



TRAUMATIC BRAIN INJURY (TBI):
THERAPY, EVALUATION AND RETURN
TO WORK
LO MOKK
LUMIUM HEAVY COM LOKUMV KE LOKUM
TED COLE, MA, DO

1

TBI

- A brain injury that is caused by an outside force

2

Two broad types of TBIs:

- Penetrating TBI
- Non-penetrating TBI

3

Two main types of damage

- Focal injury: effects one area of the brain
- Diffuse injury: effects a more widespread area

4

Types of damage

- Damage commonly seen include bleeding, tearing that injures nerve fibers, inflammation, swelling, and metabolic changes

5

Diffuse axonal injury (DAI)

- Is one of the most common types of TBIs. It involves widespread damage to the brain's white matter

6



Concussion

- Causes include a blow to the head or a rapid movement of the brain within the skull (shaking)
- A second concussion closely following the first one ("second hit") can lead to permanent damage or even death

7

Hematomas

- Bleeding in and around the brain caused by a burst blood vessel

8

Contusions

- Bruising or swelling of the brain that happens when very small blood vessels bleed into brain tissue

9

Skull fractures

- The result of blunt force trauma and can cause damage to the membranes, blood vessels, and brain under the fracture

10

Chronic traumatic encephalopathy (CTE)

- A progressive neurological disorder which appears to be caused by repeated TBIs

11

Post-traumatic dementia (PTD)

- Can happen after a single, severe TBI
- Studies show that moderate or severe TBI in early or mid-life may be associated with increased risk of dementia later in life

12



Secondary damage

- Changes that happen over a period of hours to days after the primary injury
- Can be caused by hemorrhagic progression of a contusion (HPC), disruption of the blood-brain barrier, increased intracranial pressure, infections, low blood pressure or oxygen flow, hydrocephalus, and seizures.

13

The Burden

- World wide it's estimated a TBI incidence of 939 per 100,000 population, which included 55.9 million mild and 5.48 million severe TBIs annually
- From 1990 to 2016, the incidence and prevalence of medically treated TBI rose globally by 3.6 percent and 8.4 percent

14

Who Is At Risk

- The distribution of TBI is bimodal with respect to age: the incidence of TBI is highest among the youngest and oldest age groups

15

The Cost

- In 2019 the CDC estimated that "the economic cost of injury was \$4.2 trillion, including \$327 billion in medical care, \$69 billion in work loss, and \$3.8 trillion in value of statistical life and quality of life losses"

16

Uh Oh

- Limitations in TBI surveillance are broadly recognized, and it is widely acknowledged that nearly all TBI estimates are undercounts

17

- National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Care Services; Board on Health Sciences Policy; Committee on Accelerating Progress in Traumatic Brain Injury Research and Care; Matney C, Bowman K, Berwick D, editors. Traumatic Brain Injury: A Roadmap for Accelerating Progress. Washington (DC): National Academies Press (US); 2022 Feb 1. 2, The Scope and Burden of Traumatic Brain Injury. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK580076/>

18



Concussions are common

- The Centers for Disease Control and Prevention have reported that 20% of the estimated 1.7 million concussions that occur each year are sports-related
- Many are unreported and untreated

19

- Pfister T, Pfister K, Hagel B, et al The incidence of concussion in youth sports: a systematic review and meta-analysis *British Journal of Sports Medicine* 2016;50:292-297.

20

A concussion is the most common form of traumatic brain injury, caused by a mild blow to the head.

- In 2017, approximately 2.5 million high school students in the United States reported suffering at least one concussion related to sports or physical activity in the last 12 months

21

- Toufic R, Jildeh, Kelechi R, Okoroha, Eric Denha, Christina Eyers, Ashley Johnson, Ramsey Shehab, Vasilios Moutzouros. Return to Sport Following Adolescent Concussion: Epidemiologic Findings From a High School Population. *Orthopedics*, 2020; 43 (4): e306 DOI: 10.3928/01477447-20200521-03

22

A third of children and adolescents develop a mental health problem after a concussion, which could persist for several years post-injury

- It found up to 36.7 per cent experienced significantly high levels of internalising problems such as withdrawing, anxiety, depression and post-traumatic stress and 20 per cent externalising problems such as aggression, attention problems and hyperactivity after concussion compared with healthy children or children who sustained other injuries such as an arm fracture.

23

- Alice Gomall, Michael Takagi, Thilanka Morawakage, Xiaomin Liu, Vicki Anderson. Mental health after paediatric concussion: a systematic review and meta-analysis. *British Journal of Sports Medicine*, 2021; bjsports-2020-103548 DOI: 10.1136/bjsports-2020-103548

24



American Osteopathic College of Occupational & Preventive Medicine 2026 Midyear Educational Conference

One in four children (25.3%) who have been discharged from the emergency room after a mild head injury are misdiagnosed and continue to suffer from persistent post-concussion syndrome for many years.

- This syndrome includes chronic symptoms such as forgetfulness, memory problems, sensitivity to light and noise, ADHD and even psychological problems and, instead of receiving treatment for the syndrome, they are mistakenly diagnosed as suffering from ADHD, sleep disorders, depression, etc. and given inappropriate therapy

25

- Eli Fried, Uri Balla, Merav Catalogna, Eran Kozer, Adi Oren-Amit, Amir Hadanny, Shai Efrati. Persistent post-concussive syndrome in children after mild traumatic brain injury is prevalent and vastly underdiagnosed. *Scientific Reports*, 2022; 12 (1)
DOI: 10.1038/s41598-022-08302-0

26

- This study found that people with mild traumatic brain injuries may be more likely to have cognitive impairment, cognitive decline or both one year after the injury. They were also more likely to have other symptoms like anxiety and lower satisfaction with life.

27

- Andrea Lauren Christman Schneider, et. al. TRACK-TBI Investigators. Cognitive Outcome 1 Year After Mild Traumatic Brain Injury: Results From the TRACK-TBI Study. *Neurology*, 2022 DOI: 10.1212/WNL.000000000000200041

28

Current protocols and side-line testing are inadequate

- Current protocols call for a player showing concussion symptoms to be sidelined for at least 24 hours.
- This research found that athletes with only one concussion required at least 30 days of recovery prior to returning to their sport while others who reported a second or more concussions required more recovery time

29

- "Parents need to understand that a concussion is a very serious brain injury, one which requires treatment every time a concussion is sustained. This study has revealed this type of traumatic brain injury can have a compounding effect on children that could lead to more aggressive behavior, academic problems, and social issues,"...

30



American Osteopathic College of Occupational & Preventive Medicine 2026 Midyear Educational Conference

- Gregory Knell, et. al. Association Between Concussion History and Factors Relating to Cognitive, Behavioral, and Emotional Health Among American High School Athletes: A Cross-sectional Analysis. *The American Journal of Sports Medicine*, 2020; 036354652093877 DOI: 10.1177/0363546520938776

31

Even mild concussions cause severe and long-lasting impairments in the brain's ability to clean itself of toxins, and this may seed it for Alzheimer's disease, dementia and other neurodegenerative problems

- When the brain swells, it presses against the skull, which effects tiny lymphatic vessels that clean the brain. This pressure on the vessels causes serious and long-lasting impairment of the brain's ability to purge itself of toxins

32

- Ashley C. Bolte, et. al. Meningeal lymphatic dysfunction exacerbates traumatic brain injury pathogenesis. *Nature Communications*, 2020; 11 (1) DOI: 10.1038/s41467-020-18113-4

33

The long-term risk of suicide for adults who have had a concussion is three times higher than the population norm, and the risk increases further if the concussion occurred on a weekend

- The mean time from concussion to subsequent suicide was 5.7 years. Additional concussions were associated with a further increased risk of suicide.

34

- M. Fralick, D. Thiruchelvam, H. C. Tien, D. A. Redelmeier. Risk of suicide after a concussion. *Canadian Medical Association Journal*, 2016; DOI: 10.1503/cmaj.150790

35

Damage from concussion alters the way information is transmitted between the two halves of the brain,

- Research has shown that the corpus callosum, a bundle of nerve fibers that carries signals between the brain's left and right hemispheres, is vulnerable to damage from mild traumatic brain injury, commonly known as concussion
- "We saw a correlation between white matter microstructure injury and the clinical status of the patient"

36



American Osteopathic College of Occupational & Preventive Medicine 2026 Midyear Educational Conference

- Radiological Society of North America. "Concussion alters how information is transmitted within the brain." ScienceDaily. ScienceDaily, 3 December 2019. <www.sciencedaily.com/releases/2019/12/191203082910.htm>.

37

Traumatic brain injury (TBI) during youth is associated with elevated risks of impaired adult functioning

- TBI consistently predicted later risk of premature mortality, psychiatric inpatient admission, psychiatric outpatient visits, disability pension, welfare reciprocity, and low educational attainment.
- The effects were stronger for those with greater injury severity, recurrence, and older age at first injury.

38

- Amir Sariaslan, David J. Sharp, Brian M. D'Onofrio, Henrik Larsson, Seena Fazel. Long-Term Outcomes Associated with Traumatic Brain Injury in Childhood and Adolescence: A Nationwide Swedish Cohort Study of a Wide Range of Medical and Social Outcomes. PLOS Medicine, 2016; 13 (8): e1002103 DOI: 10.1371/journal.pmed.1002103

39

These findings argue that impact sport athletes, regardless of history of concussion, have chronic problems.

- Show abnormal regulation of inflammation, less coordinated movement and abnormalities in how cells produce energy
- Increased over the course of the football season
- "This problem affects much of youth and professional impact sports in the U.S., along with training of U.S. military personnel,"

40

- Nathan W. Churchill, et. al. Neuroimaging of sport concussion: persistent alterations in brain structure and function at medical clearance. Scientific Reports, 2017; 7 (1) DOI: 10.1038/s41598-017-07742-3

41

Advanced MRI done to measure brain structure and function in 27 athletes within the first week after a concussion and again after they were medically cleared to return to play.

- Brain changes seen in the first MRI scan were still present when athletes were cleared to return to play, including:
- Persistent differences in the structure of the brain's white matter, the fibre tracts that allow different parts of the brain to communicate with each other
- Differences in brain activity, particularly in areas associated with vision and planning, with athletes that took longer to recover also showing changes in areas of the brain associated with bodily movement

42



American Osteopathic College of Occupational & Preventive Medicine 2026 Midyear Educational Conference

- Nicole L. Vike, et. al. A preliminary model of football-related neural stress that integrates metabolomics with transcriptomics and virtual reality. *Science*, 2021; 103483 DOI: 10.1016/j.isci.2021.103483

43

Head injuries can harm hundreds of genes in the brain in a way that increases people's risk for a wide range of neurological and psychiatric disorders

- Identified for the first time master genes that they believe control hundreds of other genes which are linked to Alzheimer's disease, Parkinson's disease, post-traumatic stress disorder, stroke, attention deficit hyperactivity disorder, autism, depression, schizophrenia and other disorders.

44

- Qingying Meng, et. al. Traumatic Brain Injury Induces Genome-Wide Transcriptomic, Methyloomic, and Network Perturbations in Brain and Blood Predicting Neurological Disorders. *EBioMedicine*, 2017; 16: 184 DOI: 10.1016/j.ebiom.2017.01.046

45

Traumatic brain injury is a leading cause of epilepsy

- Development of epilepsy triggered by mild traumatic brain injury may be related to an atypical response from brain cells known as astrocytes
- No treatments currently interrupt the process that the brain undergoes after injury that can eventually lead to the chronic condition of epilepsy.

46

- Oleksii Shandra, et. al. Repetitive Diffuse Mild Traumatic Brain Injury Causes an Atypical Astrocyte Response and Spontaneous Recurrent Seizures. *The Journal of Neuroscience*, 2019; 1067-18 DOI: 10.1523/JNEUROSCI.1067-18.2018

47

Unfortunately, there is no cure for concussions

- Careful observation and monitoring of the concussed patient must be done for a minimum of two weeks.

48



- "Dire effects of sports head injuries, concussions still a concern."
ScienceDaily. ScienceDaily, 19 October 2016.
<www.sciencedaily.com/releases/2016/10/161019082914.htm>

49

THERAPY

- YES, CONCUSSIONS CAN BE REVERSED!

50

Hyperbaric Oxygen Therapy (HBOT) significantly reduces astrogliosis (scarring by astrocytes) and glial scarring

- HBOT reduces inflammation and promotes neuroprotection, highlighting its potential to repair brain damage and restore function after injury

51

- da Silva SC, et. al. Hyperbaric oxygen therapy reduces astrogliosis and helps to recovery brain damage in hydrocephalic young rats. *Childs Nerv Syst.* 2018 Jun;34(6):1123-1134. doi: 10.1007/s00381-018-3803-0. Epub 2018 Apr 18. PMID: 29671042.

52

Hyperbaric Oxygen Therapy (HBOT)

- In HBOT the subject is placed in a chamber containing 100% oxygen at a pressure of more than one atmosphere absolute. This treatment is used to hasten tissue recovery and improve its physiological aspects by providing an increased supply of oxygen to the damaged tissue.
- The absolute best therapy for TBI

53

- HBOT is the absolute best therapy for TBI!

54



A RECENT THERAPY

- The first hyperbaric chamber, called the "Domicilium," was invented by British clergyman and physician Nathaniel Henshaw in 1662.

55

UHMS approved conditions

- Carbon monoxide poisoning
- Crush injuries
- Decompression sickness.
- Compromised skin grafts and flaps.
- Delayed radiation injury
- Air or gas embolism.
- Diabetic wounds that are not healing correctly
- Cyanide poisoning
- Gas gangrene
- Acute or traumatic reduced blood flow in the arteries
- Unresponsive osteomyelitis
- Flesh-eating disease (necrotizing soft tissue infection)
- Chronic infection called actinomycosis

56

Many other conditions treated worldwide

- Acquired Brain Injury (ABI)
- Autoimmune Disorders
- Birth Injury
- Brain Injury caused by Substance Abuse.
- Brain Injury from Radiation
- Concussion
- Chronic Decompression Sickness.
- Complex Regional Pain Syndrome.
- Fibromyalgia
- Anesthesia Injury
- Arthritis
- Brain Aneurysm
- Brain Injury from Chemotherapy
- Central Retinal Artery Occlusion
- Carbon Monoxide Poisoning
- Chronic Fatigue Syndrome
- Depression from Brain Injury
- Cancer

57

- Hashimoto's
- Inflammatory Conditions
- Mitochondrial Disorders
- Myofascial Pain Syndrome
- Peripheral Neuropathy Syndrome
- Reflex Sympathetic Dystrophy Syndrome
- Spinal Cord Compression Injury
- Toxic Brain Injury and more...
- Hypoxic Ischemic Encephalopathy
- Lyme Disease
- Mold Toxicity
- Near-hanging
- Post Concussion
- Post Traumatic Stress Disorder
- Shaken Baby Syndrome
- Tinnitus
- Infertility

58

Use real HBOT

- Hyperbaric treatment at minimally elevated chamber pressures (mild hyperbaric oxygen) is unproven. Mild hyperbaric oxygen therapy is currently considered to be exposures delivered at pressures lower than 1.5 ATA. Most clients in "mild hyperbaric chambers" receive breathing gas mixes well less than 95% O₂, often delivered through breathing devices such as masks that do not provide a tight seal and by the nature of their construction allow mixing of gases with the ambient chamber air, further reducing the oxygen concentration.

59

- <https://www.uhms.org/resources/featured-resources/hbo-indications.html>

60



Two types of chambers

- Mono-place
- Multi-place

61



62



63



64

Effects mediated by several pathways

- Inhibition of apoptosis, improvement of mitochondrial function, stem cell proliferation, enhancement of antioxidant defense activity, reduction inflammation, neuroprotection, transfer of mitochondria from astrocytes to neuronal cells, increased neuronal cell proliferation, improved antioxidant activity, anti-infective effects, regulates gene expression, improves immune function

65

- Irit Gottfried, et. Al. Hyperbaric Oxygen Treatment—From Mechanisms to Cognitive Improvement. *Biomolecules* 2021, 11(10), 1520; <https://doi.org/10.3390/biom11101520>

66



- Severe brain injury, a common form of clinical traumatic disease, is a critical condition. Brain injury has high disability and mortality rates and may cause respiratory tract obstruction, central apnea, pulmonary infection, epilepsy, hydrocephalus, post-traumatic syndrome, cognition and language disorders, and other sequelae that decrease the quality of life of patients

67

- Other studies reported that hyperbaric oxygen therapy could improve the indices of patients with severe brain injury, thereby significantly improving their prognosis. These findings are consistent with those of our study and indicate that hyperbaric oxygen therapy can effectively improve the prognosis of patients with severe brain injury.

68

- Xianliang Zhong, et. Al. Hyperbaric oxygen for severe traumatic brain injury: a randomized trial. Journal of International Medical Research, October 13, 2020.
- <https://doi.org/10.1177/0300060320939824>

69

Prognosis of spontaneous intracerebral hemorrhage (ICH) remains poor worldwide.

- This prospective, randomized, controlled trial included 565 patients with acute severe ICH. Participants were randomly assigned to a sham-control group (Group A) and four intervention groups: Groups B and C with 2.0 atmospheres absolute (ATA) pressure and HBOT exposure for 60 or 90 sessions, respectively; and Groups D and E with 1.5 ATA for 60 or 90 sessions, respectively. Outcome measures were modified Barthel Index (MBI) and modified Rankin Scale (mRS) scores, mortality rates at follow-up six months.

70

- In four intervention groups, MBI and mRS scores were all significantly improved, and mortality rates were all significantly decreased compared with Group A. HBOT significantly improves survival and functional outcomes of ICH.

71

- Xiaowei Li, et. Al. Hyperbaric-Oxygen Therapy Improves Survival and Functional Outcome of Acute Severe Intracerebral Hemorrhage. Archives of Medical Research, Volume 48, Issue 7, October 2017, Pages 638-652.
- <https://doi.org/10.1016/j.amrmed.2018.03.001>

72



American Osteopathic College of Occupational & Preventive Medicine 2026 Midyear Educational Conference

- In conclusion, there is an abundance of evidence for HBOT's improvement of neurological conditions in both molecular and therapeutic aspects. The main molecular changes that have been observed consist of improvements in myelination processes and mitochondrial activity, enhancement of angiogenesis, and a decrease in neuroinflammation. Therapeutic aspects include improvement of memory, cognitive and motor functions, and quality of life.

73

- Fischer, J.; Barak, B. Molecular and Therapeutic Aspects of Hyperbaric Oxygen Therapy in Neurological Conditions. *Biomolecules* 2020, 10, 1247. <https://doi.org/10.3390/biom10091247>

74

In a military veteran population nearly 70% of patients entering the Veterans Administration system with a diagnosis of TBI were still receiving treatment 4 years later

- Treatment has consisted of psychoeducational interventions, cognitive rehabilitation, psychotherapeutic approaches, integrated behavioral health interventions, and psychoactive medication administration. There is some evidence to support the use of cognitive rehabilitation approaches, limited evidence for the other three non-pharmacologic interventions, and very little evidence for psychoactive medications

75

This randomized clinical trial was undertaken to confirm or refute the efficacy of the of HBOT in persistent postconcussion syndrome (PPCS), 4-6 years after their last TBI

- Important findings in this study include significant improvements in postconcussion symptoms and seven other outcome variables [memory, cognition/speed of information processing (a computerized cognitive test battery, ANAM, developed and employed by the U.S. military for TBI), depression, anxiety, PTSD symptoms, sleep, and quality of life

76

- Paul G. Harch, et. al. Hyperbaric oxygen therapy for mild traumatic brain injury persistent postconcussion syndrome: a randomized controlled trial. *Med Gas Res.* 2020 Jan-Mar; 10(1): 8-20. doi: 10.4103/2045-9912.279978

77

Persistent post-concussion syndrome caused by mild traumatic brain injury has become a major cause of morbidity and poor quality of life

- Most of the pharmacologic and non-pharmacologic treatments have failed to demonstrate significant efficacy on both the clinical symptoms as well as the pathophysiologic cascade responsible for the permanent brain injury.

78



American Osteopathic College of Occupational & Preventive Medicine 2026 Midyear Educational Conference

- A most promising new direction is the use of hyperbaric oxygen therapy, which targets the basic pathological processes responsible for post-concussion symptoms

79

- Amir Hadanny & Shai Efrati (2016) Treatment of persistent post-concussion syndrome due to mild traumatic brain injury: current status and future directions, *Expert Review of Neurotherapeutics*, 16:8,875-887, DOI: 10.1080/14737175.2016.1205487

80

Stroke serves as a life-threatening disease and continues to face many challenges in the development of safe and effective therapeutic options

- HBOT can be used to improve oxygen flow from lungs to systemic organs and can reduce secondary brain injury effects, including apoptotic pathway initiation, oxidative stress, and rampant inflammation. By restoring oxygen tension, HBOT has been shown to restore cellular energy production, stabilize cellular calcium, decrease NADPH oxidases (NOXs) expression, and attenuate oxidative stress

81

- Blaise Cozene, et. al. An Extra Breath of Fresh Air: Hyperbaric Oxygenation as a Stroke Therapeutic. *Biomolecules* 2020, 10(9), 1279.
· <https://doi.org/10.3390/biom10091279>

82

There has been no major advancement in a quarter of a century for the treatment of acute severe traumatic brain injury (TBI)

- Studies consistently reported positive treatment effects of HBOT across a variety of outcome measures with almost no safety concerns, thus providing strong proof-of-concept evidence for treating severe TBI in the acute setting.

83

- Samuel Daly, et. al. Hyperbaric Oxygen Therapy in the Treatment of Acute Severe Traumatic Brain Injury: A Systematic Review. *Journal of Neurotrauma* VOL. 35, NO. 4.
· 15 Feb 2018 <https://doi.org/10.1089/neu.2017.5225>

84



Patients with TBI at least 3 years after the injury were treated with Hyperbaric Oxygen Therapy (HBOT).

- Those patients treated had permanent increases in blood flow to the brain that were in the normal range. In addition, speech fluency universally improved, as did memory, attention, and executive function (the ability to think rationally and effectively). Those patients who did not receive HBOT had no change in their symptoms.

85

- Barrett, K, et. al. (Undersea and Hyperbaric Medical Society, Inc. (<http://www.uhms.org>), 1998.
- <http://archive.rubicon-foundation.org/382>

86

Protocols

- Multiple protocols have been used, leading to no consensus on the best application of HBOT.

87

Equally compelling is the physiological evidence supporting the need for at least 40 HBOT sessions when contemplating growing new blood vessels for TBI

- Recent studies have demonstrated that increasing the number of HBOT sessions to 60 may be more beneficial for chronic TBI, considering the inherent progression and prolonged secondary cell death

88

- Borlongan CV, Hadanny A. Why provide 40 sessions of hyperbaric oxygen therapy to patients with traumatic brain injury? *Med Gas Res.* 2025 Mar 1;15(1):132-133. doi: 10.4103/mgr.MEDGASRES-D-24-00029. Epub 2024 Sep 25. PMID: 39436183; PMCID: PMC11515066.

89

- This author uses 1.75ata x 1h with 100% O₂
- Best to do as often as possible, although there are no studies comparing frequencies of sessions
- 1 session per weekday providing 5 sessions per week is the most common schedule

90



Impediments

- There are approximately 1,300 total hyperbaric oxygen therapy (HBOT) facilities in the United States, according to recent industry reports.
- There are about 300 independent, freestanding centers

91

- Hospital centers will not treat TBI, and only about 10% will treat emergencies
- Hospital costs are about 10x that of freestanding centers if paid out of pocket

92

OTHER THERAPIES

Pulsed Electromagnetic Field Therapy (PEMF)

- enhanced Neural Growth
- long-term, accelerated growth pattern
- influence gene expression affecting tissue regeneration

93

94

- Thomas J Goodwin. Physiological And Molecular Genetic Effects Of Time Varying Electromagnetic Fields (TVEMF) On Human Neuronal Cells. May 2003 Medicine and Science in Sports and Exercise 37(Supplement). DOI:10.1249/00005768-200505001-00867

Melatonin

- Has neuroprotective effects through its anti-inflammatory and antioxidant function, making it beneficial in reducing the reactive processes that occur after TBI

95

96



Mechanisms

- Attenuate pro-inflammatory NF κ B signaling, scavenge free radicals, decrease apoptotic cell death, and reduce the expression of abnormal proteins such as A β and p-tau.

97

- Blum B, Kaushal S, Khan S, Kim JH, Alvarez Villalba CL. Melatonin in Traumatic Brain Injury and Cognition. *Cureus*. 2021 Sep 6;13(9):e17776. doi: 10.7759/cureus.17776. PMID: 34659987; PMCID: PMC8494149.

98

Omega-3 fatty acids (n-3FA)

- Aggressive intake of omega-3 fatty acids (n-3FA) is beneficial to TBI, concussion, and post-concussion syndrome patients
- Growing clinical experience is that the brain needs to be saturated with high doses of n-3FA in order for the brain to have the opportunity to heal

99

- Michael D. Lewis. Concussions, Traumatic Brain Injury, and the Innovative Use of Omega-3s. *Journal of the American College of Nutrition*, 2016; 35(5):469
DOI: 10.1080/07315724.2016.11507962

100

Targeting mild TBI with different types of antioxidants can be a viable approach to treatment.

- Curcumin, sulforaphane, resveratrol and lipoic acid

101

Minerals

- Magnesium and zinc found to be most effective at improving both pre-clinical and clinical TBI outcome

102



- Lucke-Wold BP, et. al. Supplements, nutrition, and alternative therapies for the treatment of traumatic brain injury. *Nutr Neurosci.* 2018 Feb;21(2):79-91. doi: 10.1080/1028415X.2016.1236174. Epub 2016 Oct 5. PMID: 27705610; PMCID: PMC3491366.

103

Other agents

- Vitamin B2 (riboflavin), Vitamin B3 (nicotinamide), Vitamin B6 (pyridoxine), Vitamin B9 (folic Acid), Vitamin B12 (cobalamin), Vitamin C (ascorbic acid), Vitamin D, Vitamin E, selenium, creatine, ginseng, astaxanthin, pycnogenol

104

- Nwafor D, Goeckeritz J, Hasanpour Z, Davidson C, Lucke-Wold B. Nutritional Support Following Traumatic Brain Injury: A Comprehensive Review. *Explor Res Hypothesis Med.* 2023;8(3):236-247. doi: 10.14218/ERHM.2022.00086.

105

Psilocybin

- Assisted psilocybin use may have benefits in TBI by reducing inflammation, promoting neuroplasticity and neuroregeneration, and alleviating associated mood disorders.

106

Psilocybin acts primarily on serotonin (5-HT_{2A}) receptors

- significant improvements in cognitive function and brain scans
- stimulate neurogenesis and synaptogenesis
- lower inflammatory markers such as TNF- α , IL-6, and IL-8
- significant reductions in PTSD (up to 50%), depression (up to 65%), and anxiety

107

- Palmer C, Ferber AT, Greenwald BD. The Potential Role of Psilocybin in Traumatic Brain Injury Recovery: A Narrative Review. *Brain Sci.* 2025 May 26;15(6):572. doi: 10.3390/brainsci15060572. PMID: 40563744; PMCID: PMC12190232.

108



Vitamin D

- Vitamin D acts as a neurosteroid that reduces oxidative damage, attenuates brain edema, and inhibits the inflammatory response that causes secondary neuronal loss after TBI.

109

Vitamin D deficiency is correlated with neuroinflammation and neurocognitive defects.

- Vitamin D deficiency assessed longitudinally with measurements on admission, 7 days, and 3 months post-admission was associated with an increased likelihood of poorer Glasgow Outcome Scale-Extended (GOSE).

110

- Mahmoodkhani, Mehdi MDa et. al. Vitamin D deficiency is associated with worse neurological outcomes in moderate and severe traumatic brain injury: A prospective observational cohort study. *Medicine* 104(42):p e45202, October 17, 2025. | DOI: 10.1097/MD.00000000000045202

111

Administration of vitamin D supplements in mild-to-moderate TBI patients during the acute phase of the injury may improve long-term performance and cognitive outcomes

- The cognitive outcomes significantly improved from the first week to 3 months post TBI in the patients with vitamin D supplementation.

112

- Jong Min Lee, et. al. The Effect of Vitamin D Supplementation in Patients with Acute Traumatic Brain Injury. *World Neurosurgery*, Volume 126, 2019, Pages e1421-e1426. ISSN 1878-8750, <https://doi.org/10.1016/j.wneu.2019.02.244>.

113

- The only form of Vitamin D to use is D3, and it must be combined with K2

114



NEVER use D2!

- People taking vitamin D2 experienced a sharp drop in their vitamin D3 levels
- Vitamin D3 is superior in supporting immune and metabolic functions—Vitamin D3 stimulates genetic pathways that control inflammation, calcium absorption, and hormone regulation, while D2 lacks this same potency.

115

- Emily J G Brown, et. al. Effect of Vitamin D2 Supplementation on 25-Hydroxyvitamin D3 Status: A Systematic Review and Meta-Analysis of Randomized Controlled Trials, Nutrition Reviews, 2025; nuaf166, <https://doi.org/10.1093/nutrit/nuaf166>

116

Always use K2 with D3

- The hypothesis presented in this paper proposes the novel understanding that vitamin D exerts toxicity by inducing a deficiency of vitamin K.

117

- Masterjohn, C. Vitamin D toxicity redefined: Vitamin K and the molecular mechanism. Medical Hypotheses, Volume 68, Issue 5, 2007, Pages 1026-1034

118

- A high dose of vitamin K2 (100 mg/kg b.w.) inhibited the increase in the aortic Ca and P or in the renal Ca and P induced by vitamin D2
- A low dose of vitamin K2 (10 mg/kg b.w.) showed the same tendency

119

- Seyama, Y. Effect of vitamin K2 on experimental calcinosis induced by vitamin D2 in rat soft tissue. Int J Vitam Nutr Res., 1996;66(1):36-8.

120



K2 can also significantly reduce morbidity and mortality in cardiovascular health by reducing vascular calcification.

121

- Schwalfenberg, G. Vitamins K1 and K2: The Emerging Group of Vitamins Required for Human Health. *Journal of Nutrition and Metabolism*, vol. 2017, Article ID 6254836, 6 pages, 2017.

122

Low Dose Naltrexone (LDN)

- Naltrexone or 17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-one is a non-selective pure opioid antagonist with the highest affinity for μ -opioid receptors

123

In discrete 'low-doses' ranging from 1 to 5 mg, naltrexone acts as a glial modulator

- Glial cells are non-neuronal cells in the central (CNS) and peripheral (PNS) nervous systems that support, protect, and nourish neurons
- crucial for guiding neural development

124

Types

- Astrocytes (CNS): regulate blood flow, maintain the blood-brain barrier, and provide nutrients.
- Oligodendrocytes (CNS): Produce the myelin sheath.

125

- Microglia (CNS): Act as the immune cells of the brain, cleaning up debris and responding to injury.
- Schwann Cells (PNS): Form myelin in the peripheral nervous system.
- Ependymal Cells (CNS): Line the ventricles of the brain

126



American Osteopathic College of Occupational & Preventive Medicine 2026 Midyear Educational Conference

- LDN also reduces general inflammation, improves immune function, upregulates opioid function and decreases pain
- All of these functions are important for recovery

127

- Karlo Toljan1 and Bruce Vrooman. Low-Dose Naltrexone (LDN)—Review of Therapeutic Utilization. *Med. Sci.* 2018, 6(4), 82; <https://doi.org/10.3390/medsci6040082>

128

Previous reports indicated that mu opioid receptor (MOR) antagonists reduced neurodegeneration and inflammation after brain injury.

- Naltrexone reduced TBI-mediated neurodegeneration and inflammation, and the protective effect of naltrexone involves non-MOR and MOR mechanisms.

129

- Wang YS, Hung TW, Bae EK, Wu KJ, Hsieh W, Yu SJ. Naltrexone is neuroprotective against traumatic brain injury in mu opioid receptor knockout mice. *CNS Neurosci Ther.* 2021 Jul;27(7):831-841. doi: 10.1111/cns.13655. Epub 2021 May 21. PMID: 34018697; PMCID: PMC8193702.

130

Evidence from many studies has suggested that endogenous opioid peptides participate in a number of pathophysiological responses to brain injury.

- This provides the rationale for the use of opioid antagonists for the enhancement of neural recovery after brain injury.

131

A case is presented of an 18-year-old male who had loss of consciousness for 1 month after a severe brain injury.

- Three months of intensive rehabilitative therapies did not change his functional status.

132



- A trial of naltrexone was given while his performance in mobility, speech and overall Functional Independence Measure (FIM) scores were monitored. Results indicate an accelerated improvement in functional status and statistically improved FIM score.

133

- Calvanio R, Burke DT, Kim HJ, Cheng J, Lepak P, Leonard J, Dwyer MA, Gavande V. Naltrexone: effects on motor function, speech, and activities of daily living in a patient with traumatic brain injury. *Brain Inj.* 2000 Oct;14(10):933-42. doi: 10.1080/026990500445745. PMID: 11076138.

134

- Patients with postconcussional syndrome whose most severe symptoms were blackouts, headaches, and amnesia episodes responded to naltrexone

135

- Tennant FS Jr, Wild J. Naltrexone treatment for postconcussional syndrome. *Am J Psychiatry.* 1987 Jun;144(6):813-4. doi: 10.1176/ajp.144.6.813. PMID: 3592007.

136

Red Light Therapy

- Application of red/NIR light improves mitochondrial function (especially in hypoxic/compromised cells) promoting increased adenosine triphosphate (ATP). Nitric oxide is released locally, increasing regional cerebral blood flow.

137

These participants had experienced persistent cognitive dysfunction, ranging from 10 months to 8 years.

- All improved by at least +1 SD on the Stroop test for executive function, and/or verbal learning and memory on the California Verbal Learning Test post-LED therapy. They also reported improved sleep, and fewer post-traumatic stress disorder (PTSD) symptoms.

138



American Osteopathic College of Occupational & Preventive Medicine 2026 Midyear Educational Conference

- Naeser MA, et. al. Significant improvements in cognitive performance post-transcranial, red/near-infrared light-emitting diode treatments in chronic, mild traumatic brain injury: open-protocol study. *J Neurotrauma*. 2014 Jun 1;31(11):1008-17. doi: 10.1089/neu.2013.3244. Epub 2014 May 8. PMID: 24368233; PMCID: PMC4043367.

139

The researchers used functional MRI to gauge the effects of the light therapy, focusing on the brain's resting-state functional connectivity.

- They compared MRI results during three recovery phases: the acute phase of within one week after injury, the subacute phase of two to three weeks post-injury and the late-subacute phase of three months after injury.

140

- Patients who received low-level light therapy showed a greater change in resting-state connectivity in seven brain region pairs during the acute-to-subacute recovery phase compared to the control participants.

141

- Suk-tak Chan, et. al. Effects of Low-Level Light Therapy on Resting-State Connectivity Following Moderate Traumatic Brain Injury: Secondary Analyses of a Double-blinded Placebo-controlled Study. *Radiology*, Volume 311, Number 2
- <https://doi.org/10.1148/radiol.230999>

142

Twelve symptomatic military Veterans diagnosed with chronic TBI > 18 months post-trauma received pulsed transcranial tPBMT (tPBMT) containing 220 infrared and 180 red LEDs for 20 min, thrice per week over 6 weeks.

- Outcome measures included standardized neuropsychological test scores and qualitative and quantitative single photon emission computed tomography (SPECT) measures of regional cerebral blood flow (rCBF).

143

SPECT data clearly showed rCBF improvements in 8 of 12 participants.

- Six of 15 neuropsychological tests showed significant improvements in memory, concentration, and cognitive processing speed. All study participants verbally reported substantial reductions in many of their TBI symptoms.

144



American Osteopathic College of Occupational & Preventive Medicine 2026 Midyear Educational Conference

- Hipskind SG, Grover FL, Fort TR, et al. Pulsed Transcranial Red/Near-Infrared Light Therapy Using Light-Emitting Diodes Improves Cerebral Blood Flow and Cognitive Function in Veterans with Chronic Traumatic Brain Injury: A Case Series. *Photobiomodulation, Photomedicine, and Laser Surgery*. 2019;37(2):77-84. doi:10.1089/photob.2018.4489

145

Transcranial near-infrared low-level light therapy (LLLT) administered after traumatic brain injury (TBI) confers a neuroprotective response.

- There were statistically significant differences in the magnetic resonance imaging-derived diffusion parameters of the white matter tracts between the sham- and light-treated groups, demonstrating neuroreactivity of LLLT

146

- Figueiro Longo MG, Tan CO, Chan S, et al. Effect of Transcranial Low-Level Light Therapy vs Sham Therapy Among Patients With Moderate Traumatic Brain Injury: A Randomized Clinical Trial. *JAMA Netw Open*. 2020;3(9):e2017337. doi:10.1001/jamanetworkopen.2020.17337

147

- we analyzed white matter diffusion properties, including generalized fractional anisotropy, and the quantity of water diffusion in isotropic (i.e., isotropic diffusion) and anisotropic fashion (i.e., quantitative anisotropy, QA) for fibers crossing 11 brain areas known to be significantly affected following m TBI.

148

- Patients were given 6 weeks of daily morning blue light exposure therapy (compared to an amber-light placebo condition)

149

- We observed a significant impact of the blue light treatment (relative to the placebo) on the amount of water diffusion (QA) for multiple brain areas, including the corpus callosum, anterior corona radiata, and thalamus. Moreover, many of these changes were associated with improvements in sleep latency and delayed memory.

150



American Osteopathic College of Occupational & Preventive Medicine
2026 Midyear Educational Conference

- Bajaj S, Vanuk JR, Smith R, Dailey NS, Killgore WDS. Blue-Light Therapy following Mild Traumatic Brain Injury: Effects on White Matter Water Diffusion in the Brain. *Front Neurol*. 2017 Nov 22;8:616. doi: 10.3389/fneur.2017.00616. PMID: 29213254; PMCID: PMC5702646.

151

6 weeks of 30 min daily morning blue or placebo amber light therapy (ALT)

- Prior to and following treatment all individuals completed a comprehensive battery that included the Epworth Sleepiness Scale as a measure of self-reported daytime sleepiness. All individuals underwent a multimodal neuroimaging battery that included anatomical and resting-state functional magnetic resonance imaging.

152

- Following daily morning BLT, moderate to large increases in both gray matter volume and functional connectivity were observed in areas and networks previously associated with both sleep regulation and daytime cognitive function, alertness, and attention.

153

- BLT was associated with increased functional connectivity between the thalamus and both prefrontal and orbitofrontal cortices. Improved daytime sleepiness was associated with increased functional connectivity between attention and cognitive control networks as well as decreased connectivity between visual, motor, and attention networks

154

- Raikes AC, Dailey NS, Forbeck B, Alkozei A and Killgore WDS (2021) Daily Morning Blue Light Therapy for Post-mTBI Sleep Disruption: Effects on Brain Structure and Function. *Front. Neurol.* 12:625431. doi: 10.3389/fneur.2021.625431

155

DON'T!!!!

- Place patients on statins
- DC them if they are taking them

156



Multiple negative effects

- Inhibition of the cytochrome P450 3A4 system
- Cognitive loss
- Neuropathy
- Pancreatic and hepatic dysfunction

157

- Golomb BA, Evans MA. Statin adverse effects: a review of the literature and evidence for a mitochondrial mechanism. *Am J Cardiovasc Drugs*. 2008;8(6):373-418. doi: 10.2165/0129784-200808060-00004. PMID: 19159124; PMCID: PMC2849981.

158

These results demonstrate evidence of neurotoxicity associated with statin therapy.

- In addition, elevated oxidative stress caused by excess free radical generation was detected following simvastatin treatment

159

- Millichap, L. et. al. (2025). The effect of simvastatin induced neurotoxicity on mitochondrial function in human neuronal cells. *Toxicology Mechanisms and Methods*, 35(6), 592-603. <https://doi.org/10.1080/15376516.2025.2471807>

160

...deceptive approach statin advocates have deployed to create the appearance that cholesterol reduction results in an impressive reduction in cardiovascular disease outcomes

- ...also described how the directors of the clinical trials have succeeded in minimizing the significance of the numerous adverse effects of statin treatment

161

- Diamond DM, Ravnskov J. How statistical deception created the appearance that statins are safe and effective in primary and secondary prevention of cardiovascular disease. *Expert Rev Clin Pharmacol*. 2015 Mar;8(2):201-10. doi: 10.1586/17512433.2015.1012494. Epub 2015 Feb 12. PMID: 25672963.

162



The human brain is nearly 60 percent fat.

- Fatty acids are among the most crucial molecules that determine your brain's integrity and ability to perform.

163

- Chang CY, Ke DS, Chen JY. Essential fatty acids and human brain. *Acta Neurol Taiwan*. 2009 Dec; 18(4):231-41. PMID: 20329590.

164

25% of the cholesterol in your body is found in your brain

- In contrast to our expectations, high total cholesterol and high LDL cholesterol were associated with higher memory scores

165

- West R, et. al. Better memory functioning associated with higher total and low-density lipoprotein cholesterol levels in very elderly subjects without the apolipoprotein e4 allele. *Am J Geriatr Psychiatry*. 2008 Sep; 16(9):781-5. doi:

166

Ketogenic Diet

- Studies employing both pre- and postinjury implementation of the ketogenic diet have demonstrated improved structural and functional outcome in traumatic brain injury (TBI) models, mild TBI/concussion models, and spinal cord injury.

167

- Prins, Mayumi L. et al. The collective therapeutic potential of cerebral ketone metabolism in traumatic brain injury. *Journal of Lipid Research*, Volume 55, Issue 12, 2450-2457.

168



DC as many psych meds as possible

- Any drug effecting neurotransmitter levels will deplete the neurotransmitter system

169

- Parkinson's disease managing reversible neurodegeneration. Marty Hinz, Alvin Stein, Ted Cole, Beth McDougali, Mark Westaway. *Neuropsychiatric Disease and Treatment* 2016;12:1-13.
- Monoamine depletion by reuptake inhibitors. Marty Hinz, Alvin Stein, Thomas Uncini. *Drug, Healthcare and Patient Safety* 2011;3:69-77.
- Moncrieff, J., Cooper, R.E., Stockmann, T. et al. The serotonin theory of depression: a systematic umbrella review of the evidence. *Mol Psychiatry* 28, 3243-3256 (2023). <https://doi.org/10.1038/s41380-022-01661-0>

170

NT Repletion/Withdrawal

- 5-HTP: 150mg bid
- L-Tyrosine: 1500mg bid
- L-Cysteine: 4500mg/day
- Add multi-vitamin/mineral

171

Monitoring

- Brain Apps/Pt
- PT/OT
- Family
- Video

172

Brain Apps

- Free apps: BrainTrack, BoCA-Cognitive Monitoring
- Pay apps: CogniFit, Lumosity, Elevate, Peak, Fit Brains

173

Back to work

- Employer vs. Pt
- Employer with Pt
- Pt vs. Employer
- Pt with Employer

174



Situation determines evaluation

- If both are supporting return to work, use monitoring methods to determine initial return
- Start slow, low

175

Antagonistic

- This will often evolve into a legal battle
- Initially use same methods as cooperative

176

- An evaluation from Primary Care will rarely be accepted
- Often need evaluation from a Disability Physician
- Final determination by state-level Disability Determination Services (DDS)

177

<https://www.ssa.gov/disability/professionals/bluebook/general-info.htm>

- The SSA Blue Book lists impairments by body system, specifying the severity and duration of symptoms needed to qualify for benefits

178

Site for SSA evaluation guide

- <https://www.ssa.gov/disability/professionals/bluebook/AdultListings.htm>

179

- The Social Security Administration (SSA) defines disability as an inability to engage in any "substantial gainful activity" (SGA) due to a physical or mental impairment expected to result in death or last at least 12 months.

180



American Osteopathic College of Occupational & Preventive Medicine 2026 Midyear Educational Conference

<https://www.ssa.gov/redbook/index.html>

- The Red Book provides guidance on SSDI/SSI work incentives for employees and professionals.

181

- SSDI and SSI work incentives are Social Security Administration (gov) rules allowing people with disabilities to work and maintain benefits (cash payments, Medicaid, or Medicare). Key incentives include the Trial Work Period (TWP), which lets SSDI recipients earn any amount for 9 months (over 5 years) without losing benefits, and the Extended Period of Eligibility, providing 36 months of continued eligibility.

182

<https://adata.org/guide/ada-national-network-disability-law-handbook>

- The ADA National Network Disability Law Handbook outlines federal rights, obligations, and compliance.

183

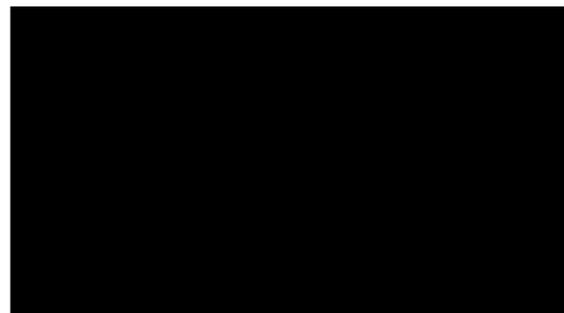
<https://www.transportation.gov/tags/disability-services-handbook>

- Department of Transportation: Disability Resource Center (DRC) Services Handbook

184

- These documents define eligibility criteria for benefits, outline legal protections, and provide guidance on accessibility, etiquette, and compliance.

185



186