

Sleep:
An Update in Clinical Management
 North Dakota Academy of Family Physicians
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Michael Howell MD-Disclosure

- Co-Creator of the SPI Sleep Journey App
- Off-Label Use
 - I will mention off-label use of dopaminergic agonists (pramipexole, ropinirole) and methadone (for RLS) as well as melatonin and clonazepam for REM sleep Behavior Disorder.

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Contents

- Recent insights on the functions of sleep
- Sleep Disorders
 - Their Burden and Impact
 - Cant Fall (or stay) Asleep
 - Too Sleepy
 - "Something Weird is Happening" Sleepwalking and related disorders

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 - STAY TUNED: Sleepwalking, Dream Enactment and Other Parasomnias (Wed 9am)

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Why do we sleep?

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Functions of Sleep

Adaptive Inactivity



Memory Consolidation

Synaptic Homeostasis

Replenish CNS ATP

Toxic Clearance

(Seigel JM, Nat Rev Neurosci 2009)





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Functions of Sleep

- Adaptive Inactivity
- Memory Consolidation
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- Replenish CNS ATP
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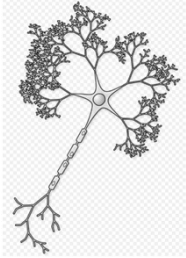


(Walker MP, Prog Brain Res 2010) Wikimedia Commons

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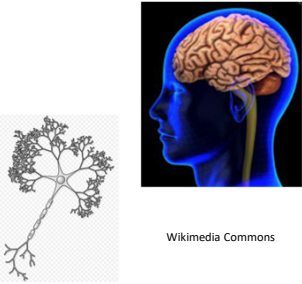


(Tononi G, Cirelli C, Eur J Neurosci 2020) Wikimedia Commons

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Synaptic Homeostasis

- Human Brain:
 - Most complicated system in the known universe
 - 100 trillion synaptic connections
 - During the day synapses are constantly growing but space is limited.
 - Synapses are pruned during deep NREM sleep leading to increased signal and decreased noise.




(Tononi G, Cirelli C, Eur J Neurosci 2020) Wikimedia Commons

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Functions of Sleep

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(Huang, Curr Top Med Chem 2011) Wikimedia Commons

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Functions of Sleep


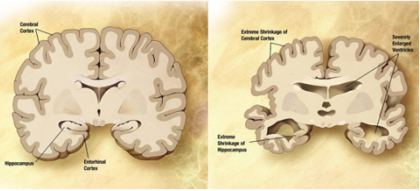
- Adaptive Inactivity
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(Nedergaard M, Goldman SA, Science 2020) Wikimedia Commons

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Sleep and Dementia

(Nedergaard M, Goldman SA, Science 2020) Wikimedia Commons

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Sleep Disorders

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- ## Sleep Disorders
- **Their Burden and Impact**
 - Cant Fall (or stay) Asleep Disorders
 - Too Sleepy Disorders

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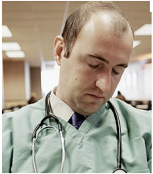
- ## The Burden of Sleep Disorders
- Inadequate and poor quality sleep is ubiquitous
 - Modern life has been structured so that sleep is dispensable
 - Exogenous light exposure is disrupting to natural circadian rhythms.
 - Caffeine is the most commonly consumed drug on the planet.
 - Consequences...

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Poor Sleep leads to... Sleepiness



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(AASM ICSD-3, 2015; Schneider, Continuum 2020)

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Poor Sleep leads to... Inattention

- Loss of vigilance




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(AASM ICSD-3, 2015; Schneider, Continuum 2020)

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Consequences of Sleepiness and Inattention



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(AASM ICSD-3, 2015; Schneider, Continuum 2020)

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The prevalence and costs of sleep disorders

1 out of every 30 drivers admit to have falling asleep in the last month while driving.

(Wickwire et al, Sleep Med Review 2016; McKinsey, Harvard Medical School 2010; National Sleep Foundation, Sleep in America Pole, 2014)

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Sleep Deprivation leads to... impulsiveness

- Poor food choices





(AASM ICSD-3, 2015; Schneider, Continuum 2020) Wikimedia Commons

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Sleep Deprivation leads to... impulsiveness

- Risk taking behaviors






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(AASM ICSD-3, 2015; Schneider, Continuum 2020)

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Poor Sleep leads to... Depressed Mood

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(AASM ICSD-3, 2015; Schneider, Continuum 2020)

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The Prevalence and costs of sleep disorders

- Sleep deprivation
 - 50-70 million Americans
- Insomnia
 - 30% of American adults have intermittent insomnia
 - 15% have chronic insomnia
 - Direct health care costs-\$3 billion
 - Indirect costs US Economy-\$32 billion

(Wickwire et al, Sleep Med Review 2016; McKinsey, Harvard Medical School 2010; National Sleep Foundation, Sleep in America Pole, 2014)

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The Prevalence and costs of sleep disorders

- Obstructive Sleep Apnea Syndrome
 - 14% of adult men
 - 5% of adult women
 - Direct health care costs-\$6 billion
 - Indirect costs US Economy-\$4 billion
 - Indirect health care costs \$60 billion
 - OSA related motor vehicle accidents-\$14 billion
 - Absenteeism \$10 billion

(Wickwire et al, Sleep Med Review 2016; McKinsey, Harvard Medical School 2010; National Sleep Foundation, Sleep in America Pole, 2014)

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The Prevalence and costs of sleep disorders

- Restless Legs Syndrome
 - 5% general population
- REM sleep Behavior Disorder-dream enactment
 - 1% General Population
 - 5% Elderly

(AASM ICSD-3 2015)

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Sleep Disorders

- Their Burden and Impact
- **Cant Fall (or stay) Asleep Disorders**
- Too Sleepy Disorders

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Cant Fall (or Stay Asleep)

- Troubles Falling Asleep
 - Hypervigilance-Psychophysiological Insomnia
 - Motor Restlessness (AKA Restless Legs Syndrome)
 - Delayed Circadian Rhythm
- Troubles Staying Asleep
 - Hypervigilance-Psychophysiological Insomnia
 - Advanced Circadian Rhythm

(AASM ICSD-3 2015)

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Troubles Falling Asleep

- Hypervigilance-Psychophysiological Insomnia
- Motor Restlessness (AKA Restless Legs Syndrome)
- Delayed Circadian Rhythm

(AASM ICSD-3 2015)

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CNS Hypervigilance-Psychophysiological Insomnia

- Difficulty falling asleep (often with trouble staying asleep as well)
 - At any time of the clock
 - 24 hour hypervigilance



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(AASM ICSD-3 2015)

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Hypervigilance: more than a nighttime problem

- Insomnia Trap
 - Impaired mood caused by a poor night of sleep.
 - Growing anxiety over the course of a day regarding impending inability to fall asleep at night.
 - Nighttime hypervigilance makes it more difficult to fall asleep.




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(AASM ICSD-3 2015)

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Bedroom Hypervigilance-A Conditioned Response




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Bedroom Hypervigilance-A Conditioned Response Requires

- Treatment requires positive conditioning of the bedroom environment
- Cognitive Behavioral Therapy for Insomnia




(Sutton, Ann Intern Med 2021) Wikimedia Commons

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Two Cardinal Rules of Cognitive Behavioral Therapy for Insomnia

- Don't go to bed unless you are sleepy
- Don't sleep outside of the bedroom




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Restlessness

- Common manifestation of atypical insomnia
- Often the only complaint is: "I cant fall asleep..."

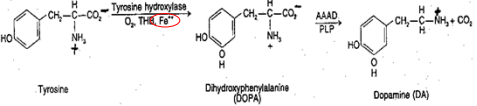


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Restlessness

- Commonly due to iron deficiency




Tyrosine $\xrightarrow[\text{O}_2, \text{THF}, \text{Fe}^{2+}]{\text{Tyrosine hydroxylase}}$ Dihydroxyphenylalanine (DOPA) $\xrightarrow[\text{PLP}]{\text{AAAD}}$ Dopamine (DA) + CO₂

(AASM ICSD-3 2015) Wikimedia Commons

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Restlessness

- **Iron Replacement**
 - Target Serum Ferritin to at least 75 micrograms/L
- Vitamin D is Synergistic




(Tutuncu M, Sleep Breath 2020; Silber MH, Mayo Clin Proc 2021;) Wikimedia Commons

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Restlessness

- **More severe cases may need Rx**
 - **gabapentin, pregabalin**
 - pramipexole, ropinerole (dopamine agonists)
 - Severe cases: methadone




(Silber MH, Mayo Clin Proc 2021) Wikimedia Commons

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Delayed Circadian Rhythm

- Common modern problem
 - May be the most common reason people have trouble falling asleep
- **Trouble falling asleep at night and sleepy in the AM**
- Living in the wrong time zone
- Delay in bodies 24 hour clock.




Galileo Spacecraft-NASA

(AASM ICSD-3 2015)

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Delayed Circadian Rhythm-Treatment

- Bright light (sunlight or 10,000 lux light box light) for 30-60 minutes in the AM.
- Melatonin small doses (0.5-1.0mg) several hours before bedtime.



Galileo Spacecraft-NASA

Zee PC and Abbott SM, Continuum 2020

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Troubles Staying Asleep



- Hypervigilance-Psychophysiological Insomnia
- Advanced circadian rhythm
- Insights from ultradian rhythms

(AASM ICSD-3 2015)

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Cant Stay Asleep-Hypervigilance

- **Unable to Stay Asleep**
 - Often combined with difficulty falling asleep
- Also a conditioned hypervigilance
 - Cognitive Behavioral Insomnia


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(AASM ICSD-3 2015)

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Advanced Circadian Rhythm

- Common problem particularly middle aged and elderly
- Trouble staying asleep but also **sleepy and tired in the evening.**
- Living in the wrong time zone
- Advance in bodies 24 hour clock.



Galileo Spacecraft-NASA

(AASM ICSD-3 2015)

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Advanced Circadian Rhythm-Treatment

- Bright light (sunlight or 10,000 lux light box light) for 30-60 minutes in the evening.
- Stop evening melatonin



Galileo Spacecraft-NASA

(Zee PC and Abbott SM, Continuum 2020)

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Advanced Circadian Rhythm-Treatment

- Melatonin small doses (0.5-1.0mg) during a middle of the night awakening.
 - Do not take before bedtime as this will make an advanced rhythm worse!



Galileo Spacecraft-NASA

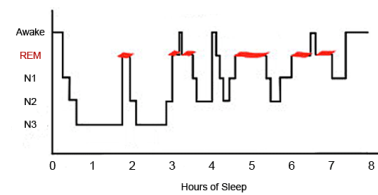
(Zee PC and Abbott SM, Continuum 2020)

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A Comment on Middle of the Night Awakenings

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Ultradian Rhythms-Normal Sleep Cycles



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- A brief awakening every 90 minutes or so does not, by itself, indicate pathology.

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Sleep Disorders

- Their Burden and Impact
- Cant Fall (or stay) Asleep Disorders
- **Too Sleepy Disorders**

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Too Sleepy

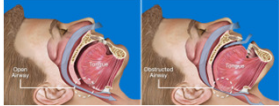
- Most Common cause for excessive sleepiness
 - Sleep Deprivation
- Obstructive Sleep Apnea
- Narcolepsy and Related Disorders

(AASM ICSD-3 2015)

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Snoring and obstructive sleep apnea (OSA)

- Collapse of the upper airway
- OSA is a common condition
 - Relative to a pliable upper airway evolved for vocalization
 - Higher risk: men, weight gain, family history, increased neck circumference.



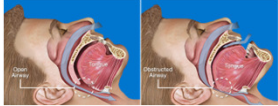
(AASM ICSD-3 2015)

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OSA-spectrum of disease

- Apnea-Hypopnea Index (AHI): number of times an individual stops breathing or nearly stops breathing per hour.
- Polysomnogram (sleep study) thresholds for diagnosis and severity (consensus based)
 - Ideal for adults: AHI < 5/hr
 - Mild: AHI 5-15/hr
 - Moderate: AHI 15-30/hr
 - Severe: AHI > 30/hr




(AASM ICSD-3 2015)

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OSA Treatment Based upon Severity

- Mild
 - Oral Appliance
 - PAP
 - Positional Therapy
- Moderate
 - Oral Appliance, PAP, Upper Airway Surgery
- Severe
 - Recommend PAP
 - Hypoglossal nerve stimulation




(Kirsch DB, Continuum 2020)

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OSA-mechanical problem in need of a mechanical solution

- Positive Airway Pressure (PAP) Therapy
 - Seals over the nose or mouth/nose.
 - Acts as a pneumatic splint to the upper airway.
- Adherence challenges
 - Works very well about 50% of the time.
 - Numerous reasons for poor adherence
 - Mask discomfort
 - Claustrophobia
 - Untreated co-morbid sleep problems
 - Nasal obstruction



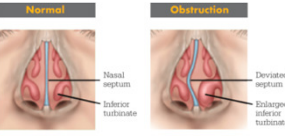
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OSA-what to do when Oral Appliance or PAP is not working

- Evaluate for possible nasal obstruction
 - Nasal endoscopy
- Relieve nasal obstruction-three benefits
 - Directly decreases AHI
 - Improve PAP and oral appliance treatment
 - Improved nasal breathing during the day



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(Kirsch DB, Continuum 2020)

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Hypoglossal Nerve Stimulation

- FDA approved therapy in 2015
- Indications
 - PAP intolerant
 - Moderate to Severe OSA
 - Non-morbidly obese patients.

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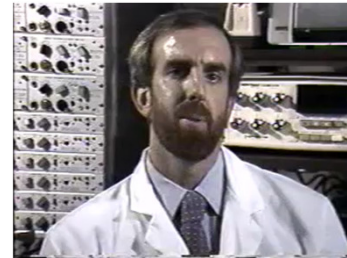
Sleepwalking and dream enactment: a preview

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Dear Dr. Howell

"I have woken to my very tall, muscular husband kneeling over me, choking me - thankfully I could get in a scream... There have been other incidents where he has punched me in the face, etc. - we have even discussed what would happen if he hurt me badly in his sleep, how he would be able to explain it to the police that he did it in his sleep - PLEASE ANY information would be greatly appreciated - I have loved this man since high school - I cant bare the thought of watching him suffer with Parkinsons!"

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(Used with permission, Dr. Carlos Schenck)

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Thank You



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