



State of the Science: HBOT 1.5 Public Policy Bulletin 10-03

Hyperbaric Oxygen Therapy Effectively Treats Traumatic Brain Injury and PTSD

Traumatic brain injury, post-traumatic stress disorder and concussive depression have been signature injuries of the war in Iraq and Afghanistan. It is consistently estimated that as many as one-third of all who have served have been injured¹. These injuries explain the increase in social problems, incarcerations, suicide, substance abuse, homelessness, disability, unemployment and a reported 9,003 active duty war veterans in wounded warrior brigades², plus high levels of undeployable service members still in the military.³ This crisis is costing the Federal Government tens of billions of dollars each year, and despite billions in research, no effective treatment solutions have been found or developed.

Fortunately, the International Hyperbaric Medical Association has affiliated physicians who have been successfully treating mild-moderate traumatic brain injury (mTBI), post-traumatic stress disorder (PTSD) and concussive depression with Hyperbaric Oxygen Therapy (HBOT). The treatment discovery was made 20 years ago, based on work of German neurosurgeons from 1977⁴. It involved HBOT at 1.5 ATA (atmospheres absolute - HBOT 1.5). Thousands of patients have received this treatment since that time and scores of physicians have replicated its positive results. Recently, this treatment has been available individuals who could pay for it; and in active duty and research environments it has been applied to selected military casualties^{5,6}.

The most recent HBOT 1.5 data presentation on blast-injured patients, March 12, 2010, at the 8th World International Brain Injury conference in Washington, D.C., demonstrated a 15 point IQ increase in 35 days, a

¹ Golding H, Bass E, Percy A, Goldberg M. Understanding recent estimates of PTSD and TBI from operations Iraqi Freedom and Enduring Freedom. JRRD. 2009; 46 (5): vii-xiii.
<http://www.warrelatedillness.va.gov/dc/docs/PTSD-TBI-estimates.pdf>.

² LTG Schoemaker, Army Surgeon General, Testimony to the House Defense Appropriations Subcommittee, April 22, 2010, http://appropriations.house.gov/index.php?option=com_jcalpro&Itemid=117&extmode=view&extid=1946

³ Zoroya, Gregg, "Army sees sharp rise in unfit soldiers, USA Today, 3/2/2010 http://www.usatoday.com/news/military/2010-03-02-unfit-soldiers_N.htm?csp=hf

⁴ Holbach KH, Caroli A, Wassmann H. Cerebral energy metabolism in patients with brain lesions of normo- and hyperbaric oxygen pressures. J Neurol. 1977 Dec1;217(1):17-30.

⁵ Harch PG, Andrews SR, Fogarty E, Lucarini J, Aubrey C, Staab PK, Van Meter KW. Hyperbaric Oxygen Therapy Treatment of Chronic Mild-Moderate Blast-Induced Traumatic Brain Injury/Post Concussion Syndrome with Post Traumatic Stress Disorder: Pilot Trial. Presented at 8th World Congress on Brain Injury, Washington DC, March 11, 2010.

⁶ Wright JK, Zant E, Groom K, Schlegel RE, Gilliland K. Case report: Treatment of mild traumatic brain injury with hyperbaric oxygen. Undersea Hyperb Med. 2009 Nov-Dec;36(6):391-9.

35 percentile increase (This is the equivalent of the difference between a construction worker and a qualified engineer.)⁷. Further, post-concussion syndrome, a very debilitating condition that 98% of blast exposed casualties suffer from⁸, was reduced by 40%, with post-traumatic stress disorder reduced by 30%, and depression, a huge problem in the blast-injured population, was reduced by 51%. All results were highly clinically significant, and statistically significant, and backed up by improvements in functional imaging⁹. Each patient had a noticeable change in their duty status, their ability to return to work or school, or their ability to return to the activities of daily living. (See Insert 3)

Over forty Active Duty and Veteran patients have been treated to date. Nearly every patient on active duty recovered sufficiently to return to duty, saving the military millions per veteran in time and replacement costs. Eighty percent of those treated have been able to return to duty, work or school. Many veterans who were discharged, and then later treated, would have been able to remain on active duty had they been treated while they were in the service. Each active duty member who recovers is worth approximately \$2.6 million¹⁰ and treatment costs are recovered within months. A military physician, treating active duty members in Florida, used the same protocol and achieved the same results by treating 7 active duty TBI/PTSD casualties, all of whom became "essentially well" (and two of whose results are displayed in attachment D). Their medical discharge boards were invariably cancelled and they returned to normal duty, usually following more than six months of non-response to the currently applied military medical protocols for TBI, PTSD and/or depression. Continuation of their careers has included their ability to redeploy, to earn promotions, to receive medals for valor, and to continue their military continuing education¹¹. Commanders who have witnessed these changes have invariably been impressed and have requested that more of their military personnel be treated.

Translating these results into DoD budget numbers is revealing. Of the 9,003 members of wounded warrior brigades (nearly a division worth), many could likely be returned to light duty in as little as 10 treatments. They could continue duty during the next months while they took 1.5 hours out of each day to report for HBOT 1.5 treatment. Most with only blast-induced concussive wounds could be returned to duty, likely between 50 and

⁷ Harch PG. Op. cit.. 2010.

⁸ <http://blogs.consumerreports.org/health/2009/05/for-iraq-veterans-headaches-continue-following-traumatic-brain-injury-soldiers-mild-head-trauma-or-b.html?resultPageIndex=1&resultIndex=1>

⁹ Apparent to the practitioner, patient, family members and respective commander, and demonstrated by an ability to return to the activities of daily living, at minimum, and usually the ability to return to duty, work, or school, depending upon the level of injury, the number of injuries, and the length of time the injury had been left biologically untreated.

¹⁰ The breakdown is \$20,000 for recruiting a new service member, \$155,000 to train a basic service member (infantry. Many schools cost much more), \$1,000,000 for 40 years of VA disability benefits for a brain injured veteran, properly paid at \$2,400 per month, and \$1 million for 40 years of lost tax revenue because the veteran is unable to work.

¹¹ Wright JK, Col, USAF, MC. Personal communication. 2010.

Non-Healing Wound to the Foot

Diabetic Foot Ulcer: This Wagner Grade III was present for one year and unresponsive to conventional therapy.



1 Day Prior to Scheduled Amputation



26 HBOT Treatments

Hyperbaric Oxygenation prevents 75% of amputations in diabetic patients. Therapy approved by CMS for Medicare upon application by IHMA to CMS for coverage, 2002.



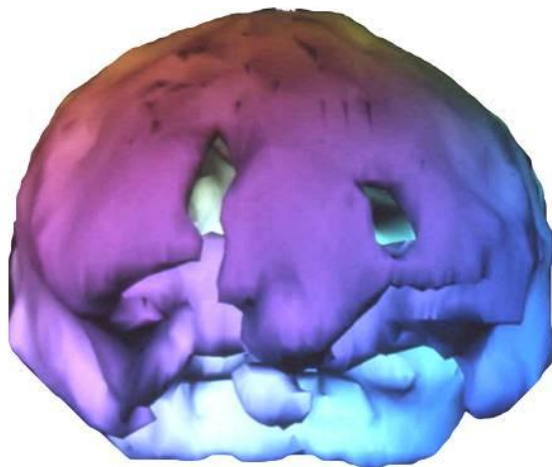
50 HBOT Treatments

These photographs are the property of Kenneth P. Stoller, MD, FAAP
Permission given by Dr. Stoller to the IHMA to publish on this CD (2004)

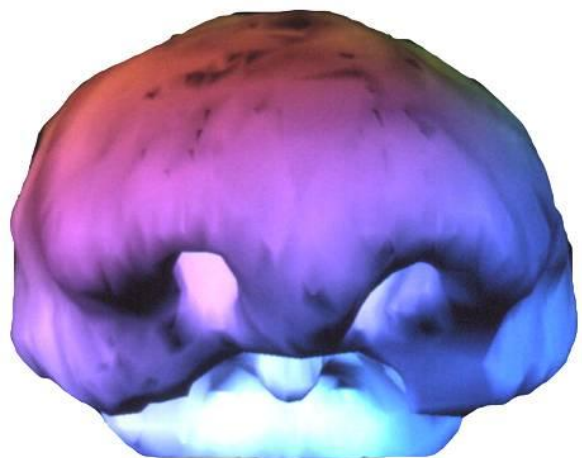


Non-Healing Wound to the Brain

Physical Abuse - 9 years after Injury - 21 y. female



Pre-HBOT 1.5

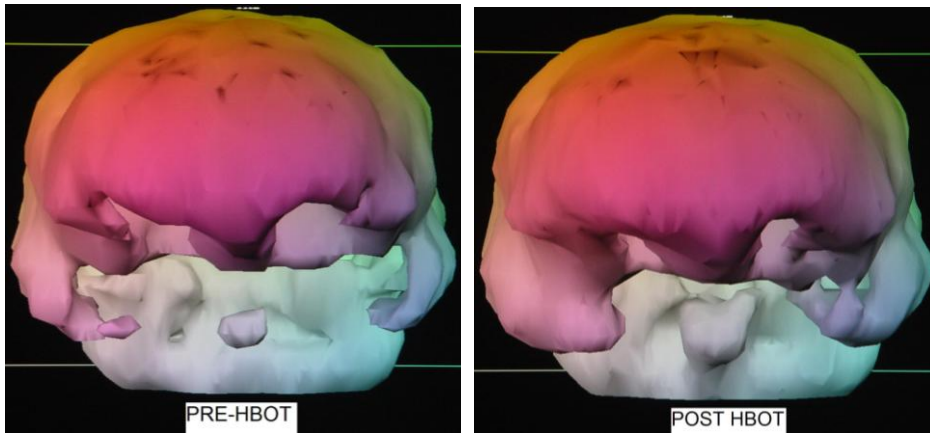


Post-HBOT 1.5

No wound will heal without oxygen. What is the difference between the diabetic non-healing foot wound and the non-healing brain injury? Essentially nothing. FDA has already approved HBOT for non-healing wounds

www.HyperbaricMedicalAssociation.org SPECT Scans © 2002 Paul Harch, M.D.

Case Report: Navy SG Meeting - Aug. 2008
25 year old Humvee Machine Gunner
6 IEDs-1 RPG hit in Two Tours in Iraq



40 HBOT 1.5 treatments (1/2 of the Protocol)

From living in a dark room, unable to go to the Mall because of PTSD, after HBOT 1.5 treatments his PTSD cleared, he turned down ½ of the offered VA disability, worked for a year, and after 40 more treatments has returned to college.

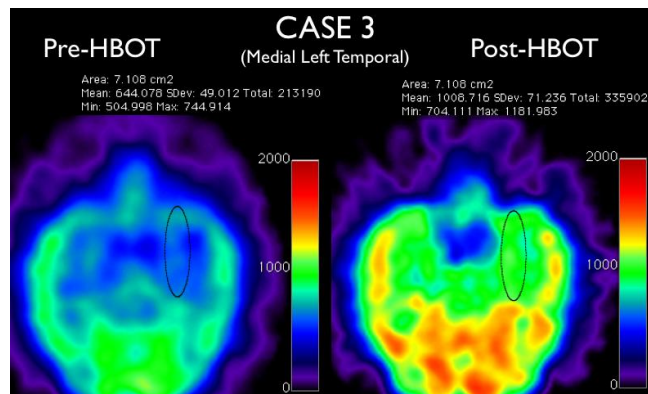
HBOT 1.5 Restores Brain Blood Flow & Doubles Metabolism

Marine Machine-gunner - August 2008 Navy SG Briefing

Scale actually goes from 0 to 2000 so it ENDS at 2000. Those pixels that are hitting near 2000 are red and are the most active, the less metabolically active are "cooler" colors of yellow, green and blue. So if you draw a line across the middle of the scale you can see what pixels are registering at 1000 by the corresponding color.

Both pre and post HBOT sets of images are exactly on the same scale. Below is a quantitative assessment that shows the actually percent increase in uptake to an area of the brain quite vulnerable to TBI. Note the mean uptake in the area went from 644 to 1008. Similar changes are evident everywhere else.

A change from green to red is a doubling of metabolism.



Analysis of blast injured veteran in LSU IRB Study # 7051: Edward Fogarty, MD, Neuro-radiologist, Chair, University of North Dakota School of Medicine, (701) 751-9579
www.HyperbaricMedicalAssociation.org

80%. Those wounded warrior brigade members, according to the DA PAM 385-40 dated 6 March 2009, are costing an estimated \$3.4 million per day (\$425 for officers and \$375 for enlisted¹². Officers are calculated at 16% of the casualties), not including the cost of ineffective medical treatments for symptoms.

If hyperbaric medicine to biologically repair these war casualties were charged at the civilian rate of \$200 per treatment, the cost per day would be \$1.7 million. If the military treated these members themselves, it would cost a maximum of \$50 per treatment (\$35 labor and \$15 for oxygen) or \$449,000 per day. After 150 days, the majority of these service members would be able to return to duty, most would be deployable, and those who could not continue their careers, potentially as low as 20%, could be discharged with lower VA disability payments than they would receive untreated. Many of those would be able to pursue educational and employment opportunities in the private sector and the residual left would be able to receive appropriate care for their disabilities. Obviously, many service members currently on light duty, and not functioning at levels they achieved prior to their injury, could also receive treatment and be appropriately improved.

It is far less expensive to provide these casualties with a biological repair than to leave them untreated. Further the cost of the current treatments is higher in one or two years for the treatments currently being used by military medicine, treatments that treat symptoms, not the cause of the than that of the permanent repair provided by HBOT 1.5.¹³ It is also possible to repair them in theater, both for acute blast injury, and also with the delayed treatment protocol. Acute treatment requires very few treatments, depending on how long treatment is delayed following the blast injury¹⁴.

There is also a tremendous savings if hyperbaric medicine were used with our wounded warriors. The first battle casualty, a U.S. Army Reserve General, blown up in Afghanistan, was treated with HBOT 1.5 while a patient at Walter Reed Army Medical Center. He received treatment from George Washington University Medical Center at the Tricare Reimbursement rate of \$250 per treatment. He spent 15 months at Walter Reed

¹² Headquarters, Department of the Army. DA PAM 385-40 6 March 2009. Army Accident Investigations and Reporting. Note: These numbers in this pamphlet have not been updated since at least 1990.

¹³ RAND Report: "Invisible Wounds of War: Psychological and Cognitive Injuries, Consequences, and Services to Assist Recovery." Tanielian, Terri; Jaycox, Lisa, April 2008, page xxii-xxiii: Two year costs within the first two years the service member returns home; PTSD \$5,904 to \$10,298 depending on whether we count the lives lost to suicide; Two year costs for major depression, \$15,461 - \$25,757; co-morbid PTSD and major depression; \$12,427 to \$16,884; One year costs for traumatic brain injury diagnosis: \$25,572 to \$30,730 in 2005 for mild cases (\$27,259 to \$32,759 in 2007 dollars), and \$252,251 to \$383,221 for moderate or severe cases (\$268,902 to \$408,519 in 2007 dollars.) These costs, largely treating symptoms, continue to have outyear costs and outyear consequences in terms of disability payments, inability to work, etc. Given that the HBOT ONE TIME cost for service members who need all 80 treatments averages \$16,000 at Medicare Reimbursement rates for a 1 hour treatment. (The cost is lower in some states and higher in urban areas, with known rates set by CMS.) Hyperbaric medicine alone, and hyperbaric medicine in conjunction with other treatments, is very cost effective. If provided acutely within hours of injury, the treatment is even more effective and massively more cost effective.

¹⁴ Colonna S, Coluccia B, Micella A, Gismondi A. [Hyperbaric oxygen therapy in acute cerebral edema]. *Minerva Anesthesiol.* 1991 Oct;57(10):976-7. Italian.

making no progress. Counting lost time and hospital costs in the Army Accident pamphlet, his first 15 months cost DoD \$400,950, with a permanent disability loss to the service of \$1.3 million. With HBOT 1.5 earlier, he would have been able to remain on active duty, a savings of \$1.3 million, but more importantly, the 5 months of recovery once he began receiving HBOT 1.5 cost \$133,650, a savings to the government of \$287,300. No other patients were treated at Walter Reed's brain injury center, despite the General's remarkable recovery that everyone on the staff. Today he has returned to the bench and is a seated judge in Florida, instead of being permanently disabled living at home.

Hyperbaric oxygen Treatment



Hyperbaric oxygen therapy (HBOT) has been approved by the FDA for 13 applications which include treating many kinds of non-healing wounds. It is the only non-hormonal biological repair and regeneration treatment approved by the FDA. Hyperbaric medicine has been used to treat neurological conditions for over 100 years. The treatment is safe with few side effects, which are rarely serious, and the treatment is far less expensive than current "symptom relief" treatments for mTBI, PTSD, or depression. Further, the mechanisms of action of the treatment are well characterized in the scientific

literature and the recoveries noted by treating physicians, patients and military commanders and family members are consistent with the known effects of this therapy. As approved, it is reimbursed by every major third party payer for a variety of conditions, including neurological indications. To date, about one third of the time, practitioners are paid for neurological treatment (brain injury). TRICARE and the Veterans Administration (VA) have paid for HBOT 1.5 neurological treatments, though they have not done so on a consistent basis, even when active duty personnel have achieved substantial recovery and returned to duty.

Scientific Evidence

There have been several important publications since 2003. These include a randomized-controlled animal study that verifies 20 years of human treatment data¹⁵. Most recently three peer reviewed articles have been published - one by a military physician – which verify that HBOT 1.5 does improve brain healing; and functional brain imaging demonstrates clearly that these effects cannot be explained by placebo^{16,17,18}. The

¹⁵ Harch PG, Kriedt C, Van Meter KW, Sutherland RJ. Hyperbaric oxygen therapy improves spatial learning and memory in a rat model of chronic traumatic brain injury. *Brain Res.* 2007 Oct 12;1174:120-9. Epub 2007 Aug 16.

¹⁶ Harch PG, Fogarty EF, Staab PK, Van Meter K. Low pressure hyperbaric oxygen therapy and SPECT brain imaging in the treatment of blast-induced chronic traumatic brain injury (post-concussion syndrome) and post traumatic stress disorder: a case report. *Cases J.* 2009 Jun 9;2:6538.

¹⁷ Wright JK. Op. cit.. 2009.

¹⁸ Rockswold SB, Rockswold GL, Zaun DA, Zhang X, Cerra CE, Bergman TA, Liu J. A prospective, randomized clinical trial to compare the effect of hyperbaric to normobaric hyperoxia on cerebral

placebo effect does not grow new blood vessels, restore apoptotic neural cells previous damaged by a lack of oxygen, nor restore neural pathways that re-enable memory and data processing ability.

Because of these scientific advances, the IHMA's sister organization, the International Hyperbaric Medical Foundation, has sponsored the National Brain Injury Rescue & Rehabilitation Observational Study, NBIRR-01 "Mild to Moderate TBI & PTSD using HBOT 1.5" research project at a network of sites across the United States¹⁹. The purpose of the project is to provide reimbursed access to biological repair treatment for traumatic brain injury and PTSD. The IRB-registered study will expand scientific knowledge relating to the efficacy of Hyperbaric Oxygen Therapy at 1.5 ATA (atmospheres absolute; HBOT 1.5) for these conditions, particularly for the kinds of blast-related brain injury experienced by combat casualties.

HBOT is the use of pressurized oxygen in an FDA-cleared medical device.

Treatment is provided in a pressure chamber that uses oxygen at greater than atmospheric pressure to saturate tissues, thus using oxygen as a medication to treat injury and disease processes. There are currently thirteen "indications" for (or applications of) hyperbaric oxygen therapy which the FDA has approved and for which Medicare reimburses²⁰. Three are for neurological injuries (decompression illness, carbon monoxide poisoning and brain abscess). Indication #6 is "arterial insufficiency" which also covers "problem non-healing wounds;" which includes conditions such as diabetic foot ulcers. Most HBOT treatments are done at 2.0 – 2.8 ATA (a measurement of oxygen dose). Clinical experience and scientific study to date shows that the brain is more responsive to oxygen at a lower 1.5 ATA dose (HBOT 1.5) in repeated treatments following the NBIRR protocol²¹.

To date, all military casualties treated in the NBIRR demonstration pilot study with HBOT 1.5 have improved and 80% of them have been able to successfully return to duty, work or school. One of these war veterans' cases has already appeared in a journal.²² Five HBOT treated active duty personnel had been returned to military active duty by April 2009. Two of them were just published in a journal article in January, 2009.²³ The NBIRR team saved the federal government over \$6.3 million in recruiting and retraining costs for treatment costs of only \$62,500.²⁴ Effective, ethical TBI and PTSD treatment is

metabolism, intracranial pressure, and oxygen toxicity in severe traumatic brain injury. *J Neurosurg.* 2009 Oct 23.

¹⁹ As each site is approved, and the study begins, their contact information will appear on www.clinicaltrials.gov. 1,000 patients will be treated. Progress can be followed at www.nbirr.org. More information is available at www.HBOT.com and www.HyperbaricMedicalAssociation.org.

²⁰ Medicare National Coverage Determinations (NCD) Manual, Publication 100-03, Section, 20.29.

²¹ Golden ZL, Neubauer R, Golden CJ, Greene L, Marsh J, Mleko A. Improvement in cerebral metabolism in chronic brain injury after hyperbaric oxygen therapy. *Int J Neurosci.* 2002 Feb;112(2):119-31.

²² Harch PG. Op. cit.. 2009. War veteran returns to work and school.

²³ Wright JK. Op. cit.. 2009. Two active duty personnel return to duty after 7 months of no progress with standard therapy.

²⁴ Military Replacement Training Costs: Per the "HBOT 1.5 Score Card," costs for recruiting a new service member, \$20,000. Basic Training, \$35,000; Infantry Training: \$150,000 Navy SEAL: \$700,000 Aircraft Pilot: \$5 million.

available now using HBOT 1.5 under IRB-oversight and pursuant to Bayesian methodologies. This is a culmination of 20 years of positive clinical results.

This memorandum outlines: 1) the current emergency involving untreated military and civilian casualties suffering from traumatic brain injury and PTSD, and how these injuries are manifesting themselves within society; 2) the scientific and clinical basis for the significant recoveries achieved by casualties of the current war treated with HBOT 1.5. 3) the most effective way to employ the current accepted uses of HBOT, including that of the NBIRR observational study, to accelerate the recovery of service members and veterans, and enhance the effectiveness of existing therapies. As a core biological repair therapy, HBOT 1.5 will integrate well into current programs for those war veterans, whether in or out of the service, as well as for civilian brain injured persons.

Appendix A: The National Emergency: Traumatic Brain Injury - Signature Injury of the Afghanistan/Iraq Wars

Almost every current war veteran exposed to a blast has a residual injury. A recent study of Fort Lewis, Washington military combatants exposed to blast showed 98% had headaches, a key symptom of Persistent Post Concussion Syndrome (PPCS) symptoms²⁵. The RAND Report (April 2008) estimated approximately 33% of all who have been deployed to Iraq or Afghanistan have one of three conditions; PTSD, major depression or TBI²⁶. That would include 541,200 war veterans as of April, 2008 and 594,000 as of May 2009. The RAND report expected National Guard injury rates to be higher. A new report issued by the National Council on Disability on March 4, 2009, admits that 20% of the 1.8 million who have served, or 360,000 service members might have suffered wartime brain injuries and that 45,000 to 90,000 may have serious, long-term disabilities from their blast injuries²⁷. It is likely these latter numbers are substantially underestimated.

For perspective, there are 154,000 homeless veterans and reports are that as many as 10% of the county jail inmates in many areas²⁸ are current Gulf War era II veterans, There is currently a 21% unemployment rate among Gulf War era II veterans ages 18-24, with a 10.6 unemployment rate for older Gulf War era II veterans. As of March, 12, 2010, 165,000 Gulf War era II veterans are unemployed and 319,000 are not in the labor force because they have given up looking for work, or are too badly injured to do work²⁹. In addition, it has been reported that as many as 16% of combat-arms active duty personnel are not deployable³⁰, likely for blast-related injuries.

Discussions with commanders, National Guard officers and war veterans indicate that about half of the National Guardsmen in states like North Dakota are symptomatic. Their specialties are combat support and combat service support. From the same sources, we have learned that nearly every single deployed combat arms service member has experienced at least one concussive blast. The NBIRR team has treated veterans with as many as 24 concussive blasts. Even a single episode of blast induced loss of consciousness or confusion may cause permanent injury to the brain.

Early in these wars it was the practice of the military to put a service member who was underperforming from a blast-induced brain injury (or PTSD) out of the service as quickly as possible. There have been persistent reports from the field about medical officials being told they are diagnosing too many brain injuries or that they must reduce the level of injury in their diagnoses and reports. To this day there are reports that if

²⁵ <http://blogs.consumerreports.org/health/2009/05/for-iraq-veterans-headaches-continue-following-traumatic-brain-injury-soldiers-mild-head-trauma-or-b.html?resultPageIndex=1&resultIndex=1>

²⁶ Tanielian, Terri & Jaycox, Lisa, Editors: Invisible Wounds of War: Psychological and Cognitive Injuries, Their Consequences and Services to Assist Recovery., RAND Corporation, April, 2008., xxi.

²⁷ Invisible Wounds: Serving Service Members and Veterans with PTSD and TBI. National Council on Disabilities. March 4, 2009. <http://www.ncd.gov/newsroom/publications/2009/veterans.doc>.

²⁸ Source: Reports from California Department of Veterans Affairs, a county in Florida, and Tulsa, Oklahoma.

²⁹ Department of Labor: Veterans Statistics, March 12, 2010. <http://www.bls.gov/news.release/vet.t01.htm>

³⁰ Zoroya, Gregg, "Army sees sharp rise in unfit soldiers, USA Today, 3/2/2010 http://www.usatoday.com/news/military/2010-03-02-unfit-soldiers_N.htm?csp=hf

someone in the service comes forward seeking treatment for their brain injury, their career is terminated and they are quickly out of the service.

Those practices are being reflected in today's headlines. The military-related suicide rate was reported at 17 per day for this population in 2005, and reports have indicated the 2005 rate may have increased in subsequent years³¹. There has been a surge of war veteran county jail inmates reported at 10% in several counties. One of city in Oklahoma saw a surge from 35 in November 2008 to nearly 200 just a few months after 3,000 Iraqi war veterans returned to the state. The divorce rate for this population is reported at 80-90%, personality changes are common and the rate of disability, substance abuse and homelessness is high. About 154,000 veterans currently are homeless³². Law enforcement department restrictions have been imposed on hiring war veterans (unlike previous wars when their experience was considered valuable). Many civilian employers, who usually find veterans above-average employees, report declining capacities in their current veteran hiring. **This is with the current "standard of care" medical palliatives that veil TBI or PTSD symptoms but do not biologically repair the underlying injuries.**

Reacting to congressional pressure, the military began keeping active duty war veterans in the service to get them "treatment," perhaps hoping they would heal by themselves or that effective healing treatments would be found. Barracks across the nation are filled with injured war veterans who are not receiving biologically repair treatment for their injuries. The National Guard casualties have simply returned to their homes with their units. If they are badly injured enough, but fortunate to have family members who can care for them, they are living in some kind of shelter. If not, they become homeless, incarcerated or commit suicide. It is a pattern seen from other wars.

Only 3% of the families in America are contributing family members to the military. Today's service member is a volunteer, not a draftee, a more professional service member who, on average, has greater morale, commitment and acquires higher skills than draftees of previous wars.

Blast-Induced TBI/PTSD Should Not be Compared to Concussive Sport Injury

The belief that, "90% of these concussed war veterans get better in six months with no treatment" is not only untrue but not based in sound science. It reflects the obsolete "belief" or "paradigm" that there is no treatment for brain injury and that blast injuries are just like concussive sports injuries. Neurology has assumed until recently that these sports concussions just get better. New reports regarding NFL players demonstrate this assumption is not true.³³

³¹ See Dr. Harch's testimony to Congress in May 15, 2009, "Off-label prescription drug use by the Department of Defense for TBI and post-traumatic stress disorder (PTSD), and the potential relationship of this drug use to the incidence of suicides in United States Service members."

Keteyian, Armen; "Suicide Epidemic Among Veterans: A CBS News Investigation Uncovers A Suicide Rate For Veterans Twice That Of Other Americans, NEW YORK, Nov. 13, 2007

http://www.cbsnews.com/stories/2007/11/13/cbsnews_investigates/main3496471.shtml

³² Peter Dougherty, Director, Veterans Affairs, Office of Homeless Veterans Programs, Interview 2009.

³³ <http://cbs5.com/sports/nfl.player.dementia.2.1219054.html>, New York, CBS News: Sep 30, 2009 "Ex-NFL Players Report Higher Rates Of Dementia."

John T. Povlishok, M.D., editor of the journal, *Neurotrauma*, presented to the December 2008 DoD HBOT Consensus Conference. He showed blasts have effects that cause multiple types of injury. These effects include things like stretching of neurons by the blast wave, sheer and twisting injuries, concussive injuries from striking solid objects or being struck by objects. The standard sports concussion model did not apply.³⁴ Further, Dr. Povlishok outlined the extensive deterioration in neural pathways that take place over just weeks following blast injuries. Since the DoD HBOT and TBI Consensus Conference, a paper on blast injury has been produced showing that blast waves cause lungs to rupture which in turn can lead to bubbles in circulation as is seen with decompression sickness (DCS).³⁵ Accordingly, if the correct acute and chronic treatment for damage caused by bubbles in the brain from DCS is hyperbaric oxygen, then it stands to reason that the correct acute and chronic treatment for damage caused by bubbles from lungs rupturing due to a concussive blast wave is also hyperbaric oxygen.

Further, brain blood flow is decoupled even in these sports concussions. Even though neuropsychological tests show a return to normal cognitive function, brain blood flow in these individuals remains decoupled. The brain is not able to control its blood circulation as it did previously. Drs. Rockswold, Harch, Orrison, and Fogarty have now all demonstrated that HBOT recouples brain-blood flow, with even a single hyperbaric treatment, thus restoring the physiology in the brain that enables the healing process³⁶.

Confusion in Diagnosis

There appears to be confusion within DoD medicine between blast-induced mild TBI and PTSD. This difficulty is found within the PTSD definition. The definition of PTSD includes symptoms commonly found in TBI (sleep cycle disruption, irritability, and difficulty in concentrating). Considering the PTSD definition was created before mild TBI and Post Concussion Syndrome were understood as they are today, this mix-up is understandable. Nonetheless, the current definition of PTSD is obscuring the diagnosis of mild TBI and branding wounded veterans of the war with emotional problems rather than physical injury.

Readiness & Retention

There is no greater threat to the All-Volunteer Force than hundreds of thousands of untreated and apparently untreatable casualties scattered throughout society. Within the services, highly qualified special operations war veterans are injured and are hiding brain injury and their compromised capacities because they dread the termination of their military careers.

Though the economy has increased the number of volunteers recently, the quality of recruits is down. There are large numbers of TBI/PTSD casualties sitting in barracks on military payroll at a cost of \$375 per day for enlisted personnel and \$425 per day for

³⁴ Povlishok, JT., Neurophysiology and Neuropathology of TBI. 5 Dec 2008. DoD HBOT in TBI Consensus Conference on Hyperbaric Oxygen Therapy in Traumatic Brain Injury. Defense Centers of Excellence.

³⁵ Reimers, Stephen, " The Case for Transient Air Embolism from Lung Injury as a Mechanism for Blast – Related Brain Injury," 2009.

³⁶ See HBOT 1.5 Restores brain Blood Flow & Metabolism, NBIRR Casualty Case Reports.

officers, with thousands of previously able men and women returned to their communities and unable to function normally³⁷. With a need to send and maintain fit troops in Afghanistan, combat readiness of the U.S. Military forces is under severe strain. For those individuals whose careers are terminated, costs are \$5 million for pilots and SOCOM personnel, \$1.3 million for special skill officers, \$845,000 for other officers, and \$500,000 for the average enlisted person³⁸. Discharging injured personnel who could be successfully treated is a huge and needless drain on federal and State resources. Further, if the services "discharge" them without acknowledging their injuries, those individuals become a burden on the States and to their home communities. This represents an unwarranted federal cost shift to the states. That shift is through incarceration, homelessness, unemployed and unemployable persons, high family levels of family disruption, and lost state and local tax revenue.

Altitude in Afghanistan

There are a considerable number of brain injured members of the Armed Forces who have been able to cope and hide their brain injury at sea level or near sea level. Now that war is moving back to Afghanistan, the lack of oxygen living at 7,000 feet and fighting at 10,000 feet will cause previously undiagnosed injuries to degrade individual capacity and performance and make apparent brain injury symptoms that were not seen at lower altitudes.³⁹ That the symptoms of these injuries will manifest at higher altitudes are well known from hypoxia studies conducted by the military in altitude chambers⁴⁰. The military commands need to be aware of this phenomena and prepare to treat these brain injured combatants in theater with HBOT 1.5. Without treatment, there will be a significant degradation of combat readiness in previously concussed individuals.

³⁷ DA PAM 385-40. op. cit. p. 7, Table 1-1

³⁸ Headquarters, Department of the Army. DA PAM 385-40 6 March 2009. Army Accident Investigations and Reporting. Note: These numbers in this pamphlet have not been updated since at least 1990.

³⁹ Ewing, R., McCarthy, D., Gronwall, D. and Wrightson, P.(1980)'Persisting effects of minor head injury observable during hypoxic stress',*Journal of Clinical and Experimental Neuropsychology*,2:2,147 — 155

⁴⁰ Goodman MD, Makley AT, Lentsch AB, Barnes SL, Dorlac GR, Dorlac WC, Johannigman JA, Pritts TA. Traumatic Brain Injury and Aeromedical Evacuation: When is the Brain Fit to Fly? *J Surg Res*; 10: 1-8. June 7, 2009.

Appendix B: Compilation of Evidence for HBOT and the 1.5 ATA Dose

HBOT is an FDA-Approved and Reimbursable Treatment for Repairing Wounds and selected Neurological Indications.

HBOT is the only non-hormonal FDA-approved treatment known to repair and regenerate human tissue.

Summary and Highlights

This is a compilation of scientific evidence for the use of hyperbaric oxygen in neurological indications extending over 100 years starting with diving and aerospace medicine.

This treatment began with using compressed air to treat neurological conditions, as it still does today. Mountain sickness is treated at high altitudes with FDA-approved 1.3 ATA compressed air. This exact same dose has been chosen by DoD medicine as a "placebo" in two studies of its current clinical trials. This is 30% more ambient oxygen, 50% more alveolar oxygen and is also under pressure where biological effects can occur due to increased concentrations of vasoactive neurotransmitters such as nitric oxide and carbon monoxide. The Lancet medical journal and other observers such as the Agency for Healthcare Research and Quality have already understood this not to be a placebo dose, but a treatment arm.

The use of this low dose treatment as a placebo has caused confusion, causing many to believe that hyperbaric oxygen is a treatment with a high placebo coefficient. This "artifact" is because of poor clinical trial design – conscious or unconscious - not because of a defect in hyperbaric oxygen.

In fact, it is impossible for oxygen to be a placebo since it is not inert (a crucial requirement of a placebo). In fact, it is involved in at least 200 cellular processes (you need a reference for this). As we warned the DoD Consensus Conference in December, 2008, use of 1.3 ATA air will likely prevent determination of placebo effects of HBOT as it did in the Collet CP study of 2001. Accordingly the Air Force's 2.4 ATA HBOT vs. 1.3 ATA hyperbaric air study that is currently underway may in fact generate a significant clinical effect in the 1.3 ATA arm. The dose of 2.4 ATA oxygen in the HBOT arm, a dose of HBOT that has never been used in chronic mild TBI post-concussion syndrome and a dose greater than the 2.0 ATA dose demonstrated to cause seizures in subacute moderate to severe TBI, is likely an overdose of oxygen. The combination of this overdose of oxygen with the 1.3 ATA hyperbaric air dose of oxygen in the control group is an intrinsic design flaw that possibly dooms the study before it starts⁴¹.

The science for HBOT 1.5 includes a randomized-controlled animal experimental trial that demonstrated the first ever improvement in chronic brain injury in mammals⁴². The

⁴¹ Bitterman H. Bench-to-bedside review: oxygen as a drug. Crit Care. 2009;13(1):205. Epub 2009 Feb 24. Review.

⁴² Harch PG, Kriedt C, Van Meter KW, Sutherland RJ. Hyperbaric oxygen therapy improves spatial learning and memory in a rat model of chronic traumatic brain

trial not only showed restored memory, it also demonstrated an increase in blood vessel density in the injured tissue area, which is consistent with the HBOT studies in which functional imaging has been used as an outcome measure. Also present is the evidence that began with the use of HBOT 1.5 in clinical practice 30 years ago as an optimum pressure for acute severe TBI treatment.⁴³ The conditions of conduct and outcomes of these cases that militate against placebo effect are described.

Much of the HBOT 1.5 research is of recent publication, including Army Medicine's verification that HBOT 1.5 repairs white matter damage in the brain.⁴⁴ Following the animal model, peer reviewed studies of blast injured veterans have appeared in 2009 and January of 2010, with the larger study being presented on March 12, 2010 at the International Brain Injury Conference. See the Abstract of The Harch 15 Patient Study at Insert 1, the Wright Study at Insert 2); The Harch Case Study at Insert 3). These cases are consistent with other cases and case series previously published in HBOT in chronic severe TBI..

When the effects are as pronounced and uniform as they are with the healing of these “non-healing” wounds in the brain, as illustrated in the above cases, fewer subjects are needed statistically to verify results. Results have been demonstrable for 20 years in functional brain imaging of the physician's choice. Dr. Orrison demonstrated at the DoD HBOT in TBI Consensus Conference that the latest imaging techniques verify results of earlier (and still valid) imaging methodologies, such as SPECT brain imaging.

Independent neuropsychological examinations, such as in the Harch 2010 study include IQ, PTSD, Depression indices, post-concussion syndrome instruments, quality of life, and return to duty work or school. Each independently verify that the healing of previous non-healing wounds in the brain is taking place. A 10% reduction is post concussion

injury. *Brain Res.* 2007 Oct 12;1174:120-9. Epub 2007 Aug 16.

⁴³ Harch, P.G., Van Meter, K.W., Gottlieb, S.F., Staab, P. (1994). HMPAO SPECT brain imaging and low pressure HBOT in the diagnosis and treatment of chronic traumatic, ischemic, hypoxic, and anoxic encephalopathies. *Undersea and Hyperbaric Medicine*, 21(Suppl), 30.

Harch, P.G., Van Meter, K.W., Neubauer, R.A., Gottlieb, S.F. (1996). Use of HMPAO SPECT for assessment of response to HBO in ischemic/hypoxic encephalopathies, in: Appendix, *Textbook of Hyperbaric Medicine*, 2nd ed. K.K. Jain (ed.), Hogrefe and Huber Publishers: Seattle (WA), pps. 480-491.

Harch, P.G. and Neubauer, R.A. (1999). Hyperbaric Oxygen Therapy in Global Cerebral Ischemia/ Anoxia and Coma, in: Chapter 18, *Textbook of Hyperbaric Medicine*, 3rd Revised Edition. K.K. Jain (ed.), Hogrefe and Huber Publishers: Seattle (WA), pps. 319-345.

Golden, Z.L., Neubauer, R., Golden, C.J., Greene, L., Marsh, J., and Mleko, A. (2002). Improvement in cerebral metabolism in chronic brain injury after hyperbaric oxygen therapy. *Intern. J. Neuroscience*, 112, 119-131.

Harch, P.G. and Neubauer, R.A. (2004). Hyperbaric Oxygen Therapy in Global Cerebral Ischemia/ Anoxia and Coma, in: Chapter 18, *Textbook of Hyperbaric Medicine*, 3rd Revised Edition. K.K. Jain (ed.), Hogrefe and Huber Publishers: Seattle (WA), pps. 223-261.

Harch, P.G., Neubauer, R.A. (2009). Hyperbaric Oxygen Therapy in Global Cerebral Ischemia/Anoxia and Coma, in: Chapter 19, *Textbook of Hyperbaric Medicine*, 5th Revised Edition. K.K. Jain (ed.), Hogrefe and Huber Publishers: Seattle (WA), pps. 235-274.

Neubauer, R.A., Gottlieb, S.F., Pevsner, N.H. (1994). Hyperbaric Oxygen for Treatment of Closed Head Injury. *Southern Medical Journal*, 87(9), 933-936.

⁴⁴ Waalkes P, Fitzpatrick DT, Stankus S, Topolski R Adjunctive HBO treatment of children with cerebral anoxic injury. *U.S. Army Medical Journal* April-June 2002:13-21

syndrome alone would be regarded as sufficient to verify clinical effect. With HBOT 1.5, that effect has been a 40% reduction on the scale. To our knowledge, no prior medical treatment or placebo has ever before demonstrated a 15 point IQ increase (35 percentile) in 30 days of neurological treatment. No other treatment provides a 51% decrease in depression or a 30% decrease in PTSD symptoms. If a single prescription drug provided even one of those results, it would be adopted immediately. When the oxygen does all of these things at once, the massed scientific evidence might otherwise prompt skepticism. However, it is well established that for other approved HBOT indications, like decompression sickness, air embolism, crush injury, blunt trauma injury, and” non-healing” or problem wounds of many kinds from diabetes to radiation necrosis, hyperbaric medicine is the only effective treatment available.

In the light of this evidence a reasonably prudent physician or executive can be amply assured in proceeding to prescribe and provide HBOT 1.5 therapy off label for a diagnosed TBI/PTSD patient. Given the known safety of the protocol, this assurance is reinforced further when balanced against the potential harm of leaving an organic brain injury untreated. With the NBIRR Project, patient outcomes are being tracked under a nationally accredited IRB-approved protocol, in the context of the other procedural safeguards inherent in current methodologies such as Coverage with Evidence Development and Bayesian Adaptive Trials. The results are expected to be acceptable to the FDA for a new on-label indication for hyperbaric medical devices.

It is important to note that failure to treat a brain injured patient and apply a biological repair to their brain injury has its own consequences. Personality changes, difficulty with impulse control, cognition deficiencies, diminished executive function, eroded activities of daily living, depression, and sleep disruption are sure to continue. Having experienced ineffective treatment, a consequent "treatment fatigue" cascade sets in with many of these patients where they refuse further treatment when offered. Brain injury patients can be helped much more effectively before the break up of their families, and the onset of unemployment, disability, homelessness, substance abuse, incarceration or suicide. Failure to treat such patients when a promising treatment exists and is available warrants the application of ethical scrutiny.

Appendix B - Section I: HBOT Dosing for Neurological Injuries

Oxygen Dosage for Brain Injury

The use of the HBOT 1.5 dose came about because of work by neurosurgeons in Germany in 1977⁴⁵. Using glucose metabolism as a marker, researchers discovered that oxygen in the brain is optimized at 1.5 ATA. Amounts over that dose in the brain cause glucose metabolism to become dysfunctional. The brain protects itself against "too much" oxygen. A higher dose does not yield optimal metabolism. Thirty years ago, hyperbaric medical practitioners in the United States began using HBOT 1.5 with acute and chronic stroke patients, with positive results. (Neubauer, 1980, Stroke)

Dr. Harch began treating patients 20 years ago with HBOT 1.5⁴⁶, based on the precedent of HBOT 1.5 established by Neubauer and the German neurosurgeons in the 1970s. The experience began with acute TBI and acute spinal cord injury patients, and was rapidly expanded to include divers with subacute and chronic brain decompression illness and eventually over 70 different neurological conditions. He treated many cases under LSU-IRB approved studies presented and published small studies of these results.⁴⁷

As a result of this successful early experience he and Dr. Sheldon Gottlieb extended the successful treatment findings to the first cerebral palsy child treated with HBOT 1.5 in North America. (see footnote 46) .His work was put to trial by the U.S. Army, at Fort Gordon, Georgia, in 2002. The Army study verified that HBOT 1.5 heals damage to white matter in the brain⁴⁸.

⁴⁵ Holbach KH, Caroli A, Wassmann H. Cerebral energy metabolism in patients with brain lesions of normo- and hyperbaric oxygen pressures. *J Neurol.* 1977 Dec 1;217(1):17-30.

⁴⁶ Harch, Paul G.; McCullough, Virginia, *The Oxygen Revolution: Hyperbaric Oxygen Therapy: The Ground Breaking New Treatment*, p. 56.

⁴⁷ Harch PG. Late treatment of decompression illness and use of SPECT brain imaging. In *Treatment of Decompression Illness, 45th Workshop of the Undersea and Hyperbaric Medical Society* (eds RE Moon, PJ Sheffield). UHMS, Kensington, 1996, 203-242.

Harch PG, Van Meter KW, Neubauer RA, Gottlieb SF. Use of HMPAO SPECT for assessment of response to HBO in ischemic/ hypoxic encephalopathies. In: Jain KK (ed). *Textbook of hyperbaric medicine, 2nd Revised Edition.* Hogrefe & Huber Publishers, Seattle WA, 1996, pp 480-491.

Harch PG, Van Meter K, Staab PK, Gottlieb SF. HMPAO SPECT brain imaging-guided hyperbaric oxygen therapy in the treatment of neurological residual of carbon monoxide poisoning. 1995 UHMS Gulf Coast Chapter Annual Meeting, New Orleans, LA, Mar 30 - Apr 2, 1995.

Van Meter K, Harch P, Weiss L, Andrews C, Simanonok J, Gottlieb S. 14 year experience of the use of a tailing of hyperbaric oxygen treatments to lessen or resolve neurologic illness (DCI) in the acute (15 day) and sub-acute (16 day to 6 month) post-injury period. 1995 UHMS Gulf Coast Chapter Annual Meeting, New Orleans, LA, Mar 30 - Apr 2, 1995.

Harch PG, Van Meter KW, Gottlieb SF, Staab P. HMPAO spect brain imaging of acute CO poisoning and delayed neuropsychological sequelae (DNSS). *Undersea & Hyperbaric Medicine*, 1994;21(Suppl):15.

⁴⁸ Waalkes P, Fitzpatrick DT, Stankus S, Topolski R Adjunctive HBO treatment of children with cerebral anoxic injury. *U.S. Army Medical Journal* April-June 2002:13-21.

In 2007, after several years of research, a series of animal experiments verified the HBOT 1.5 protocol first used in humans also proved effective in rats. The animal experiment is the first improvement of chronic brain injury in animals in the history of science and uses the HBOT 1.5 dose⁴⁹.

On August 14, 2008, Dr. Harch briefed the Navy Surgeon and the Assistant Marine Commandant, including five case studies of veterans treated with the HBOT 1.5 protocol. The five included a U.S. Army General who had received the 80 hour HBOT 1.5 protocol while a patient at Walter Reed. One of those cases was published in the Cases Journal on 12 March 2009. The subject is a former Marine who testified at the August 14, 2008 briefing (See Insert 3)⁵⁰.

When one of DoD's leading hyperbaric medicine physicians, Colonel James Wright, USAF, MC heard of Dr. Harch's work, the scientific validity of the treatment was clear. Thereafter he treated a number of active duty Air Force and SOCOM personnel under his official jurisdiction. The first of these, whose treatment began in September of 2008, was published in December 2009 (See Attachment 2). Both airmen, the first two patients treated, not only had improvement on the DoD's own neuropsych test, the ANAM, but they both were restored to duty and continued their careers. Had they not been treated, both of them would have been discharged from the service, having received a disability rating for TBI. Instead, the Air Force continues to retain their valuable expertise in their respective senior-NCO positions⁵¹.

Shortly after the initial meeting with the Surgeon General of the Navy, Dr. Harch initiated new study under an IRB from Louisiana State University with assistance from several military charities and other private sector contributors. That study has produced the current research based on 15 cases presented on the 12th of March, 2010 at the 8th World International Brain Injury Conference. The abstract is entitled "Hyperbaric Oxygen Therapy Treatment of Chronic Mild-Moderate Blast-Induced Traumatic Brain Injury/Post Concussion Syndrome with Post Traumatic Stress Disorder: Pilot Trial."⁵²(See Insert 3).

Appendix B - Section II: Scientific and Clinical Basis for the Efficacy of HBOT 1.5 Treatment

HBOT is an FDA-Approved and Reimbursable Treatment for Repairing Wounds and selected Neurological Indications.

HBOT is the only non-hormonal FDA-approved treatment known to repair and regenerate human tissue. HBOT repairs and regenerates tissue through oxygen-dependent and signaled processes, including reactivation of cellular processes damaged

⁴⁹ Harch PG, Kriedt C, Van Meter KW, Sutherland RJ. Hyperbaric oxygen therapy improves spatial learning and memory in a rat model of chronic traumatic brain injury. Brain Res. 2007 Oct 12;1174:120-9. Epub 2007 Aug 16.

⁵⁰ Harch PG, Fogarty EF, Staab PK, Van Meter K. Low pressure hyperbaric oxygen therapy and SPECT brain imaging in the treatment of blast-induced chronic traumatic brain injury (post-concussion syndrome) and post traumatic stress disorder: a case report. Cases J. 2009 Jun 9;2:6538.

⁵¹ Wright JK. Op. cit. 2009.

⁵² https://ibia.conference-services.net/programme.asp?conferenceID=1677&action=prog_list&session=6765

by hypoxia; the activation of growth factors at a DNA level; stimulation of a patient's own stem cells to cause growth and repair; and the improvement of blood supply to wounds. These salutary effects of hyperbaric oxygen can be seen in a variety of the FDA-approved indications, such as the acute wounds of traumatic loss of blood supply, traumatic hemorrhage, crush injury, and a number of neurological injuries. These effects also apply in FDA-approved conditions with chronic wounds such as diabetic foot wounds, radiation wounds, and chronic bone infections. In 1977, the British military published its finding that a 50% improvement in combat casualty care healing rates could be achieved using hyperbaric oxygen⁵³, a conclusion reinforced in Croatia in 1994⁵⁴ and Wright in 2000⁵⁵. Non-healing brain wounds respond to the correctly-pressured oxygen dose in repeated treatments in much the same manner as do non-healing diabetic foot wounds. Reimbursement for treatment of diabetic foot wounds was recently, approved by Medicare upon the IHMA's request and submission of a formal application to CMS for a National Coverage Determination. It was approved in 2003⁵⁶.

The salutary effects of HBOT apply regardless of the location of the wounds in the body. As a result, HBOT can be considered a generic drug for repair of acute and chronic wounds in the body. The application of HBOT to chronic traumatic brain injury is merely the extension of these known biological and physiological effects. When this extension is also underpinned by clinical precedent it meets the criteria for FDA-approval as an "off-label" application of an FDA-approved drug. Nearly 25% of all prescriptions are "off-label" and 80% of pediatric prescriptions are off-label. HBOT for healing wounds in the brain is not, as some have contended, experimental or investigational. Such a classification not only mischaracterizes the scientific evidence, but also unnecessarily prevents casualties from receiving this salutary therapy.

Overview of the Science: HBOT's Healing Effects

Oxygen is essential to human life. Appropriate oxygen availability is necessary to optimize bodily functions, sustain life, and repair damaged tissues⁵⁷. Oxygen normally is dissolved in the blood through the lungs and distributed throughout the body in the circulatory system. Exposing blood to higher than usual levels of oxygen through breathing oxygen under pressure increases the amount of oxygen available in the body to several times normal, with the exact increase depending on the pressure or dose at which

⁵³ Schramek A, Hashmonai M. Vascular injuries in the extremities in battle casualties. *Brit J Surg*, 1977;64:644-648.

⁵⁴ Radonic V, Baric D, Petricevic A, et al. Military injuries to the popliteal vessels in Croatia. *J Cardiovasc Surg*, 1994;35:27-32.

⁵⁵ Wright JK. "The Relevance of Hyperbaric Oxygen to Combat Medicine; RTO HFM Symposium on "operational Medical Issues in Hypo- and Hyperbaric Conditions," Toronto, Canada, 16-19 Oct 2000, RTO MP-062.

⁵⁶ See www.HyperbaricMedicalAssociation.org for the submission documentation and scientific argument, etc. CMS approved diabetic foot wound treatment in 2003. See

www.HyperbaricMedicalAssociation.org/Science for the diabetic foot wound argument. In addition, it costs about \$16,000 to rebuild a Wagner Grade III foot wound. By the time the series of surgeries are completed, it costs \$30,000 to treat this conventionally, with a cost of \$150,000 for multiple surgeries, prosthetics, etc., with the patient dead 18 months after the 2nd amputation from cardiovascular complications. It is far less expensive to treat with HBOT and prevents the cascade of events.

⁵⁷ Sheffield, P.J., *Physiological and Pharmacological Basis of Hyperbaric Oxygen Therapy, Hyperbaric Surgery*, Baker, Dirk, pp 63-109.

the treatment is conducted. When HBOT 1.5 is delivered intermittently, it saturates tissues with oxygen at approximately 7 times the normal concentration. In this context oxygen acts like an oxygen pill, stimulating healing processes like a medicinal drug⁵⁸.

The physiological processes enhanced by hyperbaric oxygen treatments are well understood and characterized in the literature.⁵⁹ Oxygen is used in over 200 cellular processes, many of which remain damaged after hypoxia.⁶⁰ Considering the well-known clinical and physiological effects of hyperbaric medicine to heal chronic wounds, the incidents of the clinical effects currently being experienced by these HBOT 1.5-treated combat veterans being attributable to placebo is inappropriate.

HBOT's healing characteristics include the ability to reduce hypoxia (low oxygen levels in damaged tissue), energize cells damaged by low blood flow, and in acute injuries, inhibit reperfusion injury (the immune response to injury). Additionally, high levels of oxygen stimulate release of stem cells from a patient's bone marrow into their circulatory system where the stem cells then home in on wounded areas of the body⁶¹. These stem cells address the tasks of repairing or replacing damaged or destroyed cells and tissue, and repairing or replacing damaged vascular systems in restoring blood flow⁶². HBOT is now viewed as a growth and repair drug by virtue of its stimulation of DNA genes that code for growth and repair hormones and their receptors^{63,64}. The net result of this stimulation is growth of new tissue, bone, skin, and blood vessels⁶⁵. This healing proceeds with mild or rare adverse side effects when established protocols are followed⁶⁶.

One of the reasons hyperbaric medicine implementation will be delayed is found in the over 40 year history of the science of treating divers for decompression

⁵⁸ Boerema I, Meyne NG, Brummelkamp WK, et al. Life without blood: a study of the influence of high atmospheric pressure and hypothermia on dilution of blood. *J Cardiovasc Surg*, 1960;1:133-146.

⁵⁹ For an extensive summary of this literature from the U.S. Air Force, see: Wright JK. "The Relevance of Hyperbaric Oxygen to Combat Medicine," Paper presented at the RTO HFM Symposium on "Operational Medical Issues in Hypo- and Hyperbaric Conditions", held in Toronto, Canada, 16-19 October 2000, and published in RTO MP-062., and Wright JK, Zant E, Groom K, Schlegel RE, Gilliland K. Case report: Treatment of mild traumatic brain injury with hyperbaric oxygen. *Undersea Hyperb Med*. 2009 Nov-Dec;36(6):391-9.

⁶⁰ Van Meter K, Sheps S, Kriedt F, Moises J, Barratt D, Murphy-Lavoie H, Harch PG, Bazan N. Hyperbaric oxygen improves rate of return of spontaneous circulation after prolonged normothermic porcine cardiopulmonary arrest. *Resuscitation*. 2008 Aug;78(2):200-14. Epub 2008 May 16.

⁶¹ Thom SR, Bhopale VM, Velazquez OC, Goldstein LJ, Thom LH, Buerk DG. Stem cell mobilization by hyperbaric oxygen. *Am J Physiol Heart Circ Physiol*. 2006 Apr;290(4):H1378-86. Epub 2005 Nov 18.

⁶² Yin D, Zhang JH. Delayed and multiple hyperbaric oxygen treatments expand therapeutic window in rat focal cerebral ischemic model. *Neurocrit Care*. 2005;2(2):206-11.

⁶³ Wu L, Pierce GF, Ladin DA, Zhao LL, Rogers D, Mustoe TA. Effects of oxygen on wound responses to growth factors: Kaposi's FGF, but not basic FGF stimulates repair in ischemic wounds. *Growth Factors*. 1995;12(1):29-35.

⁶⁴ Sheikh AY, Gibson JJ, Rollins MD, Hopf HW, Hussain Z, Hunt TK. Effect of hyperoxia on vascular endothelial growth factor levels in a wound model. *Arch Surg*. 2000 Nov;135(11):1293-7.

⁶⁵ Marx RE, Ehler WJ, Tayapongsak P, Pierce LW. Relationship of oxygen dose to angiogenesis induction in irradiated tissue. *Am J Surg*. 1990 Nov;160(5):519-24.

⁶⁶ DoD Consensus Conference White Paper, October 2008.

sickness.^{67,68,69,70,71,72} The purpose of the pressurized delivery of oxygen through HBOT was initially thought necessary to "eliminate bubbles" occurring in the blood due to inadequate decompression. For years, practitioners could not determine how burn recovery, wound healing or stroke recovery through administration of HBOT related to elimination of bubbles. By 1989, however, and now assisted by new medical scanning technologies, Navy research demonstrated that the bubbles in brain decompression sickness for the most part disappeared quickly even in the absence of treatment.^{73,74,75} Harch, investigating the reasons for the huge disparity in Navy vs. commercial and sport SCUBA treatment results, combined this Navy bubble research with other key observations and reports to convincingly argue that the primary target of Navy treatment in cases of acute brain decompression sickness was not bubbles, but the damage to blood vessels caused by the passage of bubbles. By adapting the acute treatment protocol to a lower dose of HBOT, Dr. Harch found in the early 1990s that divers with more chronic neurological injuries from decompression sickness could be rehabilitated with HBOT similarly to the rehabilitation of divers with acute injuries.

Also with the advent of advanced functional brain-imaging technologies, decompression brain damage was evaluated and found to be remarkably similar to brain damage from other causes such as TBI, stroke, and cerebral palsy. Accordingly, as cited, the potential of HBOT for treatment of other brain injuries began to be realized from the research and clinical experience of Drs. Neubauer, Harch and others. Oxygen at 1.5 ATA (HBOT 1.5) was determined to be the optimum pressure for the treatment of brain injury, combining rapid, comprehensive recovery with low risk.

The Department of Defense invited William W. Orrison, Jr., M.D., to deliver the neuroradiology presentation on December 5th, 2008 at the "HBOT in TBI" Consensus

⁶⁷ Harch PG. Late treatment of decompression illness and use of SPECT brain imaging. In Treatment of Decompression Illness, 45th Workshop of the Undersea and Hyperbaric Medical Society (eds RE Moon, PJ Sheffield). UHMS, Kensington, 1996, 203-242.

⁶⁸ Harch PG, Van Meter KW, Gottlieb SF, Staab P. HMPAO spect brain imaging of acute CO poisoning and delayed neuropsychological sequelae (DNSS). Undersea Hyperb Med. 1994;21(Suppl):15.

⁶⁹ Harch PG, Van Meter KW, Gottlieb SF, Staab P. The effect of HBOT tailing treatment on neurological residual and SPECT brain images in type II (cerebral) DCI/CAGE. Undersea Hyperb Med. 1994;21(Suppl):22-23.

⁷⁰ Harch PG, Gottlieb SF, Van Meter KW, Staab P. HMPAO SPECT brain imaging and low pressure HBOT in the diagnosis and treatment of chronic traumatic, ischemic, hypoxic and anoxic encephalopathies. Undersea Hyperb Med. 1994; 21(Suppl):30.

⁷¹ Harch PG, Van Meter KW, Gottlieb SF, Staab P. Delayed treatment of type II DCS: the importance of low pressure HBOT and HMPAO SPECT brain imaging in its diagnosis and treatment. Undersea & Hyper Med, 20(Suppl):51, 1993.

⁷² Paul G. Harch, Sheldon F. Gottlieb, Keith Van Meter, Paul K. Staab. SPECT brain imaging in the diagnosis and treatment of type II decompression sickness. Undersea Hyper Med, 1992;19(Suppl):42.

⁷³ Cockett ATK, Zehl DN, Hanley J, Adey WR, Roberts AP. Effects of emboli on the neurocirculatory system in decompression sickness. In: Trapp WG, Banister EW, Davison AJ, Trapp PA, editors. Proceedings of the 5th International Hyperbaric Congress, Vol. II, 1973. Simon Fraser University, Burnaby 2, B.C., Canada, 1974.

⁷⁴ Gorman DF, Browning DM. Cerebral vasoreactivity and arterial gas embolism. Undersea Biomed Res, 1986 Sept:13(3):317-35.

⁷⁵ Moon RE, Gorman DF. Treatment of the Decompression Disorders, Chapter 18. In: The Physiology and Medicine of Diving, 4th Edition, eds. Bennett P, Elliott D. W. B. Saunders Company, Ltd. London, 1993.

Conference. Examples of some of the hundreds of patients Dr. Harch has treated with HBOT 1.5 over the past 20 years are at www.HyperbaricMedicalAssociation.org/Science. Dr. Orrison showed functional brain scans on a series of cases, each of whom had been treated with the Harch HBOT 1.5 protocol by 3 different physicians. All patients reflected major recovery of brain function with documentary brain imaging.

Dr. Orrison's assessment of Dr. Harch's SPECT brain images is as follows:: **"Dr. Harch's use of SPECT brain imaging to examine the changes in the brain before and after hyperbaric oxygen therapy is scientifically accurate and valid. Multi-detector SPECT imaging is one of the only neuroimaging methods with sufficient utility to allow this type of longitudinal evaluation. The improvement in brain perfusion demonstrated by Dr. Harch pre- and post-HBOT is impressive and objective evidence of improved cerebral blood flow in these patients. This is the same type of change that we have recently demonstrated using the new method of whole brain CT. In addition, the clinical observations and neuro-psych testing done by numerous physicians at different locations further verifies Dr. Harch's results and correlates with the objective findings observed on the SPECT images."** ~ *William W Orrison Jr, MD*

HBOT is Safe, Effective and an Extension of Navy Diving Medicine

The HBOT 1.5 protocol is extremely safe and effective and is a direct extension of the U.S. Navy Diving Tables. In the United States Navy and nearly all other navies of the world, injured divers are treated for decompression sickness shortly after emerging from the water⁷⁶. They experience a 90% cure rate on the first treatment. As briefly mentioned above, in the late 1980s Dr. Harch found that commercial and recreational divers presenting late for treatment failed to improve as markedly as Navy divers who were usually treated with HBOT immediately. He carefully observed that the repetitive high doses of HBOT in the Navy protocol had limited effectiveness for delayed cases, especially for those with cerebral decompression illness. Borrowing from the Germans and Dr. Neubauer, he applied the HBOT 1.5 protocol for extended treatments and discovered that these divers eventually improved. Under Dr. Harch's research, these findings were then successfully applied to a multitude of other chronic neurological conditions, including TBI and PTSD. The HBOT 1.5 protocol was found to increase safety and also proved effective on subacute and chronic neurologic wounds.

Gaylan Rockswold, M.D., the neurosurgeon who used HBOT to reduce death by 59% in the most severe acutely brain injured patients concluded that "Based on our own past and continuing investigations ... placing severe TBI patients in either a monoplace or multiplace HBO chamber at 1.5 ATA for 60 minutes is a very low risk procedure."⁷⁷ **The official DoD White Paper prepared for the Consensus Conference states, "Side effects from HBOT are uncommon, and severe or permanent complications are rare, especially at the doses of HBOT used "off-label" for TBI patients (approximately 1.5 atm abs for 60 minutes.), compared to HBOT for HHS covered**

⁷⁶ Op. cit. DoD Consensus Conference White Paper, October 2008.

⁷⁷ Rockswold SB, Rockswold GL, Defillo A. Hyperbaric oxygen in traumatic brain injury. *Neurol Res.* 2007 Mar;29(2):162-72.

indications (2 to 2.4 atm abs for 120 to 90 minutes.)”⁷⁸ **For the mild traumatic brain injury patient, clinical experience demonstrates this treatment is far less risky to patients than leaving them untreated.** It is also less risky than their having been in Iraq or Afghanistan military tours, a risk for which they volunteered and for which their resulting injuries the most basic justice demands their receiving available, effective treatment.

Placebo Effect

A major argument lodged against permitting apparently HBOT 1.5 treatment for battle casualties immediately is that HBOT 1.5 might be merely a placebo effect. DoD Medicine has launched a \$20 million Clinical Trial in which 1/2 of those treated get the HBOT 1.5 dose, 1/2 get an HBOT 1.3 ATA "air" "placebo" treatment (that may render a positive clinical effect), both for 40 treatments rather than the 80 called for in the NBIRR protocol. DoD Medicine has stated that this will provide a definitive answer as to whether 40 HBOT 1.5 treatments have any effect. As critique above, this design will confuse the issue, not provide a definitive answer. Furthermore, if left, with only 40 treatments for the ensuing 5-10 years until DoD possibly does a follow-up comparator dose study of 40 vs. 80 HBOT treatments, many of these war casualties will likely have developed further problems, such as dissolved families, substance abuse, or become incarcerated or homeless. It is much more beneficial to the casualty and less risky to treat them with HBOT 1.5 for 80 treatments than to leave them untreated pending completion of design and execution of a clinical trial.

The Placebo effect is the medical phenomenon in which a person's beliefs or hopes about an inert substance or a sham therapy results in that treatment inducing the expected effects. These beliefs have effects upon the patient's health without underlying physical effects. Thirty five percent of patients are expected to get some improvement because of placebo effect.⁷⁹ HBOT 1.5 has significantly improved over 90% of the patients treated to date. Placebo effects do not cause perceptible regrowth of vasculature in the brain, or reactivate stunned neural tissue or increase brain metabolism, as independent, objective neuroimaging reveals. HBOT 1.5 causes 15 point increases in IQ, improvements on neuropsychological testing, 30% reduction on PTSD and 40% reduction in PPCS symptoms. These results exceed any other available therapy. This relief, combined with a 51% decrease in depression, has permitted 80% of those casualties treated to return to duty, work, or school. These effects are much greater than any other treatment modality used to date. The placebo effect does not explain the permanent biological repair experienced by thousands of patients with hundreds of providers over 30 years.⁸⁰

In summary, there are several reasons it is highly unlikely that improvement in war casualties treated with HBOT 1.5 is the result of a placebo effect.

⁷⁸ Op. cit., DoD Consensus Conference White Paper, October 2008.

⁷⁹ Wikipedia, "Placebo Effect"

⁸⁰ IHMA Document, October 2009, "Can Hyperbaric Oxygen Create a Placebo Effect? Basic Understanding of Scientific Methods"

- 1) Oxygen can never be a placebo because it violates one component of the placebo definition, that the substance is inert. Oxygen is a biologically active element, used in over 200 cellular processes and hence is not inert.
- 2) Placebo effects are not expected to show improvement in over 90% of the subjects treated.
- 3) Placebos do not show independently verifiable clinical effect. DoD's own invited expert, Dr. Orrison, stated showed that the latest neuroimaging techniques showed improved brain structure. A placebo does not do that. It is a clear clinical effect that rules out placebo. As John Eisenberg, MD, Ph.D., founder and director of AHRQ stated, "This is an N of 1 study where each patient serves as their own control. When there is 30 days between one image and other, and the only intervention was HBOT 1.5, the cause of the repair can only logically have been HBOT."⁸¹
- 4) The laws of physics and the gas laws show that HBOT 1.5 delivers 7 times as much oxygen to plasma as normally breathed. The known science of how oxygen works and how the body uses oxygen to heal indicates that this oxygen delivery begins healing at the DNA level, activates stem cells, and increases blood vessel density. It does this in bone, skin and other hypoxic tissues throughout the body. Why would the brain be different?
- 5) HBOT 2.0-2.4 clearly heals diabetic foot wounds. These are hypoxic wounds that we can see, and HBOT has a clinical effect. HBOT has been proven in RCTs and placebo effect was eliminated as a reason for healing. Wounds in the brain are also hypoxic wounds. It is logical that HBOT heals the hypoxic wounds in the brain and in the foot. Thus the HBOT clinical experience is consistent with the scientific validity of the rest of the HBOT treatment indications.
- 6) After 6 months, no further natural healing is expected in brain injured patients. Therefore, even years after injury, to have these injuries heal, permanently, within a 30 day period, can only be attributed to a clinical effect.
- 7) The improvement in the above cases that allowed return to duty occurred in cases that were facing being medically boarded out of the military. Few of these service members wanted this result. The desire to avoid medical boarding would tend to generate a placebo effect for every therapy prior to HBOT that was offered to these men to improve their condition. However, only HBOT 1.5 provided the objective improvement that allowed them to return to duty. The decision to return to duty was made by independent physicians who did not deliver the HBOT. These were the same physicians who were initially recommending them for a medical board. If HBOT is in fact a placebo every service member who is facing medical boarding should be offered the placebo effect of HBOT 1.5 to avoid medical boarding when all other therapies have failed.

No currently available DoD treatment for TBI/PTSD has demonstrated the improvement of HBOT 1.5 and all have both therapeutic and placebo effects. To argue, as the Surgeons General of two branches of the service have, that the greater effect of HBOT is due to placebo and that this placebo effect exceeds the therapeutic and placebo effect of

⁸¹ Meeting with Drs. Duncan, Harch and Neubauer in 2002. This is when Dr. Eisenberg ordered the HBOT 1.5 literature review on HBOT in TBI and stroke. Unfortunately it was completed after his death and did not actually examine the evidence for HBOT.

all other DoD treatments singly and in combination is scientifically implausible. When considered against the foundation evidence of HBOT's decades long known physiological effects in acute and chronic wounding this placebo argument becomes simply delusional.

Research Methodology and Medical Evidence

Research methodology has changed markedly in the past few years. Except for new molecule drug development, most discussions of FDA-approved modalities like HBOT and other devices have moved toward Bayesian Analysis**. This modality allows for determination of medical efficacy without sham or placebo treatments**. Comparative efficacy studies, for example, could put HBOT 1.5 up against the standard drug treatments the DoD and VA are using. As already discovered by the pilot studies completed, many patients need few of the prescription drugs that have been previously prescribed, and others may need some assistance with sleep or headache control, but use much less than previously used. Both of these would be a major budget savings for DoD and VA medicine. Effectively, no other treatment modality, other than HBOT 1.5, has restored the percentage, or to our knowledge, the number of TBI/PTSD casualties to duty that the IHMA-affiliated clinics have using the HBOT 1.5 protocol.

Failures of many drugs developed using the randomized clinical trial (RCT) technology have driven the FDA to seek and endorse additional scientific methods. The basic science hypothesis in an RCT is that we know nothing about a proposed methodology, even though, as in the case of hyperbaric medicine, there may be 100 years of accumulated knowledge to draw upon. This prior knowledge can be appropriately included in Bayesian study designs.

Further, a control arm or sham treatment group denies potentially effective therapy to a large number of study participants. In the case of brain injury, when it is left untreated, even for a few short months, it is devastating to the family, careers, esteem, and can be potentially life threatening to the service member and their families.

Conclusion

The risks to patients of leaving brain injuries untreated are severe and inexcusable. The effect on the Army and the other Services is degrading in many respects. That HBOT 1.5 is ethical and is safe qualifies it for use now, and makes it a logical subject of IRB-approved treatment from which data is continuously gathered and analyzed. Waiting for more definitive proof comes at the expense of hundreds of thousands of injured individuals and their families. It operates to the detriment of the readiness of the United States Armed Forces, as demonstrated by the recent increase in the number of persons in the active force who cannot be redeployed. It operates to the erosion of credibility of the Army chain of command, as well as the strength of unit readiness and cohesion.

Delay is costing millions of dollars now and inflicting untold suffering on wounded VOLUNTEERS and their families. It is incurring further millions in the out years that could be saved by applying effective treatment now. Decision makers and policy makers

have the authority to reverse the effects of the current crisis. The solution, 50+ year old hyperbaric medicine, offers a low-cost, effective, and readily deployable solution.

Dr. William A. Duncan
Vice President of Government Affairs

Attachments

Attachment 1 Harch Case Report June 9, '09

Attachment 2 Wright, Case Report: Two Airmen...

Attachment 3 Harch Abstract March 2010

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International Hyperbaric Medical Foundation

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Hyperbaric Oxygen Therapy Treatment of Chronic Mild-Moderate Blast-Induced Traumatic Brain Injury/Post Concussion Syndrome with Post Traumatic Stress Disorder: Pilot Trial

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Objectives

Mild-moderate blast-induced traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD) affect 11-28% and 13-17%, respectively, of U.S. combat troops returning from Iraq and Afghanistan. Protracted treatment for PTSD exists, but there is no effective treatment for the post-concussion syndrome (PCS) of mild-moderate TBI nor the combined diagnoses of PCS and PTSD. Based on previous case experience with PCS and an animal model we investigated the effect of hyperbaric oxygen therapy (HBOT 1.5) on symptoms, cognition, and SPECT brain blood flow in military veterans with blast-induced TBI/PCS with/without PTSD.

Method

Fifteen symptomatic U.S. military veterans with blast-induced PCS(2) or PCS/PTSD(13), diagnosed by military and/or civilian neuropsychologists and neurologists, who were average: 29.7y (21-45), 2.6y (1.24-4.75) post injury, 1 minute (13 subjects; 2 subjects 4.5 & 9h) loss of consciousness, with 3 blast TBI's (1-8) completed the study. All subjects completed cognitive testing, symptom and quality of life questionnaires, and affective measures pre and immediately post a course of forty bid, 5d/week, 1.5ATA/60 minute hyperbaric oxygen therapy treatments (HBOT). Subjects underwent SPECT brain blood flow imaging (Picker Prism 3000, 25mCi Ethyl Cysteinate Dimer) pre and post a single HBOT and post 40 HBOT's. SPECT was analyzed with Osiris software; relative standard deviation of the mean on a histogram analysis of counts in left centrum semiovale region of interest was taken pre/post Rx. Paired Student t test and Wilcoxon Signed-Ranks test (non-normally distributed data) were used for all cognitive/questionnaires.

Results

All subjects reported symptomatic improvement in the 35 day study period. Pre, post, difference, confidence interval, and p values for cognitive tests and questionnaires were: FSIQ: 95.8+/-8.4; 110.6+/-10.3, 14.8+/-7.4, 10.7-18.9, <0.001; Wechsler Memory Scale (WMS) IV delayed memory: 97.7+/-13.3, 106.9+/-15.4, 9.2+/-14.3, 1.3-17.1, =0.026; WMS Working Memory: 97.0+/-13.6, 106.9+/-13.1, 9.9+/-10.3, 4.1-15.6, =0.003(np); Stroop Color/Word: 84.3+/-12.2, 95.3+/-12.8, 11.1+/-9.2, 6.0-16.2, <0.001; TOVA variability: 64.4+/-28.7, 75.3+/-24.6, 10.9+/-20.2, -0.2-22.1, =0.045(np); Rivermead Post Concussion Symptom Questionnaire: 39.7+/-6.0, 24.1+/-12.6, -15.6+/-12.8, -22.7-(-8.5), =0.002(np); PTSD Checklist Military: 67.4+/-10.5, 47.1+/-16.0, -20.3+/-18.2, -30.4-(-10.2), <0.001; Modified Perceived Quality of Life: 81+/-37, 114+/-36, 33+/-36, 13-53, =0.003; Personal Health Questionnaire 9-Depression Index: 16.6+/-4.9, 8.2+/-4.7, -8.4+/-7.4, -12.5-(-4.3), <0.001; GAD-7 Anxiety Rating: 12.7+/-5.8, 7.9+/-5.3, -4.8+/-5.8, -8.0-(-1.6), =0.007; Percent Back to Normal: [Cognitive: 49.6+/-17.6, 67.0+/-19.4, 17.4+/-17, 7.5-27.2, =0.002], [Physical: 46.8+/-23.0, 66.3+/-18.6, 19.5+/-16, 10.3-28.7, <0.001], [Emotional: 32.5+/-20.6, 61.3+/-19.8, 28.8+/-20.9, 16.7-40.9, <0.001]. SPECT analysis on the first 5 subjects showed a reduction in the standard deviation of the mean on counts in the left centrum which corresponded to a pattern shift from heterogeneity (abnormal) to homogeneity (more normal).

Conclusions

A thirty day course of forty 1.5 ATA HBOT's demonstrated significant symptomatic, cognitive, and affective improvements in 15 U.S. military veterans with chronic blast-induced post-concussion syndrome and post-traumatic stress disorder. These findings were reinforced by quantitative and qualitative SPECT improvements.

Lay Interpretation of Preliminary Data in LSU IRB #7051 Pilot Trial Hyperbaric Oxygen Therapy (HBOT) in Chronic Traumatic Brain Injury (TBI)/Post-Concussion Syndrome (PCS) and TBI/Post-Traumatic Stress Disorder (PTSD)-Pilot Trial

The preliminary data from the LSU Pilot Trial of Hyperbaric oxygen therapy in blast-induced chronic traumatic brain injury (TBI) and post-traumatic stress disorder (PTSD) represents the first organized body of information that suggests a significant treatment effect on the conditions that present the greatest challenge to the integrity of our armed forces.

The Rand Report of 4/2008 indicated that about 33% of our military that have served in Iraq and Afghanistan have been injured or affected by TBI or PTSD or major depression. That is nearly 600,000 individuals. Traditional treatment is protracted counseling and off-label, unapproved use of FDA-black labeled psychoactive drugs that have significant side effects such as increased suicide rates. Epidemic suicide rates currently seen in war veterans from recent conflicts are consistent with the use of such medications.

In this seminal report at the 8th World Congress on Brain Injury Harch and colleagues from LSU School of Medicine, New Orleans demonstrated significant improvements in cognition, symptoms, and quality of life in 15 U.S. veterans with TBI and PTSD an average 3 years after their injury. The physicians and researchers showed that with 4 weeks of treatment using a low dose of hyperbaric oxygen therapy, a treatment used for nearly 100 years in divers and 50 years for wounds, they were able to treat these wounds in the brains of injured U.S. servicemen. Specifically, the veterans achieved substantial improvements in memory, concentration, executive function, and quality of life, and a reduction in headaches, concussion symptoms, depression, and anxiety. Specifically, the veterans achieved substantial improvements in memory, concentration, executive function, and quality of life, and a reduction in headaches, concussion symptoms, depression, and anxiety.

The average veteran experienced clinically meaningful and highly significant improvements. Their IQ increases 15 points -- a nearly 35 percentile increase. This is the IQ difference between a construction worker and an engineer. Other cognitive improvements averaged 25 percentile points. Quality of life measures, concussion symptoms, depression and anxiety indices, and the veterans own estimates of their cognitive, physical, and emotional improvements improved by 30-90%. Surprisingly, the veterans showed a 30% reduction in PTSD symptoms, a 40% reduction in post-concussion syndrome and a 51% decrease in depression and anxiety indexes. All results were clinically and statistically significant. The treatment effects are lasting and reduced or eliminated the need for other medications.

While the study did not include a control group, the magnitude of the improvement measured was striking and never before reported in the medical literature. The time course of symptoms and clinical response over the course of therapy followed a consistent pattern and was of such magnitude that the treatment results cannot be attributed to a placebo effect. Moreover, the outcome measures were supported by functional brain imaging data. This imaging data was very similar to a previous study by Harch where HBOT improved memory and blood vessel density in an animal model of traumatic brain injury. In gauging benefit relative to risk, it is notable that in both the case reports and the LSU pilot study there was no significant side effect to the treatment apart from a temporary emotional flare-up in some patients. The scientific report at the International Brain Injury Association's 8th World Congress reaffirmed earlier published peer-reviewed case reports of Harch and USAF Col. Jim Wright on brain injured U.S. servicemen.

The implication of this preliminary study is that U.S. veterans with the same conditions can safely begin treatment with this established modality, HBOT, by physician direction privately or under a national program approved by Western Institutional Review Board. This program, the National Brain Injury Recovery and Rehabilitation Project (N-BIRR) will incorporate the latest statistical design methodology that is favored by the FDA, the Bayesian Adaptive Design, to continually improve the care pathway for TBI and PTSD by comparing the efficacy of the HBOT doses and other therapies in different treatment 'arms' of the study .

With these strong positive benefits of treatment without risk, the group finds that it would not be ethical in future studies to have a control arm with sham treatment. We believe that an Institutional Review Board that is made aware of this pilot data would will find it unethical to approve sham treatment for these patients in other similar studies they may review. Therefore, our group has concluded that we must use Bayesian Adaptive Design to compare the efficacy of different doses and modalities of treatment. This will provide internal control groups for the study while optimizing in an ongoing way, the care pathway for TBI / PTSD.

March 15, 2010

Case report: Treatment of mild traumatic brain injury with hyperbaric oxygen

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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.

INTRODUCTION

Traumatic brain injury has been called one of the signature injuries of Operations Enduring Freedom and Iraqi Freedom. The RAND Report documented a 19% self-reported incidence of probable TBI among returning service members, with 320,000 probable TBI cases. Most of these cases (80%) are considered mild traumatic brain injury, or mTBI (1).

On a per-case basis, one-year costs for mTBI were estimated at \$27,259 to \$32,759 in 2007 (2). The lifetime costs of even mild TBI impairment in young service members can be deemed incalculable (3).

Mild TBI is usually characterized by a concussive event that causes a brief period of unconsciousness (lasting less than 30 minutes) or a period of confusion or amnesia lasting less than 24 hours. The Department of Defense has developed criteria for the diagnosis of mTBI, which must include one of the following:

- 1) any period of loss of or a decreased level of consciousness lasting less than 30 minutes;
- 2) any loss of memory for events immediately before or after the injury lasting less than 24 hours after the event;
- 3) any alteration in mental state at the time of the injury such as confusion, disorientation, or slowed thinking lasting less than 24 hours after the event;
- 4) transient neurological deficits (*e.g.*, weakness, loss of balance, change in vision, praxis, paresis or plegia, sensory loss, aphasia); and
- 5) normal intracranial imaging.

Findings may be transitory, and late sequelae that are not explainable by other means may qualify an individual for the diagnosis of mTBI. Patients with more than one of these findings may be assigned a higher level of TBI (4).

Since the symptoms of mTBI may develop gradually, are often subtle, and can be confused with other illness such as post traumatic stress disorder, mTBI may be unrecognized and undiagnosed (5). A concussive injury causes diffuse axonal injury, structural neuronal damage and diffuse neuronal dysfunction (6).

The symptoms of mTBI are variable and may include headache, irritability, impulsivity, anger, cognitive impairment, memory difficulty, loss of executive function, and vestibular and sleep disturbances (7). Electroencephalogram and sleep studies are usually normal. Most individuals with mTBI recover in three to 12 months, especially those who are young (8). However, some victims do not recover, or recover slowly; they are at risk for future injury and deterioration of brain function (9).

Mild TBI usually resolves without treatment within months, although approximately 20% of patients with mild TBI continue to have lingering symptoms for one year or longer after injury (1,10). Poor scores on neuropsychological testing months after injury have been correlated with poorer outcomes and unresolved symptoms (11).

Patients with several post-concussive symptoms are unlikely to improve after one year, in spite of traditional therapy (12). Treatment of mild TBI has included rest and observation, education, cognitive rehabilitation and pharmacotherapy (13).

Pharmacologic treatment may be required for control of disabling symptoms of headache, irritability, depression, and anger (14). Because of the efficacy of hyperbaric oxygen (HBO) in treating brain dysfunction from decompression sickness and carbon monoxide injuries, as well as anecdotal reports of its efficacy in treating concussive injuries, we felt HBO might prove of use in treating two airmen injured in a blast.

CASE REPORT

In January 2008 Airman B, a 23-year-old male vehicle operator, was a convoy lead vehicle commander (LVC) sitting in the passenger seat of an M915 14-ton truck. Airman C, a 22-year-old male vehicle operator, was driving the vehicle that was

attacked with an improvised explosive device (IED).

The detonation occurred on the passenger side of the vehicle, nearer to where Airman B was sitting. The vehicle was damaged, and Airmen B and C sustained concussive injuries with a sense of being dazed for several minutes. There was no known direct blow to the head for either occupant or loss of consciousness, although both occupants had tinnitus. Airman B, who was approximately 3 feet closer to the blast, suffered immediately from a severe headache. Airman C continued to drive the damaged vehicle for several minutes and had no immediate symptoms other than being slightly dazed; however, he developed a mild headache some hours later.

Later in the day, Airmen B and C reported to the medical clinic, where no additional injuries were found. They were given acetaminophen for their headaches and placed on light duty. Two weeks later their symptoms had largely resolved, and they were returned to full duty.

Three weeks post-injury both airmen noted the return of headaches, with difficulty sleeping. Airman B expressed his headache severity as 5-6 and Airman C as 4-5 (on a scale of 1-10, with 10 being the most severe pain imaginable) with headaches occurring daily and lasting for several hours. Both individuals had difficulty falling and remaining asleep, and they reported sleep duration of three to six hours per night. Additionally both individuals felt they were quick to anger and stayed angry from trivial provocations for several hours. Lack of attention to detail, forgetfulness, and fatigue were also reported by both airmen. These latter symptoms began insidiously about three weeks after injury, progressed for about two months and remained constant for the next four months, until treatment with HBO was administered.

Upon arrival at their home base, the airmen presented to the clinic complaining of headaches, fatigue, lapses in memory, irritability and sleep disturbances. Neurological exams were normal, although the airmen appeared tired. Computerized tomography of the brain, EEGs and sleep studies were normal.

On initial deployment both airmen had received the Automated Neuropsychological

Assessment Metrics test (ANAM) on 11 November 2007, two months prior to injury. This test was repeated on 21 July 2008, six months after injury. The repeat ANAM testing showed marked declines from the pre-injury baseline in several areas of measurement (*Figures 1A and 1B*, Page 394).

Airman B presented a statistically significant change in Simple Reaction Time and Matching to Sample tests, with declines in all other areas. Detailed neuropsychological testing of Airman B at six months post-injury and prior to HBO therapy revealed a diffuse or scattered pattern of deficits. Although his IQ score was within the average range, his neuropsychological functioning on a summary measure (Repeatable Battery for the Assessment of Neuropsychological Status – RBANS Form A) (15) was at just the 7th percentile.

Moreover, Airman B showed marked attention dysfunction for both auditory and visual material; cognitive processing speed was slowed and subjectively observed in casual conversation with the patient. He showed difficulty in repeating sentences and digit sequences as well as learning digit sequences over repeated trials.

Airman B also demonstrated problems in both verbal learning and visual memory. His reading speed was slowed, fingertip-tapping speed was slowed in both hands, and clerical speed for coding tasks was mildly impaired. He showed difficulty for rhythm perception and visual-motor integration for copying geometric designs. His reaction time was slowed on a computerized measure of attention. Reading level for sight words remained at the college level, but written arithmetic was at just the sixth-grade level.

Airman C presented statistically significant and drastic changes in both Simple Reaction Time modules (at the beginning and end of the battery), along with declines in all other areas except Mathematical Processing. Detailed neuropsychological testing of Airman C at the same time — prior to HBO therapy — was largely within normal limits notwithstanding problems for inconsistent attention and upper-right extremity dysfunction for grip strength and somatomotor integration. His RBANS (Form A) total score was at the 50th percentile, average range.

Initially, treatment of the headaches with ibuprofen and butalbital-aspirin-caffeine capsules (Fiorinal®) was tried, but these drugs were ineffective in relieving the pain. The airmen were placed on limited duty and daytime work only.

As the airmen had experienced at least one of the symptoms of mTBI after the blast (confusion, alteration of mental state) and their symptoms had no other reasonable explanation, they were given the diagnosis of mTBI in accordance with the Department of Defense criteria (4).

Because the two airmen had shown no improvement in their symptoms for seven months and were having difficulty performing their occupations, it was decided to begin hyperbaric oxygen treatment. Treatment with HBO was begun eight months post-initial injury. The treatment protocol was 100% oxygen for one hour at 1.5 atmospheres absolute. Treatments were given five days per week.

Clinical improvement was rapid. Airman C reported that his headaches vanished by the fifth treatment and did not return, and that he was able to sleep seven to eight hours per night uninterrupted. Airman B reported that his headaches weakened to 3-4 on a pain scale of 1-10, lasted only one to two hours instead of the previous eight to 10 hours, and that he was able to sleep eight to nine hours per night uninterrupted.

Both airmen reported that they felt more mentally alert and were less prone to forgetting, although they still did not feel “normal.” At the completion of the 40-treatment protocol, Airman C felt that his symptoms had ostensibly resolved, and Airman B felt that he was much improved, notwithstanding some lingering irritability and forgetfulness.

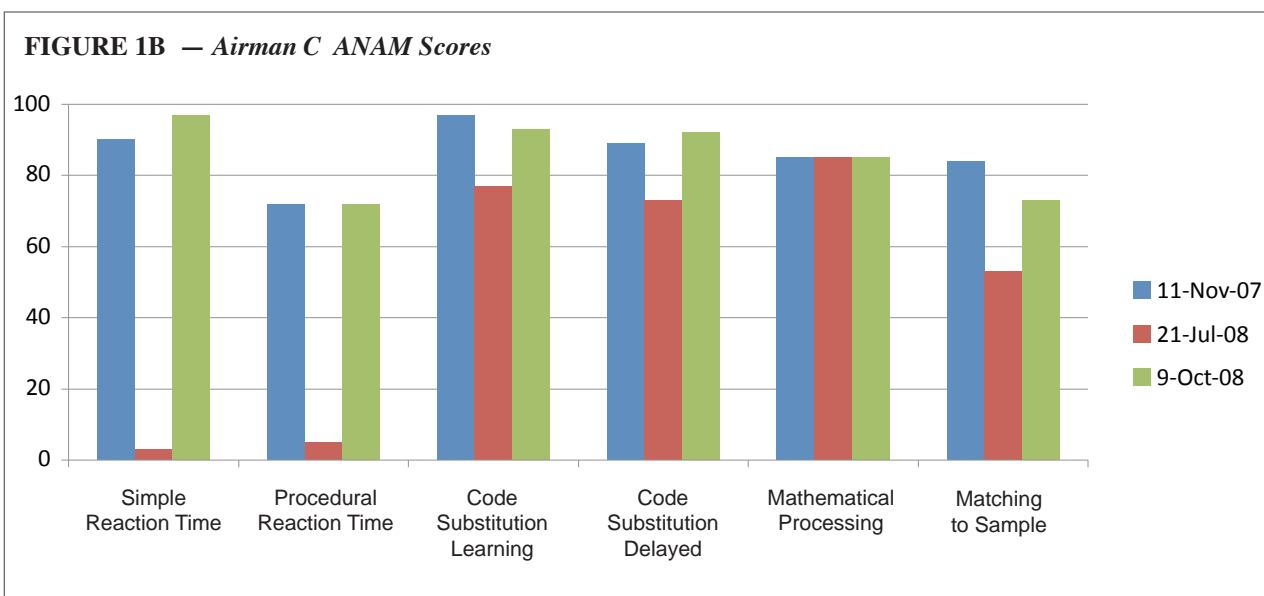
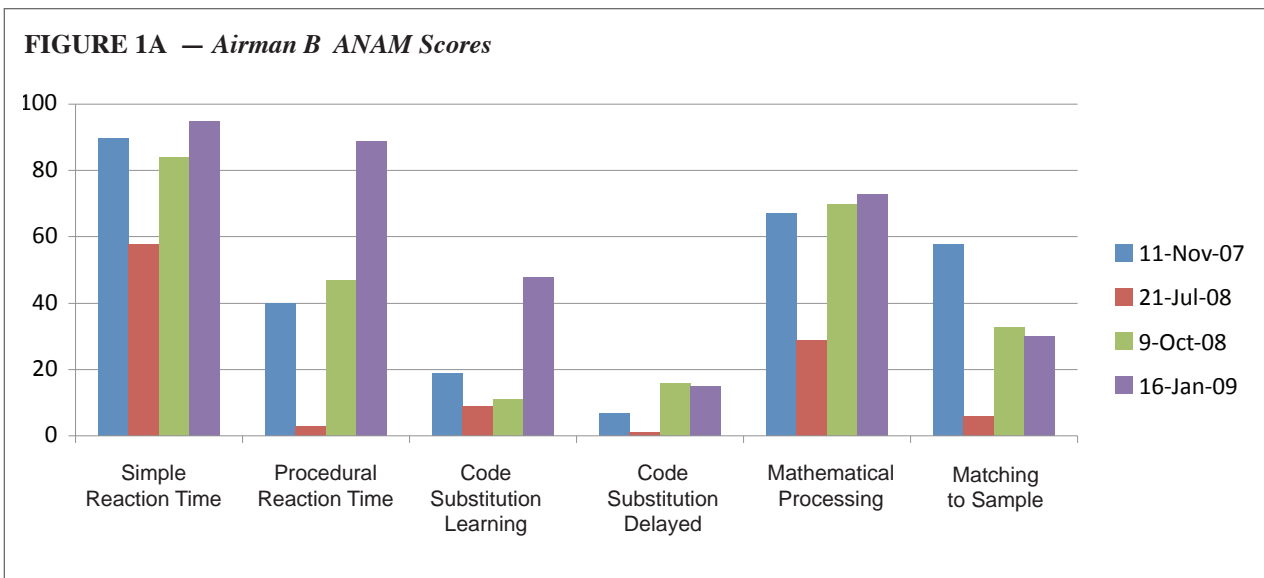
Repeat ANAM testing showed improvement in essentially all areas for both airmen. Airman C’s ANAM scores returned to pre-injury baseline levels, and Airman B’s ANAM scores returned to pre-injury levels, with no statistically significant differences in any of the tested domains (*Figures 1A and 1B*, Page 394, and *Figures 2A and 2B*, Pages 395-396).

Repeat detailed neuropsychological testing of Airman B showed improvement on some but not all

areas of cognitive functioning after HBO therapy at 10 months post-injury. His RBANS (Form B) total score was at the 12th percentile. For a patient with mild to moderate TBI, his scores improved faster than would be expected through spontaneous brain healing alone during this time interval. Areas of objective improvement included visuoconstructive abilities, fingertip-tapping speed and verbal learning/memory for word lists. His cognitive abilities status

post-HBO treatment was deemed satisfactory to continue his job duties without special monitoring.

Repeat neuropsychological testing of Airman C was generally consistent with his pre-treatment test scores. Areas of subtle improvement such as motor abilities in the dominant right hand, written arithmetic and verbal fluency were observed. His RBANS B total score was at the 47th percentile, which was not a significant change from pre-treatment testing.



Throughput scores are presented as the percentile of the comparison group of military members without TBI.

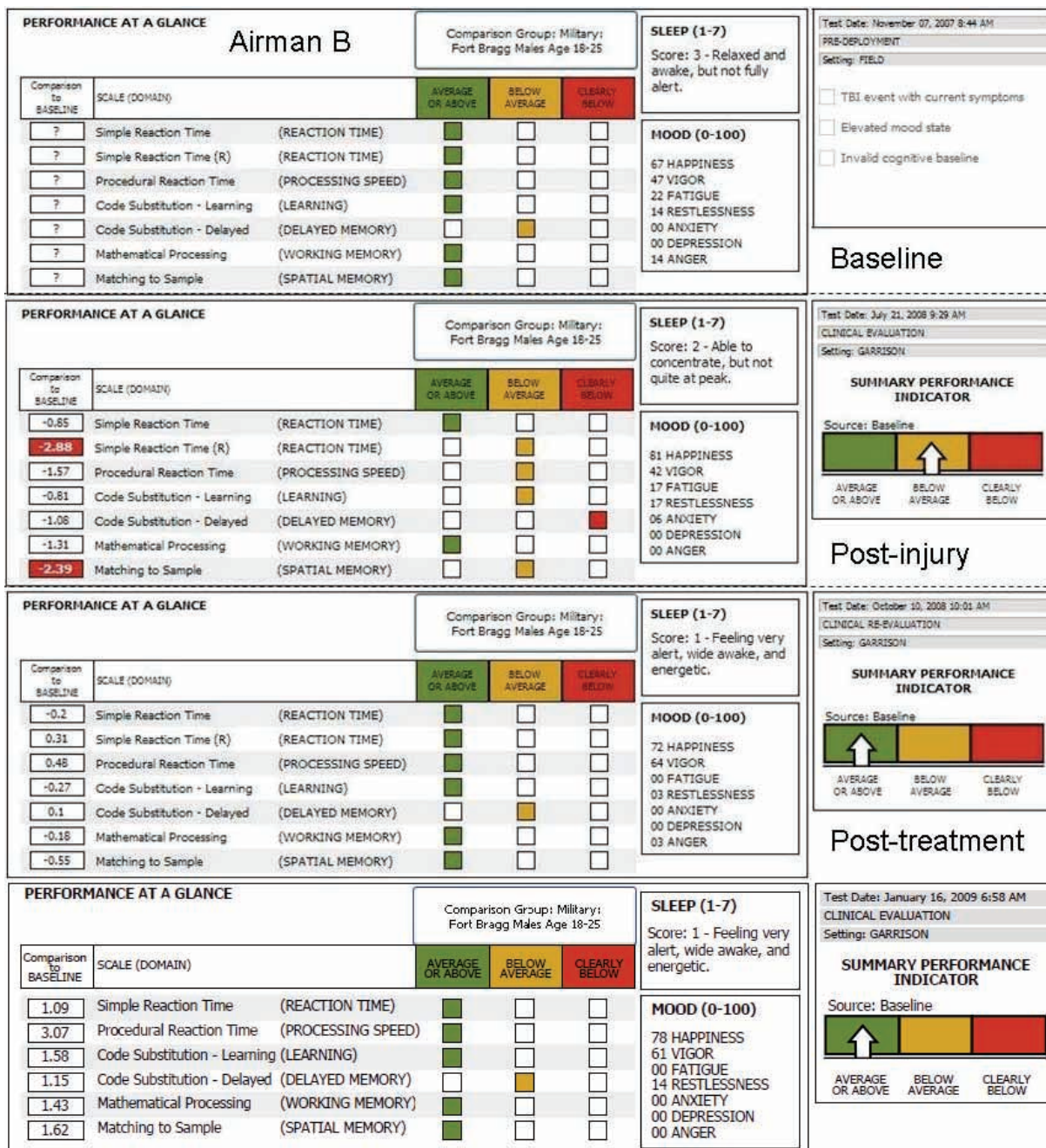


FIGURE 2A – Airman B ANAM Scores

Airman C was essentially well. Based on these results, it was decided to return Airman C to full duty, while Airman B continued hyperbaric treatment for another 40 treatments following the original treatment protocol.

Repeat ANAM testing on Airman B at the conclusion of the second set of 40 HBO treatments

showed improvement in all measures at or exceeding his pre-injury state, except for matching to sample, which was improved markedly from the injury state (Figures 1A and 2A, Page 394 and above).

Airman B reported that he had made continued improvement in cognitive function, felt much more alert and had returned to his pre-injury functional

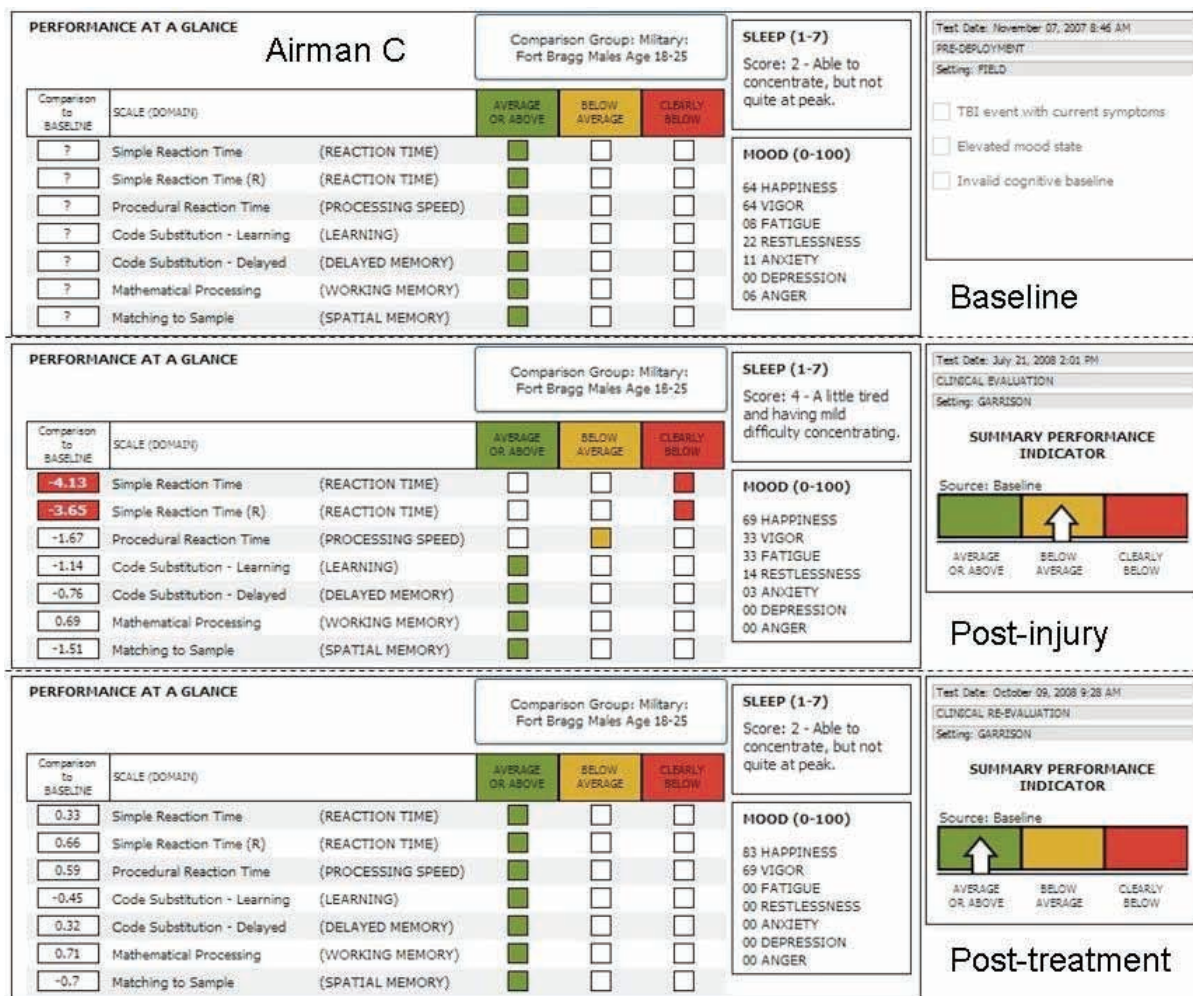


FIGURE 2B – Airman C ANAM Scores

state. He reported that he was experiencing eight hours of uninterrupted sleep per night, and that his headaches had diminished to about one per week.

He also noted the pain intensity had further decreased to 2-3 on a scale of 1-10, and that the headaches lasted two to three hours versus the original eight to 10 hours' duration.

DISCUSSION

Hyperbaric oxygen treatment has several effects that may be beneficial in treating brain injury. In animal models, HBO has been shown to enhance mitochondrial recovery and reduces apoptosis in hypoxic nerve cells (16,17). The HBO-induced improvement in mitochondrial function appears to facilitate improved cognitive recovery and reduced

hippocampal neuronal cell loss after brain injury (18).

HBO promotes neural stem cell activation and growth (19, 20), and this effect is seen in the hypoxic-damaged brain (21). HBO also alleviates hypoxic-induced myelin damage, up-regulates HIF-1 alpha-enhancing neuronal tolerance to hypoxia, and increases cellular ATP levels and cognitive recovery after concussive injury (22).

Balance beam scores in rats with cerebral contusions were improved after treatment with HBO (23). In a rat model of chronic TBI, HBO improved spatial learning and increased vascular density in the injured hippocampus (24).

Controlled human studies of the efficacy of HBO after brain injury have been few. In a study

of moderate and severe TBI using the Glasgow Coma Scale and Glasgow Outcome Scale as measures of efficacy, an HBO-treated patient showed improvement over controls (25). HBO has been shown to be clinically effective in mediating the effects of brain injury (26). While the exact mechanism is unknown, HBO is thought to restore neural pathways damaged in TBI with supporting evidence supplied from SPECT brain imaging (27).

ANAM is a library of more than thirty computer-based test modules designed for a wide variety of clinical and research applications and is the direct outgrowth of more than twenty years of computer-based test development across all service branches within the Department of Defense (28). ANAM4™ is a neurocognitive assessment tool that can be used to identify changes in a service member's cognitive function and mood state as a result of some debilitating event. The ANAM4™ TBI-MIL test battery used in this case report has been tailored to provide an instrument that is sensitive to cognitive changes that often accompany mTBI. The battery consists of a set of assessment modules that gather data on mood, processing speed (reaction time), working memory, short-term memory, spatial pattern recognition/memory and other cognitive functions. The test is designed for repeated testing and provides reliable measures when used for retesting as a measure of TBI recovery (29).

ANAM is used to establish a cognitive function baseline that can then be used for surveillance post injury or post suspected injury (30). Although not intended as a diagnostic tool *per se*, comparative performance on ANAM test modules can be helpful in confirming the diagnosis, as demonstrated in this case report. In cases with known head trauma, computer-based assessments should be supplemented with detailed neuropsychological tests tailored to the patient's presenting problems and to the specific referral question to be answered.

CONCLUSIONS

Several aspects of these two cases demonstrate the efficacy of HBO for the airmen treated. Although both airmen had stable symptoms of mTBI/post-concussive syndrome that had not improved for seven months, substantive improvement was achieved within 10 days of HBO treatment. The headaches and sleep disturbances improved rapidly while the irritability, cognitive defects and memory difficulties improved more slowly.

Fortunately, both airmen had taken the ANAM and presented objective demonstration of their deficits from TBI and their improvements after HBO treatment. Both airmen, who were injured by the same blast sitting side by side, had similar symptom complexes of TBI and improved at similar rates after initiation of HBO treatment. Neither airman had any other form of treatment for TBI. It seems unlikely to the authors that any explanation other than the HBO treatments can be offered for their improvements. ■

The views in this article are those of the authors and do not reflect the official policy of the Department of the Air Force, the Department of Defense or the U.S. Government.

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5-Feb-10

Fort Walton TBI HBOT Patient Records

Patient	Age	Rank	Service	Job	Sx	ANAM	# HBOT	Pre HBOT condn	Clinical outcome	Comments
PM	58	Bgen	Army	JAG	HA, CD, MD, A, D	not done	80, 20, 20	unable to perform ADL considered for discharge	resumed full civilian duties	medically retired prior to full HBOT
JB	24	SSgt	AF	transport	HA, CD, MD, A, I, D, SD	marked improvement	80	difficulty performing duties, unable to do CDC considered for discharge	retained, resumed full duties, promoted	
JC	24	SSgt	AF	transport	HA, CD, MD, A, I, D, SD	marked improvement	40	difficulty performing duties, unable to do CDC	retained, resumed full duties, promoted	
GA	28	Capt	AF	STO	HA, CD, SD, MD	marked improvement	40	difficulty with job tasks, memory	no difficulties, improved to pre injury condn	
SR	25	SSgt	AF	SP	HA, CD, MD, A, I, D, SD	too early for repeat	19*	considered for discharge, MEB	MEB being recalled, asked to resume full duties	
CP	25	SSgt	AF	SP	HA, CD, MD, I, D, SD	too early for repeat	23*	difficulty performing duties, unable to do CDC	resumed full duties, much improved	
KG	32	Sgt	USMC	Arty	HA, CD, MD, A, I, D, SD	much improved	40	medically retired, unable to perform ADL	performs ADL, much improved	needs 40 more HBOT
EW	33	Sgt	USMC	Recon	CD, MD	no change - pretest was excellent	40	disorganized, unable to remember simple tasks	much improved	
SH	28	TSgt	AF	CCT	HA, CD, MD, A, I, D, SD	too early for retest	35*	extremely irritable, unable to perform duties	improved	
Ken Stoller, M.D. Patient										
AC	26	Capt	Army	Field Art	A, ADL, CD, MD, SD	IMPACT vast improvement	81	unable to perform ADL	performs ADL, much improved	

Abbreviations

- * treatment in progress
- A ataxia, coordination, balance problems
- ADL activities of daily living
- CD cognitive deficit
- CDC Correspondence Study Books for On the Job Training
- D depression
- HA headache
- I irritability
- MD memory deficits
- SD sleep disturbances

Case report

Low pressure hyperbaric oxygen therapy and SPECT brain imaging in the treatment of blast-induced chronic traumatic brain injury (post-concussion syndrome) and post traumatic stress disorder: a case report

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Abstract

A 25-year-old male military veteran presented with diagnoses of post concussion syndrome and post traumatic stress disorder three years after loss of consciousness from an explosion in combat. The patient underwent single photon emission computed tomography brain blood flow imaging before and after a block of thirty-nine 1.5 atmospheres absolute hyperbaric oxygen treatments. The patient experienced a permanent marked improvement in his post-concussive symptoms, physical exam findings, and brain blood flow. In addition, he experienced a complete resolution of post-traumatic stress disorder symptoms. After treatment he became and has remained employed for eight consecutive months. This case suggests a novel treatment for the combined diagnoses of blast-induced post-concussion syndrome and post-traumatic stress disorder.

Introduction

By January, 2008 it was estimated that as many as 300,000 servicemen and women from the current Iraq and Afghanistan Wars have PTSD or major depression, 320,000 have experienced a TBI, and 82,000 have all three diagnoses [1]. Treatment is available for PTSD and depression, but there is no proven therapy for the dual diagnoses of PTSD and the residual effects of TBI, the PCS [2].

HBOT is the use of greater than atmospheric pressure oxygen in an enclosed chamber to treat basic disease processes [3]. HBOT has been traditionally applied to

certain emergent conditions and chronic wound conditions, but not to blast-induced TBI/PCS or PTSD. This case report is the first application of the authors' low pressure HBOT protocol for chronic brain injury to blast-induced TBI/PCS and PTSD. An early version of this protocol was recently reported in an animal model of chronic TBI that duplicated the human experience [4].

Case presentation

A 25-year-old retired Caucasian male U.S. Marine presented with headaches, tinnitus, and sleep disturbance. Three years before evaluation the patient sustained LOC

(a few minutes) from an IED explosion with anterograde memory loss and confusion (one hour), and persistent right ear tinnitus, headaches, imbalance, and sleep disturbance. He developed PTSD symptoms within 3 months and experienced six more explosions with near LOC within 15 months. After medical evaluation diagnoses were TBI/PCS, PTSD, depression, hearing loss, and tinnitus.

Prioritized Symptom List: 1) Constant headaches with intermittent confusion, irritability, tunnel vision, and dizziness, 2) Bilateral tinnitus, 3) Sleep disruption, 4) Left eye blurred vision, 5) Irritability, 6) Depression, social withdrawal; **Additional Symptoms:** 7) Fatigue, 8) Decreased hearing, 9) Imbalance, 10) Cognitive problems-memory, attention, decreased speed of thinking, 11) Back pain, 12) Bilateral knee pain, 13) PTSD symptoms: intrusive thoughts, combat thoughts, nightmares, tachycardia.

Med-Surg, Medications: None. **FH, ROS, and PHIS:** non-contributory or negative. **PSH:** Engaged, no children, lives with parents, 3 years college education, no tobacco or drugs, one to two beers/week. **Neuro PEx Abnormalities:** Slight deviation of right eye laterally, bilateral: decreased hearing to softly rubbing fingers at one foot, noxious response to 512 Hz tuning fork, decreased finger tapping speed, unstable: rotation exam, tandem gait, and Romberg. **Treatment and testing:** MRI brain-normal. SPECT brain imaging pre-HBOT and 72 h after the 39th HBOT. The patient underwent 39 HBOT's in 26 calendar days at 1.5 ATA/60 minutes total dive time, twice/day, five days/week in a monoplace chamber with 100% oxygen.

Outcome: Headache permanently gone after the 1st HBOT. After 12 HBOT's symptoms 3, 6, and 7 improved. At 25th HBOT absence of PTSD symptoms. Re-evaluation after 37 HBOT's: 1) 4/6 primary problems improved (#'s 1, 3, 5, 6), 2/6 no change, 2) 4/7 additional symptoms improved (7, 9, 10, 13), 3/7 no change, 3) 6/6 abnormal exam findings retested improved, 1 finding not retested (right eye deviation). SPECT: heterogeneous with bilateral frontal and temporal defects-all improved post HBOT. See: Movie 1, Figures 1 and 2. (Movie 1): Side by side Pre and Post HBOT processed transverse SPECT brain blood flow images-movie. File Format: Quicktime Video. Description of Data: Pre-HBOT scan is on the left and post-HBOT on the right. Click on either image to initialize movie. Images were obtained on a Picker Prism 3000 triple-head gamma camera. Both scans were processed by technologist PJT: 25 mCi of ECD was prepared with the standard manufacturer's kit and injected in a peripheral vein in a low noise low light area while the patient was quiet and motionless. One hour after injection acquisition proceeded with a 360 degree rotation and 40 stops, 20 seconds/stop on a 128 x 128 matrix, using low energy

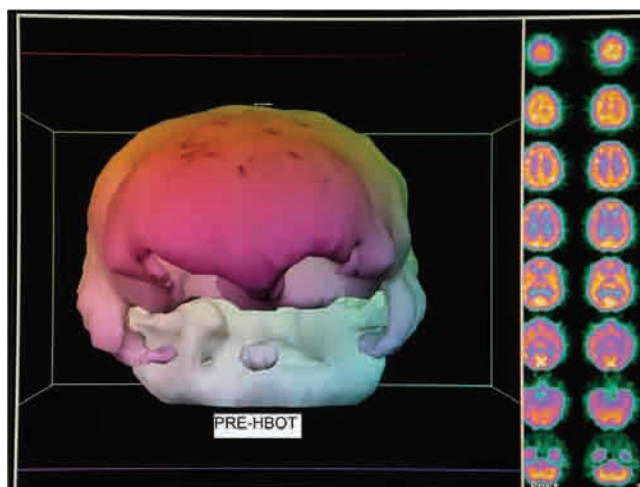


Figure 1. Pre-HBOT SPECT brain scan three dimensional surface reconstruction and processed transverse images. Note bilateral orbital frontal and temporal lobe defects and diffuse heterogeneous pattern of blood flow.

high resolution fan beam collimators. Motion correction was used for minor movement. Raw data was processed by transverse reconstruction using 360 degree filtered back projection and a ramp filter, followed by a LoPass filter, order 2.2. Cutoff was taken at the intersection of the best fit LoPass filter and noise on the power spectrum graph. Per file attenuation correction and best fit ellipse were applied. Images were oblique reformatted with slice thickness at 4 mm (2 pixels), aligned, and off-center zoom

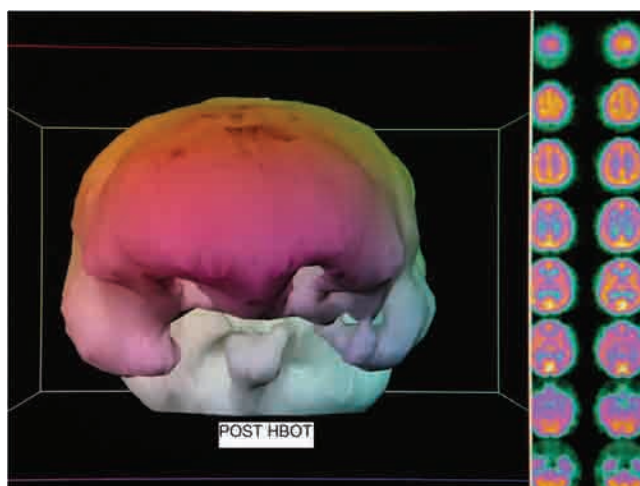


Figure 2. Post-HBOT SPECT brain scan three dimensional surface reconstruction and processed transverse images. Note relative improvement in brain blood flow to bilateral focal frontal and temporal defects and overall normalization of blood flow to a more homogeneous pattern.

applied (20 cm² area). Images were presented in all 3 orthogonal planes. Transverse processed images were analyzed with Osirix Open-source software (version 3.3.2) and windowed at a level of 1000 with a window width of 2000. They were subsequently rendered in QuickTime movie format starting from vertex and proceeding through the base of the brain. Images are in standard SPECT format and orientation. Color map is red, yellow, green, blue, and violet from highest brain blood flow to lowest. Note the marked generalized increase in perfusion on the post-HBOT scan. (Figure 1): Pre-HBOT SPECT brain scan three dimensional surface reconstruction and processed transverse images. Pre-HBOT scan was rendered in three dimensional surface reconstruction format by PJT based on the method developed and taught by Picker International using Picker software. In this method brain blood flow is computer indexed to frontal lobe blood flow. A frontal lobe surface defect was identified on a selected transverse slice. Processed/filtered transverse slices were then featured with a 100% window such that all pixels render a white image. Counts were slowly subtracted by decreasing the window threshold until the defect was visible as a full thickness black defect in the contour of the cortex. As the defect emerged and was registered in proper anatomic proportion to the rest of frontal cortical blood flow the numerical window level was taken as the determination threshold. Three separate determinations were made for each scan and the final threshold taken as an average of the three determinations. The technologist was blind to the final image reconstruction due to software restrictions that only allow threshold determination. The surface reconstruction image at this threshold is featured in the image above. Color is aesthetic. Note bilateral orbital frontal and temporal lobe defects, areas typically injured in traumatic brain injury, consistent with processed transverse images in the right hand columns. Processed images also show an abnormal diffuse heterogeneous pattern of blood flow. Description of processing is in (Movie 1). (Figure 2): Post-HBOT SPECT brain scan three dimensional surface reconstruction and processed transverse images. Three dimensional surface image was prepared in identical fashion to the image in Figure 1. Note relative improvement in brain blood flow to bilateral focal frontal and temporal defects, consistent with processed transverse images in the right hand columns. Transverse slices also show normalization of the blood flow to a more homogeneous pattern.

Discussion

The present case is the first application of the author's HBOT protocol to blast-induced TBI/PCS and PTSD. The patient's symptomatic, physical exam, and SPECT improvements are similar to ours [3,5,6,9] and others' [7,8] previous cases/case series of non-blast TBI suggesting common pathophysiology. The unexpected result was the

complete resolution of PTSD. With the overlap of symptoms, pathophysiology, and anatomy in TBI/PCS and PTSD [10] HBOT is likely impacting common shared targets in this case.

Conclusion

Thirty-nine low pressure HBOT's caused a reduction in symptoms and signs of chronic mild-moderate blast-induced TBI/PCS and PTSD. The resolution of symptoms and signs of TBI/PCS and PTSD were reflected in global and focal improvements in brain blood flow imaging, suggesting a novel treatment for these combined diagnoses.

Patient's perspective

Patient has declined to submit his perspective due to privacy concerns.

List of abbreviations

ATA, Atmospheres absolute; ECD, Ethyl cysteinate dimer; FH, Family history; HBOT, Hyperbaric oxygen therapy; HPI, History of present illness; IED, Improvised explosive device; LOC, Loss of consciousness; MRI, Magnetic resonance imaging; PCS, Post-concussion syndrome; PEx, Physical exam; PHIS, Prior head injury history; PMH, Past medical history; PSH, Personal and Social history; PTSD, post-traumatic stress disorder; ROS, Review of systems; SPECT, Single photon emission computed tomography; TBI, Traumatic brain injury.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal. In addition, this case was approved by the LSU School of Medicine's Institutional Review Board as a case report.

Competing interests

The authors declare competing interests. The primary author has a small corporation, Harch Hyperbarics, Inc. that does hyperbaric consulting. Author KVM has a corporation that leases hyperbaric oxygen chambers and a corporation that contracts to provide hyperbaric oxygen and woundcare services. None of the authors have personal or financial relationships with people or organizations that would influence the interpretation of data in this report.

Authors' contributions

PGH evaluated the patient, ordered the treatment and imaging, and wrote the draft of the manuscript. EFF analyzed and presented the SPECT imaging and assisted in writing the manuscript. PKS assisted in the treatment of the patient and assisted in writing the manuscript. KVM

assisted in development of the hyperbaric protocol and writing the manuscript. All authors read and approved the final manuscript.

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Movie 1. Side by side Pre and Post HBOT processed transverse SPECT brain blood flow images-movie. Click on this link to activate the video (MP4): <http://casesjournal.com/casesjournal/rt/suppFiles/6538/31370>

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