REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ORGANIZATION.

1. REPORT DATE *(DD-MM-YYYY)*	2. REPORT TYPE	3. DATES COVERED *(From - To)*
11/09/2018	Journal	

4. TITLE AND SUBTITLE
Chronic Decompression Illness Cognitive Dysfunction Improved with Hyperbaric Oxygen: A Case Report

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Wolf, Earl George

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
59th Clinical Research Division
1100 Willford Hall Loop, Bldg 4430
JBSA-Lackland, TX 78236-9908
210-292-7141

8. PERFORMING ORGANIZATION REPORT NUMBER
17496

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
59th Clinical Research Division
1100 Willford Hall Loop, Bldg 4430
JBSA-Lackland, TX 78236-9908
210-292-7141

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release. Distribution is unlimited.

13. SUPPLEMENTARY NOTES
Undersea and Hyperbaric Medicine

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Clarice Longoria
					19b. TELEPHONE NUMBER *(Include area code)* 210-292-7141

Chronic decompression illness cognitive dysfunction improved with hyperbaric oxygen: a case report

Kimberly R Bradley DO, MPH&TM; E. George Wolf MD; Michael F Richards MD; and Devin P Beckstrand, MD, MPH

59th Medical Wing, Undersea and Hyperbaric Medicine, Joint Base San Antonio - Lackland, TX

Running head: Chronic DCI cognitive dysfunction improved with HBO2

Corresponding author:

59th Medical Wing

E. George Wolf

59 MDSP/SGMH
2200 Bergquist Drive, Suite 1
Joint Base San Antonio - Lackland, TX 78236-9908
Office: 210.539.8018
Fax: 210.539.2122
earl.g.wolf.ctr@mail.mil

Chronic decompression illness cognitive dysfunction improved with hyperbaric oxygen: a case report

Introduction

Altitude chamber exposures are used for training to allow aircrew to experience their hypoxia and pressure effect symptoms. Decompression illness (DCI) is an umbrella term that includes decompression sickness and/or air gas embolism, both known complications that can occur subsequent to altitude chamber training or in operational aircraft when the cabin altitude is at least 18,000 feet. Compared to open water diving, the incidence of altitude chamber induced decompression illness is around 0.25% (1). Because the evolution of gas within the tissue or vasculature is being treated upon recompression from altitude reaching the surface, often these DCI symptoms will decrease or resolve altogether. Residual joint pain may be treated by breathing 100% oxygen, preferably using an aviator's mask or a continuous positive airway pressure mask. If not available, at the very least, a non-rebreather may be used, but in the best of conditions may supply around 60% inhaled oxygen. If the symptoms resolve, the patient remains on 100% oxygen for one hour longer or a minimum of two hours whichever is longer. If joint pain symptoms do not resolve by two hours, if the initial symptoms were neurological, or if any resolved symptoms recur, then recompression in a hyperbaric chamber is warranted where a US Navy treatment table 6 (TT6) is most often used for therapy. Alternate tables are available at the discretion of the hyperbaric medicine physician or chamber dive master. If symptoms persist, additional treatment "tailing dives" using US Navy treatment table 5, 6 or a treatment table 9 (45 feet of sea water (137.8 kPa) with a 30 minute oxygen period separated by a period of air breathing – a standard hyperbaric wound treatment profile) are done daily until symptoms resolve or plateau over two successive treatments.

Patient history

A 27-year-old female underwent altitude chamber training to an altitude of 25,000 feet on 26 June 2012. During the hypoxia demonstration, she experienced onset of tingling in both legs and left arm, in addition to headache, dizziness, and malaise. The physiological technicians in the chamber ensured that she started breathing 100% oxygen but her symptoms continued. She then started having difficulty responding to the attendants. She could hear them, but could not speak back. Upon compression to surface, she was examined by the local flight surgeon who confirmed her symptoms and noted she had photophobia. The patient was transported to a hyperbaric facility and received a USN treatment table 6 hyperbaric treatment. Upon returning home, she experienced new onset right hip pain (4-5/10 pain at rest) with continued headache, dizziness and generalized malaise. She visited flight medicine the next day and was transported back to the hyperbaric facility. She underwent a tailing TT5 due to right hip pain development and continued headache, and dizziness as well as a perception of decreased mental capacity. Post treatment, her symptoms resolved except for a continued moderate headache. She returned home and sent back to her unit, but not returned to flying status. The patient continued to have recurrence of intermittent paresthesia and decreased memory over the next 12 months. Her cognitive function worsened slowly over time described by her as similar to mild to moderate traumatic brain injury symptoms. The patient was evaluated by neurology, psychiatry, psychology, and aerospace medicine specialists for the continued symptoms including decreased executive function and reaction times. The brain MRI was unremarkable and normal. In addition, her echocardiogram for potential patent foramen ovale demonstrated no shunting. Medications during this time included topiramate, combination isometheptene, acetaminophen and dichloralphenazone (Midrin), combination butalbital, acetaminophen, caffeine (Fioricet), rizatriptan and naproxen for headache, trazodone for sleep issues, and sertraline for depression.

Eventually, she was referred 14 months after the incident to Wilford Hall Ambulatory Surgical Center Undersea and Hyperbaric Medicine for further evaluation.

Materials and Methods

As the patient deployed multiple times, she had a number of Automated Neuropsychological Assessments Metrics (ANAM) tests (2). ANAM was developed by the U.S. Army in the late 1990's using computer based cognitive measures and tests including attention, concentration, reaction time, memory, processing speed, decision-making and executive function. Prior to her acceptance for treatment another ANAM was administered to create a pre-treatment baseline on 25 June 2013. This was compared to her most recent pre-deployment ANAM result on 20 March 2012 (Fig 1 and 2). After local evaluation, the patient started twice daily (7 AM and 1 PM) treatments at a compression depth of 2.0 atmospheres absolute. Serial ANAM tests were done after every 10 treatments (weekly) and compared to the pre-treatment baseline and her 20 March 2012 ANAM scores. These ANAM results described in this report are compared using the tests administered on, 10 October 2013 (post 20 treatments), and the final ANAM on 5 November 2013 (39 total treatments).

Results

The ANAM on 20 March 2012 demonstrated "average or above" performance scores in all seven subtests with a sleep score of 2, and mood scores as seen in Fig 1. On 25 June 2013 performance scores were "clearly below" except for the "matching to sample" test, which was "below average" with a sleep score of 2 and considerable worsening in all mood scores (Fig 2). The serial ANAM scores improved over the first 20 treatments as seen in the ANAM on 10 October 2013 (Fig 3) with all performance scores "average or above" except for the two reaction

time scores ("below average" and "clearly below") with a sleep score of 1 and improved mood scores. She had an 11 day break to return to her home base. An ANAM was done prior to restarting hyperbaric treatments on 21 October 2013. The results demonstrated a slight deterioration with four performance scores "average or above" and three "below average" with a sleep score of 3 and some decreases in all of the mood scores except "restlessness, anxiety, and anger". The final ANAM on 5 November 2013 (Fig 4, post 39 total treatments) showed the performance scores "average or above" in all of the domains except for reaction time ("below average" and "clearly below"). These were nearly the same as the predeployment ANAM on 20 March 2012, and greatly improved compared to the pretreatment baseline ANAM on 25 Jun 13. The sleep score was 1 and the mood scores approached those of the predeployment ANAM and considerably improved from the pretreatment baseline ANAM.

Discussion

The symptoms from the altitude exposure favor air gas embolism with continued symptoms similar to traumatic brain injury from blast injuries as air emboli are produced (3-7). Both causes of air embolism recommend hyperbaric oxygen.

In spite of initial hyperbaric oxygen therapy the cognitive symptoms continued to worsen over time. Upon home base evaluation there was no shunting across the intra-atrial septum and MRI studies failed to demonstrate any pathological lesions. A pulmonary etiology could have occurred. One study of the potential use of hyperbaric oxygen for traumatic brain injury suggested a more likely benefit when symptoms were treated within 2 years of the precipitating event (8 - national meeting data presentation done June 2013). Based on this, we felt the residual DCI symptoms warranted treatment even though they initially occurred 14 months prior.

The protocol developed was based on neurological decompression sickness treatment where hyperbaric oxygen therapy is continued until the symptoms resolve or plateau. Unfortunately, the time frame was based on the number of days her base approved her temporary duty as a patient. This precipitated the twice daily hyperbaric exposures versus single day exposures and longer time to complete the same number of treatments. However, twice a day treatments are common in acute hyperbaric oxygen indications and are used on occasion in late effect of radiation injury cases (9). This demonstrates the issue of basing hyperbaric oxygen treatments to patient response in conjunction with symptom changes, laboratory or other testing as a guide to the therapy utilization.

In this case, we had an objective measure (ANAM) administered after every 10 treatments. The ANAM is designed for repeated measures testing (10), but training effect is a concern in such tests. Eonta (11) demonstrated improvement in repeated tests given back to back on the same day, but plateauing over the last 2 days (3 and 4-day studies). In this case report, it could be a factor, but likely small, as the 10-day break demonstrated a deterioration in scores followed by improvement. In addition, interval tests had individual subtests that had positive and negative changes, but with overall improvement throughout the course of treatment. Placebo effect due to "medical vacation" cannot be ruled out; however, the patient was in medical hold at her home base and not performing an active job. The demonstration that hyperbaric oxygen results in stem cell mobilization due to hyperbaric oxygen therapy may be a factor in the patient's overall cognitive improvement (12).

Would the patient improve without hyperbaric oxygen? Certainly, she may have. However, her four pre-deployment ANAM performance scores were "average or above" in all domains and the significant deterioration post incident seen in the 25 June 2013 pre-treatment scores could not

have been much worse. As the base ANAM consultant observed, the case demonstrated real changes beyond mere "training effect". How much hyperbaric oxygen therapy was increasing the slope of improvement is the question. The patient was at risk of discharge from the service from a medical evaluation board prior to her treatment. At last check, she remained on active duty.

Summary

This altitude training DCI case resulting in chronic cognitive dysfunction is the first case to our knowledge that has been treated well after the normal timeframe. The availability of pre-incident cognitive function testing allowed us to objectively measure improvement during the hyperbaric oxygen therapy series. Such monitoring can be done, especially when a baseline is available. This has potential impact for similar cognitive neurological cases in diving and altitude as well as other bubble-related etiologies, including surgical-induced air gas emboli and blast injury (13).

Disclaimer: The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense or its Components.

References

1. Rice GM, Vacchiano CA, Moore JL Jr, Anderson DW. Incidence of decompression sickness in hypoxia training with and without 30-min O2 prebreathe. Aviat Space Environ Med. 2003; 74(1):56–61.

2. http://vistalifesciences.com/anam-intro. Retrieved 16 Oct 17.

3. Phillips YY. Primary blast injuries. Ann Emerg Med 1986 Dec, 15 (12): 1446-50.

4. Argyros GJ. Management of primary blast injury. Toxicology 121 (1997) 105-115

5. Yan Z, Yuan-Guo Zhou. The past and present of blast injury research in China. Chinese Journal of Traumatology 18 (2015) 194-200

6. Clemedson CJ, Holter I, Hultman BM. Air embolism and the cause of death in blast injury. The Miltiary Surgeon, June 1954 424-437

7. Damon, E.G. and Jones, R.K. (1971) Comparative effects of hyperopia and hyperbaric pressure in the treatment of primary blast injury. Technical Report DASA 2708. Headquarters,Defense Nuclear Agency, Washington, DC.

8. Wolf EG, Baugh LM, Schubert Kabban CM, Richards MF, Prye J. Cognitive function in a traumatic brain injury hyperbaric oxygen randomized trial. UHM 2015, Vol 42 (4) Jul-Aug: 312-332.

9. Hampson NB and Corman JM. Rate of delivery of hyperbaric oxygen treatment does not affect response in soft tissue radionecrosis. UHM 2007 34 (5) 329-334)

10. http://vistalifesciences.com/research-and-publications. Retrieved 16 Oct 17.

11. Eonta SE, Carr W, McArdle JJ, Kain JM, Tate C, Wesensten NJ, et al. Automated Neuropsychological Assessment Metrics: repeated assessment with two military samples. Aviat Space Environ Med 2011; 82(1):34-9

12. Sabrina Shandley 1, E. George Wolf 2, Christine M. Schubert Kabban 3, Laura M. Baugh 4, Michael F. Richards 2, Jennifer Prye 1, Helen M. Arizpe 1, John Kalns 1. Increased circulating stem cells and better cognitive performance in traumatic brain injury subjects following hyperbaric oxygen therapy. UHM 2017, Vol. 44, No. 3

13. Kocsis JD, Tessler A. Pathology of blast-related brain injury. J Rehabil Res Dev 2009; 46(6): 667-72

HISTORY

Injury cause(s):	Resulting in:	Symptoms Right after Injury: none recorded.
None recorded.	None recorded.	Symptoms Now While Resting: none recorded.
		Symptoms Now after Exertion: none recorded.

PROVIDER OBSERVATIONS

MACE:

Interval between current and previous injury:

PERFORMANCE AT A GLANCE

Comparison Group: Military: All Services Females Age 26-30

Comparison to BASELINE	SCALE (DOMAIN)		AVERAGE OR ABOVE	BELOW AVERAGE	CLEARLY BELOW
?	Simple Reaction Time	(REACTION TIME)	■	☐	☐
?	Simple Reaction Time (R)	(REACTION TIME)	■	☐	☐
?	Procedural Reaction Time	(PROCESSING SPEED	■	☐	☐
?	Code Substitution - Learning	(LEARNING)	■	☐	☐
?	Code Substitution - Delayed	(DELAYED MEMORY)	■	☐	☐
?	Mathematical Processing	(WORKING MEMORY)	■	☐	☐
?	Matching to Sample	(SPATIAL MEMORY)	■	☐	☐

SLEEP (1-7)

Score: 2 - Able to concentrate, but not quite at peak.

MOOD (0-100)

81 HAPPINESS
69 VIGOR
08 FATIGUE
00 RESTLESSNESS
00 ANXIETY
00 DEPRESSION
00 ANGER

REFERENCE

Category lower limits for Below Average (9th percentile, 80.5 standard score) and Clearly Below Average (2nd percentile, 70 standard score) are based on Hannay, H. J., & Lezak, M. D. (2004). The neuropsychological examination: Interpretation. In M. D. Lezak, D. B. Howieson, & D. W. Loring (Eds.), *Neuropsychological Assessment* (pp. 133-156). New York: Oxford University Press.

Figure 1. ANAM on 20 March 2012

HISTORY

Injury cause(s): None recorded.

Resulting in: None recorded.

Symptoms Right after Injury: none recorded.

Symptoms Now While Resting: none recorded.

Symptoms Now after Exertion: none recorded.

PROVIDER OBSERVATIONS

MACE:

Interval between current and previous injury:

PERFORMANCE AT A GLANCE

Comparison Group: Military: All Services Females Age 26-30

Comparison to BASELINE	SCALE (DOMAIN)		AVERAGE OR ABOVE	BELOW AVERAGE	CLEARLY BELOW
?	Simple Reaction Time	(REACTION TIME)	☐	☐	■
?	Simple Reaction Time (R)	(REACTION TIME)	☐	☐	■
?	Procedural Reaction Time	(PROCESSING SPEED	☐	☐	■
?	Code Substitution - Learning	(LEARNING)	☐	☐	■
?	Code Substitution - Delayed	(DELAYED MEMORY)	☐	☐	■
?	Mathematical Processing	(WORKING MEMORY)	☐	☐	■
?	Matching to Sample	(SPATIAL MEMORY)	☐	■	☐

SLEEP (1-7)

Score: 2 - Able to concentrate, but not quite at peak.

MOOD (0-100)

44 HAPPINESS
47 VIGOR
56 FATIGUE
39 RESTLESSNESS
56 ANXIETY
56 DEPRESSION
33 ANGER

REFERENCE

Category lower limits for Below Average (9th percentile, 80.5 standard score) and Clearly Below Average (2nd percentile, 70 standard score) are based on Hannay, H. J., & Lezak, M. D. (2004). The neuropsychological examination: Interpretation. In M. D. Lezak, D. B. Howieson, & D. W. Loring (Eds.), *Neuropsychological Assessment* (pp. 133-156). New York: Oxford University Press.

Figure 2. ANAM on 25 June 2013

HISTORY

Injury cause(s):	Resulting in:	Symptoms Right after Injury: none recorded.
None recorded.	None recorded.	Symptoms Now While Resting: none recorded.
		Symptoms Now after Exertion: none recorded.

PROVIDER OBSERVATIONS

MACE:

Interval between current and previous injury:

PERFORMANCE AT A GLANCE

Comparison Group: Military: All Services Females Age 26-30

Comparison to BASELINE	SCALE (DOMAIN)		AVERAGE OR ABOVE	BELOW AVERAGE	CLEARLY BELOW
-2.83	Simple Reaction Time	(REACTION TIME)	☐	☐	☐
-2.34	Simple Reaction Time (R)	(REACTION TIME)	☐	☐	☐
-2.7	Procedural Reaction Time	(PROCESSING SPEED	☐	☐	☐
0.99	Code Substitution - Learning	(LEARNING)	☐	☐	☐
0.32	Code Substitution - Delayed	(DELAYED MEMORY)	☐	☐	☐
-0.62	Mathematical Processing	(WORKING MEMORY)	☐	☐	☐
-0.63	Matching to Sample	(SPATIAL MEMORY)	☐	☐	☐

SLEEP (1-7)

Score: 3 - Relaxed and awake, but not fully alert.

MOOD (0-100)

58 HAPPINESS
47 VIGOR
42 FATIGUE
22 RESTLESSNESS
31 ANXIETY
25 DEPRESSION
08 ANGER

REFERENCE

Category lower limits for Below Average (9th percentile, 80.5 standard score) and Clearly Below Average (2nd percentile, 70 standard score) are based on Hannay, H. J., & Lezak, M. D. (2004). The neuropsychological examination: Interpretation. In M. D. Lezak, D. B. Howieson, & D. W. Loring (Eds.), *Neuropsychological Assessment* (pp. 133-156). New York: Oxford University Press.

Figure 3. ANAM on 10 October 2013

HISTORY

Injury cause(s):	Resulting in:	Symptoms Right after Injury: none recorded.
None recorded.	None recorded.	Symptoms Now While Resting: none recorded.
		Symptoms Now after Exertion: none recorded.

PROVIDER OBSERVATIONS

MACE:

Interval between current and previous injury:

PERFORMANCE AT A GLANCE

Comparison Group: Military: All Services Females Age 26-30

Comparison to BASELINE	SCALE (DOMAIN)		AVERAGE OR ABOVE	BELOW AVERAGE	CLEARLY BELOW
-1.85	Simple Reaction Time	(REACTION TIME)	☐	■	☐
-4	Simple Reaction Time (R)	(REACTION TIME)	☐	☐	■
-1.47	Procedural Reaction Time	(PROCESSING SPEED	■	☐	☐
-0.06	Code Substitution - Learning	(LEARNING)	■	☐	☐
0.42	Code Substitution - Delayed	(DELAYED MEMORY)	■	☐	☐
0.01	Mathematical Processing	(WORKING MEMORY)	■	☐	☐
-1.07	Matching to Sample	(SPATIAL MEMORY)	■	☐	☐

SLEEP (1-7)

Score: 1 - Feeling very alert, wide awake, and energetic.

MOOD (0-100)

56 HAPPINESS
67 VIGOR
19 FATIGUE
14 RESTLESSNESS
36 ANXIETY
08 DEPRESSION
06 ANGER

REFERENCE

Category lower limits for Below Average (9th percentile, 80.5 standard score) and Clearly Below Average (2nd percentile, 70 standard score) are based on Hannay, H. J., & Lezak, M. D. (2004). The neuropsychological examination: Interpretation. In M. D. Lezak, D. B. Howieson, & D. W. Loring (Eds.), *Neuropsychological Assessment* (pp. 133-156). New York: Oxford University Press.

Figure 4. ANAM on 5 November 2013