

Progress of the Brain Injury and Mechanisms of Action of Hyperbaric Oxygen (HBO₂) for Persistent Post-Concussive Symptoms after Mild Traumatic Brain Injury (BIMA) Study

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"Any opinions, findings and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the US Army or its subordinate activities."

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Introduction

HBO₂ and mTBI

- Traumatic brain injury (TBI) referred to as “signature injury” of war on terrorism
- US Army Medical Research and Materiel Command (USAMRMC) holds FDA-IND, planned multi-year research effort to study HBO₂ on mild TBI (mTBI)
- Brain Injury and Mechanisms of Action of Hyperbaric Oxygen (HBO₂) for Persistent Post-Concussive Symptoms after Mild Traumatic Brain Injury (BIMA) study ongoing

BIMA

- Double-blind, sham-controlled RCT
 - Sham (1.2 ata air) vs. HBO₂ (1.5 ata O₂) X 60 minutes
 - 40 total sessions within a 12 week period
- N = 71 Active Duty and Veterans with mTBI randomized between Nov 2012 and May 2014
- Visit schedule: Baseline, 3 months, 6 months; telephone/computer self-report outcomes at 12 months
- Three enrolling sites
 - Ft Carson, Colorado
 - Joint Base Lewis McChord, Washington
 - Camp Lejeune, North Carolina
- Central outcomes assessment center (Ft. Carson)

BIMA Hyperbaric Chambers



HBO₂ Chamber Trailer Site
Joint Base Lewis-McCord, WA



HBO₂ Chamber

Inclusion Criteria (Selected)

- Active Duty or Veteran, ages 18-65 years
- History of one or more mTBIs
 - mTBI occurred on active duty
 - Post-concussive symptoms 3 months to 5 years after last injury
 - mTBI caused by non-penetrating trauma or blast exposure
 - mTBI resulted in loss or decreased level of consciousness (up to 30 mins); loss of memory; or alteration in mental state

Exclusion Criteria (Selected)

- Contraindications to hyperbaric pressurization and hyperbaric oxygenation or other study assessment measures
- Characteristics that may confound outcome measures
- Characteristics that may compromise study blind (e.g. prior experience with hyperbaric pressurization)

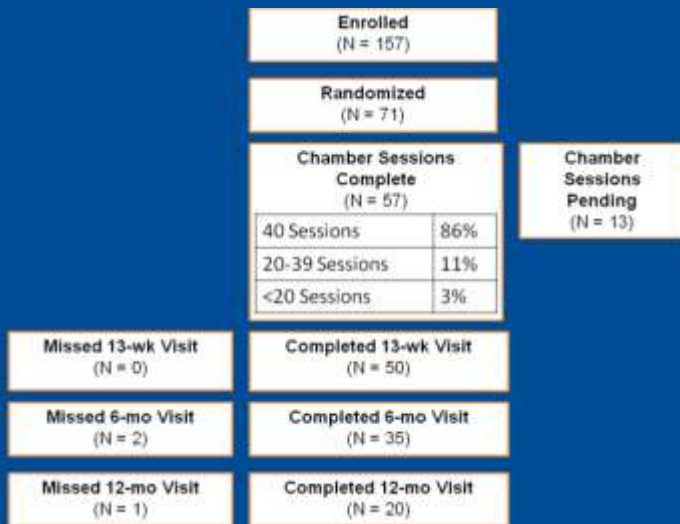
Outcome Assessments

Group	Selected Assessments
Neuropsychological	Neurobehavioral Symptom Inventory (NSI), Rivermead Post Concussive Symptoms Questionnaire (RPQ), Post-Traumatic Stress Disorder Checklist Civilian (PCL-C), Automated Neuropsychological Assessment Metrics (ANAM), World Health Organization Quality of Life (WHOQOL-BREF)
Neurological	Neurological Exam, EEG, qEEG, Dynamometer, Sharpened Romberg Test, Romberg Test, Berg Balance Scale
Neuroimaging	MRI, fMRI, CT Perfusion Angiography, Arterial Spin Labeling, Detailed Volumetric Anatomical Imaging, DTI, MR Spectroscopy

Outcome Assessments(con't)

Group	Selected Assessments
Audiology and Vestibular	Peripheral and Central Auditory Examination, Videonystagmography, Computerized Dynamic Posturography, Dynamic Visual Acuity, Rotational Vestibular Test, Dynavision
Visual Systems	Visual Acuity, Dynamic Visual Acuity, Refractive Error, Oculomotor Exam, Retinal Fundoscopy, Eye Tracking
Autonomic Function	24 Hour Holter Monitor
Sleep	Actigraph, Sleep Diary, Pittsburgh Sleep Quality Index, STOP-Bang (Sleep Apnea) Questionnaire, Restless Legs, Cataplexy, Sleep Diary
Lab	CBC, HbA1c, COHb, Creatinine, Pregnancy, Stem cells, Neuro-endocrine, Banked DNA, RNA, Serum, Plasma

Enrollment and Follow Up



Screen Failures

Pre-Screen Failure Reasons

		N (%)	
Pre-Screen Failure Reason	Second Party Inquiry	11	(8)
	Outside Recruitment Area	9	(7)
	No Interest	31	(23)
	Drug Screen Fail	4	(3)
	Claustrophobia	2	(1)
	TBI Not on Active Duty	2	(1)
	Non-Eligible Brain Injury	59	(44)
	Other	17	(13)
Total		135	(100)

Baseline Screen Failure Reasons

		N (%)	
	Voluntary Withdrawal of Consent	41	(25)
	Screen Fail	66	(41)
	Lost to Follow up	24	(15)
	Other	30	(19)
	Total	161	(100)

Baseline Characteristics

BIMA Randomized Participants (N = 71)		N (%)	
Site	Evans Army Community Hospital	34	(48)
	Madigan Army Medical Center	24	(34)
	Naval Hospital Camp Lejeune	13	(18)
Age	21-30	29	(41)
	31-40	30	(42)
	Over 40	12	(17)
Gender	Male	70	(99)
Race	White or Caucasian	59	(83)
Education	Some college or more	58	(82)

Baseline Characteristics(con't)

BIMA Randomized Participants (N = 71)		N (%)
PTSD Diagnosis	PTSD	35 (49)
Time Since Injury	Less than 1 Year	17 (24)
Type of Injury	Blast Injuries Only	23 (32)
Number of Injuries	More than 1 Injury	52 (73)
Combat experience	Yes	64 (90)
Years in Military	5 or more	55 (77)

Self-Reported Medical History

All (n = 71) randomized participants reported ongoing neurologic conditions

- 86% chronic pain
- 63% migraine headaches
- 46% motor weakness

Nearly all (99%, n = 70) randomized participants reported ongoing psychiatric conditions

- 97% sleep problems
- 72% anxiety
- 51% depression

Concomitant Medication Summary

All participants (n = 71) reported use of current medications; average medications was 8 (SD=5; Range = 1-21)

- 52% (n = 37) antidepressants
- 42% (n = 30) antimigrane medications
- 41% (n = 29) sedatives
- 32% (n = 23) narcotics

Current Therapies

63 participants reported current therapies; average number of therapies was 2 (SD=1; Range 1-7)

- 38% (n = 27) counseling
- 35% (n = 25) physical therapy
- 25% (n = 18) psychotherapy
- 21% (n = 15) occupational therapy
- 8% (n = 6) behavioral therapy
- 7% (n = 5) exercise
- 4% (n = 3) cognitive rehabilitation
- 4% (n = 3) speech therapy

Data Quality

Data capture is 99%, to date:

Missing data include

- Computerized Tomography (8 instances): Elevated creatinine
- MRI, Dynavision, Retinal Fundoscopy, Sharpened Romberg (1 instance each): Participant unable to attempt assessment

Other missing data issues

- Holter Monitor: 10% of randomized participant baseline data deemed unusable by subject matter expert

Discussion

Ambitious assessment battery

- Excellent adherence to study visit schedule
- Excellent intervention compliance
- Less than 5% completed fewer than 20 sessions or missed a 6-month visit

Potential to gain information about relationship between functional and symptomatic outcomes in mTBI population

- Challenges
 - Deployment and changing military status (follow up visits)
 - Inclusion/exclusion CT requirements
- Results will add to understanding of mTBI
- Results will add to information about HBO2/sham for mTBI

One year outcomes complete May 2015; analyze; publish