Enhanced Brain and Concussion Recovery

Round 1

Knock Out Brain Injury – An Evolving Paradigm in Healing

Alan Katz, MD, FACEP, FAAEM, UHM/ABEM

Medical Director, Hyperbaric Medical Solutions

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Alan Katz, MD, FACEP, FAAEM, UHM/ABEM

Board Certified Emergency Medicine

Board Certified Hyperbaric and Undersea Medicine

Board Certified Lobster Catcher
I Do Not have any relevant financial or other relationship or affiliation with a commercial vendor or manufacturer of medically-related products, whether referenced in this lecture or not.
Which way do you go?
Severe Head Injury

- Cerebral contusion
- Intracranial hemorrhage
- Epidural hematoma
- Subdural hematoma
- Intracerebral hematoma
- Diffuse axonal injury
We live in a world where all individuals face the risk of head injuries on a daily basis. Articles and news reports appear regularly discussing the recognition of traumatic brain injuries and the preventative measures that can be used to lessen impact. Newer modalities are emerging which will allow us to better identify injury. Multiple techniques exist to assist with brain retraining.

*Hyperbaric oxygen therapy is now emerging as the key management tool for brain repair when integrated into a comprehensive concussion recovery program.*
The paradigm of concussion care is changing rapidly leaving many unaware of the current shift toward early hyperbaric oxygen therapy.

Traditional brain imaging has been insufficient in detecting a mild traumatic brain injury. Lesser known newer techniques such as QEEG and tensor brain imaging have evolved allowing easier identification—hence easier entry into a brain injury recovery program.
Enhanced Brain and Concussion Recovery: Round 1

Knock Out Brain Injury – An Evolving Paradigm in Healing

- Learning Objectives
  - Upon completion of this lecture, participants should be better able to recognize, investigate, and treat mild traumatic brain injury.
  - All will more fully appreciate the integration of Hyperbaric Oxygen Therapy into a comprehensive brain recovery program.
Concussion

Latin verb concutere..... To shake violently
**TBI Statistics**

- 1.7 million brain injuries per year
- 75% in form of concussions or mTBI
- 230,000 to 500,000 Hospitalizations per year
- 52,000 deaths
- Economic toll of TBI exceeds $60 Billion per year
- TBI is the LEADING cause of morbidity and mortality in individuals < 45 years of age in the WORLD
Incidence

- Overall, the activities associated with the greatest number of TBI-related ED visits included bicycling, football, playground activities, basketball, and soccer.

- 71% of all sports/recreation-related TBI ED visits were males.

- 70% of sports/recreation-related TBI ED visits were persons aged 10-19 years.

- For males aged 10-19 years, sports- and recreation-related TBIs occurred most often while playing football or bicycling.

- Females aged 10-19 years sustained sports- and recreation-related TBIs most often while playing soccer or basketball or while bicycling.

Source: www.cdc.gov
Traumatic Brain Injury

Glasgow Coma Scale

“Minimal”

Mild

Mod

Severe

Sports concussion

Teasdale et al Lancet 1974; ii: 81-4

Sports concussion?
Mild TBI (mTBI)

- Any period of loss of or a decreased level of consciousness lasting less than 30 minutes
- Any loss of memory for events immediately before or after the injury lasting less than 24 hours after the event
- Any alteration in mental state at the time of the injury
- Transient neurological deficits
- >3 months: Post Concussion Syndrome
- 25% of patients continue to have symptoms after 6 months
- 70 to 90% of all TBI in the US is mTBI
TBI Pathophysiology

- Focal Ischemia

- Cerebral Vasospasm

- Vasospasm found in 25-40% of severe TBI patients
  
  - Journal of Neurosurgery, Martin, 1992
TBI Pathophysiology

Hypoxia

Multiple studies 1980 – 1999
- Adams, Van den Brink, Zhi

LOW PO2 seen within first 24 hours

Lower → worse outcome
TBI

Damage to BBB and Cellular Membranes
  - Release of glutamate from damaged cells
  - Impaired glutamate re-uptake at synapse

Failure of ATP dependent glutamate transporters
  - Membrane depolarization - enhanced glutamate release

Na+ K+ Ionic Imbalances
  - Extracellular Glutamate
    - Activation of NMDA and AMPA receptors leading to opening of calcium channels

INFLAMMATION
  - Microglial and astrocyte activation
  - ↑ Cytokines and chemokines

NECROSIS
  - Calpain Activation
  - ↑ Intracellular Calcium
    - Calcineurin Activation
  - Cathepsins
  - Lyosomal rupture

Oxidative stress
  - ROS
  - Mitochondrial dysfunction
    - Activation of Caspase and Caspase Independent Apoptosis

Intracellular Calcium

Delayed Cell Death
Neurometabolic Cascade

Increased energy demand + decreased CBF (50%) & impaired cellular efficiency

ENERGY CRISIS

Signs and Symptoms of Concussion

**Irritability**
Sadness
More emotional
Nervousness

**Drowsiness**
Sleeping more than usual
Sleeping less than usual
Difficulty falling asleep

**Headache**
Nausea
Vomiting
Dazed
Stunned
Fatigue
Light Sensitivity
Sound Sensitivity
Balance problems
Vision Problems

**Feeling "foggy"**
Feeling slowed down
Difficulty concentrating
Difficulty remembering
Confused about recent events
Answers questions slowly
Repeats Questions

*PEDiATRICS* Vol. 126 No. 3 September 1, 2010
Brain injury recovery: It’s not easy

A healthy brain utilizes \textit{ALL} energy supplied to it

15\% of the Cardiac Output

20\% of the Total Body Oxygen Consumption

25\% of the Total Body Glucose
Brain injury recovery: It’s not easy

Healing from a brain injury requires additional energy (ATP)

Energy is not in ready supply given high demands of brain tissue
In 80-90% of mTBI cases, the symptoms fade in 7–10 days.

TBI Pathophysiology

Brain Metabolism following mTBI

- Proton magnetic resonance spectroscopy
- Recovery of neuronal metabolism marker in 40 athletes following concussion
- N-acetylaspartate/creatine-containing compounds ratio
- Concussive head injury → window of brain vulnerability from cellular energetic metabolism impairment
- Symptom recovering 3-15 days
- Normalized metabolism by 30 days

*Brain 2010; 133(11): 3232-3242.*
Concussion Recovery Timeline

- **Onset**
- **Resolution**

**Typical Concussion**

**Repeat Injury**

**Post concussive Syndrome**

**Excessive exertion**
SECOND IMPACT SYNDROME

- Occurs in athletes with prior concussion following relatively minor second impact (controversial and based upon single case studies)

- Catastrophic increase in intracranial pressure due to dysfunction of autoregulation of cerebral circulation

- Most often occurs in athletes < 24 years old

LOW INCIDENCE – HIGH POTENTIAL ACUTE IMPACT

- Schneider, 1973; Saunders; 1984; Cantu, 1998. Evidence Level 4
Facts on Helmets

- Bicycle helmets are 85% effective in reducing traumatic brain injuries
- Only 40% of cyclists wear helmets

Source: www.thinkfirst.org
Use of a helmet while biking could prevent 1 injury every 4 minutes in the U.S.
2010 NFL Concussion Policy

"Once removed for the duration of a practice or game, the player should not be considered for return-to-football activities until he is fully asymptomatic, both at rest and after exertion; normal neurological examination; and normal neuropsychological testing are completed. The player is cleared to return by both his team physician(s) and the independent neurological consultant."

2018 Additional NFL Directives

- Neuropsychological testing has been expanded for all NFL players. NFL players who have been removed from a game due to a concussion will be re-tested during the season as part of the medical staff's treatment of the player and to assist in determining when players can return to practice and play. Each club will select the neuropsychological testing provider of its choice.

- Player safety rules relating to the use of the helmet will continue to be closely enforced. This will include strict enforcement of the requirement that chin straps on helmets be completely and properly buckled so that the helmet provides maximum protection.

- The NFL will continue to research and study all elements of concussions with a particular focus on long-term effects.

National Football League, November 18, 2008
Retired Players Get It

Otis Jerome Anderson “O.J.”

Bart Oates
Return to Play: Consensus Statements and Evidence Based Guidelines

Zurich Consensus Conference on Sports Concussion (2013)

- One and Done: No return until symptom free with exertion
- Individually based decisions (one size does not fit all)
- Short period of rest and slow return to activity/school

Where's the HBOT?!?

American Academy of Neuro Evidence Based Return to Play Guidelines (2013)

- One and Done: No return until symptom free with exertion
- Individually based decisions (no set timeline for safe RTP)
- HS age and younger should be managed more conservatively

Where's the HBOT?!?
Graduated RTP Protocol  
(Zurich 2012)

<table>
<thead>
<tr>
<th>Rehabilitation Stage</th>
<th>Functional Exercise Each Stage</th>
<th>Objective of Each Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Activity</td>
<td>Physical and Cognitive Rest</td>
<td>Recovery</td>
</tr>
<tr>
<td>Light Aerobic Exercise</td>
<td>Walking, swimming, stationary bike, &lt;70% maximum MR. No resistance training.</td>
<td>Increase HR</td>
</tr>
<tr>
<td>Sports Specific Exercise</td>
<td>Skating drills in ice hockey, running drills, No head impact activities</td>
<td>Add Movement</td>
</tr>
<tr>
<td>Non-contact training drills</td>
<td>Progression to more complex training drills → May start progressive resistance training</td>
<td>Exercise, coordination and cognitive load</td>
</tr>
<tr>
<td>Full-contact practice</td>
<td>Full practice (following medical clearance)</td>
<td>Restore confidence and assess functional skills by coaching staff</td>
</tr>
<tr>
<td>Return to Play</td>
<td>Normal game play</td>
<td></td>
</tr>
</tbody>
</table>

WHERE’S THE HBOT ?!!?
Heads Up: Concussion in High School Sports

- CDC program
  - Online training
  - Fact sheets
  - Symptom posters
  - Wallet cards

- Four Step Action Plan

**WHERE’S THE HBOT ??!!**
WHERE’S THE HBOT ?!!

A bump, blow, or jolt to the head can cause a concussion, a type of traumatic brain injury (TBI). Concussions can also occur from a blow to the body that causes the head to move rapidly back and forth, even if a "trip," "taking your tail ring," or what seems to be a mild bump or blow to the head can be serious.

On the lacrosse field, concussions can result from a full, hard stick to the head by the stick or ball, or from players colliding with each other or with obstacles.

RECOGNIZING A POSSIBLE CONCUSSION
To help recognize a concussion, watch for or ask others to report the following new behaviors in your athlete.

1. A forcible bump, blow, or jolt to the head or body that results in rapid movement of the head.

2. Any change in the athlete’s behavior, thinking, or physical functioning, or any other sign or symptom of concussion. (See the signs and symptoms chart.)

Athletes who experience any of the signs or symptoms listed below after a bump, blow, or jolt to the head or body may have a concussion.

- Unusual sleepiness or tiredness
- Headache
- Nausea or vomiting
- Dizziness or feeling dizzy
- Memory problems
- Disorientation
- Confusion
- Sensitivity to light or sound
- Problems with balance
- Blurred vision
-elage
- Fainting

Additional signs and symptoms may not be present immediately, but may appear over time. If your athlete shows any of these signs or symptoms, they may have a concussion. 

For more information and safety resources, visit:

www.cdc.gov/Concussion and www.usafieldhockey.org/safety

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Sports Concussion Assessment Tool 2 (SCAT2)

Standardized method of evaluating injured athletes for concussion

- Used in athletes aged from 10 years and older
- Assessment Includes:
  - Symptoms: 22 possible
  - Cognitive & Physical Assessment
    - LOC?
    - Glasgow coma scale: eye, verbal, motor
    - Orientation: Month, Date, Day of the week, year, time?
    - Immediate Memory recall: 5 word recall: (elbow, apple, carpet, saddle, bubble)
    - Concentration:
      - Repeat Digits Backwards: 3-9-7, 4-6-1-0, 2-9-6-1-4
      - Months of the year in reverse order
  - Balance
  - Coordination
Resources

SCAT3

Child SCAT3

http://bjsm.bmj.com/content/47/5/259.full.pdf

http://bjsm.bmj.com/content/47/5/263.full.pdf
Specific treatments

- Cognitive/fatigue
  - Sleep aids – melatonin
  - Possible stimulants – short term

- Migraine
  - Abortive and preventive
  - SSRIs, triptans

- Cervical
  - PT, traction

- Anxiety/Mood
  - SSRI, sleep treatment as above
  - Behavioral therapy

WHERE’S THE HBOT ?!!
Specific treatments

- **Vestibular**
  - Vestibular rehab - head coordination, balance, and gait-related exercises

- **Ocular**
  - Eye exercises involving lenses, prisms, penlights, and cover-ups designed to improve ocular function
  - Vision therapy in treating convergence and accommodative insufficiency
  - Behavioral ophthalmologist or optometrist

WHERE’S THE HBOT ?!!?
“Yo, Dewey! Got another one over here when you’re done.”
HBOT Starts Here
Improving neuropsychological function after chronic brain injury with hyperbaric oxygen.
Golden Z¹, Golden CJ, Neubauer RA

PURPOSE:
One suggested treatment for chronic brain injury (CBI) is the use of hyperbaric oxygen therapy (HBOT). The present study was an evaluation of neuropsychological improvement after HBOT in CBI patients.

METHOD:
Study 1 compared test-retest results of 21 CBI children treated with HBOT against test-retest results of 42 untreated brain injured and normal children. Study 2 compared 21 CBI adults treated with HBOT against 42 untreated normal and brain injured adults. In each study, subjects received pre and post assessments to evaluate neuropsychological function.

RESULTS:
The HBOT-treated children showed significant improvement when compared with the two control groups on measures of daily living, socialization, communication, and motor skills. The treated adults made significant gains in all neuropsychological areas tested as compared to controls.

CONCLUSION:
The studies were strongly supportive of HBOT as a treatment for lessening the neurological impact of CBI. These studies indicate that HBOT can be an effective aid in ameliorating the neuropsychological and physiological effects of CBI. The absence of a clear sham HBOT treatment group is an issue as it could be that there was a placebo effect, but it should be noted that the controls were receiving more traditional interventions during the study.
“There is a need to study the degree to which the factors of higher pressure and higher oxygen levels are responsible for the effects seen in this study. The initial emphasis has been to show that the therapy can work. Now we must determine if it is the higher oxygen levels or the higher pressure or a combination of the two is responsible for the effects seen here. It may be that a less expensive but effective treatment can be derived which relies on lower oxygen levels or lower pressure. The researcher is working on the design and implementation of such studies at present.”
Wright JK¹, Zant E, Groom K, Schlegel RE, Gilliland K.

Abstract
Two United States Air Force Airmen were injured in a roadside improvised explosive device (IED) blast in Iraq in January 2008. Both airmen suffered concussive injuries and developed irritability, sleep disturbances, headaches, memory difficulties and cognitive difficulties as symptoms of mild traumatic brain injury (mTBI). Six months after injury, repeat Automated Neuropsychological Assessment Metrics (ANAM) testing showed deterioration, when compared to pre-injury baseline ANAM assessment, in all measured areas (simple reaction time, procedural reaction time, code substitution learning, code substitution delayed, mathematical processing, and matching to sample). The airmen were treated with hyperbaric oxygen in treatments of 100% oxygen for one hour at 1.5 atmospheres absolute, resulting in rapid improvement of headaches and sleep disturbances, improvement in all symptoms and resolution of most symptoms. Repeat ANAM testing after completion of the hyperbaric treatments - nine months after initial injury - showed improvement in all areas, with most measures improving to pre-injury baseline levels. The airmen received no other treatment besides medical monitoring. Repeat neuropsychologic testing confirmed the improvement. We conclude that the improvement in symptoms and ANAM performance is most likely attributable to HBO treatment.
The effect of hyperbaric oxygen on symptoms after mild traumatic brain injury.

Wolf G¹, Cifu D, Baugh L, Carne W, Profenna L.

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 HBO(2) 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.
HBO & mTBI: Harch

A Phase I Study of Low-Pressure Hyperbaric Oxygen Therapy for Blast-Induced Post-Concussion Syndrome and Post-Traumatic Stress Disorder: Harch et al January 2012 Journal of Neurotrauma

- 15 patients symptomatic veterans w/blast injury
- Average 2.6 years post injury
- 40 treatments 1.5 ATA in 30 days
- SPECT scanning done pretreatment, after 1 treatment, and after all 40 treatments
HBO & mTBI: Harch

- Harch Phase I Study (continued)

- Significant symptomatic, cognitive, and affective improvements on an array of testing
- 30% reduction in PTSD symptoms
- IQ increased an average of 15 points
- **64% of patients able to decrease or eliminate narcotic and psychoactive medications**
- SPECT scanning documented improvement in blood flow
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.,²⁻⁴ David A. Zaun, M.S.,⁵ and Jiannong Liu, Ph.D.⁵

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

- 42 patients with mean GCS of 5.7 were prospectively randomized into two groups
- Group #1: HBOT (100% Oxygen) @1.5 ATA X 60 minutes followed by 3 hours of 100% face mask oxygen at 1.0 ATA for 3 treatments on 3 successive days
- Group #2: Standard severe TBI care (no HBOT chamber)
- Sham not needed: sedated and paralyzed
Brain tissue O2 levels increased 600% during combined treatment
Decreased intracranial pressure that lasted until next HBOT session
In post treatment period brain tissue oxygen levels remained higher by 30% vs. controls
- Peri-contusional brain with most impressive response.
Significantly improved markers of cerebral function especially in peri-contusional brain
An absolute 26% reduction in mortality for 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
Phase III study recommended for confirmation of results (It was only 3 HBOT sessions!!)
Hyperbaric Oxygen Therapy Can Improve Post Concussion Syndrome Years after Mild Traumatic Brain Injury - Randomized Prospective Trial

Rahav Roussi-Gross1, Haim Golan2,3,4, Gregori Fishlev1, Yair Bachor1, Oleg Volkov3,4, Jacob Bargan3, Mony Friedman2,5, Dan Hoefler6, Nathan Shmakovitch6, Eshel Ben-Jacob1,2,9,10, Shai Effron1,2,9,10, 1 The Institute of Hyperbaric Medicine, Assaf Harosh Medical Center, Zerifin, Israel; 2 Research and Development Unit, Assaf Harosh Medical Center, Zerifin, Israel; 3 Sacker School of Medicine, Tel-Aviv University, Tel-Aviv, Israel; 4 Nuclear Medicine Institute, Assaf Harosh 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 Orthopaedics, Head & Neck Surgery, Assaf Harosh Medical Center, Zerifin, Israel; 9 Center for Theoretical Physics, Rice University, Houston, Texas, United States of America; 10 Sackler 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 40 HBOT sessions. The HBOT protocol included 40 treatment sessions 5 days/week, 60 minutes each, with 100% oxygen at 1.5 ATA. "Mindstream" 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 NCT0075052
Hyperbaric oxygen therapy can improve post concussion syndrome years after mild traumatic brain injury - randomized prospective trial.


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.
Hbot & mTBI: Boussi-Gross

- Randomized Cross Over Controlled Study
- 56 patients with Post Concussive Syndrome (mTBI)
- 1 to 6 years post traumatic event (civilian)
- 40 sessions of HBOT
- 100% Oxygen at 1.5 ATA x 60 minutes
- SPECT Scans before & 1 to 3 weeks after treatment (blinded)
Hyperbaric oxygen may induce angiogenesis in patients suffering from prolonged post-concussion syndrome due to traumatic brain injury.
Tal S, Hadanny A, Berkovitz N, Sasson E, Ben-Jacob E, Efrati S.

PURPOSE:
Recent clinical studies present convincing evidence that hyperbaric oxygen therapy (HBOT) may be the coveted neurotherapeutic method for brain repair. One of the most interesting ways in which HBOT can induce neuroplasticity is angiogenesis. The objective in this study was to assess the neurotherapeutic effect of HBOT in post TBI patients using brain perfusion imaging and clinical cognitive functions.

METHODS:
Retrospective analysis of patients suffering from chronic neuro-cognitive impairment from TBI treated with HBOT. The HBOT protocol included 60 daily HBOT sessions, 5 days per week. All patients had pre and post HBOT objective computerized cognitive tests (NeuroTrax) and brain perfusion MRI.

RESULTS:
Ten post-TBI patients were treated with HBOT with mean of 10.3±3.2 years after their injury. After HBOT, whole-brain perfusion analysis showed significantly increased cerebral blood flow and cerebral blood volume. Clinically, HBOT induced significant improvement in the global cognitive scores (p=0.007). The most prominent improvements were seen in information processing speed, visual spatial processing and motor skills indices.

CONCLUSION:
HBOT may induce cerebral angiogenesis, which improves perfusion to the chronic damage brain tissue even months to years after the injury.
TBI: No Need to Die!

- HBOT 2017
  11th International Symposium

- A review of HBOT in Acute Severe Traumatic Brain Injury with an Extension to Acute Concussion, and an Update on Chronic Mild TBI
  -Paul G. Harch, MD
BIMA: Weaver - A Randomized trial of hyperbaric oxygen in U.S. Service Members with post-concussive symptoms

- RTC trial - 71 patients received **1.5 ATA 100% vs 1.2ATA 21%**

- Followed symptoms, quality of life, neuropsych testing, EEG, sleep, audiology, visual, lab testing, and brain imaging, at 13 weeks
- And symptom questionnaire at 6mo and 12 month.

- Found improvement in symptoms, processing speed, sleep quality, and vestibular symptoms........with greater response in the PTSD patients.

- All regressed at 6 and 12 months.
Hyperbaric Oxygen Therapy Can Induce Angiogenesis and
Regeneration of Nerve Fibers in Traumatic Brain Injury
Patients
Sigal Tal, Amir Hadanny, Efrat Sasson, Gill Suzin and Shai Efrati

- Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel
- Radiology Department, Assaf Harofeh Medical Center, Zerifin, Israel
- Sagol Center for Hyperbaric Medicine and Research, Assaf Harofeh Medical Center, Zerifin, Israel
- Faculty of Medicine, Bar-Ilan University, Ramat Gan, Israel
- Wiselmage, Hod Hasharon, Israel
- Research and Development Unit, Assaf Harofeh Medical Center, Zerifin, Israel
- Sagol School of Neuroscience, Tel-Aviv University, Tel-Aviv, Israel

15 patients treated x60 sessions at 2.0 ATA x 90min

DTI analysis
Conclusions: The mechanisms by which HBOT induces brain neuroplasticity can be demonstrated by highly sensitive MRI techniques of DSC and DTI. HBOT can induce cerebral angiogenesis and improve both white and gray microstructures indicating regeneration of nerve fibers. The micro structural changes correlate with the neurocognitive improvements.
Yellow/red show increase FA
Conclusion

HBOT can induce cerebral angiogenesis and recovery of brain microstructure in patients with chronic cognitive impairments due to TBI months to years after the acute injury. The increased integrity of brain fibers correlates with the functional cognitive improvement. The mechanism by which HBOT can induce brain neuroplasticity can be demonstrated by highly sensitive perfusion MRI and DTI. Further studies, using DTI - MRI, are needed in order to gain better understanding of the neuroplasticity effect of HBOT in a larger cohort of patients with different types of brain injuries.
What About Dose?

- Reviewed multiple trials ranging from 1.3 to 2.4

- Dr. Daphne Denham, reports that 98% of her patients [51 out of 52] treated within ten days of suffering a concussion, completely resolved their symptoms in five treatments or less when treated with escalating dose.
The Evaluation
History
Red Flags!

- Go to emergency department right away if:
  - Look very drowsy or cannot be awakened
  - One pupil (the black part in the middle of the eye) is larger than the other
  - Have convulsions or seizures
  - Cannot recognize people or places
  - Increasingly confused, restless, or agitated; rapidly worsening headache
  - Exhibits unusual behavior
  - Lose consciousness
    (a brief loss of consciousness should be taken seriously and the person should be carefully monitored)

- Weakness, numbness or decreased coordination
- Repeated vomiting or nausea
- Slurred speech
90% mTBI have oculomotor dysfunction

39% mTBI have visual field deficits

43-46% mTBI have convergence insufficiency
# Neurologic Examination

- **Cognition/ Mental Status**
  - Orientation (day, date, time, month, year)
  - Immediate memory (5 items, 3 trials)
  - Delayed recall (5 items after 5 minutes)
  - Concentration (3, 4, and 5 digits backwards, months/WORLD backwards, serial sevens)
- **Affect**
- **Coordination**
  - Finger-nose-finger/ Finger-to-nose
  - Heel-to-shin
  - Rapid finger movements
- **CN testing:**
  - EOM evaluation (nystagmus, convergence)
- **Speech**
- **Visual Fields**
- **Pupils**
- **VOMS (Vestibular/Ocular-Motor Screening)**
- **Balance assessment**
  - Modified BESS/ single leg stance
  - Tandem gait
  - Rhomberg test
Physical Examination

Dysfunction of Visual Accommodation/Convergence

Visual Accommodation

- **NPA** (Near point of accommodation)
  - Slowly move letters closer to the eye until they become blurry. Measure the distance the letters became blurry. This is the near point of accommodation.
  - Increased with dysfunction and age. Normal NPA of approximately 7cm from the bridge of the nose.

- **NPC** (Near point of convergence)
  - Note when patients lose ability maintain binocular vision
  - >6cm abnormal
BESS
Balance Error Scoring System

Screening for postural stability

- Double Leg, non-dominant leg, tandem stance
- Eyes closed
- Hard floor surface & foam surface
- Count “errors” or out of position moments:
  - Lifting hands off hips
  - Opening eyes
  - Step, stumble, or fall
  - More than 30 degrees abduction or flexion
  - Lifting foot or heel

NAMASTE
Vestibular/Oculo-Motor Screen

- Smooth Pursuit: follows a moving target while seated (3 ft from pt)
- Saccades: quickly follow a target between two points (3 ft away, 1.5 ft to right/left OR above/below eye level)
- Convergence: view a near target without double vision (target at arms length moving toward nose, >6 cm is abnormal)
- Vestibulo-ocular reflex*: ability to stabilize vision as the head moves (focus on object 3 ft away while moving head)
- Visual Motion Sensitivity*: ability to inhibit vestibular–induced eye movements using vision (rotate head and arm focus on thumb)

(Mucha, Collins et al. 2014)
Gaze Stability Exercises

Fixed/Moving targets

Variable distances from targets

Simple to complex visual backgrounds

Simple to complex surfaces during:
  - Sitting
  - Standing
  - Gait
What Structures Are Injured to the Vestibular System After Concussion?

- Actual sensors (otolith) or entire end organ gets damaged
  - Baro-trauma, blunt injury, blast/shockwave from hit

- Traction/tethering of CNVIII (vestibular-cochlear nerve)
  - From the origin of the sensor
  - In the axons of the nerve itself
  - From the insertion in the brainstem
The Vestibular – Cognition Connection

Damage to the vestibular system can directly create cognitive deficits
- Spatial navigation
- Object recognition memory
- You don’t have to have symptoms of dizziness to have the cognitive symptoms

The purpose of the otolith organ of the inner ear is assist in auto-regulation of blood flow to the head.

Injury to this organ can lead to symptoms that commonly are thought to be cerebral deficits.
The Vestibular-Autonomic Nervous System Connection

- Vestibular system lesions produce a number of injurious effects, including:
  - Disruption in the ability to rapidly adjust blood pressure
  - Respiratory muscle activity during movement and changes in posture
  - These perturbations in autonomic regulation are transient, and largely dissipate over time.
  - Could we be seeing a disruption of the vestibular system as the cause of the symptoms of concussion?
Treatment of Vestibular Dysfunction

- **Principle I**
  - Dizziness is an error message – avoidance of the symptom actually prolongs disorder.

- **Principle II**
  - Use the same treatment techniques you would use to treat an ankle sprain/strain
    - Repetitions and Sets
    - Small movements to dynamic movements
    - Symptoms as your guide
Neurocognitive Testing

- Objective measure for subtle cognitive impairments
- More sensitive than office examination
- Should NOT be used in isolation
- Helpful in the post concussion management of patients with persistent symptoms and/or a more complicated course.
- Computerized testing compares to individual's pre-season baseline
Neurocognitive Testing

Used to provide a sensitive index of higher brain functioning by measuring:

- Memory
- Attention
- Executive function
- Speed and flexibility of cognitive processing
Immediate Post-Concussion Assessment and Cognitive Testing

- ImPACT testing is a 30-45 minute neurocognitive test battery that has been scientifically validated to measure the effects of sports related concussion.
- ImPACT is available for athletes age 11 to 65
- All athletes should have a baseline test prior to playing sports:
  - Middle School & High School: test every two years
  - College: test once
  - Professional athletes: test once
- Athletes with no Baseline test: Athletes should be retested within 24-72 hours of sustaining a possible concussion.
- Athletes with a Baseline test: Athletes should be retested when they are completely symptom free.
ImPACT test:
Figure 2 Percentages of patients per score category per CNSVS domain.

Abbreviations: CNSVS, central nervous system vital signs; NCI, neurocognition index.
Clinical Advantages of Quantitative Electroencephalogram (QEEG)–Electrical Neuroimaging Application in General Neurology Practice

J. Lucas Koberda¹, Andrew Moses¹,², Paula Koberda¹,² and Laura Koberda¹,²

Abstract
QEEG-electrical neuroimaging has been underutilized in general neurology practice for uncertain reasons. Recent advances in computer technology have made this electrophysiological testing relatively inexpensive. Therefore, this study was conducted to evaluate the clinical usefulness of QEEG/electrical neuroimaging in neurological practice. Over the period of approximately 6 months, 100 consecutive QEEG recordings were analyzed for potential clinical benefits. The patients who completed QEEG were divided into 5 groups based on their initial clinical presentation. The main groups included patients with seizures, headaches, post-concussion syndrome, cognitive problems, and behavioral dysfunctions. Subsequently, cases were reviewed and a decision was made as to whether QEEG analysis contributed to the diagnosis and/or furthered patient's treatment. Selected and representative cases from each group are presented in more detail, including electrical neuroimaging with addi
DELTA (0.5-3.5 Hz)
• The SLEEP frequency

THETA (4-7 Hz)
• The RELAX frequency, dreaming

BETA (> 13 Hz)
• The GO frequency, full alertness

ALPHA (8-13 Hz)
The Awake relaxed/thinking frequency

Neurotypical

Over active / Under active
QEEG SITE CORRELATIONS

Short Term Working Memory
- Verbal Episodic Retrieval
- Cognit
- and Problem Solvi

Short Term
- Spatial/Object Retrieval
- Vigilance (Watchful
- Selective and Sustained
- Attent Areas

Sensory and Motor Functions

Langu
- Comprehension
- ral Understa
- n Sequencing
- Amygdal
- Hippocampus

Dig
- Short Term memory issues
- Self-Boundaries
- Excessive Thinki
- Inform Organization

Visual Processing
- Hallucinations
- Procedural Memory
- Dreaming

Visual Process
- Spatia Sketch
- Personality as it relates to
- Self-Concecr Victim
- Mentality
- Agnosia
- (can’t recognize objects,
- rsions, smells)
- Apra
- (inability to execute learned
- ents)
- Rum und
High Theta Activity
SPECT Scan
Investigations

- Neuroimaging (CT, MRI)

  - Use when suspicion of intracerebral structural lesion exists:
    - prolonged loss of consciousness
    - focal neurologic deficit
    - worsening symptoms
    - Deterioration in conscious state
NeuroImaging

Computed Tomography (CT)
- Not recommended for routine concussion evaluation
- Sensitive for skull fracture and intracranial hemorrhage
- Test of choice in first 24-48 hours after injury
- Will not rule out chronic subdural or neurobehavioral dysfunction

Magnetic Resonance Imaging (MRI)
- Not recommended for routine concussion evaluation
- More sensitive for cerebral contusion, petechial hemorrhage, white matter injury, posterior fossa abnormalities
- Diffusion tensor imaging may detect white matter injury better
FMRI is...

Technique used for measuring metabolic correlates of neuronal activity

- Uses a standard MRI scanner
- Acquires a series of images
- Measures changes in blood oxygenation
- Use non-invasive, non-ionizing radiation
- Can be repeated many times; can be used for a wide range of subjects
- Combines good spatial and reasonable temporal resolution
**Difference Between MRI & fMRI**

MRI studies brain **anatomy**.

**Functional MRI (fMRI)** studies brain **function**.

From: Daniel Bulte
Centre for Functional MRI of the Brain
University of Oxford
Unimanual Thumb Flexion

Right Thumb

Left Thumb
Amplified MRI
Diffusion Tensor Imaging

- Tensor is a mathematical model of directional anisotropy of diffusion

- From the tensor, we can calculate:
  - Direction of greatest diffusion
  - Degree of anisotropy
  - Diffusion constant in any direction
Diffusion Tensor Imaging

**ISOTROPIC** - Equal diffusion in all directions

**ANISOTROPIC** - Diffusion preferentially increased in some directions
Fractional Anisotropy - FA

- Measures the degree of anisotropic (unequal) diffusion in a voxel
- Ranges from 0 to 1 (no units)
  - 0 – isotropic (sphere-like)
  - 1 – Purely anisotropic (straight line)
- Can characterize demyelinating lesions, e.g., breakdown of myelin and axonal loss can reduce FA and remyelination can increase FA
- FA value of CSF = 0
Fiber Tractography / DTI - Tractography

- Technique to assess direction of white matter tracts within the brain

- Directional information from neighboring voxels is combined to estimate 3D structure of major white-matter pathways

- Voxels are connected together taking into consideration both the direction of principle vector and FA value
Clinical Applications – Normal Brain

- Fiber tracking provides critical information about white matter anatomy and connections
- Regions with similar tractographic features tend to be functionally co-activated - “neurons that fire together, wire together”
- IQ has been positively correlated with anisotropy in white matter association areas
- Reading ability has been correlated with anisotropy of left temporoparietal areas
- In the visual pathway, DTI has shown the retinotopic organization of fibers
Clinical Applications – Traumatic Brain Injury

- DTI is a useful technique to evaluate microstructural injury to the white matter fiber tracts in patients with TBI
- Decreased FA is seen in areas afflicted by TBI, that are occult on conventional MRI
- Studies suggest some correlation between findings on DTI with EEG and neuropsychological testing
- In the future, DTI may serve as a surrogate marker for closed head injury
The Puzzle:

- Public Education – “Google”
- Physician Education
  - Recognition- evaluation
  - Good History
  - Neurologic exam
  - Neurocognitive screening
  - Visual-oculo-motor exam
  - Vestibular assessment (balance)
  - Neuropsychological testing
  - Quantitative EEG testing
  - SPECT scan
  - CT/MRI
  - Diffusion Tensor Imaging – DTI scan
  - Access for HBOT
Real World Example

Hyperbaric Medical Solutions

- Since 2016 we have completed 5160 dives on a total of 120 patients for mTBI (Avg 43/pt)
  - Additionally 30 Veteran patients with TBI / PTSD, totaling approximately 1,000 dives (Avg 33/pt)
  - **59 percent were self referral / “Google”**
Our Experience

- Patient Example
  - M.G.
  - Male
  - 17 yo
## M.G.

### ImPACT® Clinical Report

<table>
<thead>
<tr>
<th><strong>Exam Type</strong></th>
<th>Baseline</th>
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<tbody>
<tr>
<td><strong>Date Tested</strong></td>
<td>07/31/2018</td>
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<tr>
<td><strong>Last Concussion</strong></td>
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<td><strong>Exam Language</strong></td>
<td>English</td>
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<td><strong>Test Version</strong></td>
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### Composite Scores

<table>
<thead>
<tr>
<th>Composite Score</th>
<th>Percentile</th>
</tr>
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<tbody>
<tr>
<td>Memory composite (verbal)</td>
<td>88</td>
</tr>
<tr>
<td>Memory composite (visual)</td>
<td>76</td>
</tr>
<tr>
<td>Visual motor speed composite</td>
<td>31.67</td>
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<tr>
<td>Reaction time composite</td>
<td>0.79</td>
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<tr>
<td>Impulse control composite</td>
<td>3</td>
</tr>
</tbody>
</table>

### Total Symptom Score

| **Total Symptom Score** | 19         |

### Cognitive Efficiency Index

| Cognitive Efficiency Index | 0.26       |

The Cognitive Efficiency Index measures the interaction between accuracy (percentage correct, reaction time) in seconds on the Symbol Match test. This score was not developed to make any normative inferences, and is included only to allow the clinician to compute a composite test to which the athlete tried to work up.

M.G.
Another Case Study

Former high functioning executive, fell and hit her head on a door frame, knocking her unconscious.

Could not walk after the event. Work up in the ER was “normal” and she was sent home.

Symptom subsequently worsened: difficulty with short term memory, concentration, attention, executive function and migraine headaches – getting lost.

Impulsivity followed and secondary depression, which lead to 2 suicide attempts.

Inpatient psych hospital for 35 days.
Case Study (cont.)

60 sessions of HBOT @1.5 ATA X 60 minutes

Significant subjective improvements in all these categories and marked objective improvement on both ImPACT testing and neuroimaging.

No further headaches

Does not get lost any more

Psychiatrist is amazed

Her life is back
Treatment with HBOT in my practice:

- Start ASAP using 1.5 ATA 100% O2 x 60
- Tx # 5-60

- Our Acute patients (<1 month) avg 5 sessions
  - Typically 1.5 ATA, however some 1.75 / 2.0 **Dr Denehem to review**

- Our Sub Acute (1 month to 6 months) avg 30 sessions plus adjunctive care (Neurofeedback, visual training etc)

- Our Chronic (6 months to many years) avg 60 sessions plus adjunctive care
S.B. 34 yo 4/24/18 vs 4/28/18 looses fight in 5th round – TKO – fights a Southpaw
D.C. 4/12/18 vs 4/28/18 Easy fight - wins in 2^{nd} round
Older ("less skilled ") fighter
Take Home:

1. A combined history, neurocognitive evaluation, and neurologic exam inclusive of vestibular and ocular evaluation in conjunction with advanced imaging and/or electrophysiological methods are required in a modern brain injury detection and recovery program.

2. Hyperbaric oxygen serves as the hub treatment for brain repair.

3. The best protocol for Hyperbaric Oxygen Therapy in brain repair has yet to be determined. What is clear is that hyperbaric oxygen therapy will serve a pivotal role.
References


- Narayana, P. (2017); White mater changes in patients with mild Traumatic brain injuries; MRI perspective. Do; 10.2217/chc-2016-0028

References (Continued)


References (Continued)


