Hyperbaric Medicine, Serotonin, and Its Effect On Neuropsychological Conditions

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OMED - Baltimore, MD - October 26, 2019
OVERVIEW

- HBOT BASIC PHYSIOLOGICAL EFFECTS
- HBOT FOR TBI
- HBOT FOR PTSD
- PATHOPHYSILOGICAL RESPONSE TO TBI AND PTSD
- SEROTONIN AND TBI/PTSD/DEPRESSION
- INCREASING SEROTONIN WITH HBOT
- TREATING TBI AND PTSD WITH SSRIS
- TREATING TBI AND PTSD WITH HBOT AND SEROTONIN PRECURSORS AND PROBIOTICS
HBOT BASIC
PHYSIOLOGICAL EFFECTS
HYPERBARIC MEDICINE (HBOT)
Basic Science and Standard Uses

A medical treatment in which a patient breathes 100% oxygen under increased atmospheric pressure.

- “Hyper” – more
- “Baric” – atmospheric pressure
- Hyperoxygenation – “high dose”
History

1928
Largest hyperbaric chamber constructed for various maladies

1937
100% O2 first used in hyperbarics for decompression sickness

1938
Used for treatment of leprosy in Brazil

1938
Used in USA to treat experimental CO poisoning in animals

1950
Used by UK to enhance tumor radio-sensitivity

1959
Boerema proved life can be sustained in absence of blood flow
History

1960s
Effectiveness shown for stroke, MS, MLS, brain ischemia, CO poisoning, gas gangrene, etc

1970s
Majority of US hyperbaric chambers were military

1980
Hyperbaric community began to develop with various organizations and certifications

1991
The National Board of Diving and Hyperbaric Medical Technology (NBDHMT) formed

2002
International Hyperbaric Medical Association (IHMA) formed
Physics

Henry’s Law of Gas Solubility

• Solubility of gas in liquid is directly proportional to partial pressure of gas above the liquid
• Increasing atmospheric pressure increases amount of gas dissolved into a fluid
• Oxygen → Blood Plasma
Physiology

What Gets Hyper-Oxygenated?

- Blood Plasma
- Cerebrospinal Fluid
- Lymph Fluid
- Clinical Hyperbaric Pressures = 7 – 22 psi
- 10–15x normal amount of O2 at 2ATA

Bypasses body’s normal system of transporting oxygen
POOR BLOOD FLOW = POOR OXYGENATION = TISSUE DAMAGE
HYPERBARIC CONDITIONS
HBOT Mechanism of Action

**Increases:**
- Collagen synthesis (fibroblast stimulation)
- Oxygen dependent killing of bacteria (antimicrobial)
- Mitochondrial ATP production (aerobic respiration)

**Decreases:**
- Lactate production and tissue acidosis
- Ischemia, cell death, and inflammation
- Leukocyte adhesion and degranulation (immune modulation)
HBOT
FDA-Approved

Drug that affects non-specific biological repair

Oxygen can never be a placebo

Only non-hormonal FDA-approved treatment known to repair and regenerate human tissue
High Dose Oxygen RX

FDA approved drug for specific diseases or injuries causing low oxygen levels/poor perfusion in the tissues

Results: Enhances and speeds up body’s natural healing process
FDA-Approved Uses

*Represent 95% of all hospital treatments

- Diabetic Wounds*
- Osteomyelitis*
- Delayed Radiation Injuries (Soft tissue/bone)*
- Compromised skin grafts/flaps*
- Decompression sickness

- Carbon monoxide poisoning
- Intracranial abscess
- Acute Arterial insufficiency
- Thermal burns
- Crush injuries, acute trauma

- Necrotizing soft tissue infections
- Exceptional blood loss anemia
- Gas gangrene
HBOT: Barriers to Access

- Limited number of FDA approved, insurance covered applications
- HBOT is non-patentable
- Research funded by nonprofits only
- No patent, no development or marketing
- Caregivers cannot take advantage of potentially effective treatments (aka HBOT for TBI)
HBOT FOR TBI
HBOT for TBI - Mechanisms

- Induces neuroplasticity
- Increases tissue oxygenation
- Generates new capillary networks
- Restores blood supply
- Increases stem cells in the blood
HBOT and Stem Cells

- 2 hours of HBOT triples the patients own circulating stem cells at 2 ATA

- 20 sessions of HBOT increases circulating stem cells to 8-fold (800%)

Thom et al., 2006
Volume Rendered Brain SPECT Perfusion Map

- 51-year-old woman
- mTBI occurred 2 years prior
Acute Rat Model of Moderate TBI

- Edema decreased in hippocampus 2wks post-HBOT; measured by DWI
- Spatial learning and memory improved
- Cognitive functioning improved significantly

**Take home:** Reducing brain inflammation with HBOT improves TBI patient post-concussive symptoms

Liu et al., 2015
HBOT FOR PTSD
PTSD: Post Traumatic Stress Disorder

Anxiety disorder triggered by exposure to a stressful event
= exaggerated response to normal and trauma-related stimuli

Concentration problems
Anxiety
Perturbed fear conditioning
Disrupted sleep
Lack of extinction of traumatic memories
Hyperarousal
Suicide ideation
Are PTSD and TBI Related?

• Symptoms of PTSD and TBI overlap

• Pathophysiological symptoms are similar:
  o Hippocampal damage is observed in both

• TBI predisposes individual to PTSD
  o PTSD can occur after TBI even if there is little or no recollection of injury

McMillan et al., 2003
HBOT for PTSD and TBI—
Treatment Mechanisms

• HBOT reduces apoptosis and inhibits inflammatory cytokines
• HBOT upregulates growth factors and antioxidant levels

Take Home:
• Similar mechanisms behind treatment benefits of HBOT for TBI and PTSD
• TBI and PTSD symptoms and treatments are synonymous
HBOT for PTSD Case Report

**Participant:** 25yr old male vet w/ PCS and PTSD

**Diagnosis:** TBI – 3yrs after LOC of several minutes from an explosion in combat

**Treatment:** Completed 39 HBOT treatments at 1.5 ATA
Results
Permanent marked improvement in the following:

- Post-concussive symptoms
- Physical exam findings
- Brain blood flow
- Complete resolution of PSTD symptoms

Patient returned to work with no issues
HBOT for PTSD and Suicidality

Participants: 30 active-duty or retired military service

Diagnosis: Moderate/Severe TBI - Blast TBIs with LOC

Treatments: 40 HBOT sessions 2x/day, 5x/week
Results

Significant improvements in the following:

- Neurological exam
- Hand motor speed/dexterity
- Quality of life
- PCS symptoms including IQ, memory, and attention
- Moods including general anxiety, PTSD, and depression
- Reduction in suicide ideation (10 of 12 patients with previous SI)

Conclusion: HBOT produces a significant drop in PTSD symptoms and suicidal ideation

Harch et al., 2017
HBOT for Blast-Induced PCS and PTSD

**Participants:** 16 military subjects, male ages 21–45

**Diagnosis:** 2.8 years post-TBI, LOC of 2 min+, PCS and PTSD

**Treatments:** 40 - 1.5 ATA/60 min HBOT sessions in 30 days

Harch et al., 2012
HBOT for Blast-Induced PCS and PTSD

**Results**

The subjects reported:

- Significant drop in depression and anxiety
- Increase in perceived quality of life
- Suicidal ideation component improved

On physical exam 15 subjects:

- Significant improvements: symptoms, neurological exam, full-scale IQ, cognitive testing, PCS and PTSD symptoms
- 64% on medication decreased or discontinued their medication

**Bottom Line:** HBOT may be better than any medication for post-concussive mood changes in TBI/PTSD patients

Harch et al., 2012
HBOT for Blast-Induced PCS and PTSD

Harch et al., 2012
HBOT Accepted By VA

Congressman Andy Biggs and Senator Kevin Cramer Introduce the TBI and PTSD Treatment Act

- Freedom to use healthcare benefits for HBOT

Several states laws require vets with PTSD be treated with HBOT

- So far there has been no money allocated to these treatments
Cost of Treatment

• 2yr taxpayer costs w/in first 2yrs service member returns home
  • PTSD: $5,904 to $10,298
  • PTSD and major depression: $12,427 to $16,884
• 1yr taxpayer costs for TBI patients:
  • mTBI: $27,259 to $32,759
  • Moderate to severe: $268,902 to $408,519
• The above costs are not for curative therapies but simple symptom management. Patients accrue other costs in the forms disability payments, inability to work, etc.
• HBOT cost for 80 treatments averages $16,000

• Bottom line: HBOT is a cost-effective, superior treatment to current VA SOC for TBI and PTSD vets
“As a TBI veteran, I received HBOT that has given me the quality of life back to enjoy time with family. My symptoms all were helped tremendously.

I have the blood flow back in my brain. The SPECT scan imaging of my brain showed that half my brain was not getting blood supply and the MRIs were all read as normal.

After HBOT, I have color in my world, and I feel like I have my life back!”
PATHOPHYSIOLOGICAL RESPONSE TO TBI AND PTSD
Neurobiochemical Cascade in TBI

Mechanical stress → Disruption to cellular membranes → Neuronal depolarization, firing, and release of neurotransmitters

Increased extracellular glutamate → Efflux of K+ with Ca2+ going intracellular → Hyperglycolysis

Kawa, 2017
Increased intracellular Ca²⁺ concentration gets sequestered by mitochondria → Oxidative metabolism gets inhibited → Energy demands must be met by glycolysis = lactate accumulation = decreased ATP production

Cell enters phase of metabolic suppression and widespread depression → Intracellular Ca²⁺ causes enzyme activation and initiation of apoptotic pathways → Immediate decreases in Mg ²⁺ slows down recovery

Kawa, 2017
Neurobiochemical Response to TBI
Disruptions in the neurobiochemical cascade of TBI lead directly to the patient's persistent emotional, cognitive, and somatic symptoms.

Further support for this conclusion:
Pre-treatment of animals with magnesium results in improved post-traumatic outcomes.

Kawa, 2017
SEROTONIN AND TBI/PTSD/DEPRESSION
Serotonin Transporter Protein (SERT) Levels Decreased in TBI

- Decreased SERT immunoreactivity in neuronal fibers
- Decreased SERT mRNA and protein expression
- Decreased SERT expression in the cerebral cortex
- Take Home: Decreased serotonin neurotransmission means increased depression with TBI patients

Abe et al., 2016
Serotonin (5HT) Origins and Functions

Origins and rate limiting steps:

• The raphe nuclei neuron cell groups, B1-B9 are the principal neurons that give rise to spinal and extensive serotonergic forebrain projections.

• These nuclei in the brain express the rate-limiting enzyme tryptophan hydroxylase 2 for 5-HT synthesis.

Functions: 5-HT regulates sleep, appetite, pain and mood.

5-HT levels are reduced in following conditions:

• Chronic stress: reduces 5-HT is found in the plasma and CSF (Gao et al., 2008).

• Depression: Decreased 5-HT transporter binding in post-mortem brains of depressed patients (Maes et al., 1995).

• "5-HT plays a role in stress and PTSD—possibly modulating the “fight-or-flight” response." (McAllister, 2011)
Neurotransmitter Systems Post-TBI

- TBI increases noradrenaline levels (and other catecholamines)
  - Increasing inflammation in the forebrain
  - Increasing anxiety-like behavior
- TBI decreases the serotonin metabolite 5-HIAA in pre-frontal cortex

**Bottom Line:**
- ↑ catecholamines + ↓ 5HT metabolism = PTSD (internal anxiety with poor ability for patient to manage)

Kawa et al., 2015
Neurotransmitters Going Awry Post-TBI

Cholinergic excess:
• Amplifies destructive effects of excitatory amino acid excesses

Cerebral monoaminergic excesses:
• Initially induced elevations of certain cerebral monoamines
• Leads to decreased cerebral glucose use
• Results in a metabolic crisis that characterizes TBI

McAllister, 2011
Neurotransmitters Going Awry Lead to Metabolic Crisis

“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
INCREASING SEROTONIN
WITH HBOT
What Raises Excitatory Neurotransmitters and Lowers Serotonin?

- **ALTITUDE**
  - Low oxygen = low serotonin
  - High altitude = high dopamine

- 25% of variation in rates of suicide could be uniquely attributed to altitude
- “With lower oxygen, the brain doesn’t make as much serotonin.”
  
  Perry Renshaw, Phd.

https://i.dailymail.co.uk/i/pix/2017/11/06/22/4615890C0000578-5055909-The-a-2_1510007823656.jpg

Kious et al., 2019
Suicide and Altitude

Suicides per 100,000 Pop.

Inhaled Oxygen Increases Serotonin

**Participants**: Six healthy participants (3 male, 3 female) breathed a 15% or 60% oxygen mixture 15 min before injection of tracer and during acquisition period.

**Observations**: Two sets of PET images were acquired

  - Before and after each of the oxygen mixtures and after reconstruction
  - All images were converted into brain functional images illustrating the brain trapping constant $K(*)$ (microL/g/min).

**Results**: Highly significant increases (50% on average) in brain serotonin synthesis ($K(*)$ values) at high (mean value of $223+/-41$ mmHg) relative to low (mean value $77.1+/-7.7$ mmHg) blood oxygen levels.

Nishikawa et al., 2005
Serotonin Increased by Oxygen: Conclusions

• Increasing blood oxygen increases 5-HT synthesis in brain
• Tryptophan hydroxylase 2 is not saturated with oxygen in brain
• Take Home: Inhaled oxygen (60%) over a short period of time rapidly increases serotonin levels in comparison to 15% inhaled oxygen
• Other studies: Support that hyperbaric medicine increases serotonin (Silliphant, 2017)
PTSD and Serotonin: New Directions for Research and Treatment

Serotonin dysfunction linked to pathophysiology of symptoms of PTSD

Higher CSF serotonin metabolites inversely correlate with impulsive behavior and severe aggression

Fluoxetine has the most published data and has been used for PTSD symptoms

Are SSRI's safe for TBI/PTSD?

Davis et al., 1997
TREATING TBI AND PTSD WITH SSRIS
SSRIs for TBI and PTSD: Danger

- Only modestly effective in reducing symptoms of severe depression
- Increase brain’s susceptibility to mood disorders after discontinuation
- Causes mature neurons to revert to an immature state and neuronal apoptosis
- **Take Home:** SSRIs deplete both catecholamines and serotonin leading to neuronal degeneration and death—DO NOT USE SSRIs FOR TBI/PTSD

Delgado et al, 2002; Wilson and Hamm, 2002
SSRI Warnings for TBI/PTSD Patients

- “The epidemic of suicides amongst military veterans is most likely due to cocktail of antidepressants. None of which are approved for treating TBI.”

- “Antidepressants increase the risk of suicidal thinking in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of any antidepressant must balance this risk with the clinical need.” –FDA warning

- Bottom Line: For TBI/PTSD patients, SSRI's = SI (suicide ideation) and depression
  - **DO NOT USE SSRIs FOR TBI/PTSD**

Delgado et al, 2002; Wilson and Hamm, 2002
Effects Of Fluoxetine on the 5-HT1A Receptor

Objective

• View effects of chronic administration of fluoxetine on cognitive performance and 5-HT1A receptor immunoreactivity following TBI

Design

• Rats received a moderate severity of lateral fluid percussive injury or sham injury 24 h after surgical preparation.
• Fluoxetine or vehicle was administered chronically on postinjury days 1–15.
Effects Of Fluoxetine on the 5-HT1A Receptor

**Results**

- Chronic fluoxetine treatment did not affect motor or maze performance.
- Injured groups showed significantly higher 5-HT1A receptor immunoreactivity.
- Fluoxetine treatment did not alter 5-HT1A receptor immunoreactivity.

**Conclusions**

- Chronic postinjury fluoxetine administration did not influence recovery.
- Injury-induced changes in the 5-HT1A receptor may contribute to TBI–induced cognitive deficit.
- **Bottom Line:** SSRIs such as fluoxetine do not increase serotonin levels long-term and have great risks for TBI/PTSD patients.
TREATING TBI AND PTSD WITH HBOT AND SEROTONIN PRECURSORS AND PROBIOTICS
Treating TBI and PTSD with Tryptophan Diet

- **Serotonin levels enhanced by carb ingestion**
  - Insulin release accelerates the serum removal of competing valine, leucine, and isoleucine
  - Increased protein in diet slows serotonin elevation so a strict Keto paleo diet is not the best

- **Tryptophan hydroxylase is the rate-limiting enzyme for serotonin production so serotonin levels are directly on bioavailable tryptophan**
  - Converts Trp to 5-HTP
  - Trp plentiful in chocolate, oats, bananas, dried dates, milk, cottage cheese, meat, fish, turkey, and peanuts.

**Take Home:** Along with turkey ingestion, a diet with some healthy carbs can improve oral tryptophan assimilation

Oral Ingestion of Tryptophan for TBI/PTSD

- Daily nutritional requirement for L-tryptophan (Trp) = 5 mg/kg
  - Most adults consume much more, up to 4–5g/d (60–70 mg/kg)
  - Ingesting L-Trp raises brain tryptophan levels and stimulates its conversion to serotonin in neurons
- Side effects at higher doses (70–200 mg/kg), include tremor, nausea, and dizziness, with a drug that enhances serotonin function (e.g., antidepressants)
- **Tryptophan can be taken as supplement (used for 50 years now)**
  - Risks: “serotonin syndrome” occurs - too much serotonin stimulation when Trp combined with serotonin drugs
  - Symptoms include delirium, myoclonus, hyperthermia, and coma
- **Tryptophan supplement dosing: Should be individualized for each patient**

Fernstrom, 2012
Oral Tryptophan (Trp) Can Increase Serotonin in Brain

- Variations in Trp concentrations in the brain found to modify the rate of 5HT synthesis in and release by neurons
- **5HT synthesis falls when brain Trp declines**
- Trp is a large neutral amino acids (LNAA) and competes with other LNAA for a shared, competitive transporter across the blood-brain barrier
- Raising plasma levels of the LNAA (other than Trp) reduces Trp transport into the brain and lowers brain (and CSF) Trp concentrations

Fernstrom, 2012
IV L-Tryptophan

- IV Trp infusion moderately increases in prolactin and GH concentration

- Subjects report feeling significantly more 'high', 'mellow', and 'drowsy' following IV Trp infusion

Charney et al., 1982
IV L-Tryptophan Study

- L-tryptophan at doses of 75 and 100 mg/kg were compared with normal saline.
  
- **Results:** ECG showed a significant increase in slow-wave activity and a trend toward decreased fast-wave activity.
  
- 100 mg/kg infusion produced a 40-fold increase in free tryptophan and an 8-fold increase in the bound form.
  
- Some impairment of a motor speed task was also noted.
  
- **Take Home:** IV L-tryptophan can be used to improve moods and possible TBI/PTSD symptoms.

Greenwood et al., 1974
L-Tryptophan More Studies Needed

The dose of Trp required to raise brain 5-HT levels is controversial.

Brain 5-HT levels elevated after Trp administration in different intensities, dependent of the brain region evaluated and the time of administration.

Further studies needed to assess dose-response of Trp administration to brain 5-HT levels.

Carneiro et al., 2018
Serotonin in the Gut

• Microbes can also alter availability of tryptophan - amino acid building block required for serotonin production
• After synthesis in intestinal enterochromaffin cells, serotonin is stored in platelets and released upon stimulation
• Estimated that 90% of the body's serotonin is made in the digestive tract
• Beneficial microbes produce short-chain fatty acids like butyrate that influence production of serotonin in enterochromaffin cells
• Take Home: A healthy gut microbiome leads to increased serotonin levels

Banskota, Ghia, and Khan. 2019
Probiotics Help Depression

- Gut probiotics play a major role in the bidirectional communication between the gut and the brain.
- Probiotics may be essential to people with depression - a metabolic brain disorder.
- **Meta-analysis showed that probiotics significantly decreased depression and psychological stress**
- *Lactobacillus* increases expression of SERT

Huang, Wang, and Hu, 2016
Increased Mean Platelet Volume and Lower Levels of Generalized Anxiety Disorder

OBJECTIVE:
• Mean platelet volume (MPV), which is indicative of platelet size, is accepted as an indication of platelet activity.

METHOD:
• Compare complete blood count especially in terms of platelet count (PLT), platelet distribution width (PDW), plateletcrit (PCT) and MPV values
• 60 GAD patients with 60 healthy controls.

RESULTS:
• MPV found to be significantly higher ($p = .008$) and platelet count found to be significantly lower in the GAD group ($p = .001$)

DISCUSSION:
• Increased MPV levels in GAD = increased platelet activation due to sympathetic system activation
• Platelet levels were found to be significantly lower in GAD
• Non-linear inverse relation between platelet volume and platelet count

Almis and Aksoy, 2018
# Increased Mean Platelet Volume and Lower Levels of Generalized Anxiety Disorder

<table>
<thead>
<tr>
<th></th>
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<th>GAD</th>
<th>Control</th>
<th>p</th>
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<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td>38.35 ± 18.97</td>
<td>34.90 ± 14.62</td>
<td>.229</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>Women (n:81)</td>
<td>38 (%63.3)</td>
<td>43 (%71.6)</td>
<td>.330</td>
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<tr>
<td></td>
<td>Men (n:39)</td>
<td>22 (%36.7)</td>
<td>17 (%28.4)</td>
<td></td>
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<tr>
<td><strong>WBC (10^9/µL)</strong></td>
<td></td>
<td>8.04 ± 1.70</td>
<td>7.88 ± 1.84</td>
<td>.623</td>
</tr>
<tr>
<td><strong>HGB (g/dL)</strong></td>
<td></td>
<td>14.01 ± 1.42</td>
<td>13.64 ± 1.54</td>
<td>.177</td>
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<tr>
<td><strong>HTC (%)</strong></td>
<td></td>
<td>42.12 ± 3.98</td>
<td>41.74 ± 5.02</td>
<td>.044</td>
</tr>
<tr>
<td><strong>RBC (10^6/µL)</strong></td>
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<td>4.86 ± 0.46</td>
<td>4.80 ± 0.55</td>
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<tr>
<td><strong>MCV (fL)</strong></td>
<td></td>
<td>85.92 ± 4.93</td>
<td>85.84 ± 5.22</td>
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</tr>
<tr>
<td><strong>PLT (10^3/µL)</strong></td>
<td></td>
<td>258.83 ± 52.41</td>
<td>297.93 ± 57.85</td>
<td>.001*</td>
</tr>
<tr>
<td><strong>RDW (fL)</strong></td>
<td></td>
<td>19.44 ± 2.10</td>
<td>19.33 ± 1.25</td>
<td>.721</td>
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<tr>
<td><strong>PCT (%)</strong></td>
<td></td>
<td>0.21 ± 0.05</td>
<td>0.20 ± 0.04</td>
<td>.112</td>
</tr>
<tr>
<td><strong>MPV (fL)</strong></td>
<td></td>
<td>8.15 ± 1.41</td>
<td>7.50 ± 1.24</td>
<td>.008*</td>
</tr>
</tbody>
</table>
Increased Platelets Leads to Increased Serotonin

- After synthesis in intestinal enterochromaffin cells, serotonin is stored in platelets and released upon stimulation
- **Hence, more platelets = more serotonin**
- Foods to increase platelets: Lean meats, beans, garlic, kale, carrots, foods rich in B9
- Don’t block platelets with Aspirin and other prescription medications (Penicillins, NSAIDS, anticonvulsants, sedatives)

Banskota, Ghia, and Khan 2019; Visentin and Liu, 2007
Hyperbaric oxygen Therapy (HBOT) is a drug that can treat many low oxygen diseases or injuries.

HBOT can effectively treat TBI and PTSD: Scientifically and cost-effectively.

TBI can be the cause of or existent concurrently with PTSD. TBI and PTSD symptoms are almost identical; therefore treatments should be very similar.

The Neurobiochemical Cascade of TBI is directly related to the post-concussive symptoms experienced by the patient. Treatment of the TBI patient's neurobiology, including ATP deficiencies, electrolytes, and neurotransmitters is essential for recovery.
Serotonin levels in the brain decrease with TBI, PTSD, depression, and chronic stress. Restoring serotonin levels is a key component to treating TBI and PTSD.

HBOT can increase serotonin levels in the brain. Inhaled oxygen can also increase serotonin.

Treatment of TBI and PTSD patients with SSRIs may result in further depression long-term or suicide. DO NOT USE SSRIs for TBI or PTSD.

Serotonin can be increased by oral tryptophan intake (turkey, carbohydrate foods or supplementation), IV tryptophan, improving the gut microbiome (with probiotics, as necessary), and improving platelet levels.
Treatment Protocols for TBI/PTSD Should Include the Following:

- **HBOT** and/or inhaled **oxygen** (home hyperbaric chambers and oxygen concentrators are options)
- Oral **tryptophan** (dosing varies: start with 500mg to 1000mg per day; take away from other proteins)
- **Carbohydrate** foods in diet and tryptophan rich foods (turkey)—modified keto diet with carbs at dinner
- **IV tryptophan** (made by compounder; dosing varies per patient: effects seen with 5mg/kg)
- Avoidance of platelet blocking medications such as aspirin or NSAIDs
- Avoidance of SSRI s
- IV and oral **supplements** foods that increase ATP, platelets, and balance electrolytes (eg. B-vitamins, minerals, especially Magnesium)
- **Intranasal therapies** (including platelet rich plasma) to enhance brain platelets (containing tryptophan), growth factors, and stem cells in the brain. These treatment bypass the BBB to get compounds to the brain (TBI Therapy's protocols at tbitherapy.com)
- **Cranial osteopathy**
Treats TBI patients by combining regenerative therapies: HBOT, stem cells, PRP, and nutritional therapies.

tbitherapy.com

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

aspenintegrativemedicine.com