Insomnia

Jonas M. Rawlins, DO, FACP

Disclosures

None


3:32

Objectives

Discuss	Discuss the underlying etiology/pathophysiology of insomnia.
Differentiate	Differentiate insomnia disorder from parasomnias, sleep related breathing disorders, and other sleep disorders.
List	List the non-pharmacologic treatments of insomnia
Explain	Explain the evidence and risks of pharmacologic treatments.

Introduction

Insomnia is the most common sleep disorder

Poses substantial burden on US healthcare system.

Linked to higher healthcare utilization and costs

Adverse Outcomes

- Reduced Quality of Life
- Cognitive function and performance
- Self-medication
- Association with suicide
- Cardiovascular risk and mortality

SLEEP, 2021, 1–9

doi: 10.1093/sleep/zsaa150
Advance Access Publication Date: 24 September 2020
Original Article

ORIGINAL ARTICLE

Insomnia with objective short sleep duration is associated with cognitive impairment: a first look at cardiometabolic contributors to brain health

Julio Fernandez-Mendoza[1,*], Fan He[2], Kristina Puzino[1], Gregory Amatrudo[1], Susan Calhoun[1], Duanping Liao[2], Alexandros N. Vgontzas[1] and Edward Bixler[1]

Definition

- A persistent sleep difficulty
- Despite adequate opportunity for sleep
- Associated with daytime dysfunction
- Can be short term (acute) or chronic
- Short term or acute (less than 3 months) usually lasts a few days or weeks and occurs in response to an identifiable stressor
- Chronic Insomnia occurs at least 3 days per week and persists for at least 3 months

Pathophysiology

Sleep is a strong and highly regulated biologic drive

The etiology of insomnia can be best seen as factors that contribute over time

Predisposing	Precipitating	Perpetuating

Predisposing factors

- Underlying medical or psychiatric conditions
- History of childhood or interpersonal trauma
- History of shift work or erratic sleep-wake patterns
- Chronic pain conditions

Common Comorbidities

Psychiatric conditions	Medical conditions	Neurologic Conditions	Medications and substances	Other sleep disorders
• Depression, • anxiety, • substance use disorders, • PTSD	• Pulmonary – COPD, Asthma, OSA • Rheumatologic – arthritis, fibromyalgia, chronic pain, Lyme disease • Cardiovascular – heart failure, ischemic heart disease, nocturnal angina, hypertension • Endocrine – hyperthyroidism, diabetes • Urinary – nocturia • GI – GERD • Cancer • Pregnancy • Dermatologic - pruritus	• Neurodegenerative disease (Alzheimer's, Parkinson's, neuromuscular • neuropathies, • hemispheric and brainstem strokes, • tumors, • Traumatic brain injuries • headache syndromes	• Stimulants, depressants, bronchodilators, antidepressants, beta antagonists, diuretics, glucocorticoids, caffeine, alcohol	• Restless leg Syndrome • Periodic Limb movement syndrome • Circadian Rhythm Sleep Wake Disorder

Precipitating events

- Events that lead to sleep disruption
  - Severe accident leading to physical injury
  - Divorce or death of spouse or close family member
  - Change in occupation such as loss of a job or transition to a new job

Perpetuating factors

Behavioral and cognitive compensatory factors

Poor sleep habits

Unrealistic expectations of sleep

Inappropriate attributions about the association of daytime symptoms and nocturnal sleep

Anxiety and worry about sleep loss

Evaluation

- History is key
- Acute or occasional insomnia – trigger or cause generally more clear
- Chronic insomnia – patterns and experiences around insomnia
- Useful tools – sleep diary (National Sleep Foundation Sleep Diary or Consensus Sleep Diary), Insomnia Severity Index

Insomnia Severity Index

Insomnia Severity Index

The Insomnia Severity Index has seven questions. The seven answers are added up to get a total score. When you have your total score, look at the 'Guidelines for Scoring/Interpretation' below to see where your sleep difficulty fits.

For each question, please CIRCLE the number that best describes your answer.

Please rate the CURRENT (i.e. LAST 2 WEEKS) SEVERITY of your insomnia problem(s).

Insomnia Problem	None	Mild	Moderate	Severe	Very Severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problems waking up too early	0	1	2	3	4

4. How SATISFIED/DISSATISFIED are you with your CURRENT sleep pattern?

Very Satisfied	Satisfied	Moderately Satisfied	Dissatisfied	Very Dissatisfied
0	1	2	3	4

5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life?

Not at all Noticeable	A Little	Somewhat	Much	Very Much Noticeable
0	1	2	3	4

6. How WORRIED/DISTRESSED are you about your current sleep problem?

Not at all Worried	A Little	Somewhat	Much	Very Much Worried
0	1	2	3	4

7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) CURRENTLY?

Not at all Interfering	A Little	Somewhat	Much	Very Much Interfering
0	1	2	3	4

Guidelines for Scoring/Interpretation:

Add the scores for all seven items (questions 1 + 2 + 3 + 4 + 5 +6 + 7) = _____ your total score

Total score categories:
0–7 = No clinically significant insomnia
8–14 = Subthreshold insomnia
15–21 = Clinical insomnia (moderate severity)
22–28 = Clinical insomnia (severe)

Ruling out another sleep disorder

- Circadian Rhythm Sleep Wake Disorders
- Sleep Disordered Breathing
- Restless Leg Syndrome
- Periodic Limb Movement of Sleep
- Parasomnias

Circadian Rhythm Sleep Wake Disorders

“Short sleeper” or short sleep duration

“Night Owl” or delayed sleep wake disorder

“Early Riser” or advanced sleep wake phase disorder

Sleep Apnea

Pauses in respirations during deep sleep that is associated with brief arousals.

STOP-BANG is an effective screening tool

One study reported OSA may be as high as 30% of patients with insomnia

Table 1. STOP-Bang inquiry

S= (Snoring) Is the snoring higher than normal speech level or high enough to be able to be heard from behind of the closed door?

T= (Tiredness) Is there a frequent tiredness or sleepiness feeling lasting the whole day?

O= (Observed Apnea) Is there anybody around you who has told your breath stopped during your sleep?

P= (Pressure) Have you got high blood pressure?

B= (BMI) Body mass index> 35/m^2

A= (Age) Age > 50

N= (Neck Circumference) Neck circumference > 40 cm

G= (Gender) Male

3 and more 'yes' answers is considered as high risk in terms of OSAS.

Restless Leg Syndrome

- Characterized by an urge to move the legs, sometimes described as creeping, crawling, itching or jitteriness of the legs
- Symptoms are typically exacerbated by periods of inactivity
- Roughly 85% of patients with RLS have difficulty falling asleep
- May also wake frequently during the night with discomfort in their legs

Periodic Limb Movements of Sleep

- Repetitive and highly stereotype limb movements during sleep
- Usually involve the legs and occasionally the arms
- Can cause or be accompanied by partial arousals
- Difficulty with sleep maintenance

Narcolepsy

- Unrefreshing or disrupted sleep
- Excessive daytime sleepiness, unplanned sleep
- Cataplexy
- Hypnogogic and or hypnopompic hallucinations
- Sleep paralysis

Role Of Polysomnography

- Sleep studies are not indicated in the routine evaluation of insomnia
- May be indicated when insomnia is:
  - Severe
  - Resistant to therapy
  - History suggests an underlying sleep disordered breathing problem eg. OSA
  - Sleep disruption is associated with unusual nocturnal activity

Wrist Actigraphy

- Monitors and stores movement data
- Can be used to monitor treatment response and to screen for other circadian disorders
- Information on sleep stages is unreliable
- Commercial products available eg. Smart phones, watches and wearables

Non pharmacologic Treatments

- Cognitive behavioral therapy for insomnia
- Brief Behavioral Therapies for insomnia
- Stimulus control
- Sleep restriction therapy
- Relaxation therapy
- Sleep hygiene

Cognitive Behavioral Therapy - Insomnia

An effective nonpharmacologic treatment that improves sleep outcomes with minimal adverse effects

Multimodal treatment combining cognitive therapies and behavioral strategies

Cognitive therapy	Stimulus control	Sleep Restriction	Sleep hygiene	Relaxation

Evaluating Sleep Treatments

- Sleep Onset Latency (SOL)
- Wake after sleep onset (WASO)
- Total Sleep time (TST)
- Sleep efficiency (SE%)

Sleep hygiene

- Recommended as an initial intervention for all adults with insomnia (not as a monotherapy)
- Exercise regularly (not within 4 hours of bedtime
- Avoid large meals before bed
- Limit fluid intake in the evenings
- Limit caffeine, tobacco and alcohol intake 4-6 hours before bed
- Use bedroom for sleep and sex only
- Maintain regular sleep-wake cycle
- Avoid daytime napping
- Environmental factors - temperature, ambient light, screens

Stimulus control

- Lie down to sleep only when feeling sleepy
- Use the bedroom for sleep and sex only
- Avoid wakeful activities at bedtime (e.g. watching television, talking on the phone, eating)
- Leave the bed if unable to fall asleep within 20 minutes and return when sleepy
- Maintain a consistent sleep wake cycle

Sleep Restriction

- Limit time in bed to the number of hours actually spent sleeping but not less than 5 hours
- May be beneficial in patients spending excessive amounts of time in bed trying to fall asleep
- Initially may worsen daytime sleepiness
- Contraindicated in bipolar disorder and epilepsy and people in high-risk occupations (eg operate heavy machinery)
- Primary care implementation a good alternative to patients unable to do formal CBTi

Relaxation therapy

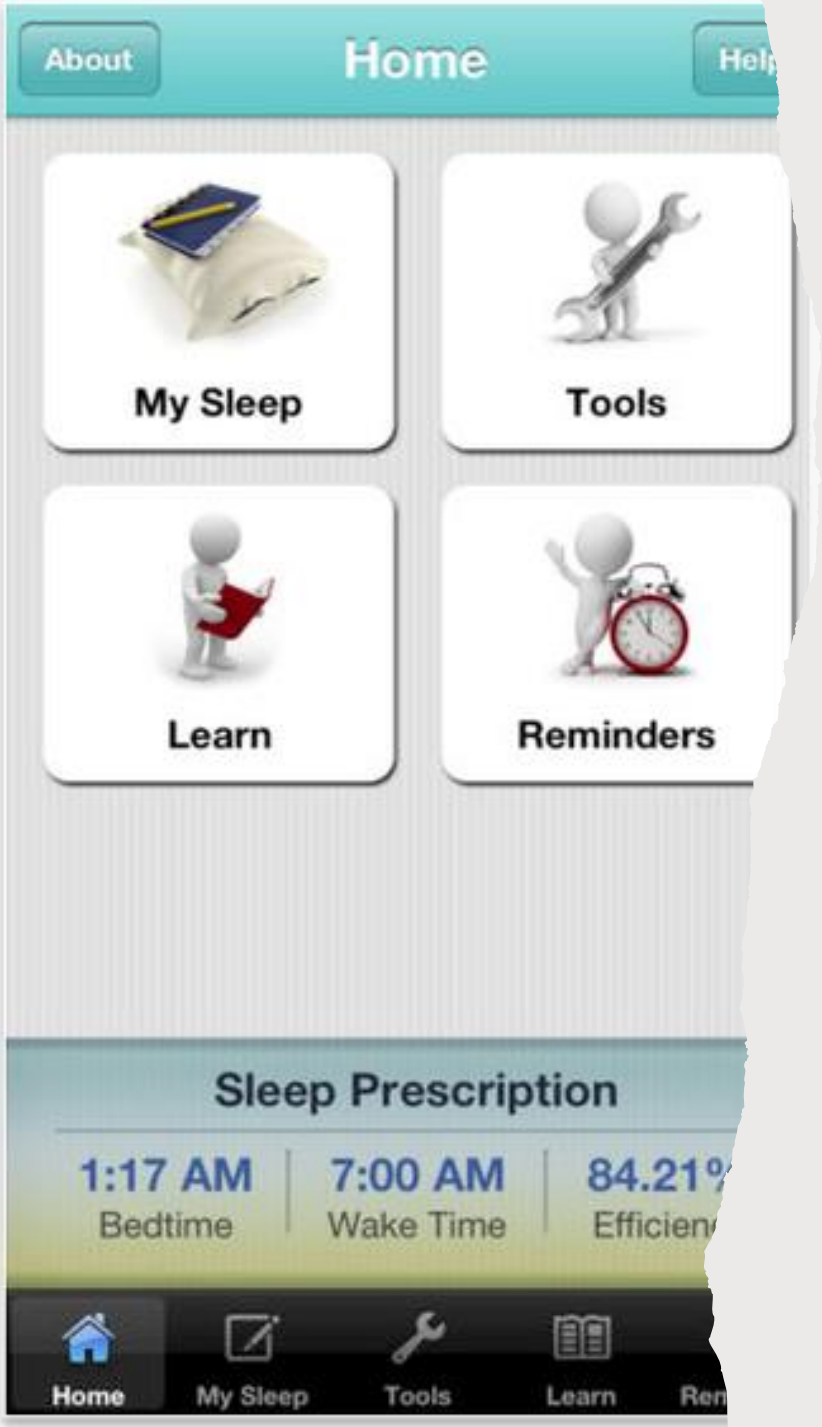
- Any activity that can limit cognitive arousal and reduce muscle tension
- Imagery training
- Hypnosis
- Meditation
- Yoga and Tai Chi
- Abdominal breathing
- Progressive muscle relaxation
- Visual or auditory biofeedback

CBTi

- Guidelines all recommend for long term approach to chronic insomnia
- Included in the above are patients already taking a hypnotic
- Cognitive therapy helps expose and address dysfunctional beliefs and attitudes about sleep and reframe negative beliefs and attitudes
- A meta-analysis found that the NNT with CBTI for improvement in ISI is 1.95, and in TST is 11.11
- RCT found that 6 weeks of CBTI produced durable benefit for 24 months
- CBTi + zolpidem (tapered after 6 weeks) led to better long-term improvement than CBTI alone or long-term PRN Zolpidem

Somryst

FDA approved digital CBTI



CBT-I Coach

Developed by the Department of Veteran Affairs and Stanford

CBT-I and Digital CBT-I

- RCT of dCBT-I showed sustained improvement in sleep efficiency after 6 weeks of treatment with sleep efficiency improving to >80% in 76% in the dCBT-I group
- Improves overall insomnia severity, sleep efficiency, sleep onset latency, soundness of sleep, restored feeling upon awakening and general fatigue
- Low cost alternative and readily available
- High adherence rate (78%) and low NNT (3.59)
- Inferior to in person face to face CBT-I

Pharmacologic Treatments of Insomnia

- Benzodiazepines
- Non-benzodiazepine Receptor Agonists
- Melatonin and Melatonin Receptor Agonists
- Dual Orexin Receptor Antagonists
- Sedative Anti-Depressants

Benzodiazepines

Temazepam

- 7.5-30 mg dose range
- 1-5 hours to max concentration
- 3.5 - 18.4 hours half-life
- Slow-intermediate – SO, SM

Triazolam

- 0.25-0.5 mg dose range
- 2 hours to max concentration
- 1.5-5.5 hours half life
- Rapid/short - SO

Non-benzodiazepine benzodiazepine receptor agonists

Zolpidem

- Immediate release sublingual 1.75- 3.5 mg
  - Rapid/ultra- short acting – for nighttime awakenings
- Oral tablet 5, 10 mg
  - Rapid/short acting – sleep onset and maintenance
- Sublingual tablet 5, 10 mg
  - Rapid/short acting – sleep onset and maintenance
- Controlled release
  - Rapid/short – 6.25, 12.5 mg – sleep onset and maintenance
- Women should use lower dose to reduce next day effects

Eszopiclone

- 1, 2, and 3 mg
- rapid/intermediate acting – sleep onset and maintenance
- Initial dose for men and women 1 mg

Zaleplon

- 5, 10 mg
- Rapid/ultra short acting - sleep onset

Dual Orexin receptor antagonists

Daridorexant

- 25, 50 mg
- Slow/long onset and duration
- Sleep maintenance

Suvorexant

- 5, 10, 20 mg
- Slow/long onset and duration
- Sleep maintenance

Lemborexant

- 5, 10 mg
- Slow/long onset and duration
- Sleep maintenance

Melatonin and Melatonin Agonists

Melatonin

- 1-3 mg
- 1-6 hr onset and 3.5-4-hour duration

Ramelteon

- 8 mg dosage
- 45 min onset and 1-2.5-hour duration
- Indicated for treatment of insomnia

Tasimelteon

- Indicated for non-24-hour syndrome, a circadian rhythm disorder that affects blind people

Sedative anti depressants

Doxepin

- 3, 6 mg
- Slow/long onset and duration
- Indicated for sleep maintenance

Not recommended

- Trazodone
- Amitriptyline
- Mirtazapine
- Seroquel

Future Advances

- Behavioral therapeutic approaches
  - Bright light therapy alone or in combo with CBT-I
  - MBSR administered in combination with CBT-I
  - In lab treatment with PSG for intense sleep retraining
  - Sleep center or hospital-based CBT-I
  - Brief Behavioral treatment for insomnia, alternative to CBT-I
- Pharmacologic
  - Orexin receptor antagonists with different receptor affinities
  - Different pharmacokinetics, such as altered time to maximum concentration or half life values
  - Different formulations to allow for different onset and offsets of therapeutic effects
  - Non reacemic mixtures of compounds for stereoisomers
- Combined
  - CBT-I combined with sedatives/hypnotics

Takeaways

Acute insomnia is insomnia lasting less than 3 months

Chronic insomnia is insomnia lasting more than 3 months

The pathophysiology of insomnia includes a state of hyperarousal complicated by predisposing, precipitating and perpetuating factors

Clinicians should focus on history to exclude other sleep disorders, notably OSA where the prevalence may be as high as 30%

CBT-I is the first line treatment recommended by the ACP and AASM due to both its efficacy and durability with low potential for side effects

Pharmacologic management of insomnia is best implemented at lowest efficacious dose and for short durations of treatment (< 6 weeks)

References

Asarnow, L. D., & Manber, R. (2019). Cognitive behavioral therapy for insomnia in depression. *Sleep Medicine Clinics*, *14*(2), 177-184.

Buysse, D. J. (2013). Insomnia. *Journal of the American Medical Association, 309*(7), 706-716.

Choi, K., Lee, Y. J., Park, S., Je, N. K., & Suh, H. S. (2022). Efficacy of melatonin for chronic insomnia: Systematic reviews and meta-analyses. *Sleep Medicine Reviews*, 101692.

Dopheide, J. A. (2020). Insomnia overview: epidemiology, pathophysiology, diagnosis and monitoring, and nonpharmacologic therapy. *The American Journal of Managed Care*, *26*(4 Suppl), S76-S84.

Edinger, J. D., Arnedt, J. T., Bertisch, S. M., Carney, C. E., Harrington, J. J., Lichstein, K. L., ... & Martin, J. L. (2021). Behavioral and psychological treatments for chronic insomnia disorder in adults: an American Academy of Sleep Medicine clinical practice guideline. *Journal of Clinical Sleep Medicine*, *17*(2), 255-262.

Kay-Stacey, M., & Attarian, H. (2016). Advances in the management of chronic insomnia. *Bmj*, *354*.

Low, T. L., Choo, F. N., & Tan, S. M. (2020). The efficacy of melatonin and melatonin agonists in insomnia–An umbrella review. *Journal of Psychiatric Research*, *121*, 10-23.

Maness, D. L., & Khan, M. (2015). Nonpharmacologic management of chronic insomnia. *American Family Physician*, *92*(12), 1058-1064.

References

Patel, D., Steinberg, J., & Patel, P. (2018). Insomnia in the elderly: a review. *Journal of Clinical Sleep Medicine*, *14*(6), 1017-1024.

Perlis, M. L., Posner, D., Riemann, D., Bastien, C. H., Teel, J., & Thase, M. (2022). Sleep and Sleep Disorders 2 Insomnia. *Lancet*, *400*, 1047-60.

Qaseem, A., Kansagara, D., Forciea, M. A., Cooke, M., Denberg, T. D., & Clinical Guidelines Committee of the American College of Physicians. (2016). Management of chronic insomnia disorder in adults: a clinical practice guideline from the American College of Physicians. *Annals of Internal Medicine*, *165*(2), 125-133.

Riemann, D., Baglioni, C., Bassetti, C., Bjorvatn, B., Dolenc Groselj, L., Ellis, J. G., ... & Spiegelhalder, K. (2017). European guideline for the diagnosis and treatment of insomnia. *Journal of Sleep Research*, *26*(6), 675-700.

Rios, P., Cardoso, R., Morra, D., Nincic, V., Goodarzi, Z., Farah, B., ... & Tricco, A. C. (2019). Comparative effectiveness and safety of pharmacological and non-pharmacological interventions for insomnia: an overview of reviews. *Systematic Reviews*, *8*(1), 1-16.

Sateia, M. J., Buysse, D. J., Krystal, A. D., Neubauer, D. N., & Heald, J. L. (2017). Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of Sleep Medicine clinical practice guideline. *Journal of Clinical Sleep Medicine*, *13*(2), 307-349.

Sutton, E. L. (2021). In the clinic Insomnia. *Annals of Internal Medicine*, *174*(3), ITC33-ITC48.

Trauer, J. M., Qian, M. Y., Doyle, J. S., Rajaratnam, S. M., & Cunnington, D. (2015). Cognitive behavioral therapy for chronic insomnia: a systematic review and meta-analysis. *Annals of Internal Medicine*, *163*(3), 191-204.