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HOUSE DEMOCRATIC POLICY COMMITTEE
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House of Representatives
COMMONWEALTH OF PENNSYLVANIA
HARRISBURG

HOUSE DEMOCRATIC POLICY COMMITTEE FORUM
Topic: Groundbreaking Traumatic Brain Scan Technology
John P. Murtha Center for Public Service and National Competitiveness
Johnstown, PA
October 12, 2017

AGENDA

10:00 a.m. Welcome and Opening Remarks

10:10 a.m. Panel from the University of Pittsburgh:

- Dr. Walt Schneider, PhD
Senior Scientist, Learning Research and Development Center
Professor of Psychology and Radiology, University of Pittsburgh
Professor of Neurosurgery, University of Pittsburgh Medical Center
Executive Board Member, Center for the Neural Basis of Cognition
- Dr. Ava Puccio, RN, PhD
Co-Director, Neurotrauma Clinical Trials Center
Assistant Professor of Neurological Surgery, University of Pittsburgh

11:10 a.m. Questions

11:50 a.m. Closing Remarks

THE GENERAL ASSEMBLY OF PENNSYLVANIA

HOUSE BILL

No. 1784 Session of
2017

INTRODUCED BY BARBIN, BARRAR, SAINATO, READSHAW, HENNESSEY,
BERNSTINE, MURT, SCHWEYER, MILLARD, SOLOMON, HILL-EVANS,
PASHINSKI, ROZZI, SCHLOSSBERG AND DRISCOLL,
SEPTEMBER 18, 2017

REFERRED TO COMMITTEE ON VETERANS AFFAIRS AND EMERGENCY
PREPAREDNESS, SEPTEMBER 18, 2017

AN ACT

1 Providing funding to the Department of Military and Veterans
2 Affairs for the purpose of providing current service members
3 and veterans with access to high-definition fiber tracking
4 brain scans and supporting ongoing clinical research in this
5 Commonwealth involving traumatic brain injuries.

6 The General Assembly of the Commonwealth of Pennsylvania
7 hereby enacts as follows:

8 Section 1. Short title.

9 This act shall be known and may be cited as the High-
10 Definition Fiber Tracking (HDFT) for Veterans Act.

11 Section 2. Definitions.

12 The following words and phrases when used in this act shall
13 have the meanings given to them in this section unless the
14 context clearly indicates otherwise:

15 "Brain scan equipment." Health care imaging equipment
16 capable of identifying brain damage by graphic depiction of
17 individual nerve tracts.

18 "Department." The Department of Military and Veterans

1 Affairs of the Commonwealth.

2 "Eligible center." A health care facility designated by the
3 department to provide access to HDFT brain scans.

4 "HDFT." A brain scan employing High-Definition Fiber
5 Tracking technology.

6 Section 3. Military members and veterans.

7 (a) Diagnosis.--Any military veteran or active duty or
8 reserve member of the United States Armed Forces or National
9 Guard who has symptoms of traumatic brain injury or
10 posttraumatic stress or evidence of combat-related concussion
11 shall be eligible to receive diagnostic treatment through the
12 use of the new HDFT technology using equipment located in this
13 Commonwealth.

14 (b) Eligible centers.--The military veteran shall visit an
15 eligible center in order to begin the process for the use of the
16 diagnostic technology.

17 (c) Brain scan equipment.--The equipment shall be purchased
18 or leased and provided to eligible centers to provide access to
19 HDFT technology throughout this Commonwealth.

20 Section 4. Regulations.

21 The department shall promulgate regulations for the
22 implementation of this act. The regulations shall allow for the
23 maximum number of military members and veterans to be able to
24 use the HDFT technology.

25 Section 5. Appropriation.

26 The sum of \$1,000,000, or as much thereof as may be
27 necessary, is appropriated to the department for the fiscal year
28 July 1, 2017, through June 30, 2018, to carry out the provisions
29 of this act.

30 Section 6. Funding.

1 (a) Eligible centers.--Five hundred thousand dollars shall
2 be distributed by the department to all eligible centers
3 proportionally based on the number of veterans and active
4 members served at each eligible center. The money received by
5 each eligible center shall be used to pay for hardware and
6 software costs of the diagnostic technology and administrative
7 expenses of the eligible center directly related to the
8 provision of HDFT scans to military members and veterans.

9 (b) Brain scan equipment.--Five hundred thousand dollars
10 shall be distributed by the department to ensure availability of
11 the diagnostic technology at eligible centers throughout this
12 Commonwealth.

13 Section 7. Effective date.

14 This act shall take effect in 60 days.

Pennsylvania House of Representatives

10/05/2017 01:33 PM

<http://www.legis.state.pa.us/cfdocs/Legis/CSM/showMemoPublic.cfm?chamber=H&SPick=20170&cosponId=24531>

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House Co-Sponsorship Memoranda

House of Representatives Session of 2017 - 2018 Regular Session

MEMORANDUM

Posted: September 12, 2017 09:52 AM
From: [Representative Bryan Barbin](#)
To: All House members
Subject: Veterans TBI Brain Scan

I have reintroduced HB1522 from the 2015-16 session. This bill provides \$500,000 for veteran brain scans and \$500,000 for necessary equipment to the Department of Military and Veteran Affairs for the purpose of providing current service members and veterans with access to high definition fiber tracking brain scans and supporting ongoing clinical research in this Commonwealth involving traumatic brain injuries and post-traumatic stress. Estimates of TBI and PTS approximate 20% of our fighting force. This technology makes the invisible wounds visible.

Please join me in sponsoring this legislation which will provide an additional means for medical care for veterans and servicemen.
[View Attachment](#)



Introduced as [HB1784](#)

PA Technology to Diagnose TBI in Veterans & Sports Injured

Walter Schneider¹ (PhD) & David Okonkwo² (MD, PhD)

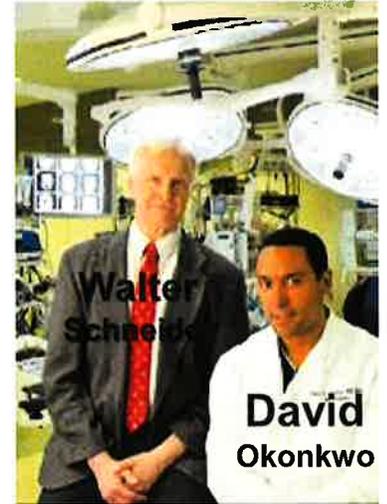
¹Professor Bioengineering, Neurosurgery, Radiology, Psychology

²Director, Neurotrauma Program & Professor Neurosurgery

University of Pittsburgh & University of Pittsburgh Medical Center

Contact wws@pitt.edu Cell 412-901-4176

Web Site TEAM-TBI.com



State Rep. Bryan Barbin

Groundbreaking traumatic brain scan technology

Oct. 122017 University of Pittsburgh-Johnstown, John P. Murtha Center

- We run a \$27 million research program in TBI with federal and foundation funding, viewed by the US Military, FBI, and Michelle Obama as the leading technology for veterans and sports TBI injury diagnosis and enabling precision medicine treatment
- We have developed the Targeted Evaluation Action and Monitoring (TEAM-TBI) program that is dramatically improving the outcomes of TBI patients and serving veterans and sports injured
- We are developing and deploying these methods in PA and Texas to provide responsible sports concussion management through deep science and dosimetry tracking from the lab to the high school football field.
- We are seeking to develop state wide TBI diagnosis and treatment centers





A TEAM-TBI Study

Ryan Soose, MD¹, Tina Harrison, BS¹, Kathryn Edelman, MS², Allison Borrasso, MS², Jane Sharpless, MS², Dana Williams, MS², Valerie Reeves, PhD³, Dan Pultz USMC⁴, Ron Poropatich, MD⁵, Sue Beers, PhD⁶, Anthony Kontos, PhD³, Micky Collins, PhD³, Walter Schneider, PhD⁴, David Okonkwo, MD, PhD²
 University of Pittsburgh Departments of Otolaryngology¹, Neurological Surgery², Orthopaedic Surgery³, Psychology⁴, Medicine⁵, Psychiatry⁶

Background

Traumatic brain injury (TBI) is a heterogeneous disorder with varying clinical profiles. Sleep disturbances are very common in chronic TBI and may secondarily impact other functional and neurocognitive outcomes of TBI. In the TEAM-TBI (Targeted Evaluation Action and Monitoring of Traumatic Brain Injury) study, participants with chronic TBI undergo a comprehensive clinical assessment, followed by adjudication of each individual's unique clinical profiles and assignment of sequenced, individualized, evidence-based treatments. TEAM-TBI participants determined to have a sleep disturbance were assigned targeted treatments over a 6-month intervention phase based on the specific nature of their sleep disorder.

Purpose

The objective of the current study was to compare sleep outcome measures after targeted sleep recommendations were made by a multi-disciplinary team and implemented over a 6-month intervention phase.

Methods

TEAM-TBI study inclusion criteria included: age 18-60 and history of TBI with refractory clinical sequelae (Post-Concussion Symptom Scale (PCSS) score > 30, more than 6-months after injury). Under an IRB-approved protocol, participants travelled to the University of Pittsburgh and underwent a 4-day comprehensive evaluation of sleep, mood, vestibular, oculomotor, cognitive, neurologic, and neuropsychological function, as well as advanced neuroimaging studies. Sleep-specific data collected included home portable sleep testing, Epworth Sleepiness Scale (ESS), Insomnia Severity Index (ISI), and Pittsburgh Sleep Quality Index (PSQI, PSQI-A). A multi-disciplinary case review then identified clinical trajectories and assigned individualized treatment recommendations. The sleep disorder diagnostic evaluation and management plan were determined by a trained sleep medicine specialist.

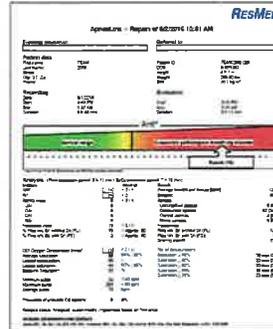


Methods Cont'd

Subjects who were adjudicated to have a sleep disturbance were further classified according to the International Classification of Sleep Disorders as having sleep-disordered breathing, insomnia, and/or other sleep medicine disorders. The sleep disordered breathing cohort was treated with positive pressure therapy, oral appliance therapy, and/or weight loss, while the insomnia cohort was treated with cognitive behavioral therapy for insomnia (CBT-I), behavioral modifications, melatonin, and/or medication recommendations. Change in sleep metrics between baseline and 6-month follow-up assessments were compared with paired t-tests.

TEAM TBI Demographic Table

| | Military | Civilian | Total |
|--------|----------|----------|-------|
| Male | 59 | 14 | 73 |
| Female | 1 | 16 | 17 |
| Total | 60 | 30 | 90 |



Results

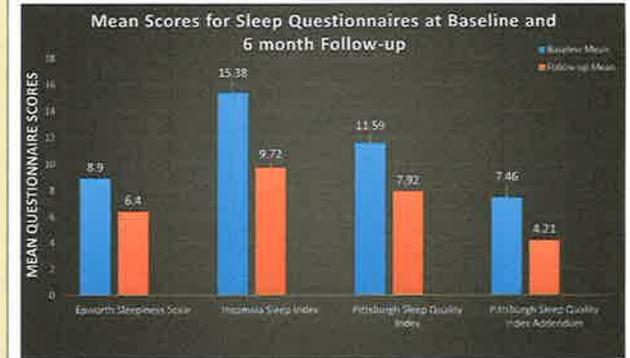
Ninety participants were enrolled, of whom 52 completed the study. Seventy-two subjects (76.5%) were identified to have a sleep disturbance, of whom 39 subjects (27 Veteran, 12 civilian subjects) have completed the 6-month intervention phase and the in-person follow-up assessment.



Results Cont'd

Compared to baseline, validated sleep questionnaires at 6-month follow-up demonstrated significant improvement in both the Veteran and civilian cohorts.

1. Mean ESS reduced from 8.9 to 6.4 (p=0.003)
2. ISI scores decreased from 15.38 to 9.72 (p<0.0001)
3. PSQI scores decreased from 11.59 to 7.92 (p<0.0001)
4. PSQIA scores dropped from 7.46 to 4.21 (p<0.0001)



Conclusion

In TEAM-TBI, chronic TBI subjects with identified sleep disorder subtypes underwent evidence-based targeted sleep interventions and demonstrated significant improvement in validated patient-reported measures of sleep quality at 6-month follow-up. TBI clinical trials must evolve towards identified clinical subgroups with targeted study interventions and disease-specific endpoints.

Support

Department of Defense Award No: W81XWH-14-2-0002 [TEAM TBI]
 Department of Defense Award No: W81XWH-12-2-0140 [HDFT Chronic]

Learn More

www.team-tbi.com
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 TEAMTBI@upmc.edu





Change in Psychological Health Following Targeted Intervention for Chronic Traumatic Brain Injury: a TEAM-TBI Study

Allison Borrasso, MS¹, Sue R. Beers, PhD¹, Yue-Fang Chang, PhD¹, Ava Puccio, PhD¹, Kathryn Edelman, MS¹, Walter Schneider, PhD¹, Anthony Kontos, PhD¹, Michael Collins, PhD¹, David Okonkwo, MD, PhD¹

¹University of Pittsburgh, Pittsburgh, PA



Background

Traumatic Brain Injury (TBI) is a heterogeneous disorder whose consequences can negatively affect individuals' physical, cognitive, social, and emotional wellbeing. U.S. military Veterans with TBI have high rates of psychological health sequelae associated with combat exposure that further complicate adjustment and reintegration to civilian life. Additionally, the staggering suicide rates among Veterans indicate a need for more effective interventions to support Veterans' psychological health.

Veterans and civilians with chronic TBI were enrolled into the Targeted Evaluation, Action, and Monitoring of Traumatic Brain Injury (TEAM-TBI) study. A 4-day comprehensive baseline evaluation identified primary areas of concern. Individualized interventions were prioritized based on input from a multidisciplinary team of clinicians. An in-person re-evaluation occurred 6-9 months later.

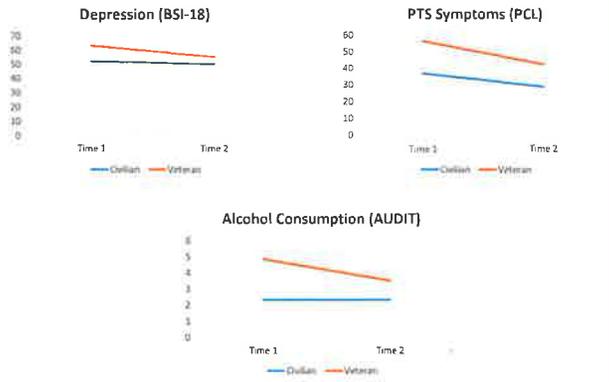
| Participant Enrollment Agenda | | | |
|--|---|---|--|
| Monday 6/22/16 | Tuesday 6/23/16 | Wednesday 6/23/16 | Thursday 6/23/16 |
| 8:00am - 9:00am Check in & registration | 8:00am - 11:00am Baseline TBI/PTSD Screening | 8:00am - 11:00am Appx. Med. Exam PTSD/PTSS Assessment | 8:00am - 11:00am Psychiatric NP Triage Psychiatric consult |
| 9:00am - 12:00pm Clinical Assessment | 11:00am - 12:00pm Goal Setting | 10:00am - 11:00am Social Assessment | 10:00am - 12:00pm Appx. Med. Exam Appx. Med. Exam |
| 12:00pm - 2:00pm Lunch | 12:00pm - 2:00pm Appx. Med. Exam PTSD/PTSS Assessment | 12:00pm - 2:00pm Social Assessment | 12:00pm - 2:00pm Appx. Med. Exam Appx. Med. Exam |
| 2:00pm - 4:00pm Individualized Intervention | 2:00pm - 4:00pm Appx. Med. Exam PTSD/PTSS Assessment | 2:00pm - 4:00pm Social Assessment | 2:00pm - 4:00pm Appx. Med. Exam Appx. Med. Exam |
| 4:00pm - 6:00pm Check out | 4:00pm - 6:00pm Appx. Med. Exam PTSD/PTSS Assessment | 4:00pm - 6:00pm Social Assessment | 4:00pm - 6:00pm Appx. Med. Exam Appx. Med. Exam |

Methods

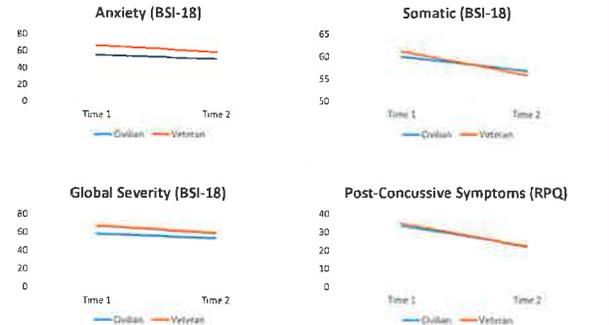
This study compared psychological health (PH) outcome measures in Veterans and civilians before and after targeted intervention and clinical coaching. Inclusion criteria were: age 18-60, history of chronic TBI, and >30 on the Post-Concussion Symptom Scale. PH variables included depression, anxiety, somatization and global severity on the Brief Symptom Inventory (BSI-18), Posttraumatic Stress Checklist (PCL), Satisfaction with Life Scale (SWLS), Alcohol Use Disorders Identification Test (AUDIT), Rivermead Post-Concussive Symptom Questionnaire (RPQ) and suicidality (BSI-18 and Patient Health Questionnaire). Data was collected in-person at baseline and follow up. Goal setting identified participants' primary concerns. Clinical coaches provided ongoing telemedicine support to help overcome obstacles, provide encouragement, assess progress, and coordinate care.

Results

- N=39; majority were Veterans (n=26), white (n=33), and male (n=29) with a mean age of 36 (min=21, max=60).
- General estimating equations (GEE) controlling for age and compliance showed a significant effect of group by time interaction for depression ($p=.03$), posttraumatic stress (PTS) symptoms ($p=.02$), and alcohol use ($p=.04$) such that Veterans showed greater improvement over time.

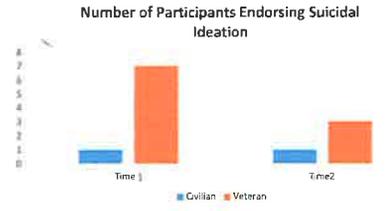


- Both groups showed significant improvement at follow up on measures of anxiety ($p<.0001$), somatization ($p=.0002$), global severity ($p<.001$), and post-concussive symptoms ($p<.001$).



Results (cont.)

- Suicidal ideation (SI) occurred in 26.92% of Veterans and 7.69% of civilians at baseline. SI decreased to 11.54% among Veterans at follow-up. There was no change in the civilian group.



- SWLS improved slightly in both groups.
- Prevalent Veteran goals = employment and mood.
- Prevalent civilian goals = employment and physical activity.

Discussion

While both groups showed improvement in PH after engaging in the TEAM-TBI care model, more significant improvements were found among Veterans for depression, PTS, and alcohol use. Suicidal ideation was more prevalent in Veterans and decreased by more than half at follow up. Results may be due to Veterans receiving prioritized PH treatment recommendations in response to meeting clinical cutoffs, along with receiving genuine concern from study clinicians and ongoing clinical coaching.

Conclusion

- Veterans had higher rates of depression, PTS, alcohol use and SI.
- TEAM-TBI incorporated a psychosocial approach to address comorbid mental health issues in Veterans with TBI.
- TEAM-TBI provided an individualized plan, clinical coaching, and a team of experienced clinicians who display genuine concern.
- Veterans' PH improved with the TEAM-TBI model of care.
- Improved PH in Veterans may facilitate increased functioning post-TBI, adjustment post-military discharge, and reduce suicide rates.

Additional Comments

Thank you to all U.S. military Veterans not only for your service to our country, but for the many sacrifices associated with your service.





Impact of Multi-Disciplinary Care and Clinical Coach Coordinators on Participant Satisfaction and Retention in TBI Clinical Trials: A TEAM-TBI Study

Kathryn Edelman, MS¹, Jane Sharpless, MS¹, Allison Borrasso, MS¹, Dana Williams, MS¹, Steven Benso, CCRN¹, Wolf Schneider, PhD², Anthony Kontos, PhD³, Michael Collins, PhD³, David Okonkwo, MD, PhD¹, Ava Puccio, PhD¹

University of Pittsburgh Departments of Neurological Surgery¹, Psychology², Orthopaedic Surgery³



Background

Traumatic Brain Injury (TBI) is a signature wound of OEF and OIF. More than 350,000 service members have been diagnosed with TBI since 2001. TBI impacts the lives of these service members across many clinical domains. A lack of precision care has hampered TBI care and clinical trials to date.

Targeted Evaluation Action and Monitoring of Traumatic Brain Injury (TEAM-TBI) is a monitored, multiple interventional research trial that identifies specific clinical profiles and assigns a sequenced, individualized, evidence-based treatment program. Clinical Coaches are assigned to each participant to coordinate treatment plans, help participants overcome obstacles, and provide support over the 6-month follow-up period.

Purpose

The objective of the current study was to assess overall participant satisfaction of the multi-disciplinary care team and approach.

Methods

Between 2014 and 2017, 90 participants (60 military, 17 female) completed the 4-day TEAM-TBI clinical intake evaluation resulting in individualized treatment recommendations. This was followed by a six-month intervention phase and an in-person follow-up. Inclusion criteria were: age 18-60, history of chronic TBI (>6 month post-injury) with refractory clinical sequelae at screening (Post-Concussion Symptom Scale [PCSS] score >30). At the conclusion of the initial and follow-up evaluations, participants completed a Satisfaction Survey which included open-ended and Likert scale questions (1-5 scale) and was administered by a team member without prior contact.

Results

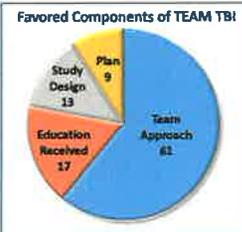
- A total of 85/90 (94%) participants completed the Satisfaction Survey at baseline which focused on the intake evaluation and approach; 90% of eligible participants also completed the follow-up time-point. 100% of participants had a mean score of 4/5 or greater across all questions at both time points; 72% had an average rating of 4.5/5 or greater.

| Participant Satisfaction Survey Results (N=85) | |
|--|---------------------------|
| Service | Average Score (1-5 Scale) |
| Consent/Meet and Greet | 4.89 |
| Accommodations | 4.66 |
| Sleep Evaluation | 4.17 |
| Concussion Clinic | 4.61 |
| MRI Research Center | 4.67 |
| Military Coordinator | 4.95 |
| Neuropsychology Testing | 4.61 |
| Goal Setting | 4.82 |
| Neurosurgery Clinic | 4.82 |
| General Questions | 4.82 |

- During the open-ended questions, 61/85 (72%) of participants cited the team approach as one of their favorite aspects of the study, 17/85 (20%) favored the education received, 13/85 (15%) highlighted the study design, and 9/85 (10%) preferred having a plan.

TEAM TBI Demographic Table

| | Military | Civilian | Total |
|--------|----------|----------|-------|
| Male | 59 | 14 | 73 |
| Female | 1 | 16 | 17 |
| Total | 60 | 30 | 90 |



- With regard to their least favorite aspects of the study, 39/85 (46%) of participants identified specific individual components of the assessment, 23/85 (27%) could not identify anything negative, 8/9 (9%) cited logistics with travelling, 7/85 (8%) struggled with the general schedule and pace, and 8/85 (9%) were "other", which included feeling overwhelmed and re-living their TBI.

Results Cont'd

- Qualitatively, the overall satisfaction scores at follow-up were very similar to baseline. When asked about motivation, 19/38 (43%) of participants said the Clinical Coach or study team was the cause of their motivation, 16/38 (36%) were motivated by getting better, and 3/38 (7%) were focused on helping others.

Testimonials

"Everyone was extremely professional and it was an overall wonderful experience. I learned a wealth of knowledge about my injuries and think that the program can do wonders for vets suffering through TBI symptoms." –34-year-old Marine Combat Veteran

"I really felt like everyone in TEAM-TBI was truly dedicated in finding out the truth behind TBI. Everyone was very genuine, kind, caring, as well as extremely patient with me. I gained knowledge about my TBI and how to manage day to day activities. I am honored to have been a part of something great." –34-year-old Navy Combat Veteran

"The quality of the staff is exceptional and definitely sets the medical standard. Where so many other medical professionals came short, TEAM-TBI has surpassed my expectations. Not only has the TEAM been able to identify my deficiencies, they came up with a solid treatment plan. Not enough good things can be said." –29-year-old Marine Combat Veteran

Conclusion

The multi-disciplinary care approach and individualized treatment plans of the TEAM-TBI study yielded high participant satisfaction scores, with strong positive feedback. The Clinical Coach component of the trial was one of the highest rated aspects of the approach and was associated with participant motivation and high retention rates. Future clinical studies and care models should consider integrating this model into standard of care for our service members with TBI.

Support

Department of Defense Award No: W81XWH-14-2-0002 [TEAM TBI]
Department of Defense Award No: W81XWH-12-2-0140 [HDFC Chronic]

Learn More

www.team-tbi.com
(412) 383-TEAM
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Objective Assessment of Psychological Health in Chronic Traumatic Brain Injury Using Magnetoencephalography: A TEAM-TBI Study

Don Krieger, PhD¹, Sue Beers, PhD², Ava Puccio, PhD¹, Allison Borrasso, MS¹, Kathryn Edelman, MS¹, Jane Sharpless, MS¹, Michael Collins, PhD³, Anthony Kontos, PhD³, Walt Schneider, PhD⁴, David Okonkwo, MD, PhD¹

University of Pittsburgh Departments of Neurological Surgery¹, Psychiatry², Sports Medicine³, Psychology⁴



Background

Magnetoencephalography (MEG) enables objective non-invasive examination of human brain function. MEG enables correlation of changes in global and regional neuroelectric activation with manifestations of neurological disorders including traumatic brain injury. Through the Targeted Evaluation, Action and Monitoring of Traumatic Brain Injury (TEAM-TBI) study, subjects with chronic TBI were assessed with MEG to identify patterns of tonic brain activation which underlie psychological health symptoms. Following 6 months of individualized, targeted interventions (including treatments for psychological health and post-traumatic stress), subjects were re-imaged with MEG. Recordings from the Cambridge(UK) Centre for Ageing and Neuroscience (CamCAN) lifespan normative cohort served as controls.

Methods

Inclusion criteria included age 18-60 and history of TBI with refractory clinical sequelae as measured by Post-Concussion Symptom Scale score > 30 more than 6 months after injury. MEG was recorded during rest from a subset of the TEAM-TBI cohort (n=60, mean age=34.9, sd=7.5, 12 female) and from a subset of the CamCAN cohort (n=75, mean age=34.3, sd=7.5, 19 female). 32 TEAM-TBI subjects have had a 6-month follow up assessment. Neuroelectric events were identified and localized to one of 155 brain regions.

Figure 1: At rest with eyes on fixation mark

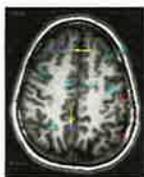
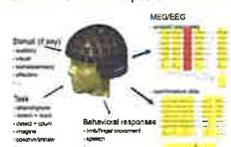


Figure 2. The raw MEG recordings were processed to extract brief neuroelectric events.

Each event:

- persisted for 0.08 seconds
- consisted of an electric current flow
- was localized within the brain with approximately 1 millimeter accuracy
- retained all frequency content from 10 to 250 Hz.
- was accepted using a statistical test with $p < 10^{-12}$

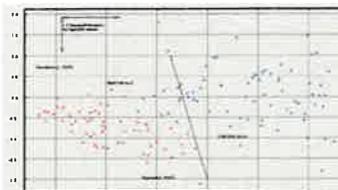
Normative patterns of neuroelectric activation were identified in the CamCAN cohort using independent components analysis (ICA). Each ICA is a set of 155 activation values, one for each brain region. The weighted sum of an individual's pattern, also 155 activation values, with one of these ICA's is a single number, called a weight.

Each weight is a measure of similarity between the individual's brain pattern and each ICA. The means of these weights differed between cohorts ($p < 0.0001$) for ICA's 1, 3, and 6 and not the other ICA's. These 3 ICA's were therefore used to classify each individual, CamCAN vs TEAM-TBI. They were also tested for correlation against the TEAM-TBI participants' Brief Symptom Inventory (BSI) Depression, Somatization, and Anxiety subscales.

Results

Figure 3a, Classification Accuracy

Using factors scores 1 and 6, 62/75 were correct for the CamCAN cohort, $p < 10^{-7}$. 59/60 were correct for the TEAM-TBI cohort, $p < 10^{-12}$. For the TEAM-TBI cohort, the correlation between factor score 1 and the BSI depression score was significant at $p < 0.01$. The correlation between factor score 6 and the BSI somatization score was also significant at $p < 0.01$.



Chronic TBI: red dots Controls: blue dots

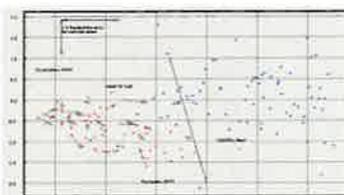


Figure 3b, Repeat Reliability

32 Team-TBI 6 month follow up studies have been obtained and processed to date. 23 of 32 show less than 1/2 standard deviation change from baseline (foot of the arrow) to follow up (head of the arrow).

Figure 3c: 9 of 32 follow-up studies show more than 1/2 standard deviation change from baseline (foot of the arrow) to follow up (head of the arrow).



The good separation from controls of those with chronic symptoms of concussion along axes which are correlated with psychological health symptoms (Figure 3a) provides a way to identify which "direction" to push the pattern of brain activity towards "normal."

The repeat reliability of the measures of brain activity over 6 months (Figure 3b) suggests the potential utility of these measures in monitoring and guiding therapies which effect brain activity, e.g. drugs and transcranial magnetic stimulation.

Figure 4, upper panel: The mean activity in each of 164 regions of interest (ROIs) was compared between a group of 55 HIV at-risk individuals and a group of 441 neurologically normal controls. Welch t-statistic was used. ROIs shown in fully saturated colors indicate $p < 10^{-6}$; those with minimal saturation, i.e. nearly white, indicate $p < 10^{-4}$. Red/blue indicate that the activity in the HIV at-risk cohort was greater/less than the activity in the control cohort.

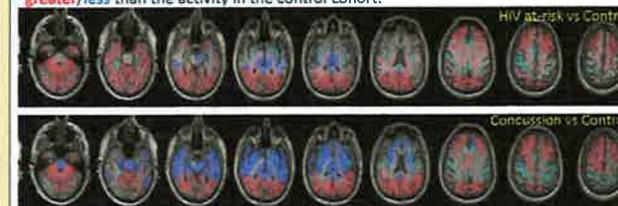


Figure 4, lower panel: The mean activity in each of 164 ROIs is compared between the TEAM-TBI baseline studies (n=73) and the 441 neurologically normal controls.

When compared to the controls, the two clinical groups (HIV and chronic TBI) had similar differences in the superior and posterior regions. However, the concussed cohort showed uniquely reduced activity in almost all frontal and temporal regions of interests. The widespread reduced regional activity may be due to compromised white matter in a significant percentage of the chronic TBI cohort.

Conclusion

- MEG-derived regional brain activity is significantly altered in patients with chronic TBI symptoms when compared to healthy controls after adjustment for age and sex. This supports the hypothesis that physiological cortical activity abnormalities may contribute to the neuropsychological symptoms following TBI.
- Regional brain activity is associated with elevated depression and somatization in chronic TBI. This support the hypothesis that TBI may induce organic, substructural, brain changes, leading to psychological health disorders.

Support

We gratefully acknowledge the contributions of James T Becker, Ben Zusman, and Ali Shields.

Department of Defense Award No: W81XWH-14-2-0002 [TEAM TBI]
Xsede - Extreme Computing and Engineering Environment: TG-IBN130001
Open Science Grid, Pittsburgh and San Diego Supercomputing Centers



High Definition Fiber Tracking (HDFT) Metrics Predict Neuropsychological Test Performance in Chronic Traumatic Brain Injury



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Background

High Definition Fiber Tracking (HDFT) is an advanced form of MRI diffusion imaging that allows for quantitative analysis of white matter tract volume and left/right brain symmetry. We examined whether HDFT could detect changes in white matter induced by traumatic brain injury (TBI) and whether those anatomical differences were associated with cognitive and/or neurological deficits in chronic TBI subjects.

Methods

Chronic (i.e., ≥ 6 months post injury) TBI adult subjects (veterans and civilians; n = 88; 18 F, mean age = 37.5) symptomatic for TBI sequelae and healthy controls (n = 82; 47 F, mean age = 32.6) completed HDFT imaging and a neuropsychological battery measuring memory, attention and executive function, and processing speed. Mayo classification procedures (Malec et al., 2007) defined TBI severity. Diffusion data were acquired on 3T Siemens Trio scanner with either a multi-shell protocol or a diffusion spectrum (DSI) imaging protocol.

HDFT metrics (Presson et al., 2016) analyzed included *spread*, or proportion of brain mask voxels contacted by at least one tract streamline measured on left and right homologues; and *symmetry*, left-right homologue correlation measured across, X/Y/Z. White matter bundles analyzed included: Arcuate Fasciculus (AF), Corpus Callosum Genu (CC G), Body (BO), and Splenium (SP), Cingulum, Corona Radiata, Corticospinal Tract (CST), External Capsule (EC), Fronto-Occipital Fasciculus (FOF), Frontal Aslant, Inferior Longitudinal Fasciculus, Optic Radiations, Superior Longitudinal Fasciculus, and Uncinate Fasciculus (UF).

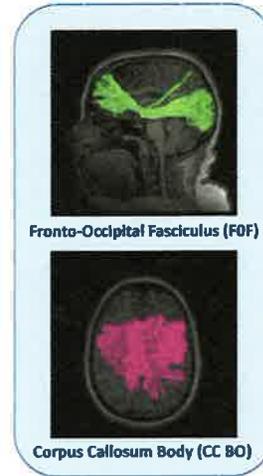
Neurological outcome instruments included Trail Making Test Part A (visual attention) and Part B (cognitive flexibility), Automated Neuropsychological Assessment Metrics System Simple Reaction Time (RT) and Two-Choice RT; Wechsler Adult Intelligence Scale-IV Processing Speed, and California Verbal Learning Test-II Long and Short Delay Free Recall (verbal memory).

| | Chronic TBI | Healthy Control | Total |
|--------|-------------|-----------------|-------|
| Male | 70 | 35 | 105 |
| Female | 18 | 47 | 65 |
| Total | 88 | 82 | 170 |

Results

The TBI group showed significantly reduced spread and symmetry for 19/28 white matter tract metrics relative to controls. Results showed significant linear correlations among HDFT metrics and test scores. Considering symmetry and spread, 7 tracts were significantly correlated with test results: FOF, CC BO, CC GE, CC SP, UF, EC, and AF.

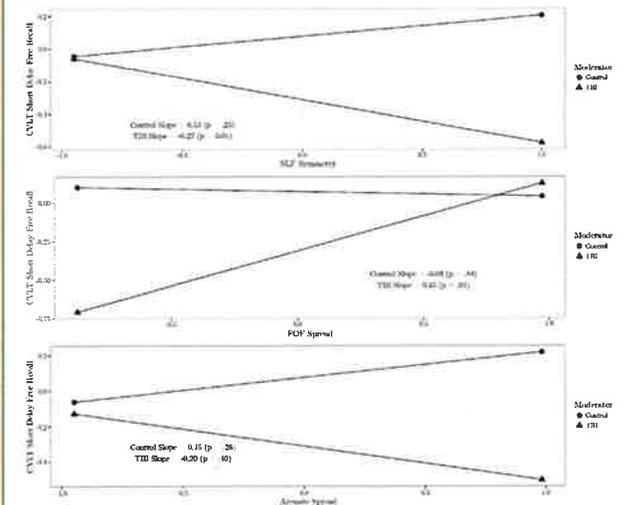
- The FOF was correlated with all cognitive variables (e.g., $r=0.38$ with WAIS-IV PSI)
- The CC BO was correlated with 7/8 cognitive variables.



| Tracts showing significant correlation with neuropsychological tests grouped by cognitive domain | | | | | | | | |
|--|-------------------------|--------|--------|----------|--------|----------|--------|----------|
| Cognitive Domain | Neuropsych Test | FOF | CC BO | CC GE | CC SP | UF | EC | AF |
| Memory | Short Delay Free Recall | Spread | Spread | Spread | Spread | | | |
| | Long Delay Free Recall | Spread | Spread | Spread | Spread | | | |
| Processing Speed | Processing Speed index | Spread | Spread | Spread | Spread | Symmetry | Spread | Symmetry |
| | Simple Reaction Time | Spread | Spread | Spread | | Symmetry | | |
| | Trail Making A | Spread | | | | | | |
| Attention/Executive Function | 2 Choice Reaction Time | Spread | Spread | Symmetry | | Symmetry | Spread | |
| | Trail Making B | Spread | Spread | | | | Spread | Symmetry |

Linear regression models found HDFT metrics (i.e., metric by tract) moderated the predictive relationship between group status and four test scores ($p=0.20-.001$) with one trend ($p=.9$) noted. The seven HDFT predictors making the greatest unique contribution to prediction of group status were spread of AF, FOF, SP, and UF and symmetry of UF, AF, and SLF.

Results Cont'd



Conclusion

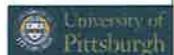
HDFT diffusion tractography metrics predicted neuropsychological test scores in the domains of verbal memory, processing speed, and attention/executive function, even after accounting for participant status and age, education, and gender. HDFT neuroimaging may provide an objective quantification of TBI injury status in symptomatic patients later in the recovery period.

Support

Department of Defense Award No: W81XWH-14-2-0002 [TEAM TBI]
 Department of Defense Award No: W81XWH-12-2-0140 [HDFT Chronic]

Learn More

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Warrior Veterans with TBI: Role of Genuine Concern in the TEAM-TBI Trial



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 University of Pittsburgh Departments of Neurological Surgery¹, Psychology², Orthopaedic Surgery³



Background

Genuine Concern (GC) is the art of making others feel valued, accepted, understood, and part of a trusting relationship. Rodgers was one of the earliest to theorize that unconditional positive regard or GC is integral to the healing process. We analyzed the impact of GC on combat Veterans participating in TEAM-TBI (Targeted, Evaluation, Action & Monitoring of Traumatic Brain Injury), a prospective, individualized, multi-interventional clinical research trial.

The TEAM-TBI principal investigators are civilians. Because of the emphasis of the project on combat Veterans, we elected to include a combat Veteran as a Military Coordinator/Coach (MCC) with 9+ years of experience working with Semper Fi Odyssey, the United States Marine Corps National Transition Program for its Wounded, Injured and Ill. A major contribution of the MCC was the commitment of Genuine Concern to the TEAM-TBI care model. For many TBI wounded Veterans, the injury was not visible like traditional wounds. Many TEAM-TBI participants reported persistent TBI symptoms and a clinical history that lacked of targeted treatment, but also lacked GC.

Purpose

Examine the impact of a MCC as a liaison between Veterans and clinical investigators, and the role of GC in a TBI research study. We hypothesized that GC enhances belief in recommended clinical treatment plans, encourages compliance, and boosts follow-up rates.



Methods

Inclusion criteria: 18–60 years of age, history of TBI after 2001, and total PCSS of 30 or greater at screening.

Exclusion criteria: Prior history of stroke or other major neurological disorder or contraindication to MR imaging.

Methods Cont'd

Self-report testimonials from Veteran Warriors participating in TEAM-TBI were collected following the initial clinical intake assessment and again at the follow-up assessment after the 6-month interventional phase of the trial. Testimonials were reviewed for impact of GC experienced by TEAM-TBI subjects from their prior health care experiences and for the GC exhibited by TEAM-TBI investigators.

The MCC actively participated in TEAM-TBI participant review meetings with clinical investigators where appropriate individualized interventions were planned. During these meetings, the MCC provided education relating to military culture and its implications, both in combat and upon return to civilian status.

| | Military | Civilian | Total |
|--------|----------|----------|-------|
| Male | 59 | 14 | 73 |
| Female | 1 | 16 | 17 |
| Total | 60 | 30 | 90 |

Results

Of the 90 TEAM TBI participants enrolled, 60 were military Veterans. Of these 60, 24 were currently active on follow-up, 3 were lost to follow-up, and 2 were withdrawn due to ineligibility. The retention rate among military Veterans eligible to complete the 6-month follow-up was 91%. The MCC and Veteran Warriors interacted over two study time points, generally on a one-to-one basis, spending an average of ten hours per participant. At study initiation, previously encountered problems were discussed, many of which could likely be attributed to lack of GC. They included lack of understanding and acceptance of current health care providers, which led to profound lack of trust.

Participants completed a satisfaction survey at the end of the in-person visit. On a Likert scale of 1 (poor) – 5 (great), participants rated the MCC on his/her comfort level of the MCC and the Usefulness of the MCC.

➤ MCC Comfort Level Average Score = 4.95/5

➤ MCC Usefulness Average Score = 4.95/5

Veteran Participant Perspective

Participant responses to the question, "How comfortable did you feel with your level of involvement with the military liaison?" from participant satisfaction survey:

"[It is] important to have a [military] liaison. He helped bring program together."

- 35 year old male Marine Veteran

"Don't know how it would be done without him; it modeled the relationship between superior officer and subordinate. He gave a good run down."

- 26 year old male Marine Veteran

"He went above and beyond. He took us out to dinner and was able to provide career resources."

- 31 year old male Navy Veteran

"Very comfortable. Dan vouched for the group and helped put me at ease."

-33 year old male Marine Veteran

"Very comfortable. He is knowledgeable and cares a lot"

-32 year old Marine Veteran

Conclusion

The TEAM-TBI model included a MCC who displayed Genuine Concern, which positively impacted participant engagement throughout the course of their enrollment. GC stimulated a trusting therapeutic alliance between Veteran participants and TEAM-TBI clinical investigators. GC also likely contributed to high compliance in the 6-month clinical intervention plan and the low lost-to-follow-up rates seen in the study. Participants indicated feeling valued, accepted, understood, and part of a trusting relationship. The Genuine Concern reported by military Veteran TEAM-TBI participants likely contributed to the strong clinical results observed in the TEAM-TBI trial.

Support

Department of Defense Award No: W81XWH-14-2-0002 [TEAM TBI]
 Department of Defense Award No: W81XWH-12-2-0140 [HDFT Chronic]

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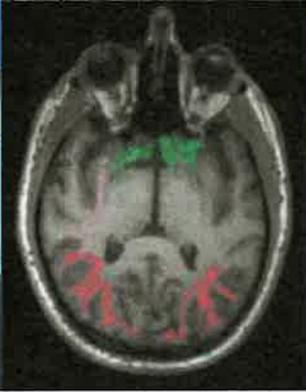
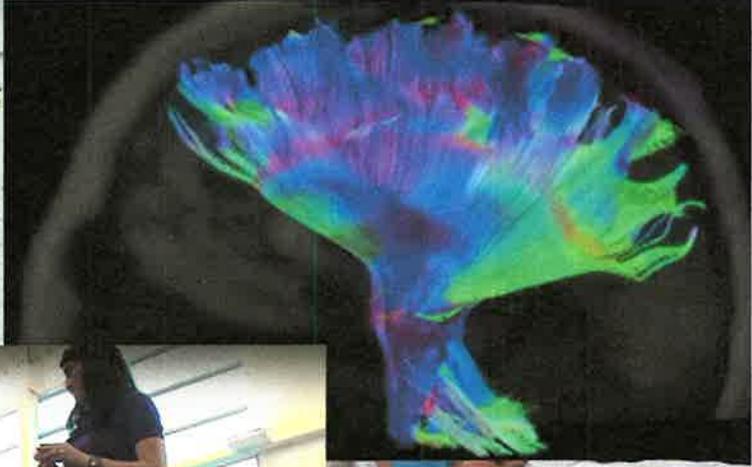


Participant Enrollment Agenda

Subject ID#: TEAM2061

Arrival Date and Time: Wings for Vets Arrive 2:36PM

| Monday | Tuesday | Wednesday | Thursday |
|---|--|--|---|
| <p>9:00am-11:30am Meet & greet Presbyterian Hospital <i>200 Lothrop St. Pittsburgh, PA 15213</i></p> <ul style="list-style-type: none"> • Agenda Review • Consent • Toolkit training • Sleep/Mood Surveys <p>11:30am – 12:30pm Military Coordinator <i>Presbyterian Hospital</i></p> <p>1:00pm – 2:00pm HDFT MRI imaging <i>Presbyterian Hospital</i></p> <p>2:30pm – 3:00pm ImPACT Testing <i>Presbyterian Hospital</i></p> <p>Overnight</p> <ul style="list-style-type: none"> • Apnea Link Assessment | <p>8:00am – 11:00am Neuropsych Testing <i>Presbyterian Hospital</i></p> <p>11:00am – 12:00pm Goal Setting <i>Presbyterian Hospital</i></p> <p>12:30pm – 3:30pm Additional brain imaging (PET/MEG/MRSI) <i>Presbyterian Hospital</i></p> <p>Overnight</p> <ul style="list-style-type: none"> • Apnea Link Assessment | <p>8:30am – 9:30am Sports Med Part 1: • History/Symptom assessment <i>Southside Concussion Clinic</i></p> <p>10:00am – 11:00am Sleep Assessment <i>Mercy Sleep Clinic</i></p> <p>12:30pm – 2:30pm Sports Med Part 2: • Exertional testing • Vestibular Assessment <i>Southside Concussion Clinic</i></p> | <p>9:30am - 10:30am Prescriptive NP Testing <i>Presbyterian Hospital</i></p> <p>10:30am – 12:30pm TEAM TBI Program Assessment Review <i>Dr. Okonkwo Presbyterian Hospital</i></p> <ul style="list-style-type: none"> • Satisfaction Survey • Blood Draw • Final Review with Coordinators • Q & A <p>1:30pm - 2:30pm Sports Med Follow-Up <i>Tentative; Appointment is as-needed</i></p> |





TEAM-TBI

NEUROSURGERY

- Ava Puccio
- Kate Edelman
- Allison Borrasso
- Jane Sharpless
- Steve Benso
- Sue Beers
- Cara Battistella
- Tom Hahner
- Maureen McAniff

BIOMARKERS

- Milos Ikonomic
- Kevin Wang – UF
- Denes Agoston-USUHS

SPORTS MEDICINE

- Micky Collins
- Anthony Kontos
- Anne Mucha
- Valerie Reeves

PET IMAGING

- James Mountz
- Chet Mathis
- Brian Lopresti
- Julie Price
- Chip Laymon
- Davneet Minhas
- Milos Ikonomic

MRI HDFT GROUP

- Walt Schneider
- Nora Presson
- Jon Chmura
- William Bird
- Gina Droeder
- Sudhir Pathak
- Emily Clarke
- Kate Fissell
- Hoby Hetherington

SLEEP

- Ryan Soose
- Tina Harrison

MEG

- Don Krieger