Characterization of Baseline EEG Abnormalities in the Brain Injury and Mechanisms of Action of Hyperbaric Oxygen (HBO_2) for Persistent Post-Concussive Symtpoms after Mild Traumatic Brain Injury (mTBI) Study (BIMA)

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Abstract

INTRODUCTION/BACKGROUND: The Brain Injury and Mechanisms of Action of HBO2 for Persistent Post-Concussive Symptoms after Mild Traumatic Brain Injury (BIMA) , sponsored by the Department of Defense (DoD) is a randomized, double-blind, sham-controlled trial of hyperbaric oxygen (HBO2) in Servicemembers with persistent post-concussive symptoms following mild TBI, undergoing comprehensive assessments. There is scant literature about EEG findings in this population, so we will report baseline clinical electroencephalography (EEG) results.
MATERIALS/METHODS: BIMA initiated September 2012, and should complete enrollment by May 2014. Clinical EEG was assessed by 3 neurologists inspecting for both inctal and interictal epileptiform abnormalities, background periodic discharges, plus localized and generalized slow wave activity. Antidepressants were continued. We recommended that narcotics and benzodiazepines be withheld the day of the EEG. Those with EEG abnormalities were compared to those without EEG abnormalities to determine if co-variants influenced abnormalities.
RESULTS: By March 06, 2014, 56 participants have had EEGs., The median age is 32 years (range 21, 49), 98% male, 29% sustained the most recent qualifying injury 3 months to 1 year prior to enrollment, 79% had at least one blast injury, and 71% had multiple injuries. None of the randomized participants had interictal epileptiform abnormalities, ictal abnormalities, or periodic discharges at baseline, while 2 (2%) and 9 (16%) of participants displayed either localized or generalized slowing of mild severity, respectively. It did not appear that concomitant antidepressant, and chronic narcotics and benzodiazepines (held on the day of the EEG) influenced results.
SUMMARY/CONCLUSIONS: In this study of participants with sequelae following mTBI, the clinical EEG interpretation was abnormal in 20%, most commonly with generalized slowing. The use of concomitant antidepressants and chronic narcotics or benzodiazepines did not seem to influence these results, suggesting that generalized slowing may be due to mTBI-related brain injury.

Introduction

- 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 HBO_2 on mild TBI (mTBI)
- Objectives of ongoing BIMA trial to select endpoints for potential Phase III efficacy trial, 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 O_2) x 60 mins, 5 days/week to 40 sessions
- N=72, Active Duty and Veterans with mTBI
- Visit schedule: Baseline, 3 and 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
- Study Timeline: 2012-2015, enrollment complete May 2014

EEG Methods

- Clinical EEG assessed by 3 neurologists inspecting for both ictal and interictal epileptiform abnormalities, background periodic discharges, localized and generalized slow wave activity.
- Concomitant medication use recorded at baseline and before EEG was performed.
- Any antidepressants were continued; narcotics and benzodiazepines were recommended to be withheld the day of the EEG
- Focus placed on determining abnormalities based on clinical read of EEG data
- Compare those with EEG abnormalities to those without to determine if concomitant medications influenced abnormalities

Acknowledgements

- This work was supported by the U.S. Army Medical Materiel Development Activity

Baseline Characteristics

BIMA Randomized Participants (N = 70)		N (%)
Site	Evans Army Community Hospital	33 (47)
	Madigan Army Medical Center	24 (34)
	Naval Hospital Camp Lejeune	13 (19)
Age	21-30	29 (41)
	31-40	30 (43)
	Over 40	11 (16)
Gender	Male	69 (99)
Race	White or Caucasian	58 (83)
Education Status	Some college or more	57 (81)

BIMA Randomized Participants (N = 70)		N (%)
PTSD Diagnosis	PTSD	35 (50)
Time Since Injury	Less than 1 Year	17 (24)
Type of Injury	Blast Injuries Only	23 (33)
Number of Injuries	More than 1 Injury	51 (73)
Combat experience	Yes	63 (90)
Years in Military	5 or more	54 (77)

Concomitant Medication Summary

All participants (n = 70) reported use of current medications; average medications was 8 (SD=5; Range = 1-21)

- xx% (N = xx) reported use of antidepressants
- xx% (N = xx) reported use of antimigrane medications
- xx% (N = xx) reported use of narcotics
- xx% (N = xx) reported use of benzodiazepines

EEG Abnormality Summaries

At baseline, of the 70 participants:

- No interictal epileptiform abnormalities
- No ictal abnormalities
- No periodic discharges

- 31% (N = 22) participants displayed slowing of mild severity
  - 1 displayed only localized slowing
  - 19 displayed only generalized slowing
  - 2 displayed both localized and generalized slowing

EEG Abnormalities by Migraine Characteristics

Variable		Presence of Any Slowing: No	Yes
Migraine Onset	N/A	14 (64)	8 (36)
	< 1 yr ago	5 (63)	3 (38)
	1 – 5 yrs ago	11 (65)	6 (35)
	> 5 yrs ago	6 (55)	5 (45)
Migraine Ongoing	No	14 (61)	9 (39)
	Yes	22 (63)	13 (37)
Migraine Severity	N/A	14 (61)	9 (39)
	No	7 (70)	3 (30)
	Yes	15 (60)	10 (40)

Displayed in each cell: N (%), where percentages are row percentages.

EEG Abnormalities by Baseline Medication Usage

Medication Usage		Presence of Any Slowing: No	Yes
Narcotics	No	29 (66)	15 (34)
	Yes	7 (50)	7 (50)
Antidepressants	No	28 (67)	14 (33)
	Yes	8 (50)	8 (50)
Antiepileptics	No	34 (62)	21 (38)
	Yes	2 (67)	1 (33)
Benzodiazepines	No	25 (57)	19 (43)
	Yes	11 (79)	3 (21)
Stimulants	No	35 (63)	21 (38)
	Yes	1 (50)	1 (50)

Displayed in each cell: N (%), where percentages are row percentages.

Generalized Slowing by Baseline Medication Usage

Medication Usage		Presence of Slowing: No	Yes
Narcotics	No	27 (64)	15 (36)
	Yes	8 (57)	6 (43)
Antidepressants	No	27 (68)	13 (33)
	Yes	8 (50)	8 (50)
Antiepileptics	No	33 (62)	20 (38)
	Yes	2 (67)	1 (33)
Benzodiazepines	No	24 (57)	18 (43)
	Yes	11 (79)	3 (21)
Stimulants	No	35 (64)	20 (36)
	Yes	0 (0)	1 (100)

Displayed in each cell: N (%), where percentages are row percentages.

Reported Medication Usage on Day of EEG Scan

- No benzodiazepine, barbiturate, or stimulant use was reported
- One participant with no EEG abnormalities reported use of antiepileptics
- Three participants reported use of narcotics, two of which displayed generalized slowing
- Three participants reported use of antidepressants, one of which displayed generalized slowing

Discussion

- In this study of participants with sequelae following mTBI, the clinical EEG interpretation was abnormal in 31%
- Most common abnormality was generalized slowing (30%)
- The use of concomitant antidepressants and chronic narcotics or benzodiazepines did not seem to influence these results
- Hence, generalized slowing may be due to mTBI-related brain injury

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