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

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Abstract

INTRODUCTION/BACKGROUND: BIMA is a Department of Defense sponsored randomized, double-blind, sham-controlled clinical trial to investigate symptomatic as well as functional responses to HBO2 in a military population with persistent post concussive symptoms following mTBI. A battery of neurological assessments is under evaluation as potential outcome measures in this population.
MATERIALS AND METHODS: BIMA initiated September 2012 and will complete enrollment May 2014. Randomized participants receive hyperbaric oxygen (HBO^2) 1.5 atm abs or sham chamber sessions at 1.2 ATA, air, for 60 minutes daily for 40 sessions. A comprehensive neurological exam, oculomotor exam, balance testing (Berg Balance Scale-BBS, Romberg Test-RT, Sharpened Romberg Test -SRT), and olfactory function (Brief Smell Identification test-BSIT) was performed at baseline. Testing is repeated at 13 weeks and 6 months post-randomization.
RESULTS: Fifty-six participants completed baseline exams. Participant characteristics included: Median age 32 years (range 21, 49), 98% male, 84% Caucasian, 45% diagnosed PTSD, 29% with most recent qualifying injury 3 months-1 year prior to enrollment, 79% >1 blast injury, and 71% with multiple injuries. On neurological exam 12% presented with tremor, abnormal facial sensation (18%), and abnormal tandem gait (12%). On oculomotor exam 79% had accommodative insufficiency with an average accommodative break of 24 cm (range 9-80 cm). 89% scored ≥ 55 with no participant scoring < 50 on the BBS. 46% scored < 30 seconds on the best trial of the SRT. RT was abnormal in 9%. On the BSIT, 16% of participants scored ≤ 9 (out of 12), about twice what is expected in a normal population.
SUMMARY/CONCLUSIONS: In BIMA participants with mTBI sequelae, the neurological examination found abnormalities across a range of testing.

Introduction

- US Army Medical Research and Materiel Command (USAMRMC) holds FDA-IND, planned multi-year research effort to study HBO2 on mild TBI (mTBI)
- BIMA objectives: Identify endpoints for future Phase III efficacy trials in mTBI, describe brain function and anatomy of military mTBI across time and between intervention groups

Study Design

- Double-blind, sham-controlled RCT
  - Sham (1.2 ata air) v. HBO_2 (1.5 ata O2) x 60 mins, 5 days/week to 40 sessions
- N=72, Active Duty and Veterans with mTBI
- Visit schedule: Baseline, 3 months, 6 months; self-report outcomes at 12 months
- Sites: Outcomes Assessment Center, Colorado; Ft. Carson, Colorado; Joint Base Lewis McChord, Washington; Camp Lejeune, North Carolina
- Enrollment complete May 2014

Baseline Characteristics

Baseline Characteristics	
Median Age (Range)	32 (21-53)
White/Caucasian	83%
Male	99%
PTSD Dx	50%
<1 Yr most recent injury	24%
Blast injury only	33%
>1 injury	73%

Neurological Exam Assessments

- Neurological Exam: Assessment of mental status, cranial nerves, motor, deep tendon reflexes, gait, cerebellar function, visual acuity, and sensory domains
- Berg Balance Scale: 14-item scale measuring impairment in balance by assessing performance of functional tasks
- 6 minute walk test: Distance walked in 6 minutes
- Dynamometer: Grip strength
- Brief Smell Identification Test (BSIT): 12 smells

Baseline Results	
Tremor	11%
Abnormal facial sensation	16%
Abnormal tandem gait	13%
Berg Balance Scale Score <55 (Range)	14% (50-56)
Mean (STD) 6 minute walk distance (feet)	1718 (346)
Mean (STD) sustained grip strength (lbs)	75.8(19.1)
Brief Smell Identification Test (BSIT) Score ≤ 9 (Range)	17% (2-12)

Oculomotor Exam

- Tests extraocular movements and smooth pursuit

Baseline Results	
Accommodative insufficiency (>8 cm)	79%
Accommodative break (cm) Mean (Range)	24.5 (9-80)

Oculomotor Exam

Romberg and Sharpened Romberg

- Sharpened Romberg Test (a): Coordination and balance while standing heel to toe with one foot in front of the other foot
- Romberg Test (b): Ability to maintain a standing posture with feet side by side

(a) (b)

Baseline Results	
Abnormal Romberg test (at least 1 of two trials)	10%
Sharpened Romberg test (< 30 seconds on best trial)	50%

Dynamic Visual Acuity

- Ability to perceive objects accurately while actively moving head

Baseline Results	
Vision loss on dynamic visual acuity testing OU	
At least one line (5 letters)	14%
At least two lines (10 letters)	3%

Dynamic Visual Acuity

Dynavision

- Large board mounted on the wall with randomly illuminating lights. Measures how well the brain and body work together to hit the illuminated lights

Dynavision Board

Baseline Results	
Self-paced Hits	
<52	3%
>52, <62	9%
>62, <72	22%
>72, <82	45%
60 second forced attention hits	
<42	6%
>42, <52	4%
>52, <62	16%
>62, <72	39%
Mean (STD) Reaction time	
Visual (seconds)	.37 (.07)
Motor (seconds)	.27 (.13)
Physical (seconds)	.64 (.18)

Summary/Conclusions

- In BIMA participants with mTBI sequelae, abnormalities are seen across a range of testing
- Accommodative insufficiency and Sharpened Romberg Test appear to have the most sensitivity to identify abnormalities in this population

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