Traumatic Brain Injury and Sleep

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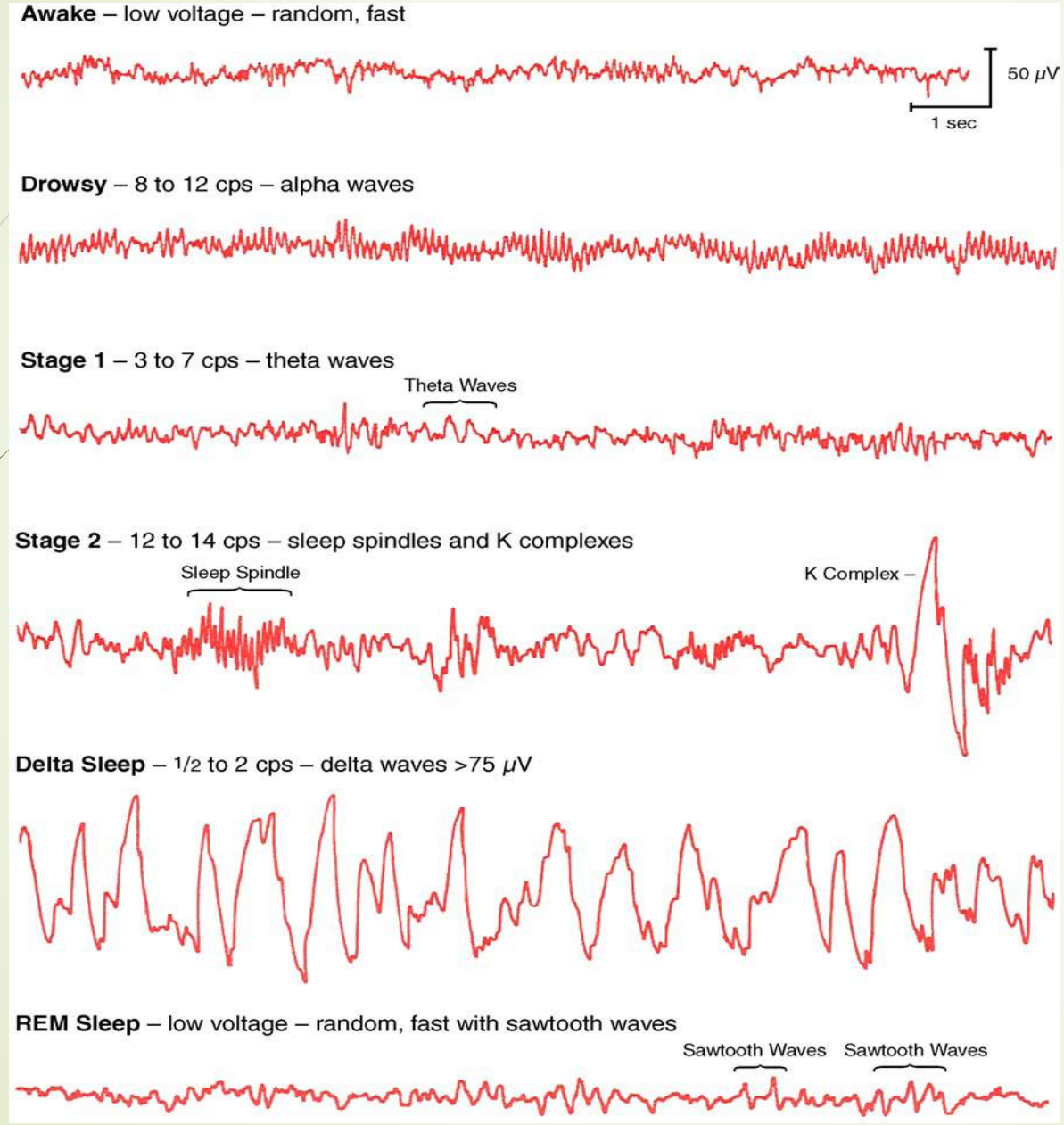
Disclosures

- Neurology
  - None
- Sleep Medicine
  - Advisory Board Honorarium- Eisai

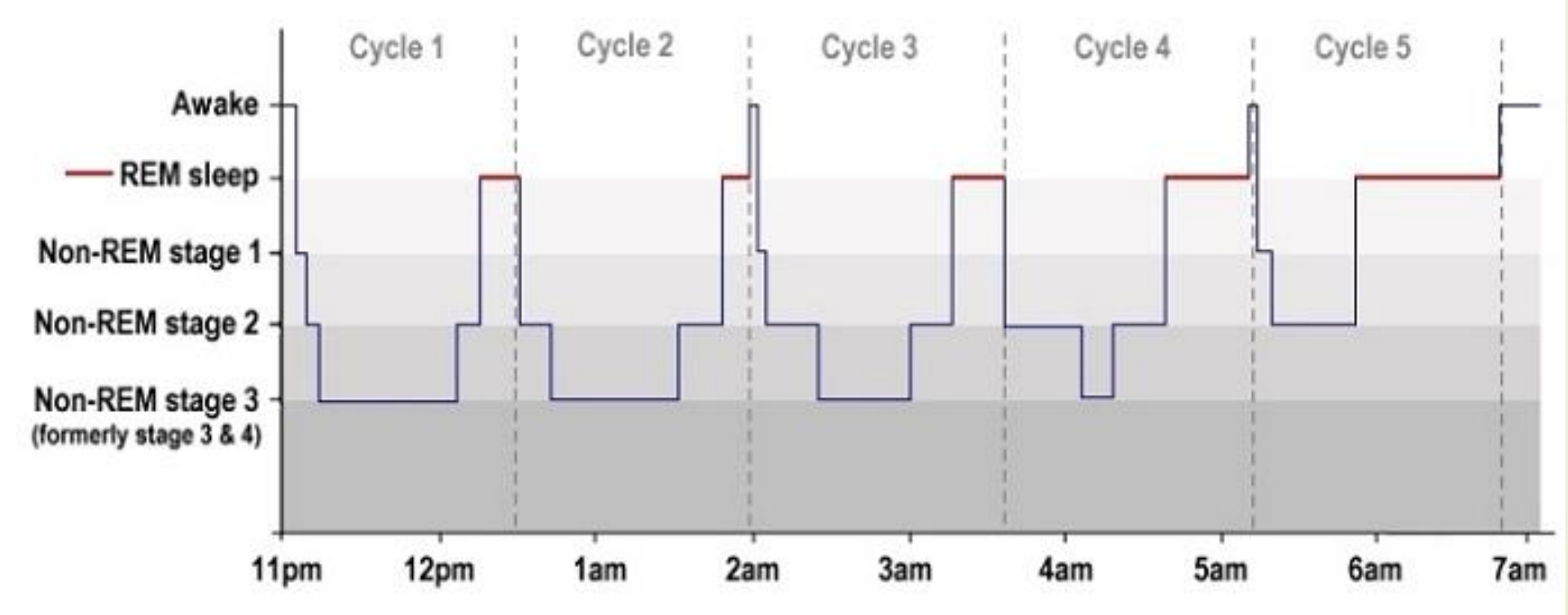
Objectives

- *At the end of this session, participants will be able to:*
  - Understand the basics of sleep physiology
  - Identify sleep disorders in the TBI population
  - Formulate an initial treatment plan for common sleep disorders

Behavioural States



Sleep Architecture



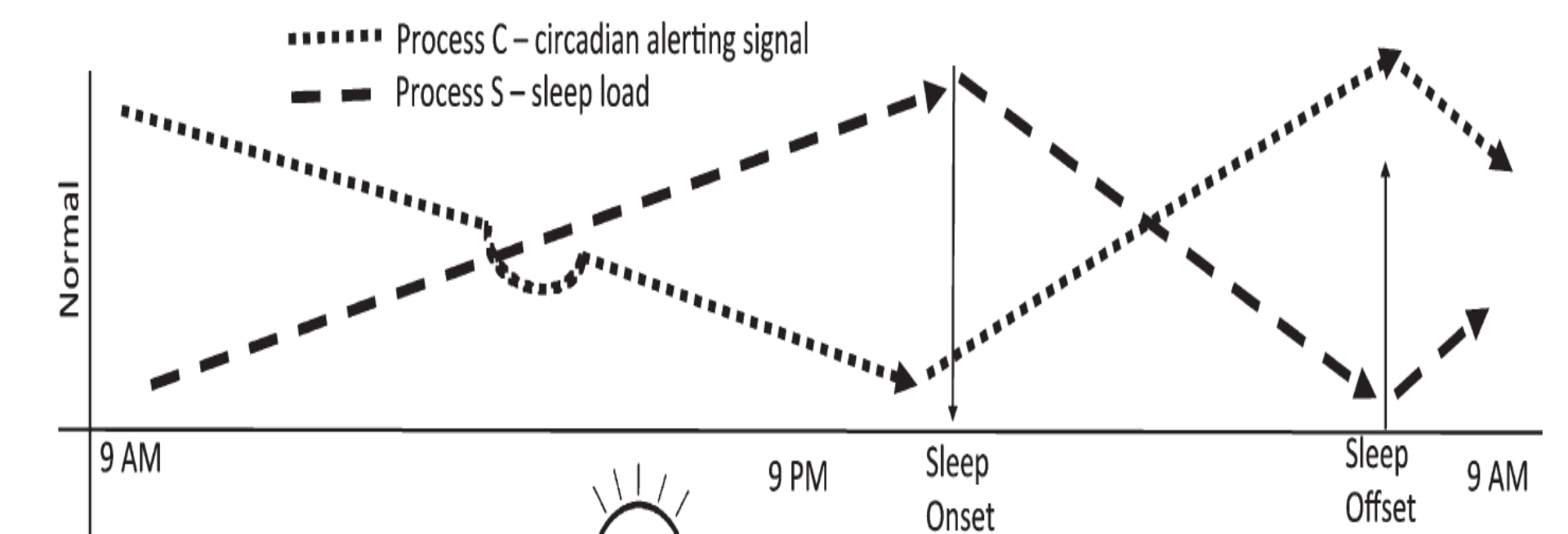
Impact of TBI on sleep architecture

Sleep parameter	Definition	Change in TBI
Wake after sleep onset (WASO)	Total awake time after initially falling asleep	Increased
Sleep efficiency	Time asleep/time in bed	Decreased
Sleep latency	Time to sleep onset	Increased
REM latency	Time to REM onset	Unchanged
Total sleep duration	Total time asleep	Decreased
N1 (5% of sleep)	Drowsy, Theta waves (4–7 Hz)	Unchanged
N2 (50% of sleep)	Sleep spindles and K-complexes	Unchanged
N3 (SWS, 15–25% of sleep)	"Deep" sleep, Delta waves (<4 Hz), Parasomnias occur	Increased
REM (20–25% of sleep)	Unregulated body temperature, motor inhibition, EEG similar to awake, rapid eye movements	Decreased

Seenivasan S, Kiley D, Kile M, Werner JK Jr. Sleep-Wake Disorders After Traumatic Brain Injury: Pathophysiology, Clinical Management, and Future. Semin Neurol. . 2025;45(3):383-400. doi:10.1055/a-2605-8706

Sleep Regulation

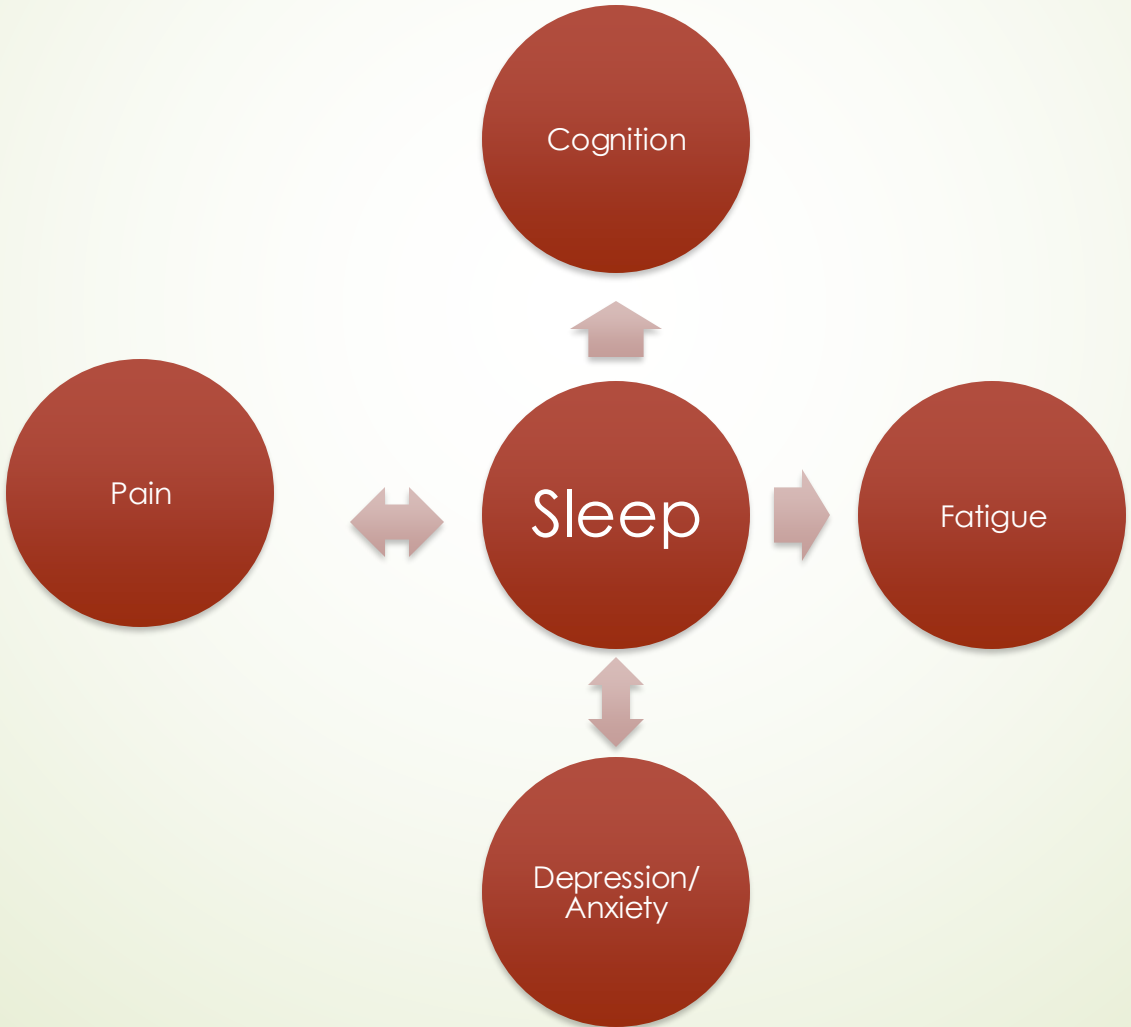
- Homeostasis (process S)
  - Sleep debt
- Circadian rhythm (process C)
  - Internal clock



Why Do We Sleep (meta-theories)?

- Ecological hypothesis
  - Rest when continued activity has decreased survival value thereby optimizing the timing/duration of behaviour
- Sleep as rest
  - Energy conservation
- Sleep as neuronal detoxification and restitution
  - Sleep removes toxins and metabolic waste
  - REM sleep involved in active mood regulation
- Learning and memory consolidation
  - REM sleep contributes to memory consolidation by cortical activation
  - Redistribution of representations during NREM sleep
- Neural network maintenance
  - Reverse learning through REM sleep
  - Strengthening of infrequently used synapses
- Immunological theory of sleep
  - Post-vaccination sleep increases immune competence
  - Chronic sleep restriction associated with low grade inflammation

Sleep influences other domains



Sleep Disorders are Common

- Sleep disturbance is frequent ~ 50-70% of TBI patients
- Sleep disorders are more common in TBI (compared to general population)

SWD	Prevalence	Prevalence TBI
Obstructive sleep apnea (OSA)	1.2–19%	23%
Central sleep apnea (CSA)	0.4%	Unknown
Insomnia	5–15%	30–65%
Pleiosomnia	NA	11–25%
Excessive daytime sleepiness (EDS) ESS > 10	5–15%	25–47%
Narcolepsy[a]	0.056%	3–4%
Restless legs syndrome (RLS)	5.5%	Unknown
Periodic limb movements of sleep (PLMS)	4–11%	7–25%
REM behavior disorder	1–7%	13%
Circadian rhythm disorder	0.2–10%	11–23%

Seenivasan S, Kiley D, Kile M, Werner JK Jr. Sleep-Wake Disorders After Traumatic Brain Injury: Pathophysiology, Clinical Management, and Future. Semin Neurol. . 2025;45(3):383-400. doi:10.1055/a-2605-8706

- Nightmares- 27% (8%)

Mathias JL, Alvaro PK. Prevalence of sleep disturbances, disorders, and problems following traumatic brain injury: a meta-analysis. Sleep Med. 2012;13(7):898-905.

Sleep Disorders

- Insomnia- difficulty sleeping when one wants to be asleep
- Hypersomnia- difficulty staying awake when one wants to be awake
- Parasomnia- abnormal/unwanted behaviours in sleep

TABLE 1] ICSD-3 Major Diagnostic Sections

Section
Insomnia
Sleep-related breathing disorders
Central disorders of hypersomnolence
Circadian rhythm sleep-wake disorders
Parasomnias
Sleep-related movement disorders
Other sleep disorders

ICSD = *International Classification of Sleep Disorders*.

Insomnia (Symptom vs. Disease)

- Insomnia
  - Difficulty initiating sleep
  - Difficulty maintaining sleep
- mTBI > moderate-severe TBI
- 46% of mTBI patients reported insomnia that persisted beyond 6 months (Questionnaire based study: Haboubi, Long, Koshy,&Ward, 2001)

TABLE 2] Insomnia

Disorder
Chronic insomnia disorder
Short-term insomnia disorder
Other insomnia disorder

Chronic Insomnia Disorder

- (A) The patient reports, or the patient's parent or caregiver observes, one or more of the following:
  - Difficulty initiating sleep
  - Difficulty maintaining sleep
  - Waking up earlier than desired
  - Resistance to going to bed on appropriate schedule
  - Difficulty sleeping without parent or caregiver intervention
- (B) The patient reports, or the patient's parent or caregiver observes, one or more of the following related to the night-time sleep difficulty:
  - Fatigue/malaise
  - Attention, concentration, or memory impairment
  - Impaired social, family, occupational, or academic performance
  - Mood disturbance/irritability
  - Daytime sleepiness
  - Behavioural problems (e.g., hyperactivity, impulsivity, and aggression)
  - Reduced motivation/energy/initiative
  - Proneness to errors/accidents
  - Concerns about or dissatisfaction with sleep
- (C) The reported sleep-wake complaints cannot be explained purely by inadequate opportunity (i.e., enough time is allotted for sleep) or inadequate circumstances (i.e., the environment is safe, dark, quiet, and comfortable) for sleep
- (D) The sleep disturbance and associated daytime symptoms occur at least three times per week
- (E) The sleep disturbance and associated daytime symptoms have been present for at least 3 months
- (F) The sleep-wake difficulty is not better explained by another sleep disorder

Sleep-Related Breathing Disorders

TABLE 3 Sleep-Related Breathing Disorders

Disorder
OSA disorders
OSA, adult
OSA, pediatric
Central sleep apnea syndromes
Central sleep apnea with Cheyne-Stokes breathing
Central sleep apnea due to a medical disorder without Cheyne-Stokes breathing
Central sleep apnea due to high altitude periodic breathing
Central sleep apnea due to a medication or substance
Primary central sleep apnea
Primary central sleep apnea of infancy
Primary central sleep apnea of prematurity
Treatment-emergent central sleep apnea
Sleep-related hypoventilation disorders
Obesity hypoventilation syndrome
Congenital central alveolar hypoventilation syndrome
Late-onset central hypoventilation with hypothalamic dysfunction
Idiopathic central alveolar hypoventilation
Sleep-related hypoventilation due to a medication or substance
Sleep-related hypoventilation due to a medical disorder
Sleep-related hypoxemia disorder

- Predisposing an individual to injury
- Pre-existing resulting in poorer outcomes
- Indirectly due to or worsened by the TBI

Sleep Apnea

- Obstructive sleep apnea
  - Weight gain due to inactivity, change in diet, or medication side effect
  - Sedatives/muscle relaxants
  - Craniofacial trauma (moderate to severe TBI)
- Central sleep apnea
  - Opioids

Central Disorders of Hypersomnolence

- EtOH, analgesics, sedating psychotropic medications, hypnotics
- Secondary Narcolepsy and Post-traumatic Hypersomnia (moderate to severe TBI)

TABLE 4] Central Disorders of Hypersomnolence

Disorder
Narcolepsy type 1
Narcolepsy type 2
Idiopathic hypersomnia
Kleine-Levin syndrome
Hypersomnia due to a medical disorder
Hypersomnia due to a medication or substance
Hypersomnia associated with a psychiatric disorder
Insufficient sleep syndrome

Circadian Rhythm Sleep Wake Disorders

- CRSWD in 26% of mTBI patients suffering from chronic insomnia
  - Zalai DM, Girard TA, Cusimano MD, Shapiro CM. Circadian rhythm in the assessment of postconcussion insomnia: a cross-sectional observational study. CMAJ Open. 2020;8(1):E142-E147.

TABLE 5] Circadian Rhythm Sleep-Wake Disorders

Disorder
Delayed sleep-wake phase disorder ★
Advanced sleep-wake phase disorder
Irregular sleep-wake rhythm disorder
Non-24-h sleep-wake rhythm disorder
Shift work disorder ★
Jet lag disorder
Circadian sleep-wake disorder not otherwise specified

Parasomnias

TABLE 6] Parasomnias

Disorder
NREM-related parasomnias
Confusional arousals
Sleepwalking
Sleep terrors
Sleep-related eating disorder
REM-related parasomnias
REM sleep behavior disorder
Recurrent isolated sleep paralysis
Nightmare disorder
Other parasomnias
Exploding head syndrome
Sleep-related hallucinations
Sleep enuresis
Parasomnia due to a medical disorder
Parasomnia due to a medication or substance
Parasomnia, unspecified

NREM = non-rapid eye movement; REM = rapid eye movement.

REM-related Parasomnias

- REM sleep behaviour disorder
  - Dream enacting behaviour
  - Can lead to injuries
  - Can be due to antidepressants
  - Association with PTSD
- Nightmare disorder
  - Diagnosis
    - Recurrent nightmares
    - Upon awakening, rapidly becoming oriented and alert
    - Causes significant distress or impairment of functioning
  - Causes
    - PTSD and other psychiatric disorders
    - Medication side effect (beta blockers, antidepressants, etc.)

Sleep-related Movement Disorders

TABLE 7] Sleep-Related Movement Disorders

Disorder
Restless legs syndrome
Periodic limb movement disorder
Sleep-related leg cramps
Sleep-related bruxism
Sleep-related rhythmic movement disorder
Benign sleep myoclonus of infancy
Propriospinal myoclonus at sleep onset
Sleep-related movement disorder due to a medical disorder
Sleep-related movement disorder due to a medication or substance
Sleep-related movement disorder, unspecified

Restless Leg Syndrome

- An urge to move the legs, usually accompanied by or thought to be caused by uncomfortable and unpleasant sensations in the legs. These symptoms must:
  - Begin or worsen during periods of rest or inactivity, such as lying down or sitting.
  - Be partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.
  - Occur exclusively or predominantly in the evening or at night, rather than during the day.
- The occurrence of the above features are not solely accounted for as symptoms of another medical or behavioural condition.
- The symptoms of RLS cause concern, distress sleep disturbance or impairment in mental, physical, social, occupational, educational, behavioural or other important areas of functioning.

- Can be secondary to psychotropic medications
  - Antidepressants
  - Antipsychotics

Periodic Limb Movement Disorder

- PLMS index >15/hr
- the PLMS cause clinically significant sleep disturbance or impairment in mental, physical, social, occupational, behavioural, or other areas of functioning
- (c) the PLMS and symptoms are not better explained by another current disorder, medical or neurological disorder, or mental disorder

- Can be secondary to psychotropic medications
  - Antidepressants
  - Antipsychotics

Sleep-related Bruxism

- Repeated teeth grinding or clenching during sleep
- Can result in:
  - Noise that disturbs the bedpartner
  - Abnormal tooth wear
  - Injury to soft tissues of the mouth
  - Morning jaw muscle pain or fatigue
  - Temporal headaches
  - Jaw locking upon awakening
- Relevant risk factors include:
  - OSA
  - Antipsychotics
  - Antidepressants
  - Severe TBI
  - Anxiety

Approach to a Diagnosis

- History (relevant to TBI population)
  - Sleep routine
  - "Review of systems"
  - Questionnaires
- Physical examination
- Investigations
  - Sleep Diary
  - Actigraphy
  - Polysomnography
  - Level 3 sleep study (home sleep apnea testing)
  - Multiple Sleep Latency Test (MSLT)
  - Maintenance of Wakefulness Test (MWT)

Sleep History

- Sleep Routine
  - Time into bed
  - Activities in bed prior to lights out
  - Lights out time (time one attempts to fall asleep)
  - Perceived latency
  - Awakenings in the night- number, duration, reasons
  - Time of final awakening
  - Time out of bed
  - Naps- time(s) and duration(s)

Sleep History

- Review of Systems
  - Snoring, witnessed apneas, morning headaches
  - Grinding or clenching (bed partner or dentist)
  - Excessive daytime sleepiness
    - Difficulty concentrating, fighting to stay awake, unintentional dozing
    - Fitness to drive
  - Motor restlessness (RLS), leg jerking/twitching (PLMD)
  - Nightmares
  - Vocal (talking, shouting) and Motor (punching, kicking) behaviours in sleep

Investigations

- Sleep diary
  - 14 day record of sleep habits
  - Identifies poor sleep hygiene
  - Better estimates total sleep time than a point estimate
  - Circadian rhythm sleep wake disorders
- Actigraphy
  - Accelerometer
  - More accurate than self-reported sleep duration

Investigations

- Polysomnography (PSG)- Level 1 sleep study
  - EEG, EMG, EKG, respiratory effort/flow, pulse oximetry
  - Helpful for diagnosing:
    - Sleep-related breathing disorders
    - Periodic limb movements in sleep
    - Bruxism
    - Parasomnias/Nocturnal seizures
    - Sleep state misperception (paradoxical insomnia)
- Level 3 sleep study (home sleep apnea testing)
  - EKG, respiratory effort/flow, pulse oximetry
  - Sleep apnea diagnosis

Investigations

- Multiple Sleep Latency Test (MSLT)
  - Preceded by 14 day sleep diary and PSG
  - 20 minute nap attempt every 2 hours x 4-5
  - Measures sleep onset latency and REM latency
  - Helpful for:
    - Diagnosis of central disorders of hypersomnolence
    - Objective confirmation of EDS
    - Fatigue vs. Sleepiness
- Maintenance of Wakefulness Test (MWT)
  - 40 minute periods every 2 hours x 4
  - Helpful for:
    - Objective confirmation of daytime alertness
    - Fitness to Drive

Treatment of Insomnia Symptoms

- Identify and treat primary sleep disorder
  - OSA
  - RLS
  - PLMD
  - Nightmare disorder
  - CRSWD
- Address psychiatric factors
  - Depression, Anxiety
- Address medical factors
  - Pain
  - Nocturia
  - GERD
  - SOB
- Chronotherapy
  - Stimulants, activating antidepressants, steroids, etc

Treatment of Insomnia Symptoms

- Sleep hygiene
  - Consistent sleep routine
  - Bed when drowsy
  - Avoid substances near bedtime (nicotine, alcohol)
  - Avoid caffeine 8 hours before bed (coffee, tea, cola, energy drinks)
  - Bed is for sleeping
  - Avoidance of electronics before bedtime
  - Limit napping
  - Supportive environment (dark, quiet, cool, safe)
  - Regular morning exercise

Treatment of Chronic Insomnia Disorder

- Cognitive Behavioural Therapy for Insomnia (CBT-I)
  - First line Treatment
  - Access Issues (trained professionals, cost, time-commitment)
  - Evidence of effectiveness in the TBI population
    - Ouellet MC, Morin CM. Efficacy of cognitive-behavioral therapy for insomnia associated with traumatic brain injury: a single-case experimental design. Arch Phys Med Rehabil. 2007;88(12):1581-92
    - Nguyen S, McKay A, Wong D, et al. Cognitive Behavior Therapy to Treat Sleep Disturbance and Fatigue After Traumatic Brain Injury: A Pilot Randomized Controlled Trial. Arch Phys Med Rehabil. 2017;98(8):1508-1517
    - Bogdanov S, Naismith S, Lah S. Sleep outcomes following sleep-hygiene-related interventions for individuals with traumatic brain injury: A systematic review. Brain Inj. 2017;31(4):422-433
    - Theadom A, Barker-Collo S, Jones K, Dudley M, Vincent N, Feigin V. A pilot randomized controlled trial of on-line interventions to improve sleep quality in adults after mild or moderate traumatic brain injury. Clin Rehabil. 2018 May;32(5):619-629
    - Malarkey ME, Fu AJ, Mannan N, et al. Internet-Guided Cognitive Behavioral Therapy for Insomnia Among Patients With Traumatic Brain Injury: A Randomized Clinical Trial. JAMA netw. open. . 2024;7(7):e2420090. doi:10.1001/jamanetworkopen.2024.20090

CBT-I

- Sleep Hygiene
  - Unhelpful sleep and lifestyle habits
- Stimulus Control Therapy
  - Conditioned arousal; weakened bed-sleep association
- Sleep Restriction Therapy
  - Excessive time in bed
- Relaxation therapeutics
  - Pre-sleep arousal; psychophysiological arousal
- Cognitive therapeutics
  - Maladaptive thoughts, beliefs, attitudes about sleep
- Sleep Education
  - Unrealistic expectations and beliefs about sleep

Treatment of Chronic Insomnia Disorder

- Melatonin
  - **Reduced melatonin production in TBI patients**

Shekleton JA, Parcell DL, Redman JR, Phipps-Nelson J, Ponsford JL, Rajaratnam SM. Sleep disturbance and melatonin levels following traumatic brain injury. Neurology. . 2010;74(21):1732-8. doi:10.1212/WNL.0b013e3181e0438b

Grima NA, Ponsford JL, St Hilaire MA, Mansfield D, Rajaratnam SM. Circadian Melatonin Rhythm Following Traumatic Brain Injury. Neurorehabil Neural Repair. 2016;30(10):972-977

  - **Nine studies were identified, 5 of which were RCTs. Melatonin was shown to improve perceived sleep quality, objective sleep duration, and sleep efficiency in adults and adolescents with sleep disturbance after mild to severe TBI.**

Cassimatis M, Browne G, Orr R. The Utility of Melatonin for the Treatment of Sleep Disturbance After Traumatic Brain Injury: A Scoping Review. Arch Phys Med Rehabil. . 2023;104(2):340-349. doi:10.1016/j.apmr.2022.09.018

- Medications
  - When treating a comorbidity
  - DORAs (dual orexin receptor antagonists)

Treatment of Sleep-related Breathing Disorders

- OSA
  - Removal of offending pharmacologic agents
  - Weight loss
  - Positional therapy
  - Mandibular Advancement Device
  - PAP therapy (CPAP, autoPAP, BiPAP)
  - Surgery
- CSA
  - Removal of offending agent
  - PAP therapy

Treatment of Central Disorders of Hypersomnolence

- Reducing offending medications/substances

- Medications
  - Wake promoting medications (Modafinil, Solriamfetol, etc.)
  - Stimulants (Methylphenidate, Dextroamphetamine, etc.)
  - Activating antidepressants (Bupropion, Venlafaxine, etc.)

Treatment of REM-related Parasomnias

- RBD
  - Reducing offending agent
  - Melatonin
  - Clonazepam
- Nightmare Disorder
  - Address underlying cause
  - Imagery rehearsal therapy (rescripting)
  - Prazosin

Treatment of Sleep-related Movement Disorders

- RLS & PLMD
  - Rule out reversible causes
  - Removing offending agents (caffeine, stimulants, antidepressants, antipsychotics)
  - Dopamine agonists
  - Alpha-2-Delta ligands
- Sleep-related Bruxism
  - Treat underlying issue such as anxiety, sleep apnea
  - Dental guard
  - Botulinum toxin
  - Could consider medications
    - Clonidine
    - Clonazepam

Conclusions

- Sleep disturbance/disorders are common in the TBI population
- Insomnia is frequent and can be persistent post concussion
- Sleep disorders in the TBI population are treatable