and irritable</td>
</tr>
<tr>
<td>• Suicidal ideation</td>
<td>• Confident</td>
</tr>
<tr>
<td>• Anosmia</td>
<td>• No thoughts of suicide</td>
</tr>
<tr>
<td>• Extreme mental fatigue</td>
<td>• Feeling of less inflammation</td>
</tr>
<tr>
<td>• PTSD</td>
<td>• Improved memory</td>
</tr>
<tr>
<td></td>
<td>• Improved sense of smell</td>
</tr>
</tbody>
</table>
TBI Therapy: Case Report 3

“The results for me have been are nothing short of MIRACULOUS! Popeye may have his spinach but I have stem cells and PRP! Yes, my brain is strong!”
**Performance Assessments**

<table>
<thead>
<tr>
<th>Session 1 (5/20/2019)</th>
<th>Target Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Reaction Time</td>
<td>236 (±32) ms</td>
</tr>
<tr>
<td>Trail Making Test A</td>
<td>N/A</td>
</tr>
<tr>
<td>Trail Making Test B</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Evoked Potentials**

- **Audio P300 Delay**
  - Test/Retest Change: 260 ms (±12%)
  - Target Range: 288–336 ms
  - N/A
- **Audio P300 Voltage**
  - Test/Retest Change: 16.7 μV (±24%)
  - Target Range: 9–19 μV
- **Boone Brain Age**
  - 23 yrs

**State (Power)**

- **CZ Eyes Closed Theta/Beta**
  - 0.7
  - Target Range: 0.1–1.6
- **F3/F4 Eyes Closed Alpha**
  - 1.2
  - Target Range: 0.9–1.1

**Front-Back (F-P) Coherence in Theta and Alpha Bands**

- **Left (Theta | Alpha)**
  - 0.31 [0.15] ≥ 0.35 [≥ 0.4]
- **Mid (Theta | Alpha)**
  - 0.28 [0.18] ≥ 0.35 [≥ 0.4]
- **Right (Theta | Alpha)**
  - 0.20 [0.08] ≥ 0.35 [≥ 0.4]

**Maximum P300 Test Depth (μV) — Range: 240–500 ms**

---

**Session 1 (6/27/2019) | Target Range**

<table>
<thead>
<tr>
<th>Performance Assessments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Reaction Time</td>
</tr>
<tr>
<td>Trail Making Test A</td>
</tr>
<tr>
<td>Trail Making Test B</td>
</tr>
</tbody>
</table>

**Evoked Potentials**

- **Audio P300 Delay**
  - Test/Retest Change: 272 ms
  - Target Range: 264–343 ms
  - N/A
- **Audio P300 Voltage**
  - Test/Retest Change: 18 μV
  - Target Range: 7–18 μV
- **Boone Brain Age**
  - 20 yrs

**State (Power)**

- **CZ Eyes Closed Theta/Beta**
  - 0.7
  - Target Range: 0.8–1.8
- **F3/F4 Eyes Closed Alpha**
  - 1.0
  - Target Range: 0.9–1.1

**Front-Back (F-P) Coherence in Theta and Alpha Bands**

- **Left (Theta | Alpha)**
  - 0.32 [0.16] ≥ 0.35 [≥ 0.4]
- **Mid (Theta | Alpha)**
  - 0.39 [0.25] ≥ 0.35 [≥ 0.4]
- **Right (Theta | Alpha)**
  - 0.20 [0.11] ≥ 0.35 [≥ 0.4]

**Maximum P300 Test Depth (μV) — Range: 240–500 ms**
Largest depths between 240-500 msec are reported. P300s typically occur between 240 and 450 msec. Probable depth and latency of true P300 is indicated on 1st page of report.

*Indicates possible artifact during late P300.

Black dotted lines at 300 msec post stimulus.
### Case Report 4: 36 year-old male vet – bomb tech

<table>
<thead>
<tr>
<th>Before Treatment:</th>
<th>After Treatment:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Headache</td>
<td>• No headaches</td>
</tr>
<tr>
<td>• Insomnia</td>
<td>• Improved sleep</td>
</tr>
<tr>
<td>• Suicide ideation</td>
<td>• No suicidal thoughts</td>
</tr>
<tr>
<td>• PTSD</td>
<td>• More energy</td>
</tr>
<tr>
<td>• Depression</td>
<td>• Able to exercise</td>
</tr>
<tr>
<td>• Fatigue</td>
<td>• Less pain</td>
</tr>
<tr>
<td>• Chronic pain</td>
<td></td>
</tr>
</tbody>
</table>
### WAVi Wellness Basic Report

**Session Number** (Created Date) | **Patient Original Title** | **Change Hrs,Sleep Since Meal**
--- | --- | ---
Session 1 (7/1/2019) | 56 yrs Baseline | N/A 4-6 10+
Session 2 (8/26/2019) | 36 yrs Baseline | N/A 7-9 10+

*See Appendix* for explanations of metrics and symbols shown on this page.

**Symbol Key:** \( \uparrow = \text{Sync blinks} \), \( \downarrow = \text{Questionable Value} \)

#### Screening Scores

<table>
<thead>
<tr>
<th>Metric</th>
<th>Session 1 (7/1/2019)</th>
<th>Session 2 (8/26/2019)</th>
<th>Target Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamilton Anxiety Rating Scale (HAM-A)</td>
<td>N/A</td>
<td>N/A</td>
<td>( \leq 17 )</td>
</tr>
<tr>
<td>Patient Health Questionnaire-9 (PHQ-9)</td>
<td>N/A</td>
<td>N/A</td>
<td>(&lt; 5 )</td>
</tr>
</tbody>
</table>

#### Performance Assessments

<table>
<thead>
<tr>
<th>Metric</th>
<th>Session 1 (7/1/2019)</th>
<th>Session 2 (8/26/2019)</th>
<th>Target Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Reaction Time</td>
<td>249 (±42) ms</td>
<td>247 (±27) ms</td>
<td>252–363 ms</td>
</tr>
<tr>
<td>Trail Making Test A</td>
<td>N/A</td>
<td>52 sec</td>
<td>38–64 sec</td>
</tr>
<tr>
<td>Trail Making Test B</td>
<td>N/A</td>
<td>57 sec</td>
<td>43–83 sec</td>
</tr>
</tbody>
</table>

#### Evoked Potentials

<table>
<thead>
<tr>
<th>Metric</th>
<th>Session 1 (7/1/2019)</th>
<th>Session 2 (8/26/2019)</th>
<th>Target Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Audio P300 Delay</td>
<td>288 ms</td>
<td>292 ms</td>
<td>250–324 ms</td>
</tr>
<tr>
<td>Test/Retest Change</td>
<td>( \uparrow 5.2 \mu V )</td>
<td>( \uparrow 7.0 \mu V )</td>
<td>( 8–21 \mu V )</td>
</tr>
</tbody>
</table>

#### State

<table>
<thead>
<tr>
<th>Metric</th>
<th>Session 1 (7/1/2019)</th>
<th>Session 2 (8/26/2019)</th>
<th>Target Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>CZ Eyes Closed Theta/Beta (Power)</td>
<td>5.0</td>
<td>4.0</td>
<td>0.9–2.1</td>
</tr>
<tr>
<td>P3/4 Eyes Closed Alpha (Magnitude)</td>
<td>1.2</td>
<td>1.2</td>
<td>0.9–1.1</td>
</tr>
</tbody>
</table>

#### Peak Frequency (7.0–13.0 Hz)

<table>
<thead>
<tr>
<th>Location</th>
<th>Session 1 (7/1/2019)</th>
<th>Session 2 (8/26/2019)</th>
<th>Target Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal</td>
<td>( \uparrow 7.0 ) Hz</td>
<td>7.0 Hz</td>
<td>9.0–11.0 Hz</td>
</tr>
<tr>
<td>Central-Parietal</td>
<td>( \uparrow 7.0 ) Hz</td>
<td>( \uparrow 7.0 ) Hz</td>
<td>9.0–11.0 Hz</td>
</tr>
<tr>
<td>Occipital</td>
<td>( \uparrow 7.0 ) Hz</td>
<td>( \uparrow 9.5 ) Hz</td>
<td>9.0–11.0 Hz</td>
</tr>
</tbody>
</table>

*Maximum P300 Test Depth (\( \mu V \)) — Range: 240–500 ms — Topo scale referenced to Session 2*

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*SYNC BLINKS REPORTED IF MAXIMUM DEPTH OF FP1 or FP2 > 20 \( \mu V \). SYNC BLINKS AFFECT FRONTAL DEPTH VALUES.*
Largest depths between 240-500 msec are reported. P300s typically occur between 240 and 450 msec. *Probable depth and latency of true P300 is indicated on 1st page of report.*

*Indicates possible artifact during late P300.*

(See Appendix)

SYNC BLINKS

[Graph and diagram showing waveforms for different locations such as F7, F3, F2, F4, F8, T3, C3, Cz, C4, T4, T5, P3, T6, O1, O2, and Central-Parietal Ave.]

Black dotted lines at 300 msec post stimulus.
Out of 100 patients treated, nearly every patient reports:

- More mental clarity
- Improved memory
- Improved executive function/decision making
- More stable emotions and less stress
- Better ability to cope with pain
- More physical and mental energy
Out of 100 patients treated, some patients report:

- Less sound and light sensitivity
- Improved eyesight
- Improved sleep and libido
- Improved motor function
  (ability to open a clenched fist, ability to walk)
- Less muscle spasticity
Conclusion: The Multimodal, Regenerative Approach is a Superior Way to Treat TBI

The practical, effective combination of multiple regenerative TBI therapies can produce synergistic benefits to the patient superior to mainstream TBI or single modality TBI treatments.
Treats TBI patients by combining regenerative therapies: HBOT, stem cells, PRP, and nutritional therapies.

tbitherapy.com

Treats chronic pain and major medical problems using modern and natural medicine.

aspenintegrativemedicine.com


