Post Viral Sleep Disturbances: *What do we know and how can we apply it to Long COVID?*

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Learning objectives

- Name three post-viral sleep disturbances
- Appreciate the value of a sleep history and when to refer a patient with long-COVID for a sleep evaluation.

Patient 1: “I’m so tired, all the time”

- A 35 year old female architect contracted COVID-19 in February 2021. She was not hospitalized or on supplemental oxygen, she was sick for a week. Other than mild obesity, she was previously healthy.
- She states that for several months now, she feels fatigued all the time. At work, she finds herself unable to focus and sometimes dozing in front of the computer or at long meetings, After work, she lacks the energy to exercise or socialize with friends. She has a hard time staying awake until her bedtime but will sometimes lie awake at night unable to fall asleep.

Patient 1: “I’m so tired, all the time”

- Physical examination
  - Vital signs are normal. PE including orthostatics are unremarkable.
- The patient has had the following work-up:
  - PHQ-9 questionnaire suggests mild/moderate depression
  - CBC, CMP, TSH, CK, AM cortisol: normal
  - CXR normal

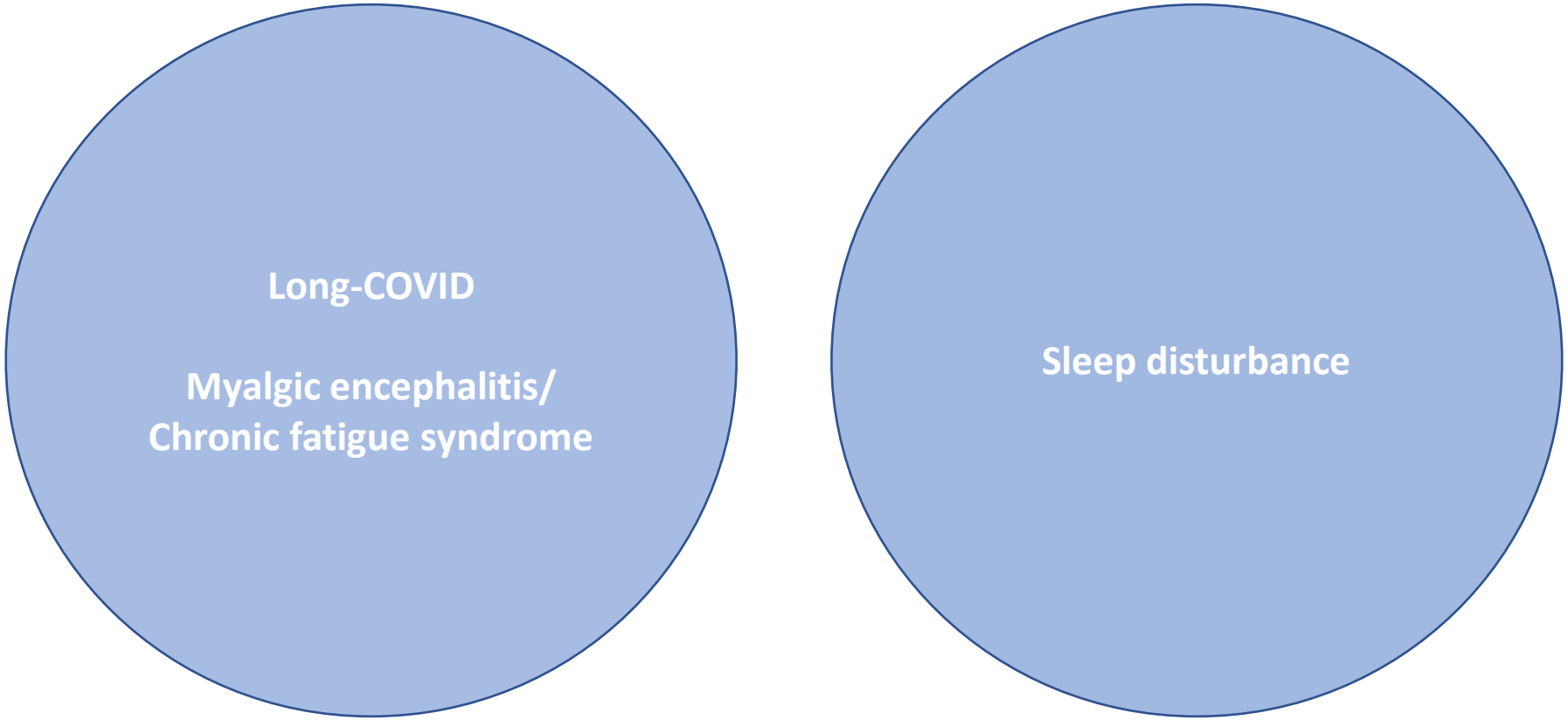
Patient 2: “My boss is going to fire me”

- 60 year old morbidly obese man with HTN, depression, asthma who contracted COVID in April 2020. Course complicated by a pulmonary embolism, pneumonia. He was hospitalized for a few days, discharged on oxygen.
- He endorses continued dyspnea with exertion since his hospitalization. He also has had excessive sleepiness, napping at least once a day. He has gained 40 pounds in the past two years.
- He was told at the hospital that he snores at night. He says that his sleep has never been refreshing but he was always able to function. He works as a cashier and his boss says if he is late or makes another error, he will get fired.

Patient 2: “My boss is going to fire me”

- Physical examination
  - Normal oxygen saturation at rest
  - Obese
  - Mild lower extremity edema, normal pulmonary/CV exam
- The patient has had the following work-up:
  - CBC, CMP, TSH, CK, AM cortisol: normal
  - CXR, CT scan, TTE normal
  - Cardiac stress test is normal
  - PFTs show mild reduction in diffusing capacity

Diagnosis


Long-COVID
Myalgic encephalitis/
Chronic fatigue syndrome
Sleep disturbance

What sleep disorders could this patient have?

- Insomnia
- Sleep apnea
- Restless leg syndrome, periodic limb movement disorder
- Parasomnia
- Circadian rhythm disorders
- Central hypersomnia (Narcolepsy, idiopathic hypersomnia)

Coronasomnia, COVID-somnia

- Constellation of sleep disorders arising as a result of the COVID-19 pandemic
  - Insomnia: difficulty falling asleep, staying asleep, awakening too early
  - Circadian dysfunction
  - Feelings of non-restorative sleep or decreased sleep quality
  - Increased nightmares

Bhat et al., Sleep Med, 2021

Associated risk factors for COVID-somnia

- Younger age (<40)
- Female gender
- Urban living
- Living in a high-risk environment for COVID-19
- Lower socioeconomic/education class
- Pre-existing psychiatric conditions
- Absence of social support
- High level of exposure to social media, news re: COVID-19

Bhat et al., Sleep Medicine, 2021

Prevalence of COVID-somnia

- Overall prevalence of 35.7% [29.4-42.4] reported sleep problems
- Patients with COVID-19: 74.8% [28.7-95.6]
- Healthcare workers: 36% [21.1-54.2] vs. general population: 32.3% [25.3-40.2]

- These rates are similar to prevalence of stress, anxiety and depressive symptoms, indicating **bidirectional** nature of sleep problems and psychological stress.

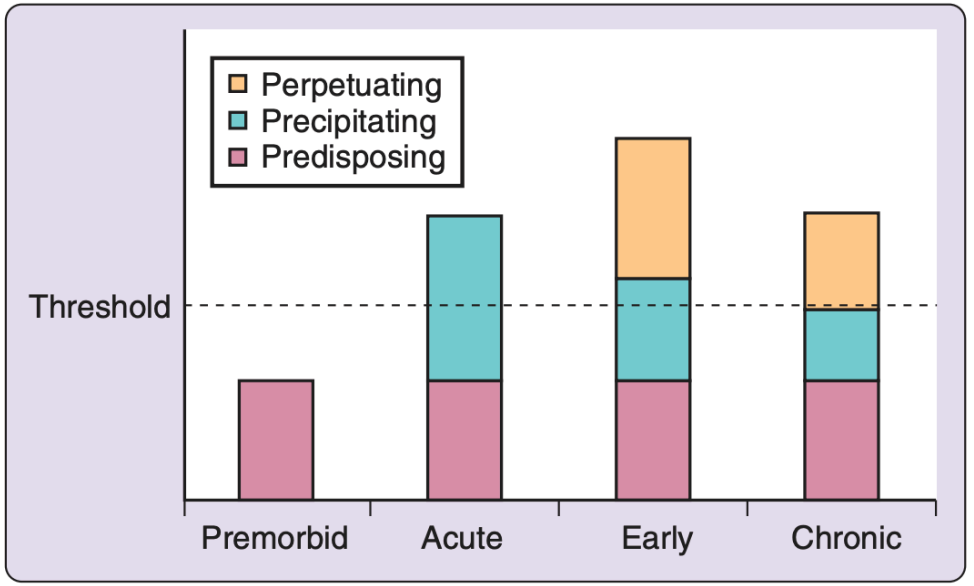
Jahrami et al., JCSM, 2021

Insomnia

- Difficulty falling asleep, staying asleep, awakening too early
- Acute vs. Chronic insomnia
  - Acute: Transient, days to weeks
  - Chronic: Symptoms >3x weekly, for >3 months
    - **Patient's adaptations to poor sleep perpetuate insomnia**

Spielman Model (3 P's) for Insomnia

- The Spielman Model (3 P's)
  - Predisposing factors
    - Personality, Social, Biological
  - Precipitating factors
    - Trauma, **illness**
  - **Perpetuating factors**
    - **Increasing time in bed**
    - **Device usage in bed**



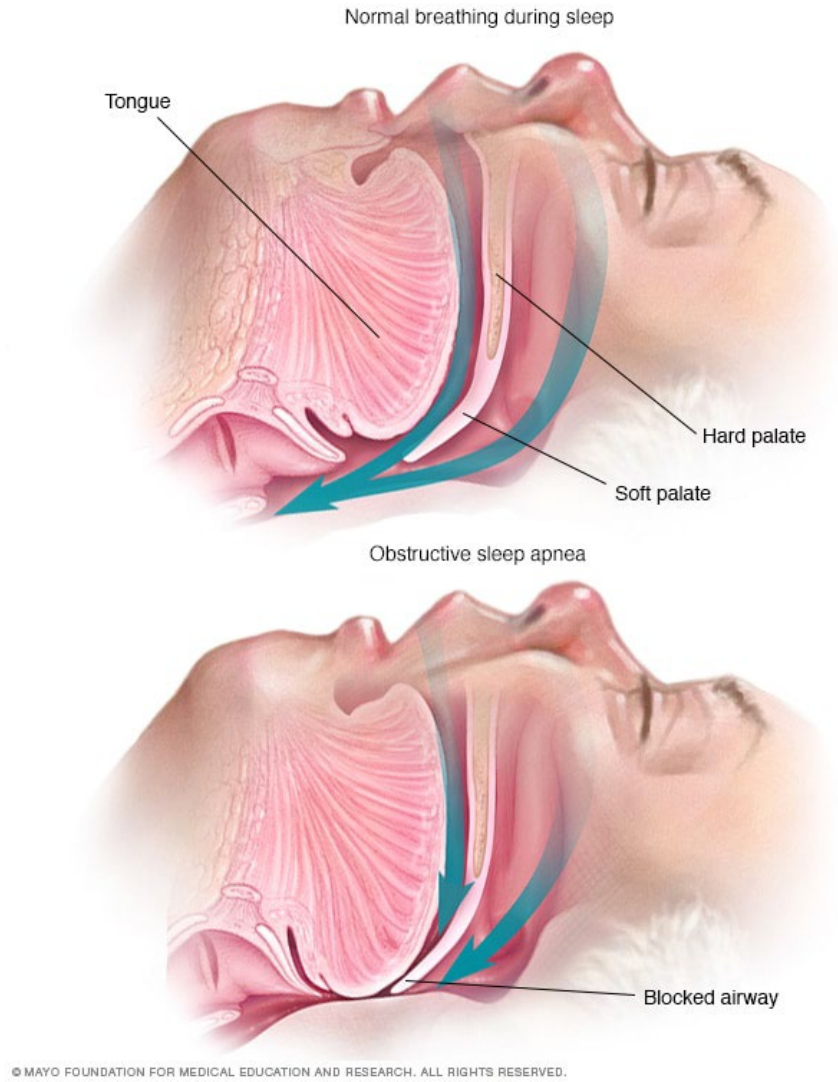
https://www.med.upenn.edu/cbti/assets/user-content/documents/ppsmmodelsofinsomnia20115theditionproof.pdf

Treatment of chronic insomnia

- No definite recommendation specifically for COVID-19 related insomnia
- Principles of general insomnia treatment:
  - **Sleep hygiene alone is ineffective**
  - Cognitive behavioral therapy for insomnia (CBTi) can be effective
    - Cognitive restructuring
    - Stimulus control
    - Sleep restriction/compression
    - Relaxation
  - Short-term pharmacotherapy for insomnia, sometimes with CBTi

Sleep apnea

- Narrowing of posterior orpharynx during sleep resulting in airway collapse leading to:
  - Intermittent hypoxemia/hypercapnia
  - Intrathoracic pressure swings
  - Arousals
  - Sleep fragmentation
- Symptoms:
  - Snoring, apneas
  - Fatigue, sleepiness, unrefreshing sleep, nighttime awakenings
- High prevalence, under-diagnosed
- Risk factors:



https://www.mayoclinic.org/diseases-conditions/obstructive-sleep-apnea/symptoms-causes/syc-20352090

COVID-19 and OSA

- Possible increased risk of death among patient with OSA who contract COVID-19
  - Obesity likely plays a significant role
  - Unclear how CPAP adherence might play a role
- Shared inflammatory mechanisms between OSA and Long-COVID, possibility of a bidirectional relationship.
  - OSA: intermittent hypoxemia, sleep fragmentation
  - Long-COVID: ?

Cade et al., AJRCCM, 2020

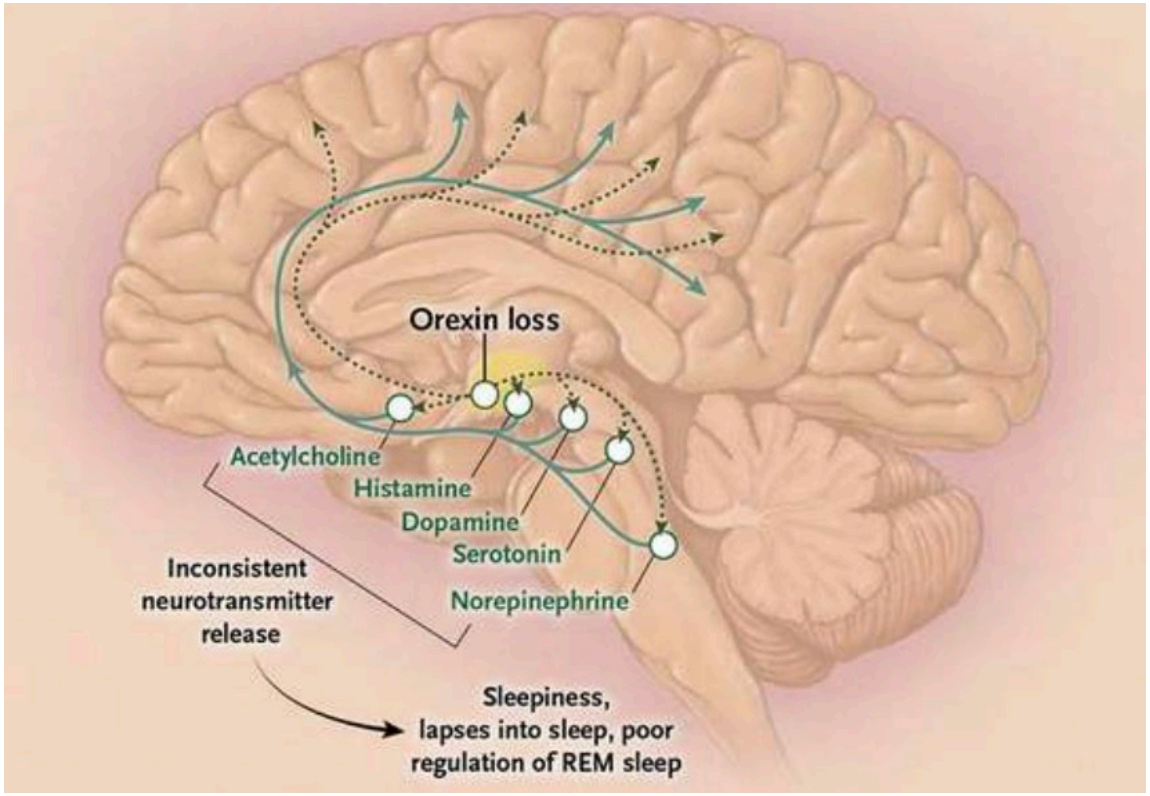
Restless leg syndrome

- An uncontrollable urge/need to move the legs, accompanied by an uncomfortable/crawling sensation.
  - Relieved by movement
  - Occurs in the evening
- One registry study showed that patients with RLS (treated with opiods) had increasing severity scores during the pandemic, with a return to normal about 6 months later.
- RLS prevalence higher among women with Long-COVID vs controls (14.8% vs. 5.7%).

Wipper et al., Sleep Med, 2022
Weinstock et al., JCSM, 2022

Narcolepsy

- Daytime sleepiness is the hallmark symptoms (*different from fatigue)
  - Cataplexy
  - Hypnagogic hallucinations
  - Sleep paralysis
- Narcolepsy type 1 (cataplexy) and type 2 (without cataplexy)
- Pathophysiology unclear:
  - Orexin
  - HLA (DQB1*0602)
  - Environmental



https://project-sleep.com/wp-content/uploads/2021/09/Science-of-Narcolepsy-Toolkit.pdf

Secondary narcolepsy

- 2009-2010 H1N1 influenza pandemic saw significant increase in pediatric cases of narcolepsy, type 1
  - Infection
  - Pandemrix (vaccine)
- T- cell mediated cytotoxicity, destruction of orexin neurons
- Narcolepsy and COVID… ?

Sleep consultation for fatigue and long-COVID

- Sleep History
  - Symptoms of sleep apnea
    - Snoring, apneas, fatigue, unrefreshing sleep, nocturia, gasping arousals, excessive sleepiness
    - STOP-BANG ≥ 3
  - Sleep schedule
    - Sleep latency, total sleep time, awakenings, naps
    - Medications, drug use, alcohol use
  - RLS symptoms, parasomnia, narcolepsy
- Examination:
  - BMI (recent weight changes?), neck circumference, Malampatti

Townsend et al., PLOS One, 2020

Sleep testing

- Home sleep test
  - Sleep disordered breathing
- In-lab overnight polysomnogram
  - Sleep disordered breathing
  - Parasomnias
  - Periodic limb movement disorder
- Multiple sleep latency test
  - Narcolepsy, idiopathic hypersomnia

Treatment

Condition	Treatment
Insomnia	CBTi Medications (sedative-hypnotics)
Sleep apnea	CPAP, Dental device, surgical options
Restless leg syndrome/periodic limb movement disorders	Medications (Dopamine agonists, gabapentinoids)
Circadian rhythm disorders	CBTi, light therapy, melatonin
Central hypersomnia	Stimulants

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