The synergistic effect of hyperbaric oxygen and virtual reality exposure therapy on mild traumatic brain injury with post-traumatic stress disorder

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Abstract

Mild traumatic brain injury (mTBI) has dramatically affected the lives of many American soldiers involved in Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND). mTBI is often exacerbated by post-traumatic stress disorder (PTSD), a condition that is five times more likely to affect soldiers that already have mTBI. Despite this, there is no current treatment for both mTBI and PTSD. Hyperbaric oxygen therapy (HBOT) and virtual reality exposure therapy (VRET) were both investigated in this study as a possible synergistic treatment for the combined diagnosis of mTBI and PTSD present in many American soldiers. Data was collected through a systematic literature review using databases such as Google Scholar, EBSCOHost, PubMed, and a variety of other journals. Data analysis involved a paired T-test with significance defined as $p<0.05$ at 95% confidence intervals. Data obtained indicated that HBOT was effective in treating mTBI symptoms, but it was ineffective in treating PTSD as quantified by the Clinician Administered PTSD Scale (CAPS) ($p=0.6330$). However, VRET was shown to be significant in reducing CAPS scores ($p=0.0014$). There were no studies available testing the effectiveness of both HBOT and VRET concurrently, so further work is needed to confirm that the combination of both can be used to treat both mTBI and PTSD.

Key terms: mild traumatic brain injury, post-traumatic stress disorder, hyperbaric oxygen therapy, virtual reality exposure therapy, military

Introduction

Mild Traumatic Brain Injury

From 2001-2014, as many as 320,000 American soldiers returned home from Iraq and Afghanistan with mild traumatic brain injury (mTBI) (Bandak et al., 2015). mTBI is caused by a bump or blow to the head and results in disruption to normal brain function (Elder et al., 2012). The most common cause of mTBI for American soldiers deployed to Afghanistan and Iraq in Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) is blast injury (Blennow et al., 2011). A blast injury is sustained through exposure to an explosion (Jianx, 2001). As illustrated in Figure 1, there are three mechanisms of blast injury that can impact the brain: primary, secondary, and tertiary (Granberg, 2010). Primary blast injury results in over-pressurization of bodily tissues (Long, 2014). This mostly impacts gas-filled organs, such as the lungs and ears. However, the immense pressure caused by explosion can also constrict the torso, impacting blood vessels (Proud, 2016). As a result, detrimental energy waves are sent to the brain, which can cause the brain to be pushed against the skull. When the brain is bruised in this way, a mTBI may occur (Scherer, 2007). Secondary blast injury is caused by debris from the blast colliding with the brain (Trudeau et al., 1998). This impact can crack the skull, which may puncture blood vessels in the

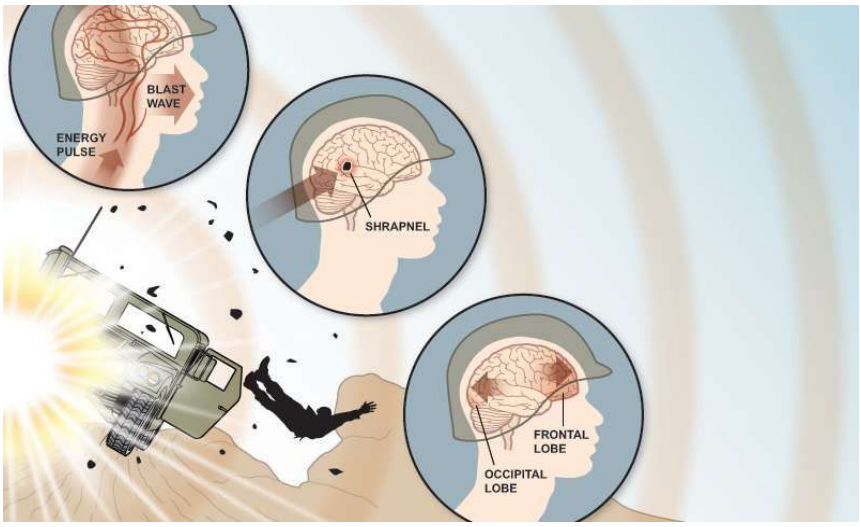

Figure 1: Effect of blast traumatic brain injury (Granberg, 2010).

brain. If blood vessels are punctured, cerebral edema may occur (Bandak et al., 2015).When cerebral edema occurs, cerebral blood flow is reduced, and this may result in a mild traumatic brain injury (Long, 2014). Lastly, the blast releases kinetic energy which can throw the body of a soldier into the air and onto the ground. When the body is thrown to the ground, the brain is slammed against the anterior and posterior sides of the skull (Scherer, 2007). This is referred to a coup-contrecoup injury, and it is also the result of a tertiary blast injury (Trudeau et al., 1998). The number of improvised explosive devices (IEDs) utilized in wartime is growing, so blast exposure in soldiers is becoming more common, increasing the frequency of mTBI (Jianx, 2001).

mTBI is a moderate form of TBI. The main difference between the two is that mTBI is defined as disorientation/loss of consciousness lasting less than thirty minutes following the initial injury (Bremner, 2016). Although, the two conditions do share the same symptoms: headache, vision problems, memory loss, dizziness, insomnia, nausea, fatigue, mood changes, depression, and anxiety (Bull, 2016). In the general population, symptoms from mTBI typically resolve themselves within a month, but symptoms from TBI typically last for six months to two years (Clasper, 2011). However, up to 15% of American soldiers experience mTBI symptoms up to one year, much longer than the typical recovery time (Elder et al., 2012). This is due to the fact that mTBI sustained during wartime are usually much more severe than those sustained by the general populations (Harch et al., 2009). Additionally, Bandak et al. showed that there are long-term effects of mTBI, such as atrophy of gray and white matter in the brain (2015). This can lead neurodegeneration, resulting in conditions such as Parkinson's disease, Alzheimer's disease, and motor neuron disease (Bandak et al., 2015). Even though mTBI symptoms may

subside after a short amount of time without treatment, there are many long-term invisible effects that are often overlooked.

Even though mTBI is a common condition among soldiers, it is often misdiagnosed since there is not a clearly defined treatment plan for the injury (Harch, 2015). This can be attributed to the fact that soldiers with mTBI appear to be uninjured in a physical sense (Liu et al., 2010). It is estimated that as many as 60% of mTBIs are missed during diagnosis (Masel, 2011). Without a proper diagnosis, it is extremely difficult for the patient to receive treatment. While the symptoms of some mTBIs may resolve themselves within a matter of months, many soldiers with mTBI may encounter severe cognitive, behavioral, and physical distress for a year or more (Obenaus, 2011). If the condition is properly diagnosed, however, current treatment options include physical rest, cognitive rest, rehabilitative therapies (occupational, physical, speech, etc.), and medication (Schwab et al., 2007). However, these treatments are extremely time-extensive and ignore the psychological side of mTBI as well as the long-term effects of the condition (Tanielian & Jaycox, 2014). mTBIs result in time away from battle and extensive suffering for American soldiers, and a treatment method that treats all aspects of the condition needs to be established.

PTSD

PTSD is a psychological disorder caused by trauma that manifests itself in haunting nightmares/memories, anxiety, insomnia, and/or social withdrawal that lasts for four or more weeks (Elder et al., 2012). Approximately 300,000 American veterans, active in battle from 2001-2004 have experienced combat PTSD (Harch et al., 2009). There are many traumatic

events experienced by soldiers during wartime; soldiers are constantly exposed to devastating and life-threatening events. While soldiers are not the only ones affected by PTSD, they are, collectively, affected by the condition the most (Mclay et al., 2011).

PTSD significantly reduces the quality of life for those who have it. When exposed to situations similar to the trauma that caused their PTSD, those affected may experience panic attacks and/or extreme anxiety (Scofield et al., 2017). Some of these situations include small spaces, places filled with large amounts of people, and exposure to loud noises (fireworks, gunshots, etc.) (Shin et al., 2009). This leads to avoiding such situations, leaving many of those with PTSD unable to ride the subway, go to work, or attend social events (Wolff, 2013). Additionally, many of those with PTSD experience terrible nightmares in which they vividly relive their trauma (Felmingham et al., 2017). As a result, insomnia may occur, which leads to even more devastating consequences such as decreased cognitive functioning (Gahm et al. 2014).

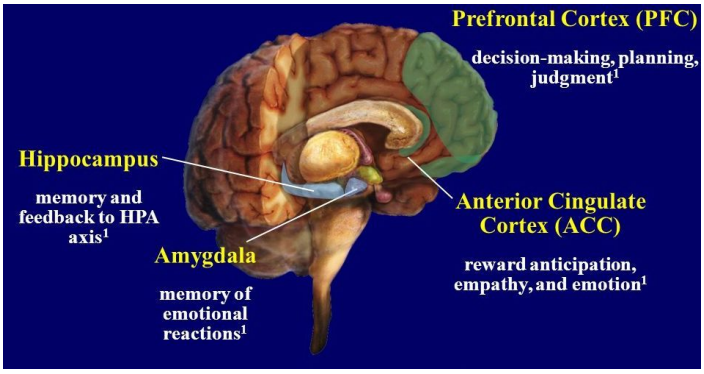

Figure 2: Areas of the Brain Implicated in PTSD (Charney et al., 2004)

As seen in Figure 2, PTSD affects structures in the brain such as the hippocampus, prefrontal cortex (PFC), anterior cingulate cortex (ACC), and amygdala (Charney et al., 2004). The hippocampus is a structure in the limbic system, a system in the brain involved with regulating emotion. Its specific function involves learning and memory (Felmingham et al., 2017). In patients with PTSD, the hippocampus has been shown to be reduced. As a result, it is difficult for those with PTSD to interpret the context of their environment as well as to be able to

differentiate between past and present experiences (Scofield et al., 2017). For example, a soldier with PTSD may be unable to listen to fireworks because it reminds him or her too much of wartime. The PFC and ACC are responsible for regulating the emotional responses caused by the amygdala (Mclay et al., 2011). The function of the amygdala is to experience and perceive emotions, particularly fear. In patients with PTSD, the PFC and ACC are remarkably reduced while the amygdala is overactive (Shin et al., 2009). Certain events may trigger PTSD symptoms in those who suffer the condition, and they may exhibit extreme fear responses. In someone without PTSD, this extreme fear would be regulated by the PFC and ACC before the amygdala is activated, resulting in little to no fear. However, since these structures are damaged in those with PTSD, simple events slightly related to the original trauma can cause severe psychological damage (Elder et al., 2012).

PTSD in soldiers is more difficult to recover from than PTSD experienced by the general population (Mclay et al., 2011). Typical treatments for PTSD, such as psychotherapy and antidepressants, are remarkably less effective in soldiers as a result. In fact, ⅔ of soldiers receiving treatment in the form of psychotherapy and/or antidepressants still displayed PTSD symptoms after the treatment was completed (Elder et al., 2012). New treatments are currently being established for military-specific PTSD, but many soldiers still suffer from the disabling condition today.

Correlation Between mTBI and PTSD

There is a proven correlation between mTBI and post-traumatic stress disorder (PTSD). Soldiers are five times as likely to have PTSD if they have suffered a mTBI. 82,000 soldiers

returning from Iraq and Afghanistan have both PTSD and mTBI (Harch 2012). There is no such correlation between mTBI and PTSD seen in the general public (Harch et al. 2009). There are three hypothesized reasons to explain the correlation between mTBI and PTSD. Since mTBI in soldiers is typically caused by a blast injury, PTSD can accompany the mTBI because the explosive blast was a traumatic experience. The blast is a life-threatening experience, and this can be very traumatic for soldiers who experience it. Additionally, after a blast injury, soldiers may have to deal with the loss of other soldiers, another traumatic event (Elder et. al, 2012). The next possible reason to explain this correlation is that the symptoms of each condition are very similar. As seen in Figure 3, symptoms such as irritability, cognitive deficits, insomnia, depression, fatigue, and anxiety are both seen in mTBI and PTSD (Stein & McCallister, 2009). It has been theorized that physicians may diagnose patients with both conditions, even if the patient only has neither or only one of the two conditions (Blennow et al., 2011). The third possibility is that PTSD is directly caused by mTBI. A mTBI could damage structures in the brain that are important for processing and responding to psychological stressors, such as the hippocampus, amygdala, and/or PFC (Clasper, 2011). Even though all mTBIs are unique, the most common damaged

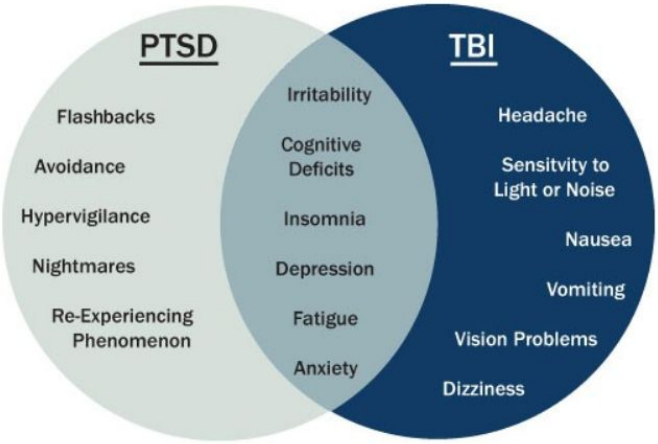

Figure 3: Venn Diagram Illustrating Similar Symptoms Between PTSD and TBI (Stein & McCallister, 2009).

structure in the brain is the PFC (Gahm et al., 2014). As mentioned above, the PFC is often reduced in patients with PTSD. This can lead to PTSD symptoms (Bull, 2016). Even though there is a proven correlation between the two conditions, there is no treatment plan currently available for the combined diagnosis of mTBI and PTSD (Campos-Pires & Dickinson, 2016).

Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy (HBOT) is a medical treatment in which a patient is exposed to 100% oxygen in a contained, pressurized environment (Liu et al., 2010). It is already a clinically proven treatment for fifteen ailments, including decompression sickness, and it is covered for these fifteen by insurance/Medicare (Masel, 2011). HBOT is a favorable treatment because it increases the concentration of oxygen gas within the blood, and this results in improved oxygenation of tissues(Uszler, 2016). The first hyperbaric oxygen chamber was created in 1662 by a British physician, but the first use of HBOT was not until the 19th century. In 1878, a French physiologist discovered that HBOT could be used to treat decompression sickness, and HBOT as a treatment method for this condition was proven in 1930 by the United States military (Harch et al., 2009). The current model for a typical hyperbaric oxygen therapy can be seen in Figure 4 (Mayo Foundation for Medical Education and Research, 2018).

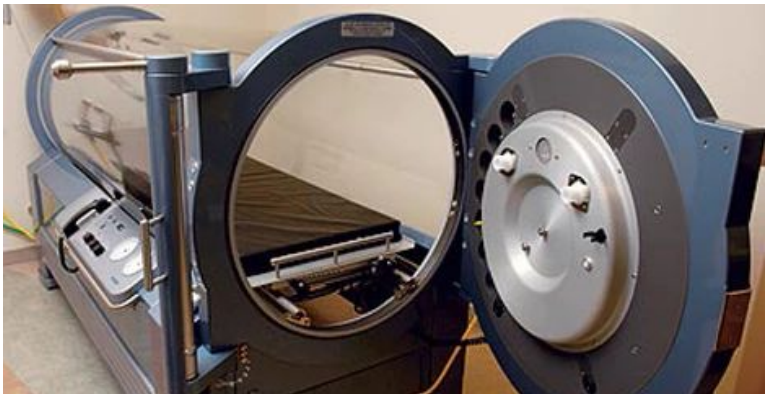

Figure 4: Image of a hyperbaric oxygen chamber (Mayo Foundation for Medical Education and Research, 2018).

While HBOT as a treatment for neurological conditions has not been widely used in the United States, it is common in countries such as China, Japan, and Russia (Harch, 2012). Countless experiments over the last forty years on the effect of HBOT on neurological disorders have shown that HBOT can be a treatment method for this condition (Scofield et al., 2017).

HBOT can be beneficial in treating mTBI. HBOT can reduce cerebral edema, which is commonly seen in mTBIs caused by secondary and tertiary blast injuries (Trudeau et al., 1998). In secondary blast injury, shrapnel from an explosion may cause a skull fracture. The broken, sharp pieces of skull may puncture cerebral blood vessels, resulting in cerebral edema (Schwab et al., 2007). Cerebral edema reduces cerebral blood flow, resulting in deoxygenation of the brain. This is detrimental to the brain, an organ that relies on constant oxygen (Scherer, 2007). HBOT can provide the much-needed oxygen to oxygen-deprived neurons and cerebral blood vessels, returning the brain back to its constant state. Cerebral edema is reduced, and the symptoms of mTBI dissipate (Proud, 2016).v A similar pathway is seen in mTBI caused by tertiary blast injury, but the difference is that cerebral edema results from damaged blood vessels caused by a coup-contrecoup injury (Obenaus, 2011). mTBI is a severely damaging disorder, and HBOT may be able to increase recovery time.

Virtual Reality Exposure Therapy

Virtual reality exposure therapy (VRET) combines virtual reality and exposure therapy, a form of behavioral therapy. Virtual reality is a computer-generated experience that can allow those who use it to simulate reality (Gahm et al., 2014). The user is transported into another reality, in which the actions the user makes in real-life (i.e. moving the head to look around) are

mimicked in the simulation (Kramer, 2013). The user wears a headset that covers both eyes which both tracks eye/head movement and acts as a video screen to allow the user to see the simulation. Typically, headphones are also worn to enhance the simulation (Mclay et al., 2011). The term virtual reality was coined by Jaron Lanier in 1987, and Nintendo created its own virtual reality gaming headset in 1995 (Rothbaum, 2005). The concept of virtual reality is widely used today in video games.

Figure 5: Image of a typical VRET session (Rizzo, 2016).

Exposure therapy involves exposing the patient to what is causing their anxiety utilizing principles of systematic desentization and the anxiety hierarchy (Creech & Misca, 2017). The patient is taught anxiety-reducing techniques and gradually exposed to the trigger of their fear/anxiety (Steenkamp et al., 2015). The patient is able to experience their fear in a safe environment with techniques that calm down their sympathetic nervous system which can decrease avoidance of these situations and decrease overall anxiety (Wang & Li, 2013). It was first established by a Joseph Wolpe, a behaviorist, in 1958 and used to treat patients with obsessive-compulsive disorder in 1970 by Stanley Rachman, a psychologist (Wolff, 2013). It is commonly used today both for OCD as well as specific phobias (Steenkamp et al., 2015).

The initial trauma that caused PTSD in soldiers may be extremely difficult to replicate in an exposure therapy setting. However, virtual reality allows the therapist to replicate the event

almost exactly, according to the patient's account of the situation (Creech & Misca, 2017). After a few sessions of teaching the patient anxiety-reducing techniques, the patient is gradually exposed to what triggered their PTSD (Mclay et al., 2011). Following the principles of systematic desentization, this occurs in small steps (Kramer, 2013). First, the patient may be exposed to the sound of fireworks. Later on, they will relive the exact situation that caused their PTSD utilizing virtual reality (Gahm et al., 2014). A typical session of VRET can be seen in Figure 5 (Rizzo, 2016). VRET is typically conducted in 12-16 sessions, which is much shorter than the typical 20-24 sessions prescribed for traditional psychotherapies. This makes VRET an effective, quick, and relatively inexpensive treatment for PTSD in soldiers (Wang & Li, 2013).

The Gap in Current Research

There is not currently a treatment for both mTBI and PTSD, despite the proven correlation between the two conditions in soldiers. Many soldiers do not undergo treatment, resulting in long-term irreversible brain damage and a decreased quality of life. However, this does not need to be the case. This paper will discuss and investigate the possible synergistic effect of HBOT and VRET in order to treat both mTBI and PTSD.

Purpose

The purpose of this study is to explore the validity of the synergistic effect of hyperbaric oxygen and virtual reality exposure therapy on mild traumatic brain injury with post-traumatic stress disorder. These conditions reduce the quality of life for many American soldiers and veterans, so the implementation of an effective treatment plan is pertinent.

Research Question

Is there a synergistic effect between hyperbaric oxygen and virtual reality exposure therapy on the treatment of mild traumatic brain injury with post-traumatic stress disorder in soldiers?

Hypotheses

Alternative

The combination of HBOT and VRET will have a significant effect on mTBI with PTSD in soldiers.

Null

The combination of HBOT and VRET will not have a significant effect on mTBI with PTSD in soldiers.

Methods

Data was collected from various peer-reviewed papers and analyzed using systematic data analysis. The papers were found through various including Google Scholar and EBSCOhost, using keywords “hyperbaric oxygen therapy”, “virtual reality therapy”, “PTSD”, “traumatic brain injury in soldiers”, “mild traumatic brain injury in soldiers”, “PTSD and mTBI”, and “hyperbaric oxygen therapy and mild traumatic brain injury”. Additional papers were found through the references of articles discovered through these online databases.

Selection Criteria

All data in this study was extracted from peer-reviewed studies no more than ten years old to ensure current research. Additionally, the subjects tested in these studies were all current/past members of the American military in OEF, OIF, and/or OND.

In the studies focusing on HBOT, subjects had to have sustained a mTBI from a blast injury during wartime. Subjects also had to be diagnosed with both mTBI as well as PTSD. Subjects had to be tested prior to and following the study utilizing subject-reported mTBI symptom questionnaires and the Clinician Administered PTSD Scale (CAPS).

There is not one effective way to quantifiably measure mTBI, and many studies used a combination of cognitive, behavioral, and physical tests to quantify mTBI. However, subject-reported mTBI symptom questionnaires summarized the results of these tests and were commonly present throughout different studies, so they were analyzed in this paper.

The Clinician Administered PTSD Scale (CAPS) is the currently acceptable quantifiable scale for PTSD according to the U.S. Department of Veterans Affairs. It is a 30-question test administered by clinicians and clinical researchers. Each question corresponds to a specific criterion of symptoms. The questions are answered by the patient with a scored response of 0-5, with 0 meaning the symptom is completely absent and 5 meaning the symptom is extreme. To be diagnosed with PTSD, patients must have at least one Criterion B symptom, one Criterion C symptom, two Criterion D symptom, and two Criterion E symptoms as well as meet Criterion F (condition has lasted at least four weeks) and Criterion G (condition results in severe distress/impairment). An overall score of 25 or higher can be used to officially diagnosis PTSD, but scores of 47 and higher (signifying extreme PTSD) are most common in soldiers.

In the studies focusing on VRET, subjects also had to be diagnosed with both mTBI as well as PTSD. Subjects had to be tested prior to and following the study utilizing CAPS.

Papers were excluded if they did not meet these requirements. Eleven data sets were included and thirteen data sets were excluded.

Data Analysis

Paired t-tests for the initial research question were performed in Microsoft Excel to determine if the data was significant. Significance was defined as a p-value<0.05 at 95% confidence intervals.

Results

Table 1. The effect of HBOT on specific symptoms of mTBI as self-reported by patients

Symptom	Improved	No Change	Declined	p-Value
Headache	80% (12/15)	20% (3/15)	0% (0/15)	0.0140
Sleep disruption	93% (14/15)	7% (1/15)	0% (0/15)	0.0001
Memory	72% (13/18)	28% (5/18)	0% (0/18)	0.0500
Cognition	94% (15/16)	6% (1/16)	0% (0/16)	0.0001
Energy level	80% (8/10)	20% (2/10)	0% (0/10)	0.0500
PTSD stress	20% (1/5)	80% (4/5)	0% (0/5)	0.2080
Irritability	73% (8/11)	27% (3/11)	0% (0/11)	0.1377
Photophobia	67% (6/9)	33% (3/9)	0% (0/9)	0.3466

This data was extracted from a sample size of twenty total subjects from six total studies. Not all patients experienced all of the following symptoms, so there is a different patient size for each symptom. The table includes the percentage of subjects that indicated that a particular symptom improved, did not change, or declined following HBOT treatment. The fractions inside the parentheses following the percentages indicate the number of subjects that indicated that a particular symptom improved, did not change, or declined following HBOT treatment out of the total subjects that experienced the specific symptom. Following HBOT treatment, almost all

symptoms improved, except for PTSD. Most symptoms improved over 70% following HBOT. No subjects reported that their symptoms had no change following HBOT treatment. The p-values for all but 3 symptoms (PTSD stress, irritability, and photophobia) were significant with a value of over 0.05.

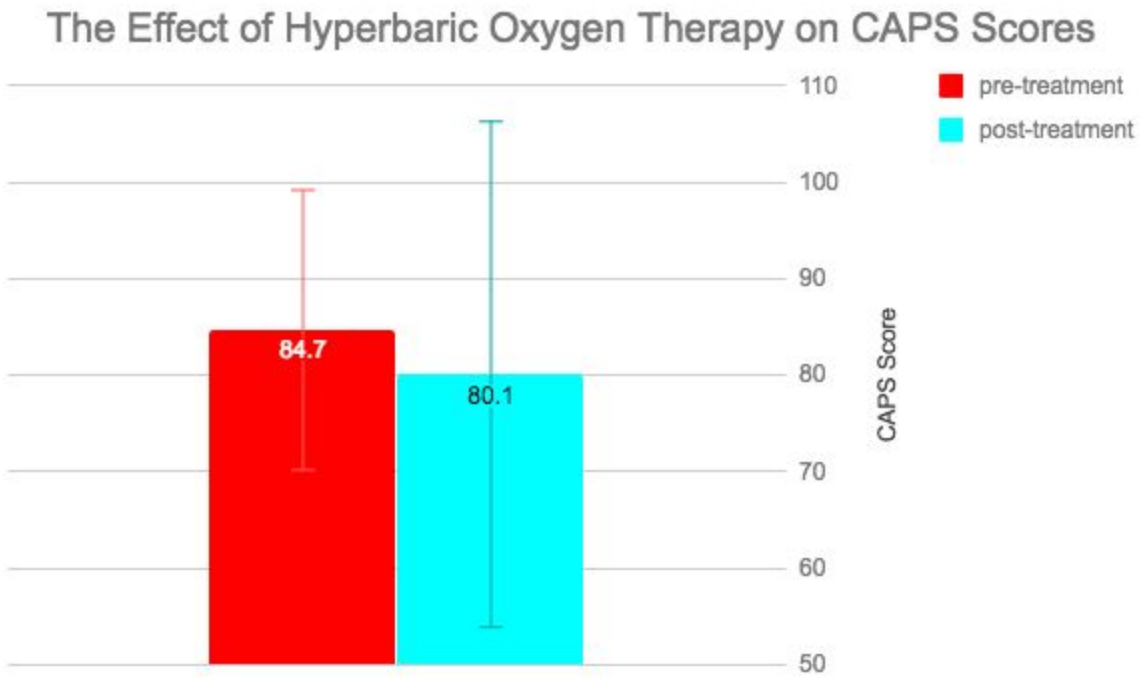

Figure 6: **The effect of hyperbaric oxygen therapy on CAPS scores.** Bars indicate standard deviation *shows insignificant difference (p=0.663)

This bar graph indicates the effect of HBOT on CAPS scores. CAPS scores were collected and averaged from six studies with a total of 20 subjects across all studies. Before treatment, the average CAPS score was 84.7, with a standard deviation of 14.1. After HBOT treatment, the average CAPS score was reduced to 80.1, with a standard deviation of 26.2. The p-value was 0.663, meaning the effect of HBOT on CAPS scores was insignificant.

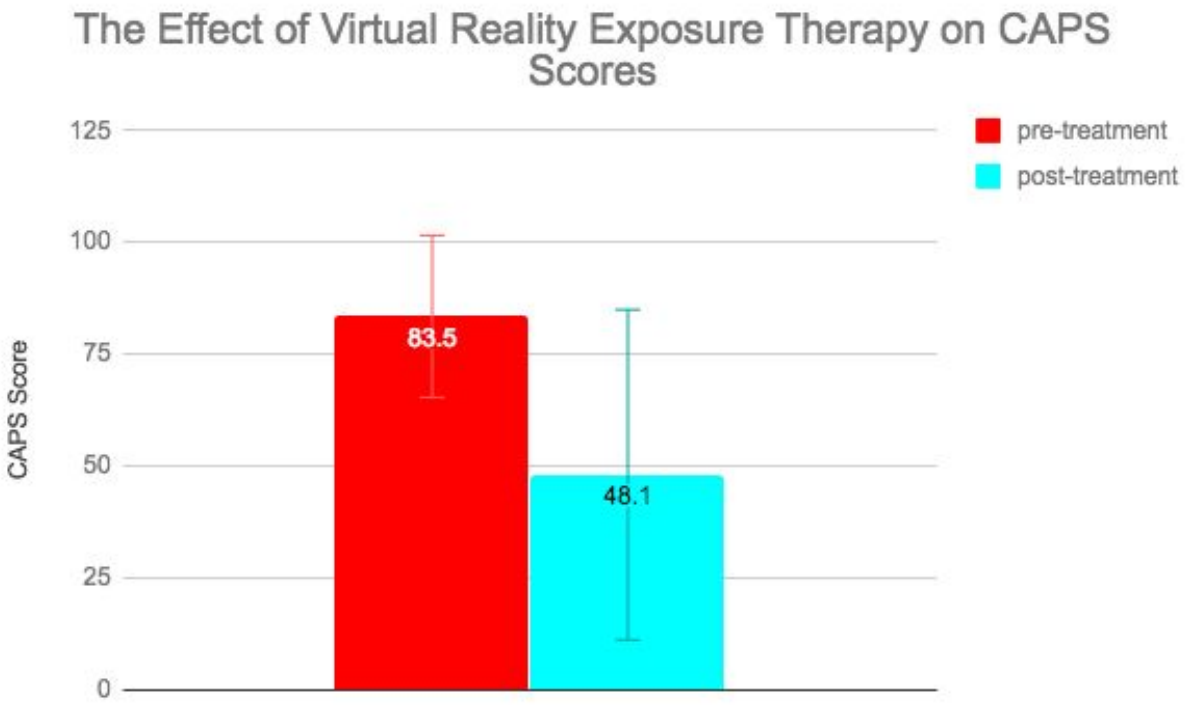

Figure 7: **The effect of virtual reality exposure therapy on CAPS scores.** Bars indicate standard deviation *shows significant difference (p=0.0014)

This bar graph indicates the effect of VRET on CAPS scores. CAPS scores were collected and averaged from five studies with a total of 16 subjects across all studies. Before treatment, the average CAPS score was 83.5, with a standard deviation of 14.1. After HBOT treatment, the average CAPS score was reduced to 48.1, with a standard deviation of 36.9. The p-value was 0.0014, meaning the effect of VRET on CAPS scores was significant.

DISCUSSION

The number of American soldiers/veterans with mTBI is increasing due to growing risk of blast exposure on the battlefield. Additionally, the rate of PTSD in soldiers is rising because the two conditions are correlated in soldiers. However, many current treatment options are

ineffective for mTBI and PTSD. There is no current treatment plan for the combined diagnosis of both conditions. The combination of HBOT and VRET pose as a possible treatment for mTBI and PTSD.

Data was analyzed from studies on the effectiveness of HBOT alone and the effectiveness of VRET alone. There have been no studies done on both treatment concurrently. The results of the data collected concerning the effect of HBOT on mTBI and PTSD indicated that hyperbaric oxygen therapy was an effective treatment for mTBI but not for PTSD. The data analyzed was subject-reported symptom questionnaires and CAPS scores pre- and post-treatment. After the treatment was over the experimenters asked the subjects if specific symptoms had improved, declined, or stayed stagnant. For seven out of the eight symptoms, there was at least 65% improvement post-HBOT. This resulted in p-values of less than 0.05 for all but three symptoms, which means that the data was significant. The one symptom that did not improve on average for most of the subjects tested was PTSD stress. 80% of subjects reported that their symptom of PTSD stress was unchanged after treatment. This result correlated with the CAPS score results, in which the effect of HBOT on CAPS scores was insignificant ($p=0.663$).

HBOT has been shown to be effective in reducing cerebral edema, brain swelling that can be caused by mTBI. By providing oxygen to the brain, unoxygenated neurons and blood vessels become oxygenated, reducing cerebral edema. This explains why symptoms such as headache, memory loss, and low energy level were improved after HBOT treatment because they were a direct result of the cerebral edema. However, PTSD typically causes changes in the brain such as increased activity in the amygdala and decreased activity in the hippocampus and PFC. HBOT has not been researched in repairing damaged neural structures that were not damaged by lack of

oxygen. As a result, HBOT had no effect on PTSD symptoms because the treatment is not an effective way to treat the root cause of the disorder.

The results of the data collected concerning the effect of VRET on PTSD show that VRET is an effective treatment for PTSD. The effect of VRET on mTBI was not included because there has been no researched effect of VRET on mTBI. CAPS scores in soldiers improved from pre-VRET to post-VRET. It was also a significant difference with a p-value of 0.0014. However, the mean CAPS score post-treatment was still 48.1 which is still categorized as extreme PTSD. Possibly, the mean number of treatments of VRET prescribed to a patient needs to increase to lower this number to under 25, the benchmark for PTSD diagnosis. However, VRET did still result in a significant improvement because the average starting CAPS score was 83.5, meaning that there was a 35.4 (27%) improvement pre-treatment to post-treatment.

The changes in the brain as a result of VRET have not been researched. However, as a result of this paper, it can be hypothesized that VRET decreases the activity of the amygdala and increases the activity of the hippocampus and PFC. These structures are typical damaged in those with PTSD, causing PTSD symptoms such as jumpy anxiety and social withdrawal. Since VRET had such a significant effect in reducing CAPS scores, it is highly likely it influenced brain activity in such a way.

CONCLUSION

The increasing number of mTBIs seen in American soldiers/veterans as well as the high correlation between mTBI and PTSD necessitates a treatment plan that treats both conditions.

This systematic data review provides evidence to support the hypothesis that the combination of HBOT and VRET have a significant effect on treating mTBI and PTSD. The p-values gathered from the t-tests conducted confirm this significance. HBOT reduces most symptoms of mTBI except for PTSD stress. This result is confirmed by a lack of significance of HBOT on CAPS scores post-treatment. However, VRET does have a significant effect on lowering CAPS scores post-treatment. The two treatments should be looked at as a possible treatment option for soldiers/veterans currently suffering from both mTBI and PTSD to increase their quality of life and to reduce negative long-term effects.

FURTHER WORK

The studies investigated in this paper either focused on solely HBOT or solely VRET. To accurately judge whether or not there is a synergistic effect between the two, a study needs to be conducted in which patients with mTBI and PTSD are treated with both treatments concurrently. In this study, the brains of each patient should be analyzed via magnetic resonance imaging (MRI) to determine a baseline of damage caused by each condition. Additionally, a symptom questionnaire as well as a CAPS test should be administered to each patient to, again, determine a baseline. Then, the patients should receive 20-40 sessions of HBOT and 6-12 sessions of VRET in order to maximize the effectiveness of each treatment. After the treatment is over, all diagnostic tests should be repeated to analyze the effect of each of the treatments. Special attention should be noted to structures in the brain such as the amygdala, hippocampus, and PFC in MRI scans. If there is a significant difference between patients pre- and post- treatments ($p<0.05$ at 95% confidence intervals), there would be a valid synergistic effect between both HBOT and VRET.

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References

Bandak, F., Ling, G., Bandak, A., & Lanerolle, N. D. (2015). Injury biomechanics, neuropathology, and simplified physics of explosive blast and impact mild traumatic brain injury. *Handbook of Clinical Neurology Traumatic Brain Injury, Part I,*89-104. doi:10.1016/b978-0-444-52892-6.00006-4

Berridge, C. W. (2009). The Locus Coeruleus-Noradrenergic System and Stress: Implications for Post-Traumatic Stress Disorder. *Post-Traumatic Stress Disorder,*213-230. doi:10.1007/978-1-60327-329-9_10

Blennow, K., Jonsson, M., Andreasen, N., Rosengren, L., Wallin, A., Hellström, P. A., & Zetterberg, H. (2011). No neurochemical evidence of brain injury after blast overpressure

by repeated explosions or firing heavy weapons. *Acta Neurologica Scandinavica,123*(4), 245-251. doi:10.1111/j.1600-0404.2010.01408.x

Bremner, J. D. (2016). PTSD and mild traumatic brain injury. *Posttraumatic Stress Disorder,*317-344. doi:10.1002/9781118356142.ch13

Bull, A. M. (2016). Biomechanics in Blast. *Blast Injury Science and Engineering,*17-31. doi:10.1007/978-3-319-21867-0_2

Campos-Pires, R., & Dickinson, R. (2016). Modelling Blast Brain Injury. *Blast Injury Science and Engineering,*173-182. doi:10.1007/978-3-319-21867-0_14

Clasper, J. (2011). Blast and ballistic injury. *Oxford Medicine Online*. doi:10.1093/med/9780199550647.003.012006

Creech, S. K., & Misca, G. (2017). Parenting with PTSD: A Review of Research on the Influence of PTSD on Parent-Child Functioning in Military and Veteran Families. *Frontiers in Psychology,8*. doi:10.3389/fpsyg.2017.01101

Elder, G. A., Dorr, N. P., Gasperi, R. D., Sosa, M. A., Shaughness, M. C., Maudlin-Jeronimo, E., . . . Ahlers, S. T. (2012). Blast Exposure Induces Post-Traumatic Stress Disorder-Related Traits in a Rat Model of Mild Traumatic Brain Injury. *Journal of Neurotrauma,29*(16), 2564-2575. doi:10.1089/neu.2012.2510

Fishbein, D. (n.d.). Understanding the Role of Anterior Cingulate Cortex Function in Risky Decision Making by Drug Abuser. *PsycEXTRA Dataset*. doi:10.1037/e582892013-001

Gahm, G., Reger, G., Rizzo, A., Koenen-Woods, P., & Skopp, N. (2014). Comparing Virtual Reality Exposure Therapy to Prolonged Exposure in the Treatment of Soldiers with PTSD. doi:10.21236/ada613612

Harch, P. G., Fogarty, E. F., Staab, P. K., & Meter, K. V. (2009). 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 Journal,2*(1), 6538. doi:10.4076/1757-1626-2-6538

Harch, P. G. (2015). Hyperbaric oxygen in chronic traumatic brain injury: Oxygen, pressure, and gene therapy. *Medical Gas Research,5*(1). doi:10.1186/s13618-015-0030-6

International Symposium on Clinical Neuroscience: Traumatic Brain Injury and Neurodegeneration Case Study Abstracts. (2015). *International Symposium on Clinical Neuroscience: Traumatic Brain Injury and Neurodegeneration Case Study Abstracts*. doi:10.3389/978-2-88919-706-4

Jianx, I. C. (2001). Cognitive deficits following blast injury-induced neurotrauma: Possible involvement of nitric oxide. *Brain Injury,15*(7), 593-612. doi:10.1080/02699050119009

Kohda, K., Kato, K., & Kato, N. (n.d.). Studies on Pathophysiology of PTSD Using the SPS Model. *Ptsd,*55-59. doi:10.1007/4-431-29567-4_6

Kramer, M. (2013). Virtual Reality Exposure Therapy vs. Prolonged Imaginal and In-Vivo Exposure with Combat Veterans with Complex PTSD. *PsycEXTRA Dataset*. doi:10.1037/e608922012-010

Liu, L., Zhou, B., & Liu, B. (2010). Effect of hyperbaric oxygen on cerebral oxygen saturation in patients with sub-acute traumatic brain injury. *Critical Care,14*(Suppl 1). doi:10.1186/cc8526

Long, J. B. (2014). Blast-Induced Acceleration in a Shock Tube: Distinguishing Primary and Tertiary Blast Injury. doi:10.21236/ada613618

Masel, B. E. (2011). Hyperbaric Oxygen Therapy for Traumatic Brain Injury: Still an Enigma. *Archives of Physical Medicine and Rehabilitation,92*(9), 1519-1521. doi:10.1016/j.apmr.2011.06.011

Mclay, R. N., Wood, D. P., Webb-Murphy, J. A., Spira, J. L., Wiederhold, M. D., Pyne, J. M., & Wiederhold, B. K. (2011). A Randomized, Controlled Trial of Virtual Reality-Graded Exposure Therapy for Post-Traumatic Stress Disorder in Active Duty Service Members with Combat-Related Post-Traumatic Stress Disorder. *Cyberpsychology, Behavior, and Social Networking,14*(4), 223-229. doi:10.1089/cyber.2011.0003

Obenaus, A. (2011). Neuroprotective Strategies after Repetitive Mild Traumatic Brain Injury. doi:10.21236/ada566666

Peterson, A. L., Mclean, C., Lichner, T., Mintz, J., & Foa, E. (n.d.). Massed Prolonged Exposure Therapy for PTSD Delivered to Active Duty Soldiers: Predictors of Treatment Completion and Outcome and Comparison. *PsycEXTRA Dataset*. doi:10.1037/e533652013-061

Proud, W. G. (2016). The Fundamentals of Blast Physics. *Blast Injury Science and Engineering,*3-16. doi:10.1007/978-3-319-21867-0_1

Rothbaum, B. (2005). Virtual Reality Exposure Therapy for the Treatment of PTSD. *PsycEXTRA Dataset*. doi:10.1037/e517292011-401

Roy, M. J., Rizzo, A., Difede, J., & Rothbaum, B. O. (2016). Virtual Reality Exposure Therapy for PTSD. *Oxford Medicine Online*. doi:10.1093/med/9780190205959.003.0013

Scherer, M. (2007). Gait rehabilitation with body weight-supported treadmill training for a blast injury survivor with traumatic brain injury. *Brain Injury,21*(1), 93-100. doi:10.1080/02699050601149104

Schwab, K. A., Ivins, B., Cramer, G., Johnson, W., Sluss-Tiller, M., Kiley, K., . . . Warden, D. (2007). Screening for Traumatic Brain Injury in Troops Returning From Deployment in Afghanistan and Iraq. *Journal of Head Trauma Rehabilitation,22*(6), 377-389. doi:10.1097/01.htr.0000300233.98242.87

Scofield, D. E., Proctor, S. P., Kardouni, J. R., Hill, O. T., & Mckinnon, C. J. (2017). Risk Factors for Mild Traumatic Brain Injury and Subsequent Post-Traumatic Stress Disorder

and Mental Health Disorders among United States Army Soldiers. *Journal of Neurotrauma,34*(23), 3249-3255. doi:10.1089/neu.2017.5101

Shin, L. M. (2009). The Amygdala in Post-Traumatic Stress Disorder. *Post-Traumatic Stress Disorder,*319-334. doi:10.1007/978-1-60327-329-9_15

Steenkamp, M. M., Litz, B. T., Hoge, C. W., & Marmar, C. R. (2015). Psychotherapy for Military-Related PTSD. *Jama,314*(5), 489. doi:10.1001/jama.2015.8370

Tanielian, T., & Jaycox, L. H. (n.d.). Invisible Wounds of War Psychological and Cognitive Injuries,Their Consequences, and Services to Assist Recovery: Summary. *PsycEXTRA Dataset*. doi:10.1037/e527612010-001

Trudeau, D. L., Anderson, J., Hansen, L. M., Shagalov, D. N., Schmoller, J., Nugent, S., & Barton, S. (1998). Findings of Mild Traumatic Brain Injury in Combat Veterans With PTSD and a History of Blast Concussion. *The Journal of Neuropsychiatry and Clinical Neurosciences,10*(3), 308-313. doi:10.1176/jnp.10.3.308

Uszler, J. M. (2016). Neurophysiologic SPECT Brain Function Imaging and Hyperbaric Oxygen Therapy. *Textbook of Hyperbaric Medicine,*91-97. doi:10.1007/978-3-319-47140-2_10

Wang, G., & Li, L. (2013). Virtual Reality Exposure Therapy of Anxiety Disorders. *Advances in Psychological Science,20*(8), 1277-1286. doi:10.3724/sp.j.1042.2012.01277

Wolff, K. (2013). Post-Traumatic Stress Disorder in Female Military. *Encyclopedia of Women in Todays World*. doi:10.4135/9781412995962.n648

Zuj, D. V., Felmingham, K. L., Palmer, M. A., Lawrence-Wood, E., Hooff, M. V., Lawrence, A. J., . . . Mcfarlane, A. C. (2017). Neural activity and emotional processing following military deployment: Effects of mild traumatic brain injury and posttraumatic stress disorder. *Brain and Cognition,118*, 19-26. doi:10.1016/j.bandc.2017.07.001