



**Sleep and Mild Brain Injury  
Clinical and Research Updates**

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## SLEEP RESPONSE TO MTBI: WHO, WHAT, WHY

> *J Neurotrauma*. 2022 Jan;39(1-2):172-180. doi: 10.1089/neu.2021.0295. Epub 2021 Nov 23.

### Characterizing Sleep and Wakefulness in the Acute Phase of Concussion in the General Population: A Naturalistic Cohort from the Toronto Concussion Study

Catherine Wiseman-Hakes <sup>1,2</sup>, Evan Foster <sup>1,3</sup>, Laura Langer <sup>1</sup>, Tharshini Chandra <sup>1</sup>, Mark Bayley <sup>1,4</sup>, Paul Comper <sup>1,5</sup>

Affiliations + expand  
PMID: 34714132 DOI: [10.1089/neu.2021.0295](https://doi.org/10.1089/neu.2021.0295)

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## WHO, WHAT, WHY

### Who?

- In the acute stage (up to one week post) ; > 80% report immediate changes in sleep
- Females more severe than males (but a universal response)

### What?

- Increased sleep need, reduced day-time wakefulness
- Associated with headaches, ( $r=0.43$ ,  $p < 0.0001$ ), overall pain ( $r=0.42$ ,  $p < 0.0001$ )

### Why?

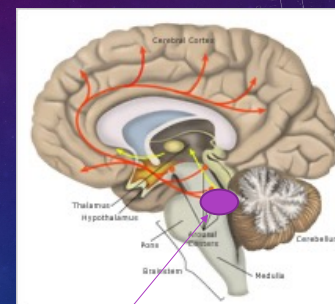
- Two possible underlying mechanisms
  - Biomechanical
  - Neuroprotective

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## BIOMECHANICAL INJURY

- Mechanism of injury during a TBI/concussion creates biomechanical forces exerted on the head and neck which can lead to transient or permanent physiological changes in the brain.
- Hypothalamus is particularly vulnerable to injury which can lead to alterations in the sleep-wake cycle and sleepiness
- Three key structures involved in the sleep wake system are particularly vulnerable to injury



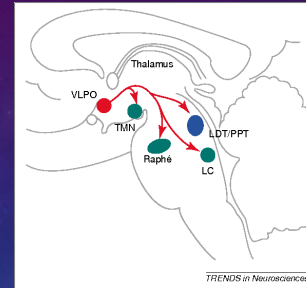
Locus Coeruleus: Maintaining alertness, vigilance: Ascending arousal system

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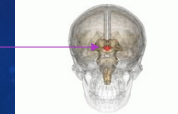
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## BIOMECHANICAL INJURY AFFECTS THE THALAMUS AND HYPOTHALAMUS

- **The Locus Coeruleus:**
- **The Ventral Lateral Pre-optic Nucleus (VLPO):**
- **Pineal Gland:** responsible for production and release of melatonin



VLPO  
Nucleus..  
Maintaining sleep



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## NEUROPROTECTIVE: WHY SLEEP IS IMPORTANT FOR RECOVERY


- Changes in sleep immediately following a concussion (or brain injury of any severity) may also be neuroprotective: Why?
- Brain's glucose is replenished during slow wave sleep, and, 2.The brains' actual glucose requirements during sleep are significantly less
- Metabolic Cascade: The initial ionic flux and glutamate release result in significant energy(glucose) demands and a period of metabolic crisis for the injured brain. (Giza and Hovda 2014)
- Quantitatively, cerebral glucose metabolic rates are 11% lower in stage 2 sleep (Maquet 1992) and ~ 40% lower in slow wave sleep (Maquet 1990) as compared to resting wakefulness.

Wiseman-Hakes et al. 2022 <https://pubmed.ncbi.nlm.nih.gov/34714132/>

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## WHO IS AT RISK: CURRENT FINDINGS FROM OUR LAB



The Hull-Ellis Concussion  
and Research Clinic

- By **8 weeks** post mTBI, those whose sleep will return to 'normal', i.e. pre-injury sleep, are typically on a recovery trajectory. (n=221, 66% female).
- Those at risk include:
  - Females ( $p < 0.01$ ): It's Physics! Biomechanics, body weight & size, vulnerability of the neck
  - History of pre-injury depression ( $p < 0.01$ )
  - Concurrent neck pain ( $p < 0.01$ )

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## LONGER TERM PERSISTENT SLEEP DISORDER: RISK AND CONTRIBUTING FACTORS

- Neck issues
- Chronic neuroinflammation (Zheng et al, 2022 Frontiers in Immunology)
- Mood (Wiseman-Hakes et al., 2015)
- Presence of (or development of) Obstructive Sleep Apnea
- Circadian Rhythm Sleep Phase Shift (Zalai et al., 2020 CMA Open Access)
- Reduced Melatonin production (Duclos et al., 2013, Grima et al, 2018).
- Interested readers see:
  - Toccalino, Wiseman-Hakes & Zalai, 2021  
<https://pubmed.ncbi.nlm.nih.gov/33843391/>
  - Wickwire et al. 2016 <https://link.springer.com/article/10.1007/s13311-016-0429-3>

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## CONSIDERATIONS FOR NON-PHARMACOLOGICAL MANAGEMENT

- Currently, there is no gold standard protocol (either pharmacological or non-pharmacological) for the treatment of insomnia after mTBI (or TBI of any severity for that matter)
- Anecdotally, pharmacological interventions are not well tolerated and have negative side-effect such as fatigue, day-time sleepiness, reduced alertness, cognitive 'dulling'
- Zopiclone (eszopiclone), often prescribed, is contra-indicated with opioids, and also has withdrawal effects. Furthermore, it may help initially with 'falling asleep', however has not been found to be efficacious in maintaining sleep over time
- A non-pharmacological, individualized approach should be considered

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## EVIDENCE BASED NON PHARMACOLOGICAL MANAGEMENT

- Assessment and management of neck/whiplash issues and associated soft tissue injury
- Sleep hygiene
- Yoga Nidra and Meditation (Rush 2019, Barrett 2020)
  - <https://www.sciencedirect.com/science/article/pii/S2666354622000114?via%3Dihub>
  - <https://sleep.biomedcentral.com/articles/10.1186/s41606-017-0009-4>
- Looking to the Gut Microbiome
  - <https://www.frontiersin.org/journals/psychiatry/articles/10.3389/fpsyt.2019.00164/full>

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## EVIDENCE BASED NON-PHARMACOLOGICAL MANAGEMENT

Mood and Stress Management: reducing oxidative stress and the neuroinflammatory cascade

- Breathwork <https://pubmed.ncbi.nlm.nih.gov/35213875/>
- <https://pubmed.ncbi.nlm.nih.gov/25234581/>
- Acupuncture:
  - <https://www.ncbi.nlm.nih.gov/pmc/articles/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3156618/>
  - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7658634/>
- Anti-inflammatory diet: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7658634/>
- Dietary Supplements
  - Magnesium and Zinc <https://pubmed.ncbi.nlm.nih.gov/21226679/>
  - Ashwagandha <https://pubmed.ncbi.nlm.nih.gov/32818573/>
  - Melatonin (BUT... it is NOT a sleep aid... AND there are vast differences in quality and bioavailability) <sup>11</sup>

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