Annals of Case Reports
Suzin G, et al. Ann Case Rep: 9: 101729
www.doi.org/10.29011/2574-7754.101729
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Research Article

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Hyperbaric Oxygen Therapy for Military Post-Traumatic Stress Disorder in Elderly Veterans: Case Studies, Literature Review, and Discussion

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Citation: Suzin G, Doenyas-Barak K, Hadanny A, Elamir M, Miller R, et al (2024) Hyperbaric Oxygen Therapy for Military Post-Traumatic Stress Disorder in Elderly Veterans: Case Studies, Literature Review, and Discussion. Ann Case Report. 9: 1729. DOI:10.29011/2574-7754.101729

Received: 25 March 2024, **Accepted:** 30 March 2024, **Published:** 02 April 2024

Abstract

Post-traumatic stress disorder (PTSD) remains a prevalent and debilitating condition among military personnel and veterans, with significant impacts on mental, physical, and social well-being. This report follows the efficacy of hyperbaric oxygen therapy (HBOT) in treating persistent PTSD in elderly veterans. Two patients aged 60 and 77, with over two decades of PTSD symptoms, underwent a comprehensive HBOT protocol. The treatment resulted in significant improvements across clinical, cognitive, and neurological domains. Both individuals exhibited substantial reductions in PTSD symptom severity, marked improvements in emotional regulation, and enhanced cognitive functioning post-HBOT. Neuroimaging showed an increased brain activity, particularly in regions associated with memory, attention, and emotional regulation. These findings underscore the potential of HBOT as a novel therapeutic approach for elderly individuals with persistent PTSD, even decades after the traumatic event and will be discussed within the framework of the Hyperoxic-Hypoxic paradox.

Keywords: TR-PTSD; HBOT; Cognition; SPECT.

Introduction

Epidemiological studies consistently highlight a high prevalence of post-traumatic stress disorder (PTSD) among military personnel and veterans, impacting up to 30% of those with combat experience [1]. Furthermore, among elderly veterans aged 60 years or older receiving treatment in the VA, the prevalence of combat-related PTSD was found to be 17% for sub-threshold PTSD and 5% for full PTSD [2]. It is assumed that 33% of people suffering from PTSD in the general population are treatment- resistant to all treatment approaches, and 50% are resistant to Cognitive Behavioural Therapy (CBT) approaches [3]. The occurrence of PTSD varies based on the specific conflict and the intensity of combat exposure [4]. Combat- related PTSD significantly affects individuals' mental and physical health, along with their social functioning and overall quality of life [5]. The enduring impact of PTSD on the elderly, persisting for decades after the traumatic event, has been extensively investigated within the framework of maintaining both medical and cognitive well-being. Cumulative data indicates that PTSD increases the likelihood of progressing to dementia. In a retrospective cohort study involving over 180,000

veterans (average age 68.8 years) without dementia initially, those diagnosed with PTSD exhibited an approximately twofold increase in the risk of developing dementia over a 7-year period compared to the control group (HR 2.41; CI, 2.24–2.39). Importantly, this increased risk persists even after excluding individuals with a history of head injury, depression, or substance use disorder [6,7]. In recent years there is cumulative data on the neuroplasticity effect of dedicated protocols of hyperbaric oxygen therapy (HBOT) [8,9]. The new protocol of HBOT, utilizing the so-called Hyperoxic-Hypoxic paradox, was found to induce, stem cells proliferation, mitochondrial proliferation as well as mitochondria migration from glia cells to neuronal cells, to reduce inflammation and to improve induction of HIF and VEGF culmination in angiogenesis and neurogenesis [10]. Clinically, HBOT was found to improve neurocognitive function of patients after traumatic brain injuries [11], post-stroke patients [12] and elderly subjects with age-related decline. Recently HBOT was found to alleviate PTSD symptoms of veterans suffering from treatment-resistant PTSD [13]. The clinical improvement correlated with brain activity as evaluated using functional MRI. The clinical results remained persistent throughout the 2-year follow-up period [13]. The effect of HBOT on elderly individuals with treatment resistant PTSD (TR-PTSD), decades after the traumatic event, have yet to be documented. In this report, we describe two cases of elderly clients over the age of 60, with TR-PTSD, treated with HBOT.

Methods

Two elderly veterans, age 60 and 68 years old, suffering from military related PTSD for over 2 decades, were referred for treatment in the AVIV clinic at the Villages, Florida USA. Clinical, cognitive and brain imaging-based evaluation were done at baseline and following the treatment course.

Treatment

The HBOT protocol included 60 daily sessions, five days a week administrated using a Multiplace chamber, AVIV model 287000 (Fink Engineering, Australia). Each session comprised of 90 minutes of exposure to 100% oxygen at 2 ATA, with five-minute air breaks every 20 minutes. Compression/decompression rates were 1.0 m/min.

Evaluation Tools

To monitor baseline and post-treatment functioning, a battery of tests was administrated, including the Clinician-Administered PTSD Scale for DSM-5 (CAPS-V) questionnaire for evaluating the severity of PTSD symptoms, psychological symptoms questionnaires including Patient Health Questionnaire-9 (PHQ-9) and The General Anxiety Disorder 7-Item Scale (GAD7), Pittsburgh sleep quality questionnaire (PSQI), cognitive function using the Neurotrax computerized battery and the Cambridge Neuropsychological Test Automated Battery (CANTAB). Brain single photon emission computed tomography (SPECT) imaging was used to evaluate brain metabolism. Evaluations were performed at baseline and 1-4 weeks after the last HBOT session.

CAPS-V

Changes in PTSD symptom severity were measured using the clinician-administered PTSD scale (CAPS-V). CAPS-V comprises of 30 items, with 20 items reflecting the severity of DSM-V PTSD. Symptom Scores range from 0 to 80, with higher scores indicating more severe PTSD symptoms [14].

PHQ9

A 9-item questionnaire utilized by clinicians to assess the severity of depressive symptomatology. Each of the 9 questions is equal to one point. The threshold of 5 is used for clinical diagnosis of depression. Higher scores indicate more severe depression [15].

GAD7

A 7-item questionnaire utilized by clinicians to assess the severity of various anxiety disorders. Each of the 7 questions is equal to one point. The threshold of 4 is used for clinical diagnosis of anxiety. Higher scores indicate a more severe anxiety disorder [16].

PSQI

A 19-item self-rated questionnaire used to assess sleep quality and disturbances over a one-month time period. The scoring of the PSQI questionnaire involves assessing seven components of sleep quality, with higher scores indicating poorer sleep quality [17]. The threshold of 5 is used for clinical diagnosis of low sleep quality.

Neurotrax

Changes in cognitive performance was monitored using the Neurotrax Computerized Cognitive Assessment Battery. This assessment evaluates various cognitive domains including memory, executive function, attention, information processing speed, and motor skills. Cognitive scores were normalized for age, gender and educational levels [18]. The participants completed validated alternate test forms of the Neurotrax test battery at baseline and post-HBOT, to allow for iterative administrations with minimal learning effects. Test-retest reliability of the tests were found to be high in both normal and injured populations, without significant learning effects except in the VF and VS domains that were not evaluated in the current study.

CANTAB

Cognitive performance was also monitored using several tasks from the CANTAB battery. These tests included the MTT

task, which evaluates measures of focused attention, information processing speed, cognitive flexibility and the PAL task which measures spatial episodic memory [19]. Notably, the patients were given different test versions of the CANTAB test battery at baseline and after the control/HBOT period, to allow repeated administrations with minimal learning effects. The current version of CANTAB has no population norms for either parameter.

Brain SPECT

Brain single photon emission computed tomography (SPECT) was conducted with 925–1,110 MBq (25–30 mCi) of technetium-99m-Ethyl-cysteinate-dimmer (Tc-99m-ECD) at 40–60 min post injection, using a dual detector gamma camera (ECAM or Symbia T, Siemens Medical Systems) equipped with high resolution collimators. Data was acquired in 3-degree steps and reconstructed iteratively by the Chang method (μ=0.12/cm) attenuation correction. Pre- and post-treatment SPECT were normalized to the maximal uptake in the cerebellum. SPECT images were reoriented into Talairach space using NeuroGam (Segami Corporation, Culombia, MS, USA) for identification of Brodmann cortical areas, and to compute the mean perfusion in each Brodmann area.

Results

Case #1

A 77-year-old veteran was evaluated after suffering from debilitating symptoms of PTSD for decades, resistant to Selective Serotonin Reuptake Inhibitors (SSRIs) and to Eye Movement Desensitization and Reprocessing (EMDR) currently being administered. At his baseline evaluation he conveyed a long-life battle with emotional difficulties going back to the Vietnam War. During those days he served as a marine sniper inside the enemy frontline. He was 21 when witnessed multiple cases where comrades were shot dead in front of him. He recalls being in constant danger, feeling a continuous threat to his life. After discharge from the marines, he constantly fought to obtain balance and quality of life but repeatedly failed due to haunting symptoms. He was married twice before meeting his current wife. He had a hard time keeping a steady job, crippled with intrusive thoughts about the war and flashbacks. He was hyper vigilant, demonstrated periodical outbursts towards his wife, with an enhanced startle effect to sudden noise and avoidance from social encounters and crowded places. He fought insomnia and self-medicated with daily consumption of alcohol in addition to prescribed SSRI's. Physically, he suffered from neck and back pain preventing him from engaging with his long-life habit of playing golf. His chronic medications included statin, bisphosphonates, and SSRI and vitamin supplements. His pre-treatment evaluation, 56 years after traumatic event, revealed the severances of his condition. He showed signs of moderate depression and anxiety, moderate PTSD symptomatology with a CAPS-V of 46 and suffered from substantial sleep disturbances (See Table 1). His cognitive tests revealed changes in sustained attention, slow information processing speed and declined spatial memory, which correlate with accelerated age-related cognitive decline (See Table 2). SPECT imaging showed severe focal decreased cortical uptake throughout the frontal lobes and to a lesser extent over the parietal lobes followed by the temporal lobes. Following completion of the HBOT protocol, the results showed a significant improvement in his performance encompassing cognition, neurological and psychological aspects. As detailed in table 3, his PTSD symptoms were alleviated to complete resolution. His CAPS-V score has gone from 46 (moderate PTSD) to 3 (no PTSD). Importantly, there was a significant decrease in intrusive symptoms and hypervigilance. Concordantly, his PHQ-9 and GAD-7 scores indicated a relief in depression and anxiety symptomatology (See Table 1). It was notable that within the cognitive realm, he has shown growth in multiple domains including learning of new verbal information (increase of 5.4 standard score), improvements in spatial memory (spatial span advanced from 6 to 8 figures) and information processing speed (reaction time decreased from 918 milliseconds to 831 milliseconds) (See Table 2). His brain SPECT showed improvement in metabolic function ranging from 6-20% including the orbitofrontal areas and prefrontal cortex, corresponding to the limbic system, emotional regulation, attention and decision making (See Figure 1 and Table 3.)

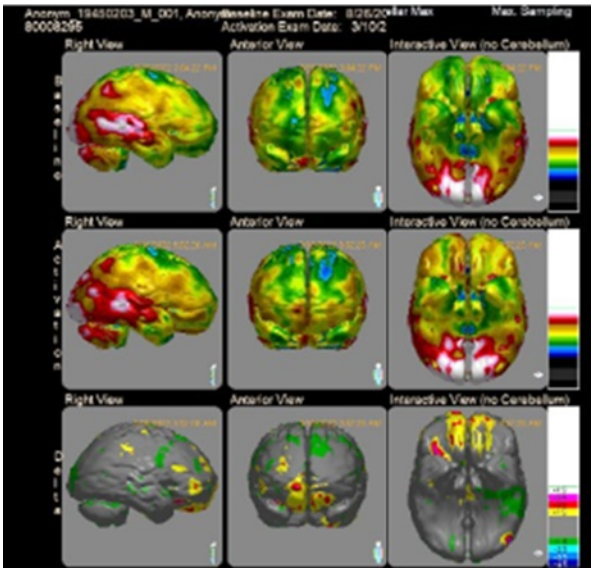

Figure 1: Case #1 SPECT images (upper row – before HBOT; Middle row- after HBOT; Lower row – Delta change).

In his own words, he described his post-treatment self as "being a different person". In a follow up conversation 6 months post-program he reported the persistence of the beneficial effects

of HBOT and said that "I have been living in the past and now living in the present". He mentioned that he can see the beauty of life – "I'm not in the threat anymore". He stopped using SSRI's and was surprised how calmly he dealt with a recent tragedy, after a close family member passed away.

Case #2

A 60-year-old Air Force veteran with a background in medical training, was referred to the AVIV clinic due to her long-term TR-PTSD symptoms, resistant to weekly counselling sessions and SSRI's. Following her high school graduation, she married and subsequently enlisted in the Air Force, where she received training as a medic. Over the years she was deployed to missions in the Middle East where she was exposed to bombing and people who were shot. In one noticeable event, she was asked to pull apart the corpse of a mother clinging to the bodies of her two severely burnt children. After serving in the Air Force for over 20 years, she retired without officially reporting signs of PTSD. She reported feeling 'normal' throughout her military career, unaware of what anxiety truly meant. Following her retirement, she pursued further education and earned the title of Nurse Practitioner, subsequently joining the staff of an intensive care unit. Unexpectedly, this new career path became the catalyst for the relative delayed onset of her full-blown PTSD. She experienced a significant debilitation in her ability to perform daily living tasks, characterized by a growing sense of irritability, a heavy burden of guilt, persistently low morale, and overwhelming shame. Her once-routine meals were now disrupted as she couldn't bear to consume meat or witness the act of tearing chicken from its bone during dinner. Adding to her torment, she began experiencing frequent nightmares, haunted by disturbing visions of the mother and her tragically burnt children. She horrifically referred to this haunting figure as 'MOTHER'. Ultimately, she found herself unable to continue her work in the trauma unit and was forced to resign. Her husband insisted that she get help. When presented to the Aviv Clinic she reported a past medical history significant for post-traumatic stress. Within the cognitive realms she reported difficulties with memory and attention, forgetting events, occasional brain fog, restlessness, and distractibility. She reported a past medical history notable for A-Fib s/p ablation, menopause, sleep disturbances, back pain, and anxiety. Before coming to the AVIV clinic she was treated with blood thinners, drugs for treating hypertension and sleeping pills. As summarized in Table 1. Her clinical screening unveiled profound intrusive symptoms, mild depression and severe anxiety indicators, sleep disturbances, and heightened hyper arousal including unmanageable irritability, anger, and restlessness, all significantly impacting both social and occupational aspects of her life. Her cognitive assessment results, summarized in Table 2, displayed below-average scores in the domains of divided attention and information processing speed, suggesting a decline in these areas. Her brain MRI revealed no signs of acute intracranial infarction, mass effect, or abnormal enhancement. There was minimal evidence of chronic microangiopathic white matter ischemic change. On her SPECT scan, there was mild to moderate decreased cortical activity, with focal areas of severely decreased cortical activity observed bilaterally in the frontal lobes. Additionally, mild to moderate decreases in cortical uptake/activity were noted over the parietal, temporal, and left cerebellar lobes. During the HBOT course, she went from experiencing distressing nightmares, to the emergence of memories from her past, including memories of playing with a childhood friend in a playground. Subsequently, the nightmares stopped, and she started recollecting happier memories from her earlier years. Gradually, her internal turmoil unraveled, bringing her a sense of peace and the gradual resolution of emotional knots that had plagued her. After completing the HBOT protocol, she repeated the comprehensive assessment battery, 12 weeks after her last HBOT session. As summarized in Table 1, She has made substantial progress in her emotional well-being and overall mental health following treatment, as reflected in her scores. She reported significant improvements in emotional regulation, sleep quality, and a remarkable reduction in anxiety and self-blame. Moreover, her clinical assessments demonstrate marked improvements. Her CAPS-V symptoms score decreased significantly from 34 to 10, indicating substantial relief, manifesting in less intrusions, less avoidance and less symptoms of heightened arousal (see Table 1). Her cognitive progress is evident in the assessment results, with notable improvements in information processing speed progressing from a low average (89.6) to an above average score (105.3). Notably, her cognitive flexibility (See table 2: 'MTTLMTM') substantially improved, highlighting her enhanced ability to adapt to changing demands and suppress habitual responses. Comparing pre-treatment and post-treatment brain imaging, substantial improvements were observed. SPECT imaging revealed heightened activity (9% to 18%) in Frontal, Parietal, and Temporal areas, correlating with enhanced working memory, coordination, attention, and language comprehension (See Figure 2 and Table 3.). These findings collectively signify significant positive changes in clinical, cognitive and neurological function following the treatment.

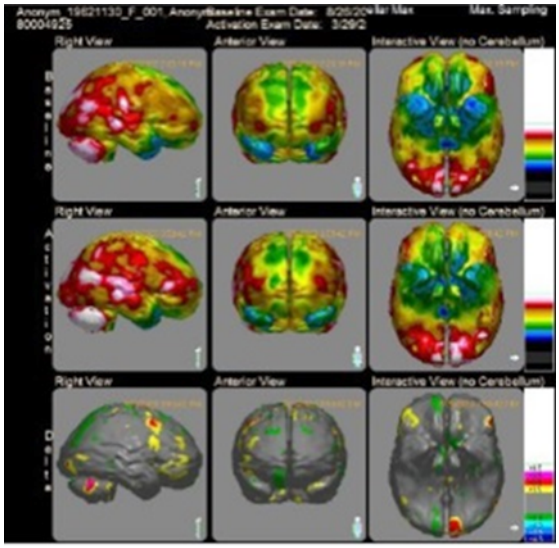

Figure 2: Case #2 SPECT images (upper row – before HBOT; Middle row- after HBOT; Lower row – Delta change).

To summarize, she has experienced a significant transformation in her overall well-being since receiving treatment. Her nightmares, once occurring 2-3 times a week, have become rare occurrences. Her sleep quality has improved to the extent that she's tapering off the sleeping pill, resulting in more refreshing mornings and more energy during the day. Additionally, she has rediscovered her motivation for sports, engaging in water volleyball, tap dancing, and jazz dancing. According to her, the treatment has been a life-changing experience.

Symptoms	Case #1		Case #2	
	PRE	POST	PRE	POST
CAPS-V (Severity Score)	46	3	34	10
PHQ-9	12	5	5	2
GAD-7	11	4	17	3
PSQI	8	13	9	7

Table 1: Scores from clinical questionnaires. CAPS-V (Clinician administered PTSD Scale); PHQ-9 (Patient Health Questionnaire); GAD-7 (The Generalized Anxiety Disorder Scale); PSQI (Pittsburgh Sleep Quality Index).

Function		Case 1		Case 2	
		pre	post	pre	post
Neurotrax	Attention	104.9	107.9	101.5	101.5
	Processing Speed	98.8	101.3	89.6	105.3
	Verbal Memory	108.7	114.1	112.2	115.9
CANTAB	MTTLM (ms.)	917.57	831.21	631.71	571.03
	MTTLMTM (ms.)	1192.16	1147.55	775.53	640.97
	PALNPR	6	8	8	8
	PALTEA	40	15	6	6

Table 2: MTTLM (Mean Latency of response time in MTT task); MTTLMTM (Mean latency of response time on Multitask Trials in MTT task); PALNPR (Longest Sequence Reached on PAL task); PALTEA (Estimated Error Numbers on PAL Task).

Brain region		Brain function	Pre	Post	% change
Case 1	BA 4 R	Motor function of limbs and face muscles	0.75	0.8	6.62%
	BA 11 L	Reward, emotion, connected to the limbic system	0.71	0.8	13.45%
	BA 11 R	Reward, emotion, connected to the limbic system	0.71	0.85	20.33%
	BA 19 L	Associative Visual Cortex	1.07	1.17	9.81%
	BA 24 R	Attention	0.68	0.8	17.10%
	BA 25 R	Emotion Regulation, Decision making	0.8	0.92	14.88%
	BA 36 R	Memory	0.63	0.72	14.50%
	BA 44 R	Language comprehension and Speech	0.82	0.89	8.74%
Case 2	BA 17 R	Primary visual cortex	1	1.12	12.00%
	BA 21 L	Face recognition, word meaning (reading)	0.91	1.01	10.99%
	BA 28 R	Spatial memory, directionality	0.62	0.73	17.74%
	BA 28 R	Language comprehension and speech	0.82	0.95	15.85%
	BA 28 L	Spatial memory, directionality	0.65	0.72	10.77%
	BA 37 L	Visual memory	0.87	0.95	9.20%
	BA 44 R	Language comprehension and speech	0.81	0.93	14.81%
	BA 46 R	Working memory, decision making	0.82	0.91	10.98%

Table 3: SPECT scores per Broadmann area.

Discussion

PTSD has long-lasting effects that significantly impact quality of life, cognitive functions, and social and occupational performance, persisting decades after the traumatic event. The article presents two cases of veterans at the ages of 60 and 77 years, suffering from military-related TR-PTSD who were successfully treated with HBOT many years after experiencing PTSD-related insults. The clinical improvement was found related with enhancements in the relevant brain regions, as demonstrated by brain SPECT imaging. These case studies further support findings from a previous study by Doenyas-Barak et al. (2022) [20], which demonstrated that HBOT can induce neuroplasticity and alleviate PTSD symptoms in veterans suffering from TR-PTSD, with the effects of treatment persisting longitudinally post-treatment. However, it's noteworthy that individuals older than 60 were excluded from that study, therefore, the mean patient age was 36. In the cases presented here, we observe that the beneficial effects of HBOT were evident even in individuals in their seventh decade of life and even decades after the initial trauma. These case studies align with previous research demonstrating the advantages of employing the Hyperoxic-hypoxic paradox [13] in treatment resistant conditions. Physiological barriers that previously hindered any clinical impact of pharmacological or psychotherapeutic interventions are now overcome, establishing a distinct timeframe during which such interventions may prove considerably more potent. Additionally, the beneficial effects of HBOT on cognition, which is of significant importance after the 6th decade of life, further enhance processing resources, facilitating emotional regulation and thereby improving the daily life performance beyond the alleviation of the PTSD symptoms. The prospect of treating PTSD, even decades after the traumatic event, offers new hope for patients experiencing persistent symptoms unresponsive to other forms of treatment. Elderly patients with PTSD are particularly vulnerable to cognitive decline, dementia, cardiovascular disease, and suicidal tendencies [21-23]. Providing treatment for these individuals can alleviate emotional burdens on their caregivers and reduce economic strain on the healthcare system.

In conclusion, TR-PTSD veterans may be due to functional and structural brain changes, particularly within the frontolimbic

circuitry, that may persist many years after the traumatic exposure [24]. These brain alterations underscore the potential utility limitation of the current available psychological and pharmacological interventions. The dedicated HBOT protocols activate a paucity of cellular mechanisms, promote neuroplasticity and the regaining of function in key brain regions. This presents a promising avenue for the treatment of PTSD. Given its potential to alleviate biological constraints that impede clinical improvement, HBOT may contribute to symptoms alleviation decades following the traumatic events beyond the 6th decade of life. Subsequent research should monitor the aging trajectories of elderly individuals with PTSD to determine whether, following treatment, they demonstrate reduced susceptibility of transitioning to dementia.

Disclosure

Author Contributions: Conceptualization, G.S. and S.E.; Writing-original draft preparation, G.S.; writing—review and editing, S.E, K.D.B, A.H. M.E and R.M; supervision, S.E.

Funding: This research received no external funding.

Ethical Considerations: Informed consent for publication was obtained from both participants in a written format. All personal identifying information was removed from the manuscript.

Data Availability Statement: Data supporting the study results can be provided followed by request sent to the corresponding author's e-mail.

Acknowledgments: We would like to express our gratitude to Dave Globig, Dion Atchison, Lisa Lynn, Dr. Ankita Shukla, Dr. Randy Brown, Aaron Tribby, John Horsley, Cheyene Emmons, and Loredana Caprio for their dedication during the treatment of Case 1 and Case 2.

Conflict of interest statement: GS and AH are employees and shareholders at AVIV scientific Ltd. SE is a shareholder and head of medical advisory board of Aviv scientific Ltd. ME and RM are employees at AVIV clinics.

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