

Impact of Sleep on Treatment & Recovery in Veterans with TBI and PTSD

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DISCLOSURES

Presenters have no financial interests to disclose.

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OBJECTIVES

- ① Provide an overview of the quality of sleep in returning Veterans with TBI and PTSD.
- ② Discuss how sleep disturbance affects everyday functioning and outcome in Veterans with TBI and PTSD.
- ③ Describe measurement tools for sleep assessment and treatment outcome monitoring.
- ④ Review current treatment options for sleep disturbance in TBI and PTSD.

POLL QUESTION

What is your primary role in VHA?

Select all that apply:

- ☐ VA researcher
- ☐ Clinician
- ☐ Nurse
- ☐ Trainee
- ☐ Other — if selected 'other', please write your response into Q&A box

SLEEP IN TBI & PTSD

Part 1

SLEEP IN RETURNING VETERANS

Sleep Disturbances in TBI:

- Sleep problems are common in Veterans with TBI, including those with mild (m)TBI
- Both sleep quality (self-reported trouble sleeping) and quantity (sleep duration) are affected, and have been associated with mental health symptoms (Seelig et al. 2010).
- Overall, 25–81% of post-acute TBI patients experience prolonged or permanent sleep disturbances - regardless of localization, severity, or time since TBI.
- These sleep problems are chronic and have been shown to persist at 6 months and up to 5 years post-TBI.

(Mathias & Alvaro, 2012; Baumann et al., 2007; Castriotta et al., 2007; Kempf et al., 2010)



<http://www.bumc.bu.edu/busm/files/2015/09/COM-sad-soldier-US-Marine-Corps-e1441128953101.jpg>

SLEEP IN TBI

Prevalence of Sleep Disturbances in TBI:

- Meta-analysis (N=1706) of TBI and sleep literature (1990-2011) found (Mathias & Alvaro, 2012):
 - In studies using objective sleep measures and formal diagnostic criteria the prevalence of sleep disturbances: **53%**.
 - Compared to the general population, TBI group was:
 - significantly more likely to experience sleep disturbances
 - more than **12 times** more likely to have diagnosed sleep disorders.
- The Armed Forces Health Surveillance System reported **sleep disorders** among the **most common TBI sequelae** in the active duty Armed Forces service members between 2000-2012 (AFHSC, 2013).
- In a sample of 114 returning Veterans with blast-induced mTBI - **77%** reported subjective sleep difficulties. (Farrell-Carnahan, Franke, Graham, and McNamee, 2013)

SLEEP IN TBI

Common Sleep Disturbances in TBI:

- Daytime sleepiness
- Nighttime sleep disturbance

Common post-TBI sleep-wake disturbances (SWDs):

- Poor nocturnal sleep quality
- Hypersomnia
- Excessive daytime sleepiness
- Impaired daytime vigilance
- Circadian rhythm phase shift

(Ayalon et al., 2007; Baumann, 2012; Baumann, Werth, Stocker, Ludwig, & Bassetti, 2007; Kempf, Werth, Kaiser, Bassetti, & Baumann, 2010; Ponsford, Parcell, Sinclair, Roper, & Rajaratnam, 2013).

SLEEP IN TBI

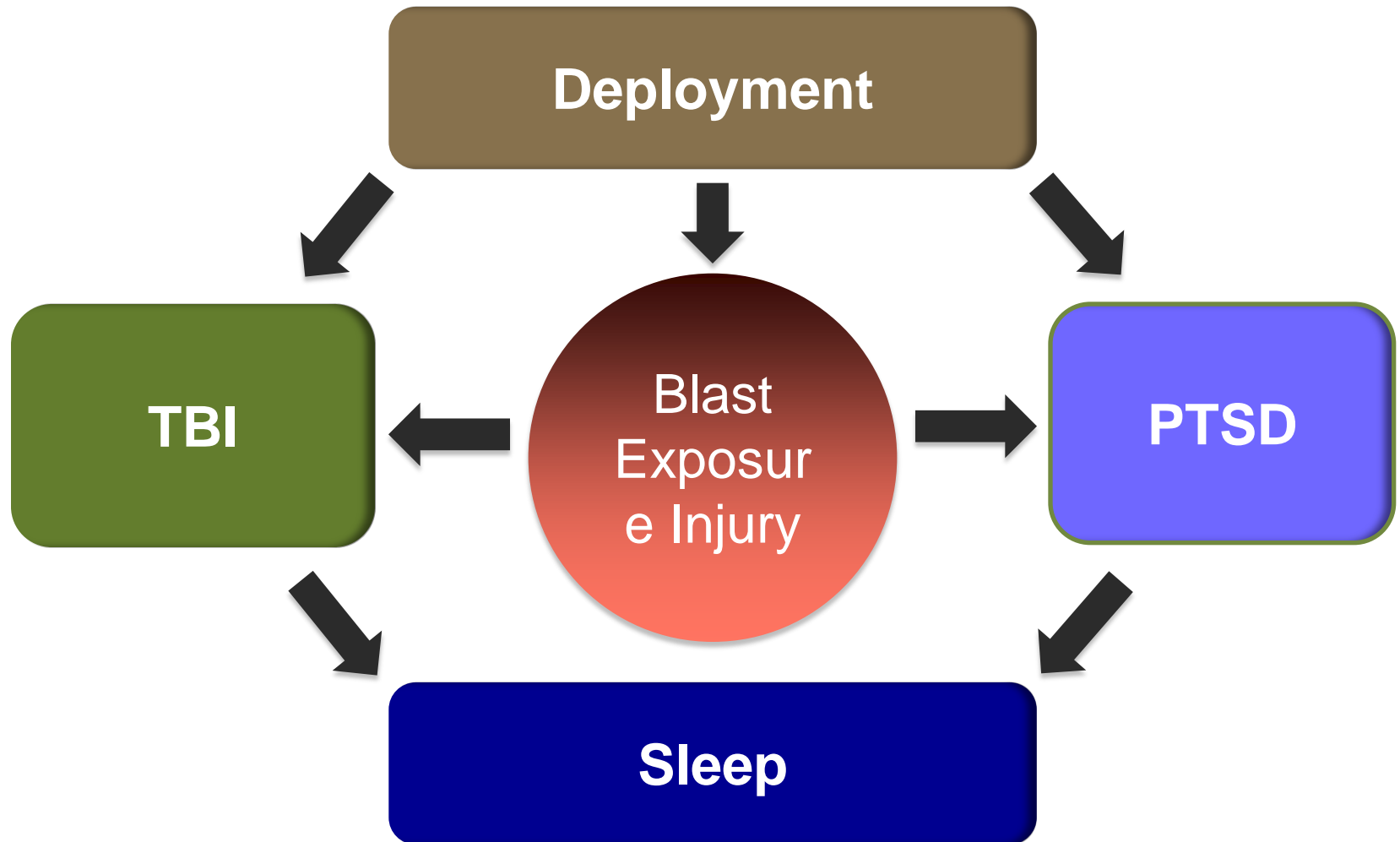
Common Sleep Disturbances in TBI: Objective Sleep Studies

Patients with TBI exhibit:

- reduced sleep efficiency
- increased wakefulness after sleep onset
- increased sleep onset latency
- alterations in sleep architecture:
 - less REM sleep, more time in “light” Non-REM sleep
- more frequent insomnia

(Baumann et al., 2007; Collen, Orr, Lettieri, Carter, & Holley, 2012; Mathias & Alvaro, 2012; Ponsford et al., 2012; Shekleton et al., 2010)

Complicating Factors



SLEEP IN PTSD

Sleep Disturbances in PTSD:

- Sleep disturbance is one of the core features of PTSD. (Calhoun et al., 2007; Dagan, Zinger, & Lavie, 1997)
- Approximately 70% of patients with PTSD have co-occurring sleep problems. (K. A. Babson & Feldner, 2010)
- PTSD has been associated with:
 - reduced sleep efficiency,
 - increased sleep latency,
 - increased sleep fragmentation, and
 - greater night-to-night variability in sleep.

(Breslau et al., 2004; Calhoun et al., 2007; Habukawa, Uchimura, Maeda, Kotorii, & Maeda, 2007; Mellman, Kulick-Bell, Ashlock, & Nolan, 1995; Straus, Drummond, Nappi, Jenkins, & Norman, 2015)

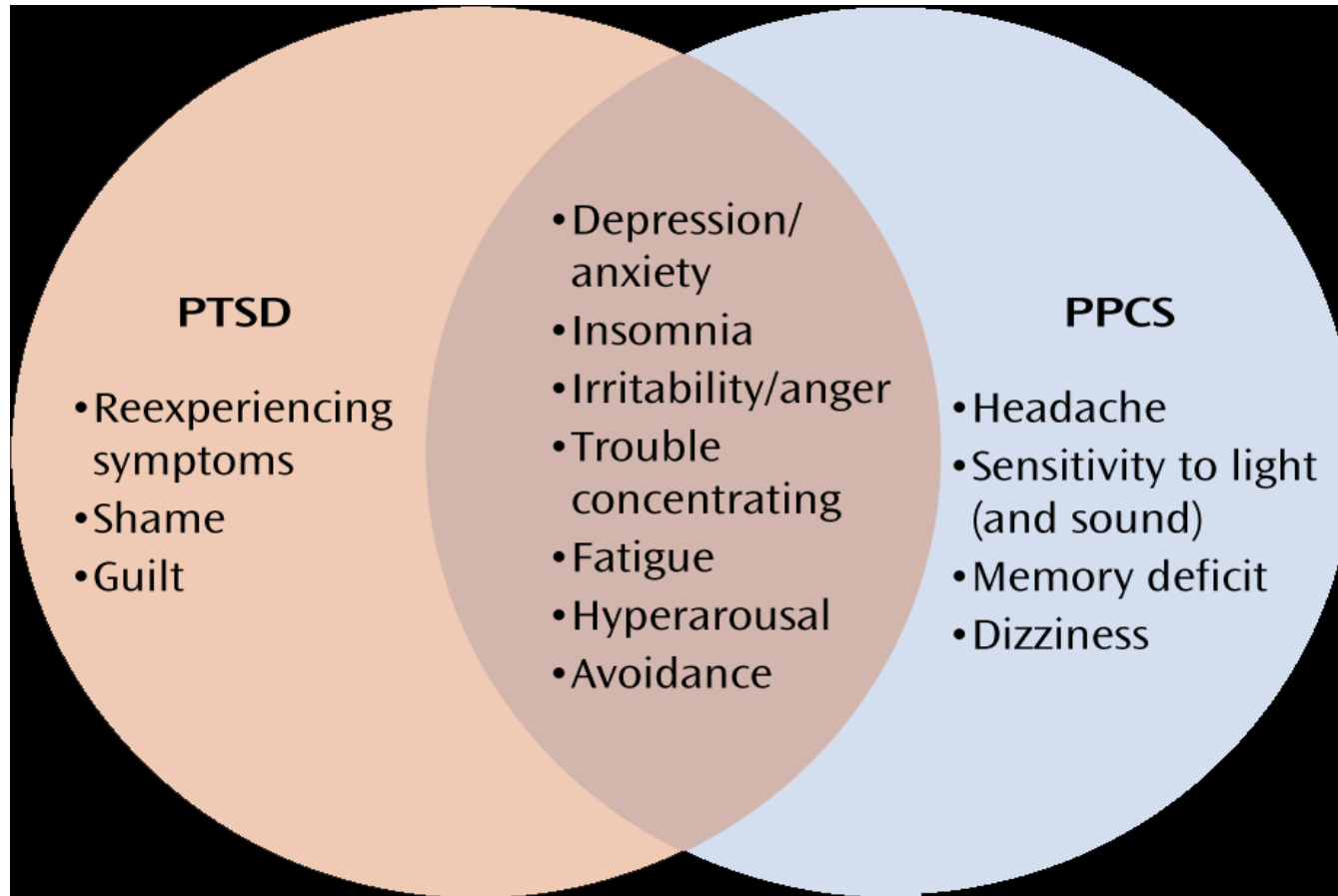
SLEEP IN PTSD

Sleep Problems: a Risk Factor for Development and Maintenance of PTSD

- Sleep disturbance may be *a risk factor for development of PTSD* following trauma exposure (Bryant et al., 2010; Gehrman et al., 2013; Gerhart et al., 2014; Kobayashi & Mellman, 2012; Koffel et al., 2013; Spoormaker & Montgomery, 2008; Swinkels et al., 2013; Wright et al., 2011).*
- Gerhart et al. (2014): initial sleep problems predicted increased PTSD and depression at 6 month follow-up [a longitudinal study of sleep and trauma-related distress].
- Koffel et al. (2013): found pre-deployment sleep complaints uniquely predicted PTSD and depression up to two years after deployment [follow-up study].
- These findings suggest that pre-trauma sleep disturbance predicts later development of PTSD following exposure to trauma.

* Reviewed in: Gilbert, K., Kark, S.M., Gehrman, P., & Bogdanova, Y. (2015). Sleep Disturbances, TBI and PTSD: Implications for Treatment and Recovery. *Clinical Psychology Review*, 40, 195-212.

PTSD & PERSISTENT POST-CONCUSSIVE SYNDROME: OVERLAPPING SYMPTOMS



Additional Sleep Problems:

- Hypersomnia
- Sleep misperceptions
- Circadian disorders

SLEEP IN TBI & PTSD

- Few studies have compared individuals with co-occurring PTSD and TBI to those with TBI or PTSD only.
 - The overlap between TBI and PTSD combined with other confounding deployment- and post-deployment-related factors, present significant methodological challenges.
 - Sleep disturbance may also mediate the effect of mTBI on the development of PTSD and may be an early indicator of risk for PTSD and depression in blast-exposed Veterans.
(Macera et al., 2013)
 - Sleep problems may be an risk factor for development of PTSD or depression in TBI
(Maguen, Lau, Madden, & Seal, 2012).
 - Sleep problems can be considered a separate post-deployment health problem, distinct from PTSD, TBI, and depression (Maguen, Lau, Madden, & Seal, 2012).
- **Early identification and treatment of sleep disturbance may potentially prevent the development and improve the outcome of mental health disorders, such as PTSD.**

SLEEP & EVERYDAY FUNCTIONING IN VETERANS WITH TBI & PTSD

Part 2

SLEEP IN TBI

Sleep Problems Affect Recovery and Functional Status in Veterans with TBI:

- Exacerbate symptoms of TBI (pain, cognitive deficits, fatigue, irritability) (Ouellet & Morin, 2007)
- Increase neuropsychiatric symptoms (depression, apathy, anxiety) post-TBI (Rao et al., 2014)
- Impair cognitive (working memory) functioning (Bogdanova et al., 2013)
- Negatively impact participation & outcome in TBI treatment (Worthington & Melia, 2006)
- Independently predict poorer functional and social outcomes post mTBI (Chan & Feinstein, 2015)

SLEEP IN TBI

Impact of Sleep on Cognition in TBI

- Cognitive deficits (attention, concentration, and executive dysfunction) are the primary complaints post-TBI.
- Few studies have examined the association between poor sleep following TBI and cognition.
- There is evidence that these deficits may be exacerbated by poor sleep.
- Bloomfield and colleagues (2010) examined whether sleep difficulties exacerbate deficits in sustained attention following TBI:
 - Separated TBI participant into good and poor sleepers subgroups, based on both subjective and objective measures of sleep.
 - Poor sleepers performed significantly worse on measures of sustained attention.

SLEEP IN PTSD

Sleep Problems Affect Cognitive Function in PTSD:

- Few studies have examined specific components of cognitive difficulties in PTSD, including attention, executive function, and learning, with respect to poor sleep.
- One recent study demonstrated a relationship between sustained attention, verbal memory, and objectively measured sleep in PTSD.
- A full night's sleep (approximately 7 hours or greater) mitigated attention errors in PTSD.

SLEEP IN TBI & PTSD

Sleep Problems & Cognitive Function in TBI/PTSD:

- A large proportion of Veterans coming from the OEF/OIF/OND combat arenas present with both PTSD and mTBI.
- Approximately 40% of PTSD-mTBI Veterans report severe sleep disturbances (Wallace et al., 2011) and cognitive problems (Schiehser et al., 2011; Spencer, Drag, Walker, & Bieliauskas, 2010).
- The examination of the relation between their cognitive difficulties and sleep problems is particularly important.
- One study examined the relationship between sleep, PTSD symptom severity, daily cognition, and quality of life in OEF/OIF/OND Veterans with blast exposure and persistent cognitive complaints (Kark et al., 2013):
 - Veterans with PTSD had worse sleep on subjective and objective measures of sleep
 - Poor sleep was related to worse daily cognition, low level of community integration, and reduced satisfaction with quality of life.

SLEEP AND FUNCTIONAL STATUS

Sleep Problems Affect Recovery and Functional Status in Returning Veterans

- **Poor sleep independently predicts:**
 - development of depression (Baglioni et al., 2011; Jackson et al., 2014)
 - development of PTSD (Bryant et al., 2010; Gehrman et al., 2013)
 - changes in post-deployment depression and PTSD symptoms (Wright et al., 2011)
 - suicide risk in clinical and non-clinical populations (Pigeon et al., 2012; Ribeiro et al., 2012)
 - post-deployment community integration (Kark et al., 2013)
- **Poor sleep negatively impacts outcome in PTSD treatment.** (Nappi et al., 2012)

SLEEP AND FUNCTIONAL STATUS

Sleep and Everyday Functioning in Returning Veterans

- Veterans with sleep difficulties report ***lower quality of life*** and more ***severe fatigue, pain, PTSD, and depressive symptoms*** compared to those without sleep difficulties. (Lang, Veazey-Morris, & Andrasik, 2014; Wallace et al., 2011)
- Poor sleep quality was associated with ***PTSD, panic disorder, depression, suicidal ideation, and risky drinking behavior*** in Iraq/Afghanistan Veterans. (Swinkels et al., 2013)
- Sleep disturbances were more related to ***low satisfaction with life and post-deployment community integration*** than other symptoms of PTSD in returning Veterans with blast exposure (Kark et al., 2013).

SLEEP: ASSESSMENT & MONITORING

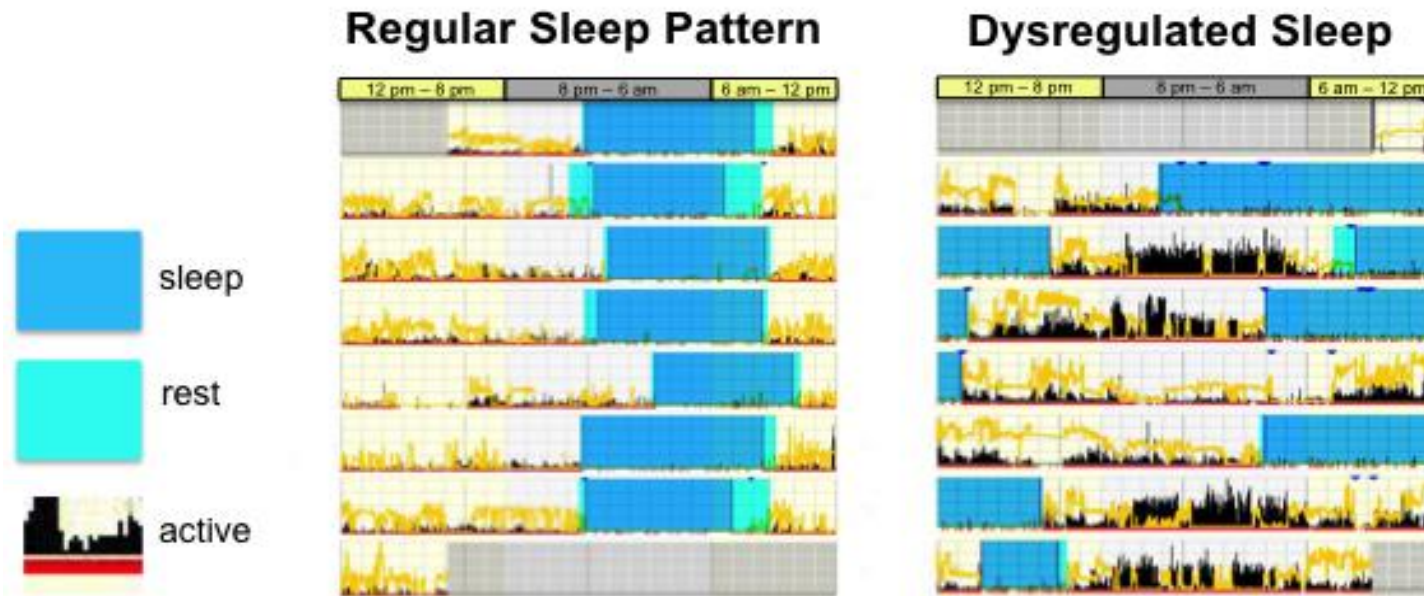
Part 3

SLEEP ASSESSMENT & MONITORING

Actigraphy:

- Objective measure of sleep quality
- Reliable indicator of global sleep parameters: total sleep time, sleep onset latency and sleep efficiency (Bloomfield et al., 2010; Sadeh & Acebo, 2002)
- Allows for more ecologically-valid data collection and prolonged sleep recording compared to polysomnography (PSG)
- Actigraph, a wrist-worn activity monitor with a built-in accelerometer, allows unrestrained registration of activity in patients' natural surrounding
- Useful tool for sleep evaluation and treatment monitoring

ACTIGRAPHY



Actigraphy readings collected for 7 days by an Actigraph (watch-accelerometer).

ACTIGRAPHY MEASURES

Actigraphy (ACT) Measure	Definition
Total Sleep Time (ACT Total Sleep Time), mins	Total time scored as sleep
Wake After Sleep Onset (ACT WASO), mins	Total time spent awake after sleep initiation and before final awakening
Sleep Efficiency (ACT Sleep Efficiency), %	Total Sleep Time/Total Time in Bed
Fragmentation Index	An index of restlessness measured by number of 1-min periods of immobility relative to the total number of immobility phases

SLEEP EFFICIENCY & PTSD

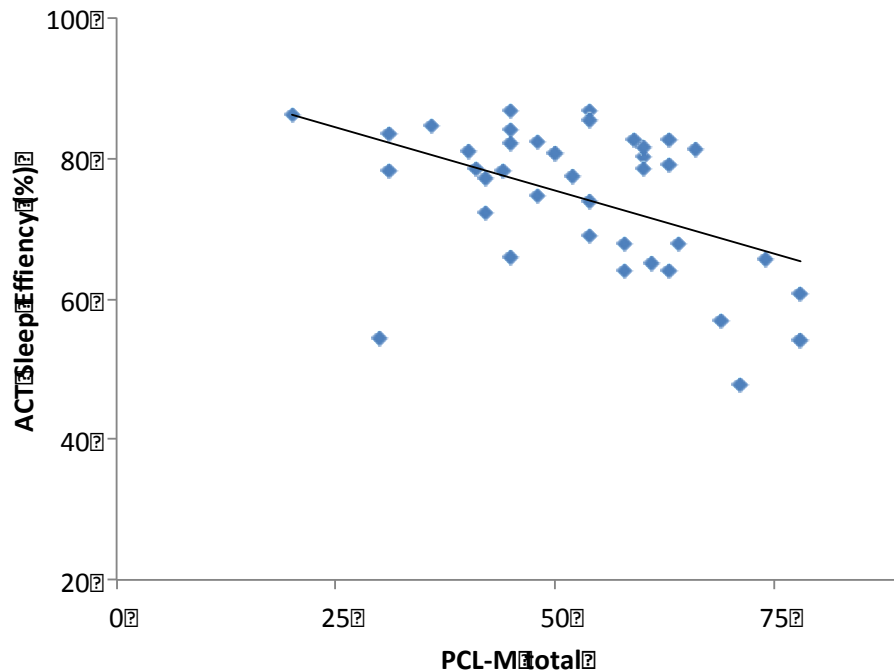
	All	PTSD	No PTSD	<i>p</i>
N	39	23	16	
PSQI total	12.0 (3.8)	13.3 (3.3)	10.1 (3.7)	0.009
ACT Total Sleep Time (m)	349.9 (70.7)	334.9 (76.1)	371.2 (57.7)	ns
ACT WASO (m)	42.4 (20.3)	42.2 (21.3)	42.2 (19.4)	ns
ACT Sleep Efficiency (%)	74.4 (10.3)	71.9 (10.8)	78.1 (8.4)	0.049
ACT Fragmentation Index	19.1 (7.4)	19.7 (6.7)	18.1 (8.4)	ns

PSQI - Pittsburgh Sleep Quality Index; ACT - Actigraphy

- Kark et al (2013) evaluated sleep in Veterans with blast exposure (N=39)
- Subjective (PSQI) and Objective (Actigraphy) sleep quality measures
- Found greater self report **sleep disturbance** [PSQI, Total] and **reduced Sleep Efficiency** [ACT-SE] in Veterans with PTSD (n=23) compared to no PTSD (n=16)

Sleep efficiency & ptsd

PTSD and ACT Sleep Efficiency



- PTSD symptom severity negatively correlated with ACT Sleep Efficiency ($p = 0.002$), but not Total Sleep Time (Kark et al., 2013)

It is important to evaluate the quality of sleep in patients with PTSD, as it may provide clinically important information.

SLEEP IN TBI & PTSD: Current Treatment Options

Part 4

SLEEP TREATMENT

Why is it important to treat Sleep Disorders in TBI and PTSD?

- Sleep is among the primary symptoms in TBI and PTSD and one of the mediating factors affecting the level of severity and treatment outcome of both conditions
- Poor sleep remains at clinical levels even after the resolution of mTBI or PTSD
- Sleep is critical for restorative processes and neural repair
- Sleep is important for cognitive, psychological and physical functioning

Few treatments & rehabilitation protocols target sleep as a primary symptom.

SLEEP TREATMENT

Sleep Interventions in TBI & PTSD

- Traditionally, treatment of sleep disorders has been rooted in pharmacology.
- However, pharmacologic treatment for sleep is not generally recommended in TBI:
 - Pharmacologic agents may negatively impact neural recovery following TBI
 - Side effects may further impair cognition and daytime alertness. (Larson & Zollman, 2010; Flanagan et al., 2007)
- Recently developed non-pharmacologic interventions have potential for treating sleep in TBI and TBI/PTSD:
 - Cognitive behavioral treatment for insomnia (CBT-I)
 - Neuromodulation (LED and TMS)

CURRENT GUIDELINES

- The current practice guidelines developed by the Standards of Practice Committee of the American Academy of Sleep Medicine recommend using ***psychological and behavioral interventions*** for the treatment of chronic primary insomnia (Standard) and secondary insomnia (Guideline) (Morgenthaler et al., 2007).
- No guidelines specific to treatment of sleep disorders following mTBI have been established (Marshall et al., 2012).
- Recommendations for sleep disorders have been adopted from current practice guidelines outside of the TBI field.
- Practice guidelines for incorporation of sleep interventions into management of PTSD are yet to be established (Germain et al., 2013).

NON-PHARMACOLOGIC INTERVENTIONS

Cognitive Behavioral Treatment for Insomnia (CBT-I)

Behavioral
Intervention

behavioral treatment for insomnia:

CBT-I

Cognitive Behavioral Treatment for Insomnia (CBT-I):

- A psychotherapeutic treatment (4-8 sessions) that has successfully treated insomnia principally in non-TBI populations.
- Utilizes *stimulus control*, *sleep restriction*, and *cognitive restructuring* techniques to alter and improve sleep behaviors and thoughts related to poor sleep. (Mitchel et al., 2012)
- In a CBT-I study with mild to severe TBI patients (n=11), sleep efficiency increased by an average of 13.7% from baseline to 3-month follow-up and reductions in sleep disturbance were associated with decreased fatigue. (Ouellet & Morin, 2007)
- However, the *cognitive restructuring* component of CBT-I **may be challenging** for a person with cognitive (attention, executive function) or self-monitoring deficits, which are frequently associated with TBI.

behavioral treatment for insomnia

Web-based, Tele-health & Computerized CBT-I delivery:

- There is emerging evidence that web-based CBT may be effective in improving the sleep and associated daytime functioning of adults with insomnia (Espie et al., 2012).
- Three recent studies demonstrated improved sleep in adults with chronic insomnia following:
 - up to 8 weekly sessions of telephone-delivered CBT-I (Arnedt et al., 2013) or
 - five weeks of computerized CBT-I (Vincent & Walsh, 2013) or
 - six weeks of unsupported, internet-delivered self-help CBT-I (Lancee, van den Bout, van Straten, & Spoormaker, 2012)
- That would be important to evaluate whether such protocols can be utilized in treating returning Veterans and military personnel.
 - One recent study reported efficacy of a behavioral intervention for insomnia in OEF/OIF/OND Veterans that involved: one in-person and three telephone sessions, as well as electronic delivery components (Epstein et al., 2013).

NEUROMODULATION: TMS

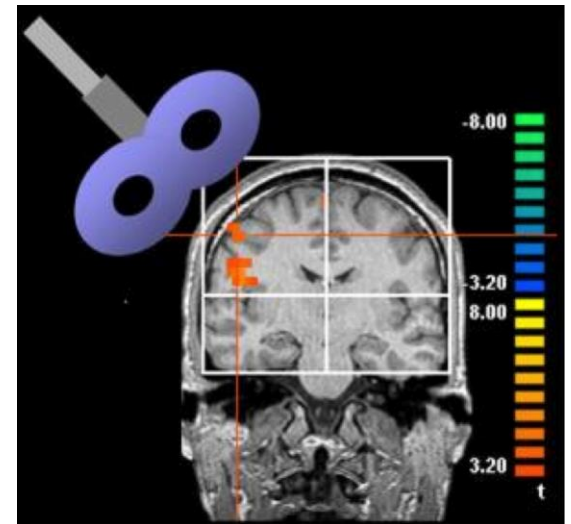
Transcranial Magnetic Stimulation (TMS)

Novel Intervention

NEUROMODULATION: TMS

Transcranial magnetic stimulation (TMS):

- Non-invasive way to stimulate specific brain areas through the scalp using magnetic fields.
- Stimulation of pre- and post- synaptic cells can increase the efficacy of synaptic transmission, which is an underlying principle of the modulating effects of TMS. (Pascual-Leone et al., 2011)
- TMS may target multiple symptoms and enable more successful treatment of patients with mTBI, PTSD and depression.



Neuroimaging-guided TMS

NEUROMODULATION: TMS

TMS for neuropsychiatric symptoms in TBI & PTSD

Therapeutic application of repetitive (r)TMS:

- Depression (reviewed in Rossi et al, 2009)
- PTSD (Boggio et al., 2010; Cohen et al., 2004; Watts et al., 2012)
- mTBI cognitive symptoms (Bogdanova et al., 2015a).
- Sleep disturbance in Veterans with blast TBI & PTSD (Bogdanova et al., 2015b):
 - Double-blind, randomized controlled pilot efficacy study
 - A series of daily rTMS sessions for 1-week
 - Improvement in sleep quality and a significant reduction in PTSD symptoms
 - Further controlled studies are needed to evaluate the effect of this neuromodulation intervention on sleep in TBI and PTSD

NEUROMODULATION: LED

Red / NIR Light-emitting Diode (LED) Therapy

Novel Intervention

NEUROMODULATION: LED

Low-Level Light Therapy: Light-emitting diode (LED) therapy

- LED is a non-invasive, portable and relatively inexpensive treatment modality.
- LED is a painless, non-thermal neuromodulation treatment that directly targets cellular functioning of injured brain cells.
- *Therapeutic utility* of LED treatment has been demonstrated in psychiatric (depression) and neurologic disorders (mild to moderate TBI; Naeser et al., 2014), and rehabilitation (rev. in Hashmi et al., 2010).



SLEEP TREATMENT WITH LEDS

There is emerging evidence for the therapeutic utility of LED treatment for:

- Sleep in healthy adults (Zhao et al., 2012)
- Insomnia (Xu et al., 2002).
- Sleep in patients with moderate chronic TBI (Bogdanova et al., 2014, 2015)
- Cognitive function in chronic TBI (Naeser et al., 2011; Naeser et al., 2014).
- Mood and PTSD symptomatology in moderate chronic TBI (Naeser et al., 2011; Naeser et al., 2014; Bogdanova et al., 2015)

LED Therapy Intervention:

- Non-thermal neuromodulation device
- Treatment schedule: 18 sessions (3x/week for 6 weeks)



Red/NIR Transcranial
LED cluster head



Actiwatch

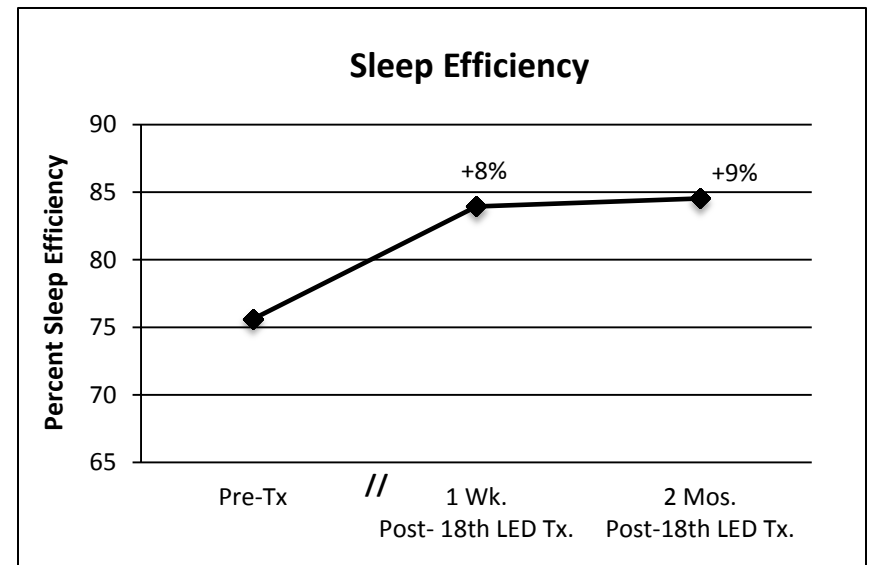
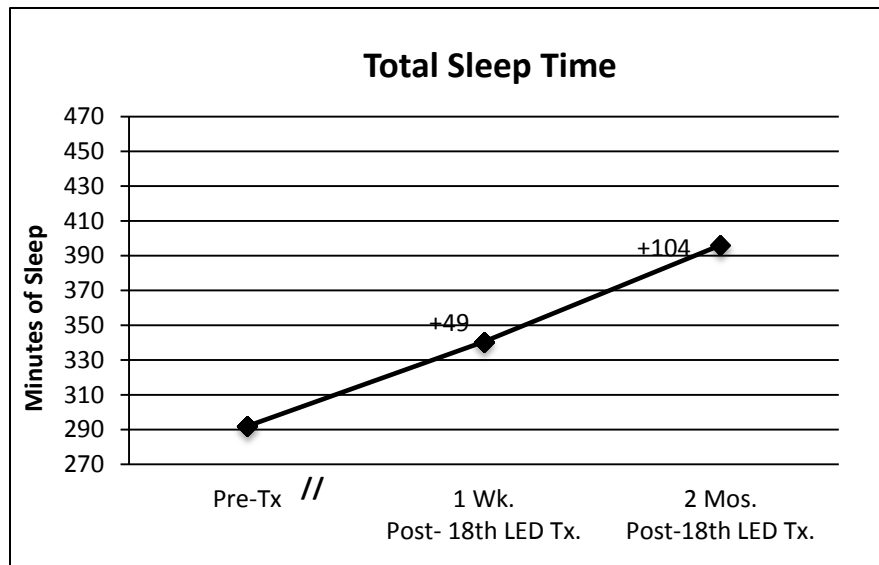
SLEEP TREATMENT WITH LEDS

- **Recent pilot LED treatment trials reported:**
 - Improvement in sleep and other TBI associated symptoms in chronic mild and moderate TBI (Bogdanova et al., 2014; 2015).
 - Improved sleep and PTSD symptoms following the red/near infra-red ***transcranial*** LED treatment in patients with chronic moderate TBI and comorbid PTSD (Bogdanova et al., 2014).
- Results suggest that sleep efficiency (measured with actigraphy) can be changed by transcranial LED treatment in patients with chronic TBI:
 - sleep efficiency increased one week post-LED treatment and
 - was maintained at 2-month follow-up.

TRANSCRANIAL LED TREATMENT, CASE 1

Actigraphy Sleep Data

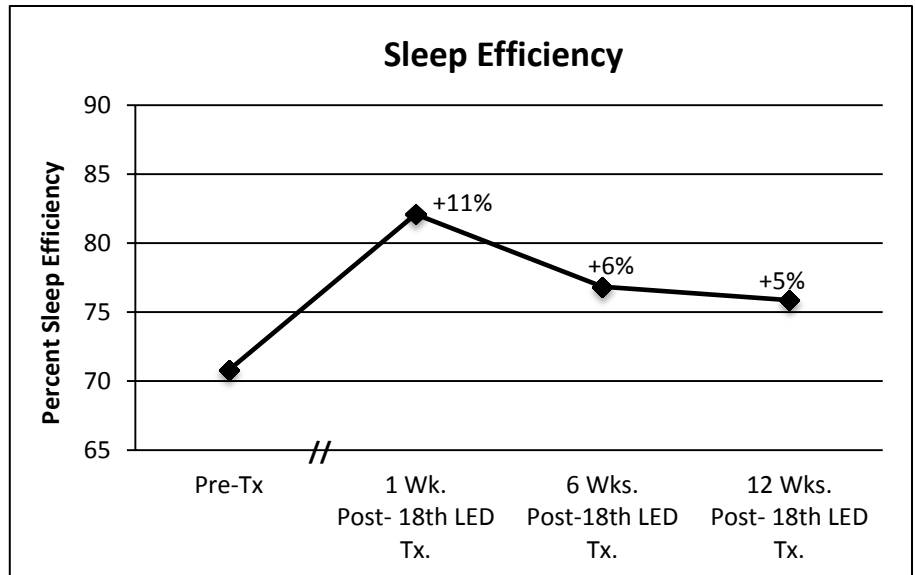
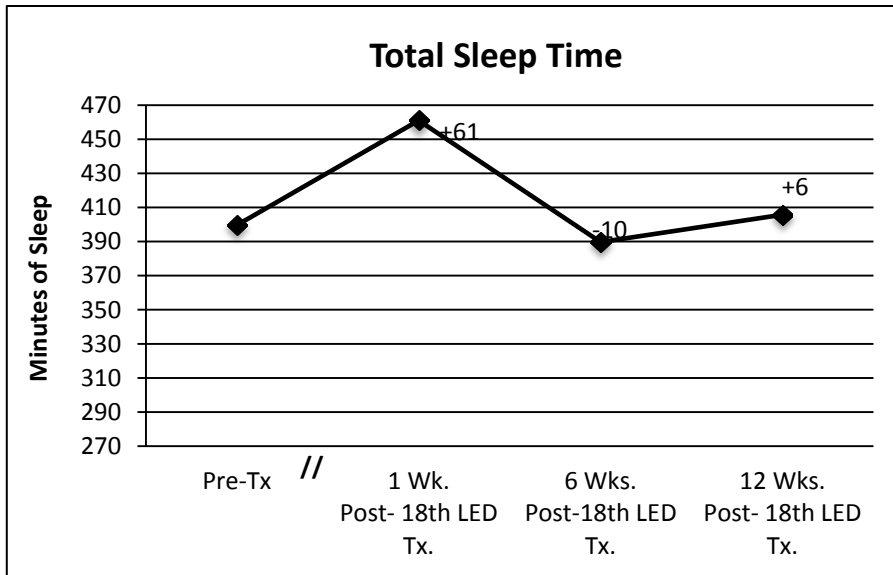
23 Yr M Non-veteran with Moderate TBI
13 Mo. Post- Bicycle/Car Accident
Pre- and Post- 18 Transcranial LED Treatments



INTRANASAL LED TREATMENT, CASE 2

Actigraphy Sleep Data

24 Yr F Non-veteran with Mild TBI
3 Yrs Post- most recent TBI (4 Sports related Concussions)
Pre- and Post- 18 Intranasal LED Treatments



SLEEP TREATMENT: CHALLENGES & FUTURE DIRECTIONS

Part 5

Part 5

CHALLENGES

- Despite its high prevalence, few treatments and rehabilitation protocols target sleep as a primary symptom.
- Patients with dual diagnosis of PTSD and TBI have difficulty with treatment compliance (PTSD symptoms, executive functioning deficits).
- There are no evidence-based treatment protocols available to address the multiple cognitive and sleep problems in Veterans with TBI and PTSD.
- There is a need for research to identify best practices for treatment of patients with mTBI and associated comorbidities, such as PTSD and sleep disturbance (Report of VA Consensus Conference, 2010).

Multimodal therapeutic approach

Combined Interventions:

- Neuromodulation treatment combined with behavioral intervention may provide an enhanced ***multimodal therapeutic approach***, specifically tailored to address multiple issues: sleep problems, TBI and PTSD.
- Combined interventions have potential to:
 - ***enhance*** efficacy of sleep treatment in TBI and comorbid PTSD
 - ***reduce*** PTSD symptoms
 - ***promote*** recovery after TBI
 - ***optimize*** outcome in injured returning Veterans



FUTURE DIRECTIONS

CLINICAL:

- Evaluation and treatment of sleep problems in TBI and PTSD should become an integral part of clinical management of these disorders.
- Using non-pharmacological interventions and neuromodulation techniques to enhance the treatment and promote recovery in Veterans with TBI and PTSD.

RESEARCH:

- Future research efforts should target the development of sleep-focused interventions and multi-modal treatment programs adjustable to the specific needs of Veterans with multiple comorbidities, such as TBI, PTSD, and sleep disturbance.
- RCTs to investigate specific effects of neuromodulation and combined interventions on sleep and other neuropsychiatric symptoms in Veterans.

Questions/Comments?

Thank You!

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