

Cutting Through the Controversy: The Roll of Hyperbaric Oxygen Therapy (HBOT) in the Treatment of Traumatic Brain Injury

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DISCLOSURES

- San Francisco Institute for Hyperbaric Medicine
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- Scott Sherr, MD Independent Consulting
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- Sequoia Hospital Redwood City - Hospitalist



OBJECTIVES

- **Overview**
- What is HBOT
- Placebos and Shams: HBOT trial design
- TBI & HBOT
- Side Effects
- Cost
- Locations



HOW IS TBI CURRENTLY TREATED?

- Acute Hospital Care
- Rehabilitation: Speech, PT, OT, job training, cognitive/behavioral therapy, support groups.
- “Off Label” Drugs:
 - Antipsychotics
 - Amphetamines
 - Narcotics
 - Anti-Seizure Medications
 - Sleep Medications
 - Antidepressants: Black Box Warnings

No drug is FDA approved to treat TBI





HBOT: **It Heals Wounds**

FDA APPROVED* FOR HBOT:³

- **Delayed Radiation Injury**
- **Diabetic Foot Ulcers**
- **Refractory Osteomyelitis**
- **Sudden Sensorineural Hearing Loss**
- **Crush Injury, Compartment Syndrome, and other Acute Traumatic Ischemias**
- **Skin Grafts and Flaps**
- **Air or Gas Embolism**
- **Gas Gangrene**
- **Decompression Sickness**
- **Severe Anemia**
- **Necrotizing Soft Tissue Infections Thermal Burns**
- **Central Retinal Artery Occlusion**
- **Carbon Monoxide Poisoning and Smoke Inhalation**

*Insurance will cover some or all of the cost of treatment



INVESTIGATIONAL HBOT INDICATIONS

- **Traumatic Brain Injury***
- Stroke*
- Cerebral Palsy*
- Reflex Sympathetic Dystrophy (CRPS)*
- Surgical Recovery*
- Hip Osteonecrosis*
- Inflammatory Bowel Disease (UC, Crohn's)*
- Cancer*
- Stem Cell Yield*
- Cognitive Enhancement
- Lyme Disease
- Migraine Headaches
- Parkinson's disease
- Alzheimer's disease
- Rheumatoid Arthritis
- Osteoarthritis
- Multiple Sclerosis
- Heart Disease
- And more...

***Best data to support use**





FUNCTIONAL BRAIN IMAGING:

**Measuring blood flow and metabolic activity
patterns in the brain**

**SPECT Scans
Functional MRI**

PATIENT W.S.

- Former high functioning executive, falls and hits her head on a door frame, knocking herself unconscious.
- She could not walk after the event. Work-up in the ER was normal and she was sent home.
- Over the next 3 months, her symptoms worsened: difficulty with short term memory, directions, concentration, and severe migraine headaches.



W.S. (CONT.)

- Impulsivity followed and severe depression, which led to 2 suicide attempts.
- Inpatient psych hospital for 35 days.
- Sent home on an antipsychotic, antidepressant, narcotic, and a sleep aid medications.



W.S. (CONT.)

- Amen Clinic evaluation including SPECT imaging
- 80 sessions of HBOT @1.5 ATA X 60 minutes
- Dramatic improvements in all **subjective** categories and marked **objective** improvement on ImPACT testing
- No further headaches
- She does not get lost any more
- She can concentrate
- Depression is gone
- Off most of her medications



PATIENT J.R.

- 65 y/o Army Veteran with TBI & PTSD since 1972 with terrible nightmares, a violent temper, and a history of domestic violence.
 - After 20 HBOT treatments his nightmares went away and never came back.
 - After 40 treatments, his aggression went away completely.



PATIENT P.R.

- 18 y/o male in a MVA with severe TBI, nonverbal partial quadriplegic, “given up” on by rehab specialists.
 - Walking with a cane & conversant after 120 HBOT treatments



RECOVERY FROM A TBI: IT'S NOT EASY¹

A healthy brain utilizes ALL energy
supplied to it

15% of the Cardiac Output

20% of the Total Body Oxygen Consumption

25% of the Total Body Glucose

5 to 10% of neurons are active at any one time

RECOVERY FROM A TBI: IT'S NOT EASY¹

Healing from brain injury requires additional energy (Oxygen  ATP)

This energy is not in ready supply given already high metabolic demands of brain tissue.



HBOT: It Heals Wounds

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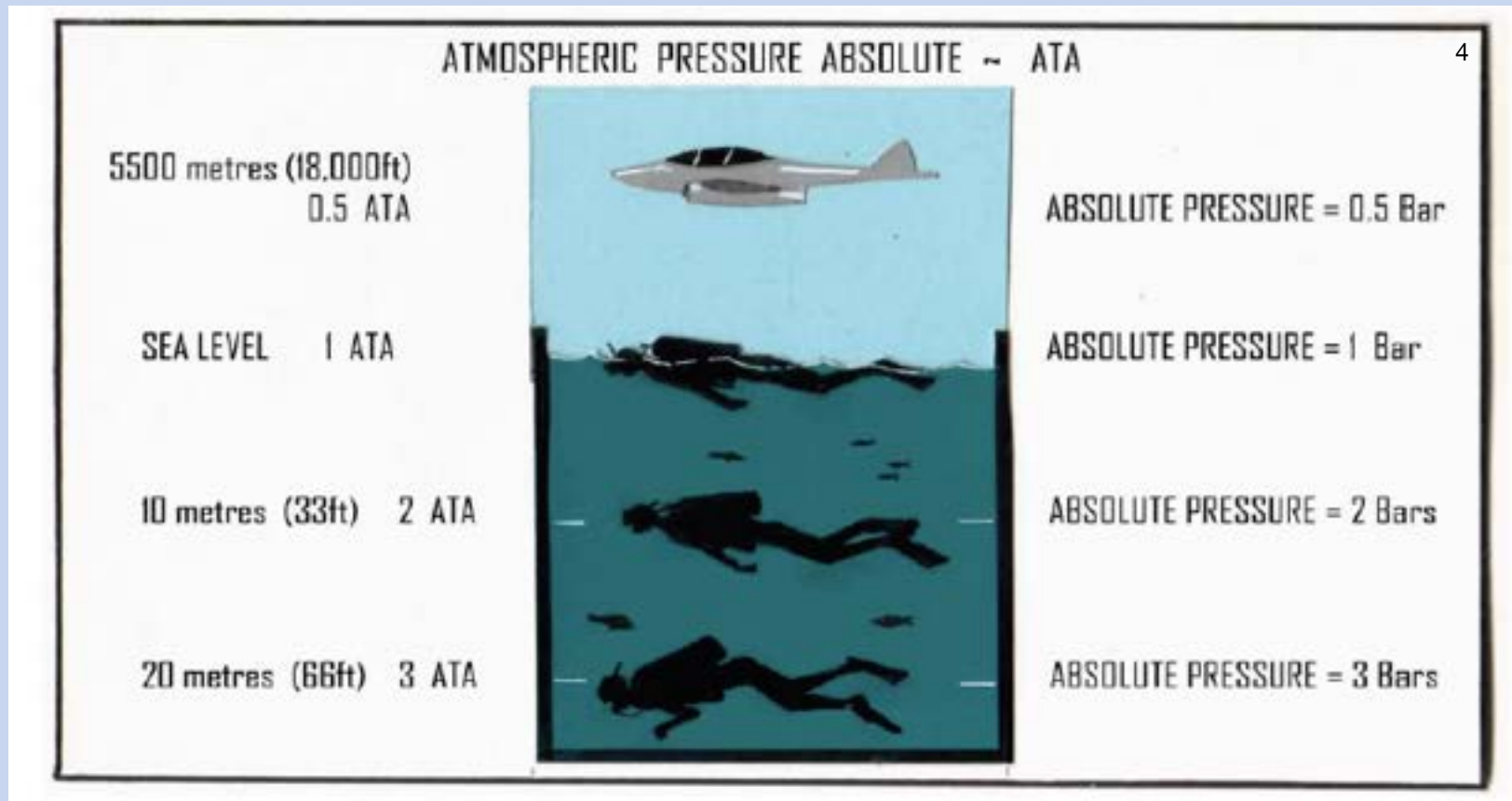
WHAT IS IN THE AIR?²

- 21% Oxygen
- 78% Nitrogen
- Argon, Krypton, CO₂, Neon, CO, Methane, Xenon, Hydrogen, Helium, and others
- Highest place on earth?
 - Mt. Everest: 29,035 feet above sea level
- Lowest place on earth?
 - Dead Sea: 1,371 feet below sea level
 - <http://www.deadsea-health.org/>



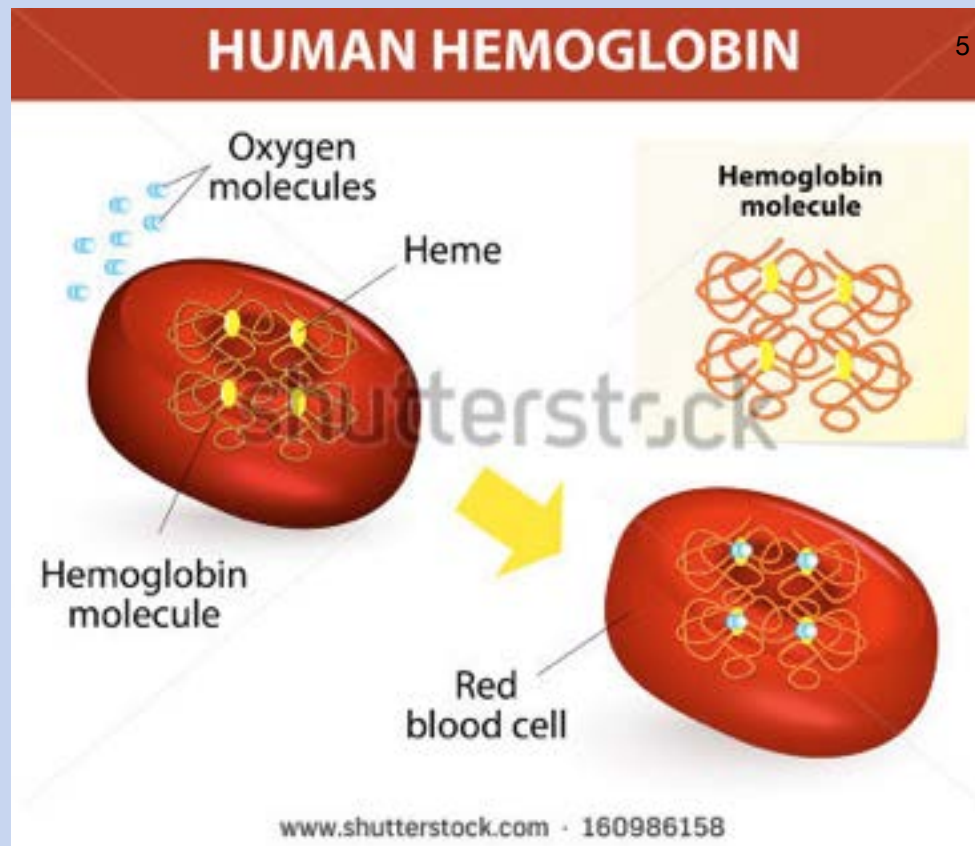
HBOT DEFINITION:³

- The intermittent administration of 100% **Oxygen** at higher-than-atmospheric **pressure**.



HBOT: IT'S NOT ABOUT THE RBC

- Hemoglobin is **already** 97% saturated with oxygen at sea level.

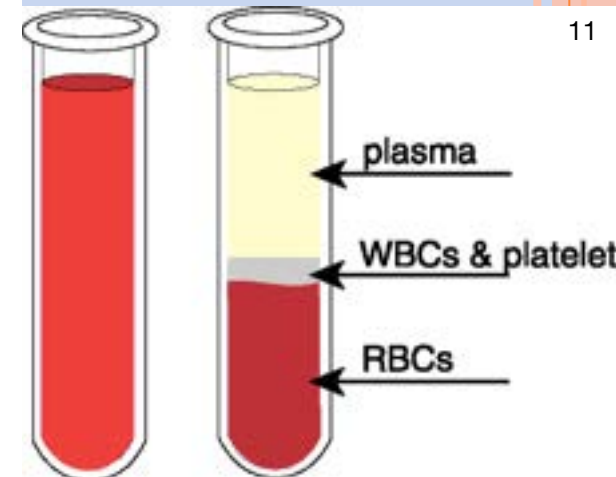
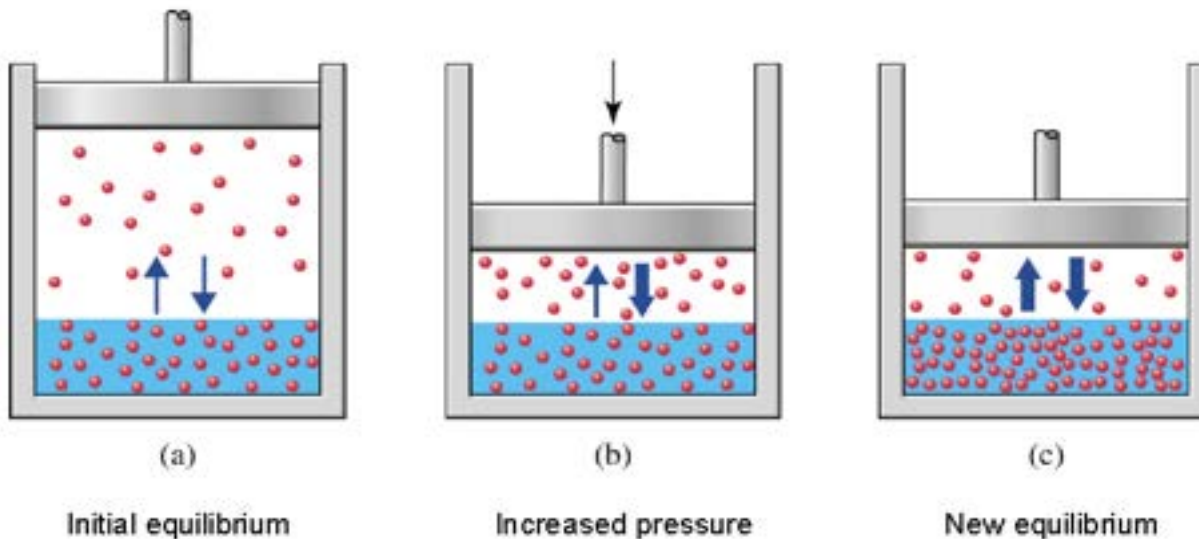


HBOT: PRESSURE IS KEY

- Effect of HBOT is due to its ability to supersaturate the blood plasma with oxygen via Henry's Law.

Gas Solubility – Effect of Pressure

6



11

MULTIPLACE CHAMBER^{7,8}



MONOPLACE CHAMBER





SUPER-SATURATING PLASMA WITH OXYGEN

3,9,10

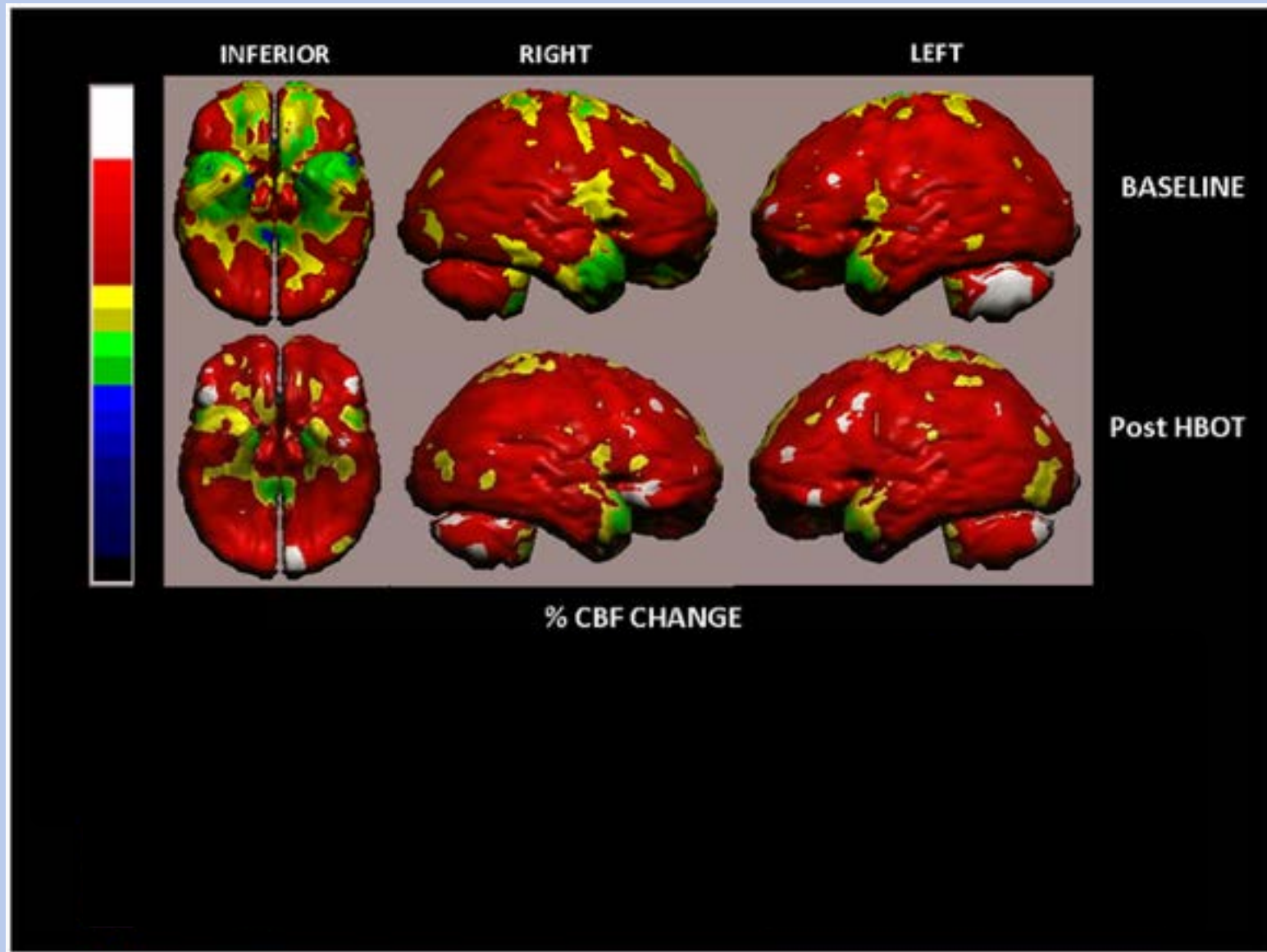
Acute Ischemic Injury
Cellular Metabolism
DNA

HBOT & TBI: MECHANISMS^{1,3,11,13,} OF HEALING

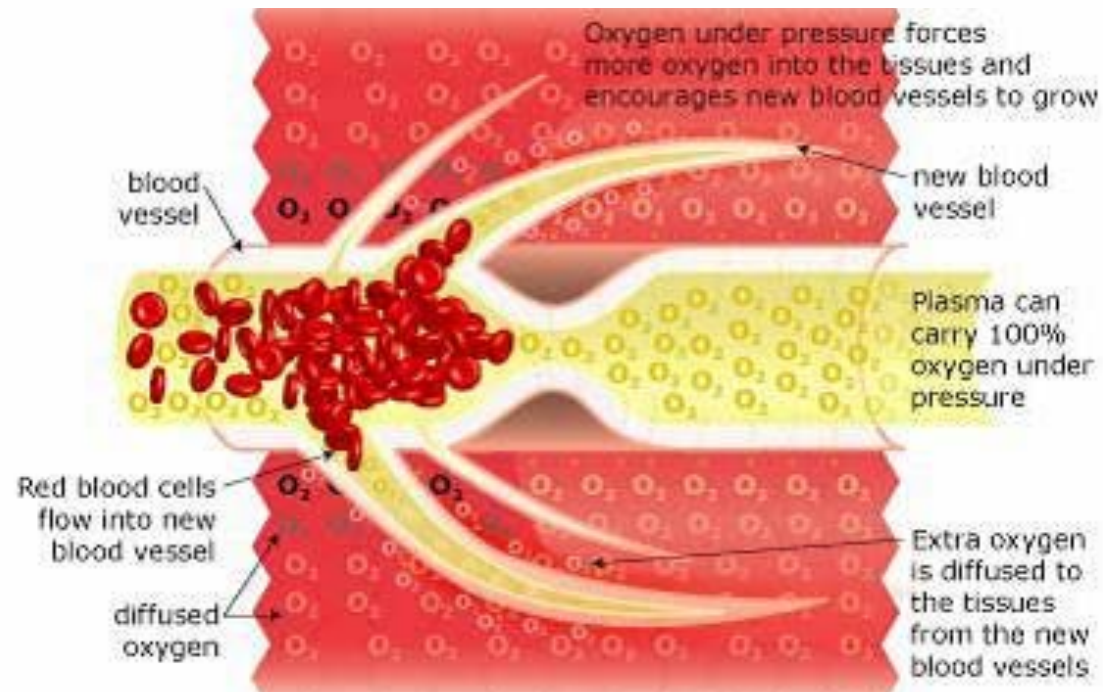
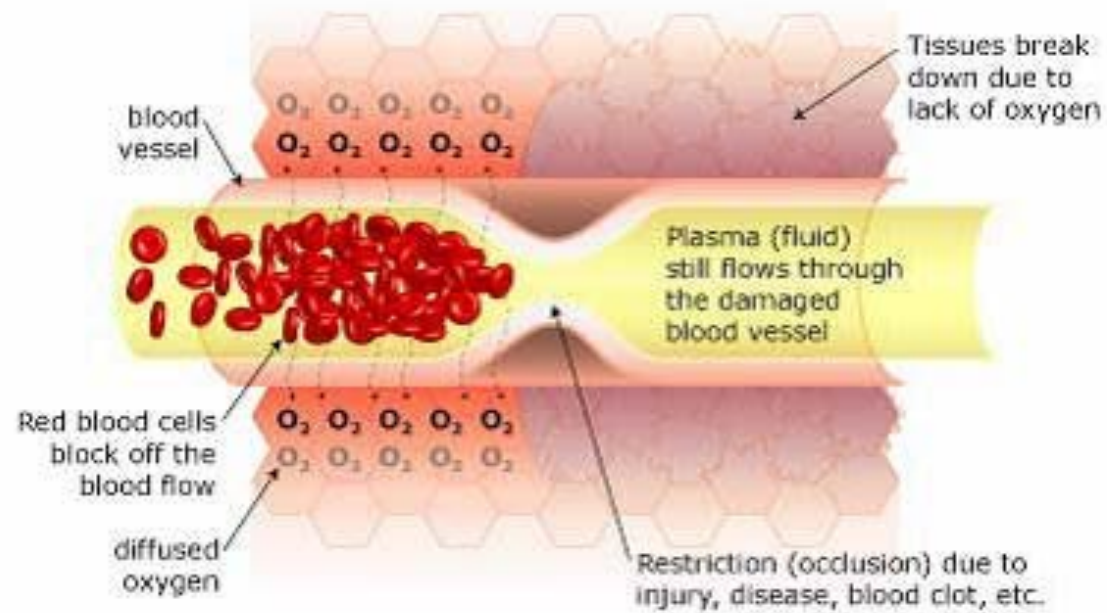
- HBOT in acute TBI
 - Decreasing intracranial pressure
 - Decreasing inflammation
 - Preventing Apoptosis
 - Protecting peri-contusional tissue from secondary ischemia
 - Ramps up efficiency of wound healing
 - Stem cell mobilization to damaged tissue
- HBOT in chronic TBI:
 - Regeneration of “**stunned**” axons & glia in peri-contusional tissue
 - Angiogenesis
 - Stem cell mobilization and proliferation to damaged tissue
 - Preventing apoptosis



Figure 9. Volume rendered Brain SPECT perfusion maps of Example 2.



Boussi-Gross R, Golan H, Fishlev G, Bechor Y, Volkov O, et al. (2013) Hyperbaric Oxygen Therapy Can Improve Post Concussion Syndrome Years after Mild Traumatic Brain Injury - Randomized Prospective Trial. PLoS ONE 8(11): e79995. doi:10.1371/journal.pone.0079995
<http://127.0.0.1:8081/plosone/article?id=info:doi/10.1371/journal.pone.0079995>



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PLACEBO: A MEDICALLY INEFFECTIVE TREATMENT

²

An effective placebo simulates treatment in all ways EXCEPT for the intervention in question

A placebo is called a sham when a procedure is involved

PLACEBOS & SHAMS: HBOT TRIAL DESIGN

Tx Group

15



Control Group

16



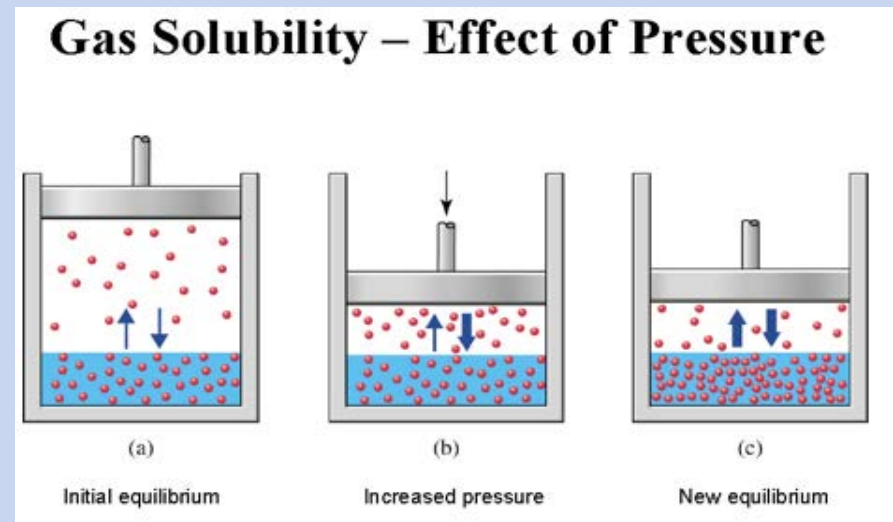
The problem with HBOT trial design is that you have EARS and can sense pressure changes!



PLACEBOS & SHAMS: HBOT TRIAL DESIGN

- 1.2 to 1.3 ATA is the minimum pressure needed to “feel it” in your ears
- An increase in pressure by ANY AMOUNT will also increase dissolved O₂ into circulation ¹⁷
- Even small changes in air pressure can have measurable effects on human physiology ¹
- **HBAT 1.3ATA: 43% more O₂ in blood**
- **HBOT 1.5ATA: 700%**
- **HBOT 2.4ATA: 1200%**

HBAT of 1.3 ATA is the sham treatment in military trials





PLACEBOS & SHAMS: HBOT TRIAL DESIGN

A sham group that receives ANY increase in pressure, oxygen, and/or nitrogen will NOT be a true sham

They all have physiologic effect

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- **TBI & HBOT**
 - **HBOT heals**
 - HBOT heals? The military trials
- Protocol
- Side Effects
- Cost
- Locations



HBOT & TBI: EVIDENCE

- HBOT heals:
 - **Rockswald et al. (RCT)- Acute, Severe TBI**
 - **Boussi-Gross et al. (RCT) –Mild TBI (mTBI)**
 - Harch (Observational) –Mild TBI
 - Boussi-Gross et al. (RCT) –Stroke



ACUTE, SEVERE TBI

J Neurosurg 118:1317–1328, 2013

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A prospective, randomized Phase II clinical trial to evaluate the effect of combined hyperbaric and normobaric hyperoxia on cerebral metabolism, intracranial pressure, oxygen toxicity, and clinical outcome in severe traumatic brain injury

Clinical article

*SARAH B. ROCKSWOLD, M.D.,¹⁻³ GAYLAN L. ROCKSWOLD, M.D., PH.D.,^{3,4} DAVID A. ZAUN, M.S.,⁵
AND JIANNONG LIU, PH.D.⁵

¹Department of Physical Medicine and Rehabilitation and ³Division of Neurosurgery, Department of Surgery, Hennepin County Medical Center; Departments of ²Medicine and Rehabilitation and ⁴Neurosurgery, University of Minnesota, Minneapolis, Minnesota; and ⁵Analytical Services, Chronic Disease Research Group, Minneapolis Medical Research Foundation, Minneapolis, Minnesota



ROCKSWALD ET AL.

ACUTE, SEVERE TBI

- 42 patients with mean GCS of 5.7 were prospectively randomized into two groups:
- HBOT (100% Oxygen) at 1.5 ATA x 60 minutes followed by 3 hours of 100% face mask oxygen at 1.0 ATA on 3 successive days
- Standard TBI care (No HBOT chamber)
- Sham not needed: sedated and paralyzed



ROCKSWALD ET AL.

ACUTE, SEVERE TBI

- Brain tissue PO₂ levels increased 600%
- **Peri-contusional brain** tissue had PO₂ levels 20% higher than control lasting until next treatment
- **Decreased intracranial pressure** that lasted until next HBOT session
- Significantly **improved markers of cerebral metabolism** especially in peri-contusional brain
- It was safe: no increase in markers of lung or brain toxicity



ROCKSWALD ET AL. ACUTE, SEVERE TBI

HBOT Safe
HBOT Neuro-protective

—
Improved Mortality
Improved Outcomes

- An absolute **26% reduction** in mortality in the combined HBO2/NBH group ($p = 0.048$)
 - 16% of patients died in HBOT group
 - 42% died in the control group
- An absolute **36% improvement in favorable outcome** using the sliding dichotomized GOS ($p = 0.024$) as compared with the control group.
- Phase III study recommended for confirmation of results



HBOT & MTBI

OPEN ACCESS Freely available online

PLOS ONE

Hyperbaric Oxygen Therapy Can Improve Post Concussion Syndrome Years after Mild Traumatic Brain Injury - Randomized Prospective Trial

Rahav Boussi-Gross^{1,3}, Haim Golan^{3,4,5}, Gregori Fishlev¹, Yair Bechor¹, Olga Volkov^{3,4}, Jacob Bergan¹, Mony Friedman¹, Dan Hoofien^{6,7}, Nathan Shlamkovitch⁸, Eshel Ben-Jacob^{2,5,9,10*}, Shai Efrati^{1,2,3,10*}

1 The Institute of Hyperbaric Medicine, Assaf Harofeh Medical Center, Zerifin, Israel, **2** Research and Development Unit, Assaf Harofeh Medical Center, Zerifin, Israel, **3** Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel, **4** Nuclear Medicine Institute, Assaf Harofeh Medical Center, Zerifin, Israel, **5** The Raymond and Beverly Sackler Faculty of Exact Sciences, School of Physics and Astronomy, Tel-Aviv University, Tel-Aviv, Israel, **6** Department of Psychology, The Hebrew University of Jerusalem, Jerusalem, Israel, **7** The National Institute for the Rehabilitation of the Brain Injured, Tel-Aviv, Israel, **8** Otolaryngology, Head & Neck Surgery, Assaf-Harofeh Medical Center, Zerifin, Israel, **9** Center for Theoretical Biological Physics, Rice University, Houston, Texas, United States of America, **10** Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel

Abstract

Background: Traumatic brain injury (TBI) is the leading cause of death and disability in the US. Approximately 70-90% of the TBI cases are classified as mild, and up to 25% of them will not recover and suffer chronic neurocognitive impairments. The main pathology in these cases involves diffuse brain injuries, which are hard to detect by anatomical imaging yet noticeable in metabolic imaging. The current study tested the effectiveness of Hyperbaric Oxygen Therapy (HBOT) in improving brain function and quality of life in mTBI patients suffering chronic neurocognitive impairments.

Methods and Findings: The trial population included 56 mTBI patients 1–5 years after injury with prolonged post-concussion syndrome (PCS). The HBOT effect was evaluated by means of prospective, randomized, crossover controlled trial: the patients were randomly assigned to treated or crossover groups. Patients in the treated group were evaluated at baseline and following 40 HBOT sessions; patients in the crossover group were evaluated three times: at baseline, following a 2-month control period of no treatment, and following subsequent 2-months of 40 HBOT sessions. The HBOT protocol included 40 treatment sessions (5 days/week), 60 minutes each, with 100% oxygen at 1.5 ATA. "Mindstreams" was used for cognitive evaluations, quality of life (QOL) was evaluated by the EQ-5D, and changes in brain activity were assessed by SPECT imaging. Significant improvements were demonstrated in cognitive function and QOL in both groups following HBOT but no significant improvement was observed following the control period. SPECT imaging revealed elevated brain activity in good agreement with the cognitive improvements.

Conclusions: HBOT can induce neuroplasticity leading to repair of chronically impaired brain functions and improved quality of life in mTBI patients with prolonged PCS at late chronic stage.

Trial Registration: ClinicalTrials.gov NCT00715052

HBOT & mTBI: BOUSSI-GROSS ET AL.

- 56 patients with Post Concussive Syndrome (mTBI)
- **1 to 6 years** post traumatic event (civilian)
- Prospective Randomized Cross Over Control Study: both groups treated at different times
- 40 sessions of HBOT
- HBOT (100% Oxygen) at 1.5 ATA x 60 minutes
- **SPECT Scans** before & 1 to 3 weeks after treatment (blinded)



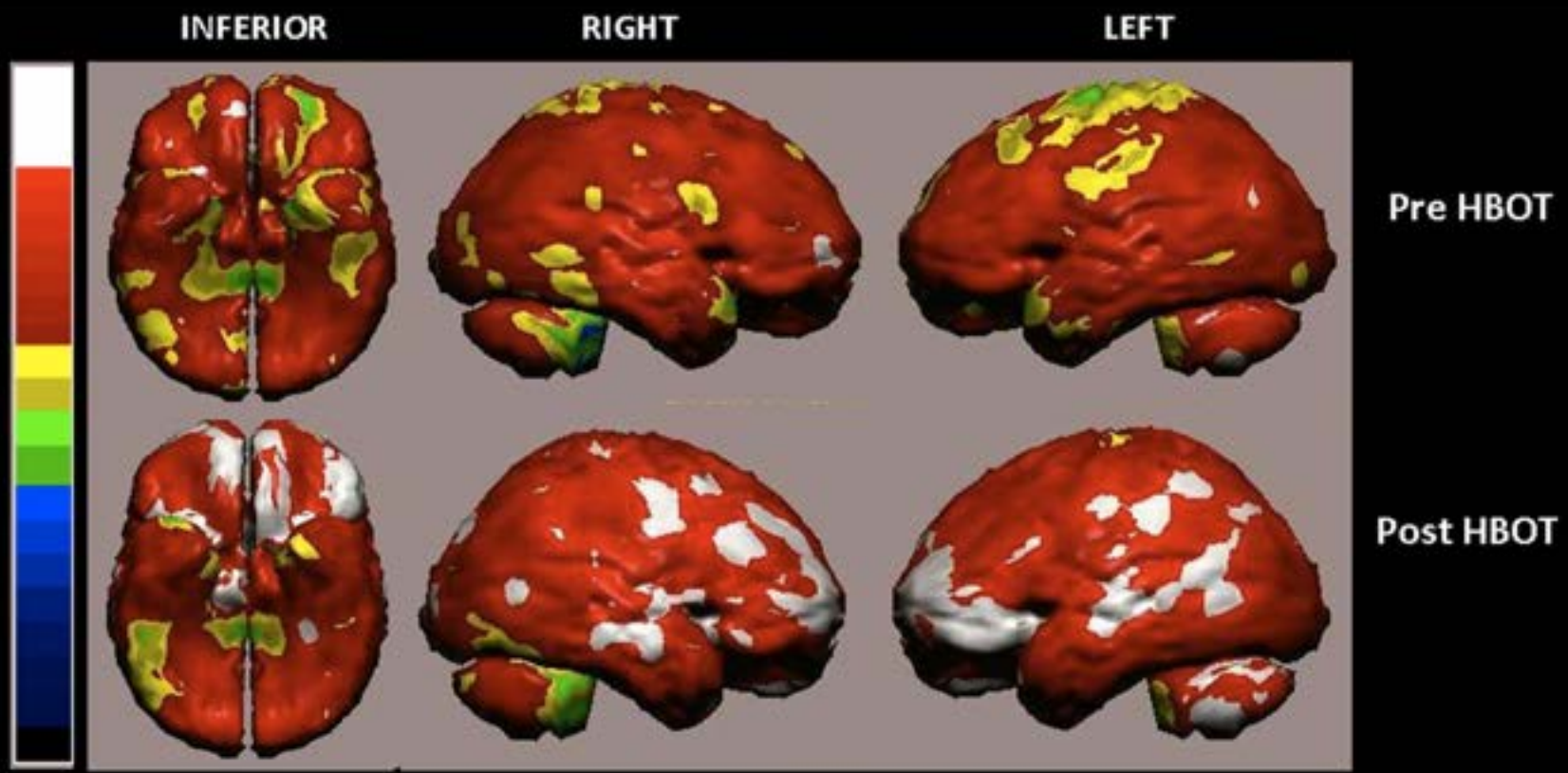
HBOT & MTBI: BOUSSI-GROSS ET AL.

HBOT significantly improved:

- Information processing speed
- Attention
- Memory
- Executive function
- SPECT Scans
- Quality of Life (QOL on EQ-5D & EQ-VAS score)

Objective Tests

Significant improvements in blood flow on SPECT Scans correlated to areas of improvement on cognitive testing → **Reactivation of “stunned” brain**



51-year-old woman from the treated group suffering mTBI that had occurred 2 years prior to inclusion in the study

HBO & MTBI: HARCH ET AL.

After 1 HBOT



After 40 HBOT



OBJECTIVES

- What is HBOT
- Placebos and Shams: HBOT trial design
- **TBI & HBOT**
 - HBOT heals!
 - **HBOT heals? The military trials**
- Protocol
- Side Effects
- Cost
- Locations



HBOT & TBI: EVIDENCE

- HBOT heals? Military trials of HBOT safety and feasibility in mTBI
- Conclusions: HBOT safe, feasible, but **no effect**
 - Wolf et al. (RCT)
 - Miller et al. (RCT)
 - Cifu et al. (RCT)
 - Churchill et al. (RCT)

No
functional
imaging

All studies included a sham group that was NOT a true sham

Sham received Increased Pressure, Increased Oxygen, and/or Increased Nitrogen ALL which have physiologic effect



MILITARY HBOT TRIALS

Flawed Study Designs = Flawed Conclusions

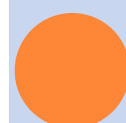
**All groups that received increased oxygen
(HBAT or HBOT) improved**

The Effect of Hyperbaric Oxygen on Symptoms after Mild Traumatic Brain Injury

George Wolf,¹ David Cifu,^{2–4} Laura Baugh,^{1,5} William Carne,^{3,4,6} and Leonardo Profenna¹

Abstract

In this single-center, double-blind, randomized, sham-controlled, prospective trial at the U.S. Air Force School of Aerospace Medicine, the effects of 2.4 atmospheres absolute (ATA) hyperbaric oxygen (HBO₂) on post-concussion symptoms in 50 military service members with at least one combat-related, mild traumatic brain injury were examined. Each subject received 30 sessions of either a sham compression (room air at 1.3 ATA) or HBO₂ treatments at 2.4 ATA over an 8-week period. Individual and total symptoms scores on Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT[®]) and composite scores on Post-traumatic Disorder Check List-Military Version (PCL-M) were measured just prior to intervention and 6 weeks after completion of intervention. Difference testing of post-intervention means between the sham-control and HBO₂ group revealed no significant differences on the PCL-M composite score ($t = -0.205$, $p = 0.84$) or on the ImPACT total score ($t = -0.943$, $p = 0.35$), demonstrating no significant effect for HBO₂ at 2.4 ATA. PCL-M composite scores and ImPACT total scores for sham-control and HBO₂ groups revealed significant improvement over the course of the study for both the sham-control group ($t = 3.76$, $p = 0.001$) and the HBO₂ group ($t = 3.90$, $p = 0.001$), demonstrating no significant HBO₂ effect. Paired t-test results revealed 10 ImPACT scale scores in the sham-control group improved from pre- to post-testing, whereas two scale scores significantly improved in the HBO₂ group. One PCL-M measure improved from pre- to post-testing in both groups. This study showed that HBO₂ at 2.4 ATA pressure had no effect on post-concussive symptoms after mild TBI.



HBOT & MTBI: WOLF ET AL.

- 2 groups:
 - “Treatment” 100% oxygen @ 2.4 ATA X 90 minutes
 - “Sham” compressed air @ 1.3 ATA X 90 minutes
- 50 patients
- 30 sessions
- 3 to 71 months post event
- ImPACT and PCL-M testing before and 6 weeks after.



HBOT & mTBI: WOLF ET AL.

- Conclusion:
 - HBOT safe, feasible, but not effective
 - No difference in improvement between Sham vs. Treatment groups but...
 - **“Both groups improved more than what would be expected greater than 6 months after mTBI”**



TABLE 2. IMPACT SCALE MEANS FOR SHAM-CONTROL AND HBO₂ GROUPS AT BASELINE AND POST-TREATMENT INTERVAL.

Symptom	Control baseline	Control 6 weeks post	P value	HBO ₂ baseline	HBO ₂ 6 weeks post	P value
Headache	3.4	2.0	0.002*	3.3	2.6	ns
Nausea	1.1	0.9	ns	0.2	0.4	ns
Vomiting	0.0	0.0	ns	0.0	0.0	ns
Balance	1.4	1.0	ns	1.5	1.2	ns
Dizziness	1.3	1.2	ns	0.9	1.2	ns
Fatigue	3.4	1.7	0.005*	3.1	2.6	ns
Trouble falling asleep	4.2	2.2	0*	4.2	2.7	0.01*
Sleeping more than usual	0.7	0.3	0.038*	0.2	0.7	ns
Sleeping less than usual	1.2	0.5	0.038*	1.8	0.6	0.03*
Drowsiness	3.3	1.4	ns	1.9	2.5	ns
Sensitivity to light	2.2	1.8	ns	1.9	1.8	ns
Sensitivity to noise	1.7	0.9	ns	1.5	1.7	ns
Irritability	2.3	1.3	0.032*	3.0	2.7	ns
Sadness	1.3	0.5	0.029*	1.3	1.5	ns
Nervousness	1.6	0.8	0.046*	2.0	1.0	ns
Emotionality	0.8	0.3	0.046*	1.3	0.9	ns
Numbness	2.0	0.9	ns	1.7	0.8	ns
Slower than usual	1.4	0.5	0.01*	1.2	1.4	ns
Feeling foggy	1.2	1.3	ns	1.3	1.5	ns
Concentration problems	3.0	2.5	ns	2.9	2.5	ns
Trouble remembering	4.8	2.8	ns	2.8	2.8	ns
Visual problems	1.0	0.8	ns	0.8	0.8	ns

*p = significant.

TABLE 3. PCL-M MEANS FOR SHAM-CONTROL AND HBO₂ GROUPS AT BASELINE AND POST-TREATMENT INTERVAL.

Symptom	Control baseline	Control 6 weeks post	P value	HBO ₂ baseline	HBO ₂ 6 weeks post	P value
Composite score	48.9	40.6	0*	50.0	41.6	0*
Re-experiencing	2.2	2.0	ns	2.8	2.2	ns
Avoidance	3.3	2.9	ns	3.3	2.5	ns
Arousal	4.2	2.8	0*	3.8	2.6	0.001*

*p < 0.05.

ImPACT
(TBI)

PCL-M
(PTSD)

HBOT & MTBI: WOLF

Study Limitations:

- **1.3 ATA breathing compressed air is NOT a placebo: 43% increase in oxygen plasma concentration**
- 30 treatments
- 2.4 ATA is likely too much pressure
- No functional brain imaging
- Follow up data not yet published



Original Investigation

Effects of Hyperbaric Oxygen on Symptoms and Quality of Life Among Service Members With Persistent Postconcussion Symptoms

A Randomized Clinical Trial

R. Scott Miller, MD; Lindell K. Weaver, MD; Nazanin Bahraini, PhD; Susan Churchill, APRN-NP; Robert C. Price, MD; Virginia Skiba, MD; James Caviness, MD; Scott Mooney, PhD; Brian Hetzell, MS; Jun Liu, PhD; Kayla Denu, BA; Richard Ricciardi, PhD; Susan Francisco, MD; Nicole C. Close, PhD; Gerald W. Surratt, MD; Corinna Bartos, MD; Margaret Ryan, MD; Lisa A. Brenner, PhD; for the HOPP5 Trial Team

IMPORTANCE Improvement has been anecdotally observed in patients with persistent postconcussion symptoms (PCS) after mild traumatic brain injury following treatment with hyperbaric oxygen (HBO). The effectiveness of HBO as an adjunctive treatment for PCS is unknown to date.

OBJECTIVES To compare the safety of and to estimate the efficacy for symptomatic outcomes from standard PCS care alone, care supplemented with HBO, or a sham procedure.

DESIGN, SETTING, AND PARTICIPANTS Multicenter, double-blind, sham-controlled clinical trial of 72 military service members with ongoing symptoms at least 4 months after mild traumatic brain injury enrolled at military hospitals in Colorado, North Carolina, California, and Georgia between April 26, 2011, and August 24, 2012. Assessments occurred before randomization, at the midpoint, and within 1 month after completing the interventions.

← Invited Commentary page 53

+ Supplemental content at
jamanetwork.com



HOPPS TRIAL

- 3 groups:
 - No HBOT
 - 1.2 ATA + pressurized air (Sham)
 - 1.5 ATA + 100% Oxygen.
- Conclusions:
 - HBOT group significantly improved
 - Sham group also significantly improved
 - Both Sham & HBOT improved significantly vs. no HBOT
 - Trend towards greater effect in **HBOT group**, but no significant difference between groups.
 - Placebo effects responsible for improvements





MILITARY HBOT TRIALS

Flawed Study Designs = Flawed Conclusions

**All groups that received increased oxygen
(HBAT or HBOT) improved**

HBOT & TBI: CLINICAL TRIALS

- BIMA: Completion date estimation: 12/2014
- NBIRR: under review for publishing
- Enrolling (now or soon):
 - **LSU HBOT:** enrolling
 - Joe Namath HBOT trial: former NFL players
 - **UTAH HYBOBI II:** enrolling soon
 - University of Washington: HBOT + Stem Cell Therapy
 - University of MN (Acute, Severe TBI)
 - Hyperbaric Medical Solutions in NY: Acute concussion and HBOT



OBJECTIVES

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- **Protocol**
- Side Effects
- Cost
- Locations



HBOT & TBI PROTOCOL

- Acute, Severe TBI: (inpatient HBOT)
 - HBOT 1.5 ATA X 60 minutes + 100% FIO2 @1.0 ATA X 3 hours on at least 3 successive days
- Acute mTBI (concussion)
 - HBOT 1.5 ATA X60 minutes for 2 to 10 sessions?
- Chronic TBI:
 - Neurocognitive testing
 - SPECT Scanning
 - HBOT 100% oxygen 1.5 ATA X 60 minutes for 40 sessions
 - Treatments are done in **succession (5 to 6 days per week) because of the cumulative nature of HBOT**
 - Up to 120 sessions may be helpful
 - HBOT maintenance treatment? Possible role for soft chambers?



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HBOT COMMON SIDE EFFECTS

- **Ear Barotrauma:** Completely preventable!!
- Vision Changes: Myopia
- Increased Insulin Sensitivity
- Claustrophobia
- Time consumption...



HBOT RARE SIDE EFFECTS

- Oxygen Seizures
- Pulmonary Toxicity
- Pneumothorax
- Fire



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HBOT COST

- Insurance Coverable Conditions
 - **Free standing clinics cost patients (and insurance companies) less money.**
 - Copays
- Investigational Conditions: CLINICS ONLY
 - \$200-\$350 per treatment
 - Cash / Credit
 - Payment plans
 - Crowdfunding
 - Nonprofit 501c3



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- Cost
- **Locations**



HBOT LOCATIONS

- Bay Area/San Jose:
 - Bay Area Hyperbarics- Thank you!
 - Regional Medical Center
 - Stanford
- San Francisco/Oakland
 - New HBOT center opening in 2015
 - San Francisco Institute for Hyperbaric Medicine
 - Hyperbaric Oxygen Clinic of SF
 - St. Francis Medical Center
- Marin:
 - Advanced Hyperbarics
- New York
 - Hyperbaric Medical Solutions (NYC 2015, Long Island)
- Virtual
 - IntegrativeHBOT.com



BAY AREA PARTNERS

- Amen Clinic: San Francisco
 - <http://www.amenclinics.com/san-francisco/>
- One Hit Away Foundation
 - <http://www.onehitaway.org/>
- Dr. Mark Renneker





HBOT:
It Heals Wounds
Safely

THANK YOU



REFERENCES:

1. Hyperbaric Oxygen Therapy Can Improve Post Concussion Syndrome Years after Mild Traumatic Brain Injury - Randomized Prospective Trial Boussi-Gross R, Golan H, Fishlev G, Bechor Y, Volkov O, et al. (2013) Hyperbaric Oxygen Therapy Can Improve Post Concussion Syndrome Years after Mild Traumatic Brain Injury - Randomized Prospective Trial. PLoS ONE 8(11): e79995. doi: 10.1371/journal.pone.0079995
2. wikipedia.com
3. uhms.org
4. <http://www.scubadivingsarasota.info/wp-content/uploads/2010/02/Atmospheric-Pressure-absolute1.png>
5. shutterstock.com
6. https://classconnection.s3.amazonaws.com/27/flashcards/592027/png/gas_solubility-effect_of_pressure1334408405264.png
7. http://1.bp.blogspot.com/-WzT8oJKBsM0/T0EkVC_SUpI/AAAAAAAAAqM/erEZNuYuR9o/s1600/2827aead-d86a-413e-9428-2116b09587b5.jpg
8. <https://www.virginiamason.org/Hyperbaric>
9. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3082642/>
10. <http://www.ncbi.nlm.nih.gov/pubmed/19015983>
11. A prospective, randomized Phase II clinical trial to evaluate the effect of combined hyperbaric and normobaric hyperoxia on cerebral metabolism, intracranial pressure, oxygen toxicity, and clinical outcome in severe traumatic brain injury. J Neurosurg. 2013 Jun;118(6):1317-28. doi: 10.3171/2013.2.JNS121468. Epub 2013 Mar 19. Rockswold SB1, Rockswold GL, Zaun DA, Liu J.

12. <http://www.abovetopsecret.com/forum/thread919105/pg3>
13. <http://www.ncbi.nlm.nih.gov/pubmed/17934837>
14. <http://www.healingchambers.com.au/what-is-hyperbaric-oxygen-therapy-2/22-ways/>
15. hyperbaricmedicalsolutions.com
16. <http://www.palmbeachpost.com/photo/news/local/royal-palm-beach-girl-11-recovering-from-having-pa/pXFXR/>
17. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3837504/>
18. A phase I study of low-pressure hyperbaric oxygen therapy for blast-induced post-concussion syndrome and post-traumatic stress disorder. J Neurotrauma. 2012 Jan 1;29(1):168-85. doi: 10.1089/neu.2011.1895. Epub 2011 Nov 22. Harch PG1, Andrews SR, Fogarty EF, Amen D, Pezzullo JC, Lucarini J, Aubrey C, Taylor DV, Staab PK, Van Meter KW.
19. The effect of hyperbaric oxygen on symptoms after mild traumatic brain injury. J Neurotrauma. 2012 Nov 20;29(17):2606-12. doi: 10.1089/neu.2012.2549. Epub 2012 Nov 9. Wolf G1, Cifu D, Baugh L, Carne W, Profenna L.
20. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3837504/>
21. The effect of hyperbaric oxygen on persistent postconcussion symptoms. J Head Trauma Rehabil. 2014 Jan-Feb;29(1):11-20. doi: 10.1097/HTR.0b013e3182a6aaf0. Cifu DX1, Hart BB, West SL, Walker W, Carne W.
22. Effects of hyperbaric oxygen on symptoms and quality of life among service members with persistent postconcussion symptoms: a randomized clinical trial. JAMA Intern Med. 2015 Jan 1;175(1):43-52. doi: 10.1001/jamainternmed.2014.5479. Miller RS1, Weaver LK2, Bahraini N3, Churchill S4, Price RC5, Skiba V6, Caviness J7, Mooney S8, Hetzell B9, Liu J9, Deru K4, Ricciardi R10, Fracisco S11, Close NC12, Surrentt GW5, Bartos C6, Ryan M7, Brenner LA3; HOPPS Trial Team.

REFERENCES

23. <https://clinicaltrials.gov/ct2/show/NCT01611194>
24. <https://clinicaltrials.gov/ct2/show/results/NCT01306968?sect=X01256#all>
25. <http://www.tbiwashington.org/documents/LindellWeaverBIMASeattleTBI23white.pdf>
26. <http://www.ncbi.nlm.nih.gov/pubmed/23682548?dopt=Abstract>
27. <http://clinicaltrials.gov/ct2/show/NCT01986205>

The Effect of Hyperbaric Oxygen on Persistent Postconcussion Symptoms

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William Carne, PhD

Background: The high incidence of persistent postconcussion symptoms in service members with combat-related mild traumatic brain injury has prompted research in the use of hyperbaric oxygen (HBO₂) for management. **Objective:** The effects of HBO₂ on persistent postconcussion symptoms in 60 military service members with at least 1 combat-related mild traumatic brain injury were examined in a single-center, double-blind, randomized, sham-controlled, prospective trial at the Naval Medicine Operational Training Center at Naval Air Station Pensacola. **Methods:** Over a 10-week period, subjects received a series of 40, once-daily, hyperbaric chamber compressions at 2.0 atmospheres absolute (ATA). During each session, subjects breathed 1 of 3 preassigned oxygen fractions (10.5%, 75%, or 100%) for 60 minutes, resulting in an oxygen exposure equivalent to breathing surface air, 100% oxygen at 1.5 ATA, or 100% oxygen at 2.0 ATA, respectively. Individual, subscale and total item responses on the Rivermead Postconcussion Symptom Questionnaire and individual and total Posttraumatic Disorder Checklist-Military Version were measured just prior to intervention and immediately postintervention. **Results:** Between-group testing of pre- and postintervention means revealed no significant differences on individual or total scores on the Posttraumatic Disorder Checklist-Military Version or Rivermead Postconcussion Symptom Questionnaire, demonstrating a successful randomization and no significant main effect for HBO₂ at 1.5 or 2.0 ATA equivalent compared with the sham compression. Within-group testing of pre- and postintervention means revealed significant differences on several individual items for each group and difference in the Posttraumatic Disorder Checklist-Military Version total score for the 2.0 ATA HBO₂ group. **Discussion:** The primary analyses of between group differences found no evidence of efficacy for HBO₂. The scattered within group differences are threatened by Type 2 errors and could be explained by nonspecific effects. **Conclusion:** This study demonstrated that HBO₂ at either 1.5 or 2.0 ATA equivalent had no effect on postconcussion symptoms after mild traumatic brain injury when compared with sham compression. **Key words:** *hyperbaric oxygen therapy, postconcussion syndrome, traumatic brain injury*



HBOT & MTBI: CIFU

- All received 2 ATA with varying oxygen concentrations for 40 treatments
- Study was safe & feasible
- “No effect” of HBOT on TBI or PTSD symptoms on various subjective testing during, 1 week after, and 3 months post treatment
- For all patients in the study, there was an improvement for working memory, executive function, delayed verbal memory, and verbal fluency

Increased Pressure, Increased Oxygen, and/or Increased Nitrogen ALL have physiologic effect = No true placebo