

Returning to form: Factors affecting sleep disturbance duration and recovery following traumatic brain injury



Nicholas R. Griffin¹, Emerson Wickwire², David M. Schnyer¹, Wayne A. Gordon³, Pratik Mukherjee⁴, David O. Okonkwo⁵, Alex B. Valadka⁶, Mary Vassar⁴, John Yue⁴, Geoffrey T. Manley⁴

1. The University of Texas at Austin. 2. University of Maryland. 3. Icahn School of Medicine at Mount Sinai, New York, NY. 4. University of California, San Francisco. 5. University of Pittsburgh. 6. Virginia Commonwealth University.

Introduction

- After traumatic brain injury (TBI), 40 to 75 percent of patients suffer from newly arising sleep disturbances¹⁻⁴
- Sleep disturbances include increased sleep time (hypersomnia) or decreased sleep time (trouble falling asleep)^{5,6}.
- While most sleep disturbances decrease in the time following injury, up to 25% of patients report sustained sleep disturbances after 1 year or more^{3,7}.
- Depression and anxiety are often comorbid with post-TBI sleep disturbances, and have been observed to exacerbate each other over time⁸.
- We aim to further examine the relationship between post-TBI sleep disturbances and comorbid mood disturbances.
- Hypotheses:
 - 1. Sleep disturbance at 6 month follow up is positively associated with injury severity.
 - 2. Comorbid depression/anxiety will inhibit recovery from sleep disturbances.

<u>Methods</u>

Participants

- 286 adults were selected from a total of 599 participants consented 200 male, mean age = 43.04, SD = 17.62, fluent English speakers.
- Recruitment from four nationwide Level 1 trauma centers within 24 hours of injury.
- Inclusion criteria: 18+ years of age, acute brain CT, ability to provide consent.
- Exclusion criteria: pregnancy, incarceration, significant physical trauma, debilitating mental health disorders or neurological disease, MRI contraindications, pre-existing conditions which interfere with assessments (see Fig 1).

Measures

- Demographic and injury severity were assessed at hospital intake.
- Outcome assessment (OA) measures collected 3- and 6 months post-injury.

Injury Severity Measures

- Glasgow Coma Scale (GCS): Measures level of consciousness, from 3 (most severe injury) to 15 (normal function).
 - Scores ≥ 13 are classified as mTBI, scores < 13 classified as TBI.
- Injury Severity Score (ISS): Index of physical injury, from 1 (least severe) to 75 (most severe).

Outcome Measures

- Glasgow Outcome Scale Extended (GOSE): 8-point Likert scale ranging from 1 (death) to 8 (upper good recovery).
- Brief Symptom Inventory 18 (BSI-18): Assessment of psychological distress across the global severity index (GSI), and depression, anxiety, and somatization sub-scores.

 Total Number of Participants Consented:
 Reason for Exclusion from Analyses
 Missing Arrival GCS
 Attrition = 3 Mo
 - Collected at 6 month follow up.
- Sleep Disturbances: Binary reports of 4 sleeprelated complaints after injury, assessed at 3 month and 6 month follow-ups, including:
 - Sleeping Less Than Usual
 - Sleeping More Than Usual
 - Trouble Falling Asleep
 - Diurnal Drowsiness

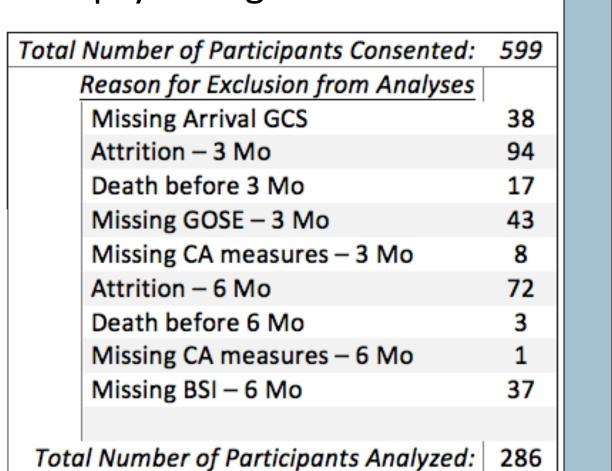


Figure 1. Reasons and counts for participant exclusions

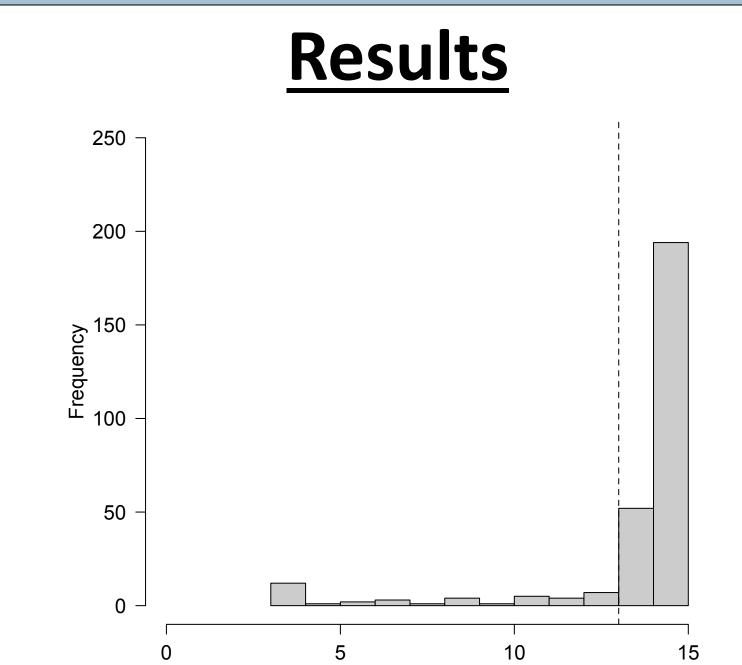


Figure 2. Distribution of GCS scores.

- GCS (overall mean: 13.84, SD = 2.79) classified 254 mTBI and 32 TBI.
- Because of the high number of mild TBI patients, the main analyses focus only on the mTBI group.

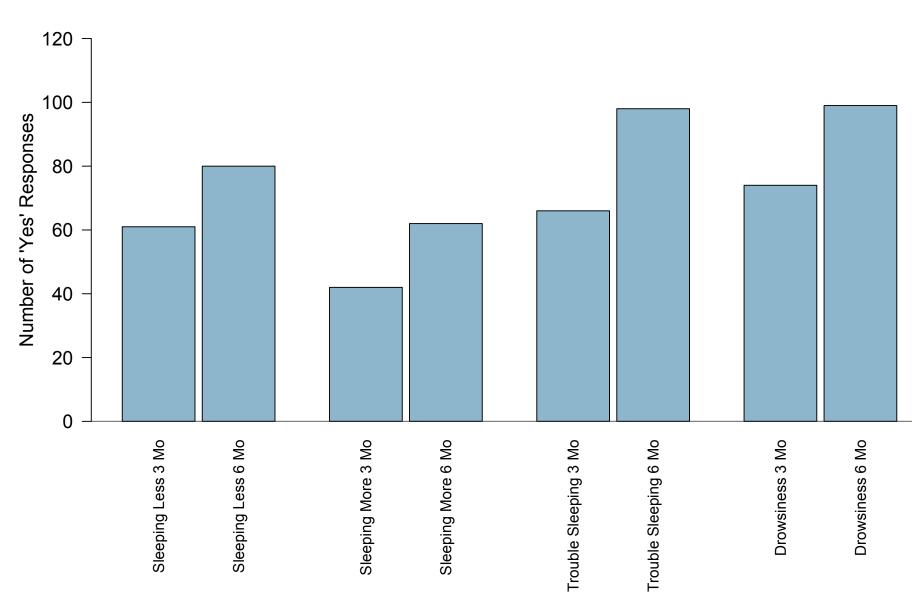


Figure 3. Number of "Yes" responses to each of the sleep disturbance measures.

• Significantly greater proportion of participants report each of the sleep disturbances at 6 months than at 3 months ($\chi^2(1, N=254) < 4.3$, p's < .04).

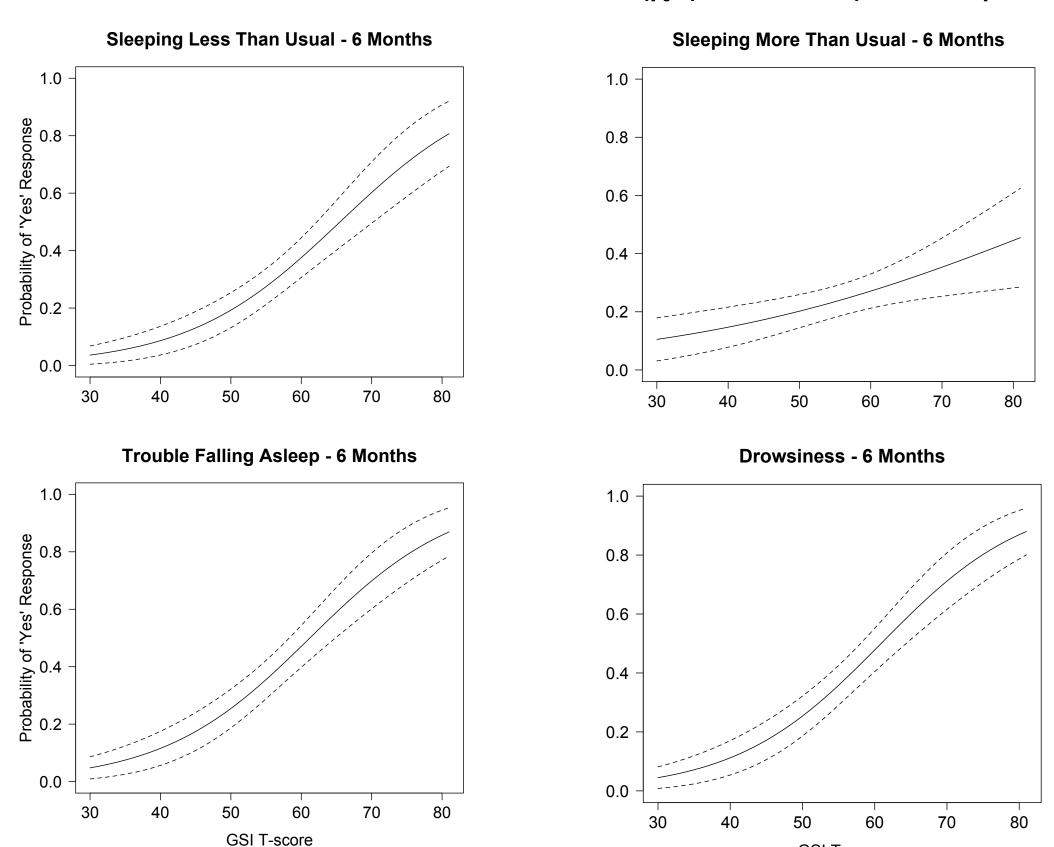


Figure 4. Probability of "Yes" responses to sleep disturbance measures by TBI group and GSI t-score.

- Increasing GSI significantly predicts increasing depression, anxiety, and somatization BSI-18 sub-scores (r(284) > .83, p's < .001). Thus, the GSI was the sole measure of psychopathology used in subsequent models.
- Increasing GSI significantly predicts increasing probability of all sleep disturbance measures at 6 months post-injury (b's > .03, z's > 2.43, p's < .02).

Results (continued)

GSI Mediation Models

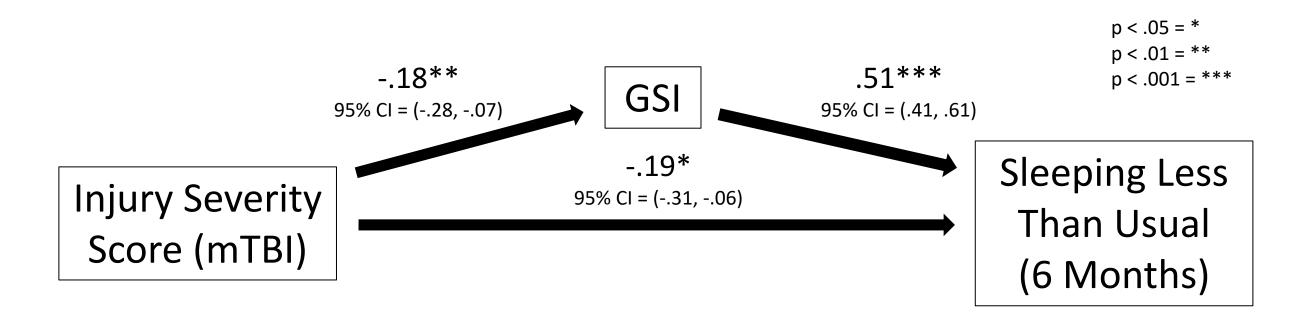


Figure 5. Mediation of GSI on the relationship between ISS and Sleeping Less Than Usual.

- Significant independent negative prediction of ISS on Sleeping Less Than Usual at 6 months post-injury for mTBI participants (b = -.05, z = -3.03, p = .002).
- Effect of ISS on Sleeping Less Than Usual is partially mediated by GSI.

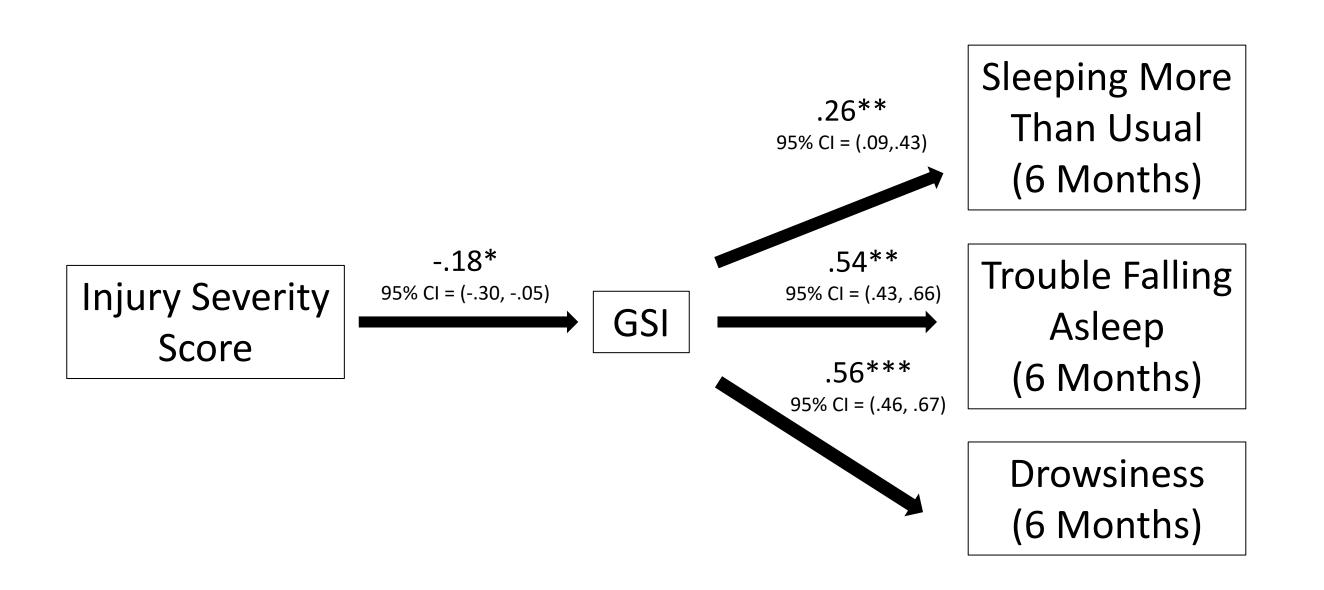


Figure 6. Effect of ISS on GSI, and subsequent effects of GSI on Sleeping More Than Usual, Trouble Falling Asleep, and Drowsiness.

- No independent predictions of increased ISS on increases in remaining 6-month post-injury sleep disturbance measures were significant (b's < .06, z's < 1.45, p's > .15).
- ISS negatively predicts GSI, which significantly predicts increased reports of Sleeping More Than Usual, Trouble Falling Asleep, and Drowsiness.
- Mediation models including direct unidirectional paths from ISS to each sleep disturbance measure were conducted, each returning non-significant results for the direct ISS to sleep disturbance paths (b's < -.03, z's < 1.56, p's > .12).

Discussion

- With the exception of ISS significantly predicting Sleeping Less Than Usual in mTBI participants, injury severity did not directly predict sleep disturbances.
- Reports of sleep disturbances increased over time for mild TBI patients as overall physical outcomes simultaneously improved.
- Global Severity Index of psychological distress mediated the models predicting sleep disturbance support of depression perpetuating sleep disturbances.
- Greater awareness of injury-related deficits TBI patients may have given rise to increased GSI and sleep disturbance¹⁰.

References

1. Mathias, J. L. & Alvaro, P. K. Prevalence of sleep disturbances, disorders, and problems following traumatic brain injury: A meta-analysis. *Sleep Med.* (2012). doi:10.1016/j.sleep.2012.04.006
2. Parcell, D. L., Ponsford, J. L., Rajaratnam, S. M. & Redman, J. R. Self-reported changes to nighttime sleep after traumatic brain injury. *Arch. Phys. Med. Rehabil.* (2006). doi:10.1016/j.apmr.2005.10.024
3. Mahmood, O., Rapport, L. J., Hanks, R. A. & Fichtenberg, N. L. Neuropsychological Performance and Sleep Disturbance Following Traumatic Brain Injury. *J Head Trauma Rehabil* 19, 378–390 (2004).
4. Williams, B. R., Lazic, S. E. & Ogilvie, R. D. Polysomnographic and quantitative EEG analysis of subjects with long-term insomnia complaints associated with mild traumatic brain injury. *Clin. Neurophysiol.* (2008) doi:10.1016/j.clinph.2007.11.003.

5. Orff, H. J., Ayalon, L. & Drummond, S. P. A. Traumatic Brain Injury and Sleep Disturbance: A Review of Current Research. *J Head Trauma Rehabil* 24, 155–165
6. Ayalon, L., Borodkin, K., Dishon, L., Kanety, H. & Dagan, Y. Circadian rhythm sleep disorders following mild traumatic brain injury. *Neurology* (2007). doi:10.1212/01.wnl.0000258672.52836.30
7. Parcell, D. L., Ponsford, J. L., Redman, J. R. & Rajaratnam, S. M. Poor Sleep Quality and Changes in Objectively Recorded Sleep After Traumatic Brain
8. Wickwire, E. M. *et al.* Sleep, Sleep Disorders, and Mild Traumatic Brain Injury. What We Know and What We Need to Know: Findings from a National Working Group. *Neurotherapeutics* (2016). doi:10.1007/s1331

9. Shekleton, J. et al. Sleep disturbance and melatonin levels following traumatic brain injury.

10. Baumann, C. R., Werth, E., Stocker, R., Ludwig, S. & Bassetti, C. L. Sleep-wake disturbances 6 months after traumatic brain injury: A prospective study. Brain (2007). doi:10.1093/brain/awm109

