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 deeemed 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 phamacotherapy (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 t o 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 l evels, 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.

FIGURE 1A — *Airman B ANAM Scores*

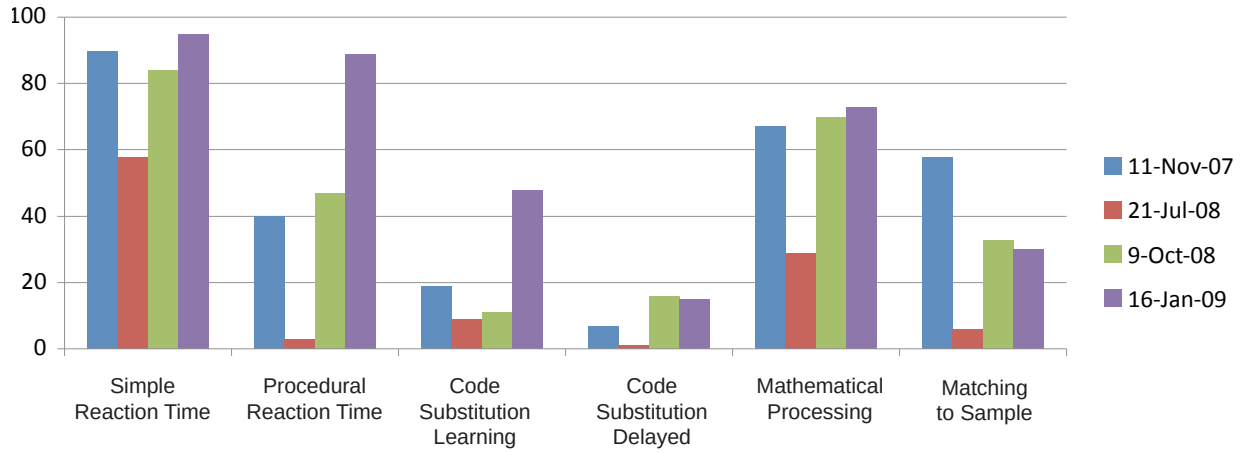
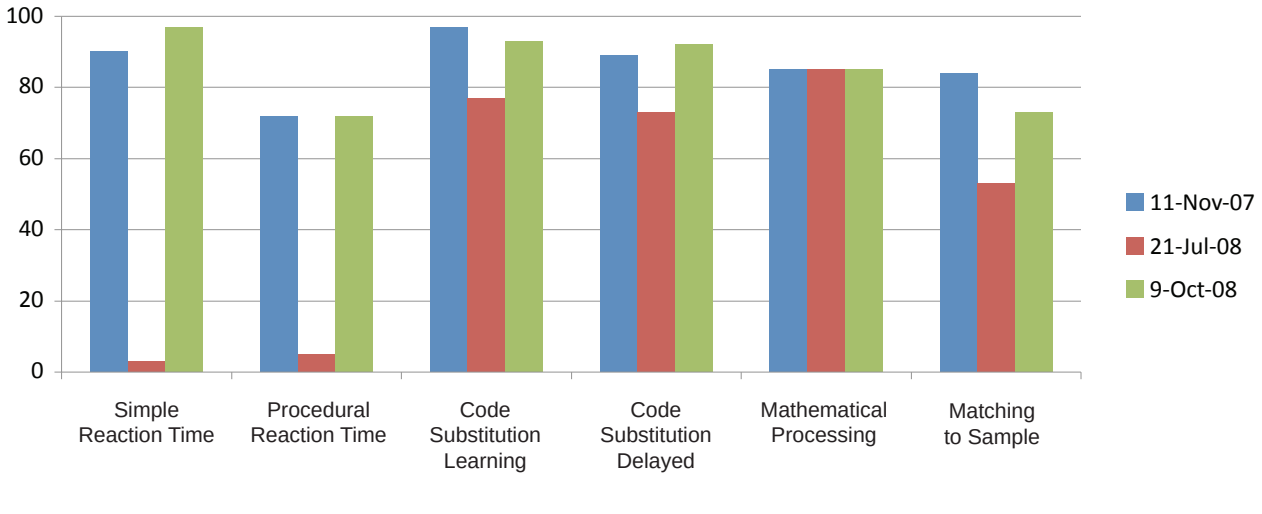


FIGURE 1B — *Airman C ANAM Scores*



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

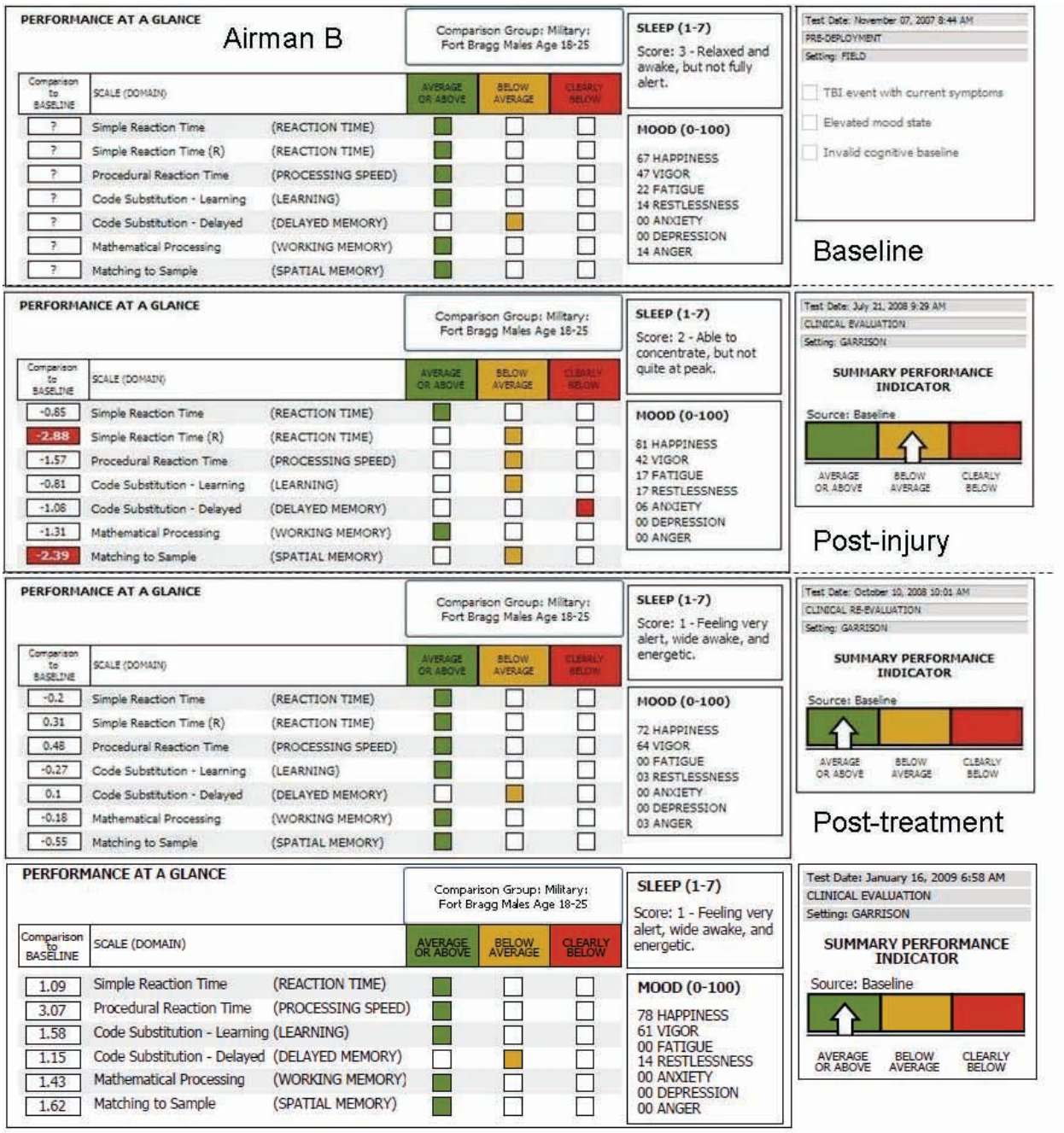


FIGURE 2A — *Airman B ANAM Scores*

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

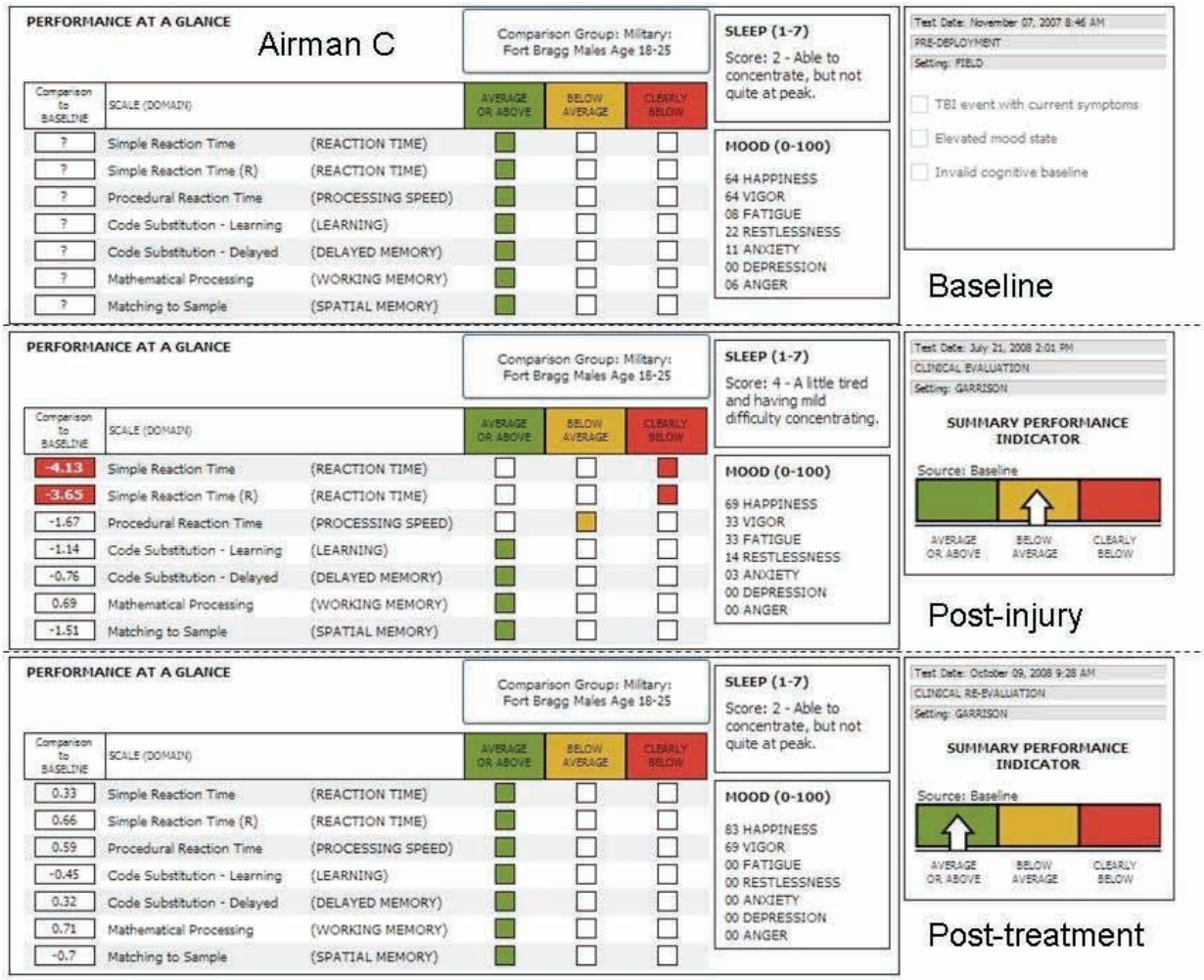


FIGURE 2B — *Airman C ANAM Scores*

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.

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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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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 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

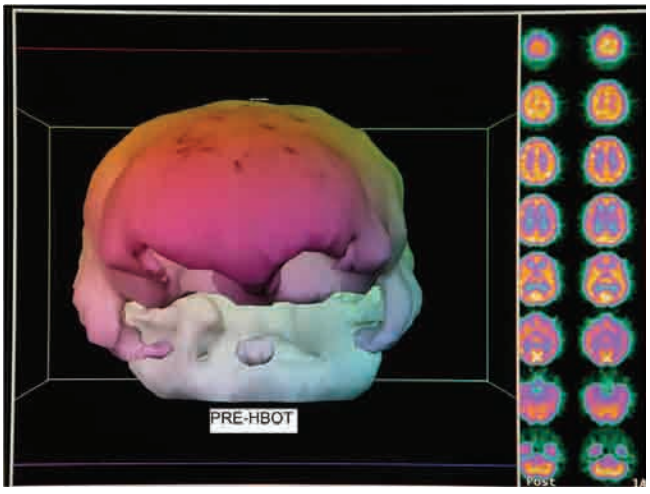

Figure 1. Pre-HBOT SPECT brain scan three dimensional surface reconstruction and processed transverse images. Note bilateral orbital frontal and temporal lobe defects and diffuse heterogeneous pattern of blood flow.

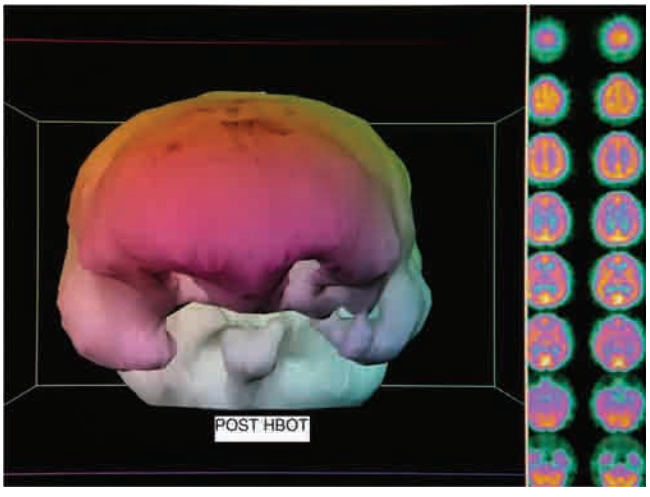

Figure 2. Post-HBOT SPECT brain scan three dimensional surface reconstruction and processed transverse images. Note relative improvement in brain blood flow to bilateral focal frontal and temporal defects and overall normalization of blood flow to a more homogeneous pattern.

applied (20 cm^2 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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