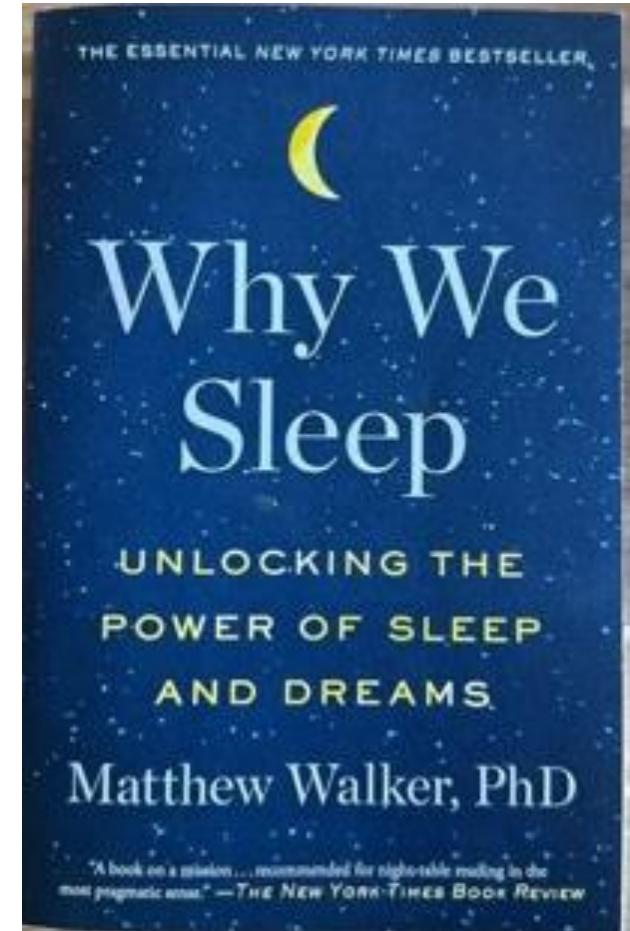
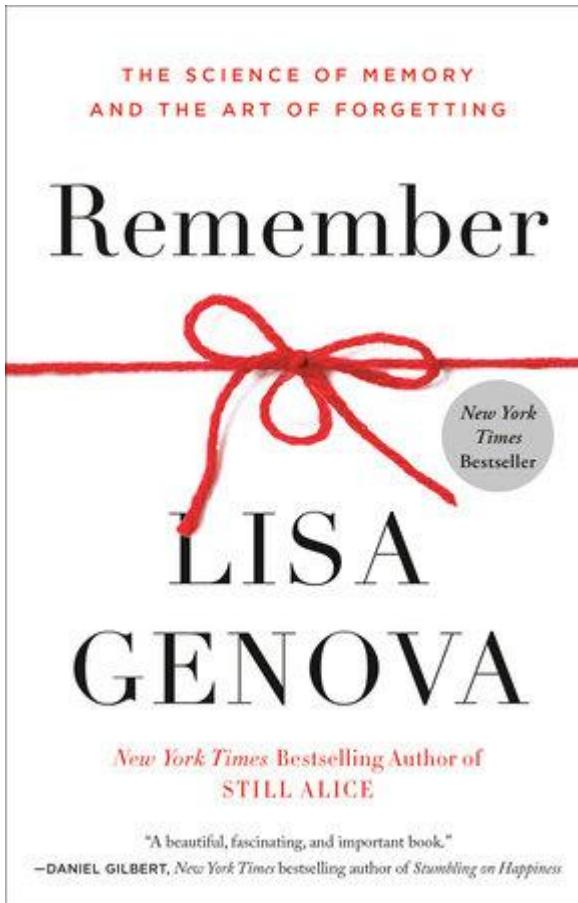
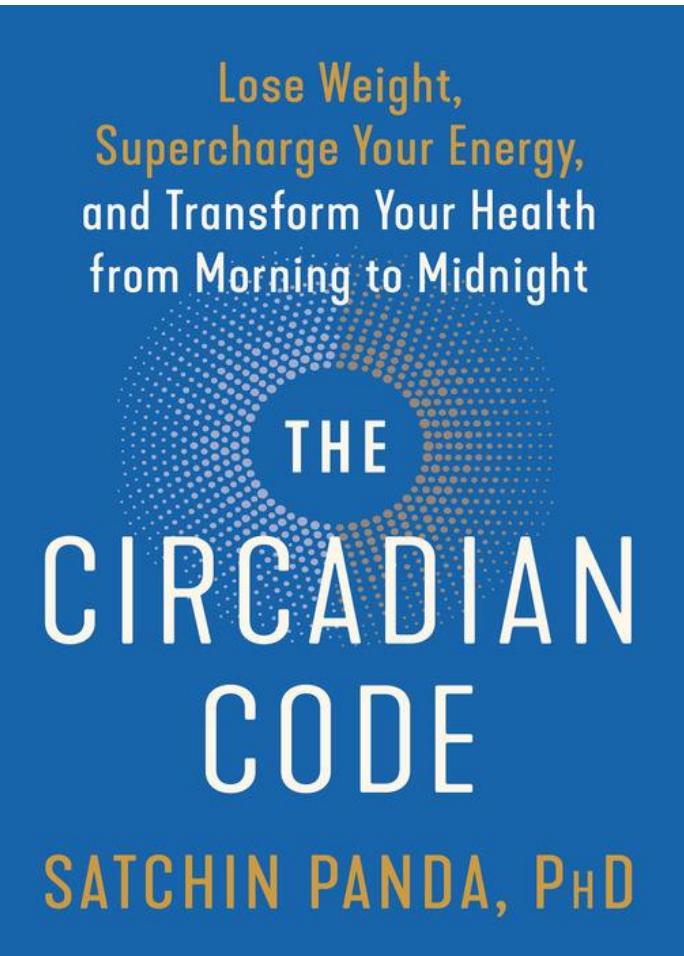


Getting In and Out of the Opioid Use Disorder Roundabout

Bill Davies PAC BS



Disclosures: None



BUSINESS LAW

PREHISTORIC GOGLING



Identifying those Co-Travelers (Medical Conditions) with Modifiable Therapies to Tx OUD

1. Pain, Opioids and ID Co-Travelers in the Painful Commute

2. Finding the Signs to Guide your Decisions



3. Help Getting Them Up and Out





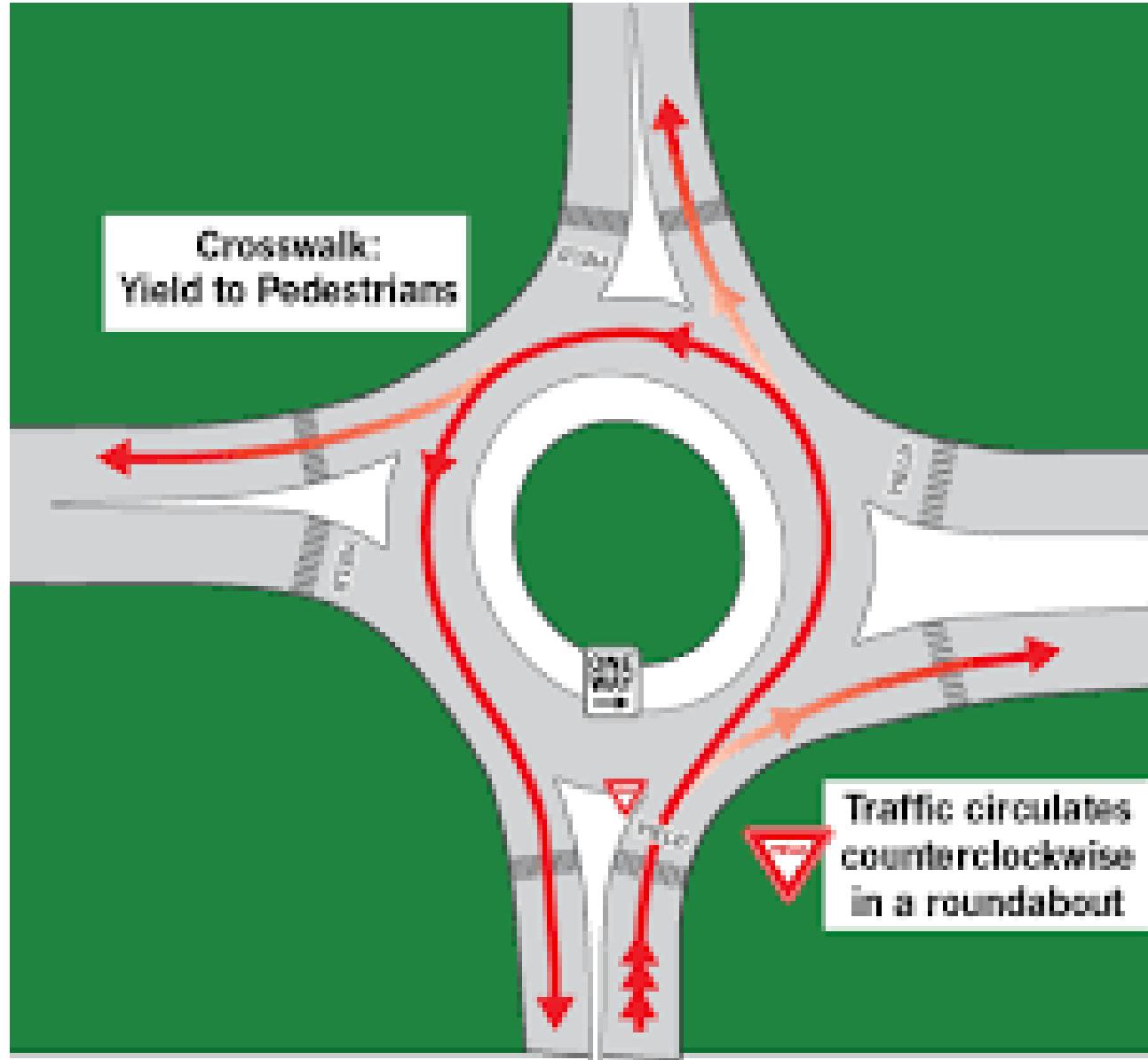
Audience Participation

What Do We Know about how People feel about Roundabouts?

Results from Polling 20 Individuals on their Reactions to Roundabouts

- Confusing
- Dread
- Anxious
- Aggressive
- Avoidance
- Go slow and then Fast
- Don't look Back
- Angry
- Panic
- Fearful
- Tense Up
- Hold my Breath
- Despair
- Accelerate
- Distain
- Unsafe





Yield to all traffic before entering roundabout



Audience Participation

What Do Chronic Pain/Opioid Users feel about their Daily Life?

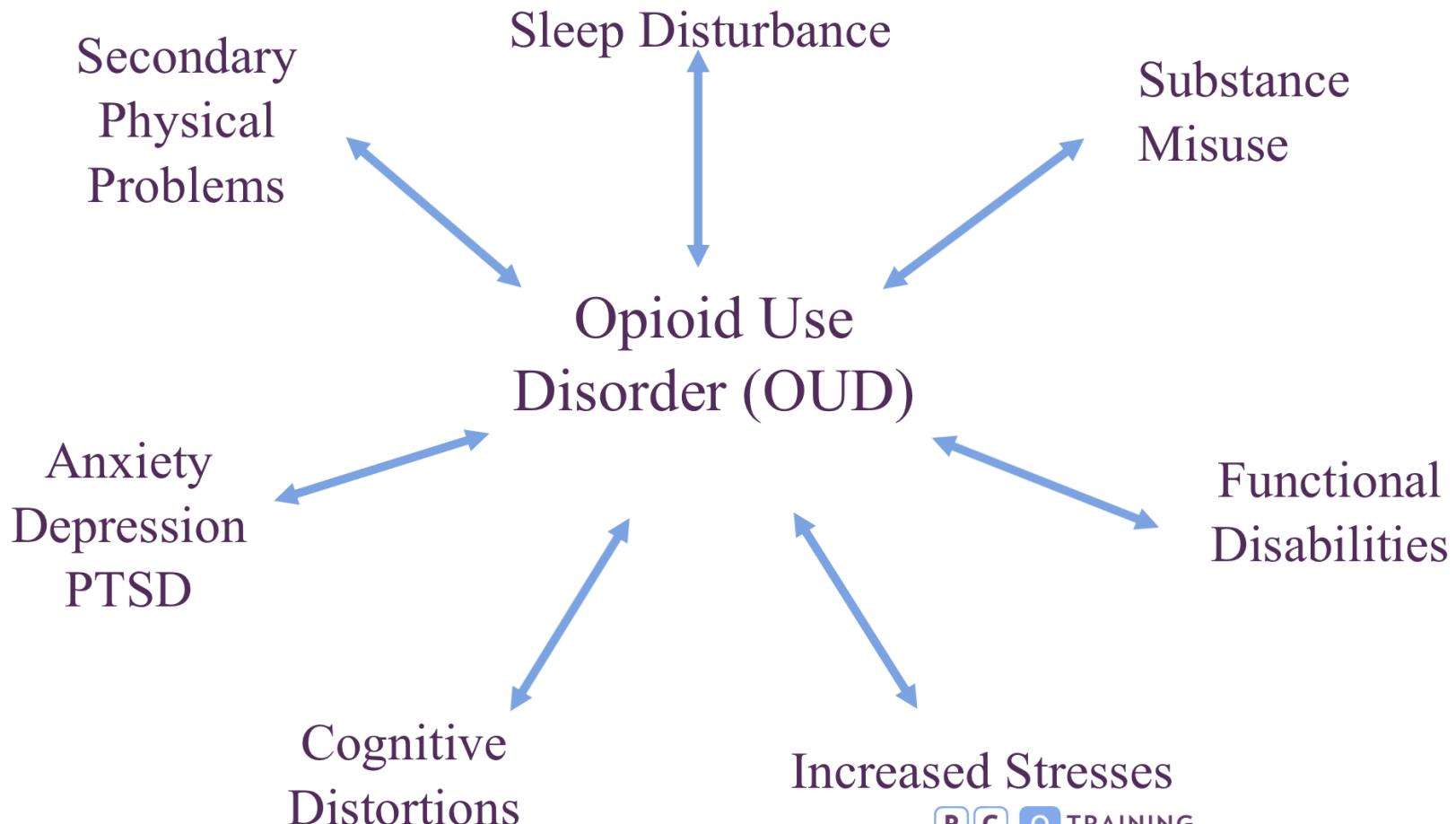
Individual's Report Reactions to Their Lives with Pain and OUD (Highjacked Emotions)

- Confusing
- Dread
- Anxious
- Aggressive
- Avoidance
- Goes from slow to then Fast
- I Don't look Back
- Angry
- Hopeless
- Panicky
- Fearful
- Tense Up
- Hold Breathing
- Despair
- Accelerate temper
- Distain
- Unsafe

We know this about Pain and UOD Patient's Issues?

- Varied Presentations
- Complex Painful Disorders
- Treatment Complexities
- Contributing physiological issues
- Confounding behavioral sequela
- Bidirectional with All Bodies System
- **Pre existing Conditions are Critical to ID**
- Patient's understanding is difficult: ? wants/needs

As a chronic condition, OUD shares similar challenges as persistent pain

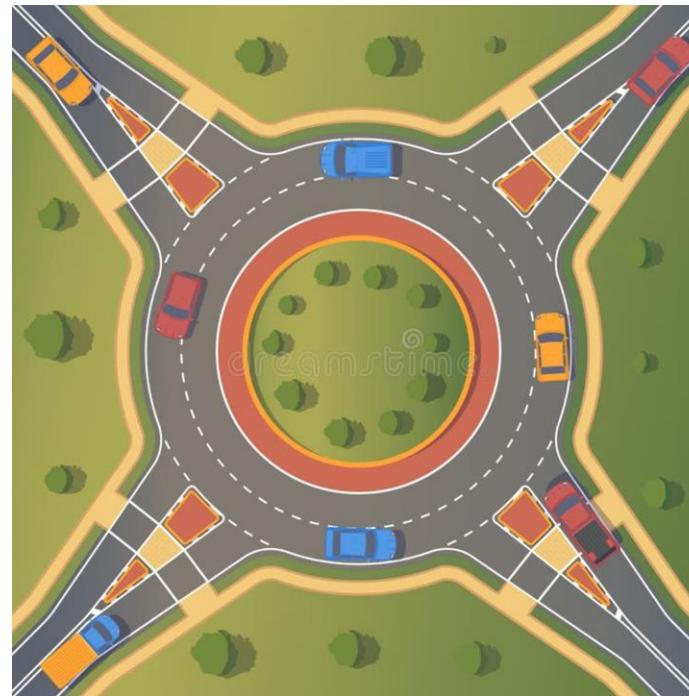


Addictive Behaviors share key Neurobiological features

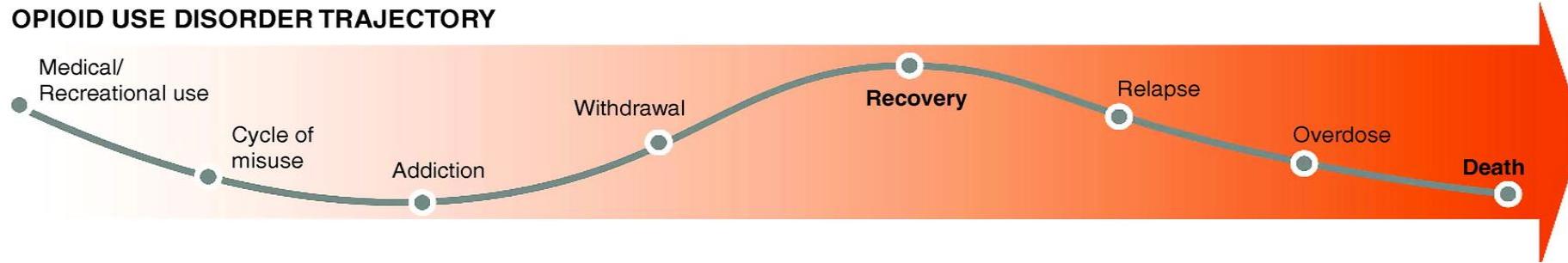
- **Involve pathways of reward and reinforcement by:**
 - neurotransmitter dopamine and prefrontal cortex
- **Brain's learning mechanism** (conscious/unconscious)
- **Mental health issues**
 - Likely accompany
- **Often accompanied by**
 - undiscovered health conditions
 - (Todays Discussion)
- **Cognitive drives:**
 - Past Memories, rewards and motivations
- Are Continued to be pursued despite Physical and psychological harm

When Encountering Roundabout what do we do?

- Slow Down
- Look left and Right
- Count the Lanes
- Look Behind, Look Ahead
- Seek a best or better pathway



OPIOID USE DISORDER TRAJECTORY



- ✓ Identifying those Co-Travelers (Medical Conditions)
- ✓ Changing the Trajectory and Outcomes

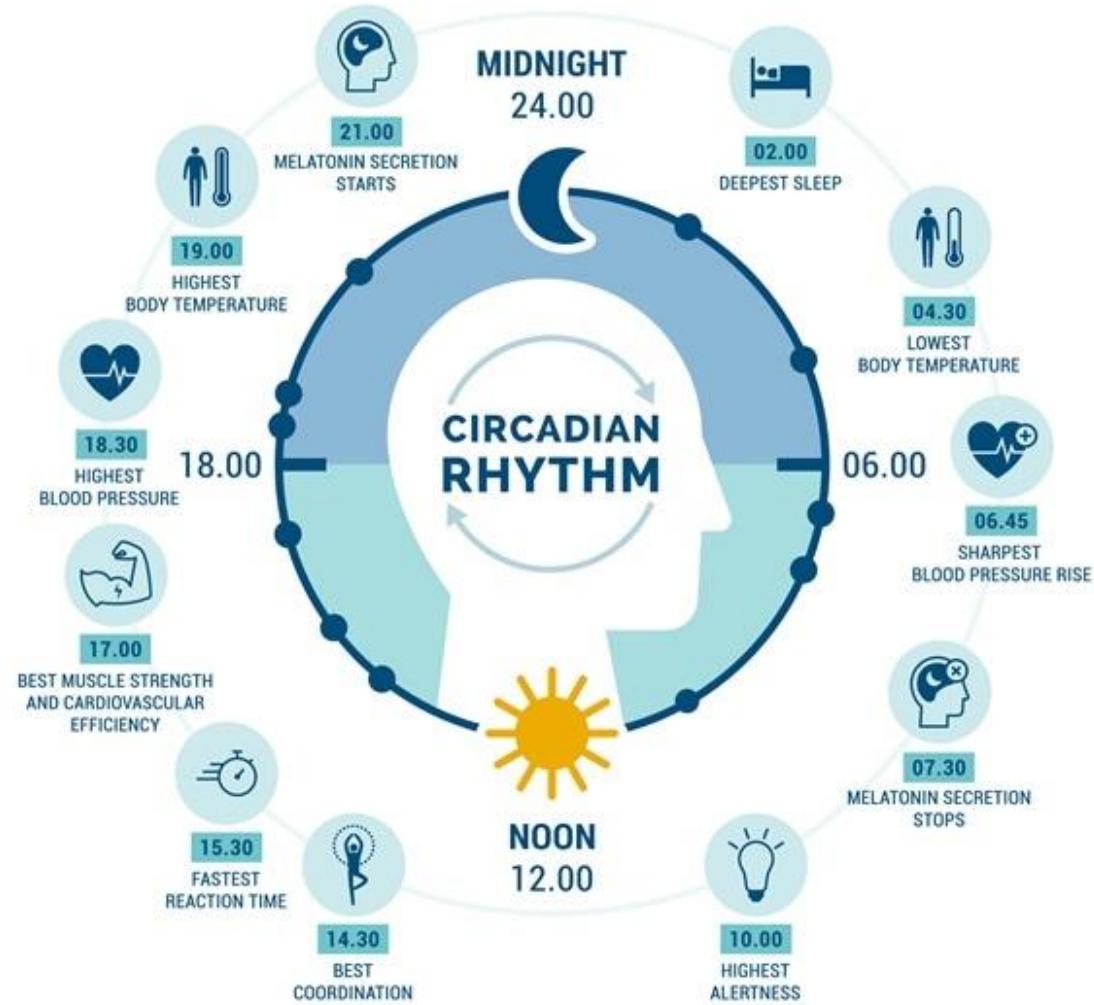


The clocks that time us

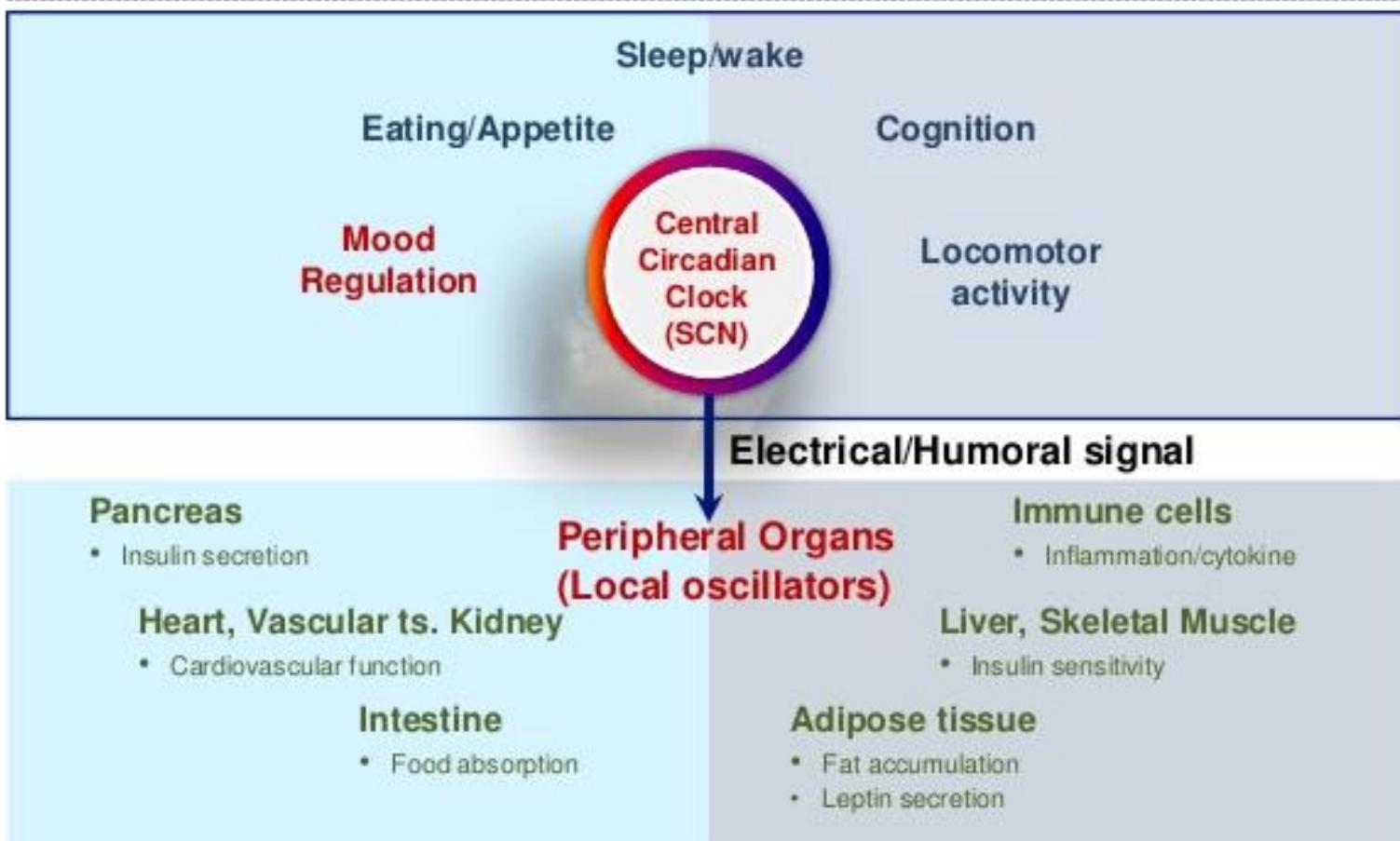
Circadian Clock/Rhythm: the Body's Biological Clock



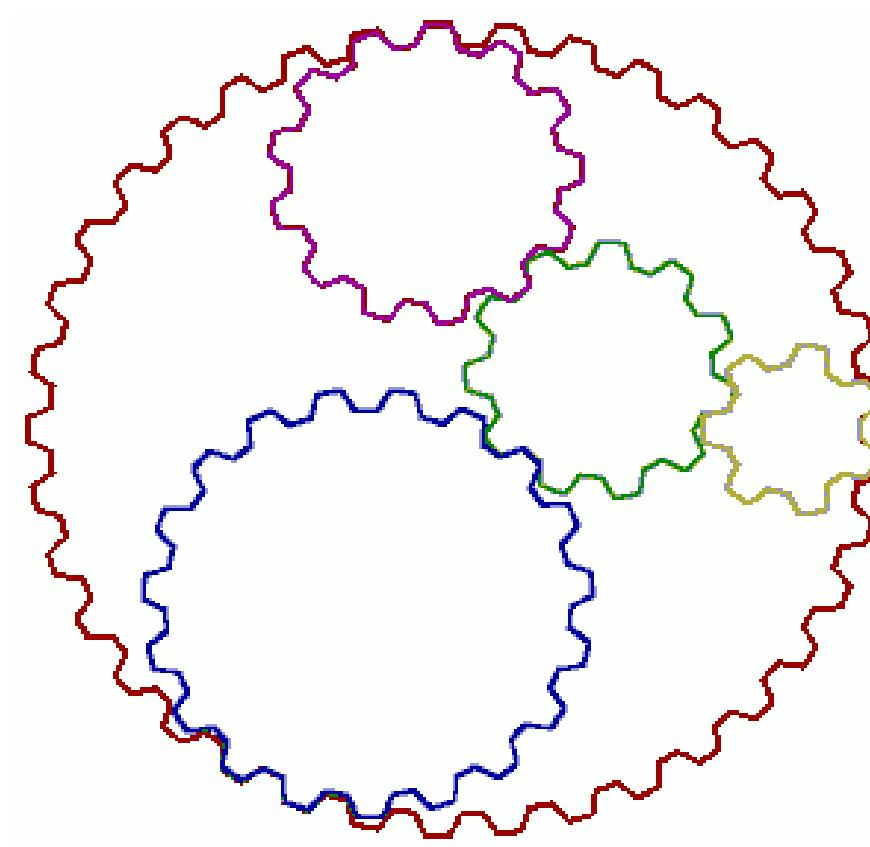
1. Virtually every cell in the body contains its own circadian clock machinery
2. controls levels of hormones important for the sleep-wake cycle.



Circadian clock system



Circadian Rhythm



The clocks that time us

Circadian Rhythms in Pain Disorders

1. Circadian clock regulates:

➤ key physiological processes (**Genes**)

➤ maintains cellular, tissue, and systemic homeostasis. **Genes**

➤ Immune activation has been closely linked to **neurodegeneration**.

➤ Circadian regulation of brain cells implicated in role of systemic inflammation on **neurodegeneration**

2. Disruption of influences key activities involved in:

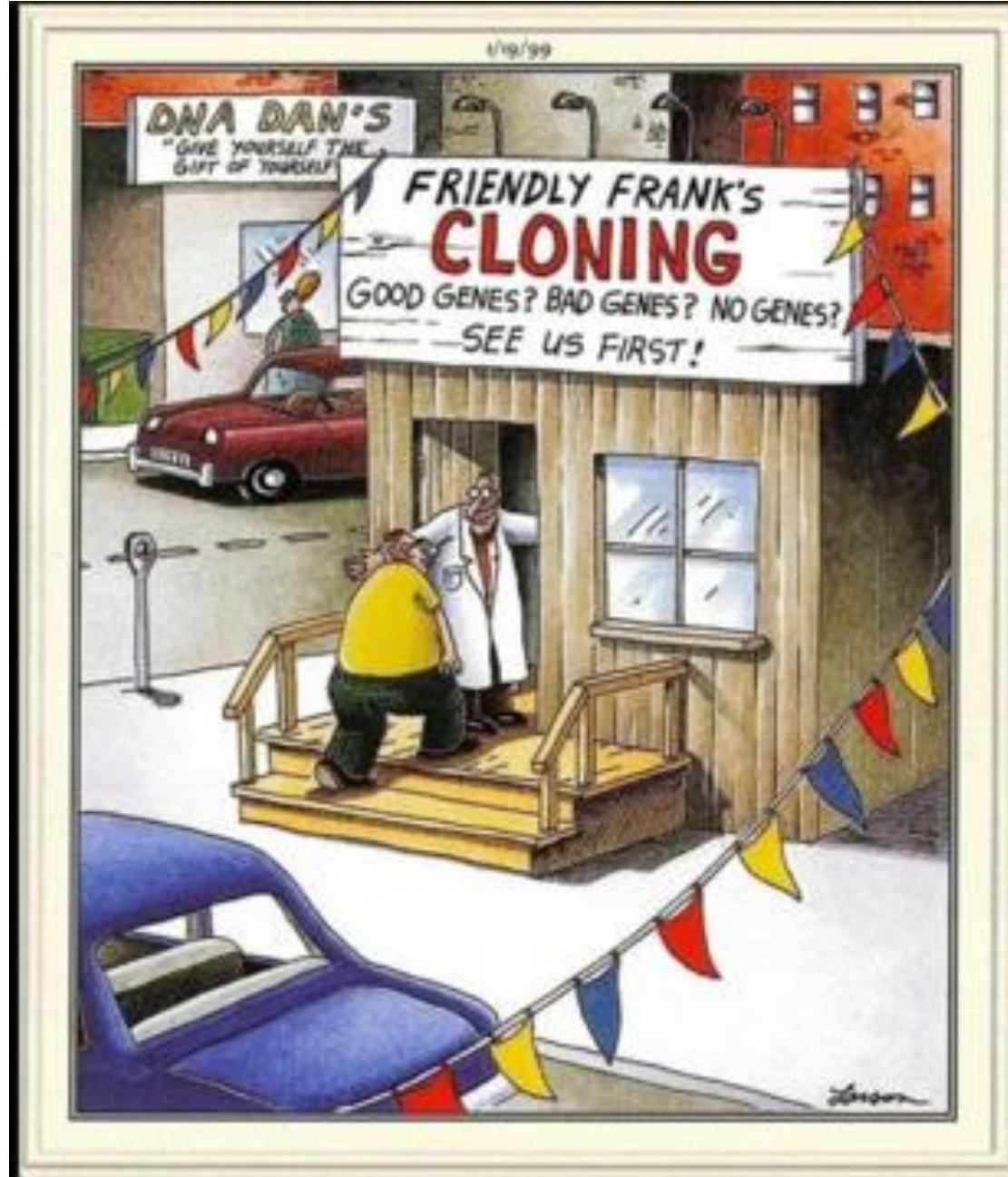
➤ immune response

➤ molecular rhythm disruptions

➤ brain function.

• **Circadian clocks regulates**

- Pain,
- opioid analgesia
- opioid reward processing



Circadian Rhythm Disruptors 1

- Lifestyle habits (**Social jet lag**)
- Lifestyle habits can raise your risk for circadian rhythm disorders.
- include:
 - Alcohol, Chronic caffeine use
 - Frequent air travel
 - Illegal drug use
 - Lack of exposure to natural light during the day
 - Unhealthy sleep habits

Other Disorders

- **Autism spectrum disorders**
- **Certain genetic conditions**, such as Smith-Magenis syndrome, Angelman syndrome, and Huntington's disease
- **Conditions that affect eyesight**, such as blindness and macular degeneration,
- **Conditions that cause damage to the brain**, such as traumatic brain injuries, strokes, and brain tumor
- **Mental health conditions**, such as bipolar disorder, major depression, obsessive-compulsive disorder, and schizophrenia, which raise the risk of delayed sleep-wake phase disorder
- **Neurodegenerative** diseases

Circadian Rhythm Disruptors 2

- Cancer
- Alcohol
- Poor liver function
- Leaky Gut
- Depression
- Low Melatonin Production
- Shift work
- Loss of Sleep wake regulators
- Altered adenosine levels
- **Pain / OUD, medications**
- Irregular metabolism in the day/night
- Micro awakening
- Altered sleep REM/SWS structures
- Parasomnia
- Snore, SRBD
- Insomnia
- Traumatic Disorders
- Molecular rhythm disruptions

Circadian rhythms of opioid analgesia



❑ Pain behavior varies across the day

- Variations in diurnal rhythms of acute pain also exist

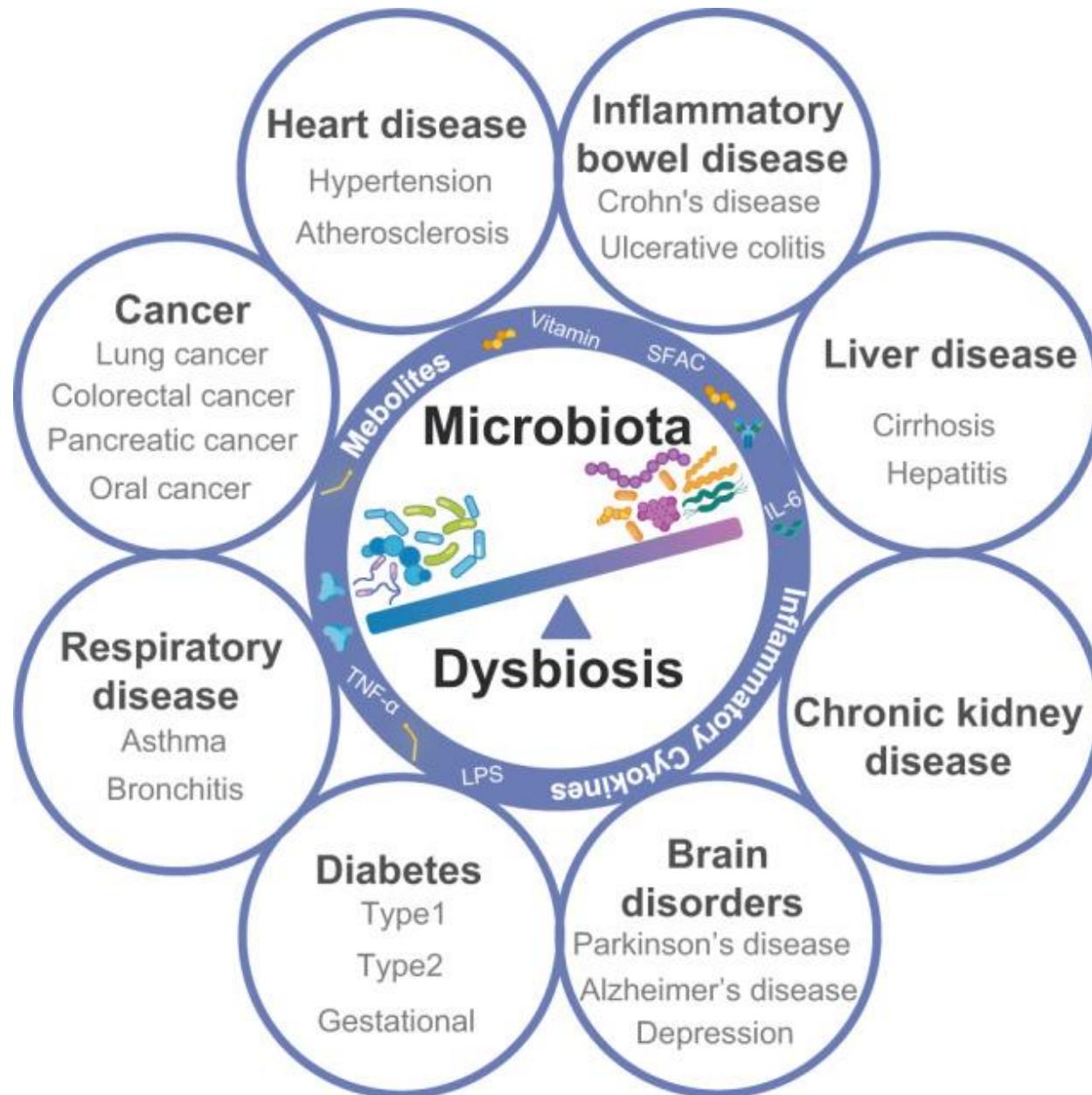
❑ Efficacy of opioid analgesics also varies across the day

1. biliary colic and labor pain peak at night, whereas post-operative pain peaks in the morning
2. trigeminal neuralgia pain peak in the morning,
3. neuropathic pain and TMJ pain peak in the night at 20:00 h

•Correcting Circadian Misalignment: Keeping the Clock in Time



1. **Keep** a regular meal schedule, especially if you are a shift worker or sleep at irregular times of the day or night. **time-restricted eating (TRE)**
2. **Start** a regular bedtime routine. Sleep in a cool (96), quiet place and follow a relaxing bedtime routine that limits stress. These practices, along with regular sleep and waking times, can help you fall asleep faster and stay asleep longer. **(correcting phase shift)**
3. **Avoid** daytime naps, especially in the afternoon. **Limit to 20-30 min**
 1. However, shift workers may benefit from a short nap before the start of their shift.
4. **Get** regular physical activity. You may recommend getting regular physical activity during the daytime and avoiding exercising close to bedtime, which may make it hard to fall asleep.
5. **Limit** caffeine, alcohol, nicotine, and some medicines, especially close to bedtime.
6. **Manage** your exposure to light. Light is the strongest signal in the environment to help reset your sleep-wake cycle.
 - Dim lighting for a period before bed may also help reduce the symptoms of a circadian rhythm disorder.



Gut bacteria (microbiome) both **produce and respond** to the same neurochemicals used by brain to regulate mood and cognition

GABA
serotonin
norepinephrine dopamine
acetylcholine melatonin

How to heal from pain, inflammation and autoimmunity...



Seek Help from Nutrition
(NielsenNutrition.com)

Feed the Body

Drink ½ body weight in water (up to 100 ounces)

Sleep 8 hours a night

Practice mindfulness

Eat anti-inflammatory food:

Fats: fish, chia, flax, coconut oil, walnuts

Fruits: look for color and vibrancy, berries, pineapple

Vegetables: green leafy, broccoli, bok choy

Herbs / spice: ginger, rosemary, turmeric, cinnamon, basil, clove

Heal Leaky Gut

Bone broth

Aloe, DGL, Glutamine, Zinc

Eliminate processed sugar

Rest, de-stress

Balance microbiome

Identify underlying triggers (virus, food sensitivities etc)

Address digestion

Give the body a break: Gluten Free / Dairy Free

Fermented Foods (need base / barrier)

Lacto / bacillus probiotics

Extra Support

Turmeric (golden milk, Inflama-Complete – must be quality: rhizome extract)

Dark Cherry Juice

Epsom Salt Baths

Arnica

Chamomile

Essential oil

Heat / Cold therapy: sauna, cryo or at home

Avoid: artificial sweeteners & additives that destroy the microbiome AND increase inflammation

Avoid: artificial sweeteners & additives that destroy the microbiome AND increase inflammation



Circadian Misalignment Traffic Jam



This thing we called Sleep



Sleep's Mechanisms

Physiology and Neurochemistry regulation

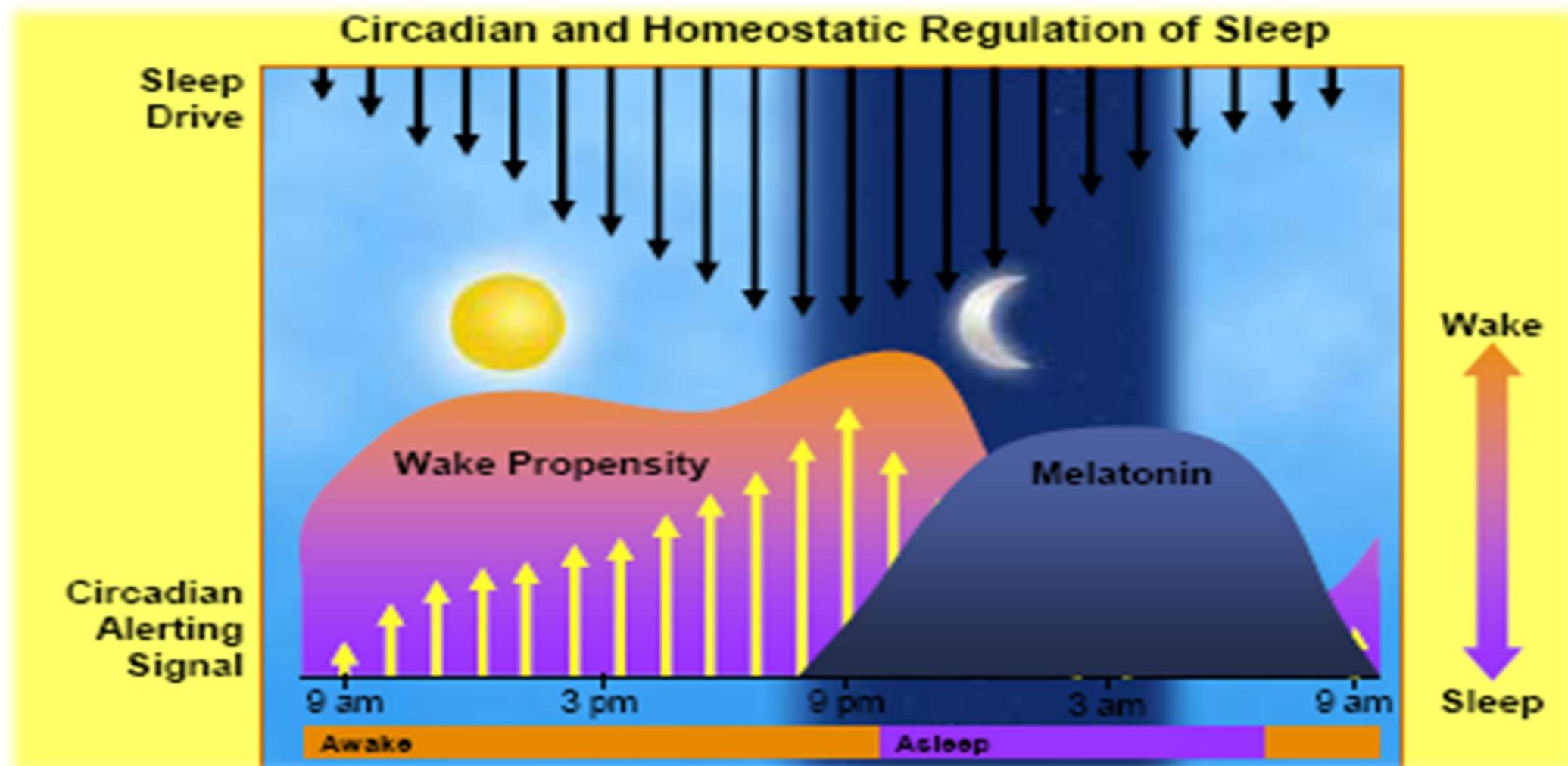
Circadian rhythm and Homeostasis drives

The wake-sleep circuit

categorized within 3 major factors

1. Circadian rhythms:
 - **daily cycles of sleep-wakefulness**
2. Homeostatic drive:
 - the need to sleep that accumulates as a function of prolonged wakefulness
3. Allostatic signaling :
 - the adaptation of sleep and wakefulness to
 - External &
 - behavioral events

Sleep Wake Cycle



Disorders impacting Sleep?

- Sleep-disordered breathing
- Central disorders of hypersomnolence
- Circadian rhythm sleep-wake disorders
- Sleep-related movement disorders
- Pain (OUD)
- Medications
- Addictions (?)
- Parasomnias
 - **abnormal and undesirable behaviors during sleep** and are thought to be due to the sleep state instability.
- PTSD
- CHF
- COPD
- Microbiome
- CVA
- Mood Disorders

Sleep-Wake Disorders and Chronic Pain: Reciprocal and Interactive Effects

As the patient spend **more time in Bed**

- Basic circadian cycle is **disrupted**
- Basic physiologic rhythm of sleep is **lost**

Lack of movement and sleep leads to

- more pain
- further sleep disruption
- dysphoria
- more fatigue.
- Sleep deprivation produces hyperalgesia changes according to most studies

Common Responses and Symptoms of Sleep Disorders

- Emotional signs include:
 - sadness
 - anger
 - denial
 - fear
- These may lead to:
 - nightmares
 - insomnia
 - difficulty with relationships
 - emotional outbursts
- Common physical symptoms:
 - dizziness
 - altered sleep patterns
 - changes in appetite
 - headaches
 - gastrointestinal problems
- Co-Psychological disorders may include:
 - PTSD
 - TBI (all concussions)
 - depression
 - anxiety
 - dissociative disorders
 - substance abuse problems

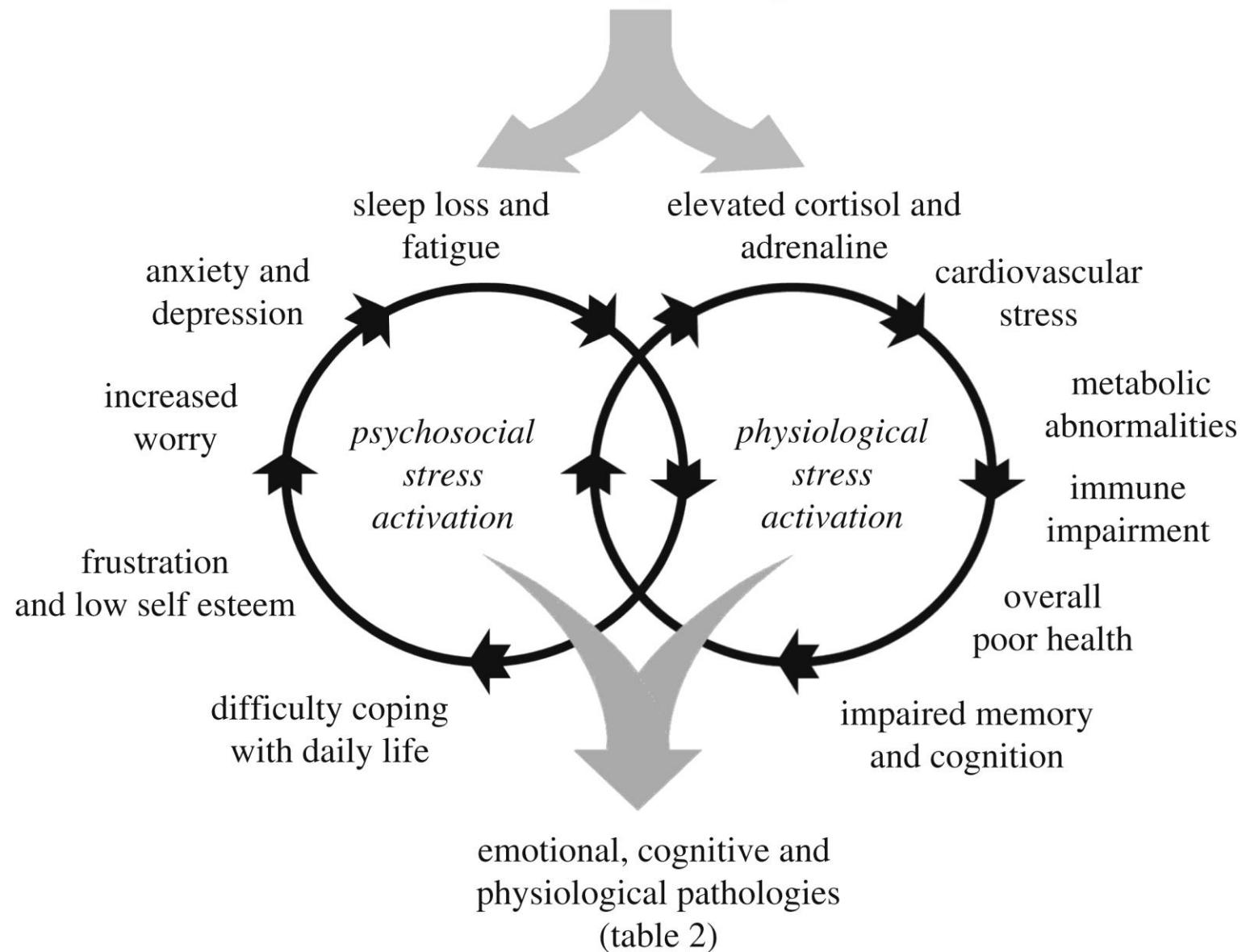
Sleep Debt's impact: Brain, Mind, and Amygdala

1. **functional deficit** occurs between:
 - amygdala
 - ventral anterior cingulate cortex (vACC),
(voice of reason and calm)
2. which can result in decreased mood and can cause the amygdala to have
heightened responses to negative stimuli
3. reduces the ability of the medial prefrontal cortex (MPFC) to suppress activity in the amygdala, leading to **emotional instability**
4. A prolonged deprivation of rapid eye movement (REM) sleep is associated:
 1. functional changes:
_in multiple brain regions
 2. altered receptor activity:
leads to mood alterations such as anger

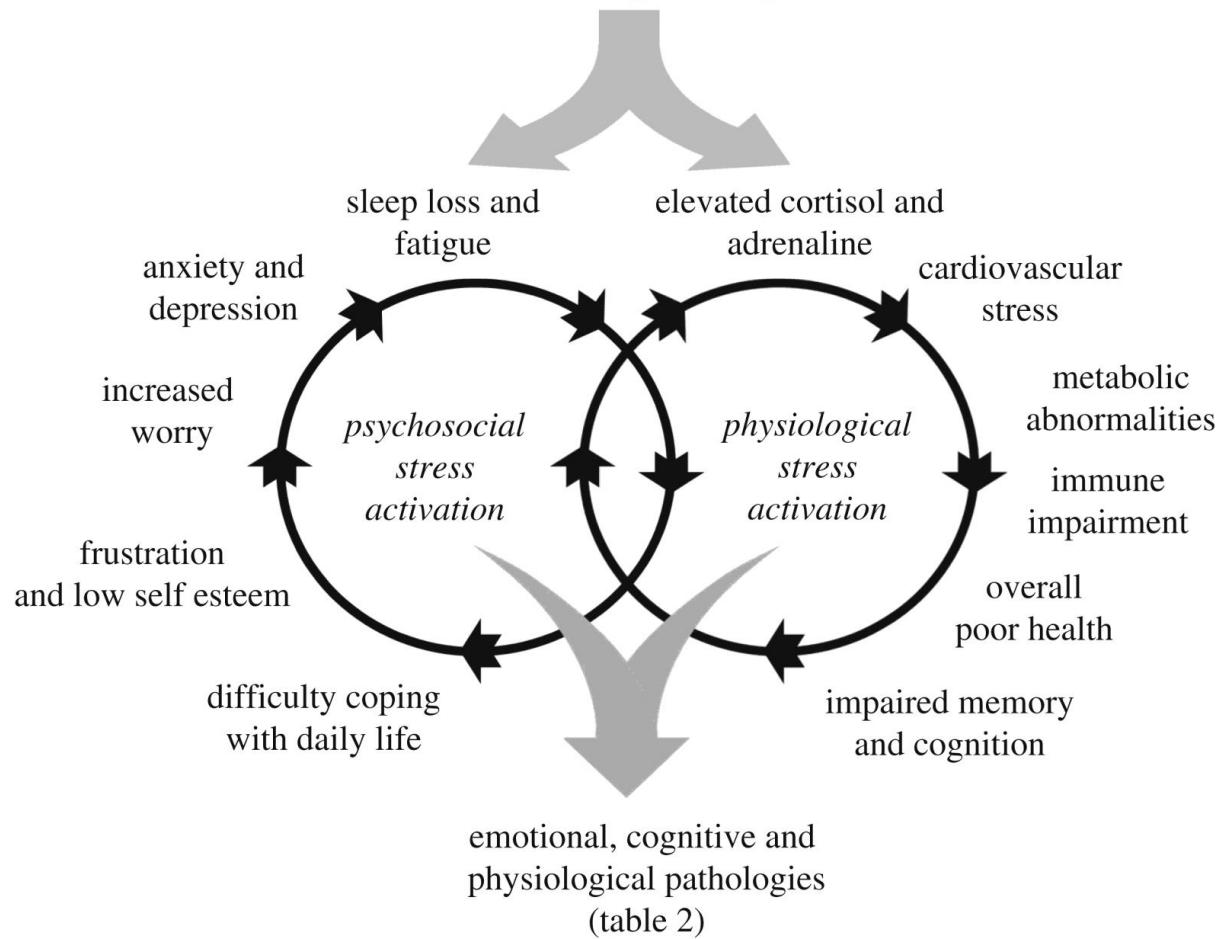
Sleep Disorder's Impact

- Up to 70 million people in the US
- ~45 million people in Europe have a chronic sleep disorder that impacts daily functioning and health
- There are ~100 sleep disorder classifications
- Associated with increased activity of:
 - **sympathetic nervous system !**
 - **hypothalamic–pituitary–adrenal axis !**
 - **metabolic effects!**
 - **changes in circadian rhythms!**
 - **proinflammatory responses!**

chronic sleep disruption



chronic sleep disruption



Sleep is a key determinant of Brain Health linked OUD

- Sleep deficiency is an important correlate of OUD.
-
- Associated with overlapping cognitive deficits:
 1. executive function
 2. reward processing
- Deficiency leads to **desperation**
- A growing scientific consensus has identified sleep as a
- **critical component of OUD, during:**
 - active disease state
 - during recovery
- Patients with OUD identified sleep disturbance as a
 - **primary contributor to relapse and treatment attrition**

Biochemical Pharmacology of **Sleep/Pain** Receptors, Neurotransmitters and Neuropeptides

Sleep

- Dopamine
- Histamine
- **Serotonin**
- Adenosine
- **Melatonin**
- **GABA**

- Norepinephrine
- Acetylcholine
- Interleukin-1
- Prostaglandins
- Neuropeptides
- Orexin

Pain

- Glutamate
- **GABA**
- Opioid peptides
- IL- 6
- Cannabinoids
- Leptin
- **Orexin**
- **melatonin**

The **INSOMNIA SCREENING QUESTIONNAIRE** is a **screening tool** used to guide the providers in the clinical evaluation of **insomnia and many under current sleep impacting issues**



- Is a screening tool used to guide the providers in the clinical evaluation of sleep and insomnia.
- It is used to screen for a primary sleep disorders

Diagnostic Domains:

- 1) Insomnia: Q 3, 4 or 5
- 2) Psychiatric Disorders: Q 6-9
- 3) Circadian Rhythm Disorder: Q10
- 4) Movement Disorders: Q11-12
- 5) Parasomnias Q13
- 6) Sleep Disordered Breathing (Sleep Apnea): Q14-16

insomnia screening questionnaire - JPS Health Network

https://www.jpshealthnet.org/sites/default/files/insomnia_screening_questionnaire.pdf



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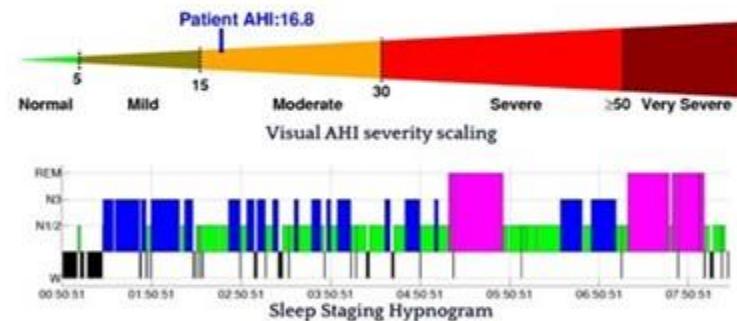


Home Sleep Study - Analysis & Interpretation

Patient Name DOB Age Study Date Interp. Physician		Study ID Sex BMI Patient Code Interp. Date	
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[REDACTED] underwent a level II diagnostic home sleep study using a Zmachine Synergy device on 09/17/2023 to explore the possibility of obstructive sleep apnea among other differential diagnoses for sleep disorders. Raw data was reviewed epoch by epoch for diagnosis and recommendation.

Summary of Findings



Recording Time	Sleep Time	AHI	RDI	ODI	REI	Snoring
1370.3 min. (over 3 nights)	386.3 min. (1 night)	16.8/hr	17.4/hr	13.8/hr	15.6/hr	8.9% of TST
Mean Heart Rate	CAI	Supine AHI	Supine RDI	Mean SpO ₂	Lowest SpO ₂	Time in SpO ₂ < 89%
70.9 bpm	0.2/hr	17.5/hr	18.3/hr	92.3%	82%	1.2% of TST
		REM AHI	REM RDI			
		27.8/hr	28.5/hr			

AHI = Apneas + Hypopneas per hour of sleep. All apneas and hypopneas are at least 10 seconds in duration, and hypopneas are scored with a minimum 3% associated desaturation. ODI = Oxygen desaturations of at least 3% from baseline per hour of sleep.



Findings and Interpretation

- The findings on this night of the study, out of 3 reviewed, was deemed most representative.
- This study was technically adequate. No technical issues were noted.
- Sleep fragmentation was noted.
 - Broken sleep was closely associated to respiratory events.
- RDI (respiratory disturbance index) most accurately reflects the patient's clinical picture.
 - On this basis, there is evidence for the presence of sleep apnea.
- Respiratory events increased in the supine position (18.3/hr) compared to the non-supine positions (16.2/hr).
- REM sleep demonstrated a higher presence of respiratory events (28.5/hr) compared to NREM stages of sleep (14.3/hr).
- 1 central apneas noted, resulting in a central apnea index of 0.2/hr.
 - These appeared after arousals, and are considered within the realm of normal.
- Total of 4.5 minutes at or below 89%.
 - The longest duration of an SpO₂ at or below 89% was 0.4 minutes.
- Snoring was noted for 34.3 minutes (8.9% of total sleep time).
- Heart rate evaluation demonstrated expected fluctuations within the scope of normal parameters for this patient's history and sleep study.

Diagnosis

- Moderate Obstructive Sleep Apnea sleep apnea
- Sleep fragmentation

Recommendations

- AutoPAP 5-18 cm H₂O to begin, with in-office pressure adjustment determined at follow-up visits as indicated.
- Recommend hybrid/combination full-face mask (i.e. Philips DreamWear Full Face mask, ResMed AirFit F30i, Fisher & Paykel Evora Full Face Mask, or similar) to start; may be changed per patient preference provided no contraindications are present.
- As an alternative to PAP therapy, this study meets the requirements of medical necessity for use of a mandibular advancement device/oral appliance therapy (OAT), which has supporting evidence to benefit those with mild or moderate obstructive sleep apnea.
- Weight management is a key component of treating sleep apnea. Ensure a strong diet and regular exercise regimen to optimize overall sleep.
- Review sleep hygiene techniques and optimize sleep environment.
- Recommend follow-up with Sleep Specialist for initial PAP adherence and monitoring at 1 month, 3 months & 12 months after PAP initiation.

Electronically Signed 2023-10-06, 12:21 by
Ankur N. Patel, MD MS
Sleep Medicine Physician
Wellness Institute for Sleep and Health

Modifying Sleep Environment (Supportive Therapies)



- **Body Temperature:**
 - Room Thermal Controls (96)
 - Anxiety elevates temperature
- **Bed and Positionings (HOB)**
- **Exercise/Movement**
 - Promotes sleep depth and quality
- **Auditory Exposure:**
 - Rhythmic Auditory Stimulation (RAS)
- **Visual Therapies :**
 - (modify circadian cycles)
 - <https://justgetflux.com/research.html>

Rhythmic Auditory Stimulation (RAS) involves synchronizing the patient
(Stroke and Sleep rehab)



Your Ears always Hearing

(6) Reasons Why White Noise Helps You Sleep



- **Helps you build a bedtime ritual.**
- **Keeps your bedroom CALM**
- **Shuts down your busy brain.**
- **Once you're asleep, you'll stay asleep.**
- **You'll sleep more soundly.**
- **You can bring white noise anywhere.**



Other substance use is common in OUD and may also contribute to sleep/circadian deficiency

- the rate of **cigarette smoking** among individuals with OUD far exceeds that of the general population.
- Nicotine:
 - ❖ lengthens sleep onset latency
 - ❖ decreases total sleep duration (particularly during deeper sleep stages)
- Withdrawal triggers awakenings

- 1) alcohol and cocaine use disorders are highly comorbid in OUD
- 2) associated with poorer OUD outcomes.
 - Alcohol, a depressant,
 - ❖ **may** promote the initiation of sleep.
 - ❖ **but** it is very disruptive during the second half of sleep
 - (e.g., **increased wake after sleep onset, nightmares, decreased slow wave sleep**) and contribute to SDB
 - Cravings, reflux, hangover, depression, ect

Take home points:

Circadian system, Pain system, and Opioid processing pathways form a spiraling and disruptive feedback loop

- Sleep deprivation and circadian disruption predisposes individuals to
 - future and or worsening pain control,
 - impaired cognitive function,
 - metabolic dysregulation and
 - Opioid craving and relapse
 - confounding addictive patterns (OUD).
- Sleep disturbances history can complicate the course of recovery from pain and substances.
- Suspect it in all pain disorders
 - (Sleep Consult)
- Correcting Circadian Misalignment:
 - Requires intensive counseling
 - Pt motivation
- Non-pharmacologic intervention:
 - Brief Behavioral Therapy (BBT) effective in reducing acute and chronic pain conditions, plus Opioid over use
- NIH committed \$25 million to fund a research program entitled “Sleep dysfunction as a core feature of opioid use disorder and recovery”

Any Questions?

Bill Davies, BS, PAC, Education

